Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

______________________________ ________________

Marina Bruck Date

Whose Job Is It Anyway? An Analysis of Views on Responsibility of Vector Control and Hotspots of Acceptance of *Wolbachia* Suppression Among Communities Organized to Prevent Arboviruses (COPA) Study Participants in Ponce, Puerto Rico

By

Marina Bruck

Master of Public Health

Department of Epidemiology

Kenneth G. Castro, MD

Committee Chair

Laura Adams, DVM

Committee Member

Whose Job Is It Anyway? An Analysis of Views on Responsibility of Vector Control and Hotspots of Acceptance of *Wolbachia* Suppression Among Communities Organized to Prevent Arboviruses (COPA) Study Participants in Ponce, Puerto Rico

By

Marina Bruck

Bachelor of the Arts
University of Florida
2018

Thesis Committee Chair: Kenneth G. Castro, MD

An abstract of

a thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

Master of Public Health

in the Department of Epidemiology

2020

Abstract

Whose Job Is It Anyway? An Analysis of Views on Responsibility of Vector Control and Hotspots of Acceptance of *Wolbachia* Suppression Among Communities Organized to Prevent Arboviruses (COPA) Study Participants in Ponce, Puerto Rico

By Marina Bruck

Background: Dengue is one of the world's most widespread arthropod-borne viral (arboviral) diseases, endemic in more than 100 countries. An estimated 390 million dengue infections occur every year. In the search for a sustainable vector control mechanism, scientists identified a way to reduce *Aedes* mosquito populations by introducing *Wolbachia*, a naturally occurring endosymbiotic bacterium. Community engagement for novel vector control methods is crucial to gain support for long term success of the intervention.

Methods: *Communities Organized to Prevent Arboviruses* (COPA) is a community-based cohort study being conducted by the CDC Dengue Branch, the Puerto Rico Vector Control Unit and Ponce Health Sciences University to evaluate acceptability, feasibility and impact of a novel vector control method while conducting disease and vector surveillance in Ponce, Puerto Rico. The COPA knowledge, attitudes, and practices (KAP) survey asked about perceived risk and burden of arboviral disease, personal investment, and vector control practices. A subset of participants was provided an explanation of novel vector control methods including *Wolbachia* suppression and surveyed on their acceptance of the techniques. In this report, these factors will be assessed for association with acceptance of the *Wolbachia* suppression. Additionally, the thirty-eight community clusters will be analyzed to identify different levels of acceptance.

Results: With an overall baseline participant response rate of 74%, a total of 1,357 eligible COPA participants between 21-50 years of age provided responses to the KAP and novel vector control method acceptance surveys. Of the participants, 36.9% were male and 63.1% were female. A total of 922 (67.9%) respondents expressed acceptance of the *Wolbachia* suppression program. Of the thirteen variables tested, annual income and repellant use were found to have a statistically significant association with acceptance. Those with an income of $40,000 or above were 1.13 times as likely [95% CI: 1.03, 1.23] to accept *Wolbachia* suppression than those who earned less than $40,000 annually. Those who reported repellant use were 1.09 times as likely to be accepting of *Wolbachia* suppression [95% CI: 1.01, 1.18]. No significant hot or cold spots for acceptance of this intervention were detected in the cluster analysis.

Whose Job Is It Anyway? An Analysis of Views on Responsibility of Vector Control and Hotspots of Acceptance of *Wolbachia* Suppression Among Communities Organized to Prevent Arboviruses (COPA) Study Participants in Ponce, Puerto Rico

By

Marina Bruck

Bachelor of the Arts
University of Florida
2018

Thesis Committee Chair: Kenneth G. Castro, MD

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

Master of Public Health

in the Department of Epidemiology

2020

Acknowledgements

I would like to thank Dr. Ken Castro for his guidance and for sharing his expertise with me throughout this process. His encouragement and patience made this thesis possible.

I would also like to thank Dr. Gabriela Paz-Bailey, Dr. Laura Adams, Dr. Tyler Sharp and Emma Little, MPH for allowing me to become involved in their work and continuing their guidance after I had left Puerto Rico.

Table of Contents

1. Introduction

1.1 Dengue as a Global Problem

Dengue is one of the world's most widespread arthropod-borne viral (arboviral) infectious diseases, endemic in more than 100 tropical and subtropical countries and causing over $2 billion dollars a year in the Americas alone, excluding vector control costs(1). An estimated 390 million dengue infections occur every year, with about 96 million annually manifesting in recognizable clinical symptoms, commonly known as dengue fever(2). While the majority of dengue infections are asymptomatic or subclinical, a small percentage progress to more severe disease, which can lead to fatal complications such as severe bleeding, plasma leakage, respiratory distress and are commonly designated as severe dengue(3). While other major global infectious diseases are on the decline(2), the World Health Organization (WHO) reports a 30-fold increase in Dengue virus (DENV) global incidence between 1962 and 2012(4). A member of the *Flaviviridae* family, there are four dengue serotypes (DENV-1, DENV-2, DENV-3, DENV-4), all of which can circulate simultaneously in dengue-endemic countries(5). Immunity for the virus is type-specific, meaning that repeat infection of dengue is not only possible, but it has been seen that progression to more serious symptoms occurs more frequently with secondary DENV infection by a different serotype(6).

1.2 Aedes Mosquitoes

Aedes mosquitoes are insect vectors responsible for the spread of multiple diseases that have continued to emerge and reemerge all over the globe, namely DENV, Zika virus (ZIKV), chikungunya virus (CHIKV) and yellow fever virus (YFV)(7).

Although DENV is transmitted primarily via the *Aedes aegypti* mosquito, a mosquito that feeds during the day and resides in urban environments, transmission by *Aedes albopictus*, a typically rural vector that has adapted to urban environments, has increased(8). *Ae. aegypti* can be widely found throughout the Caribbean, the Southeastern United States, South America, European countries bordering the Mediterranean (Turkey, Greece, Cyrus, Croatia, Albania, Italy, Spain, France) and the Portuguese coast, Central and Southeast Asia, Oceania, and all throughout Sub-Saharan Africa(9). Meanwhile, *Ae. albopictus* has a broader distribution across the United States, the southern Canadian border, Western Europe and the Balkans but a narrower distribution than *Ae. aegypti* across East Africa(9). The two vectors have similar distributions across Asia and Oceania(9). The global spread of *Aedes* mosquitoes has been enhanced by land cover changes, commercial transportation, expansion of vector habitats and a multitude of other factors that increase opportunity for human-vector contact(9). *Ae. albopictus* is considered an invasive species, aided by the observation that these mosquitoes have shown the ability to adapt to urban habitats normally inhabited by *Ae. aegypti(8)*. In addition to differences in feeding patterns, typical habitats and geographic spread, DENV outbreaks caused by *Ae. aegypti* are epidemiologically different than DENV outbreaks caused by *Ae. albopictus (10)*. Outbreaks caused by *Ae. aegypti* tend to be more sustained and explosive in number of infections, while in areas where *Ae. albopictus* is the only DENV vector, outbreaks are relatively smaller and less frequent(10). As the climate continues to move towards warmer and wetter patterns, there is greater potential for spread of *Aedes* mosquitos to areas that have never been at risk for local dengue transmission (9).

