

From Efficacy to Effectiveness: The Pragmatic Clinical Trial

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The Big Picture

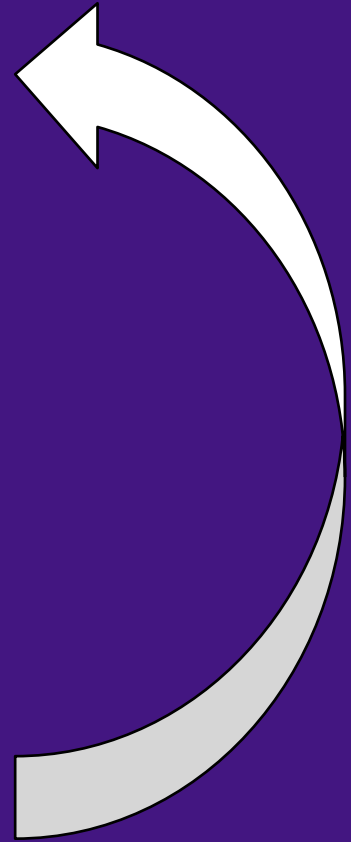
Comparative Effectiveness



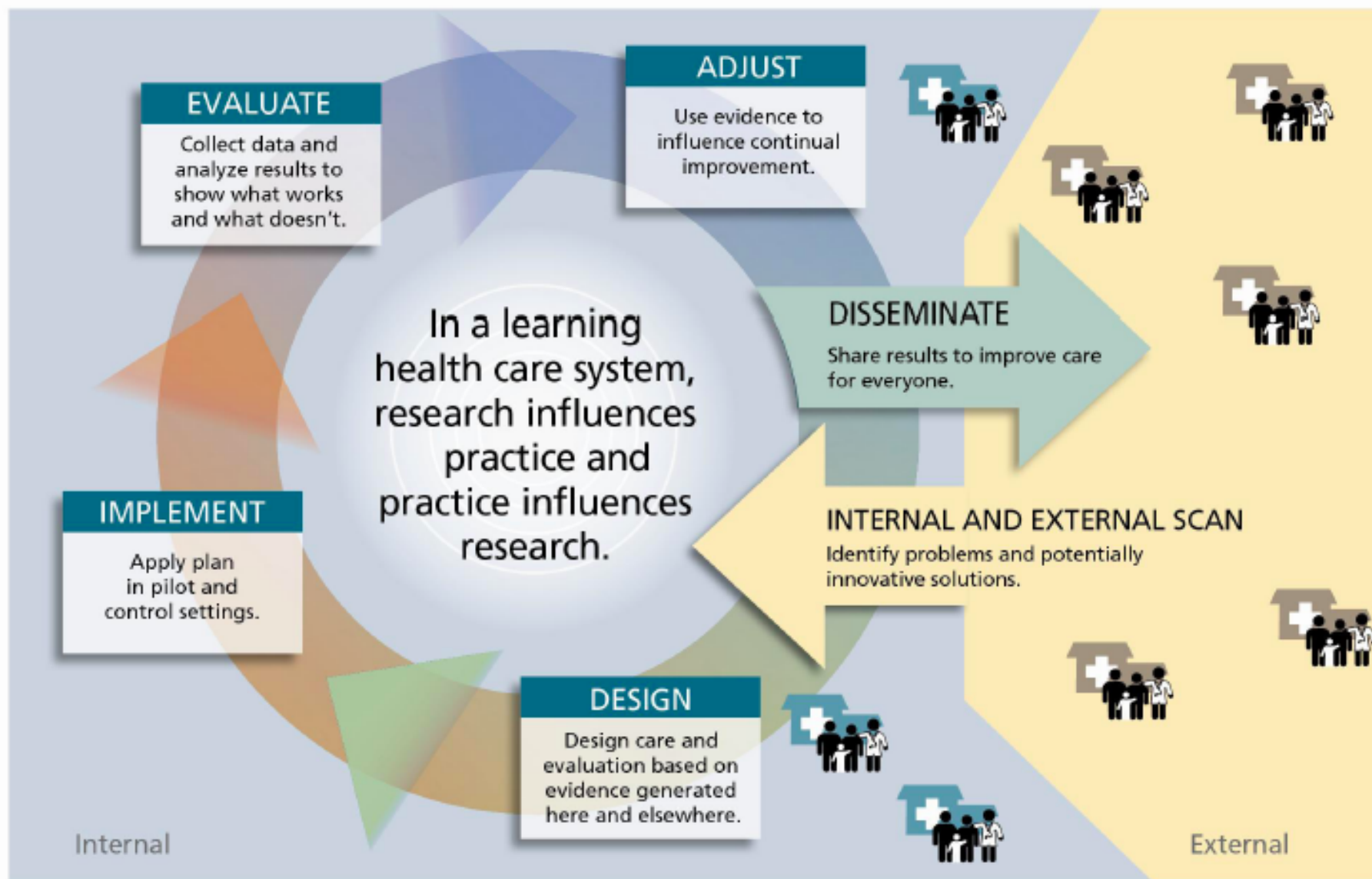
Evidence Based Practice



Health Policy



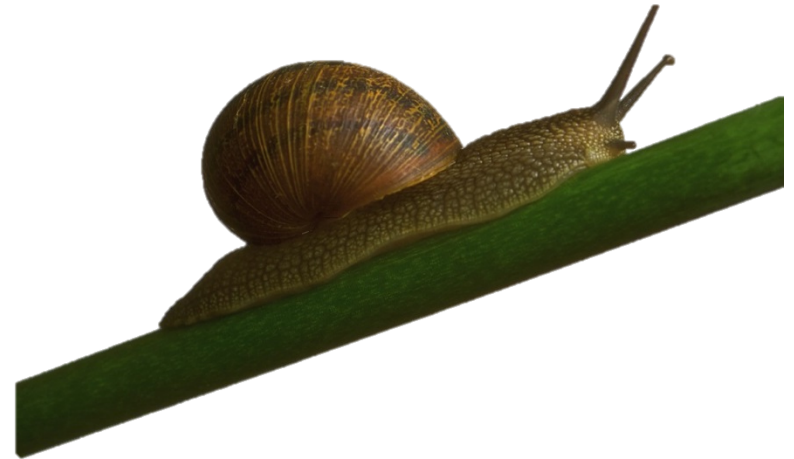
Learning health care systems



So we need to generate
evidence

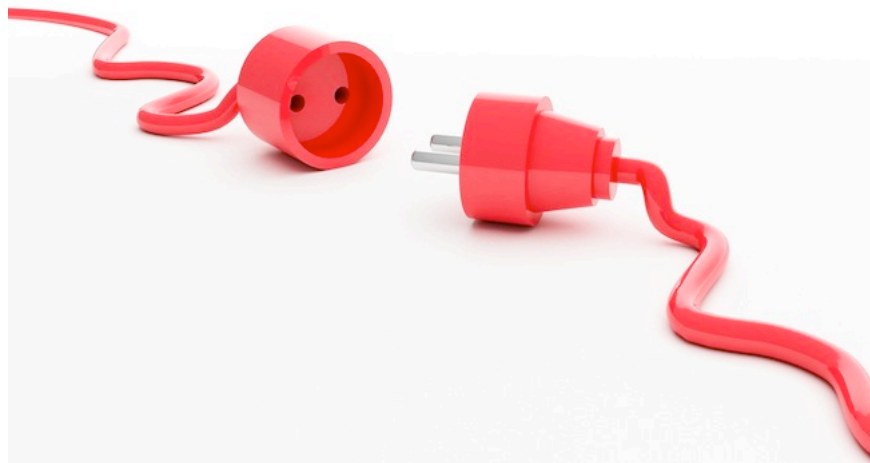
Challenge #1: Clinical research is slow

- Traditional RCTs are slow and expensive—and rarely produce findings that are easily put into practice.
- In fact, **it takes an average of 17 years** before research findings lead to widespread changes in care.



Challenge #1: Clinical research is slow

“...rarely produce findings that are easily put into practice.”



Efficacy vs. Effectiveness

Efficacy vs. Effectiveness

- Efficacy: can it work under ideal conditions
- Effectiveness: does it work under real-world conditions



Challenge #2: Clinical research is not relevant to practice

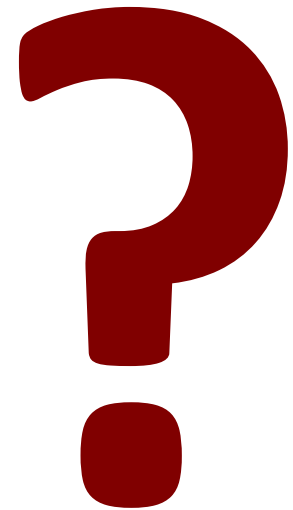
- Traditional RCTs study efficacy of txs for carefully selected populations under ideal conditions.
- Difficult to translate to real world.
- When implemented into everyday clinical practice, often see a “voltage drop” — dramatic decrease from efficacy to effectiveness.

