International Journal of Research Publication and Reviews, Vol 5, no 4, pp 9461-9472 April 2024

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Assessing Vulnerability to Dengue Virus Infection in the Tropical Rainforest Region of Southern Nigeria using the Water Associated Disease Index (WADI)

Brian O. Onyeke

MSc Public Health, University of Suffolk, United Kingdom
Email: brianonyeke@gmail.com

ABSTRACT

Vulnerability to dengue virus (DENV) infection among children and adults in the tropical rainforest region of Southern Nigeria was assessed using the WADI. The WADI vulnerability framework identified environmental (climate, population density, and land use), economic (water access and housing quality), and social (age, sex, education, and healthcare access) determinants of dengue based on composite indicators of exposure and susceptibility within the population, where exposure represents environmental conditions conducive for the presence and transmission of DENV, while susceptibility represents the existing economic and social conditions that render a population sensitive to dengue. Findings revealed that warm temperatures, rainfall, humidity, intensive land use, and high population density supports DENV development and survival of *Aedes aegypti*, indoor and outdoor water containers create breeding sites for vectors, and slums and squatter settlements increase susceptibility to dengue. It concludes that in the absence of readily available vaccine and limited resources to treat or combat dengue in the study area, accurate identification of areas most vulnerable to dengue and timely delivery of interventions to prevent, mitigate, and manage the disease is crucial. Ability to read and understand public health messages regarding dengue prevention, early recognition of symptoms, and adequate healthcare are recommended to reduce fatality.

Keywords: dengue, exposure, rainforest, susceptibility, vulnerability, water-associated diseases

HIGHLIGHTS

- Lack of accurate diagnosis for dengue fever makes it an under-reported disease in Nigeria.
- Environmental, economic, and social factors make inhabitants of tropical rainforest regions vulnerable to dengue.
- Children below 12 years in the study area are at most risk of severe dengue.
- Education and improved access to healthcare is necessary to control the spread of DENV.
- Identification of most vulnerable areas and timely intervention can prevent and mitigate dengue.

INTRODUCTION

Access to safe and clean water is a key requirement for maintaining public health. The relationship between water and good health, characterised by access to safe and clean water through source water protection, treatment, and sanitation is the foundation of a healthy population. Water availability is a primary determinant for addressing the issues of global poverty, and many diseases are associated with its contamination. Diseases associated with water contamination include diarrhoea, cholera, typhoid, shigella, polio, meningitis, hepatitis, schistosomiasis, dengue, fluorosis, campylobacteriosis, etc. (UNU-INWEH, 2011; WHO, 2018a). Water-associated diseases threaten the health and well-being of billions of people worldwide and are most prevalent in tropical and sub-tropical regions especially developing countries (WHO, 2012). They are spread by a range of transmission routes including ingestion of contaminated water, contact with contaminated water, and exposure to disease-carrying vectors (such as mosquitoes) that depend upon water to survive. Water-associated diseases are linked to approximately 3 million deaths annually and countless hours of lost productivity and illness (WWAP, 2009). Intensified by poor water and waste management, uncontrolled urbanisation, high population density, and changing climate conditions, water-associated diseases are of increasing concern in a rapidly changing and increasingly globalised world (Fullerton, Dickin, & Schuster-Wallace, 2014).

About 10 percent of the global burden of disease could be prevented by improved access to safe water, sanitation and hygiene, and better water management (Prüss-Ustün, Bos, Gore, & Bartram, 2008). The incidence of dengue has recently grown rapidly putting more than half the world's population at risk (WHO, 2018b). It is endemic in over 120 countries, including Southeast Asia and Western Pacific, the Caribbean, Latin America, and some regions in the United States, Africa, and the Middle East (Brady *et al.*, 2012). Dengue is estimated to infect about 400 million people and cause 250,000-500,000 cases of severe dengue annually, leading to hundreds of thousands of hospitalisations, countless hours of lost productivity, and approximately 20,000 deaths per year (Suaya *et al.*, 2007; Bhatt *et al.*, 2013).

Dengue has seen a 30-fold upsurge worldwide between 1960 and 2010, due to increased population growth rate, global warming, unplanned urbanisation, inefficient mosquito control, frequent air travel, and lack of healthcare facilities (Gubler, 1998; WHO, 2009; Guzmán *et al.*, 2010). However, it remains an under-reported disease in Nigeria with most cases often undiagnosed, misdiagnosed as malaria or referred to as fever of unknown cause due to lack of awareness by healthcare providers and poor surveillance by public health authorities (Ayukekbong, 2014).
The aim of this study is to assess vulnerability to dengue virus (DENV) in the tropical rainforest region of Southern Nigeria by analysing environmental factors (climate, population density, and land use), economic factors (water access and housing quality), and social factors (age, sex, education, and healthcare access). These factors represent the environmental, economic, and social conditions which render a population vulnerable to dengue virus infection. It seeks to increase the level of knowledge and awareness of dengue in Nigeria within the health sector and the general public.

LITERATURE REVIEW

Definition of Dengue

Dengue is a mosquito-borne tropical disease caused by the dengue virus that affects infants, young children and adults. The clinical features of dengue ranges from a self-limited illness known as dengue fever to a potentially deadly complication called severe dengue (WHO, 2009). Dengue fever is a flu-like illness with symptoms such as high fever, headache, retro-ocular pain, nausea and vomiting, muscle and joint pains, skin rash, and swollen glands, which usually begin 3-14 days after infection (Gubler, 2010; Kularante, 2015). Dengue fever may develop into severe dengue (dengue haemorrhagic fever or dengue shock syndrome) due to plasma leakage, fluid accumulation, respiratory distress, severe bleeding, and organ impairment (WHO, 2018b). Dengue virus is transmitted by several species of the *Aedes* genus of mosquito (mainly *Aedes aegypti*). There are four (4) antigenically distinct dengue virus (DENV) serotypes: DENV-1, DENV-2, DENV-3, and DENV-4 (Kurane, 2007; WHO, 2009). DENV are RNA viruses that belong to the *Flavivirus* genus of the *Flaviviridae* family, which also includes West Nile virus, tick-borne encephalitis virus, yellow fever virus, zika virus, and several other viruses which may cause encephalitis (Dengue Virus Net, 2018; WHO, 2011). DENV is transmitted to humans through bites of infected female *Aedes* mosquito (WHO, 2001). A dengue vaccine, Dengvaxia (CYD-TDV) has been registered in some dengue endemic countries for use in individuals aged 9-60 (WHO, 2016).

Classification of Dengue

The traditional World Health Organization (WHO) 1997 case definition classifies dengue as: dengue fever, dengue haemorrhagic fever, and dengue shock syndrome (WHO, 2009; CDC, 2013).

1997 Dengue Case Definition
Dengue Fever (DF) is most commonly an acute febrile illness defined by the presence of fever and two or more of the following (but not meeting the case definition of dengue haemorrhagic fever):
Retro-orbital or ocular pain

- Headache
- Rash
- Myalgia
- Arthralgia
- Leukopenia
- Haemorrhagic manifestations (e.g. positive tourniquet test, petechiae, purpura/ecchymosis, epistaxis, gum bleeding, blood in vomit, urine, or stool; or vaginal bleeding).

