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Zika Virus Outbreak & Zika Congenital Syndrome

Regional Situation and Response

PAHO

Regional Meeting on the IBP Initiative, 15 June 2016
Lima, Peru

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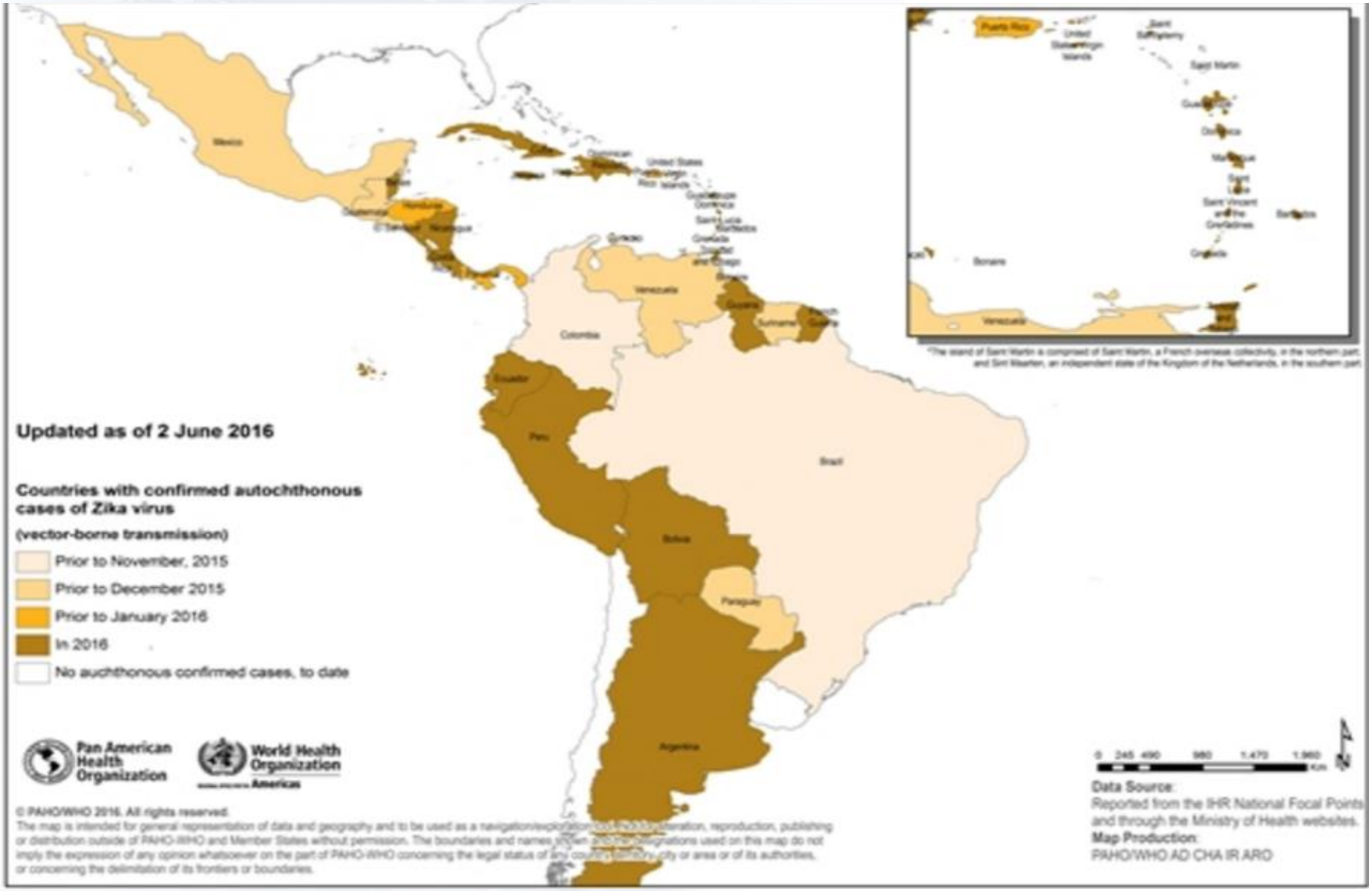
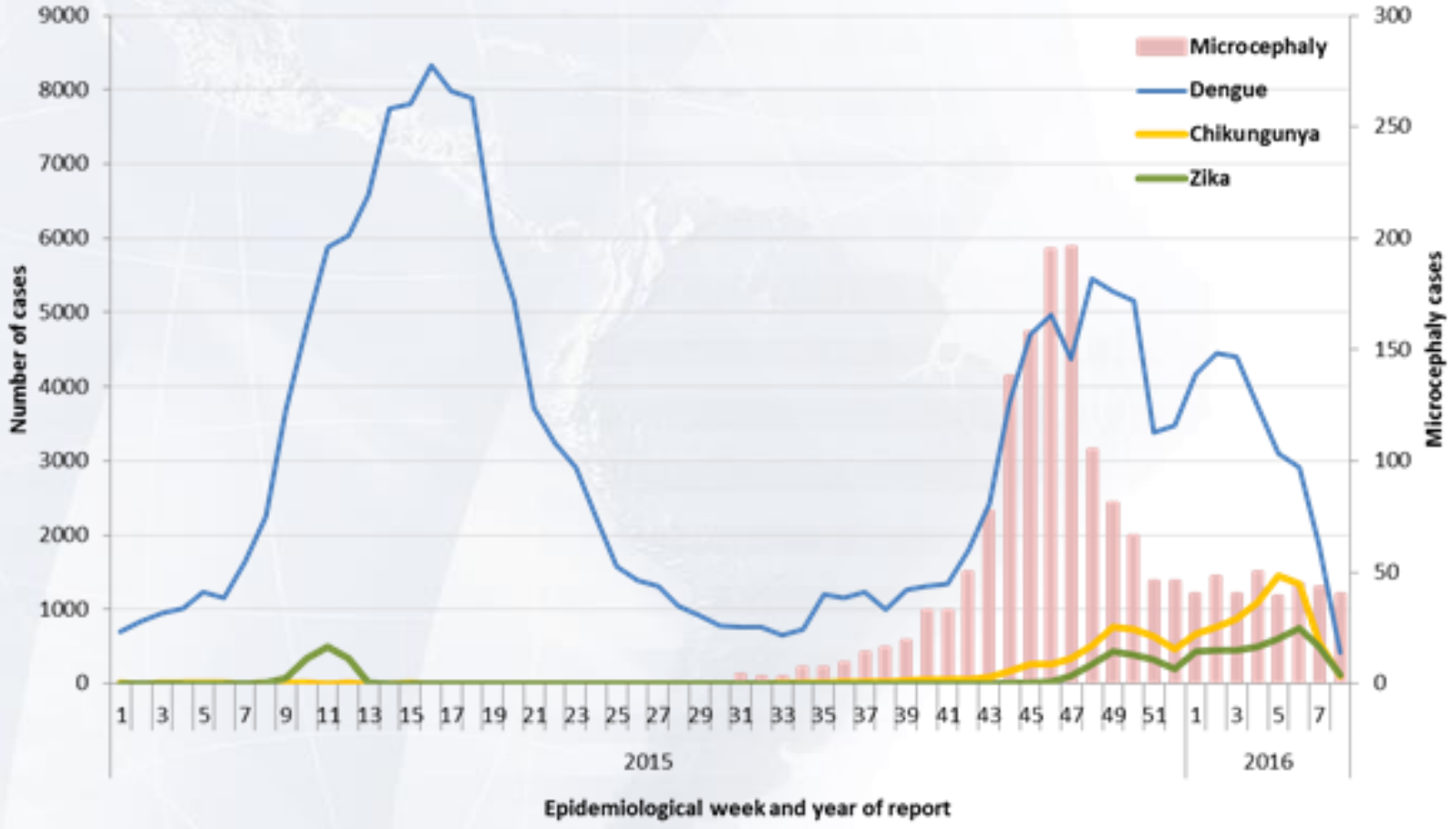
ZIKV Transmission



