



The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard Bioethics Collaborative

Thursday, February 25th, 2021 | 1:00PM-4:00PM ET
Virtual Meeting

Decentralized Clinical Trials Meeting Summary

1. Introduction

Decentralized clinical trials (DCTs), also referred to as “remote,” “virtual,” or “hybrid” clinical trials, are executed in whole or in part through remote modalities, such as telemedicine, smart phone applications, mobile health wearables, or health care providers who travel to participants’ homes. The February 25th, 2021, meeting of the MRCT Center Bioethics Collaborative convened attendees to examine the ethical challenges presented by DCTs.

2. Meeting Summary

General Considerations

Two general considerations emerged from the discussion. First, participants appeared to share a sense that DCTs should not be held to a different ethical standard than “traditional” clinical trials. Second, there was an acknowledgment that ethical challenges are raised by the specific methods and modalities used to facilitate DCTs. These methods and modalities may be used in all types of studies, including ones that retain a significant in-person element. Because of this, it is imperative to specify which methods and modalities we have in mind when discussing the ethical challenges presented by DCTs.

Generally, DCTs were seen as advantageous primarily for patient-focused reasons, as a way of reducing participant burden, time, and costs and increasing access to research. It was noted, however, that there is little rigorous empirical work to support this sense and few studies have surveyed participants to understand their experiences, preferences, or concerns about DCTs.

Home Visits

Bioethics Collaborative attendees considered the challenges that may arise during home visits in DCTs. Privacy challenges arise when neighbors and other community members observe health care workers visiting participants’ homes, allowing inferences and assumptions about the participant’s health that may be sensitive and risk stigma. While meeting attendees agreed that home visits in DCTs may serve a justice-promoting function (thereby increasing research access), individuals who lack basic utilities, space, and comforts may not wish an unfamiliar person in their home but not feel empowered to say so.



These concerns highlight the importance of establishing relationships of trust between home health care researchers and participants, as well as the wider community; how to build such trust was a recurrent theme of the afternoon. Attendees suggested that health care providers could—or should—spend time getting to know the research participant before starting study procedures; that time, however, is often not compensated. In addition, there may be a more natural affinity if the provider is of similar background to the participant, a possibility that has implications for workforce development.

From the perspective of home health care staff, safety concerns can provide obstacles to study conduct. A lack of internet access or cellular coverage at a participant's home may prevent a visiting study nurse from reporting adverse events or communicating with the PI in a timely fashion, and there may even be situations in which healthcare workers visiting a home feel isolated, unsafe, or threatened due to erratic participant behavior or psychosocial conditions.

The home context may also complicate interactions between researchers and participants in more subtle ways, such as when individuals who previously consented to participate in research appear disinterested or disengaged once study team members arrive at their home. Participants may be more hesitant to express their desire to withdraw from the research to study staff who are already in their home. Conversely, study staff may understandably struggle with how to approach seemingly ambivalent or uninvested participants during home visits.

Attendees suggested that Institutional Review Boards (IRBs) may not appreciate these and other considerations and that review of home health care visits in DCTs may require attention to a different set of issues than those typically considered in standard IRB review of research sites and conduct.

Mobile Health Technologies

In the context of DCTs using mobile health technologies, concerns about justice may arise when individuals lack access. To some extent, sponsors and researchers are able to mitigate these issues by providing the necessary devices and software to research participants. As an additional measure, providing education and technical support further combats disparities in digital access. One attendee noted that education and technical support should be made available to both research participants and study staff, as it should not be assumed that research staff are familiar with the rapidly expanding number of devices and software platforms that can be used in DCTs.

More difficult to overcome are issues of justice raised by disparities in digital connectivity (e.g., Internet access, cellular coverage, etc.). One attendee recommended that research stakeholders might mitigate issues of connectivity by providing research participants with devices outfitted with multi-carrier SIM cards. Multi-carrier SIM cards allow a device to connect to the cellular carrier that provides the best service in a given location. Practical technological solutions deserve sustained exploration at the sponsor level.

