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Response to Dawson et al

To the Editor—Dawson et al [1] raise 3 concerns about human challenge trials to assess the efficacy of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines. First, that current scientific understanding is insufficient to know all the risks to volunteers, including potential long-term effects. However, assuming that the effects of artificial infection resemble those of natural infection, there is substantial evidence that, so long as only young and healthy people are recruited [2–5], the risk of death is comparable to that of live kidney donation [6–8]. Known and unknown nonlethal complications following infection are also possible, but based on the evidence to date, among young people, complications within the duration of follow-up that has been possible in the first months of this pandemic are likely to remain rare. It would be imperative that volunteers in challenge studies have a clear understanding of the known risks and of the possibility of yet unrecognized risks. That includes long-term risks whose frequency is unknowable, a familiar complication inherent in all first-in-human trials—including any phase III trials of novel SARS-Cov-2 vaccines.

Second, Dawson et al [1] question whether autonomous decision making by volunteers overrides concerns about risk, given that "people often make decisions in irrational or idiosyncratic ways," suggesting that irrational decisions are likelier in this case than elsewhere. We note that >28 000 individuals have already declared willingness to participate in SARS-Cov-2 challenge trials [9] and we think it unlikely that all of these are acting irrationally. Of course, not all may be suitable for a challenge trial, and a thorough informed consent process should make a determination on each selected candidate. Procedures for obtaining fully comprehending consent, familiar to research ethics since the 1980s, have been well established for novel interventions, including those for which risks are ill defined. Dawson et al note, "Given the inherent uncertainty in vaccine development, this kind of optimistic bias could lead people to take risks without seeing the associated benefits" [1]. However, this concern could apply to first-in-human vaccine trials, and even in phase 3 SARS-Cov-2 vaccine trials, there is, for example, an uncertain risk of the vaccine inducing enhancing coronavirus disease 2019 (COVID-19) disease [10].

Third, Dawson et al consider that the conduct of challenge studies would imperil public confidence in the COVID-19 research enterprise, potentially undermining the global response to the COVID-19 pandemic [1]. This we question. So long as investigators are open about the possibility of rare events occurring and this is made public knowledge, if these events do occur rarely (as might also happen in conventional vaccine trials), we think it unlikely that COVID-19 research or public health response would be affected, even if a rare volunteer did experience serious disease or death as a result of participation.

We recognize that challenge trials would raise fewer ethical worries if it were possible to exclude all volunteers at high

risk of serious disease, including those genetically predisposed, or if curative treatments existed. But they are already justified, both for keeping the risks to validly-consenting volunteers tolerable, and because the risks to volunteers must be balanced against the societal value of reducing the time required to identify efficacious vaccines against a disease that is causing a massive and relentless daily toll.

Notes

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Testing for Novel Coronavirus Antibodies: A Necessary Adjunct

We read with interest the article by Cowling and Aiello [1] about the use of proactive public health measures to help slow the spread of the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) over the world. The size of this pandemic and the exorbitant increase in number of patients seems to have become unstoppable. More than 200 countries are now involved in this emergency, and, as of 30th May 2020, about 6.1 million persons have tested positive and > 360 000 patients have died [2].

It now seems clear that the implementation of such measures has unfortunately not been sufficient to contain the outbreak, considering that this dramatic increase in numbers occurred within only a few months after the first case in Wuhan, China [3]. This new endemic disease has proved itself not only a worldwide clinical disaster but also an economic disaster. It caused the lockdown of economic activities and the collapse of worldwide markets [4].

Furthermore, the numbers of individuals infected are difficult to estimate, owing to the presence of both SARS-CoV-2–positive asymptomatic individuals and symptomatic, self-isolating individuals in whom nasopharyngeal swab samples were not obtained. Many experts estimate that the real number of persons positive for SARS-CoV-2 is underreported by up to 10-fold [5, 6].

The problem of asymptomatic individuals spreading SARS-CoV-2 is critical. Knowing the number of truly infected people is important not only for epidemiological reasons but also in order to restart the world economy, which would otherwise be blocked until an uncertain date in the future. The most feasible solution to knowing how many people have actually been infected lies in the possibility of carrying out large-scale serosurveys, evaluating