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CASE AND COMMENTARY: PEER-REVIEWED ARTICLE

Should Children Be Enrolled in Clinical Research in Conflict Zones?

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Abstract

This commentary examines 4 ethical issues in a case of clinicians considering conducting research on children in conflict zones: (1) whether any time or resources should be taken away from treating acute injuries in order to conduct research; (2) obtaining consent for children to participate in research, which is particularly challenging given that children can be separated from parents or guardians; (3) whether the research is feasible at the moment, since starting research that stands little chance of being completed is ethically questionable; and (4) maintaining neutrality, impartiality, and humanity. Research that puts participants and researchers at risk of additional harm must be considered carefully. Here, we propose that both research and clinical care might occur simultaneously when researchers engage humbly with involved communities as the research is being designed, conducted, and reported in order to understand and resolve ethical issues involved.

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Case

Dr P is a physician and researcher from an East African country that has been immersed in violence and civil conflict for years. He and his colleagues work in the region with an international nonprofit organization that both provides health care services and aims to strengthen the evidence available to guide practitioners during humanitarian crises. Dr P and colleagues care for many adults and children injured by violence and are concerned about availability of interventions for diseases endemic to the region. Many children hospitalized for war injuries also have infectious diseases, such as HIV/AIDS, malaria, and tuberculosis. Dr P and colleagues consider researching these diseases' prevalence among children in the region and whether and to what extent current policies address their needs. Some enthusiastically support these research ideas, but others question whether clinical research during conflict would be the best use of clinicians' time and skills.

Dr P and colleagues form a team to collectively consider practical and ethical issues they could face when conducting research. One plan that emerges during their meetings

includes enrolling children arriving at the hospital and sampling their blood, monitoring children who test positive for an infectious disease, and evaluating how well current policies support clinicians' capacity to offer evidence-based interventions and psychosocial care. Since children often arrive at the hospital accompanied not by their parents but by other relatives or adults, parental informed consent might not be possible. Although consent from an adult relative accompanying a child is standard for medical interventions in the region, some team members wonder whether a child's assent to participate in research or an adult relative's consent to enroll a child in research would be ethically sufficient. Assuming consent can somehow be appropriately secured, some team members worry that it's not ethical to even attempt research that might not even be feasible because participants' blood samples can deteriorate and expire while being transported to the capital city for analysis. Long transportation delays are not easily averted in the region due to security incidents, roadblocks, and ambushes. Even assuming good blood sample preservation and analysis, test results (normally available 14 days after collection) will need to be conveyed to children's parents by research team members who travel to their villages. If the children's parents have been killed and no guardian is present, it's unclear whether keeping newly orphaned children in a research protocol is ethically appropriate.

Dr P and colleagues remain neutral about the region's conflict, but the government has authority over the hospital, and nearby villages are controlled by antigovernment rebel forces. Rebel groups have not objected to villagers seeking care at the hospital, but if researchers are viewed as government collaborators or agents reporting on rebel activities, everyone in the hospital could be at risk of violence. Another complexity is that the government's Ministry of Health, which would have to approve a research protocol, might oppose any project it sees as beneficial to the interests of people living in rebel-held regions.

Although convinced that children with infectious diseases are not adequately cared for under existing policies, Dr P and colleagues believe that the capacity to respond to need can't be improved without a good evidence base that research would likely establish. They are also convinced that it is ethically problematic to wait until conflict ends to conduct research that could lead to improvements, and so Dr P and colleagues continue to deliberate about what they should do.

Commentary

Conducting research in a conflict zone raises many practical and ethical challenges. Conflict varies in its nature and scale, ranging from open military warfare to other forms of armed conflict and communal violence. The 2021 Council for International Organizations of Medical Sciences consensus statement on clinical research in low-resource settings addresses concerns of working among armed populations and during riots in its comments on conflict.[1] The challenges include concerns for safety and security, lack of scientific capacity or ethical oversight, practical limitations that might compromise study quality, and political pressures and barriers.[2] However, research during conflict can be beneficial when conducted appropriately and ethically.[3] The difficulty is finding the balance between challenges and benefits, which requires careful and humble reflection on each situation's details and application of research ethics frameworks.[1,4,5] With this particular case, we will comment on 4 ethical issues, although more could be considered.

