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Zika Preparedness Latin American Network

16 June 2016

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Umeå Centre for Global Health Research
Epidemiology and Global Health

Preparedness Latin American Network
ZikaPLAN

Call for proposals Feb. 2016	Deadline April 2016	Review finalized July 2016	Starting date Oct. 2016	…

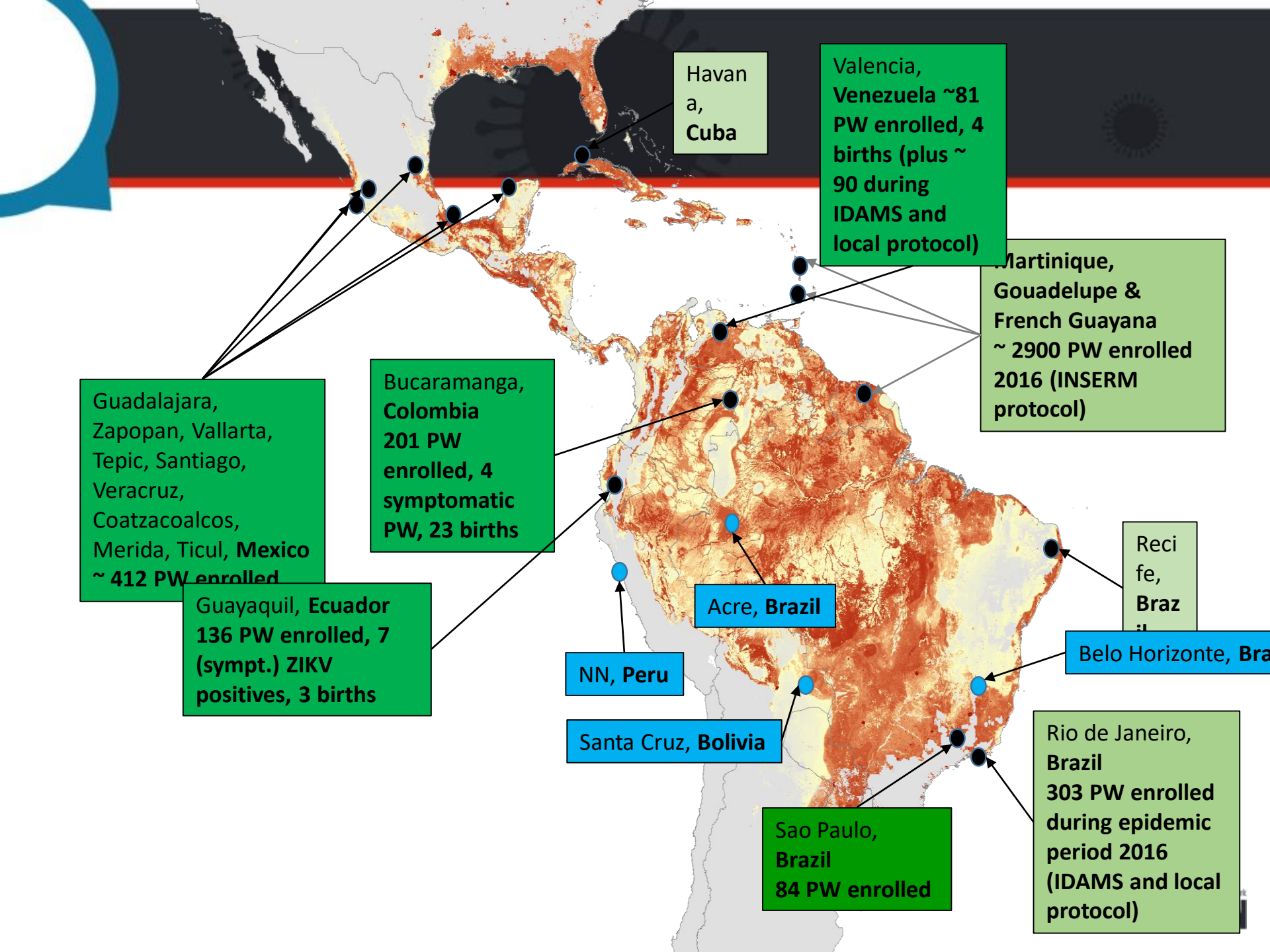
ZIKAction

CO: Carlo Giaquinto, University of Padua / PENTA Foundation, Italy

Preparedness Latin American Network ZikaPLAN

CO: Annelies Wilder-Smith, Umea University, Sweden

CO: Xavier de Lamballerie, Aix-Marseille University / INSERM, France


Havana, **Cuba**
Valencia, **Venezuela ~81 PW enrolled, 4 births (plus ~ 90 during IDAMS and local protocol)**
Martinique, Gouadelupe & French Guayana ~ 2900 PW enrolled 2016 (INSERM protocol)
Guadalajara, Zapopan, Vallarta, Tepic, Santiago, Veracruz, Coatzacoalcos, Merida, Ticul, **Mexico ~ 412 PW enrolled**
Bucaramanga, **Colombia 201 PW enrolled, 4 symptomatic PW, 23 births**
Guayaquil, **Ecuador 136 PW enrolled, 7 (sympt.) ZIKV positives, 3 births**
Acre, **Brazil**
Recife, **Braz**
Belo Horizonte, **Bra**
NN, **Peru**
Santa Cruz, **Bolivia**
Rio de Janeiro, **Brazil 303 PW enrolled during epidemic period 2016 (IDAMS and local protocol)**
Sao Paulo, **Brazil 84 PW enrolled**

Harmonization of data and a roadmap towards data sharing

1. To harmonize the protocols and standardize the tools for data capture and data management
   - 1.1. Harmonization of protocols
   - 1.2. Standardization of data capture tools and data management
2. To set up joint harmonized platforms for clinical research
   - 2.1. To set up a reciprocal clinical monitoring platform
   - 2.2. To set up a joint laboratory diagnostics EQA platform
   - 2.3. To set up a virtual joint biobanking platform
   - 2.4. Establishing principles of governance for the joint virtual biobanking platform
3. To share data in real time in the collaborative environment of the three EC-funded consortia
   - 3.3. Monitoring enrolment and accrual of patients across geography
   - 3.4. Joint analysis plan

Comparison between 3 EU Zika consortia

ZIKAlliance

- **Asymptomatic PW cohorts:**
- **Children cohorts**
- **Natural history cohorts**
- **Seroprevalence studies**
- **Virology and Basic Science**
- **Modelling**
- **Entomology**
- **Preparedness network**

