

# Ethical issues arising in research into health and climate change

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## Dengue and climate change: exploring bioethical challenges in global health research

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### Brief description of context

Dengue is a mosquito-borne infectious disease primarily transmitted by *Aedes aegypti* and *Aedes albopictus* [1]. It is highly prevalent in regions across the Global South, particularly in South Asia and South America. The global incidence of dengue has increased dramatically, with over 6 million cases reported in 2023 and nearly 5 million by mid-2024 alone [2], a significant rise from the 500,000 cases recorded in 2000. Symptoms range from mild fever to severe complications (in 5% of cases), including hemorrhage, organ failure, and shock [2,3]. In 2023, dengue caused over 6,000 deaths globally [3].

Historically, dengue has been confined to the Global South; however, in recent years, developed countries have reported an increase in autochthonous cases. In 2023, 122 autochthonous cases were documented in Europe, doubling the incidence from 2022 [4]. Climate change significantly impacts vector-borne diseases, as temperature affects both the life cycle and survival of mosquitoes. *Aedes* mosquitoes cannot survive in winter climates, and their longevity increases when temperatures range between 20°C and 30°C. Higher dengue incidence has also been linked to annual rainfall exceeding 500 mm. Due to climate change, *Aedes albopictus* has now been found in Europe and the U.S. [5].

Since only symptomatic treatment is available and the spread of dengue is facilitated by climate change, primary prevention, such as vaccination, emerges as a key area for medical research. The French pharmaceutical company Sanofi developed the vaccine *Dengvaxia*®, which is currently used for preventing secondary dengue in individuals who have already been infected (seropositive). Clinical trials conducted in Latin America and South Asia demonstrated that the vaccine reduces severe disease in these cases. However, despite these trials being performed in the Global South, *Dengvaxia*® is primarily available in the U.S. and Europe, with limited access in Latin American and South Asian countries where dengue remains a significant health threat [6].

At the end of 2023, the World Health Organization's Strategic Advisory Group of Experts on Immunization (SAGE) approved *Qdenga*®, a vaccine developed by the Japanese pharmaceutical company Takeda, for primary prevention of dengue, including those at risk of initial infection who have not been previously infected (seronegative), in areas with high dengue burden and transmission. It is currently available only in Indonesia, Brazil, and Europe [7,8], despite clinical trials being conducted in Latin American and South Asian countries [9].

### Discussion of ethical issues

Climate change is a challenge that the entire world is currently facing, and its impacts are expected to intensify in the coming years. However, it predominantly affects regions where socioeconomic and health conditions are already compromised: the Global South. Dengue, a neglected tropical disease, is causing a steady rise in cases in endemic countries. Furthermore, the Global North is also beginning to express concern, as autochthonous cases are increasing in regions where climate change has created favorable conditions for the vector's development.

This situation brings forth several ethical concerns:

### **1. Justice and fairness in the research agenda**

The increase in dengue cases in endemic areas and its potential for global spread are serious concerns. Dengue highlights the critical need for both vaccines and proactive environmental interventions. Primordial prevention, aimed at eliminating or reducing risk factors by addressing underlying conditions, plays a crucial role in responding to the impacts of climate change. This approach complements vaccines, which are primarily developed by large pharmaceutical companies in the Global North, often driven by economic interests. While primary prevention through vaccination remains essential, the substantial influence of these companies on vaccine development raises ethical concerns, as clinical trials are frequently conducted in Low- and Middle-Income Countries (LMICs), where disease burden is highest, but immediate vaccine access is not guaranteed.

A serious ethical issue arises in Honduras, where local individuals participated in clinical trials for the *Dengvaxia*® vaccine. Although effective in seropositive individuals, these trials showed an increased risk of severe dengue for seronegative participants. Despite its approval for secondary dengue, *Dengvaxia*® remains unavailable in Honduras and other trial locations, providing no tangible benefit to these populations. Barriers include high costs, inadequate infrastructure, and limited resources for pre-vaccination screening to ensure its safe administration. Additionally, there is no public record of compensation or benefits for participants who may have experienced adverse effects, nor evidence of local partnerships to secure these benefits, as recommended by the Council for International Organizations of Medical Sciences (CIOMS) guidelines. This lack of support highlights ethical concerns, as populations involved in vaccine development do not benefit, revealing research-driven inequities influenced by economic interests [10,11].

