EVIDENCE-BASED PUBLIC HEALTH POLICY FOR ZIKA INFECTION MANAGEMENT IN MALAYSIA

Wong Chin Mun1, Rozita Hod[1], Mohd Rohaizat Hassan[1], Nadia Aqilla Shamsusah[2], Hani Kartini Agustar[2] and Sharifah Ezat Wan Puteh[1]

[1]Faculty of Medicine, Universiti Kebangsaan Malaysia, Cheras, Kuala Lumpur; [2]Faculty of Science and Technology, Universiti Kebangsaan Malaysia, Bangi, Selangor, Malaysia

Abstract. Zika has re-emerged as a pandemic between year 2007-2018. Research progress on Zika is much slower in the Asia region compared to America counterpart and there is much under-reporting and inadequate preparedness for any future Zika outbreak. A review of current disease management policies/guidelines can provide evidence-based information to improve preparedness and response to Zika epidemic in Malaysia. A systematic literature search using a Population, Intervention, Comparison, and Outcome (PICO) framework and a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) workflow across four scientific databases and snowball sampling review of guidelines from international health authorities yielded 189 relevant articles from 2013-2018, from which 37 articles screened by titles fulfilling inclusion and exclusion criteria were subjected to abstract scrutiny, resulting in eight articles for full text analysis using a Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment system of Cochrane's checklist. Meticulous, systematic quality ratings conducted by independent reviewers yielded four important Zika intervention domains. Narrative and qualitative assessments on their effectiveness in intervention and relevant public health effects were evaluated. Two domains, namely, vaccine development and blood product management, were rated as having a high quality of evidence, and therefore considered critically important to the management of Zika and were strongly recommended for implementation by the Ministry of Health, Malaysia. The other two domains, vector control and family planning, were deemed important and were recommended, if feasible, for inclusion into a Zika management program. In conclusion, evaluation of the scientific quality in disease management produced four domains, inclusion of which into public health policies should strengthen the preparedness and management of future Zika epidemic in Malaysia.

Keywords: disease outbreak management, Malaysia, science-based public health policy, Zika infection, Zika surveillance

Correspondence: Rozita Hod, Department of Public Health, Faculty of Medicine, Universiti Kebangsaan Malaysia, Cheras Federal Territory Kuala Lumpur 56000, Malaysia
Tel: +60 19 607 3701   E-mail: rozita.hod@ppukm.ukm.edu.my

INTRODUCTION

Zika, a century-old re-emerging infectious disease has drawn much global attention during 2007-2018 due to new discovery of its association with microencephaly of newborns and Guillain-Barré syndrome (an acute, symmetrical and ascending paralysis) (WHO, 2016). This phenomenon is associated with Zika virus of Asian lineage, which was transmitted to the Latin America region during international sport events (Musso, 2015; Hu *et al*, 2019). This evolved Zika virus of Asian lineage, P6-740, responsible for global public health emergency, was believed to have originated in 1966 from an existing Malaysian strain (Pond, 1963; Lim *et al*, 2017; Hu *et al*, 2019). Surprisingly, the Asia region has greatly lagged in case reporting and research into Zika disease, presumably owing to under-identification of the Zika virus and its disease syndrome (Heang *et al*, 2012; Lim *et al*, 2017; Wongsurawat *et al*, 2018; Woon *et al*, 2019). Symptoms of Zika infection are mild (fever, rash, headache, joint pain, conjunctivitis, and muscle pain) and its genome is similar to that of dengue virus (Kochakarn *et al*, 2016).

From 85 systematic reviews of Zika disease (from 2013 to 2018), there was only one from Southeast Asia (Wong *et al*, 2016). However, the climate of Southeast Asia is suitable for growth and breeding of Zika virus-carrying *Aedes* and related spp, and thus there should be an abundant presence of Zika virus in the sylvatic cycle (Leung *et al*, 2015; Kuadkitkan *et al*, 2020). However, public health policies of Zika disease management in this region are not as established as in the American and the European regions, due to reasons described above.

