MULTI-REGIONAL CLINICAL TRIALS
THE MRCT CENTER OF BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

October 10th 2024

Health Literacy Month Webinar Series Q&A

Session 1: Designing Impactful Informed Consent Processes that Empower Participants

During the October 10th, 2024 webinar, several questions were posed by the audience. Following the webinar, the panelists responded to those audience questions. The following responses were prepared by:

- Sylvia Baedorf Kassis **(SBK)**, Program Director, MRCT Center
- Marianna Azar **(MA)**, Program Specialist, Division of Education and Development, Office of Human Research Protections (OHRP), HHS
- Katherine Blizinsky **(KB)**, Director of Policy, NIH All of Us Research Program

These responses are intended to accompany the webinar recording. The responses reflect the opinions of the panelists and do not necessarily reflect the positions of Brigham and Women's Hospital, Mass General Brigham, Harvard University, or HHS.

Below, the audience comment or question is quoted as written during the webinar. The panelist who commented on each question is indicated. In many cases, the questions and responses have been edited for clarity.

1. **The comment about legal-sounding language is a huge battle with Sponsors. How do we educate Sponsors and not just sites or how do sites communicate with Sponsors to address this concern?**

   SBK: This is an area of continued dialogue and conversation with the sponsors with whom we work, and an area where we continue to champion the use of understandable information given in plain language—even in the use of legalese.

   MA: The OHRP Participant-Centered Informed Consent training program (https://www.hhs.gov/ohrp/education-and-outreach/human-research-protection-

training/participant-centered-informed-consent-training/index.html) names study funders among the target audience. Anyone in the research community who plans, writes, or reviews consent forms for research involving human participants stands to benefit from taking a participant-centered approach to the development of consent documents.

2. Should the training include use of AI-generated text, vetting and verifying its appropriateness?

SBK: Any use of AI-generated text should be reviewed by a person for accuracy and clarity.

MA: AI is a tool that can be used to generate plain-language consent forms. Echoing MRCT Center's point, review by a human for accuracy, clarity, completeness, and so on is needed at this juncture.

3. Do you have suggestions or resources for opt out parental permission forms? Any input or thoughts on "assents?"

SBK: Parental permission forms and assents can follow the regulations around Key Information in order to provide the critical information that will support a person making an informed decision about whether or not to participate. Assent form creation should take into account the age of the participants being asked to assent in order to be effective.

KB: As previously mentioned, age-appropriateness is critical to developing an informed assent process, and that can be a very nuanced endeavor, given people's rapid change in sophistication and intellectual complexity, particularly as children reach the age of majority. It can be helpful to have different assent materials and/or processes based on age groups, such as 7-12 years old and 13 years old to the age of majority. Additionally, timeliness should be taken into account. For example, detailing every aspect of participation over the course of a lengthy study at the point of enrollment may not enable the pediatric participant to provide as meaningfully informed assent as providing brief just-in-time assent immediately prior to a particular research activity.

All of Us is also wrestling with several other considerations as we develop our pediatric participation model. Importantly, these considerations include determining the appropriate course of action when child and parent/guardian wishes do not align.

Parents/guardians often have a legal right to prohibit their children from participating, but there is not always a clear course of action when the child dissents but the parent/guardian is permissive. While the conditions different studies entail will contextually shape the proper route to take, every study will have to address what constitutes dissent on the part of a child, how that may change as a child ages, and how much weight to grant that dissent at different ages given what the research may involve. Study teams should consider the effect on the child of potential parent/guardian-child conflict, as well as the validity of the research outcomes if children are participating involuntarily.

MA: Note that "opt-out consent" is not referenced in the HHS regulations. OHRP is aware that this term is sometimes used by investigators or IRBs to describe a process in which consent or parental permission requirements have been altered or waived, or for which the requirement to document consent or parental permission has been waived. The term "passive consent" is sometimes used in research with children to describe situations in which the investigator can assume that a parent is permitting a child to participate. For example, researchers collecting survey and behavioral data from children at school provide parents with information regarding the study by mail and ask the parent(s) to return a form if they do not want their child to participate. Sometimes, this practice is referred to as an opt-out procedure, which is not consistent with the regulatory requirement for seeking and obtaining parental permission. If the IRB determines that the conditions for waiver of parental permission can be met, then the IRB could waive the requirement for parental permission under 45 CFR 46.408(c) or 45 CFR 46.116(c) or (d). Even though not required by the regulations, an IRB may require that parents be given the opportunity to refuse permission even when the IRB has waived the regulatory requirement to obtain parental permission.

4. Is there a work-around for the "digitally excluded patient" in the development phase?

SBK: A digitally excluded patient is someone who experiences challenges accessing digital health tools and information. The challenges include access, skills, confidence and motivation (https://digital.nhs.uk/about-nhs-digital/corporate-information-and-documents/digital-inclusion/what-digital-inclusion-is). Knowing more about the intended participants can support a multi-faceted approach to inclusion. The need for and feasibility of in-person or telephone-based recruitment, consent, and on-study conversations to support enrollment and persistence in the study should be considered.