ZIKAction

- **Asymptomatic PW cohorts:**
- **Children cohorts**
- Case-control studies

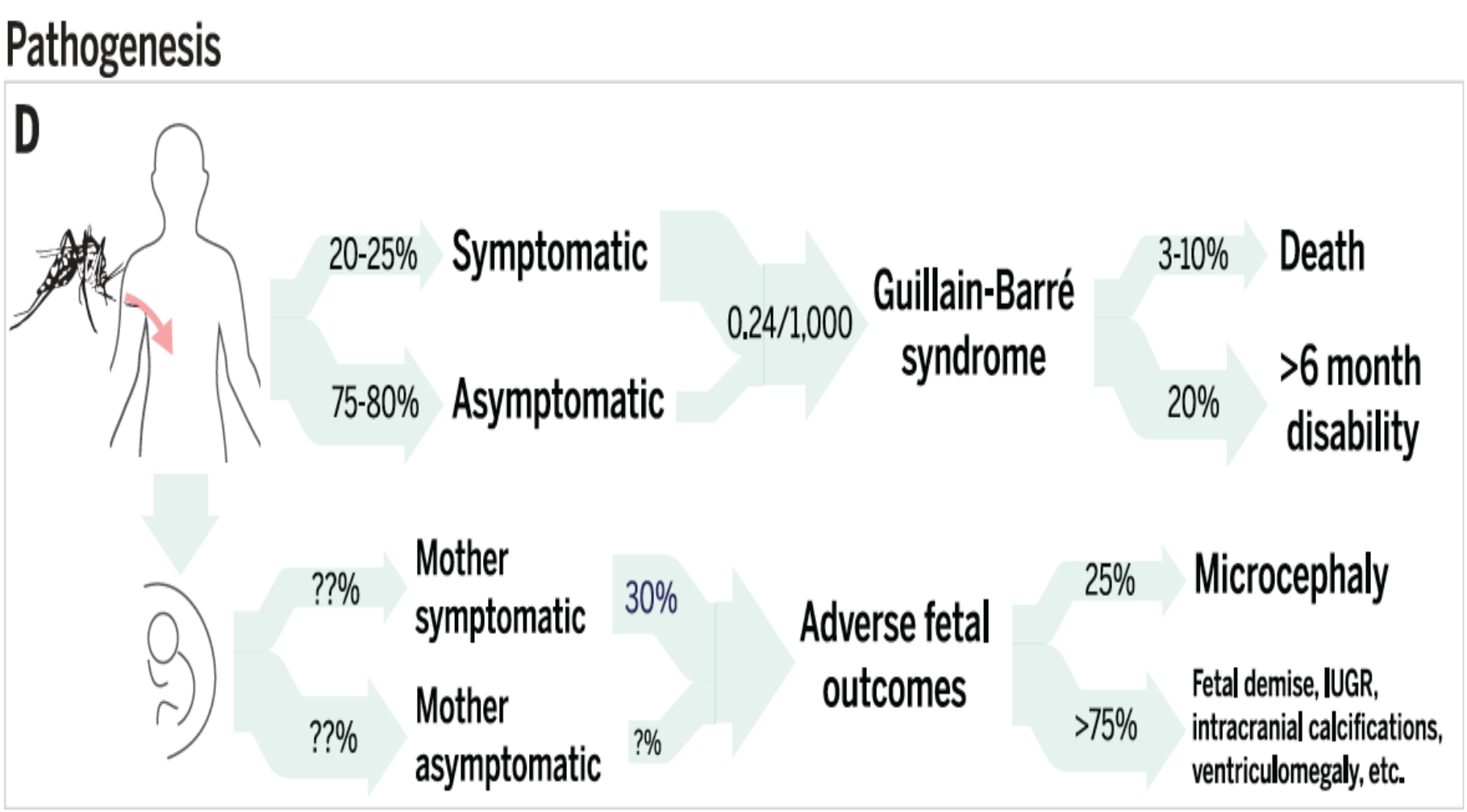
Preparedness network

ZIKAPlan

- Symptomatic PW cohorts:
- **Children cohorts**
- Seroprevalence
- Modelling
- Birth defect surveillance
- Travellers cohorts
- Neuro-Zika
- Entomology

Preparedness network

What are the attack rates?



Asymptomatic to symptomatic ratio and its impact on CZS

Asymptomatic Prenatal Zika Virus Infection and Congenital Zika Syndrome

Enny S. Paixao,[1] Wei-Yee Leong,[2] Laura C. Rodrigues,[1,a] and Annelies Wilder-Smith[1,2,3,a]

Prospective studies (442-2596 pregnant women with lab confirmed ZIKV)

38-61% of pregnant women with lab confirmed Zika infection are symptomatic

5-6% of symptomatic infections result in CZS

5-7% of asymptomatic infections result in CZS

What are the implications?

All pregnant women need to be screened

High bar for vaccine development: sterilizing immunity needed?

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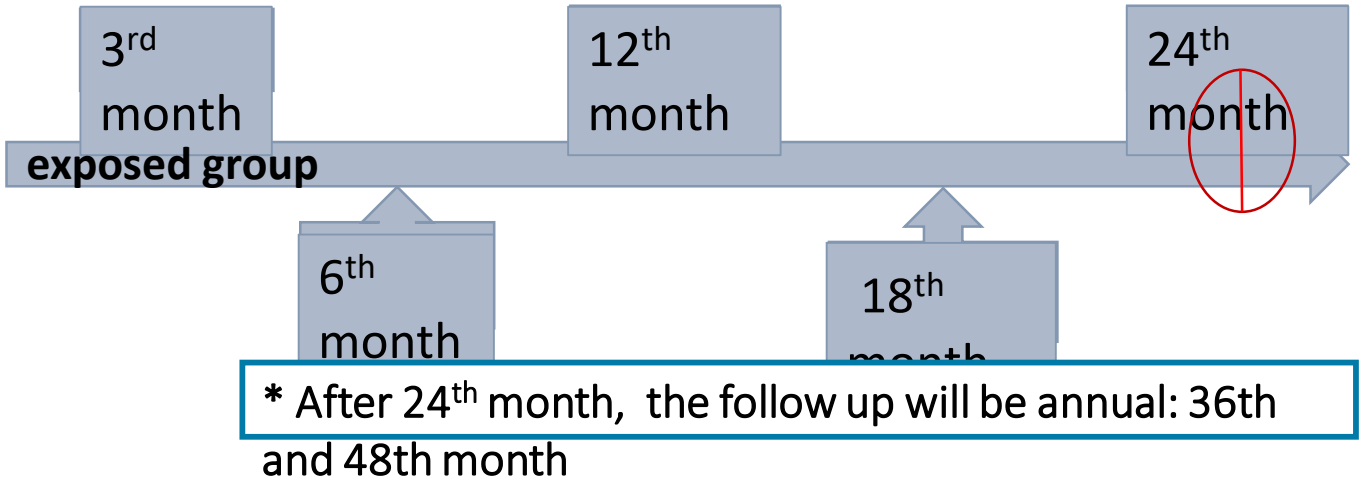
Objectives, Study population and data collection

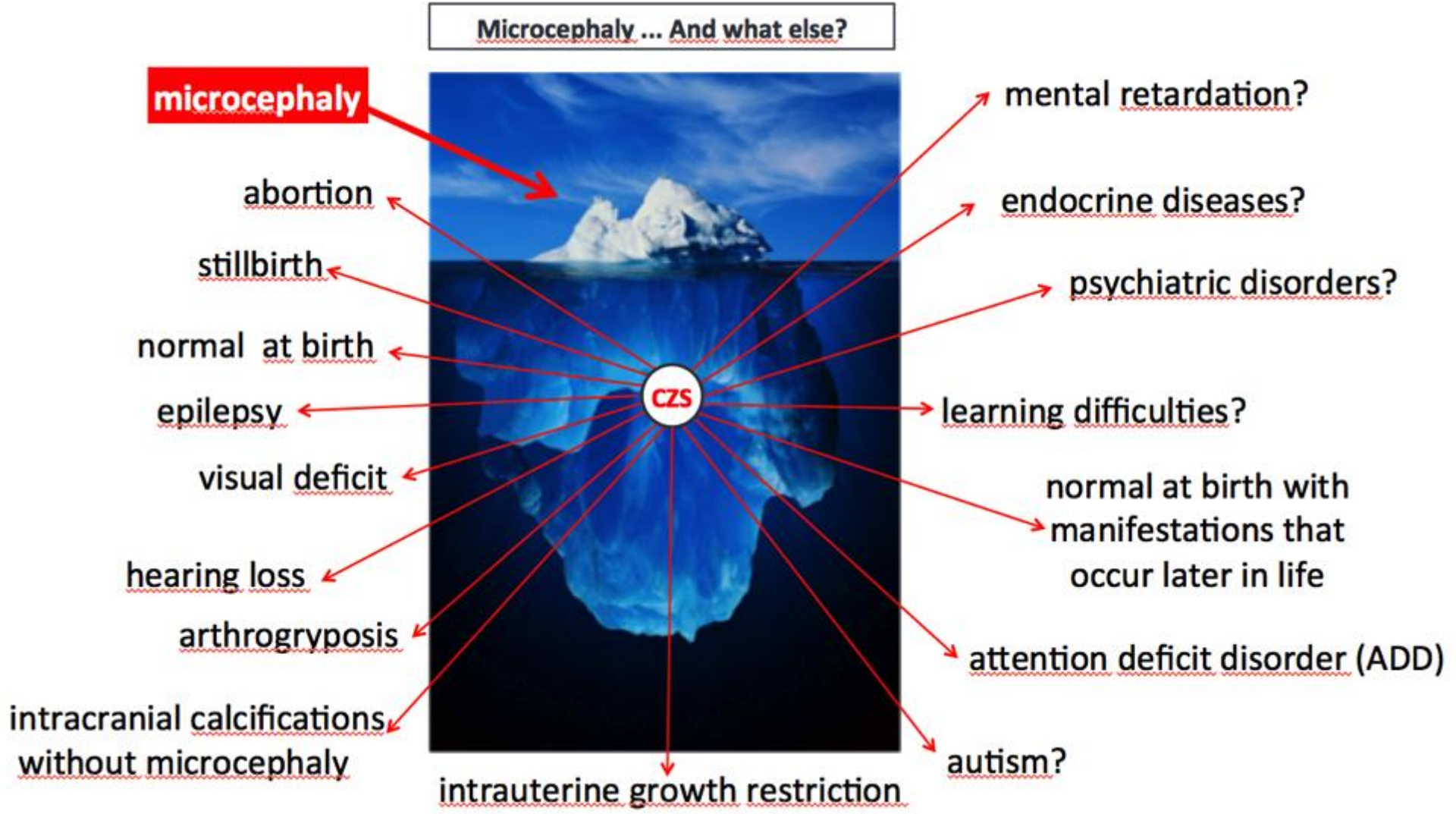
Sources: (1) infants who have been followed since the beginning of the epidemic; (2) case-control study

