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Clinical Research Ethics Question of the Month: Intermittent Cognitive Impairment

By Norman M. Goldfarb

You are the chairperson of an IRB. You have learned that one of the sites in a study your IRB approved has enrolled study participants who, because of inconsistent blood flow to their brains, have inconsistent cognitive ability.

Question 1. How much does this situation concern you?

Of the 50 respondents, 60% would have a lot of concern, 36% would have some concern, and 4% would not be concerned.

One respondent said, "Many factors can cause inconsistent cognitive ability: sleep deprivation, narcolepsy, anxiety, PTSD, ICD, Bipolar, ADD, etc. These conditions could mimic fluctuations in cognition, but they aren't conditions that one would necessarily exclude across the board.

One respondent said, "I think it would depend on whether the subject had an authorized representative there who had reviewed the original informed consent and co-signed it after it had been explained."

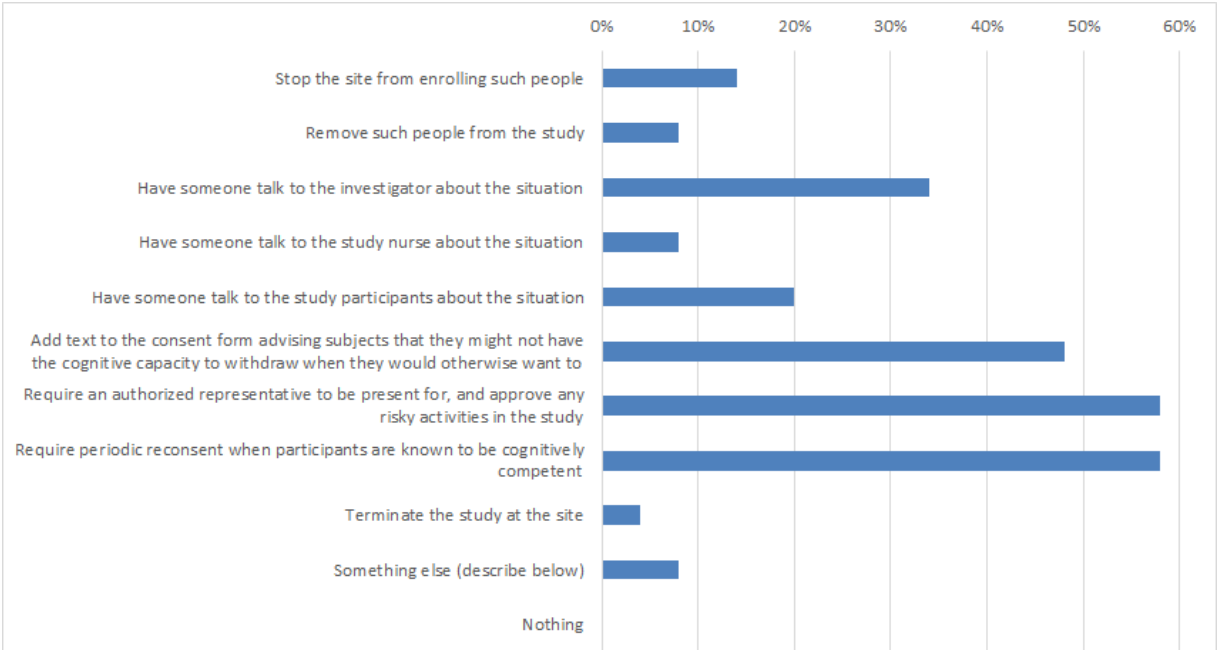
Question 2. How concerned are you that study participants will not be able to make a timely decision to withdraw from the study?

Of the 50 respondents, 60% would have a lot of concern, 32% would have some concern, and 4% would not be concerned.

One respondent said, "As long as the person is aware of the variation in their cognitive ability, is not decisionally/intellectually impaired, and as long as they are NOT consented during a period of diminished cognition, I'd say the consent is legit."

One respondent said, "Unless there are ongoing mental state assessments, participants could continue on treatment well past the time they would if they were in full control of their faculties."

Question 3. What action, if any, should your IRB take?



Fifty-eight percent of respondents would require an authorized representative to be present for and approve any risky activities in the study, 58% of respondents would require periodic reconsent when participants are known to be cognitively competent, .and 48% of respondents would add text to the consent form advising subjects that they might not have the cognitive capacity to withdraw when they would otherwise want to. Only 14% of respondents would stop the site from enrolling such people, and only 8% would remove such people from the study.

One respondent said, "I don't think people should be excluded from the opportunity to consider research opportunities because they have fluctuations in cognitive ability. I think the point of consent is what is important here. Are they competent when they consent? Does a person without these fluctuations think about their level of commitment to study participation every minute of every hour of every day? I think some fluctuation is acceptable."

One respondent asked, "What does the protocol permit? If cognitive impairment is exclusionary, the subjects should be notified and terminated, and the site terminated."

Discussion

All three Belmont principles come into play into this scenario. The principle of beneficence suggests that we should protect subjects without the capacity to protect themselves. The principle of justice suggests that we should make every reasonable effort to allow these subjects to participate in the study if that's what they want to do. The principle of respect for persons suggests that we should make every reasonable effort to let the subjects make their own decisions about participating in the study.

The key question is whether the subjects' intermittent cognitive incapacity is actually interfering with their ability to withdraw consent when it actually matters, e.g., prior to a

risky procedure. Everyone has cognitive impairment when they are sleeping, and that does not raise ethical concerns. A majority of respondents would address this concern by (a) requiring an authorized representative to be present for and to approve any risky activities in the study and (b) require periodic reconsent when participants are known to be cognitively competent. These extra protections seem adequate and reasonable.

Next Month's Question

You are on a committee tasked with advising the FDA on whether certain past actions unrelated to clinical research, e.g., an incident of sexual misconduct, a racist statement, or a business transaction with an unsavory government, should disqualify a physician from conducting clinical studies. Where would you draw the line? Read the full question and give us *your* answer at https://www.surveymonkey.com/r/QHDTH83.

Author

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