



Bioethics

ISSN: 2989-5448 (Online)

Publisher: Tomorrow's Research Publications (TRP)

An International Peer-Reviewed Open Access Journal

Policy Analysis

Vulnerability and Exploitation in Clinical Trials Conducted in Low-Income Settings

Ingrid Ramirez^{1*}, Etienne Zielinska² and Agnieszka Zielinska³¹Department of Philosophy, Loire University Center for Clinical Ethics, France²Department of Public Health Ethics, Vistula Institute of Philosophy and Medicine, Poland³Department of Philosophy, Vistula Institute of Philosophy and Medicine, Poland

ABSTRACT

Clinical trials conducted in low-income countries raise a persistent worry that sponsors are drawn there by lower costs and thinner oversight, and that consent from populations dependent on the trial for care cannot bear the ethical weight placed on it.

This review traces that worry from the 1990s standard-of-care debate over placebo-controlled perinatal HIV-transmission trials through the fair-benefits and responsiveness frameworks it produced, distinguishing vulnerability, a diminished capacity to protect one's own interests, from exploitation, taking disproportionate advantage of that diminished capacity.

It then examines how dependency on a trial for basic healthcare strains standard consent doctrine, how undue inducement can render modest incentives effectively irresistible, and how uneven regulatory oversight and unenforced post-trial access commitments leave gaps that procedural safeguards alone do not close.

We argue that vulnerability and exploitation are frequently conflated, and that a population can be vulnerable without being exploited when investigators calibrate design, consent, and benefit-sharing to that vulnerability rather than taking advantage of it.

We conclude that defensible research in low-income settings requires standard-of-care justification, negotiated benefit-sharing, consent suited to conditions of dependency, and credible local oversight operating together, not as substitutes for one another.

Keywords: research ethics; clinical trials; exploitation; vulnerability; global health

Citation: Ramirez I, Zielinska E and Zielinska A (2026) Vulnerability and Exploitation in Clinical Trials Conducted in Low-Income Settings. *Bioethics*. 1(1):01-05.

Corresponding Author: Ingrid Ramirez

E-mail Address: i.ramirez@lucce.fr

Article History: Received 8 December 2025 | Accepted 18 March 2026 | Published 09 June 2026

Copyright: © 2026 Ingrid Ramirez, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited (<https://creativecommons.org/licenses/by/4.0/>).

INTRODUCTION

Clinical research has always needed people willing to bear risk so that others, later, will not have to. The

trouble starts when the people bearing the risk and the people who stand to benefit are not the same population, and when the gap between them tracks income, education, and access to care rather than anything relevant to the science itself. This is the recurring worry about trials sited in low-income settings: that sponsors are drawn there less by scientific need than by lower costs, thinner regulatory scrutiny, and research-naïve populations who will consent to almost anything that looks like access to medical attention [1,2]. Commentators have repeatedly noted that for many potential participants in such settings, a clinical trial is sometimes the only realistic way to access medical treatment at all, which is precisely what makes the ethics of enrollment there so different from enrollment in a well-resourced health system [3]. The concern is not new -- it goes back at least to the perinatal HIV-transmission trials of the mid-1990s -- but it has not gone away, and every subsequent wave of globalized research, from HIV prevention studies to the multinational trials now routinely conducted across South Asia and sub-Saharan Africa, has reopened the same question in a new register [4].

The ethical vocabulary here divides into two related but distinct ideas: vulnerability and exploitation. Vulnerability describes a diminished capacity to protect one's own interests, whether through poverty, illiteracy, limited healthcare alternatives, or dependence on the researcher for care that is otherwise unavailable. Exploitation describes what happens when someone takes advantage of that diminished capacity to secure a benefit disproportionate to what the other party receives in return [5]. A population can be vulnerable without being exploited, if researchers respond to that vulnerability with extra protection rather than opportunism; and, more controversially, a transaction can be exploitative even when both sides describe themselves as better off for having entered into it, since a fair-seeming exchange to a desperately poor participant may still divide the benefits of the underlying research unfairly [6]. Untangling these two ideas, and asking what obligations they generate for sponsors, investigators, and host governments, is the task of this review.

