STUDENT PAPER 1

Radicalizing Clinical Trial Ethics through Community Partnership: Limitations and Strategies for Change

Researcher: Brooke Danielle Daggao Johnson

Abstract

Clinical trials are crucial in developing safe medical treatments and combating diseases. However, the ethical considerations surrounding research involving human subjects have been an ongoing topic of debate. Existing ethical policies aim to ensure the accuracy of research findings and protect the well-being of participants. Nevertheless, these policies have been rooted in Western scientific and medical systems, which historically exploited communities for the benefit of privileged individuals and capital accumulation, perpetuating domination and settler colonialism. While ethical policies alone cannot erase these harmful legacies, they have globally failed at holding researchers, companies, and institutions accountable for their impact on communities. This failure has led to exploitation and unintended harm in disenfranchised communities with under-resourced health systems and limited access to healthcare resources. To address these challenges, this literature review proposes integrating stricter regulations, transparent disclosure of trial results, and comprehensive post-trial care. Additionally, it advocates for including community partnerships in clinical trial ethics policies to prioritize community needs and promote accountability. By examining qualitative studies on the perspectives of patients, researchers, and clinicians involved in clinical trials, as well as the current state of clinical trial ethics policies, this paper suggests a partnership-based approach that can facilitate the development of new treatments while addressing historical legacies of exploitation and harm in disenfranchised communities worldwide.

Introduction

Clinical trials are crucial for advancing safe medical treatments and addressing widespread diseases. However, testing and developing clinical interventions for humans present certain risks that raise ethical challenges and concerns. Adherence to clinical trial ethics ensures research accuracy and participant protection. Although the primary aim of clinical research is to advance general knowledge of how the human body reacts to disease, participants may not directly benefit. By following ethics policies, researchers can mitigate harm and maintain participant dignity. Nevertheless, debates over these ethical policies persist, with concerns about exploiting vulnerable populations under current guidelines (Egharevba, E., & Atkinson, J., 2016).

Vulnerable communities often face risks in clinical trials, highlighting the need for more robust ethical frameworks and accountability. By employing the framework of structural violence, this paper will examine the unethical aspects of contemporary clinical trials that emphasize the necessity for stricter regulations, transparent disclosure of trial results, and post-trial care to protect vulnerable populations and uphold ethical standards. In addition, this paper will explore the importance of community partnerships in clinical research ethics, proposing their integration to safeguard against exploitation. Such partnerships provide mutual benefits and deeper insights into community needs that would help address ethical concerns.

Furthermore, this paper suggests a strategy for embedding partnerships in clinical ethics policies, including equitable profit distribution. While recognizing the differences between communities worldwide, this paper aims to highlight the need for further research to examine the impact of partnerships and the integration of community partnerships in specific countries, governments, and cultural/social contexts. By analyzing the ethical issues in clinical trials conducted worldwide, we can gain valuable insights that inform ethical guidelines and policies for clinical trials.

Historical Ethical Guidelines and Their Limitations:

The establishment of the Nuremberg Code in 1947 and the Helsinki Declaration in 1964 marked significant milestones in medical research ethics. These guidelines set standards for ethical conduct in research involving human subjects. Despite their authority, there remain gaps in their application, particularly in trials involving under-resourced communities. These gaps highlight a disconnect between ethical guidelines and practical implementation (Mahmood, 2012; Negri, 2017). Biomedical research is increasingly conducted in locations with under-resourced health systems, whether through the globalization of clinical trials in underdeveloped countries or the implementation of clinical trials in developed countries -- like the United States-- where health systems may be under-resourced. The alarming number of unethical medical experiments within vulnerable communities has drawn public attention. These experiments disregard internationally-agreed medical ethics and human rights principles, causing severe concern (Negri, 2017). Consequently, while these principles are universally essential and relevant, they are especially crucial in clinical research, particularly in vulnerable communities where fundamental principles are often disregarded (Negri, 2017). Before delving into the failures of clinical trial ethics policy in protecting such communities, it is essential to define what constitutes a vulnerable community in a clinical trial and how we will examine these failures through the lens of structural violence.

Vulnerable Populations and Structural Violence:

I) What Defines a Vulnerable Community?

Whether in developing countries or affluent nations, vulnerable communities lack the resources and representation within robust structures to achieve long-term sustainability. They often find themselves in precarious situations due to economic conditions, cultural backgrounds, physical environments, and social and familial networks (Pacheco-Vega et al., 2018). Conversely, powerful entities like industries and governmental institutions influence these communities by leveraging their control through government access, knowledge, and resources (Kingori, 2015). In the context of clinical trials, vulnerable communities refer to those with under-resourced health systems and limited access to healthcare resources. Such is evident in clinical trials where these communities risk exploitation by the biomedical research industry to gain access to healthcare. Despite healthcare advancements, stark disparities remain in both developed and developing countries. These disparities are highlighted by countries like the USA, where high healthcare spending contrasts with poor health outcomes, illustrating widespread health and economic inequalities domestically and internationally (Benatar, 2002; Kingori, 2015).

II) What is Structural Violence?