This situation demands a review of current public health policy of Zika management system in Malaysia to improve response and control of Zika cases. Research-based public health policy reviews have now been used to strengthen the gap in evidence-based policy by assessing evidence-based medicine (Masood *et al*, 2018). This study sought to identify domains of public health responses in global management of Zika virus infection, with the aim to provide suggestions on the suitability of these domains to be included in Zika surveillance, response and management systems in a Malaysian setting.

MATERIALS AND METHODS

Literature search

Systematic search related to relevant articles from four major search engines (COCHRANE library, Ovid Medline, PubMed, and Science Direct) were carried out using a Boolean search strategy. A concept involving population, intervention, comparison, and outcome (PICO) (Ferreri *et al*, 2009) was applied to generate relevant keywords for the systematic review to ensure adequate coverage of literature search for articles published from 2013 to 2018 (Table 1). Ethical consideration is not applicable for a systematic review.

As policies of disease management differ according to countries, some documents used as reference for policy formation may not be present in the scientific databases. Thus, a snowball sampling was used to obtain documents/guidelines not found in the scientific databases searched but present in international organizations such as the Centers for Disease Control and Prevention (CDC), the United States

Table 1

Population, intervention, comparison, and outcome keywords used in screening of publications on global management of Zika virus infection (2013-2018)

Keyword	Sub-theme	Synonyms
Patient/problem	Zika infection	Zika virus infection
		Zika virus transmission
		Zika local transmission
		Zika outbreak
Intervention	Country policy	Country plan
		Health strategy
		Ministry of Health proposed action
		Public health blueprint
		Public health approach
		Public health Zika prevention program
		Zika screening system
		Zika screening guidelines
		Zika prevention theory
		Public health response
		Public health preparedness and response
		Border control
		Travel medicine
		Travel safety

Table 1 (cont)

Keyword	Sub-theme	Synonyms
Comparison	WHO	Global
		Region
		Europe
		USA
		Developed countries
		WPRO
Outcome	Zika screening	Prevent mosquito bite
	Prevent mosquito transmission	Prevent mosquito transmission
	Prevent sexual transmission	Prevent *Aedes* mosquito bite
	Prevent blood transmission	Prevent mosquito transmission
	Prevent maternal to child transmission	Mosquito transmission
	Zika vaccination	Prevent *Aedes* mosquito transmission
	Knowledge, attitude and practice	Vector control
		Aedes vector control
		Protected sex
		Safe sex practice
		Delay pregnancy
		Antenatal ultrasound scan
		Transplacental transmission
		Amniotic fluid transmission
		Mother to child transmission
		Maternal to child transmission
		Seminal fluid infection
		Hematospermia
		Blood product safety
		Blood product screening
		Transfusion safety
		Transfusion screening
		Symptomatic screening
		Laboratory confirmation
		ZIKV antibody testing
		Prophylaxis
		Behavior medicine
		Behavior intervention
		Increase awareness
		No *Aedes* sp, Dengue or Zika infection

USA: United States of America; WHO: World Health Organization; WPRO: Western Pacific Region; ZIKV: Zika virus

Food and Drug Administration (US FDA) and World Health Organization (WHO).

A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was used to assist workflow of the search for articles. Keywords used to search for the articles are: "Zika infection" or " Zika outbreak" or "Zika virus transmission" or "Zika local transmission" and "Zika Screening" or "Prevent mosquito transmission" or "Prevent Sexual transmission" or "Prevent blood transmission" or "Prevent maternal to child transmission" or "Zika Vaccination" or "Knowledge, attitude, practice" and "developed and developing countries" or "US WHO" or "CDC" or "PAHO" or "WPRO" and "Country plans" or "Health strategy" or "Ministry of health proposed action" or "Public health blueprint" or "Public health approach" or "Public health Zika prevention program" or "Zika screening system" or "Zika screening guidelines" or "Zika prevention theory" or "Public health response" or "Public health preparedness and response" or "Border control" or "Travel medicine" or "Travel safety".

Article selection and data extraction

Inclusion criteria for article search in this systematic review are: (i) full text, primary research articles on countries policy, guidelines, strategies in use/ proposed; (ii) clinical management policy; (iii) reported at least one outcome pertaining to intervention program (reduced transmission and/or reduced morbidity); (iv) articles published in 2013-2018; and (v) public health tools. Exclusion criteria are: (i) reviewed articles and those lacking original research work or empirical data; (ii) studies conducted in animals, genetics or genomics, and laboratory experiments; and (iii) clinical updates, opinions, editorials and perspectives. Articles that are duplicates or similar were excluded.

