ETHICAL DILEMMA OF CONDUCTING RESEARCH AND PUBLIC HEALTH INTERVENTIONS IN EMERGING DISEASES: THE CASE OF COVID-19 (SHORT COMMUNICATION)

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ABSTRACT
In the recent past, epidemics (such as Covid-19, SARS, Ebola, and MERS) have posed ethical dilemma to health professionals where research and public health programs have to be undertaken concurrently. Clinical research is essential for the development and administration of safe and effective diagnostics, therapeutics and vaccine products. Clinical research should therefore be of scientific and societal value, and should be carried out with the highest scientific validity standards before the vaccines/drugs are used for interventions in public health programmes. In epidemics, however, there emerges an urgent need to control the spread diseases Activities during epidemics end up as hybrids of research and public health intervention. This raises ethical concerns about validity, as well as the ethical obligations that come with conducting research and public health intervention programs. This is because the ethical obligations of conducting research differ from those of carrying out public health programmes. Since determining the techniques or combination of tools and approaches that will ensure that epidemics do not resurge or spread in the future is difficult, a balanced framework with justifications and ethical obligations to address both research and health intervention programmes in epidemics is required. Failure to adhere to the current research regulations puts at risk lives of study participants, while failure to undertake the public health interventions/programmes can lead to high rates of mortality due to rapid spread of diseases during epidemics. Regulations, guidelines and institutional reviews of research conventions should therefore be evaluated and reconfigured in order to address or accommodate the ethical uncertainties and inadequacies encountered in public health intervention programmes in epidemics.
Keywords: Ethical obligations, Research, Public Health programmes, Covid-19.

INTRODUCTION

The scale with which public health professionals are implementing strategies to control Corona virus disease 19 (Covid-19) diagnosis, treatment, and prevention raises several ethical concerns. It's difficult to tell the difference between research and public health initiatives. As part of the public health control responses to the pandemic, programs that are being researched are also being implemented (Bierer *et al*, 2020). This appears to have been the trend of events in previous epidemic disasters such as HIV/AIDS, Ebola, Severe Acute Respiratory Syndrome (SARS), and Middle East Respiratory Syndrome (MERS) (WHO, 2016). Ethical concerns, uncertainties, and deficiencies arise because guidelines for conducting research are assumed to be sufficient in implementation of public health programs (including how they are conducted, governed, and communicated to relevant populations). This paper reviewed the dilemma the health professionals face and discusses possible solutions to the problems. The guiding review questions for this paper were: How can we safely conduct research and public health programs during epidemics without being deemed to be violating ethical issues? What are the research priorities and barriers for vaccines and public health interventions in epidemics? In the future, what needs to be changed, how can it be changed, and who monitors compliance with the changes?

Various foundational and contemporary literature on health research demonstrate the importance of adhering to ethical guidelines such as obtaining individual informed consent, voluntarily enrolling participants in research, anonymity, and confidentiality (Holland, 2017). These guidelines regulate the conduct of research in order to protect the interests of research subjects and to prevent ethical wrongdoing (WHO, 2016). In many ways, as explained by previous researchers -Childress & Bernheim, 2008; Daniels, 2000; Friedman, 2008; Kass, 2001; and Thompson *et al*., 2006, and proponential research ethical guidelines (Belmont Report of 1979), these guidelines are similar as adopted in previous international ethical guidelines. The guidelines are based on the assumption that there is enough time to conduct research, particularly clinical trials. The guidelines were primarily intended to protect the rights of individual research participants. This claim is supported by other guidelines in ethical scrutiny conventions such as the Nuremberg Code of 1946, the World Medical Association's (WMA) Declaration of Helsinki of 2013, the Council on International Organizations of Medical Sciences'

(CIOMS) International Ethical Guidelines on Biomedical Research involving Human Subjects (CIOMS) of 2016 and others (Vaughn,2017; Wassertheil-Smoller & Smoller, 2015). Personal liberty is prioritized over public health in the guidelines, which are deemed to be universal principles that cut across cultural lines. In the event of an epidemic, however, controlling the spread of a disease becomes the top public health priority. Public health programs must ensure that disease, as in epidemics, does not spread through evidence based interventions developed from research. Public health ethics has yet to provide relevant methods for maximizing benefits for a large population, particularly when programs restrict and contradict civil liberties enjoyed during research (for instance, anti-smoking regulations, mandatory use of seat belts or helmets, mandatory use of masks) or involve liberty-limiting measures.