Research on dengue vaccines illustrates how the health research agenda related to climate change could be shaped. As global temperatures rise and weather patterns shift, vector-borne diseases like dengue, malaria, zika, and chikungunya are likely to spread to previously unaffected areas, especially in the Global North. To prevent these diseases from escalating into global health crises, research should prioritize and enhance systematic prevention strategies—such as vaccine development, vector control, and surveillance—in the Global South, where the burden of vector-borne diseases is highest and climate change could further deepen health inequities.

### **2. Research governance**

Due to their geographical position and socioeconomic conditions, LMICs are often selected as ideal populations for studying climate change-related diseases, such as dengue, before these diseases spread to other regions. Although vector control measures—such as insecticide-treated bed nets, indoor residual spraying, larviciding, environmental sanitation, and community education—have been implemented, their effectiveness varies significantly depending on local environmental factors, political commitment, and the sustainability of interventions. In regions like Honduras, the limited success of these measures is often attributed to inadequate public health strategies and insufficient resources, compromising their long-term impact. This highlights the need for vaccine development as a complementary and potentially more sustainable preventive approach for diseases like dengue.

The development of clinical trials in dengue-endemic countries is ethically justifiable only if proportionate benefits are delivered to participants and their communities, as greater exposure allows for larger sample sizes and more precise results. However, it is important to consider that participants may face adverse effects during or after participation, often within health systems that are not adequately equipped to manage complications effectively. This situation raises another ethical concern that needs to be addressed before conducting research.

For this reason, it is essential for international health organizations, in collaboration with national governments, to develop and apply policies that regulate and protect the interests of the most affected populations. When successful results are achieved, these vulnerable populations should not only serve as study subjects but also be among the first to benefit from scientific advances. Organizations such as the World Health Organization (WHO) and international funding agencies, in coordination with pharmaceutical companies, should prioritize the distribution of benefits to countries with the highest disease burden, rather than those with greater economic power but a lower burden of disease.

The *Qdenga*® vaccine exemplifies ethical challenges in access to essential vaccines. Despite its proven efficacy and safety, its prohibitive cost—driven by Takeda Pharmaceuticals' monopoly—prevents inclusion in LMICs' national immunization programs without substantial external funding, meanwhile, wealthier countries with lower disease burdens offer *Qdenga*® to travelers to endemic areas. This highlights a major ethical concern: economic barriers limiting equitable access to life-saving interventions for populations most in need. International organizations like the WHO and the Global Alliance for Vaccines and Immunization (GAVI) have worked to subsidize and negotiate lower vaccine prices for LMICs, as seen with the COVAX initiative, which supplied billions of COVID-19 doses to these countries. However, sustained support is needed to ensure similar access to essential vaccines for diseases like dengue, which disproportionately impact LMICs.

The ethical implications of conducting research in LMICs, particularly regarding benefit-sharing and justice, are well-documented in bioethics literature. According to CIOMS guidelines, both the host country and the study population should equitably benefit from research outcomes [12]. This is especially relevant given the historical imbalance where vulnerable populations have seldom benefited from advances achieved through research conducted in their regions. Effective research partnerships should include diverse stakeholders, such as governments, academic institutions, and community representatives, to ensure that research priorities and benefits align with local needs. For developing countries, capacity-building for critical thinking and negotiation is fundamental to addressing these disparities and establishing equitable research partnerships [13]. Ethical obligations in infectious disease research further emphasize the need for a fair distribution of benefits, particularly for those most vulnerable to climate change and other global health challenges [14].

A collaborative approach, coordinated by international agencies such as the WHO or regional health organizations, in partnership with local entities that understand the specific needs and vulnerabilities of their populations, has the potential to promote more sustainable and ethical research practices. This initiative requires dedicated funding and support from local governments, cooperative agencies, and international health organizations. Facilitating discussions with diverse stakeholders, including working groups, can help identify effective governance models. Nonetheless, implementing these recommendations presents significant challenges, and sustained commitment, along with accountability mechanisms, will be essential to ensure that all participants fulfill their roles.

### **Conclusion and recommendations**

In conclusion, the dengue case study exemplifies how climate change-related diseases attract research interest from the Global North, with LMICs often serving as primary study populations. However, funding typically prioritizes marketable products like vaccines, often driven by the economic interests of large pharmaceutical companies, leaving these interventions less accessible in the most affected areas. At the same time, preventive efforts addressing root causes receive comparatively less support. This imbalance underscores the need for sustainable funding strategies that prioritize and address long-term disease burdens in vulnerable regions.