“If we want more evidence-based practice, we need more practice-based evidence.”

Green, LW. American Journal of Public Health, 2006.

Challenge #3: The evidence paradox

- >18,000 RCTs published each year—plus tens of thousands of other clinical studies.
- Yet systematic reviews consistently find not enough evidence to effectively inform clinical decisions providers and patients must make.



The solution?
A solution?
An approach?

The solution?
A solution?
An approach?

Pragmatic Trials

Pragmatic vs. Explanatory Trial

- Explanatory trials
 - Examine efficacy
 - Conducted under ideal conditions
 - Explain mechanisms
- Pragmatic trials
 - Determine comparative effectiveness (CER)
 - Routine practice
 - Aim to help providers, patients, and policy makers choose between interventions

Pragmatic Trials
Large Simple Trials
Effectiveness Trials

Explanatory Trials

- If and how an intervention works
- Control for as many biases and confounders as possible
- Maximize intervention's effect

Pragmatic Trials

- Size: huge $n \rightarrow$ robust estimates, heterogeneity
- Endpoints: patient oriented with minimal adjudication
- Setting: integrated into real world
 - Non-academic centers
 - Leverage digital data
 - Patients as partners

MYTHBUSTERS.

DON'T TRY THIS AT HOME!*



MYTHBUSTERS.

