Response to Hasford and to Spinola et al

To the Editor—We proposed human challenge trials (HCTs) as a possible alternative or complementary to conventional Phase 3 trials for expedited SARS-Cov-2 vaccine efficacy testing [1]. Hasford [2] argues that a large, simple, randomized trial, as proposed by Yusuf et al [3], could work better. We note that the latter design is similar to that implemented by the WHO for the SOLIDARITY platform trial [4]. If vaccine efficacy can be assessed rapidly in such trials then HCTs might prove unnecessary, but preparing for HCTs would still be a valuable hedge against the possibility of too low an incidence of COVID-19 in field trials in such a fluid situation.

Spinola et al argue that HCTs are generally limited to diseases which can be fully treated. We recognize that SARS-CoV-2 is not in that category, but have explained elsewhere why the risks remain tolerable [5, 6]. We note also that , since we wrote our original paper, two specific therapies have been shown to reduce the risks to patients hospitalised with COVID-19 [7, 8], and it is possible that further treatments will be developed in the coming months that reduce the risks even further. It is true that we necessarily have no information on the long-term outcomes associated with SARS-CoV-2 infections. The informed consent statement must include specification that there may be long-term effects of which we are currently unaware. As we explained elsewhere, this in no way invalidates participants' informed consent [9]. Nor does the uncertainty otherwise make the trials impermissible [10]. We agree with Spinola et al that such trials should not target minority groups for recruitment [5].

Spinola et al argue that "it is unlikely that a SARS-CoV-2 model could be ready to evaluate vaccines for years." But the circumstances of the COVID-19 pandemic have changed the paradigm for the time it takes to develop and test new vaccines. If sufficient resources are devoted to developing HCTs for SARS-CoV-2, then we believe they could be available much sooner. Of note is the recent report that HCTs might be conducted at Oxford University "by the end of this year".[11]

Spinola et al are also concerned that HCTs would not provide adequate data regarding vaccine safety and that, even with a parallel large short-term safety trial, such testing could not detect long-term adverse effects. However, even in the type of conventional phase 3 trial that it is hoped might produce efficacy data in 3-6 months sufficient to justify widespread vaccine use [4], longer-term adverse effects will remain unknown, and must necessarily be studied in post-licensure studies.

References

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