

# THE ETHICS AND REGULATORY LANDSCAPE: IS A MASSIVE PUBLIC CAMPAIGN NEEDED?

SHARON TERRY AND ROB CALIFF

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# Our national clinical research system is well-intentioned but flawed

- High percentage of decisions not supported by evidence\*
- Health outcomes and disparities are not improving
- Current system is great **except**:
  - Too slow, too expensive, and not reliable
  - Doesn't answer questions that matter most to patients
  - Unattractive to clinicians & administrators

**We are not generating the evidence we need to support the healthcare decisions that patients and their doctors have to make every day.**

Which treatment is best for whom?

High-quality evidence is scarce: <15% of guideline recommendations are supported by high-quality evidence

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ORIGINAL CONTRIBUTION

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# Scientific Evidence Underlying the ACC/AHA Clinical Practice Guidelines

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Pierluigi Tricoci, MD, MHS, PhD

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Joseph M. Allen, MA

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Judith M. Kramer, MD, MS

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Robert M. Califf, MD

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Sidney C. Smith Jr, MD

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**C**LINICAL PRACTICE GUIDELINES are systematically developed statements to assist practitioners with decisions about appropriate health care for spe-

**Context** The joint cardiovascular practice guidelines of the American College of Cardiology (ACC) and the American Heart Association (AHA) have become important documents for guiding cardiology practice and establishing benchmarks for quality of care.

**Objective** To describe the evolution of recommendations in ACC/AHA cardiovascular guidelines and the distribution of recommendations across classes of recommendations and levels of evidence.

**Data Sources and Study Selection** Data from all ACC/AHA practice guidelines issued from 1984 to September 2008 were abstracted by personnel in the ACC Science and Quality Division. Fifty-three guidelines on 22 topics, including a total of 7196 recommendations, were abstracted.

*Tricoci P et al. JAMA 2009;301:831-41*



# Do We have a Problem?

## ARGUMENT FOR **YES**

We lack evidence for most health and healthcare decisions

Ignorance in medical practice is dangerous

“Research exceptionalism” is paralyzing learning

## ARGUMENT FOR **NO**

We have a history and a rationale for ethical oversight of research to prevent harm to research subjects

Practice is governed by the “doctor-patient” relationship

The system is working

# Office of Human Research Protections

- Questions raised about comparison of accepted approaches to clinical care in practice
- Particular concerns about consent
  - When is it necessary?
  - When can it be modified?
  - Is randomization itself a risk?
- A diversity of opinions expressed at a public hearing at HHS
- Summary document from the meeting is pending and expected any day

# The Common Rule

- The Federal Policy for the Protection of Human Subjects or the “Common Rule” was published in 1991 and codified in separate regulations by 15 Federal departments and agencies, as listed below. The HHS regulations, 45 CFR part 46, include four subparts:
  - subpart A, also known as the Federal Policy or the “Common Rule”;
  - subpart B, additional protections for pregnant women, human fetuses, and neonates;
  - subpart C, additional protections for prisoners;
  - and subpart D, additional protections for children.
- <http://www.hhs.gov/ohrp/humansubjects/commonrule/>

# The Common Rule

- 7 CFR Part 1c      Department of Agriculture
- 10 CFR Part 745      Department of Energy
- 14 CFR Part 1230      National Aeronautics and Space Administration
- 15 CFR Part 27      Department of Commerce
- National Institute of Standards and Technology
- 16 CFR Part 1028      Consumer Product Safety Commission
- 22 CFR Part 225      Agency for International Development (USAID)
- 24 CFR Part 60      Department of Housing and Urban Development
- 28 CFR Part 46      Department of Justice
- National Institute of Justice
- 32 CFR Part 219      Department of Defense
- 34 CFR Part 97      Department of Education
- 38 CFR Part 16      Department of Veterans Affairs
- Office of Research Oversight
- Office of Research and Development
- 40 CFR Part 26      Environmental Protection Agency
- Research and Development
- 45 CFR Part 46      Department of Health and Human Services
- 45 CFR Part 690      National Science Foundation
- 49 CFR Part 11      Department of Transportation
  - <http://www.hhs.gov/ohrp/humansubjects/commonrule/>

