

Reflections on research ethics in a public health emergency: Experiences of Brazilian women affected by Zika

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Abstract

In Brazil, the epicenter of the Zika crisis, brown, black, and indigenous poor women living in municipalities with scarce resources were disproportionately affected. The gendered consequences of the epidemic exposed how intersectional lenses are central to understand the impact of public health emergencies in the lives of women and girls. The demand for Zika-affected children and women to be research participants is relevant for an ethical analysis of participant protection procedures during a crisis. We investigated how women experienced research participation by analyzing their narratives. Two-year-long longitudinal qualitative study in Brazilian sites located in the epidemic's epicenter was performed using mixed methods: ethnography with women from two distinct states and individual semi-structured interviews with five women in different Zika-affected states, four of which were community leaders. All women in the study were mothers or grandmothers of Zika-affected children. Thematic analysis was used for data evaluation. Women perceived being pressured to participate in research and a lack of benefit sharing. Structural determinants of gender inequality, such as its effect on power distribution, were found to impact research participant protection. Formal procedures for research protocols approvals were insufficient in protecting participants because these instruments were unable to account for structural aspects. Communitarian mobilization, through WhatsApp groups, was found to be an important mechanism to create conditions to challenge oppressive structures. Strengthening public health, effective community-based participation in research planning and implantation of ethical strategies that promotes gender equality can have transformative effect on unequal power structures and promote participant protection.

KEYWORDS

community engagement, public health emergency responses, research ethics, vulnerability, Zika

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1 | INTRODUCTION

The outbreak of microcephaly cases in Brazil initially detected in 2015 and later linked to the Zika virus brought global scientific interest to the most affected areas.¹ The scientific race to investigate the bodies of the women and children affected was intensified in February 2016 with the declaration of the Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO).² Although Zika virus had been known to science since the 1950s, prior to the Zika epidemic in Brazil, nothing was known about Zika virus effects on women, pregnancy, embryo, fetus, or child development, and what later became known as congenital Zika syndrome (CZS).³ The sexual and reproductive effects of Zika were an unexpected novelty to scientists and clinicians worldwide.⁴ The Zika epidemic and its consequences are a gendered issue.⁵

According to the last cumulative data published by the WHO, Brazil has the highest number of CZS cases and Zika infection in the world.⁶ After four years of the epidemic, Brazil continues to be the epicenter of CZS and Zika infections. Zika virus and its mosquito vector circulate in Brazil to this day, and new cases of CZS are diagnosed every year.⁷ There is a positive correlation among Zika, poverty, CZS cases, poor infrastructure, and lack of basic sanitation.⁸ It should come with no surprise that most CZS cases are concentrated in the Brazilian Northeast, one of the regions with the lowest HDI (Human Development Index) and highest rates of

adolescent pregnancies in the country.⁹ Other important factors contribute to this picture, such as gender inequality along with lack of access to sexual and reproductive health (SRH), safe abortions, and information.¹⁰

The most affected are young, poor, black, brown or indigenous women and girls with little formal education living in remote cities and in situation of extreme poverty in Brazil.¹¹ The majority of them depend on the public health system (Sistema Único de Saúde-SUS) for care, and caregivers of affected children are mostly women.¹² That is, women and girls who have been facing historical and structural layers of vulnerability. Together with their children, women live taxing days filled with itineraries of care and many unknowns.¹³ Yet, all that is known about this novel global phenomenon of a mosquito-borne disease found to have significant sexual and reproductive consequences come from the participation of women and children for the advancement of science.¹⁴ The hope in science as a way to find answers, along with feelings of altruism, was an important mechanism for many women when deciding to collaborate with researchers, allowing for invasive procedures on themselves and their children.¹⁵

The Brazilian historical past as a colony and the persistence of coloniality with the maintenance of subservient relationship to the world's power and economic leaderships has enabled paternalistic, racist, and misogynistic values to shape relations.¹⁶ Historically we have seen that science and healthcare practice are not immune to this.¹⁷ From the biomolecular mechanism of the virus to the social impacts of the epidemic, multinational, multidisciplinary global research consortiums were avidly seeking participants.¹⁸ However,

¹Oliveira, J.F., de, Pescarini, J.M., Rodrigues, M. de S., Almeida, B., de A., Henriques, C.M.P., Gouveia, F.C., et al. (2020). The global scientific research response to the public health emergency of Zika virus infection. *PLoS One*. 15(3):e0229790. Retrieved June 11, 2022, from <https://doi.org/10.1371/journal.pone.0229790>

²World Health Organization. (2016). WHO statement on the first meeting of the International Health Regulations (2005) (IHR 2005) Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformations. Retrieved February 24, 2022, from [https://www.who.int/news-room/detail/01-02-2016-who-statement-on-the-first-meeting-of-the-international-health-regulations-\(2005\)-\(ihr-2005\)-emergency-committee-on-zika-virus-and-observed-increase-in-neurological-disorders-and-neonatal-malformations](https://www.who.int/news-room/detail/01-02-2016-who-statement-on-the-first-meeting-of-the-international-health-regulations-(2005)-(ihr-2005)-emergency-committee-on-zika-virus-and-observed-increase-in-neurological-disorders-and-neonatal-malformations)

