Human Challenge Trials for a COVID-19 Vaccine: Should we bother about exploitation?

Victor Chidi Wolemonwu*

Keywords: Human challenge trials, COVID-19, Vaccine ethics, Research ethics, Bioethics, Global poverty

INTRODUCTION

Safe and effective vaccines are yet to be developed and distributed for the treatment of the virus that causes COVID-19. "Vaccine trials are notoriously lengthy, with optimistic estimates of 12 to 18 months to vaccine rollout."[1] Safe and effective vaccine development within the shortest possible time requires adopting a medical research strategy like human challenge trials. A few weeks ago, experts in the fields of bioethics, philosophy, medicine, computer sciences - some of whom are Nobel Laureates - and some prominent businessmen sent a signed letter to Dr. Francis Collins, the Director of the National Institutes of Health (NIH), calling on the government to embark on human challenge trials to accelerate the development and distribution of a COVID-19 vaccine. According to the 125 signatories to the letter, human challenge trials are indispensable during the COVID-19 pandemic as successful development of vaccines through this method would help improve human health and well-being, and save countries from a looming social and economic meltdown.[2] Human challenge trials involve fewer participants, are not restrained by the rate of natural infections, and can be completed in much less time than conventional vaccine trials.[3] There is a potential projection that if vaccines are not developed quickly, the global poverty index may increase from 600 million pre-pandemic to one billion before the end of 2020.[4]

Some bioethicists argue that government and medical scientists should adhere strictly to the best ethical standard to ensure that research volunteers are not exploited in any way despite the severity of the pandemic.[5] The 125 experts that signed the letter to the NIH recognize the need to mitigate any possible ethical issue of exploitation that might arise if the government endorses human challenge trials. Though the letter fails to highlight and address the ethical issue of possible incentivization of the human challenge trials, I argue that advertised incentives as a recruitment strategy undermine the the benefit of recruiting individuals

* Victor Chidi Wolemonwu, PhD Researcher, MA, ACMLB, Department of Philosophy, University of Sheffield, UK

to participate out of altruism. Given the high poverty index rate, the government and medical scientists could, in effect, be taking advantage of the vulnerability of those who are socially and economically impoverished, treating them as mere means to some scientific end.

ANALYSIS

Human Challenge Trials: Mitigating Possible Exploitation

Challenge trials involve a deliberate exposure of healthy research participants to pathogens to study how people contract the disease and how resistance can be attained in order to develop a vaccine. These trials have proven useful in the past for the advancement of scientific knowledge through the development of vaccines for cholera, malaria, and smallpox. Some bioethicists caution about the reliance on human challenge trials to address the COVID-19 pandemic. Shah et al. contend that "given the stakes of exposing volunteers to potentially fatal risks, it would be a mistake to rush the implementation of challenge trials without adequately considering what it will take for them to make a difference."[6] Their concern stems from the fact that little is known about COVID-19 and there is no standard treatment.

The experts highlighted four basic criteria to ensure that human challenge trials meet high ethical standards. The criteria are that only young, healthy participants should be enrolled; the highest quality medical care should be provided for participants; the ethical and scientific review must be of the highest standard; and the autonomy of participants must be respected. These principles are aimed at mitigating ethical challenges that had arisen in the past, especially, the issue of lack of consent and the risk of exposure of research participants to harm. Additionally, this paper explores compensation as an incentive to participate.

I. Age of Permissible Participation

The experts noted that potential participants should be healthy youths who are within the age range of 20 and 29 because they are less likely to die of the virus when exposed. Some bioethicists and scientists agree with this requirement. Verity et al., for instance, argue that the fatality ratio of people within that age range is .0778–.398 (.193 per cent).[7] According to some reports, healthy persons of 19 years and under may be less likely to suffer adverse events like hospitalization or death when they are infected with COVID-19. However, those in the age range of 20 to 44 years seem to be at higher risks for hospitalization, ICU admission, or death (due to the devastating consequences of the virus like cardiac complications, multisystem inflammatory syndrome, or stroke).[8] So, there is no guarantee that the participants in that age range will be free from any adverse events when they are exposed to the virus. To be valid, researchers will have to address the problem of applying the results to the elderly population. If the participants are all 29 and under, a vaccine may produce either better, stronger antibodies or weaker and fewer antibodies in them than in the elderly. Transparency about research limitations is crucial.