NB: Anorexia, nausea, abdominal pain, and persistent vomiting may also occur but are not case defining criteria for DF.
Dengue Haemorrhagic Fever (DHF) is characterised by all of the following:

- Fever lasting from 2-7 days
- Evidence of haemorrhagic manifestations or a positive tourniquet test
- Thrombocytopenia
- Evidence of plasma leakage shown by haemo-concentration, pleural effusion, or ascites.

Dengue Shock Syndrome (DSS) has all the criteria of DHF plus circulatory failure as evidenced by:

- Rapid and weak pulse and narrow pulse pressure, or
- Age-specific hypotension and cold, clammy skin and restlessness.

The 1997 WHO dengue case definition is limited in terms of its complexity and applicability. This limitation led to a new WHO classification for dengue severity in 2009 which is divided into: dengue without warning signs, dengue with warning signs, and severe dengue (WHO, 2009; CDC, 2013).

2009 New Dengue Case Definition

Dengue without warning signs - fever and two of the following:

- Nausea/vomiting
- Rash
- Aches and pains
- Leukopenia
- Positive tourniquet test.

Dengue with warning signs - dengue (as defined above) with any of the following:

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation (e.g. ascites, pleural effusion)
- Mucosal bleeding
- Lethargy/restlessness
- Liver enlargement (greater than 2cm)
- Laboratory: increase in haematocrit concurrent with rapid decrease in platelet count.

NB: Warning signs require strict observation and medical intervention.

Severe dengue - dengue with at least one of the following:

- Severe plasma leakage leading to shock (dengue shock syndrome) or fluid accumulation with respiratory distress
- Severe bleeding (as evaluated by a clinician)
- Severe organ involvement (i.e. AST or ALT 1000 or greater, impaired consciousness, organ failure).

While WHO still support both case definitions, there is a move towards using the 2009 case definition due to its ease of use (Epocrates, 2018). The revised classification have a high potential for facilitating dengue case management and surveillance, and more sensitive than the 1997 case definition for timely recognition of disease (Barniol *et al*., 2011).

Aetiology of Dengue

Dengue infection is caused by the dengue virus (DENV). There are four antigenically different serotypes of the dengue virus namely: DENV-1, DENV-2, DENV-3, and DENV-4 (Normile, 2013; *Mustafa et al., 2015*). DENV is an RNA virus of the family *Flaviviridae*; genus *Flavivirus*. Other members of the same genus include yellow fever virus, West Nile virus, St. Louis encephalitis virus, Japanese encephalitis virus, tick-borne encephalitis virus, Kyasanur forest disease virus, and Omsk haemorrhagic fever virus, and are mostly transmitted by arthropods (mosquitoes and ticks), hence referred to as arboviruses (Gould & Solomon, 2008). The primary vector of dengue is the *Aedes aegypti* mosquito; a daytime feeder that breeds inside and outside the home in containers holding water. *Aedes aegypti* prefers to lay its egg in artificial water containers, to live in close proximity to humans, and to feed on humans rather than other vertebrates (Gubler, 2010). Its peak biting periods are early in the morning and in the evening before dusk (WHO, 2012), but may bite and thus spread infection at any time of the day (CDC, 2010).

Other *Aedes* species that transmits dengue include *Aedes albopictus, Aedes polynesiensis* and *Aedes scutellaris* (WHO, 2009). Recovery from infection by any one serotype gives lifelong immunity to that specific serotype, but short-term immunity to other serotypes which lasts only a few months (Webster *et al.,* 2009; WHO, 2009; WHO, 2011). Subsequent infection with a different serotype increases the risk of developing severe dengue (WHO, 2018b). Dengue virus infection presents with a diverse clinical picture that ranges from asymptomatic illness to dengue fever (DF) to the severe illness of dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS) (WHO, 2009). Studies have shown that infection with either the DENV-1 or DENV-2 serotype may result in more severe infections (Guzmán *et al.*, 1999; Pichainarong *et al.*, 2006). International travel and transportation of goods has helped the spread of both the vector and the virus, making dengue a global infection (WHO, 2011). Some serotypes have sylvatic cycles spent between wild animals and humans (Wilder-Smith & Gubler, 2008). Humans are the primary host of the dengue virus (Gould & Solomon, 2008; WHO, 2009) but it also circulates in non-human primates (WHO, 2011). The dengue virus is transmitted to humans through the bite of an infected female *Aedes* mosquito. *Aedes* also transmits chikungunya, yellow fever and zika virus (WHO, 2018b). The mosquito becomes infected with the dengue virus when it takes a blood meal from a person infected with dengue fever, usually during the initial 2-10 day febrile period when large amounts of DENV are in the blood (CDC, 2014).

The virus develops in the cell lining its midgut, and after an additional 8-12 days spreads to other tissues including the mosquito's salivary glands and subsequently released into its saliva, thus, capable of transmitting the virus to other humans for the rest of its life, which might be a few days or a few weeks (CDC, 2014; Gubler, 2010), and to the next generation of mosquitoes (WHO, 2001). The incubation period is usually 4-7 days but can also range from 3-14 days (WHO, 2016). Infected symptomatic or asymptomatic humans are the main carriers and multipliers of the virus, serving as a source of the virus for uninfected mosquitoes, and can transmit the infection (for 4-5 days; maximum 12) via *Aedes* after the first symptoms appear (WHO, 2018b). Dengue can also be transmitted via infected blood products, mucocutaneous exposure, needle stick injury, organ transplants or blood transfusions from infected donors (Chen & Wilson, 2004; Stramer *et al.*, 2012; Wilder-Smith, Chen, Massad, & Wilson, 2009). Vertical transmission (from mother-to-child) during pregnancy or at birth has also been reported (CDC, 2014; Wiwanitkit, 2009).

Pathogenesis of Dengue

The pathogenesis of dengue is linked to the host immune response, which is triggered by infection with the dengue virus (Stephenson, 2005). Host factors that affect the severity of dengue infection include race, age, genetic factors and nutritional status (Guzmán *et al.*, 1990). Primary infection is usually benign in nature; however, secondary infection with a different serotype or multiple infections with different serotypes can cause severe infection that is classified as either dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS), depending on the clinical signs (WHO, 2009). Infants can develop severe dengue infection during a primary infection due to transplacental transfer of maternal antibodies from an immune mother, which subsequently amplifies the infant's immune response to the primary infection (Whitehorn & Simmons, 2011). Cells of the monocyte-macrophage lineage are the major sites of viral replication, but the virus can infect other tissues in the body such as the liver, brain, pancreas, and heart (Jessie, Fong, Devi, Lam, & Wong, 2004; Weerakoon *et al.*, 2011; Whitehorn & Simmons, 2011). DHF and DSS are associated with vascular leak causing increase in haematocrit and development of pleural effusions or ascites. There is also severe thrombocytopenia and coagulation disorder (WHO, 2011). In severe infection, loss of intravascular fluid leads to tissue hypoperfusion, resulting in lactic acidosis, hypoglycaemia, hypocalcaemia, and finally multiple organ failure (WHO, 2011). Co-infection with zika or chikungunya virus (or both) is possible (Hajra, Bandyopadhyay, & Hajra, 2016; Villamil-Gómez, González-Camargo, Rodriguez-Ayubi, & Zapata-Serpa, 2016). Co-infection with malaria is also possible (Magalhaes *et al.*, 2014).

