COMIRB Guidance: Conducting research with adults with impaired decisional capacity

Adults who lack capacity to provide informed consent are considered a vulnerable population in research and are excluded from most studies. However, certain research—particularly studies investigating conditions like Alzheimer's disease or dementia, and studies involving trauma patients—may require the participation of adults who lack capacity to consent to generate meaningful findings. When such studies are proposed, COMIRB will conduct a thorough review to ensure the protocol includes appropriate ethical safeguards for enrolling and protecting these participants.

What is decisional capacity?

For the purpose of this guidance, decisional capacity refers to a research participant's ability to make an informed decision about whether or not to participate in a study. Specifically, it refers to the ability to comprehend the nature and purpose of the study, the risks and benefits of participation, and the ability to make a reasoned decision to participate or to refuse. Decisional capacity should not be confused with a legal determination of incompetence.

Impaired decisional capacity may be due to a chronic or acute medical condition, a stressful event, intoxication or other circumstance. Decisional capacity may be temporary, may fluctuate, or may decline over time. While some medical conditions are associated with cognitive impairment, decisional capacity can vary patient-to-patient, and circumstance-to-circumstance. For example, a participant with cognitive impairment may have capacity to provide informed consent for a research survey and not have capacity to provide informed consent for a complex clinical trial.

Including or excluding adults with impaired decisional capacity

There is nothing wrong with incidental inclusion of participants with cognitive impairment as long as they have capacity to provide informed consent and can complete the study.

For research seeking to enroll participants who lack the capacity to provide informed consent, the protocol should explain why it is appropriate and necessary to include these participants. COMIRB will consider issues such as, but not limited to, the following:

- The extent to which the research investigates the underlying cause of the incapacity,
- The extent to which the research questions are answerable in those who have capacity to consent,
- The risks and benefits of the research.

Assessing decisional capacity

Specific plans for assessing decisional capacity are protocol-specific. Assessments should be more rigorous as the risks and complexity of the research increases. In general, assessments should cover four domains for decisional capacity:

- Understanding: ability to comprehend information about the study; can be assessed by asking the individual to repeat or paraphrase information back to the person obtaining consent or assessing capacity.
- Appreciation: how an individual uses their understanding of the research and relates this to their own personal circumstances and belief systems; can be assessed by inquiring about any doubts the individual has about the information presented to them, and about the individual's perspective on the likely outcome or consequences of participation.
- Reasoning: ability to provide logic and rationality in weighing participation and alternatives; can be assessed by inquiring about the individual's ability to identify risks, benefits and rational reasons for one's choice.
- Communicating a choice: ability to convey a decision about participation.

Note that a quiz alone assesses comprehension but does not assess capacity.

For more risky or complex research, a more formal assessment should be performed by trained clinicians using validated capacity assessment instruments such as those below. (This is not a comprehensive list.)

- [1]UCSD Brief Assessment of Capacity to Consent (UBACC)
- [2]MacArthur Competence Assessment Tool (MacCAT)

In some cases it may be appropriate for capacity to be assessed by an independent party outside of the research team.

Research teams can also rely on a documented clinical decision regarding capacity in the medical record if that is still active.

Obtaining informed consent from a Legally Authorized Representative (LAR)

To enroll a participant lacking capacity to provide informed consent, a Legally Authorized Representative* may provide informed consent on behalf of the participant. Examples of an LAR include a court-appointed guardianship or someone with a Medical Durable Power of Attorney (MDPOA) for the participant. Research teams can rely on a documented LAR in the medical record if that is still current. Most healthy adults do not have an LAR.

*The federal regulations use "legally authorized representative" as a generic term, with the specific definitions left to state law where the research is conducted. If you are directing research in other states, be aware that who qualifies as a legally authorized representative varies state-to-state. For example, some states have specific laws for a "surrogate" to provide consent for research.

Obtaining informed consent from a Proxy

Colorado state law allows for proxy decision makers for medical treatment. Proxy decision makers can be used to provide consent for a participant who lacks capacity for research as long as the research holds a prospect of direct benefit to participants. The proxy decision-maker may be "the patient's spouse; either parent of the patient; any adult child, sibling, or grandchild of the patient; or any close friend of the patient." The law prescribes a specific process by which clinicians may attempt to identify a proxy decision-maker; this process is described in detail at Colorado Revised Statute 15-18.5-103 (full text available here). Research teams can rely on a documented proxy in the medical record if that is still current.

Regaining capacity

In the event that a participant regains capacity after being initially enrolled by a proxy or LAR, the participant should be informed about the research and asked if they wish to continue in the study. If the participant consents to continue in the study, the participant must sign the informed consent form. Conversely, if the participant wishes to be withdrawn, the study team must respect the participant's wishes.