# The Common Rule

- Although they have not issued the Common Rule in regulations, three other departments and agencies comply with all subparts of 45 CFR part 46. These include:
  - The Central Intelligence Agency, by executive order, must comply with all subparts of 45 CFR Part 46. (Executive Order 12333, paragraph 2.10)
  - The Department of Homeland Security, created after issuance of the Common Rule, has chosen to apply all subparts of 45 CFR part 46 to its human research activities. (6 U.S.C. section 112)
  - The Social Security Administration was separated from HHS in 1994 and, absent action by the Administrator, must apply all regulations that applied to SSA before the separation. (42 U.S.C. section 901)
    - <http://www.hhs.gov/ohrp/humansubjects/commonrule/>



ANPRM for Revision to Common Rule  
**HHS Announces Proposal to Improve Rules  
Protecting Human Research Subjects**  
*Changes under consideration would ensure  
the highest standards of protections for  
human subjects involved in research, while  
enhancing effectiveness of oversight*

July 22<sup>nd</sup>, 2011; still waiting!

Ethics Supplement:  
*Survey to Assess Ethical Framework of  
Minimal Risk Studies*



# Overview

- Address the ethical gray space related to the interface of minimal risk research and quality improvement studies as they would be applied to Learning Health Systems
  - Identify if a common ethical framework exists
  - Survey IRB chairs, leaders of healthcare quality improvement programs, and patients
  - Common constructs evaluated across all 3 surveys

# Attitudes about the Ethics of Research on Medical Practices (RoMP)

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David Magnus PhD



**Spectrum**

The Stanford Center for Clinical and Translational Education and Research

Benjamin S. Wilfond MD



Treuman Katz Center  
for Pediatric Bioethics



**ITHS**

Institute of Translational Health Sciences  
Scientists helping scientists improve health

**UW Medicine**  
SCHOOL OF MEDICINE

# Study Aims

Objective: To better understand how patients, their surrogates, the general public, and IRB members view ethical implications of randomization within usual clinical practices.

Aim 1: Assess and compare attitudes of potential research subjects towards risks and benefits of, and towards informed consent for participation in, research on medical practices.

- 1a) Adults and parents of children who are active health care users

- 1b) A nationally representative population sample.

- 1c) Determine the factors, such as perceived health status, health care utilization, trust, parental status, education, or socioeconomic status, that are associated with attitudes about the acceptability and expectations related to research on medical practices.

Aim 2: Assess attitudes of IRB members towards risks and benefits of, and towards informed consent for participation in, research on medical practices.

# Research Questions

- How do these stakeholders value and weigh tradeoffs between autonomy, risks, quality of care, and other characteristics of this specific class of clinical research?
- How do these stakeholders view different approaches to notifying, informing, and engaging patients and communities about the design of, and informed consent for, such research?



# **Decision Autonomy in Pragmatic Clinical Trials**

## ***Supplement to the TiME Trial***

Scott Halpern, MD, PhD

Laura Dember, MD

Susan Ellenberg, PhD

Steven Joffe, MD, MPH

Jason Karlawish, MD

# Aims

- Aim 1: Assess qualitatively how patients treated with hemodialysis and their providers value physician autonomy to choose among treatment strategies that are within the range of the standard of care
- Aim 2: Quantify how curtailing treatment autonomy influences patients' and providers' willingness to participate in RCTs, and whether these influences differ in research vs. clinical care settings
- Aim 3: Measure the extent to which requirements for informed consent modify patients' and providers' concerns regarding the curtailment of treatment autonomy in research and clinical care





# NIH Collaboratory

Health Care Systems Research Collaboratory

## **Collaboratory Coordinating Center**

Jeremy Sugarman, MD, MPH, MA

Kevin Weinfurt, PhD



# Overarching Goal

To improve understanding of when and how different stakeholders believe research testing or comparing interventions that are each considered standard of care are acceptable and when traditional or modified approaches to consent for it should be sought.

# Revised Specific Aims

- **AIM 1:** Collect rich qualitative data from multiple stakeholders patients to identify the broad range of attitudes, beliefs, and preferences concerning the need for research in different usual care settings and related consent issues.
- **AIM 2:** Systematically identify the factors that influence U.S. adults' beliefs concerning research and consent in different usual care situations.
- **AIM 3:** Convene a summit meeting to share emerging results and findings from related projects.
- **AIM 4:** To elicit stakeholders' views concerning the appropriate models of oversight and consent for research on standard health care practices.