³Dick, G.W., Kitchen, S., & Haddow, A. (1952). Zika Virus (I). Isolations and serological specificity. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 46(5):509–520; Baud, D., Gubler, D.J., Schaub, B., Lanteri, M.C., & Musso, D. (2017). An update on Zika virus infection. *Lancet*. 390(10107):2099–2109; de Oliveira, W.K., de França, G.V.A., Carmo, E.H., Duncan, B.B., de Souza Kuchenbecker, R., & Schmidt, M.I. (2017). Infection-related microcephaly after the 2015 and 2016 Zika virus outbreaks in Brazil: a surveillance-based analysis. *Lancet*. 390(10097):861–870; Martines, R.B., Bhatnagar, J., de Oliveira Ramos, A.M., Davi, H.P.F., Iglezias, S.D.A., Kanamura, C.T., et al. (2016). Pathology of congenital Zika syndrome in Brazil: a case series. *Lancet*. 388(10047):898–904.

⁴Vélez, A.C.G., & Diniz, S.G. (2016). Inequality, Zika epidemics, and the lack of reproductive rights in Latin America. *Reproductive Health Matters*. 24(48):57–61.

⁵Ibid; Wenham, C., Nunes, J., Correa Matta, G., de Oliveira Nogueira, C., Aparecida Valente, P., & Pimenta, D.N. (2020). Gender mainstreaming as a pathway for sustainable arbovirus control in Latin America. *PLoS Neglected Tropical Diseases*. 14(2):1–7; Davies, S.E., & Bennett, B. (2016). A gendered human rights analysis of Ebola and Zika: Locating gender in global health emergencies. *International Affairs*. 92(5):1041–1060.

⁶World Health Organization/PAHO. (2018). Zika cases and congenital syndrome associated with Zika virus reported by countries and territories in the Americas, 2015–2018. Cumulative cases. Retrieved April 28, 2022, from https://www.paho.org/hq/index.php?option=com_docman%26view=download%26category_slug=cumulative-cases-pdf-8865%26alias=43296-zika-cumulative-cases-4-january-2018-296%26Itemid=270%26lang=en

⁷Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. (2021). Boletim Epidemiológico: Situação epidemiológica da síndrome congênita associada à infecção pelo vírus Zika, 2015 a 2020. 4(52). Retrieved April 28, 2022, from https://www.gov.br/saude/pt-br/media/pdf/2021/fevereiro/11/boletim_epidemiologico_svs_4.pdf

⁸Wenham, et. al., op. cit. note 5.

⁹Brasil. IPEA. Desenvolvimento Humano Nas Macrorregiões Brasileiras. 2016. Available at <http://repositorio.ipea.gov.br/bitstream/11058/6217/1/Desenvolvimento%20Humano%20nas%20macrorregi%C3%B5es%20brasileiras.pdf>. Accessed: 28 April. 2022; Brasil.

Ministério da Saúde. Secretaria de Vigilância em Saúde. Sistema de Informações sobre Nascidos Vivos – SINASC. Retrieved April 28, 2022, from <http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sinasc/cnv/nvuf.def>

¹⁰Vélez & Diniz, op. cit. note 4; Wenham, et. al., op. cit. note 5; Diniz, D., & Brito, L. (2016). Epidemia provocada pelo vírus Zika: informação e conhecimento. *Revista Eletrônica de Comunicação Informação e Inovação em Saúde*. 10(2):1–5.

¹¹Brasil.Ministério da Saúde. Secretaria de Vigilância em Saúde, op. cit. note 7; Wenham, et. al., op. cit. note 5; Ambrogi, I.G., Brito, L., & Diniz, D. (2021). The vulnerabilities of lives: Zika, women and children in Alagoas State, Brazil. *Cadernos de Saúde Pública*. 36(12):e00032020.

¹²Ambrogi, Brito and Diniz (2021), op. cit. note 11; Freitas PSS, Soares GB, Mocelin HJS, Lamonato LCXL, Sales CMM, Linde-Arias AR, et al. How do mothers feel? Life with children with congenital Zika syndrome. *Int J Gynecol Obstet*. 2020;148(S2):20–8.

¹³Freitas, et. al., op. cit. note 12; Diniz, D., & Brito, L. (2019). Uma epidemia sem fim: zika e mulheres. In T. Rifiotis & J. Segata (Eds.). *Políticas etnográficas no campo da moral*. Porto Alegre: UFRGS. pp. 169–181; Diniz, D. (2016). Zika: Do Sertão nordestino à ameaça global. Rio de Janeiro: Civilização Brasileira.

¹⁴Ibid.

¹⁵Ibid; Fleischer, S. (2022). Fé na ciência? Como as famílias de micro viram a ciência do vírus Zika acontecer em suas crianças no Recife/PE. *Anuário Antropológico*. 47(1):170–88.

¹⁶Rego, S., & Palácios, M. (2016). Ethics, global health and Zika virus infection: a view from Brazil. *Revista Bioética*. 24(3):430–4.

¹⁷Rego, S. (2005). A formação ética dos médicos: saindo da adolescência com a vida (dos outros) nas mãos. Editora FIOCRUZ; Brandt, A.M. (1978). Racism and Research: The Case of the Tuskegee Syphilis Study. *Hastings Center Report*. 8(6):21; Rodriguez, M.A., & Garcia, R. (2013). First, do no harm: The US sexually transmitted disease experiments in Guatemala. *American Journal of Public Health*. 103(12):2122–6.

