

# **Epidemiology of Zika Infection and Pregnancy in Brazil**

**Zika virus in the Americas: an HHS expert consultation to  
accelerate the development of countermeasures**

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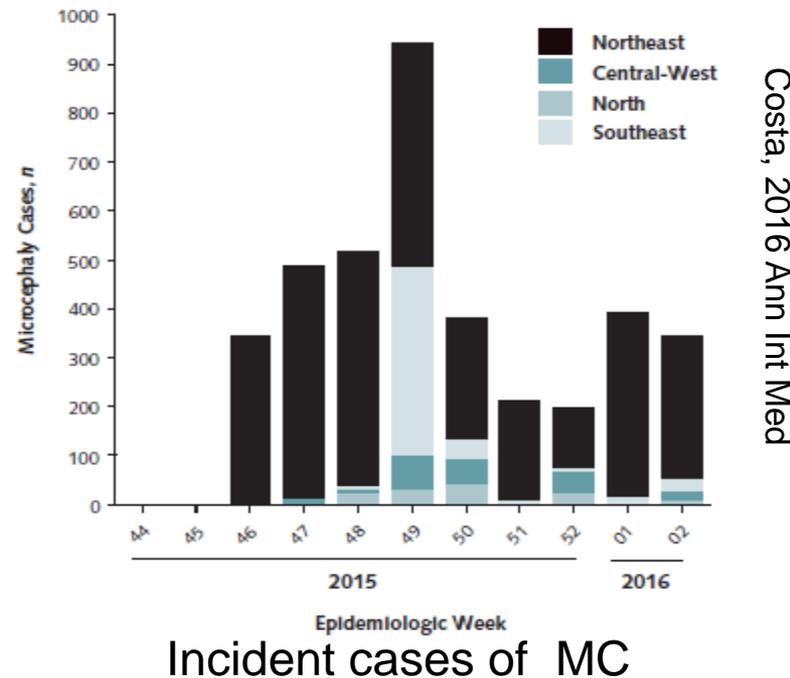
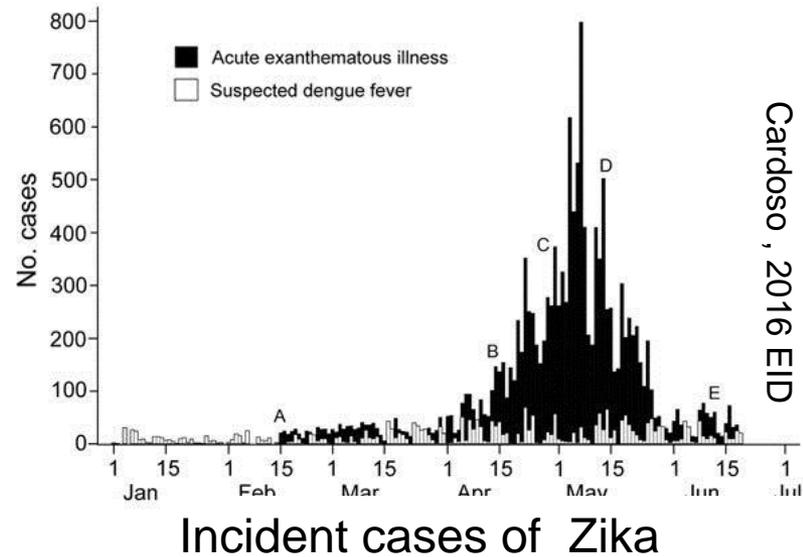
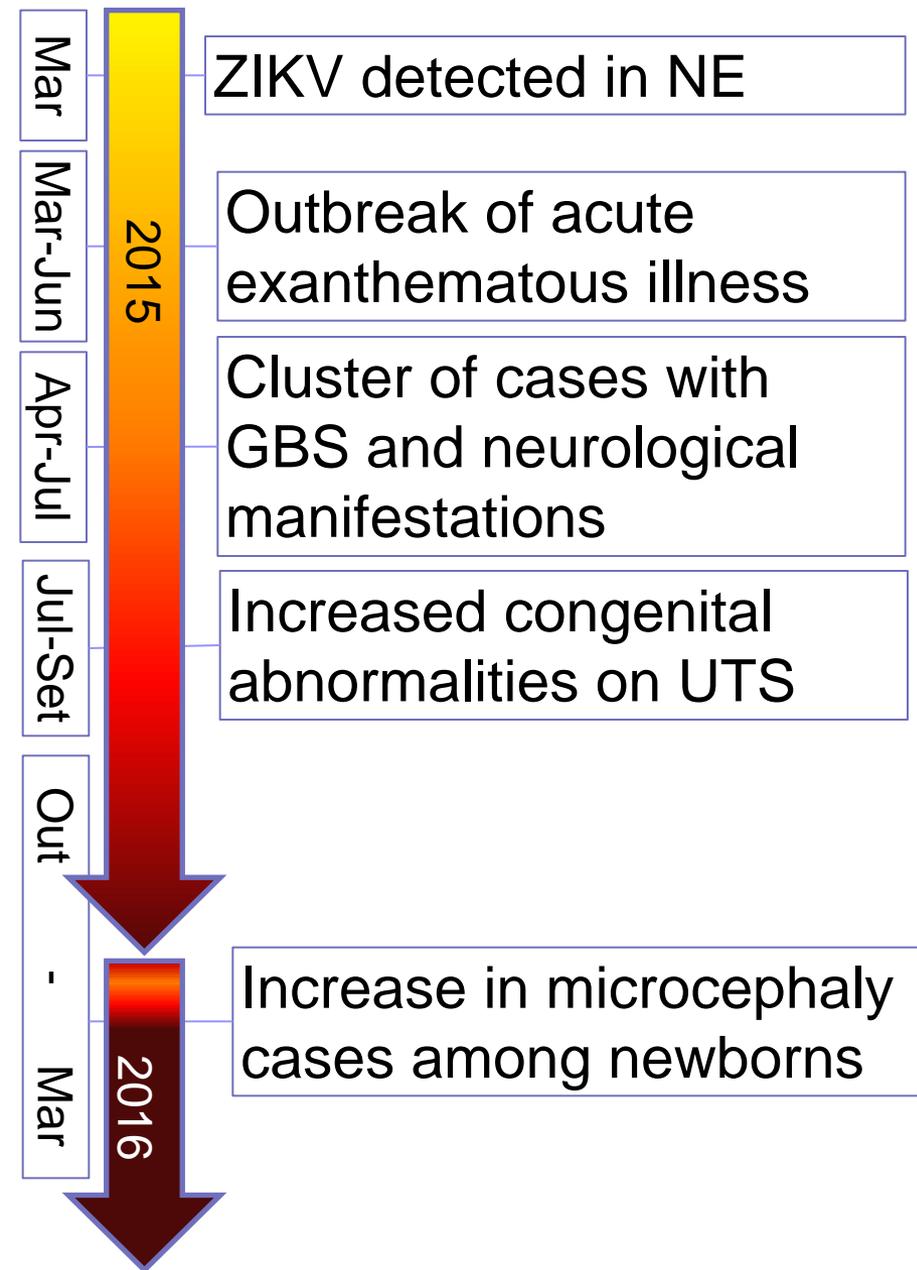
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# Zika infection and Microcephaly in Brazil