The exploitation experienced by vulnerable communities in clinical trials exemplifies 'structural violence'—harm caused by societal structures, such as political and economic systems, rather than direct physical violence (Farmer et al., 2006). These structures hinder basic human needs, impacting the well-being of individuals (Farmer et al., 2006). It is difficult to assign blame, as this harm arises from systemic issues rather than individual actions. In domestic politics, it manifests in decisions like healthcare funding, which can unevenly affect different groups and lead to disparities in access to essential services. Alternatively, structural violence can manifest as under-resourced health systems and limited access to healthcare resources (Brown et al., 2018). Current ethical policies in clinical trials often overlook the biosocial aspects of health and tend to favor market interests over those of community participants. Vulnerable communities often end up in the same or worse conditions post-trial, thereby perpetuating health disparities and physical suffering (Farmer et al., 2006; Brown et al., 2018). Meanwhile, research institutions and pharmaceutical companies often profit from these trials, which underscores the need to evaluate the broader societal, economic, and political factors.

The globalization and privatization of clinical trials have introduced significant ethical and legal challenges, particularly in countries with weak regulatory frameworks. These countries often exhibit higher rates of poverty and illiteracy, making their communities more vulnerable to exploitation in clinical research (Negri, 2017). Furthermore, the shift in clinical trial management and oversight from government bodies, like the CDC in the United States, to private entities—including pharmaceutical companies, universities, contract research organizations, and commercial Institutional Review Boards (IRBs)—intensifies these issues especially in lower-income countries (Negri, 2017; Spellecy et al., 2024). In the U.S., commercial IRBs often prioritize regulatory compliance over ethical concerns, with their business models discouraging thorough reviews due to cost, potentially compromising participant safety for financial gain (Spellecy et al., 2024). Furthermore, assessing IRB quality and managing conflicts of interest pose difficulties, with large IRBs reluctant to undergo research that could question their effectiveness in protecting participants' rights (Klitzman et al., 2020). This issue draws attention as the FDA proposed a rule in 2020 to mandate single IRB reviews for multisite clinical trials to speed up reviews and reduce costs, likely favoring the usage of commercial IRBs (Spellecy et al., 2024). The COVID-19 pandemic exemplified the issues surrounding the privatization of clinical trial oversight and weak regulatory frameworks. The COVID-19 outbreak posed considerable obstacles for research ethics committees (RECs) as they sought to navigate the need for swift evaluation of COVID-19 studies while ensuring thorough deliberation regarding associated risks and advantages (Burgess et al., 2023). A 2021 study examining COVID-19 clinical trials revealed inconsistencies in phase definitions and enrollment criteria globally, risking participants' well-being due to limited access to treatment and insufficient discussions on vulnerabilities in informed consent processes (Buruk et al., 2021). In the U.S. during the COVID-19 pandemic, the FDA's relaxed standards under Operation Warp Speed led to ethical concerns. Despite limited research on participant harm or compensation, reports emerged of adverse events linked to Emergency Use Authorization (EUA)-approved COVID-19 vaccines (Classen, 2021). Another example includes a New England Journal of Medicine (NEJM) case report on COVID-19 presymptomatic transmission that was discredited due to not adequately interviewing the patient being studied, and other studies faced critique for methodological flaws such as double reporting and misrepresenting data (Hashem et al., 2020). The global trend of prioritizing profits in clinical trials, with inadequate oversight and relaxed ethics policies, compromises participant safety and informed consent, raising profound ethical concerns about participant exploitation and the integrity of research (Negri, 2017; Sarwar, 2019). Such scenarios underscore the need for a comprehensive reevaluation of the privatization of clinical trial oversight and sponsorship and its implications for research ethics and participant protection.

Thus, this paper delves into the ethical dilemmas faced in international research through the lens of structural violence, highlighting how poverty and limited healthcare access increase risks for vulnerable participants. This paper will analyze the harms inflicted by clinical trials under current ethical frameworks, aiming to illuminate how these policies fall short in protecting communities, especially the vulnerable, from harm.

Exploring Structural Violence in Clinical Trials within Vulnerable Communities

I) The Issue of Informed Consent

The issue of informed consent in clinical trials is a complex and multifaceted problem that often perpetuates structural violence against communities through structural coercion. Central to this issue is ensuring that participants have the health literacy necessary to provide informed consent. Such is exacerbated by the lack of scientific knowledge among the general population, which impedes their understanding of the potential long-term effects of participation in clinical trials (Lamkin & Elliot, 2018). Medical anthropologists argue that consent should not be treated merely as a bureaucratic procedure but should instead encompass broader societal, economic, and political factors influencing individuals' autonomy (Varma et al., 2021). Such understanding is crucial to recognizing the link between consent and exploitation, especially in the context of larger societal forces (Lamkin & Elliot, 2018). Exploitation in clinical trials extends beyond inadequate compensation or overt coercion; it includes situations where participants face undue influence from excessively enticing rewards, leading to compromised decision-making and increased risks for harm (Lamkin & Elliot, 2018; Mngadi et al., 2017). Although not all incentives are problematic, the role of independent ethics reviews in safeguarding against such influences is critical. However, these reviews may not always account for every individual's unique circumstances (Mngadi et al., 2017).