Articles that passed all criteria were subjected to full review and critical appraisal by two independent reviewers, who extracted data from the selected article using COCHRANE checklist (Review Manager 5.3). Each article was extracted for data regarding the leading author, year of publication, study design, sampling population, interventional tool, domain, health impact imposed, and public health implications.

Quality of reporting assessment

Quality of each article was evaluated using Cochrane Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment (Ryan and Hill, 2016). GRADE assessment system rates quality of evidence of an article based on eight criteria: risk of bias, indirectness, inconsistency, imprecision, and publication bias, large effect, dose-response gradient, and plausible confounding would change the effect.

There are six types of risk of bias: i) selection bias (random sequence generation and allocation

concealment), ii) performance bias (blinding of participants and personnel), iii) detection bias (blinding of outcome assessment), iv) attrition bias (incomplete outcome data), v) reporting bias (selective reporting), and vi) other bias area not within the range of coverage of the other type of biases, such as confounding effects (Ryan and Hill, 2016). Risk level of "low" or " unclear" or "high" is then designated (The Cochrane Collaboration, 2014), and finally, a global rating is given to each article. Adjustment of quality based on the number of risk of bias in each level was used to obtain a final quality of evidence as follows (Ryan and Hill, 2016): article(s) with >3 "high" risk bias is (are) considered as "poor quality", with <4 "low" risk bias + >2 "high" risk bias rating as "moderate quality" and <4 "low" risk bias + <2 "high" risk bias rating as "good quality".

All selected articles were analyzed with other seven GRADE Assessment System criteria of quality of evidence as mentioned using narrative (qualitative) and quantitative (rating score) GRADE assessment. Presence of the first five criteria in the GRADE assessment system resulted in an upgrade of score while absence of the last three criteria in the system downgraded the score (Ryan and Hill, 2016). The final quality of evidence for each outcome is graded as "high", "moderate", "low", or "very low", reflecting the degree of confidence obtained in the effect estimate (Ryan and Hill, 2016). A "high" quality evidenced

outcome means all potential problems that affect the quality of evidence reported in the particular research area have been identified and assessed, and future research is highly unlikely to be needed to change the confidence of effect estimate (Ryan and Hill, 2016), while the converse needs to be applied for a "very low" quality outcome.

A Review Manager software package (RevMan 5.3) (The Cochrane Collaboration's software, Copenhagen, Denmark) was used in the generation of figures and tables of the risk bias assessment (Julian and Sally, 2014).