## Summary

- **Timeline** of Zika infection and Microcephaly (MC)
- **Case definitions** for MC
- **Baseline and magnitude** of MC outbreak
- Evidence for the **time** of introduction of ZIKV
- Evidence for the **association** between Zika infection and MC
- Knowledge **Gaps**

# Timeline from the Zika Epidemic in Brazil





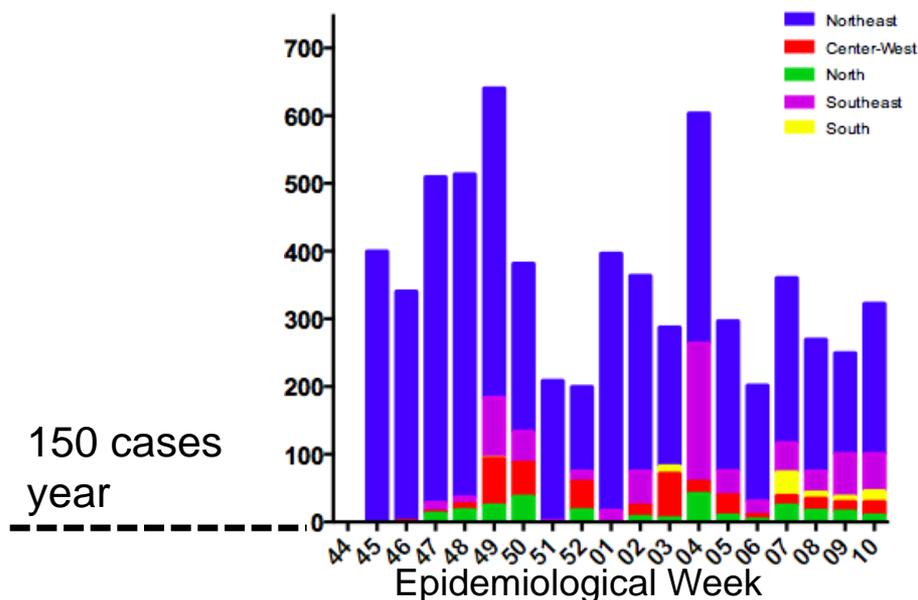
# How to interpret reported numbers?