II. Protection of Participants from Harm

The experts suggested that participants should be provided with the highest quality medical care and also be monitored frequently to mitigate any possible harm that may arise due to their exposure to the virus. Nir Eyal et al. note that "any volunteers in whom infection was confirmed (during the challenge trials) should receive excellent care for COVID-19, including *priority for any scarce life-saving resources*, in state-of-the-art facilities."[9] It is not clear how proper resource distribution would be made between challenge trials and other

medical emergencies. Many hospitals in the US and other parts of the world with high incidents of COVID-19 are overwhelmed by an increasing number of patients in ICUs and other inpatient units with COVID-19. There are scarcities of medical care facilities and resources as hospitals and ICUs are under intense pressure due to the surge.[10] It is reasonable to use resources for challenge trials but in some areas, there are not available resources. It is also important to ensure that adequate provisions, both in terms of health facilities and manpower are made available for the care of patients already in precarious situations whether due to COVID-19 or other diseases like cancer. An increase in the number of fatalities has occured when there were fewer resources to cater to the health and well-being of critically ill patients with COVID-19 and other chronic ailments.[11] Prioritizing the health and well-being of volunteers for challenge trials over those of critically ill COVID-19 patients is morally problematic. To resolve this moral dilemma, the challenge trials must take place where there are ample hospital beds, critical care doctors, and where a surge in COVID-19 cases is not expected. Some states within the US and some countries have flattened their curve, are past the overwhelming volume of hospital stays, and have state-of-the-art medical facilities. The trials should take place where other patients' care will not have to be compromised and where the research participants will have access to care.

III. Standard of ethics boards

The experts also suggested that ethical and scientific review must be of the highest standard. Beyond the usual FDA and IRB review process, they suggested a robust public discussion and an additional independent ethics and science taskforce.[12] However, it is unclear how this will pan out. Also, the letter did not explain whether consensus-based ethical decision making would be adopted to resolve conflicting moral issues that may arise during the review process. The challenge with a consensus-based ethical decision is that members may agree with it without recourse to whether such decision is morally appropriate. Members may agree because they want to act in solidarity with the proposer of the decision or because they have a special stake in the outcome. To avoid decisions that do not comport with proper ethics, a decision-making procedure with accountability is required.

IV. Respect for participants' autonomy

The experts emphasized that the autonomy of participants must be respected. Although voluntary informed consent is necessary as it tends to protect the rights of research participants to accept risks, participants may make irrational decisions.[13] Individuals who are incompetent to make decisions like children should be excluded. Researchers should provide a tool to ensure that potential participants understand the risks of participation. "The wish of informed volunteers to participate in the trial ought to be given substantial weight."[14]

There is an ethical concern about enrolling volunteers who may want to participate in the challenge trials due to some motivations other than altruism. Some may have a psychological misconception of risk or desire to take on risk; others are motivated by compensation. Researchers should assess autonomy to be certain that participants understand risks and have freely decided to participate.

V. Ethical Concern about Advertised Financial Incentives

The success of clinical research depends on the availability of participants. According to the Council for International Organizations of Medical Sciences (CIOMS) ethical guidelines, financial or material incentives are

essential aspects of clinical research.[15] Incentives induce individuals to get involved in something inherently good. The inherent goodness of clinical research is that it is scientifically and socially valuable as long as there is a sound research design.[16] The compensation is made to attract participants who are altruistic and who believe in the research goals or who have certain qualities the researchers need. According to Dickert and Grady, incentives are like wages because although research participation does not require much expertise, it, however, requires "time, effort, and the endurance of undesirable or uncomfortable procedures."[17] As unskilled labour, researchers and their sponsors are ethically required to pay participants incentives "on a scale commensurate with that of other unskilled but essential jobs."[18] Some see compensation as coercive undermining the voluntary aspect of informed consent.[19] Some bioethicists, however, contend that the use of incentive as a recruitment strategy is morally problematic because it seems to reduce research participation to a kind of commercialized venture where services are paid for.

Many research participants are desperately looking for ways to address their economic needs. Employing incentives as a recruitment strategy targets vulnerable, and economically impoverished groups. Financial incentivization in clinical research is morally problematic because it is used to "attract the poor and socially disadvantaged, while those who profit most from the outcome of these studies are the better-off members of society."[20] Researchers should not approach vulnerable groups that may be incentivized by desperation and more tempted to ignore the risks. There is significant debate over whether compensation for clinical trial participation is ethical. Compensation can be appropriate if it is not coercively high. To ensure enough participants and that low-income people have the opportunity to participate, the challenge trials should compensate to cover their living expenses or any lost income but should not offer additional payments that could be coercive.

CONCLUSION

The COVID-19 pandemic has worsened the global poverty. Adopting an expedient research procedure like human challenge trials which would accelerate vaccine development for COVID-19 is morally imperative. Volunteers who participate in the challenge trials should be motivated to advance human health and well-being rather than driven by their economic needs. It is morally necessary to eliminate the possibility of motivations based on financial desperation, or a distorted understanding of the risks. Researchers must use fair methods to attract those able to digest the scientific risks and societal benefits while avoiding taking advantage of marginalized groups.

[1] Weinberg, Justin, "Philosophers, Epidemiologists & Others Call for Human Challenge Trials for COVID-19 Vaccine," Daily Nous, July 16, 2020, https://dailynous.com/2020/07/16/philosophers-epidemiologists-others-call-human-challenge-trials-covid-19-vaccine/.