Reported cases of Dengue, Chikungunya, Zika virus and microcephaly in Pernambuco state, Brazil by EW, 2015 to 2016



First reports in Brazil:
Unusual increase of newborns with microcephaly

Photo credit: Image provided by mother of newborn (Rio de Janeiro, Brazil), with authorization for dissemination exclusively among public health workers.

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Causal relationship between prenatal ZIKV infection and microcephaly and other severe brain anomalies

(updated 13 April 2016, NEJM)

- **High rate of MC in mothers tested ZIKV +**
- **MC phenotype observed in Brazil is consistent with Fetal Brain Disruption Sequence**
  - **Destruction of the fetal brain tissue by ZIKV followed by collapse of the skull**
- **ZIKV RNA as been found in:**
  - **Amniotic Fluid of fetuses with MC**
  - **Brain Tissues of fetuses and infants with MC**

- Greater Risk is 1st trimester (mostly weeks 7-13) in some case as late as week 18
- Preliminary report: 30% of fetuses with abnormalities detected in utero in pregnant women ZIKV +
- High proportion of fetal loss and fetal deaths in pregnant women infected between week 6 - 32
- Ocular anomalies in 35% of children with MC

Table 1. Shepard's Criteria for Proof of Teratogenicity in Humans as Applied to the Relationship between Zika Virus Infection and Microcephaly and Other Brain Anomalies.*

Criterion No.	Criterion	Evidence	Criterion Met?
1	Proven exposure to the agent at one or more critical times during prenatal development	On the basis of case reports, case series, and epidemiologic studies of microcephaly that are associated with laboratory-confirmed or presumed Zika virus infection, the timing of Zika virus infection associated with severe microcephaly and intracranial calcifications appears to be in the late first or early second trimester.[14-20]	Yes
2	Consistent findings by ≥2 high-quality epidemiologic studies, with control of confounding factors, sufficient numbers, exclusion of positive and negative bias factors, prospective studies if possible, and relative risk ≥6	On the basis of data from Brazil, the temporal and geographic association between Zika virus illness and cases of microcephaly is strong.[1] Two epidemiologic studies have been published. In a study in Brazil[14] that used a prospective cohort design, 29% of women with Zika virus infection at any time during pregnancy had abnormalities on prenatal ultrasonography, some of which have not been confirmed postnatally. In a study in French Polynesia,[2] retrospective identification of eight cases of microcephaly and the use of serologic and statistical data and mathematical modeling suggested that 1% of fetuses and infants born to women with Zika virus infection during the first trimester had microcephaly; the risk ratio in this analysis was approximately 50, as compared with the baseline prevalence of microcephaly. No other epidemiologic studies have examined this association to date.	Partially
3	Careful delineation of clinical cases; a specific defect or syndrome, if present, is very helpful	The phenotype has been well characterized in fetuses and infants with presumed congenital Zika virus infection, including microcephaly and other serious brain anomalies, redundant scalp skin, eye findings, arthrogryposis, and clubfoot.[15,20-23] The phenotype in some infants appears to be consistent with the fetal brain disruption sequence,[20,22] which has been observed after infection with other viral teratogens.[24]	Yes
4	Rare environmental exposure that is associated with rare defect	Reports of fetuses and infants with microcephaly who are born to women with brief periods of travel to countries with active Zika virus transmission are consistent with Zika virus being a rare exposure.[16,20,23] The defect, congenital microcephaly, is rare, with a birth prevalence of approximately 6 cases per 10,000 liveborn infants, according to data from birth-defects surveillance systems in the United States.[25]	Yes
5	Teratogenicity in experimental animals important but not essential	No results of an animal model with Zika virus infection during pregnancy and fetal effects have yet been published.	No
6	Association should make biologic sense	Findings are similar to those seen after prenatal infection with some other viral teratogens (e.g., cytomegalovirus, rubella virus).[26] Animal models have shown that Zika virus is neurotropic,[27,28] which supports biologic plausibility. Evidence that Zika virus infects neural progenitor cells and produces cell death and abnormal growth,[29] along with evidence of Zika virus in brains of fetuses and infants with microcephaly, on the basis of immunohistochemical staining and identification of Zika virus RNA and live virus,[16,17,19] provides strong biologic plausibility.	Yes
7	Proof in an experimental system that the agent acts in an unaltered state	This criterion applies to a medication or chemical exposure, not to infectious agents.	NA

* The criteria listed here were proposed by Shepard.[9] Criteria 1, 2, and 3 or criteria 1, 3, and 4 are considered to be essential, whereas criteria 5, 6, and 7 are helpful but not essential. Partial evidence is insufficient to meet a criterion. NA denotes not applicable.