TRY THIS AT HOME!*

DO



Key features of most PCTs



Use of electronic health records (EHRs)

- EHRs allow efficient and cost-effective, recruitment, participant communication & monitoring, data collection, and follow up



Randomization at clinic or provider level

- Protocols can be tailored to local sites and can adapt to changes in a dynamic health care environment

But EMRs Have Their Limitations

Data Quality Issues with Death

- Unambiguous- should be easy
- Pts died prior to index visit
- Pts had visits after death
 - 1.4% of those who died subsequently had visits

Pragmatic vs. Explanatory Trials

CMAJ

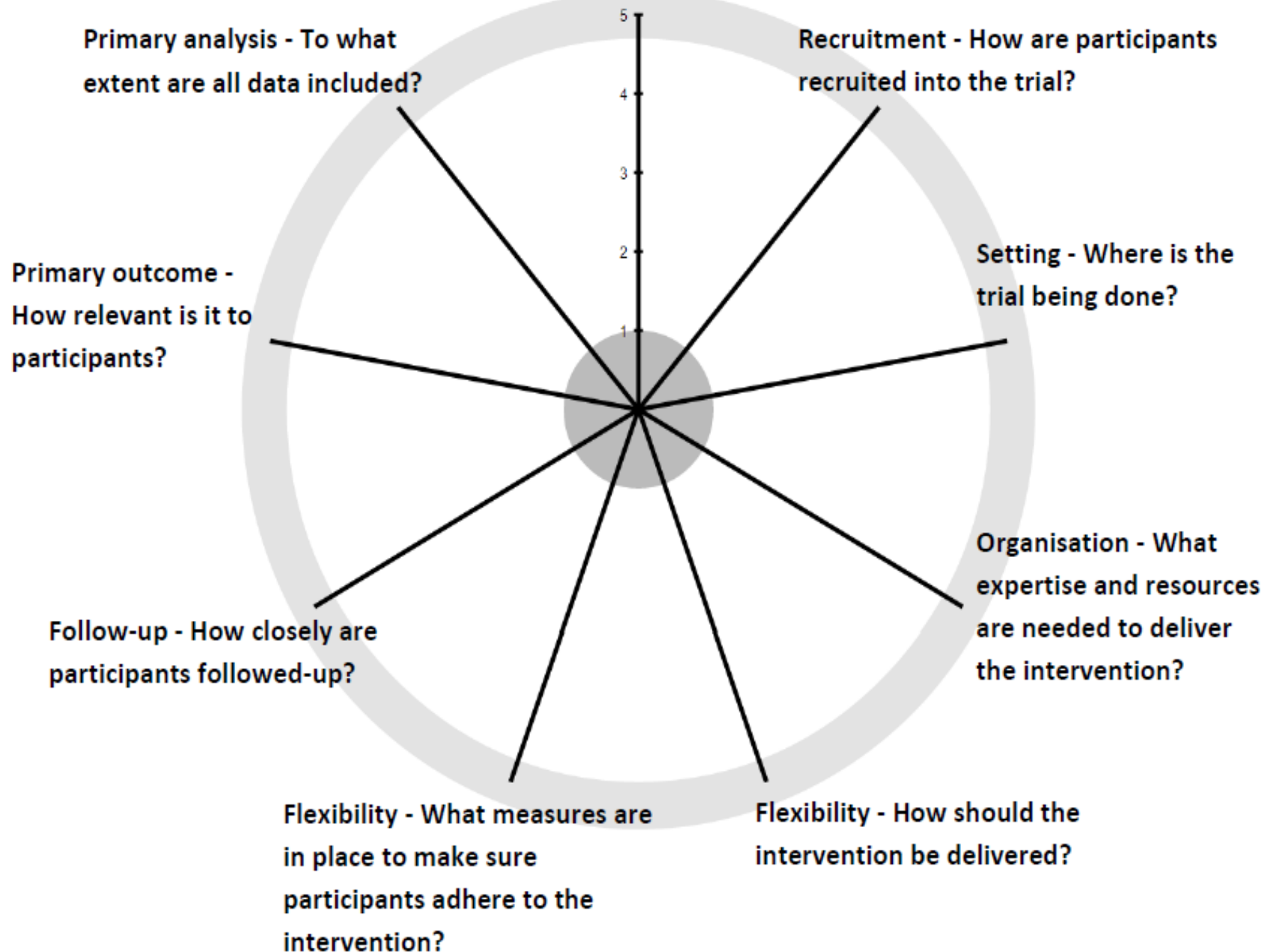
ANALYSIS

A pragmatic–explanatory continuum indicator summary (PRECIS): a tool to help trial designers

Kevin E. Thorpe MMath, Merrick Zwarenstein MD MSc, Andrew D. Oxman MD, Shaun Treweek BSc PhD, Curt D. Furberg MD PhD, Douglas G. Altman DSc, Sean Tunis MD MSc, Eduardo Bergel PhD, Ian Harvey MB PhD, David J. Magid MD MPH, Kalipso Chalkidou MD PhD

Published at www.cmaj.ca on Apr. 16, 2009. An abridged version of this article appeared in the May 12 issue of *CMAJ*. This article was published simultaneously in the May 2009 issue of the *Journal of Clinical Epidemiology* (www.jclinepi.com).