# Topics

- **Definition of minimal risk**

- **Co-Lead** – Robert Califf, MD
- **Co-Lead**-- John Lantos, MD
- Rosemary Madigan, RN, MS, MPH
- Sarita Wahba, MSPH, MS
- Dave Wendler, MA, PhD

- **The research/QI distinction in practice**

- **Lead** – Kevin Weinfurt, PhD
- Andrew Brickman, PhD
- Daniel Davis, PhD
- Sarah Greene, MPH
- Jonathan Finkelstein, MD, MPH
- Daniel Ford, MD, MPH
- Sarah Pallin, MPH

- **Waiver or modification of consent/Alternate models of notification**

- **Lead** – Ross McKinney, MD
- Laura Beskow, PhD
- Jessica Burris
- Clara Filice, MD, MPH, MHS
- Daniel Ford, MD, MPH
- John Lantos, MD
- Bray Patrick-Lake, MS
- Mark Pletcher, MD
- Brian Rath, Esq
- Hollie Schmidt, MS

# Topics

- **Data monitoring in PCTs**

- **Lead** – Susan Ellenberg, PhD
- Richard Culbertson, PhD
- Jim Sabin, MD

- **Achieving IRBs harmonization and efficiency in PCTs**

- **Lead** - John Lantos, MD
- Jeremy Corsmo, MPH
- Rachael Fleurence, PhD
- Stephanie Gaudreau
- Raffaella Hart, CIP
- Pearl O'Rourke, MD
- Bray Patrick-Lake, MS
- Todd Rice, MD

- **Vulnerable subjects in CRTs**

- **Lead – Needed**
- Jonathan Finkelstein, MD, MPH
- James Fischer, PHARM.D., FCCP
- Peg Hill-Callahan
- Rachel Lally, MPH
- Amanda Terry, MA, CRA
- Roberta Tovey, PhD
- Mary Jane Welch, DNP, APRN, BC, CIP

# Topics

- **Gatekeepers in PCTs**
  - **Lead – Needed**
  - Robert Califf, MD
  - Amanda Terry, MD, CRA
  - Susan Surovec
  - Danielle Whicher, PHD, MHS
- **Identifying direct and indirect subjects/participants in CRTs/Risk and benefit balance assessment**
  - **Lead – Needed**
  - Kelly Edwards, PhD, MA
  - Megan Gauvey-Kern
  - Debbe McCall, MBA
  - Jaye Bea Smalley
  - Carl Stepnowsky, PhD
- **FDA regulated products and PCTs**
  - **Lead – Monique Anderson, MD**
  - Denise Cifelli, MS
  - Sheila Fireman, MA, JD
  - Caroline Miner, MA
  - Nancy Stade, JD