1. Born with microcephaly
2. **Born to infected women**



Principal outcomes to be compared: **evolution of head circumference, clinical, dental and neurological disorders, neurodevelopment, epilepsy, ophtalmologic and audiologic impairment, death.**

ZikaPLAN

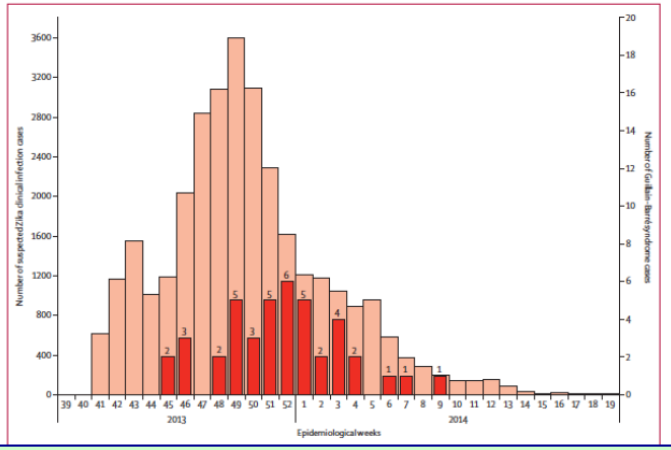

Microcephaly ... And what else?
microcephaly
abortion
stillbirth
normal at birth
epilepsy
visual deficit
hearing loss
arthrogryposis
intracranial calcifications without microcephaly
CZS
intrauterine growth restriction
mental retardation?
endocrine diseases?
psychiatric disorders?
learning difficulties?
normal at birth with manifestations that occur later in life
attention deficit disorder (ADD)
autism?

ZikaPLAN

GBS during outbreak of Zika Infection in French Polynesia (2013-2014)

[Population census 2012: 268,270 inhabitants]
Lancet February 29, 2016

- **Risk of GBS was 0.24 per 1000 Zika infections (1 per 4000 infected patients)**
- Mean Age **42 ys** (IQR 36-56)
- 31 Men (74%)
- History of viral illness in **88%**
- Median of **6 days** [IQR 4-10] before onset of GBS
- Median Progression of neuro symptoms to nadir was 4 days [IQR 4-9]
- Plateau phase 4 days [IQR 3-10]
- Clinical outcome 3 months after:
  - **24 (57%)** patients were able to walk without assistance



Clinical Features

- Generalized muscle weakness **74%**
- Inability to walk **44%**
- Facial palsy **64%**
- Admission to ICU **38%**
- Respiratory support **29%**
- Neurophysiology (37 cases) consistent with Acute Motor Axonal Neuropathy (**AMAN**)

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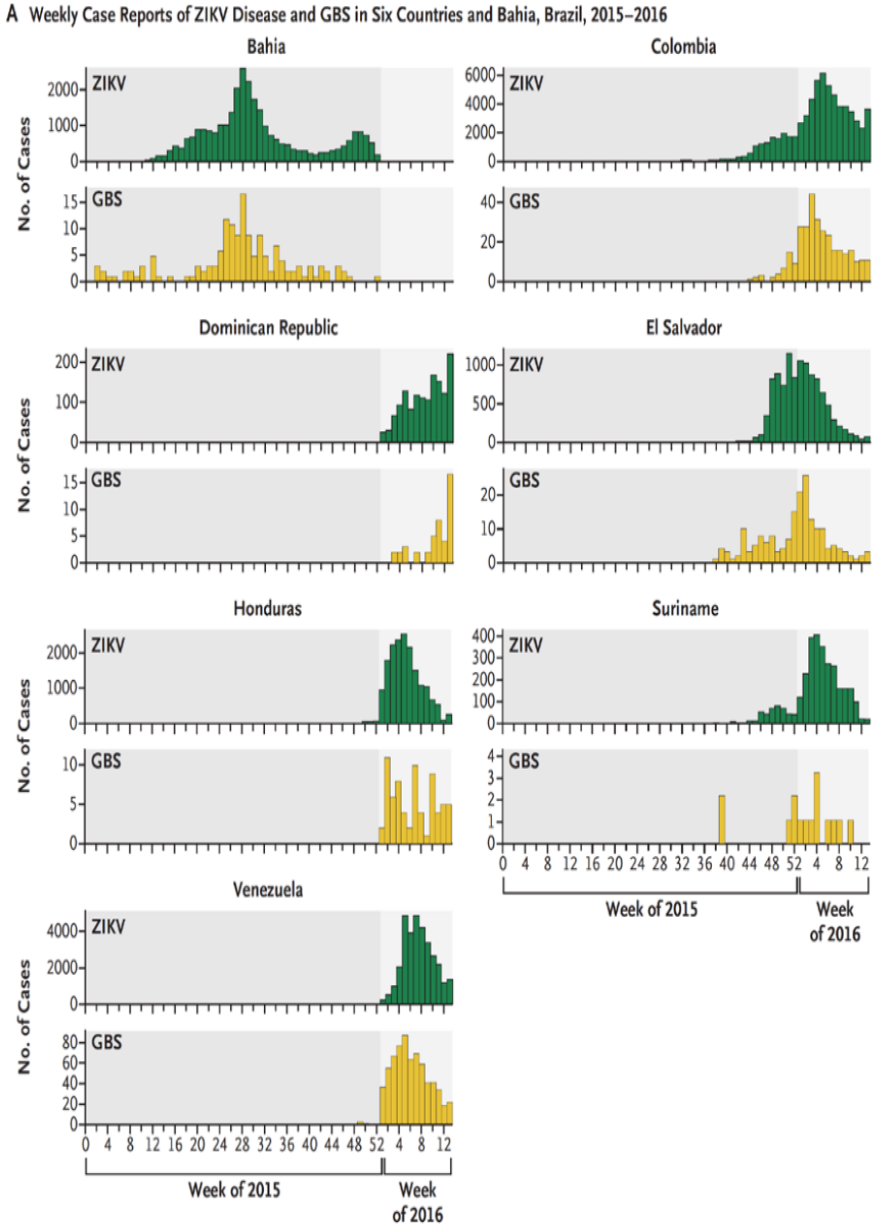
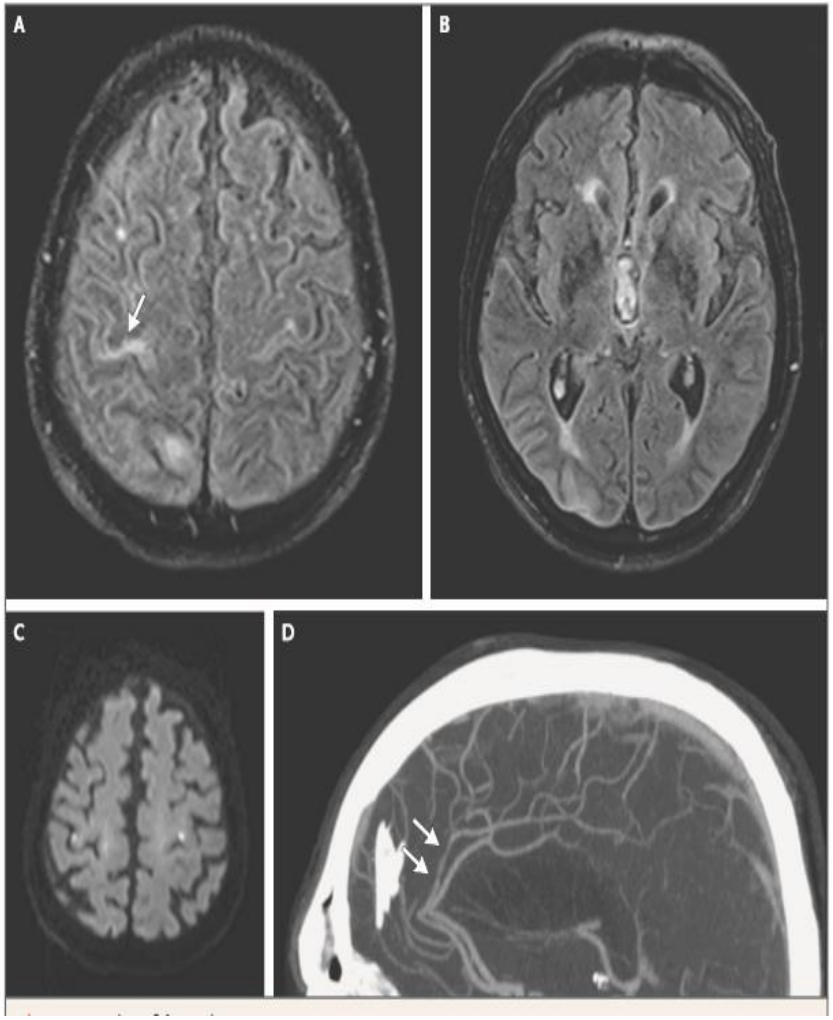
2016:
GBS in times of Zika