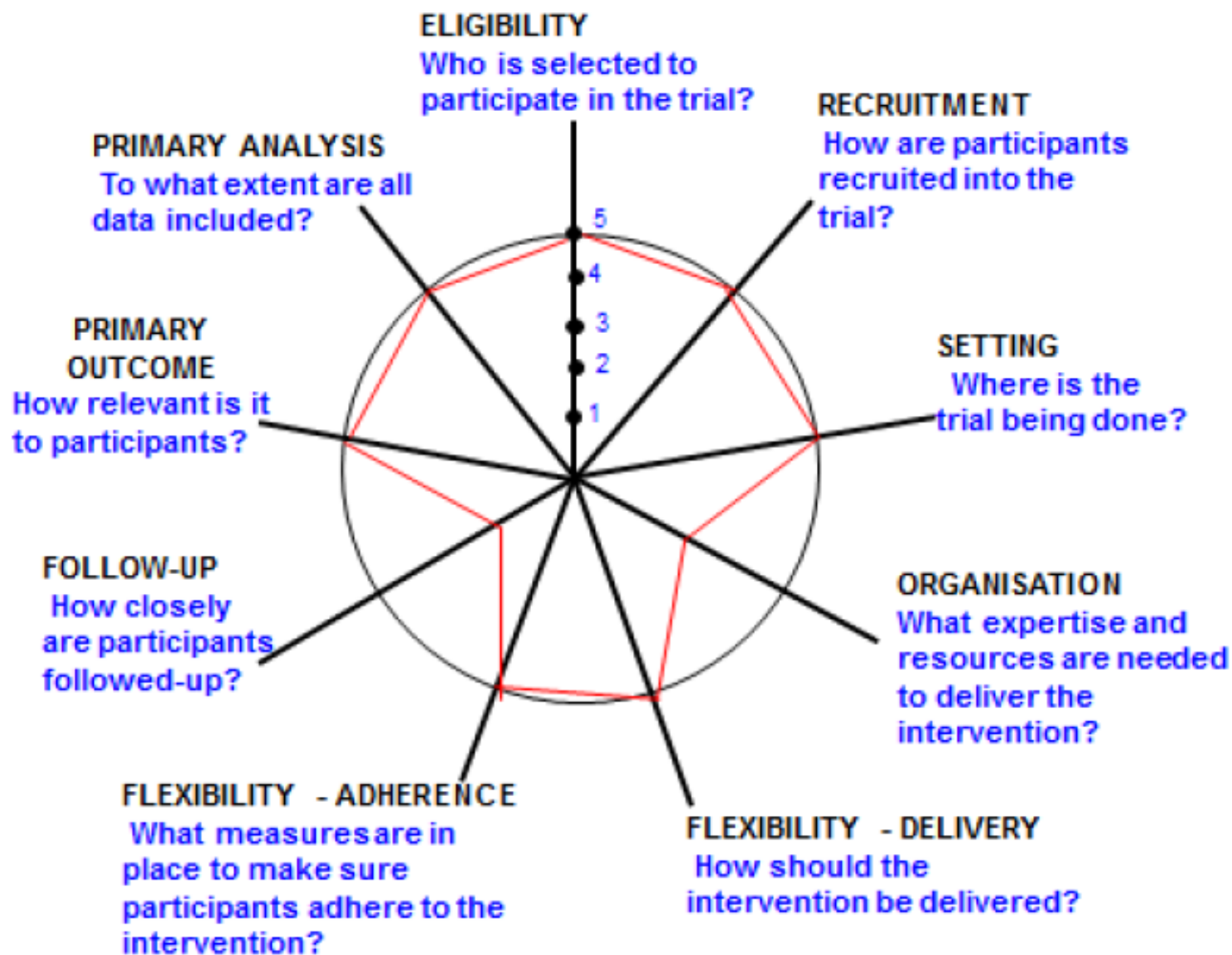
Eligibility – Who is selected to participate in the trial?



Pragmatic vs. Explanatory

1. Eligibility
2. Recruitment
3. Setting
4. Organization
5. Flexibility-intervention
6. Flexibility-adherence
7. Follow-up
8. Primary outcome
9. Primary analysis (? includes all data?)

Example from: Little P, Moore M, Kelly J, Williamson I, Leydon G, McDermott L, Mullee M, Stuart B: Ibuprofen, paracetamol, and steam for patients with respiratory tract infections in primary care: pragmatic randomised factorial trial. BMJ 2013, 347:f6041.



Example of Pragmatic Trial- Lumbar Imaging with Reporting of Epidemiology (LIRE)

LIRE (pronounced leer)- From the French verb, “To Read”



LIRE Funded by NIH Health Care Systems Research Collaboratory

- Supported by the NIH Common Fund
- Goal: improve the way (pragmatic) clinical trials conducted
- Build infrastructure for CER

nihcollaboratory.org



The Collaboratory

 This section only[Home](#)[About Us](#)[Project Cores And Working Groups](#)[Demonstration Projects](#)[Resources](#)[Calendar](#)[Directory](#)

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upcoming events

- Collaboratory Grand Rounds: 3/1/13
- Collaboratory Grand Rounds: 3/8/13
- Special Session – Collaboratory Grand Rounds: 3/18/13

twitter



NIH_CommonFund New Innovator, Dr. Sabeti! MT

news

02/26/13: [White House announces new public access policy for scientific research](#)

new resources

ARCHIVE: Collaboratory Grand Rounds: 2/15/13, Richard Platt

ARCHIVE: Collaboratory Grand Rounds: 1/18/13, Lynn DeBar

ARCHIVE – Collaboratory Grand Rounds: 1/11/13, Eric Larson

ARCHIVE: Collaboratory Grand Rounds: 2/8/13, David Murray

Phenotype KnowledgeBase (PheKB)

A Framework for Patient and Consumer Engagement in Evidence Generation (pdf)