RESULTS

Selection of publications

A total of 189 studies, including 60 from non-science databases, were screened by titles and abstracts using the search criteria by one reviewer, from which 27 articles were then subjected to full review and critical appraisal by two independent reviewers, resulting in 11 articles for screening of relevance and quality by the reviewer team who screened out three articles (Fig 1). Among the eight articles selected, three were randomized control trials (RCTs), three quasi CTs and two cohort studies. Narrative analysis of intervention tools and relevant health effects included risk communication and multidisciplinary collaboration, plan-do-study-act (PDSA) framework application, family planning services provision and impact evaluation, Zika
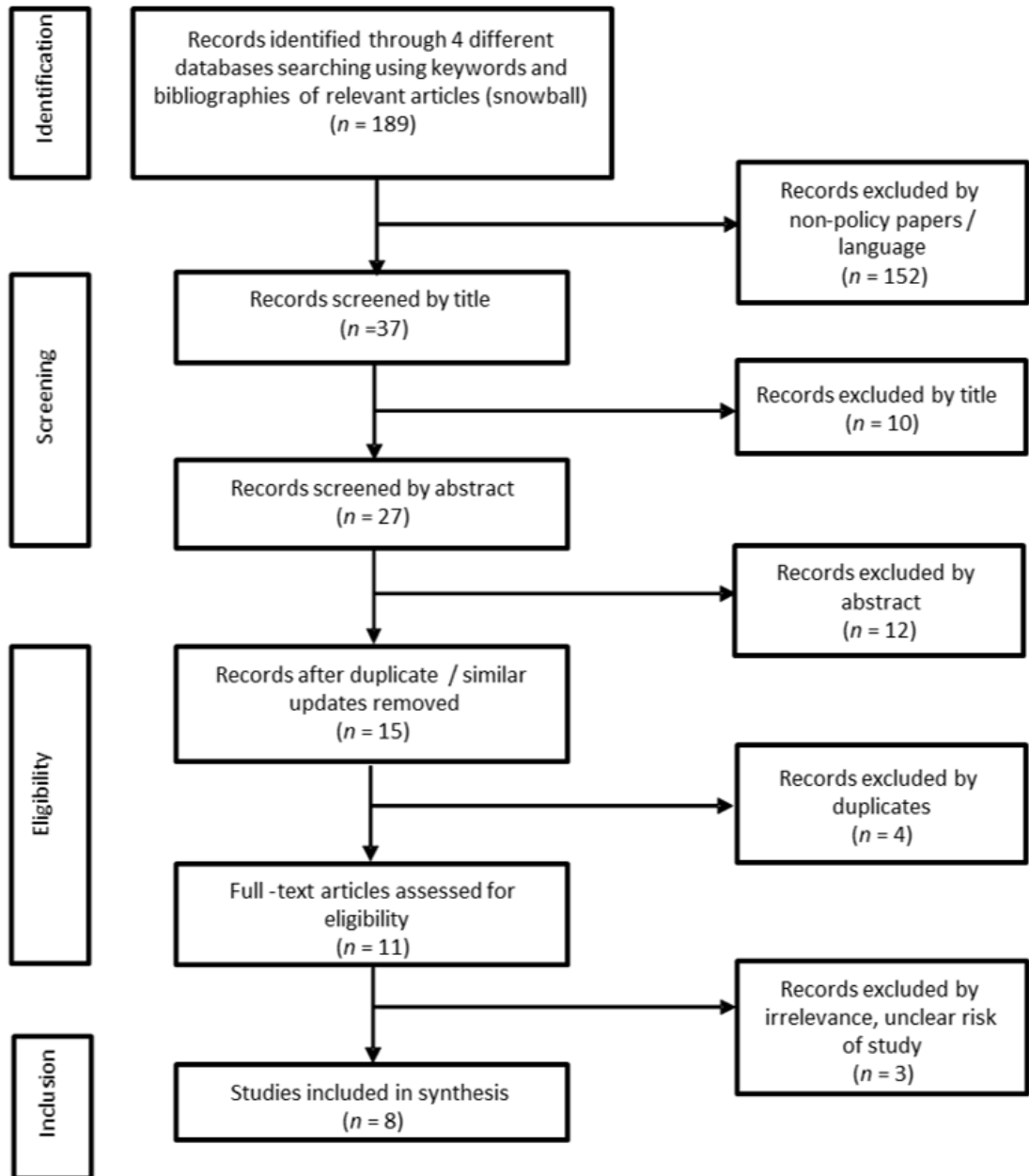
Fig 1 - Workflow of selection process of publications on management of Zika virus infection (2013 - 2018)

screening protocol for pregnant women, blood product management during outbreak, clinical trials on vaccination and on vector control (Table 2). Figure 2 showed the quality rating of the final 8 articles with different risk levels represented by the colour of the circle. Each circle represented a category of bias evaluated for that article.

Domain identification

Four domains were identified from evaluation of the eight publications, namely, vector control, family planning, blood product management, and vaccination development.

Vector control

For effective vector control, Rodriguez-morales *et al* (2016) proposed the use of Geographic Information System (GIS)-based mapping system as Zika virus epidemiological maps to aid public health preparedness and control measure. The overlaying of various maps allowed visualization of correlations among climate of municipality, incidence, presence of vector, number of pregnant women, timing of diagnosis, and availability of diagnostic tool (RT-PCR). Application of GIS is similarly used as a risk mapping tool for Dengue infection in Malaysia (Aziz *et al*, 2012). The use of informative technology enables better monitoring of vector distribution and provides a more meaningful and effective disease monitoring and prevention.