Risk Factors to Dengue in Nigeria

Dengue is an endemic disease in Nigeria, yet it is under-reported and routine diagnosis is neglected. The diagnosis is further complicated by the fact that dengue fever mimics malaria fever and the prevalence of dengue-malaria co-infection is high. Due to the significant endemicity of malaria in Nigeria, most "febrile illnesses" including dengue are misdiagnosed and treated as malaria (Ayukekbong, 2014). The factors responsible for dengue incidence are complex. However, factors such as population density, inadequate water supply and waste management, lack of effective control programs, climate change and poor socio-economic status are identified as key determinants for dengue transmission worldwide (Guzmán & Kouri, 2002; Torres & Castro, 2007). The risk factors to dengue virus infection in Nigeria can be broadly classified into environmental factors, economic factors, and social (demographics) factors as follows:

Environmental Factors: Environmental factors consists of climatic factors and socio-environmental factors

- ***Climatic factors*:** Temperature, precipitation (rainfall) and humidity are important climatic factors for the growth and dispersion of the mosquito vector and potential of dengue outbreaks (Urbanová, 2016). The availability of favourable breeding grounds for *Aedes* enhances the spread of DENV. The ideal temperature range for the survival of *Aedes aegypti* through all development stages is between 20-30°C (Morin, Comrie, & Ernst, 2013). Models have determined that at below temperatures of 20°C and higher than 34°C, *Aedes* mosquito cannot reproduce in substantial numbers (Focks, Brenner, Hayes, & Daniels, 2000). Humidity is also linked to *Aedes* prolificacy (Canyon, Hii, & Muller, 1999). Nigeria, like other tropical regions has two seasons - rainy season and dry season. Due to water requirements of mosquitoes for breeding, the incidence and, in particular, epidemic of dengue is very high during the rainy season (Keating, 2001). However, after a certain threshold is reached additional rainfall floods breeding habitats and washes eggs and larvae away (Arcari, Tapper, & Pfueller, 2007; Poveda *et. al.*, 1999). This results in reduced exposure during extremely heavy rainfall events such as monsoon rains due to destruction of vector eggs and larvae.

- ***Socio-environmental factors*:** Non-climatic environmental factors associated with the spread of dengue include high population density and residential land use intensification (Banu, Hu, Hurst, & Tong, 2011). 40 percent of the population in developing countries lives in urban areas, which is projected to rise to 56 percent by 2030 largely due to rural-urban migration (UN Population Division, 2002). Rural-urban migration is due to both "push" (seeking better earning avenues) and "pull" (seeking better amenities such as education, healthcare, etc.) factors. The inability of government to provide matching civic amenities and infrastructure to accommodate the influx generates unplanned settlements with inadequate potable water, poor sanitation including solid waste disposal, and poor public health infrastructure which raises the potential for *Aedes aegypti* breeding to a high level and makes the environment for dengue transmission conducive (Bohra & Andrianasolo, 2001; WHO, 2011). The rapid, unplanned growth of urban centres in Nigeria combined with inadequate water supply and sewage systems have great influence on the transmission of dengue (Ayukekbong, 2014). Rapid population movement intensifies land use by converting lands in urban and suburban areas into residential uses. Increased housing provides an abundance of breeding sites for *Aedes* which prefer to live in close proximity to humans who serve as host to dengue virus (Ooi & Gubler, 2009).

Economic factors: Economic factors that affect the abundance of *Aedes aegypti* mosquitoes and influence disease transmission include housing with unhygienic living conditions and poor household design. The presence of solid waste around the household and prolonged storage of water for domestic use can create potential breeding grounds for *Aedes aegypti*, thereby increasing the transmission of dengue infections (Mondini & Neto, 2007; Nagao *et al.*, 2003). The poor drainage system and inadequate waste disposal practices among low income communities in Nigeria result in the presence of stagnant water bodies and water collected in waste metal containers and discarded vehicle tyres which serve as breeding sites for *Aedes* mosquito vectors which transmit dengue virus (Baba & Talle, 2011).

Social (demographics) factors: Demographics such as age, sex, race, and education are often significantly related to dengue virus incidence. Recent studies show that DHF & DSS is prevalent among children below 15 years of age in Northern Nigeria (Bello, Aminu, & Jatau, 2016; Hamisu et al., 2017) compared to Southern Nigeria where it is prevalent in adults aged 21-60 years (Adeleke et al., 2016; Adesina & Adeniji, 2016; Kolawole et al., 2017). Majority of the studies in Nigeria demonstrate a higher prevalence of dengue infection among females (Idris, Baba, Thairu, & Bamidele, 2013; Bello et al., 2016; Hamisu et al., 2017; Kolawole et al., 2017), however, a male preponderance was noticed in studies conducted in North Central Nigeria (Adedayo et al., 2013; Ugwu, Vem, Nimzing, & Anejo-Okopi, 2018). African descent populations have an innate resistance to severe dengue infection. Observations in Cuba and Haiti reveal epidemiological evidence that black individuals are at lower risk for severe dengue cases compared to white individuals, and this has been used to support the hypothesis that specific genomic difference among different racial groups is a risk factor for DHF and DSS (Guzmán et al., 1999; Halstead et al., 2001; Leslie, 2011; Sierra, Kouri, & Guzmán, 2007). This may provide an explanation as to why outbreaks of DHF and DSS have been under-reported in Africa (Amarasinghe et al., 2011). Data on the relationship between education and dengue in Nigeria is scanty. But studies in other developing countries suggest that level of education significantly affect individual's knowledge, attitudes and practices (KAPs) regarding dengue prevention and control. People with low education are at greater risk of dengue infection (Tran et al., 2003; Diaz-Quijano et al., 2018).

METHODS

Study Setting

This paper assessed vulnerability to dengue virus infection in the tropical rainforest region of Southern Nigeria, specifically Cross River state. The tropical rainforest region is characterised by hot, humid and very wet climate with rainfall throughout the year and no distinct dry season. Each month has an average rainfall of at least 60mm (2.4in) (McKnight & Hess, 2000).

Vulnerability Assessment

Vulnerability is defined as "the degree to which a system is susceptible to or unable to cope with adverse effects" (McCarthy, 2001). In most cases, vulnerability is determined by considering dimensions of exposure and susceptibility, and ability to adapt or cope with a hazard (Adger, 2006). In the context of water-associated disease, vulnerability is determined by a population's exposure to conditions that support the presence and transmission of a water-associated pathogen, and susceptibility to social, cultural, and economic conditions that shape sensitivity to a water-associated pathogen (Fullerton *et al.*, 2014). Vulnerability assessment is an approach used to describe the potential for harm from a diverse range of hazards at local, regional, national or global scales (Birkmann, 2007). Because measures of exposure and susceptibility are often multi-dimensional, indicators are commonly used as proxies to allow for the simplification and integration of diverse measures into a composite index (Hahn, Riederer, & Foster, 2009). This vulnerability assessment employed a range of environmental, economic, and social factors as indicators of vulnerability.