Título

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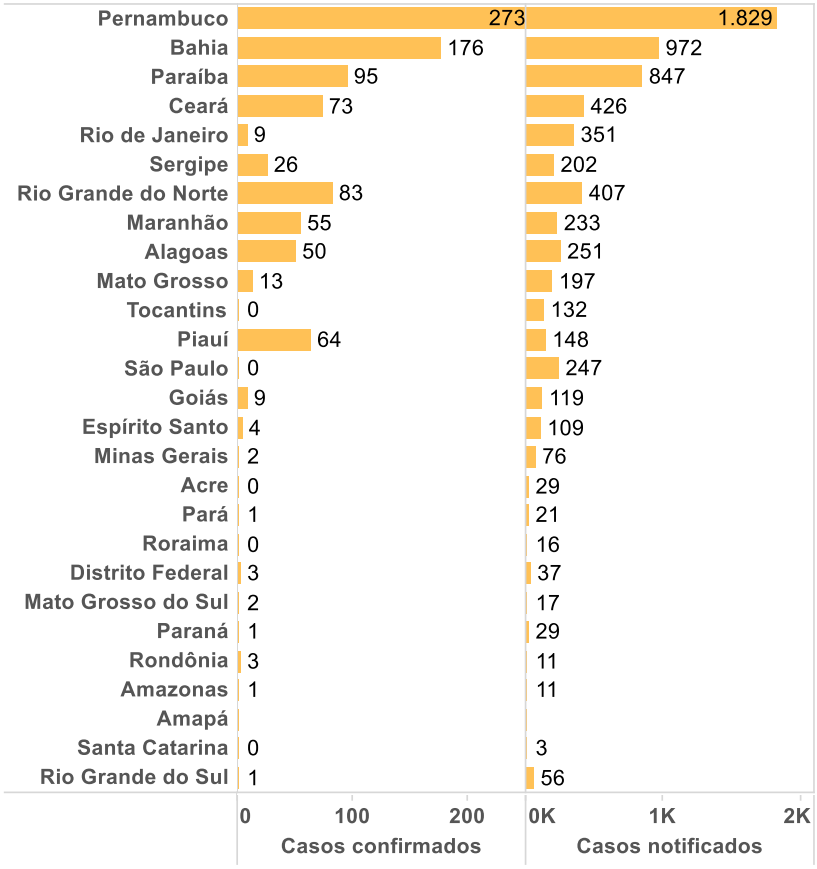
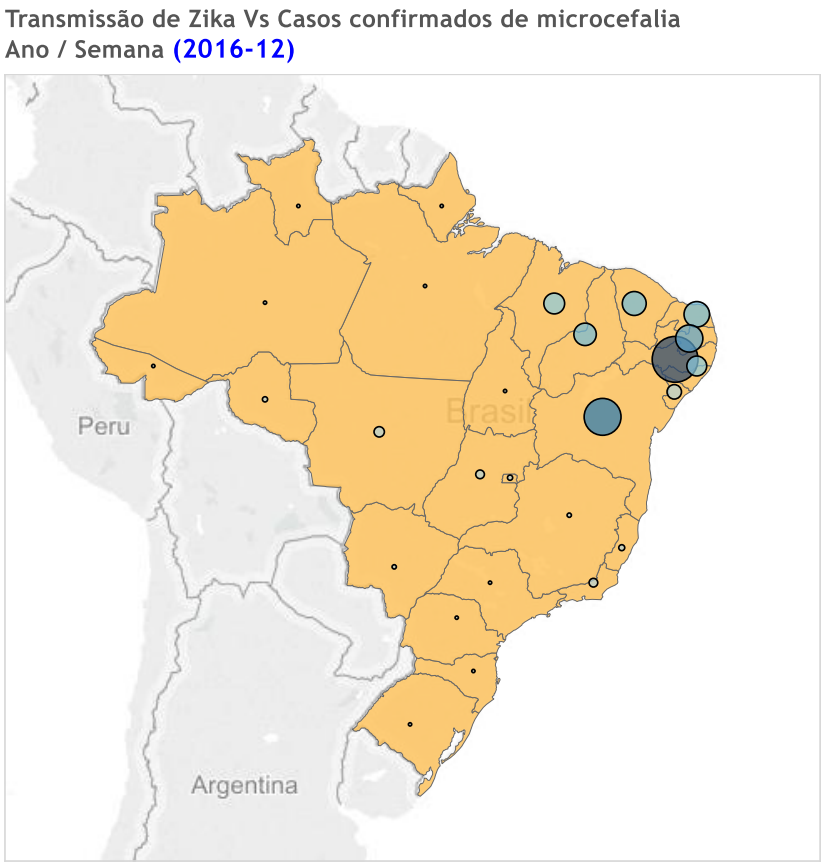
Casos notificados e confirmados de microcefalia por semana epidemiológica, Brasil.