Anders *et al* (2018) described the first field trial of biological control of *Aedes aegypti*, in Yogyakarta City, Indonesia by measuring efficacy of deployment of *Wolbachia* bacteria-mosquitoes to reduce their ability of Zika virus transmission. *Wolbachia*-infected Ae. aegypti are deployed across intervention clusters within a six to nine months period until prevalence in trapped Ae. aegypti reaches 60-80%. The Institute for Medical Research (IMR) Malaysia also has conducted a *Wolbachia*-infected insect project since 2016 and a two-stage release of *Wolbachia*-infected vectors was carried out over a four-week period to achieve higher success rate of infected Ae. aegypti to induce cytoplasmic incompatibility of the vector for Dengue control (Nazni *et al*, 2019), a strategy that can be applied to control Zika infection.

Family planning: pre-pregnancy and antenatal management

Family planning is an important management aspect for Zika infection control because transmission can occur both through intercourse and vertically to offspring (Musso *et al*, 2015). Four articles selected described family planning as a policy for management of Zika infection. For example, Forman *et al* (2017) emphasized the importance of multi-agencies collaboration through a modified PDSA framework for Zika-related family planning in individual with infection risk; and Rao *et al* (2017) proposed a proper algorithm of antenatal Zika virus screening to detect high risk cases. CDC has produced a screening algorithm and health education for

Table 2

Descriptive analysis of eight publications selected for scrutiny of information on successful management of Zika virus infection (2013 – 2018)

Reference	Study design	Sample population	Interventional tool	Domain	Health effect outcome	Public health implication
Rico *et al* (2016)	Random controlled trial	Hospitals and the American Red Cross in Puerto Rico (*n* = 7)	Platelet component production with amotosalen + UV-A pathogen reduction technology (INTERCEPT™ Blood System, Cerus Corp,Concord, CA) to reduce risk of transfusion-transmitted infection during ongoing CHIKV/DENV/ZIKV epidemic	Blood products management	Adequate safe platelet supply during Zika outbreak to reduce risk of blood transmission	An alternate technology to help supplying enough platelets to patients during Zika outbreak during which FDA requests Puerto Rico and certain counties in Florida to cease collecting blood until investigational donor screening test for ZIKV RNA is implemented or until implementation of an approved or investigational pathogen reduction technology.
Rodriguez-Morales *et al* (2016)	Retrospective cohort	La Guajira, Colombia	Used GIS mapping to analyze incidence rate of Zika infection in La Guajira municipalities, Colombia from 2015 to 2016	Vector control	Identified risk area and disease burden	Propose using GIS-based epidemiological maps to allow to integration of preventive and control strategies and public health policies for Zika transmission

Table 2 (cont)

Reference	Study design	Sample population	Interventional tool	Domain	Health effect outcome	Public health implication
Dehlendorf *et al* (2017)	Quasi random controlled trial	Southern states of USA	Integrated Zika-related family planning care through collaboration and communications with multi-agencies	Family planning: pre-pregnancy and antenatal management	Minimized sexual transmission of Zika virus	Integrate family planning into Zika response policy through proactive communication and collaboration
Forman *et al* (2017)	Quasi random controlled trial	Hospital and its network of community health centers for a large and diverse immigrant population (*n* = 1)	Implementation of universal prenatal screening	Family planning: pre-pregnancy and antenatal management	Detection of Zika virus affected pregnancies and management at hospital setting	Use of a modified PDSA cycle framework as emergency preparedness and response strategy to increase prenatal screening rate for pregnant patients at risk of exposure to Zika virus, thereby providing key lessons for emergency preparedness in heterogeneous, safety-net hospital settings
Rao *et al* (2017)	Cohort	Pregnant women with potential Zika virus exposure in a single perinatal referral center (*n* = 185)	Performed antenatal scan to detect possible Zika infection in pregnant women exposed to Zika virus infection during Zika outbreak	Family planning: pre-pregnancy and antenatal management	Early detection of fetal or neonatal infections for prompt management	Identify potential markers for fetal Zika virus infection and correlate with neonate outcome to provide an algorithm for timing and frequency of neonatal screening in pregnancy with potential Zika virus exposure

