Zika virus in the South-East Asia Region

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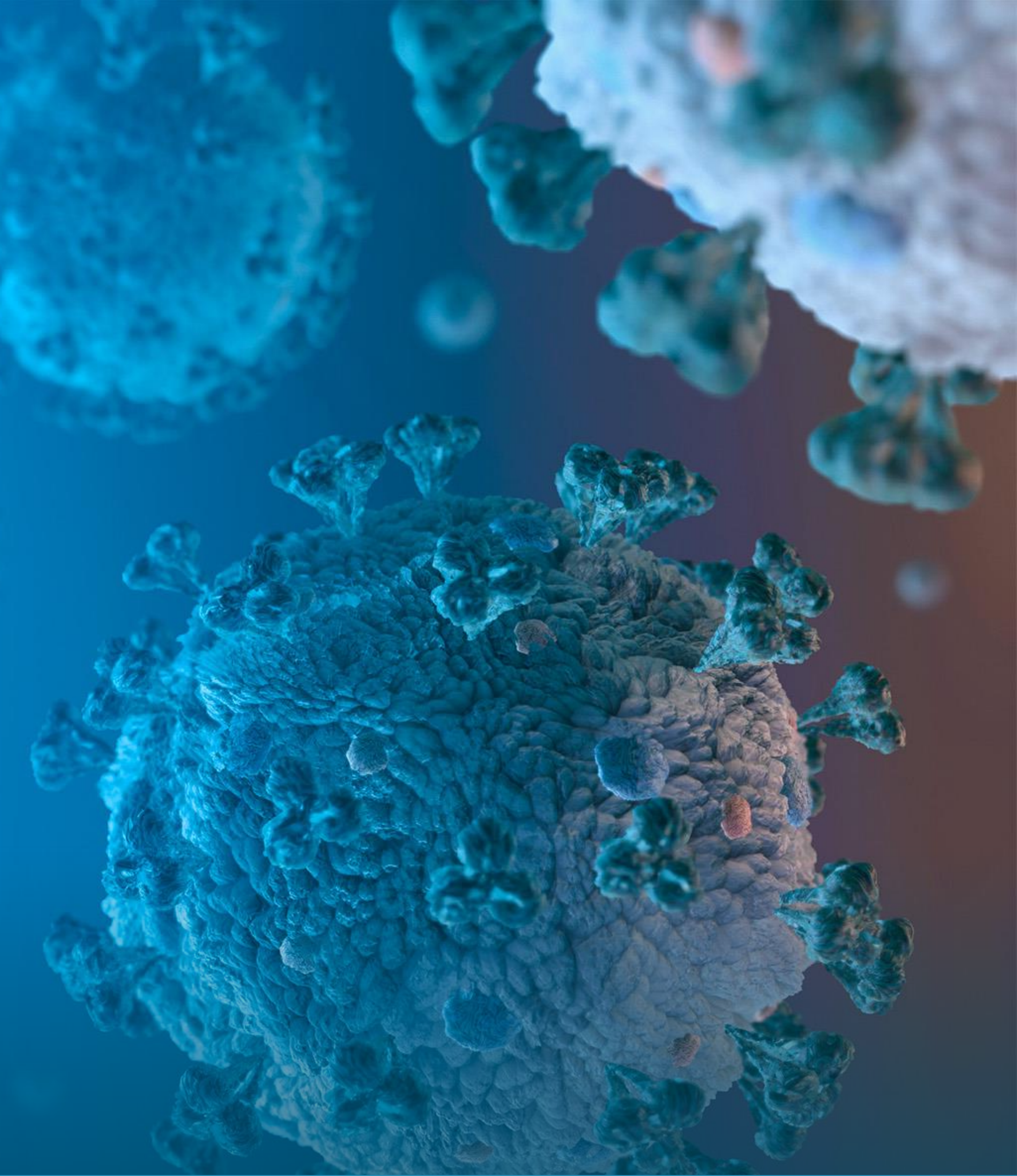


World Health Organization
REGIONAL OFFICE FOR South-East Asia

Reporting of ZIKV infection in South-East Asia

	Country	Year reported
1	Bangladesh	2016
2	Bhutan	
3	DPR Korea	
4	India	1954
5	Indonesia	1981

	Country	Year reported
6	Maldives	2015
7	Myanmar	2016
8	Nepal	
9	Sri Lanka	2023
10	Thailand	2013
11	Timor Leste	

Bangladesh

2016

- First case of ZIKV infection in an old blood sample collected from a 67 years old male who had never been overseas (https://www.reuters.com/article/us-health-zika-bangladesh-idUSKCN0WO0VJ)

India

1954

NIV Pune reported anti-ZIKV antibody in 16.8% of samples tested however, high cross-reactivity with DENV and other flaviviruses

2016

Sentinel surveillance initiated

2017

First cases reported (Ahmedabad, Gujarat and Chennai)

2018

Largest outbreak (283 cases in Rajasthan, Gujarat and Madhya Pradesh)

2021

First reports in Kerala (13 cases)

Outbreaks in Uttar Pradesh and Maharashtra

2022

First report of a case in Karnataka

2023

First report (informal) of a case in Mumbai

Zika virus: Current concerns in India - PMC (nih.gov)
Potential Zika virus spread within and beyond India | Journal of Travel Medicine | Oxford Academic (oup.com
Zika virus in India: past, present and future | QJM: An International Journal of Medicine | Oxford Academic (oup.com)
Zika Virus Disease – India (who.int)
Detection of Zika virus disease in Thiruvananthapuram, Kerala, India 2021 during the second wave of COVID-19 pandemic - PMC (nih.gov)
Frontiers | Zika a Vector Borne Disease Detected in Newer States of India Amidst the COVID-19 Pandemic (frontiersin.org)
79-year-old Mumbai's first Zika patient, recovered fully | Mumbai News - Times of India (indiatimes.com)

Indonesia

1981

First report of Zika virus disease (Central Java)

2013 to 2015

Reported cases among returning travelers

2014

Seroprevalence surveys in 14 provinces: 662 samples from children aged 1-4 years (9.1%) and 870 samples from those aged 5-9 years (9.2%)

2016

Isolation of ZIKV in a 27-year-old male resident, central Sumatra (JMB-185 strain not closely related to the Brazilian ZIKV associated with microcephaly) and may have been circulating in the region, including Indonesia since 2000

https://www.sciencedirect.com/science/article/abs/pii/0035920381901000
The current status of Zika virus in Southeast Asia - PMC (nih.gov)
Zika virus, a cause of fever in Central Java, Indonesia - PubMed (nih.gov)
Zika virus infection acquired during brief travel to Indonesia - PubMed (nih.gov)
ZIKA VIRUS INFECTION IN AUSTRALIA FOLLOWING A MONKEY BITE IN INDONESIA - PubMed (nih.gov)
Isolation of Zika Virus from Febrile Patient, Indonesia - PMC (nih.gov)

Zika Virus Seropositivity in 1-4-Year-Old Children, Indonesia, 2014 - PubMed (nih.gov)
Spatiotemporal Heterogeneity of Zika Virus Transmission in Indonesia: Serosurveillance Data from a Pediatric Population - PMC (nih.gov)
Genomic characterization of Zika virus isolated from Indonesia - ScienceDirect

Maldives

June 2015

- Laboratory-confirmed case of ZIKV disease in a 37 year-old Finnish male who returned home after working for 6 months in Maldives. Developed flu-like symptoms, rash and eye pain. Positive for ZIKV by RT-PCR (in urine sample not in serum). DENV IgG and IgM positive; Dengue NS-1 Negative. (Eurosurveillance | Zika virus infection in a traveller returning from the Maldives, June 2015)

2016 & 2017

- Three cases positive out of 651 cases tested. (https://health.gov.mv/en/publications/situation-update-on-zika-virus-disease-in-the-maldives)

Myanmar

2017

- Analysis of 462 samples from patients and asymptomatic people from 2004-2017: confirmed ZIKV infection among 4.9% of patients with dengue symptoms and 8.6% of asymptomatics (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5930904/)

Sri Lanka

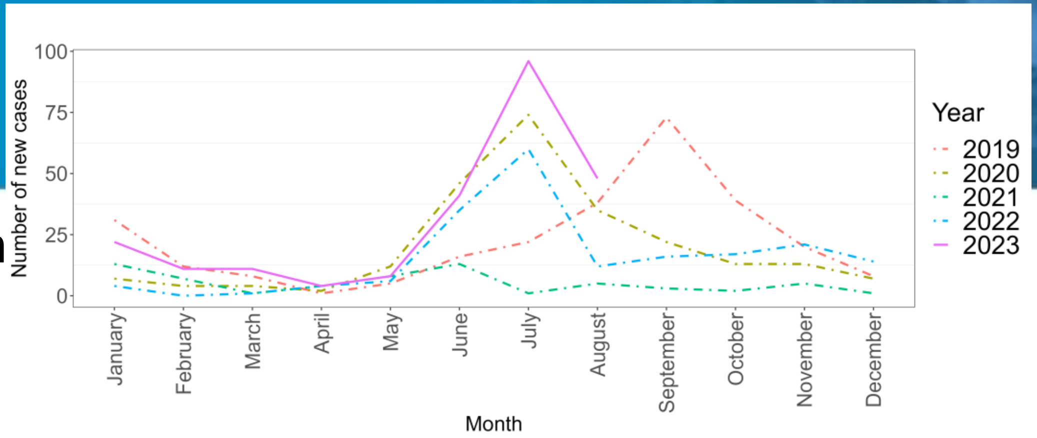
2023

- 595 samples collected from suspected dengue patients from 2017 to 2019 in two tertiary care hospitals: 2.9% of the sample were confirmed of having ZIKV infection (https://www.sciencedirect.com/science/article/pii/S1876034123002484?via%3Dihub)

