

Appendix

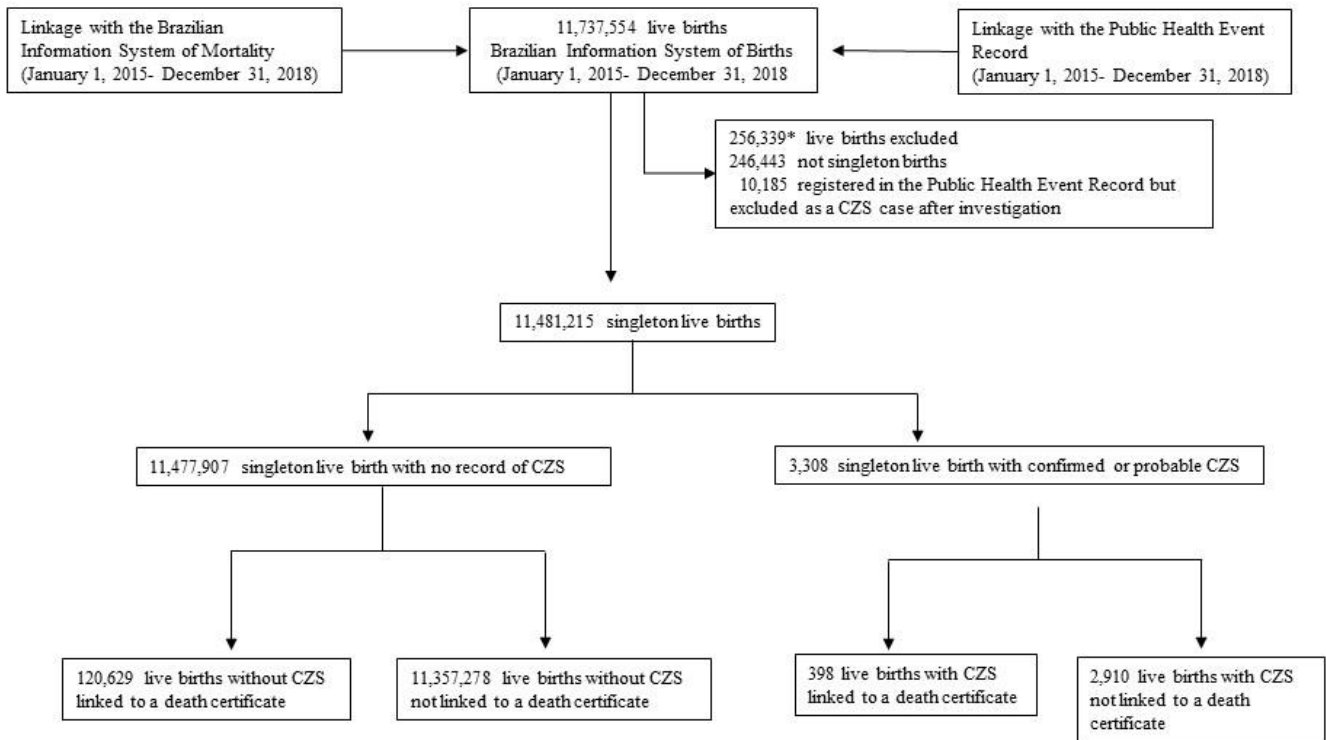
Congenital Zika Syndrome: A Nationwide Cohort Study in Brazil, 2015-2018

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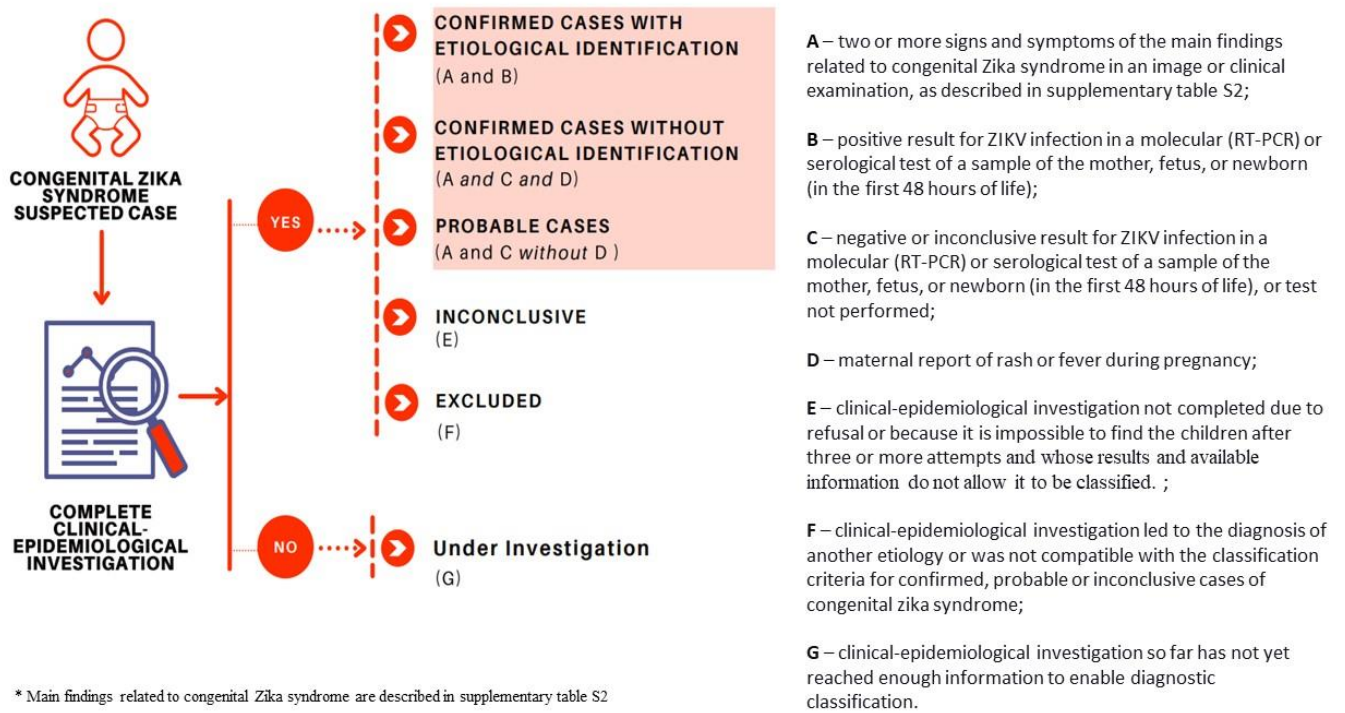
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Figure S1. Flowchart study population Brazil, 2015-2018.