Table 2 (cont)

Reference	Study design	Sample population	Interventional tool	Domain	Health effect outcome	Public health implication
Anders *et al* (2018)	Random controlled trial	A network of primary care clinics in a single site in Yogyakarta, Indonesia	Deployment of *Wolbachia*-infected vectors to endemic sites	Vector control	Reduced *Aedes* sp vector load	Guide future planning for large scale deployment of *Wolbachia* as cost-effectiveness measure for vector control in Zika endemic area
Gaudinski *et al* (2018)	Random controlled trial	Subjects (*n* = 125): Clinical trial team VRC 319 enrolled participants (*n* = 80); 20/group), VRC 320 enrolled participants (*n* = 45; 15/centers)	Received intramuscular injection of vaccine (4 mg)	Vaccination	Vaccine safety (local and systemic reactogenicity day-7 and day-28 post-vaccination), immunogenicity at week-4 post-last vaccination	Development of Zika vaccine research based on vaccine safety
Lathrop *et al* (2018)	Quasi random controlled trial	Females in Puerto Rico (*n* = 21 and 12)	Implemented LARC method (reversible) to reproductive age women at Zika infection in epidemic region during outbreak	Family planning: pre-pregnancy and antenatal management	Prevented sexual transmission of Zika infection in epidemic region during outbreak by providing contraceptive service for free	Free provision of contraception through provider reimbursements and infrastructure supported by agency to improve effectiveness and coverage of family planning in zika endemic areas

CHIKV: Chikungunya virus; DENV: Dengue virus; FDA: Food and Drug Administration; GIS: geographic information system; LARC: long-acting reversible contraception; PDSA: plan-do-study-act; UV-A: ultraviolet A; ZIKV: Zika virus

Fig 2 - Risk of biases among eight selected publications on management of Zika virus infection (2013- 2018)

Green circle: low risk; Red circle: high risk; Yellow circle: unclear risk

pregnant women and men both symptomatic and asymptomatic of infection (CDC, 2017). The algorithm has been used in Latin America and European Union regions where active circulation of Zika infection exists (Musso, 2015).

Blood product management

The certification of blood product safety is of critical concern, particularly during a Zika outbreak and subsequent endemic period. Determination of safety of blood products received and distribution must be prioritized against

critical need of supply. Rico *et al* (2016) described applying amotosalen and UV-A pathogen reduction (PR) technology to sterilize available platelet components during Zika outbreak in tertiary hospitals in Puerto Rico, successfully reducing risk of transfusion-transmitted infection.

Vaccination

Two vaccine trial teams reported good immunogenicity and vaccine safety, and effective local and systemic reactogenicity post-vaccination (Gaudinski *et al*, 2018). However, vaccine development requires many phases of clinical trials and involves large healthcare expenditure (Graves, 2016). Anti-ZIKV vaccination has yet to prove a correlational protective effect from adverse fetal outcome, and further trials are required to demonstrate vaccine effectiveness (Gaudinski *et al*, 2018).

A global rating of the importance to public health outcome and recommendation of action(s) were assigned to each domain according to guidelines of The Cochrane Collaboration (2014). For Zika disease management, blood product management and vaccination development were rated high in quality and considered of "critical importance" for disease management, and vector control and family planning for Zika-infected individual rated moderate and considered "important" (Table 3).

DISCUSSION

This study employs an evidence-based (health technology) assessment of a pandemic communicable disease using an epidemiological method to propose a health management action that should lead to a revision of policy towards control of Zika infection in Malaysia, which could be applicable to the whole Southeast Asian region.

Vaccine implementation was rated as a "critically important" domain for Zika management. Malaysia is a country which practices compulsory vaccination schedule for all new-born citizens in the country as a public health measure to curb deadly infectious diseases (Ministry of Health Malaysia, 2015). However, vaccine development for Zika virus has not drawn much interest from the public as the local National Flavivirus Surveillance only reported one new case during the previous five years (2016-2020), without any reported Zika virus-related microencephaly and Guillain-Barré Syndrome (Ministry of Health Malaysia, 2019a). Dengavaxia, a vaccine developed for Dengue infection has been used as a model for development of a Zika vaccine (Musso *et al*, 2015; Baud *et al*, 2017). However, Dengavaxia has recently met resistance for recommendation to the public due to safety issue on sero-negative Dengue patient, while efficacy in sero-positive Dengue patients is unclear, as cross-reactivity may occur (WHO, 2018).