¹⁸ZIKAlliance (org.). ZIKAlliance: A Global Alliance for Zika Virus Control and Protection. Retrieved April 29, 2022, from <https://zikalliance.tghn.org/>; ZikaPLAN (org.). ZikaPLAN: Preparedness Latin American Network. Retrieved April 29, 2022, from <https://zikaplan.tghn.org/>; ZIKAction (org.). International ZIKAction Consortium. Retrieved April 29, 2022, from <https://zikaction.org/>

it is ethically relevant that research involving those most affected by Zika are in the context of the intersectionality of poverty, unmet health and socio-economic needs, racial and gender disparities, and low levels of formal education.¹⁹

How investigational practices are experienced by women affected by Zika and impact theirs and their children's lives become an important question. Although the international interest in Zika has decreased significantly, women and families affected continue to have unanswered questions, many unmet needs, and rights violated. This study aims to explore some of the impact and make ethical considerations regarding research practices in a region with significant needs and inequalities during a public health emergency.

Research during crisis with populations that are historically in vulnerable contexts should raise important ethical considerations. With an intersectional feminist approach,²⁰ anchored on the concept and praxis of reproductive justice (RJ) that encompasses reproductive health, reproductive rights, and social justice,²¹ this longitudinal study investigated how Zika-affected women experienced research as participants. We paid particular attention to research participant protection processes such as informed consent and benefit-sharing, and what impact research participation had on their lives, from the time of the scientific race furor to years later.

2 | METHODOLOGY AND MATERIALS

This is a mixed-methods longitudinal qualitative study performed during 2017-2019 with Brazilian women affected by Zika. In order to examine how participation or invitation to participate in research affected the women, two methods were utilized: ethnography with women from two Brazilian states and individual semi-structured interviews with five women in five different Brazilian states. The focus was on their experiences when they participated or were invited to participate in research during the Zika epidemic. One or more members of the research team followed women during their daily routines intermittently throughout these years. They accompanied the women at home or at the community associations of mothers and caregivers of children affected by Zika. Observations also involved the digital space of groups in WhatsApp, a popular messaging phone application in Brazil, where many mothers and caregivers share their experiences, questions, and advice amongst themselves.

It has been already reported on how community settings, like community associations and WhatsApp groups, that gathered the

women affected by Zika "hosted the science of Zika virus".²² These meeting places provided a hub where researchers, health providers, community members, politicians, members of the media and affected women gathered and exchanged information about a wide variety of subjects including about research participation options. Some members of this research group also had known some of the participants since 2016 given prior advocacy activities during Zika outbreak and research,²³ this permitted a trust building and strengthening of a longitudinal relationship between researchers and affected women.

WhatsApp groups administrators, who are mothers, grandmothers, or caregivers of Zika-affected children, met during the fieldwork and invited some of the research team members to participate in the online application. The observations on WhatsApp focused on topics regarding research participation, such as being approached to participate in research, return of exam results done during research participation, as well as any return of information acquired through research or benefit sharing. This acquaintanceship with their experiences since the Zika virus entered their lives during this part of the study was fundamental to develop the semi-structured guide. For all interactions, the reason for the presence of a research member was explained, and permission was granted for the qualitative study about their experiences. Many interactions happened in community settings such as associations, rehabilitation centers, and/or other events. The research team also used these moments to explore the women's perceptions regarding research, and more specifically, investigate their experiences and the significance of the informed consent form in their lives. At times, we asked permission to gather a group of women for narrative-oriented conversations on this topic or to listen to them individually.

Semi-structured interviews were conducted with five women, mothers, or grandmothers of a child affected by the Zika virus. They lived in five different Brazilian states; each of these locations was majorly affected by the Zika epidemic and had women's associations centered around children affected by Zika.²⁴ Four of the women interviewed were leaders of these associations and were considered community leaders by their peers. The interviews were 30-60 minutes long and took place in a location of the women's choosing. Some were at the women's homes, some at the community association centers. Although they were semi-structured and topic-guided, the rapport established during previous interactions with the women allowed the interviews to occur as conversations. The interview instrument was elaborated to explore women's perceptions and understandings when participating or when asked to participate in research regarding Zika on them or their children. Questions regarding their emotions, reactions, and implications concerning the informed consent form were investigated. From there, topics that

¹⁹Wenham, et. al., op. cit. note 5.

²⁰Ibid; Larson, E., George, A., Morgan, R., & Poteat, T. (2016). 10 Best resources on... intersectionality with an emphasis on low- and middle-income countries. *Health Policy Plan.* 31(8):964-9; Diniz, D. (2014). *Perspectivas e articulações de uma pesquisa feminista*. In C. Stevens, S. Rodrigues de Oliveira, & V. Zanello (Eds.), *Estudos feministas e de gênero: articulações e perspectivas*. Ilha de Santa Catarina: Mulheres. pp. 11-21.

²¹Ross, L.J. (2017). *Reproductive justice as intersectional feminist activism*. Souls. 19(3):286-314; Ross, L.J. (2006). *Understanding Reproductive Justice: Transforming the Pro-Choice Movement*. *Off Our Backs*. 36(4):14-9.

²²Fleischer, op. cit. note 15.

²³Diniz & Brito, op. cit. note 10; Ambrogi, Brito, & Diniz, op. cit. note 11; Diniz & Brito, op. cit. note 13.