1.3 Climate Change and Mosquitoes

Ae. aegypti is primarily confined to subtropical and tropical climates, such as that of Puerto Rico, whereas *Ae. albopictus* can be found in more temperate climates, due in part to the fact that their eggs can survive colder temperatures than adult mosquitoes. (10, 11). Two climate factors that directly affect mosquito populations are temperature and rain precipitation patterns(12). Warmer and wetter climates provide ideal conditions for *Aedes* breeding and oviposition (laying of eggs)(10). Some of the warmest tropical environments such as the northern region of the Amazon, South East Asia and sub-Saharan have been identified as the most suitable places for *Ae. aegypti* oviposition(10). Overall distribution of oviposition suitability for *Ae. albopictus* is similar, with the main difference being in the hottest regions, where *Ae. albopictus* has reduced survival when compared to *Ae. aegypti*(10).

Hurricanes and typhoons, both common in regions that are inhabited by *Aedes* mosquitoes, often result in an increased number of mosquitoes in the weeks following, and have the potential to exacerbate the spread of arboviral diseases, though this link has not yet been described(12). In September 2017, Puerto Rico was hit by two consecutive hurricanes, Irma and Maria(12). By utilizing mosquito traps already in place, population estimates revealed that the number of mosquitoes sharply increased in the five weeks following the hurricanes, though this total count included *Culex* mosquitoes, which do not carry DENV(12). Although no arboviruses were detected in the *Ae. aegypti* mosquitoes post-hurricane(12), climate conditions causing stronger and wetter storms may have implications on arbovirus outbreaks in the future.

1.4 Vector Control Methods: Past, Present and Future

Historically, *Aedes* vector control has relied heavily on synthetic insecticides and environmental management of breeding sites(13). Environmental management, which entails identification, reduction and removal of breeding sites can be time consuming and inefficient, especially since the climate in which *Aedes aegypti* thrives experience heavy rainfall(13). Heavy insecticide use (DDT, pyrethroids, carbamates, organophosphates)(8) carry the risk of passing on insecticide-resistant alleles, creating populations of resistant vectors(14). Resistance to the four main classes of insecticides has been detected in *Aedes* populations across the Americas, Asia, and Africa(15). Aside from challenges in vector control, it has been shown that in dengue-endemic communities, there is a limited sense of security and low acceptance towards the spraying of insecticides(7). Insecticide resistance, inefficient environmental management and low community buy-in are just some of the challenges vector control professionals are facing. In the search for a sustainable vector control mechanism, scientists identified a way to decrease *Aedes* population numbers by introducing *Wolbachia*, a naturally occurring endosymbiotic bacterium found in about 40% of all insects(16). When a male *Ae. aegypti* mosquito is infected with the *Wolbachia* bacterium and subsequently mates with a female mosquito in the wild, the eggs laid by the female will be sterile and therefore never hatch, due to the cytoplasmic incompatibility caused by the bacterium(16).This technique, known as "*Wolbachia* suppression", will effectively reduce the population over time as long as the *Wolbachia*-infected male mosquitoes continue to be released(16). As this is a novel vector control strategy and requires the *Wolbachia* infected mosquitoes to be released into the community, community awareness and acceptability are crucial to the success of the program.

1.5 Puerto Rico's Arbovirus History and Controversy Over Vector Control

Dengue epidemics in Puerto Rico have followed a pattern of occurring about every 3–5 years(11), with the most recent outbreaks occurring in 2007, 2010 and 2012–2013(17, 18). The island also experienced a CHIKV outbreak in 2014, followed by a ZIKV outbreak in 2016(12). The official history of dengue in Puerto Rico began in 1899, when the first case was documented on the island(19). A 1963 DENV outbreak of about 27,000 cases prompted the Puerto Rico Department of Health (PRDH) to request assistance from the Centers for Disease Control and Prevention (CDC)(19). From that point on, outbreak response plans included insecticide spraying, community cleanup campaigns, and programs designed to educate the public about community-based vector control(19). This program framework, developed with the help of a medical anthropologist hired in 1986, became the basis for the WHO global dengue control strategy and expanded to countries such as Colombia and Indonesia(19). However, becoming a world-recognized program did not come without trial and error, particularly when it came to the spraying of insecticides to prevent and control outbreaks. An attempt made between 1965 and 1969 to curb *Ae. aegypti* populations through spraying the insecticide malathion failed to eliminate the vector, and in an even greater failure, resistance to malathion was detected in *Ae. aegypti* following the campaign(19). Another malathion insecticide spraying attempt was made during the 1977 dengue epidemic, where this insecticide was sprayed from trucks and airplanes over some areas in San Juan, where other areas served as the control regions(19). No difference in number of dengue cases was detected between the treated and untreated areas(19). These data supported the results of extensive research conducted in the 1980s on the use of insecticides on *Ae. aegypti* populations, where no effects on epidemiological trends were detected based on use of insecticides(19).

Public awareness and support of vector control methods has been an issue for Puerto Rico in the past. During the 2016 Zika outbreak, Puerto Rico reported 35,395 confirmed and probable symptomatic Zika virus disease cases, accounting for 97% of all ZIKV infections in the United States territories, which includes American Samoa and the U.S Virgin Islands(20). CDC, in collaboration with PRDH, planned to conduct aerial spraying of the organophosphate Naled in an attempt to reduce the risk of Zika (21). The proposed intervention was met with objections stemming from a history of distrust in the federal government from local leaders and citizens who were concerned about Naled's efficacy and safety (22). Aside from Naled failing to curb a dengue outbreak in 1987, protesters called attention to a pattern of the island being used as a testing ground for the United States, including when the US military tested out the biological weapon "Agent Orange" in the Puerto Rican jungles prior to using it in Vietnam(23). The future of successful vector control in Puerto Rico depends on gaining community trust and educating the public about novel vector control methods that are safer and more sustainable.

1.6 Communities Organized to Prevent Arboviruses

Communities Organized to Prevent Arboviruses (COPA) is a community-based cohort study being conducted by the CDC Dengue Branch, the Puerto Rico Vector Control Unit (VCU) and Ponce Health Sciences University (PHSU) to evaluate acceptability, feasibility and impact of a novel vector control method while conducting surveillance for arboviral infections and vector populations in Ponce, Puerto Rico. Ongoing surveillance is required due to the high proportion of asymptomatic infections and poor correlation between mosquito indices and dengue transmission, which make it challenging to use historical data to predict effectiveness of vector control programs. In addition to surveillance, COPA aims to assess the acceptability of vector control methods, both traditional and novel, by conducting a Knowledge, Attitudes and Practices (KAP) survey of community members (Appendix A). This information can provide insight into the characteristics of participants who practice vector control at home and those who are aware and accepting of novel vector control methods, namely *Wolbachia* suppression.

