Enrolling Children with Mitochondrial Disease in a Research Biobank:

The Challenge of Meaningful Assent

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"Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. " - The Belmont Report: Ethical principles and Guidelines for the Protection of Human Subjects of Research, 1979.[1]

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Mitochondrial Disease Biobank

Analytic Goals

- Understand the importance of assent as an adjunct to traditional informed consent
- Identify components of meaningful assent
- Discuss qualities to consider when evaluating whether a child is able to assent

Assent is a child's affirmative agreement to participate in research.[2]

- The idea that children should have a say in whether to participate in research emerged after the publication of the Belmont Report in 1979.[3]
- It is an addition to, and not a substitute for, consent given by the child's legal guardian.
- The goal of assent is to give children some control over their bodies. Obtaining assent demonstrates that, although children are not competent to make medical decisions themselves, they still are humans deserving of respect.

When is assent used?

- The federal law governing research on human subjects states that, when reviewing research protocols involving children, "[T]he IRB shall determine that adequate provisions are made for soliciting the assent of the children…"[4]
- It is unclear what constitutes "adequate provisions." The only other guidance the statute offers is that when determining whether a child is capable of assenting, the IRB "shall take into account the ages, maturity, and psychological state of the children involved."[5]

Who can provide assent?

- The core question is whether a child has the capacity to provide assent for a specific research project. **Capacity** is the ability to understand information that is relevant to making a specific decision.[6] While **competence** is an absolute legal standard, capacity can vary depending upon the task in question.[7]
- In order to streamline assent processes, many research protocols correlate capacity with a certain age. There is no consensus regarding the age at which capacity develops.[8]
- The dispute over capacity for assent stems in part from disagreement over what a child needs to understand in order to provide meaningful assent. The ability to appreciate the concrete process involved in research participation (filling out a form, giving a blood sample) develops much earlier than the child's ability to engage in more abstract though about possible research outcomes (~11 years).[9]
- According to statute, our IRB is given the task of ensuring that protocols have properly chosen an age at which children are able to assent for a particular project. Despite the fact that our protocol was vague about the assent process, we were not given any input by our IRB regarding assent.

Methods

We solicit assent from participants ages 12-18. Much has been written about the appropriate minimum age for assent, and we chose age 12, which is on the higher edge of the minimum age spectrum, since many children with mitochondrial diseases experience cognitive delays.[10]

All assent for this project is obtained through direct conversation between the child and a Biobank staff member, either in person or via phone (and in one instance, via an ongoing e-mail exchange with a 17 year old participant). We considered allowing parents to fill out the consent form with their child, but decided that the potential for parental influence, however benign, would be too great. When the child is not available in person, we rely upon the parent's reporting as to whether the child is able to take part in a discussion about assent. All participants are reconsented at age 18.

So far, all of the children (n=11) approached have demonstrated appropriate understanding of Biobank enrollment, and have agreed to participate. Assent is not a useful research protection unless it means something- merely soliciting a child's assent is not enough. In this project, the child has veto power in regards to research participation: any child who refuses to grant assent is not enrolled in the Biobank, even if parental consent has been granted.

Further improving the current process

- ✓ Re-evaluate current research regarding children's cognitive development to determine whether lowering the project's assent age is appropriate
- ✓ Solicit assent from all children in the targeted age range, regardless of reported neurological status. At this time, we only solicit assent if the child is between 12-18 years of age, and a parent or guardian states that the child has the capacity to assent.
- ✓ Engage the IRB in an ongoing conversation about best practices for obtaining assent

Discussion

It has been almost thirty years since 45 CFR §46.408 became law, yet most researchers are no clearer on what it means for child assent than they were in 1981. The Common Rule, as the law is known, requires adequate provisions be made for soliciting child assent, but without consensus, implementation varies widely, subject to the attention and understanding of institutional IRBs.

Mayo Clinic Mitochondrial Disease Biobank staff seek assent from children between the ages of 12 and 18 years old who are interested in enrolling. This age range was chosen after consideration of both the average child's cognitive development as well as the cognitive challenges that children with mitochondrial disease often face. Reasonable people could disagree with the standard we have set, and as such, it is important to keep apprised of data related to children's capacity for decision-making. Institutional IRBs should act as a partner when researchers must make difficult decisions about assent.

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7. Buchanan, A. Mental capacity, legal competence and consent to treatment. J R Soc Med. 2004 Sep;97(9):415-20
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