²⁴Matos, S.S., & Silva, A.C.R., da. (2020). "Nada sobre nós sem nós": associativismo, deficiência e pesquisa científica na Síndrome Congênita do Zika vírus. *ILHA Revista de Antropologia*. 22(2):132-68.

emerged related to being part of a scientific investigation were further explored.

All interviews were recorded and transcribed for later analysis. Measures to maintain confidentiality were taken by codifying the interviews and transcriptions with numbers and by not utilizing any identifying information in the description of the data. For the fieldwork with ethnography-based narrative-oriented conversations, field notes taken by the researchers were shared via password-protected files and did not contain any identifying information; dates and the state where the interaction happened were the only localizing information. Thematic analysis was used when evaluating the data.²⁵ Two researchers coded the interviews, and concepts were grouped to form themes. This allowed for a conceptual understanding of the themes that emerged from the data without being previously formulated by the researcher.²⁶ With this method, a reflective interpretation of the concepts found in the data was possible. In this analysis three themes emerged: perception of being pressured for research participation; perception of lack of benefits in research; effects of structural determinants of gender inequality on research participant protection.

Whenever possible and appropriate, researchers engaged in benefit-sharing practices, providing information regarding social benefits available to the women or orienting them to resources where they could find a requested support, like pro-bono lawyers or medical orientation. Plans to return research findings were discussed with the interviewed women. A digital copy of the final product in accessible language and individual conversations via WhatsApp were agreed as possible means for reporting the research findings.²⁷ The research protocol was reviewed and approved by the Escola Nacional de Saúde Pública Sergio Arouca -ENSP/Fiocruz Research Ethics committee- CAAE: 73740017.0.0000.5240. This study complied with the International Ethical Guidelines for Health-related Research Involving Humans. Both written and oral informed consent were used as a continuous process, according to the level of literacy of the participants and given the low-risk level of this type of qualitative research interaction that mostly happened in community settings. Furthermore, it was very similar to the interactions that generally happened in their gatherings and with people in their community.

3 | RESULTS & DISCUSSION

Although an important characteristic of this research is its longitudinal aspect, most of the women's narratives were related to experiences lived during the peak of the epidemic and the correlated scientific rush for answers. Some of the women's perspectives

regarding their and their children's participation in research changed as a result of their interaction with researchers and the study procedures they experienced over the years. Initially, closer to the first outbreak, science was an important source of hope, and there was great attention paid to the scientific authorities. While the hope in science persisted, questions regarding research's potential to positively impact their lives started to arise, and the ideas surrounding the investigational process started to change.

By sharing discontent with previous experiences as research participants there was the realization of a collective experience that was unique to them—being affected by the Zika epidemic in Brazil. With the recognition of being engaged in a community, they started to question and challenge the ways procedures were being carried out—refusal to participate in further research was the ultimate manifestation against the lived research experiences.²⁸ An outcome with important ethical implication as it can lead to loss of a community's engagement with science as a mechanism to find reliable answers to problems in society, opening precedent for other types of, perhaps less predictable, explanations to take on this role.²⁹

3.1 | Perception of being pressured for research participation

Microcephaly was one of the most identifiable signs of Zika virus effect on the fetus. However, it soon became evident that the effects of the virus on the fetus can involve other organs, such as eyes and joints.³⁰ The Zika virus infection consequences on the developing fetus or child are understood as a syndrome, with multiple systems affected in variable degrees. This novel syndrome brings challenges to biomedical research that is usually not extensively interdisciplinary, and specialties are focused on a specific aspect of the physiology. Lack of coordination and sharing of information among research teams can raise important ethical issues when there is a novel syndrome with multiple effects on one person, one body.

Most of the Zika-related cases were concentrated in low-resource regions, and affected women were referred to university hospitals or research institutions. These places became the reference centers for the care of women and children affected by Zika. Pediatric and other specialists would be available only a few days of the week or month, and all those in need of a visit would be scheduled on those days. Many women and children live far away from the reference centers and depend on state or municipal chartered transportation.³¹ Coordination of care occurred so all of the Zika-affected cases would be seen on the same day.

²⁵Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, 3(2):77–101.

²⁶A. Strauss & J. Corbin, (Eds.). (2008). *Pesquisa Qualitativa: técnicas e procedimentos para desenvolvimento de teoria fundamentada*. (Transl. Luciane de Oliveira da Rocha). 2nd ed. Porto Alegre: Artmed.

²⁷Taylor J. (2019). Reporting research findings to participants is an ethical imperative. *BMJ*, 367:l6324.

²⁸Fleischer, op. cit. note 15.

²⁹Diniz & Brito, op. cit. note 13.

³⁰Moore, C.A., Staples, J.E., Dobyms, W.B., Pessoa, A., Ventura, C. V., Da Fonseca, E.B., et al. (2017). Characterizing the pattern of anomalies in congenital zika syndrome for pediatric clinicians. *JAMA Pediatrics*, 171(3):288–95; Musso, D., Ko, A.I., & Baud, D. (2019). Zika Virus Infection — After the Pandemic. *The New England Journal of Medicine*, 381(15):1444–1457.

³¹Ambrogi, Brito, & Diniz, op. cit. note 11.