A Framework for Patient and

the nih collaboratory

Rethinking Clinical Trials

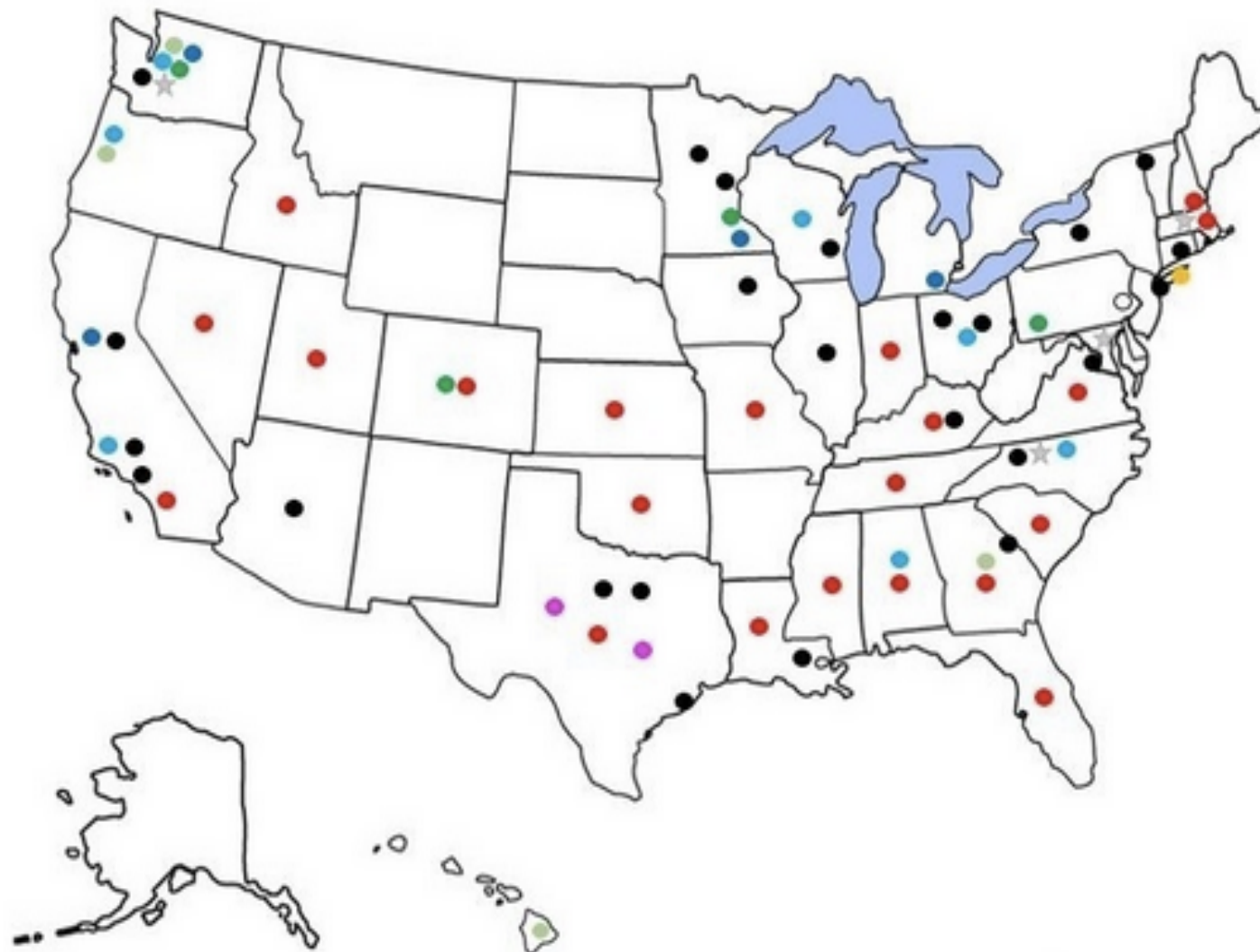
Supported by the Common Fund at the National Institutes of Health, the **Health Care Systems Research Collaboratory** is intended to improve the way clinical trials are conducted by creating a new infrastructure for collaborative research. The ultimate goal is to ensure that healthcare providers and patients can make decisions based on the best available clinical evidence.

The NIH HCS Research Collaboratory includes a Coordinating Center that provides national leadership and technical expertise in all aspects of research with healthcare systems. The Coordinating Center will make data, tools, and resources from these projects available to the greater research community to facilitate a broadened base of research partnerships with health care systems.

The NIH HCS Research Collaboratory also supports the design and rapid execution of several high-impact **Pragmatic Clinical Trial Demonstration Projects** (*listed below*) that will address questions of major public health importance that engage health care delivery systems in research partnership.