Community engagement for novel vector control methods has been used in other settings as well, including developers of genetically engineered mosquitoes, particularly in low-and-middle income countries to ensure sound and ethical research, but also to gain community support for the long term success of the intervention (24). The race to find effective and accepted replacement methods for insecticides has been a large part of the vector control movement. Camino Verde ("The Green Way") is a feasibility study conducted in regions of Nicaragua and Mexico, both dengue endemic countries, designed to create an alternate, insecticide-free strategy(25). The researchers hypothesized that informed community mobilization increases the effectiveness of dengue control with the objective of developing a sustainable, community based approach to limit the need for insecticides(25). The intervention consisted of a baseline survey, education, *Ae. aegypti* ecosystem changes and intercommunity visits to share experiences between groups(25).

By the end of the fourth year of the study, twice as many intervention households were participating in community dengue control practices than control households(25).

The COPA KAP survey asks participants if they are familiar with the novel vector control methods of sterile insect technique, *Wolbachia* suppression and larvicides, along with questions about perceived risk and burden of arboviral disease in the community, personal investment, and vector control practices. Interviewers then provide participants with a brief explanation of the novel techniques. In this paper, demographic and KAP factors will be assessed for association with acceptance of the *Wolbachia* suppression technique. Additionally, the thirty-eight clusters identified for the study will be analyzed to identify different levels of acceptance for *Wolbachia* suppression. Geographic clustering of behaviors can provide valuable insight into resource allocation, effectiveness of interventions, and the distributions of health related behaviors(26), such as in one study that looked at geographic clustering and measles vaccination in US counties and found that unvaccinated children and adolescents were clustered disproportionately within certain US counties with respect to the fraction of the national population that those counties represent(27). A similar principle can be applied to *Wolbachia* suppression acceptance rates found by the COPA study to assess differences between communities and identify opportunities for effective implementation of public health interventions.

2. Methods

This study was granted exempt status by the Emory University Institutional Review Board. The data analysis described in this report uses a subset of deidentified data collected by the CDC Dengue Branch in San Juan, Puerto Rico, in collaboration with Ponce Health Sciences University (PHSU). Thirty-eight community clusters were chosen in Ponce, Puerto Rico, the second largest city on the island, based on their location, presence of natural or man-made barriers that separate them from other communities, and percentage of inhabitants living under the poverty level. The study described in this report uses the data collected with the baseline enrollment questionnaire, including demographic information, KAP questions pertaining to risk and transmission of arboviruses, and level of support for novel vector control methods. The questionnaire was administered by trained Spanish-speaking interviewers using the Spanish version of the survey found in the Appendix (Appendix A). COPA participants whose birthdate fell on an odd calendar date were eligible to complete the novel vector control methods interview asking about previous knowledge and acceptance of novel methods after being provided a brief explanation of each. Participants described in this report were all 21-50 years of age at the time of baseline enrollment and completed the novel vector control methods interview, resulting in a total of 1,357 participants.

2.1 Demographic / KAP variables

Thirteen demographic and KAP variables were analyzed for association with acceptance of *Wolbachia* suppression by using SAS Version 9.4 to calculate Mantel-Haenszel risk ratio estimates. The demographic variables assessed were sex, age, education level, annual income, and employment environment. The KAP variables assessed were the belief that mosquitoes can transmit disease, perception of arboviruses as a problem in the community, belief that it is worth spending time and money on vector control, annual household expenditure on vector control, having used insect repellant in the past month, having utilized a mosquito net in the past year, opinion of government involvement in vector control, and having previously heard of mosquitoes deliberately infected with *Wolbachia*. All participant responses were included in the overall analysis; however, missing data and non-responses were removed from calculations at the variable level. Collapsing the “Age”, “Education Level”, and “Annual Income” variables was done to remain consistent with other current unpublished works from the CDC Dengue Branch for the purpose of future collaboration and publication.

Sex and Age

Participants had the option to either answer male, female, or other. In this subset, all participants either answered male or female. Age was recorded as a continuous variable and then grouped into ten-year age categories (21-30, 31-40, 41-50).

Education Level

Ten options were provided for indicating highest level of education completed. The options were “No Schooling”, “Special Education”, “Grades 1-5”, “Grades 6-8”, “Grades 9-11”, “completed High School/GED”, “Technical/ Associate’s Degree”, “Bachelor’s Degree”, “Post-graduate Degree”, and “Professional Degree”. For the purposes of this study, these responses were grouped into “Lower Education”, which included “No Schooling”, “Special Education”, grades 1-11”, “completed High School/GED” and “Technical/Associate’s Degree”, and “High Education” which included everyone who has completed a bachelor’s degree or a post-graduate degree above that.

Annual Income

Annual income was recorded categorically (less than $10,000, $10,000 - $19,000, $20,000 - $29,000, $30,000 - $39,000, $40,000 - $49,000, $50,000 - $59,000, $60,000 - $69,000 and greater than or equal to $70,000). Participants also had the option to answer with monthly income. These responses were multiplied by 12 and recoded into the appropriate “annual income” category. This variable was then dichotomized into “Less than $40,000” and “$40,000 or above”. The variable was dichotomized in order to create a proxy for socioeconomic status (SES), similar to the education level variable previously described.

Employment Environment

This variable was only recorded for participants that responded to the employment status question with “Full-time”, “Part-time”, “Student” or “Work Study”. Those excluded responded to the employment status question with “Business Owner”, “Casual or Informal Work”, “Retired”, “Unemployed”, “Unable to work due to health problems”, “Homemaker” or “Other” A total of 629 participants remained for analysis after applying these exclusion criteria, who then had the opportunity to describe their employment environment as either “Primarily Indoors”, “Primarily Outdoors”, “Other” or “Varies”. The responses were then categorized into “Indoors” and “Other”, which included “Primarily Outdoor”, “Other” and “Varies” to represent whether participants experience a level of high or low exposure to mosquitoes while at work without explicitly asking so.

Transmission/Risk/Community Burden of Arboviruses

Three KAP questions were designed to assess knowledge of how arboviruses are transmitted, perceived personal risk and perception of arboviruses as a problem in their community. The first was a dichotomous yes/no question asking if the participant believes that mosquitoes can transmit disease. The second question asked about personal perceived risk of contracting each of the following diseases: Zika, dengue and chikungunya. Response options were “None”, “Low” or “High”. Variables were recoded into a single “risk” variable. Participants who responded with “None” or “Low” to any of the three diseases were categorized into the “None/Low” category, while those who responded “High” to any of the three were categorized into the “High” category. The third question asked if the participant if they believe that diseases transmitted by mosquitoes are a problem in their community in a yes/no format.