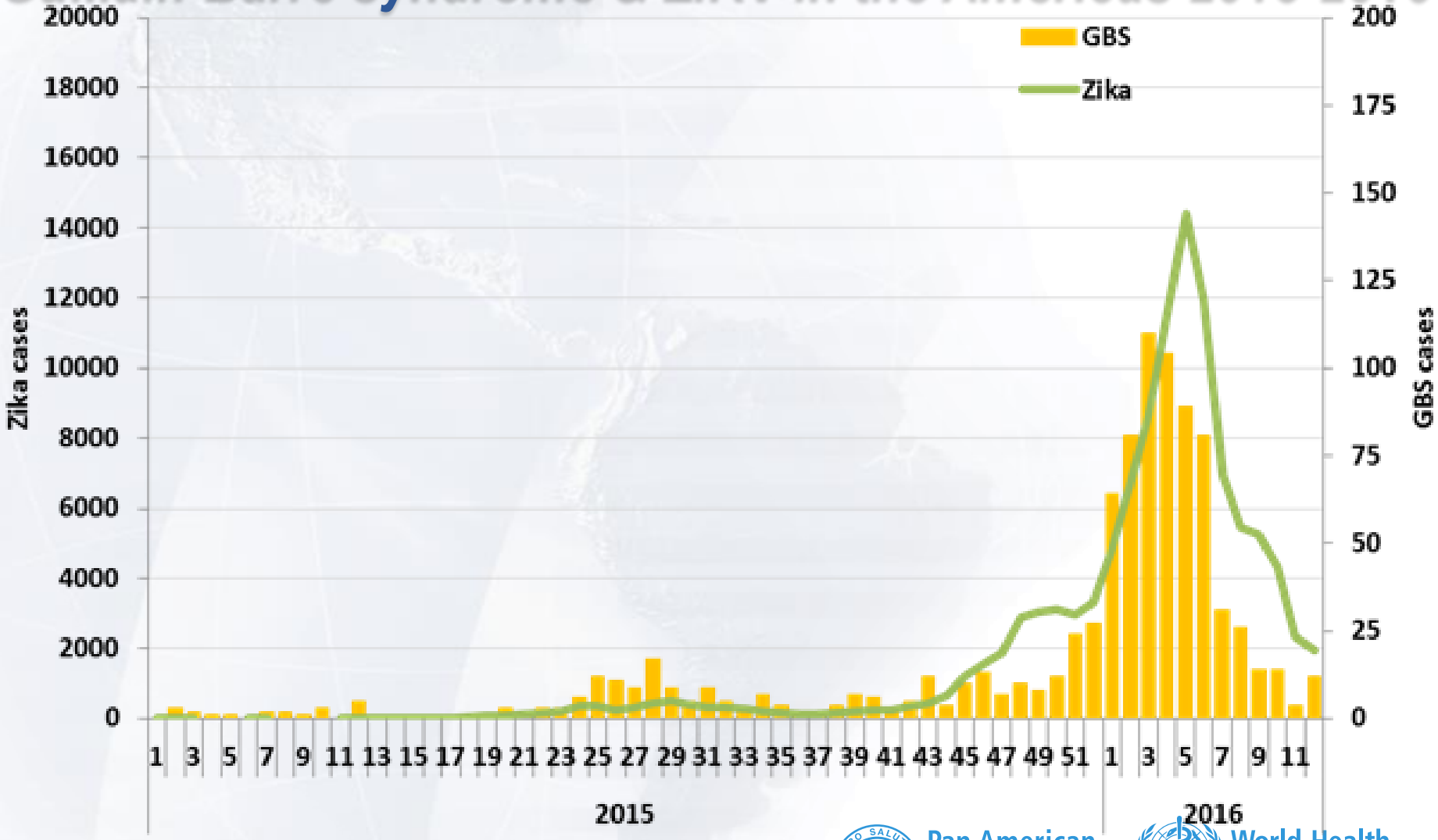
Fonte: Informe epidemiológico de casos de microcefalia no Brasil. Ministério da Saúde. Brasil
Elaboração: Sala de situação Vírus Zika - OPAS/OMS Brasil

Countries, territories and areas reporting microcephaly and /or CNS malformation cases potentially associated with Zika virus infection (updated 09 June 2016).