The concept of "structural coercion" is critical in this regard, as it acknowledges the role of structural elements, such as the absence of universal healthcare or the need for consistent medication, in shaping participants' choices. These factors often leave research participation as the only feasible means for many to secure income and healthcare, even when participants are fully aware and capable of understanding the study details (Lamkin & Elliot, 2018). A common misunderstanding in clinical trials, such as the RHDGen genomic study at the University of Cape Town, is about the potential benefits of participation. Driven by unmet healthcare needs, participants frequently mistake research for opportunities for diagnosis or treatment. The term "diagnostic misconception" refers to the failure to differentiate between research and clinical diagnosis, whereas "therapeutic misconception" describes the belief that research participation will directly benefit the participant. For instance, individuals with heart disease participating in the RHDGen trial hoped it might lead to improved treatments for rheumatic heart disease, although there was no intent of benefit to the trial's participants (Masiye et al., 2017). Similarly, research on COVID-19 in South Africa highlighted ethical challenges, including how the fear of the disease could exacerbate therapeutic misconceptions and question the efficacy of consent processes during such crises

(Burgess et al., 2023). Ultimately, ensuring informed consent in clinical trials, particularly for vulnerable communities, demands a thorough understanding of the impact of structural coercion and the broader societal, economic, and political factors at play. Consent should not be seen as a mere formality but as a process deeply intertwined with the larger context in which individuals make informed decisions.

II) The Issue of Diversifying Clinical Trials

The limited diversity in clinical trials presents significant moral, scientific, and medical challenges. Homogeneous participant demographics, such as uniformity in age, sex, or race/ethnicity, can skew results and limit the generalizability of clinical knowledge. In the U.S., advancements in clinical and scientific knowledge have not equally benefited minorities like African Americans and Hispanics compared to white populations (Curr Probl Cardiol, 2019). Efforts to diversify clinical trial participants, especially in terms of race/ethnicity, are ongoing. However, focusing narrowly on recruitment diversity can inadvertently reinforce structural violence and racial biases in research. Discussions about racial diversity often lean towards racial or ethnic determinism, emphasizing genetic differences while neglecting significant social and structural factors. For instance, a study sequencing the genomes of African American and Latino children with asthma identified genetic variants affecting lung capacity and immune response, impacting the effectiveness of albuterol in Black and Brown children compared to white children. However, these findings overlook the role of structural racism, such as living in areas with poor air quality due to systemic inequalities (Varma et al., 2021).

Race, a social construct, reflects lifelong social experiences, yet it is often misused in research to infer disease causality. Clinicians and researchers must move beyond the overemphasis on race as a primary factor and understand broader social contexts affecting patient health and care quality (Cooper et al., 2018). Despite concerns about using race as a genetic basis in research, such practices continue, and current clinical trial ethics policies fail to address the consequent ethnic determinism and structural violence.

BIPOC communities, often more vulnerable, face challenges like lack of informed consent in clinical trials. Institutional racism in the U.S. leads to segregation and poor healthcare access, job opportunities, and socioeconomic status for these communities, resulting in adverse health outcomes. The COVID-19 pandemic has exacerbated these disparities. An example can be found in the University of California San Diego's Phase III AstraZeneca vaccine trial, which took place in National City. This region, which is predominantly Latino and was severely affected by COVID-19, was offered free healthcare during the two-year trial, which may have significantly influenced the desire to consent for uninsured participants. While aimed at increasing diversity, this approach overlooks systemic inequalities affecting these communities (Varma et al., 2021).

In conclusion, the lack of diversity in clinical trials has profound implications for scientific and medical knowledge, especially for communities of color. While strides have been made to diversify trial participants, a singular focus on recruitment diversity under existing ethics policy may perpetuate ethnic determinism. BIPOC communities face multifaceted barriers, making them more susceptible to participating in clinical trials. Ethical policies must address these societal issues, ensuring equitable and ethical conduct of clinical trials while safeguarding vulnerable communities and striving for participant diversity. in long-term harm or reduced quality of life. Thus, addressing these ethical issues is paramount in modern clinical trials.

III) The Ethics of Post-Trial Access and Care

The absence of post-trial care for participants is a significant ethical concern and a large form of structural violence. Participants are often left without access to potentially beneficial treatments or support after trials, exposing them to risks and harm. The concept of post-trial care is broader than the accessibility of a therapeutic, which specifically involves providing access to an investigational drug or intervention. Post-trial care encompasses a range of responsibilities, including arranging clinical care or social services, referring participants to appropriate follow-up care or alternative interventions, and providing support to transition from research to healthcare sectors. It is important to offer post-trial care consistently and in accordance with ethical research principles (Cho et al, 2018). However, in both developed or under-developed countries, clinical trials are not required to provide post-trial care (Mahmood, 2012). The absence of mandated post-trial care leaves participants vulnerable to the effects of experimental drugs, often resulting in long-term harm or reduced quality of life. Thus, addressing these ethical issues is paramount in modern clinical trials.

