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A Historical and Political Review of the Response to the 2015-2016 Zika Outbreak in Puerto Rico

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ABSTRACT

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The Zika virus was first identified in 1948 but was relatively unknown until 2015, when Brazil began to report a significant increase in the numbers of babies with congenital defects. It is a virus that is primarily transmitted by mosquitos and primarily effects the nervous system. With its tropical climate and constant mosquito presence, Puerto Rico was the location of a massive outbreak during 2015-2016. However, the response to the outbreak faced several hurdles despite Brazil already reporting an increase in microcephaly. The purpose of this review is to examine the political and historical factors that hampered the initial response to the 2015 Zika outbreak in Puerto Rico and how they affected the perceived risk of the Zika virus. It is crucial that intensive health education campaigns and vaccine development continue in order to ensure that a second outbreak does not occur and result in a greater number of babies diagnosed with Congenital Zika Syndrome.

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Author's Statement Page

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Background

In April 1947, a team of scientists studying yellow fever virus in the Zika forest of Uganda discovered a "hitherto unrecorded virus" in a rhesus monkey. Due to the location of its discovery it was named the Zika virus. In January 1948, a second discovery of the virus was made in the *Aedes africanus* mosquito at the same research site. Four years later, at the Ugandan Virus Research Institute, neutralizing antibodies were found in 6 of 99 humans tested near the Institute, though none had symptoms of a disease (Dick, Kitchen, & Haddow, 1952). In 1964, when a researcher working with the virus developed a headache, slight fever, and a rash that the first human case of Zika virus was laboratory-confirmed. From the 1960s to the 1990s, antibodies in humans were confirmed in laboratories after testing local residents, but there were only 14 documented active cases of the disease (Cohen, 2016; Duffy et al, 2009; Faye et al., 2014).

In 2007, an outbreak of a disease similar to dengue occurred on the Island of Yap in Micronesia (WHO, 2016a). As reported by Duffy et al. (2009), when blood samples were tested the doctors realized the illness was not dengue. Samples were sent to the Centers for Disease Control and Prevention (CDC), which determined the pathogen was the Zika virus. Duffy's team confirmed of the 185 cases, 49 cases were Zika, and 59 cases were categorized as probable. The researchers conducted household surveys and discovered Zika antibodies in 414 of 557 residents. This data was used for population estimates, and researchers concluded that 73% of residents had been infected with the Zika virus. This was the first major, documented outbreak of Zika virus in human populations. Cases of Zika continued throughout the Pacific Ocean, but the 2015 outbreak in Brazil captured the attention of the international community. In 2015, it is estimated between 440,000 and 1,300,000 cases of Zika infection occurred in Brazil (Heukelbach et al.,

2016). On April 7, 2016 the World Health Organization reported that during the span of January 1, 2007 to April 6, 2016, the Zika virus had made its way across 62 countries and territories (WHO, 2016b). The purpose of this review is to examine the political and historical factors that hampered the initial response to the 2015 Zika outbreak in Puerto Rico and how they affected the perceived risk of the Zika virus.

Transmission Routes

The Zika virus is most commonly spread through the bite of an infected mosquito from the *Aedes* genus, either the *Aedes aegypti* or *Aedes albopictus.* These are the same species of mosquitos that transmit dengue and chikungunya viruses. The *Aedes aegypti* is more likely to spread Zika virus because they prefer to feed on humans whereas the *Aedes albopictus* feeds on other animals as well (CDC, 2016a). Female mosquitos require blood to lay their eggs, and the *Aedes aegypti* typically lays its eggs in artificial or natural water containers because these are located within human populations (CDC, 2012).

The Zika virus can also be transmitted to a fetus by a pregnant mother. If a woman contracts the Zika virus while pregnant, it can be passed to the fetus (CDC, 2016b). This transmission route is concerning since it can result in severe birth defects in the fetus. The most documented birth defect is microcephaly (CDC, 2016b). The fetus is born with a head significantly smaller than that of a healthy baby of the same age and sex, usually due to improper or insufficient brain development. Viral cases are more often the result of brain shrinkage because of significant tissue death. Microcephaly can result in a variety of deformities and disabilities, such as blindness, hearing loss, impaired cognition, seizures, impaired motor functions, delayed speech, and other brain abnormalities. Microcephaly is a lifelong condition and there is no standard treatment (CDC, 2016c).

The Zika virus can also be transmitted through sexual intercourse. An infected individual can pass it to their partners via semen or vaginal fluids. It can spread before onset of symptoms, while it is symptomatic, and after symptoms disappear. Sexual transmission of the Zika virus has been documented between males-to-males, males-to-females, and females-to-males. Though no female-to-female cases have been documented, it is still "biologically plausible" (CDC, 2016d). Approximately 80% of those infected with Zika will never develop symptoms, and the only cases that can be verified as sexually transmitted are those where only one partner has visited or lived in an area with active Zika transmission and have been laboratory-confirmed for the Zika virus. As of August 26, 2016, there were 17 documented cases of sexually transmitted Zika infections across 11 countries (WHO, 2016d).

Blood transfusions are a fourth possible transmission route. Many Zika infected individuals are asymptomatic, and it is possible they could donate blood without knowing they were infected (CDC, 2016e). After the outbreak in French Polynesia, a sample of 1,505 blood donations given between November 13, 2013 and February 17, 2014 were tested for the Zika virus, with 2.8% testing positive. At the time of publication, none of the blood recipients were infected with Zika, but studies are still ongoing (Musso et al., 2014). However, Brazil has reported a number of cases that can be plausibly linked to infection via blood transfusion (Barjas-Castro et al., 2016; Motta et al., 2016).