With this, there was also a concertation of Zika researchers seeking for participants. After participating in dozens of studies, women started feeling pressured by the researchers waiting in the hospital's halls. One of the women interviewed described her experience, which she noted other women shared, as an “*excess of exposure*” to research solicitations and participation. Going for a medical appointment and being approached by several different research teams asking for their names and personal information was experienced as “*a mafia of research*”. She further explained the experience as “*everyone is traumatized*”. The segmented approach to research coordination seems to have contributed to this type of experience.

3.2 | Perception of lack of benefits in research

Science provided many answers that aided in the understanding of what had happened to them, their pregnancies, and their children. Women appreciated when the scientific way of inquiry and investigations provided information that made sense in helping explain how the mosquito-borne infection changed their lives. They also knew and understood that science was pervasively present in their routines. As one woman explained: “*Research can help our children a lot, they can bring a lot of benefits, right?!.*” Among the multiple medications, medical procedures, and CZS's signs and symptoms, women knew the importance of observation and the study of events that posed questions to which answers were needed.³² Research participation, however, needed to be applicable in their lives; the meaning of science was derived from the potential and/or perceived benefits it would bring to their children.

Coupled with feeling overwhelmed and pressured with multiple research participations, women usually said that these studies had “*no meaning*” to them. When asked why they felt that way, the answer was related to the lack of “*benefit*”. At first sight, this could be thought of as an issue of “*therapeutic misconception*”, where research participants fail to recognize the difference between research procedures and health care by understanding that the purpose of the study is to benefit those enrolled.³³ However, women thought of research benefits not as a direct or immediate benefit, but as something well-founded scientifically and that would provide improvements in the future that would come to be.

In addition, the lack of benefit was related to the absence of result dissemination, benefit-sharing, or follow-up from the researchers. As another woman explained, “*This research was not important to me at all. I would like to be informed of what happened, but for me, it was not worth it.*” Women's experience with research was profoundly marked by the absence of findings dissemination or any action that could be understood as benefit sharing. A prominent and recurring

complaint in the interviews was that the results from all the exams, imaging, and testing done on their bodies or biological samples collected from them and their children were never returned to them. The women also expressed sadness and indignation that the outcomes of the investigations were never shared. Similar findings regarding this have been recently presented elsewhere.³⁴

This must be understood in the context of these women's lives. They are the primary caregivers of children with significant specialized needs and with many pathologies that are mostly unknown, even to the medical experts. They know the value of science, and they participated in the studies hoping the research would bring benefits. Benefit-sharing has been described as “*the sharing of whatever accrues from the utilization of biological resources, community knowledge, technologies, innovations or practices*”.³⁵ Benefit, in benefit-sharing, is defined as anything that “*contributes to the well-being of an individual and/or a given community (e.g., by region, tribe, disease-group, etc.)*”.³⁶ One participant explained it well: “*many researchers had some benefit. I am not saying financially, but they had some benefit in evaluating our children, and we did not have any benefit*”. Sharing of findings is an ethical imperative already announced in the Declaration of Helsinki, but it is also to be understood as one of the possible ways to share benefits.³⁷ Even if it is a null finding, participants should be informed and thanked.³⁸ When studies are carried out without any recognition of the women's efforts and benefits never reach them, there is a transformation on how research is perceived from something potentially beneficial that carries hope to meaningless.

3.3 | Effects of structural determinants of gender inequality on research participant protection

Emerging diseases in emergency situations in which resources are scarce and people live with many unmet needs can shift perspectives and dispute the boundaries that distinguish medical care from research.³⁹ We identified a couple of factors that made this

³⁴Fleischer, op. cit. note 15.

³⁵Organization of African Unity Scientific, Technical and Research Commission. (2008). African model legislation for the protection of the rights of local communities, farmers, and breeders, and to the regulation of access to biological resources. The OAU's Model Law.

³⁶HUGO Ethics Committee. (2000). Hugo Ethics Committee statement on benefit sharing April 9, 2000. *Clinical Genetics*. 58(5):364–366.

³⁷Taylor, op. cit. note 27; World Medical Association Declaration of Helsinki. (2018). Ethical principles for medical research involving human subjects. Retrieved May 2, 2022, from <https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>

³⁸HUGO, op. cit. note 36; Editorial. (2018, November 13). How a simple ‘thank you’ could improve clinical trials. *Nature*. 563(7731):293–294.

³⁹Henderson, et. al., op. cit. note. 33; Nuffield Council on Bioethics. (2020). Research in global health emergencies: ethical issues. Nuffield Council on Bioethics. Retrieved June 11, 2022, from <https://www.nuffieldbioethics.org/publications/research-in-global-health-emergencies/>; National Commission for The Protection of Human Subjects of Biomedical And Behavioral Research. Office of The Secretary. (1979). The Belmont Report: Ethical principles and guidelines for the protection of human subjects of research. Washington, DC. Retrieved June 11, 2022, from <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html>; Helgesson, G. (2019). Can and should the research–therapy distinction be maintained? Reflections in the light of innovative last-resort treatment. *Research Ethics*. 15(2):1–14.

³²Fleischer, op. cit. note 15; Diniz & Brito, op. cit. note 13; Diniz, op. cit. note 13.