Personal Investment and Practice in Vector Control

Five KAP variables selected for this analysis pertain to personal practices in vector control. The first is a dichotomous yes/no question asking if the participant believes it is worth it to invest time and money to control mosquitoes. The second is a question about personal expenditure. This variable was created by summing the amount of money reportedly spent per household on exterminators and mosquito control products; responses were grouped into categories of less than \$120 (the median amount) or ≥ \$120. The third KAP variable is a dichotomous yes/no asking if the participant used mosquito repellant in the past 30 days. Participants were also asked how frequently they used a mosquito net in the past year. Those who responded with “Never” or “Rarely” were categorized as “No Use” while those who responded with “Monthly”, “Weekly” or “Daily” were categorized as “Yes”. The variables described in this section, particularly those about using repellant and mosquito nets, serve as a proxy for independent vector control and protection measures. The last KAP question asked participants who they believe has the responsibility of implementing vector control: the government/department of health or themselves.

Previous Knowledge of Wolbachia Mosquitoes

The final question asked participants if they had ever head of mosquitoes with *Wolbachia* before. Those who responded “No” or “Unsure” were grouped together, while the second group included all participants who answered “Yes”.

2.2 Acceptance Rate of Wolbachia Suppression by Community Cluster

In order to assess acceptance of *Wolbachia* suppression by community cluster, a new dataset was created by aggregating the number of participants who responded in support of the technique and dividing by the total number of participants per cluster who fit the criteria of this analysis. This provided a ratio of acceptance of *Wolbachia* suppression for each of the 38 clusters (Figure 1). In the majority of cases, participants in this subset reside independently of each other. There are only a few observations in which participants shared a residence with another participant, suggesting that conducting a Getis-Ord Gi* Hotspot Analysis by community cluster may be more informative than a household-level cluster analysis. Cluster acceptance rate visualization and Getis-Ord Gi* Hotspot Analysis was done using ArcMap 10.6.1.

3. Results

During baseline enrollment, 23,830 households were visited, of which 2,281 (9.5%) agreed to participate. The household-level response rate was 20% and the participant-level response rate was 74%. A total of 4,090 participants were enrolled, of which, 1,357 (33%) met the inclusion criteria for the vector control interventions interview. Among the 1,357 respondents, 922 (67.9%) indicated acceptance of *Wolbachia* suppression as an intervention to control mosquito vectors.

3.1 Sex

Participants were 36.9% were male and 63.1% female (Table 1). Among the male participants, 70.5% responded as accepting of *Wolbachia* suppression, as did 66.5% of female participants (Table 2). Females were 0.94 times less likely to be accepting of *Wolbachia* suppression as men [95% CI: 0.88, 1.02] (Table 2), though this difference was not statistically significant.

3.2 Age

Age of participants follows a normal distribution with a median age of 37 years [IQR: 28-44]. For the analysis, ages were grouped into three classes with 31.0% of participants aged 21 to 30 years old, 30.0% of participants aged 31 to 40 years old and the remaining 39.0% participants aged 41 to 50 years old (Table 1). Of participants 21-30 years old, 68.6% responded in acceptance of *Wolbachia* suppression, as did 68.3% of participants 31-40 years old and 67.2% of participants 41-50 years old (Table 2). There was no statistically significant difference detected in acceptance of *Wolbachia* suppression by these three age groups (Table 2).

3.3 Education Level

A total of 868 (64.6%) of participants reported an education level below completing a bachelor's degree, with the remaining 479 (35.6%) reporting as completing a college degree or above (Table 1). Of those in the "Lower Education" category, 68.1% reported acceptance of *Wolbachia* suppression, as did 67.4% of the "High Education" category. Participants in the "High Education" group were 0.99 times less likely to report acceptance [95% CI: 0.92,1.07], though education level showed no statistically significant association with acceptance of *Wolbachia* suppression (Table 2).

3.4 Annual Income

After calculating and categorizing annual income, 84.7% of participants reported an income of less than $40,000 (Table 1). Among those, 67.0% reported acceptance of *Wolbachia* suppression (Table 2). An annual income of $40,000 or above was reported by 15.3% of participants (Table 1), 75.5% of whom reported acceptance of *Wolbachia* suppression for vector control (Table 2). Those with an income of $40,000 or above were 1.13 times as likely [95% CI: 1.03, 1.23] to accept *Wolbachia* suppression than those with a lower income, with the results indicating a statistically significant association between income and acceptance of this vector control intervention (Table 2).

3.5 Employment Environment

A total of 629 (46.4%) participants fit the inclusion criteria for the employment environment variable based on their response to the employment status question. Of these, 69.5% described their employment environment as primarily indoors (Table 1) and among them, 69.1% reported acceptance of *Wolbachia* suppression (Table 2). Of the remaining 30.5% that described their employment environment as primarily outdoors or varied (Table 1), 67.7% reported acceptance of *Wolbachia* suppression (Table 2). There was no statistically significant association between type of employment environment and acceptance of this vector control modality [RR: 0.98, 95% CI: 0.87, 1.10] (Table 2).

3.6 Knowledge of Disease Transmission

When asked if they believed that mosquitoes transmit diseases, only 4.8% of participants responded with “No” (Table 1). Of those who responded with “No,” 59.4% indicated acceptance of *Wolbachia* suppression, as did 68.5% of participants who knew that mosquitoes transmit disease (Table 2). There was no statistically significant association detected between believing that mosquitoes can transmit disease and *Wolbachia* suppression acceptance [RR: 1.15, 95% CI: 0.94, 1.42] (Table 2).

3.7 Perception of Risk

A total of 322 (31.3%) of participants indicated that they believe they have a high risk of contracting a disease transmitted by a mosquito (Table 1). Of those indicating high perceived risk of infection, 70.2% reported acceptance of *Wolbachia* suppression, as did 68.3% of those who believing their risk of infection is little to none (Table 2). Though the majority of participants believed they had low risk for contracting mosquito-borne disease, there was no statistically significant association detected between perception of disease risk and *Wolbachia* suppression acceptance [RR:1.02, 95% CI: 0.94, 1.12] (Table 2).

3.8 Arboviruses as a Community Issue

When asked if they believe arboviruses are a problem in their community, 69.6% of participants indicated that they feel it is a problem (Table 1), 69.6% of whom expressed acceptance of *Wolbachia* suppression (Table 2). Of those who do not see arboviruses as an issue in their community, 65.3% indicated acceptance (Table 2). No statistically significant association was found between perception of arboviruses as a community problem and acceptance of this intervention [RR:1.7, 95% CI: 0.98, 1.16] (Table 2).

