Then, Now and the Future: Ethics and Regulatory Challenges in Pragmatic Clinical Trials

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Background Conditions

- There is a broad moral claim to obtain evidence to improve clinical practice since most decisions are now made without reliable evidence to know which choices optimize health.

- Technology permits conducting large scale research and cohort finding for rare diseases and special populations, often with minimal incremental risks and burdens and less cost.
An Ethics Framework for a Learning Health Care System: A Departure from Traditional Research Ethics and Clinical Ethics

BY RUTH R. FADEN, NANCY E. KASS, STEVEN N. GOODMAN, PETER PRONOVOST, SEAN TUNIS, AND TOM L. BEAUCHAMP
March 2013

Study of Babies Did Not Disclose Risks, U.S. Finds
By SABRINA TAVERNISE

Study of premature babies with Children’s Mercy input sparks debate

Feds Fault Preemie Researchers For Ethical Lapses
By RICHARD SACK

Parents Not Informed Premature Babies at Risk in Study

Slide courtesy of Steven Joffe, MD, MPH
Major Areas of Controversy

• Consent
• Risks and benefits
• Standard of care
Alternative Bioethical Views

The OHRP and SUPPORT — Another View
Ethics and Regulatory Issues in the Collaboratory

- Multi-stakeholder conversations at the planning stage convened by the Ethics & Regulatory Core
  - Investigators and research teams
  - Sponsors
  - IRBs
  - Regulators
- Minutes reviewed and posted
- Updates following project implementation

https://rethinkingclinicaltrials.org/demonstration-project-ethics-and-regulatory-documentation/
Public Meeting August 28, 2013

Public Meeting Transcript
A transcript for the meeting has been posted. View transcript here or in PDF format (PDF - 940 KB). OHRP staff created this transcript from the video captions by correcting transcription errors and identifying the speakers. The caption text accompanying each video is unedited.

August 26, 2013 – Full Meeting Agenda
A full agenda for the August 28, 2013 public meeting has been added to the docket, and is available at this page of the docket.

August 21, 2013 - Information on viewing the August 28, 2013 HHS Public Meeting on Protections of Human Subjects and Research Studying Standard of Care Interventions
For those who cannot attend the August 28, 2013 HHS Public Meeting on the Protections of Human Subjects and Research Studying Standard of Care Interventions, HHS is providing an option to view the public meeting via live streaming technology. To view the HHS public meeting live on August 28, 2013, go to the HHS live streaming site at www.HHS.gov/live, then hit the “Click to Play” arrow.

On August 16, 2013, HHS added to the docket a basic agenda for the meeting. The basic agenda is available in PDF or Microsoft Word format at this page of the docket.

In a Federal Register notice on June 26, 2013 (PDF - 107 KB), HHS announced a public meeting to be held on August 28, 2013, to seek public input and comment on how certain provisions of the Federal policy for the protection of human subjects should be applied to research studying one or more interventions which are used as standard of care treatment in the non-research context.

http://www.hhs.gov/ohrp/newsroom/rfc/Public%20Meeting%20August%2028,%202013/aug28public.html
IOM/NAM Workshop

Meeting

Ethical Review and Oversight Issues in Research Involving Standard of Care Interventions: A Workshop

When: December 2, 2014 - December 3, 2014 (8:30 AM Eastern)
Where: National Academy of Sciences Building (Lecture Room) · 2101 Constitution Avenue, NW, Washington, DC 20418

Topics: Biomedical and Health Research, Public Health
Activity: Ethical Review and Oversight Issues in Research Involving Standard of Care Interventions: A Workshop
Board: Board on Health Sciences Policy

Other Meeting Resources

- Agenda
- Videos
+ Presentations

Workshop in Brief

Standard of Care - Workshop in Brief

Committee Information

- Committee Roster

EXPLORING THE ETHICAL AND REGULATORY ISSUES IN PRAGMATIC CLINICAL TRIALS
LEADING A SERIES OF 3 ARTICLES ON DIFFERENT ASPECTS OF THIS TOPIC

COLUMN
Clinician Trialist Round 2B: WhenRCT Participants are Lost to Follow-Up, Part I: Why Even a Few Can Matter
M. Halp, P. Albanese, and D. I. C. B. Jett

TRIBUTE
An Interview with David Sackett
M. Halp and P. Albanese
Clinical Trials Special Series
Guest Editors: Jeremy Sugarman and Robert Califf

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

http://ctj.sagepub.com/content/early/recent
INTRODUCTION

Ethics of research in usual care settings: Data on point

Jeremy Sugarman MD, MPH, MA
Signals from Early Empirical Research

• At least a substantial minority of people want to be meaningfully engaged in research decision-making
  – Regardless of risk
  – Regardless of health care norms
• It is unclear if the nature of these activities were clearly understood and their best interests were not compromised
• Since requiring traditional written consent may compromise some research this issue must be better understood
Subsequent Issues

• Standards for data monitoring
  – Points to consider
  – Sample charter
• Incidental findings/PCT collateral findings
• Payments and incentives

https://rethinkingclinicaltrials.org/cores-and-working-groups/regulatory-ethics/
Now and on the Horizon

• Ethics in research design
  – Stepped wedge
  – Implementation science
• Responding to PRO signals
• Disclosure and authorization alternatives
  – Opting out
  – Broad notification
• Clinicians obligations to participate
• Data sharing

https://rethinkingclinicaltrials.org/cores-and-working-groups/regulatory-ethics/
Concluding Comments

• Addressing the ethical and regulatory challenges of PCTs is surprisingly complex
• The well-rehearsed habit of ‘adding protections’ in research ethics may not be actually be providing needed protections and may inadvertently stymie important research efforts
• Additional data and deliberation should help inform the development of appropriate policies and procedures