Exploring Changes to Clinical Trial Ethics Regulation

The current framework of clinical trial ethics has proven insufficient in safeguarding vulnerable individuals from harm. Consequently, clinical trials today are marred by structural violence and exploitation, evident in issues like informed consent, issues related to diversifying trial participants, and lack of post-trial care. Vulnerable communities face significant risks of physical exploitation, which underscores the urgency of reforming ethics regulations to prevent future harm and ensure participant protection. In the following section, this paper will explore potential modifications to current ethical regulations and oversight for clinical trials worldwide

I) Disclosure of all Clinical Trial Results

Randomized clinical trials (RCTs) are pivotal for substantiating treatment efficacy and guiding clinical practice. However, their success hinges on the willingness of human subjects to participate, often without prior understanding of potential benefits and risks. Investigators and sponsors must adhere to high ethical standards and transparently publish results, irrespective of the outcome, as failing to do so impedes scientific progress and compromises participant trust. The World Health Organization and the Food and Drug Administration Amendments Act of 2007 advocate for mandatory disclosure and sharing of clinical trial results, yet issues like premature discontinuation and non-publication persist (Khan et al., 2021). Research indicates a bias toward publishing positive outcomes (Khan et al., 2021). Publishing RCT results in medical journals ensures rigorous peer review, minimizing bias, and ensuring accuracy.

To empower informed decision-making and enhance participant safety, accessible information on experimental treatments is essential. Patient expectations, concerns about limited knowledge, potential side effects, and randomization impact their enrollment decisions (Ventz et al., 2021). Implementing permeable trial designs, releasing data summaries at intervals, enables ongoing patient and physician engagement (Ventz et al., 2021). However, ethical, organizational, and statistical considerations are vital during policy implementation (Ventz et al., 2021).

The failure to publish clinical trial data deprives physicians and patients of crucial safety insights and perpetuates inequalities. Rigorous peer review through journal publication is imperative. Falling short of these standards obstructs scientific advancement, undermines participant dedication, and leaves others with incomplete information. Permeable designs can bridge this gap with careful planning. Researchers must surmount challenges to enhance clinical research efficacy and protect communities and participants from harm (Ventz et al., 2021).

II) Post-Trial Access and Care in Medical Research Ethics

The concept of post-trial access to therapeutics, rooted in the Declaration of Helsinki, highlights the ethical need to provide participants with ongoing access to beneficial treatments post-research. While emphasized in the 2000 and 2013 versions of the Declaration, this concept lacks clarity regarding eligibility criteria, the scope of access, and responsibility for provision (Hellman et al., 2022). Additionally, the Universal Declaration on Bioethics and Human Rights broadens the scope beyond just drug availability, suggesting responsibilities for funders, researchers, and governments in ensuring access to beneficial interventions post-trial. The Council for International Organizations of Medical Sciences (CIOMS)/WHO guidelines similarly assign researchers and sponsors responsible for providing and monitoring beneficial drugs. However, ambiguity persists in legal and ethical guidelines about the specifics of access duration, conditions, and accountable parties (Iunes et al., 2019).

Research Ethics Committees (RECs) play a pivotal role in mandating post-trial access plans in research protocols, yet enforcing these plans remains a challenge, particularly post-trial (Iunes et al., 2019). RECs are encouraged to consider post-trial access seriously and reject applications that do not adequately address local participants' needs (Andanda & Wathuta, 2017). Governments and RECs are urged to integrate mechanisms within regulations to ensure compliance with these ethical requirements (Hellman et al., 2022).

Beyond mere access, post-trial care encompasses a broader range of respons-ibilities, including medical and social support, follow-up treatment, and alternative interventions for research participants. This comprehensive care is essential for a smooth transition from research to standard healthcare, particularly for trials with limited or no long-term treatment access. It is vital to recognize and address the varying needs of participants, especially those with limited healthcare access, to prevent exploitation and uphold ethical standards. This approach ensures that all participants receive equitable post-trial support regardless of their healthcare coverage, aligning with ethical research principles and reducing healthcare disparities (Cho et al., 2018).

Innovative methods of integrating post-trial access include the implementation of open-label clinical trials, which may take the form of extension studies or rollover studies, where investigational medicines are provided to all participants. These trials are particularly valuable when an ongoing collection of safety or efficacy data is beneficial. Additionally, post-trial access programs serve as a crucial avenue for providing investigational medicines to patients who have completed a trial when no further research data on efficacy is needed, with ongoing safety monitoring through agreements with treating physicians. Patient support programs represent another vital strategy utilized in some countries to ensure that approved medicines, which might not be accessible to some patients due to financial constraints or lack of health plan coverage, are available. These diverse approaches are instrumental in extending the benefits of clinical research to participants after the trial's conclusion, firmly grounding post-trial access initiatives in ethical research practices (Kelman et al., 2018). However, post care access can be a factor posing undue influence or coercion for participation or continuing participation in a clinical trial. Hence, the issue of post-trial access to treatment should be carefully evaluated, depending upon the therapeutic area as well as severity of the condition (Doval et al., 2015). Thus, there needs to be more research examining the implication of post-trial access and informed consent.