Treating Injuries vs Conducting Research

Dr P and his colleagues are trying to decide how to allocate their limited time, energy, and resources between treating acute, conflict-related injuries and addressing unmet needs of children with acute and chronic infectious diseases through research. Some of the clinicians believe evidence from research is needed to determine whether existing policies and interventions address the needs of infected children. As the Active Learning Network for Accountability and Performance in Humanitarian Action notes: "The failure to generate and use evidence in policy and response makes humanitarian action less effective, less ethical and less accountable."[6] Research in conflict zones might be needed to determine if interventions effective in other settings remain effective in conflict settings and, if not, what adaptations are necessary for conflict zones. However, some could argue that research is of low priority since it might provide little direct benefit to the children living in the conflict zone. At best, it might show that disease prevalence is higher than previously documented, that current policies are not working well, or that changes are needed that might benefit other children. When the needs of conflict-injured children are compared to those of other children who might benefit in the future from research, the urgency of their situation might seem to outweigh the long-term needs of children in the region. Others might argue that only treating the children's injuries is an overly short-sighted approach. If the clinicians focus exclusively on conflict injuries, children might afterwards get sick and die from communicable diseases and thus have little overall benefit from the clinical resources they received.

Ethical dilemmas often are portrayed as one option vs another, especially when both options are ethical but prioritize different ethical principles. Rather than pitting one option against the other, clinicians creatively considering other options might identify an alternative that satisfies both ethical commitments, although perhaps not completely. Instead of viewing this case as an "either-or" dilemma in which the clinicians should *either* care for patients *or* do research, a "both-and" approach would allow the clinicians to strive *both* to care for patients *and* to do research. Whether this approach is practically feasible will depend on resources and context. Perhaps Dr P and his colleagues could split their time between clinical care and research, or perhaps one clinician could be freed up to focus on research while others cover that clinician's patient responsibilities.

However the team allocates resources, good reasons are needed to justify conducting research during conflict. Addressing research in humanitarian emergencies, the United Nations' Inter-Agency Standing Committee stated: "If the research question could be answered in a nonemergency setting, then it should not be answered in an emergency setting."[7] Yet to simply "export" health interventions shown to be effective in "stable"—typically high-income—countries to conflict settings without evaluating their effectiveness is also problematic.[8] Doing so would only continue the regrettable status quo of using public health interventions in humanitarian crises that have little—and low-quality—evidence to support them.[9] Sometimes medical interventions or procedures are tried in humanitarian settings that in reality are experimental and should instead be used in research protocols, complete with ethical review. Conducting research in conflict zones raises many challenges, but if care is being provided, research to evaluate its effectiveness and safety might be feasible and ethical.

Children as Subjects

Informed consent is internationally accepted as an ethical requirement to participate in research.[1,4,5] Since participating in research is voluntary, informed consent is a way to

respect people's right to decide for themselves if they wish to be involved. Children's participation in research requires additional ethical scrutiny, especially in humanitarian and conflict settings.[10,11] Policies typically state that parents or guardians may give consent for a child to participate in research on the assumption that they know the child's best interests. The age at which children may give consent varies depending on the age of majority in a country. Below the age of majority, even when parents or guardians give consent, a child's assent or agreement might be sought, although some cultures do not believe assent is necessary or appropriate.[12] In some cultures, parents or guardians might not like researchers obtaining assent from a child if they believe children cannot understand research. Others might be offended by researchers' obtaining assent from children if doing so suggests that the parents' consent was insufficient. However, if children are not consulted, they might feel coerced into participating and not engage fully with the researchers.

The case of Dr P is further complicated by the fact that children often are separated from their parents during conflicts. Excluding them from research until they are old enough to consent might deny them the benefits that such research might generate.[13] It could be argued that children separated from their parents should not participate in research, as they might have been traumatized by the conflict and be unable to give authentic consent if no adult can give consent for them. However, people who have experienced traumatic events can understand the purpose of research and truly consent to participate.[14] The difficult circumstances that the children have been through—perhaps forced to leave their homes, knowing their parents have died, becoming their siblings' caretaker—might have accelerated their maturation and left them more capable of consenting than other children of similar ages.