Conceptual Framework of Vulnerability

The Water Associated Disease Index (WADI) conceptual framework of vulnerability to dengue was applied in this study (Fullerton *et al.*, 2014). WADI integrates a range of environmental, economic, and social components to assess the vulnerability of communities and regions to water-related diseases in the face of global changes such as increasing urbanisation, land use intensification and climate change (Dickin, Schuster-Wallace, & Elliot, 2013; Fullerton *et al.*, 2014). The WADI framework of vulnerability relies on composite indicators of exposure and susceptibility, where susceptibility represents the existing economic and social conditions that render a population sensitive to dengue, while exposure represents environmental conditions conducive to the presence and transmission of the dengue virus within the population. In order to identify key indicators of susceptibility and exposure that describe vulnerability to dengue, a conceptual framework of vulnerability to dengue (Figure 1) was developed based on literature review. The framework identifies the determinants of exposure and susceptibility that together describes the linkages between human, vector and virus elements in the dengue transmission cycle. While by no means comprehensive, it identifies key factors and interactions that contribute to dengue presence and transmission.

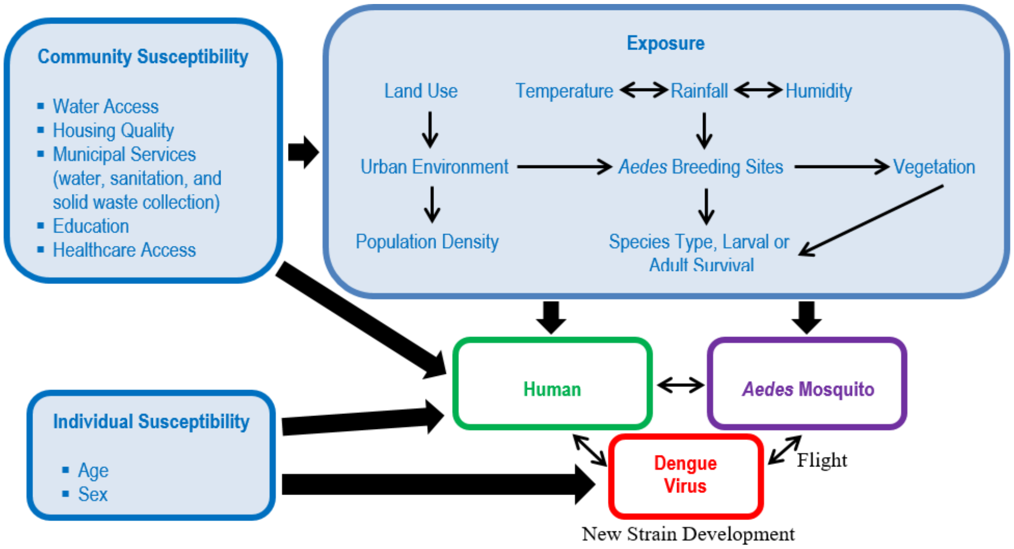

Figure 1: WADI conceptual framework of vulnerability to dengue

Data Sources

The selection of data to measure these indicators was based on the quality and availability of datasets identified from publicly accessible data repositories online. In order to identify datasets to populate the indicators, search terms were used to identify website with relevant datasets. Data were sourced from the following databases: WorldClim global climate grids, Globcover land cover map, UN DESA Population Division, WHO/UNICEF Joint Monitoring Programme, WHO World Health Statistics, WHO Global Health Observatory, and UNESCO Institute for Statistics. Data for each indicator measure were obtained from original sources where available, i.e. in a situation where the same dataset appears on multiple data platforms, the organisation responsible for collecting the data was used as the original source. Datasets used to assess vulnerability to dengue were based on the conceptual framework (Figure 1) and availability of freely accessible data, and also observed values which were used to populate indicators. The datasets are listed in Table 1.

Table 1: Components of WADI-Dengue Vulnerability Assessment

VULNERABILITY COMPONENT	CATEGORY	FACTOR	INDICATOR	INDICATOR MEASURE	ACTUAL VALUE	RATIONALE FOR INCLUSION
EXPOSURE	Environmental	Climate	Temperature	Mean annual temperature	27.18°C	Temperatures between 20-30°C is ideal for *Aedes* proliferation (Morin *et al.*, 2013)
			Rainfall	Mean annual rainfall	2,796mm	Wet conditions provide favourable breeding site for *Aedes* (Keating, 2001)
		Population density	Population density	People/square km	265 people/sq. km (NDRDMP, 2006)	Densely populated areas increase the potential for *Aedes* breeding and dengue transmission (WHO, 2011)
		Land use	Type of land use	Forest, mixed vegetation, cropland, or urban land uses	Forest, mixed vegetation, cropland - 40% Urban land uses - 60%	*Aedes* mosquito prefer to live in urban environments in close proximity to humans (Ooi & Gubler, 2009)

SUSCEPTIBILITY	**Economic**	**Water access**	**Access to affordable, reliable water source**	**Unimproved water source**	**65% of households store water in containers for drinking and pour flush toilets**	**Lack of access to water supplies necessitates prolonged storage of water which create potential breeding grounds for *Aedes* (Mondini & Neto, 2007)**
		Housing quality	**Housing construction and solid waste collection**	**Unimproved sanitation facilities**	**75% of houses lack adequate waste disposal facilities**	**Poor drainage system and inadequate waste disposal practices create breeding sites for *Aedes* (Baba & Talle, 2011)**
	Social (demographic)	**Age**	**Children, Youths, Adults**	**Children <15 years Youths 21-40 years Adults 41-60 years**	**55% DHF & DSS (<15 years) 21% DHF & DSS (21-40 years) 24% DHF & DSS (41-60 years)**	**DHF and DSS in Nigeria is significant in individuals <15 and 21-60 years (Adeleke *et al.*, 2016; Bello *et al.*, 2016; Hamisu *et al.*, 2017; Kolawole *et al.*, 2017)**
		Sex	**Male, Female**	**Male < 21 yrs. Male 21-40 yrs. Male 41-60 Female < 21 yrs. Female 21-40 yrs. Female 41-60 yrs.**	**12% DF (Male < 21 yrs.) 31% DF (Male 21-40 yrs.) 19% DF (Male 41-60 yrs.) 10% DF (Female < 21 yrs.) 15% DF (Female 21-40 yrs.) 13% DF (Female 41-60 yrs.)**	**Both male and female populations are susceptible to dengue in Nigeria (Adedayo *et al.*, 2017; Hamisu *et al.*, 2017; Ugwu *et al.*, 2018).**
		Education	**Illiterate, primary education, secondary education**	**Female progression to secondary school**	**35% of females progress to secondary school after completing primary education**	**Level of education significantly affects individual's knowledge, attitudes and practices (KAPs) regarding dengue prevention and control. (Tran *et al.*, 2003)**
		Healthcare access	**Access to nearby healthcare services**	**Physician density**	**0.395 physicians/1,000 people (WHO, 2010)**	**Physician density indicates availability and accessibility of healthcare (Fullerton *et al.*, 2014)**

Indicator Selection Criteria

To determine the best data to measure indicators of vulnerability to dengue, it was necessary to set indicator selection criteria to guide the assessment and selection process. Indicator selection criteria ensure measures are selected systematically based on their quality and appropriateness (Cole, Eyles, & Gibson, 1998). Measures for this study were selected based on their ability to meet indicator criteria outlined by Garriga and Foguet (2010), and their ability to closely describe the indicator they are chosen to represent. Where no exact measures are available, proxies were used to describe indicators, for example, in the case of healthcare access. In other instances, some indicators were measured by extracting closely related measures as potential indicator measures where the optimal indicator measure is unavailable (female education could be measured using female literacy rate but due to data unavailability female progression to secondary school was used).