Historical anchors matter for how this debate is argued today. The Nuremberg Code's insistence on voluntary consent was written directly in response to coercion under conditions of total power imbalance [7], and the Belmont Report's principle of justice was formulated partly to ask why the burdens of research had so often fallen on groups unlikely to share in its benefits [8]. International research did not invent this asymmetry, but it can sharpen it: a trial conducted in a low-income country routinely involves a sponsor from a wealthy country, a product priced for wealthy-country markets, and a host population whose main point of contact with the health system may be the trial itself. Table 1 sets out the major sources of vulnerability that recur in this

literature alongside the safeguards most commonly proposed for each, and Figure 1 places those sources on a schematic axis of how severely each tends to compromise voluntary, informed participation.

THE STANDARD-OF-CARE DEBATE

The clearest flashpoint in this literature is the 1994 to 1997 controversy over placebo-controlled trials of short-course antiretroviral regimens to prevent mother-to-child HIV transmission in several African and Asian countries. Zidovudine's efficacy against perinatal transmission had already been established in a trial conducted in the United States and France, yet several subsequent trials in lower-income settings randomized women to placebo rather than to the already-proven regimen, reasoning that the local standard of care was no treatment at all and that a placebo arm was therefore not withholding anything women would otherwise have received [4]. Critics, writing in the same journal within months, argued that this reasoning imported a double standard directly into trial design: no ethics committee would have approved a placebo arm against a proven HIV intervention in a wealthy-country population, and using local poverty as the justification for a design that would be unacceptable elsewhere was exploitation dressed up as pragmatism [1]. Defenders of the trials replied that a genuinely applicable standard of care had to be sensitive to what was actually deliverable within the host country's health infrastructure, since a trial arm built around a regimen no local program could realistically sustain after the study ended would produce a result of no practical use to the population that bore its risks [9].

Neither side of that exchange has been fully vindicated by subsequent practice, but the debate reshaped how sponsors and reviewers now think about "standard of care" in international research: not as a single global benchmark, nor as whatever happens to be locally available, but as a question that has to be argued for explicitly, trial by trial, with reference to what a positive result could plausibly do for the host population [10]. That reframing has not eliminated disputes over placebo use in resource-limited settings, but it has made it much harder for a sponsor to justify a lower-protection design purely by appeal to local scarcity without also explaining what benefit the host population stands to gain from participating.

FRAMEWORKS FOR FAIR BENEFIT AND RESPONSIVENESS

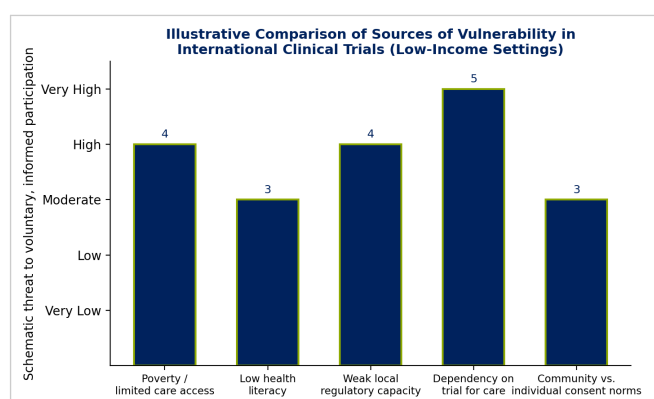
Partly in response to that debate, a body of work emerged proposing that the ethical acceptability of externally sponsored research in a low-income country should depend on demonstrable, negotiated benefit to the host population, not merely on the adequacy of informed consent. One influential proposal specified benchmarks that a study had to meet -- including collaborative partnership with local investigators, a

favorable balance of risk and benefit judged by local as well as sponsor standards, and responsiveness to the health needs of the host community -- arguing that consent alone could not carry the full ethical weight that an earlier, more general account of what makes any clinical research ethical had placed on it [11,12]. A companion "fair benefits" framework went further, proposing that researchers negotiate, transparently and in advance, what the host community and its participants would receive in return for hosting the trial, whether that took the form of improved local healthcare infrastructure, training, or guaranteed post-trial access to an effective intervention [13].

Table 1. Major sources of vulnerability identified in international clinical trials conducted in low-income settings, and the safeguards most commonly proposed in response.