3.9 Personal Investment of Time and Money

Almost all (95.3%) participants indicated that they believe that it is worthwhile to spend time and money to control mosquitoes (Table 1). Of those, 68.0% indicated acceptance, while 68.8% of those who do not believe it is worth spending time and money to control mosquitoes also indicated acceptance (Table 2). No statistically significant difference in acceptance of *Wolbachia* suppression was found between groups [RR: 0.99, 95% CI: 0.84, 1.17] (Table 2).

3.10 Annual Household Expenditure on Mosquito Control

Participants whose annual expenditure on mosquito control was less than the median amount of $120 represented 62.2% of the total participants (Table 1), of whom 67.7% indicated acceptance (Table 2). The association between annual expenditure and acceptance of *Wolbachia* suppression was not found to be statistically significant [RR: 1.04, 95% CI: 0.96, 1.12] (Table 2).

3.11 Use of Repellant

A total of 751 (55.6%) participants responded that they had used mosquito repellant in the past 30 days (Table 1). Of those who reported using repellant, 70.6% reported acceptance of *Wolbachia* suppression, as did 64.7% of those who reported no use of repellant in the past 30 days (Table 2). Those who reported repellant use were 1.09 times as likely to be accepting of *Wolbachia* suppression [95% CI: 1.01, 1.18 ,] (Table 2); there appears to be a statistically significant relationship between use of repellant in the past 30 days and acceptance.

3.12 Use of a Mosquito Net

In addition to repellant use, participants were also asked about their frequency of mosquito net use in the past year. Only 2% indicated that they had used a mosquito net either monthly, weekly or daily (Table 1). Of those, 55.6% responded in support of *Wolbachia* suppression (Table 2). There appears to be no statistically significant association between frequency of use of mosquito nets and acceptance [RR: 0.81, 95% CI: 0.58, 1.14] (Table 2).

3.13 Role of Government/Department of Health in Vector Control

A total of 84.6% of participants responded that they believe that the government/department of health should have some role in vector control (Table 1) and of those, 67.4% responded as accepting of *Wolbachia* suppression (Table 2). Those who said the government/department of health should have some role in vector control were 0.92 times less likely to respond in acceptance of *Wolbachia* suppression than those who do not believe that the government should have a role, though there is no statistically significant association between opinion on the role of the government and acceptance [95% CI: 0.84, 1.01] (Table 2).

3.14 Previous Knowledge of Wolbachia-Infected Mosquitoes

Only 4.6% of participants indicated that they had previously heard of mosquitoes deliberately infected with *Wolbachia* (Table 1); 73.0% of those participants said they accept *Wolbachia* suppression (Table 2). Among participants who had not previously heard of mosquitoes with *Wolbachia*, 67.7% said they would be accepting after hearing a brief explanation. No statistically significant association was detected between whether participants had previously heard of mosquitoes with *Wolbachia* and acceptance [RR: 1.08, 95% CI: 0.92, 1.26] (Table 2).

3.15 Acceptance of Wolbachia Suppression by Community Cluster

Aggregation of total participants that indicated acceptance of *Wolbachia* suppression per cluster and dividing by the total of participants from each cluster allowed for the comparison between clusters by rate of acceptance. The lowest rate of acceptance was found in cluster JC02 with a rate of 41% and the highest rate of acceptance was found in cluster MA01 with a rate of 84% (Figure 1). Two thirds (66%) of the clusters had acceptance rates between 60% and 75%, and 84% of clusters had acceptance rates between 50% and 75% (Figure 1). The Getis-Ord Gi* Hotspot Analysis was conducted in an effort to identify statistically significant hotspots based on which cluster and neighboring clusters have a high incidence value of acceptance of *Wolbachia* suppression compared to the expected value. Due to the lack of variation in acceptance rates between community clusters, the Getis-Ord Gi* Hotspot Analysis did not return any noteworthy results.

4. Discussion

COPA aims to reduce transmission of arboviral diseases such as dengue, Zika and chikungunya by conducting ongoing entomologic and arboviral incidence surveillance, along with engaging the public and implementing effective and sustainable novel vector control methods such as *Wolbachia* suppression. This analysis was performed to better understand participants' knowledge, attitudes, practices, and perceptions toward vector control and arboviral disease risk, and how those factors influence acceptance of novel vector control methods.

The aim of this study was to assess which of the selected demographic and KAP factors are associated with acceptance of *Wolbachia* suppression. The demographic factors selected for analysis included sex, age, education level, annual income, and employment environment. Of these factors, only annual income had a statistically significant association with acceptance of *Wolbachia* suppression, as participants with income >$40,000 were more likely to be accepting than those ≤$40,000. This association may indicate that those of a higher SES have a better understanding of the possible benefits of *Wolbachia* mosquitoes, or that they have more trust in government interventions than those with a lower income. An analysis of association between income level and vector control practices and perceptions could provide further insight. The KAP factors assessed in the analysis were specifically chosen to analyze personal perception of risk, arboviruses as an issue in the community, who should oversee vector control and personal protection behaviors. Of these factors, only use of repellent in the past 30 days had a statistically significant association with acceptance of *Wolbachia* suppression, as participants who reported repellant use were more likely to accept *Wolbachia* suppression. Future studies may consider examination of other variables that assess personal protective behaviors and additional variables that may be influenced by income levels, such as the association between acceptance and hiring an exterminator, installing screens in the home or having air conditioning throughout the house. It may also be useful to develop methods and programs to reach groups that were shown to have lower rates of acceptance, such as those who earn less than $40,000 a year or those who do not believe that mosquitoes can transmit diseases.

Following this analysis of association between demographic/KAP variables and acceptance, the data was aggregated by cluster to attempt to identify any hotspots or cold spots of *Wolbachia* acceptance. Since there was little variation in acceptance rates between clusters, no hot or cold spots were able to be detected by the Getis-Ord Gi* test. These relatively high acceptance rates throughout Ponce indicate a readiness and interest amongst participants for the novel vector control technique, though assessing the KAP factors is still valuable to develop targeted ways to further increase overall acceptance.

One important limitation of this study is associated with the relatively low household-level participation (20%) and lack of generalizability across the island of Puerto Rico. Ponce, located on the southern coast of the island, is the second largest municipality in Puerto Rico, behind San Juan, with a population of about 186,400(28). San Juan, on the other hand, has a population of over 400,000(28). Puerto Rico’s 78 municipalities range from these well populated coastal cities to rural towns(28).While the results from the COPA study may provide some information that can be used to implement and assess vector control across the island, each municipality must be treated differently. Additionally, members of the selected communities who chose not to respond to the survey may have different views on acceptance of *Wolbachia* suppression. Furthermore, the individual associations found in these high acceptance rate community clusters may not represent associations to be found in other communities with lower acceptance rates.