The debate on whether ethical scrutiny conventions for research should also apply to public health intervention programs in epidemics remains unresolved. The catastrophic threat posed by epidemics is the impetus for this debate. Epidemics such as Covid-19, HIV/AIDS, Ebola, SARS, and MERS emerge unexpectedly, spread quickly, and have the potential to wipe out the entire human race if public health disease management decisions are not made quickly. Such decisions are made to protect human life. The decisions frequently do not adhere to the established research conventions of ethical scrutiny (Sambala *et al*, 2019), resulting in an ethical quandary. The debate here is between emphasizing individual rights versus emphasizing public health ethics as a societal responsibility to protect and promote population health (Buchanan & Miller, 2006). But even with current scientific knowledge, decisions for research and public health interventions in epidemics frequently still involve trade-offs involving health and non-health risks and benefits on both sides. A case in point is the recent Covid-19 pandemic.

By March 2020, more than 300,000 registered clinical trial studies had been conducted worldwide in the aftermath of the Covid-19 pandemic (Clinical Trials.gov. 2020). Aside from clinical trials, there were numerous trial and error therapeutics, interventions and misinformation about Covid-19 (Biere *et al*, 2020). The results of clinical trials were three vaccines recommended by the World Health Organization (WHO) to aid in disease control (Pfizer-BioNTech vaccines by Moderna, AstraZeneca/Oxford, and Jansen) (WHO, 2021; MHRA,2021). However, even with these vaccines, there are several unresolved issues (including ethical issues) regarding their use. These have made some people hesitant to get vaccinated. But then, the question here is, when some people refuse to take the Covid-19 vaccines, whose rights and interests do we consider first during such public health challenges: the non-compliant and potentially infectious or those of the general public that need protection?

The development of Covid-19 vaccines is a remarkable accomplishment. However, it is unclear how long the vaccines will provide personal protection or whether they will completely protect against new variants - (Some reports have associated the vaccines with blood clots; in other cases, fully vaccinated persons have contracted the virus and died of Covid-19). Comprehensive research and testing are still required to combat new variants, control outbreaks, protect people who have not been immunized and promote long-term wellness. Ideally, this means that the vaccines are still experimental (trial vaccines), but are being used for research as well as public health interventions. This raises two fundamental ethical issues in the control of epidemics. First, should we disregard individual rights, as well as the risks posed by trial vaccines and interventions, due to the catastrophic nature of a disease? Second, when should an experimental vaccine become a routine immunization vaccine, particularly during epidemics? Addressing these ethical concerns and uncertainties is beneficial in ensuring vaccine safety, removing uncertainties, and reducing vaccine hesitancy.

One argument in favor of the decision to immediately use COVID-19 vaccines (as well as other vaccines used in epidemic emergencies) before comprehensively ascertaining their efficacy is that vaccines are a global public good (WHO,2016). The vaccines are intended to reduce the mortality and suffering that may occur as a result of the fast spread of epidemics. Such an argument justifies vaccine regulatory accommodation (Emergency Use Authorization- EUA) and provides the moral resolve to use vaccines as Public Health interventions in emergencies (FDA,2020). However,although this is a compelling argument, the resolution does not alleviate safety concerns or uncertainty about the future of research participants or the general public. Given the number of lives lost during the Covid-19 pandemic over a short period of time on the global stage, one can understand the emergency authorization; it is a difficult decision to make. Perhaps this is why the WHO global ethics expert team group formed to provide guidance for COVID-19 pandemic clinical trials neither supports nor opposes the possibility of interventions such as challenge trials being conducted in the Covid 19 pandemic (Bierer *et al*,2020). The problem with such noncommittal decisions and accommodations is that

they allow for misinformation, which may lead to the promotion of certain therapeutic approaches for which there is little data. One such case was the use of the oral drug hydroxy-chloroquine to treat Covid-19. Hydroxy-chloroquine is an approved drug for treatment of malaria and lupus. Covid-19 patients were thought to benefit from the drug, possibly to save their lives. Despite the lack of efficacy data, the FDA granted the drug an EUA (Facher, 2020) with little information on immediate and long-term patient outcomes. Nobody knows what long-term effects it has on the Covid-19 patients. This is an example of why there is a need for reforms that take into account the safety of public health interventions by examining what should be included in research regulations and health programs during epidemics.

