NIH Collaboratory

Health Care Systems Research Collaboratory

Rethinking Clinical Trials®

Ethical and Regulatory Oversight Considerations

Julie Kaneshiro, MA
Office for Human Research Protections

Kevin Weinfurt, PhD
Duke University School of Medicine

Essentials of Embedded Pragmatic Clinical Trials Seminar

Learning goal

Learn about the regulatory and ethical considerations specific to conducting ePCTs

Important things to know

- Ethical analysis for ePCTs is a work in progress
- Federal and local policies and/or their operationalization regarding the oversight of ePCTs are in flux
- There is often confusion and misunderstanding about ePCTs on the part of patients, providers, IRBs, and DSMBs

ePCTs are motivated by ethical imperatives

ePCTs also raise interesting ethical and regulatory questions

Evolving understanding of unique ethical/regulatory issues for ePCTs

- Informed consent
- Data monitoring
- Defining minimal risk
- Research/quality improvement distinction
- Vulnerable subjects
- IRB harmonization
- Identifying direct and indirect subjects
- Gatekeepers
- FDA-regulated products
- Nature of ePCT interventions
- Privacy

Resources: Regulatory & ethical challenges of ePCTs

Introduction

and

Informed Consent

From the *Living Textbook of Pragmatic Clinical Trials*
www.rethinkingclinicaltrials.org

Resource: Additional readings on regulatory/ethical considerations

Special Issue of Clinical Trials

From the *Living Textbook of Pragmatic Clinical Trials*
www.rethinkingclinicaltrials.org

Current ethics/regulatory in flux

Determining if the Common Rule applies

- ✓ The activity is conducted or supported by HHS
- ✓ The activity is non-exempt human subjects research

To determine whether the activity is non-exempt human subjects research, **ask these questions:**

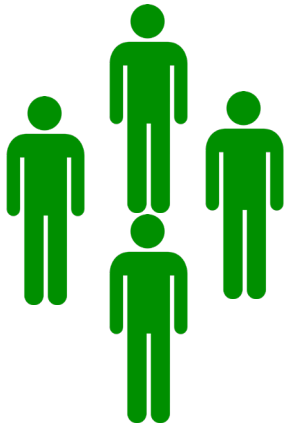
1) Does the activity involve **research**?
2) Does the research involve **human subjects**?
3) Is the human subjects research **exempt**?

Does the ePCT involve a research intervention?

Definition of research:

Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge

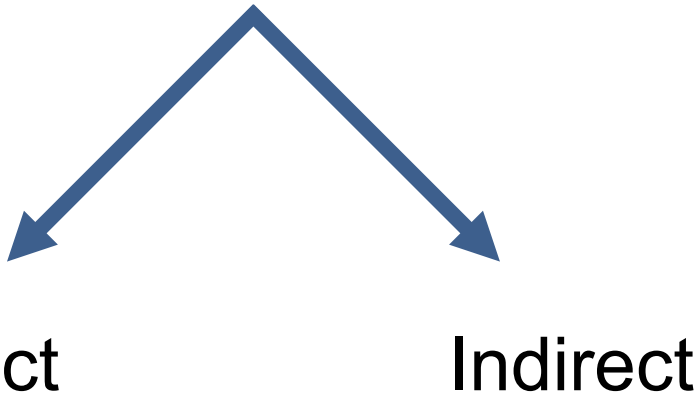
Regulatory & ethical challenges of ePCTs



Ethical, not regulatory, question:

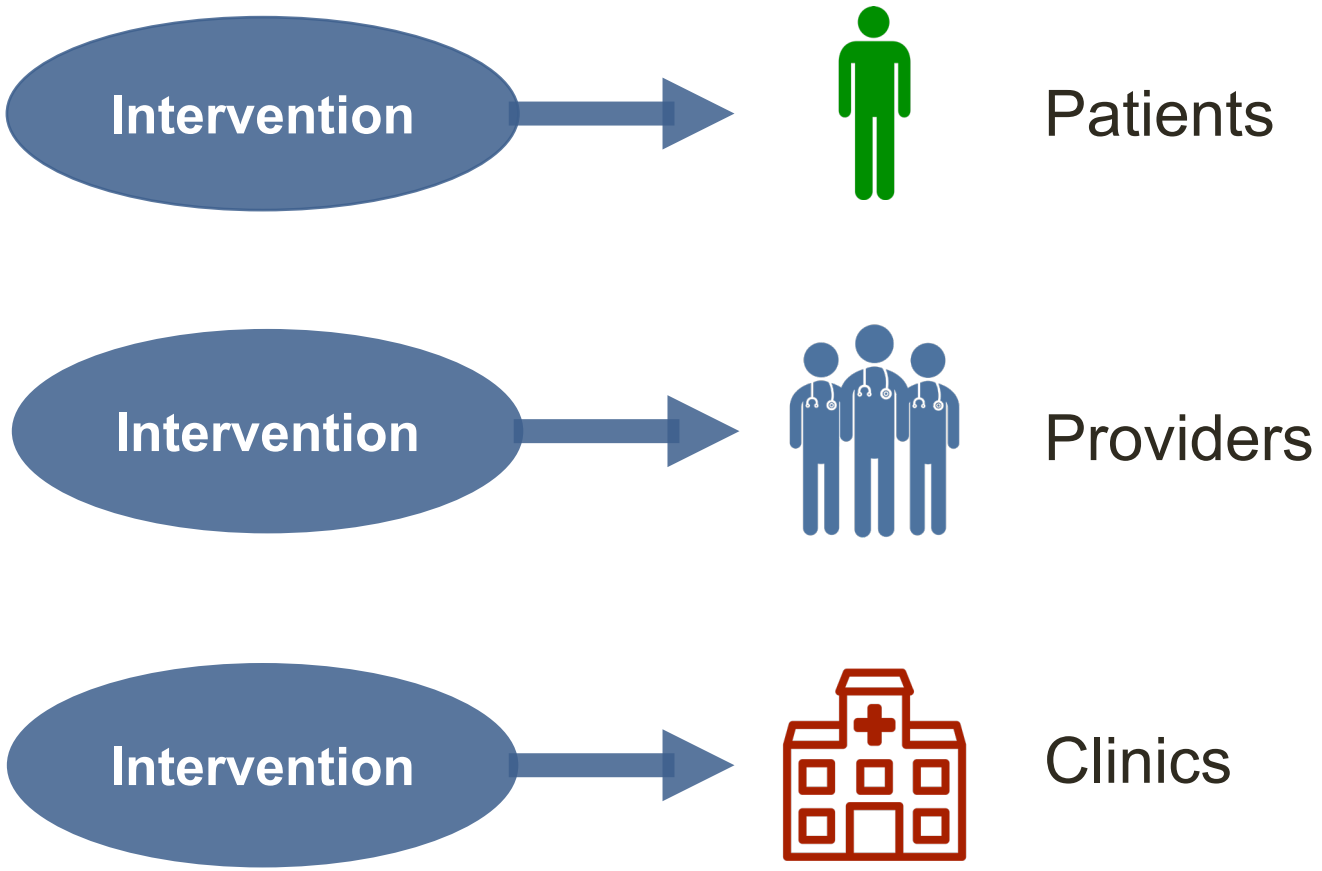
Whose rights and welfare need to be protected?