Given these considerations, innovative adaptations of ethics guidelines—such as allowing relatives to give consent for children's participation in research—might be reasonable, especially if accepted in the region. Some cultures are highly individualized and insist on individuals deciding for themselves. Other cultures value wider family and community interactions and decision making.[12] Children going to medical facilities are sometimes accompanied by elders or community leaders, who may be called "uncle" out of respect for their position. Such practices further complicate obtaining consent. In such situations, those beyond the nuclear family could be assumed to know the children well and to be able to make decisions based on the children's best interests. These issues remain challenging and far from clear-cut, with local context and level of risk being important to consider.

To address issues of consent for orphaned children and those unaccompanied by parents, the researchers should spend time getting to know the participant community.[13] Community engagement helps researchers avoid pursuing methods that turn out to be unacceptable or impractical in the community. In particular, participatory research methods are increasingly seen as important ways to ensure community values and culture are understood and respected.[15] During researchers' interactions with the community, challenges and concerns can be raised and potential problems mitigated or avoided. Such discussions will reveal what method of seeking consent or assent is acceptable in that community. This approach can also help children feel comfortable, as they know the approach has been agreed upon by the community and the researchers.

Research Feasibility

Even if ethical issues can be resolved satisfactorily, the feasibility of the research must be investigated carefully. Humanitarian organizations and individuals working in conflict zones might be overstretched and underresourced to the extent that conducting research might not be feasible.[8] The case of Dr P described challenges of transporting samples, poor infrastructure, and security issues. Without practical solutions to such problems, the research might have to be adapted or abandoned.

Before conducting clinical research in conflict zones, researchers should assess the opportunities and the challenges (including methodological, logistical, political, and ethical challenges) to help them decide whether it is feasible to conduct ethical research in that place at that time. A thorough situation analysis should also include assessment of stakeholders' attitudes and beliefs about conducting research in conflict zones, the availability of research assistants from within the community affected by the conflict (who could collect data using their social networks), and assessment of the risk-benefit ratio of the proposed research by maintaining risk registers and conducting regular risk assessment during service delivery. Various tools and checklists are also available to help with assessments and planning, such as the guidelines of the International Institute of Social Studies.[16]

To justify the risk of harm and use of resources, especially in a conflict zone, the research should be able to make a meaningful contribution to practice. Conducting unfeasible research has ethical implications, since starting an unfeasible study would waste resources.[16] Furthermore, conducting an unfeasible study might leave communities distrustful of researchers or even clinicians, which could impede realization of the benefits being sought. However, such challenges should not lead to research being immediately abandoned, as alternative means and additional resources could be pursued to address the difficulties.

Researchers should also consider that the needs and research questions arising in resource-limited environments might be more amenable to study using different research methodologies, such as observational studies or adaptive trial designs.[17] Snowball sampling methodology, for example, increases the likelihood of addressing distrust and suspicion when stakeholders in conflict zones are introduced by a trusted social network.[18] Conducting research ethically in conflict settings requires significant effort and flexibility, as well as sufficient resources and expertise, and is urgently needed in many areas. Research teams should ensure that their project is feasible and their team is well prepared before starting research projects.

Interacting With Authorities

The final ethical issue to be considered here is the role of authorities. Humanitarian organizations working in conflict settings find themselves walking a tightrope between various authorities. Getting the balance wrong can have fatal consequences for those working for humanitarian organizations and those they seek to help. Providing medical care to the injured can be seen as much more beneficial than conducting research. The collection of information or biological samples might be viewed with suspicion unless the researchers and participating communities have a clear understanding of the study. Researchers have been killed due to misunderstandings or malicious rumors about the goals of their study.[19] Much can be learned about the ethics of conducting research from past experiences, an example being research carried out during the 2014 to 2016 Ebola epidemic.[17,20]

The risks for researchers working in conflict settings have been studied.[21,22] In addition to the researchers themselves, others associated with them can be put at heightened risk. In the case of Dr P, the hospital could be attacked if it is viewed as collaborating with one side or the other in the conflict. The attacks on health care facilities reported in Syria are a terrible reminder that those who seek to care for the sick and injured are no longer viewed as entitled to protection in the eyes of some combatants.[23] Instead, they might become direct targets of violence or threatened with violence if they treat certain people or don't treat others. Such risks must be considered when decisions are being made about research in conflict settings.

