WHO ZIKV Individual Participant Data Consortium: Progress to date and next steps

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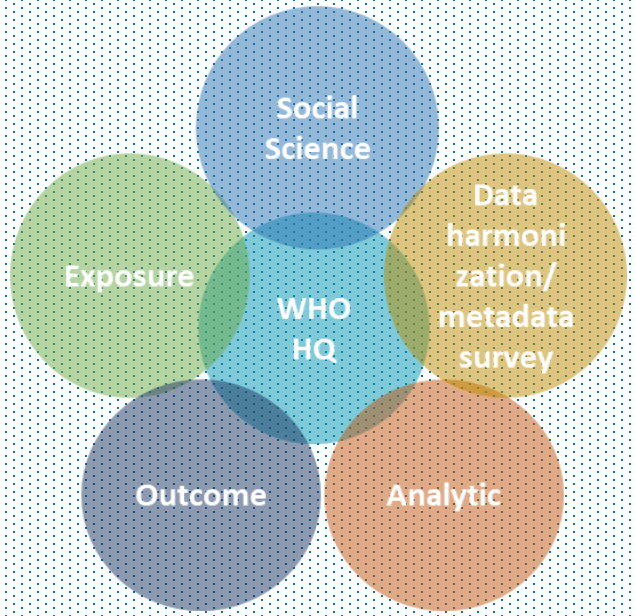
WHO ZIKV consortium

Established in 2017 by the PAHO/WHO, the **ZIKV Individual Participant Data (ZIKV-IPD) Consortium** harmonizes global research on Zika virus in pregnancy.

The Consortium initiative arose from a meeting of international organizations and Ministries of Health in June 2016 to coordinate and harmonize ZIKV-related research efforts

It collaborates with international organizations to develop and validate prognostic models for predicting adverse pregnancy outcomes, guiding healthcare practices.

Consortium organization



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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).

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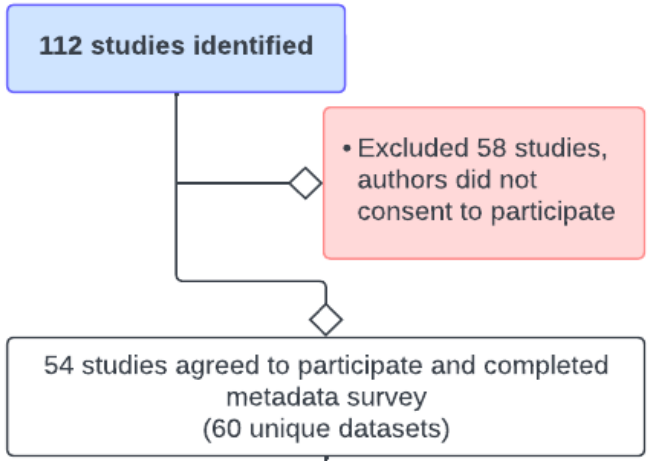
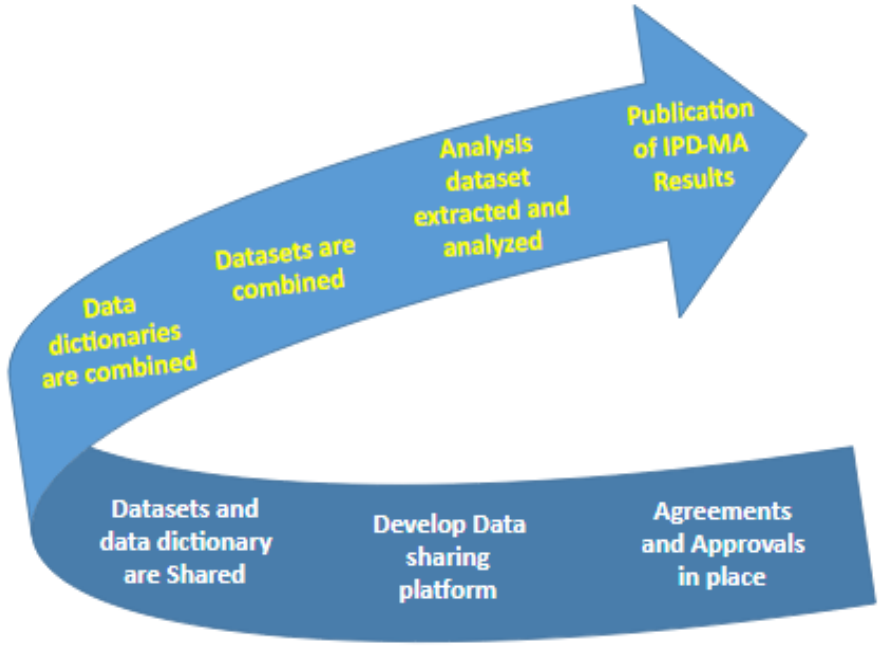
WHO - ZIKA IPD Consortium Process