KB: While *All of Us* is a digital-first program, we have some lessons learned for bridging the digital divide. Possibly the largest hurdle is informed consent. As has been mentioned, *All of Us* has physical enrollment sites where a potential participant can have an *All of Us* staff member walk them through the informed consent process on a digital device in person. However, this still leaves out individuals not located near a physical location or who cannot travel to one. Screen sharing tele- or video conference capabilities that enable study staff to walk the individual through informed consent and reduce the individual's digital interaction needs down to providing their digital signature may help bridge the divide for many people. Participation in participant provided data collection activities, such as surveys, can be bridged by Computer Assisted Telephone Interviews. In these, the study staff ask the study participant survey questions via telephone and record their responses directly into the participant's digital study account. These are some of the steps *All of Us* have considered or taken, but different solutions may be helpful for different studies. Community and subject matter expert input can assist study staff to find the most effective solutions for their research populations.

5. **This is in regard to the electronic consent process in the presence of a digital divide. There are people who opt for the electronic versus the traditional consent process, but there are situations where individuals who opt for this process, do not have access to sufficient secure internet, using public WiFi. How do you recommend to address the issue of unauthorized 3rd party access to confidential information shared and sent through the electronic process.**

   KB: This is tremendously difficult, and I would certainly point people towards the resource Marianna mentions below. Different studies will need to consider the approaches that work for them, but *All of Us* has largely addressed the issue by providing people with physical locations where they can safely and securely engage with the program. These are largely healthcare provider organizations, offering in-person enrollment and engagement sites throughout the country, but we also have community partner organizations–such as a network of local library-based engagement sites–and our mobile engagement unit (the *All of Us* Bus) that can also provide safe digital spaces.

   MA: As this is a question regarding best practices, I recommend reviewing the content associated with OHRP's 2019 Exploratory Workshop on Privacy & Health Research in a Data-Driven World - https://www.hhs.gov/ohrp/education-and-outreach/exploratory-workshop/2019-workshop/index.html. Also, the following SACHRP recommendations on internet research may be relevant here - https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2013-may-20-letter-attachment-b/index.html.

6. How do you manage videos and other materials for participants who may not be English speakers?

KB: *All of Us* is currently fully available in two languages - English and Spanish. At this time, our content, including scripts for our videos, is developed first in English and subsequently translated into Spanish. For more nuanced or complex materials, we have a Cultural Awareness Committee consisting of consortium members representing many different backgrounds review the materials for cultural competency and relevance. The Spanish translation itself has two phases. In the first phase, a qualified translator translated the English content into Spanish. In the second phase, our Spanish Translation Committee, consisting of individuals representing fluency in Spanish from multiple different Spanish-speaking countries, reviews the initial translation and makes changes as needed to ensure the content is broadly understandable across different dialects. Finally, for our video content, Spanish-speaking individuals provide the verbal content (animated videos) or appear directly in the videos (live-action videos). Because of the complexity of the study, we are limited in our ability to provide extensive support for languages beyond English and Spanish. However, we have several community partners who are leading efforts to build engagement tools for other language groups.

7. If participants fail the formative evaluation, what happens?

KB: We view the consent-embedded formative assessments as teaching tools, one last opportunity to make sure people get key information before they make an important participation decision. Each assessment consists of four to five binary-choice questions focusing on key information in the informed consent documentation. After an individual provides an answer to a question, whether correct or incorrect, the program provides them with feedback. When the person answers correctly, the program reinforces that correct answer by briefly reiterating the salient point(s). When the person answers incorrectly, the feedback includes both the correct response and supporting information to help the individual understand the issues more fully.

The vast majority of people across all consent modules answer all the assessment questions correctly, but about 5% of people incorrectly answer at least one question on at least one assessment. We have implemented a formative assessment precisely for the purpose of catching that 5% of prospective participants. There are many possible reasons why people might answer questions incorrectly, but particularly with a study that is as

complicated and involved as *All of Us*, where there's a lot of information for prospective consenters to digest, we would prefer to overly inform and ensure people who need it get that final clarification opportunity. For more information, please visit our website, where we have posted our core protocol. Conceptual details about the formative assessment can be found at the end of Section 6.6.1.

8. How do you check the health literacy levels of the informed consent document? Do you use software or patient inputs via a patient advocacy group?

SBK: Overall, we advise obtaining feedback on the information and materials from the intended user community. Even one unaffiliated review can help identify areas that need clarification. In terms of readability formulas, the Simple Measure of Gobbledygook (SMOG) is useful in assessing health-related documents (https://www.readabilityformulas.com/articles/how-to-use-smog-readability-formulas-on-health-literacy-materials.php#google_vignette). This requires longer text, however, and thus is not ideal or accurate for shorter materials, which is why external review is so important.