ZIKA
STRATEGIC RESPONSE PLAN

REVISED FOR JULY 2016 – DECEMBER 2017

World Health Organization

June 2016

Photo: PAHO/Harold Ruiz

ABOUT THIS STRATEGIC RESPONSE PLAN

Zika virus and its complications such as microcephly and Guillain-Barré syndrome represent a new type of public health threat with long-term consequences for families, communities and countries.

The *Zika Strategic Response Plan, Revised for July 2016 – December 2017*, updates the previous *Strategic Response Framework and Joint Operations Plan, January – June 2016*, to guide the continuing international response to Zika virus infection, its complications and consequences. The plan provides the basis for coordination and collaboration among WHO and its partners so that countries' preparedness and response capacities are supported to the fullest extent possible.

The *Zika Strategic Response Plan, Revised for July 2016 – December 2017* focuses on:

- Preventing and managing medical complications caused by Zika virus infection by targeting pregnant women, their partners, their households and their communities and expanding health systems' capacities for that purpose.
- Integrated mosquito management, sexual and reproductive health counselling as well as health education and care within the social and legal contexts of each country.

Zika Strategic Response Plan
16 June 2016
WHO/ZIKV/SRF/16.3

TABLE OF CONTENTS

FOREWORD BY

THE DIRECTOR- GENERAL

The Zika virus outbreak in the Americas shows how a disease that had not caused an outbreak for six decades can become a global health emergency. In 2015, suspected congenital malformations and other neurological complications were detected in the Americas and linked to Zika virus. In an interconnected world characterized by profound mobility, Zika has spread dramatically across central and southern America and more recently to other regions, including Asia and Africa. Its risk profile has changed from a mild threat to one with serious consequences. There is now scientific consensus that Zika virus is a cause of microcephaly and Guillain-Barré syndrome. Several factors have combined to make this situation one that requires a collaborative and concerted global response, including:

- the potential for further international spread given the wide distribution of competent vectors,
- the lack of population immunity, which allows the disease to spread quickly,
- the absence of vaccines, specific treatments and rapid diagnostic tests, and
- inequalities in access to sanitation, information and health services in affected areas.

Since the publication of the first Zika Strategic Response Plan in February this year, much has been learned about Zika virus infection, how it spreads, the consequences of infection**,** and priorities for its control. Experts believe that if the virus is capable of causing such severe abnormalities as microcephaly, it is likely to cause additional neurological problems that will become apparent as children develop. Mosquito control efforts alone are unlikely to provide the short-term solution to prevent the proliferation of this virus, while vaccination development could take at least 36 months.

This Zika virus strain and its complications represent a new type of public health threat which requires a unique and integrated strategy that places support for women and girls of child-bearing age at its core. The spread of Zika virus will have long-term health consequences for families, communities, and countries whose health systems will be challenged to care for children born with these complications for years to come.

This revised Strategic Response Plan includes a greater focus on preventing and managing the medical complications caused by Zika virus infection and expanding health systems' capacities for that purpose. Risk communications targeting pregnant women, their partners, their households and their communities will be central to prevention efforts to ensure they have the information they need to protect themselves. Other elements of the plan include integrated vector management, sexual and reproductive health counselling and services, health education and care within the social and legal contexts of each country.

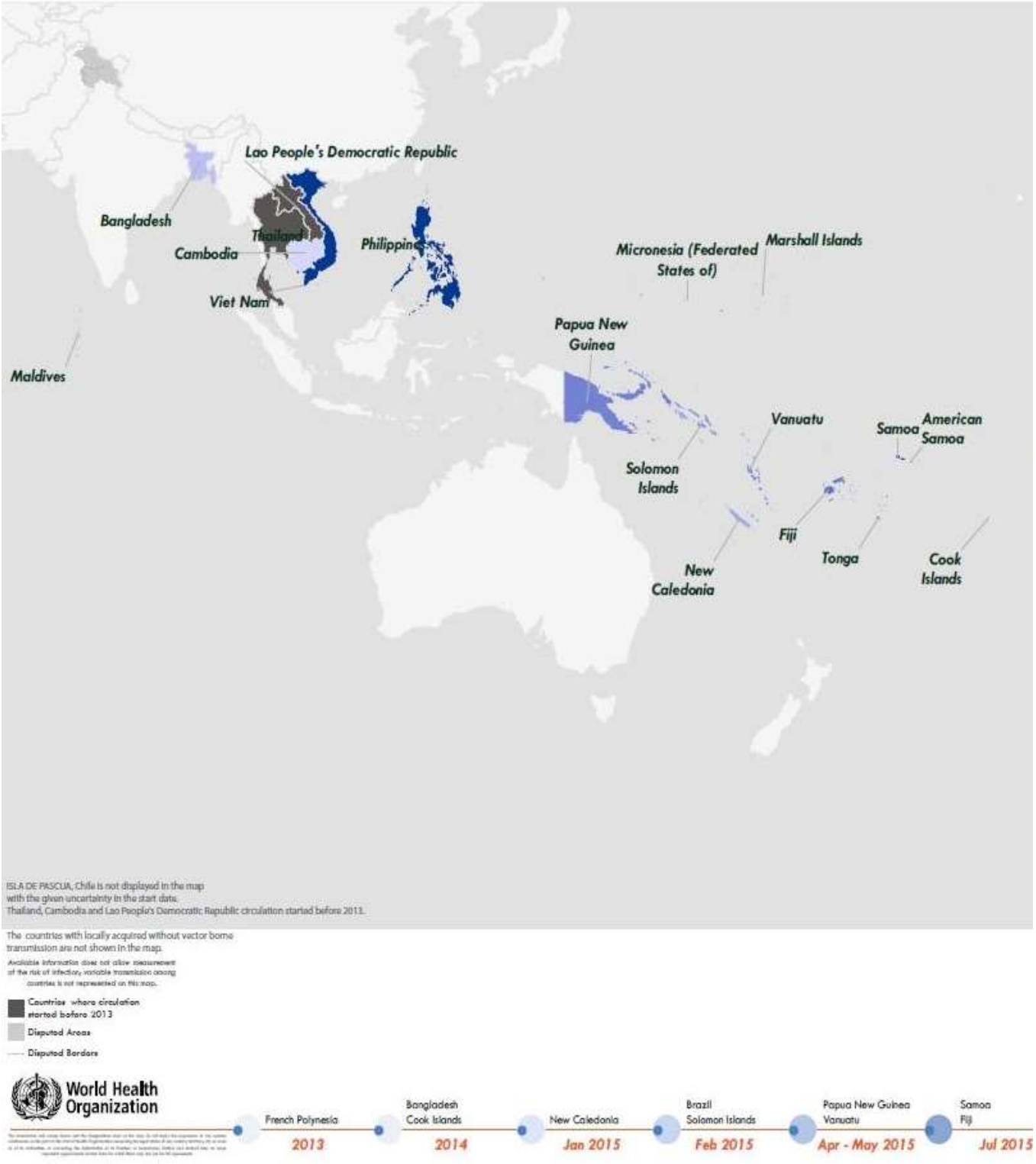
Significant funding gaps existed for the full implementation of the Strategic Response Plan published in February 2016, for both WHO and its partners. Coherent funding mechanisms are essential for successful implementation of this revised Strategic Response Plan and can catalyse national financing for multi-level responses to Zika. In May 2016, the United Nations Secretary-General established a Multi-Partner Trust Fund for this purpose.

Few health threats are local anymore, and few health threats can be managed by the health sector acting alone. I would like to take this opportunity to recognise and thank all the partners involved for their collaboration and considerable efforts in support of this revised global Strategic Response Plan.

Dr. Margaret Chan
Director-General, WHO

ZIKA VIRUS

Fig. 1. Countries, territories and areas showing the distribution of Zika virus, 2013-2016



Oct -Nov 2015	Dec 2015	Jan 2016	Feb 2016	Mar 2016	Apr - May 2016
El Salvador	French Guiana	Bolivia (Plurinational State of)	Ecuador	Peru	Micronesia (Federated States of)	Argentina
Guatemala	Honduras	United States Virgin Islands	Guyana	Marshall Islands	Vietnam	Grenada
Mexico	Martinique	Dominican Republic	Jamaica	Saint Vincent and The Grenadines	Cuba	Saint Barthelemy
Paraguay	Panama	Costa Rica	Curaçao	Sint Maarten	Philippines	Belize
Suriname	Puerto Rico	Guadeloupe	American Samoa	Trinidad and Tobago		Saint Lucia
Venezuela (Bolivarian Republic of)		Saint Martin	Haiti	Aruba		
Colombia		Nicaragua	Tonga	BONAIRE, Netherlands		
Cabo Verde		Barbados				
		Maldives				

OVERVIEW OF THE SITUATION

This *Zika Strategic Response Plan - Revised for July 2016 to December 2017*, comprises of the *Strategic Response Framework* and *Joint Operations Plan*, and has been developed to guide the international response and joint actions against Zika virus infection, its complications and consequences. It provides the basis for coordination and collaboration with partners so that countries' preparedness and response capacities are supported to the fullest extent possible. The document will be updated regularly.

BACKGROUND

Zika virus is mostly transmitted through the bite of an infected mosquito, primarily *Aedes aegypti* – the same vector that transmits chikungunya, dengue and yellow fever. *Aedes albopictus* can also transmit the disease and further studies are in progress to better understand its role in the transmission of Zika virus. This virus may also be transmitted through sexual intercourse. Zika virus disease has a similar epidemiology, clinical presentation and transmission cycle in cities and towns as chikungunya and dengue, although the illness is generally milder.

Symptoms of Zika virus disease include mild fever, skin rash, conjunctivitis, muscle and joint pain which normally last for 2 to 7 days. There is no specific treatment but symptoms are normally mild and can be treated with common fever medicines, rest and drinking plenty of fluids.

Zika virus was first identified in 1947 in a monkey in the Zika forest of Uganda and it was first identified in humans in 1952 in Uganda and the United Republic of Tanzania. Over the following half century, Zika virus has been causing sporadic disease in Africa and Asia. Outbreaks were reported for the first time from the Pacific in 2007 and 2013 in Yap Island (Federated States of Micronesia) and French Polynesia, respectively. The virus subsequently spread to other Pacific islands, including New Caledonia, Cook Islands, Easter Island (Chile), Fiji, Samoa, Solomon Islands and Vanuatu. The geographical range of Zika virus has been steadily increasing ever since (see Fig. 1).

The current Zika virus outbreak and its association with an increase in microcephaly, other congenital malformations and Guillain-Barré syndrome (GBS), have caused increasing alarm in countries across the world, particularly in the Americas. Brazil announced a national public health emergency in November 2015.

An International Health Regulations (IHR, 2005) Emergency Committee met on 1 February 2016, and WHO declared the recent clusters of microcephaly and other neurological disorders in Brazil (following a similar cluster in French Polynesia in 2014) a Public Health Emergency of International Concern. In the absence of another explanation for the clusters of microcephaly and other neurological disorders, the IHR Emergency Committee recommended enhanced surveillance and research and aggressive measures to reduce infection with Zika virus, particularly amongst pregnant women and women of child-bearing age.

The third meeting of the Emergency Committee (EC) convened by the Director-General under the International Health Regulations regarding microcephaly, other neurological disorders and Zika virus, held on 14 June 2016, concurred with the international scientific consensus, reached since the Committee last met, that Zika virus is a cause of microcephaly and GBS, and, consequently, that Zika virus infection and its associated congenital and other neurological disorders is a Public Health Emergency of International Concern. The Committee restated the advice it provided to the Director-General in its 2nd meeting in the areas of public health research on microcephaly, other neurological disorders and Zika virus, surveillance, vector control, risk communications, clinical care, travel measures, and research and product development.

The Committee reaffirmed its previous advice that there should be no general restrictions on travel and trade with countries, areas and/or territories with Zika virus transmission.

Based on this advice the Director-General declared the continuation of the Public Health Emergency of International Concern. The Director-General reissued the Temporary Recommendations from the 2nd meeting of the

Committee, endorsed the additional advice from the Committee's 3rd meeting, and issued them as Temporary Recommendations under the IHR (2005).

ZIKA VIRUS TRANSMISSION

In February 2015, Brazil detected cases of fever and rash that were laboratory-confirmed to be Zika virus in May 2015. In December 2015, there were 56 318 suspected cases of Zika virus disease in 29 states in Brazil.

As of 15 June 2016, 60 countries and territories have reported mosquito-borne transmission, of which 46 countries are experiencing the first outbreak of Zika virus since 2015, with no previous evidence of circulation (see Fig. 2 on the next page).

Non vector-borne Zika virus transmission, most probably via a sexual route, has been documented in 10 countries: Argentina, Canada, Chile, France, Germany, Italy, New Zealand, Peru, Portugal and the United States of America. It is assumed that sexual transmission is ongoing in countries which report local transmission by mosquitoes.

INCREASE IN MICROCEPHALY, OTHER NERVOUS SYSTEM MALFORMATIONS AND PREGNANCY-RELATED COMPLICATIONS

A recently published modelling study conducted in French Polynesia, where a documented outbreak of Zika virus infection occurred in 2013, retrospectively estimated the risk to be 95 cases of microcephaly per 10 000 women infected during the first trimester.[1] According to another study, 29% of Zika virus-positive pregnant women were found to have fetal abnormalities on ultrasonography.[2] There is a wide range of incidents of complications associated with Zika infection during pregnancy which is as yet not confirmed.

As of 15 June 2016, microcephaly and other central nervous system malformations potentially associated with Zika virus infection or suggestive of congenital infection have been reported by 12 countries or territories (Brazil, Cabo Verde, Colombia, El Salvador, French Polynesia, Marshall Islands, Martinique, Panama, Puerto Rico, Slovenia, Spain, and United States of America). Three of those countries, namely, Slovenia, Spain and United States of America, reported microcephaly borne from mothers with travel history to countries with ongoing Zika virus transmission.

