WHO EPI-WIN Seminar
Zika: Ten years after the public health emergency

Zika Research Priorities for Preparedness and Response

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Zika and associated complications:
Public Health Emergency of International Concern (PHEIC)

2015-2016 WHO declared public health emergency

- Rapid surge in global attention, investment, research, response
  - transmission
  - pathogenesis
  - spectrum of disease
  - diagnostics
  - vaccines
  - prevention and control

End of the PHEIC – persistent challenges

Zika transmission declined. The Zika agenda was left unfinished.

- No vaccines
- No monoclonal antibodies
- No therapeutics
- No diagnostics for routine screening of asymptomatic pregnant women
- Limited global surveillance and laboratory infrastructure, esp. outside the Americas

Unprepared for re-emergence in the future

End of an emergency ≠ end of a response

Challenges of detecting and studying Zika transmission and disease

- 50-80% of infections asymptomatic
- Most infections mild and self-limited
  - Don’t present to medical care
- Not detected or reported with low transmission
- Microcephaly affects a small percent of affected pregnancies
- Affected infants are born months after intrauterine exposure

In the absence of large outbreaks, Zika virus and congenital Zika syndrome will likely evade detection.

Diagnostics: Key barrier for clinical care, surveillance, research

Challenges with existing laboratory assays

- Acute infections diagnosed by PCR
  - Highly specific, but technically complex
  - 3-5 day window of detection
  - Useful only for recent, symptomatic infections
- Serology (antibody) tests: cross-react with Zika, dengue, other orthoflaviviruses
  - IgG - long-lasting antibody, can't differentiate recent infection
  - IgM - indicates more recent infection, but may persist for months; may reflect infection prior to pregnancy
- No current test recommended for routine screening of asymptomatic pregnant women.

Improved diagnostics needed for surveillance, clinical management, research, development of vaccines, therapeutics, monoclonal antibodies.

Zika Vaccines and Monoclonal Antibodies

Zika vaccine development – active area early in the epidemic:

- 22 vaccines advanced to Phase I clinical trials
- Several types of candidates: inactivated virion, live-attenuated, mRNA, DNA, virus-vectored, recombinant peptides
- Many novel approaches in preclinical development
- Important decline in public and private investment after transmission declined

Prophylactic monoclonal antibodies:

- Used for multiple other pathogens (RSV, SARS-CoV-2, ebola, etc.)
- Promising potential for rapid deployment, including use in pregnant women - if available, affordable, and manufactured at scale

Decline in ZIKV incidence: major barrier to large clinical trials, reaching clinical endpoints. Need to prepare sites now for clinical trials in future outbreaks.

Research priorities for Zika epidemiology, transmission, and pathogenesis

Limited information on Zika transmission and disease in Africa and SE Asia

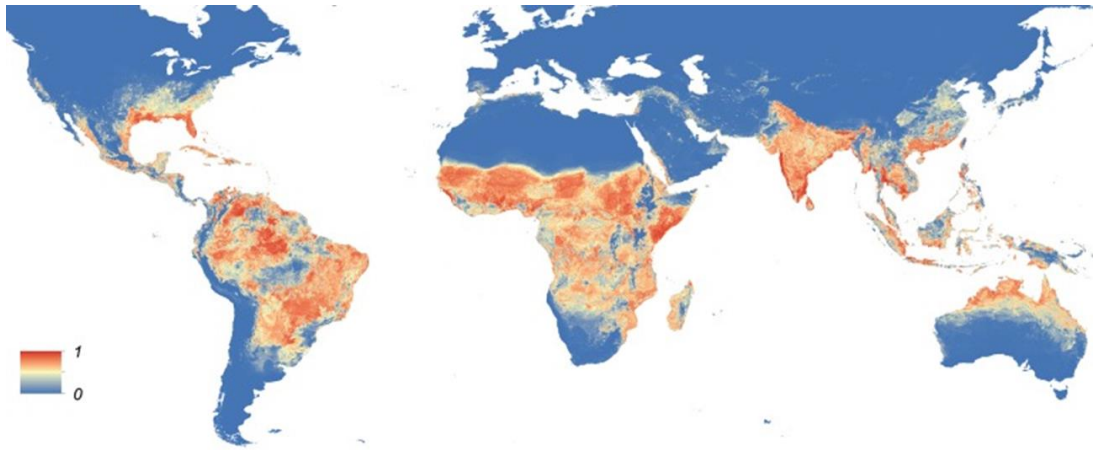
- Pre-epidemic Asian strain:
  - Continues to circulate in SE Asia
  - Limited surveillance on infection and birth outcomes
  - Thailand studies confirmed cause of microcrephaly
- African lineage Zika virus – little known:
  - Rare, sporadic case reports
  - Sentinel surveillance needed to identify cases and outcomes
  - Animal models – possible increased virulence vs. Asian lineage