Definition I

Definition II

Definition III

Up to Dec 8, 2015    12/08/15 - 03/09/16    03/09/16 to date



**6,671 notified cases**

2,378 (36%) Investigated  
 907 (38%) **Confirmed** MC or CNS alteration  
 1,471 (62%) Discarded  
 4,293 (64%) under investigation

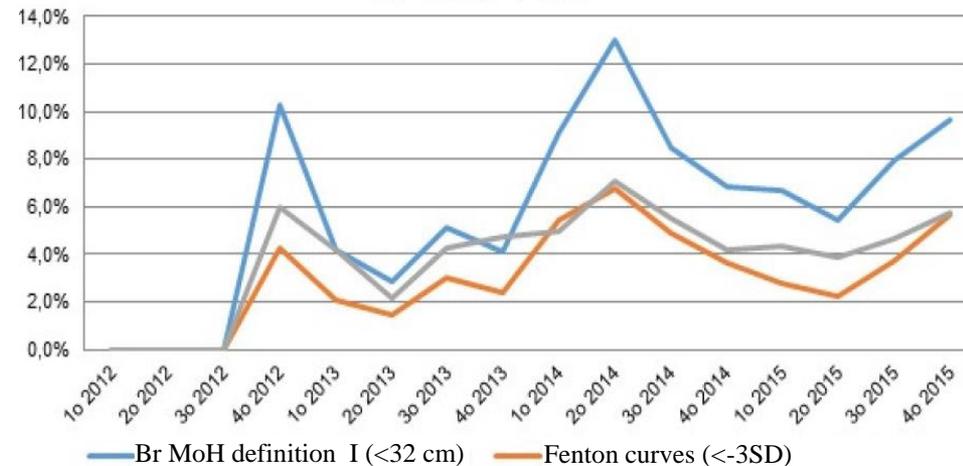
- I ≤33 cm for term newborn babies of both sexes; <-2 SD of Fenton reference for preterm babies
- II ≤32 cm for term newborn babies of both sexes; <-2 SD of Fenton reference for preterm babies
- III ≤31.9 cm and ≤31.5cm for term neonates for respectively, males and females; <-2 SD InterGrowth for preterm babies

# Baseline data and outbreak magnitude

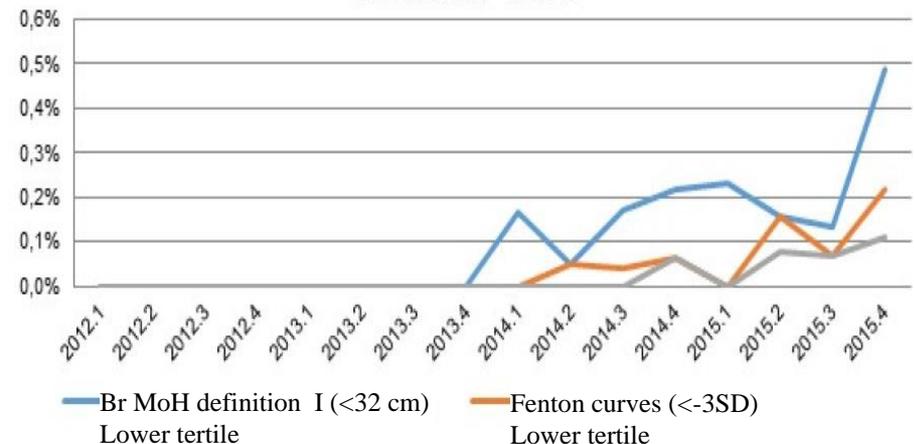
## The case of Paraíba State

- Retrospective study on 21 hospitals:
  - Jan 2012 to Dec 2015
  - 10% of the dataset
  - n= 16,208
- Higher incidence than expected
- Temporal oscillation
- Peak of “extreme” cases of microcephaly late 2015