Placental insufficiency, intra-uterine growth restriction, intra-uterine fetal death and spontaneous abortion have been reported as potential outcomes of Zika virus infection. More neurological complications are still being discovered as the nature and extent of Congenital Zika Syndrome is not yet defined.

INCREASE IN GUILLAIN-BARRÉ SYNDROME, OTHER NEUROLOGICAL SYNDROMES AND NON-NEUROLOGICAL COMPLICATIONS

Between October 2013 and April 2014, French Polynesia experienced the first Zika virus outbreak ever recorded in the territory. During the outbreak, 42 patients were admitted to a hospital with GBS. This represents a 20-fold increase in the number of people with GBS in French Polynesia compared with the previous four years. A published a case-control study[3] of these data showed a strong association between Zika infection and GBS. All 42 people with GBS were also confirmed for Zika virus infection. Based on a 66% attack rate[4] of Zika virus infection in the general population, judged from a survey of blood serum, the risk of GBS was estimated to be 2.4 per 10 000 Zika virus infections.[5]

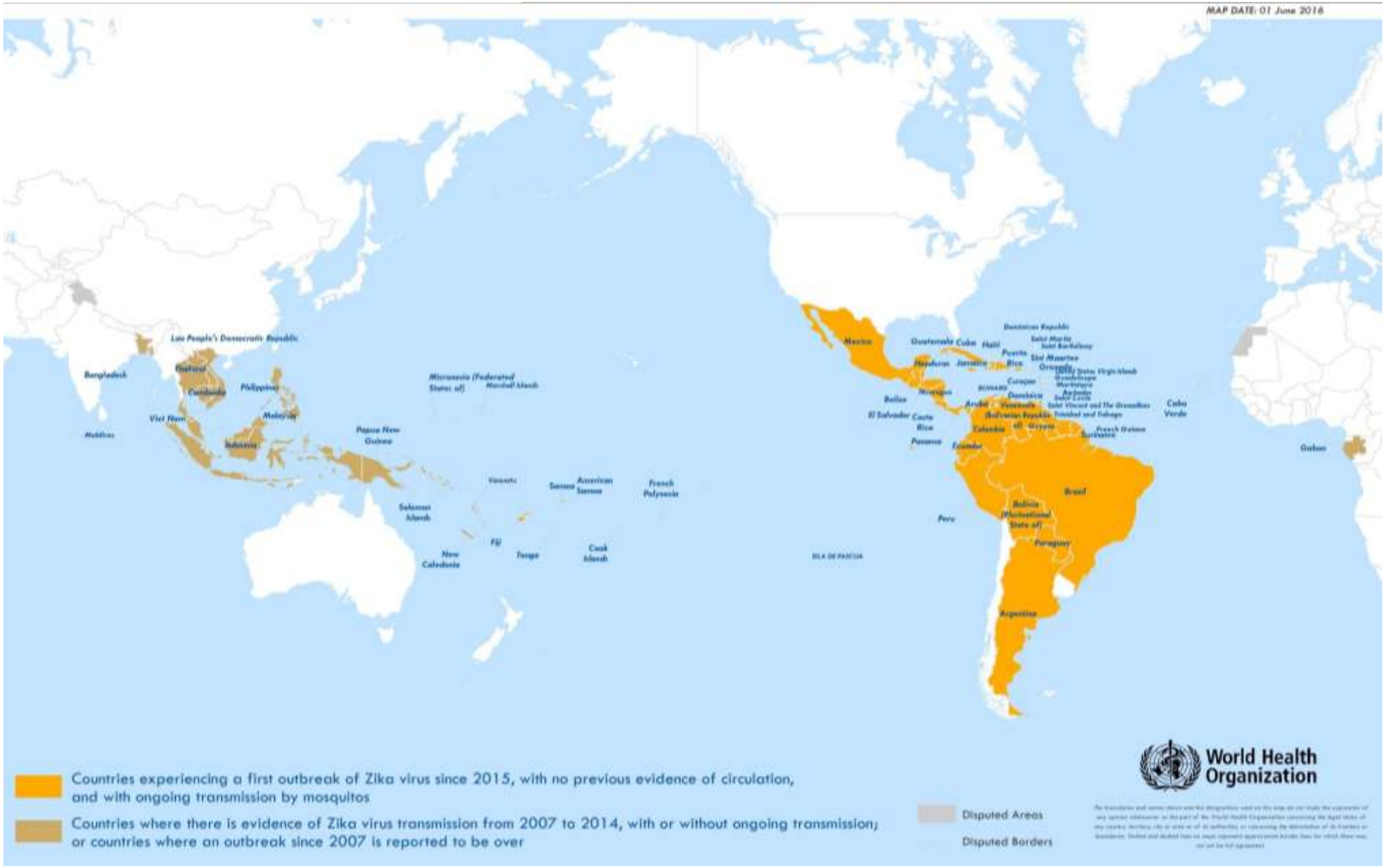
As of 15 June 2016, 13 countries and territories worldwide have reported an increase in the number of people with GBS and/or laboratory confirmation of Zika virus infection among people with GBS. These countries/territories are: Brazil, Colombia, Dominican Republic, El Salvador, French Guiana, French Polynesia, Haiti, Honduras, Martinique, Panama, Puerto Rico, Suriname and Venezuela.

There were also reports of other neurological disorders associated with Zika virus infection: an acute myelitis case in a 15-year old girl from Guadeloupe and a meningoencephalitis case in an 81-year old man.[6,7] Additionally, non-neurological complications have also been reported, including thrombocytopenia.[8]

[1] Johansson, Michael A. et al. "Zika And The Risk Of Microcephaly". New England Journal of Medicine (2016). doi: 10.1056/nejmp1605367.
[2] Brasil, Patrícia et al. "Zika Virus Infection In Pregnant Women In Rio De Janeiro — Preliminary Report". *New England Journal of Medicine* (2016): n. pag.

[3] A study that compares patients who have a disease or outcome of interest (cases) with patients who do not have the disease or outcome (controls).
[4] The measure of frequency of disease, or speed of spread, in an at-risk population.
[5] Cao-Lormeau, Van-Mai et al. "Guillain-Barré Syndrome Outbreak Associated With Zika Virus Infection In French Polynesia: A Case-Control Study". The Lancet 387.10027 (2016): 1531-1539.
[6] Mécharles, Sylvie et al. "Acute Myelitis Due To Zika Virus Infection". The Lancet 387.10026 (2016): 1481.
[7] Carteaux, Guillaume et al. "Zika Virus Associated With Meningoencephalitis". New England Journal of Medicine 374.16 (2016): 1595-1596.
[8] Sarmiento-Ospina, Andrea et al. "Zika Virus Associated Deaths In Colombia". The Lancet Infectious Diseases 16.5 (2016): 523-524.

Fig. 2. Global status of Zika virus



FUTURE PROJECTION AND RISK ASSESSMENT

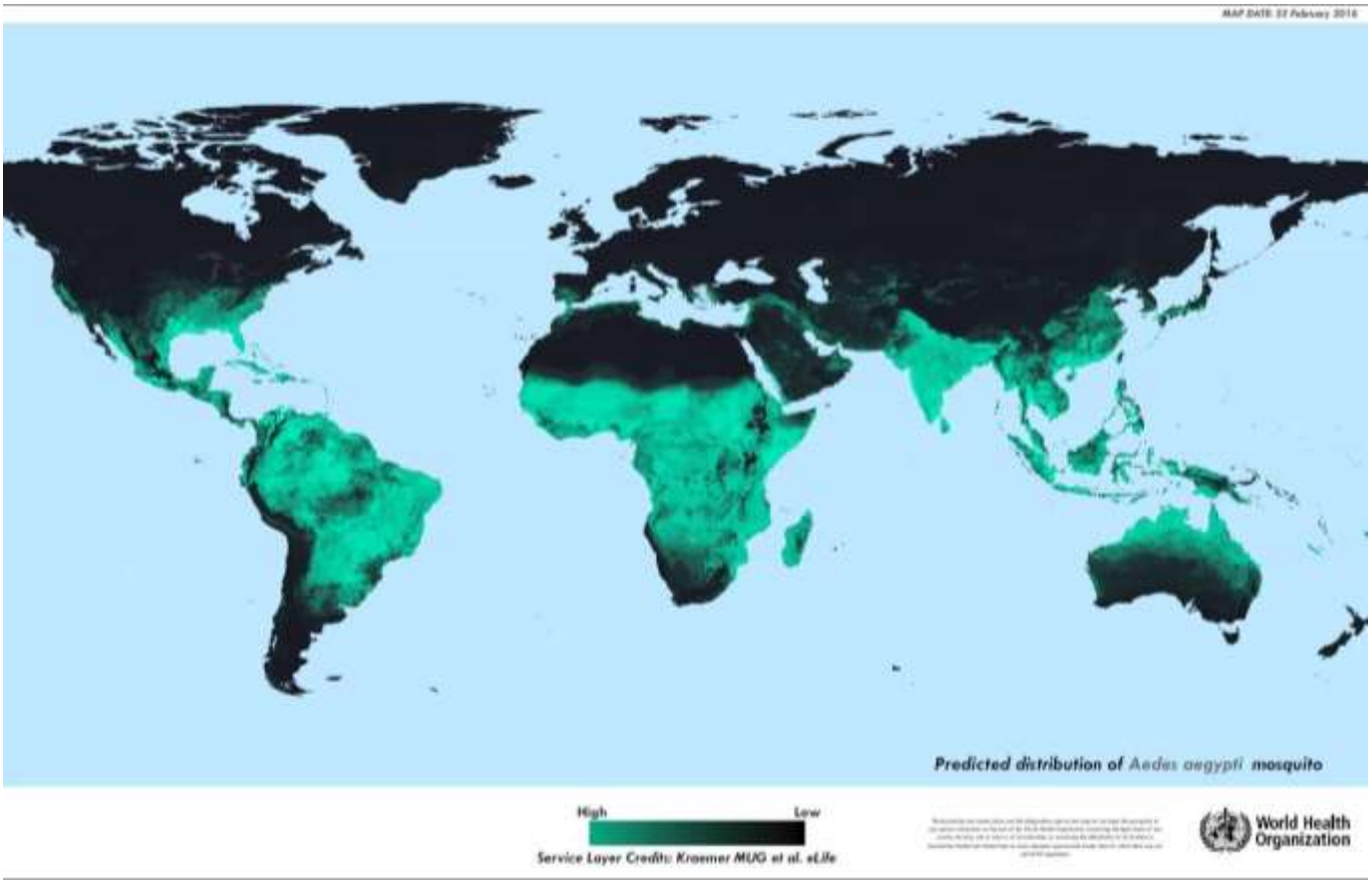
Vigilance needs to remain high. Zika virus continues to spread geographically to areas where competent vectors are present (see Fig. 3).

Major epidemics of Zika virus disease may occur globally since environments where mosquitoes can live and breed are increasing due to recent trends including climate change, rapid urbanization and globalization. It is anticipated that Zika virus will continue to spread and can reach all countries and territories where *Aedes aegypti* mosquitoes are found. Other *Aedes* mosquitoes are believed to be competent vectors for Zika virus and to have a much farther geographical reach. For example, *Aedes albopictus* is found in temperate climates. Furthermore, the Zika outbreak is likely to have a more negative impact on poor and marginalized communities, not only due to poor living conditions and infrastructure (e.g. breeding sites in stagnant water), but also insufficient access to information, and resources for prevention and care.

On 18 May 2006, a risk assessment by WHO Regional Office for Europe (EURO) estimated that the majority of countries in Europe had either low (22 countries) or moderate (18 countries) likelihood of transmission, if the virus is imported during 2016.[9] Three geographical areas with established *Aedes aegypti* populations were categorized as having a high likelihood for transmission: Madeira Island, and the Black Sea coastal areas of both Georgia and the Russian Federation. Other WHO regional offices have been conducting and are updating their risk assessments on a regular basis.

In May 2016, studies confirmed that the Zika virus that is currently circulating in Cabo Verde likely originated from Brazil. Zika virus has long been present on the African continent, but this is the first time that a Zika strain responsible for outbreaks linked to neurological disorders and microcephaly has been detected in an African country. Accordingly, risk assessments and preparedness activities are required.

Fig. 3. Predicted distribution of the *Aedes aegypti* mosquito



[9] http://www.euro.who.int/en/media-centre/sections/press-releases/2016/05/zika-virus-expected-to-spread-in-europe-in-late-spring-and-summer-overall-risk-low-to-moderate

These strains have been introduced by travellers to other countries inhabited by mosquito vectors, in Asia for example, but no local outbreaks of neurological disease linked to Zika virus have been reported so far. As these outbreaks occurred more recently, such neurological cases would not be expected until later in the year.

STATUS OF THE RESPONSE

The Pan American Health Organization (PAHO) and WHO's operational response began long before the declaration of the Zika outbreak as a Public Health Emergency of International Concern and has accelerated since. On 14 February 2016, WHO launched a global Strategic Response Framework and Joint Operations Plan to guide international coordination.

In February 2016, 23 partners were identified as working with WHO to implement the Strategic Response Framework. This number has now increased to over 60. UNICEF, for example, is working in 21 countries at both community and policy level to control the spread of Zika virus and mitigate its impact by safely engaging communities and children in mosquito control, provide care and support for affected children and families, and drive the much needed development of easy-to-use tools to diagnose infection and vaccines to prevent Zika virus disease.

The global response to Zika is coordinated from WHO headquarters in Geneva. The agency has activated an Incident Management System (IMS) in its headquarters and regional offices as part of its new Health Emergencies Programme. The system enables a dedicated incident manager based at WHO headquarters to draw on expertise and resources from across the entire Organization.