Adverse Outcomes

Guillain-Barré Syndrome

Most of the potential adverse outcomes from Zika infection have been neurological. The virus attacks the nervous system, but there is no evidence supporting the Zika virus will permanently damage any other organs. On July 17, 2015, Brazil reported a significant increase in

the number of neurological disorders in individuals with a history of Zika infection, many confirmed to be Guillain-Barré syndrome (GBS) (WHO, 2016a). GBS is an auto-immune disorder, and the infected person's immune system begins attacking the peripheral nerves. Typically, the first symptoms are tingling and weakness in the extremities and the face, but this can progress to paralysis of these muscles (WHO, 2016c). Chest muscles can also be affected, and 25% of patients have difficulty breathing. Of those that need to be intubated, 60% will suffer from major complications, such as sepsis, pneumonia, and pulmonary embolism. Though 95% of patients will recover, 20% will remain severely disabled (Yuki & Hartung, 2016). During the 2013 outbreak, French Polynesia reported a 20% increase in the number of new GBS cases (Oehler et al., 2014). Dos Santos et al. (2016) studied the trends of Zika infection and GBS cases in Brazil, Colombia, Venezuela, El Salvador, the Dominican Republic, Suriname, and Honduras and found as the incidence of Zika increases so does the incidence of GBS. This is also true for decreases in incidence. On April 7, 2016, the WHO's Weekly Situation Report stated there was a causal link between Zika virus and GBS (WHO, 2016b).

Birth Defects

In October 2015, the Brazilian Ministry of Health reported a significant increase in the number of babies born with microcephaly in areas with high Zika transmission (WHO, 2016a). By testing their amniotic fluid, two pregnant women whose fetuses were microcephalic tested positive for Zika virus RNA. Further research revealed that

> [a]mong a cohort of 35 infants with microcephaly born during August–October 2015 in eight of Brazil's 26 states and reported to the registry, the mothers of all 35 had lived in or visited Zika virus-affected areas during pregnancy, 25 (71%) infants had severe microcephaly (head circumference

> >3 SD below the mean for sex and gestational age), 17 (49%) had at least one neurologic abnormality, and among 27 infants who had neuroimaging studies, all had abnormalities (Schuler-Faccini et al., 2016, para. 1).

Shortly after, Brazil reported blood and tissue of two microcephalic stillborn fetuses and a microcephalic newborn who died almost immediately after birth all tested positive for Zika virus RNA (Kleber de Oliveira et al., 2016; Schuler-Faccini et al., 2016). A larger cohort study was conducted in which 72 of 88 pregnant women tested positive for Zika. Of the 72 women, 42 received ultrasounds, which revealed fetal abnormalities in 12 (29%) fetus' (Brasil, et al., 2016). This discovery lead to a retrospective study on the outbreak in French Polynesia that found an association between Zika infection in pregnant women and microcephaly in the fetus. Cauchemez et al. (2016) reported within a 23-month study period, 8 cases of microcephaly were detected. Seven of these cases revealed that the mother was infected by Zika during the first trimester. The final results indicated there is a 1% increased risk for microcephaly in Zika infected women. The baseline prevalence in French Polynesia was 2 cases of microcephaly per 10,000 newborns, but during the outbreak it was 95 per 10,000 newborns. In terms of future pregnancies, there is no documented evidence a previous Zika infection will have any effect on future pregnancies (CDC, 2016f). On April 13, 2016, the CDC confirmed via a media statement there is a causal link between Zika infection and microcephaly in fetuses (CDC, 2016b). A review of existing data conducted by Rasmussen et al. (2016) also supported a causal relationship. A Zika infection during pregnancy has also been tied to pregnancy loss and on June 16, 2016, the CDC announced it would start reporting all pregnancies with laboratory-evidence of Zika that results in poor outcomes (CDC, 2016l).

Though microcephaly might be the most conspicuous of the birth defects associated with Zika virus, it is certainly not the only one. Researchers at the CDC are now calling this pattern of birth defects Congenital Zika Syndrome, which have been grouped into five types:

(1) "Severe microcephaly with partially collapsed skull
(2) Thin cerebral cortices with subcortical calcifications
(3) Macular scarring and focal pigmentary retinal mottling
(4) Congenital contractures
(5) Marked hypertonia and symptoms or extrapyramidal involvement" (Moore et al., 2017, p. 293).

The long-term effects on fetuses who were exposed to Zika virus in utero is still not known, and researchers acknowledge that though a baby might not display signs of any congenital defects at birth, it is still possible that problems may develop later in life (Sun, 2016a; CDC, 2017a). A lot of data also remains unpublished (Costello et al., 2016).

Puerto Rico

On August 12, 2016, at the request of Puerto Rico Governor Alejandro García Padilla, the Department of Health and Human Services declared a public health emergency in response to the Zika outbreak. There were 10,690 laboratory-confirmed cases, including 1,035 pregnant women (Monroe, 2016; Nather, 2016; Steenhuysen, 2016). This declaration allows Puerto Rico to apply for additional federal funds to hire and train new workers for vector control and health education. It also allows for health workers to be temporarily reassigned to aid in the response (Nather, 2016; Steenhuysen, 2016; Wisconsin Health Association, 2016).

As of November 11, 2016, Puerto Rico had "the largest number of laboratory-confirmed cases" (Lozier et al., 2016, para. 7). Between November 1, 2015 and October 20, 2016, there

were 62,500 suspected cases of Zika virus diagnosed in Puerto Rico and 29,345 (47%) were confirmed via laboratory testing. This was an incidence rate of 844 cases per 100,000 population. Females were diagnosed more often than males with 18,384 (63%) confirmed and presumed cases (Lozier et al., 2016). This was also the case for outbreaks in El Salvador, the Island of Yap, and Brazil. A study conducted in Brazil hypothesized women are more likely to be exposed to the *Aedes* mosquito because they are more likely to stay-at-home, where these mosquitoes tend to be found around containers of stagnant water. Women were also more likely to seek out health care with symptom onset, especially if they were of child-bearing age (Coelho et al., 2016).

