Department of Bioethics, National Institutes of Health Clinical Center, Bethesda, MD, USA
Fogarty International Center, National Institutes of Health, Bethesda, MD, USA

Correspondence to: D Wendler
dwendler@nih.gov

Cite this as: *BMJ* 2021;372:n541
http://dx.doi.org/10.1136/bmj.n541
Published: 04 March 2021

Avoiding exploitation in multinational covid-19 vaccine trials

Low and middle income countries must benefit, not just participate

Alexander A Iyer, Joseph Millum, Christine Grady, David Wendler

Highly efficacious vaccines for covid-19 are now being distributed in high income countries. At the same time, multinational covid-19 vaccine trials continue—and new trials are being planned—around the world.[1]

People in high income countries who have access to efficacious vaccines may be unwilling to enrol or remain in trials testing unproved vaccines—especially trials with a placebo arm. As a result, ongoing and future multinational covid-19 vaccine trials may have to rely on participants from low and middle income countries (LMICs), where access to vaccines remains limited. It is critical to ensure that trials do not exploit these individuals and countries.

The fact that most people in LMICs lack access to covid-19 vaccines results from unjust wealth differences between countries, and from high income countries purchasing a disproportionate share of global vaccine supplies.[2] However, responding to this injustice by declining to enrol people from LMICs would be problematic. First, it would deny them the potential benefits of receiving an investigational vaccine. Second, it could impede the development of additional covid-19 vaccines, including those with high value for LMICs in particular. For example, vaccines that do not require ultracold storage could contribute substantially to tackling the pandemic in countries where some existing vaccines cannot be distributed.[3]

A better approach is to design multinational vaccine trials to avoid worsening existing injustices and mitigate them when possible. Most importantly, these trials should not exploit individuals, communities, or countries that lack access to covid-19 vaccines. Recent reports from LMICs raise concerns in this regard,[4] highlighting a need for clear guidance.

Exploitation occurs when trial participants or host communities do not benefit fairly given the burdens and risks they face, and the benefits others receive from their participation. A trial that enrolled participants largely from LMICs but made any resulting vaccine available only in high income countries, would be exploitative. To avoid exploitation, multinational covid-19 vaccine trials should satisfy several requirements in addition to those that apply to all clinical trials (such as informed consent and fair participant selection).[5] Funders, regulators, and review committees should ensure that sufficient oversight and accountability mechanisms are in place to see that these requirements are satisfied in practice.

First, trials should be responsive to host countries' health needs.[6] Evaluating a vaccine that would be cheaper, easier to distribute, or more effective against local SARS-CoV-2 variants could satisfy this condition. In addition, while global vaccine scarcity persists, evaluating any vaccine that could be used in host countries would be locally responsive.

Second, vaccines that are found to be safe and effective should be made available in host countries.[6] When most or all of a trial's participants come from LMICs, these countries should receive correspondingly higher priority for any resulting vaccine. If a trial does not yield an effective vaccine, host countries should benefit in other ways, such as through improvements to health infrastructure.

Third, trials should not make participants substantially worse off. To this end, consent processes should warn participants not to assume they will receive an effective vaccine, and to avoid risky behaviour throughout the trial. Participants should receive high quality healthcare if they develop covid-19, and free treatment for any research related harms. When trial participation ends, individuals should be informed whether they received the covid-19 vaccine or a control intervention, and counselled about future options, including any risks associated with receiving a different vaccine.

Fourth, trials should be planned and conducted in partnership with host countries. Host countries should help determine the acceptability of proposed trials, the type and magnitude of benefits they will receive, and the steps needed to ensure a trial does not undermine local health systems.[6]

Fifth, investigators, sponsors, and funders should be transparent and explain to the public why testing additional vaccines is valuable after effective vaccines have been identified.

Even when the above conditions are satisfied, multinational covid-19 vaccine trials may be perceived as unfair if most participants come from LMICs. Investigators, sponsors, and funders should consider ways to balance enrolment by increasing recruitment and retention of participants from outside LMICs.

For example, investigators might encourage trial participants who become eligible for a covid-19 vaccine outside of research to defer receiving it and continue to participate in the trial. This can be appropriate for people who would not face excessive risks as a result, such as those at low risk for severe covid-19. A second, and potentially supplementary approach, would be to guarantee that, once the trial ends, all participants will be offered an effective vaccine. A third option would be to stipulate that all participants who become eligible for vaccination outside of research will be unblinded and, if in the

placebo arm, offered the investigational vaccine with continued follow-up.

Even as safe and effective covid-19 vaccines are deployed, there remains substantial value in developing additional vaccines. With careful steps to avoid exploiting people in LMICs, multinational trials can offer an ethical way to accomplish this goal.

Competing interests: We have read and understood BMJ policy on declaration of interests and have no interests to declare. The writing of this editorial was supported by NIH intramural funds but the views expressed are the authors and do not represent the positions or policies of the National Institutes of Health, the Department of Health and Human Services, or the United States Government.

Provenance and peer review: Not commissioned; externally peer reviewed.

We thank Larry Corey, Phil Krause, John Mascola, Mary Marovich, Hilary Marston, and Merlin Robb for valuable discussion of these issues.

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