ZIKA VIRUS: PATIENT EDUCATION RECOMMENDATIONS

By

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Abstract

As the current growing threat to maternal-fetal health, the most recent and largest outbreak of the Zika virus has introduced the devastating fetal effects of microcephaly and other central nervous system deficits. Therefore, the need for appropriate recognition, treatment, management, and prevention of the Zika virus prompts the necessity for further education and high quality level research to be conducted and utilized. A search of the literature using the databases PubMed, UptoDate, and CINAHL was conducted for articles published between 2009 and 2016. In addition, key informant interviews from various specialties including clinical genetics and public health were conducted. The proposed best practice recommendations for education regarding the Zika virus and appropriate prevention and treatment methods are outlined in an electronic education module that would be delivered to patients and their families prior to visiting their healthcare providers. As the Zika virus continues to spread and further research is conducted regarding its teratogenic effects, the need for concise and effective education is critical in order to raise awareness and conversely decrease the potential for maternal exposure and adverse fetal outcomes.

Keywords: fetal teratogens, Zika, Zika virus
Chapter 1

Zika Virus: Patient Education Recommendations

The purpose of this thesis is to create best practice recommendations for teaching pregnant patients how to prevent exposure to the Zika virus and what to expect if exposure is suspected. There are approximately 6 million pregnancies each year in the United States (Centers for Disease Control and Prevention [CDC], 2015). Gestational and fetal health is a significant portion of the healthcare system, and a new threat to maternal-fetal health has emerged. Having an evidence-based practice to follow is incredibly important in education and delivery of effective healthcare. However, behaviors and substances that can influence both fetal health, maternal health, and obstetric outcomes are prominent in society. These detrimental behaviors and substances, known as teratogens, include smoking, drinking alcohol, various prescription and illicit drugs, infectious diseases, as well as different medical conditions such as obesity (CDC, 2015). These teratogens cause an array of birth defects that are evident in 1 in every 33 babies born in the United States each year (CDC, 2015). Therefore, many different variables during the gestational period pose significant detrimental risks to the health of the fetus and the mother. The CDC (2015) states that “the ideal result is a full-term pregnancy without unnecessary interventions, the delivery of a healthy baby, and a healthy postpartum period in a positive environment”. However, viruses and diseases that may seem common to the mother can potentially have harmful effects on the fetus’s development and overall health. Therefore, research, interventions, and education are important in the prenatal healthcare system as well as generalized society to reduce the frequency of teratogenic effects on the developing fetus.
However, an unpredictable threat that may emerge during pregnancy involves the maternal contraction of a virus or infectious disease. In today’s healthcare realm, the most media-prominent virus is the Zika virus. Due to the great concern that has erupted and the growing rates of infection across the world, many issues regarding the Zika virus itself and its fetal effects have been highlighted in the media. However, the most recent outbreak is not the first occurrence of the Zika virus, only the largest. The Zika virus was first discovered in 1947 in the Zika Forest near Entebbe, Uganda (Gozlan, 2016). A team from the East African Virus Research Institute were in the Zika Forest looking to study the epidemiology of the yellow fever virus. Studying the vector relationship between rhesus monkeys and the *Aedes simpsoni* mosquito, the researchers were able to isolate two viral strains that had caused fevers in the test subjects, and found that the two were identical. They named the virus Zika, appropriate for the location of its finding and noting its difference from the yellow fever virus. Further testing revealed that pathologic effects from the virus were confined to the central nervous system as found when no signs or symptoms were experienced from intraperitoneal inoculation as compared to degenerative cerebral symptoms form intracerebral inoculation (Gozlan, 2016). This unique characteristic indicated to researchers that the newly discovered virus was different, however no clinical symptoms were found in the testing mice nor the rhesus monkeys beyond a fever.

In 1954, the first clinical symptoms of Zika virus including a fever and headache were reported in a 10-year-old girl in Nigeria (Gozlan, 2016). She recovered completely in 6 weeks, however, in 1956, William Bearcroft, a researcher at the West African Council for Medical Research Laboratories in Lagos, Nigeria, wanted to know more. Bearcroft inoculated a human volunteer with the Zika virus. The patient reported a fever, headache, malaise, nausea, and
vertigo, but by the seventh day reported feeling quite well (Gozlan, 2016). Between 1958 and 2002, a total of 606 additional strains of Zika virus were isolated and reported by the World Health Organization (WHO) (Gozlan, 2016). Various strains have been identified in Central, East, and West Africa, as well as various countries through Southeast Asia. Despite the vast amount of strains and evident spread throughout the world, only 14 sporadic human infections of Zika virus were reported between 1958 and 2002 (Gozlan, 2016). However, in 2007, 48 cases were confirmed in Yap Island in Micronesia, the largest clustered amount of outbreaks for the singular cause of Zika virus (Gozlan, 2016). Moving into October of 2013 to March of 2014, French Polynesia experienced a significant outbreak of over 28,000 cases with individuals expressing symptoms including fever, a maculopapular rash, and nonpurulent conjunctivitis (Gozlan, 2016). Although a staggering number, it is presumed to be an underestimate due to the mildness of symptoms or complete lack of symptoms altogether. In addition, the first reports of potentially finding Guillain-Barré syndrome to be a symptom of the Zika infection concerned health officials and scientists alike as this had never been seen before.

Moving forward, other territories in the South Pacific reported additional cases through July 2014, concerning health officials of the ease of transmission for the Zika virus. In addition, remote cases in Norway, France, Japan, and Australia were identified in travelers and reflected the ability for different species of the *Aedes* mosquito to be vectors of the virus despite no other surrounding or infiltrating diseases (Gozlan, 2016). In early 2015, cases of patients with similar symptoms to Zika virus grew in numbers as the months progressed and became evident in northeastern Brazil. Upon investigation and viral DNA sequencing, it was confirmed that Zika had reached South America, presumably by the recently held 2014 World Cup due to the varying strains present and wide-spread infection. However, the cases in Brazil seemed to be
distinguished by the possibly connected cases of microcephaly in newborns. By November of 2015, the Brazilian Ministry of Health declared a public health emergency as the number of cases of microcephaly presumably linked with Zika virus continued to grow by the day (Gozlan, 2016).

The Zika virus is a flavivirus in the Flaviviridae family and is transmitted by the Aedes species mosquitos (Peterson, Jamieson, Powers, & Honein, 2016). This positive, single-stranded, enveloped RNA virus is vectored by ticks and mosquitos that also carry Yellow Fever, Dengue Fever, Japanese encephalitis, and West Nile Viruses (CDC, 2014). Therefore, many similarities can be found between Zika virus and the stated viruses such as geographical distribution and rate of transmission between hosts and infected persons. In addition, the Zika virus’s epidemiology is similar to chikungunya virus in the sense that when discovered less than a century ago until now, Zika has been relatively isolated and controlled to a small segment of the world. However, now it is growing and chikungunya is still considered a global health problem as it is incredibly prevalent and limited treatment is available. Therefore, the urgency to address the current Zika outbreak and obtain a better understanding of how to treat and prevent the further spread of the virus is vitally important.

With that said, in order to understand the extent of severity and correlating clinical and fetal effects, the method of transmission of the Zika virus must first be addressed. As previously stated, Zika virus is carried by Aedes species mosquitos and shares many characteristics of other similar viruses. In the Asian and African strands, Zika virus circulates between nonhuman primates and forest-dwelling species of Aedes mosquitoes in a sylvatic transmission cycle (Peterson et al., 2016). Essentially, the mosquitos located in the tropical areas feed on primates that are infected with the virus. From there, subsequent primates that are bitten by the same now-
infected mosquitoes acquire the virus and perpetuate the cycle further. In the chance that an infected mosquito feeds on a human in the area, that human now acquires the virus and acts as a host similar to the primates. However, unlike the primates, the human has the ability to travel great distances and across oceans. Seeing as the most likely human beings to be in tropical areas specifically with known infected primates and mosquitoes are researchers, these researchers bring the virus back to their home countries. In these broadened locations, the local Aedes species mosquitoes now perpetuate a new cycle that involves using humans as feeding reservoirs rather than primates. Therefore, in these suburban and urban settings, the chief Aedes species mosquitoes include *A. aegypti* and *A. albopictus*, both known species to reside in the Americas (Peterson et al., 2016). Furthermore, these species are known to feed in the daytime, live in close proximity with human habitation, have a nearly imperceptible bite, and maintain a high vectorial capacity (Peterson et al., 2016). This means that the mosquitoes found in inhabited and densely populated areas are able to ingest and transmit large proportions of the specific virus and often do so due to feedings consisting of biting multiple humans and several times a day.