As reported by the Puerto Rican Health Department (2016a), during November 1, 2015 and December 22, 2016, 2,591 pregnant women displayed evidence of Zika. They either tested positive, were presumed positive for Zika, or presumed positive for arbovirus. Of those, 1,537 (59.3%) were symptomatic and 1,054 (40.7%) were asymptomatic. During this time, there were also seven live births of fetuses that had a birth defect consistent with Zika infection, three loss of pregnancies of fetuses with a congenital defect consistent with Zika infection, and two lost pregnancies where the fetal tissue tested positive for Zika virus.

On October 28, 2016, Puerto Rico reported the first case of Zika-associated microcephaly in a live birth (Politico, 2016). However, the first case of microcephaly in a Zika-positive fetus occurred in May 2016 (Aljazeera, 2016). In order to protect the privacy of the mothers and children, the CDC is not reporting data on birth defects in the territories (CDC, 2017b) but Ellington et al. (2016) predicts an interquartile range of 100 to 270 babies will be born with Zika-associated microcephaly before mid-2017. On April 18, 2017, Helen Branswell reported that only 16 cases of birth defects had been attributed to Zika virus. She reports that an unnamed, former US official said that Puerto Rico underreporting the issue. The individual states a much

higher number of babies with typical Zika birth defects but officials have not labeled them Congenital Zika Syndrome (CZS). The CDC and the PRHD have different inclusion criteria for CZS (CDC, 2017b).

By December 1, 2016, of 172 patients reported to the GBS Surveillance system, 81 tested positive for Zika, presumed positive for Zika, or presumed positive for flavivirus. Of these 81, 67 were diagnosed with GBS and the remaining 14 were diagnosed with other neurologic conditions (PRHD, 2016b). Of the 34 patients diagnosed between January 1 and July 31, 2016 with GBS and with positive or presumed Zika infection, 21 required intensive care in hospitals. One patient died after developing a severe case of thrombocytopenia while being treated (Dirlikov et al., 2016a; Dirlikov et al., 2016b).

Methods

The information was compiled using formal and informal data sources. Formal data sources were gathered from online, peer-reviewed journals accessed via PubMed and Galileo, a database for the University System of Georgia that provides access to a variety of scholarly journals, such as the *New England Journal of Medicine*, *PLoS Neglected Tropical Diseases*, *Social Science and Medicine*, and others. When searching Galileo, the discipline parameters were restricted to biology, environmental sciences, health and medicine, history, public health, social sciences and humanities, sociology. Main keywords used were zika, Puerto Rico, Brazil, microcephaly, sterilization, oral contraception, Vieques, history, United States, response, naled, skepticism. Online periodicals were also searched to gather information on current events and the public's attitude and response to the Zika outbreak. It provides information in a more real-time perspective that cannot be accomplished by peer-reviewed articles.

Literature Review

The World Health Organization states "the context of people's lives determine their health" (n.d., para. 3). Addressing a health crisis from one perspective may alleviate the problem but sustainable change requires an examination of multiple factors that may be influencing a population's health (HealthyPeople.gov, n.d.).

Economic

Currently, Puerto Rico has a $70 billion debt and is unable to make payments. Its status as a territory prevents it from declaring bankruptcy and receiving additional aid from the US government (Alvarez & Goodnough, 2015; Respaut, 2016; Walsh, 2016). In order to handle the spiraling debt and in response to Puerto Rico's noncompliance with Federal statutes, regulations, or terms of conditions of a Federal Award, on June 30, 2016, the US passed the Puerto Rico Oversight, Management and Economic Stability Act (PROMESA). Noncompliance allows the federal government to implement any remedies that may be legally available (Office of Management and Budget, n.d.). PROMESA created a financial oversight board, prevented creditors from taking action against the island, and allowed for the restructuring of debt (PROMESA, 2016). This was met with mixed reactions by Puerto Ricans. The governor, the non-voting elected representative, and businesses were supportive of PROMESA but other political leaders and much of the Puerto Rican population fiercely protested the measure (Allen, 2016). Protests occurred in Manhattan, New York and across the island, chanting colonialism (Dayen, 2016; Mijente, 2016; Walsh, 2016). However, even some critics acknowledge action was necessary and perhaps austerity measures were the only recourse (Walsh, 2016). Other critics hold firm the bill completely undermines democracy (Dayden, 2016; Telesur, 2016; Suarez & Allen, 2016).

Much of this debt is a result from healthcare costs. Prior to the Zika outbreak, the Puerto Rican healthcare system was already under significant strain. Because of high rates of poverty and unemployment, Medicaid covers almost half of Puerto Ricans, but the Medicaid financing rules are different compared to the rest of the United States (Alvarez & Goodnough, 2015; Newkirk II, 2016; Respaut, 2016). For Puerto Rico, the federal matching assistance percentage (FMAP) is fixed at 55%, but for the states, it can range from 50-83% depending on that state's per capita income (Evans et al, 2016; Congressional Research Service, 2016). If Puerto Rico's FMAP was based on its per capita income, the federal government would be paying 83% of its Medicaid costs (Government Accountability Office, 2014). Medicaid and CHIP federal funds are also capped for Puerto Rico and all other territories. In FY 2015, the Medicaid federal funds were capped at $329 million and CHIP was capped at $183 million (MACPAC, 2016). As of June 2015, there were 1,671,657 Medicaid and CHIP enrollees, which is approximately half of the population (Medicaid, n.d.). Through the Patient Protection and Affordable Care Act (ACA), Puerto Rico was able to receive an additional $803 million (Kaiser Family Foundation, 2016a; Congressional Research Service, 2016). The total available ACA Medicaid funding is $6.4 billion to be used from July 1, 2011 and September 30, 2019 but the Centers for Medicare and Medicaid project this will run of by the end of 2017 (Congressional Research Service, 2016; Kaiser Family Foundation, 2016a; United States Senate: Committee on Finance, 2016).