Thailand

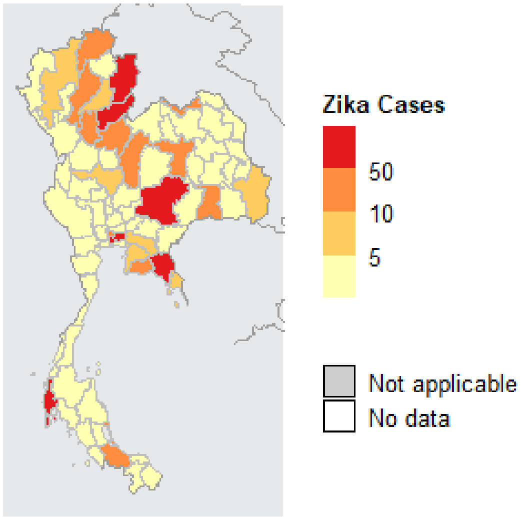
- Endemic in Thailand with peaks in case reporting usually seen in June & July coinciding with the wet season.
- Phylogenetics suggest ZIKV has been circulating in Thailand since at least 2002.
- As of 21 August, 241 cases have been reported in 2023 from 22 provinces with the highest number reported from Chanthaburi (n=76)
- <u>As per the 2016-2022 databases</u>
  - Of 241 ZIKV-infected pregnant women, three delivered babies with microcephaly
  - Of 77 infants born to ZIKV-infected pregnant women, four evidence of developmental abnormalities at 2-year follow-up
  - 15 infants had congenital abnormalities associated with ZIKV infection
  - Five of 145 cases of ZIKV-infection had Guillain-Barré syndrome.

[Long-term circulation of Zika virus in Thailand: an observational study - The Lancet Infectious Diseases]
[Summary of the situation from disease surveillance 506 (moph.go.th)]



Thailand: Zika cases by province

2019-2023



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Data Source: World Health Organization
Map Production: WHO Health Emergencies Programme

Laboratory capacity for diagnosis of arboviral infections

Country	CHIKV					DENV						ZIKV				
Bangladesh*	A	M	G	N	P	A	M	G	N	P						P
Bhutan	A	M	G		P	A	M	G		P						
India	A	M	G		P	A	M	G		P			M			P
Indonesia		M	G		P	A	M	G	N	P	S					P
Maldives					P	A	M	G		P						P
Myanmar	A	M	G			A	M	G		P						
Nepal	A	M	G		P	A	M	G		P						P
Sri Lanka					P	A	M	G		P	S					P
Thailand		M	G	N	P	A	M	G	N	P		A		G	N	P
Timor Leste						A	M	G	N	P	S					

Source: Arboviral surveillance and control capacity survey

A	Antigen
M	IgM
G	IgG
N	Neutralizing Antibody
P	RT-PCR or other nucleic acid amplification test
S	Viral gene/ genome sequencing

Limitations

- Although serological studies suggest the presence of ZIKV infection in the South-East Asia region since as early as 1950's, case reporting is sporadic.
- Serological assays are used in identification of ZIKV infection. They may be cross-reactive with other circulating Flaviviruses (especially, DENV and JEV). Therefore, interpretation of test results should be done cautiously
- Underreporting/ low case detection may happen
  - Non-availability of ZIKV infection surveillance system
  - Less likely to be ZIKV infection to be included in differential diagnosis
  - Asymptomatic, mild, afebrile or atypical presentation
- In this context, the epidemiology of ZIKV and the disease burden in the region is poorly understood

Acknowledgement

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Thank you

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Case, Entomological and Wastewater Surveillance of Zika

A Multi-Disciplinary Approach

30 August 2023

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Environmental Health Institute

WHO Collaborating Centre for Reference and Research of Arbovirus and their Associated Vectors

National Environment Agency

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Re-emergence of Zika in Singapore 2023

After outbreak of ~500 cases in 2016-17, only sporadic cases were reported, with no constant transmission

2016-2017: Large outbreak of more than 500 cases

Outbreak of Zika virus infection in Singapore: an epidemiological, entomological, virological, and clinical analysis

*The Singapore Zika Study Group**

2019: 12 Cases, one small cluster of 3 cases

THE STRAITS TIMES — SINGAPORE

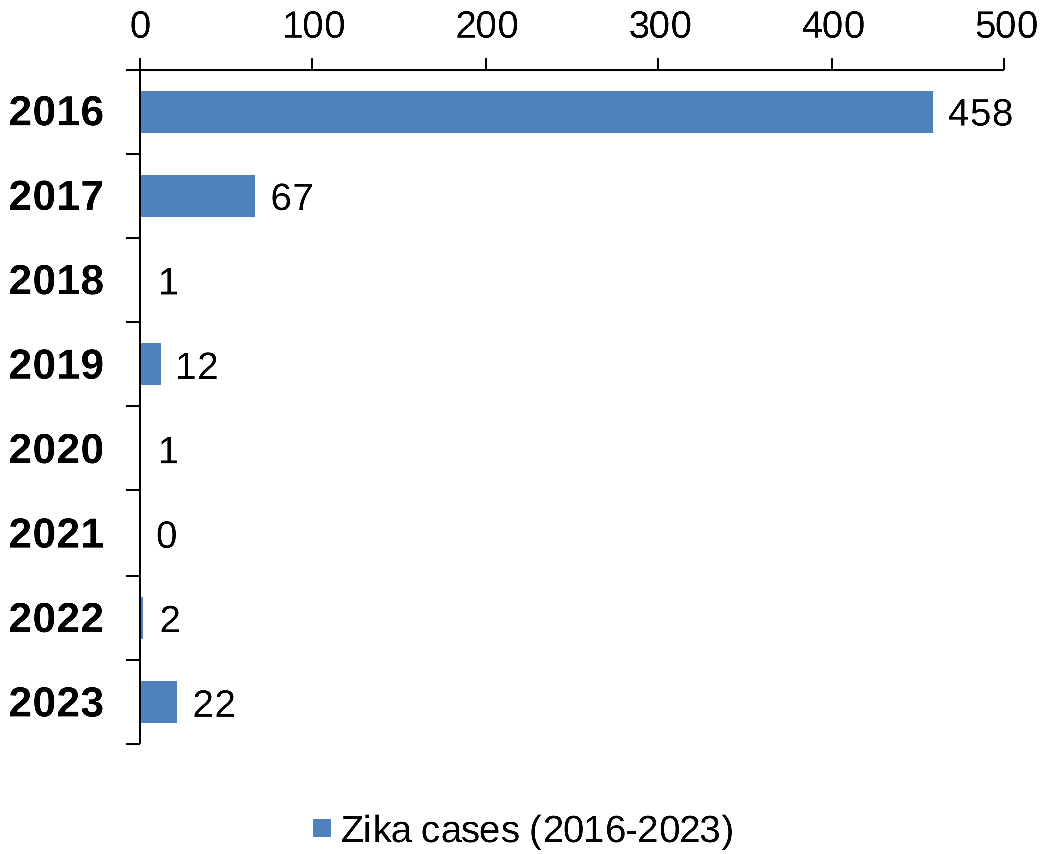
3 Zika cases confirmed in Serangoon Gardens, first cluster in Singapore in 2019

2023: 22 Cases with 15 in one cluster

Singapore

22 Zika cases in Singapore in the first half of 2023: Grace Fu

Most of these were found in a cluster in Kovan, while the remaining cases were isolated.

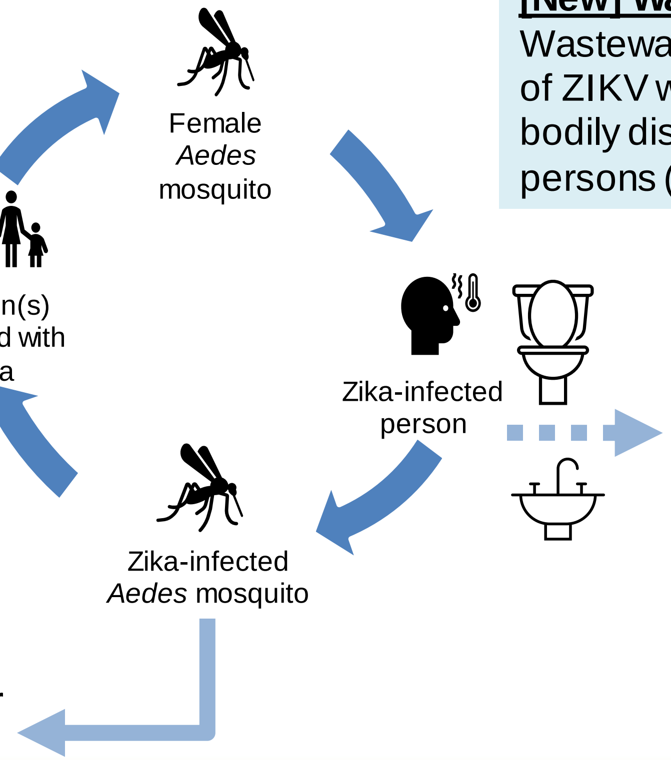


Case, entomological and wastewater surveillance for enhanced monitoring

- Commenced entomological and wastewater testing for Zika virus (ZIKV) RNA in the area of concern
- Leveraged existing capabilities and infrastructure for outbreak monitoring

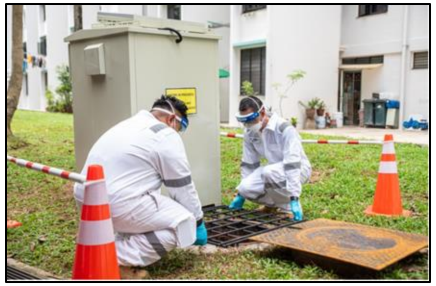
Case Surveillance
- Healthcare practitioners and community alerted of the situation to facilitate early detection

Entomological Surveillance
- Collection and testing of *Aedes* mosquitoes from areas with reported clusters