Index Construction

In order to construct the index and create map outputs, thresholds were applied to each indicator measure to standardise data to a range from 0 to 1, and converted into a raster format using the geographic information system (GIS) ArcGIS software version 10 (Esri, Redlands, CA) in order to visually communicate temporal changes in vulnerability to dengue. Exposure component raster layers containing pixels representing a value from 0 to 1 were developed for each month of the year, resulting in 12 temperature, 12 precipitation, and 12 humidity layers. Susceptibility component raster layers also containing pixels representing a value from 0 to 1 were created by normalisation of component data using the Human Development Index approach, where x represents the factor in question, and x_{min} and x_{max} represent the lowest and highest value in the dataset respectively:

Susceptibility component $x = (x - x_{min}) / (x_{max} - x_{min})$

An overall score of vulnerability for dengue in the area were based on the weightings of exposure and susceptibility indicators to determine the optimal contribution of each to the WADI-Dengue.

GIS layers produced in the index construction were used for map creation. While many vulnerability assessment approaches provide tabular outputs, visualisation is an important part of the WADI methodology because it allows users to gain a better grasp of the spatial distribution of regions of high or low vulnerability as they can easily interpret outputs.

RESULTS AND DISCUSSION

Exposure indicators including climatic conditions such as temperature, rainfall and humidity influence the growth and development of *A. aegypti* mosquitoes. Mean annual temperature of 27.18°C was recorded in the study area. Increasing temperature has a combined effect of impacting virus development as well as vector survival. Mean annual rainfall of 2,796mm was recorded. Rainfall was positively correlated with mosquito reproduction rates and dengue transmission. The high level of moisture (humidity) observed in the area due to ample rainfall also support *Aedes* survival and reproduction. A positive correlation between incidence of dengue and population density was observed in the study area. The incidence of dengue was found to be higher among people living in built environment compared to forested and vegetative environments.

Susceptibility to dengue is very high in the study area. Indoor and outdoor water storage for purposes of drinking or for using pour flush toilets increases susceptibility because use of water storage containers creates potential breeding sites for *A. aegypti*. Poor housing quality typical of slums, squatter settlements and rapidly expanding urban communities increases susceptibility to dengue. Housing lacking window and door screens allow free passage of mosquitoes. Porous floors, unplastered walls, or untiled bathrooms increases humidity indoors and is conducive to vector survival. 75 percent of houses in the study area lack adequate waste disposal facilities; dump sites can collect water and provide breeding sites for mosquitoes. The risk of dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) was observed to be higher in children (55%) than adults due to capillary fragility in children. Males between 21-40 years (31%) were found to be most vulnerable to dengue fever (DF). This is likely as a result of young males being more engaged in outdoor activities such as farming, fishing, and animal husbandry which make them susceptible to dengue infection.

Increases in adaptive capacity were observed in families with increased female education and literacy. Adaptive capacity is the ability or potential to cope with a hazard and to reduce the likelihood of harmful effects (Hinkel, 2011). Females are largely responsible for domestic water-related tasks such as water collection and storage, and food preparation. Being able to read and understand public health messages regarding dengue prevention and early recognition of symptoms enhances resilience to the disease.

Females who have progressed to secondary education (35%) are associated with positive health outcomes, and in poor households this education offers a protective effect. Adequate access to healthcare creates resilience to water associated disease, and reduces dengue fatality significantly. Delays in presentation for medical attention, diagnosis and appropriate care result in deaths especially among infants and children.

CONCLUSION AND RECOMMENDATIONS

With no readily available vaccine and limited resources to treat or combat the spread of dengue in the study area, preventive measures aimed at lowering the burden of disease is the best alternative. A water-associated disease such as dengue requires accurate identification of areas most vulnerable, and the timely delivery of interventions to prevent, mitigate, and manage the disease in those areas. In order to effectively direct resources for disease control, it is crucial to understand key disease determinants and dynamics, and the differential distribution of vulnerability. Planning is needed in areas that do not currently experience circulating dengue viruses but that are characterised by favourable exposure and susceptibility conditions. As vulnerability to dengue is dependent upon conditions for mosquito vector survival, rising temperatures caused by climate change - especially increases in minimum temperatures may lead to expansion of areas of vulnerability to dengue, and may elevate vulnerability in regions that are currently endemic. Conversely, more frequent and intense rainfall events may actually decrease amounts experienced and may actually decrease exposure to dengue by preventing larval survival in outdoor breeding areas. Furthermore, ability to read and understand public health messages regarding dengue prevention, early recognition of symptoms, and adequate healthcare are recommended to reduce fatality.