[2] Open Letter, "Challenge Trials for COVID-19," *1 Day Sooner*, July 2020, https://1daysooner.org/openletter.

[3] Ferguson, Kyle and Caplan, Art, "Accepting the Challenge: COVID Vaccine Challenge Trials Can Be Ethically Justified," *The Hasting Centre*, June 29, 2020, https://www.thehastingscenter.org/accepting-the-challenge-covid-vaccine-challenge-trials-can-be-ethically-justified/.

[4]Business Standard, "Study says global poverty may surge to over 1 billion, warns Asian nations,", June 12, 2020, https://www.business-standard.com/article/pti-stories/study-warns-of-poverty-surge-to-over-1-billion-due-to-virus-120061200112_1.html.

[5] Mateus, Benjamin, "Human challenge trials are being pushed to develop a vaccine against the coronavirus," *World Socialist Web Site*, May 5, 2020, https://www.wsws.org/en/articles/2020/05/05/vacc-m05.html.

[6] Shah, Seema K. et al., "Before Deliberately Infecting People with Coronavirus, Be Sure It's Worth It," *The New York Times*, June 2, 2020, https://www.nytimes.com/2020/06/02/opinion/coronavirus-vaccine-challenge-trials.html?action=click&module=Opinion&pgtype=Homepage.

[7] Verity, Robert et al., "Estimates of the severity of coronavirus disease 2019: a model-based analysis," *The Lancet: Infection Diseases*, Vol 20, (March 2020): 669-677, https://doi.org/10.1016/ S1473-3099(20)30243-7, 673.

[8] Radcliffe, Shawn, "Nearly 40% of Those Hospitalized for COVID-19 Are Under 55," *Health Line*, March 19, 2020, https://www.healthline.com/health-news/covid-19-isnt-just-dangerous-for-older-adults.

[9] Eyal, Nir et al., "Human Challenge Studies to Accelerate Coronavirus Vaccine Licensure," *The Journal of Infectious Diseases*, Vol. 221, (May 2020): 1753.

[10] Phua, Jason et al., "Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations," *The Lancet: Respiratory Medicine*, Vol 8, (May 2020): 506-17. https://doi.org/10.1016/S2213-2600(20)30161-2; Aziz, Shadman et al., "Managing ICU surge during the COVID-19 crisis: rapid guidelines," Intensive Care Medicine. Vol. 46, No. 7, (2020): 1303-1325, doi:10.1007/s00134-020-06092-5.

[11] Leclerc, Thomas et al., "Prioritisation of ICU treatments for critically ill patients in a COVID-19 pandemic with scarce resources," *Anaesthesia, Critical Care Pain Medicine*, Vol. 39, No. 3, (June 2020): 334, DOI: 10.1016/j.accpm.2020.05.008.

[12] Open Letter, "Challenge Trials for COVID-19."

[13] Dawson, Liza et al., "Severe Acute Respiratory Syndrome Coronavirus 2 Human Challenge Trials: Too Risky, Too Soon," *The Journal of Infectious Diseases*, Vol. 222, (June 2020): 514–6, DOI: 10.1093/infdis/jiaa314.

[14] Open Letter, "Challenge Trials for COVID-19." For more on ethical guidelines on human challenge trials, cf. World Health Organization. Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants. Geneva: World Health Organization; 2011; Expert Committee on Biological Standardization. Human Challenge Trials for Vaccine Development: regulatory considerations. Geneva: World Health Organization, 2016.

[15] CIOMS-WHO, *International Ethical Guidelines for Health-related Research Involving Humans*, 4th. Geneva, 2016.

[16] Grant, Ruth W. and Sugarman, Jeremy, "Ethics in Human Subjects Research: Do Incentives Matter?," *Journal of Medicine and Philosophy*, Vol. 29, No. 6, (December 2004): 726.

[17] Dickert, Neal, Grady, Christine, "What's the Price of a Research Subject? Approaches to Payment for Research Participation," *The New England Journal of Medicine*, Vol. 341 No. 3, (November 1999): 199.

[18] Dickert and Grady, What's the Price of a Research Subject?," 200.

[19] Malmqvist, Erik, "Paid to Endure: Paid Research Participation, Passivity, and the Goods of Work," *The American Journal of Bioethics*, Vol. 19, No. 9 (August 2019): 11.

[20] Faden, Ruth R. et al., *A History and Theory of Informed Consent* (Oxford: Oxford University Press, 1986), 354. Kaewkungwal et al. also argued raised concerned about the ethical permissibility of targeting the economically impoverished population for human challenge trials. For more on this view, cf. Kaewkungwal, Jaranit et al. 2019. "Conducting human challenge studies in LMICs: A survey of researchers and ethics committee members in Thailand." Plos One, 14(10): e0223619.https://doi.org/10.1371/journal.pone.0223619.