Since February 2016, the United Nations Deputy Secretary-General has convened monthly coordination meetings to provide a forum at the principals' level for UN system coordination and information-sharing. At the working level, WHO has also been holding regular meetings with partners of the Inter-Agency Standing Committee to disseminate information, seek input from partners and create a transparent approach to the response.

Governments of Colombia, Dominican Republic, Ecuador, El Salvador and Jamaica have all advised women to postpone becoming pregnant until more is known about the virus and its complications. However, it is important to note that this is not necessarily an option for women who live in contexts where the majority of pregnancies are unplanned, access to contraceptives and sexual and reproductive health services are limited, and sexual violence is prevalent. The US Centers for Disease Control and Prevention (CDC) has issued a level 2 travel warning, which includes recommendations that pregnant women consider postponing travel to any area with ongoing Zika virus transmission.

An effective public health response needs to be consistent with human rights, including the rights of men and women to be informed of, and have access to, safe, effective, affordable and acceptable methods of contraception, without discrimination. These should include emergency contraception, maternal healthcare and safe abortion services (where it is legal) and post-abortion services.

WHO has established a Zika response portal on its website. This is a central point of reference for partners that shows in real time who is doing what, where, and when, at the global, regional and national levels. More than 500 partner activities and associated budgets are now being tracked through the tool. This helps to ensure that efforts are directed where they are most needed, duplications and deficits are minimised, and the cost-effectiveness of activities is boosted accordingly.

In addition to expert fact-finding and advisory missions to affected countries, including to Cabo Verde, WHO, in collaboration with other agencies and following meetings and consultations with more than 250 experts, has published and/or updated 16 guidance documents. The guidance covers all aspects of the response and is available in several languages.[10] Additionally, other partners have led interagency collaboration on communications materials, including a guidance and resource package for country offices for Zika coordination, planning, key messages and actions.[11]

Based on the recommendations from the IHR Emergency Committee meeting on 14 June 2016, WHO has issued no general restrictions on travel or trade with countries, areas and/or territories with Zika virus transmission. However, WHO is advising pregnant women not to travel to areas with ongoing Zika virus oubreaks, and for all returning travellers to practice safer sex, including through the correct and consistent use of condoms, or abstain from sex for at least 8 weeks. If men experience symptoms (rash, fever, arthralgia, myalgia or conjunctivitis) then they should adopt safer sexual practices or consider abstaining for at least 6 months. This advice is based on the increased risk of microcephaly and other congenital malformations in babies born to pregnant women infected with Zika virus.

FUNDING REQUIREMENTS

The support already received from donors has been crucial to enable a rapid and effective Zika response during the first months of the response, and WHO and partners are grateful to all donors who have contributed so far. However, funding needs have been largely unmet, both for WHO and for its partners. For instance, WHO and PAHO required US$ 25 million to fund its emergency response to

[10] http://www.who.int/csr/resources/publications/zika/en/
[11] http://www.who.int/csr/resources/publications/zika/community-engagement/en/

Zika from January to June 2016. From there onwards, WHO has received just over US$ 4 million.

As part of the Zika response from July 2016 to December 2017, WHO and its partners have immediate priority areas for funding, which include preventing and managing the medical complications caused by Zika virus infection, expanding health systems' capacities, sexual and reproductive health, risk communication targeting pregnant women, and integrated vector management.

As the Zika response moves from an acute emergency setting to a longer-term programmatic approach, funding sources will also need to shift from emergency to longer-term national and international development and technical assistance programmes, especially in the areas of maternal and child care and sexual reproductive health.

Therefore, it would be useful to assess the short, medium and long term economic impact of Zika and to develop an investment case covering all areas of the strategy – in particular, for the care and support of children and families affected. This information should be used to advocate for sustained funding from international and national sources.

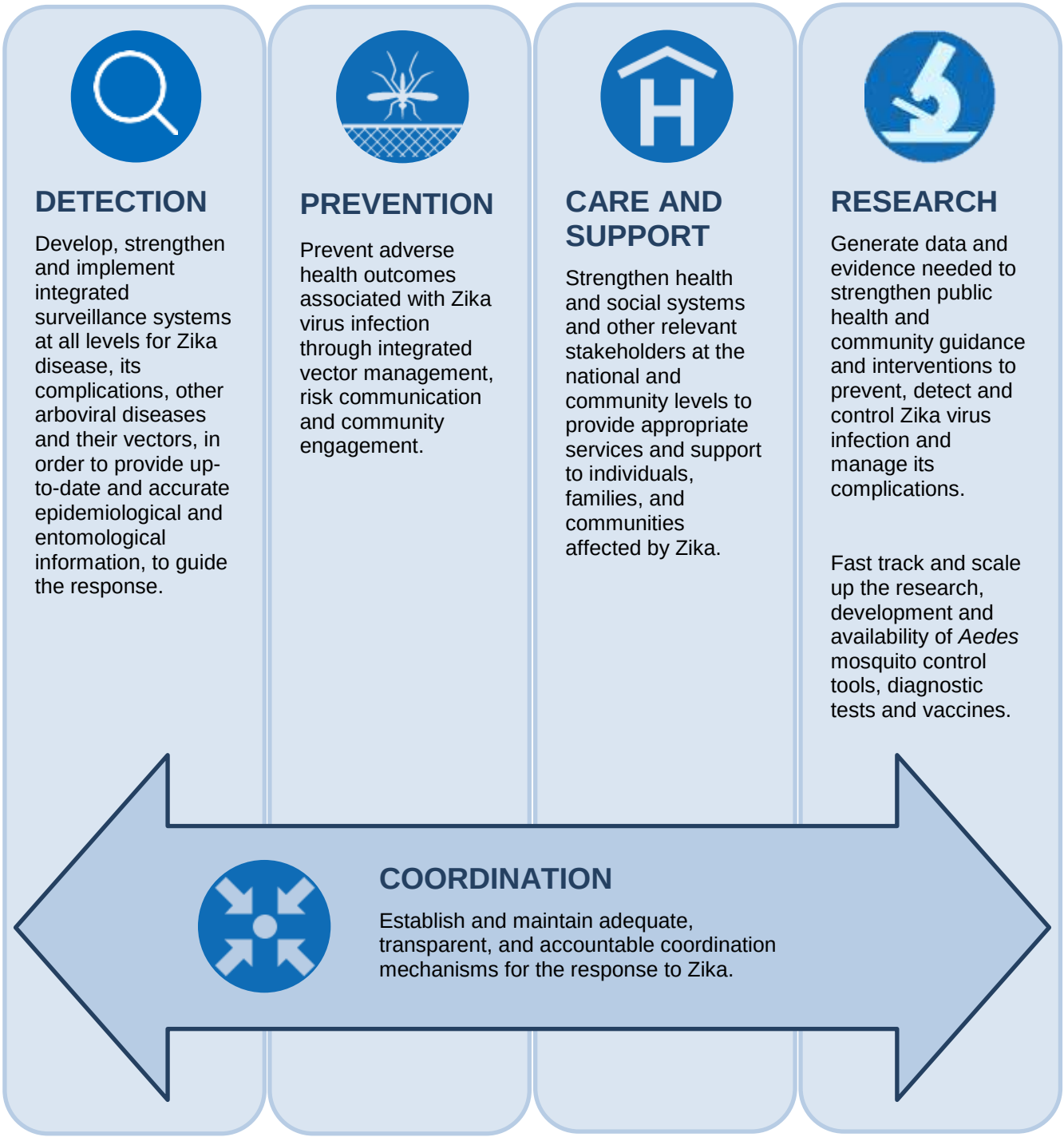
Coherent fundraising mechanisms are essential which can complement and catalyse national financing for the multi-levelled response to Zika. In May 2016, the United Nations Secretary-General established a Zika Multi-Partner Trust Fund (MPTF) for this purpose. The aim of the Zika MPTF is to generate, manage and ensure the effective use of resources necessary to achieve the goal and strategic objectives of the Zika Strategic Response Framework as outlined below. The Zika MPTF is a critical part of the financing for the overall Zika response. It aims to provide:

- a mechanism for a coordinated, flexible and rapid UN response, through a common financing instrument, which supplements the financing mechanisms of the UN agencies, funds and programmes;
- a cross - UN perspective, which allows identification of the areas of greatest need and highest priority for funding and which facilitates a coherent UN System contribution to the overall Zika response;
- a proven, accountable, transparent and cost-effective financial instrument for the mobilization of funding from Member States, regional legislative bodies, inter-governmental and non-governmental organizations, businesses and individuals; and
- a results-based management system to enable monitoring of the impact of the Fund's contribution to the Zika response.

STRATEGIC

OBJECTIVES

The overarching goal of this strategy is to support national governments and communities to prevent and manage the complications and mitigate the socio-economic consequences of Zika virus infection.



The revised Zika Strategic Response Framework reflects an approach that addresses the social, economic and environmental determinants of health and incorporates a human rights, equity and gender equality perspective.

This framework has been informed by a number of developments since February 2016. More organizations and countries are now involved in the response, from 23 to over 60. Yet, activities proposed by WHO and its partners have been underfunded to date, and without sufficient funding the response is likely not to succeed.

Knowledge has evolved about Zika virus infection and its complications. The vast majority of infections go undetected. Some sources report that four out of five people with Zika virus infection do not develop symptoms. However, there is now scientific consensus that Zika virus is a cause of microcephaly and Guillain-Barré syndrome, and links to other neurological complications are being investigated. Furthermore, mounting increasing evidence has shown that sexual transmission of Zika virus is possible and more common than previously assumed.

We have a better understanding of which components of the response have and have not been effective and why. For example, mosquito control will continue to be an important component of the response but more work is needed to identify and overcome the limitations of mosquito control to reduce transmission and for personal protection, such as insecticide resistance and the barriers to comprehensive and sustained implementation.

Furthermore, in anticipation of the further spread of the virus and its broadening impact, the Strategic Response Framework will also support analysis and preparedness activities in countries that do not yet report local transmission of Zika virus.

TARGET POPULATIONS

The revised Zika Strategic Response Framework focuses on these target populations:

- pregnant women and women and girls of childbearing age, particularly in areas where Zika virus is circulating;
- partners of pregnant women and women and girls of childbearing age;
- babies and children with complications from Zika virus infection;
- people with Guillain–Barré syndrome and other neurological complications;
- families and communities affected or at risk; and
- travellers going to and returning from Zika affected areas.

STAKEHOLDERS

In areas with ongoing Zika transmission:

- policy-makers and other public figures at national, state and local levels;
- healthcare (doctors, nurses, etc.) and social system workers (community health workers, etc.);
- staff from other public services critical for prevention (environmental agencies, education, interior, etc.) or care and support (social services, social protection, education, etc.);
- all parties involved in integrated vector management
- civil society organizations such as religious groups, village groups, nongovernmental organizations, businesses and public and private institutions; and
- local and international organizations involved in reproductive health and family planning services.

In areas without ongoing Zika transmission:

- national policy-makers;
- healthcare and social system workers;
- travel and health authorities;
- travellers; and
- the air, shipping and tourism industries.

And, social and news media in all areas.

RESPONSE

STRATEGY

To achieve the objectives, WHO and partners have devised the following strategies.

DETECTION

Develop, strengthen and implement integrated surveillance systems at all levels for Zika disease, its complications, other arboviral diseases and their vectors, in order to provide up-to-date and accurate epidemiological and entomological information, to guide the response.

Surveillance for Zika will include the following activities, which may need to be adjusted to respond to new knowledge:

- finalising the definition of Zika virus disease and its complications;
- enhancing surveillance globally, not just in the Americas, since it is uncertain to what extent and where Zika virus will spread, including making point-of-care tests available to frontline providers for accurate diagnoses;
- integrating the capacity for surveillance and control for all diseases transmitted by *Aedes* mosquitoes, in particular Zika, chikungunya, dengue and yellow fever. This may lead to much greater efficiencies in the long term, though it may dilute efforts, increase costs and complicate capacity building in the immediate term.
- strengthening pre-natal and neonatal surveillance which is linked to Sustainable Development Goal 3, "Ensure healthy lives and promote well-being for all at all ages";
- strengthening surveillance for Guillain-Barré syndrome (GBS) and other known neurological consequences of Zika virus infection;
- developing a clear algorithm for reporting suspect cases at various levels of healthcare: community (including Community Event Based Surveillance), primary care and specialist referral, as well as any measures put in place at points of entry for detecting and reporting cases among cross-border and international travellers; and
- strengthening surveillance of the *Aedes* mosquitoes by engaging communities in activities such as mapping *Aedes* breeding sites and undertaking actual surveillance themselves.

Recent research has demonstrated that community-based, integrated control of *Aedes aegypti* to prevent dengue, when thoroughly implemented, is able to reduce mosquito density and also the transmission of the virus.[12,13,14] Civil society organizations can play an important role in:

- strengthening communities´ capacity to participate actively in community surveillance;
- creating demand for Zika virus diagnosis from the at-risk populations and dispellings rumors and fears;
- strengthening the number and capacities of laboratories; and
- setting criteria for diagnostic tests.

PREVENTION

Prevent adverse health outcomes associated with Zika virus infection through integrated vector management, risk communication and community engagement.

In view of the continued spread of the disease and the mosquitoes increasing resistance to insecticides, there is a need to generate robust evidence on the effectiveness of mosquito control strategies as they are rolled out.

