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OPINION ARTICLE

Zika virus emergency in Brazil: scientific challenges and early developments [version 1; peer review: 1 approved, 1 approved with reservations]

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Abstract

The epidemic of microcephaly and other congenital abnormalities associated with Zika virus which emerged in Brazil now threatens different countries worldwide. Since the declaration of a National Public Health Emergency, the Brazilian government has implemented a response plan in which the research agenda is central. Developments were achieved in four main areas of the agenda: 1) virological, clinical and epidemiological studies, 2) alternative vector control strategies, 3) development and evaluation of diagnostic tests, and 4) development and evaluation of vaccines. National and international collaborative networks have played an important role in the race against the clock to quickly translate the results of R&D initiatives into public policies. It is paramount that the lessons learned from Zika lead to fast and effective responses to future epidemics.

Keywords

Zika virus , epidemic , microcephaly , Aedes Aegypti , vector control , scientific agenda

This article is included in the **Emerging Diseases and Outbreaks** gateway.

Open Peer Review

Approval Status ? ✓

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Any reports and responses or comments on the article can be found at the end of the article.

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In the last decades, Brazil has faced different arbovirus epidemics. However, none of them had the complexity of Zika virus and associated diseases. In April 2015, the first cases of the virus were reported in the country¹. Initially, the occurrence was considered to be of no greater threat than dengue or chikungunya. Nonetheless, by the end of October, the number of microcephaly cases started to rise sharply, which triggered a thorough investigation and subsequently the declaration of a National Public Health Emergency^{2,3}. On December 5, the President of Brazil launched the National Microcephaly Response Plan, involving 19 institutions and structured on three pillars: 1) vector control, 2) health care, and 3) research & education².

The research agenda focused on four main areas: 1) virological, clinical and epidemiological studies, 2) alternative vector control strategies, 3) development and evaluation of diagnostic tests, and 4) development and evaluation of vaccines. After almost one year since the reporting of the first cases of microcephaly associated with Zika in the country, many developments in the agenda were achieved and other challenges emerged:

1) Virological, clinical, and epidemiological studies – Researchers in Brazil were able to characterize transplacental Zika transmission and its influence in halting neurological development^{4,5}. These findings supported campaigns to increase awareness and protection of pregnant women against mosquitoes. Although Zika seems to be the main culprit of microcephaly increase, other cofactors are under investigation, what may lead to new policies to tackle other risk factors⁶. Recent studies also suggest that the consequences of Zika infection go beyond microcephaly, pointing out the need to further characterize syndromes and related diseases as well as to revise diagnostic and management protocols⁷.

2) Alternative vector control strategies – After the Zika emergency was declared, a range of new vector control strategies were proposed, which target different phases of the mosquito life cycle and different settings. The Brazilian Ministry of Health has been promoting effectiveness evaluations of promising strategies, including Wolbachia-infected mosquitoes and mosquito-driven dissemination of pyriproxyfen^{8,9}. These studies will provide invaluable information to improve *Aedes* control policies in Brazil. Entomological studies have also been investigating if *Aedes Aegypti* is the only Zika virus vector in Brazil¹⁰. This is a crucial point because other mosquito species have different breeding and feeding habits; in which case, the results of these studies may have an important impact on vector control measures.

3) Development and evaluation of diagnostic tests – Since the first cases of Zika have been identified there has been an ongoing effort to improve molecular tests and to develop highly sensitive and specific serological tests, with limited cross-reaction with other arbovirus, allowing point-of-care utilization¹¹. Candidates have arisen from private and public initiatives, which are being validated and evaluated with support from the Brazilian Ministry of Health. The inclusion of such tests in the public health system will require training of health professionals and modifying follow-up protocols.

As the spectrum of Zika consequences widens, so does the need for detection and treatment.

4) Development and evaluation of vaccines – The development of an effective and secure vaccine against Zika has been one of the main goals worldwide. Different research groups are working on that, including groups in Brazil. Nonetheless, only one vaccine candidate has received FDA approval to initiate a phase I clinical trial¹². Brazilian governmental bodies, such as the National Research Ethics Council, the National Clinical Trials Registry and the National Health Surveillance Agency, developed task-forces to timely evaluate research projects, clinical trials, and products related to Zika virus and associated diseases.

It has also been a race against the clock to quickly translate the results of R&D initiatives into public policies. For this purpose, the Brazilian Ministry of Health set up the Zika and Related Diseases Specialists Network, fostering greater collaboration between researchers and decision makers¹³. The joint effort between the Ministries of Health; Science, Technology, Innovation and Communication; and Education also made possible the launching of an open call for strategic research projects to tackle this emergency.

International research collaborations were established with partners such as the Center for Diseases Control, the World Health Organization, the US National Institutes of Health and the British Council. Since WHO declared a Public Health Emergency of International Concern, new communication channels have also been built between Ministries of Health from different countries¹⁴. As the world becomes more interconnected and urbanized, it is likely that many other epidemics will follow. Therefore, it is paramount that lessons learned from Zika lead to fast and effective responses to future global threats.

Author contributions

Tazio Vanni contributed to conception, drafting, and submission of the manuscript.

Karlos Diogo Chalegre contributed to the conception and drafting of the manuscript.

Camile Giaretta Sachetti contributed to the conception and drafting of the manuscript.

Pedro Reginaldo dos Santos Prata contributed to the conception and drafting of the manuscript.

Marco Antônio de Araújo Fireman contributed to the conception and drafting of the manuscript.

Competing interests

No competing interests were disclosed.

Grant information

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Open Peer Review

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Luciano A. Moreira

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General comment

Vanni *et al.* describe in this manuscript what has been, the Brazilian Government response, since the declaration of the National Public Health Emergency due to Zika. It is well written, concise and indicates the Brazilian Government is aware and is trying to tackle the Zika epidemics by using a multidisciplinary approach. It is important to guarantee though continuous funding for these different strategies.

Specific comment

Second paragraph: It is not clear whether the research agenda falls into the third pillar described by the authors on paragraph 1 3) Research & education. If yes, where education is inserted in the four main areas?

Competing Interests: I am the Lead Scientist of the Eliminate Dengue Brazil and the Brazilian Ministry of Health has been funding the Wolbachia approach since 2012, in Brazil.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 08 August 2016

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Below my considerations. I believe that the article can be indexed with minor adjustments.

I do not agree with the statement: "In the last decades, Brazil has faced different arbovirus epidemics. However, none of them had the complexity of Zika virus and associated diseases". Dengue has caused and still causes serious public health and has much higher mortality rate in Brazil.

The article cites many epidemiological bulletin of the Ministry of Health. This is important, but it has some articles that deserve to be mentioned. As an example, we have published papers citing cases of Zika in Brazil (RN and BA) before the publication of the Ministry of Health report.

Even with all the advances cited by the authors I believe that it is necessary to mention the delay in the release of funds for research on Zika in Brazil.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Comments on this article

Version 1

Author Response 10 Aug 2016

Tazio Vanni, Brazilian Ministry of Health, Brazil

It is worth noting that community health workers have played a major role not only in vector control measures, but also in identifying and providing health care to patients affected by Zika and associated diseases. Evaluations of different strategies involving community health workers were encouraged to take part in the abovementioned open call.

Competing Interests: None

Reader Comment 07 Aug 2016

Enrique Barros, Universidade de Caxias do Sul, Brazil

This is a good summary the latest research developments in the Zika struggle. I wonder why there is no reference to research on potential roles and cost effectiveness of the internationally acclaimed community health workers/Family Health Strategy in helping combat this epidemic.

Competing Interests: None.

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