Principal Investigator	Institution	Project
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NIH Health Care Systems Research Collaboratory



★ Collaboratory Coordinating Center

● LIRE – Lumbar Image Reporting and Epidemiology

● SPOT – Suicide Prevention Outreach Trial

● TSOS – Trauma Survivors Outcomes and Support

○ TIME – Time to Reduce Mortality in End-Stage Renal Disease (sites to be selected from units across all 50 states)

● STOP CRC – Stop Colorectal Cancer in Priority Populations

● PPACT – Collaborative Care for Chronic Pain

● PROVEN – Pragmatic Trial of Video Education in Nursing Homes

● ABATE – Active Bathing to Eliminate Infection

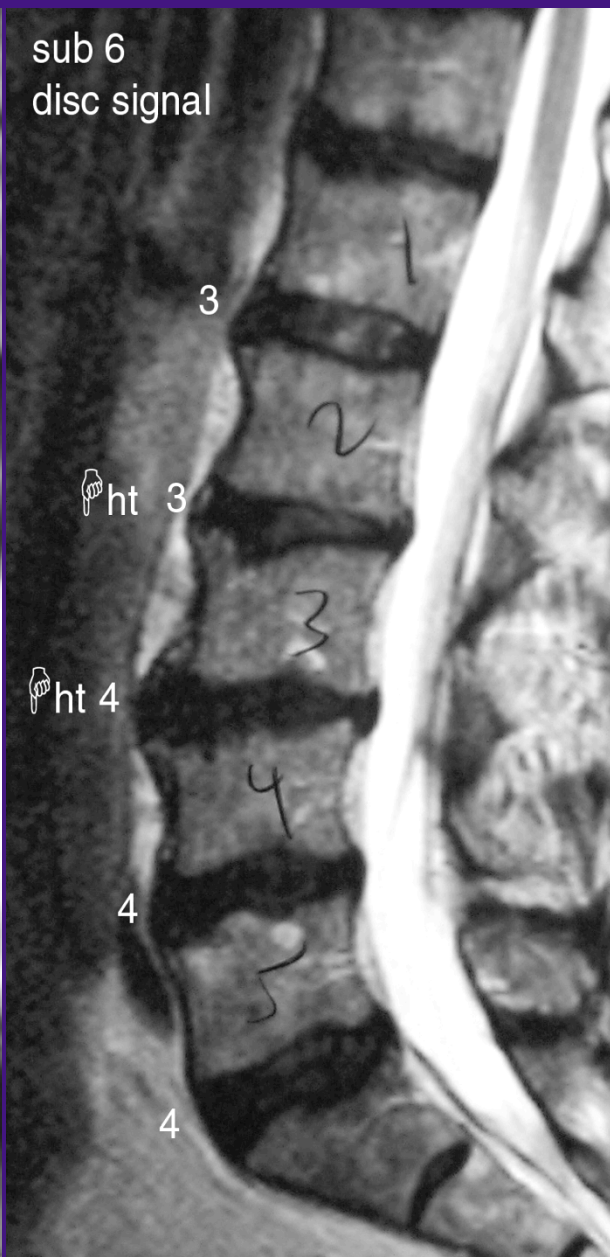
● ICD-Pieces – Improving Chronic Disease Management with Pieces

Additional sites to be determined

Background and Rationale

- Lumbar spine imaging frequently reveals incidental findings
- These findings may have an adverse effect on:
 - Subsequent healthcare utilization
 - Patient health related quality of life