Controlling the spread of Zika virus requires a multi-faceted approach, which should not only be concerned with vector control, but also with protecting individuals, especially pregnant women and women of reproductive

[12] Toledo, Maria E. et al. "Evidence On Impact Of Community-Based Environmental Management On Dengue Transmission In Santiago De Cuba". Tropical Medicine & International Health 16.6 (2011): 744-747.
[13] Kittayapong, P., et al., Suppression of dengue transmission by application of integrated vector control strategies at sero-positive GIS-based foci. American Journal of Tropical Medicine and Hygiene (2008): 78: 70-76.
[14] Andersson, Neil et al. "Evidence Based Community Mobilization For Dengue Prevention In Nicaragua And Mexico (Camino Verde, The Green Way): Cluster Randomized Controlled Trial". BMJ (2015): h3267.

age, from infection and preventing unwanted pregnancies through supporting access to equitable sexual and reproductive health services. This approach includes:

- implementing integrated vector management (IVM) to efficiently and judiciously use resources, defined as "a rational decision-making process for the optimal use of resources for vector control";
- targeting all life stages of the *Aedes* mosquito: egg, larva/pupa and the adult;
- reducing the risk of sexual transmission and other possible routes of transmission;
- coordinating, collaborating and partnering with stakeholders from government (municipalities, ministries of education, health, social services, water and sanitation, etc.) and civil society (NGOs, private sector, faith-based associations, churches, etc.);
- engaging and empowering communities, private sectors, etc. in mosquito control and prevention behaviours at the environmental, household, schools, businesses, personal levels, etc.; and
- developing relevant risk communication and behaviour change strategies and materials.

The aim of IVM is to improve the efficacy, cost-effectiveness, ecological soundness and sustainability of mosquito control. The main elements of an IVM strategy are:

- **advocacy, risk communication for behaviour change and community engagement and legislation** – the promotion of these principles in development policies of all relevant agencies, organizations and civil society; the establishment or strengthening of regulatory and legislative controls for public health; and the empowerment of communities;
- **collaboration within the health sector and with other sectors**[15] – the consideration of all options for collaboration within and between public and private sectors; planning and decision-making delegated to the lowest possible administrative level; and strengthening communication among policy-makers, managers of programmes for the control of vector-borne diseases, and other key partners;
- **integrated approach to disease control** – ensuring the rational use of available resources through the application of a multi-disease control approach; integration of non-chemical and chemical vector control methods ; and integration with other disease control measures;
- **evidence-based decision-making** – adaptation of strategies and interventions to local vector ecology, epidemiology and resources, guided by operational research and subject to routine monitoring and evaluation;
- **capacity-building** – the development of essential infrastructure, financial resources and adequate human resources at national and local levels to manage IVM programmes, based on a situation analysis.

The IVM approach may be different in countries at risk but not currently affected by Zika virus. The global response to Zika, therefore, needs to be much more sensitive to village, district, national and regional contexts to ensure that risk assessments, preparedness and response activities are equitable and cost-effective. The context depends on the density of *Aedes* populations and other factors such as seasonality, urban or rural status, or local understanding and beliefs of the causes of diseases and conditions. Specifically, climate and environmental information can be used to better target the timing and geographic location of vector control interventions[16].

Effective and sustained risk communication and community engagement allow individuals and communities at risk of exposure to, and infection with, Zika virus to take informed decisions to protect themselves and their loved ones from the disease and its complications. Risk communication and community engagement for protection against Zika virus can be organized around the following seven pillars:

1. community actions to control the day-biting *Aedes* vector (such as eliminating breeding sites) and personal protective actions (such as sleeping under a net) to prevent the bite of this mosquito;
2. age-appropriate and culturally acceptable health education for anyone who may be sexually active, accompanied by counselling and health services as appropriate;
3. risk communication for healthcare workers, who need the knowledge, tools and skills to effectively and empathetically counsel, advise and offer appropriate services;
4. national and local risk communication and community engagement plans with all relevant stakeholders for effective and proactive action against this threat;
5. information and education so that travellers and their sexual partners know and understand the risks, and also to prevent unnecessary negative decisions for travel and trade;
6. operational research to understand knowledge, attitudes and practices and so inform ongoing interventions; and
7. coordination amongst key responders, such as affected governments, UN, NGOs and other international agencies, national and local actors, researchers and social science networks.

[15] Such as health, water management, education, military (if relevant), and meteorological, including at the ministerial level.

[16] Munoz, Angel et al. "The Latin American and Caribbean Climate Landscape for ZIKV Transmission." (2016) Columbia University Academic Commons: http://dx.doi.org/10.7916/D8X34XHV.

Risk communication and community engagement should remain flexible enough to change focus, and to track and anticipate new demands that are likely to arise, such as the introduction of new interventions including the use of Wolbachia-infected mosquitos, irradiated mosquitos and the trials and introduction of new vaccines and treatments.

CARE AND SUPPORT

Strengthen health and social systems and other relevant stakeholders at the national and community levels to provide appropriate services and support to individuals, families, and communities affected by Zika.

Care and support needs to focus primarily on the needs of:

- women and girls of childbearing age and children born with complications from Zika virus infection;
- families and communities at risk and affected; and
- people with Guillain–Barré syndrome and other neurological complications, including acute disseminated encephalomyelitis and meningoencephalitis.

Over the next eighteen months it will be important to enable nations and communities to strengthen and develop their health and social services to respond to the short- and long-term medical complications and socio-economic consequences of Zika infection. This includes:

- providing equitable access to quality sexual and reproductive healthcare and services for all women and adolescent girls of reproductive age in Zika-affected areas, including access to family planning, counselling, contraceptive services, including emergency contraception, and supplies, quality prenatal care, quality obstetric care, safe abortion services (where legal), and post-abortion care;
- identifying and treating people with Zika virus infection complications, regardless of gender and disability;
- addressing the psychological and economic impact of the complications, in part by providing adequate psychosocial and mental health support;
- dealing with the long-term implications of children affected by microcephaly and other complications;
- ensuring that migrants, refugees, asylum seekers, internally displaced persons as well as hidden, poor, marginalised or hard-to-reach populations are included in national response plans, and relevant activities are carried out in coordination with local authorities and partners;
- addressing non-medical consequences of the virus such as stigma, reduced income and increased poverty;
- considering removing financial and other barriers for effective access to essential health services;
- giving pregnant women access to point-of-care technology for detecting Zika virus infection and, if such is the case, access to counselling and psychosocial advice, and, if possible, to ultrasonography to monitor fetal growth; and
- developing capacities to recognize and care for patients with GBS, particularly severe GBS requiring ventilatory support.

Perinatal and paediatric care should include early screening and support to individuals and families affected by foetal or newborn complications. Children born with microcephaly and other congenital disorders may develop mental disorders, major neurological disorders or intellectual disabilities which are life-long and require extra care.

Furthermore, all children born to women infected with Zika should be monitored closely for complications for at least three years. There is emerging evidence that children born to women infected by Zika during pregnancy may develop neurological complications over time, even if they are born without microcephaly.

Health and social service systems need to urgently adjust now and develop intersectoral response mechanisms including non-clinical support and stigma reduction for families and children affected, longer term special education as well as targeted social protection measures for families affected by Zika. The aim should be to ensure that children with complications due to maternal Zika virus infection achieve their full potential through rehabilitative services, early stimulation, social assistance and protection, psychosocial support and specialized healthcare and education. Because families affected by adverse neurological or other congential malformations from Zika virus infection will receive reduced income due to the need to care for affected children and bear other direct or indirect financial costs, governments could consider providing special support to the families affected by Zika.

Multiple disciplines will be required to ensure the effective delivery of essential health services and management of Zika complications both in the immediate and long-term, as advised by WHO guidelines and administered by a competent and skilled health and social care workforce. Emphasis should be placed on timely and targeted information regarding accessibility, quality and effectiveness of Zika-related services and commodities as well as reconfiguring the health services to ensure timely access to a pyramid of quality care as close as possible to the affected households.

RESEARCH

Generate data and evidence needed to strengthen public health and community guidance and interventions to prevent, detect and control Zika virus infection and manage its complications.

Fast track and scale up the research, development and availability of Aedes mosquito control tools, diagnostic tests and vaccines.

The goal of the WHO Zika Virus Research Agenda[17] is to support the generation of evidence needed to strengthen essential public health guidance and actions to prevent and limit the impact of Zika virus and its health complications, particularly related to pregnant women and children.

Gaps in the research related to Zika virus were identified by a process initiated from the WHO Region of the Americas – the region at the centre of the current crisis. At regional level, this process identified priority research and development needs in:

- characterizing Zika virus infection including investigating public health and clinical implications;
- describing the dynamics of arbovirus epidemics in the Americas region and characterizing arbovirus vectors; and
- developing and enhancing laboratory platforms to support surveillance.

This process was complemented by consultative meetings convened by WHO at global level to further expand on these identified areas. Meetings were convened to discuss research, vector control and the management of complications associated with Zika virus infection. These highlighted additional global research needs, including:

- developing diagnostic products with very good performance and increasing access to common standards, methods and reference materials to facilitate this development;
- developing a vaccine, with a focus on protecting pregnant women and their babies;
- developing effective therapeutics for both Zika virus and complications;
- holding cohort studies of pregnant women (infected and non-infected with Zika virus) to better understand the outcomes of Zika virus infection on pregnancy as well as child health and developmental outcome long-term;
- piloting new vector control tools;
- developing a causality framework to evaluate the association between Zika virus and neurological disorders; and
- understanding the natural history of Zika virus infection and identifying risk factors for severe complications.

Most importantly, the research required to address Zika virus have been influenced by the unfolding human cost of the epidemic. At the fore are the stories of families of infants born with microcephaly and other congenital syndromes, whose conditions are now being linked to maternal infection with Zika virus during pregnancy. Many of these infants will be at risk of learning difficulties and developmental delays and disabilities (e.g. motor, language) at birth and as they grow older, that will require life-long specialized care and psychosocial support for these children and their families.

Beyond the purely health-related considerations, research is needed around gender, disability, and economic, social, environmental and behavioural considerations for the response (e.g. the PAHO-supported socioeconomic impact assessment), including modelling of potential scenarios to estimate the impact of spread and the economic, as well as human, costs. Research into the gender dimensions of the Zika response should include an assessment of Zika on the primary caregivers in Zika affected households.

There is also a need to undertake more research around the behaviours associated with mosquito control, and around care and support for families and children affected by Zika. The WHO research agenda spells out the need to conduct systematic research that tracks the perception of risk, and the uptake of protective behavior; this will enable the development of effective risk communication and community engagement around vector control, stigma, reduced income and increased poverty.

Within IVM, it will be necessary to validate in field pilots innovative mosquito control methods, such as Sterile Insect Technique (SIT). In addition, the relationship between vector population abundance and Zika transmission remains to be quantified. Studies should aim to collect new vector and clinical datasets carefully matched temporally and spatially. Spatial heterogeneity and transmission at sites other than the home must be considered.

[17] Within the two research objectives, WHO's Zika Virus Research Agenda is referred to, and further expanded upon in the next section of this document and Annex C.

COORDINATION

Establish and maintain adequate, transparent, and accountable coordination mechanisms for the response to Zika.

Coordination mechanisms need to:

- move away from an emergency framework to a longer term programmatic approach;
- cover a range of international and national responders, including national authorities, partners and stakeholders such as UN agencies, the Global Outbreak Alert and Response Network (GOARN), public health research partners, national and international NGOs, regional networks and R&D partners; and
- ensure appropriate representation from diverse social groups which are impacted by Zika virus. Asylum seekers, refugees, internally displaced and migrants should be represented in the coordination mechanisms, including at local levels.

Of tantamount importance is political leadership at national, state and local levels. The response should not be left to the health authorities alone to manage. The highest authority at each level should lead and hold all sectors (such as health, water, sanitation, education and social services) to account, and consideration should be given to cross-border surveillance and coordination mechanisms.

WHO and its partners are working closely with the Inter-Agency Standing Committee (IASC), the UN country teams (UNCTs), and the UN Office for the Coordination of Humanitarian Affairs (OCHA) to ensure coordination mechanisms are interoperable with existing humanitarian response and development systems. WHO and its partners are also working to strengthen existing coordination mechanisms as necessary in order to clarify division of labour amongst partners to avoid duplication and to ensure all programmatic areas are covered at global, national and local levels, as well as ensure effective information sharing mechanisms with low transactions costs.

Now that it is apparent that a longer term approach to Zika is required, WHO will transition its leadership in the response to Zika from an emergency Incident Management System to a more programmatic approach through 2016. However, during this transition period the incident management teams within WHO will continue to ensure regular communication between headquarters, regional and country offices, and close coordination with partners across all sectors and services at global, national and local levels. Some WHO regional offices and partners have prepared specific strategies which complement this global strategy and plan and reflect considerations specific to each geographic area.

Another aspect of coordination is to ensure that Zika surveillance and response will work in conjunction with other established disease control programmes, especially malaria, dengue, chikungunya, acute flaccid paralysis (AFP), and maternal and child health programmes.

COUNTRY

CONTEXT

The current cluster of microcephaly and other neurological complications that is linked to Zika virus infection affects countries differently. Hence, the response strategy needs to be tailored to meet specific needs.

The response objectives and the strategy outlined above to meet them are being implemented through intervention packages tailored to each context (see Table 1 below) in line with national and sub-national response strategies. Risks are assessed to identify areas and populations at high risk of infectionand medical complications, and to assess the capacity of health and social systems to respond.

COUNTRY CLASSIFICATION

There are four contexts classified according to the risk of occurrence of complications associated with Zika virus infection, as follows:

1. Countries reporting Zika virus transmission and increased rates of complications
2. Countries reporting Zika virus transmission only
3. Countries where competent vectors are present
4. All other countries

It is important to note a country may contain more than one classification within its borders.

Countries reporting Zika virus transmission and increased rates of complications

Countries reporting Zika virus transmission and increased rates of congenital malformations and neurological syndromes require a full-scale response. This will include enhanced surveillance and outbreak response, community engagement, mosquito control and personal protective measures, provision of sexual and reproductive health services, care for people and families with potential complications, field investigations and public health research towards better understanding of risk and mitigation measures.