The accelerated approval and novelty of the Covid-19 vaccine creates significant uncertainty and may exacerbate existing vaccine-related fears and hesitancy. Lack of coordination among research groups could be the major impediment to establishing a process of sufficient clarity and uniformity. There is now a growing body of literature recognizing the need for public health scientists to be more involved in containing the spread of emerging infectious diseases as well as the long-term safety of vaccines for human populations (Bierer et al, 2020; WHO,2021).

DISCUSSION

The COVID-19 pandemic has fundamentally altered how epidemic research and public health interventions must be carried out. Because it is difficult to predict the techniques or combinations of tools or approaches that will ensure that epidemics do not occur or spread in the future, public health scientists have a moral obligation to address these concerns and uncertainties. These concerns and uncertainties are critical to future public health intervention programmes and should therefore be addressed.

There is an urgent need for a framework that addresses both research and public health interventions. Although researchers are engaged in lab research to develop vaccines, clinical research to test treatment strategies, surveys to assess risk perceptions of infections, and mixed methods designs to understand social, behavioral, and educational factors related to the disease, research remains deficient of the ethical requirements for public health programs during epidemics. There exist a variety of ethical decision-making frameworks that use various moral theories in an attempt to balance individual interests against public health goals in epidemics. Among these are Kass's 2001six-step analytical framework, Daniels's 2000 accountability for reasonableness framework, Childress and Bernheim's 2008 framework, and the recent Ubuntu's 2018 framework (Sambala *et al*, 2020). However, none of these frameworks provide a sufficient and balanced justification for promoting specific values and ethical features relevant to both research and public health programmes, as well as the rights inherent in both (Sambala *et al*, 2020).

One of the contentious issues to consider in epidemics is when an experimental vaccine or drug should become a routine vaccine. This problem could be solved by establishing a 'threshold' for vaccines as a justification for rolling out vaccines (implementation of mass immunization). This necessitates sufficient clarity as well as a uniformity threshold. Such data is derived from process and evidence standards for regulatory approvals (including accommodated authorizations) of new vaccines and drugs. The clarity and uniformity of a vaccine inform on its efficacy and effectiveness. Evidences should specify how much and what types of cumulative data are required to make an accommodation decision.

Much of the work that public health workers do is directly related to research and must be evidence-based health practice. It is therefore unethical to refuse to conduct research for health practice before implementing interventions within the profession. However, although there is a demand on health professionals to justify and base their practice on robust research-based interventions, time in epidemic situations limits this opportunity. None the less, it is still critical to base any health practice interventions on research. The solution here would be to coordinate the decisions made by health scientists. Strategies for engaging health scientists more fully are therefore required. In the context of epidemics, strategies are required to engage health scientists more fully in order to effectively address the associated issues related to improved decision-making skills, evidence-based practice, and patient care improvement.

Ethical dilemmas are significant, particularly in light of the recent Covid-19 responses, where there were many 'trial and error' interventions with unknown outcomes (Biere *et al*, 2021). The corona virus was discovered in 2002, so it is not a new discovery (Fung and Liu, 2019). The virus was expected to cause an epidemic at some point; however, even with prior knowledge, the world community was unprepared when the epidemic occurred. This was due to a lack of research capacity in most developing nations and non-prioritization of the disease by developed nations. This is the reason why in the Covid 19 pandemic, there were gaps, ambiguities, and lack of consistency in research and intervention processes. The majority of these deficiencies can be

dealt with by solving global inequalities in vaccine research and development, manufacturing capacity, and improving collaboration among health research scientists.

Clinical research should be rigorous, of scientific and societal value, and carried out with the highest scientific validity standards (CIOMS, 2016). The standard procedures for blinding to treatment assignment, randomization, and controls must be followed. Regardless of time constraints, clinical research is clearly required to address complex issues associated with disease infections and patients' safety. However, existing research procedures, mechanisms, and guidance may not be applicable in the case of emerging epidemics. In epidemics, the priority is to find a vaccine or a cure and to stop the disease from spreading (Sambala *et al*, 2020). Inadequacies in procedures could be addressed through evidentiary standards that necessitate reforms (regulatory reforms, system redesign, or process innovation) and by identifying new procedures/mechanisms that can be included in the conventions of ethical scrutiny for public health programs. Researchers should consider reviewing generic protocols for conducting research in epidemic/pandemic situations in preparation, which can be quickly altered and reviewed for specific situations.