This case study also points to the multiple conflicts of interest that can arise in research conducted in conflict settings. Countries affected by internal conflict and violence might require all research studies to be approved or licensed by a government agency. That same government might have a vested interest in certain issues not being researched or, if they are, in ensuring that the findings are not reported in ways that criticize the government, its policies, or its allies.[24] In some cases, these constraints might prevent studies from getting the necessary approvals. Researchers might have to consider the risk of conducting such studies without the required approvals (with the result that their studies might be shut down before they are completed), of their organization being forced to leave the country after reporting the results, or of the research team experiencing violence or imprisonment.[24]

Conclusion

The ethical and practical challenges of conducting research in conflict settings should not lead to it being abandoned; creative approaches should be explored to manage time, find resources, and adapt protocols as needed. Before designing studies, it is essential for researchers to engage involved communities, even those in conflict, to understand their needs and relevant cultural practices and concerns. Such engagement must be undertaken with humility.

Research with children is an important way to address their needs (understood holistically) with evidence-based interventions and policies. Viewing them as too vulnerable to participate in research might further marginalize them and leave their treatment without supportive evidence. Although including children raises additional ethical challenges, such as informed consent, these can be addressed through meaningful engagement with the community, parents, and other authorities.

Significant efforts might be required to establish researchers' independence from the conflict. Some living in conflict zones might not accept that neutrality is possible, and hence research in these settings has inherent dangers. So, too, does providing health care.[25] Both health care and research have the potential to benefit the community greatly. Ensuring research is conducted ethically is one way to minimize the risks for everyone involved.

References

1. Council for International Organizations of Medical Sciences (CIOMS) Working Group. *Clinical Research in Resource-Limited Settings: A Consensus by a CIOMS Working Group*. Council for International Organizations of Medical Sciences; 2021. Accessed July 12, 2021. https://cioms.ch/wp-content/uploads/2021/06/CIOMS_ClinicalResearch_RLS.pdf