In addition to mosquito transmission, Zika virus has also been found to be sexually and vertically transmitted. As stated by Peterson et al. (2016), “replicative viral particles, as well as viral RNA — often in high copy numbers — have been identified in sperm, and viral RNA of Zika virus has been detected up to 62 days after the onset of symptoms” (para. 13). However, the risk factors regarding severity and length of infectivity have not yet been determined for Zika, which poses further questions and concerns for couples who may have traveled in the previous year or are in areas where Zika is rapidly spreading. Please see Appendix A for a detailed timeline of the Zika Virus transmission.
An interesting component of this Zika outbreak deals with the timing and location of world events. The 2016 Summer Olympics were held in Rio, and many individuals from various countries expressed concerns and severe reservations in regards to traveling to Rio to participate in the games. In order to understand the measures taken to deem the Rio games safe to attend, Brazilian officials and world health leaders worked to discuss and assess the reality for potential infection. Please see Appendix B for a timeline of events and actions taken by Brazilian officials leading up to the 2016 Olympic games.

Understanding the timeline of events that occurred from the Brazilian point of view helps to understand the conversation and measures being taken around the world. According to the WHO expert panel on Zika, it was concluded that hosting the Olympics in August -- during the Brazilian winter -- meant the mosquito population would be smaller, and intensified mosquito-control measures to be in place around the competition venues "should further reduce the risk of transmission" (Sun, 2016). In addition, Tom Frieden, director of the U.S. Centers for Disease Control and Prevention, stated there was no public health reason to postpone or move the games (Sun, 2016). Furthermore, Frieden said about 20% of the world lives in a Zika-affected region, and 30% of global travel already is "in and out of Zika-affected areas of the world" (Sun, 2016) He said the proportion of travel affected by the Olympics, which was expected to draw up to 500,000 visitors, is "very marginal." A further breakdown of the travel analysis associated with Zika states,

“Chad, Djibouti, Eritrea, and Yemen, are unique in that they do not have a substantial number of travelers to any country with local Zika virus transmission, except for anticipated travel to the Games. These four countries were represented by a combined total of 19 athletes (plus a combined delegation of about 60 persons), a tiny fraction of the 350,000–500,000 visitors
expected at the Games. Overall travel volume to the Games represents a very small fraction (<0.25%) of the total estimated 2015 travel volume to Zika-affected countries, highlighting the unlikely scenario that Zika importation would be solely attributable to travel to the Games” (Sun, 2016).

Seeing as Zika virus poses many risks to global health as a whole, many different disciplines of study have become concerned regarding the progression of this outbreak. In an interview with Dr. William Dobyns of Seattle Children’s Research Institute, Dr. Dobyns stresses the severity of the situation by highlighting the potential for extensive brain destruction to developing fetuses (Aleccia, 2016). He states that the effected fetuses are likely to have severe neurological and developmental delays and may not be able to walk, talk or feed themselves and many will die shortly after birth (Aleccia, 2016). In addition, the presence of Fetal Brain Disruption Sequence on scans from fetuses in Brazil potentiate the possibilities of the unknown potential related to Zika. Therefore, it is evident that the Zika virus and the threats that it poses to the global medical community are not something to be ignored. Health experts say Zika virus is not expected to hit the U.S. as hard as places such as Brazil due to the mosquito control and the ability of many people to avoid insect bites in the United States. However, the state of the unknown continues to persist and pose challenging questions to health officials and everyday citizens alike.

As previously stated, Zika is not a new virus. However, the current outbreak is one that substantially surpasses those of the past. For example, Rasmussen (2016) stated that no reports of adverse pregnancy or birth outcomes were noted during previous outbreaks of Zika virus disease in the Pacific Islands (p. 1981). Therefore, a clinical question to address in regards to this outbreak is what has been done to combat outbreaks of this magnitude with sources similar to
Zika? Viruses that share similar biologic properties and manifestations include Dengue, Chikungunya, and Cytomegalovirus (CMV). For example, CMV shares a similar pathogenicity as ZIKV has shown, causing loss of neural stem cells or intermediate progenitors, the building blocks of the developing brain, due to infection, which may have potential effects on brain size and maturation (Cheeran et al., 2009). Similarities between these viruses prompt the question of whether or not similarities can be drawn between treatment methods, prevention, and community education. For example, Rasumssen (2016) confirmed that there is a causal relationship between prenatal Zika virus infection, microcephaly and other serious brain anomalies through completing Shepard’s criteria for proof of teratogenicity. Therefore, by looking at other studies and outbreaks caused by other viruses, it could be thought that a treatment plan could be developed.

However, the trouble with this proposal is that Zika has presented a number of abnormalities and significant risks that have not previously been addressed. For example, the link between Guillain–Barré Syndrome (GBS) and Zika virus was considered after a sparingly few cases appeared during the previous Zika outbreaks. However, now that it is a prominent component of today’s outbreak, it is important to understand why and how this connection occurs. Guillain-Barre is an autoimmune condition in which the individual’s immune system inappropriately attacks components of their peripheral nerves. Furthermore, antibodies produced in response to an infection cross-react with peripheral nerve components, and therefore incorrectly attack local cells as compared to the invading cells. Symptoms usually start with symmetrical weakness or tingling in the legs and subsequently spread to the arms and face. For some people, these symptoms can lead to paralysis of the legs, arms, or muscles in the face. However, most people afflicted recover in a few weeks with self-limiting symptoms. The few
cases associated with the 2014 outbreak in French Polynesia established a link, however the
current outbreak has a growing body of evidence to confirm the link. In addition, other
flaviviruses such as Dengue and Campylobacter jejuni infections have confirmed links to
correlating GBS infections, indicating the similarities between Zika and previously studied viral
correlations. Understandably, as the incidence of Zika increases in countries in South and Central
America, so does the incidence of GBS.

In addition, in a study by Cao-Lormeau et al. (2016), all of the patients involved in the
study with GBS had neutralizing antibodies against Zika. In addition, 39 out of 42 of the study
participants had Zika IgM, and 37 had experienced mild-flu like symptoms a week prior to GBS
symptoms, indicating Zika infection. Of all of these patients, there were no deaths, however the
link between Zika and GBS was scientifically established.

On a cellular level, GBS and Zika appear to play interchanging cause and effect roles on
one another. From the World Health Organization’s Zika Virus Vaccine Target Product Profile
(TPP), it states that “Molecular mimicry between Zika and naturally occurring glycolipids on
host cells has been postulated to play a role in an autoimmune response to gangliosides. This
leads to an increased incidence of neurological complications related to Zika infection, but a
direct viral effect cannot currently be excluded either. The latter is suggested by rapid onset of
GBS after Zika infection” (WHO, 2016a, p. 2). Therefore, it is clear that the immunologic
properties of Zika directly affect the body’s susceptibilities to other potential pathogenic
conditions.