Ideally, research should also assess the impact of an application on decision making using the best available evidence, and such an application should be pursued vigorously and routinely by health researchers in collaboration with physicians. To determine whether a vaccine provides 'real-life' protection against the etiologic agent, Phase III clinical trials require the recruitment of a much more diverse cross-section of the population (and for a period long enough as evidence for the drug/vaccine efficacy). However, in an emergency such as in epidemics, such a threshold is constrained by the amount of time available to prevent the loss of human lives. Adequate subgroup analyses are required, especially in phase III research studies. Groups were not adequately represented in Phase III vaccine trials, as it is now in the Covid-19 situation. Extraneous variables may confound study results if supportive care standards are not consistent across sites. Even so, if supportive care standards are unattainable in low-resource settings (such as developing countries), study findings may not be generalizable to these contexts. To the greatest extent possible, local researchers should be involved in the design, implementation, analysis, reporting, and publication of outbreak-related research. Local researchers can help ensure that studies respond sufficiently to local circumstances and demands, and that they can be implemented efficiently without harming the pandemic response.

Researchers must ensure that the host community understands the nature of the implementation program, as well as the associated risks and potential harms, when conducting clinical trials. This procedure necessitates the use of numerous resources, including time. During epidemics, regulations should strive to conserve resources while also protecting subjects from unintentional exposure to those who are asymptomatic but infected with a disease such as COVID-19. To achieve this, it would be necessary to improve transparency, clarity, and accountability to relevant authorities, as well as the social value of supplementing public health intervention programs. Individual participants' voluntarism would have to be ensured. This could be accomplished by reducing arbitrary, unfair, and discriminatory practices and developing the appropriate procedures and mechanisms to achieve these goals for health programs (including best utilization of existing procedures, guidance, institutional capacities)

Timing is another common issue in epidemic research: even impressively accelerated vaccine studies may reach a critical stage just as the first wave of infection is coming under control. This makes determining whether the vaccine provides protection much more difficult and time-consuming, because research participants are far less likely to be infected. In the case of the Covid-19 pandemic, flexibility and reconsideration were required because not only did the intensity and severity of infection vary over time and by location, but also because knowledge of the disease and understanding of its treatment (prevention) grew.

CONCLUSIONS

The difficulties in determining definitive solutions to these ethical uncertainties and inadequacies, such as the ethics of infectious disease research and control, actually reflect conflicts between Bioethics and the newer field of Public health ethics. Current research conventions, such as regulations, guidelines, institutional reviews, and ethics, fail to adequately address ethical issues in epidemic control. Ethical disagreements arise regarding the best strategies for reducing disease burden, particularly when the strategies have not been proven in a given context, the safety of research/interventions and the priorities and barriers for research on vaccines/drugs during epidemics. The core goals of ethical scrutiny in research and the implementation of public health intervention programs need to be redesigned. According to Vaughn (2017), if the proponents of research ethical guidelines had considered ethical

debates in infectious diseases at the time of the research guidelines development, ideas of informed consent, confidentiality, and distributive justice might have been construed differently than they are now. Since research and public health interventions in epidemics occur at the same time, the conventions should instill reforms, procedures, and mechanisms necessary to achieve the goals of research and implementation public health programs. This reconfiguration should also strive to ensure that clinical trials are conducted in a safe and efficient manner during epidemics.

As the Covid-19 pandemic recedes, a global health treaty for epidemic emergencies may be required. Within the context of epidemics, strategies are required to more fully engage health research scientists and public health practitioners in order to effectively address associated issues such as coordination, improved decision-making skills, evidence-based practice, and patient care improvement. These should include relevant obligations, who should hold them, relevant authorities, and accountability. As a result, the capacities and authorities required to implement any new or newly configured approaches will need to be considered. To accelerate progress in appraisals to address/accommodate ethical uncertainties and inadequacies, there is a need for leadership, preparation, and planning, as well as the need to apply what has been learned in case another epidemic occurs or, in the absence of another epidemic, to the next pandemic.

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