dos Santos T. et al. August 31, 2016
The NEW ENGLAND JOURNAL of MEDICINE
DOI: 10.1056/NEJMc1609015

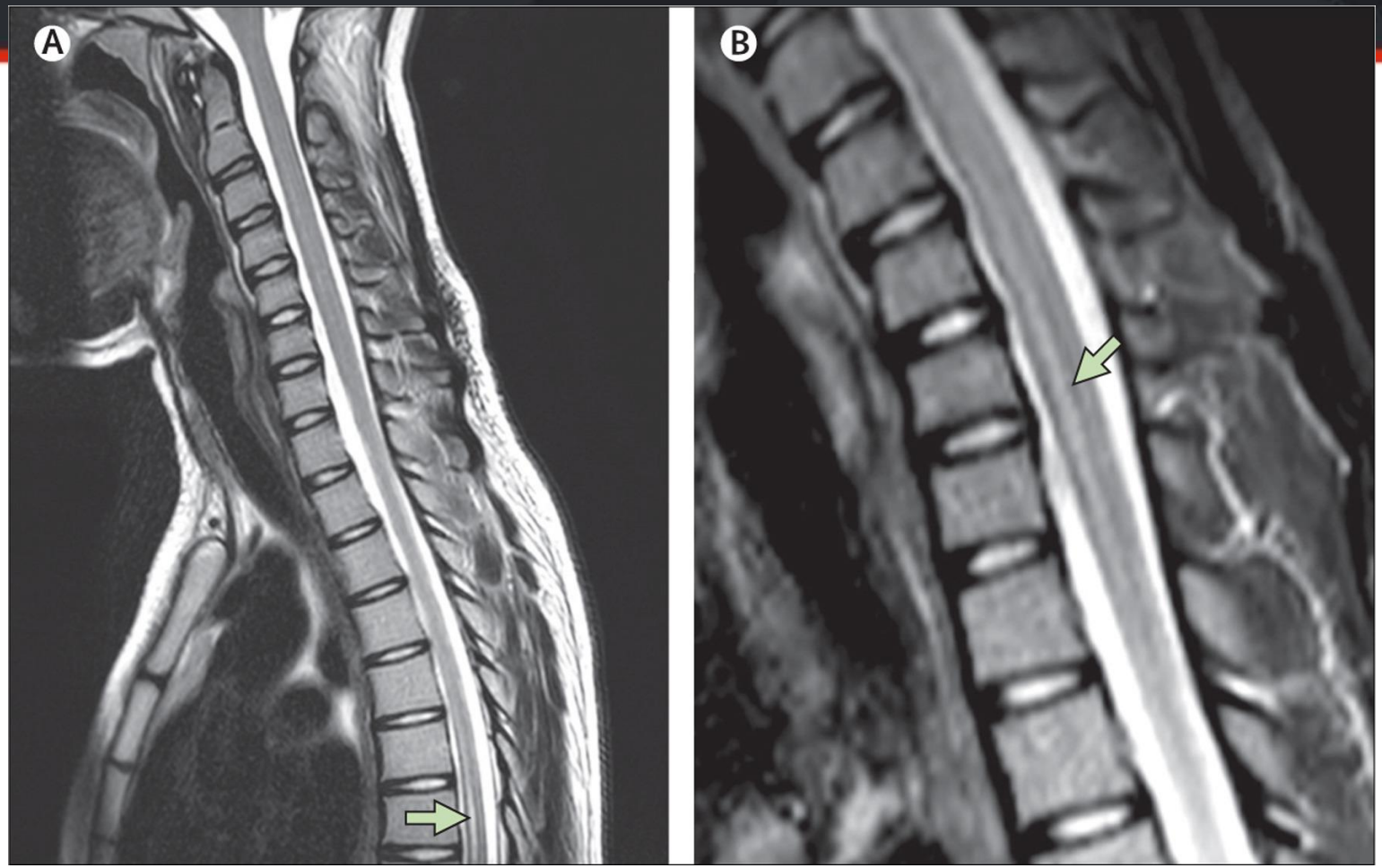
Zika Meningoencephalitis



- 81-year-old man admitted to ICU 10 days after a 4-week cruise in the area of New Caledonia, Vanuatu,
- Febrile (39.1° C) and comatose (GCS 6) with left hemiplegia and paresis of the right upper limb.
- Transient rash within the next 48 hours.
- CSF: WCC 41
  - (with 98% polymorphonuclear cells), protein 76 mg/dL, CSF/blood glucose ratio 0.75.
- CSF positive Zika RT-PCR assay and culture for ZIKV

Carteaux March 2016 NEJM

Acute myelitis due to Zika virus infection



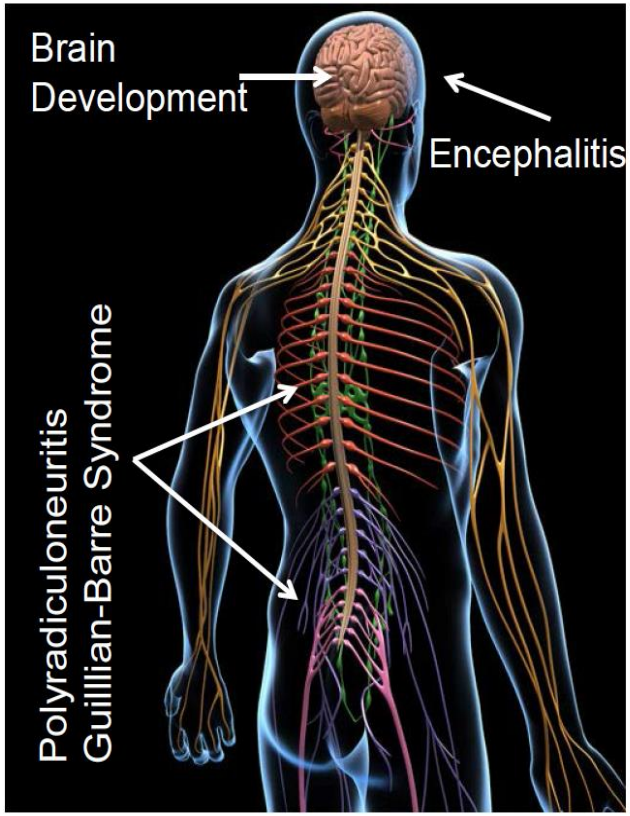
15 yo female, Left hemiparesis, back and arm pain, conjunctival injection, no fever

Mecharles et al. Lancet Published Online: 03 March 2016

Neurological Problems Presumed to be Associated with Zika Infection

Peripheral Nervous System Involvement:

- **Guillain-Barre Syndrome**
  - Acute Demyelinating Polyneuropathy
  - Acute Motor Axonal Neuropathy
  - Miller-Fisher variant
- **Neuropathies**



