

# 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

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## Study of Babies Did Not Disclose Risks, U.S. Finds

By SABRINA TAVERNISE

## THE KANSAS CITY STAR.

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NEWS

## Study of premature babies with Children's Mercy input sparks debate

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## Feds Fault Preemie Researchers For Ethical Lapses

by RICHARD KNOX

April 10, 2013 3:14 PM

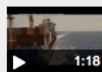
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1:18

## Parents Not Informed Premature Babies at Risk in Study



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ANALYSIS AIR DATE: April 11, 2013

## Hospitals Dispute Failure to Disclose Clinical Study Risks for Premature Infants

The Washington Post PostTV Politics Opinions Local Sports National World

## Health & Science

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## Watchdog agency criticizes ethics of study of premature infants

The New York Times

## The Opinion Pages

WORLD U.S. N.Y. / REGION BUSINESS TECHNOLOGY

EDITORIAL

## An Ethical Breakdown

Rethinking Clinical Trials

March 2013

Slide courtesy of Steven Joffe, MD, MPH

# Major Areas of Controversy

- Consent
- Risks and benefits
- Standard of care

# Alternative Bioethical Views

THE NEW ENGLAND JOURNAL OF MEDICINE

CORRESPONDENCE



The OHRP and SUPPORT

THE NEW ENGLAND JOURNAL OF MEDICINE

CORRESPONDENCE



June 2013

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 Hearing

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## 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](http://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

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## Meeting



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## 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](#)



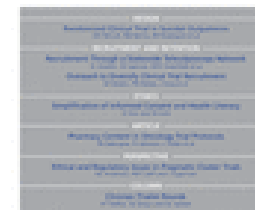
Sugarman J, Califf RM. Ethics and regulatory complexities for pragmatic clinical trials. *JAMA* 2014; 311: 2381-2382.

Anderson M, Califf R, Sugarman J, for the NIH Health Care Systems Research Collaboratory Cluster Randomized Trial Workshop. Ethical and regulatory issues of pragmatic cluster randomized trials in contemporary health systems. *Clin Trials* 2015; 12: 276-286.

VOLUME 12, NUMBER 3, JUNE 2015 ISSN 1745-0145

## CLINICAL TRIALS

Journal of the Society for Clinical Trials



Full contents are listed on the back cover

SCT



VOLUME 12, NUMBER 5, OCTOBER 2015 ISSN 1740-7745

# CLINICAL TRIALS

Journal of the Society for Clinical Trials

EXPLORING THE ETHICAL AND REGULATORY ISSUES  
IN PRAGMATIC CLINICAL TRIALS  
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Part I: Why Even a Few Can Matter  
M Walsh, PJ Desveaux and DL Sackett

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An Interview with David Sackett  
RB Haynes and SN Goodman