In the hopes to prevent further fetal deaths and complications as a result of Zika, the
development of a vaccine has become a pressing issue for scientists and legislators alike. As
discussed by Rubin et al. (2016), now that fetal findings and the transmission of Zika have been established, the major concern is to find proper diagnostic tests and treatments to prevent further exposure. In June 2016, Inovio Pharmaceuticals received approval from the FDA to launch a phase 1 clinical trial of a DNA-based vaccine that it is developing with GeneOne Life Science for Zika (Schniring, 2016). This trial consists of 40 human volunteers with the goal of the vaccine to trigger antibody and T-cell responses. Depending on trial results and completion time, the possibility for a potential vaccine to be released could be as soon as summer of 2017. Another DNA-based Zika vaccine developed by the National Institute of Allergy and Infectious Diseases (NIAID) is also looking to enter into Phase 1 clinical trials within the year of 2016. The World Health Organization’s Zika Virus Vaccine Target Product Profile states that the vaccine intention is to “protect against congenital Zika virus syndrome for use during an emergency using a live, attenuated viral vaccine platform” (WHO, 2016a). Their vaccine development is geared towards women of childbearing age to prevent the occurrence of congenital Zika. However, if supply permits, men of the same age would be the second-tier recipients due to the ability for sexual transmission. Therefore, the first priority is to prevent Zika associated diseases, with the second priority being routine immunization to develop population immunity. Although there is great potential, the WHO states “it is currently unknown whether previous infection with or vaccination against other flaviviruses might impact the severity of infection of Zika. The role of potentially cross-reactive antibodies in disease prevention or enhancement is still unclear (WHO, 2016a, p. 3). The NIAID’s vaccine platform includes a DNA-based live-attenuated vaccine similar to the Dengue vaccine. In addition, an investigational vaccine that uses a genetically engineered version of vesicular stomatitis virus as well as a whole-particle inactivated viral vaccine are being researched and developed to not only combat a Zika outbreak,
but also to understand other similar outbreaks and treatments. Due to the ambition of these intentions, the vaccines will likely not be available for several years. In the meantime, the next step to take involves preventative measures and successful symptomatic management for those afflicted.

Moving forward to the present, Zika virus is rapidly spreading to the United States. In particular, 707 travel associated cases and 105 locally acquired cases have been reported throughout the state of Florida as of October 6, 2016 (CDC, 2016). Florida is significant in the fact that prior to August 2016, locally acquired cases in the United States were solely attributable to the territory of Puerto Rico. As of October 6, 2016, Puerto Rico had a documented 23,665 locally acquired cases (CDC, 2016). However, now that there is confirmation of local transmission and a significant amount of people have been affected, the need for proper recommendations and control measures is imperative to the population’s health. In addition, travel associated cases being reported has also grown. States such as Texas has 218 cases, California has 277 cases, and New York has 837 cases as of October 2016 (CDC, 2016).

Significance to Healthcare

As of February 2016, Brazil estimated approximately 1.3 million cases of Zika have presented and contribute to the massive endemic that appears to be unfolding (Gozlan, 2016). Due to this large and growing number of infected people, the concern turns to the result of fatal microcephaly and the teratogenic health complication that is poses. The large amount of people affected relates to the amount of fetuses possible effected, and potentially harmed. The physical and psychological harms Zika virus has shown to cause on a developing fetus will be outlined, as
well as what the world can possibly expect from this rapidly spreading virus and how to combat its prevalent and fetal threatening inoculation.

Conclusion

Seeing as the presence of Zika virus is rapidly growing in today’s world health environment, the need for effective and universal prevention and treatment is imperative. Although there have been prior outbreaks and Zika is not a new virus necessarily, this is the largest effect science has seen. Therefore, studying both the history of the virus and the present situation set the stage for a promising result. This thesis will address best practice recommendations for teaching pregnant patients how to prevent exposure to the Zika virus and what to expect if exposure is suspected.
Chapter 2

This chapter is a review of various evidence based research studies and expert opinions regarding the genetic history, clinical manifestations, epidemiology, and case studies regarding Zika virus. Databases used for the search include PubMed, UptoDate, and CINAHL and articles published between 2009 and 2016. Key terms that were used include ‘fetal teratogens’, ‘zika’, and ‘zika virus’. In addition, the Centers for Disease Control and Prevention (CDC), World Health Organization (WHO), and the Society for Maternal and Fetal Medicine (SMFM) issued several reports and statistics that were utilized as supporting evidence to research found and clinical scenarios used within this review.

Zika Virus Transmission and Symptoms

In a case study regarding two American scientists, these scientists had worked in a village in Senegal in 2008 and experienced a vast amount of bites from *Aedes* mosquitos. Upon returning to their homes, both individuals began to experience symptoms six to nine days after their return. One of the scientists experienced swollen ankles, maculopapular rash along his torso, fatigue, arthralgia, prostatitis, aphthous ulcers on his lips, hematospermia, and a headache (Foy et al., 2011). The other scientist experienced similar symptoms of a maculopapular rash on his torso, fatigue, a headache, and swelling and arthralgia in the wrists, knees, and ankles (Foy et al., 2011). These symptoms for both patients developed within one week of returning to America and lasted approximately one week. In addition, the wife of the first scientist developed symptoms similar to both patients within ten days of her husband returning and engaging in sexual intercourse prior to the onset of the husband’s clinical symptoms. Her symptoms included malaise, chills, extreme headache, photophobia, muscle pain, maculopapular rash on her torso,
apthous ulcers on her inside lip, arthralgia, and conjunctivitis (Foy et al., 2011). Within one week her symptoms resolved as well, with their children not experiencing any form of illness or discomfort. These findings support the probability that Zika was sexually transmitted from the researcher to his wife, as well as the findings that hemagglutination inhibition antibody titers and virus neutralizing titers were highly elevated above background levels for Zika and yellow fever virus from blood draws during all of the patient’s acute phases and convalescent phases (Foy et al., 2011). Therefore, this information, coupled with the fact that at that time no strains of Zika virus were found in America or carried by mosquitos in the patient’s home town, it is highly likely that Zika was sexually transmitted to the patient’s wife. However, further exploration and testing is necessary seeing as no other flavivirus has been known to be sexually transmitted.

Regarding vertical transmission, the transfer of the virus from the mother to the fetus, the main concern regarding Zika is the dismal fetal effects that have become prominent in the most recent outbreak. Various reports regarding fetal demise, microcephaly, and other genetic anomalies have been reported and are increasing in number. Therefore, the importance of understanding how Zika affects the fetus and potentially what complications will result is rapidly escalating. Previous Zika reports did not include accounts of pregnancy complications or fetal effects, therefore puzzling scientists and public health officials alike. However, the vast amount of information and research that is being conducted during the current outbreak is incredibly helpful in deciphering what is occurring on a scientific level.

**Zika Virus and Fetal Complications**

Addressing the most prominent complication in the current outbreak, the study conducted by Tang et al. (2016) analyzed and established a controllable experimental model system to
investigate the impact and mechanism of the Zika virus on human brain development. By doing this, the researchers hoped to reveal a scientific explanation for the microcephaly cases in children of Zika infected mothers. Conducted at the University of Florida, the researchers used human induced pluripotent stem cells (hiPSCs) as an in vitro model to investigate the link between Zika and effects on neuronal cells. Using a common strain of Zika, MR766, the researchers introduced the strain to several human cell lines to evaluate the level of susceptibility of each kind. Interestingly, the embryonic kidney cell line showed low permissiveness to Zika, indicating further complications beyond neural effects could be seen in the future (Tang et al., 2016). To directly evaluate the effects on neural cells, inoculation of Zika cells was introduced to incubated human cortical neural progenitor cells (hNPCs) for two hours and then titered over three days. What was found was that Zika infected up to 90% of the hNPCs within 72 hours, effectively limiting the ability for a fetus’s brain to brow (Tang et al., 2016). For example, after infecting the encountered hNPCs, Zika-infected hNPCs produce infectious Zika particles, dysregulating the cell cycle and transcription of hNPCS, and effectively causing cell death. In addition, the study revealed that hNPCS are a direct cell target of Zika, further supporting the findings of intrauterine brain growth restriction and overall fetal demise.