Disc Degeneration in Asx

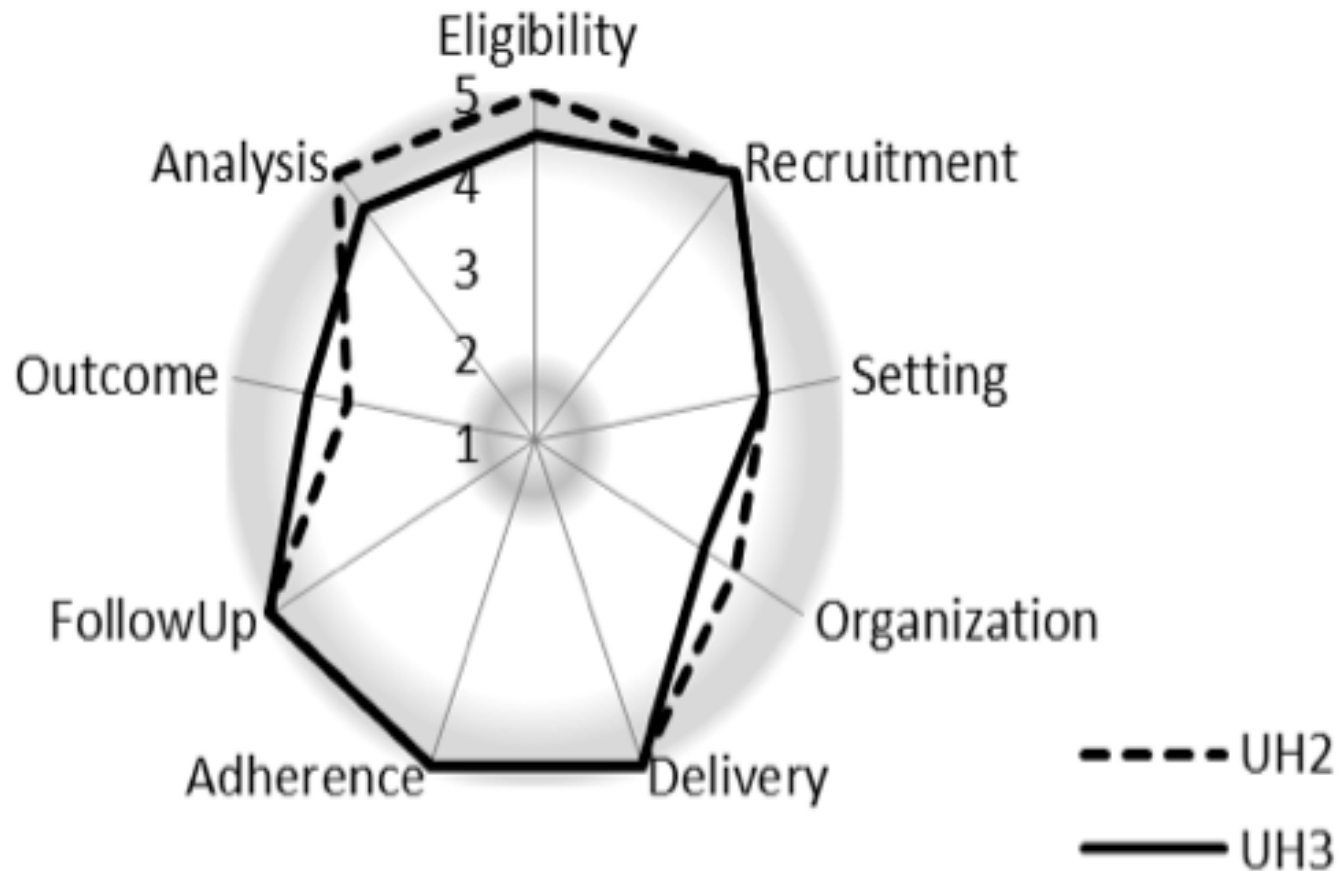


Hypothesis

- Inserting benchmark information into reports will influence subsequent management of primary care patients with LBP
 - Fewer subsequent imaging tests
 - Fewer referrals for minimally invasive pain treatment
 - Fewer referrals to surgery
 - Less narcotic use

LIRE PRECIS

LIRE



The Intervention

Comment

The following findings are so common in normal, pain-free volunteers that while we report their presence, they must be interpreted with caution and in the context of the clinical situation. Among people between the age of 40 and 60 years who do not have back pain, a plain film x-ray will find that about:

- 8 in 10 have disk degeneration
- 6 in 10 have disk height loss

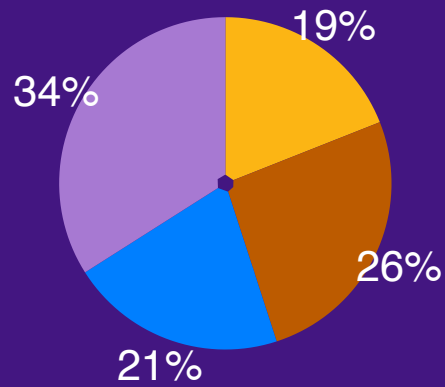
Note that even 3 in 10 means that the finding is quite common in people without back pain.

Participating Systems

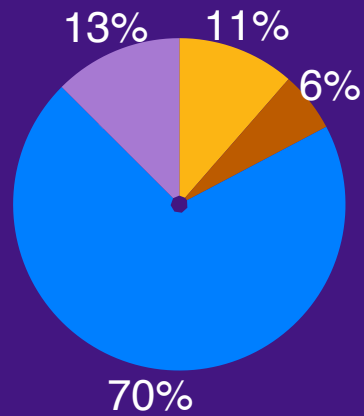
Name	# Primary Care Clinics (Randomized)	# PCPs (Randomized)
Kaiser Perm. N. California	20	865
Henry Ford Health System, MI	26	228
Group Health Coop of Puget Sound	19	245
Mayo Health System	36	345
Total	101	1683

LIRE: Enrollment

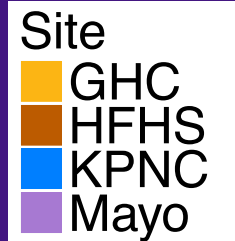
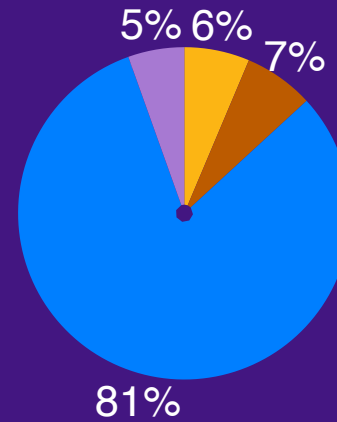
Clinics (n = 100)



Providers (n = 3,195)



Patients (n = 245,586)



LIRE- Primary Outcome

- What we want to know: how patient's back pain is doing
 - Back pain-related disability: Roland-Morris Disability Questionnaire
 - Back and leg pain: pain NRS
 - HRQoL
- How do we get this data?
 - Ask the patient: Pt Reported Outcome

Are PROs Pragmatic?

- Barriers:
 - Time to get
 - # of personnel
 - Finding and contacting
 - \$\$
- For 100s -> 😊
- For 1,000s -> 😐
- For >100,000s -> ☹️

LIRE- Primary Outcome

- A single metric of overall intensity of resource utilization for spine care based on CPTs converted to RVUs
- Passively collected from EHR

Key Pragmatic Aspects of LIRE

- Broad inclusion criteria
- Waiver of consent/minimal risk
- Simple, easily implementable intervention
- Passive collection of outcomes

Patient-Centered Outcomes Research Institute



Patient-Centered Outcomes Research Institute

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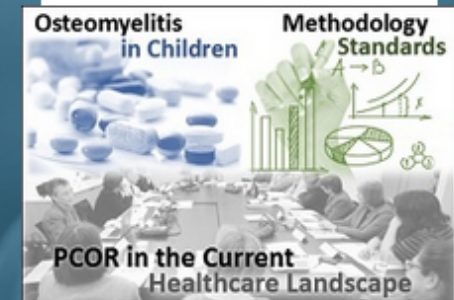
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Examining Coordinated Care

Do patient outcomes improve when care providers team up in a coordinated program?