* The exclusions do not sum to 256,339 because a record may be multiples and excluded as a CZS case after investigation
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Figure S2. Flowchart for classification criteria for congenital Zika syndrome



*Based on the Brazilian Ministry of Health Guideline

Table S1: Mortality risk by age group among singleton live births in the cohort-linked data (CZS confirmed cases only), Brazil, 2015-2018.

Live births	Live births with CZS	Live births without CZS	HR for mortality (95% CI)
Neonatal mortality (up to 27 days)			
Neonatal deaths	123	80,006	
Deaths per 1,000 PY	639.01 (535.50-762.54)	95.7 (95.0 - 96.3)	6.6 (5.5-7.9)
Post-neonatal mortality (28-364 days)			
Post-neonatal deaths	119	32,175	
Deaths per 1,000 PY	51.98 (43.43-62.21)	3.5 (3.5 - 3.6)	15.3 (12.8-18.3)
Infant mortality (up to 364 days)			
Infant deaths	242	112,181	
Deaths per 1,000 PY	97.3 (85.7-110.3)	11.3 (11.2 - 11.3)	9.2 (8.1-10.4)
Mortality after one year (12-36 months)			
Deaths after 1 year	57	8,448	
Deaths per 1,000 PY	14.01 (10.9-18.3)	0.7 (0.7-0.8)	19.8 (15.2-25.7)
Total mortality (up to 36 months)			
Total Deaths	299	120,629	
Deaths per 1,000 PY	45.8 (40.9-51.3)	5.6 (5.6-5.7)	10.2 (9.1-11.5)

PY= person years

*Confirmed cases only

Table S2: Main findings in infants with congenital Zika syndrome (translation from material published by the Brazilian Ministry of Health)¹

Most common findings identified prenatally			
<i>Structural CNS/cranial</i>	<i>Facial dysmorphia</i>	<i>Neurologic sequelae</i>	<i>Other</i>
Microcephaly/microencephaly	Flat face	Static position of hands and feet (indicative of arthrogyposis)	Polyhydramnios
Craniofacial disproportion	Retrognathia		
Prominent occipital bone	Hypotelorism		
Misshapen cerebellar vermis	Redundant scalp		
Ventriculomegaly (mild, moderate, severe), ex vacuo/hydrocephalus			
Brain calcifications, diffuse			
Ventricular synechiae			
Agenesis of the corpus callosum			
Schizencephaly/porencephaly			
Cerebral cortex thinning			
Microphthalmia			
Most common findings identified at birth or within the first month of life			
<i>Structural CNS/cranial</i>	<i>Neurosensory sequelae</i>	<i>Neurologic sequelae</i>	<i>Other</i>
Microcephaly	Retinal mapping changes	Changes in muscle tone	
Craniofacial disproportion	Lesions of retinal epithelium/ unusual pigmentation	Changes in posture	
Brain calcifications	Retinal atrophic circular lesions	Hyperexcitability/hyperirritability	
Abnormal cortical development/ polymicrogyria/simplified gyri	Optic nerve changes (hypoplasia, partial/complete atrophy, increased papillary excavation)	Epileptic seizures	
Cortical thickening, frontoparietal	Alteration of visual function	Difficulties with suck and swallow	
Ventriculomegaly	Alteration of auditory function	Joint contractures	
Hypoplastic brain stem	Abnormal eye movements		
Hypoplastic cerebrum/alterations posterior fossa			
Hypoplastic corpus callosum			
Retinal and optic nerve anomalies			
Findings identified after the first month of life			
<i>Structural CNS/cranial</i>	<i>Neurosensory sequelae</i>	<i>Neurologic sequelae</i>	<i>Other</i>
		Most frequent	
Craniofacial disproportion	Visual changes (inattention)	Dysphagia	Congenital hip dislocation
Changes in HC due to hydrocephalus	Strabismus, nystagmus	Epilepsy/spasms	

Brain calcifications
Dysmorphic corpus callosum
Ventriculomegaly

Changes in retinal mapping
Alteration of auditory function

Irritability
Hypertonia
Persistent primitive reflexes

Frequent

Sensorineural hearing loss

Rare

Microphthalmia
Coloboma

Cryptorchidism
Hypospadias

Cataract
Glaucoma

CNS – central nervous system
HC – head circumference

Reference

1. Ministério da Saúde (BR). *Orientações integradas de vigilância e atenção à saúde no âmbito da Emergência de Saúde Pública de Importância Nacional*. Ministério da Saúde. (2017).