Weaknesses of the study included the facts that although performed with the most common strain of Zika, the exact strains currently circulating through the affected areas continue to change. Therefore, strengths of the study included identification of the cellular principles of Zika, however application to the current outbreak will require further testing and confirmation through case studies and serum samples to confirm the pathogenesis. In addition, the populations in which Zika may effect moving forward are composed of varying genetic makeups, which can dramatically impact the biochemical reactions associated with introduction of the virus into each
individual. However, significant support for the connection between neural cell dysregulation and corresponding developmental impairments is evident and introduces many questions including long term consequences if the child were to survive due to the significant physical and cognitive defects. In addition, application to the adult population and the potential link with Zika and Guillain-Barre’s syndrome constitutes a significant concern seeing as an established connection between neural cell dysregulation and death has been found.

In order to accurately study the current strain and effects that are being reported, the study conducted by Mlakar et al. (2016) analyzed one case study of a woman who terminated her pregnancy after an ultrasound confirmed her baby had microcephaly and several comorbidities. Living in Brazil, the mother experienced a rash and fever at the end of her first trimester yet ultrasounds at the 14th and 20th week showed no fetal abnormalities. However, during the 29th gestational week, the mother reported reduced fetal movement and the ultrasound revealed intrauterine growth retardation, numerous calcifications in the placenta, confirmed microcephaly, moderate ventriculomegaly, and a very low transcerebellar diameter (Mlakar et al., 2016). Following the elective termination of the pregnancy at 32 weeks, an autopsy was performed on the child where the entire Zika genome was found from serum samples in the fetal brain tissue. In addition, various tests were conducted to further analyze the organs, tissues, and serum of the child including electron microscopy, indirect immunofluorescence, TRIzol Plus RNA purification, real-time RT-PCR, and one-step RT-PCR.

Similar to the study by Tang et al. (2016), supportive evidence for neurotropic and teratogenic nature of the virus were found in all parts of the brain. In addition, the autopsy revealed microcephaly, micrencephaly, cerebral cortex and subcortical white matter calcifications (as well as placental), open sylvian fissures, agyria, hydrocephalus of the lateral
ventricles, and degeneration of brain stem and spinal cord (Mlakar et al., 2016). All other organs revealed no levels of Zika virus or abnormalities. However, this is a weakness of the study seeing as it is only one mother-baby couplet and further damage is a potential result seeing as further development could not be studied due to termination of the pregnancy. Overall, further evidence strengthens the link between microcephaly and Zika, with many unknown possibilities being revealed and addressed through further study of the virus’s pathogenic potential.

In the study conducted by Calvet et al. (2016), two women from Brazil were analyzed, examined and tested for Zika infection and the correlating fetal effects. One woman presented at 10 weeks while the other woman presented at 18 weeks gestation, both with fever, myalgia, and a rash characteristic of Zika. The woman who presented at 18 weeks with systemic effects received an ultrasound at 21 weeks gestation where fetal anomalies including microcephaly, ventriculomegaly, and partial agenesis of the cerebellar vermis were found (Calvet et al., 2016). At 27 weeks gestation, the microcephaly was confirmed along with relevant dilation of ventricles, asymmetry of hemispheres, and hypoplastic cerebellum with complete absence of the cerebellar vermis (Calvet et al., 2016). The baby was delivered at 40 weeks gestation with head a head circumference below the 3rd percentile and an incredibly low potential to thrive. The woman who presented at 10 weeks with systemic effects received an ultrasound at 25 weeks where severe hypoplasia of the cerebellar vermis, enlargement of the posterior fossa, and microcephaly was found (Calvet et al., 2016). The baby was also delivered however presented with severe ventriculomegaly, microphthalmia, cataracts, and severe arthrogryposis in all extremities (Calvet et al., 2016). Amniotic fluid samples from both patients at 28 weeks confirmed Zika, however maternal urine and serum samples were negative for the virus and systemic effects had dissipated by that time.
This study also ruled out the question of whether the specific Zika strain circulating in Brazil during the 2015 outbreak was a recombinant strain combined with other flaviviruses or whether it was singular in origin. This was suspected due to the new presentation of adverse fetal effects such as microcephaly and fetal demise that had otherwise not been present in other Zika outbreaks in the past 70 years. However, quantitative reverse transcription PCR and viral metagenomic next-generation sequencing confirmed the absence of other flavivirus or infiltrating viruses in the extracted genome of both the mother’s and the amniotic fluid samples. In addition, this was the first study to entirely isolate the complete Zika genome solely from amniotic fluid gathered during gestation. This confirms that transplacental transmission is entirely possible and supported by evidence.

In the report by Schuler-Faccini et al. (2016), increased findings of microcephaly in Brazil resulted in the Brazil Ministry of Health investigating the possible association with Zika virus. The task force that was created to investigate this outbreak of microcephaly and the potential correlation with increased Zika virus presence included clinical geneticists, obstetricians, pediatricians, neurologists, and radiologists to investigate all babies born with microcephaly and women suspected of being inoculated with Zika. Due to the concern regarding inconsistent reporting regarding what in particular specified microcephaly, the definition for Zika virus-related microcephaly was established to be a head circumference less than two standard deviations below the mean for sex and gestational age at birth of the affected child (Schuler-Faccini et al., 2016, pp. 59). Therefore, this establishment of a standardized measurement with which to classify the microcephaly cases aided in the accuracy and continuity among the reported cases. Therefore, the task force within Brazil that was recording these cases found that in the first 35 cases of microcephaly, 71% of the infants had severe microcephaly (>3 standard
deviations below the mean), approximately half of the reported cases had at least one neurologic anomaly, and 74% of the mothers reported a rash during pregnancy (Schuler-Faccini et al., 2016, pp. 59). In addition, CT scans and cranial ultrasounds consistently revealed brain calcifications and ventricular enlargement due to cortical and subcortical atrophy (Schuler-Faccini et al., 2016, pp. 60). Further diagnostics also revealed 31% of cases had excessive scalp skin and 1% had congenital contractures (Schuler-Faccini, 2016, pp. 60). The abundance of scalp skin indicates that cerebral development was inhibited but not growth of the scalp skin. In addition, congenital contractures further point to nervous system involvement and the direct effects the Zika virus has on neuronal development as compared to other forms of development.

Weaknesses of this study include the fact that until November of 2015, there was no established protocol or standard with which to report microcephaly in healthcare settings. Therefore, the risk for physicians or parents not understanding the situation or seeing it as otherwise normal may have underscored the amount of reports that were actually made. In addition, in many of the birthing centers in Brazil, head circumference may not have been routinely taken. This also causes a problem for underreporting of potential cases and further inconsistent reporting of microcephaly due to people’s unawareness of what to report and lack of information. In regards to the maternal symptom of a rash as observed in many of the mothers studied, self-reporting of the rash and duration of symptoms as compared to observation and evaluation by healthcare professionals introduces the potential for error and inconsistency between mothers. Therefore, the need for further evaluation and standardized assessments of both fetal and maternal involvement is necessary to better understand the implications of Zika.

In the study by Melo et al. (2016), two pregnant women from the state of Paraiba, Brazil that were associated with the large amount of women who reported symptoms similar to those
reported by Zika infected-persons were evaluated. The interesting component of this study was that the two women’s blood levels were evaluated for Zika virus and no detection as made despite prior symptoms indicating a prior infection of Zika. However, evaluation of the two women’s amniotic fluids were evaluated and testing revealed the presence of Zika virus. This was the first indication of intrauterine transmission of the virus and the correlating effects that can be made despite indirect inoculation.

The first woman’s fetus presented with a head circumference 2.6 standard deviations below normal, brain atrophy with coarse calcifications of the white matter of the frontal lobes, corpus callosal and vermian dysgenesis, and enlarged cisterna magna (Melo et al., 2016). These findings are consistent with previous cerebral deformities and developmental delays that had been seen with other cases of microcephaly. The second woman’s fetus presented with a head circumference 3.1 standard deviations below normal, asymmetric cerebral hemispheres, displacement of the midline, absence of corpus callosum and thalami, and calcifications around the lateral and fourth ventricles (Melo et al., 2016). These findings were also consistent with previous Zika-induced microcephaly cases and highlight the impact that intrauterine transmission has on the brain development of a fetus. This is significant due to the unlikelihood of intrauterine infections such as Cytomegalovirus affecting brain development. However, severe cerebral and neural impairments are being consistently seen in Zika cases. Weaknesses of the study include the fact that only two women were evaluated in this study. However, detailed reports aid researchers in evaluating the consistent and inconsistent symptoms that are being seen with the most recent Zika outbreak.