Countries reporting Zika virus transmission only

For countries that are already experiencing transmission of Zika virus, the first priority is to enhance surveillance for both Zika virus infection and potential complications to establish a baseline. Increasing community awareness and engagement in mosquito control and personal protective measures, provision of sexual and reproductive health services and understanding the risks associated with Zika virus infection are also priorities. Governments of these countries should make plans for coping with possible congenital complications and neurological syndromes and set up a rapid response mechanism.

Countries where competent vectors are present

For countries that have a documented presence of *Aedes* mosquitoes but no evidence of Zika transmission or increased rates of complications, the priority would be to enhance surveillance and mosquito control within existing programmes. Additionally, governments should prepare plans and train staff of all sectors to rapidly roll out the response in the case of an outbreak.

All other countries

All other countries should engage in risk communications targeting the public regarding trade and travel, and reduce fear and misconceptions about imported cases whilst conducting surveillance activities to detect imported cases.

COUNTRY PREPAREDNESS

Unaffected and at-risk countries need to prepare their health systems for the potential consequences of a Zika virus outbreak. The preparedness activities undertaken by countries should derive from a systematic country-level risk assessment. All countries should assess the public health impact of Zika virus on the basis of their available response capacity, and the presence of contributing factors for Zika virus transmission.

Factors related to local Zika virus transmission include, but are not limited to, presence of *Aedes aegypti* and *Aedes albopictus*, suitable climatic conditions for competent vectors and other vulnerability factors such as population density, air and shipping connectivity, seasonality and urbanization. Factors related to capacity of countries to respond rapidly to local Zika virus transmission and adverse consequences of Zika virus infection include, but are not limited to, vector management, access to personal protection and sexual and reproductive health services,

surveillance, laboratory capacity, risk communication and community engagement, the existence of emergency care services capable of managing cases of Guillain-Barré syndrome, and capacity to roll out integrated care and support for children with severe disabilities. Evaluations should additionally be sensitive to local variables at village, district, national and regional levels in order to ensure risk assessments, preparedness and response activities are equitable.

Countries with documented or suspected presence of the competent vectors should establish and strengthen integrated vector management activities to prevent local transmission of Zika virus. This group of countries should also reinforce their surveillance systems to ensure prompt detection of local transmission of Zika virus and be ready to report to WHO according to current recommendations. These countries should also ensure they can identify Zika virus, and if they cannot, establish protocols for shipping samples abroad for testing. Capacity for risk communication and community engagement should also be enhanced, so that populations can make informed decisions in order to protect themselves and others from infection, mitigate the effects of Zika virus and the complications of the disease. In addition, countries should strengthen health and social systems and services to ensure that sufficient care can be provided to people and families with potential complications, should an outbreak occur.

Countries without the presence of a competent vector should focus on risk communication for travel health, as well as to reduce fear and counter misconceptions about the virus. A principal objective of risk communication is to allow individuals to make informed decisions about their travel and lifestyles in order to protect their health and the health of others. Engaging with health professionals is key for ensuring early detection of imported cases of Zika virus disease and potential complications. Countries in this group that wish to establish laboratory capacity should follow WHO and CDC guidance on laboratory diagnosis of Zika virus infection, whereas countries that do not wish to do so should ensure that they have established protocols for shipping samples abroad for diagnosis.

Preparedness strategies should be implemented through intervention packages tailored for each country context.

Table 1. Preparedness activities according to country context

Response strategy	Countries with competent vectors*	Other countries
Coordination	✓	✓
Emergency risk communications and community engagement	✓	✓
Laboratory	✓	✓
Surveillance and case management	✓	✓
Health and social systems and services strengthening	✓	
Integrated vector management	✓	

**includes countries with previous Zika transmission but not currently experiencing an outbreak*

RESPONSE

MONITORING

Effective response operations depend on continuous, regular and detailed monitoring, analysis and reporting.

OBJECTIVES

Monitoring and analysis of the response, as well as reporting on the response:

- enables all partners involved to have a common understanding of the situation, examine whether sufficient progress has been made against the plan to reach the strategic objectives and make evidence-based decisions for the direction of the response; provides an overview of trends and is used to adjust needs, targets and funding required; and
- allows the leadership to review the progress of the overall response and make adjustments, as necessary.

The present response strategy is being continually assessed to address changing circumstances and/or new evidence.

COUNTRY PREPAREDNESS[18]

Surveillance indicators

- Percentage of countries where the baseline rate of microcephaly has been established
- Percentage of countries where the baseline rate of Guillain-Barré syndrome has been established
- Percentage of countries with laboratory capacity RT-PCR and ELISA + PRNT (plaque-reduction neutralization tests) in country or with system in place for accessing laboratory confirmation services abroad

Response indicators

- Percentage of Zika associated Guillain-Barré syndrome having been hospitalised
- Percentage of microcephaly cases in live births in settings of Zika virus transmission having had neuro-imaging
- Percentage of pregnant women with confirmed Zika infection having had ultra-sound screening
- Percentage of countries with a risk communication strategy and/or implementation plan
- Percentage of countries having routine vector surveillance
- Percentage of countries having assessed resistance to insecticide
- Percentage of sites with vector control activities that report impact of vector control measures.

REPORTING[19]

Countries are invited to provide an update on surveillance, response and impact indicators every 2 weeks. WHO is working to provide Member States with recommendations on strengthening surveillance and reporting systems in the context of the Zika virus outbreak.

Reported country information will be collated and presented in WHO's weekly Zika situation report which is disseminated through the WHO website and email to partners. Some information will be aggregated (for instance as a percentage of countries), others will be presented country by country.

As part of comprehensive response monitoring, WHO requests partners to regularly report on their response activities taking place at the global, regional and country levels through the 4Ws online portal which can be found at this link: http://who.int/emergencies/zika-virus/response/4w/en/.

To be added to the distribution list or to provide response monitoring information, please email zikainfo@who.int.

[18] Detailed descriptions of these indicators can be found at Annex B.

[19] Surveillance data are not listed here. Detailed information and reporting requirements are found in "Surveillance for Zika infection, microcephaly and Guillain-Barré syndrome". (6 April 2016) http://www.who.int/csr/resources/publications/zika/surveillance/en/

SUMMARY OF

REQUIREMENTS

FUNDING NEED[20] (US$)[21]	NUMBER OF PARTNERS	GEOGRAPHIC SCOPE
121.9M	>60	Global

WHO will continue to work with all partners to update and consolidate the needs and requirements across the response based on this Strategic Response Framework.

Fig. 4. Resource requirements by objective[22]

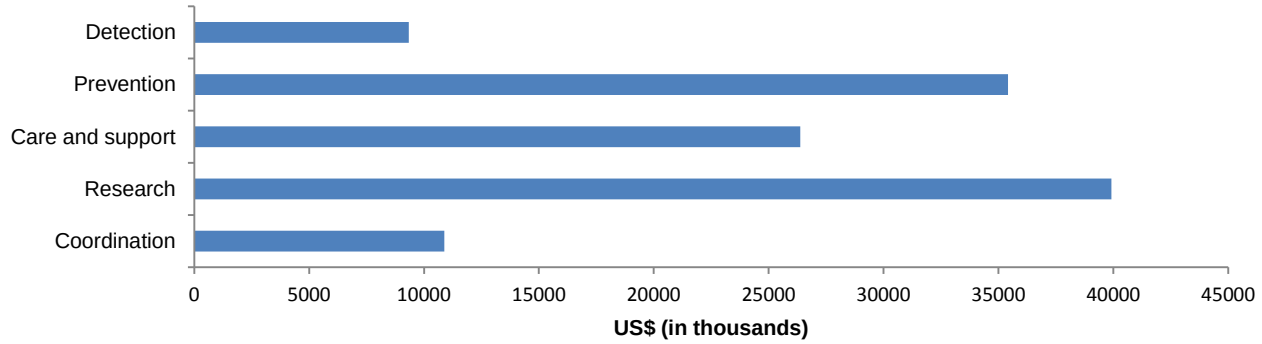
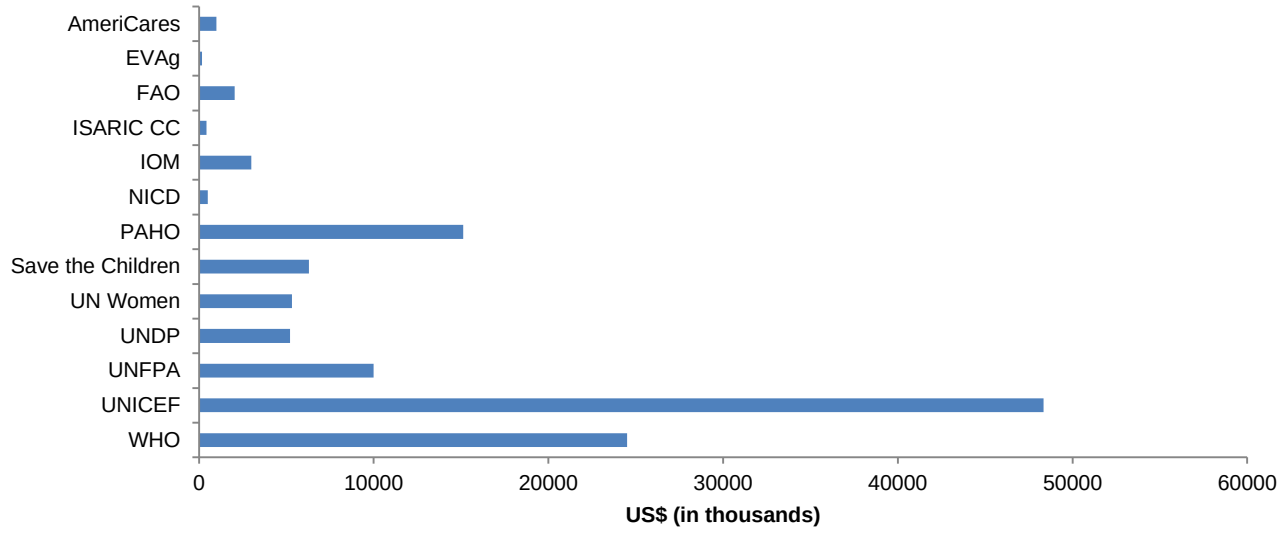


Fig. 5. Resource requirements by organizations[23]



[20] The funding figures above represent requirements for WHO and its partners between July 2016 to December 2017, but are not exhaustive for this time period. It is expected that these figures will be revised on a regular basis as each organization develops their plans.
[21] US$ = United States dollar.
[22] Figures 4 and 5 summarize the needs and requirements identified to date by objective and organization, and do not include any figures for requirements or received funding over the period of the previous strategy.
[23] Please refer to Annex A for full names of organizations.

PART II:
JOINT OPERATIONS PLAN

Detection

Prevention

Care and support

Research

Coordination

REQUIREMENTS (US$)

9.3M

STRATEGIES

1 Assessment and implementation of preparedness measures

2 Laboratory and diagnostics

3 Surveillance and monitoring

CONTACT
Dr. Stéphane HUGONNET

hugonnets@who.int

DETECTION

Develop, strengthen and implement integrated surveillance systems at all levels for Zika virus disease, its complications, other arboviral diseases and their vectors, in order to provide up-to-date and accurate epidemiological and entomological information, to guide the response.

There is a significant cross-over between prevention and detection within the IVM model, integrating surveillance with prevention methods.

In areas where there is little or no virus transmission, risk assessments should be regularly performed based on the epidemiological situation, exposure and contextual factors, including the public health capacity to respond to a Zika virus outbreak.

Furthermore, existing surveillance systems should be enhanced for early detection and reporting of Zika virus and unusual clusters of neurological disorders or neonatal malformations, including both event-based and indicator-based surveillance systems.

Timely notification of any event compatible with Zika virus is important, and in particular any associated with neurological disorders and neonatal malformations through established channels, including IHR.

In those areas conducting preparedness, work capacities should be mapped for disease and vector surveillance, laboratory diagnosis, IVM and emergency risk communication for Zika virus, microcephaly and other neurological syndromes. Also, it is advised that inter-country training and missions should be conducted in order to enhance laboratory capacity in member states.

The establishment or strengthening of event-based or syndromic surveillance should be supported, potentially targeting specific groups for surveillance, such as pregnant women through ante- and post-natal care, as is the case in Jamaica. Furthermore, regional, country and more local plans should be established for a sentinel based surveillance system for congenital birth abnormalities and Guillain-Barré syndrome. Existing lab based disease specific surveillance systems (e.g. measles, polio) should be facilitated to detect Zika virus infection and associated disorders.

For the surveillance system to be effective, demand generation activities should be rolled out, to allay fear of people affected by the virus, as well as individual advice and counseling in the case of positive results, particularly for pregnant women or families of children with microcephaly.

Finally, the development and roll-out of rapid diagnostic tests should be supported, and an awareness of the need and conditions for early diagnoses of Zika virus infection and its complications should be generated.

Table 2. Strategies and indication of organizations involved in detection

Strategy	Organizations
Assessment and implementation of preparedness measures	PAHO, UNICEF, UNFPA, WHO, WFP
Laboratory and diagnostics	ESR New Zealand, EVAg, Institut Pasteur, NICD, PAHO, HHS/CDC, WHO
Surveillance and monitoring	FAO, IOM, UNICEF, UTMB, WHO

REQUIREMENTS (US$)

35.4M

STRATEGIES

1 Community engagement

2 Integrated vector management

3 Public health risk communication

CONTACT
Dr. William PEREA CARO

pereaw@who.int

PREVENTION

Prevent adverse health outcomes associated with Zika virus infection through integrated vector management, risk communication and community engagement.