REFERENCES

1. Adedayo, F., Nioma, I., Olanrewaju, M. B., Adeyinka, A., & Ebele, A. (2013). Serological evidence of recent dengue virus infection among febrile children in a semi arid zone. *American Journal of Infectious Diseases, 9*(1), 7-10. doi:10.3844/ajidsp.2013.7.10
2. Adeleke, M. A., Muhibi, M. A., Ajayi, E. I. O., Idowu, O. A., Famodimu, M. T., Olaniyan, S. O., & Hassan, A. N. (2016). Dengue virus specific immunoglobulin G antibodies among patients with febrile conditions in Osogbo, Southwestern Nigeria. *Tropical Biomedicine, 33*(1), 1-7. Retrieved August 17, 2018, from https://www.researchgate.net/publication/295693688_Dengue_virus_specific_Immunoglobulin_G_antibodies_among_patients_with_febrile_conditions_in_Osogbo_Southwestern_Nigeria
3. Adesina, O. A., & Adeniji, J. A. (2016). Incidence of dengue virus infections in febrile episodes in Ile-Ife, Nigeria. *African Journal of Infectious Diseases, 10*(1), 21-24. doi:10.4314/ajid.v10i1.4
4. Adger, W. N. (2006). Vulnerability. *Global Environmental Change, 16*(3), 268-281. doi:10.1016/j.gloenvcha.2006.02.006
5. Amarasinghe, A., Kuritsky, J. N., Letson, G. W, & Margolis, H. S. (2011). Dengue virus infection in Africa. *Emerging Infectious Diseases, 17*(8), 1349-1354. doi:10.3201/eid1708.101515
6. Arcari, P., Tapper, N., & Pfueller, S. (2007). Regional variability in relationships between climate and dengue/DHF in Indonesia. *Singapore Journal of Tropical Geography, 28*, 251-272.
7. Ayukekbong, J. A. (2014). Dengue virus in Nigeria: Current status and future perspective. *British Journal of Virology, 1*(4), 106-111. doi:10.13140/rg.2.1.4784.7520
8. Baba, M. M., & Talle, M. (2011). The effect of climate on dengue virus infections in Nigeria. *New York Science Journal, 4*(1), 28-33. Retrieved August 31, 2018, from http://www.sciencepub.net/newyork/ny0401/05_4179ny0401_28_33.pdf
9. Banu, S., Hu, W., Hurst, C., & Tong, S. (2011). Dengue transmission in the Asia-Pacific region: Impact of climate change and socio-environmental factors. *Tropical Medicine and International Health, 16*(5), 598-607. doi:10.1111/j.1365-3156.2011.02734.x
10. Barniol, J., Gaczkowski, R., Barbato, E. V., da Cunha, R. V., Salgado, D., Martinez, E., … Jaenisch, T. (2011). Usefulness and applicability of the revised dengue case classification by disease: multicenter study in 18 countries. *BMC Infectious Diseases, 11*(106), 1-12. doi:10.1186/1471-2334-11-106
11. Bello, O. A., Aminu, M., & Jatau, E. D. (2016). Seroprevalence of IgM antibodies to dengue fever virus among patients presenting with symptoms of fever in some hospitals in Kaduna State, Nigeria. *International Journal of Science and Research, 5*(3), 1255-1259. Retrieved August 17, 2018, from https://www.ijsr.net/archive/v5i3/NOV162015.pdf
12. Bhatt, S., Gething, P. W., Brady, O. J., Messina, J. P., Farlow, A. W., Moyes, C. L., … Hay, S. I. (2013). The global distribution and burden of dengue. *Nature, 496*(7446), 504-507. doi:10.1038/nature12060
13. Birkmann, J. (2007). Risk and vulnerability indicators at different scales: Applicability, usefulness and policy implications. *Environmental Hazards, 7*(1), 20-31. doi:10.1016/j.envhaz.2007.04.002
14. Bohra, A., & Andrianasolo, H. (2001, November 5-9). *Application of GIS in modelling of dengue risk based on socio-cultural data: Case of Jalore, Rajasthan, India*. Paper presented at the 22nd Asian Conference on Remote Sensing, Singapore. Retrieved October 4, 2018, from https://www.crisp.nus.edu.sg/~acrs2001/pdf/096bohra.pdf
15. Brady, O. J., Gething, P. W., Bhatt, S., Messina, J. P., Brownstein, J. S., Hoen, A. G., … Hay, S. I. (2012). Refining the global spatial limits of dengue virus transmission by evidence-based consensus. *PLOS Neglected Tropical Diseases, 6*(8), e1760 (1-15). doi:10.1371/journal.pntd.0001760
16. Canyon, D. V., Hii, J. L. K., & Muller, R. (1999). Adaptation of *Aedes aegypti* (Diptera: Culicidae) oviposition behavior in response to humidity and diet. *Journal of Insect Physiology, 45*, 959-964.
17. Centers for Disease Control and Prevention. (2010). *Travelers' health: Dengue in tropical and subtropical regions*. Retrieved August 27, 2010, from https://wwwnc.cdc.gov/travel/notices/watch/dengue-tropical-sub-tropical
18. Centers for Disease Control and Prevention. (2013). *Dengue: Clinical description for case definitions.* Retrieved August 4, 2018, from https://www.cdc.gov/dengue/clinicalLab/caseDef.html
19. Centers for Disease Control and Prevention. (2014). *Dengue: Epidemiology.* Retrieved August 9, 2018, from https://www.cdc.gov/dengue/epidemiology/index.html
20. Chen, L. H., & Wilson, M. E. (2004). Transmission of dengue virus without a mosquito vector: Nosocomial mucocutaneous transmission and other routes of transmission. *Clinical Infectious Diseases, 39*(6), e56-e60. doi:10.1086/423807
21. Cheng, J. J., Schuster-Wallace, C., Watt, S., Newbold, K., & Mente, A. (2011). *Summary analysis: Quantifying water supply, sanitation and the Millennium Development Goals.* Hamilton, Canada: United Nations University.
22. Cole, D.C., Eyles, J., & Gibson, B. L. (1998). Indicators of human health in ecosystems: What do we measure? *Science of the Total Environment, 224*(1-3), 201-213. doi:10.1016/S0048-9697(98)00350-7
23. Dengue Virus Net. (2018). *Dengue Virus Information.* Retrieved August 2, 2018, from https://www.denguevirusnet.com/dengue-virus.html
24. Diaz-Quijano, F. A., Martínez-Vega, R. A., Rodriguez-Morales, A. J., Rojas-Calero, R. A., Luna-González, M. L., & Díaz-Quijano, R. G. (2018). Association between the level of education and knowledge, attitudes and practices regarding dengue in the Caribbean region of Colombia. *BMC Public Health, 18*(143), 1-10. doi:10.1186/s12889-018-5055-z