³³Henderson, G.E., Churchill, L.R., Davis, A.M., Easter, M.M., Grady, C., Joffe, S., et al. (2007). Clinical Trials and Medical Care: Defining the Therapeutic Misconception. *PLoS Medicine*. 4(11):e324. Retrieved June 11, 2022, from <https://doi.org/10.1371/journal.pmed.0040324>

distinction difficult for women, and as a result, affected research participant protection processes. One factor was the fact that care and research were reported to happen simultaneously. One woman told us: *"It is all mixed together. You do not know the difference because you are in a doctor's appointment, and at the same time, there are tons of questions. At the same time, people are filling out questionnaires with you, and in the same room, your son is being seen [by a health provider]. So, you cannot separate what day is research and what day is regular medical treatment"*. Adequate communication and time for the decision have all been characterized as important issues to attend to when doing research with humans in order to allow for suitable informed consent, particularly in public health emergencies.⁴⁰ But the distinction difficulty goes beyond just the participant-researcher dyad; it has to do with the broader contexts and power structures.

With years gone by since the epidemic, women reported that the quality of the children's care in the health facilities had decreased significantly. When studies were abundant, children would be evaluated *"right away,"* and the *"mother"* would leave the hospital after a visit with *"something"*. The *"something"* most of the time referred to an evaluation result or requests for further examinations. Women complained that this type of attention has *"stopped"* completely; imaging evaluations that would be performed expeditiously, currently *"take five months"*, according to them. They related that this change is due to a lack of financial resources from the international organizations, that are no longer doing research in the centers. Again, confusion between care and research experienced by the women is not a straightforward case of 'therapeutic misconception' but informed by many structural factors that can involve a strategic choice for better care and some evaluation of risk and benefits that goes beyond the clinical assessment.⁴¹ Especially considering that CZS is a novel condition, and the majority of affected women are poor with difficult access to health care, the alternative to research might be an *"empty choice"*, a concept that highlights how choice cannot be uncoupled from structural factors that effectively limit or eliminate options.⁴²

Women in this study described multiple times how the informed consent form did not carry any other meaning to them other than being a required procedure. As a woman told us, *"You go for an appointment, and even before the visit starts, there are five or six different types of researchers asking you questions. One study is for this,*

and another is for that. A ton of forms that you have to sign right away. No one explained what it was regarding, and I would just start signing." Some reported that signing these papers, even without understanding what they meant, seemed to be a way to guarantee the best care for their child. When asked about the informed consent papers, many women did not have the forms; a few reported losing them or throwing them away; some said they were never given a copy. Others signed the form but did not know how to read what was stated in there. This demonstrates some insufficiencies in the research participant protection process.

Informed consent is a mechanism intended to guarantee the opportunity to choose to participate or not in a study.⁴³ The idea of choice can be problematic because it would also require an analysis of individual freedom and structural power dynamics.⁴⁴ Choice cannot be assessed just from within the researcher-participant relationship. It has been argued that poverty and social exclusion lead to vulnerabilities in medical research because of the impacts on health inequalities and diminished autonomy.⁴⁵ Inequality and powerlessness lived by the women due to patriarchal, racist, classist, political, social, and economic structures add important layers of vulnerabilities to their lives.⁴⁶

In this scenario, even more conservative definitions of 'coercion' and 'undue influence' can happen almost seamlessly. According to the Belmont Report, 'coercion' and 'undue influence' would only happen when participant's voluntariness is affected by an *"overt threat of harm"* or *"excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance"*.⁴⁷ Even within these narrow definitions, women described situations that would fit these constraints. As when they were told by the principal investigator of one research, who is also their personal clinician, that they should not participate in studies led by other researchers. Or when a health provider from the public service announced on the WhatsApp groups about task force days for examination and stated: *"You have to participate in these tests"* without saying that the tests were part of a study.

There are at least three important ethical considerations to be made here: 1- In most cases, given the scarcity of resources and their remote locations, Zika-affected children and women receive care on set task force days.⁴⁸ Announcements on WhatsApp about the task force days for regular routine care are common, so distinguishing if the encounter would be for regular care or for research before making plans to go is essential. 2- Answers to inquiries regarding whether these tests were part of a research protocol or regular care were not shared in the group and only provided individually to the women who asked. 3- Most of the affected women and children are

⁴⁰Nuffield Council on Bioethics, op. cit. note 39; Sullivan, M., Kone, A., Senturia, K.D., Chrisman, N.J., Ciske, S.J., & Krieger, J.W. (2001). Researcher and Researched-Community Perspectives: Toward Bridging the Gap. *Health Education and Behavior*, 28(2):130-149; Falb, K., Laird, B., Ratnayake, R., Rodrigues, K., & Annan, J. (2019). The ethical contours of research in crisis settings: five practical considerations for academic institutional review boards and researchers. *Disasters*, 43(4):711-26.

⁴¹Mfutso-Bengo, J., Ndebele, P., Jumbe, V., Mkunthi, M., Masiye, F., Molyneux, S., et al. (2008). Why do individuals agree to enrol in clinical trials? A qualitative study of health research participation in Blantyre, Malawi. *Malawi Medical Journal*, 20(2):37-41; Ravinetto, R.M., Afolabi, M.O., Okebe, J., Van Nuil, J.J., Lutumba, P., Mavoko, H.M., et al. (2015). Participation in medical research as a resource-seeking strategy in socio-economically vulnerable communities: Call for research and action. *Tropical Medicine & International Health*, 20(1):63-6.