A retrospective case study by de Fatima Vasco Aragao et al. (2016) analyzed 23 children in Pernambuco, Brazil that had congenital infections associated with the Zika outbreak. Through
ZIKA VIRUS: PATIENT EDUCATION RECOMMENDATIONS

cerebral spinal fluid serological testing and physical examination, all of the study children that were found positive for infectious diseases that are known to cause microcephaly such as toxoplasmosis, cytomegalovirus, rubella, syphilis, and HIV were excluded. In addition, as per the Brazilian Ministry of Health’s protocol, the definition of microcephaly was changed from a head circumference of 33 cm or less to 32 cm or less for infants of gestational age of 37 weeks or more (de Fatima Vasco Aragao, 2016). For preterm infants, the definition includes the head circumference being more than two standard deviations below the mean for the infant’s gestational age and sex. With these classifications, 23 infants were identified and 15 underwent CT scans, seven underwent both CT and MRI scans, and one underwent only an MRI scan.

From the CT scans, all 22 had calcifications between cortical and subcortical white matter, 21 had malformations of cortical development, 20 had a decreased brain volume, 19 had ventriculomegaly, and 11 had hypoplasia of the cerebellum or brainstem (de Fatima Vasco Aragao, 2016). From the MRI scans, all eight had calcifications between the cortical and subcortical white matter, malformations of cortical development occurring predominantly in the frontal lobes, and ventriculomegaly (de Fatima Vasco Aragao et al., 2016). In addition, seven of the eight children had enlarged cisterna magna, seven had delayed myelination, and six had a moderate to severe decrease in brain volume, simplified gyral pattern, and abnormalities of the corpus callosum (38% hypogenesis and 38% hypoplasia) (de Fatima Vasco Aragao et al., 2016). These radiological findings help scientists to better establish the consistent malformations that are being seen in infants infected with Zika. Although a small sample size and all participants originating from the same geographical area, and therefore most likely the same strain of Zika, these results pose important radiological clarifications of what is being seen in cases of Zika-related microcephaly. In addition, further testing will be important to establish standardized
results with which to compare other radiological information obtained from infants with microcephaly and Zika-infected mothers.

A cohort observational study in Bahia, Brazil by Reefhuis et al. (2016) analyzed the relationship between the trimester of exposure to Zika virus and the correlating effects seen in both the mothers and the infants. Based upon reported evidence and data gathered by the World Health Organization, a graphical schematic was created to project months when births with exposure to Zika in different trimesters can be expected from the women studied in Bahia, Brazil. This can help associate the reports of highest amount of cases of microcephaly with periods of exposure. This will also help scientists analyze the difference between severity of symptoms and the period and rate of infection.

As found in the study, the period of highest Zika activity across all cohorts studied was March 22–May 31, 2015 (Reefuis et al., 2016). Although mostly speculative, overall findings indicate that the period of highest risk for severe effects of Zika correspond to exposure during the first and early second trimester (Reefhuis et al., 2016). Using the graphical schematic developed in this study, speculation regarding varying degrees of severity can be better associated with period of exposure and therefore significant data can be developed. Based upon dates of conception and consistent use of full term gestation as predictive timelines, the estimated trimester in which the mother may have been effected can be corresponded with the due date and therefore help to project when another influx of cases of microcephaly may be seen. Although mostly speculative at this point with a limited amount of detail available to evaluate the findings, the analysis will be beneficial to not only develop preventative measures but also potentially identify mothers who may be infected and are not aware.
An individual case study of a twenty-year-old woman from Salvador, Brazil was conducted by Sarno et al. (2016) to evaluate a fetus for Zika infection-related symptoms. The woman reported an asymptomatic pregnancy along with negative results for HIV, HTLV, hepatitis C, and TORCH infections. During the eighteenth week of gestation the fetus showed low fetal weight and intrauterine growth restriction. Further ultrasounds at the 26th and 30th week revealed severe microcephaly along with hydranencephaly with minimal residual cortical parenchyma, intracranial calcifications and destructive lesions of posterior Fossa, hydrothorax, ascites and subcutaneous edema (Sarno et al., 2016). At the 32nd gestational week the ultrasound revealed fetal demise and an induced delivery occurred. Serum analysis was performed on extracts of the cerebral cortex, medulla oblongata, and cerebrospinal and amniotic fluid. This analysis revealed the presence of Zika, however extracts of the heart, lung, liver, vitreous body of the eye and placenta did not.

These results pose many questions seeing as the occurrence of hydrops fetalis and fetal demise had not been well-reported or documented prior to these findings. The way in which Zika may cause these occurrences is unknown and would require further testing. However, the absence of other complicating factors and the similarity in nervous system abnormalities that have been seen in other Zika-affected fetuses stimulates the argument that there may be more to the Zika effects than previously reported. Future examinations of stillbirths and spontaneous abortions from similar Zika-affected areas is necessary to be able to further study these additional complications. Overall, the scientific evidence surrounding this most recent Zika outbreak points to the possibility that additional complications may be present than previously thought.

**Zika Virus Related Complications in Adults**
As seen with the many questions regarding Zika, what exactly can occur due to a Zika infection is unknown. The most recent outbreak has seen the common occurrence of mild adult symptoms such as rash, arthralgia, and fever and detrimental fetal symptoms such as microcephaly and various cerebral deformities. However, the first known Zika-linked death was reported in April of 2016 in Puerto Rico. A 70-year-old male had previously been infected with Zika due to the large presence of the virus in Puerto Rico. After experiencing the mild symptoms for approximately one week, he reported feeling better and returning to his usual activities. However, several days following a week of recovery the man experienced abnormal bleeding and returned to the hospital.

He was diagnosed with immune thrombocytopenic purpura, a condition where the body’s immune system attacks the platelets, the clotting components of the blood. Scientists and healthcare providers are unsure why or the frequency of when these complications occur with Zika. During the 2007 outbreak in French Polynesia, very few cases of a possible link between Zika and Guillain-Barre, a condition where a person’s antibodies attack their own nerve cells and therefore can cause permanent paralysis, were seen. However, in the most recent outbreak there have been limited reports of any further complications beyond the devastating fetal effects. This man’s report of the possibility of Zika-caused deaths sparks the need for prevention and further research regarding the effects and relationship of Zika and the body. Although it may be too soon to tell, the effects that Zika may inflict upon individuals extends beyond what has been seen in the past.

**Standardized Fetal Head Circumference Measurements to Identify Zika Related Complications**
In an observational data analysis study, the need for universal standards in head circumference measurements was argued to be necessary in order to accurately and consistently measure microcephaly cases and diagnose them accordingly. According to (Victora et al., 2016), between August 2015 and January 30, 2016, 4,783 cases of microcephaly were reported, including newborn and fetal losses. From there, 404 cases were confirmed microcephaly, and 17 cases were confirmed to be a result of Zika virus infection. However, what studies and reporters found was that there were inconsistent measurements surrounding what was determined to be microcephaly. Therefore, on December 8, 2015, Brazil’s Ministry of Health revised their definition of microcephaly to read that a diagnosis must be a result of a head circumference equal or less than 32 cm (Victora et al. 2016). Prior to this clarification and blatant categorization, varying scientists and physicians were categorizing microcephaly to be less than or equal to 33 cm. Therefore, this brings concerns of the validity of the measurements that have been reported in relations to Zika related microcephaly. Therefore, the recommendation that Victora et al. (2016) makes is to include a standardized diagnostic criteria for microcephaly as under two standard deviations from the expected head circumference for age and gender. In addition, The SMFM published their guidelines which state that “isolated fetal microcephaly should be defined as fetal head circumference greater than three standard deviations or more below the mean for gestational age, and the diagnosis of pathologic microcephaly is considered certain when the fetal head circumference is greater than five standard deviations below the mean for gestational age” (SMFM, 2016, para. 3). Using these guidelines, better measurements can be made by the recommended applications for calculation and uniform InterGrowth growth standards. Using the uniformity of this scale and cross-reference reliability, a standardized understanding of the
requirements for microcephalic cases can be used to filter a more statistically reliable and congruent database of this outbreak’s cases.

