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Social Value, Beneficial Information, and Obligations to Participants in a Trial of Novel COVID-19 Vaccines

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The case describes researchers who are seeking ethics guidance on communicating with participants in a phase-1 COVD-19 vaccine trial about FDA-authorized COVID-19 vaccines (Wilfond, Duenas, and Johnson 2023). The researchers want help choosing among three options they have identified for encouraging participants to obtain one of the authorized vaccines. We argue that research ethics consultants should consider going beyond this question to address another ethics concern the researchers might have overlooked.

The case states that interim data suggest some of the COVID-19 vaccines being tested in the trial likely are less effective than authorized vaccines and have different side-effect profiles. All U.S. adults became eligible to receive an authorized vaccine around the time the trial began in April 2021 (Hunnicutt 2021), a fact likely known to trial participants. Ethical and regulatory standards require that the researchers inform participants about the interim data so they can make

decisions that align with their values and preferences. However, the case notes that the interim data are disappointing for only *some* of the trial vaccines, implying that some of the other trial vaccines still might show promise as potential alternatives or additions to authorized vaccines.

If some of the trial vaccines remain viable candidates, the researchers should consider whether continuing the trial would be justified and whether to offer some participants the option to continue without receiving an authorized vaccine. This entails weighing the potential scientific and social value of continuing the trial against the risks of continued exposure to COVID-19 without protection from a proven vaccine. Presumably the researchers thought the trial vaccines could offer advantages over the authorized vaccines, otherwise beginning the trial in April 2021 would not have been justified (Wendler and Rid 2017). Continued data collection from participants who received a still-viable trial vaccine could be valuable for future research and development, but their receiving an authorized vaccine likely would confound assessment of the trial vaccine. As in any ongoing trial of investigational products, there is uncertainty: the trial vaccines might be ineffective or less effective than authorized vaccines in protecting against COVID-19. If some trial vaccines still have potential social value and continuing the trial could inform their assessment, then offering some participants the option to continue in the trial without receiving an authorized vaccine might be justified.

Participants who received the still-viable vaccines may choose, if fully informed, to continue in the trial recognizing they are taking a chance that they will lack protection from COVID-19. Offering an option to participate in a vaccine trial while forgoing standard preventive interventions, such as an authorized vaccine, is commensurate with other kinds of research. For example, a study might compare an investigational treatment to a standard-of-care intervention for a serious disease (e.g., cancer, HIV), provided that participants are fully informed and competent to make an independent decision about their participation (CIOMS 2016). Furthermore, the circumstances of

any participants who received a still-viable vaccine have not changed radically since the trial began: COVID-19 remains a serious risk, proven effective vaccines are available, and the value of the trial vaccines is uncertain. If it was permissible to ask these participants to forgo receiving an authorized vaccine in the beginning, it might be permissible to ask them to continue to do so. The ethical acceptability of this risk also might depend in part on individual participants' risk profiles regarding COVID-19 infection.

The existence of a public health emergency and grave concerns about the consequences of the COVID-19 pandemic justifiably have highlighted the need to ensure equitable access to safe and effective vaccines, based on considerations of justice and beneficence. At the same time, people may choose to defer the adoption of protective measures in the service of a worthy cause such as the advancement of socially valuable scientific research. The ethical justification for continuing this trial depends on the potential scientific and social value of the data to be collected, the amount of incremental risk assumed by participants who delay vaccination, and assurances of their understanding and voluntary participation (Wendler et al. 2020).

The three options formulated by the researchers for communicating with participants about authorized vaccines are relevant for participants in any trial arms that are permanently discontinued and for participants who received a still-viable trial vaccine but choose to leave the trial to receive an authorized vaccine. These options involve different approaches to sharing information or expertise to assist participants or their providers with optimizing decisions about authorized vaccines.

There is precedent in existing bioethics scholarship for researchers to provide expertise-specific assistance to study participants. Considerations of beneficence support such provision of information under certain conditions, such as informing participants about incidental findings in genomics research (PCSBI 2013). Many argue that researchers have a bounded responsibility to

inform study participants of findings that would enable participants to protect themselves or others from harm. However, there is little ethical reason to disclose if participants have expressly stated they do not want information about incidental findings, or if such findings lack clinical interpretability and would only increase participants' anxiety (Jarvik et al. 2014). Some bioethicists also have argued that researchers might have obligations based on relationships they have established with study participants to provide ancillary care beyond what is specified in a study protocol (Richardson and Belsky 2004; Merritt, Taylor, and Mullany 2010). Ancillary care obligations might be stronger when study participants have assumed risks and burdens for the sake of research, as is the case in the trial of novel COVID-19 vaccines.

If the researchers' special expertise enabled them to provide information needed for participants' medical care that others could not provide, there could be a strong argument from considerations of beneficence and duties of ancillary care that the researchers should assist participants by providing this information. However, it seems highly unlikely that the researchers would have uniquely beneficial information to offer participants in this case, let alone information that would help with selecting an authorized vaccine. Although the researchers have expertise in infectious disease generally and COVID-19 in particular, they do not have special knowledge to inform selection of a particular authorized vaccine beyond what generally is available to healthcare providers. And unless a participant had an adverse event that clearly can be tied to receiving a trial vaccine (an unlikely circumstance), the researchers would not have specific information from the trial itself that would be useful for selecting an authorized vaccine for the participant.

Given the researchers' lack of uniquely beneficial information for trial participants about selecting an authorized COVID-19 vaccine, Option 1 is most appropriate in that it recommends that participants consult with their primary care providers, rather than the researchers. While sometimes it can be reasonable for researchers to step outside their research role to share valuable

health information, they likely do not have such information in this case. Option 1 is not entirely satisfactory, however, since it ignores the potential social value of continuing the trial with participants who received still-viable vaccines. The research ethics consultants therefore should engage with the researchers to determine whether there is still social value in continuing the trial, and if so, on how to communicate responsibly with participants who received still-viable vaccines about their options for continuing in the trial and delaying receipt of an authorized vaccine.

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