The finding of a statistically significant association between acceptance of *Wolbachia* suppression and higher income as well as recent use of insect repellant may reflect spurious associations and would require further analysis to determine their significance in the context of acceptance of *Wolbachia* suppression. Another limitation of this analysis is the exclusive reliance on bivariate analyses to identify statistically significant associations, and the absence of a multivariate logistic regression analysis to assess association between the collected variables and acceptance of *Wolbachia* suppression while exploring for any effects caused by effect measure modification or confounding, such as possible interaction between income and recent repellant use.

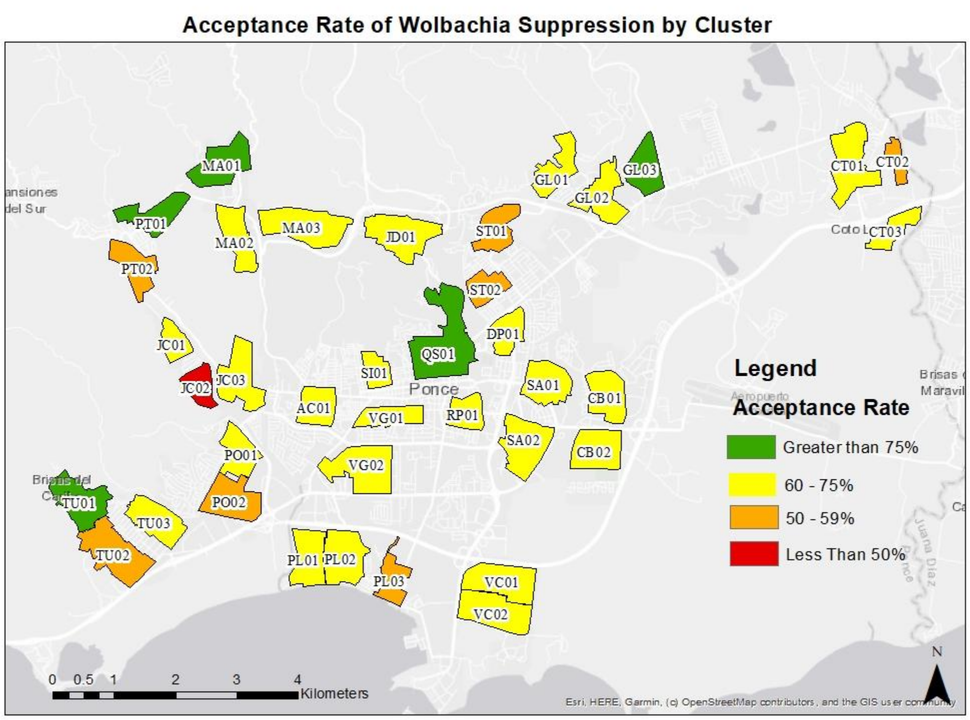
Our analysis uncovered that 67.9% of respondents were accepting of *Wolbachia* suppression, suggesting a relatively large overall acceptance of this novel vector control in this community in southern Puerto Rico. Effective and safe novel vector control methods such as *Wolbachia* suppression have the potential to relieve some of the burden caused by arboviral diseases in places such as Puerto Rico, but the key to their success lies greatly in building trust with communities and engaging all involved, as COPA intends to accomplish.

Table 1. Demographic/ KAP Descriptive Analysis	
Variable	**N (%)**
Total	**1,357**
Sex	
Men	501 (36.9)
Women	856 (63.1)
Age	
21-30	420 (31.0)
31-40	407 (30.0)
41-50	530 (39.0)
Education Level	**1,347**
Lower Education	868 (64.4)
High Education	479 (35.6)
Annual Income	**1,256**
Less than $40,000	1064 (84.7)
$40,000 or Above	192 (15.3)
Employment Environment	**629**
Primarily Indoors	437 (69.5)
Primarily Outdoors/ Varied	192 (30.5)
Believe Mosquitoes Transmit Disease	1277 (95.2)
Perceived Risk of Getting a Disease from Mosquitoes	**1,029**
None/Low	707 (68.7)
High	322 (31.3)
Perception of Arboviruses as an Issue in the Community	**1,287**
Perceive Arboviruses as an Issue in Community	896 (69.6)
Expenditure of Time and Money for Vector Control	**1,346**
Believe it is Worth Investing Time and Money for Vector Control	1283 (95.3)
Annual Household Expenditure on Mosquito Control	**1,256**
Less than $120	781 (62.2)
$120 or Above	475 (37.82)
Personal Repellant Use in Past 30 Days	**1,350**
Have Used Repellant in Past 30 Days	751 (55.6)
Use of Mosquito Net in Past Year	**1,350**
Have Used Mosquito Net in Past Year	27 (2.0)
Role of Government/ Department of Health in Vector Control	**1,322**
Believe Government/Dept of Health Should Have Some Responsibility in Vector Control	1119 (84.6)
Have Previously Heard of Mosquitoes with *Wolbachia*	63 (4.6)

Table 2. Estimated Mantel-Haenszel Risk Ratios (RR) and 95% Confidence Intervals (CI)				
Variable	**Acceptance of *Wolbachia* Suppression N (%)**	**Total N**	**RR**	**95% CI**
Sex				
Men[r]	353 (70.5)	501		
Women	569 (66.5)	856	0.94	0.88, 1.02
Age				
21-30[r]	288 (68.6)	420		
31-40	278 (68.3)	407	0.99	0.91, 1.09
41-50	356 (67.2)	530	0.98	0.90, 1.07
Education Level[a]				
Lower Education [r]	591 (68.1)	868		
High Education	323 (67.4) .2)	479	0.99	0.92, 1.07
Annual Income				
Less than $40,000[r]	713 (67.0)	1064		
$40,000 or Above	145 (75.5)	192	1.13	1.03, 1.23
Employment Environment [b]				
Primarily Indoors[r]	302 (69.1)	437		
Primarily Outdoors/Varied	130 (67.7)	192	0.98	0.87, 1.10
Believe Mosquitoes Transmit Disease				
No[r]	38 (59.4)	64		
Yes	875 (68.5)	1277	1.15	0.94, 1.42
Perceived Risk of Getting a Disease from a Mosquito				
None/Low[r]	483 (68.3)	707		
High	226 (70.2)	322	1.02	0.94, 1.12
Perceive Arboviruses as a Problem in the Community				
No[r]	256 (65.3)	392		
Yes	624 (69.6)	896	1.07	0.98, 1.16
Believe it is Worth Investing Time and Money for Vector Control				
No[r]	44 (68.8)	64		
Yes	873 (68.0)	1283	0.99	0.84, 1.17
Annual Household Expenditure on Mosquito Control				
Less than $120[r]	529 (67.7)	781		
$120 or Above	334 (70.3)	475	1.04	0.96, 1.12
Have Used Repellant in Past 30 Days				
No[r]	388 (64.7)	600		
Yes	530 (70.6)	751	1.09	1.01, 1.18

Have Used Mosquito Net in Past Year				
No[r]	899 (68.2)	1318		
Yes	15 (55.6)	27	0.81	0.58, 1.14
Believe Government/Dept of Health Should Have Some Responsibility in Vector Control				
No[r]	148 (72.9)	203		
Yes	754 (67.4)	1119	0.92	0.84, 1.01
Have Previously Heard of Mosquitoes with *Wolbachia*				
Never/Unsure[r]	876 (67.7)	1294		
Yes	46 (73.0)	63	1.08	0.92, 1.26
[r]=Reference Group **[a]= Group Includes Special Education, No Education, Grades 1-11, Completed High School/GED, and those with a Technical or Associate Degree** **[b]= Group Only Includes Individuals Who Responded to Employment Status with "Full time", "Part-time", "Student" or "Work/Study"**				

Figure 1.