**Guidelines for Prevention and Treatment of Zika Virus**

With the influx of information and expanding clinical body of evidence, the presentation and treatment of Zika poses a challenging question to public health officials. Organizations such as the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) have issued various statements regarding the general recommendations and guidelines that have been deemed the most appropriate in regards to Zika prevention and treatment at this time. In summary, for men and women who have exhibited the signs of Zika as previously discussed, men should wait at least six months after the onset of the symptoms to engage in unprotected sex and women should wait at least eight weeks after the onset of their symptoms and/or possible exposure before trying to get pregnant (CDC, 2016). In addition, the WHO recommends using condoms or simply abstaining from sexual activity while there is suspected or confirmed active Zika transmission in the individual’s area (WHO, 2016b). In terms of prevention, the WHO (2016b) recommends simple daily modifications such as wearing long sleeves and pants, using window screens and insect repellent containing DEET, sleeping under mosquito nets, and closing doors and windows. Furthermore, seeing as vaccine development is ongoing and yet to be completed, current treatment recommendations from the WHO include getting plenty of rest, drinking enough fluids, and treating pain and fever with common medicines until the symptoms subside (WHO, 2016b). Overall, the body of research and recommendations continue to evolve as new information is studied and revealed.
Conclusion

Overall, the evidence that is presented in chapter 2 comes from a variety of case studies and outlines the detrimental effects that Zika has caused to a developing fetus and infant. In particular, it is known that there is an established relationship between Zika and detrimental neuronal effects, as well as a relationship between maternal contraction and various forms of transmission. However, there is still a great deal of information that is unknown about Zika. For example, the evidence that has been presented is based off of individual case studies that reflect a lower level of clinical evidence. Therefore, randomized control trials and experimental studies are indicated for the future to help support a larger body of evidence for the scientific understanding of Zika. Furthermore, little is known about the long term effects of Zika. The discussion of how long Zika resides in the body, how severe developmental delays may be, and how much support a child born with Zika may need in the future is unknown. In addition, the development of the Zika vaccine is currently ongoing, however it is not known when it will be completed and available to the public, as well as how effective it will be. Finally, a major factor in maternal-child health resides in the discussion of whether or not breastfeeding can transmit Zika and cause the same detrimental neural effects to children as if they were to be congenitally or locally infected. All of these questions remain to be answered, and will continue to be addressed as further studies and information is gathered regarding Zika and those affected.
Chapter 3

Chapter 2 introduced studies that outline the epidemiology, clinical manifestations, and generalized concerns that have arose from the presence of Zika virus in today’s global health realm. Chapter 3 will provide best practice recommendations for teaching pregnant patients how to prevent exposure to the Zika virus and what to expect if exposure is suspected. The target population for these recommendations is intended to be healthcare providers and staff who educate and closely work with pregnant individuals. However, preventative measures and the recommendations for screening are intended to go beyond the pregnant population to encompass all people in order to minimize the risk of infection and transmission. These recommendations are both evidence based and expert opinion seeing as Zika’s effects are still partially unknown and certain research studies have not been able to be conducted as of yet.

The mode in which this information would be delivered to patients would be via an electronic health module that would be completed prior to a patient seeing their primary or perinatal healthcare provider. The educational module would be composed of information directed towards all pregnant women and their families, whether they are exposed, infected, or suspected of infection, with information revolving around preventative measures to avoid contracting Zika. In addition, the information presented would be evaluated and modified based upon the health literacy of the population of patients that attend the clinic where the module would be implemented.

By instilling this process of introductory education prior to the patient seeing the physician, the hope is that any questions the patient or family member may have regarding Zika prevention and treatment would be addressed while the patient is with the provider. Furthermore,
the module would be designed based upon the progressive levels of prevention. These levels of prevention and corresponding recommendations are outlined here:

**Primary Prevention**

As previously stated, there are several guidelines and recommendations that have been issued by the CDC and WHO in terms of preventative measures. In addition to these previously stated recommendations, according to the British Medical Journal, men returning from travels should refrain from sexual activity for twenty-eight days and if an infection is suspected, they should refrain from sexual activity for six months (Ahmad, Amin, & Ustianowski, 2016). For women traveling, they should delay conception for twenty-eight days after traveling as well. For general preventative measures, recommendations such as wearing long-sleeved shirts and long trousers simply decrease the risk of exposure and being bitten. In addition, staying in places that use window and door screens to keep mosquitoes outside or have closed windows and air conditioning are recommended. Mosquito bed-nets as well as mosquito repellents that contained 50% DEET should be used, applying it after sunscreen to ensure effectiveness (Ahmad, Amin, & Ustianowski, 2016). To further decrease the potential risk, treating clothing with permethrin can repeal mosquitoes in a way that does not require additional application of products to the skin or home (Ahmad, Amin, & Ustianowski, 2016). A preventative measure that had been found effective for CMV included the use of an Autocidal Gravid Ovitrap (AGO) to attract and capture the female *Aedes aegypti* mosquitoes that are responsible for transmission of infectious agents to humans (Lorenzi, Major, Acevedo, et al., 2016). These traps reduced the density of these mosquitoes tenfold in the test communities as compared to the communities without traps (Lorenzi, Major, Acevedo, et al., 2016). Therefore, these preliminary findings suggest AGO
traps might reduce virus transmission by reducing mosquito density. This could also be a simple preventative measure to implement both in home and community settings.

**Secondary Prevention**

In terms of communicating with the public regarding how to monitor themselves and their fetuses regarding the potential dangers of Zika virus, the Society for Maternal and Fetal Medicine released a statement regarding ultrasound screenings for pregnant women. The statement included the guidelines that if the fetal head circumference is more than two standard deviations below the mean head circumference size for that fetus’ gender and age, a detailed neurosonographic examination is recommended to be performed (SMFM, 2016, para. 4). If following the neurosonopraphic examination intracranial anatomy is found to be normal, a follow up ultrasound in three to four weeks is recommended so that the physician can closely monitor for any changes or negative deviations from the normal (SMFM, 2016, para. 6). If evidence of maternal Zika virus infection is found, serial ultrasounds every three to four weeks is recommended so that maternal and fetal status can be closely monitored and interventions enacted as soon as possible. In addition, the statement expanded along the lines of manifestations that would be found if pathologic microcephaly, as compared to nonpathological microcephaly that is not a direct cause of Zika virus, would include a sloping forehead and therefore highly raise suspicion that Zika is a possible source of infection (SMFM, 2016, para. 3). Finally, regulations that were issued to be followed regarding the evaluation of microcephaly stated that isolated fetal microcephaly should be greater than three standard deviations below the mean for gestational age, and pathologic microcephaly should be greater than five standard deviations below the mean for gestational age (SMFM, 2016, para. 3). This further highlights the dramatic physical abnormalities that may occur as fetal effects as a result of Zika infection. Overall,
precautionary measures to avoid being in mosquito-infested areas and minimize mosquito exposure should be taken. However, in the event that a pregnant woman is at risk, the Society for Maternal and Fetal Medicine has outlined guidelines to be followed to ensure the highest level of care is provided.