Gravitrap for *Aedes* mosquitoes

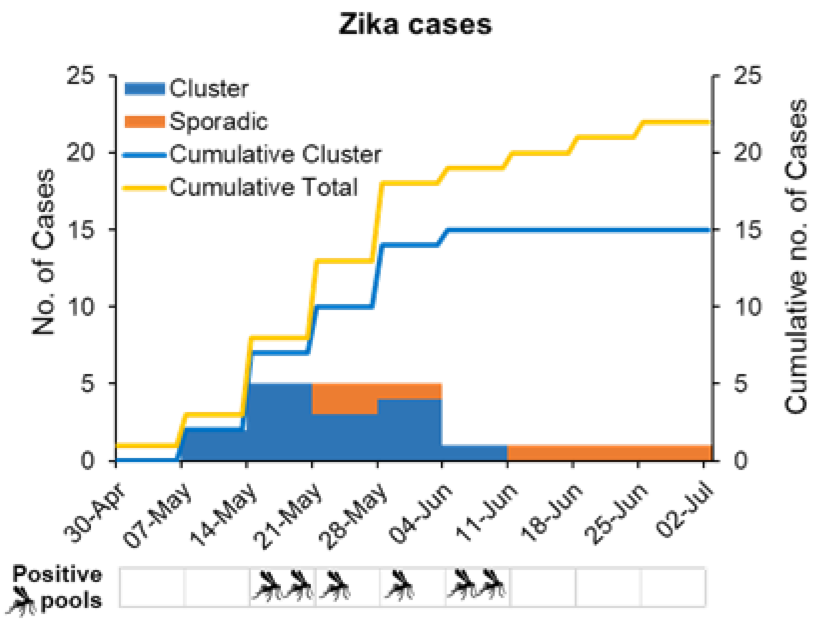
[New] Wastewater Surveillance
Wastewater sampling and testing of ZIKV which may be shed via bodily discharges of infected persons (e.g. urine)

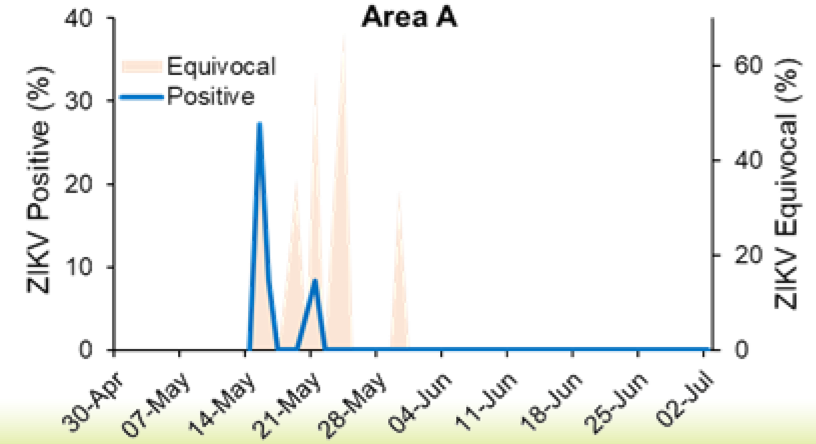


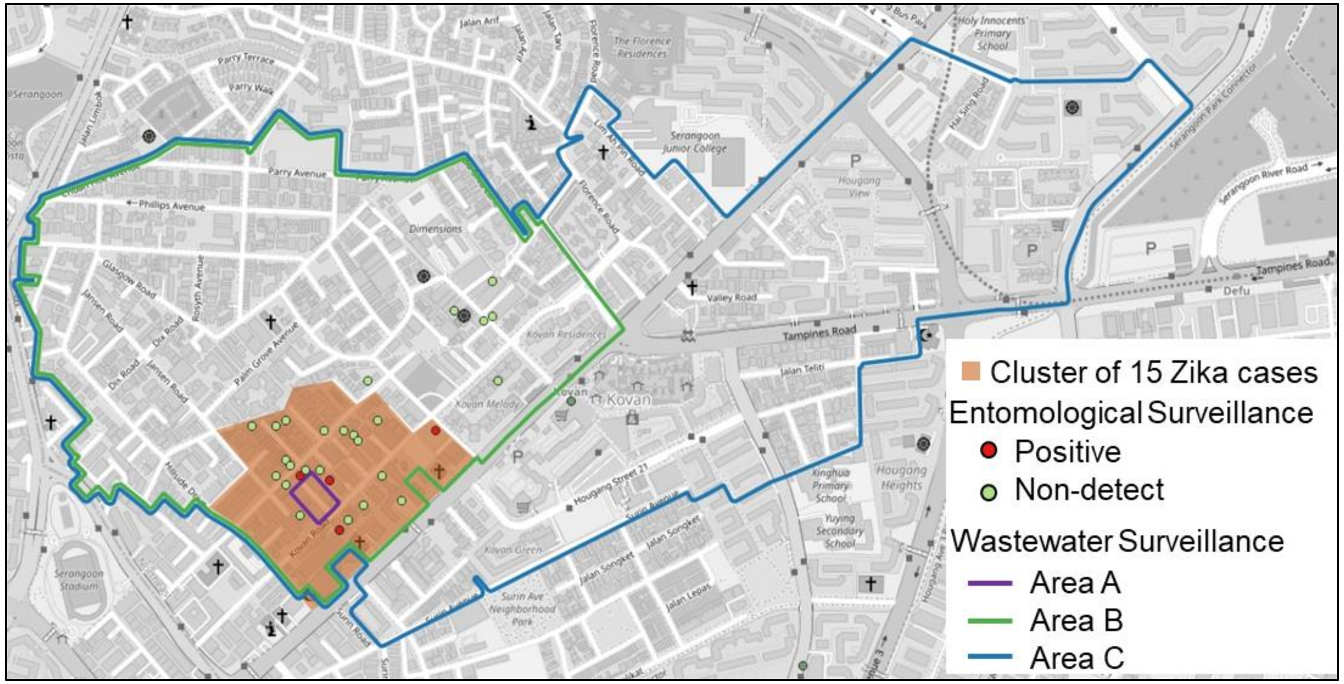
Wastewater Autosampler

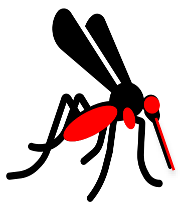
Information guides:
- Risk communications
- Vector control
- Further surveillance

Positive ZIKV wastewater signals corroborates rise in cases at cluster; *A. aegypti* & *A. aegypti* with ZIKV positive heads/thoraces & abdomens





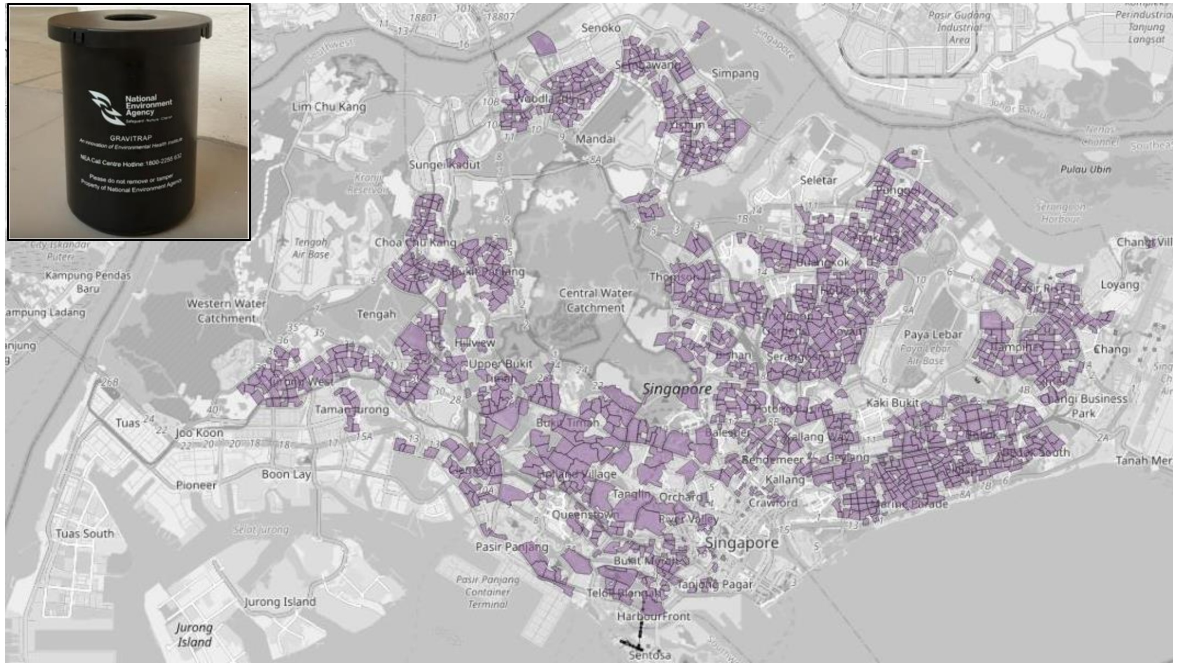




Positive Aedes spp.	Head/thorax & Abdomen	Abdomen	Not able to dissect
A. aegypti	1	0	2
A. albopictus	1	1	1

Non-detection of ZIKV RNA in wastewater & mosquito samples from other sites

Restriction of positive signals to within the neighbourhood suggests limited transmission of Zika



ZIKV RNA not detected in other wastewater samples

- Leveraged COVID-19 wastewater network of 500 autosamplers
- ~3800 samples tested from May – July 23

