

Brief Communication

Lessons Learned From The COVID-19 Pandemic on Ethical Review and Regulatory Oversight of Clinical Trials

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Abstract

The COVID-19 pandemic revealed significant challenges and opportunities in the ethical review and regulatory oversight of clinical trials. This paper outlines essential lessons learned, emphasizing the need for adaptable ethical and regulatory frameworks, supported by comprehensive guidelines, to effectively address future public health emergencies.

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Introduction

Following the outbreak of COVID-19 in December 2019, there was an unprecedented global effort to address the overwhelming impact of the pandemic. This led to a significant increase in all areas of research including clinical trials which overwhelmed ethical and regulatory approval processes which were only designed to function within stable research environments. The system faced serious challenges in responding to the higher volume of clinical and public health research during the pandemic.

In the first 100 days of the pandemic, more than 500 Randomized Clinical Trials (RCTs) had already been registered on ClinicalTrials.gov and the World Health Organization International Clinical Registry Platform (1). However, not all of these trials were completed due to several challenges. COVID-19, not only had it brought several challenges to the ethical and regulatory oversight but also brought opportunities with valuable lessons learned to prepare for future similar outbreaks and pandemics.

This article aims to highlight some of the challenges, opportunities, and lessons learned particularly regarding ethical and regulatory oversight of clinical trials during the COVID-19 epidemic.

Challenges

During infectious disease outbreaks of public health importance, health institutions and ministries of health have moral obligations to gather information as rapidly as possible, to inform the ongoing public health response, and to enable scientific evaluation of new interventions being tested.

During the COVID-19 pandemic, the most demanding challenge for ethics committees was the need to accelerate the review process of the protocols submitted to learn more about infectious agents and to inform policy decisions. This raised ethical concerns and necessitated the need to put in place policies and innovative informed consent processes consistent with social distancing. The whole undertaking might have potentially compromised the quality of informed consent processes, including limiting the potential for rigorous or authentic community/stakeholder engagement (2).

In many settings, ethics committees confronted challenges in their deliberations on research ethics, due to the overlapping public and global health ethical issues that emerged alongside and consequent to the COVID-19 pandemic (3). Additionally, the committees encountered complexities in conducting risk-benefit

analysis with the constantly evolving standards of treatment and new data (4) and tried to deal with the various ethical dilemmas related to more complex clinical trial designs, such as adaptive clinical trial design.

The impact was substantial, particularly in clinical trials. The prioritization of COVID-19 research, along with the suspension of non-COVID-related research including therapeutic clinical trials, and research on HIV and TB raised critical questions regarding public health equity(3). There has been discontinuation of trials; suspensions; participant recruitment challenges; resource allocation; changes in guidelines; changing landscape of participants follow-up; exclusive use of virtual platforms; delay in study timelines and increased protocol deviations (5). Similarly, COVID-related trials were also impacted due to the suspension of trials as guidelines were updated. The impact on COVID-19 trials was attributed to social distancing, quarantine, remote follow-up, use of virtual platforms, new and rapidly evolving clinical trial designs, gaps in ethical review guidelines, lack of capacity to review new designs and oversight, and the challenges in separating research activities from clinical service or public health activities (6). Even though COVID-19 has affected low and middle-income countries, efforts in clinical research in these resource-constrained settings were very limited (7).

Opportunities

The increase in research activities during the COVID-19 pandemic has brought meaningful changes in various aspects of health research approaches, through the introduction of new research designs, networking, and harmonization of guidelines.

All stakeholders of research including, ethics committees, regulatory bodies, data monitoring committees (DMCs), and funders have stepped up efforts to the urgency of the situation, with many countries implementing a fast-track procedure for review and authorization of clinical trials (1). It has been shown that adaptive platform trials embedded in routine clinical care have efficiently and largely contributed to evidence generation and created synergies for collaborations. The lockdown and social distancing measures have accelerated the implementation of innovative and remote approaches to conducting clinical trials.

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Lessons learned

Drawing from the challenges faced and the opportunities accrued, the following lessons can be recapitulated to bolster future endeavors in clinical and public health research.

1) The health research ethics committees develop procedures to ensure appropriate, expedient, and flexible mechanisms and procedures for ethical review and oversight and expand opportunities for joint or centralized approval processes.

2) Stakeholders and the research community are better off by investing in large-scale clinical trials that can promote international collaboration instead of isolated single-center trials, and coordination can generate more impactful results. The use of adaptive/platform trial designs and decentralized clinical trials (DCTs) promoted by social distancing has also been recommended for maximizing flexibility in the conduct of trials without compromising their integrity and validity (8).

3)The globalization of clinical trials and the increased opportunity for networking should be harnessed by strengthening the capacity of developing countries for research through training and increasing their engagement in research. Noting that developing countries are marginalized in research activities, especially in conducting clinical trials (9), there is a critical need for enhanced capacity-building efforts. Developing countries have severe gaps in clinical research infrastructure and lack systems for preparedness. Global support is needed to ensure increased opportunity for networking by way of globalization of clinical trials; harmonization of standards; development of responsive systems instituting robust yet flexible regulatory guidelines, enhancing public engagements, capacity building, and international partnerships enabling information sharing and resource utilization. These initiatives should be supported by developing robust national guidelines and leadership in these countries. Within the research community, there is a crucial need for fostering collaboration and coordinated responses to surmount future global public health crises (7).

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