Table 3

Overall quality rating according to domain/outcome of eight publications selected for scrutiny of information on successful management of Zika virus infection (2013 - 2018)

Quality criteria (summary of scores from GRADE analysis)	Relative importance	Quality of evidence (one circle per outcome)	Recommendation
Outcome # 1: Vector control			
Anders *et al*, 2018 (+3)	Important	⊕⊕⊕ Moderate	Suggests considering this public health measure in policy
Rodriguez-Morales *et al*, 2016 (-2)			
Outcome # 2: Family planning			
Dehlendorf *et al*, 2017 (-2)	Important	⊕⊕⊕ Moderate	Suggests considering this public health measure in policy
Forman *et al*, 2017 (-3)			
Lathrop *et al*, 2018 (+3)			
Rao *et al*, 2017 (-5)			
Outcome # 3: Blood product management			
Rico *et al*, 2016 (+2)	Critical	⊕⊕⊕⊕ High	Should consider this public health measure in policy
Outcome # 4: Vaccination			
Gaudinski *et al*, 2018 (+2)	Critical	⊕⊕⊕⊕ High	Should consider this public health measure in policy

GRADE: Grading of Recommendations Assessment, Development and Evaluation assessment from Cochrane handbook (Ryan and Hill, 2016)

Challenges in Zika virus vaccine development are (i) need for a more comprehensive information on evolution of epidemiology of Zika virus, (ii) low interest in funding due to mild clinical presentation in ZIKV-infected adults, (iii) growth of anti-vaccine group in the community, (iv) issue of halal production of vaccine, (v) lack of local vaccine manufacturing industry, and (vi) lack of study of local Zika virus infection prevalence (Hombach *et al*, 2016). These challenges discourage consideration of anti-ZIKV vaccination as a crucial

component in health policy for Zika infection. New clinical applications using monoclonal antibodies targeting NS3 (non-structural) region and E (envelope) proteins of Zika virus may assist in Zika infection treatment and thereby allay fears against a Zika vaccine (Lin *et al*, 2018).

Blood product management is another "critically important" domain for Zika infection management. The National Blood Bank has not included Zika infection screening as part of the routine screening tests of blood products in Malaysia (Ministry of Health Malaysia, 2014). Contaminated blood products were reported to transmit Zika infection (Williamson *et al*, 2017). Asymptomatic donors further pose diagnostic challenge to blood screening (Gillian *et al*, 2017). Laboratory capacity building to detect ZIKV infected blood products should include FDA guidelines on safe blood product management and cost-benefit study of additional procurement of nucleic acid tests for blood donor-screening (Stone *et al*, 2017; US FDA, 2018a; US FDA, 2018b). Our study finds blood product/blood-donor screening during a Zika outbreak is a crucially recommended domain of disease management to prevent devastating health trust bankruptcy owing to contaminated blood transmission to a vast population. However, the country must first establish seroprevalence of autochthonous Zika transmission for blood donor screening, as ZIKV RNA detection using the costly

RT-qPCR method is low (0.16%) in absence of an epidemic (which rises to 3%) (Magnus *et al*, 2018). Rico *et al* (2016) described treating platelets with amotosalen combined with UV-A, a pathogen reduction technique, is an efficient management procedure to curb possible shortage of blood products during a Zika virus outbreak.

Vector control was rated as an "important" domain by disease management policy/ guideline articles on Zika infection management, but vector requires meticulous and sustainable effort, as Zika virus has been isolated from 19 different vector species, most predominant being Ae. aegypti and Ae. albopictus (Muktar *et al*, 2016). Vector control efforts in urban settlement is handicapped by unintegrated town planning and water shortage (WHO, 2012; Alphey *et al*, 2013). Absence of local water supply in Selangor state has led to a habit of storing water, creating potential breeding sites of mosquitoes (Zulzaha, 2015) and irresponsible construction contractors often leave behind open water receptacles (Zhaki *et al*, 2020). Long working hours of urban dwellers leave little time for effective search and destroy of vector breeding sites (Manogaran *et al*, 2017). These factors have made Selangor state with the highest prevalence of dengue fever, a proxy of Zika infection (Ahmad *et al*, 2018). Urbanization of rural areas increases prevalence of both infectious and non-communicable diseases (Wong *et al*, 2018), a condition worsen by a low

level of environmental awareness (Mei *et al*, 2016). Integrated vector management involving multi-stakeholders is the determinant of success (WHO, 2012).