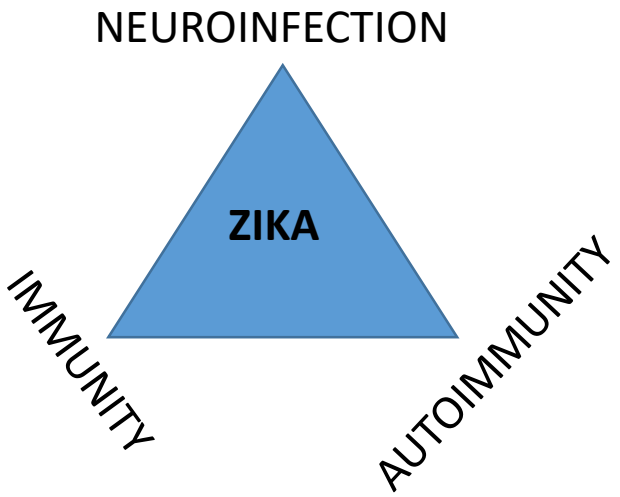
Central Nervous System Involvement:

- Encephalitis
- Myelitis
- Optic neuritis

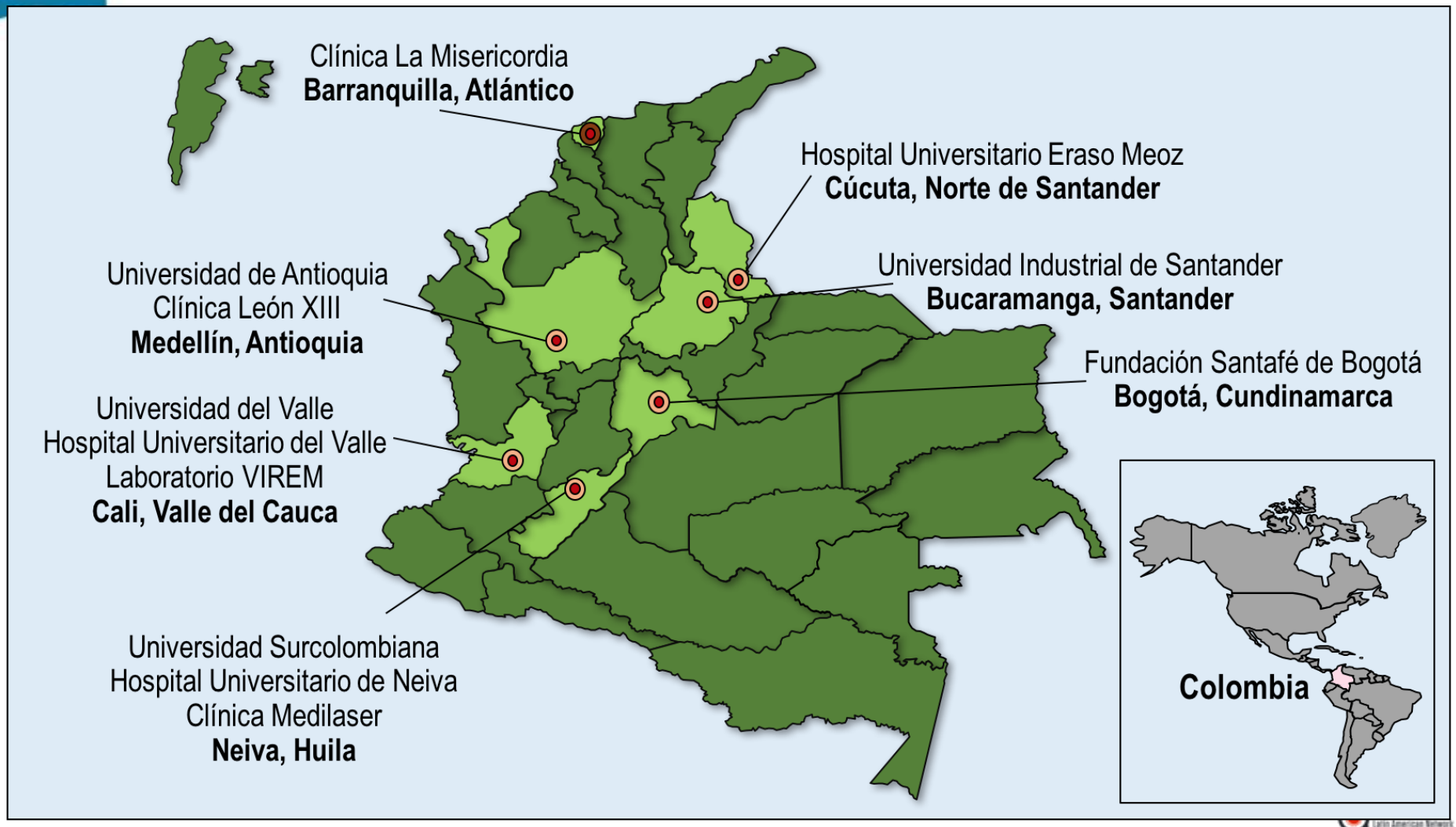
Immune Mediated Pathogenesis vs Direct Viral Neuropathogenicity or Both

What is causing Neuro-Zika?

DIRECT INFECTION? ⟷ PARAINFECTION? ⟷ POST-INFECTIOUS AUTOIMMUNITY?