Integrating Partnerships within Clinical Trial Ethics

While updating ethical regulations and imposing sanctions against misconduct is crucial, establishing partnerships with vulnerable communities is vital to safeguard them from exploitation and unethical practices in clinical trials. Community partnerships contribute to achieving study goals and improving participation, but their role in upholding ethical principles and best practices is also critical yet often undervalued (Adhikari et al., 2019). Research highlights the effectiveness of collaborations between developed nations' researchers and sponsors and those in developing nations, including policymakers and local communities. These alliances are instrumental in preventing exploitation and ensuring research is both beneficial and culturally appropriate, addressing specific health concerns within these communities (Sarwar, 2019; Seifer et al., 2010). This collaborative model is equally relevant in affluent nations, as vulnerable groups exist across various socio-economic spectrums. In developed countries, such as the US, successful participatory research models in cancer clinical trials, especially those focusing on ethnic minorities and low-income groups, demonstrate the value of engaging communities throughout the research cycle (Seifer et al., 2010).

Furthermore, government reports emphasize the importance of community involvement in all phases of clinical research, from design to implementation, outreach, and recruitment. Despite these recommendations, a gap exists in systematically incorporating these principles into national policy and industry reforms (Seifer et al., 2010). Therefore, our next section will explore the pivotal role of community partnerships in ensuring ethical, informed consent and effective oversight in clinical trials, underscoring the ethical benefits of such integrations.

I) Community Partnerships, Informed Consent, and Ethical Review

Ethical health research hinges on valid informed consent, which involves providing comprehensive information, ensuring participant understanding, and facilitating voluntary decision-making. Community engagement enhances this process by offering valuable insights into the clarity and rationale of studies. These insights help tailor materials and methods of information delivery to suit local languages, literacy levels, and cultural norms. Such insights often go beyond mere translation, incorporating locally relevant analogies, imagery, and demonstrations (Adhikari et al., 2019). Federal regulations require all U.S. Institutional Review Boards (IRBs) to include at least one "unaffiliated member," reflecting practices endorsed by international bodies like the World Health Organization. However, research reveals that these community members need to be more utilized, as they tend to serve in limited capacities that do not fully leverage their potential to represent community interests or counteract institutional biases (Lidz et al., 2012). Future research is needed to explore this and to formalize their role in emphasizing the human subject issues from a participant's viewpoint, particularly in the consent process and confidentiality protections (Lidz et al., 2012).

Moreover, IRBs often need help in discerning whether non-affiliated or non-scientific members genuinely represent specific communities, exacerbated by difficulties in identifying and trusting appropriate community representatives. Such is highlighted by instances where IRBs have mistakenly trusted representatives lacking essential cultural knowledge, underlining the complexity of community dynamics and the risk of misrepresentation (Klitzman, 2012). Addressing these challenges, Community Engagement Studios (C.E. Studios) emerge as a potent mechanism for enhancing community involvement in research. Inspired by the award-winning Clinical and Translational Research Studio, which offers researchers specialized guidance from academic experts through in-person meetings, C.E. Studios adapt this model to include patients or community stakeholders as experts. Each C.E. Studio convenes a unique panel of stakeholders representing the researcher's target population. These stakeholders contribute firsthand knowledge and lived experience of specific conditions or communities. As consultants rather than research subjects, they provide valuable feedback during in-person meetings (Joosten et al., 2015). This approach not only refines research designs but also boosts participant engagement and develops supportive frameworks through the insights of these 'expert' community members, as evidenced by their positive feedback and willingness to re-engage (Nielson et al., 2020). Similarly, citizen science projects offer a novel method for community participation in research by encouraging public contributions to scientific endeavors. These projects empower individuals and marginalized groups to influence scientific inquiry, thereby democratizing science and potentially enhancing precision medicine through collaborative data collection (Petersen et al., 2020).

The "shared decision-making" model further exemplifies an enhanced approach to informed consent, focusing on collaborative communication between clinicians and patients to meld evidence with individual values and preferences. In addition, patient decision aids, offering balanced, evidence-based insights into treatment options, have been proven to elevate patient knowledge and involvement in decision-making, leading to a better understanding of evidence, clarified personal values, and heightened participation in decision-making processes (Spatz et al., 2016). Implementing these strategies necessitates close coordination with ethics committees and adherence to regulatory standards, sometimes requiring compromises to maintain ethical research practices (Adhikari et al., 2019).

By identifying and mitigating overlooked risks and adapting to protect participants, community partnerships uphold the integrity of clinical trials, contributing to the advancement of ethical research and benefiting a wide range of communities. Community partnerships, coupled with shared decision-making and patient decision aids, can improve informed consent and the ethics of clinical trials.

II) Implementation of Community Partnerships and Challenges

Effective community partnerships in research require establishing trust with underserved communities through a comprehensive strategy. A comprehensive strategy should include collaborative planning, continuous consultation, and joint involvement in all research phases, from data analysis to result dissemination. However, building these relationships is time-consuming and sensitive to setbacks (Petereit & Burhansstipanov, 2008). Integrating patients effectively necessitates prioritizing training, resource allocation, and fostering attitudes that support collaboration (Parry et al., 2020). Researchers must actively involve patients in all aspects of research, supported by organizational policies that encourage shared goals, effective communication, mutual respect, and learning. Providing patient-centered research training and resources is crucial for meaningful patient engagement and recognizing the value of their contributions throughout the research process (Parry et al., 2020).