⁴²Kingori, P. (2015). The 'empty choice': A sociological examination of choosing medical research participation in resource-limited Sub-Saharan Africa. *Current Sociology*, 63(5):763-778.

⁴³The Belmont Report, op. cit. note 39.

⁴⁴Kingori, op. cit. note 42.

⁴⁵Popay, J. (2010). Understanding and tackling social exclusion. *Journal of Research in Nursing*, 15(4):295-297.

⁴⁶Ibid; Alvarez-Castillo, F., & Feinholz, D. (2006). Women in developing countries and benefit sharing. *Developing World Bioethics*, 6(3):113-21.

⁴⁷The Belmont Report, op. cit. note 39.

⁴⁸Diniz & Brito, op. cit. note 13.

dependent on the public health system to keep immunization report cards and other public health records up to date. These records used to be required to receive certain public social benefits and enroll in school.⁴⁹

To evaluate the structural character of the power dynamics in place when studies are conducted primarily with women and children living a public health crisis due to a novel disease, we need to depart from narrowly focusing on the participant-researcher dyad.⁵⁰ Particularly in these situations where there are marked inequalities, the concept of 'structural coercion' is important to understand the experiences lived by the women and children. Structural coercion shifts the focus from the individual and accounts for the broader social, economic, political, and cultural contexts that take part in a person's decision to enroll in a study.⁵¹ This concept is based on the understandings of 'structural violence' as harmful social arrangements that "are structural because they are embedded in the political and economic organization of our social world; they are violent because they cause injury to people".⁵²

Aspects of 'structural violence' and patriarchal structures present in our society are exposed when some of the women described feelings of objectification of their children's bodies and issues. The ethical implications of perceiving objectification during research are related to human dignity and autonomy, as objects are understood as not human and not able of decision making.⁵³ One woman reported: "Nowadays, there are physicians that do not even look at my child. They do not find it as important because the [research] boom stopped". Many women reported feeling "used" and that their children are not "guinea pigs".⁵⁴ One woman said: "During research, you feel like an object, right? Because, you know, they poke the children a lot". While this points to a lack of recognition, it also claims it,⁵⁵ exposing the ethical impact of oppressive structures in research practices.

The justification used by one of the women interviewed about not having another option to obtain specialty care than by signing the research papers shows how 'structural coercion' works on vulnerabilities. 'Structural coercion' can be identified when a woman related that she would not question the physician because he/she would not allow for that kind of intimacy or rapport. On other occasions this woman explained that she did not find it was really necessary to ask anything to the doctor. The narrative of something that is not allowed as unnecessary exposes the coercive forces that go beyond the participant-researcher relationship. Points to gendered social and

economic power dynamics outside the dyad that affects the participant-researcher relationship. More importantly, the intervention to transform this also lies outside of the participant-researcher relationship.⁵⁶

A fundamental factor to diminish 'structural violence' as already reflected by Paul Farmer, is the guarantee of rights.⁵⁷ The provision of healthcare by the Brazilian public health care system (SUS), allows women to decline research. As exemplified when one of the women explained feeling that the care tied with research had worsened, as a result she stopped taking her child to the research hospital and would instead go to another public hospital to obtain care. If free accessible public health were not an option, it is possible that her decision would be a different one. In fact, that has been observed in the cases when specific interventions are not available in the public system but attainable via study enrollment.⁵⁸ This adds evidence to the fundamental role of SUS along with other social and economic protections in the prevention of 'structural violence', 'structural coercion', and social exclusion, also guaranteeing rights and improving research.⁵⁹

It did not take long for women to organize WhatsApp groups, one of the main ways of communication, to talk about their feelings regarding the investigational work performed on their children's bodies as well as their own. Women felt the importance of the recognition of their identity and autonomy.⁶⁰ These feelings of disrespect, collectively shared, as they reflected on their experiences in groups, was a motivational basis for collective action.⁶¹ One of the women explained a shared sentiment that the researchers have been more careful after they collectively complained. Others said that many women stopped participating in research all together. These attitudes can be interpreted as a "collective fight for recognition".⁶²

4 | FINAL CONSIDERATIONS

The excessive and concerted research solicitations and participation coupled with the lack of recognition and benefit-sharing were some of the reasons many women affected by Zika attributed to declining participation in latter studies. More importantly, it demonstrates how women themselves value their participation in research and understand that they were alienated from obtaining any return for their efforts. Our findings corroborate with what has already been shown about women, particularly poor women in Global South, being excluded from benefit-sharing and having their needs neglected.⁶³ It also draws attention to the ill effects of uncoordinated and

⁴⁹Brasil. (2004). Casa civil. Portaria nº 5.209, de 17 de setembro de 2004. Regulamenta a Lei nº 10.836, de 9 de janeiro de 2004, que cria o Programa Bolsa Família, e dá outras providências. Brasília, 2004. Retrieved June 11, 2022, from http://www.planalto.gov.br/ccivil_03/_ato2004-2006/2004/decreto/d5209.htm#:text=Regulamenta%20a%20Lei%20no,que%20he%20confere%20o%20art

⁵⁰Fisher, J.A. (2013). Expanding the Frame of "Voluntariness" in Informed Consent: Structural Coercion and the Power of Social and Economic Context. *Kennedy Institute of Ethics Journal*, 23(4):355–379.

⁵¹Ibid.