Healthcare System Infrastructure

Medical students and doctors are leaving in droves for higher salaries and to escape the growing economic crisis (Alvarez & Goodnough, 2015; Félix & Suárez, 2015; Kilpatrick, 2015). According to the Puerto Rican Surgeons and Physicians Association, 864 doctors left the island in 2014 and 2015 (Parés Arroyo, 2016a; Sierra-Zorita, 2016). Waiting lines to see a doctor can

last hours and there's no guarantee that the physician will be able to attend everyone. In order to see a specialist, it can take months to get an appointment because of the shortages. (Allen, 2016; Félix & Suárez, 2015; Margolis, 2016; Reitman, 2016). Patients are even being recommended to go to the mainland to receive treatment, if possible (Coto, 2016c; Respaut, 2016). The healthcare infrastructure is also suffering under the financial crisis. As a significant portion of the population is covered by Medicaid, many providers are dependent on these payments to keep services available but they are never reimbursed (Kilpatrick, 2015; Margolis, 2016). This had led to layoffs and a shortage of medical supplies (Margolis, 2016). Hospitals have closed floors, lowered the retirement age, and cut benefits. On April 29, 2016, it was reported by the chief executive of Puerto Rico's Association of Hospitals that over 3,000 hospital employees had been laid off in the past year (Parés Arroyo, 2016b). Santa Rosa Hospital even had its power shut off for a few hours as it struggled to reach an agreement with the island's power company. The power company is $9 billion in debt and the hospital is $4 million in debt to the power company (Associated Press, 2016; Margolis, 2016).

Political

On February 22, 2016, President Obama's administration requested Congress for over $1.8 billion in emergency funds to combat the growing outbreak of Zika, both domestically and internationally. The emergency funds would be used (1) for vaccine research and diagnostic development, (2) for mosquito surveillance and control, (3) for education for health providers, women, and partners, (4), for improvement of health services and support for low-income pregnant women, and (5) to help Zika-affected countries better control transmission (Obama White House Archives, n.d.). In his letter to the Speaker, President Obama specifically requested additional Medicaid funding for Puerto Rico and other U.S. territories to aid in providing health

services for pregnant women at risk for infection or those who have already been diagnosed. These funds would also be used to fund health services for children with microcephaly (Obama White House Archives, 2016). However, this request was stalled in Congress until September 28, two days before the end of the fiscal year, when $1.1 billion was finally approved to fight the Zika virus (Kaplan, 2016). A major reason the funding stalled was a provision added by House and Senate Republicans that would block any clinics associated with Planned Parenthood from receiving funds. Democrats were unwilling to approve the bill as long as this provision was included because it would restrict women's access to contraception. This resulted in both parties blaming the other for playing politics at the expense of those at risk (Kaplan, 2016; Kodjak, 2016; Sullivan 2016; Werner, 2016). This provision was eventually dropped which resulted in the passing of the bill. The funding was also stalled while members of the House Committee on Appropriations suggested that funds dedicated to the Ebola response be repurposed toward the Zika response (United States House of Representatives: Committee on Appropriations, 2016). However, former CDC Director Tom Frieden stated in a press briefing this unspent money was to be used for prevention efforts in case Ebola makes another appearance and that "we can't be letting down our guard in one place to fight another battle" (CDC, 2016h). This was echoed by Sylvia Burwell, the Secretary of the Department of Health and Human Services (Bichell, 2016; Eilperin & Snell, 2016).

Historical

Though there are a number of additional occasions that have resulted in a complex relationship between the United States and Puerto Ricans residents, only Vieques Island, birth control, and sterilization are reviewed here. In his speech to the House of Representatives over Zika funding, Rep. Luis V. Gutiérrez (D-IL) references Vieques and forced sterilization as events

that have influenced how many Puerto Ricans perceive the Zika threat (2016). As the transmission of the Zika virus is environmental and currently the greatest threat to future generations of Puerto Ricans, reviewing these events is crucial to understanding the context in which Puerto Ricans interpret the actions of the United States.

Vieques Island

Vieques Island is 33,000 acres and is located approximately 6 miles off the southeastern coast of Puerto Rico. Beginning in 1941, the US began the expropriation of 26,000 acres of land for Naval and Marine Corps training. The east side of island was used for bombing and shelling practice that occurred 120-180 days per year while the west was used as weapons storage and waste disposal (Epting, 2015; Medina et al., 2014; Withers, 2013).

For decades, the navy continued to test weapons despite protests from the residents and a lawsuit filed by the Puerto Rican government. It was not until the death of civilian security guard David Sanes Rodriguez on April 19, 1999 the protests received international attention and the military's activities were eventually stopped (COHA, 2011; Epting, 2015, Withers, 2013). On May 1, 2003, the US Navy left Vieques and most of the land was designated as a wildlife refuge under the US Department of Fish and Wildlife. Though the island is no longer being used to test weapons, clean-up efforts are severely hindered because human activity is restricted on wildlife refuges (COHA, 2011; McCaffrey, 2009). The land was also not returned to the residents. They still do not have access and are unable to develop it (Berman Santana, 2006). The island had a history of agriculture and fishery before the naval occupation, (Epting, 2015; McCaffrey, 2009) and the majority of residents view the Department of Fish and Wildlife as the most recent oppressor in continued US control of the land (Davis, Hayes-Conroy, & Jones, 2007; McCaffrey, 2009).

