PRAGMATIC TRIALS AND THE LEARNING HEALTHCARE SYSTEM

INSIGHTS FROM YEAR 1 OF THE NIH COLLABORATORY

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President and CEO
Faculty/Presenter Disclosure

Speaker Sean Tunis has **no** potential for conflict of interest with this presentation....

other than receiving grant funding from the NIH for work on the Collaboratory coordinating center

Numerous unrestricted grants from payers and life sciences companies, none related to products discussed in the talk
IF RCTS WERE 60’S ROCK STARS

1965

2013
RISING STARS

Big Data

Modeling

Advanced Obs
Probably not yet time to retire the RCT but need to (continue to) re-invent it
COMMONLY CITED LIMITATIONS OF RCTS

- Expensive
- Limited external validity
- Lengthy start up and enrollment
- Costly infrastructure, often not sustained
- Generally, current approach leaves too many gaps in evidence on important questions
Effectiveness of 3000 treatments as reported in randomised controlled trials selected by Clinical Evidence. This does not indicate how oftentimes treatments are used in healthcare settings or their effectiveness in individual patients.
The NIH Collaboratory Program

- Five year initiative funded by NIH Office of Director
  - Coordinating Center and seven demo PCTs
- Aim is to expand infrastructure for highly efficient PCTs through partnership with health care systems
  - Develop tools, policies, best practices to rapidly scale up from initial demo projects
  - Seek exponential increase in efficiency of conducting PCTs
Learning health care systems

In a learning health care system, research influences practice and practice influences research.

EVALUATE
Collect data and analyze results to show what works and what doesn’t.

ADJUST
Use evidence to influence continual improvement.

IMPLEMENT
Apply plan in pilot and control settings.

DESIGN
Design care and evaluation based on evidence generated here and elsewhere.

DISSEMINATE
Share results to improve care for everyone.

INTERNAL AND EXTERNAL SCAN
Identify problems and potentially innovative solutions.

Internal

External
Collaboratory Organization
Health Care Systems Research Collaboratory

1. Pragmatic trial design
2. Electronic health record as core data collection instrument
3. At least 2 integrated health systems collaborating to answer the question
   * Many applications—7 funded to go forward with planning phase
Partnering NIH Institute / Center

- NIDDK

Primary Goal

- Evaluate the effects on mortality, hospitalizations and quality of life of an extended duration of thrice weekly maintenance hemodialysis sessions

Sample

- 5100 patients initiating maintenance hemodialysis treatment at participating facilities within two large dialysis provider organizations
- 322 dialysis facilities
Randomization Strategy
- Cluster randomization of dialysis facilities to extended treatment duration or usual care

Data Sources
- EHRs from dialysis provider organizations
- Quality of life questionnaires

Strategies to Improve Efficiency
- Outcomes ascertained using data available from routine clinical care through data elements common to all sites
- No on-site study personnel required
Nighttime Dosing of Anti-Hypertensive Medications
(University of Iowa)

Partnering NIH Institute / Center
- NHLBI

Primary Goal
- Determine impact of nighttime dosing of anti-hypertensive medications on rates of adverse cardiovascular (CV) events (AMI, CVA, CHF admissions, and coronary and peripheral revascularization).

Sample
- 1100 patients with HTN and 1 or more other conditions that increase CV risk in primary care, cardiology, and nephrology clinics at the Univ. of Iowa and Duke.
Nighttime Dosing of Anti-Hypertensive Medications (University of Iowa)

Randomization Strategy
- Patient-level

Data Sources
- University of Iowa and Duke EMRs (Epic)
- Personal health records to collect PROs, treatment adherence, and out of system adverse events.

Strategies to Improve Efficiency
- Identification of eligible patients through EMR
- Enrollment of patients through study website or central coordinator accessible via toll free telephone line
- Informed consent obtained using interactive online module
PROGRESS TO DATE

• Promising start toward substantially increase capacity to conduct RCTs, integrated with delivery of care

• Some major challenges identified
  – Current human subjects oversight regulations don’t deal well with integration of research and practice
  – Business case for HCS is unclear

• Addressing major limitations of RCTs may reframe debate around use of alternative methods
WILL THIS APPROACH PRODUCE FAIR COMPARISONS?

“You can't always get what you want
But if you try sometimes well you might find
You get what you need.”

Mick Jagger, Keith Richards
THANKS!

LOOKING FORWARD TO QUESTIONS AND DISCUSSION
BACKUP SLIDES
Required Characteristics of PCTs (per RFA)

- Test interventions that are broadly applicable to multiple health systems
- Address issues of major public health importance
- Engage partnership with health care delivery system
- Utilize information that is captured by EMRs or other extant systems and require minimal adjudication
- Minimal exclusion criteria to maximize diversity and generalizability
- Incorporate rigorous prospectively identified controls (preferably by randomization)
Required Characteristics of PCTs (cont.)

- Maximize external validity by testing generalizability across distinct health care settings and populations
- Address and overcome key barriers to conducting research in healthcare settings
- Test interventions that are relatively simple, do not require a complex infrastructure for implementation, and that can be reliably delivered by providers
- Should allow for interventions to be implemented with flexibility by practitioners to mimic practice
Demonstration Projects

- Nighttime Dosing of Anti-Hypertensive Medications (University of Iowa)
- Population-Based Prevention of Suicide Attempts (Group Health Cooperative)
- Lumbar Imaging with Reporting of Epidemiologic Data (University of Washington)
- Collaborative Care for Chronic Pain in Primary Care (Kaiser Permanente Center for Health Research)
- Active Bathing to Eliminate Infection Trial (UC Irvine)
- Time to Reduce Mortality in End-Stage Renal Disease (TiME) Trial (University of Pennsylvania)
- STOP Colon Cancer (Kaiser Permanente)
NIH Health Care System Collaboratory

- Collaboratory Coordinating Center
- Nighttime Dose of Anti-Hypertensive Medications
- Prevent Suicide Attempt
- Reduce Mortality in End Stage Renal Disease (sites to be selected from units across all 50 states)

- Stop Colon Cancer in Priority Populations
- Chronic Pain in Primary Care
- Reduce Infections and Readmissions
- Lumbar Image Reporting and Epidemiology

Additional sites to be determined
High Level Summary

• We have the technical capacity as a country to increase high quality evidence to inform practice by a log order or more

• The NIH HCS Collaboratory is in a great position to assist in the effort by capturing the essence of practical HCS research and providing the knowledge to others
  • Demonstration projects
  • Knowledge repository
  • Proselytizing

• At one year every component of the Collaboratory sees a valid and interesting function

• The main unsettled factor has been the regulatory and ethics framework
Ethical / Regulatory Questions

- Is the research vs. quality improvement divide reasonable in today’s “datafied” environment?
- What is minimal risk?
- When can consent be waived?
- When is modified “practical consent” appropriate?
- In a cluster RCT, what are practical methods to:
  - Notify
  - Facilitate autonomous participation
  - Feasibility allow an individual to “opt out”