Appendix A

Form Approved
OMB Control No.: 0920-1254
Exp. date: 3/31/2022

KAP: Adults and Adolescents

1. If you could **change** or **improve** three things in your community, what would they be?
Do not read the options; it is okay if they only provide 1-2 answers.

- ☐ Standing water
- ☐ Environmental/Pollution
- ☐ Stray animals
- ☐ Crime/Gangs/Safety
- ☐ Potable water distribution
- ☐ Drugs
- ☐ Electricity
- ☐ Teen pregnancy
- ☐ Sexually transmitted diseases/HIV
- ☐ Diseases transmitted by mosquitoes (dengue, Zika, chikungunya)
- ☐ Debris
- ☐ Lack of sewage system
- ☐ Children's health
- ☐ Maintenance of green spaces
- ☐ Flies, no-see-ums, other insects
- ☐ Mosquitoes
- ☐ Homelessness
- ☐ Trash removal
- ☐ Messy or dirty neighborhood
- ☐ None
- ☐ Other: ___________________

2. *In the **last 12 months**,* since this month of the past year, which of the following sources have you used to **obtain health information**?
Probe if necessary. Select all that apply.

- ☐ School
- ☐ Brochures
- ☐ Internet
- ☐ Children
- ☐ Newspapers/magazines
- ☐ Official spokespeople
- ☐ Health professionals
- ☐ Radio
- ☐ Social networks (Facebook, Twitter, Instagram)
- ☐ Community meetings
- ☐ TV
- ☐ Neighbors
- ☐ WhatsApp

3. Do you think that **mosquitoes transmit** diseases?

☐ Yes | ☐ No

4. *In the **next 12 months**,* how much risk do you think there is in this house of becoming sick with:

a. Dengue	☐ High | ☐ Low | ☐ None ☐ None because I have had it
b. Zika	☐ High | ☐ Low | ☐ None ☐ None because I have had it
c. Chikungunya	☐ High | ☐ Low | ☐ None ☐ None because I have had it

5. Would you go to the doctor if you thought you had chikungunya, dengue, o Zika?

☐ Yes | ☐ No | ☐ Only if the symptoms were severe

KAP: Adults and Adolescents

6. Do you think that diseases transmitted by mosquitos such as dengue, Zika and chikungunya are a problem in your community?

☐ Yes | ☐ No

7. Have you used **mosquito repellent** in the ***last 30 days***?

☐ Yes | ☐ No

7a. What **type of repellant** have you used to prevent mosquito bites?

- ☐ Citronella
- ☐ Store-bought spray (Off)
- ☐ Cream
- ☐ Towelettes
- ☐ Natural/Artisanal/ Homemade repellants
- ☐ Other: ___________

8. In the ***last 12 months,*** how often have you used a **mosquito net**?

- ☐ Daily
- ☐ One time per week
- ☐ One time per month
- ☐ Rarely
- ☐ Never

9. **Where** do mosquitoes bite you most frequently?
Read the options. Select all that apply.

- ☐ Around the house outside
- ☐ Inside the house
- ☐ Work
- ☐ School
- ☐ Community sports field
- ☐ Somewhere else in the community
- ☐ Somewhere else outside of the community
- ☐ Mosquitoes do not bite me

A **mosquito-breeding site** is anything that retains water that enables mosquitoes to reproduce. Mosquitoes can even reproduce in an area as small as a bottle cap.

10. Currently, what are the **most common** mosquito **breeding sites** in this community?
Select all that apply, do not read the options.

- ☐ Hollow trees
- ☐ Abandoned houses
- ☐ Neighbors' houses
- ☐ Garbage containers
- ☐ Drains
- ☐ Debris from hurricane
- ☐ Tires
- ☐ Other containers
- ☐ Pools in abandoned houses
- ☐ Untreated pools
- ☐ Septic tanks
- ☐ Ground (floor)
- ☐ Rooves
- ☐ There are no breeding sites
- ☐ Other: ___________________

11. Do you think controlling **mosquito-breeding sites** is a good strategy to prevent mosquito-borne diseases?

☐ Yes | ☐ No

12. *In the **last 12 months***, have you **spoken** with any of the following people about how to **control** mosquitoes?

a. Your family	☐ Yes | ☐ No
b. Your neighbors	☐ Yes | ☐ No
c. Your community	☐ Yes | ☐ No

13. Do you think that **your community should do more** to **control** mosquitoes?

☐ Yes | ☐ No

14. Who do you think is **responsible** for **controlling** mosquitoes?

a. The government and/or the Department of Health?	☐ Yes | ☐ No
b. You?	☐ Yes | ☐ No

15. Do you think it is worth it to **invest time and money** each month to **control mosquitoes** inside and outside the house?

☐ Yes | ☐ No

16. Did you know that we would be here in your community?

☐ Yes | ☐ No

16a. How did you find out that we would be in your community?

☐ Through the community leader
☐ Informational flyer
☐ Through someone else
→Who? ____________________
☐ Facebook
→ Which page? ____________________
☐ Loud speaker
→ Where? ____________________
☐ Radio
→ Which station? ____________________
☐ Street banner
☐ Newspaper
→ Which one? ____________________
☐ Other: ____________________

2. Have you ever heard of mosquitoes with ***Wolbachia***?

☐ Yes | ☐ No | ☐ Doesn't know | ☐ No response

Interviewer read the following:

- Wolbachia is a bacterium that lives inside many insects, including some mosquito species.
- Wolbachia does not cause disease in humans and its use is safe for people, animals and the environment.
- There are many types of Wolbachia. Some types of Wolbachia can be used to control Aedes aegypti mosquitoes and the viruses they transmit.
- Since this type of Wolbachia has not been found in Aedes aegypti mosquitoes, scientists have introduced this bacterium in the mosquitoes in a laboratory.

Mosquitoes with *Wolbachia* can be used in two different ways.