The Agency for Toxic Substances and Disease Registry (ATSDR) conducted a series of reviews to determine if any health effects resulted from the naval activity. The first review done in 2001 did not find an association between the bombings and the disproportionately high disease prevalence among island residents compared to mainland Puerto Rico. The report stated that the levels of compound explosives and heavy metals found in environmental samples were not hazardous to the health of the residents (Berman Santana, 2006; Withers, 2013). However, a 2007 report by the Puerto Rico Department of Health revealed that Vieques residents have "25% higher infant mortality rates, 16% higher asthma rates, 27% higher cancer rates, 28% higher diabetes rates, 95% higher cirrhosis of the liver, and 38% higher hypertension rates" than those on mainland Puerto Rico (Medina et al., 2014). Other ecological studies report similar findings (Baver, 2006; Davis, Hayes-Conroy, & Jones, 2007; Wilcox, 2001; Yelin & Miller, 2009). In 2009, the ASTDR reopened the investigation into Vieques after the director of agency was called up to defend against various claims of inadequate review (Withers, 2013). The agency issued a press release stating it had changed its previous conclusions and there were too many gaps in the data to determine health effects (ATSDR, 2009). In 2011 and 2013, the ATSDR again reviewed the data and reported that the "findings of these studies indicate elevations in chronic disease prevalence, cancer incidence, and cancer mortality among the population between Vieques and the rest of Puerto Rico" (ATSDR, 2013, p. 163) but there was insufficient data to link naval activity with these disparities (ATSDR, 2011; Medina et al, 2014). However, outside researchers have heavily criticized the methodology of these investigations (Davis, Hayes-Conroy, & Jones, 2007; Epting, 2015; McCaffrey, 2009). In 2010, Dr. John Wargo, a professor at Yale University who has worked with the EPA, FDA, WHO, and other Congressional committees, testified his evaluation of the ATSDR's public health assessments to the Subcommittee on Investigations and

Oversight, House Committee on Science and Technology, U.S. House of Representatives. He criticizes the agency for relying on data collected by others and not conducting their own studies. The reports were not peer-reviewed and the samples sizes were small (1-12) samples. He also states the agency failed to assess how food contamination could lead to additional exposure and failed to collect soil contamination data (Testimony of John P. Wargo, 2016). Diaz and Massol-Deya (2003) found that plants on Vieques had much higher concentrations of lead (10x) and cadmium (3x) when compared to plants on mainland Puerto Rico. Hair samples were tested in women of reproductive age on the island and 26.8% had levels of mercury that are considered unsafe for a developing fetus. In northeastern Puerto Rico, a heavily industrialized area, only 6.6% of women had unsafe levels (Ortiz-Roque & Lopez-Rivera, 2004). In 2005, a class action lawsuit was filed by three-fourths of the island's residents—about 7,000 people—seeking reparations but the case was dismissed on the grounds of "sovereign immunity," meaning it is protected from lawsuits (Baynes, 2012; Forsythe, 2012).

Sterilization

In the early 1900s, there was a global rise in the eugenics movement. The "American ruling class" promoted the theory that only the fittest should reproduce in order to decrease the number of undesirables (Bauza, 1994; Mass, 1977). Marginalized women were forcibly sterilized all over the United States (Denbow, 2014; Schoen, 2001). At this time, Puerto Rico was suffering from a failed single-export economy and had high rates of unemployment and poverty (Mass, 1997). Therefore, officials decided the most direct intervention would be to target population growth. This began in 1937, when Law 116 was passed in Puerto Rico legalizing the sterilization of those who were mentally ill, intellectually disabled, epileptic, and those considered sexual degenerates (Bauza, 1994; Ley Num. 116, 1937; Mass, 1977). Fifty-three birth

control clinics were opened in the late 1930s, despite pushback from the Catholic Church and anti-colonialists. At hospitals and at the clinics, sterilization became the most promoted form of birth control offered to women (Presser, 1969; Warren et al., 1986). Healthcare workers ventured into rural areas to target the poorest women and encourage sterilization. Some local governments even subsidized the cost of the operation. Though consent was needed by the woman and her husband, it was often sought immediately after childbirth, when both were distracted and preoccupied (Bauza, 1994; Mass, 1977). There were reports in later years where women did not understand the procedure was permanent and expressed regret at their decision (Bauza, 1994; Reilly, 2015).

Though some women felt coerced, it is import to note many sought out the procedure. However, their motivations were not driven by a desire to limit the size of their family. Mass (1977) concluded it was more due to a lack of other options. Post-natal care, child-health care, and maternal-care services were expensive and insufficient. Abortions were expensive, illegal, and resulted in a prison-sentence. Other birth control options were not readily available. The pill was controversial and carried severe side-effects and intra-uterine devices were expensive and follow-up-care was difficult to obtain. Though a large portion of women chose to be sterilized, their decisions were routed in poverty, lack of healthcare, lack of education, gender roles, and racism (Martinez, 2009). It was estimated in 1994 that 45.1% of Puerto Rican women aged 15-49 had been sterilized. This was the highest in the world. The next highest was the Dominican Republic at 39.0% and for comparison, the United States was 23.4%. This same survey estimated in 2015, 36.6% of Puerto Rican women aged 15-49 were sterilized. Only India was higher at a rate of 39.0%. 21.8% of American women reported sterilization (United Nations, 2015).

Oral Contraceptive

In 1951, Margaret Sanger, the founder of the Planned Parenthood Federation of America, approached Dr. Gregory Pincus on developing a birth control pill for women. At the time, Dr. Pincus was an endocrinologist known for achieving *in vitro* fertilization in rabbits. In order to fund Pincus's research, Sanger turned to fellow activist Katharine McCormick, who had inherited millions of dollars upon her husband's death. Eventually, Pincus brought in gynecologist and infertility specialist John Rock to conduct preliminary testing. Rock's patients were trying to get pregnant and while experimenting with progesterone and oestrogen, he discovered they had a contraceptive effect (Dhont, 2010; Marks, 1999; Roberts, 2015). These trials were conducted on patients without their informed consent (Christin-Maitre, 2012; Dhont, 2010; Marks, 1999; Roberts, 2015). Informed consent laws did not exist at this time and the women were told this would aid fertility once the trial was complete (Roberts, 1999). Pincus and Rock conducted preliminary trials on infertile women to determine if the hormones would successfully halt ovulation. Small-scale trials continued in Worchester, Massachusetts and New York City, New York under the guise of fertility treatments (Marks, 1999). The results were promising but without large scale human trials, the pill would never receive FDA approval for contraceptive reasons. However, the trials could not be conducted in the United States because of the Comstock Laws, which prohibited the distribution of contraceptives and information about them (Roberts, 2015). Therefore, the trials were conducted in Puerto Rico because contraceptive was legal and the population was mostly stationary. It was also close to the US which would allow close supervision (Dhont, 2010; Liao & Dollin, 2012; Marks, 1999). Since birth control clinics already existed it was not difficult to gain access to women who were already trying to avoid pregnancy (Liao & Dollin, 2012; Marks, 1999; Roberts, 2015). The researchers viewed the island as an ideal setting because of its growing, yet impoverished population (Liao & Dollin,

