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Details of the Collaborative Activity

2019-20

Name of the Collaborating Institute: Ann & Robert H Lurie's Children's Hospital of Chicago Foundation, Chicago

Name of collaborating department from YDU: Center for Ethics

Activities:

Joint Research and Publications:

Dr. Vina Vaswani, Centre for ethics participated in an invited workshop at Lurie's Children's Hospital, Notth western University in Chicago between 3rd -5th June 2019. The collaborative discussions resulted in two joint publications. Travel fund to attend the workshop was granted by Greenwall Foundation and Wellcome Trust

1. Vina V, Abha S, Seema KS, Ricardo P, Annette R, Informed consent for controlled human infection studies in low- and middle-income countries: Ethical challenges and proposed solutions, *Bioethics, Special Issue: Ethics of Human Challenge* Trials, Aug Aug 2020, Wiley

2. Seema KS, Franklin GM, Thomas CD, Devan D, Claudia E, Holly FL, Euzebiusz J, Nancy SJ, Dorcas K, Melissa K, Jonathan K, Douglas M, Matthew JM, Sean CM, Ricardo P, Thomas LR, Meta R, Abha S, Katherine S, Micheal JS, Vina V, Annette R, Ethics of controlled human infection to address COVID-19, *Science*, 2020, 368 (6493);832-4

ATTESTED
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Ann & Robert H. Lurie
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April 16, 2019

Dear Dr. Vina Vaswani,

As a collaborator on: *A new ethical and regulatory framework for the use of human challenge studies on emerging infectious diseases*, we invite you to join us for an in-person workshop at Lurie Children's Hospital & Northwestern University in Chicago, Illinois from June 3-5, 2019. At this workshop, we will review the manuscripts written on the various components of the framework, including the one you have co-authored, and ask you to share the results of your analysis with the group. We will also discuss how to consolidate these distinct efforts into one unified document which will serve as the framework. In collaboration with the World Health Organization, we will begin the process of developing international ethical guidelines for human challenge studies.

Funding for your travels will be provided by the Greenwall Foundation and Wellcome Trust. In addition to travel expenses, funding for your food and accommodations for the duration of the workshop will also be provided by the Greenwall Foundation and Wellcome Trust.

We truly appreciate your participation in this endeavor to date, and we hope that you will be able to join us at the workshop.

Sincerely,

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Bioethics / Early View

SPECIAL ISSUE: ETHICS OF HUMAN CHALLENGE TRIALS

Informed consent for controlled human infection studies in low- and middle-income countries: Ethical challenges and proposed solutions

Vina Vaswani, Abha Saxena, Seema K. Shah, Ricardo Palacios, Annette Rid

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Abstract

In controlled human infection studies (CHIs), participants are deliberately exposed to infectious agents in order to better understand the mechanism of infection or disease and test therapies or vaccines. While most CHIs have been conducted in high-income countries, CHIs have recently been expanding into low- and middle-income countries (LMICs). One potential ethical concern about this expansion is the challenge of obtaining the voluntary informed consent of participants, especially those who may not be literate or have limited education. In some CHIs in LMICs, researchers have attempted to address this potential concern by limiting access to literate or educated populations. In this paper, we argue that this practice is unjustified, as it does not increase the chances of obtaining valid informed consent and therefore unfairly excludes illiterate populations and populations with lower education. Instead, we recommend that investigators improve the informed consent process by drawing on existing data on obtaining informed consent in these populations and interventions aimed at improving their understanding. Based on a literature review, we provide concrete suggestions for how to follow this recommendation and ensure that populations with lower literacy or education are given a fair opportunity to protect their rights and interests in the informed consent process.

POLICY FORUM

RESEARCH ETHICS: COVID-19

Ethics of controlled human infection to address COVID-19

High social value is fundamental to justifying these studies

By Seema K. Shah, Franklin G. Miller, Thomas C. Darton, Devan Duenas, Claudia Emerson, Holly Fernandez Lynch, Euzebiusz Jamrozik, Nancy S. Jecker, Dorcas Kamuya, Melissa Kapulu, Jonathan Kimmelman, Douglas MacKay, Matthew J. Memoli, Sean C. Murphy, Ricardo Palacios, Thomas L. Richie, Meta Roestenberg, Abha Saxena, Katherine Saylor, Michael J. Selgelid, Vina Vaswani, Annette Rid