In line with integrated vector management (IVM) principles, the following major actions have been identified:

- promote advocacy, social mobilization and regulatory control for public health and empowerment of communities, to enhance community participation and to improve efficiency and sustainability of mosquito control interventions;
- plan and implement mosquito control operations as part of the emergency response to outbreaks;
- develop and standardize guidelines for *Aedes* mosquito surveillance and control and support implementation at different levels of administration with a focus on larval source management;
- facilitate the establishment of a global entomological laboratory network which will assist in processing specimen for species identification and incrimination of *Aedes* species;
- strengthen *Aedes* mosquito surveillance and update distribution maps of all arboviral diseases; and
- routinely monitor resistance to insecticides and investigate resistance mechanisms involved so as to inform actions for resistance management.

It is necessary to view integrated vector management through the lens of prevention of arboviral diseases more generally, and to deploy cost-effective and sustainable vector control interventions. Strengthened inter- and intrasectoral coordination, partnerships and community participation are possible through a multisectoral action framework such as that developed by UNDP and the Roll Back Malaria Partnership for malaria.[24] Supporting ministries of education and school administrators to incorporate education on arboviral diseases transmitted by *Aedes aegypti* and *Aedes albopictus* and how to prevent its spread, into school curriculums can also help to galvanize the engagement of communities through children as agents of change.

The promotion of individual and community behaviours to control mosquitoes and to protect against mosquito bites, particularly targeting women of reproductive age and their male sexual partners, requires an understanding that people will find such behaviours hard to consistently adopt, not least due to factors associated with cost, access to sexual and reproductive health services, access to potable water and sanitation and adequate housing.

Interventions need to be gender-sensitive to promote safer sexual behaviours, such as correct and consistent use of condoms to reduce the risk of sexual transmission of Zika virus, and in acknowledgement that some cultural and legal contexts can result in women not being able to control decisions related to their pregnancies.

Careful risk communication around the use of pesticides will be important to provide appropriate messages to communities, as much as possible to avoid rumours and contribute to building trust among authorities. An emphasis should be placed on highlighting the risks of pesticides whilst providing pragmatic advice on which is the most appropriate and how best to use them. Systemic and sensitive perception mapping is important to identify harmful beliefs and misperceptions, which in turn can help guide the response.

[24] Multisectoral Action Framework for Malaria. http://bit.ly/1YbRpsF

Some families and households are already adopting and using methods of mosquito control that are available through the market or private sector, such as sprays and bed nets. However, the most economically deprived are at the same time the most vulnerable and do not have access to those measures.

Efforts at household level must be accompanied with community and municipality actions to improve access to water, waste and water management, and safe storage of water and sanitation. These environmental and structural actions are the key for sustainable vector control.

Given the nature of the mosquito, it is important that people, particularly pregnant women, are aware of the patterns of mosquito biting, when they are most vulnerable, the efficacy of the methods, and need for any additional protection. Dialogue with the private sector is required to harmonise and standardize messaging around protection modalities and methods.

There is clear evidence that health-seeking behaviours are fundamental to the control of the spread of diseases and epidemics, and community engagement is key to preventing transmission. The Social-Ecological Model (SEM) provides a systematic framework to overcome barriers to the adoption of behaviours in the prevention and control of the spread of Zika virus. Further, as outlined in the inter-agency guidance on risk communication and community engagement, interventions to engage communities should follow standard evidence-based planning, implementation and monitoring steps, beginning with sound research of prevailing risk perception attitudes and knowledge, practices and socio-cultural customs around vector control and personal protection measures, taking account of sexual transmission of Zika virus.

Table 3. Strategies and indication of organizations involved in prevention

Strategy	Organizations
Community engagement	AmeriCares, Jhpiego, Save the Children, PAHO, UNDP, UNFPA, UNICEF, UN Women, WHO
Integrated vector management	AmeriCares, FAO, IAEA, International Medical Corps, Institut Pasteur, Malteaser International, PAHO, UNDP, UN Women, WHO
Public health risk communications	FAO, IOM, NICD, PAHO, Save the Children, UNFPA, UNHCR, UNICEF, UN Women, WHO

Coordination within the government, among UN agencies and other partners including those in charge of mass media and social media platforms is critical to ensure transparency, active listening to understand community concerns and to manage any misinformation that may be circulating due to the newness of the disease. Local partnerships especially at the community level are essential to ensure communication platforms, messages and listening to community concerns is in real time, situated in the specific context and is culturally appropriate.
Behavioural change programmes should be designed to take into account the availability of services and commodities, and WHO and its partners should look to motivate and persuade communities to act on vector control where the services and commodities are available.

Healthcare workers need to be provided with credible and consistent information in order to give appropriate advice, such as that relating to access to pregnancy terminations, contraception (with an emphasis on condom use to avoid sexual transmission of Zika), and what actions men can take to limit the risks. As well as sexual and reproductive health services, including access to contraceptives and condoms (to prevent sexual transmission), diagnostic services for early detection of Zika virus infection and its complications, including fetal abnormalities during pregnancy, should be considered.

Prevention and preparedness efforts also need to target hidden or hard to reach populations, such as refugees and people on the move, and those with difficult access to information. For example, risk communication may need to be developed specifically for points of entry or cross border communication mechanisms. Of particular concern are the most vulnerable populations in urban slums and other densely populated peri-urban areas; not only are they at higher risk of being infected because of the environment they live in, but they are less likely to have access to the protection measures.

Travel advisory information should be developed both for travel between countries, and within countries where there are areas of high transmission. UNICEF is raising awareness and sharing timely information on the spread of disease, and how it can be prevented through personal protection and community-based vector control measures – including through the use of innovative technology, such as U-report. 122 million people have now been reached with preventive messages through mass, social and digital media in 12 countries, with highest outreach in Brazil, Mexico, Colombia, and Cuba.

REQUIREMENTS (US$)

26.4M

STRATEGIES

1 Access to health and social care

2 Delivery of health and social care

3 Health and social systems strengthening

CONTACT
Dr. Anthony COSTELLO

costelloa@who.int

CARE AND SUPPORT

Strengthen health and social systems and other relevant stakeholders at the national and community levels to provide appropriate services and support to individuals, families, and communities affected by Zika.

In countries affected by congenital Zika cases, governments should consider establishing a pyramid of care and support that builds on community networks and community health workers to provide the most basic support, complemented by strengthening the capacity of primary care providers and supported by referral care for providing high end diagnostic, monitoring and corrective services.

Governments should look to provide a package of support services (counselling, and social protection) for families to care for affected children and address the impact of microcephaly, other congenital anomalies and neurological conditions. In order to ensure adequate financing of these services, goverments should develop investment cases to estimate the costs associated with the response.

Communication with the public on raising awareness of the neurological impact of maternal Zika virus among children, and advocacy with policy makers on the support required to families will be crucial to provide an appropriate response. With engagement of women and communities as partners in the Zika response, it is possible to augment Zika-related services for addressing sexual and reproductive needs, promoting support to the women who have given birth to and care for children with microcephaly, and preventing discrimination against infected women and people living with disabilities.

Existing capacities and needs should be assessed to guide health system strengthening, particularly around ante-natal, birth and post-natal care, neurological and mental health services, safe conception services, contraception, quality obstetric care and safe abortion. Specific actions as a result could include ensuring access to contraceptive services and supplies, training a network of providers for counselling services, and training to health professional on Zika's gender dimensions in order to equip them with appropriate preventive measures and quality and effective services.

Information sharing between clinicians, surveillance and laboratory should be strengthened to contribute to filling information gaps on Zika virus infection and its association with neurological disorders or neonatal malformations.

WHO Headquarters will look to hold a global technical meeting on health system assessment approaches and global outbreaks, and provide technical support on health systems related needs to affected regions.

Table 4. Strategies and indication of organizations involved in care and support

Area of intervention	Organizations
Access to health and social care	UNICEF, UN Women, WHO
Delivery of health and social care	AmeriCares, Save the Children, PAHO, UNFPA, UNICEF, UN Women, WHO
Health and social systems strengthening	AmeriCares, NICD, PAHO, PHAC, Save the Children, UNFPA, UNICEF, UN Women, WHO

Examples of planned activities include:

- Regional WHO offices to provide technical support on laboratory strengthening, including training in collecting and handing Zika virus specimens and ensuring laboratories have appropriate materials and experience.
- UNICEF will conduct awareness raising activities, supporting improvements to access for services, promoting multisectoral care and support, and strengthening community and peer support mechanisms.
- Save the Children will provide special protection measures for populations at risk and implement non-clinical support services for children with Zika-related conditions and their families.

REQUIREMENTS (US$)

39.9M

STRATEGIES

1 Development and dissemination of vaccines and point-of-care diagnostics

2 Development and dissemination of vector control tools

3 Guidance and protocols

4 Public health research

CONTACT
Dr. Nathalie BROUTET

broutetn@who.int

Dr. Bernadette MURGUE

murgueb@who.int

RESEARCH

Generate data and evidence needed to strengthen public health and community guidance and interventions to prevent, detect and control Zika virus infection and manage its complications.

Fast track and scale up the research, development and availability of Aedes mosquito control tools, diagnostic tests and vaccines.

Research activities are covered in greater detail in WHO's Zika Virus Research Agenda, which is outlined in this section and broken down further in Annex D. In addition to identifying priority research gaps, a need was also identified to align the research and response of partners at all levels in order to implement effective and coordinated international research, and to provide the supportive functions to enable robust research to take place.

Coordination will be critical to address the research priorities identified and to harmonise the efforts of partners across countries, regions and institutions. Key actors will need to collaborate on scientific research projects and will also need to work with responders to translate research findings into improved public health responses.

The following functions have been identified to enable research coordination and management, and will be key to supporting the research identified in the Zika Virus Research Agenda.

Research and partner coordination

Close partner coordination and collaboration is required to ensure that research and response activities are aligned to agreed global priorities within the Research Agenda. This will require strengthening mechanisms to implement collaborative international research, share and access data, and disseminate preliminary research findings.

Common platform for standardized processes, protocols and tools, and for sharing specimens, data and information

Global, regional and national actors will require clear and standardized protocols to effectively detect, track and monitor Zika virus infection including complications.

Harmonization is required to assure the accuracy of data collection, to increase power of research and to improve both quality assurance and quality control. Standardized protocols will be required for biological sampling, sample storage, shipment and transport, testing, record taking and data entry. Shared platforms will include common repositories for data, research outcomes and findings, and dissemination strategies will be put in place to enable the sharing of preliminary research findings and data.

Training and capacity building for research and public health response

The execution of new and harmonized tools, standards, processes and protocols requires enhanced training of users including laboratory technicians, public health workers, clinicians and others. Training is also required at local level for public health responders working on clinical management of Zika virus and its complications, vector control and risk communications.

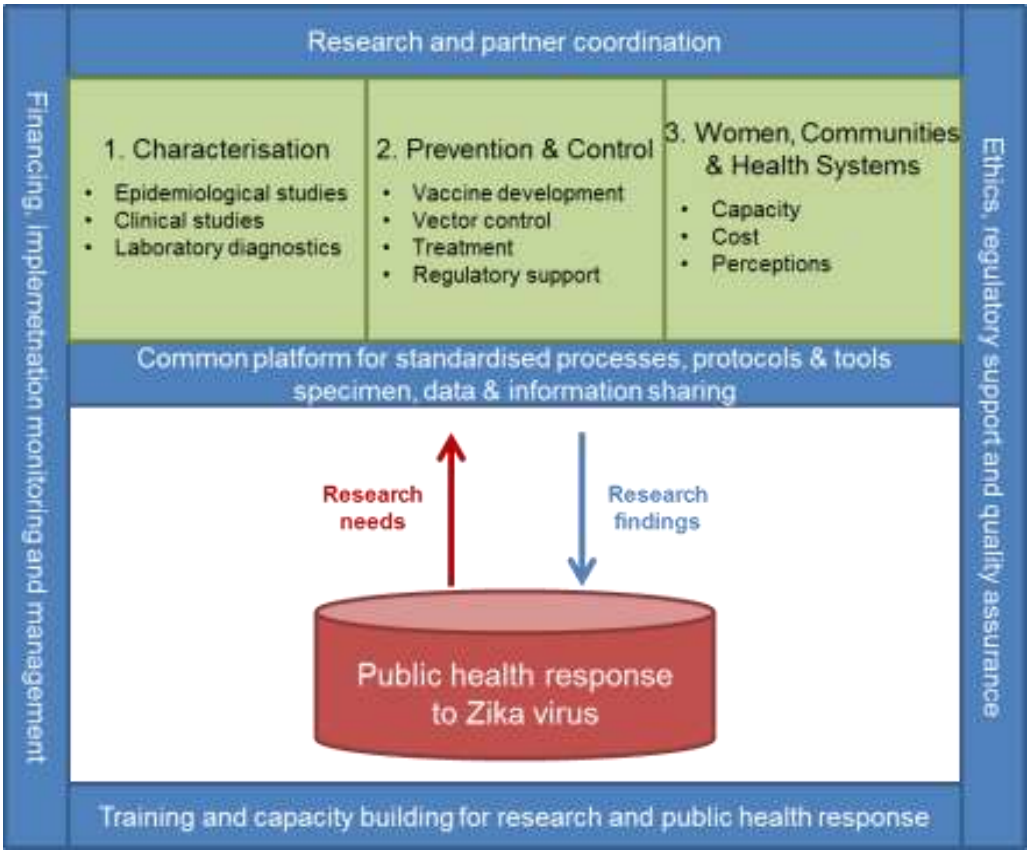
Financing, implementation monitoring and management

Financing will be sought to initiate and maintain work in the Research Agenda over an anticipated timeframe of June 2016 to December 2018. Support will be sought from key funding partners and donors, and robust mechanisms established to ensure transparent monitoring, management, reporting, and accountability of funds and activities.