However, inadequate patient preparation and resource limitations can hinder effective collaboration. Insufficient preparation leaves patients under-equipped, risking misunderstandings and unmet expectations. This gap and resource constraints create a power imbalance and complicate fair compensation for patient partners. Addressing these issues involves clear education, role definition, and comprehensive preparation for researchers and patients, enhancing patient contributions and ensuring a meaningful partnership experience (Bird et al., 2019).

III) Ethical Considerations in Profit Distribution

Beyond engagement, ethical community partnerships in clinical research should ensure equitable benefit sharing. It is uncertain if clinical trial insights will return to the communities, such as through subsidized medications or intellectual property rights (Fox, 2020). However, concerns arise as pharmaceutical and biotech firms often collaborate with various entities, including direct-to-consumer (DTC) genetic testing companies, to compile extensive datasets without the consent of the DNA contributors, who consequently do not share in the profits (Ahmed & Shabani, 2019). Policymakers bear the responsibility of safeguarding vulnerable populations from exploitation and guaranteeing their benefit from research participation. Such requires adopting platforms like LunaDNA, a community-owned biomedical research initiative employing a fractional-ownership model, which distributes profits among DNA contributors. Additionally, establishing community trusts in partnership with the NIH and pharmaceutical firms can facilitate subsidized drug access and community reinvestment in genomic research (Fox, 2020). Nonetheless, the viability of such incentives hinges on adequate financial backing, exemplified by LunaDNA's closure on January 31, 2024, due to insufficient revenue (Grinstein, 2024). Consequently, further research is needed for sustainable funding mechanisms for equitable benefit-sharing initiatives. Ethical partnerships should aspire to ensure that communities derive direct benefits from their participation, whether through data control, intellectual property rights, or community-oriented advantages (Fox, 2020)

Conclusion

Clinical trials are crucial in developing safe medical treatments and addressing prevalent diseases afflicting human society. The existing regulations governing modern clinical trials have proven inadequate in protecting the most vulnerable individuals. However, there is still hope for improvement. To safeguard vulnerable populations and maintain ethical standards, it is imperative to strive for more stringent regulations, transparent disclosure of trial results, and comprehensive post-trial care.

Furthermore, integrating community partnerships into clinical research ethics policies is crucial. By establishing partnerships with vulnerable communities, we can protect them from exploitation and unethical conduct during clinical trials. These partnerships foster a deeper understanding of community and patient needs, address potential issues, and benefit participants and researchers. Moreover, it is essential to include profit distribution to participants as an integral component of community partnerships.

Since this review provides an overview of clinical trial ethics worldwide, further research is needed to explore the impact of partnerships and the integration of community partnerships within specific countries, governments, and cultural/social contexts. Additionally, more focus should be directed toward stricter regulations, oversight and examining their effectiveness in communities globally.