1. As certain infectious diseases are increasing due to climate change, particularly in regions where they are already prevalent, we recommend further research in these areas, adhering to international ethical guidelines like those from CIOMS, to ensure that research benefits are shared equitably with local populations. By upholding ethical standards, we can help ensure that communities most

affected by climate change-related diseases not only participate in the research but also receive direct benefits from its outcomes.

2. As the burden of neglected tropical diseases disproportionately impacts LMICs, we recommend that stakeholders in LMICs actively negotiate with research entities to ensure that research priorities and outcomes align with local health needs. Such collaborations should be supported by capacity-building initiatives that empower LMICs to secure outcomes that genuinely benefit their communities. Guided by CIOMS principles and a commitment to ethical reciprocity, this approach will help ensure that international research efforts address the real challenges associated with climate change-related diseases in the most affected regions.

## References

1. World Health Organization. Dengue: guidelines for diagnosis, treatment, prevention and control. Geneva: WHO; 2009. Available at: <https://tdr.who.int/publications/m/item/2009-10-01-dengue-guidelines-for-diagnosis-treatment-prevention-and-control>
2. European Centre for Disease Prevention and Control. Dengue worldwide overview. [Internet: Last update April 2024]. Available at: <https://www.ecdc.europa.eu/en/dengue-monthly>
3. George, A. M., Ansumana, R., de Souza, D. K., Niyas, V. K. M., Zumla, A., & Bockarie, M. J. (2024). Climate change and the rising incidence of vector-borne diseases globally. *International journal of infectious diseases: IJID: official publication of the International Society for Infectious Diseases*, 139, 143–145. <https://doi.org/10.1016/j.ijid.2023.12.004>
4. Brem J, Elankeswaran B, Erne D, Hedrich N, Lovey T, Marzetta V, Tarrago Salvado L, Züger C, Schlagenhauf P. Dengue “homegrown” in Europe (2022 to 2023). *New Microbes and New Infections*. 2024;56:101205. <https://doi.org/10.1016/j.nmni.2023.101205>
5. Rocklöv J, Tozan Y. Climate change and the rising infectiousness of dengue. *Emerg Top Life Sci*. 2019;3(2):133–42. <https://doi.org/10.1042/ETLS20180123>
6. Tully D, Griffiths CL. Dengvaxia: the world’s first vaccine for prevention of secondary dengue. *Therapeutic Advances in Vaccines and Immunotherapy*. 2021;9:1–8. <https://doi.org/10.1177/25151355211015839>
7. World Health Organization (WHO). WHO prequalifies new dengue vaccine. 2024. Available from: <https://www.who.int/news/item/15-05-2024-who-prequalifies-new-dengue-vaccine>
8. Wilder-Smith A, Ooi EE, Horstick O. Brazil to start widespread dengue vaccinations. *Lancet*. 2024;403(10387):424-426. [https://doi.org/10.1016/S0140-6736\(24\)00046-1](https://doi.org/10.1016/S0140-6736(24)00046-1)
9. Patel, S. S., Rauscher, M., Kudela, M., & Pang, H. Clinical Safety Experience of TAK-003 for Dengue Fever: A New Tetravalent Live Attenuated Vaccine Candidate. *Clin Infect Dis*. 2023;76(3) e1350–e1359. <https://doi.org/10.1093/cid/ciac418>
10. World Health Organization (WHO). Vaccines and immunization: Dengue. 2024. Available from: <https://www.who.int/news-room/questions-and-answers/item/dengue-vaccines>
11. PLOS Neglected Tropical Diseases. The Impact of the Newly Licensed Dengue Vaccine in Endemic Countries. *PLoS Negl Trop Dis*. 2024;18(4) <https://doi.org/10.1371/journal.pntd.0005179>

12. Council for International Organizations of Medical Sciences (CIOMS). *International Ethical Guidelines for Health-related Research Involving Humans*. Geneva: CIOMS; 2016. Available from: <https://cioms.ch/publications/guidelines/>
13. Macpherson CC. Research ethics guidelines and moral obligations to developing countries: Capacity-building and benefits. *Bioethics*. 2019;33:389–395. <https://doi.org/10.1111/bioe.12577>
14. Selgelid MJ, Jamrozik E. *Ethical Challenges in Infectious Disease Control: A Bioethical Perspective*. *Bioethics*. 2017;34(4):797–806. <https://doi.org/10.1111/bioe.12802>