[SEE WHAT RESEARCHERS ARE LEARNING](#)



PCORI

- Independent non-governmental organization
- Goal to help patients, clinicians, purchasers and policy makers make better informed health decisions
- Spearheading CER and pragmatic trials

PCOR Trust Fund

- 2010-2012: \$210 million
- 2013: ~\$320 million
 - \$150 million general revenues
 - \$1/Medicare beneficiary + private plans
- 2014-2019: ~\$650 million/yr
 - \$150 million general revenues
 - \$2/beneficiary
- PCORTF not authorized after 2019

PCORI National Priorities

- Comparative Assessments of Prevention, Diagnosis, and Treatment Options
- Improving Healthcare Systems
- Addressing Disparities
- Accelerating Patient-Centered and Methodological Research

Stakeholder Engagement Essential



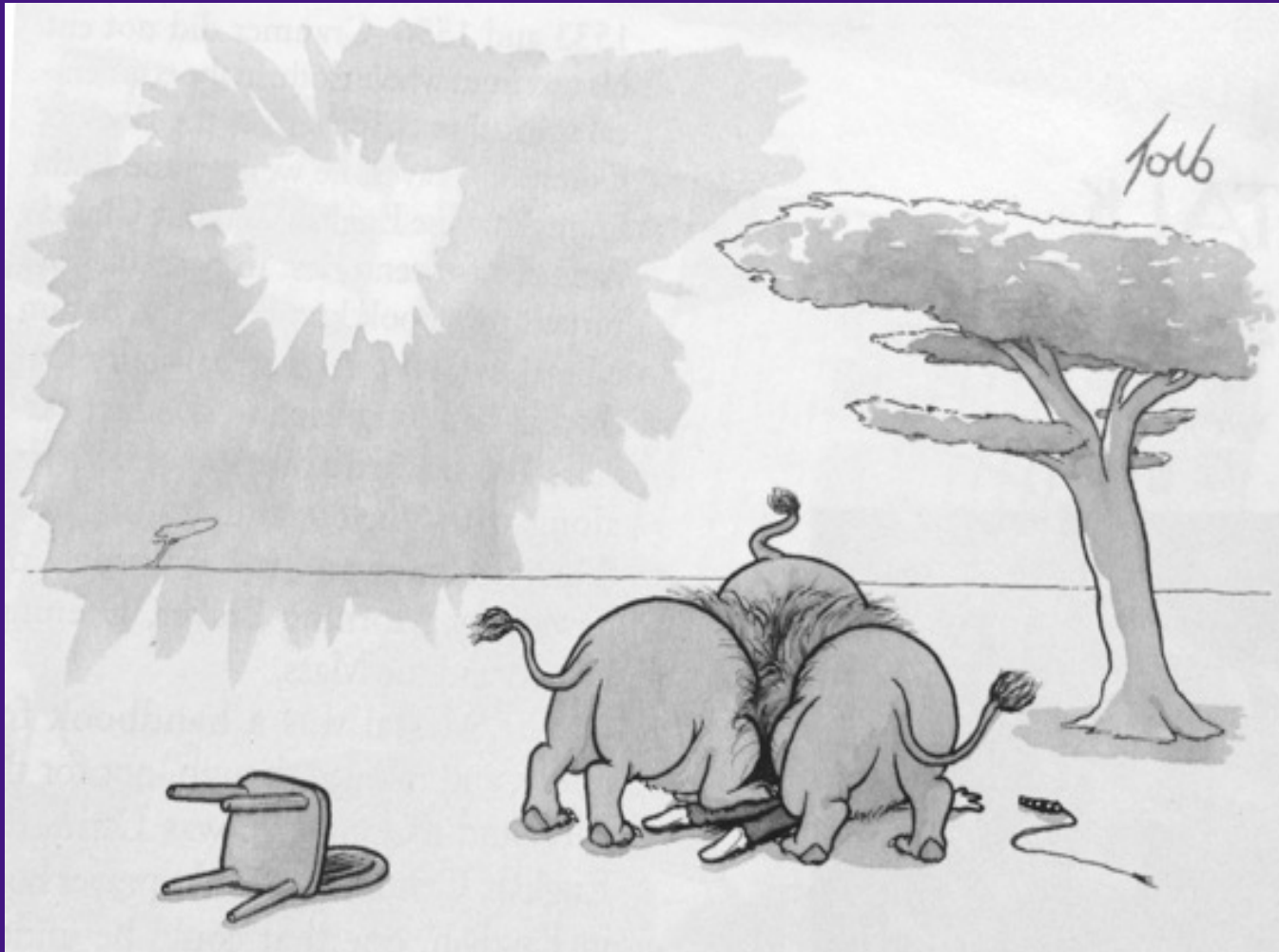
What Is Stakeholder Engagement?

- Participation in formulation of research questions
- Defining essential characteristics of study participants, comparators, and outcomes
- Monitoring of study conduct and progress
- Interpretation/dissemination of results

Take Home Points

- Pragmatic vs. Explanatory trials and the PRECIS tool
- NIH Health Care Systems Collaboratory
- PCOR and PCORI

Explanatory vs. Pragmatic Trials



The Great Zeferelli's chair worked a lot better
in controlled conditions.