A foundational requirement of ethical research is that persons provide informed consent. Yet, there are exceptions that promote valuable research without unduly compromising participants’ interests. Applicable regulations for federally funded research permit waiver or alteration of consent requirements when certain conditions are met, including that the research poses no more than minimal risk to participants and that it would be impracticable to do without waiver or alteration (1). Determining whether these regulatory standards are met has become increasingly challenging during the coronavirus disease 2019 (COVID-19) pandemic.

As seen in the cases discussed below, studies that were or would have been eligible for consent exceptions before the pandemic may now have heightened risks, rendering exceptions no longer appropriate. Alternatively, studies previously ineligible for consent exceptions may now qualify because the pandemic has rendered what counts as minimal risk more expansive or because COVID-19 limits the practicability of doing research using traditional consent processes. Guidance is needed about how the circumstances of a pandemic influence the applicability of regulatory standards for consent exceptions.

**Minimal Risk**

Before the pandemic, our institutional review board (IRB) approved a trial comparing smoking cessation interventions among older, underserved adults. The study was approved using opt-out consent, a type of consent alteration. Participants must submit samples in person or via a mobile laboratory. Although typically a low-risk activity, during the pandemic, the risks associated with submitting samples may be higher than before. To determine whether opt-out consent remains appropriate, the IRB must determine whether the study remains minimal risk.

The Common Rule defines a minimal-risk study as one in which “the probability and magnitude of harm or discomfort anticipated...are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests” (2). This definition has been criticized as ambiguous because it cannot be understood without specifying whose daily life serves as the benchmark (3).

Everyone’s risks of daily life have increased during the pandemic, but this has occurred unequally. Relevant to the smoking cessation example, older adults and those with many of the comorbidities brought about by smoking are at greater risk for severe COVID-19 and death. Underserved communities have disproportionately been harmed. On its face, such heterogeneity of risk could support an account of minimal risk in which research-related risks are assessed against the daily lives of the target study population. Yet, this would allow those who experience heightened daily risks to be exposed to greater risks under a minimal-risk standard than those who experience lower daily risks—potentially exploiting differences attributable to structural racism and health disparities.

To avoid the problem of affording less protection to disadvantaged populations, many ethicists advocate for using the daily lives of healthy persons living in safe environments as a universal benchmark. Thus, during COVID-19, IRBs assessing minimal risk would be expected to draw comparisons to the daily risks encountered by healthy young adults.

What does this mean for the smoking cessation trial? The IRB now needs to determine whether research-related laboratory visits—and associated severe acute respiratory syndrome coronavirus 2 infection risk—increase participants’ risks beyond what healthy young adults encounter. Because contacts are minimized during mandatory lockdowns and stay-at-home orders, an IRB may determine that the study exceeds minimal risk if it encourages contacts that would otherwise be avoided. However, as communities reopen and contacts increase, benchmark risks also increase such that participants’ interactions with laboratory personnel observing infection precautions could be deemed minimal risk. Alternatively, an IRB may consider whether the higher risks for severe disease in older, underserved adults make the study greater than minimal risk regardless of extant public health advisories. These are challenging decisions.

Coronavirus disease 2019 may also sometimes make consent exceptions easier to justify. Because the benchmark risks have increased during the pandemic, more risks may be subsumed under minimal risk. For example, some IRBs have historically been reluctant to permit investigators to use electronic health records to identify persons eligible for research and to then send text messages to these persons to document study enrollment unless they actively decline. Yet, big data use for purposes like contract tracing, often without consent, has heightened the privacy risks of daily life during the pandemic. Perhaps for this reason, some IRBs—including the IRB at our institution—are now permitting use of electronic health records and text messaging to enroll participants using opt-out consent, an approach deemed both minimal risk and adequately protective of participants’ rights and welfare.
Exceptions to consent also require that the study would be impracticable if traditional consent were required. Notably, this is not a question of ability to obtain a wet signature; video conferencing and electronic signatures make traditional consent possible while following infection precautions (4). However, because COVID-19 has hampered in-person recruitment, studies may not achieve adequate enrollment if traditional consent is required given the less personal nature of remote consent approaches.

Imagine a minimal-risk study of stored biospecimens in which investigators record participant identifiers and link specimens with electronic health records and claims data. Ordinarily, research staff would approach patients in clinic waiting rooms, which often achieves high rates of consent. However, because of COVID-19 visitor restrictions, staff are excluded from waiting rooms. They may instead call or e-mail patients about the study, but they anticipate less success in recruitment. Their concern is not that patients would decline to participate if contacted but that they would be harder to reach. Would a consent exception be appropriate?

In answering this question, note that the regulations regarding consent exceptions focus on whether a study is practicable if traditional consent is required, which may be influenced by the practicability of securing consent, as well as other factors. Such judgments entail a degree of subjectivity but commonly encompass considerations such as whether plausible consent approaches would compromise scientific validity by reducing enrollment or introducing bias due to selective enrollment (5). If requiring traditional consent makes the study impracticable in these ways, an IRB may reasonably grant a consent exception (6), even if no such exception would be granted in nonpandemic circumstances.

CONCLUSION

Coronavirus disease 2019 has influenced minimal risk and practicability determinations. We suggest that IRBs review newly submitted protocols with this in mind and also revisit previously approved protocols to determine whether consent exceptions remain appropriate or may be newly granted. As the pandemic continues, additional guidance from bioethicists and regulators will help determine the best path forward.
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