Countries reporting congenital syndrome associated with Zika virus	Number of confirmed cases to date
Brazil	1,551
Colombia	7
Martinique[2]	4
Panama	5
Puerto Rico[3]	1
United States[4]	2

Neurological Anomalies

Guillain-Barré syndrome & ZIKV in the Americas 2015-2016



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Zika virus Knowledge Gaps to be addressed

Regional research agenda was developed by PAHO:

- **Define absolute risk of neurological malformation in fetus by gestational age**
- **Describe the clinical spectrum of the Zika congenital syndrome**

- Understand the role of the different modes of transmission: sexual, vector
- Characterize the dynamics of arboviruses co-circulating in same sub-regions: DENV, CHIKV, ZIKV, YFV, others…..and study the vector competency
- New serological tests to improve detection in context of high circulation of other flaviviruses

- New tools for vector control
- Need of financing and coordination

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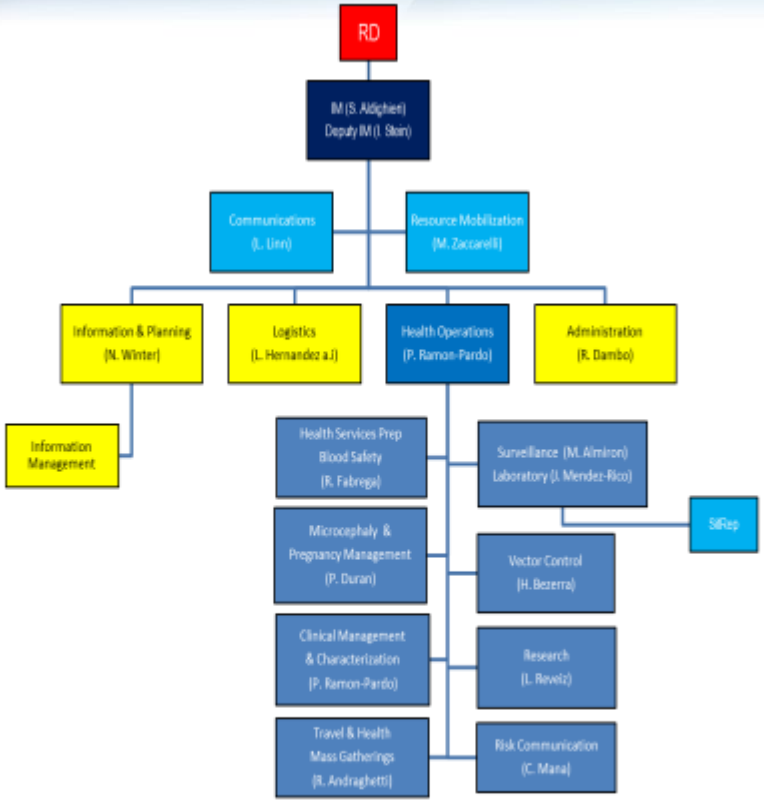
Some considerations regarding the regional context……

- Current incidence is difficult to gauge:
  - ZIKV infections are non specific and mild
  - Laboratory constraints including cross reactivity issues
- However we know that millions of ZIKV infections are expected at short and medium term (DENV & CHIKV incidence is a proxy, speed of regional spread of CHIKV is also a proxy)
- Long term outlook of ZIKV in LAC is uncertain (despite expected herd immunity…)

PAHO Zika Incident Management System (IMS)

- Activated in December 2015
- Full operations: 1 February 2016
- Reports to PAHO Director
- Articulates work of all PAHO technical departments
- 25 IMS staff full time + 5 EOC staff
- Coordinates implementation of the Regional Strategy through 28 COs
- Linked to the WHO IMS activated at HQ and 5 other regions



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PAHO and regional Zika response activities