References

1. Ahmed, E., & Shabani, M. (2019). DNA data marketplace: An analysis of the ethical concerns regarding the participation of the individuals. Frontiers in Genetics, 10. https://doi.org/10.3389/fgene.2019.01107
2. Andanda, P., & Wathuta, J. (2018). Human dignity as a basis for providing post-trial access to healthcare for research participants: A South African perspective. Medicine, Health Care and Philosophy, 21(1), 139–155. https://doi.org/10.1007/s11019-017-9782-1
3. Benatar, S. R. (2002). Reflections and recommendations on research ethics in developing countries. Social Science & Medicine, 54(7), 1131–1141. https://doi.org/10.1016/S0277-9536(01)00327-6
4. Bird, M., Ouellette, C., Whitmore, C., Li, L., Nair, K., McGillion, M. H., Yost, J., Banfield, L., Campbell, E., & Carroll, S. L. (2020). Preparing for patient partnership: A scoping review of patient partner engagement and evaluation in research. Health Expectations, 23(3), 523–539. https://doi.org/10.1111/hex.13040
5. Brown , G. W., McLean , I., & McMillan , A. (2018). structural violence. A Concise Oxford Dictionary of Politics and International Relations. https://www.oxfordreference.com/display/10.1093/acref/9780199670840.001.0001/acref-9780199670840-e-1775;jsessionid=9859873220402576296D5D71624836CB
6. Burgess, T., Rennie, S., & Moodley, K. (2023). Key ethical issues encountered during covid-19 research: A thematic analysis of perspectives from South African Research Ethics Committees. BMC Medical Ethics, 24(1). https://doi.org/10.1186/s12910-023-00888-y
7. Buruk, B., Guner, M. D., Ekmekci, P. E., & Celebi, A. S. (2021). Comparison of Covid-19 studies registered in the Clinical Trial Platforms: A research ethics analysis perspective. Developing World Bioethics, 22(4), 217–230. https://doi.org/10.1111/dewb.12333
8. Cho, H. L., Danis, M., & Grady, C. (2018). Post-trial responsibilities beyond post-trial access. The Lancet, 391(10129), 1478–1479. https://doi.org/10.1016/S0140-6736(18)30761-X
9. Classen, J. B. (2021). US COVID-19 Vaccines Proven to Cause More Harm than Good Based on Pivotal Clinical Trial Data Analyzed Using the Proper Scientific Endpoint, "All Cause Severe Morbidity." Trends Int Med. 2021; 1(1): 1-6.
10. Cooper, R. S., Nadkarni, G. N., & Ogedegbe, G. (2018). Race, Ancestry, and Reporting in Medical Journals. JAMA, 320(15), 1531. https://doi.org/10.1001/jama.2018.10960
11. Doval, D., Shirali, R., & Sinha, R. (2015). Post-trial access to treatment for patients participating in clinical trials. Perspectives in Clinical Research, 6(2), 82. https://doi.org/10.4103/2229-3485.154003
12. Egharevba, E., & Atkinson, J. (2016). The role of corruption and unethical behaviour in precluding the placement of industry sponsored clinical trials in sub-Saharan Africa: Stakeholder views. Contemporary Clinical Trials Communications, 3, 102–110. https://doi.org/10.1016/j.conctc.2016.04.009
13. Farmer, P. E., Nizeye, B., Stulac, S., & Keshavjee, S. (2006). Structural Violence and Clinical Medicine. PLoS Medicine, 3(10), e449. https://doi.org/10.1371/journal.pmed.0030449
14. Fox, K. (2020). The Illusion of Inclusion—The "All of Us" Research Program and Indigenous Peoples' DNA. New England Journal of Medicine, 383(5), 411–413. https://doi.org/10.1056/NEJMp1915987
15. Hashem, H., Abufaraj, M., Tbakhi, A., & Sultan, I. (2020). Obstacles and considerations related to clinical trial research during the COVID-19 pandemic. Frontiers in Medicine, 7. https://doi.org/10.3389/fmed.2020.598038
16. Henderson, G. E., Churchill, L. R., Davis, A. M., Easter, M. M., Grady, C., Joffe, S., Kass, N., King, N. M. P., Lidz, C. W., Miller, F. G., Nelson, D. K., Peppercorn, J., Rothschild, B. B., Sankar, P., Wilfond, B. S., & Zimmer, C. R. (2007). Clinical Trials and Medical Care: Defining the Therapeutic Misconception. PLoS Medicine, 4(11), e324. https://doi.org/10.1371/journal.pmed.0040324
17. Ioannidou, E., & Feine, J. S. (2020). Black Lives Matter Is About More Than Police Behavior. JDR Clinical & Translational Research, 5(4), 288–289. https://doi.org/10.1177/2380084420952788
18. Iunes, R., Uribe, M. V., Torres, J. B., Garcia, M. M., Alvares-Teodoro, J., De Assis Acurcio, F., & Junior, A. A. G. (2019). Who should pay for the continuity of post-trial health care treatments? International Journal for Equity in Health, 18(1), 26. https://doi.org/10.1186/s12939-019-0919-0
19. Jonathan Grinstein, P. (2024, January 19). Total eclipse of lunadna: Once touted genome data sharing platform goes dark. Inside Precision Medicine. https://www.insideprecisionmedicine.com/topics/precision-medicine/total-eclipse-of-lunadna-once-touted-genome-data-sharing-platform-goes-dark/
20. Joosten, Y. A., Israel, T. L., Williams, N. A., Boone, L. R., Schlundt, D. G., Mouton, C. P., Dittus, R. S., Bernard, G. R., & Wilkins, C. H. (2015). Community engagement studios. Academic Medicine, 90(12), 1646–1650. https://doi.org/10.1097/acm.0000000000000794
21. Kelman, A., Kang, A., & Crawford, B. (2018). Continued access to investigational medicinal products for clinical trial participants—an industry approach. Cambridge Quarterly of Healthcare Ethics, 28(1), 124–133. https://doi.org/10.1017/s0963180118000464
22. Khan, M. S., Shahid, I., Asad, N., Greene, S. J., Khan, S. U., Doukky, R., Metra, M., Anker, S. D., Filippatos, G. S., Fonarow, G. C., & Butler, J. (2021). Discontinuation and non-publication of heart failure randomized controlled trials: A call to publish all trial results. ESC Heart Failure, 8(1), 16–25. https://doi.org/10.1002/ehf2.13099
23. Kingori, 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. https://doi.org/10.1177/0011392115590093