1. Identification



2. CONTRIBUTION



To note

- Secure web-based data platform (OpenClinica) used for data upload

3. HARMONIZATION

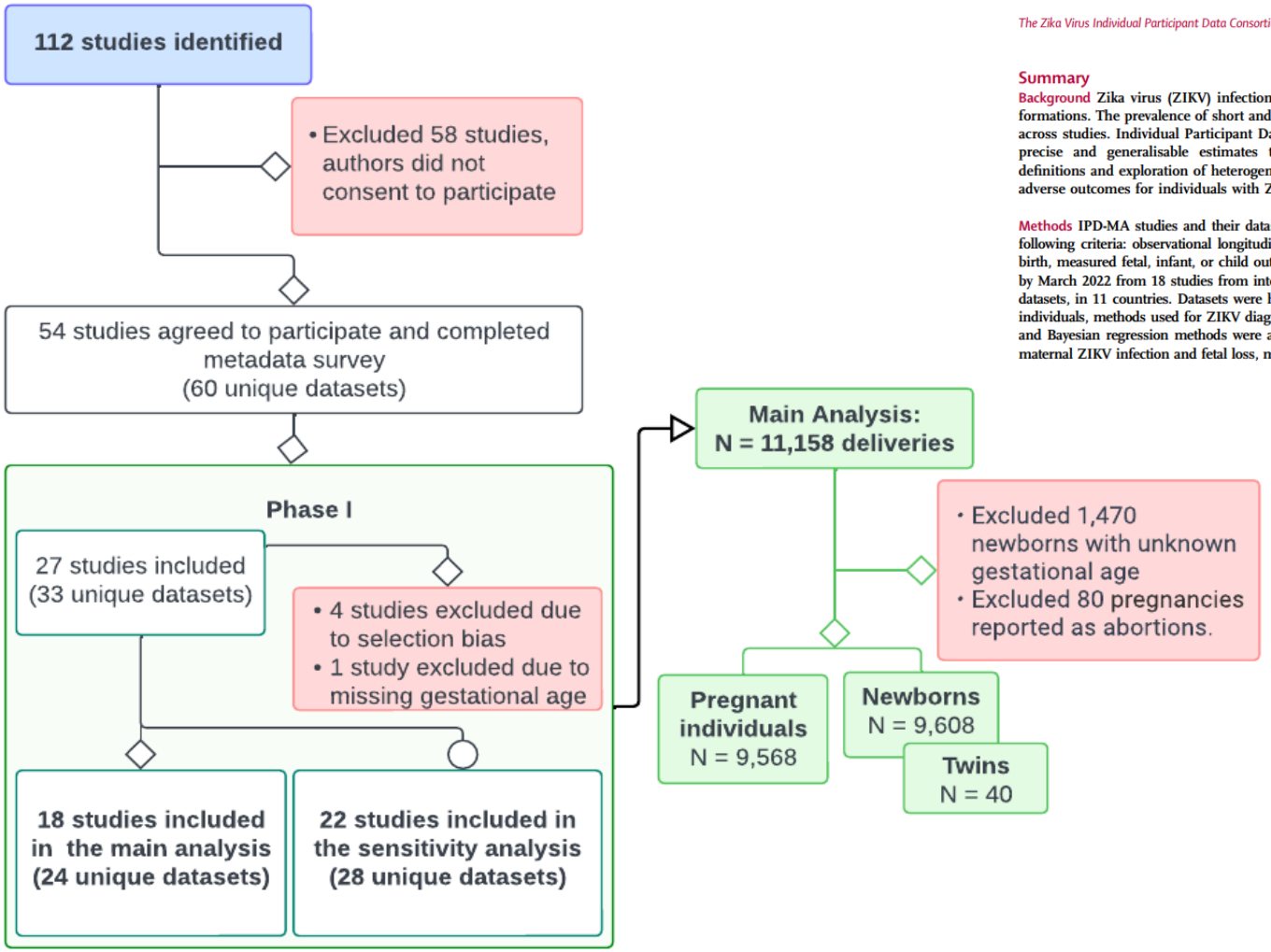
Master codebook

2020: Master codebook 236 variables

2022: Master codebook (expanded)

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

Phase I Results paper



Adverse fetal and perinatal outcomes associated with Zika virus infection during pregnancy: an individual participant data meta-analysis

The Zika Virus Individual Participant Data Consortium[e]

eClinicalMedicine
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Summary

Background Zika virus (ZIKV) infection during pregnancy is associated with an increased risk of congenital malformations. The prevalence of short and long-term consequences, however, remains uncertain due to heterogeneity across studies. Individual Participant Data Meta-Analysis (IPD-MA) offers an alternative approach to provide more precise and generalisable estimates through data harmonisation across studies, allowing for standardised definitions and exploration of heterogeneity. This project was undertaken to estimate absolute and relative risks of adverse outcomes for individuals with ZIKV infection during pregnancy.

Methods IPD-MA studies and their datasets were identified through a systematic search conducted in 2018 with the following criteria: observational longitudinal or surveillance-based studies investigating ZIKV during pregnancy or at birth, measured fetal, infant, or child outcomes, and included at least 10 participants. Here we used IPD data shared by March 2022 from 18 studies from international health organisations and research networks, comprising 24 unique datasets, in 11 countries. Datasets were harmonised with standardised definitions, using variables related to pregnant individuals, methods used for ZIKV diagnoses, fetal characteristics and outcomes, and pooled for analysis. Frequentist and Bayesian regression methods were applied to estimate outcome prevalence and evaluate the association between maternal ZIKV infection and fetal loss, microcephaly and congenital zika syndrome as primary outcomes.