# Topics

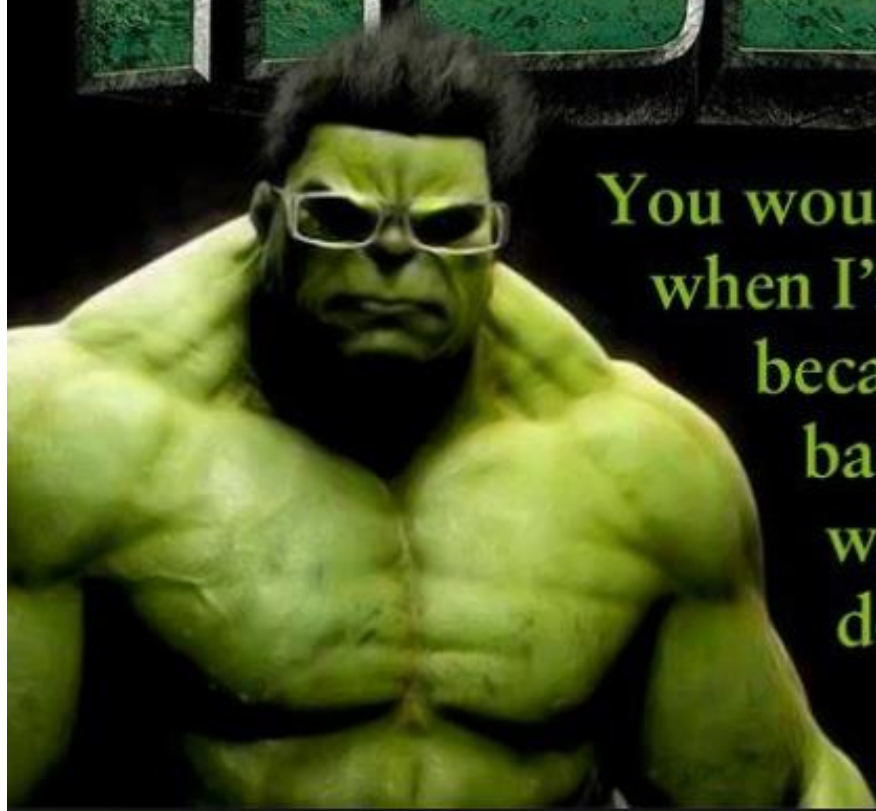
- **Ethics and the nature of interventions in PCTs (eg, physician vs. patient)\***
  - **Lead – Needed**
  - Zia Agha, MD
  - Kathryn James, PA, MPH
  - Lindsay Kindler, PhD, RN, CNS
  - C. Egla Rabinovich, MD, MPH
  - Carol Somkin, MD, MPH
- **Privacy**
  - **Lead – Deven McGraw, JD**
  - Jeremy Sugarman, MD, MPH, MA
- **Plain Language Product Reviewers**
  - Geraldine Bliss, MS
  - Mary Elkins Melton
  - Dena Rifkin, MD, MS
- **Internal/Independent Reviewer**
  - Arthur Caplan, PhD

# Summary

- Our research system is only answering a fraction of the questions that are critical to inform practice and health decisions by patients
- The system is complex, highly regulated and resistant to change
- A combination of new guidances and substantial empirical data will influence the landscape for the foreseeable future, but there is no assurance that these different inputs will be mutually reinforcing
- The clinical research community is not in a good position to advocate for changes that would increase knowledge because of accusations of self serving behavior
- **A strong and well-informed patient voice is needed!**



# THE CREDIBLE HULK



You wouldn't like me  
when I'm angry  
because I always  
back up my rage  
with facts and  
documented  
sources.

# Time to Take Action!

- Unacceptable:
  - Lack of evidence for accepted approaches
  - Disparities
  - Lack of responsiveness to the shifting regulatory foundation
  - Lack of engagement on part of the stakeholders/public



There is no deli line, if patients don't do this, no one will (can)!



# ***What if a learning health\_\_\_\_\_ system was powered by people?***

- ***What if the public was part of better innovation in health?***

Accelerating breakthroughs. Driving accepted practice comparison. Understanding the continuum from health to illness. Understanding health and healthcare services from the lens of patient's needs.

- **Health accessible to all.**

# Let's Get Organized!

- Large and well coordinated advocacy effort
- Deep disease specific advocacy expertise has been honed for 50 years
- Issues are too big for one network or org
- Need collaboration to awaken public: ultimately benefiting all who suffer, or who will suffer
- Harness power of networks at same time we create PCORnet and other networks.
- No network will succeed without equal power of advocacy

# Precedents

- AIDS
- Cancer Activism
- Coalition for Genetic Fairness

# Call to Action

- Series of webinars, flash meetings
- Gather stories
- Craft main messages
- Ready responses to various regulatory communications
- Plan action steps, create toolkits
- Educate stakeholders, including the public
- Garner attention of major spokespersons
- Educate policymakers
- Place blogs, articles, and social media elements
- Campaign, campaign, campaign – this is our moonshot

# Questions

- Can we all step up beyond disease, cause, organizations? **We have to – this is too critical to let anything get in the way**
- Who funds? **Who cares is who funds: money from philanthropists, sweat equity from foundations**
- How will organization of the effort be managed? **Create a coalition with shared, but accountable, leadership.**
- What is it really trying to accomplish that Research!America and other advocacy orgs aren't already doing? **More than increasing funding for federal agencies: awakening public to two secrets – 1) Medicine is not evidence based; 2) People have to participate, no other choice.**
- Who are we really trying to influence? **Policy makers, regulators, the public, researchers, clinicians, advocates**
- Do patients agree on autonomy vs societal good tradeoffs? **No, excellent point for deliberation.**





# What do we have to lose?

# Everything.