Ethical issues arising in research into health and climate change

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Clinical trials, environmental harms and the response-ability to act

Brief description of context

Clinical trials are critical for the evaluation of health interventions. At the same time, trials contribute to environmental harms: approximately 38,000 new trials were registered globally on Clinicaltrials.gov in 2022, each with an estimated greenhouse gas emission footprint of ~80 to over 2000 tonnes carbon dioxide equivalent (CO_2e; herein: emissions; 80 tonnes is equivalent to driving a car ten times around the planet) (D'Souza and Samuel 2023). Emissions arise at each stage of a clinical trial: when distributing or implementing interventions; conducting trials, including facility energy consumption and researchers' and participants' travel; and laboratory and other analyses, including data storage and processing during and following trials. Clinical trials also have wider neglected environmental harms associated with resource use and hazardous and non-hazardous waste production.

There is growing interest in reducing clinical trial-associated emissions ('mitigation'). In high-income countries (HICs) including the UK, tools for assessing emissions associated with different trial processes are becoming increasingly available, and guidance to support reducing trial-associated emissions are being developed (Griffiths et al. 2024).

While moves to reduce trial emissions are escalating in HICs, particularly in the UK, ethical scholarship has attended little to questions of moral obligations and responsibilities associated with trial emission mitigation. The moral obligation question requires considerable unpacking and is not the focus of this paper. Rather, taking this moral obligation as given, this paper focuses on questions of who should be morally responsible for emission mitigation. It situates itself within the broader ethics scholarship that stresses that environmental harms should be addressed through collective responsibilities (Schinkel 2011, Young 2011, Galvin and Harris 2014, Jamieson 2015), and specifically where responsibilities are attributed proportionally to ability–an approach most prominently put forward by Marion Young (2011). This scholarship also aligns with sociologists who argue that responsibilities require a capacity to act; being responsible is being 'response-able'–being able to respond (Haraway 2016). To explore this, this paper aims to understand which actors are best positioned to reduce clinical trials emissions.

Discussion of ethical issues

This paper draws on a WHO-commissioned project which is aiming to develop globally applicable recommendations for clinical trial emissions mitigation, and involved talking to a range of clinical trial actors. These actors are distributed across the research ecosystem, including funders, researchers, research organisations, publishers, national and international regulators, and ethics committees. Our focus was on those designing, developing and conducting trials in HIC and Low and Middle Income Country (LMIC) settings. We spoke to trial sponsors, primary investigators (PIs), and research site managers in 12 countries (UK (n=8), Kenya (n=3), South Africa (n=2), Malaysia (n=2), and one each from The Netherlands, Germany, Brazil, India, Nepal, Zambia, Gabon, and Ethiopia), including 15 men and 8 women.

Key findings:

1. **Whose responsibility? Maximal preparedness for regulated trials**

PIs, CROs (contract research organisations) and sponsors must adhere to compliance-based protocols when designing and overseeing clinical trials. This requires adherence to a range of stringent regulations to ensure any trial's efficacy, quality and safety. Particularly for regulatory

trials, i.e., when sponsors are trialling an intervention for regulated use, a culture of nervousness and 'panic' has developed, with actors concerned that any small error in trial processes/practices can result in an invalid trial. In response, PIs, CROs and sponsors are designing/conducting trials with maximum preparedness. Those working at research sites provided examples of over-packaging of goods and repeat inspections of host trial sites. Frequent research site visits to verify labs, check compliance, and confirm data entry leads to high flying-related emissions when sites are overseas. Cluster visits, i.e., visiting several closely distanced sites at a time to reduce flying, can mitigate some emissions, but are not always possible. Digital communication also reduces flying, but a lack of digital infrastructure and problems with connectivity–including regular power cuts–remain prevalent at many LMIC sites. Finally, maximal preparedness is associated with evermore data collection 'just in case', leading to data analysis with increasingly energy-intensive algorithms and AI because of technical feasibility rather than a necessity to answer trial research questions.

2. **The intersection of responsibility with capacity, trust and colonialism**

Site visit frequency is a particular issue for LMIC-based research sites where a lack of capacity and/or skills require regular oversight to ensure the trial is running to stringent protocols and standards. This lack of capacity is also associated with the flying of samples back to the sponsor's lab for processing, and the flying of engineers to regularly fix broken machines. A move to de-centralised trials to increase capacity (and reduce emissions) is emerging, but sub-zero sample storage remains limited at many research sites in LMICs, as are concerns that research site-based analyses will be inferior to those conducted at the host's lab. A further concern is the potential for the samples to offer medical insights remaining unrealised due to inferior analysis capabilities at LMIC sites, potentially leading to wasted resources. The balance between building capacity at research sites (and the co-benefits of decreasing flights and the de-colonisation of research conduct); versus the need for sponsors, PIs and/or CROs to verify correct trial conduct is difficult for study participants to clearly articulate.

3. **Trial research site lack of 'response-ability'**

Trial research site managers face constraints and/or tensions when considering trial emission mitigation which makes it difficult for them to be response-able for reducing trial-associated emissions. First, their facilities are often housed in larger institutions that have control over making decisions about (renewable) power usage. Second, trial sponsors (academic/industry) design stringent protocols to ensure a trial's rigour, validity and patient/participant safety, with which research sites must comply: environmental harms can only be considered if part of the protocol, and such considerations are nearly always not included. Third, when competing for a clinical trial contract, a lack of incentives are provided to incorporate more expensive low-emission or low-resource options, making it difficult for trial sites to prioritise these options.

4. **Responsibility for 'getting it right first time'**[1]

Whilst many long-established standards for testing and diagnostics exist across a variety of scientific processes, newer testing and diagnostics can at times be a 'wild west' of different standards and thresholds. Despite this, examples were provided of PIs using such newer techniques during trial conduct. This presents obstacles in generating reproducible and valid data, and potentially wastes resources.

Conclusions and recommendations

The broader clinical trial landscape reveals PI/sponsors acting with maximal preparedness to ensure trials are conducted in line with regulatory requirements and, in turn, these actors requiring research sites to follow strict protocols. At the same time, examples of poorly designed trials exist, leading to wasted resources.

[1] https://gettingitrightfirsttime.co.uk/

Recommendations:

1. Sponsors and PIs should be responsible for not only ensuring that clinical trials are well-designed from the outset (appropriate research questions, not replicating existing research, efficient & well-designed trial methodology), but also that standards of testing and diagnostics being utilised within the trial, and the standards against which the scientific community will consider the results of the trial, are relevant (Dickersin and Mayo-Wilson 2018). Funders and journal editors share this responsibility by making sure such practices are incentivised and implemented.

2. Mitigation concerns cannot be separated from the chain of nervousness and maximal preparedness in the broader clinical trial ecosystem. While the need to maintain patient/participant safety is of utmost importance, some LMIC-based trial site practices, while not described above, already mitigate emissions by accident due to a lack of resources. Lessons can be learned regarding how to move from maximal preparedness to resourcefulness without impacting trial safety.

3. Sponsors, PIs and funders should promote trial emission mitigation by (where relevant) supporting investment in renewable energy, digital infrastructures and capabilities, and skilling workers through decentralised trials. REC/IRBs could also play a role, with examples provided of some RECs in LMICs requiring capacity building as an aspect of receiving approval. Co-benefits include the promotion of socially just, de-colonised research processes.

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