⁵²Farmer, P.E., Nizeye, B., Stulac, S., & Keshavjee, S. (2006). Structural violence and clinical medicine. *PLoS Medicine*, 3(10):1686–1691.

⁵³Freire, P. (2005). *Education for critical consciousness*. London: Continuum.

⁵⁴Diniz & Brito, op.cit. note 13.

⁵⁵Diniz & Brito, op. cit. note 10.

⁵⁶Fisher, op. cit. note 50.

⁵⁷Farmer, P. (2005). *Pathologies of Power: Health, Human Rights, and the New War on the Poor*. Berkeley: University of California Press.

⁵⁸Kingori, op. cit. note 42; Fisher, op. cit. note 50.

⁵⁹Popay, op. cit. note 45; Farmer, op. cit. note 57.

⁶⁰Honneth, A. (2009). *Luta por reconhecimento: a gramática moral dos conflitos sociais*. (Transl. Luiz Repa). São Paulo: Editora 34.

⁶¹Ibid.

⁶²Ibid.

⁶³Alvarez-Castillo & Feinholz, op. cit. note 46.

unchecked scientific races in public health emergency settings and the importance of community participation in all phases of study design and implementation.⁶⁴

The ethical protection of research participants goes beyond typical bureaucratic procedures, such as the approval of research protocols by a local Research Ethics Committees. Our findings support what has already been described as a significant limitation of consent; by itself, it is insufficient for ensuring ethical research practices.⁶⁵ Although our study is limited by its purposive sampling, we focused on the longitudinal experiences of women with leadership roles in the community. Women experienced exclusion from all sorts of research-related benefits which implicated on how they interacted with research, highlighting the importance of benefit sharing.⁶⁶ We were able to identify that there are structural issues that affect research participant protection.

Consequently, interventions should address the broader context of inequalities and injustices. Particularly, in public health emergency settings, in which situations of vulnerability are aggravated, attention should be paid to the participants and their communities in evaluating the structural power dynamics that affect research participation. In the context of poverty, social exclusion, and many unmet needs, even community engagement can be insufficient in preventing vulnerabilities from exploitation and structural coercion.⁶⁷ Yet, our findings point to the importance of having research protocols that are community-based designed, involving the community and grassroots movements.⁶⁸ The building of a collective engagement was a powerful mechanism to challenge oppressive structures and initiate change. Community-based participatory strategies share feminist values, promoting shifts in power and transforming oppressive structures.⁶⁹

Now, women living the Zika legacy of caring for their families and having their sexual and reproductive health and rights under threat are experiencing yet another unprecedented public health emergency due to the SARS-CoV-2 virus. The COVID-19 pandemic has further disproportionately impacted women and girls, deepening vulnerabilities and worsening inequalities.⁷⁰ Our findings add evidence to the importance of having a gender-transformative approach, placing women and girls at the center of public health emergency responses, not only to improve research participant protection but also to

advance gender equality and prevent vulnerabilities and exploitation. In places with marked inequalities, such as Brazil in the Global South, a feminist approach is fundamental to appreciate the intersecting oppressions that disproportionately affect women and girls. This lens should be used in all public health emergency preparedness and response phases, including research planning and execution. Research should also be developed and performed in ways centered on women and girls, safeguarding their rights, and ensuring gender equality.

CONTRIBUTORS

All authors contributed equally to this manuscript. Sergio Rego did not directly participate in data collection. Otherwise, Ilana Ambrogi, Luciana Brito, and Sergio Rego participated in all phases of the study, interpreted the data, critically revised the manuscript, approved the final version, and agreed to be accountable for all aspects of the work.

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CONFLICT OF INTEREST

None to declare.

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⁶⁴Sullivan, op. cit. note 40; Nuffield, op. cit. note 39; Martinez, L.S., Russell, B., Rubin, C.L., Leslie, L.K., & Brugge, D. (2012). Clinical and Translational Research and Community Engagement: Implications for Researcher Capacity Building. *Clinical and Translational Science*, 5(4):329–332.

⁶⁵Nuffield Council on Bioethics, op. cit. note 39.

⁶⁶Alvarez-Castillo & Feinholz, op. cit. note 46.

⁶⁷Nyirenda, D., Sariola, S., Kingori, P., Squire, B., Bandawe, C., Parker, M., et al. (2020). Structural coercion in the context of community engagement in global health research conducted in a low resource setting in Africa. *BMC Medical Ethics*, 21(1):90.

⁶⁸Nuffield Council on Bioethics, op. cit. note 39; Anoko, J.N., Barry, B.R., Boiro, H., Diallo, B., Diallo, A.B., Belizaire, M.R., et al. (2020). Community engagement for successful COVID-19 pandemic response: 10 lessons from Ebola outbreak responses in Africa. *BMJ Global Health*, 4(Suppl 7); Shah, S.K., Miller, F., & Fernandez Lynch, H. (2020). The role of community engagement in addressing bystander risks in research: The case of a Zika virus controlled human infection study. *Bioethics*, 34(9):883–892.

⁶⁹Wenham, et al., op. cit. note 5; Diniz, op.cit. note 20; Anoko, et al., op.cit. note 68.

⁷⁰Wenham C, Smith J, & Morgan R. (2020). COVID-19: the gendered impacts of the outbreak. *Lancet*. 395(10227):846–848.

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