2012; Roberts, 2015). They also wanted to test if uneducated women would be able adhere to the regime of an oral contraception. The first round of volunteers were drawn from a public housing project full of individuals that had recently been moved from a slum (Liao & Dollin, 2012; Marks, 1999). The women who became part of the study were mostly illiterate, and many were unaware that this was a clinical trial. Though the participants were supposedly told it was trial, there were no forms to sign and many did not understand and later felt deceived. These women were already visiting birth control clinics and were desperate for ways to control their fertility (Liao & Dollin, 2012; Marks, 1999).

Of the study pool, 100 women were recruited for the experimental pool and 125 for the control group (Roberts, 2015). Within the first month, 30 women had withdrawn from the trial due to negative publicity, husband's objections, and/or negative side effects (Marks, 1999). In the first six months, 12 of the original 100 had withdrawn due to negative side effects. These effects included nausea, headaches, dizziness, and vomiting (Christin-Maitre, 2012; Marks, 1999). However, Pincus believed the symptoms to be psychosomatic and continued to accept new participants (Geampana, 2016; Marks, 1999; Roberts, 2015). By this time, only around 20 of the original 100 remained. The number of participant dropouts was so significant the investigators used number of menstrual cycles as opposed to the number of women in their publications (Marks, 1999; Roberts, 2015). In 1960, the pill was FDA approved for contraceptive use and as early as 1962, Searle, the pharmaceutical responsible for production and distribution, had received 132 reports of blood clots; 11 of which resulted in death. They maintained that there was no conclusive proof the pill was responsible for those deaths (Geampana, 2016). Investigators were dismissive of the women's complaints and continued to administer the pill. According to Marks (1999), this dismissive attitude was typical of the time. Today, Puerto Rican

women are still critical of this experiment, and those who lived through still express trauma when reflecting on that time (Carroll, 2016; Laureano, 2010; Quintanilla, 2004).

Environmental

The *Aedes aegypti* mosquito has a constant presence on the island and mosquito-borne illness are commonplace. The residents were dismissive because dengue and chikungunya have more serious symptoms and are just considered part of life on the island (Call, 2016a; McNeil, 2016a; Sifferlin, 2016a; Sun, 2016b). As reported by journalist John Call, in an interview with an expectant mother, she states,

> "It's never going to be gone. Why now do we have to have this massive fumigation? So when the government signed the emergency act that will provide a lot of federal funds towards Zika that's when I was like – hmm, follow the money maybe? Is it something more about getting money?" (2016a, para. 24).

She was initially worried about Zika but after she tested negative, she began to question the motivations of government and healthcare professionals (Call, 2016a). Another expectant mother, who is a nurse by trade, tested positive in her first trimester but has had normal tests, also questions if the threat is truly as severe as portrayed. She does not deny that a threat exists but she believes it is being exaggerated (Call, 2016b). Jason Beaubien (2016), another journalist, reports of speaking with a father, who knows he should be worried about Zika but the 2014 chikungunya outbreak was much worse and he shrugs off any concern. The apathy was exacerbated by disagreement among health professionals on the severity of the problem. Some grew frustrated, trying to convince the populace of the seriousness of the disease. A state epidemiologist says she has never before seen a mosquito-borne virus that has the ability to cross the placenta to the fetus (Beaubien, 2016). But some local health professionals expressed doubt,

stating the projected numbers were an exaggeration (Coto, 2016a; McNeil, 2016b; Silverman, 2016). Though they agree it is a problem, many doctors did not believe that it is a major one (Beaubien, 2016; Coto, 2016a).

Naled is an insecticide that is primarily used to kill mosquitoes, though it is also used in agriculture. For mosquito control, naled is disseminated as an ultra-low volume (ULV) spray. The aerosol droplets contain a small amount of the active ingredient, which kills mosquitos on contact. Though the EPA has ruled naled safe if used correctly, there is debate on whether it is truly safe. The EPA states that because it is unlikely people will come into direct contact with naled, there is no real health risk as a result of spraying (EPA, 2017). The CDC also advocates the safety of naled. Their website states that the amount sprayed is so minor that "all scenarios and exposures were hundreds or thousands of times below an amount that might pose a health concern" (CDC, 2016g). It does recognize that at high doses, naled can cause significant health problems, such as nausea, dizziness, convulsions, respiratory paralysis, and death. In contrast to the EPA and the CDC, the European Union has banned naled because the "scenarios evaluated in the human health risk assessment as well as in the environmental risk assessment showed a potential and unacceptable risk. Furthermore, the evaluation has not demonstrated sufficient efficacy" (The European Commission, 2012).

