NIH Collaboratory

Health Care Systems Research Collaboratory

Rethinking Clinical Trials®

Topic 6: Measuring Outcomes

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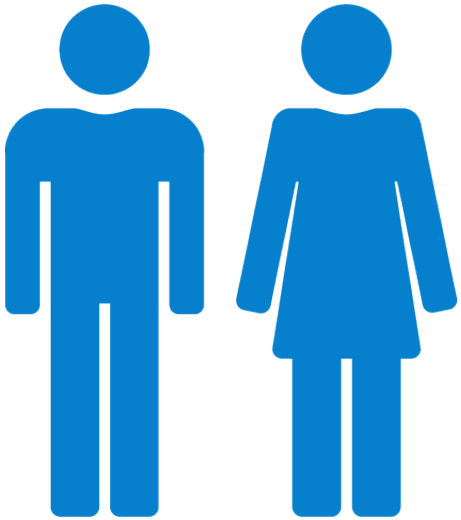
Collaboratory ePCT Training Workshop

Outline

- Definitions
- The electronic data puzzle
- Caveats for EHR data in research
- Possible sources of error
- Data quality assessment recommendations
- Clinical phenotypes
- Reporting guidelines for PCTs
- Patient-reported outcomes
- Conclusions & recommendations

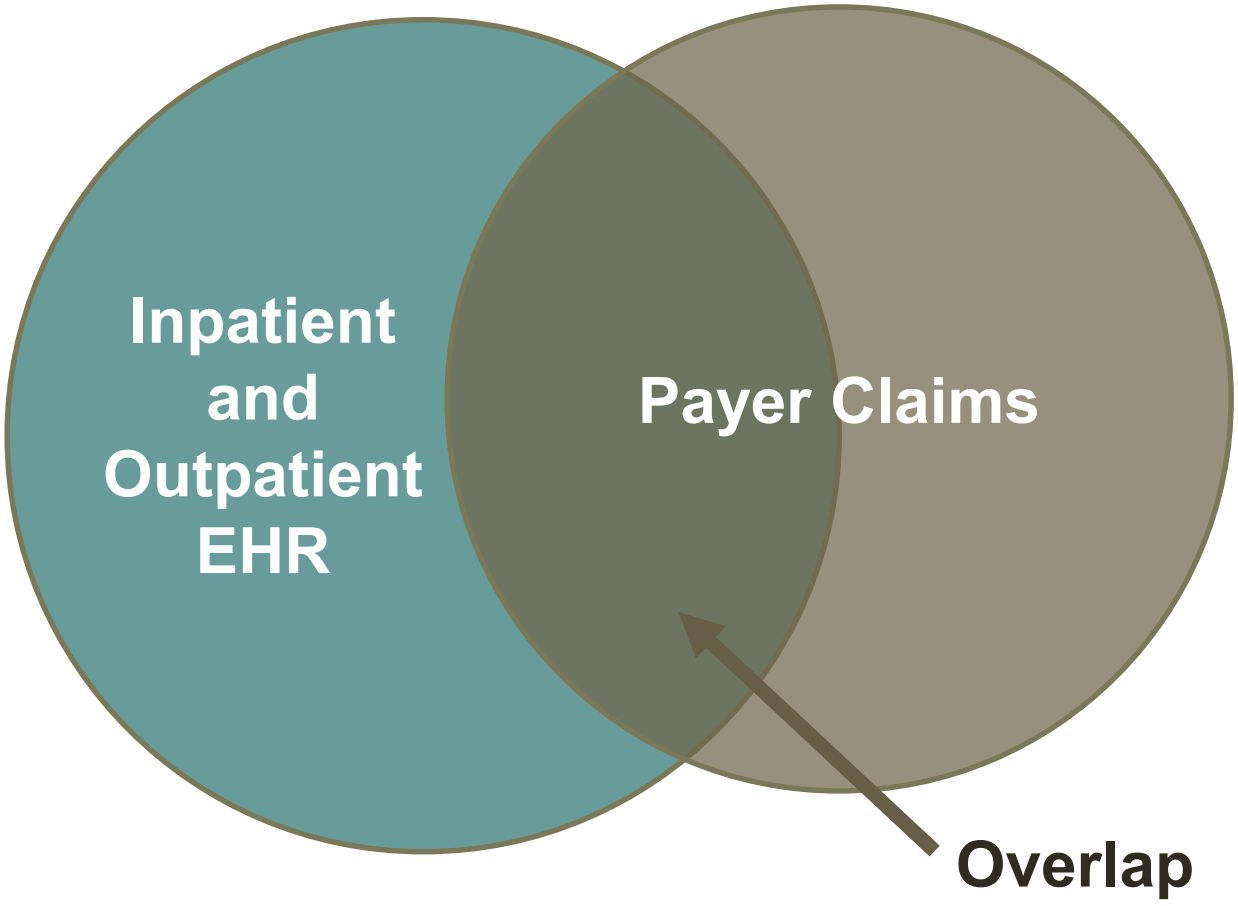
Outcomes vs endpoints



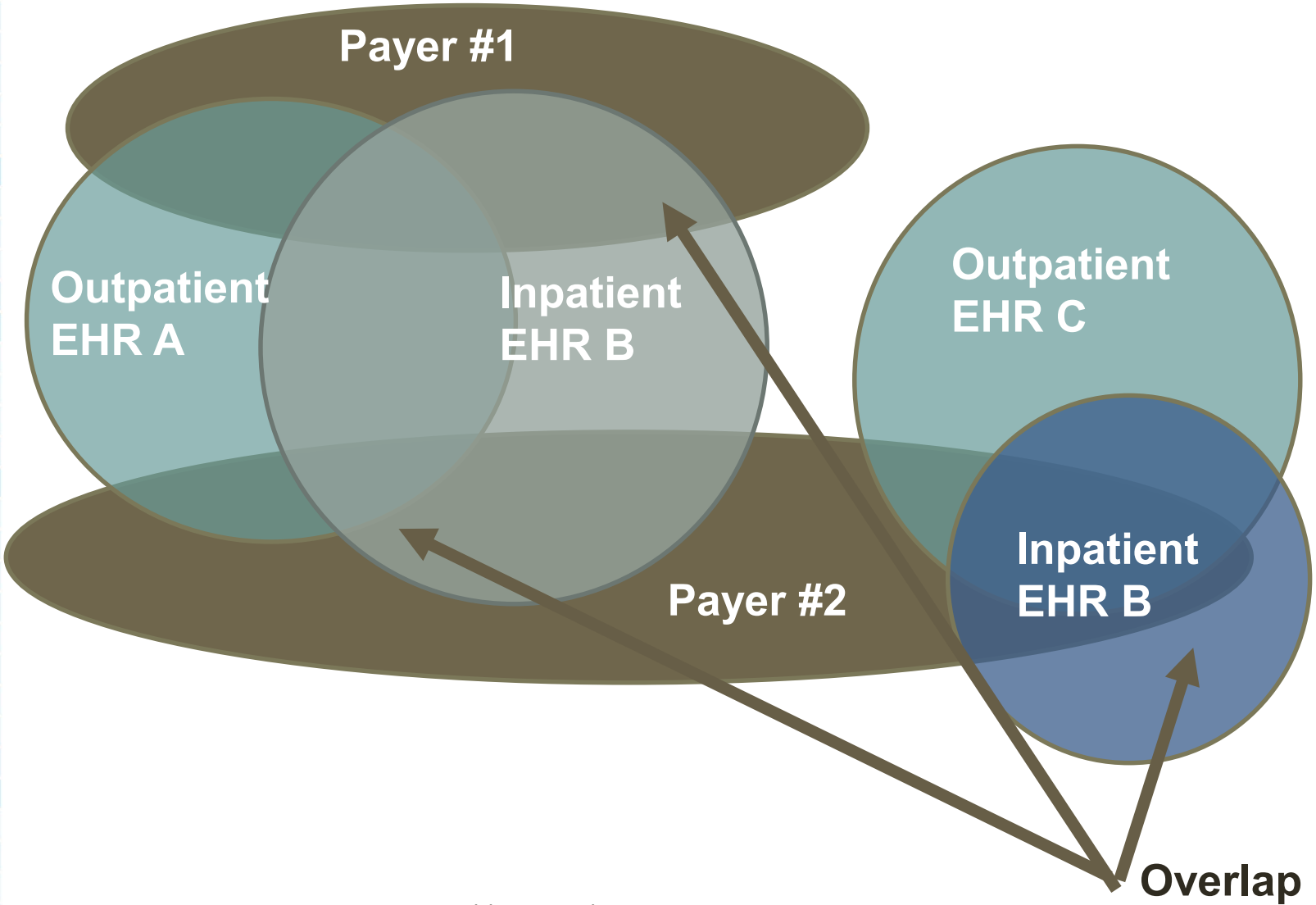
- Direct
- Surrogate
- Composite

Where is the signal?

- EHR (laboratory values, treatments, etc)
- Claims data (does the event generate a bill?)



Reality is not straightforward



Source: Greg Simon, MD, Group Health Research Institute

Data sources for endpoints in PCTs

