Using IPD-MA to inform the public health response to ZIKV

Nathalie Broutet
Caron Kim, Lauren Maxwell, João Paulo Souza
on behalf of the ZIKV IPD Consortium
Understanding ZIKV
How IPD-MA can help
1. Estimate the absolute and relative risks of microcephaly and other adverse perinatal outcomes by trimester of infection, rash, viremia, concurrent or prior flavivirus infection (dengue, yellow fever vaccination, ZIKV), and other co-factors

2. Identify factors that modify women’s risk of ZIKV-related fetal or neonatal outcomes, including microcephaly

3. Develop and validate a risk prediction tool to inform decision making by pregnant women, couples planning a pregnancy, and healthcare providers and/or resource mobilization
Reach the sample size necessary for precise and accurate risk estimates.
Explore sources of heterogeneity and effect measure modification

<table>
<thead>
<tr>
<th>Year</th>
<th>Participants (no)</th>
<th>Deaths (no)</th>
<th>Deaths from external causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
<td>9183</td>
<td>557</td>
<td>68</td>
</tr>
<tr>
<td>1995</td>
<td>9328</td>
<td>574</td>
<td>68</td>
</tr>
<tr>
<td>1997</td>
<td>4963</td>
<td>217</td>
<td>29</td>
</tr>
<tr>
<td>1998</td>
<td>9335</td>
<td>401</td>
<td>64</td>
</tr>
<tr>
<td>1999</td>
<td>4657</td>
<td>176</td>
<td>19</td>
</tr>
<tr>
<td>2000</td>
<td>5144</td>
<td>194</td>
<td>47</td>
</tr>
<tr>
<td>2001</td>
<td>8940</td>
<td>211</td>
<td>44</td>
</tr>
<tr>
<td>2002</td>
<td>795</td>
<td>106</td>
<td>19</td>
</tr>
<tr>
<td>2003</td>
<td>719</td>
<td>106</td>
<td>23</td>
</tr>
<tr>
<td>2004</td>
<td>3858</td>
<td>30</td>
<td>5</td>
</tr>
<tr>
<td>Overall</td>
<td>68 222</td>
<td>2552</td>
<td>386</td>
</tr>
</tbody>
</table>

Cancer death

Deaths (no) | Hazard ratio (95% CI)
--- | -------------------
557 | 1.06 (0.97 to 1.16)
574 | 1.00 (0.92 to 1.09)
217 | 1.10 (0.97 to 1.25)
401 | 1.13 (1.03 to 1.24)
176 | 1.10 (0.96 to 1.26)
194 | 1.12 (0.98 to 1.27)
211 | 1.11 (0.96 to 1.27)
106 | 1.19 (1.00 to 1.43)
30  | 1.42 (1.09 to 1.86)
386 | 1.14 (1.04 to 1.13)

Deaths from external causes

Deaths (no) | Hazard ratio (95% CI)
--- | -------------------
68 | 1.05 (0.81 to 1.36)
68 | 1.24 (1.01 to 1.51)
29 | 1.18 (0.86 to 1.61)
64 | 1.50 (1.27 to 1.78)
19 | 1.42 (1.02 to 1.98)
47 | 1.11 (0.85 to 1.44)
44 | 1.40 (1.11 to 1.76)
19 | 0.74 (0.39 to 1.43)
23 | 1.17 (0.80 to 1.71)
5  | 1.48 (0.83 to 2.63)
386 | 1.14 (1.04 to 1.13)

Hazard ratio

http://www.bmj.com/content/bmj/345/bmj.e4933/F2.large.jpg?width=800&height=600
Facilitate sensitivity analyses
Identify pregnancies at the highest risk of CZS
Standardized protocols and IPD

Standardization facilitates:

• Pooling data across studies to ensure precise and accurate estimates of relative and absolute risks of ZIKV-related outcomes

• Ensuring results are due to differences in the epidemiology and pathology of ZIKV infection and not due to differences in data collection methods

• Coordination of research to improve efficiency and produce timely information to shape the public health response to emergency
<table>
<thead>
<tr>
<th>Research protocol</th>
<th>What will the studies measure?</th>
</tr>
</thead>
</table>
| Cohort study of Pregnant Women                       | • Measure ZIKV infection in pregnant women  
• Describe the clinical spectrum of ZIKV Infection in pregnant women  
• Identify, describe and quantify the spectrum of congenital deficiencies, including microcephaly, in the fetuses/offspring of ZIKV-infected women |
| Case-control study for microcephaly and congenital ZIKV syndrome | • Identify and quantify risk factors for microcephaly and congenital ZIKV syndrome                                                                                                                                               |
| Case-control study for Guillain-Barré Syndrome and GBS-like syndrome | • Identify and quantify risk factors for Guillain-Barré Syndrome and GBS-like syndrome                                                                                                                                           |
| Cohort study of newborns of pregnant women with ZIKV | • Identify, describe and quantify the spectrum of congenital deficiencies, including microcephaly, in the fetuses/offspring of ZIKV-infected women                                                                                   |
| Virus survival in body fluids                        | • Measure ZIKV in different body fluids of confirmed ZIKV patients at different time points                                                                                                                                       |
| ZIKV Seroprevalence study general population         | • Estimate seroprevalence of ZIKV in all age groups of the general population living in exposed and non-exposed areas                                                                                                            |
Support and harmonization of research in countries: Standardized research protocols

A document summarizes the ongoing efforts of the World Health Organization and Pan American Health Organization, Institut Pasteur and the networks of Fiocruz, CONISSE and ISARIC to generate standardized clinical and epidemiological research protocols and questionnaires to address key public health questions. Specifically, data collected using the standardized protocols will be used to refine and update recommendations for prevention of Zika virus spread, surveillance and case definitions for microcephaly, to help understand the spread, severity, spectrum and impact on the community of ZIKV and to guide public health measures, particularly for pregnant women and couples planning a pregnancy.

Read summary
pdf, 407kb
15 pages

Creating a central repository for ZIKV data
The global response to ZIKV
In the shadow of Ebola

http://i.huffpost.com/gadgets/slideshows/359890/slide_359890_4018996_free.jpg
Seyllou/AFP/Getty Images
ZIKV IPD Consortium

ZIKAlliance

IDAMS

CDC

Institut Pasteur

European Commission

ISARIC

Instituts thématiques

Inserm

Centers for Disease Control and Prevention

Preparedness Latin American Network

ZikaPLAN

NIH

National Institutes of Health

ZIKAAction
Acknowledgements

wellcome trust