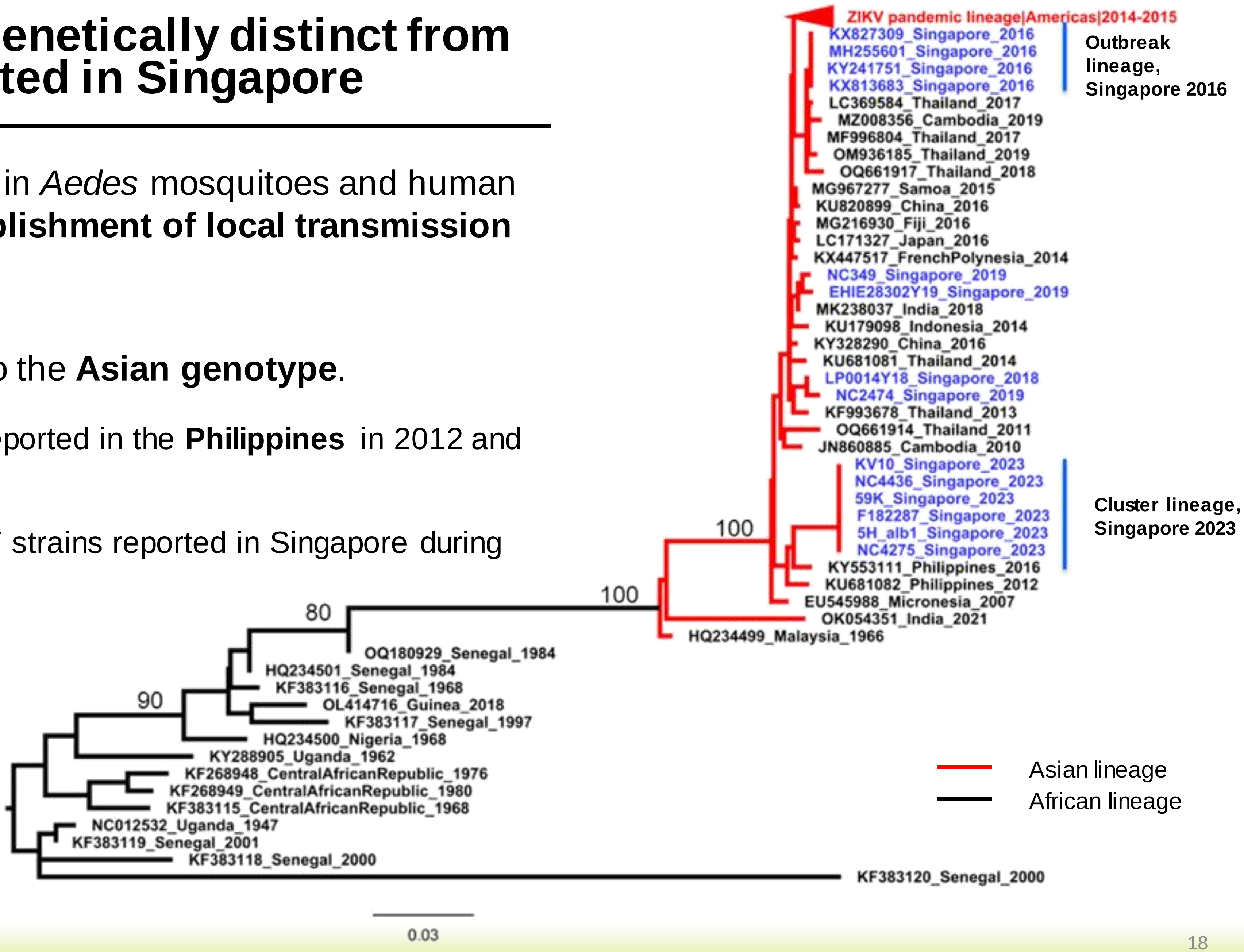
No positive mosquitoes in areas with sporadic cases

- Leveraged network of 70,000 Gravitraps deployed islandwide to monitor *Aedes* population
- Screened only samples from areas with cases
- ~1800 samples from April – July 23

ZIKV strain in 2023 is genetically distinct from previous strains reported in Singapore

- **Identical *E* gene sequences** in *Aedes* mosquitoes and human samples **confirmed the establishment of local transmission of ZIKV**.

- 2023 ZIKV strains belonged to the **Asian genotype**.
    - Genetically closest to ZIKV reported in the **Philippines** in 2012 and 2016.
    - Genetically distinct from ZIKV strains reported in Singapore during the **outbreak in 2016**.



ZIKV envelope gene-based phylogenetic tree constructed with Maximum Likelihood

Summary

- Low seroprevalence of Zika in Singapore
  - 3.3% ZIKV IgG ELISA positive, of which 34% had neutralising antibodies using ZIKV PRNT
  - Serosurvey of ~3,600 healthy blood donors in 2017

- Sporadic cases reported, with no constant Zika transmission

- Presence of competent vectors necessitates case, vector and wastewater surveillance

- Wastewater surveillance as a novel, non-intrusive approach to monitor the spread of Zika

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Zika Virus Disease in the Region of the Americas

Thais H. dos Santos

Advisor, Surveillance & Response to Arboviral Diseases

August 2023

PAHO Pan American Health Organization World Health Organization REGIONAL OFFICE FOR THE Americas

Introduction of Zika Virus in the Region of the Americas, 2014

- **On March 3, 2014, Chile reported autochthonous ZIKAV transmission on Easter Island**. The presence of the virus was detected until June of that year on the island.

- **In March 2015, Brazil reported a large outbreak of exanthematic disease** (7,000 cases between February and April).

- **On April 29 2015, the first cases of Zika were confirmed in the State of Bahia** in the northeast of the country.

- **On May 7, PAHO issued the epidemiological alert "Zika virus infection",** describing the disease and giving recommendations for its surveillance, case management, and prevention and control actions.

Alerta Epidemiológica

Infección por virus Zika

7 de mayo de 2015

La Organización Panamericana de la Salud (OPS) / Organización Mundial de la Salud (OMS) recomienda a sus Estados Miembros que establezcan y mantengan la capacidad para detectar y confirmar casos de infección por virus Zika, tratar a los pacientes, implementar una efectiva estrategia de comunicación con el público para reducir la presencia del mosquito transmisor de esta enfermedad, en especial en las áreas en las que está presente el vector.

Resumen de la situación

https://www.who.int/news-room/feature-stories/detail/the-history-of-zika-virus

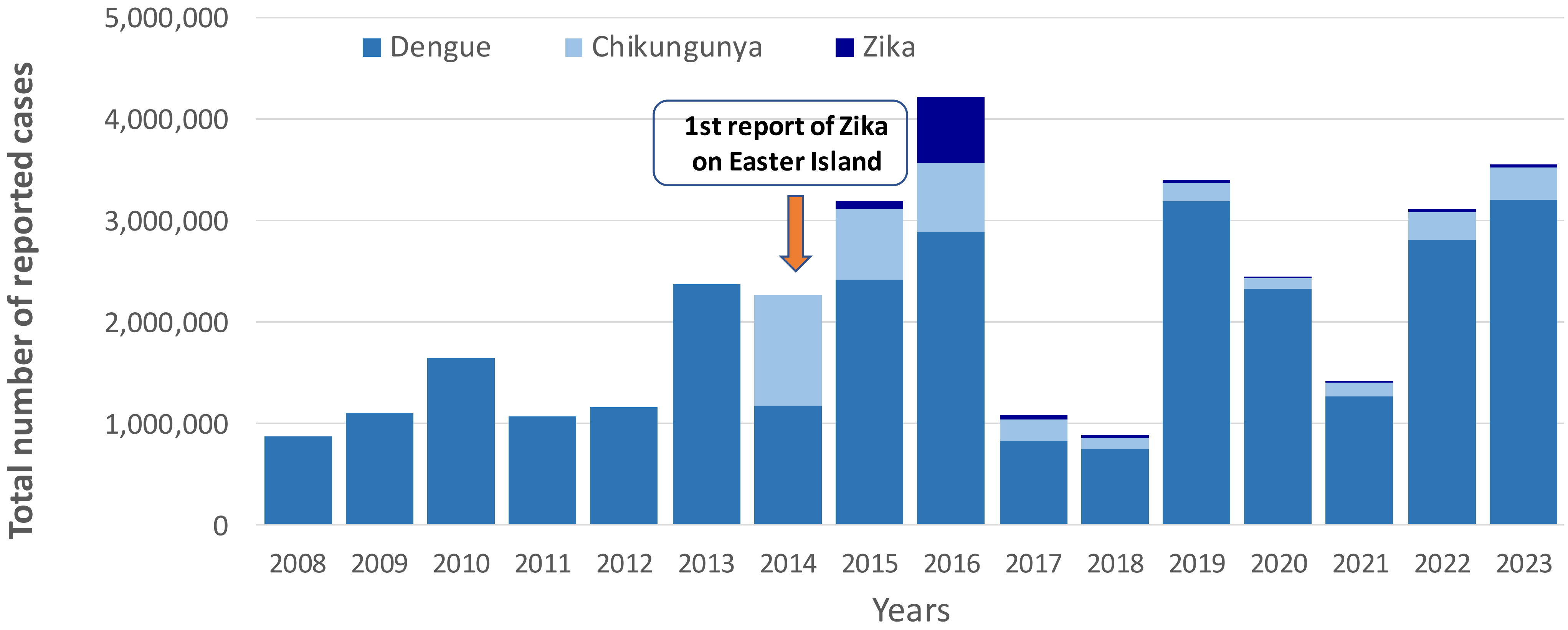
Association of Zika Virus with Guillain-Barré Syndrome and Microcephaly

- On July 9, 2015, Brazil described an association between ZIKAV infection and Guillain-Barré syndrome; 26 cases of GBS with confirmation of Zika were identified in Bahia.
- On October 23 of the same year, the country notified PAHO of an unusual increase in microcephaly cases since August and identified its association with Zika infection.
- In Brazil, as of week 1 of 2016, **3,530 cases of microcephaly** were registered (including 436 deaths), the annual average from 2010 to 2014 was **163 cases**.
- The observed increase in neurological disorders and neonatal malformations led to the declaration of a **Public Health Emergency of International Concern on February 1, 2016**