Types of participants in an ePCT

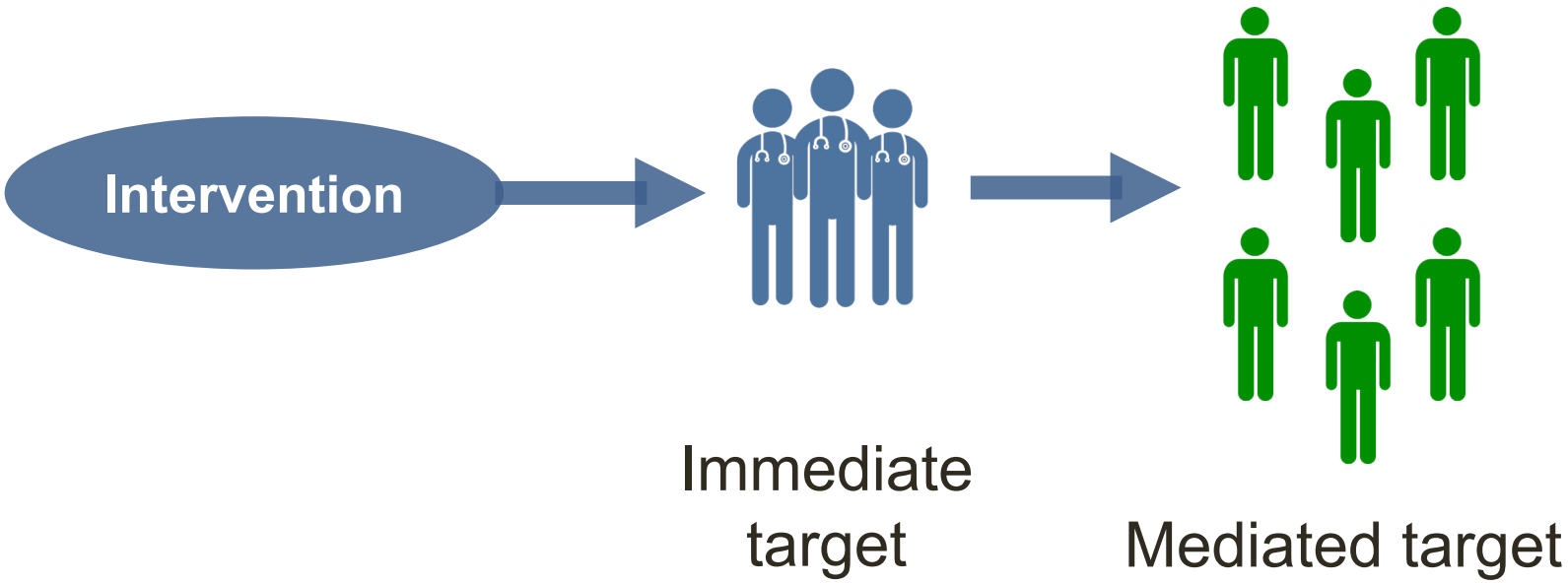


Direct participants

Immediate or mediated targets of the intervention

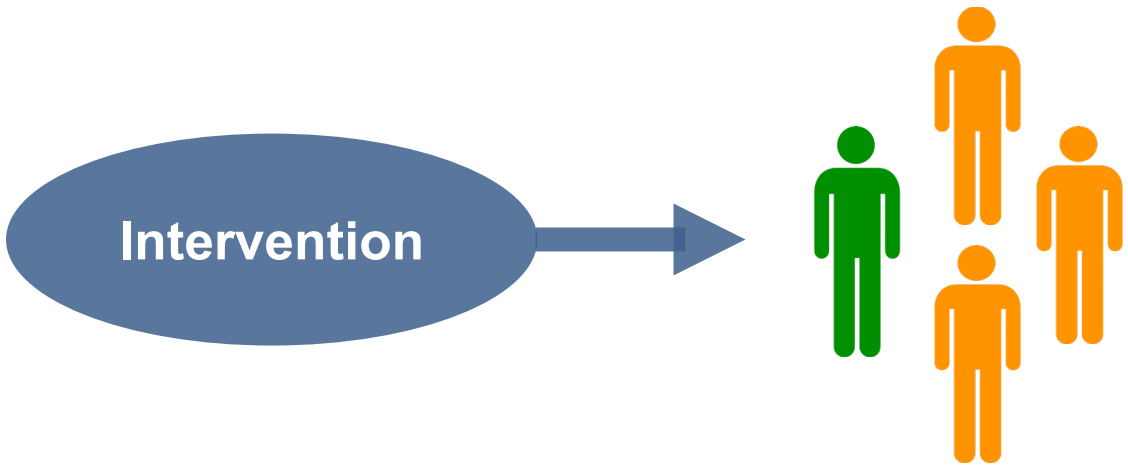


Direct participant



Indirect participants

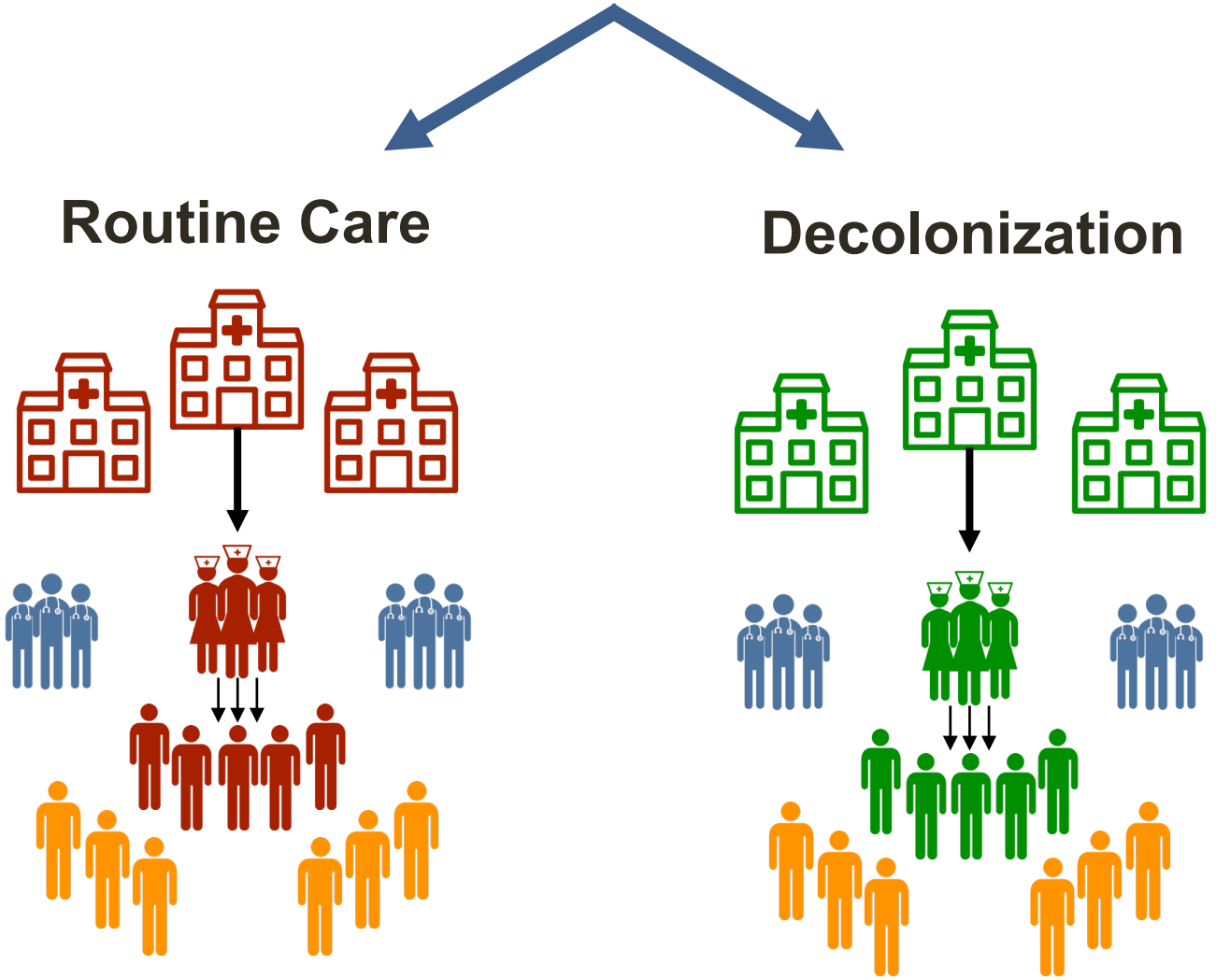
People affected by routine exposure to the environment (eg, family/caregivers)



Case study from NIH Collaboratory: Active Bathing to Eliminate (ABATE) Infection

- Cluster trial comparing 2 quality improvement strategies to reduce multidrug-resistant organisms and healthcare-related infections in non-ICU population
- 53 hospitals
- 331,584 patients