"The first challenge in using big biomedical data effectively is to identify what the potential sources of health care information are and to determine the value of linking these together."

Finding the Missing Link for Big Biomedical Data
(See Figure 1)

Griffin M. Weber, MD; Kenneth D. Mandl, MD, MPH; Isaac S. Kohane, MD, PhD

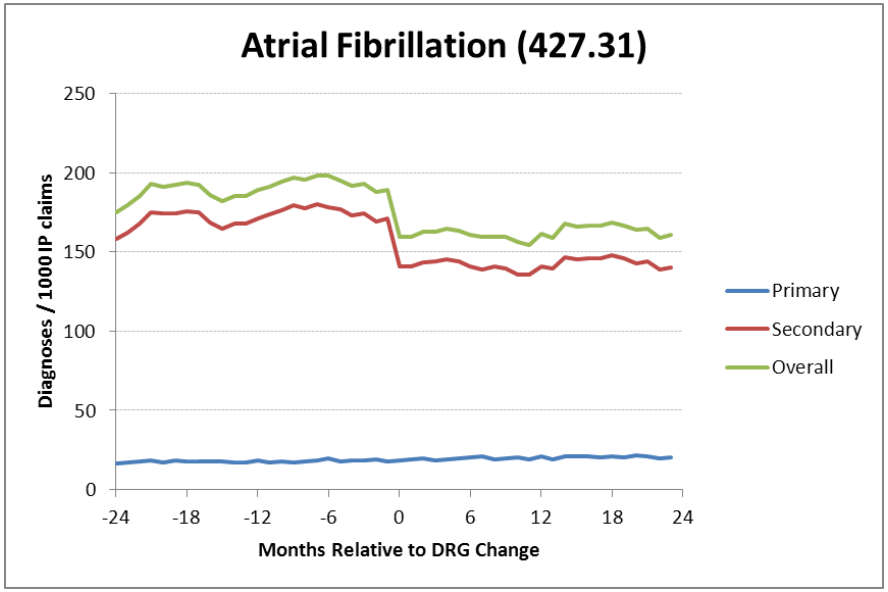
JAMA. 2014;311(24):2479-2480. doi:10.1001/jama.2014.4228