GBS and other neurological complications

Congenital Zika Syndrome

Total Number of Reported Cases of Arboviruses in the Region of the Americas, 2008 – 2023 (EW31)



- In the period from 2015 to 2023, **cases of Zika virus disease represent 5.78% of reported cases of arboviral diseases**

Fuente: Plataforma de Información en Salud (PLISA)

Spread of Zika Virus in the Region of the Americas, 2015-2016

October 2015

October-December 2015

January-March 2016

April – June 2016

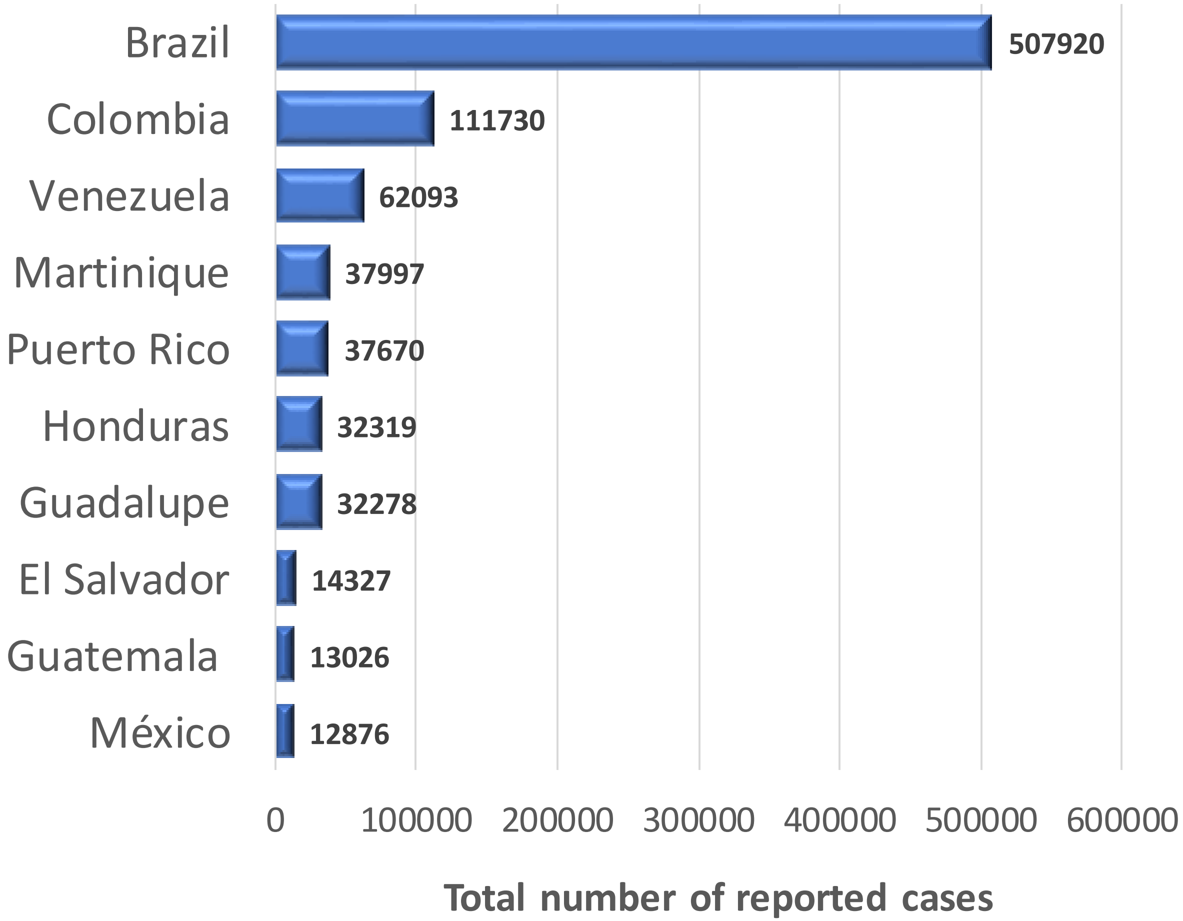
July-September 2016

October-December 2016

- From 2015 to 2016, 48 countries were affected

https://www.ais.paho.org/phip/viz/ed_zika_countrymap.asp

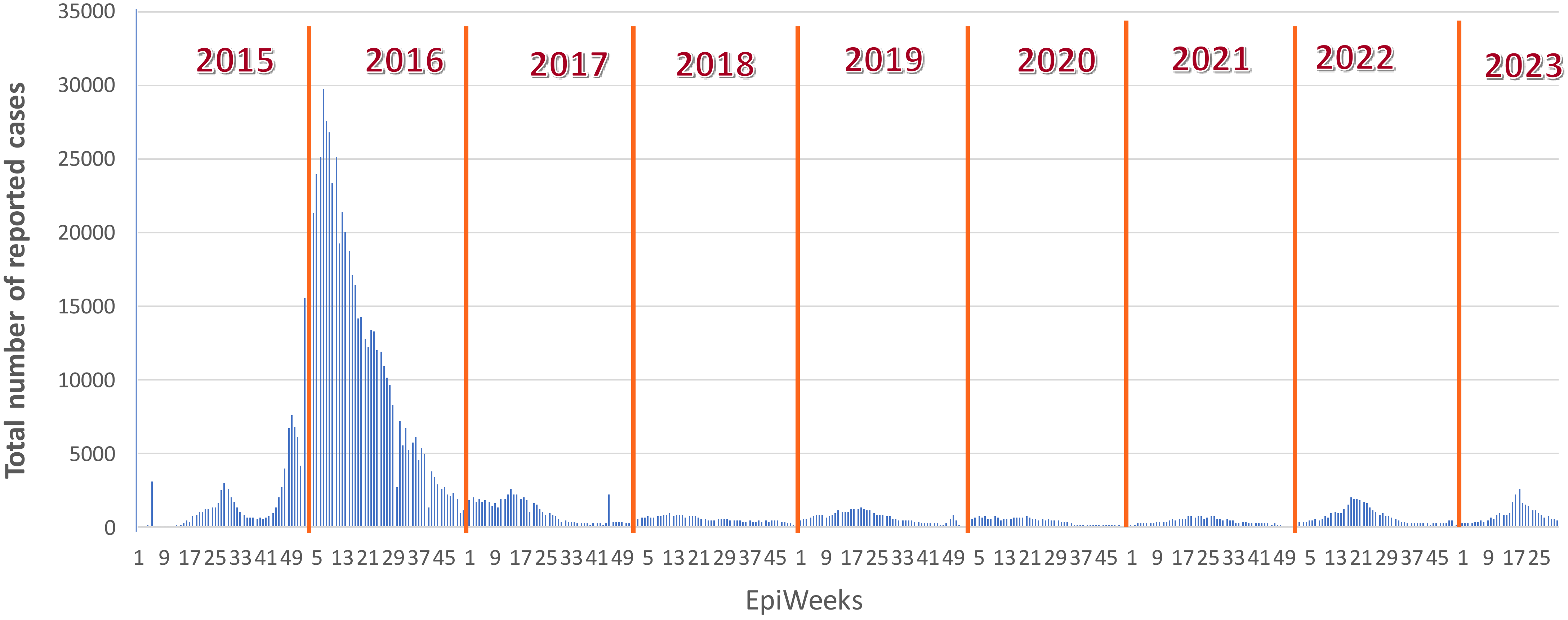
Zika Virus Disease Cases in Most Affected Countries in the Region of the Americas, 2014-2023(EW31)



- ❑ Ten countries concentrate 89% (862,236) of the cases of Zika virus disease reported in the Region in the period from 2014 to 2023 (EW31).
- ❑ In the period, Brazil concentrated 52% (507,920) of the cases in the Region, followed by Colombia with 12% and Venezuela with 6%.
- ❑ Martinique and Guadeloupe have the highest incidence due to the epidemics that occurred in 2016; subsequently no case report
- ❑ Although Brazil reports the highest number of Zika cases, it ranks fourth in incidence with 57 cases per 100,000 population.

Source: Health Information Platform (PLISA), PAHO /OMS

Zika Virus Disease Cases in the Region of the Americas, 2015 - 2023 (EW31)



- Since its initial detection, 935,9999 cases of Zika were reported (27% only have been lab confirmed, 8-35)
- 78% of cases were reported in the years 2015 and 2016
- The highest incidence occurred in 2016 with 67.5 cases per 100,000 pop, compared to 2.76 per 100,000 pop for 2023

Source: Health Information Platform (PLISA), PAHO /OMS

Case Definition (2022)

Case	Definition
Suspected case+	A person who has a sudden-onset exanthema* that is not explained by other medical conditions and who (or his or her sexual partner) resides in or has visited epidemic or endemic areas during the two weeks prior to the onset of symptoms and has two or more of the following: **1.** Itching **2.** Conjunctivitis (non-purulent/hyperemic) **3.** Joint pain **4.** Myalgia **5.** Periarticular edema **6.** Fever
Probable case	Suspected case of Zika that also has: • Detection of anti-ZIKV IgM in a single serum sample (collected during the acute or convalescent phase), with negative results for other endemic flaviviruses *or* • Epidemiological link to a confirmed case
Confirmed case	Patient who meets the criteria of a suspected case and has laboratory confirmation of recent ZIKV infection, i.e., presence of: • ZIKV RNA or isolation in serum or other samples (e.g., urine, saliva, tissues or whole blood, CSF), or • positive anti-ZIKV IgM antibodies and plaque reduction neutralization test (PRNT) for ZIKV titers ≥10 and without titers for other flaviviruses, or • In deceased patients, molecular detection of the viral genome from autopsy tissue, fresh or paraffin with in situ hybridization tests.

