ETHICAL RESPONSIBILITIES TOWARD INDIRECT AND COLLATERAL PARTICIPANTS IN PRAGMATIC CLINICAL TRIALS

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March 18, 2016 NIH Collaboratory and PCORnet Grand Rounds
FUNDING AND DISCLOSURES

- The views presented here are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health or the Patient-Centered Outcomes Research Institute (PCORI), its Board of Governors or Methodology Committee, or other participants in the National Patient-Centered Clinical Research Network (PCORnet).

- Jaye Bea Smalley is an Engagement Officer at the Patient-Centered Outcomes Research Institute. Maria W Merritt, Sana Al-Khatib, Debbe McCall, Karen Staman, and Carl Stepnowsky have no conflicts of interest.

- This work is supported by the National Institutes of Health (NIH) Common Fund, through a cooperative agreement (U54 AT007748) from the Office of Strategic Coordination within the Office of the NIH Director.
KEY ISSUES

• Research subjects, or “direct participants,” have been explicitly defined in the context of cluster randomized trials as:
  ➢ Individuals being directly intervened upon and/or
  ➢ Individuals from whom personal identifiable data are being collected for the purposes of the research

• Common rule does not provide clarity around various types of environmental manipulation

• Guidance from the SACHRP encompasses both immediate and mediated exposure
KEY ISSUES

• Ottawa Statement restricted to immediate exposure
• Unique nature of PCTs—typically imbedded in the delivery of care and require a systematic approach to identifying participants
• PCTs often expose individuals intentionally and unintentionally to environmental manipulation
• Purpose of PCTs is to generate evidence for healthcare decision makers, clinicians, patients, and others
SCOPE

- To examine how to act properly toward people affected by the conduct of a pragmatic clinical trials
- Consider the unique nature of pragmatic clinical trials
- Expand the concept of research participation
- Distinguish among three categories of research participants
SCOPE

- Explore what participation mean for the ethical responsibilities of PCT investigators and other PCT leadership
- Consider the ethical implications—not regulatory—of involving indirect and collateral participants
- Communication and dissemination strategies for informing and engaging participants
- Promote public trust and understanding for PCTs
KEY FINDINGS

• Risks and benefits to which all participants are exposed should be weighed to ensure that their rights and welfare are protected accordingly.

• Regardless of distinctions among participants, there should be no distinction in our imperative to build trust and consider protections for all participants.

• Types of participants in PCTs vary considerably and each trial must be carefully reviewed in consideration of identifying all participants.
DISTINCT CATEGORIES OF RESEARCH PARTICIPANTS

- Direct participants
- Indirect participants
- Collateral Participants
DIRECT PARTICIPANTS

**Definition:** 1. Individuals being intentionally targeted by a study intervention, whether through immediate or mediated exposure
2. Individuals on whom personal identifiable data are being collected for the purposes of the PCT

DIRECT PARTICIPANTS

Responsible parties: IRB
Action: No additional recommendations
Definition: Individuals (other than direct participants) whose rights and welfare may be affected by the intervention through their routine exposure to the environment in which the intervention is being deployed.
**Indirect Participants**

**Responsible parties** Gatekeepers

**Action:**
- Investigators, IRBs, health systems leadership and others engaged in research enterprise should work to identify and delineate risk
- PCT information should be adequately communicated and disseminated to indirect participants, and to the institutionally defined leadership and officials who bear responsibility
**COLLATERAL PARTICIPANTS**

**Definition:** Patient and other stakeholder communities who may be affected by the occurrence and findings of PCTs.

COLLATERAL PARTICIPANTS

**Responsible parties:** Gatekeepers, patient groups, community members

**Action:**

- Patient and stakeholder engagement in research process
- Effective communication and dissemination of research information
- Educate communities about the lack of evidence for healthcare decision-making
- Further research is required to evaluate when and how to engage collateral participants
EXAMPLE OF COLLATERAL PARTICIPANTS

- PCORI’s Patient-Centered Outcomes Research Network (PCORnet) and the member Clinical Data Research Networks (CDRNs) and Patient-Powered Research Networks (PPRNs)
- PCORnet’s first clinical trial for the Optimal Aspirin Dose for Patients with Coronary Artery Disease
- PCORI’s Advisory Panels
The **Pragmatic Trial of Video Education in Nursing Homes (PROVEN)** trial is underway to evaluate the effectiveness of advance care planning (ACP) videos in reducing hospitalizations, hospice election, and other burdensome transitions among seriously cognitively and functionally impaired nursing home residents with multiple co-morbidities served by two large health-care systems.
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<th><strong>DIRECT</strong></th>
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<td>The patients in the intervention of the systems participating in the trial and nursing home staff who receive training on delivering video intervention</td>
<td>All other nursing home staff and patients’ families</td>
<td>Other nursing home professionals, attorneys involved in ACP, community members, and caregiver advocacy groups who work with patients their families, and professional associations for nursing home administrators and staff</td>
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The **Lumbar Imaging with Reporting of Epidemiology (LIRE)** trial is underway to reduce overtreatment of back pain patients. In this study, at clinics randomly assigned to receive the intervention, epidemiologic benchmarks are inserted into lumbar spine imaging reports to provide context to the findings.
## CASE STUDY

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<td>Patients of primary care providers, primary</td>
<td>Informatics personnel, radiologists, healthcare operations</td>
<td>Community members served by the hospital, patients with a similar condition, and professional associations for healthcare providers</td>
</tr>
<tr>
<td>care providers, physician assistants and</td>
<td>personnel, healthcare operations personnel, relevant department</td>
<td></td>
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<tr>
<td>other non-physician primary care providers.</td>
<td>chairs, non-trial patients in need of services</td>
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The Active Bathing to Eliminate Infection (ABATE) trial is underway to reduce multidrug-resistant organisms and hospital infections by comparing usual bathing of non critically ill hospitalized patients to universal bathing with chlorhexidine plus nasal mupirocin for those who are carriers of methicillin-resistant Staphylococcus aureus (MRSA).
## Case Study

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<td>Patients in the control and intervention units of the hospitals participating in the trial. Nurses and nursing assistants (received protocol training)</td>
<td>All other hospital staff and patient visitors to participating units, and healthcare facilities that receive transferred patients from participating hospitals</td>
<td>Other hospital units, the community served by the hospital, and the professional associations for healthcare providers</td>
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CONCLUSION

- These distinctions aim to support PCT funders, sponsors, investigators, host sites, patient/caregiver organizations, and other interested parties in acting rightly toward various people affected in various ways by PCT research programs.

- Identifying participants is an important first step in the early phases of a PCT.

- Educate those engaged on the urgent need for evidence based practices and the opportunity to address evidence gaps through PCTs.

- If culture change occurs such that participants are indeed more active participants in the process, we hope all participants, direct, indirect, or collateral, will be empowered and informed.
Robert Califf and Jeremy Sugarman provided input on earlier versions of this article.

Thanks also goes to Tammy Reece, Susan Huang, Jeffrey Jarvik, and Vince Mor for their assistance with the development of this article.

The authors would also like to acknowledge the important contributions of two anonymous reviewers.