24. Klitzman, R. (2012). Institutional Review Board Community members. Academic Medicine, 87(7), 975–981. https://doi.org/10.1097/acm.0b013e3182578b54
25. Klitzman, R., et al., "When IRBs Say No to Participating in Research about Single IRBs," Ethics & Human Research 42, no. 1 (2020): 36-40. doi: 10.1002/eahr.500041
26. Lamkin, M., & Elliott, C. (2018). Avoiding Exploitation in Phase I Clinical Trials: More than (Un)Just Compensation. Journal of Law, Medicine & Ethics, 46(1), 52–63. https://doi.org/10.1177/1073110518766008
27. Mahmood K. Forewarned is forearmed! unethical drug trials in the developing countries. J Dow Uni Health Sci 2012; 6(3):79-81.
28. Masiye, F., Mayosi, B., & de Vries, J. (2017). "I passed the test!" Evidence of diagnostic misconception in the recruitment of population controls for an H3Africa genomic study in Cape Town, South Africa. BMC Medical Ethics, 18(1), 12. https://doi.org/10.1186/s12910-017-0175-z
29. Mngadi, K. T., Singh, J. A., Mansoor, L. E., & Wassenaar, D. R. (2017). Undue inducement: A case study in caprisa 008. Journal of Medical Ethics, 43(12), 824–828. https://doi.org/10.1136/medethics-2016-103414
30. Negri, S. (2017). Unethical Human Experimentation in Developing Countries and International Criminal Law: Old Wine in New Bottles? International Criminal Law Review, 17(6), 1022–1048. https://doi.org/10.1163/15718123-01761352
31. Nielson, C., Huang, Y., Kull, C. A., & Park, A. H. (2020). Utilizing Community engagement studios to inform patient experience in a Multicenter Randomized Control Trial. International Journal of Pediatric Otorhinolaryngology, 133, 110007. https://doi.org/10.1016/j.ijporl.2020.110007
32. Pacheco-Vega, R., & Parizeau, K. (2018). Doubly Engaged Ethnography: Opportunities and Challenges When Working With Vulnerable Communities. International Journal of Qualitative Methods, 17(1), 160940691879065. https://doi.org/10.1177/1609406918790653
33. Parry, M., Bjørnnes, A. K., Toupin-April, K., Najam, A., Wells, D., Sivakumar, A., Richards, D. P., Ceroni, T., Park, M., Ellis, A. K., Gilron, I., & Marlin, S. (2020). Patient Engagement Partnerships in Clinical Trials: Development of Patient Partner and Investigator Decision Aids. The Patient - Patient-Centered Outcomes Research, 13(6), 745–756. https://doi.org/10.1007/s40271-020-00460-5
34. Petereit, D. G., & Burhansstipanov, L. (2008). Establishing Trusting Partnerships for Successful Recruitment of American Indians to Clinical Trials. Cancer Control, 15(3), 260–268. https://doi.org/10.1177/107327480801500310
35. Petersen, C., Austin, R. R., Backonja, U., Campos, H., Chung, A. E., Hekler, E. B., Hsueh, P.-Y. S., Kim, K. K., Pho, A., Salmi, L., Solomonides, A., & Valdez, R. S. (2019). Citizen science to further precision medicine: From vision to implementation. JAMIA Open, 3(1), 2–8. https://doi.org/10.1093/jamiaopen/ooz060
36. Saleh, A., Saelens, B., Hayes, M., The Health Equity Community Advisor, & Coker, T. R. (2022). Community Partnership Guide for Engaging with Academic Researchers. Progress in Community Health Partnerships: Research, Education, and Action, 16(1), 129–134. https://doi.org/10.1353/cpr.2022.0012
37. Sarena D. Seifer, Margo Michaels, & Stacy Collins. (2010). Applying Community-Based Participatory Research Principles and Approaches in Clinical Trials: Forging a New Model for Cancer Clinical Research. Progress in Community Health Partnerships: Research, Education, and Action, 4(1), 37–46. https://doi.org/10.1353/cpr.0.0103
38. Sarwar, Ev. (2019). Ethical Dilemmas Associated With Profit-Driven Research in Developing Countries. The Journal of Healthcare Ethics & Administration, 5(1), 22–35. https://doi.org/10.22461/jhea.1.71622
39. Spatz, E. S., Krumholz, H. M., & Moulton, B. W. (2016). The New Era of informed consent. JAMA, 315(19), 2063. https://doi.org/10.1001/jama.2016.3070
40. Spellecy, R., Thompson, N., & Nattinger, A. B. (2024). A proposal by the U.S. Food and Drug Administration for reliance on single institutional review boards: Proceed only with caution. Annals of Internal Medicine. https://doi.org/10.7326/m23-2152
41. Varma, S., Vora, K., Fox, K., Berkhout, S., & Benmarhnia, T. (2021). Why Calls to Diversify Trial Populations Fall Short. Med, 2(1), 25–28. https://doi.org/10.1016/j.medj.2020.12.012

Brooke Johnson

Biography

I am a Global Health major graduating in 2024 and the founder of UCSDs' first Black Pre-Medical/Health organization. My undergraduate research in the Rivera-Chavez lab focuses on the infection dynamics of bacteriophages that infect Vibrio cholera. I aspire to become a physician-scientist, committed to ensuring equitable treatment for all patients and instigating meaningful advancements in healthcare and scientific research. My current interests lie in enhancing the ethical framework of clinical trials, fueled by my passion for microbiology and medicine.

Acknowledgements

I extend my heartfelt gratitude to my advisor, Dr. Miranda Hua Wu, and to programs such as Global Health Horizons Honors Thesis, McNair, TRELS, and BUMMP for their unwavering belief in me and for guiding my development as a researcher. I am deeply thankful to my family for their support, which enabled me to become the first in our family to graduate from university. Lastly, I am grateful to all my mentors who have significantly contributed to my personal and professional growth.

> *"Research practices should prioritize the well-being and autonomy of marginalized communities. Updating ethical regulations and imposing sanctions against misconduct is crucial, but establishing partnerships with vulnerable communities is vital to safeguard them from exploitation and unethical practices."*