+ A suspected case is also considered to be any pregnant woman who has an acute onset exanthema* that is not explained by other medical conditions and who (or her sexual partner) resides in or has traveled in the previous 14 days to an area with Zika transmission. Do confirmatory testing for Zika and other exanthematous diseases (e.g., measles, rubella).

* The exanthema is usually maculopapular, cephalocaudal distribution and accompanied by pruritus.

PAHO Pan American Health Organization World Health Organization Americas

PAHO 120th ANNIVERSARY

Considerations

- With the exception of Canada, Chile (Mainland), and Uruguay, all countries and territories in the Region of the Americas have reported autochthonous cases of Zika virus disease.
- The years of 2015 and 2016 were the years with the highest number of cases; 78% of cases since the introduction of ZIKAV to the Region
- Despite the reduction in incidence since 2016, it is necessary to maintain continued information sharing, even in light of waning interest and considering the accumulation of susceptible people
- It is necessary to establish a system for detection and reporting of cases with neurological conditions and congenital malformations associated with ZIKAV
- An adequate and sufficient laboratory diagnosis must be maintained for the timely detection of ZIKAV circulation that guides control actions.

PAHO 120th ANNIVERSARY

Thank you
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Obrigada
Merci

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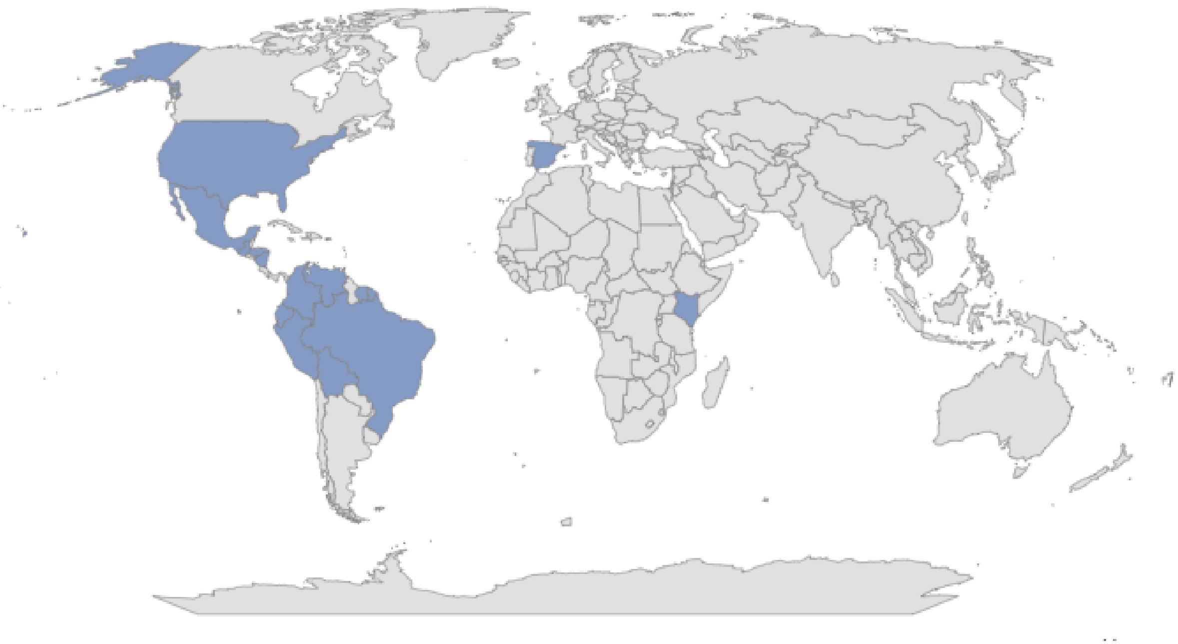
ZIKV IPD-MA Project

EPI-WIN WEBINAR
Zika virus



Ricardo Ximenes

On behalf of the WHO IPD-MA group

ZBC-Consortium

Zika Brazilian Cohorts Consortium

human reproduction programme hrp 50
research for impact
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ZIKV IPD-MA Objectives

Objective 1

Estimate the **absolute and relative risks of fetal infection**; **miscarriage** (<20 weeks gestation), **fetal loss** (≥ 20 weeks gestation**), microcephaly**, and **other manifestations** of CZS and later developmental delays for women who do and do not experience ZIKV infection during pregnancy.

Objective 2

Identify **factors that modify** women's risk of adverse ZIKV-related fetal, infant, and child outcomes and infants' risk of infection (e.g. **gestational age** at time of infection, **clinical or subclinical illness**, concurrent or prior **arbovirus exposure**, other **congenital infections**, and other posited effect measure modifiers).

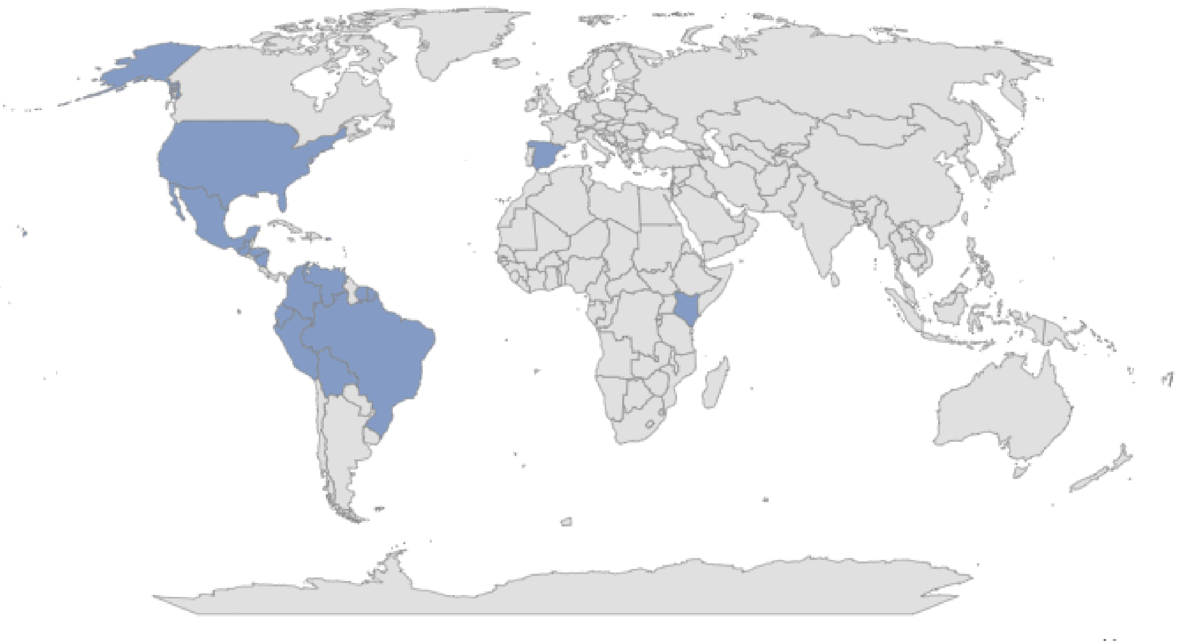
Objective 3

Use information on the relative importance of different effect measure modifiers identified in Objective 2 to **decompose the total effect** of ZIKV infection during pregnancy on adverse fetal, infant and child outcomes into (1) **the direct effect of ZIKV**; (2) **the indirect effect of ZIKV** as mediated by the effect measure modifier of interest (eg, DENV, CHIKV or STORCH pathogens) and (3) **the effect of the interaction** between ZIKV and the mediator of interest.

Objective 4

Develop and validate a **risk prediction tool** to identify pregnant women at **a high risk of an adverse ZIKV related outcome** and to inform couples planning a pregnancy, healthcare providers and/or resource mobilization (eg, vector control strategies; antenatal care; open access to contraception).

ZIKV IPD-MA Project Overview



human reproduction programme hrp 50

research for impact

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64 **participating sites**

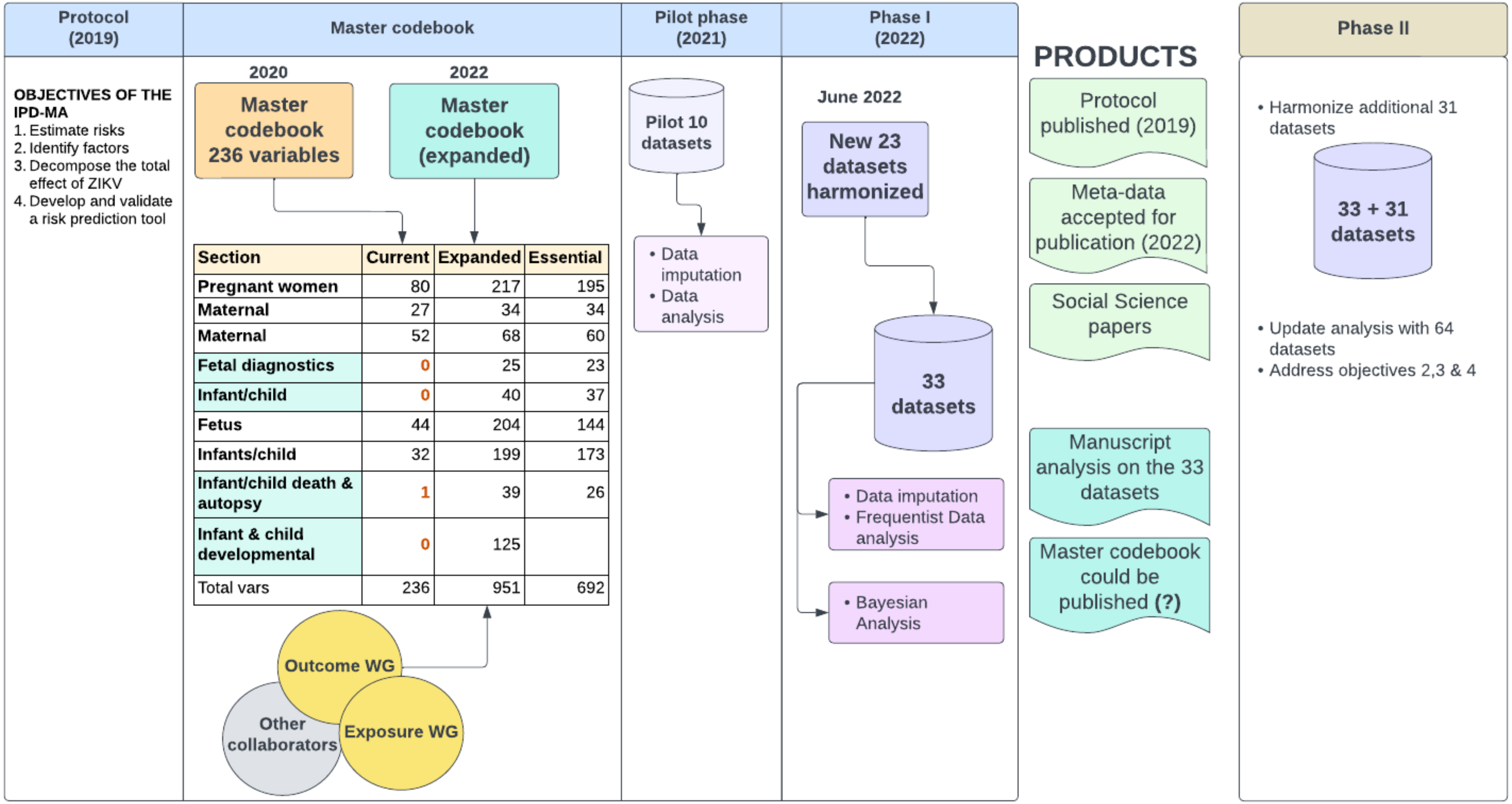
22 **participating countries and territories**