**Tertiary Prevention**

Figure 1 features a schematic of Zika treatment and the current steps being taken to treat and prevent further transmission according to the British Medical Journal. Seeing as there is still a great amount of uncertainty and unknown knowledge associated with Zika virus, the need to promptly recognize, treat, and prevent its spread is imperative to public health control and maintenance. Therefore, the use of recommended treatment guidelines and systematic care can promote the most consistent and accurate approach to Zika treatment across the world.

According to the CDC, proper practices for pregnant women vary based upon the woman’s status. For asymptomatic exposed women, in less than two weeks since exposure it is suggested...
to have serum and urine testing, and return 2-12 weeks after exposure for IgM antibody testing. For symptomatic exposed women, IgM antibody testing rRT-PCR serum and urine, and serial ultrasounds are suggested. For prenatal management of women with Zika, serial ultrasounds and an amniocentesis if necessary are suggested. For postnatal women with Zika, fetal tissue samples, cord blood, Wharton’s jelly, maternal blood, and fetal blood are all tested to reveal presence or absence of Zika (Oduyebo, 2016). In addition, the US Department of Health and Human Services is also releasing funding to help prevent pathogenic dissolution in the blood supply. This is incredibly important for global health prevention, especially in areas with a high Zika incidence rate such as Puerto Rico.

**Conclusion**

As recommendations and data continue to evolve, medical practice will continue to see success and failures in terms of treatment and spread of Zika. With that, the available data will also evolve. Seeing as current data and recommendations are chiefly based on lower quality level research such as case studies and expert opinion, as information and additional statistics are acquired, they will provide a higher quality level of research. Therefore, despite the increasing level of understanding and information that is being released, additional time and data will provide a more accurate and conclusive depiction as to what Zika truly means in the public health realm and how health care providers can safely and effectively approach treatment and prevention methods.
Chapter 4

The educational module that is proposed would be delivered to patients in the clinic setting via an electronic tablet in the waiting room of the clinic. The front desk staff at the clinic would provide the patient and their family with the tablet after they have checked-in for their appointment, providing the instructions of how to use the tablet if they are unfamiliar and noting that it would take a maximum of ten minutes to complete. With consideration for health literacy and health communication, the educational module would be written at a sixth grade reading level and available in English and Spanish so that it is accessible to many different people and personal backgrounds. Education would be provided to the front desk staff prior to the implementation of this process so that they were familiar with the module, the electronic tablet, and who to contact if any questions arose from patients that they were not able to answer.

To guide the implementation and evaluation process of the educational module for patients and families prior to seeing their providers in a clinic setting, the Health Belief Model was utilized. This framework is directed towards education and behavior and is based upon the principles of cognitive theories. Mental processes such as thinking, reasoning, hypothesizing, or expecting are critical components of cognitive theories, which are often termed value expectancy models because they propose that behavior is a function of the degree to which individuals value an outcome (Skinner et al., 2015, p. 76). For health-related behaviors, the value is avoiding illnesses and staying or recovering well. In relation to Zika, the amount of value pregnant patients and their families place on the prevention and proper detection of Zika-related symptoms, the Health Belief Model would propose that this would directly correlate with their interest and participation in the educational module and asking questions during their time with the provider.
Skinner et al. (2015) proposes that the Health Belief Model illustrates how people will be more likely to engage in a health-related behavior if they understand the relationship between perceived susceptibility, perceived severity, perceived threat, perceived benefits, and perceived barriers. For example, once a pregnant woman completes the educational module in the waiting room of the clinic, she will understand her risk of contracting Zika based upon the information provided. If she lives in an area near large amounts of standing water, or if she spends a considerable amount of time outside without wearing protective clothing or bug deterrents, she will have a higher perceived risk than someone who does not have these same risk factors. Based upon the Health Belief Model, this understanding of her perceived susceptibility would be considered a “cue to action” and therefore drive her to take action such as asking further questions about prevention to her provider (Skinner et al., 2015). In addition, based upon the Health Belief Model, the perceived severity, meaning “the belief about the seriousness of contracting an illness or condition or of leaving it untreated, including physical consequences”, will greatly influence the individual’s subsequent actions (Skinner et al., 2015, p 77). Many pregnant mothers are typically already highly concerned about the safety of their babies during pregnancy. Therefore, introducing information about Zika prior to them visiting a health-care provider would further initiate a conversation about preventative measures and screening methods.

To evaluate the educational module’s effectiveness, a proposed survey conducted prior to the educational module and after the educational module would be distributed when the patient arrives and leaves the clinic office. The survey would consist of three to five questions and would be directly based upon the information that is delivered in the module. This survey would be delivered via the same tablet that the educational module is completed on, and would take a
maximum of five minutes to complete as there would only be three to five questions. Therefore, the patient would arrive at the clinic, check in with the front desk staff for their appointment, receive the electronic tablet, complete the pre-survey, complete the educational module, visit with the provider for their healthcare appointment, then complete the post-survey on the electronic tablet prior to leaving the clinic. The evaluation would be to see how the beliefs of the individual have changed in regards to the information known prior to completing the module, and then subsequently after completing the module and attending their healthcare appointment with the provider. For example, the questions would be phrased in such a way that requires the individual to reflect on whether or not their beliefs in regards to Zika and their personal susceptibility have changed based upon the information provided. The survey would be given on the same electronic device that the module would be delivered from, therefore eliminating the cost for any printed materials or additional devices to be utilized.

Overall, the need for patient education regarding the growing presence of Zika is critical to ensure that all measures are taken by healthcare staff and the public alike to prevent further fatal and detrimental effects of Zika from occurring. The open communication between providers and patients during clinic visits following the completion of the educational module would allow for the opportunity for health care providers to emphasize the importance of the information and clarify any inconsistencies that patients may have heard or read from popular media. In addition, it would allow for a general of awareness of Zika to be present in the clinical setting, and therefore potentially increase the amount of screening and prevention measures that can be taken in the general public. In addition, the heightened need to discuss patients’ travel history and home environment would be addressed as these factors directly relate to the susceptibility of the patient to be exposed to Zika, as well as preventative measures that can be taken for prevention.
Conclusion

Overall, Zika virus has played a large role in the past two years of medical history. Since the beginning of the most recent outbreak’s impact on society, it has caused a tremendous amount of fear and anxiety due to the high potential for fetal anomalies and death. This places a large amount of stress on individuals and families with the hope of pregnancy and the creation of a family, as well as on the healthcare system to provide a cure or “quick fix” in order to correct the problems. As with all good things, the solution is not one that comes quickly. Rather, with time and understanding of the nature of the virus and its effects, scientists and healthcare providers will be able to identify the most appropriate prevention measures, treatments, and education to provide. For now, the importance of communicating what is known, what can be done, and what is being studied is vital in the prevention of a further progression of the outbreak.
References


Figure 1. Retrieved from http://static.www.bmj.com/content/bmj/352/bmj.i1062/F2.large.jpg?width=800&height=600


Appendix A

Timeline of Events in Brazil

November 2015: Brazil declares public Health emergency declared

January 2016: CDC warns pregnant women about traveling, International Olympic Committee releases statement on Zika and Brazil to institute preventative measures

February 2016: WHO declares a public health emergency, The organizing committee for the Games announces that it will install screens to block mosquitoes in communal areas "where required" but will charge national delegations to have the screens placed on athletes' rooms.