Family planning receives much research attention, attested by 50% of the articles selected in our study, owing to the health and mental burden of families with ZIKV-associated microcephaly in newborns from infected mothers (WHO, 2016). Malaysia does not incorporate Zika screening in routine antenatal check-up based on initial announcement that Zika is an imported infection (Ministry of Health Malaysia, n.d.). However, local transmission was accepted when a case was reported in an infected navy officer in Perak state who had prior history of jungle trekking in the local forest (Ministry of Health Malaysia, 2019), confirming the occurrence of sylvatic to urban cycle of Zika transmission, previously reported in primates (Woon *et al*, 2019). Updated guidelines for Zika screening released in 2018 only recommended antenatal screening for women returning from high-risk countries (excluding local travel) (Ministry of Health Malaysia, 2019b). The guideline was based on current reported incidence in the country, which probably is under reported due to inclusion of non-pertinent targets in the surveillance (Ministry of Health Malaysia, 2016). Plan-do-study-act cycle is therefore important to improve disease management workflow through continuous evaluation and monitoring.

Although Malaysia provides free antenatal care and family planning to all citizens (Ministry of Health Malaysia, n.d.), multi-agency involvement in communication on risks of sexual route of ZIKV transmission would be more sustainable as community participation is higher (Parks and Lloyd, 2004).

In addition, timing and mode of family planning are essential factors to ensure maximum effectiveness of protection towards ZIKV vertical transmission, while not disrupting a population fertility rate (CDC, 2016). Pomar *et al* (2018) reported 21% of severe complications and 14% fetal lost in Zika positive pregnancies in French Guiana, and termination of pregnancy for Zika-related microencephaly conception is practiced in Latin America to reduce psychological stress of the family and to reduce neonatal care cost. However, termination of pregnancy in an Islamic country is a controversial option, antenatal Zika virus screening for patients just returned from Zika endemic countries should be included into a management workflow. Patients with confirmed Zika-positive status should be referred for proper family counselling (CDC, 2017). Currently, there is no implementation of antenatal ultrasound scans for microencephaly screening for mothers with Zika infection in Malaysia. Timing of antenatal ultrasound screening for Zika-related microencephaly is suggested to be offered after 20 weeks of gestation or

approaching the third trimester (Ahmad *et al*, 2016). Once microencephaly is detected, anti-ZIKV IgM/IgG screening should be performed and mothers referred for specialist care.

GRADE assessment is gaining popularity as it enables comprehensive and systematic review of a disease, health technology and/or health policy evaluation (Zähringer *et al*, 2020). Going forward, serology of Zika infection in Malaysia should be increased to establish benchmark of the four suggested disease prevention domains, as seroprevalence of Zika infection in Malaysia is most likely under-reported, similar to other Southeast Asian countries (Perng *et al*, 2019).

The study noted a paucity of publications solely devoted to policy for Zika virus infection, probably owing to variations in policy content among different governments and country regulators' interests, which depend on government structure and funding allocation, disease burden and public health capacity of each country. Adoption of guidelines for Zika treatment and control depend on national health authorities and disease burden in the country/region.

In conclusion, the study identifies four domains essential for Zika disease management, namely, vaccination, blood product management, vector control and family planning. Evidence-based public health policies on Zika management will facilitate the Ministry of Health Malaysia in prioritizing domains important to disease prevention and control pertinent to the local situation, leading to efficient execution of disease management programs and workflow to better prepare public awareness of Zika infection that has garnered international concern owing to the Asian origin of the virus.

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CONFLICTS OF INTEREST DISCLOSURE

The authors declare no conflicts of interest.

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