33,061 **pregnant women**

11,030 **ZIKV+ pregnant women**

18,281 **children**

Milestones and Future Work



Section	Current	Expanded	Essential
Pregnant women	80	217	195
Maternal	27	34	34
Maternal	52	68	60
Fetal diagnostics	0	25	23
Infant/child	0	40	37
Fetus	44	204	144
Infants/child	32	199	173
Infant/child death & autopsy	1	39	26
Infant & child developmental	0	125	
Total vars	236	951	692

ZBC-Consortium

Zika Brazilian Cohorts Consortium

Objective

To estimate the **risk of adverse outcomes** among offspring of women with **RT-PCR-confirmed ZIKV infection** during pregnancy and to **explore heterogeneity** between studies

Ximenes et al., Microcephaly Epidemic Research Group (MERG). Zika virus infection in pregnancy: Establishing a case definition for clinical research on pregnant women with rash in an active transmission setting. PLoS Negl Trop Dis. 2019 Oct 7;13(10):e0007763. doi: 10.1371/journal.pntd.0007763. PMID: 31589611; PMCID: PMC6797234.
Ximenes RAA, Miranda-Filho DB *et al.* , Risk of adverse outcomes in offspring with RT-PCR confirmed prenatal Zika virus exposure: An individual participant data meta-analysis of 13 cohorts in the Zika Brazilian Cohorts Consortium. Lancet Reg Health Am. 2023 Jan;17:100395. doi: 10.1016/j.lana.2022.100395. Epub 2022 Nov 28. PMID: 36714276; PMCID: PMC9880800.

Zika Brazilian Cohorts Consortium

ZBC-Consortium

Cohort	Study population	Recruitment dates	ZIKV RT-PCR + pregnant women, n (%)
North Region			**404 (26.0%)**
Belém	Pregnant women with rash	October 2015–December 2017	82 (5.3%)
Manaus	Pregnant women with rash	December 2015–January 2017	322 (20.7%)
Northeast Region			**157 (10.1%)**
Campina Grande	Pregnant women with rash	November 2015–October 2016	33 (2.1%)
Recife - MERG	Pregnant women with rash	December 2015–June 2017	108 (7.0%)
Salvador	Pregnant women with rash	February 2016–November 2016	16 (1.0%)
Central-West Region			**87 (5.6%)**
Tangará da Serra	Pregnant women with rash	January 2016–December 2016	36 (2.3%)
Goiânia	Pregnant women with rash	March 2017–March 2019	51 (3.3%)
Southeast Region			**900 (58.2%)**
Rio de Janeiro – Ped UFRJ	Pregnant women with rash	November 2015–May 2016	30 (1.9%)
Rio de Janeiro – DMP UFRJ	Pregnant women with rash	April 2016–Present	7 (0.4%)
Rio de Janeiro – IFF-Fiocruz	Pregnant women with rash	September 2015–March 2017	241 (15.6%)
São José do Rio Preto	Pregnant women with rash	February 2016–June 2016	57 (3.7%)
Jundiaí	Pregnant women with high-risk and/or rash	March 2016–August 2018	55 (3.6%)
Ribeirão Preto	Pregnant women with rash	December 2015–July 2016	510 (33.0%)
Total			**1548 (100.0%)**

Abbreviations: DMP UFRJ, Departamento de Medicina Preventiva, Universidade Federal do Rio de Janeiro; IFF-Fiocruz, Oswaldo Cruz Foundation's Fernandes Figueira Institute; MERG, Microcephaly Epidemic Research Group; PED UFRJ, Departamento de Pediatria, Universidade Federal do Rio de Janeiro.

Table 1: Women with RT-PCR-confirmed ZIKV infections during pregnancy participating in studies of the ZBC-Consortium.

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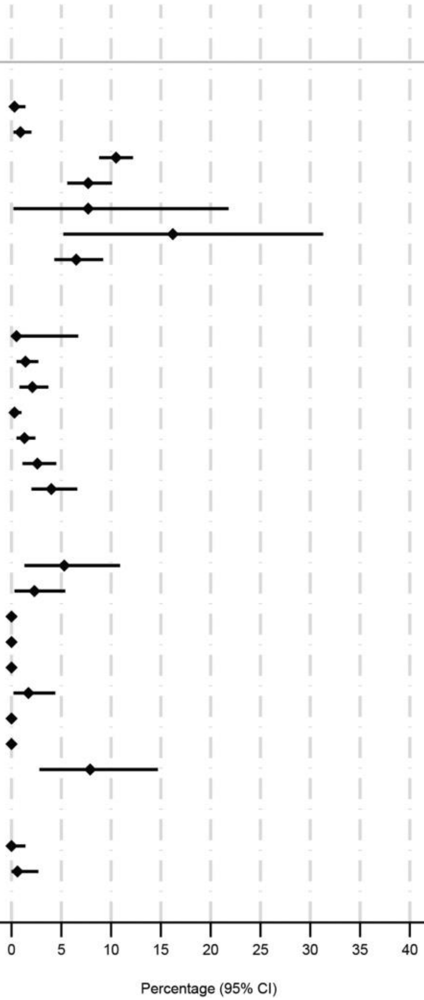
Group and outcome	Timing	Cases	Total	Absolute risk (95% CI)
OUTCOME AT DELIVERY				
Stillbirth	Birth assessment	25	1557	0.300 (0.000, 1.400)
Miscarriage	At the end of pregnancy	38	1557	0.900 (0.200, 2.000)
Preterm Delivery (<37 weeks)	Birth assessment	166	1459	10.500 (8.800, 12.200)
Low Birthweight (<2500g)	Birth assessment	125	1466	7.700 (5.600, 10.100)
Low Birthweight (<=-2SD)	Birth assessment	120	1341	7.700 (0.200, 21.800)
Small for Gestational Age	Birth assessment	197	1341	16.200 (5.200, 31.300)
Large for Gestational Age	Birth assessment	104	1341	6.500 (4.300, 9.200)
MICROCEPHALY AND CRANIOFACIAL DISPROPORTION				
Craniofacial Disproportion	First assessment	11	330	0.500 (0.000, 6.700)
Moderate Microcephaly	First assessment	24	1059	1.400 (0.500, 2.700)
Moderate Microcephaly	Any assessment	35	1124	2.100 (0.800, 3.700)
Severe Microcephaly	First assessment	13	1059	0.300 (0.000, 1.000)
Severe Microcephaly	Any assessment	28	1124	1.300 (0.500, 2.400)
Microcephaly of Any Severity	First assessment	37	1059	2.600 (1.100, 4.500)
Microcephaly of Any Severity	Any assessment	63	1124	4.000 (2.000, 6.600)
NEUROIMAGING OUTCOMES				
Calcifications	First assessment	27	565	5.300 (1.300, 10.900)
Ventriculomegaly	First assessment	18	565	2.300 (0.300, 5.400)
Cerebellum Hypoplasia/Atrophy	First assessment	5	565	0.000 (0.000, 0.500)
Corpus Callosum Agenesis or Dysgenesis	First assessment	3	565	0.000 (0.000, 0.100)
Corpus Callosum Hypoplasia	First assessment	1	565	0.000 (0.000, 0.001)
Diffuse Cortical Atrophy	First assessment	16	565	1.700 (0.200, 4.400)
Mega Cisterna Magna	First assessment	4	565	0.000 (0.000, 0.300)
Lissencephaly	First assessment	1	565	0.000 (0.000, 0.001)
At Least One Abnormal Result*	First assessment	27	565	7.900 (2.800, 14.700)
ARTHROGRYPOSIS AND ORTHOPEDIC ALTERATION				
Orthopedic alteration	First assessment	7	391	0.000 (0.000, 1.400)
Arthrogryposis	First assessment	5	248	0.600 (0.000, 2.700)



The absolute risk

<u>Microcephaly</u>

- At birth or at the first evaluation: **2.6%**
- At any time during follow-up: **4.0%**