MICROCEPHALY

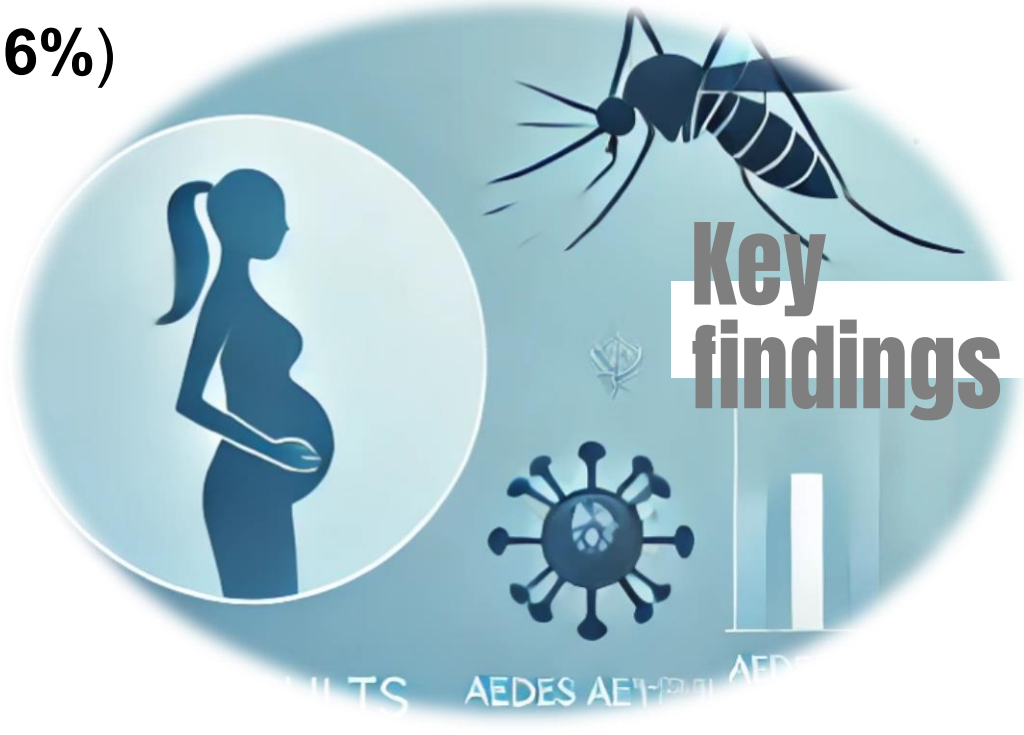
Estimated at **3%** (95% Confidence Interval: **2% - 5%**)

Fetal Loss

Estimated at **4%** (95% Confidence Interval: **2% - 6%**)

Congenital Zika Syndrome (CZS)

Increased risk observed, highlighting potential severe outcomes in affected pregnancies



Next steps: Phase II

- Data acquisition and harmonization of remaining studies
- Continue conducting the short- and long-term risk analysis in the complete set of participant studies
- Address the statistical challenges related to under and over reporting in surveillance-based studies
- Address measurement error

Acknowledgement

Many thanks to ZIKV Consortium participating members

Below are the coordinating team, working groups, and their members:

Coordinating team: Broutet N, Carabali M, Jaenisch T, Kara E, Kim C, Maxwell L, Sayers J, Silva R, Thwin SS, and Ximenes R.

Exposure working group: Alger J, Alvares DR, Brasil P, Calvet G, Cerigo H, Cunha A, da Veiga AG, LaBeaud D, Marques E, Martelli CT, Mattar S, Passos SD, Rabe I, and Scalabrin D defined exposure variables for data harmonization.

Outcome working group: Araújo TVB, Arrieta G, Avelino-Silva V, Bardají A, Bertozzi A, Blackmon K, Buekens P, Cachay R, Clemente NS, da Costa PS, de Siqueira I, DeBiasi RL, Duarte G, Eickmann S, Fumadó V, Gerardin P, Hofer C, Holband N, Lee E, Lopez-Medina E, Miranda-Filho DB, Mojica CB, Moreira ME, Mulkey SB, Mussi-Pinhata M, Noel T, Pomar L, Prata-Barbosa A, Sohan K, Soria-Segarra C, Soriano-Arandes A, Ticona JPA, Valencia D, Viñuela-Benéitez C, and Vouga M defined outcome variables for data harmonization.

Analytic working group: Benedetti A, Caicedo-Castro I, Campbell H, Damen JAAG, Debray T, de Jong V, Gibbons L, Gustafson P, Hofer C, Montarroyos U, Moons K, Munoz J, and Wei Y conducted statistical analysis and results synthesis.

Data harmonization working group and metadata survey: Cerigo H, De La Hoz-Siegler I, Levis B, Rosenberger KD, Shreedhar P, and Tobian F worked on data harmonization and metadata survey.

Social Science working group: Campos M, Daza M, Gama G, Hormiga C, Marban-Castro E, Matta G, Melo A, Mercado M, Montoya MCM, Paiva E, and Petra P focused on the qualitative research related to the social impact of the Zika virus and reviewed the manuscript.

Thank you

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