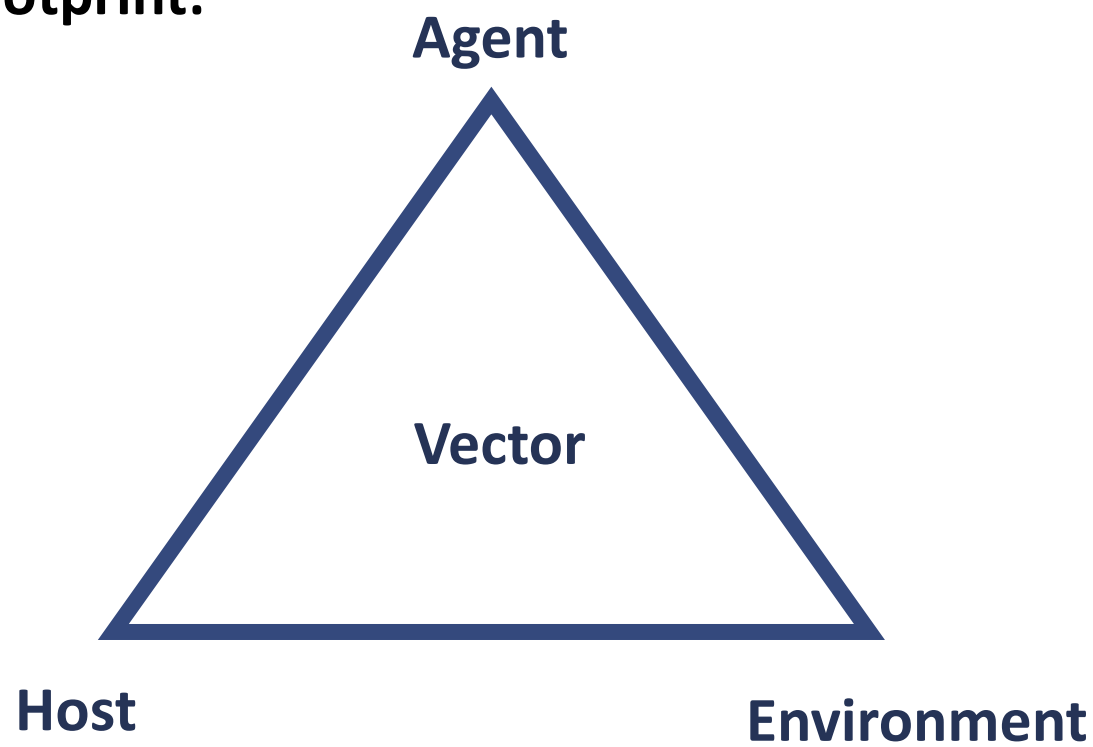
    Fetal loss rather than birth defects?

Acceleration of Aedes-borne epidemics: dengue, Zika, chikungunya, yellow fever

Common factors fueling expansion of vector footprint:

- Climate change
- Migration, urbanization
- Poverty
- Crowding
- Water and sanitation





Research priorities for vector control and understanding interactions of vector-host-animal reservoirs

- Strengthen evidence base for current vector control strategies (larvicides, residual spraying, sanitation)
- Multiple promising new technologies – need for accelerated innovation and moving to scale
- Investigate potential unintended consequences of targeted strategies on vectors, disease transmission, ecology
- Build global capacity in entomology and research in vector surveillance and control, and interactions with emergence of human disease