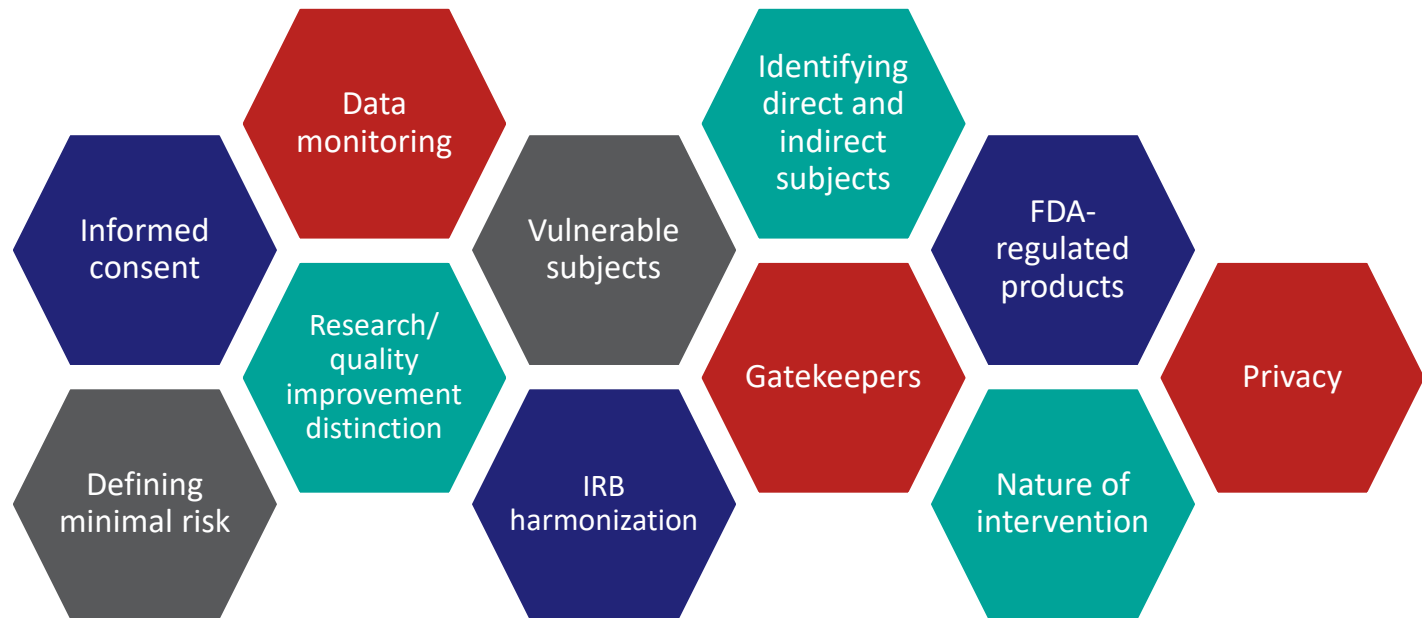
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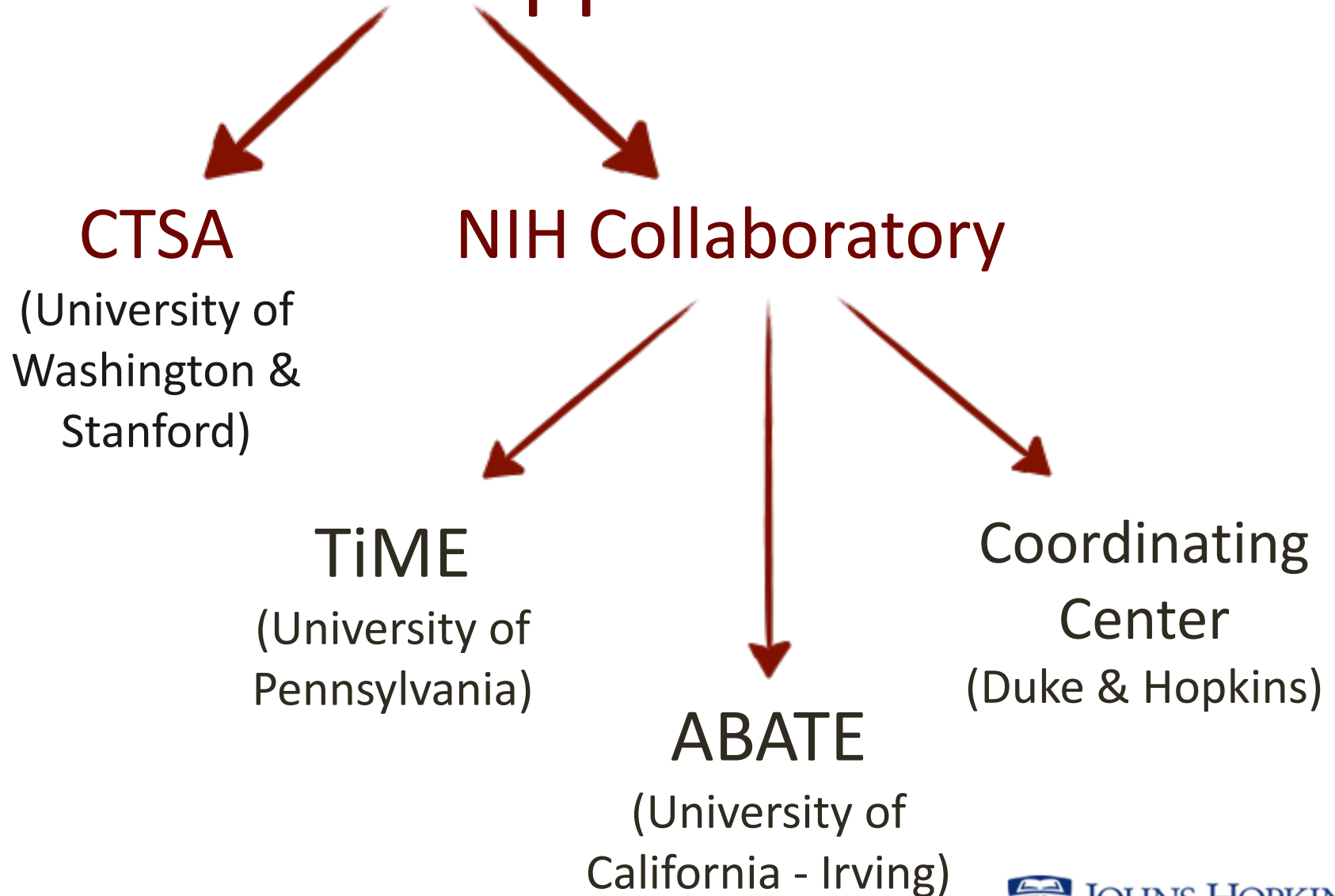
# *Clinical Trials* Special Series

Guest Editors: Jeremy Sugarman and Robert Califf



<http://ctj.sagepub.com/content/early/recent>

# NIH Ethics Supplements



AJOB EMPIRICAL BIOETHICS  
2016, VOL. 7, NO. 2, 71–75  
<http://dx.doi.org/10.1080/23294515.2016.1152104>

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## INTRODUCTION

# Ethics of research in usual care settings: Data on point

Jeremy Sugarman MD, MPH, MA

Downloaded from <http://ajob.sagepub.com> at 10:52 10 May 2016

# 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

# 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