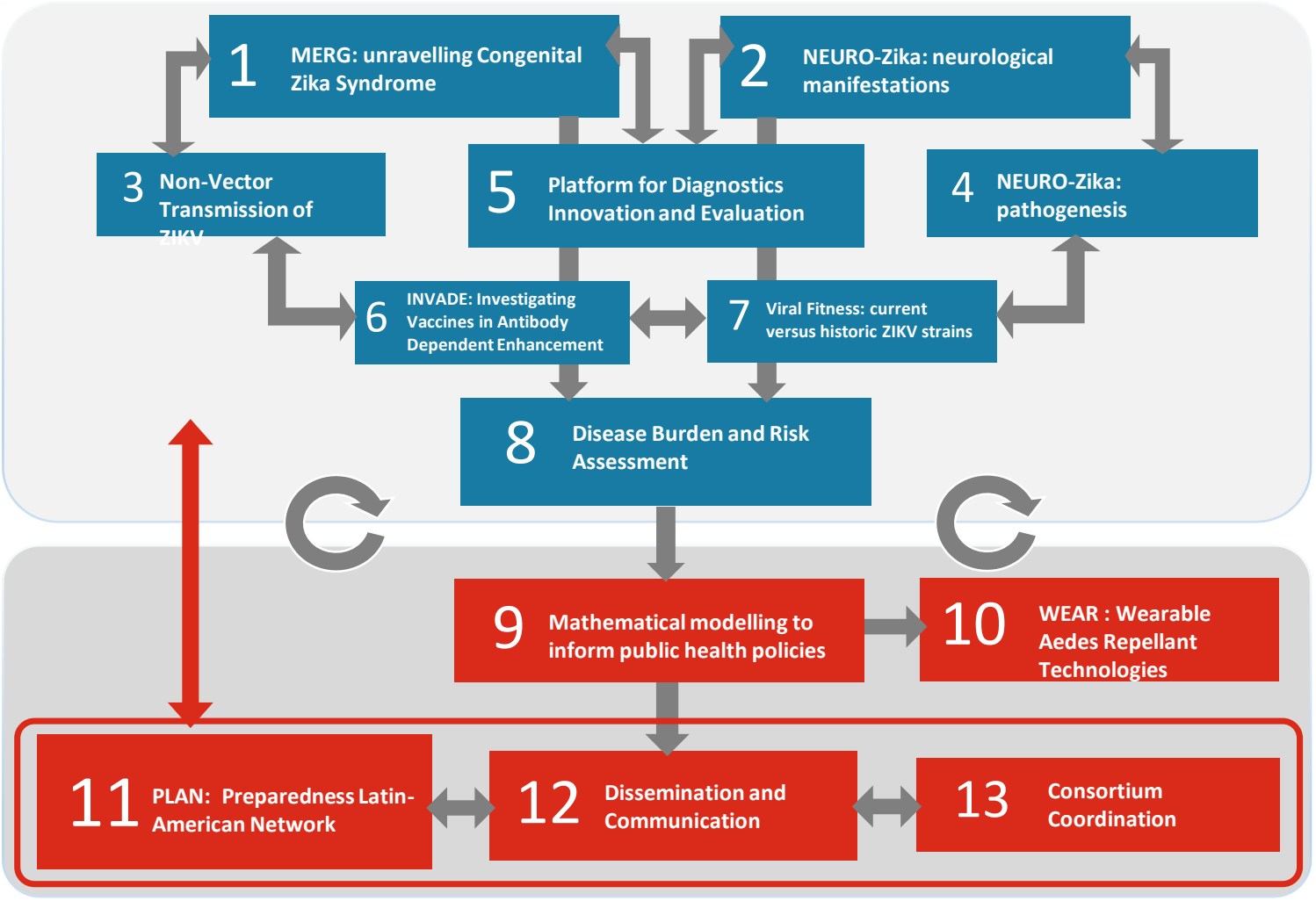


NEAS network in Colombia



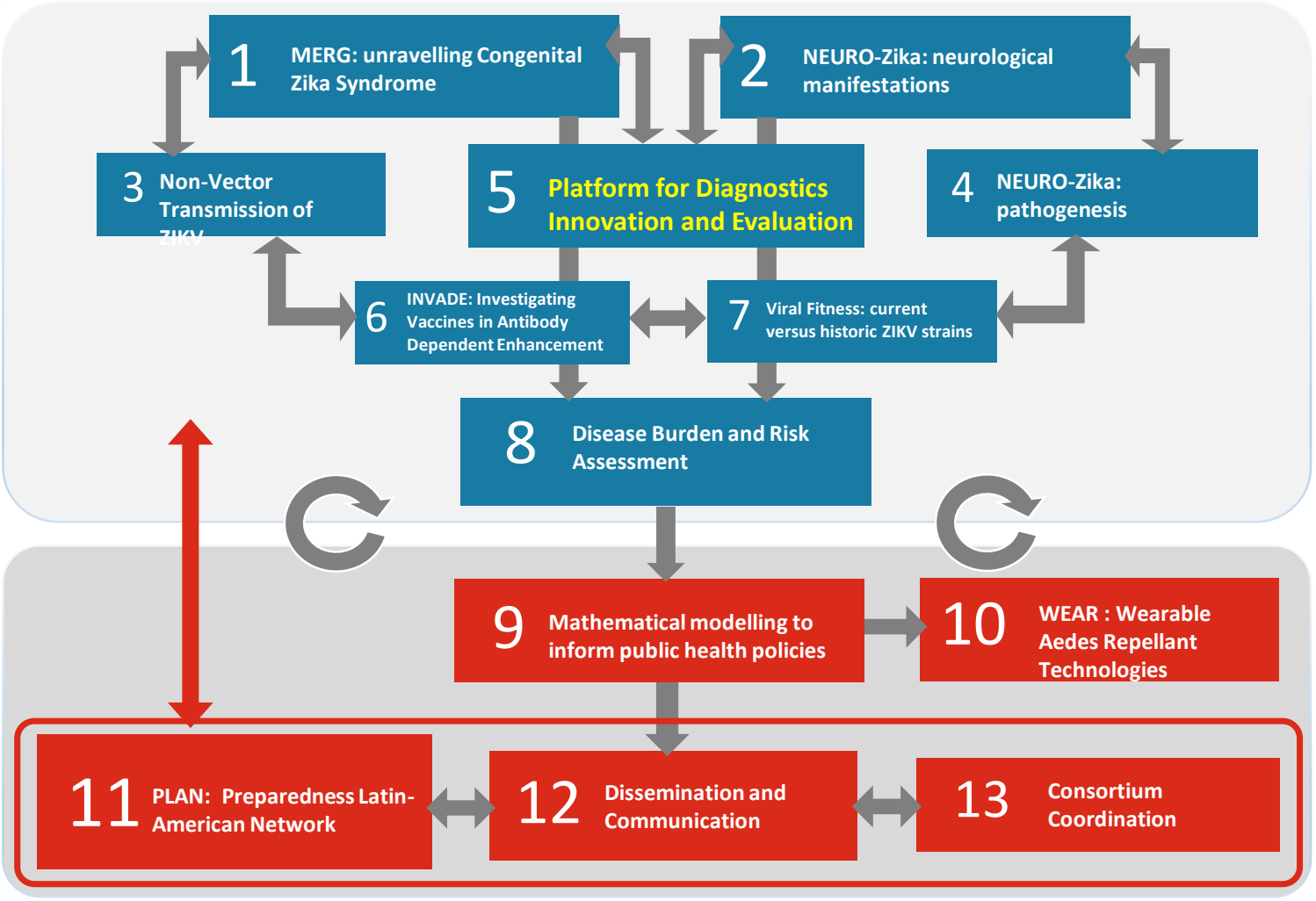
NEAS – COLOMBIA collaborating centers

Overall structure of the work plan



ZikaPLAN

Overall structure of the work plan



ZikaPLAN

ZikaPlan Bio-Bank: Guiding Principles and Governance

Guiding principles for the ZikaPLAN Biobank:

- Transparency
- Fairness: equal access by public and private test developers, small and large companies
- Respect national laws with regard to the transport or use of patient samples

Virtual bank concept to maximise contributions and minimise transport

A Steering Committee provides oversight with regard to:

- Virtual bank inventory
- Request for reference materials/panels
- Request for evaluations or access to collection/evaluation sites

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Diagnostics: Quality Cascade

1. Reference Panels (strains)
2. Development/Validation Panels (specimens)
3. Evaluation Panels

Design & Manufacture

Approval for use

4. Verification Panels

Availability in market

Procurement

5. Proficiency Panels

3.1. Quality of tests and testing

Storage

3.2. Quality of diagnosis

Performance

3.3. Data management

Algorithms used

Result reporting & record

ZikaPLAN evaluation platform

WP 5 Biobanking/Evaluation sites: criteria for selection

- Senegal, Colombia, Cuba (RELDA), Switzerland

Protocols for evaluation

- Review CDC and WHO PQ protocols, harmonize and publish
- All evaluation sites will obtain ethics approval for using the archived specimens and consensus protocol for evaluation

Request for evaluations

- Call for evaluation: Terms of agreement with companies
- Requests will be reviewed by the Steering Committee
- If approved, developers/manufacturers will be referred to the evaluation sites