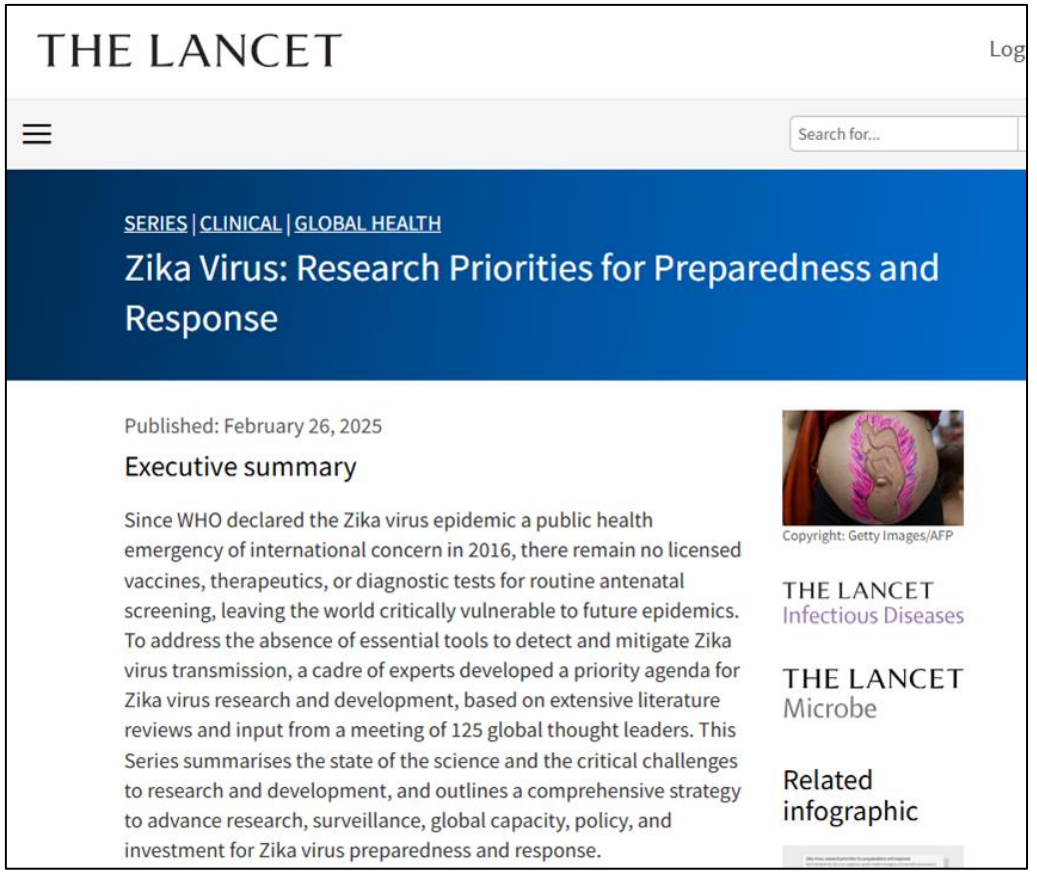
A structured approach to Zika research priorities
Expert meeting - Wellcome Trust, London December 2023

Literature review, draft strategy, stakeholder meeting:

- Address scientific and systems barriers
- Diagnostics
- Vaccines
- Monoclonal antibodies
- Therapeutics
- Animal models
- Biorepositories and specimen sharing

Published in joint series of T*he Lancet Infectious Diseases* and *The Lancet Microbe*
https://www.thelancet.com/series-do/zika-virus

Meeting report on integrated research agenda for mosquito-borne arboviruses. Ulrich et al., *Open Forum Infectious Diseases*, July 2025



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Need for public awareness and continued investment

- Critical need for continued investment in research, surveillance, global capacity
- Advance visibility and engagement of governments, foundations, the public

- Major new award by Wellcome Trust:
  - Funded 5 large global networks
  - Accelerating science of diagnostics, genomic epidemiology, animal reservoirs, global transmission, esp. Africa and Asia
  - Sustaining visibility and investment critical to advance science needed for global preparedness and response