Development of an effective vaccine is the clearest path to controlling the coronavirus disease 2019 (COVID-19) pandemic. To accelerate vaccine development, some researchers are pursuing, and thousands of people have expressed interest in participating in, controlled human infection studies (CHIs) with severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2) (*1, 2*). In CHIs, a small number of participants are deliberately exposed to a pathogen to study infection and gather preliminary efficacy data on experimental vaccines or treatments. We have been developing a comprehensive, state-of-the-art ethical framework for CHIs that emphasizes their social value as fundamental to justifying these studies. The ethics of CHIs in general are underexplored (*3, 4*), and ethical examinations of SARS-CoV-2 CHIs have largely focused on whether the risks are acceptable and participants could give valid informed consent (*1*). The high social value of such CHIs has generally been assumed. Based on our framework, we agree on the ethical conditions for conducting SARS-CoV-2 CHIs (see the table). We differ on whether the social value of such CHIs is sufficient to justify the risks at present, given uncertainty about both in a rapidly evolving situation; yet we see none of our disagreements as insurmountable. We provide ethical guidance for research sponsors, communities, participants, and the essential independent reviewers considering SARS-CoV-2 CHIs.

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SUFFICIENT SOCIAL VALUE

CHIs have a long, complicated history. They have contributed to substantial improvements in clinical and public health practice, including the recent licensure of two vaccines (*5*), but also involved some unethical research (*3*). The first step in justifying SARS-CoV-2 CHIs, especially as they would involve major uncertainty and controversy, is to demonstrate their high social value. Crucially, SARS-CoV-2 CHIs should address relevant, unresolved scientific questions in rigorously designed and conducted experiments.

SARS-CoV-2 CHIs could have high social value in several ways. For example, they could help prioritize among the almost 100 investigational vaccines and over 100 experimental treatments for COVID-19 currently in development. CHIs could help identify the most promising agents, which would inform the design of larger trials, guide decisions to scale up manufacturing early, and thereby accelerate product development and implementation. If they saved even a few months of vaccine development (*1*), SARS-CoV-2 CHIs would contribute to faster control of the pandemic and reduce the need for, and associated costs of, physical distancing measures, providing substantial benefits for much of the world's population (including the most vulnerable).

To achieve high social value in this way, coordination of stakeholders is essential. Sponsors of SARS-CoV-2 CHIs should delineate a credible path forward from CHIs to rigorous field studies, and eventually toward scaled-up production. This is a considerable challenge given the rapidly evolving research response to the pandemic; many approaches to accelerating product development are already appropriately being pursued in parallel. It is therefore essential to plan and evaluate SARS-CoV-2 CHIs as a complement, not an alternative, to these other approaches and ensure that CHI results are integrated into the dynamic COVID-19 research landscape. For example, the World Health Organization is convening sponsors of SARS-CoV-2 CHIs to increase transparency and promote coordination. Research sponsors should lead by establishing and enforcing standards for rapid data collection, dissemination, and sharing that permit aggregation of results across CHIs. Medical journals should require compliance with these standards before accepting manuscripts. Regulatory agencies should collaborate with sponsors, researchers, and policy-makers to define how CHI data will inform or modify larger trials, licensure, and manufacturing. Finally, sponsors and governments should implement mechanisms to ensure widespread, equitable access to proven products whose development was accelerated by SARS-CoV-2 CHIs. Such wide-ranging stakeholder coordination is difficult but important to demonstrate high social value. Though not achieved for proposed Zika virus CHIs during the 2015–2016 epidemic, it did occur later (*6*).

SARS-CoV-2 CHIs could have high social value in other ways, and individual CHIs could address multiple scientific questions. For example, CHIs could clarify dynamics of infection, viral pathogenesis, and risk of vaccine pathogenesis or identify correlates of protection—all of which could inform the development and implementation of vaccines. CHIs could also illuminate poorly understood parameters for modeling the pandemic and public health responses, including who is infectious and when and how infections occurred. This information is difficult to collect by observation alone, and existing animal models do not fully replicate clinical disease seen in humans. Additionally, if the pandemic wanes before larger trials are completed, SARS-CoV-2 CHIs could be critical for advancing research until the next outbreak, as with Zika virus (*6*). All of these paths to high social value would require similar, extensive coordination with relevant stakeholders.

SARS-CoV-2 CHIs admittedly have limited generalizability, as they would need to be conducted with low-risk populations (see below) with a non-natural mode of infection. Therefore, although some propose replacing efficacy trials with SARS-CoV-2 CHIs (*1*), it is more likely that CHIs accelerate vaccine or treatment development by informing larger trials, not by making such trials redundant. Yet almost all disease models or trial designs require some extrapolation or further testing. For example, field trials with frontline workers could also accelerate vaccine development, but they would not include older, retired individuals.

Thus, there are many potential ways in which SARS-CoV-2 CHIs could have high social value. Before their initiation, it is essential that the given social value is judged as compelling enough to justify its pursuit.

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