



COVID-19 and the ethics of human challenge trials

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During the past year COVID-19 changed the lives of people globally. Its threat to health and economy triggered an unprecedented global research response, which resulted in the speedy development of various vaccines as well as rapid testing and assessment of medication. In the meantime, however, the healthcare system had to deal with surging numbers of COVID-19 patients. The resolve to achieve progress in research and the need to provide patient care under testing circumstances triggered a variety of ethical difficulties.

Ethical challenges

The first three papers in the current issue highlight some of the ethical questions triggered by COVID-19. Solbakk et al. (2021) advance arguments against controlled human infection studies making a case for upholding well-established research ethics guidelines, even under exceptional pandemic circumstances. Da Silva et al. (2021) look at problems in academic publishing such as keeping up the rigor of peer review and the quality of editorial decision making when dealing with a significantly increased manuscript flow and facing the urgency to work faster rather than slower. They advance six recommendations in order to “minimize risks of publishing questionable original research on public health research related to COVID-19” (*ibid.*). Rashi (2021), finally, tackles the dangers that health care workers and their families are exposed to because of COVID-19. Should these risks be accepted by health care workers? What are the justifications for the professional obligation to continue work under circumstances of increased risk? When do working conditions become unacceptably dangerous?

The case against exceptionalism

This editorial focuses on the first paper by Solbakk et al. (2021) about human challenge trials, i.e., experiments where human participants are intentionally exposed to pathogens. The pandemic has triggered a debate about these studies with advocates and opponents advancing a variety of arguments (see *ibid.* table 2 for references). Yet, our authors are not in favour of allowing any “ethical exceptions or shortcuts” (*ibid.*). On the contrary, especially when it comes to COVID-19 research they deem it pivotal to stick to existing research ethics guidelines, “the *priority of the individual principle*” being “the most fundamental” (*ibid.*). The interests of individual trial participants should always trump those of society. Variations of this principle can be found in the different versions of the Declaration of Helsinki and in the UNESCO Universal Declaration on Bioethics and Human Rights.

It remains unclear whether the authors assert that challenge trials are categorically unethical or whether their claim is restricted to the specific case of COVID-19. The first interpretation is suggested where they generically claim that the primacy of the interests of individual research participants should be upheld whatever the circumstances. “There is no exception for times of crisis, or for instances where societal interests are large” (*ibid.*). The second interpretation is implied where they declare that the principle “... prohibits the conduct of SARS-CoV-2 challenge studies at the present time where the challenge virus would be the native virus with full virulence and where there is no rescue treatment yet available” (*ibid.*). The two clauses indicate that if the challenge virus were not fully virulent and/or there was a rescue treatment, challenge trials might be acceptable after all. Be this as it may, two questions must be clearly distinguished.

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Are violations of research ethics norms ever acceptable?

The authors' emphasis on the importance of upholding existing research ethics norms is commendable. Whenever the common good is severely threatened, people and institutions tend to focus more on consequentialist reasoning. They suddenly seem to be less offended by violations of deontological norms, which would be upheld emphatically under normal circumstances. This mechanism generally occurs in times of war, terror attacks or severe public health threats. Unfortunately, however, it often appears to be difficult to scale back the norm violations after circumstances have normalized again. Because of institutional inertia, for instance, it is difficult to redirect policies in large organizations after they have accepted norm encroachments for the greater good. So, there are long-term perils involved in accepting norm infringements or rule adjustments under extraordinary circumstances. These hazards caution against insouciantly accepting such transgressions in exceptional circumstances. It also means that whenever temporary violations of a particular norm were to be accepted, the specifics of the justifying circumstances should be stipulated, and a return path towards respect of the norm at hand should be detailed in advance.

Which research ethics norms are violated by challenge trials?

Solbakk et al. (2021) claim challenge trials would contravene the norm that societal interests should yield to those of individuals. Is such a norm violation unavoidable though? Or would it also be perfectly possible for such trials to respect the priority of individual interests? Just imagine that individual participants of a certain study had an altruistic motivation for their choice to get involved, thereby aligning their individual interests with those of society. The ensuing

harmony between individual and societal interests seems to allow for controlled human infection studies after all—absent any other counter arguments of course.

Likewise, considerations of proportionality do not seem to prohibit controlled human infection studies categorically. The norm of proportionality only permits such trials where the potential societal benefits of the research outweigh the risks to participants. But scenarios are imaginable where pandemic circumstances were so severe that the societal benefits of a controlled infection study would more than offset the risks to trial participants. Equally, it is not obvious that controlled challenge trials would necessarily violate the requirement of informed consent, that they would inevitably amount to torture, or unavoidably disrespect human dignity. So, whilst it might be the case that a specific challenge study would violate a particular widely accepted research ethics standard, the generic claim that challenge studies categorically infringe certain core research ethics norms and would thus be unethical seems unsubstantiated.

References

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