Indirect participants: ABATE example



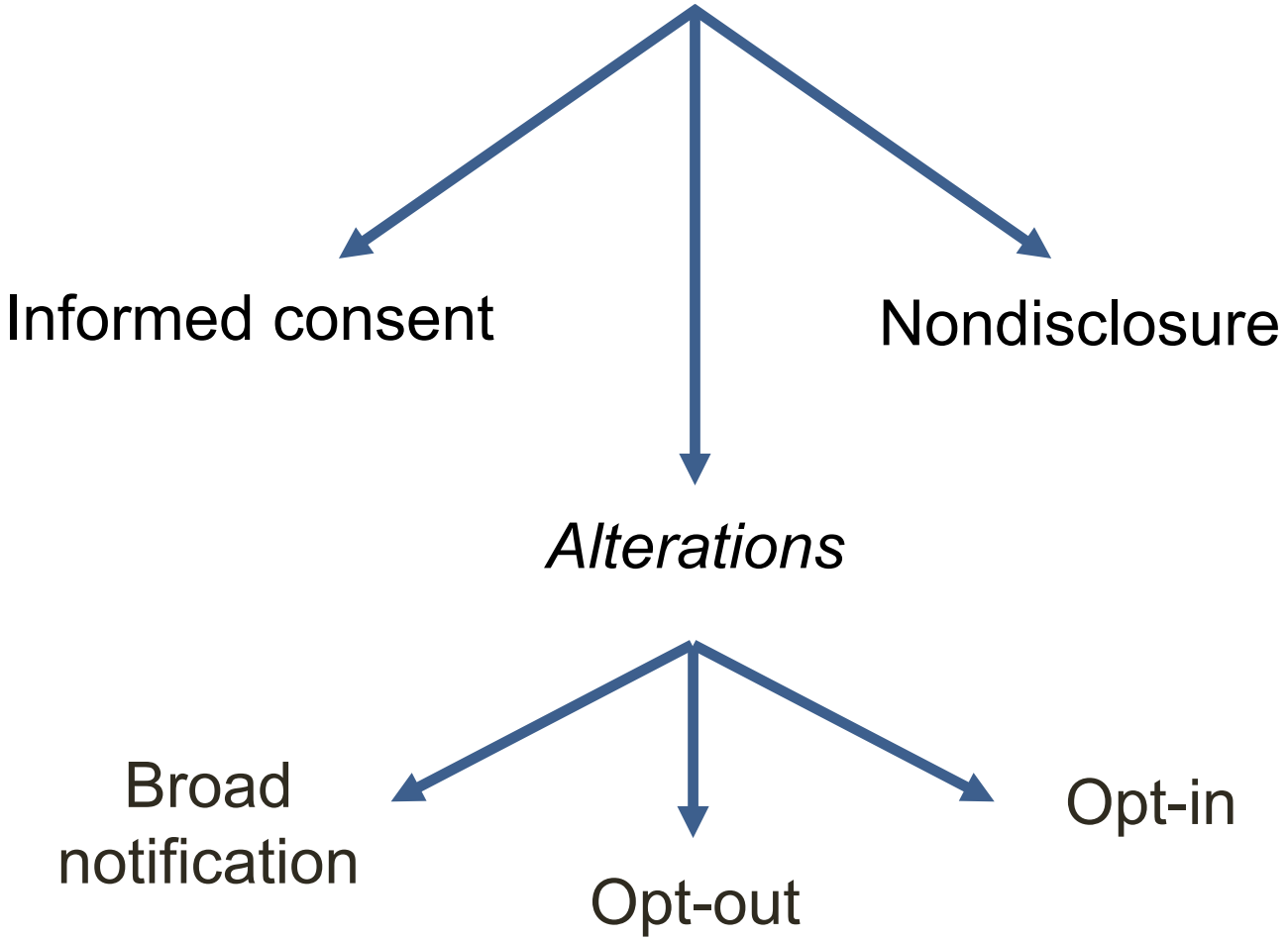
Regulatory Perspective: *Who are the subjects in ePCTs?*

Definition of human subject:

Human subject means a living individual about whom an investigator conducting research:

- Obtains **information or biospecimens** through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
- Obtains, uses, studies, analyzes, or generates **identifiable private information or identifiable biospecimens**

Approaches to notification & authorization



Resource: Regulatory and ethical challenges of ePCTs

Consent, Disclosure, and Nondisclosure

From the *Living Textbook of Pragmatic Clinical Trials*
www.rethinkingclinicaltrials.org

Resource: Alternative approaches

Alternative Approaches to Disclosure and Authorization

From the *Living Textbook of Pragmatic Clinical Trials*
www.rethinkingclinicaltrials.org

Working with human subjects oversight bodies

- Institutional review boards (IRBs)
- Data monitoring committees (DMCs)
  - Data safety and monitoring boards (DSMBs)

Requirement for single IRB review

Applicability

- U.S. institutions engaged in cooperative research for the portion of the research conducted in the United States
- Does not apply:
  - When more than single IRB review is required by law (including tribal law)
  - Whenever any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context

Compliance date for sIRB provision: ***January 20, 2020***

Data monitoring committee

Group of experts that reviews the ongoing conduct of a clinical trial to ensure continuing patient safety as well as the validity and scientific merit of the trial

Unique considerations for monitoring ePCTs

- Poor adherence to intervention: problem or finding?
- Inference about adverse events
  - Availability of clinical data to assess relatedness
  - Should adverse events still be monitored?
- Limited or delayed access to study outcomes during study conduct
- Are interim analyses actionable?

Adapted from Greg Simon, PCT Grand Rounds, December 8, 2017

Important things to do

- Designate someone to track local and federal regulatory developments and serve as liaison with regulatory/oversight bodies
  - You can contact OHRP for guidance
- Budget sufficient time for proactive education and negotiations with relevant regulatory/oversight bodies
- Identify all parties who might be affected by the study and its findings; consider protections

OHRP Contacts and Resources

- Please contact us or submit your questions to OHRP@hhs.gov
- Visit OHRP website at www.hhs.gov/ohrp
- Bookmark this page for quick reference to OHRP resources on the revised Common Rule: www.hhs.gov/ohrp/education-and-outreach/revised-common-rule/index.html

OHRP PUBLIC OUTREACH WEBSITE

www.hhs.gov/About-Research-Participation

Resources for the public to learn about participating in research and making informed decisions

Videos

Information

Tools

OHRP Office for Human Research Protections | *Protecting Human Subjects in Research*