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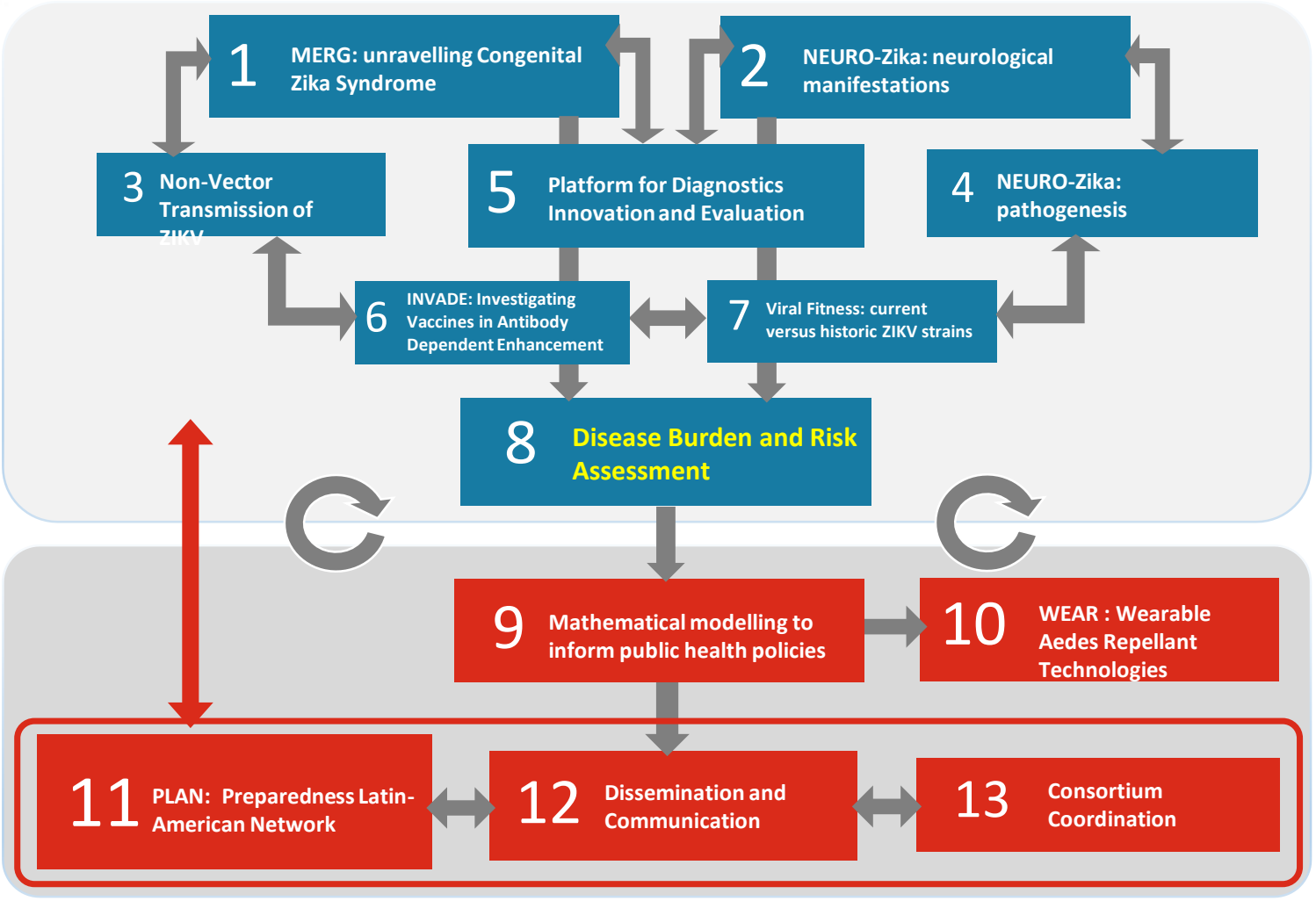
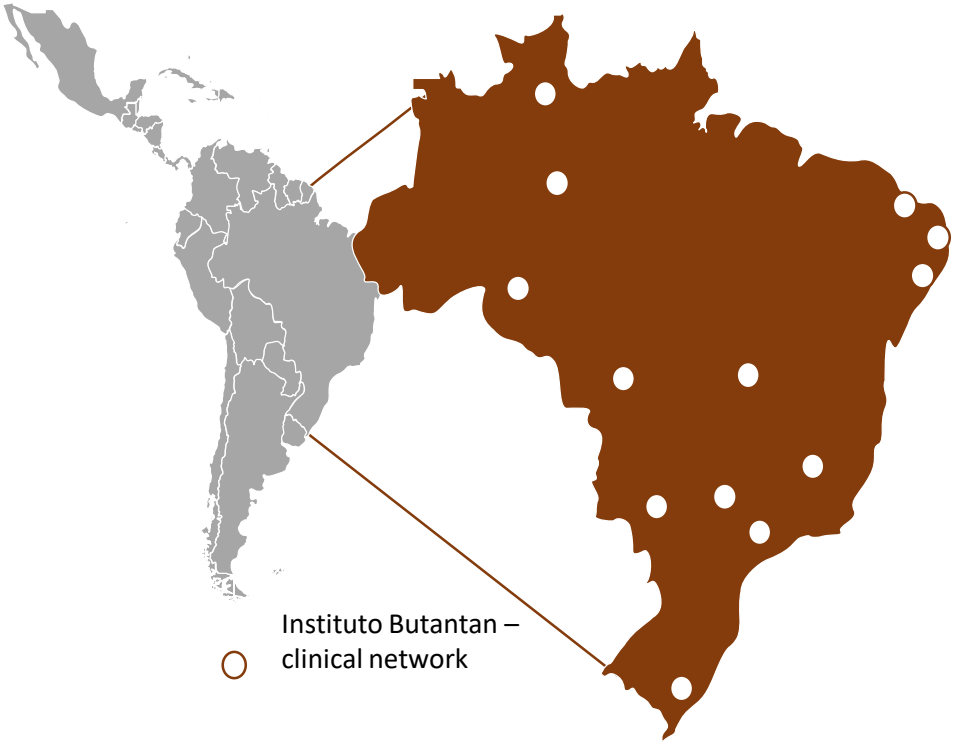
Overall structure of the work plan



ZikaPLAN

Prospective cohort study involving 17,000 subjects aged 2-59 in 14 different geographic locations in Brazil



14 Clinical Sites in Brazil

- *Boa Vista*
- *Mananus*
- *Porto Velho*
- *Cuiabá*
- *Campo Grande*
- *Brasília*
- *São José do Rio Preto*
- *São Paulo (2): Hospital das Clínicas – FMUSPand Santa Casa de Misericóridua*
- *Porto Alegre*
- *Belo Horizonte*
- *Aracajú*
- *Recife*
- *Fortaleza*

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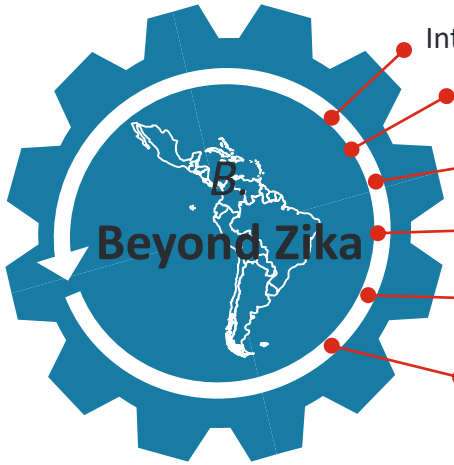
ZikaPLAN objectives

Addressing knowledge gaps and needs in key areas of interest to the current Zika Outbreak:

- Congenital Zika Syndrome(CZS)
- Neurological complications
- Pathogenesis
- Non-vector transmission
- Diagnostic tools
- True burden of disease
- Viral fitness

Building a sustainable Latin-American EID Preparedness and Response capacity



- Inter-Epidemic Research Plan
- Policy briefs and Recommendations
- Network building
- Training and Capacity Building
- Dissemination and Communication
- Sustainability Strategy

ZikaPLAN

NOVEL INTERVENTIONS FOR PREVENTION OF Aedes-transmitted diseases such as Zika and dengue



Pattamaporn Kittayapong[1], Phanthip Olanratmanee[1], Pongsri Maskhao[2], Peter Byass[3], Valérie Louis[4], James Logan[5], Duane Gubler[6], and Annelies Wilder-Smith[3,4]

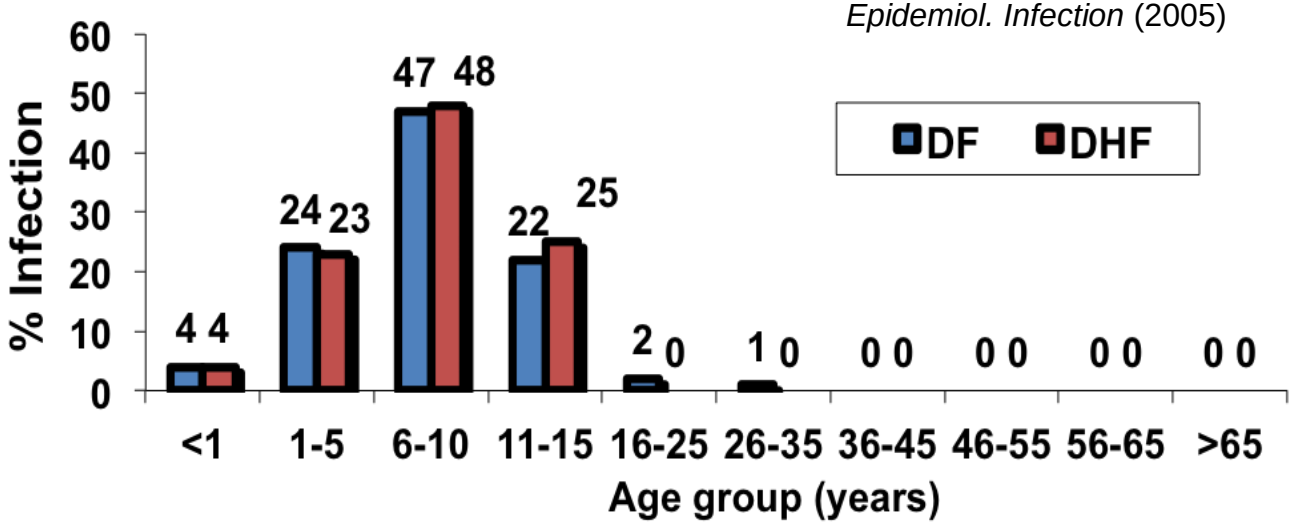
[1]Center of Excellence for Vectors and Vector-Borne Diseases, Faculty of Science, Mahidol University at Salaya, Nakhon Pathom, Thailand; [2] Faculty of Humanities and Social Sciences, Rajabhat Rajanagarindra University, Chachoengsao, Thailand; [3]Center for Global Health Research, Department of Public Health and Clinical Medicine, Umea University, Sweden; [4]Institute of Public Health, Heidelberg University Medical School, Germany; [5]Department of Disease Control, London School of Hygiene and Tropical Medicine, [6]Emerging Infectious Diseases Program, Duke-NUS, Singapore