Temporal distribution of microcephaly cases in Paraíba - Brazil

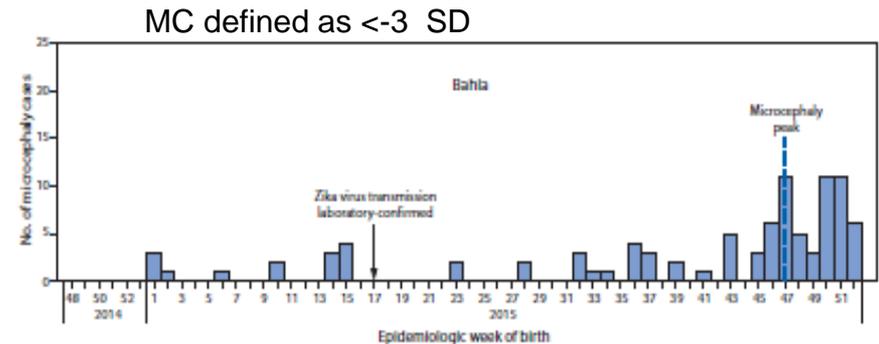
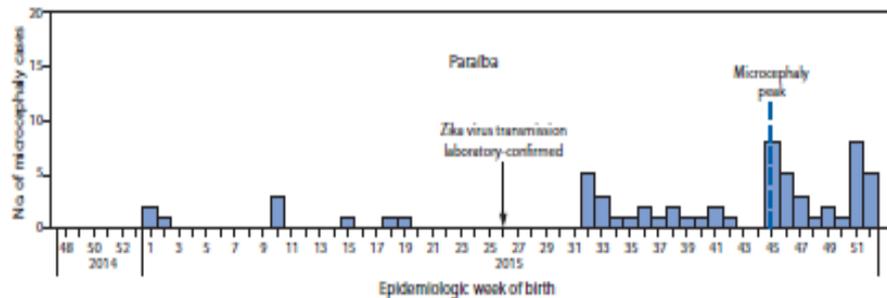


Temporal distribution of extreme cases of microcephaly in Paraíba - Brazil



# Evidence for the time of introduction of ZIKV

Increase of cases of MC since Oct 2015 (de Oliveira MMWR 2016)



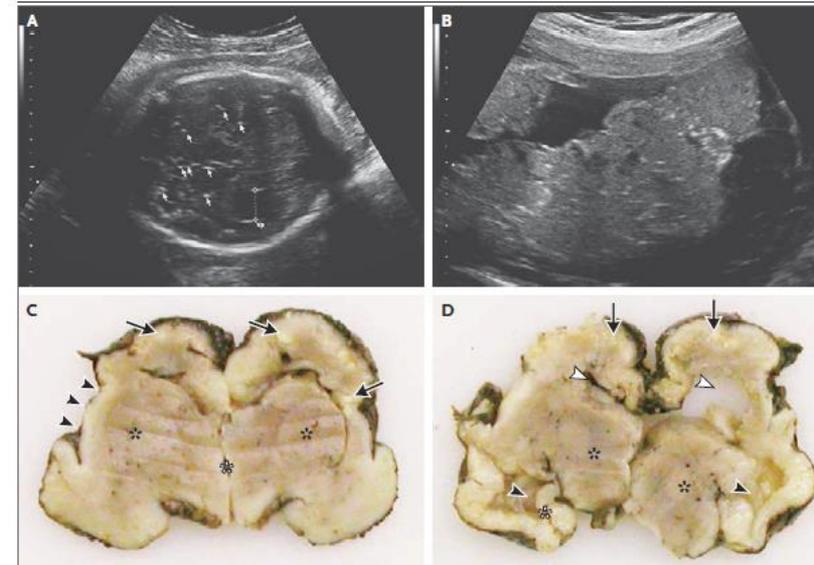
Single introduction of ZIKV between May-Dec 2013 and early 2014 (Nunes SCIENCE 2016)