In response to the Zika outbreak in Puerto Rico, the EPA sprayed naled in 14 *Aedes aegypti* mosquito populations in February and March of 2016 with a 100% mortality rate (EPA, 2017). However, when the CDC recommended that Puerto Rico spray naled to reduce the mosquito populations, the citizens protested so severely the Governor's advisor for the Zika epidemic resigned citing a vicious environment (McNeil, 2016b). It was also discovered the CDC had already imported naled onto the island without first consulting the Governor. This led

to massive resistance which resulted in the CDC apologizing and shipping the naled back to the US (Coto, 2016b; McNeil, 2016b). Many Puerto Ricans saw this as confirmation that the US planned to spray without their knowledge or approval. Even some Puerto Rican health professionals were unconvinced that the US was not attempting to conduct experiments and participated in the protests (Beaubien, 2016; McNeil, 2016b; Viglucci, 2016). Naled has also been sprayed in the Miami-area of Florida but it was requested and approved by health officials. Many of the cities' residents have protested its use, citing the health risks and its ban in the EU. There was a short delay to begin spraying as health and government officials considered alternatives but they ultimately decided to go ahead and spray areas where the mosquito has been found (CBS Miami, 2016; Luscombe, 2016; Karimi & Visser, 2016).

According to some Puerto Ricans, the CDC was not transparent in their actions or forthcoming with the risks associated with naled. On July 21, 2016, the Municipality of San Juan and its Mayor Carmen Yulin Cruz Soto filed a lawsuit in federal court against the CDC and its director Tom Frieden, the Commonwealth of Puerto Rico and its officers, Governor Alejandro Garcia Padilla, Secretary of the Department of Agriculture Myrna Comas, and Secretary of the Department of Health Ana Rius-Armendariz. The lawsuit states that the citizens are "seeking relief from defendants' intended actions which will pose a significant risk to the well-being of several species of fish, wildlife, and plants" and "to prevent defendant The Center for Disease Control and Prevention (hereinafter "CDC") to implement its plan to carry aerial spraying within the San Juan territorial jurisdiction and across Puerto Rico without first complying with environmental laws and regulations," specifically citing the Endangered Species Act and the National Environmental Policy Act. The following day, Puerto Rican Governor Alejandro García Padilla stated that the Puerto Rican government would not allow naled to be sprayed (Coto,

2016b; McNeil, 2016b). Instead, *Bacillus thuringiensis* subspecies *israelensis* (Bti), a naturally occurring bacteria, will be used to control the mosquito population (Coto, 2016b; Silverman, 2016). Bti spores produces toxins that kill mosquito larvae but it does not affect adult mosquitos (EPA, 2016). On September 23, 2016, in a press briefing, Director Tom Frieden discussed the effectiveness of using a combination of naled and Bti and though he understood the residents' concerns about naled, he stated that a lack of awareness of microcephaly probably influenced the reaction (CDC, 2016k) and that perceptions would change once the babies with microcephaly were born (Fox & Angulo, 2016).

Implications

The long-term health outcomes for babies with CZS are not entirely known yet (Reilly & Rappaport, 2017). According to the CDC, microcephaly can be an isolated condition or it can co-occur with other birth defects. Microcephaly can usually be detected in a fetus via an ultrasound but in other babies, it does not become apparent until after birth when their heads stop growing (CDC, 2016c). Babies diagnosed with CZS will require care from multiple doctors and should start therapy as soon as possible. Early intervention services can provide cognitive, social, emotional, and physical resources for these babies and their parents (CDC, 2017c). All infants born to mothers with laboratory evidence of Zika should receive a physical examination, head ultrasound, hearing, eyesight, and neurologic assessment, and Zika virus testing (CDC, 2017d). If the infant has laboratory evidence of Zika infection but does not display any abnormalities associated with CZS, additional monitoring is recommended for possible delayed onset (CDC, 2017e; Russell et al., 2016). Families should also be involved in monitoring for feeding, growth, and sleep problems, irritability, and seizure recognition (CDC, 2017f; Russell et al., 2016). The babies are still too young to determine if being exposed to the Zika virus in utero will cause

learning disabilities or other development delays later in life (Peñaloza & Allen, 2017; Reilly & Rappaport, 2017; Rosen, 2016; van der Linden, 2016; WHO, 2016e). Puerto Rico's Health Department plans to monitor babies born to Zika infected mothers or babies exposed perinatally up until 3 years of age (CDC, 2017g).

Treatment for babies with CZS will also have a huge impact on the families of these babies, private insurers, and public health care systems. In a web briefing with the Kaiser Family Foundation, former CDC director Dr. Tom Frieden states the Center for Birth Defects at the CDC estimates the lifetime care of a child with a congenital defect can have a lifetime cost between $1 million to $10 million (Kaiser Family Foundation, 2016b). As a significant portion of Puerto Rican's have Medicaid as their insurer, they would rely on Medicaid to pay for treatment. But with the current Medicaid funding crisis, additional funds are necessary. Of the emergency funds allocated for the Zika response, President Obama requested $246 million be directed to the Centers for Medicare and Medicaid Services (CMS) but this was not addressed in the proposals from Congress (Wexler, Oum, & Kates, 2016). However, on January 18, 2017, CMS announced $60.6 million will be directed at Puerto Rico. These funds will be used to support prevention activities and health services to those affected by the Zika virus (CMS, 2017).

Public Health Response

In response to the growing diagnoses of Zika in Puerto Rico, the PRHD and CDC implemented vector-control programs, improved diagnostic tests, and implemented a number of surveillance systems for pregnant women, contraception use, and GBS cases. On September 27, 2016, the CDC announced it would provide funding to establish the first Vector Control Unit (VCU) in Puerto Rico. The VCU is responsible for overseeing the implementation of integrated mosquito control activities. These activities include reducing the mosquito population,

community engagement, and health education (CDC, 2016i). The PRHD and Women, Infant, and Child (WIC) clinics developed a vector control program that is home-based and targeted toward pregnant women. One method of reducing the mosquito population is to remove, cover, or treat standing water where mosquitos lay their eggs. Another method is through the use of insecticides and larvicides. Insecticides kill the adult mosquitos and larvicides kill the mosquito larve (CDC, 2017h). The WIC clinics contact known pregnant women and offer services to remove water containers, to spray insecticide, and to apply larvicide. They partnered with the Department of Housing to implement these services (Dirlikov et al., 2016b).