- Regional Surveillance under IHR (monitoring Zika virus spread, detecting GBS increase and congenital neurological malformations)
- Publication of Epi updates and maps
- Development / Review / Publication of technical guidelines (WHO and PAHO)
- Coordination of partners through PAHO COs and HQ (UN agencies, GOARN, other partners)
- Organize inter-country trainings: Laboratory, Arbovirus Surveillance, Vector Control, Research Protocols, Health Services strengthening, Pregnant women and Children management
- Strategic Fund for insecticides / larvicides and Procurement of laboratory reagents, Immunoglobulins

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PAHO and regional Zika response activities

- Support to National Zika Plans through PAHO COs
- Deployment of multidisciplinary teams to key and prioritized countries (20 teams in 17 countries up to 08 April 2016). Follow-up missions targeting identified gaps. Expertise includes:
  - Epi Surveillance / Laboratory
  - Strengthening of Health Services
  - Case management / clinical characterization: GBS, MC, Zika congenital syndrome
  - Reproductive Health
  - Risk Communication
  - Vector Control
  - Research protocols

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KEY FACTS on ZIKAV

WHERE PAHO HAVE WORKED

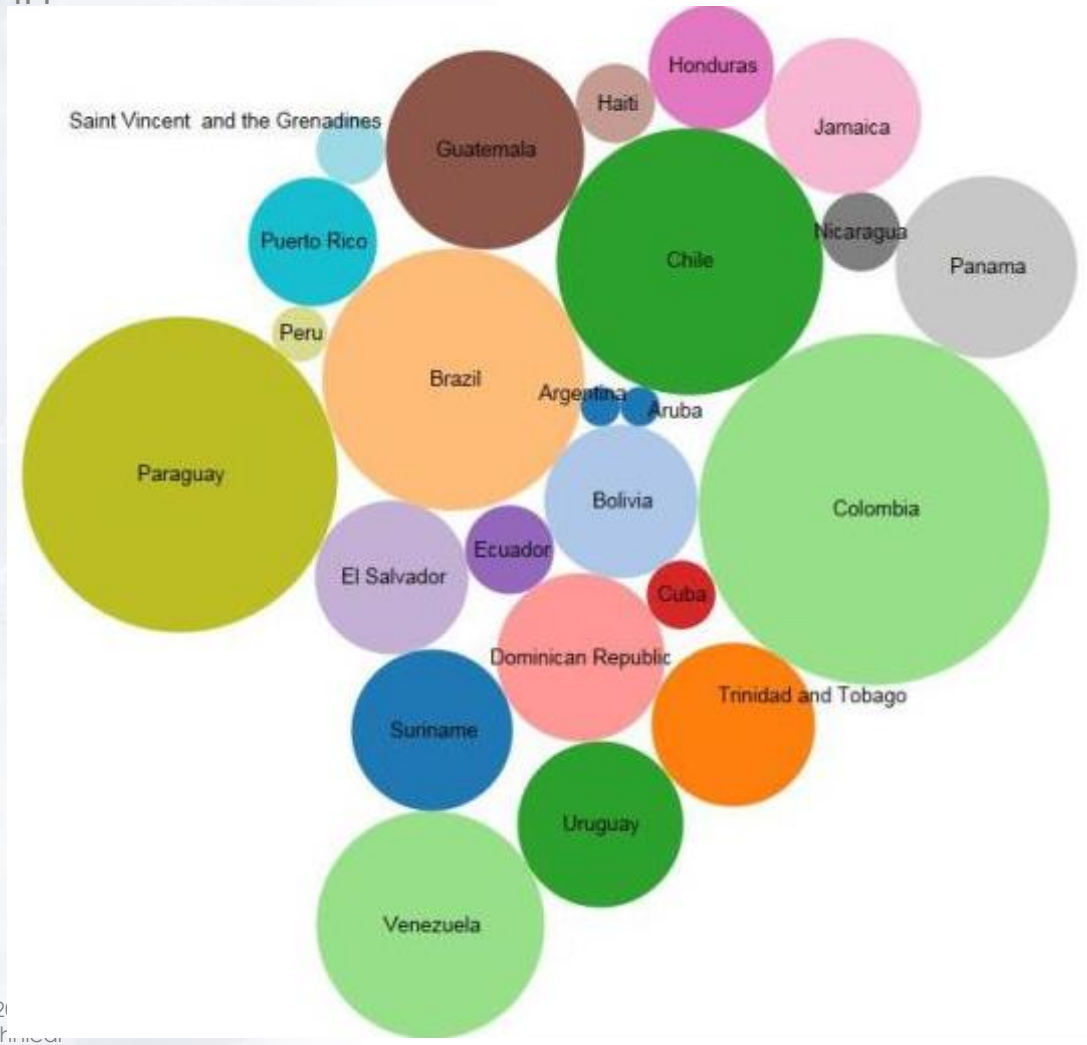
PAHO has carried out activities in

24 COUNTRIES in LAC

Totalizing approximately

933 days

of technical work
on those priority countries.



Source: PAHO database of missions and contracts
Information is based on official missions financed by PAHO, during 2