- Increase in air passengers to Brazil from ZIKV endemic areas

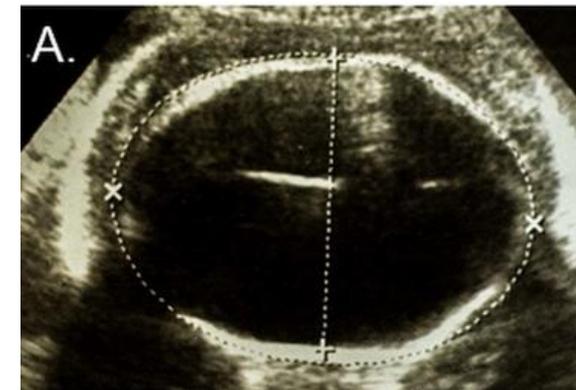
# Evidence for the association between Zika infection during pregnancy and microcephaly

- Higher incidence of MC in newborns from regions where a previous outbreak of ZIKV was described (de Oliveira MMWR 2016; Teixeira AJPH 2016)
- Presence of the virus in the amniotic fluid and tissues on newborns with MC (Calvet, 2016; Oliverira, 2016; Mlakar 2016)
- Case report providing evidence of an association with
  - Fetal demise (MMWR)
  - Spontaneous abortions
  - Hydrops fetalis and hydranencephaly (Sarno PLoS NTD 2016)

## Zika Virus Associated with Microcephaly



Mlakar, 2016 NEJM

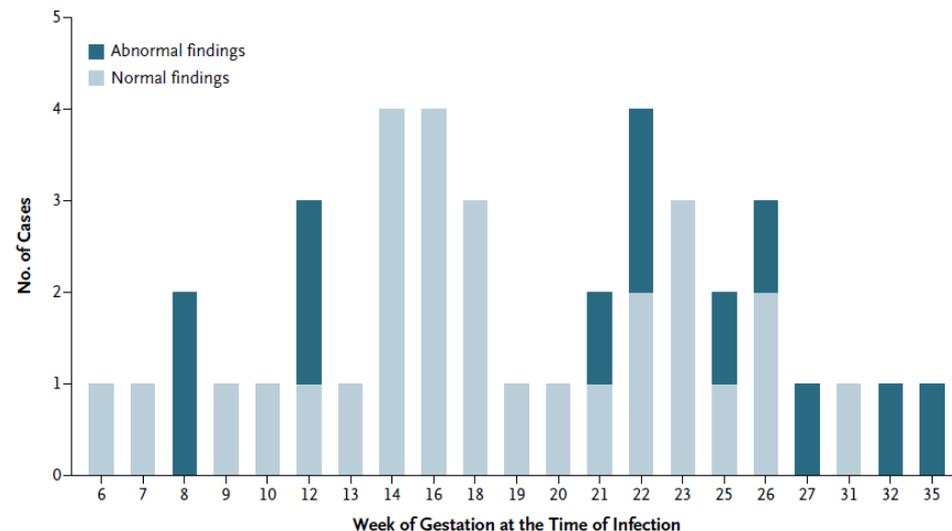


Sarno, 2016 PLOS NTD

# Evidence for the association between Zika infection during pregnancy and microcephaly (II)

Prospective evaluation of ZIKV infection during pregnancy likely to be associated with mild and severe outcomes (Brasil et al, NEJM 2016)

- Cohort of 88 pregnant women with fever/rash Sep 2015 -Feb 2016
- 72 (82%) tested positive ZIKV
- Fetal death: 2/72 (3%)
  - Infected at w25 and w32
- Fetal abnormalities: 12/42 (29%)
  - 5 MC (infected w8-w26)
  - 7 other outcomes



# Zika Congenital Syndrome?: Questions and Challenges

- Association between ZIKV and congenital defects?:
  - Persistence of interuterine infection?
  - Risk period of transmission, mechanism and cofactors?
- Diagnostics has been the key barrier
- Natural history:
  - Rates of vertical transmission after infection of mother
  - Development of severe sequelae after congenital infection
- Spectrum of the disease manifestations
  - Manifestations in newborns without microcephaly:
  - Restricted to the CNS?
- Prognosis
  - Sequelae (seizures, hydrocephalus), development?
  - Interventions to families and address stigma