Health education has been a crucial aspect of managing the Zika outbreak. It provides knowledge, develops skills, and increases self-efficacy toward healthy behaviors. The PRHD has made health education materials available at health care facilities and all entry ports. The PRHD and WIC clinics have also developed and implemented health education classes for pregnant women (Dirlikov et al., 2016b). With assistance from the CDC and other partners, the PRHD has also implemented a messaging campaign known as "Asi es Como Detenemos el Zika," or "This is How We Stop Zika." The campaign promotes community engagement and the use of social media to educate the public about Zika and encourage active participation in prevention efforts. The website provides links to information on how to protect yourself, your partner, your home, and the community. It also includes digital images, posters, web badges, a video, and toolkits for event hosting and social media. The toolkits include provide instructions on how to organize community clean-up days and build-it yourself prevention kit events. The kits include bed nets, mosquito repellent, larvicidal tablets, and condoms (This is How We Stop Zika, n.d.).

In order to minimize the number of babies born with Zika virus–associated birth defects, increasing access contraceptives is crucial. It provides women the ability to prevent or delay

pregnancy. Approximately 65% of pregnancies in Puerto Rico are unintended. Women face barriers of high-costs, contraception shortages, lack of education about contraception options, and lack of contraceptive delivery sites (CDC, 2016j; Li et al., 2017; Tepper, 2016). The "Zika Contraception Access Network" (Z-CAN) was established to increase the access of contraception. The Z-CAN program provides enrolled women access to the contraception of their choice at no cost to them. It also trains medical professionals how to provide birth control (CDC, 2016j; CDC Foundation, 2016).

As an international response, 18 different entities are working on a vaccine for Zika virus. Significant progress has been made because researchers have been able to build on the existing work on other flavivirus vaccines (Mukherjee1 & Khera, 2017). On June 20, 2016, Inovio Pharmaceuticals, Inc. received approval from the Food and Drug Administration to conduct a clinical trial for a Zika vaccine. The first round of human clinical trials with 40 subjects in the United States and Canada with a start date of July 2016 and an anticipated study completion date of December 2017 (NCT02809443). In August 2016, Inovio began a second Phase 1 clinical trial in Puerto Rico. This study is currently in the process of recruiting 160 volunteers who were previously infected with dengue. The estimated completion date of this trial is May 2018 (NCT02887482).

Florida's Response

In the continental US, only Florida and Texas have reported cases of locally-acquired Zika through the ArboNET surveillance system. According to the CDC, as of April 26, 2017, Texas had reported 6 cases of presumed local mosquito-borne infection and Florida 218 (CDC, 2017j). However, Florida's Department of Health reported in 2016 alone, there were 285 locally-acquired infections and 2 cases in 2017 as of May 2, 2017 (2017). On February 3, 2016, Florida

Governor Rick Scott declared a public health emergency in 4 counties that reported Zika infection. At that time, there were only 9 cases and all were travel-related but the purpose was to be prepared for when local-transmission was confirmed (2016a). The following day, his office announced a request for the federal government to supply Zika antibody testing kits (Governor Rick Scott, 2016b). Then on May 12, 2016, he expanded his request to include Zika preparedness kits as well as funding for mosquito surveillance, mosquito population control, and laboratory resources (2016c). When this failed to happen in a timely manner, Governor Scott announced on June 23, 2016 that by executive order, he would authorize $26.2 million of emergency state funds to be used in the Zika response (2016d). On July 29, 2016, four locally-acquired cases were confirmed in Miami-Dade and Broward counties, both of which are in southern Florida (Florida Department of Health, 2016). Florida health officials went door-to-door for outreach and to collect urine samples and other information (Goldschmidt, 2016). They also set up a temporary clinic at the Miami Beach Police Department (Luthra, 2016). On December 12, 2016, Florida was reported Zika-free by US health officials. Dr. Lyle Petersen, director of the CDC's Division of Vector-Borne Disease, also credits the aerial spraying of naled as a major contributor to stopping the outbreak. He believes without the use of naled, the outbreak would have continued (Kay, 2016). The rapid response was commended by former CDC Dr. Frieden (Preidt, 2016). This differed from the response in Puerto Rico because Florida took immediate, aggressive action as soon as cases were confirmed.

Conclusion

Dr. Lyle Petersen, , has said that the Zika virus is "probably the most complicated issue CDC has ever faced. Everything is not straightforward and every single center at CDC is involved, which is unprecedented" (Sifferlin, 2016b). It is crucial to continue casting a wide net

in the response. The factors to consider when developing a risk communication campaign are the public's trust in authorities, the emotional response, the proximity to the risk, the severity of the risk, the tolerability of the risk, and their history with the risk and the risk communicators (Janoske, Liu, & Sheppard, 2012). This review addressed how the political, economic, and historical relationship between the US and Puerto Rico has led to a skepticism of government agencies and their message. The constant presence of mosquitos and mosquito-borne illnesses on the island has resulted in a dismissive attitude toward the true risk. Health agencies must continue to implement intensive health education campaigns to try to convey the true risk associated with Zika infection.

A critical need to continue combating the Zika virus is grants to continue research on the virus and a vaccine as well as continue developing and implanting health education programs. If the most recently proposed healthcare bill to repeal the ACA were successful, it would eliminate the Prevention and Public Health Fund for FY2019 and onwards (Energy and Commerce Committee, 2017). This fund was created to improve the public health system by investing in prevention and public health programs. In FY2016, 12% of the CDC's budget was supplied through this fund (CDC, 2017i). If it were to be eliminated, it would have a massive, negative impact on the health agencies across the states and territories that depend on federal funding for comprehensive public health campaigns (Sun, 2017c). Without the funding to develop health education campaigns, further study the virus, and develop a vaccine, everyone would be at risk. Zika is a quiet disease and has the potential to infect a significant amount of the population before health officials are aware of an outbreak. Therefore, preventive actions are necessary to stop the next outbreak.

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