25. Dickin, S. K., Schuster-Wallace, C. J., & Elliot, S. J. (2013). Developing a vulnerability mapping methodology: Applying the Water-Associated Disease Index to dengue in Malaysia. *PLOS One, 8*(5), e63584 (1-11). doi:10.1371/journal.pone.0063584
26. Epocrates. (2018). *Dengue fever definition.* Retrieved August 2, 2018, from https://www.online.epocrates.com/diseases/119721/Dengue-fever/Definition
27. Focks, D. A., Brenner, R. J., Hayes, J., & Daniels, E. (2000). Transmission thresholds for dengue in terms of Aedes aegypti pupae per person with discussion of their utility in source reduction efforts. *American Journal of Tropical Medicine & Hygiene, 62*, 11-18.
28. Fullerton, L. M., Dickin, S. K., & Schuster-Wallace, C. J. (2014). *Mapping global vulnerability to dengue using the Water-Associated Disease Index.* Hamilton, Canada: United Nations University.
29. Garriga, R. G., & Foguet, A. P. (2010). Improved method to calculate a water poverty index at local scale. *Journal of Environmental Engineering, 136*(11). doi:10.1061/(ASCE)EE.1943-7870.0000255
30. Gould, E. A., & Solomon, T. (2008). Pathogenic flaviviruses. *Lancet, 371*(9611), 500-509. doi:10.1016/S0140-6736(08)60238-X
31. Gubler, D. J. (1998). Dengue and dengue hemorrhagic fever. *Clinical Microbiology Reviews, 11*(3), 480-496. Retrieved August 31, 2018, from https://cmr.asm.org/content/cmr/11/3/480.full.pdf
32. Gubler, D. J. (2010). Dengue viruses. In B. W. J. Mahy & M. H. V. van Regenmortel (Eds.), *Desk encyclopedia of human and medical virology* (pp. 372-382). Boston, MA: Academic Press. Retrieved August 31, 2018, from http://www.pdf.to/bookinfo/desk-encyclopedia-of-human-and-medical-virology.pdf/
33. Guzmán, M. G., Alvarez, M., Rodriguez, R., Rosario, D., Vázquez, S., Valdés, L., … Kouri, G. (1999). Fatal Dengue Hemorrhagic Fever in Cuba, 1997. *International Journal of Infectious Diseases, 3*(3), 130-135. doi:10.1016/S1201-9712(99)90033-4
34. Guzmán, M. G., Halstead, S. B., Artsob, H., Buchy, P., Farrar, J., Gubler, D. J., … Peeling, R. W. (2010). Dengue: A continuing global threat (Supplemental material). *Nature Reviews Microbiology, 8*(12), S7-S16. doi:10.1038/nrmicro2460
35. Guzmán, M. G., & Kouri, G. (2002). Dengue: An update. *Lancet Infectious Diseases, 2*(1), 33-42. doi:10.1016/S1473-3099(01)00171-2
36. Guzmán, M. G., Kouri, G. P., Bravo, J., Soler, M., Vazquez, S., & Morier, L. (1990). Dengue hemorrhagic fever in Cuba, 1981: A retrospective seroepidemiologic study. *The American Journal of Tropical Medicine & Hygiene, 42*(2), 179-184. doi:10.4269/ajtmh.1990.42.179
37. Hahn, M. B., Riederer, A. M., & Foster, S. O. (2009). The livelihood vulnerability index: A pragmatic approach to assessing risks from climate variability and change – A case study in Mozambique. *Global Environmental Change, 19*(1), 74-88. doi:10.1016/j.gloenvcha.2008.11.002
38. Hajra, A., Bandyopadhyay, D., & Hajra, S. K. (2016). Zika virus: A global threat to humanity: A comprehensive review and current developments. *North American Journal of Medical Sciences, 8*(3), 123-128. doi:10.4103/1947-2714.179112
39. Halstead, S. B., Streit, T. G., Lafontant, J. G., Putvatana, R., Russell, K., Sun, W., … Watts, D. M. (2001). Haiti: Absence of dengue hemorrhagic fever despite hyperendemic dengue virus transmission. *The American Journal of Tropical Medicine and Hygiene, 65*(3), 180-183. doi:10.4269/ajtmh.2001.65.180
40. Hamisu, T. M., El-Yuguda, A. D., Abubakar, M. B., Shettima, Y. M., Maina, M. M., Zanna, M. Y., … Terhemen, I. C. (2017). Prevalence of dengue virus infection among febrile outpatients attending University of Maiduguri Teaching Hospital in Borno State, Nigeria. *IOSR Journal of Dental and Medical Sciences, 16*(6), 155-159. doi:10.9790/0853-160603155159
41. Hinkel, J. (2011). Indicators of vulnerability and adaptive capacity: towards a clarification of the science–policy interface. *Global Environmental Change, 21*, 198-208.
42. Idris, A. N., Baba, M. M., Thairu, Y., & Bamidele, O. (2013). Seroprevalence of dengue type-3 virus among patients with febrile illnesses attending a tertiary hospital in Maiduguri, Nigeria. *International Journal of Medicine and Medical Sciences, 5*(12), 560-563. doi:10.5897/IJMMS2013.0994
43. Jessie, K., Fong, M. Y., Devi, S., Lam, S. K., & Wong, K. T. (2004). Localization of dengue virus in naturally infected human tissues, by immunohistochemistry and in situ hybridization. *Journal of Infectious Diseases, 189*(8), 1411-1418. doi:10.1086/383043
44. Keating, J. (2001). An investigation into the cyclical incidence of dengue fever. *Social Science and Medicine, 53*(12), 1587-1597. Retrieved August 31, 2018, from https://eurekamag.com/pdf/003/003641684.pdf
45. Kolawole, O. M., Seriki, A. A., Irekeola, A. A., Bello, K. E., & Adeyemi, O. O. (2017). Dengue virus and malaria concurrent infection among febrile subjects within Ilorin metropolis, Nigeria. *Journal of Medical Virology, 89*(8), 1347-1353. doi:10.1002/jmv.24788
46. Kularante, S. A. (2015). Dengue fever. *BMJ, 351*, h4661. *doi:10.1136/bmj.h4661*
47. Kurane, I. (2007). Dengue hemorrhagic fever with special emphasis on immunopathogenesis. *Comparative Immunology Microbiology & Infectious Diseases, 30*(5-6), 329-40. doi:10.1016/j.cimid.2007.05.010
48. Leslie, T. E. (2011). Dengue fever and the quandary of race. *Latin American and Caribbean Ethnic Studies, 6*(3), 283-309. doi:10.1080/17442222.2011.617590
49. Magalhães, B. M. L., Siqueira, A. M., Alexandre, M. A. A., Souza, M. S., Gimaque, J. B., Bastos, M. S., … Mourão, M. P. G. (2014). *P.vivax* malaria and dengue fever co-infection: A cross-sectional study in the Brazilian Amazon. *PLOS Neglected Tropical Diseases, 8*(10), e3239. doi:10.1371/journal.pntd.0003239
50. McCarthy, J. J. (Ed.). (2001). *Climate change 2001: Impacts, adaptation, and vulnerability: Contribution of Working Group II to the third assessment report of the Intergovernmental Panel on Climate Change.* Cambridge, MA: Cambridge University Press.
51. McKnight, T. L. & Hess, D. (2000). *Physical geography: A landscape appreciation*. Upper Saddle River: Pearson Prentice Hall.

