VIEWPOINT

CLIMATE CHANGE AND HEALTH

Clinical Research Risks, Climate Change, and Human Health

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For clinical research to be deemed ethically acceptable, it is necessary that a study have a favorable benefit-risk ratio.[1] This requirement is met when risks and harms are minimized, potential benefits are maximized, and the potential benefits outweigh the potential risks.[1]

In evaluating the risks of clinical research, institutional review boards (IRBs) and ethics committees concentrate primarily on those risks related to the health of participants. However, when calculating the potential benefits, they expand their purview to include the health of nonparticipants, including those from both present-day as well as future generations.[1] The focus on risks to participants is understandable, given that history's most egregious research-related harms have directly affected research participants. Nonetheless, it stands to reason that if present-day and future-generation nonparticipants matter when calculating the potential health benefits of clinical research, then present-day and future-generation nonparticipants should also matter when calculating the health risks and harms associated with clinical research. Not to do so gives rise to a risk-benefit calculation—and clinical research conduct—that is unbalanced, misguided, and does not properly respect the rights, safety, and welfare of nonparticipants and future generations.

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Health risks and harms associated with clinical research include, among other issues, those associated with anthropogenic climate change. (Clinical research is associated with a range of environmental and other harms, such as those related to extraction of resources, exploitation of labor, and the production of [toxic] waste, but this is beyond the scope of this Viewpoint.) Climate change has long been linked with catastrophic health harms. Since 2019, the World Health Organization has listed "air pollution and climate change" as the greatest threat to global health,[2] and people around the world have already begun to experience some of the worst air quality, wildfires, extreme temperatures, flooding, and droughts recorded in recent human history. Furthermore, the situation is only getting worse: between 2030 and 2050, climate change is expected to cause 250 000 additional deaths per year from malnutrition, malaria, diarrhea, and heat stress.[3] Clinical trials contribute substantially to greenhouse gas emissions, with carbon emissions of the 350 000 national and international trials registered on ClinicalTrials.gov—just a subset of clinical trials globally—being estimated at 27.5 million tons, which is just less than one-third of the total annual carbon emissions of Bangladesh, a country of 163 million people.[4]

Given these current and impending harms, the scientific community, policymakers, IRBs, and ethics committees can no longer claim ignorance of the fact that human activity—including clinical research—negatively affects both participants and nonparticipants alike, and it is untenable to omit these effects when calculating the potential benefits and risks of conducting clinical research. Of course, simply calculating the carbon footprint associated with clinical trials is not enough: to be ethically acceptable, the carbon footprint of clinical trials—and the related harms of clinical research—must be minimized to maximize the net benefits of research. While there is a range of possible approaches to achieve this behavior change within the research community, as stewards of ethical research, IRBs and ethics committees have an important role to ensure the benefit-risk ratio is upheld within research practice. To fulfill this role, IRBs and ethics committees must ensure that research studies (1) calculate and minimize the carbon dioxide equivalent (CO_2e) emissions associated with a clinical study, (2) disclose the associated carbon footprint of their research, and (3) have a feasible mitigation and carbon offset plan for those CO_2e emissions that cannot be reduced to ensure that their study achieves net-zero CO_2e emissions. IRBs and ethics committees may then make research ethics approval contingent, in part, on meeting these 3 conditions. It is important to note that many carbon offset plans do little to address the effects of carbon use. As such, they should be a last resort, and the companies chosen to offset CO_2e emissions must be effective at doing so.

Because IRBs and ethics committees do not presently calculate the potential benefits and risks of research in a manner that considers climate change in this way, a sense of urgency to correct this matter is needed, including developing user-friendly tools for trialists to effectively calculate the carbon impact of their study. At the same time, implementing these requirements should not be rushed, should be carried out in consultation with key stakeholders—eg, funders, sponsors, investigators, governmental agencies, participants, and communities—and needs to be introduced in a fair and equitable manner so that important clinical research is able to proceed in a timely fashion and in such a way that certain regions, countries, and groups conducting clinical research are not disproportionately negatively affected. Importantly, regulations should not be implemented in a way that would

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place undue disadvantage on particular groups or communities, nor as a tick box that would lead to a compliance-based approach with little impact on CO_2e emissions; IRB and ethics committee members must remain vigilant to the spirit of what is trying to be achieved.

To give an example, even if a clinical trial research proposal scores well with a favorable benefit-risk ratio because it takes nonparticipant harms into consideration through low-carbon measures, the research itself must be scientifically sound and likely to produce value; the alternative is wasted resources and emissions. In fact, it is now well established that many clinical trials conducted today are uninformative; ie, clinical trials may be conducted in a manner in which (1) the study hypothesis does not address an important and unresolved scientific, medical, or policy question; (2) the study is not designed to provide meaningful evidence; (3) the study design is not feasible; (4) the study is not conducted and analyzed in a scientifically valid manner; or (5) the study does not report its methods and results accurately, completely, and promptly.[5] Uninformative research is more common than previously realized, and it has been reported, for example, that 3 of 4 clinical trials related to heart disease, diabetes, and lung cancer conducted in the US are "a waste of time and money."[6]

In engaging and conversing with stakeholders, it is important to note that requiring researchers to be mindful of ways they may reduce the carbon impact of their clinical study, calculate and disclose the associated carbon footprint of their research, and have a feasible mitigation and carbon offset plan to ensure that their study achieves net-zero CO_2e emissions, is best understood not as a new requirement but rather as an existing requirement that has not been realized, operationalized, and enforced. The idea that such harms are worth taking seriously, and that "medical research should be conducted in a manner that minimizes possible harm to the environment,"[7] has existed in the World Medical Association's Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects for approximately 50 years.

What is needed, then, is less uninformative clinical research, more informative clinical research, and a strategy to ensure that clinical research does not compromise the safety, rights, and welfare of nonparticipants and future generations. Society is at a critical reflection point, where various industries and sectors—including the health care sector—are transitioning and targeting to get to net-zero emissions: the time has come for the clinical research ecosystem to do the same.

ARTICLE INFORMATION

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