Ethics, regulatory support and quality assurance

The potential impact of Zika virus infection for pregnant women and their babies raises additional ethical and regulatory complexities for research in this field. Public health decisions may have to be made on an urgent basis and in the context of scientific uncertainty. Establishing a sound basis of ethics, regulatory support and quality assurance for the Research Agenda will be key to enabling researchers and decision-makers to lead an evidence-based and robust response to the challenges posed by Zika virus.

Fig. 6. WHO Zika Virus Research Agenda Implementation Framework



The coordination and management elements described above form the key support structure for the overall implementation of the WHO Zika Virus Research Agenda. The proposed research areas and the coordination and management functions that enable them are shown in the Implementation Framework (see Fig. 6).

In this Implementation Framework, three prioritised research areas have been identified: 1) Characterisation, 2) Prevention and Control, and 3) Health Systems are coordinated by an overall research and partner coordination function. The research areas are supported by common platforms for standardized processes, protocol and tools, and specimen, data and information sharing. These platforms allow needs from the public health response to flow up to and inform research activities, and will also enable research findings to guide and improve the international response.

Training and capacity building for research and public health response forms the foundation of the Implementation Framework. Developing these skills in the key workforce involved in

implementing the Research Agenda – laboratory technicians, clinicians, responders and others – is fundamental to making the Research Agenda operational and achieving its aims.

The management and administration of the Research Agenda is supported by two cross-cutting functions encompassing financing, implementation monitoring and management as well as ethics and quality assurance. These functions will provide the necessary organizational support required to run this major international project, as mechanisms to ensure that the highest levels of quality and accountability are maintained.
Other planned activities include:

- UNICEF has been engaging with WHO, PAHO, the US Government, other partners and industries to help drive the rapid development of Zika diagnostics and vaccines. The target product profile for diagnostics was finalized and published on 13 April 2016, defining the desired characteristics of point-of-care Zika diagnostic tests, to detect active infection and prior infection.
- A target product profile is under development for Zika Vaccines. The TPP has been submitted for public consultation. The final TPP is planned for release by the end of June 2016. A consultation has occurred in June 2016 which examined the regulatory expectations for Zika virus vaccine use.
- Additionally, a programme of work is under development, including demand and procurement forecasts, industry consultation, advance procurement-like mechanisms, support to WHO technical assessment, as well as R&D procurement
- Activities will be done in close coordination with WHO as technical lead with PAHO, UNFPA, UNICEF and other key actors; as well as fairly and transparently with industries.
- UNDP with partners (such as the IFRC) is examining the socioeconomic, gender and broader human development impacts that Zika has had on those infected by the virus, their households, their communities, and their respective national, regional and local institutions.
- EVAg consortium is providing efficient assays reagents to the healthcare organizations and products to the pharmaceutical industry for the preparation of new drugs and vaccines.[25,26]

Table 5. Strategies and indication of organizations involved in research

Area of intervention	Organizations
Development and dissemination of vaccines and point-of-care diagnostics	UNICEF, UTMB, WHO
Development and dissemination of vector control tools	Institut Pasteur, NICD, PAHO, UNICEF, WHO
Guidance and protocols	ECDC, Heart to Heart International, Institut Pasteur, ISARIC CC, UNICEF, WHO
Public health research	ESR New Zealand, Institute Louis Malarde, Institut Pasteur, ISARIC CC, PAHO, Time Z Consortium, UNDP, UNFPA, UNICEF, UN Women, UTMB, WHO

[25] Dye, Christopher et al. "Data Sharing In Public Health Emergencies: A Call To Researchers". *Bulletin of the World Health Organization* 94.3 (2016): 158-158.
[26] Huzly, Daniela et al. "High Specificity Of A Novel Zika Virus ELISA In European Patients After Exposure To Different Flaviviruses". *Euro Surveill.* 21.16 (2016): n. pag.

REQUIREMENTS (US$)

10.9M

STRATEGIES

1 Inclusion of vulnerable communities

2 International coordination

3 International Health Regulations

4 Support to national coordination

CONTACT
Mr. Ian CLARKE

clarkei@who.int

COORDINATION

Establish and maintain adequate, transparent, and accountable coordination mechanisms for the response to Zika.

To ensure effective internal coordination, and support coordination and collaboration of partners and stakeholders, WHO has established incident management teams in support of governments at the global, regional and country level, as required. These teams are operating using an incident management structure, with regular communication between incident managers at different levels and close operational coordination with partners at all levels.

WHO is ensuring that partners are kept aware of the latest situation through conducting regular briefings, holding partner coordination calls, sharing information, and providing regular situation updates. Partners are encouraged to send updates on their key Zika activities to the WHO incident management team for inclusion in the global weekly situation reports.

WHO will continue to coordinate closely with the Inter-Agency Standing Committee (IASC) and other partners through regular targeted outreach, periodic general information sessions to the entire IASC community.

To support countries and affected populations effectively, WHO is working closely with national authorities and a broad range of partners on the development of the strategic response priorities, and mapping multisectoral and multidisciplinary capacities. WHO is coordinating with partners in conducting assessments, developing technical advice and guidance, and delivering critical interventions and support to countries.

At the country level, WHO is working through the regular UN country team structures, according to the principles of partnership of humanitarian clusters.

Coordination activities are broadly divided between those activities designed to help support member states coordinate their own internal response to this outbreak, and those activities designed to coordinate the global or regional response.

Table 6. Strategies and indication of organizations involved in coordination

Area of intervention	Organizations
Inclusion of vulnerable communities	Save the Children, UNFPA, UNICEF, UN Women, WHO
International coordination	PAHO, UNFPA, UNICEF, UN Women, WHO
International Health Regulations	WHO
Support to national coordination	Save the Children, UNDP, UNFPA, UNHCR, UNICEF UN Women, WHO

The coordination activities in support of governments have a significant overlap with the other sections above, and include:

- enhancing the promotion of personal protection measures and vector management, building on existing community mobilization programmes of Member States;
- ensuring the integration of gender dimensions in the development of comprehensive national Multi-Sector Risk Assessments between UNICEF, WHO, UN Women and UNFPA for communication and social mobilization, care for mothers and children and WASH support;
- supporting the national gender machinery and civil society, especially women's organizations, in mobilizing joint and aligned efforts at community level;
- advocating for wide and affordable access to comprehensive Sexual and Reproductive Health information complying with the Montevideo Consensus and Action Plan to the public authorities;
- supporting the monitoring and evaluation of national and regional Zika virus Action Plans;
- providing technical support to countries to develop, review and implement contingency plans for epidemic and pandemic response;
- enhancing the communication capacity of healthcare personnel and volunteers; and
- ensuring that a risk communications plan, that can be used to communicate with the public and stakeholders during a potential Zika virus infection, has been developed.

Activities in support of coordinating the global and regional response include:

- ensuring regional and global incident command structures can support coordination for preparedness and response;
- interpreting, translating, and disseminating of information products, guidance and publications concerning Zika;
- supporting to member states regarding the measures to be adopted in relation to mass gatherings and sporting events;
- conducting inter-country trainings to prioritized countries & territories in support of surveillance activities;
- advocating for national, regional and local governments to implement their obligations in all areas and coordinate implementation support;
- leveraging of sustainable national and international resources for all areas of the Zika Control and mitigation plan;
- monitoring, evaluating and knowledge sharing around national and regional prevention and control strategies; and
- advocating at regional, national and local level for the inclusion of refugees in national response plans.

PART III: ANNEXES

ANNEX A
PARTNER ORGANIZATIONS

Table 7. Partners contributing to the Zika activities database (4Ws)

Organization
AmeriCares
Australasian Society for Infectious Diseases
Australian Cerebral Palsy Alliance
Child Fund International
Cruz Roja Boliviana
Curtin and PathWest
European Centre for Disease Prevention and Control (ECDC)
European Virus Archive goes Global
Food and Agriculture Organization of the United Nations (FAO)
Heart to Heart
Institut Pasteur
Institute of Environmental Science and Research, New Zealand (ESR)
International Atomic Energy Agency (IAEA)
International Federation of Red Cross and Red Crescent Societies
International GBS Outcome Study
International Medical Clinic
International Organization for Migration (IOM)
International Severe Acute Respiratory and Emerging Infection Consortium Coordinating Centre (ISARIC CC)
Jhpeigo
Malteser International
Marie Bashir Institute for Infectious Disease and Biosecurity
National Institute for Communicable Diseases, South Africa (NICD)
National Institute of Infectious Diseases, Japan
New South Wales Public Health Library
Pan American Health Organization (PAHO)
Peruvian Red Cross
Public Health Agency of Canada
Save the Children
UN Development Programme (UNDP)
UN High Commissioner for Refugees (UNHCR)
UN International Children's Emergency Fund (UNICEF)
UN International Strategy for Disaster Reduction (UNISDR)
UN Population Fund (UNFPA)
UN Women
Universal Postal Union
University of Sydney
University of Texas Medical Branch – Research (UTMB)
University of the West Indies
US Centers for Disease Control and Prevention (CDC)
US Department of Health and Human Services (US HHS)
World Food Programme (WFP)
World Health Organization, including regional offices
World Vision

ANNEX B
PARTICIPATING ORGANIZATIONS' FUNDING REQUIREMENTS[27]

Table 8. Organization's requirements by objectives

ORGANIZATION / Objective	**Total Requirements (US$)**
AMERICARES	**1 000 000**
Prevention	1 000 000
EUROPEAN VIRUS ARCHIVE GOES GLOBAL (EVAg)	**178 200**
Prevention	165 000
Care and Support	13 200
FOOD AND AGRICULTURAL ORGANIZATION OF THE UN (FAO)	**2 050 000**
Detection	300 000
Prevention	1 750 000
INTERNATIONAL ORGANIZATION FOR MIGRATION (IOM)	**3 000 000**
Detection	1 000 000
Prevention	2 000 000
INTERNATIONAL SEVERE ACUTE RESPIRATORY AND EMERGING INFECTION CONSORTIUM (ISARIC)	**429 527**
Research	429 527
INSTITUT PASTEUR	***Undisclosed***
Research	
NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES, SOUTH AFRICA (NICD)	**500 000**
Detection	500 000
PAN AMERICAN HEALTH ORGANIZATION (PAHO)	**15 115 000**
Detection	2 665 000
Prevention	5 715 000
Care and Support	4 680 000
Research	915 000
Coordination	1 140 000
SAVE THE CHILDREN	**6 300 000**
Prevention	3 024 000
Care and Support	2 772 000
Coordination	504 000
UN DEVELOPMENT PROGRAMME (UNDP)	**5 204 500**
Prevention	4 129 500
Research	200 000
Coordination	875 000
UN POPULATION FUND (UNFPA)	**10 000 000**
Prevention	1 300 000
Care and Support	8 700 000

[27] The funding figures below represent requirements for WHO and its partners between July 2016 to December 2017, but are not exhaustive for this time period. It is expected that these figures will be revised on a regular basis as each organization develops their plans.

UN HIGH COMMISSIONER FOR REFUGEES (UNHCR)	***Undisclosed***
Prevention	
Coordination	
UN INTERNATIONAL CHILDREN'S EMERGENCY FUND (UNICEF)	**48 340 000**
Detection	1 600 000
Prevention	11 180 000
Care and Support	7 420 000
Research	25 410 000
Coordination	2 730 000
UN Women	**5 329 300**
Prevention	20 000
Care and Support	984 300
Research	632 000
Coordination	3 693 000
US CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)	***Undisclosed***
Detection	
Prevention	
Research	
WHO	**24 496 755**
Detection	3 276 225
Prevention	5 133 150
Care and Support	1 803 892
Research	12 338 450
Coordination	1 945 038
Grand Total	**121 943 282**

Table 9. Objective's requirements by organization

OBJECTIVE / Organization	**Total Requirements (US$)**
DETECTION	**9 341 225**
FAO	300 000
International Organization for Migration	1 000 000
NICD	500 000
PAHO	2 665 000
UNICEF	1 600 000
US CDC	*Undisclosed*
WHO	3 276 225
PREVENTION	**35 416 650**
AmeriCares	1 000 000
EVAg	165 000
FAO	1 750 000
International Organization for Migration	2 000 000
PAHO	5 715 000
Save the Children	3 024 000
UNDP	4 129 500
UNFPA	1 300 000
UNHCR	*Undisclosed*
UNICEF	11 180 000
UN Women	20 000
US CDC	*Undisclosed*
WHO	5 133 150
CARE AND SUPPORT	**26 373 392**
EVAg	13 200
PAHO	4 680 000
Save the Children	2 772 000
UNFPA	8 700 000
UNICEF	7 420 000
UN Women	984 300
WHO	1 803 892
RESEARCH	**39 924 977**
Institut Pasteur	*Undisclosed*
ISARIC	429 527
PAHO	915 000
UNDP	200 000
UNICEF	25 410 000
UN Women	632 000
US CDC	*Undisclosed*
WHO	12 338 450
COORDINATION	**10 887 038**
PAHO	1 140 000
Save the Children	504 000
UNDP	875 000
UNHCR	*Undisclosed*
UNICEF	2 730 000
UN Women	3 693 000
WHO	1 945 038
Grand Total	**121 943 282**