52. Mondini, A., & Neto, F. C. (2007). Socioeconomic variables and dengue transmission. *Revista de Saúde Pública, 41*(6), 1-7. doi:10.1590/S0034-89102007000600006
53. Morin, C. W., Comrie, A. C., & Ernst, K. (2013). Climate and dengue transmission: Evidence and implications. *Environmental Health Perspectives, 121*(11-12), 1264-1272. doi:10.1289/ehp.1306556
54. *Mustafa, M. S., Rasotgi, V., Jain, S., & Gupta, V. (2015). Discovery of fifth serotype of dengue virus (DENV-5): A new public health dilemma in dengue control. Medical Journal Armed Forces India, 71(1), 67-70. doi:10.1016/j.mjafi.2014.09.011*
55. Nagao, Y., Thavara, U., Chitnumsup, P., Tawatsin, A., Chansang, C., & Campbell-Lendrum, D. (2003). Climatic and social risk factors for *Aedes* infestation in rural Thailand. *Tropical Medicine & International Health, 8*(7), 650-659. doi:10.1046/j.1365-3156.2003.01075.x
56. *Normile, D. (2013, October). Tropical medicine: Surprising new dengue virus throws a spanner in disease control efforts. Science, 342(6157).* Retrieved October 31, 2013, from http://www.science.sciencemag.org/content/342/6157
57. Ooi, E. E., & Gubler, D. J. (2009). Dengue in Southeast Asia: Epidemiological characteristics and strategic challenges in disease prevention (Supplemental material). *Cadernos de Saúde Pública, 25*(1), S115-S124. doi:10.1590/S0102-311X2009001300011
58. Pichainarong, N., Mongkalangoon, N., Kalayanarooj, S., & Chaveepojnkamjorn, W. (2006). Relationship between body size and severity of dengue hemorrhagic fever among children aged 0-14 years. *Southeast Asian Journal of Tropical Medicine & Public Health, 37*(2), 283-288. Retrieved October 2, 2018, from http://www.tm.mahidol.ac.th/seameo/2006_37_2/07-3680.pdf
59. Poveda, G., Graham, N. E., Epstein, P. R., Rojas, W., Velez, I. D. *et al.* (1999) Climate and ENSO variability associated to malaria and dengue fever in Colombia. In: Proceedings of the 10th Symposium Global Change Studies. Boston: *American Meteorological Society*, 173-76.
60. Prüss-Ustün, A., Bos, R., Gore, F., & Bartram, J. (2008). *Safer water - better health: Costs, benefits and sustainability interventions to protect and promote health*. Geneva: World Health Organization.
61. Sierra, B., Kouri, G., & Guzmán, M. G. (2007). Race: a risk factor for dengue hemorrhagic fever. *Archives of Virology, 152*, 533-543. doi:10.1007/s00705-006-0869-x
62. Stephenson, J. R. (2005). Understanding dengue pathogenesis: Implications for vaccine design. *Bulletin of the World Health Organization, 83*(4), 308-314.
63. Stramer, S. L., Linnen, J. M., Carrick, J. M., Foster, G. A., Krysztof, D. E., Zou, S., … Tomashek, K. M. (2012). Dengue viremia in blood donors identified by RNA and detection of dengue transfusion transmission during the 2007 dengue outbreak in Puerto Rico. *Transfusion, 52*(8). doi:10.1111/j.1537-2995.2012.03566.x
64. Suaya, J. A., Shepard, D. S., & Beatty, M. E. (2007). Dengue: Burden of disease and costs of illness. In TDR. Report of the Scientific Working Group Meeting on Dengue (pp. 35-49).
65. Torres, J. R., & Castro, J. (2007). The health and economic impact of dengue in Latin America. *Cadernos de Saúde Pública, 23*(S1), S23-S31. doi:10.1590/S0102-311X2007001300004
66. Tram, T. T., Anh, N. T. N., Hung, N. T., Lan, N. T., Cam, L. T., Chuong, N. P., … Heegaard, E. D. (2003). The Impact of Health Education on Mother's Knowledge, Attitude and Practice (KAP) of Dengue Haemorrhagic Fever. *Dengue Bulletin, 27*, 174-180.
67. Ugwu, B. K., Vem, S. T., Nimzing, L., & Anejo-Okopi, A. J. (2018). Dengue virus antibodies in patients presenting with pyrexia attending Jos University Teaching Hospital, Jos, Nigeria. *Saudi Journal of Pathology and Microbiology, 3*(1), 47-55. doi:10.21276/sjpm.2018.3.1.9
68. UN Population Division (2002). *World Urbanization Prospects: The 2001 revision*. New York City, NY: United Nations. Retrieved from http://info.k4health.org/pr/m16/m16chap1_1.shtml
69. United Nations University - Institute for Water, Environment and Health. (2011). *Understanding the water-health nexus: Perceived local linkages between water, environment and health*. Hamilton, Canada: United Nations University.
70. Urbanová, K. (2016). *Analysis of risk factors associated with dengue in Southeast Asia* (Master's thesis, Mendel University in Brno, Czech Republic). Retrieved August 6, 2018, from http://is.mendelu.cz/lide/clovek.pl?zalozka=13;id=48222;studium=73226;zp=55828;download_prace=1;lang=en
71. Villamil-Gómez, W. E., González-Camargo, O., Rodriguez-Ayubi, J., Zapata-Serpa, D., & Rodriguez-Morales, A. J. (2016). Dengue, chikungunya and zika co-infection in a patient from Colombia. *Journal of Infection & Public Health, 9*(5), 684-686. doi:10.1016/j.jiph.2015.12.002
72. Webster, D. P., Farrar, J., & Rowland-Jones, S. (2009). Progress towards a dengue vaccine. *Lancet Infectious Diseases, 9*(11), 678-687. doi:10.1016/S1473-3099(09)70254-3
73. Weerakoon, K., Kularatne, S. A. M., Edussuriya, D.H., Kodikara, S. K. A., Gunatilake, L. P. G., Pinto, V. G., … Gunasena, S. (2011). Histopathological diagnosis of myocarditis in a dengue outbreak in Sri Lanka, 2009. *BMC Research Notes, 4*(268), 1-6. doi:10.1186/1756-0500-4-268
74. Whitehorn, J., & Simmons, C. P. (2011). The pathogenesis of dengue. *Journal of Vaccine, 29*(42), 7221-7228. doi:10.1016/j.vaccine.2011.07.022
75. WHO/UNICEF. (2013). *Progress on Drinking Water and Sanitation: 2012 Update*. Retrieved October 6, 2013, from https://www.wssinfo.org/documents-links/documents/
76. *Wilder-Smith, A., Chen, L. H., Massad, E., & Wilson, M. E. (2009). Threat of dengue to blood safety in dengue-endemic countries. Emerging Infectious Diseases, 15(1), 8–11. doi:10.3201/eid1501.071097*

77. Wilder-Smith, A., & Gubler, D. J. (2008). Geographic expansion of dengue: The impact of international travel. *Medical Clinics of North America, 92*(6), 1377-1390. doi:10.1016/j.mcna.2008.07.002
78. *Wiwanitkit, V. (2009). Unusual mode of transmission of dengue. Journal of Infection in Developing Countries, 4(1), 51-54. doi:10.3855/jidc.145*
79. World Health Organization. (2001). *Water-related diseases: Dengue and dengue haemorrhagic fever*. Retrieved August 5, 2018, from https://www.who.int/water_sanitation_health/diseases-risks/diseases/dengue/case/en/
80. World Health Organization. (2009). *Dengue: Guidelines for diagnosis, treatment, prevention and control* (New ed.). Geneva, Switzerland: Author.
81. World Health Organization. (2011). *Comprehensive guidelines for prevention and control of dengue and dengue haemorrhagic fever* (Rev. ed.). New Delhi, India: World Health Organization, Regional Office for South-East Asia.
82. World Health Organization. (2012). *Global strategy for dengue prevention and control, 2012-2020*. Geneva, Switzerland: Author.
83. World Health Organization. (2016, July 29). Dengue vaccine: WHO position paper. *The Weekly Epidemiological Record, 30*(91), 349-364. Retrieved August 20, 2018, from http://www.who.int/wer/2016/wer9130.pdf
84. World Health Organization. (2018a). *Water related diseases: Information sheets*. Retrieved October 4, 2018, from http://www.who.int/water_sanitation_health/diseases-risks/diseases/diseasefact/en/
85. World Health Organization. (2018b). *World Health Organization fact sheets: Dengue and severe dengue*. Retrieved October 4, 2018, from http://www.who.int/en/news-room/fact-sheets/detail/dengue-and-severe-dengue
86. World Water Assessment Programme. (2009). *The United Nations World Water Development Report 3: Water in a Changing World*. Paris, France: UNESCO Publishing .