Additional considerations

If a participant with cognitive impairment has the capacity to provide informed consent, they retain the right to consent on their own behalf and neither an LAR nor a proxy may provide consent on their behalf. However, it may be appropriate to involve an LAR or caregiver in the consent process if the participant's capacity is expected to decline during the course of the study.

Assent

When consent must be obtained from an LAR or a proxy, sometimes it is possible to obtain the assent of the adult participant. Assent in this context means simply an "affirmative agreement" to participate in the research. Since these participants do not have capacity to understand, appreciate, reason, and express a choice about joining the research, their capacity to assent may also be compromised. For this reason COMIRB does not generally require assent forms for adults. Rather, when possible, the study team should help inform the participant about the study as best they can. During the consent process with the LAR or proxy the study team should remain cognizant and respectful of any wishes expressed by the participant. For those adult participants who are able to provide it, the study team should obtain their *affirmative agreement* verbally or otherwise to join the research. If the study team observes dissent from the participant, that is, an objection to participation, the study team should respect their dissent and not enroll them or withdraw them.

For clinical trials that must be conducted in compliance with ICH-GCP, the participants should be informed about the trial in a manner that facilitates their understanding and, if capable, the participant should sign and date the informed consent form. In this context, COMIRB interprets "capable" as meaning that the participant is 1) able to express an affirmative agreement to participate and 2) able to sign and date the consent form.

Writing the protocol

Every protocol submitted to COMIRB should explicitly address the issue of decisional capacity in the "Description of Population to be Enrolled" section. If you do not intend to enroll participants lacking capacity to provide informed consent, this can be addressed by simply listing "Able to provide informed consent" among the inclusion criteria.

For research that enrolls participants lacking capacity to consent, or screens a significant number of participants who might lack capacity to provide consent, the protocol should include the following, as appropriate:

- A clear explanation of why it is appropriate and necessary to include participants who lack capacity to consent.
- A description of how decisional capacity will be assessed prior to initial consent, and identification (by name or role) of the members of the research team who will perform this assessment.
- If a recognized, validated decisional capacity instrument will be used, it should be specifically named with a citation in the protocol, but need not be attached to the submission.
- A description of how decisional capacity will be periodically assessed over the course of the study.
- In situations (e.g., acute trauma) where a participant's capacity to consent may improve during the study, a statement that participants who regain capacity will be asked to provide informed consent to continue in the study if they were enrolled with the consent of an LAR or proxy, and if the participant declines they will be withdrawn for the research.
- For participants whose decisional capacity is expected to decline over the course of the study, describe plans to obtain consent from a LAR or proxy for the participant to continue in the study.
- For participants who will require assistance from a caregiver to complete the study, describe plans to obtain consent from the caregiver at the beginning of the study.
- If informed consent will be obtained from an LAR or proxy, a description of that consent process.
- If some participants may be able to provide assent, verbally or otherwise, describe the assent process.

The following paragraphs may be helpful for the protocol, depending on the specifics of the study. The PI is responsible for editing them for specific protocols. For example, references to proxy consent may not be included in protocols that hold no prospect of direct benefit to participants.

> *Informed Consent: Informed consent must be obtained before any study specific procedures are done. In the case where the participant is unable to provide consent, the participant's proxy or legally authorized representative (LAR) may provide consent for the patient.*

The investigator (or designee) will give the participant or participant's proxy or LAR the IRB-approved consent form to review. The study will be explained to the participant, and/or the participant's proxy or LAR in language they can understand and their questions will be answered. The consent process will be carried out in accordance with federal regulations, state laws and institutional policies. A copy of the signed consent form will be provided to the participant or the participant's proxy or LAR and will be included in the participant's medical record.

Participants will be assessed for return of decisional capacity regularly during study participation. The participant will be informed about the study if and when they become able to provide informed consent, and the participant will be given the opportunity to continue study participation or withdraw. If the participant consents to continue in the study, the participant will be requested to sign a consent form according to the process above. If consent is denied by the participant, they will be withdrawn from the study however, data obtained under LAR consent will be retained. If a participant dies before becoming able to consent, data obtained under LAR consent will be retained.

References

1. Jeste DV, Palmer BW, Appelbaum PS, Golshan S, Glorioso D, Dunn LB, Kim K, Meeks T, Kraemer HC. A new brief instrument for assessing decisional capacity for clinical research. Arch Gen Psychiatry. 2007 Aug;64(8):966-74. doi: 10.1001/archpsyc.64.8.966. PMID: 17679641.
2. Grisso T, Appelbaum PS, Hill-Fotouhi C. The MacCAT-T: a clinical tool to assess patients' capacities to make treatment decisions. Psychiatr Serv 1997; 48:1415–1419.