March 2016: Zika panel created by Olympic committee

April 2016: only half of the tickets are sold for the August games, people worry that it may be due to Zika, Brazilian House votes to impeach President Dilma Rousseff, South Korea unveils uniforms for Olympic games and calls them “Zika-proof”

May 2016: Harvard's Public Health Review publishes a commentary by a Canadian professor, Amir Attaran, who states the games should be moved or postponed (Olympic committee says that games will proceed as planned), President officially impeached, Australian Olympic teams provided with Zika-proof condoms coated with an antiviral, USA Swimming moves training out of Puerto Rico to Atlanta due to training concerns, Dr. Tom Frieden, director of the U.S. Centers for Disease Control and Prevention, says, "There is no public health reason to cancel or delay the Olympics”, A group of more than 100 prominent doctors and professors signs a letter submitted to WHO Director-General
Margaret Chan, saying the Summer Games should be postponed or moved "in the name of public health"

• WSJ: athletes debating on whether or not to attend the Rio Olympics due to Zika

May 2016: Paul Gasol, a Spanish basketball player, says everyone thinking of going to Brazil should think about the risk of attending the games this year


June 2016: The new health minister for Brazil goes on the record as saying the chance of catching Zika during the Olympics is "almost zero”, WHO says there is a very low risk that the games will spread Zika virus

June 2016: athletes such as golfers Rory McIlroy, Jordan Spieth, Dustin Johnson, Lee-Anne Pace, Jason Day, Shane Lowry, Marc Leishman, Vijay Singh, Tejay van Garderen (cycling), and news anchor Savannah Guthrie, Milos Raonic (tennis) all will not be playing in this year’s games
Appendix B

Graphical Timeline of Transmission

Zika Transmission April 2016- April 2017

- As of April 27, 2016
  - US States (FL, CA, NY)
    - Travel-associated Zika virus disease cases reported: 426
    - Locally acquired vector-borne cases reported: 0
  - US Territories (PR, VI, AS)
    - Travel-associated cases reported: 3
    - Locally acquired cases reported: 596

- As of June 01, 2016
  - US States
    - Travel-associated cases reported: 618
- Locally acquired vector-borne cases reported: 0
- Total: 618  
  - Sexually transmitted: 11
  - Guillain-Barré syndrome: 1

  **US Territories**
  - Travel-associated cases reported: 4
  - Locally acquired cases reported: 1,110
  - Total: 1,114
  - Guillain-Barré syndrome: 8

  o As of June 8, 2016
    - **US States**
      - Travel-associated cases reported: 691
      - Locally acquired vector-borne cases reported: 0
      - Total: 691  
        - Sexually transmitted: 11
        - Guillain-Barré syndrome: 2

    - **US Territories**
      - Travel-associated cases reported: 4
      - Locally acquired cases reported: 1,301
      - Total: 1,305
      - Guillain-Barré syndrome: 7

  o As of June 22, 2016
    - **US States**
      - Locally acquired mosquito-borne cases reported: 0
      - Travel-associated cases reported: 819
      - Laboratory acquired cases reported: 1
      - Total: 820  
        - Sexually transmitted: 11
        - Guillain-Barré syndrome: 4

    - **US Territories**
      - Locally acquired cases reported: 1,854
      - Travel-associated cases reported: 6
      - Total: 1,860
      - Guillain-Barré syndrome: 7

  o As of July 13, 2016
    - **US States**
      - Locally acquired mosquito-borne cases reported: 0
      - Travel-associated cases reported: 1,305
      - Laboratory acquired cases reported: 1
      - Total: 1,306  
        - Sexually transmitted: 14
        - Guillain-Barré syndrome: 5

    - **US Territories**
• Locally acquired cases reported: 2,905
• Travel-associated cases reported: 11
• Total: 2,916
  ▪ Guillain-Barré syndrome: 12
  - As of July 20, 2016
    - US States
      • Locally acquired mosquito-borne cases reported: 0
      • Travel-associated cases reported: 1,403
      • Laboratory acquired cases reported: 1
      • Total: 1,404 ▪ Sexually transmitted: 15
      • ▪ Guillain-Barré syndrome: 5
    - US Territories
      • Locally acquired cases reported: 3,815
      • Travel-associated cases reported: 12
      • Total: 3,827*
      • ▪ Guillain-Barré syndrome: 14
  - As of July 27, 2016
    - US States
      • Locally acquired mosquito-borne cases reported: 0
      • Travel-associated cases reported: 1,657
      • Laboratory acquired cases reported: 1
      • Total: 1,658 ▪ Sexually transmitted: 15
      • ▪ Guillain-Barré syndrome: 5
    - US Territories
      • Locally acquired cases reported: 4,729
      • Travel-associated cases reported: 21
      • Total: 4,750*
      • ▪ Guillain-Barré syndrome: 17
  - As of August 17, 2016
    - US States:
      • Locally acquired mosquito-borne cases reported: 14
      • Travel-associated cases reported: 2,245
      • Laboratory acquired cases reported: 1
      • Total: 2,260 ▪ Sexually transmitted: 22
      • ▪ Guillain-Barré syndrome: 7
    - US Territories
      • Locally acquired cases reported: 8,000
      • Travel-associated cases reported: 35
      • Total: 8,035*
• Guillain-Barré syndrome: 25
  ○ As of September 7, 2016
    ▪ US States
      • Locally acquired mosquito-borne cases reported: 43
      • Travel-associated cases reported: 2,920
      • Laboratory acquired cases reported: 1
      • Total: 1,658
        ○ Sexually transmitted: 24
        ○ Guillain-Barré syndrome: 7
    ▪ US Territories
      • Locally acquired cases reported: 15,809
      • Travel-associated cases reported: 60
      • Total: 4,750
      • Guillain-Barré syndrome: 31
  ○ As of October 5, 2016
    ▪ US States
      • Locally acquired mosquito-borne cases reported: 105
      • Travel-associated cases reported: 3,712
      • Laboratory acquired cases reported: 1
      • Total: 3,818
        ○ Sexually transmitted: 30
        ○ Guillain-Barré syndrome: 13
    ▪ US Territories
      • Locally acquired cases reported: 24,118
      • Travel-associated cases reported: 83
      • Total: 24,201
      • Guillain-Barré syndrome: 39
  ○ As of October 26, 2016
    ▪ US States
      • Locally acquired mosquito-borne cases reported: 139
      • Travel-associated cases reported: 3,951
      • Laboratory acquired cases reported: 1
      • Total: 4,091
        ○ Sexually transmitted: 33
        ○ Guillain-Barré syndrome: 13
    ▪ US Territories
      • Locally acquired cases reported: 28,627
      • Travel-associated cases reported: 96
      • Total: 28,723
- Guillain-Barré syndrome: 43

  - As of December 7, 2016
    - US States
      - Locally acquired mosquito-borne cases reported: 185
      - Travel-associated cases reported: 4,389
      - Laboratory acquired cases reported: 1
      - Total: 4,575
        - Sexually transmitted: 38
        - Guillain-Barré syndrome: 13
    - US Territories
      - Locally acquired cases reported: 33,712
      - Travel-associated cases reported: 126
      - Total: 33,838
      - Guillain-Barré syndrome: 50
  - As of February 22, 2017
    - US States
      - Locally acquired mosquito-borne cases reported: 221
      - Travel-associated cases reported: 4,747
      - Laboratory acquired cases reported: 1
      - Total: 5,041
        - Sexually transmitted: 44
    - US Territories
      - Locally acquired cases reported: 35,304
      - Travel-associated cases reported: 143
      - Total: 35,447
  - As of April 5, 2017
    - US States
      - Locally acquired mosquito-borne cases reported: 222
      - Travel-associated cases reported: 4,901
      - Laboratory acquired cases reported: 1
      - Total: 5,197
        - Sexually transmitted: 45
    - US Territories
      - Locally acquired cases reported: 36,361
      - Travel-associated cases reported: 143
      - Total: 36,504
  - As of April 19, 2017
    - US States
      - Locally acquired mosquito-borne cases reported: 223
• Travel-associated cases reported: 4,939
• Laboratory acquired cases reported: 1
• Total: 5,238
  o Sexually transmitted: 46
  ◦ US Territories
    • Locally acquired cases reported: 36,426
    • Travel-associated cases reported: 143
    • Total: 36,569
  o As of April 26, 2017
  ◦ US States
    • Locally acquired mosquito-borne cases reported: 224
    • Travel-associated cases reported: 4,963
    • Laboratory acquired cases reported: 1
    • Total: 5,264
      o Sexually transmitted: 46
  ◦ US Territories
    • Locally acquired cases reported: 36,432
    • Travel-associated cases reported: 143
    • Total: 36,575