ANNEX C
PARTICIPATING ORGANIZATIONS' FUNDING REQUIREMENTS

Table 10. Description of surveillance indicators

Indicator	Comments	Numerator	Denominator
Percentage of countries where the baseline rate of microcephaly has been established	Establishing a baseline for microcephaly is a surrogate of the capacity of the surveillance system to detect any increase in the incidence of microcephaly and other congenital abnormalities and occurrence of the Zika congenital syndrome. Countries should ideally base this on a cut-off using -2 standard deviations from the WHO growth reference standards or for preterm infants, using the Intergrowth-21 standards at birth. The baseline can be established through retrospective study, review of charts, nationwide or in selected sites, and can be presented as a rate or number of expected cases per a given time period.	# of countries where the baseline rate of microcephaly has been established. Source: MoH	# of countries which have reported vector-borne autochthonous Zika virus transmission since 2007. Source: WHO
Percentage of countries where the baseline rate of Guillain-Barré syndrome has been established	Establishing a baseline for Guillain-Barré syndrome is a surrogate of the surveillance of GBS and capacity to detect any increase in the incidence of GBS. The baseline can be established through retrospective study, review of charts, nationwide or in selected sites, and can be presented as a rate or number of expected cases per a given time period.	# of countries where the baseline rate of Guillain-Barré syndrome has been established. Source: MoH	# of countries which have reported vector-borne autochthonous Zika virus transmission since 2007. Source: WHO
Percentage of countries with Zika virus laboratory capacity in country or with system in place for accessing laboratory confirmation services abroad.	This measures the capacity of the country to diagnose cases of Zika virus infection or establish the association between the infection and complications. The capacity can be in country, or through a formal arrangement with a laboratory outside the country.	# of countries with laboratory capacity (RT-PCR and ELISA + PRNT) in country or with system in place for accessing laboratory confirmation services abroad. Source: MoH	# of countries where Zika virus competent vectors are present. Source: WHO

Table 11. Description of response indicators

Indicator	Comments	Numerator	Denominator
Percentage of Zika associated Guillain-Barré syndrome having been hospitalised	This is a surrogate marker for access to healthcare as all GBS cases should be hospitalised. It focuses on GBS and not the other neurological complications (eg. meningoencephalitis) as one assumes that if patients with GBS access care, those with other neurological complications do as well. This indicator shall be reported on by countries with Zika virus vector-born transmission.	# of Zika associated Guillain-Barré syndrome cases which have been hospitalised Source: MoH	# of Zika associated Guillain-Barré syndrome cases. Source: MoH
Percentage of microcephaly cases in live births in settings of Zika virus transmission having had neuro-imaging	This is a surrogate marker for access to healthcare as all cases of microcephaly should have neuro-imaging tests. If they had the test, one assumes that they were referred and managed in a reference health structure. This indicator shall be reported on by countries with Zika virus vector-born transmission.	# microcephaly cases in live births which had neuro-imaging Source: MoH	# microcephaly cases in live births Source: MoH
Percentage of pregnant women with confirmed Zika infection having had ultra-sound screening	This is a surrogate marker for access to healthcare. Women with confirmed Zika infection should be monitored which includes ultrasound screening. This indicator shall be reported on by countries with Zika virus vector-born transmission.	# of pregnant women with confirmed Zika infection who had ultra-sound screening. Source: MoH	# of pregnant women with confirmed Zika infection. Source: MoH
Percentage of countries with a risk communication strategy and/or implementation plan	The availability of a risk communication strategy and/or implementation plan is a distant but measurable surrogate for risk reduction interventions and behavioural changes.	# of countries which have a written communication strategy and/or implementation plan. Source: MoH	# of countries which have reported vector-borne autochthonous Zika virus transmission. Source: WHO
Percentage of countries having routine vector surveillance	Surveillance may serve to identify areas of high-density infestation or periods of mosquito population increase. In areas where the vector is no longer present, entomological surveillance is critical in order to detect new introductions rapidly before they become widespread and difficult to eliminate.	# of countries which have a routine vector surveillance programme in place. Source: MoH or Ministry of environment	# of countries where Zika virus competent vectors are present. Source: WHO or Ministry of environment
Percentage of countries having assessed vector resistance to insecticide	The initial and continued susceptibility of the vector to specific insecticides is of fundamental importance for the success of larviciding or adulticiding operations. The development of resistance may lead to failure of the control programme unless it is carefully monitored and a timely decision is made to use alternative insecticides or control strategies.	# of countries which have assessed insecticide resistance at least once in the past 12 months Source: MoH or Ministry of environment	# of countries where Zika virus competent vectors are present. Source: WHO or Ministry of environment
Percentage of sites with vector control activities that report impact of vector control measures.	All sites with vector control activities should monitor the impact of the interventions, at least with a sentinel site. The impact can be measured by the % decline in the number of larvae or adults collected, depending on the intervention.	# of sites reporting the impact of control measures Source: MoH or Ministry of environment	# of sites where vector control measures are implemented Source: MoH or Ministry of environment

ANNEX D
WHO ZIKA VIRUS RESEARCH AGENDA

As part of the *WHO Zika Virus Research Agenda* and within the WHO's *R&D Blueprint for Action to Prevent Epidemics*[28], WHO has identified research activities in five areas where the Organization is best placed to provide international leadership and to leverage its convening power.

1. CHARACTERIZATION

There is an urgent need to better understand and characterize Zika virus infection and its complications. This including investigating the association between Zika virus infection and its complications and understanding the natural history of disease and pathology.

Key research areas include: epidemiological studies to strengthen global epidemiological data on Zika virus infection and support modelling and future projections of presumed congenital Zika virus syndrome; clinical studies to determine causality and characterization of complications; and laboratory diagnostics.

1.1 Epidemiological studies

1.1.1 Retrospective seroprevalence survey of Zika virus infection in frozen sera kept in bio-bank from other studies, such as clinical trials for vaccine.

1.1.2 Support to prevalence survey in population or communities representative of general population, using PCR and IgG.

1.1.3 Characterization and risk of infection in other countries (baseline of epidemiology of Zika virus, sentinel surveillance activities).

1.2 Clinical studies

1.2.1 Support for development and implementation of cohort studies that will be selected:

i. To explore the risk of adverse outcomes of pregnancy (including all congenital abnormalities) in pregnant women infected with Zika virus infection compared with non-infected women; early pregnancy initiated cohort study of pregnancy outcomes in the context of Zika virus.

ii. Follow-up for at least two years of babies and infant born from infected mother and non-infected mothers.

iii. To study complication of Zika virus infection in adult men and women (autoimmune-mediated disorders such as GBS).

1.2.2 Persistence of Zika virus in body fluids of patients with acute infection or convalescents. Research on viral persistence in a cohort of men and women and regular testing of their body fluids (e.g. blood, semen, vaginal fluids, urine, saliva, breast milk) to explore risk of onwards transmission.

1.2.3 Natural history/clinical characterization studies, including

[28] http://www.who.int/csr/research-and-development/blueprint/en/

biological sampling and follow up of patients with Zika virus infection to understand full spectrum of the virus infection, risk factors and evolution of complications. The study is also expected to provide insights for the timing and means for potential clinical and therapeutic interventions, and to contribute revised case definition for surveillance.

1.3 Laboratory diagnostics

1.3.1 Conduct and maintain a landscape analysis of commercially available tests.

1.3.2 Establish a consultative process to develop a target product profile for Zika virus diagnostics to detect active infection and evidence of prior infection.

1.3.3 Implement an Emergency Assessment procedure for timely availability of quality assured diagnostics for Zika virus.

1.3.4 Develop WHO biological standards.

2. PREVENTION AND CONTROL

1.4 Vaccine development

2.1.1 Conduct and update a landscape analysis of approaches taken by commercial, governmental, academic and any other known entities towards the development of Zika virus vaccine candidates.

2.1.2 Develop a target product profile for a Zika virus vaccine for use in the emergency context and future outbreaks, targeted at the protection of women of child-bearing age and pregnant women.

2.1.3 Develop regulatory considerations for Zika virus vaccines.

2.1.4 Identify barriers to expedite and support the development of prioritised vaccine candidates, and collaborate with partners on the development and provision of reference materials.

2.1.5 Provide technical advice for clinical trials of prioritised candidates.

1.5 Vector control

The vector control research priorities aim at evaluating community directed interventions and establishment of vector control surveillance system

2.1.6 Conduct and update a landscape analysis of commercially available tests.

2.1.7 Maintain landscape and support development of intervention options until sufficient development is achieved for deployment.

2.1.8 Identify operational considerations for comparative and multi-centre controls for vector control trials.

2.1.9 Research on the impact of insecticide resistance on vector control efficacy.

2.1.10 Research on new indicators for entomological surveillance.

2.1.11 Investigations on community-based vector control approaches, taking into account social and cultural differences.

2.1.12 Identification of secondary vectors that may play a role in

Zika virus dynamics.

2.1.13 Support pilot implementation of new vector control tools for Zika virus (e.g. Wolbachia, transgenic mosquitoes).

2.1.14 Evaluation of a prioritized selective vector control approach with existing tools targeting pregnant women.

2.2 Treatment

2.2.1 Conduct and update a landscape analysis of potential therapeutics and small molecule prophylaxis.

2.2.2 Maintain landscape and promote development of intervention options until sufficient regulatory approval.

2.2.3 Establish a Consultative Working Group for the prioritisation of therapeutic and prophylactic candidates.

2.3 Regulatory support

2.3.1 Establish regulatory support for vaccines, diagnostics and therapeutics and prepare and characterize reference reagents.

3. WOMEN, COMMUNITIES AND HEALTH SYSTEMS

3.1 Perceptions and behaviours

3.1.1 Using social science methods, assess perceptions and behaviours related to pregnancy in the context of Zika of a) community members (women, men adolescents) and b) healthcare policymakers, programme managers and service providers. Key issues to be addressed include: perceptions of risk; decision-making paradigms; roles and responsibilities of the health system versus roles and responsibilities of women and their families; pregnancy management and demand for sexual reproductive health services (including attitudes about, access to, and utilisation of contraception and safe abortion, both legal and illegal); care-seeking behaviour during pregnancy and perceptions of quality of care; care for affected children; and perceived psychosocial effects on women, families and communities.

3.1.2 Evaluate the availability of contraception and assess abortion services across health services in relation to demand. Establish a network of sentinel sites to monitor contraceptive trends (demand, supply, utilisation) in Zika virus affected countries.

3.1.3 Coordinate and synthesise community-level operational research (qualitative and quantitative) conducted by partners, including Knowledge, Attitudes and Perceptions (KAP) surveys on Zika virus, prevention, treatment, sexual reproductive health, vector control and other topics as identified during the response.

3.2 Capacity of health system

Research activities will build on country assessments undertaken by PAHO/AMRO and the WHO guidance on Guillain-Barré syndrome, pregnancy management, breast feeding, microcephaly and others.

3.2.1 Bottleneck analysis to determine key barriers, potential drivers and priority issues for improving compliance with the issued guidance and ensuring successful uptake/implementation of the guidance.

3.2.2 Family planning counselling, contraceptive services, post-abortion care and, where legally available, abortion services.

4. COORDINATION AND MANAGEMENT

4.1 Common platform for standardized processes, protocols and tools, and for sharing specimens, data and information

4.1.1 Develop case definitions for surveillance, public health, laboratory and individual diagnosis.

4.1.2 Define full spectrum of complications in newborn clinical data collection and evaluation of surveillance reports to define 'presumed congenital Zika virus syndrome'. Data collection training to describe the broad range of clinical manifestations and abnormalities being observed.

4.1.3 Develop and implement standardized protocols for biological sampling, storage, shipment and transport, and other relevant topics. Support the development of bio-banking.

4.1.4 Develop generic protocols for six types of study that will be implemented by countries to address key research priorities:

- cross sectional prevalence survey
- cohort studies of pregnant women
- cohort studies of neonates and infants
- case control studies for risk factors of microcephaly
- case control studies of GBS
- persistence of Zika virus in body fluids of patients with acute infection.

4.1.5 Generic protocol on natural history/clinical characterization studies, including biological sampling and follow up of patients with Zika virus infection to understand full spectrum of the virus infection, risk factors and evolution of complications. The study is also expected to provide insights for the timing and means for potential clinical and therapeutic interventions, and to contribute revised case definition for surveillance.

4.1.6 Inventory of on-going of research projects and activities on Zika, and observed complications.

4.1.7 Individual patient data (IPD) meta-analysis of pregnant women and adult and infant cohorts in areas with Zika transmission.

4.1.8 Develop platforms to support ongoing systematic reviews of available evidence to contribute to the Zika virus causality framework. Systems should be developed for continuous and efficient updates of the evidence that can be adapted for future outbreaks of new and emerging communicable diseases.

4.2 Training and capacity building for research and public health response

4.2.1 Assess the capacity of health workers to address clinical complications related to Zika Virus including management of pregnant women, management of infants born with neurological complications, including microcephaly management of children and adults with neurological

complications, including Guillain-Barré syndrome.

4.2.2 Evaluate health workforce strategies related to vector control in and around surrounding areas of health facilities.

4.2.3 Call for grants to support countries to address their own research priorities (published by the Special Programme of Research, Development and Research Training in Human Reproduction (HRP)[29] and Special Programme for Research and Training in Tropical Diseases (TDR)[30]).

4.2.4 Coordinate planning and implementation of strengthened laboratory capacity and infrastructure in Zika virus endemic regions.

5. RESEARCH SUPPORT ACTIVITIES

5.1 Ethics

5.1.1 Establish an ethics working group to develop guidance on ethics and Zika virus for public health professionals and researchers that will support surveillance and public health research activities, including for the governance of bio-banks.

5.1.2 Conduct scoping reviews on ethics and Zika virus, including the outcome of relevant ongoing research on ethical issues raised by the Zika virus epidemic.

5.1.3 Support accelerated ethics review at global and regional levels to assure a rapid and timely turnover for all Zika virus related activities (both research and surveillance) that require ethics approval.

5.1.4 Strengthen national research ethics committees to conduct timely and efficient ethics review of Zika virus related research protocols, and national bioethics commissions to provide ethics related advice to their governments.

[29] http://www.who.int/reproductivehealth/about_us/hrp/en/
[30] http://www.who.int/tdr/en/

This report is produced on behalf of the WHO Outbreaks and Health Emergencies Programme and partners.

This document provides the WHO Outbreaks and Health Emergencies's shared understanding of the crisis, including the most pressing health needs, and reflects its joint health response planning.


www.who.int


http://www.who.int/emergencies/zika-virus/en/


@WHO