Missions are considered trainings, workshops, conferences and tech... support carried out by PAHO experts.

This chart consider missions finished, as of 2 June 2016.

Chart not contemplating missions to PAHO HQ in Washington DC

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HOW MANY PAHO EXPERTS

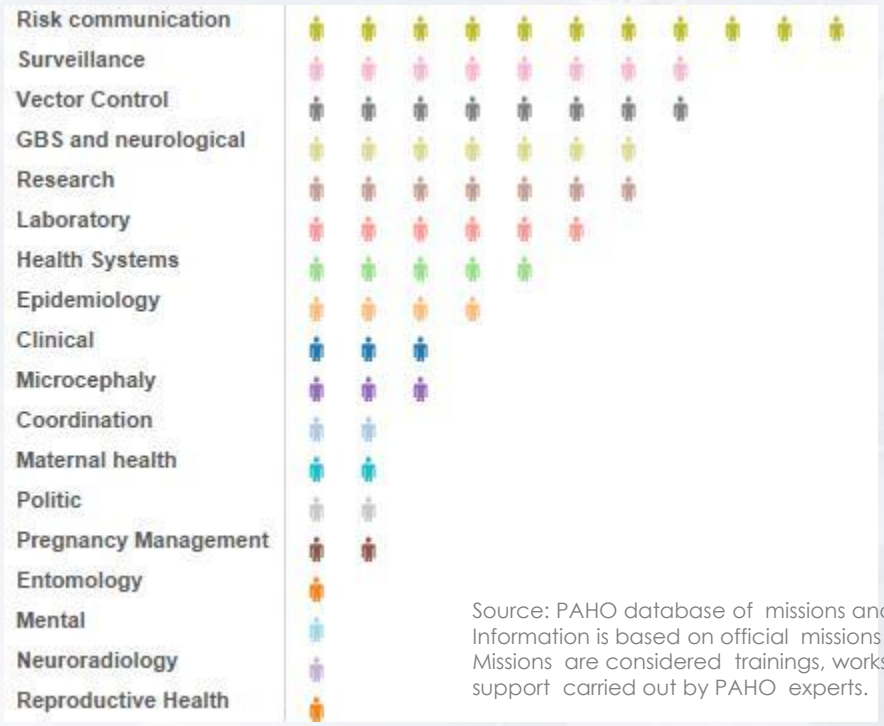
KEY FACTS on ZIKAV

PAHO has mobilized/hired

81 EXPERTS

Working in

18 TECHNICAL AREAS



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Regional Response challenges (some…)

- MS “political” management of deformities related to ZIKV
- Transition from 15 years unique Dengue surveillance to multi arbovirus surveillance (DENV + CHIKV + ZIKV + YFV + MAYV + OROV + SLV….)
- Numerous Bottle Necks for ZIKV PCR (SinglePlex X 3), complex transition to MultiPlex and Zika IgM, needs for follow-up missions at medium term
- Health Services limited knowledge of GBS characterization and management, needs for deployment of experts at medium term
- Change of paradigm for Vector Control: from house to house to protection of pregnant women and new methodologies (GMM, *Wolbachia*)
- Multiple research protocols in multiple countries…….

Criteria :

• Populations < 2,000 m (CIESIN, Columbia University)

• Limited by Northern and Southern limits 10 C isotherms (no survival of Aedes aegypti during winter)

• Areas with compatible climates (classification of Köppen-Geiger)

Criteria for assessing the population at risk for arboviruses transmitted by *Aedes aegypti* in the Americas (draft version 11/04/2016)