Source of vulnerability	How it compromises participation	Commonly proposed safeguard
Poverty / limited healthcare access	Trial participation may be the only realistic route to medical attention, making refusal costly rather than neutral	Guaranteed standard of care and post-trial access negotiated before enrollment
Low health literacy	Formal disclosure may not translate into genuine understanding of risk, randomization, or placebo	Iterative, community-appropriate consent processes rather than a single disclosure event
Weak local regulatory capacity	Ethics review may face less scrutiny or resourcing than in the sponsor's home country	Independent local ethics committee capacity-building and external oversight
Dependency on the trial for care	Undue inducement: ordinary incentives can become effectively irresistible	Benefit-sharing negotiated in advance rather than treated as an incidental payment
Community vs. individual consent norms	Individual consent may bypass or conflict with community decision-making structures	Layered consent that respects community consultation without overriding individual refusal

Figure 1. Schematic comparison of how severely different sources of vulnerability are judged, in the literature reviewed here, to threaten voluntary and informed participation in international clinical trials (illustrative rating scale, not derived from a single empirical study).



These frameworks were an advance over consent-only

accounts, but they have also drawn a specific objection: that "fair benefits" risks becoming a negotiated price for participation rather than a correction of underlying injustice, since a population that lacks basic healthcare access to begin with is in a weak bargaining position even when the negotiation itself is procedurally transparent [14]. On this view, responsiveness requirements are necessary but insufficient, because they operate within, rather than against, the background inequality that makes low-income settings attractive to sponsors in the first place. A more general treatment of exploitation in research reaches a similar conclusion from a different angle: that a transaction can satisfy every procedural safeguard on the books and still be exploitative if the division of benefits between sponsor and host population is disproportionate to their respective contributions [15].

CONSENT UNDER CONDITIONS OF DEPENDENCY

Standard consent doctrine assumes a participant who can weigh risks and benefits and decline without cost. That assumption is strained when trial participation is, for many enrollees, their only realistic point of access to medical attention, diagnostic testing, or medication of any kind. Under those conditions, refusal is not a neutral option; it is a decision to forgo the only care on offer, which makes the voluntariness of consent doubtful even when every disclosure requirement has technically been satisfied [16]. Community and family-based decision-making common in many low-income settings complicates the individualist model further, since a study team obtaining consent only from an individual participant may be bypassing the decision-making structure the community itself regards as legitimate, while a study team that defers entirely to community leaders risks overriding individuals who would have declined on their own.

Undue inducement is the sharpest version of this problem: a modest payment or in-kind benefit that would be an unremarkable courtesy to a well-resourced participant can function, for someone with no other route to treatment, as an offer too significant to refuse on the merits of the study alone [5]. Ethnographic accounts of trial recruitment in low-income settings describe participants who understand perfectly well that they are subjects of an experiment and who enroll anyway, not out of confusion about the trial's purpose but because the alternative is no care whatsoever -- a pattern that sits uneasily with a consent framework built around the idea that a truly voluntary choice requires a reasonable alternative to accepting [17].

REGULATORY OVERSIGHT AND POST-TRIAL OBLIGATIONS

Weak or under-resourced regulatory and ethics-review infrastructure in many low-income countries has

repeatedly been identified as a structural driver of exploitation risk, independent of any individual sponsor's intentions. A trial that would face searching scrutiny from a well-staffed ethics committee in a high-income country may pass with comparatively little friction where committees are newer, less resourced, or under pressure to attract international research investment [18]. International guidance has moved to address this gap directly: the most recent revisions of the Declaration of Helsinki require that research be responsive to the health needs of the population in which it is conducted, and the CIOMS guidelines add detailed provisions on the ethics review capacity that host countries need in order to make that requirement more than aspirational [19,20].

Post-trial access is the second recurring regulatory gap: an intervention proven effective in a low-income host population is not thereby guaranteed to remain available to that population once the trial ends, particularly where the sponsor's commercial market lies elsewhere [21]. Both the Declaration of Helsinki and the CIOMS guidelines now call for post-trial access arrangements to be planned before a study begins rather than negotiated, if at all, after results are known, but enforcement of that expectation varies enormously by country and by sponsor, and a purely aspirational commitment written into a protocol is not the same thing as a binding one [20]. Commentators reviewing multinational trial practice across a range of middle-income settings have argued that the ethical questions genuinely differ by country and cannot be resolved by a single global rule, since a health system's capacity to sustain a proven intervention after a trial ends is itself a local, empirical fact rather than a matter that a universal guideline can settle in the abstract [10].