Hypothesis: Impregnated school uniforms reduce the incidence of dengue infections in school children

Medical Hypotheses (2011) 861–862

A. Wilder-Smith [a,*], A. Lover [b], P. Kittayapong [c], G. Burnham [d]

Anatapreecha and *et, al. Epidemiol. Infection* (2005)



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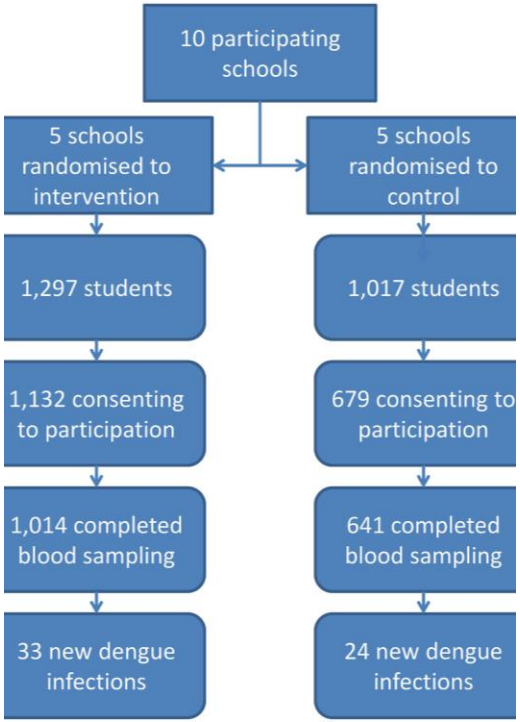
PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Mitigating Diseases Transmitted by *Aedes* Mosquitoes: A Cluster-Randomised Trial of Permethrin-Impregnated School Uniforms

Pattamaporn Kittayapong[1,2]*, Phanthip Olanratmanee[3], Pongsri Maskhao[4], Peter Byass[5], James Logan[6], Yesim Tozan[7,8], Valérie Louis[7], Duane J. Gubler[9], Annelies Wilder-Smith[5,6,10,11]*



SCHOOL UNIFORM PROCESSING

Collecting, coding & packaging school uniforms

Courier pick-up & shipping for permethrin-impregnation

Marking and school delivery

PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Mitigating Diseases Transmitted by *Aedes* Mosquitoes: A Cluster-Randomised Trial of Permethrin-Impregnated School Uniforms

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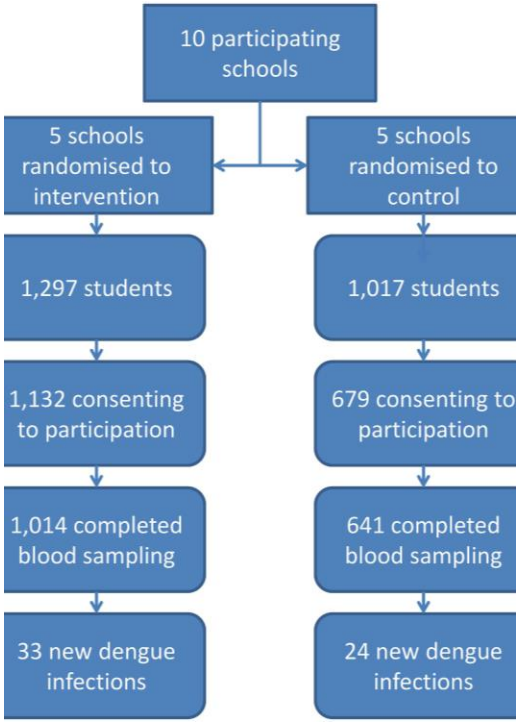


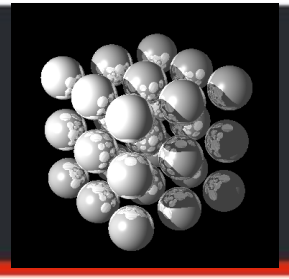
No difference in the attack rate

Why?

Rapid washing out of permethrin

Longer lasting insecticides, applications for maternity clothing, for tourists

ZikaPLAN: Wash-resistant clothing



Investigate new wash-resistant technologies that are currently under development

Fibres that contain novel silica shells, that can be weaved into clothing to maintain slow release of repellents over multiple washes

Cone tests, arm-in cage tests, GC and HPLC analysis to determine release rates from the fabric after multiple washes (0-100 washes)

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Networks, networks, networks

Birth defect surveillance

NEAS

Evaluation platform-laboratory network

Vector hub

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Introducing... REDe

Research Capacity Network

Research Capacity Network

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groups » Research Capacity in Latin America - what is missing? » Welcome to REDE! Tell us what you need in your area

Bienvenidos a REDE. Esperamos poder trabajar juntos en crear una red integrada
cientifica y ayudara a mejorar las capacidades para investigaciones futura

Introduciendose
Hablando donde se encuentra
Comentandonos tres opiniones que consideran generarion un cambio en la
area?

Esperamos escuchar de ustedes!
El Equipo Editorial

Welcome to REDE everybody. We look forward to working together to create an in
will bring together the research community and help to build capacity for future re

Introducing yourself
Telling us where you are
Telling us what three things would make a difference to research capacity in your are

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What are you looking for? SEARCH

REDe

Research Capacity Network

THE PREPAREDNESS RESEARCH CAPACITY NETWORK FOR THE EU ZIKA CONSORTIA

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Home

This is the working space for REDe, the research capacity network that is run by the three EU Zika consortia; ZikaPLAN, ZikAlliance and ZikAction. The aim is to build strong partnerships between all research sites running Zika studies in Latin America and the Caribbean so we can work together and develop a sustainable platform for research that can respond to future outbreaks.

REDe Resources

Access resources to guide, teach, support and train you and your team in setting up and running high quality studies.

LEARN MORE

GHN_EDITORS

Build your professional profile and CV

MEMBERSHIP LEVEL:

SUBMISSION REQUIRED

REDe
Research Capacity Network

REDe aims to build a strong & sustainable network which will be led by core centres of excellent within the region.

These regional centres will coordinate and implement all sorts of capacity development activities such as:

- Workshops
- Mentoring schemes
- Focussed training session
- Online courses

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ZikaPLAN

e-Learning short courses through the Global Health Network

Conducting Clinical Research:

1. Introduction to Clinical Research – ***EACCR***
2. ICH Good Clinical Practice – ***MRC The Gambia***
3. The Research Question – ***Expert driven content***
4. The Study Protocol: Part one – ***Expert driven content***
5. The Study Protocol: Part two – ***Expert driven content***
6. Data Safety Monitoring Boards for Clinical Trials – ***Expert driven content***
7. Introduction to Informed Consent – ***MRC The Gambia***
8. Introduction to Data Management for Clinical Research Studies - ***DNDi, UCT***
9. Introduction to Collecting and Reporting Adverse Events – ***MRC The Gambia***

Specialist Topics:

1. Introduction to Good Clinical Laboratory Practice – ***Gates Foundation GHCC***
2. Ethics of Ancillary Care in Research – ***John Hopkins University***
3. Introduction to Reviewing Genomic Research – ***Expert driven content***
4. The Retrospective Treatment Outcome Study for Traditional Medicines – ***Expert driven content***
5. How to Conduct GCP Inspections/Audits at the Clinical Investigator Site – ***Expert driven content***
6. Ethics & Best Practice in Data Sharing in Research – ***Expert driven content***
7. Children and Clinical Research – ***Nuffield Council on Bioethics***

Preparedness Latin American Network ZikaPLAN

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