Interviewer: Show the visual aid for male mosquitoes with Wolbachia.

Interviewer read the following:

- This technique can be used releasing **only male** *Aedes aegypti* mosquitoes carrying Wolbachia. Male mosquitoes do not bite. Female mosquitoes carrying Wolbachia are not released. When it is used this way, it is considered a sterile insect technique.
- Male mosquitoes with Wolbachia have been used in California and the Florida Keys and have been approved for evaluation in Miami, FL.
- When male mosquitoes carrying Wolbachia mate with wild females without Wolbachia, these female mosquitoes without Wolbachia lay their eggs, but these don't hatch.
- This technique requires the release of lots of male mosquitoes with Wolbachia. These mosquitoes need to be released several times per week for a prolonged period to keep the mosquito populations low.
- Mosquito population will eventually increase again when the releases of mosquitoes carrying Wolbachia stop.

2a. Would you support the use of male mosquitoes with *Wolbachia*?

Interviewer: Read the responses.

☐ Support
☐ Neutral
☐ Oppose →
☐ No response

2b. What are the reasons you oppose?

Interviewer: Do not suggest responses. Choose all reasons mentioned below. Use "other" for reasons not listed.

☐ Environmental impact
☐ Wild animal health
☐ Human health
☐ Pet health
☐ Don't think it is/would be effective in this community
☐ Not a community priority/arboviruses are not a concern here
☐ Concerned about safety of use of mosquitoes with *Wolbachia*
☐ Other: ______________________________

References

1. Shepard DS, Coudeville L, Halasa YA, et al. Economic impact of dengue illness in the Americas. *Am J Trop Med Hyg* 2011;84(2):200-7.
2. Bhatt S, Gething PW, Brady OJ, et al. The global distribution and burden of dengue. *Nature* 2013;496(7446):504-7.
3. WHO. *Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control*. World Health Organization, 2009:3-14.
4. WHO. *Global Strategy for Dengue Prevention and Control, 2012–2020 WHO, Geneva 2012*. 2012.
5. Simmons CP, Farrar JJ, Nguyen v V, et al. Dengue. *N Engl J Med* 2012;366(15):1423-32.
6. Murphy BR, Whitehead SS. Immune response to dengue virus and prospects for a vaccine. *Annu Rev Immunol* 2011;29:587-619.
7. Roiz D, Wilson AL, Scott TW, et al. Integrated Aedes management for the control of Aedes-borne diseases. *PLoS Negl Trop Dis* 2018;12(12):e0006845.
8. Auteri M LRF, Blanda V, Torina A.. t. . Insecticide Resistance Associated with kdr Mutations in Aedes albopictus: An Update on Worldwide Evidences. *Biomed Res In* 2018.
9. Kamal M, Kenawy MA, Rady MH, et al. Mapping the global potential distributions of two arboviral vectors Aedes aegypti and Ae. albopictus under changing climate. *PLoS One* 2018;13(12):e0210122.
10. Brady OJ, Golding N, Pigott DM, et al. Global temperature constraints on Aedes aegypti and Ae. albopictus persistence and competence for dengue virus transmission. *Parasit Vectors* 2014;7:338.
11. Mendez-Lazaro P, Muller-Karger FE, Otis D, et al. Assessing climate variability effects on dengue incidence in San Juan, Puerto Rico. *Int J Environ Res Public Health* 2014;11(9):9409-28.
12. Barrera R, Felix G, Acevedo V, et al. Impacts of Hurricanes Irma and Maria on Aedes aegypti Populations, Aquatic Habitats, and Mosquito Infections with Dengue, Chikungunya, and Zika Viruses in Puerto Rico. *Am J Trop Med Hyg* 2019;100(6):1413-20.
13. Benelli G JC, Walker T. . Biological Control of Mosquito Vectors: Past, Present, and Future. *Insects* 2016;7.
14. David MR GG, Valle D, Maciel-de-Freitas R. . Insecticide Resistance and Fitness: The Case of Four Aedes aegypti Populations from Different Brazilian Regions. *Biomed Res Int* 2018.
15. Moyes CL VJ, Martins AJ, et al. . Contemporary status of insecticide resistance in the major Aedes vectors of arboviruses infecting humans. *PLoS Negl Trop Dis* 2017;11.
16. Dutra HL, Rocha MN, Dias FB, et al. Wolbachia Blocks Currently Circulating Zika Virus Isolates in Brazilian Aedes aegypti Mosquitoes. *Cell Host Microbe* 2016;19(6):771-4.
17. Noyd DH, Sharp TM. Recent Advances in Dengue: Relevance to Puerto Rico. *P R Health Sci J* 2015;34(2):65-70.
18. Sharp TM, Hunsperger E, Munoz-Jordan JL, et al. Sequential episodes of dengue--Puerto Rico, 2005-2010. *Am J Trop Med Hyg* 2014;91(2):235-9.
19. Sharp TM, Ryff KR, Santiago GA, et al. Lessons Learned from Dengue Surveillance and Research, Puerto Rico, 1899-2013. *Emerg Infect Dis* 2019;25(8):1522-30.
20. 2016 Case Counts in the US. Center for Disease Control and Prevention. (https://www.cdc.gov/zika/reporting/2016-case-counts.html). (Accessed).

21. McNeil DG. A Mosquito Killer, Unwelcome to Many. The New York Times September 17, 2016, 2016.
22. Silverman E. CDC Backs Down on Proposal to Use Controversial Insecticide to Thwart Zika. *STAT*, 2016.
23. McNeil DG. Zika Cases in Puerto Rico are Skyrocketing. The New York Times July 30, 2016, 2016.
24. Meghani Z, Boete C. Genetically engineered mosquitoes, Zika and other arboviruses, community engagement, costs, and patents: Ethical issues. *PLoS Negl Trop Dis* 2018;12(7):e0006501.
25. Andersson N, Arostegui J, Nava-Aguilera E, et al. Camino Verde (The Green Way): evidence-based community mobilisation for dengue control in Nicaragua and Mexico: feasibility study and study protocol for a randomised controlled trial. *BMC Public Health* 2017;17(Suppl 1):407.
26. Liu Y, Croft JB, Wheaton AG, et al. Clustering of Five Health-Related Behaviors for Chronic Disease Prevention Among Adults, United States, 2013. *Prev Chronic Dis* 2016;13:E70.
27. Smith PJ, Marcuse EK, Seward JF, et al. Children and Adolescents Unvaccinated Against Measles: Geographic Clustering, Parents' Beliefs, and Missed Opportunities. *Public Health Rep* 2015;130(5):485-504.
28. Portal Oficial del Gobierno de Puerto Rico. Gobierno de Puerto Rico. (www2.pr.gov/Directorios/Pages/DirectoriodeMunicipios.aspx). (Accessed April 10, 2020).