CONCLUSION

Vulnerability and exploitation are not the same wrong, and treating them as interchangeable has made this literature harder to resolve than it needs to be. A population can be genuinely vulnerable -- poor, under-resourced, dependent on the trial for care -- and still be treated fairly, if investigators respond to that vulnerability with a design, a consent process, and a benefit-sharing arrangement calibrated to it rather than one that simply takes advantage of the leverage vulnerability creates. The standard-of-care debate, the fair-benefits and responsiveness frameworks it produced, the persistent difficulty of securing genuinely voluntary consent under conditions of dependency, and the uneven state of regulatory oversight and post-trial obligation are best read not as separate controversies but as four facets of the same underlying question: what does a sponsor from a wealthy country owe to a population it recruits from a poor one. No single procedural fix -- better consent forms, a fair-benefits negotiation, a stronger local ethics committee -- answers that question on its own. What the literature surveyed here suggests instead is that

defensible research in low-income settings requires all of these safeguards working together, and a background willingness on the part of sponsors and regulators to treat responsiveness to host-population need as a condition of doing the research at all, not as a courtesy extended once the trial has already been designed around other priorities.

DECLARATIONS

Acknowledgements

The authors are grateful to colleagues in their respective philosophy and public health ethics departments for comments on earlier drafts of this review.

Funding

This review received no external funding.

Conflict of Interest

The authors declare no conflicts of interest relevant to this work.

Author Contributions

Ingrid Ramirez conceived the review, drafted the sections on the standard-of-care debate and fair-benefits frameworks, and coordinated the final manuscript. Etienne Zielinska developed the sections on consent under conditions of dependency and undue inducement and critically revised the manuscript for content. Agnieszka Zielinska contributed the analysis of regulatory oversight and post-trial obligations and verified the reference list. All authors read and approved the final manuscript.

Ethics Statement

As a literature review synthesizing previously published, publicly available research and policy analysis, this article did not involve new data collection from human participants and did not require institutional ethics committee approval.

Data Availability

No new data were generated or analyzed for this review. All sources discussed are cited in the reference list and are publicly available through their respective publishers.

REFERENCES

1. Angell M (1997) The ethics of clinical research in the Third World. *New England Journal of Medicine*.
2. The ethical implications of clinical trials in low- and middle-income countries. *American Bar Association, Human Rights Magazine*.
3. The ethics of global clinical trials: in developing countries, participation in clinical trials is sometimes the only way to access medical treatment (2015) *EMBO Reports*,

- DOI:[10.15252/embr.201540398](https://doi.org/10.15252/embr.201540398).
4. Lurie P, Wolfe SM (1997) Unethical trials of interventions to reduce perinatal transmission of the human immunodeficiency virus in developing countries. *New England Journal of Medicine*.
 5. Resnik DB (2003) Exploitation in biomedical research. *Theoretical Medicine and Bioethics*.
 6. Ballantyne A (2010) How to do research fairly in an unjust world. *American Journal of Bioethics*.
 7. The Nuremberg Code (1947) Trials of War Criminals before the Nuremberg Military Tribunals.
 8. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1979) The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research.
 9. Varmus H, Satcher D (1997) Ethical complexities of conducting research in developing countries. *New England Journal of Medicine*, DOI:[10.1056/NEJM199710023371411](https://doi.org/10.1056/NEJM199710023371411).
 10. Dal-Re R, Jha V, Lv J, Chaudhury RR, Wang Y, Perkovic V (2016) International trials in middle-income countries: different local scenarios require different ethical approaches. *Journal of the Royal Society of Medicine*, DOI:[10.1177/0141076815608854](https://doi.org/10.1177/0141076815608854).
 11. What makes clinical research in developing countries ethical? The benchmarks of ethical research (2004) *The Journal of Infectious Diseases*.
 12. Emanuel EJ, Wendler D, Grady C (2000) What makes clinical research ethical? *JAMA*.
 13. Fair benefits for research in developing countries (2002) *Science*.
 14. London AJ (2005) Justice and the human development approach to international research. *Hastings Center Report*.
 15. Wertheimer A (2011) *Rethinking the Ethics of Clinical Research: Widening the Lens*. Oxford University Press.
 16. Macklin R (2004) *Double Standards in Medical Research in Developing Countries*. Cambridge University Press.
 17. Petryna A (2009) *When Experiments Travel: Clinical Trials and the Global Search for Human Subjects*. Princeton University Press.
 18. Ethical considerations of clinical trials in the developing world (2009) *Transactions of the Royal Society of Tropical Medicine and Hygiene*.
 19. World Medical Association (2013) World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*.
 20. Council for International Organizations of Medical Sciences (CIOMS) (2016) *International Ethical Guidelines for Health-related Research Involving Humans*. CIOMS, Geneva.
 21. Annas GJ (2009) Globalized clinical trials and informed consent. *New England Journal of Medicine*.