The risk of severe microcephaly < than that of moderate microcephaly

<u>Brain imaging abnormalities</u>

- At least one: **7.9%**
  - Calcification: 5.3%
  - Ventriculomegaly: 2.3%

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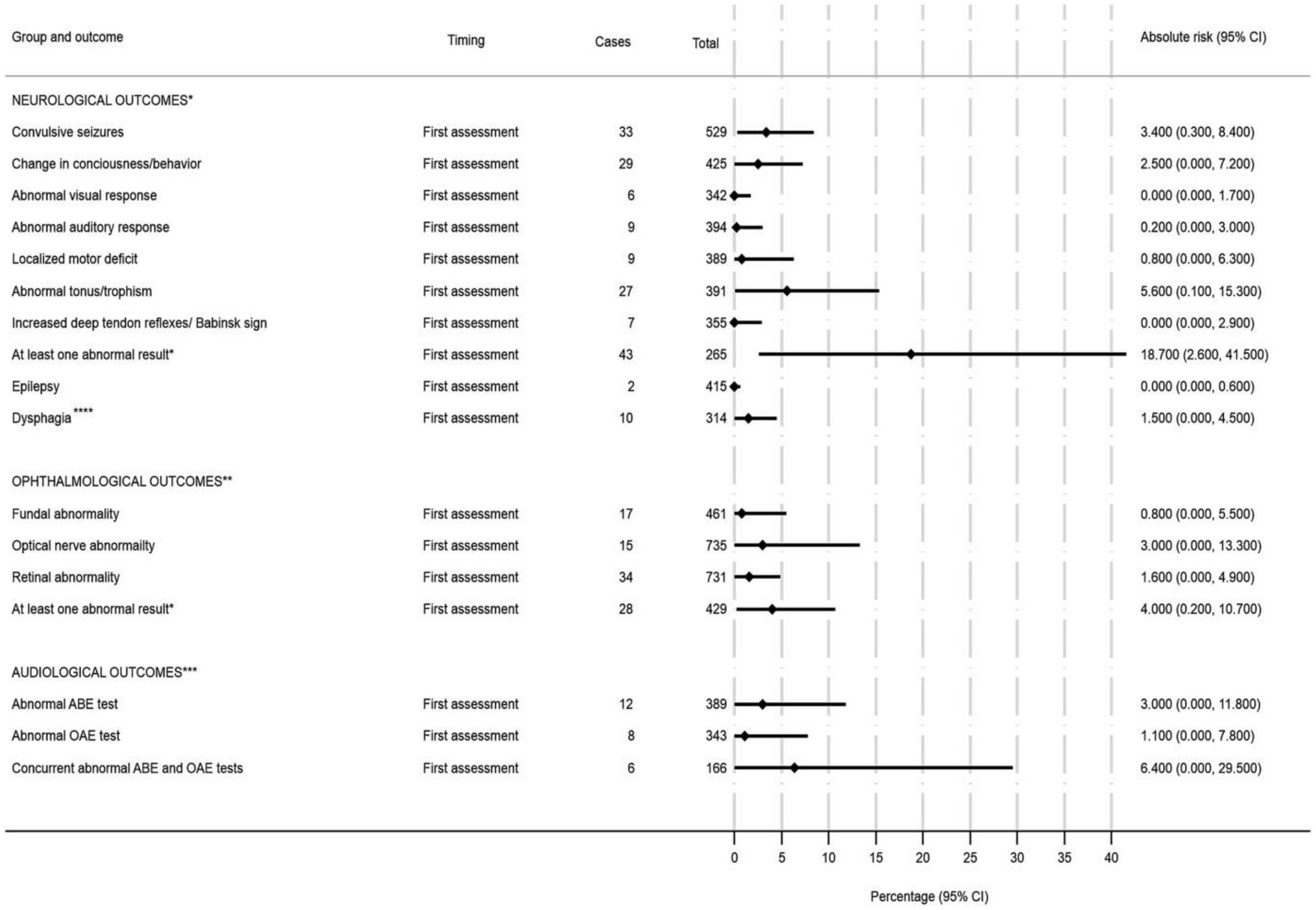

The absolute risk

Neurological outcomes

- At least one abnormal result: **18.7%**

abnormal tonus/trophism: 5.6%
convulsive seizures : 3.4%
change in consciousness/behavior: 2.5%

Ophthalmological outcomes: **4.0%**

Audiological outcomes: **6.4%**

Overall risk (at least one: microcephaly, neuroimaging, neurological, or ophthalmic abnormalities)

- at first evaluation: **24.7%**
- At any time: **31.5%**

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	Microcephaly at birth or first evaluation		
	n/N (%)	OR (95% CI)[b]	p-value
Timing of infection in pregnancy[a]			
First trimester	18/169 (10.6%)	7.52 (2.75–20.6)	<0.001
Second trimester	7/364 (1.9%)	1.23 (0.42–3.57)	0.706
Third trimester	7/441 (1.5%)	1.0	
Missing trimester	5/85	–	–
Highest educational attainment			
Primary education	12/362 (3.3%)	0.80 (0.27–2.30)	0.673
Secondary education	16/382 (4.2%)	1.01 (0.36–2.83)	0.978
University or postgraduate	5/121 (4.1%)	1.0	–
Missing education	4/193	–	–
Skin color			
Branca (White)	16/348 (4.6%)	1.0	–
Parda (Mixed)	8/270 (3.0%)	0.56 (0.22–1.42)	0.219
Preta (Black)	4/79 (5.1%)	1.11 (0.29–4.21)	0.876
Other	0/8 (0%)	–	–
Missing skin color	6/354	–	–
Region			
Northeast	6/115 (5.2%)	1.0	–
North	8/128 (6.2%)	1.21 (0.41–3.60)	0.730
Central-West	3/83 (3.6%)	0.68 (0.17–2.81)	0.595
Southeast	20/732 (2.7%)	0.51 (0.20–1.29)	0.158

	Brain imaging abnormalities after birth		
	n/N (%)	OR (95% CI)[b]	p-value
Timing of infection in pregnancy[a]			
First	25/138 (18.1%)	17.1 (3.82–76.6)	<0.001
Second	12/254 (4.7%)	3.66 (0.79–17.0)	0.098
Third	2/154 (1.3%)	1.0	

[a]Timing of infection was based on date of rash and/or positive ZIKV RT-PCR test. [b]Estimated using multilevel mixed effects logistic regressions allowing for within-study correlations.

Table 3: Associations (i) between microcephaly and trimester of infection, maternal education, skin color, and geographic region and (ii) between brain imaging abnormalities and trimester of infection in children born to women with RT-PCR-confirmed ZIKV infections during pregnancy participating in studies of the ZBC-Consortium.

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Added value of this study

- **One-third of liveborn children** with prenatal ZIKV exposure present with **at least one abnormality** compatible with congenital infection
- Birth evaluations may **underestimate** the risk of **ZIKV-related microcephaly.**
- The risk of **ZIKV-related microcephaly** is relatively **homogeneous** across study sites and does not appear to be modified across geographic, educational, or racial/ethnic groups.

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Implications of this study

- Need of a **multi-disciplinary health team** available to prenatally exposed children born during the Zika pandemic of 2015–2017.

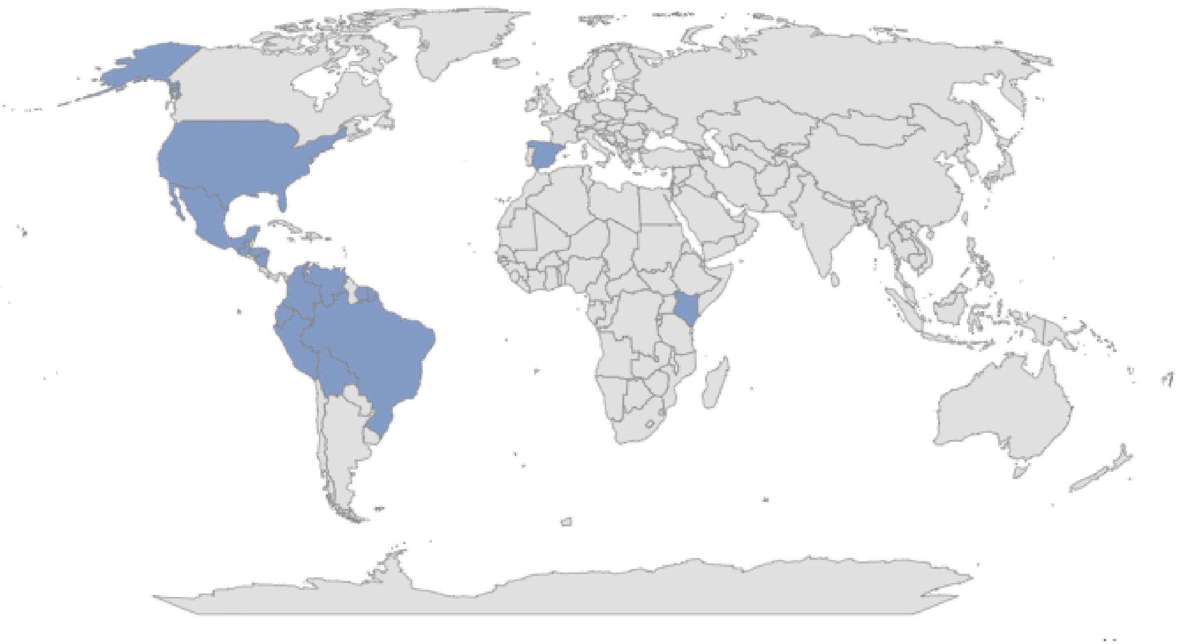
- Study of **the long-term consequences** of Zika virus infections during pregnancy for school-aged children and their families in Brazil.

- Efforts toward developing affordable and accurate **ZIKV diagnostic and screening tests** remain critically important.

- The use of these tests for **early detection** of circulating ZIKV **in communities** to enable rapid deployment of public health measures for averting new epidemics

ZIKV IPD-MA Project

EPI-WIN WEBINAR
Zika virus



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