2. Ford N, Mills EJ, Zachariah R, Upshur R. Ethics of conducting research in conflict settings. *Confl Health.* 2009;3:7.
3. Goodhand J. Research in conflict zones: ethics and accountability. *Forced Migr Rev.* 2000;8:12-15.
4. Declaration of Helsinki. World Medical Association. Adopted June 1964. Amended October 2013. Accessed July 12, 2021. https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
5. Mezinska S, Kakuk P, Mijaljica G, Waligóra M, O'Mathúna D. Research in disaster settings: a systematic qualitative review of ethical guidelines. *BMC Med Ethics*. 2016;17:62.
6. Knox Clarke P, Darcy J. *Insufficient Evidence? The Quality and Use of Evidence in Humanitarian Action*. Active Learning Network for Accountability and Performance in Humanitarian Action (ALNAP); 2014. Accessed July 12, 2021. https://reliefweb.int/sites/reliefweb.int/files/resources/alnap-study-evidence.pdf
7. Reference Group for Mental Health and Psychosocial Support in Emergency Settings. Recommendations for conducting ethical mental health and psychosocial research in emergency settings. Inter-Agency Standing Committee; 2014. Accessed July 12, 2021. https://interagencystandingcommittee.org/system/files/1._iasc_recommendations_for_ethical_mhpss_research_in_emergency_settings_0.pdf
8. Kohrt BA, Mistry AS, Anand N, Beecroft B, Nuwayhid I. Health research in humanitarian crises: an urgent global imperative. *BMJ Glob Health*. 2019;4(6):e001870.
9. Blanchet K, Ramesh A, Frison S, Warren E, et al. Evidence on public health interventions in humanitarian crises. *Lancet*. 2017;390(10109):2287-2296.
10. Berman G, Hart J, O'Mathúna D, et al. What we know about ethical research involving children in humanitarian settings: an overview of principles, the literature and case studies. Innocenti working paper 2016-18. Office of Research, UNICEF; 2016. Accessed July 12, 2021. https://www.unicef-irc.org/publications/pdf/IWP_2016_18.pdf
11. Wessells M. Reflections on ethical and practical challenges of conducting research with children in war zones: toward a grounded theory. In: Mazurana D, Jacobsen K, Gale LA, eds. *Research Methods in Conflict Settings: A View from Below*. Cambridge University Press; 2013:81-105.
12. Vreeman R, Kamaara E, Kamanda A, et al. Community perspectives on research consent involving vulnerable children in western Kenya. *J Empir Res Hum Res Ethics*. 2012;7(4):44-55.
13. Embleton I, Ott MA, Wachira J, et al. Adapting ethical guidelines for adolescent health research to street-connected children and youth in low- and middle-income countries: a case study from western Kenya. *BMC Med Ethics*. 2015;16:89.
14. O'Mathúna D. Conducting research in the aftermath of disasters: ethical considerations. *J Evid Based Med*. 2010;3(2):65-75.
15. O'Mathúna D. The dual imperative in disaster research ethics. In: Iphofen R, Tolich M, eds. *SAGE Handbook of Qualitative Research Ethics*. SAGE; 2018:441-454.
16. Hilhorst D, Hodgson L, Jansen B, Mena R. Security guidelines for field research in complex, remote and hazardous places. International Institute of Social

Studies, Erasmus University Rotterdam; 2016. Accessed July 12, 2021. https://repub.eur.nl/pub/93256/Fieldwork_security_guidelines.pdf
17. Alirol E, Kuesel AC, Guraiib MM, de la Fuente-Núñez V, Saxena A, Gomes MF. Ethics review of studies during public health emergencies—the experience of the WHO Ethics Review Committee during the Ebola virus disease epidemic. *BMC Med Ethics.* 2017;18:43.
18. Cohen N, Arieli T. Field research in conflict environments: methodological challenges and snowball sampling. *J Peace Res*. 2011;48(4):423-435.
19. Yimer G, Gebreyes W, Havelaar A, et al. Community engagement and building trust to resolve ethical challenges during humanitarian crises: experience from the CAGED Study. *Confl Health.* 2020;14:68.
20. Schopper D, Ravinetto R, Schwartz L, et al. Research ethics governance in times of Ebola. *Public Health Ethics*. 2017;10(1):49-61.
21. Mazurana D, Jacobsen K, Gale LA, eds. *Research Methods in Conflict Settings: A View from Below*. Cambridge University Press; 2013.
22. Byrne S, Elcheroth G, Gabriel S, Goetschel L, Hagmann T, Santschi L. A conflict sensitive approach to field research: doing any better? *Swiss Acad Rep*. 2017;12(5):1-40. Accessed July 12, 2021. https://www.swisspeace.ch/assets/publications/downloads/Articles/50ed664095/A-conflict-sensitive-approach-to-field-research-17-swisspeace-laurent_goetschel.pdf
23. Spagat M. Attacks on medical workers in Syria: implications for conflict research. *PLoS Med*. 2018;15(4):e1002560.
24. Thomson SM. "That is not what we authorised you to do…": access and government interference in highly politicised research environments. In: Sriram CL, King JC, Mertus JA, Martin-Ortega O, Herman J, eds. *Surviving Field Research: Working in Violent and Difficult Situations*. Routledge; 2009:108-123.
25. Coupland R, Breitegger A. *Health Care in Danger: The Responsibilities of Health-Care Personnel Working in Armed Conflicts and Other Emergencies*. International Committee of the Red Cross; 2012. Accessed July 12, 2021. https://shop.icrc.org/download/ebook?sku=4104/002-ebook

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Editor's Note

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