Issues of justice and access also arise in DCTs due to the paucity of technologies available in languages other than English. While translation can mitigate some of the issues, it is not always



an easy fix. For example, it would be insufficient to translate a mobile application used in a DCT without also translating other aspects of the technology or the platform used to run the app. Additionally, translation capabilities may often be constrained for iconographic languages or languages that read from right-to-left. Attendees noted that technology companies are increasingly aware of the limitations posed by offering products exclusively in English; hope was expressed that technologies may soon be more widely available in non-English languages.

Questions of trust resurfaced in the discussion on mobile technologies. Among other issues, sponsors should qualify mobile technology vendors on trustworthiness and transparency, such as ensuring that participant data will not be shared with other parties. While IRBs also play a role in evaluating mobile technologies, IRBs often may struggle to review DCTs that use mobile technologies: each mobile technology has a unique privacy policy and/or end-user license agreement, often containing different substantive privacy and confidentiality risks. These agreements are often lengthy and complex, and they may contain exculpatory language that is prohibited by US regulations governing research with humans. Meeting attendees suggested that IRBs could perhaps adapt by reviewing and approving a set of different general types of remote modalities that are appropriate for use in DCTs, working toward templated approaches to conceptualizing the risks and disclosing them in consent forms

Flexibility

Flexibility will foster respect and trust: providing research participants with choices, when possible, is important, such as whether they prefer to visit a research site, use a remote modality, or have a home visit for all or some of their study visits. Research participants might appreciate the opportunity to exercise choice and exert control. Offering these flexibilities also minimizes assumptions about participant wishes and burdens, particularly in advance of feedback about participant experiences.

One Bioethics Collaborative attendee shared a compelling anecdote to illuminate how DCTs may shift, but not reduce, participant burden. The attendee was a clinical trial participant who had an adverse event related to the investigational product. At a significant distance from the research site, and on advice of the study investigator, they received treatment at a local hospital; the emergency treatment led to billing issues that remained unresolved for two years. The lack of affiliation between the local hospital and the research site left the attendee unsupported to navigate and resolve the billing issues. While these types of events are unpredictable, research participants appropriately anticipate that the research team will help them navigate situations related to their research participation.

Changing Roles and Responsibilities

As the roles of the research site and the investigator change in DCTs, sponsors may assume some of the responsibilities typically held by these parties such as compliance with local laws, a responsibility traditionally executed by the research site. Sponsors in DCTs may be directly involved in participant recruitment, perhaps entering into arrangements with clinical laboratories, pharmacies, and primary care providers, among other health care providers, to screen patient



information and alert patients to clinical trial opportunities. While these actions may expedite the recruitment process and increase access to trials, they change research relationships.

The potential for direct sponsor interactions with participants raises novel ethical and practical questions. Unlike an investigator, the sponsor is not in a treatment relationship with the participant, and whether the interaction would be interpreted as the practice of medicine should be considered. Sponsors do not have a fiduciary relationship with participants. The Secretary's Advisory Committee on Human Research Protections will soon release a draft guidance document on the increasing role of the sponsor in DCTs.

Conclusions

Bioethics Collaborative attendees appreciated the ethical challenges posed by DCTs as well as the likely benefits. Researchers, sponsors, IRBs, and participants will utilize and continue to improve the methods and approaches of DCTs to increase their flexibilities and advantages.

3. Potential Future Work

- Explore and summarize evidence on research participant experiences with the various methods and modalities used in DCTs, and call for further empirical research if necessary:
 - Caution stakeholders from prematurely calling the methods and modalities in DCTs successes without evidence of the participant experience across various populations
 - Build a points-to-consider list on the potential challenges presented by home visits and mobile technologies
 - Advance the argument for why it may be best to give research participants the flexibility to determine whether they visit a research site, use a remote modality, or have a home visit for all or some of their study participation.