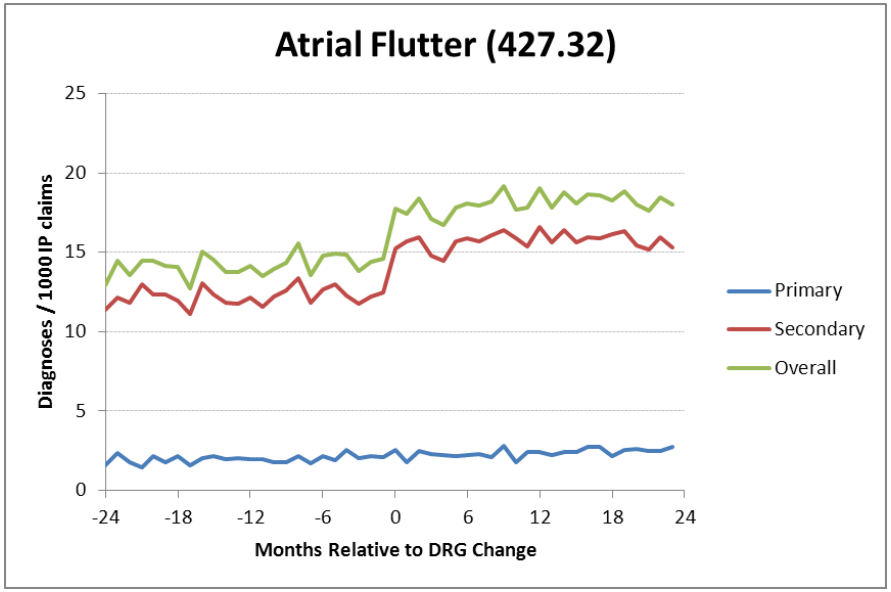
Data sources for endpoints in ePCTs

- EHR or ancillary health information systems
- Patient report
- Patient measurement

Caveats when using EHR data for endpoints (selected)

- Data may be transformed/coded for purposes other than research & clinical care





Brad Hammill, unpublished

Caveats when using EHR data for research (selected)

- Data captured in clinical notes may not be available
- EHRs are often highly customized
- EHRs may present multiple sources of similar data

Source: Hersh WR et al. Med Care 2013;51:S30-S37.

Caveats when using EHR data for research (selected)

"EHRs may present multiple sources of data that affect data provenance."

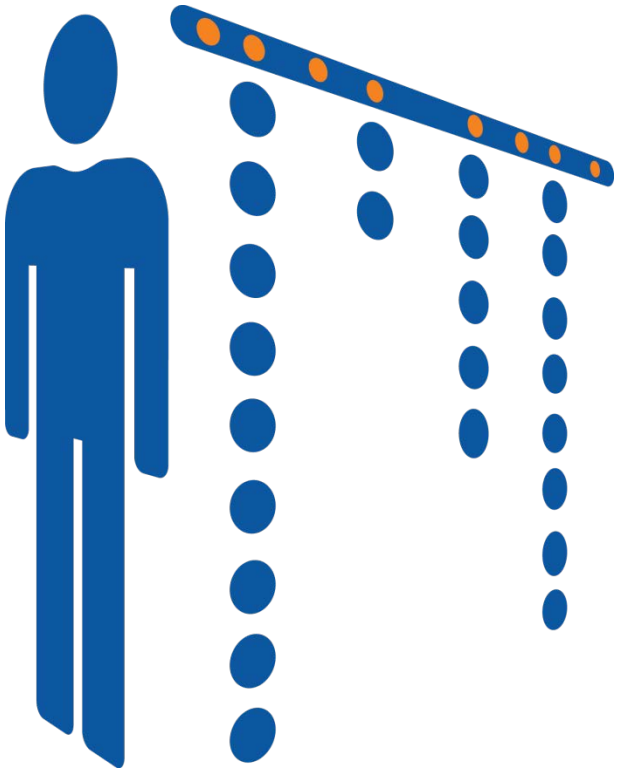
Caveats for the Use of Operational Electronic Health Record Data in Comparative Effectiveness Research *(See Figure 1)*

William R. Hersh, MD, Mark G. Weiner, MD, Peter J. Embi, MD, MS, Judith R. Logan, MD, MS, Philip R.O. Payne, PhD, Elmer V. Bernstam, MD, MSE, Harold P. Lehmann, MD, PhD, George Hripcsak, MD, MS, Timothy H. Hartzog, MD, James J. Cimino, MD, and Joel H. Saltz, MD, PhD

Med Care. 2013 Aug; 51(8 0 3): S30–S37
doi: 10.1097/MLR.0b013e31829b1dbd

Caveats when using EHR data for research (selected)

- EHRs often do not tell a complete story

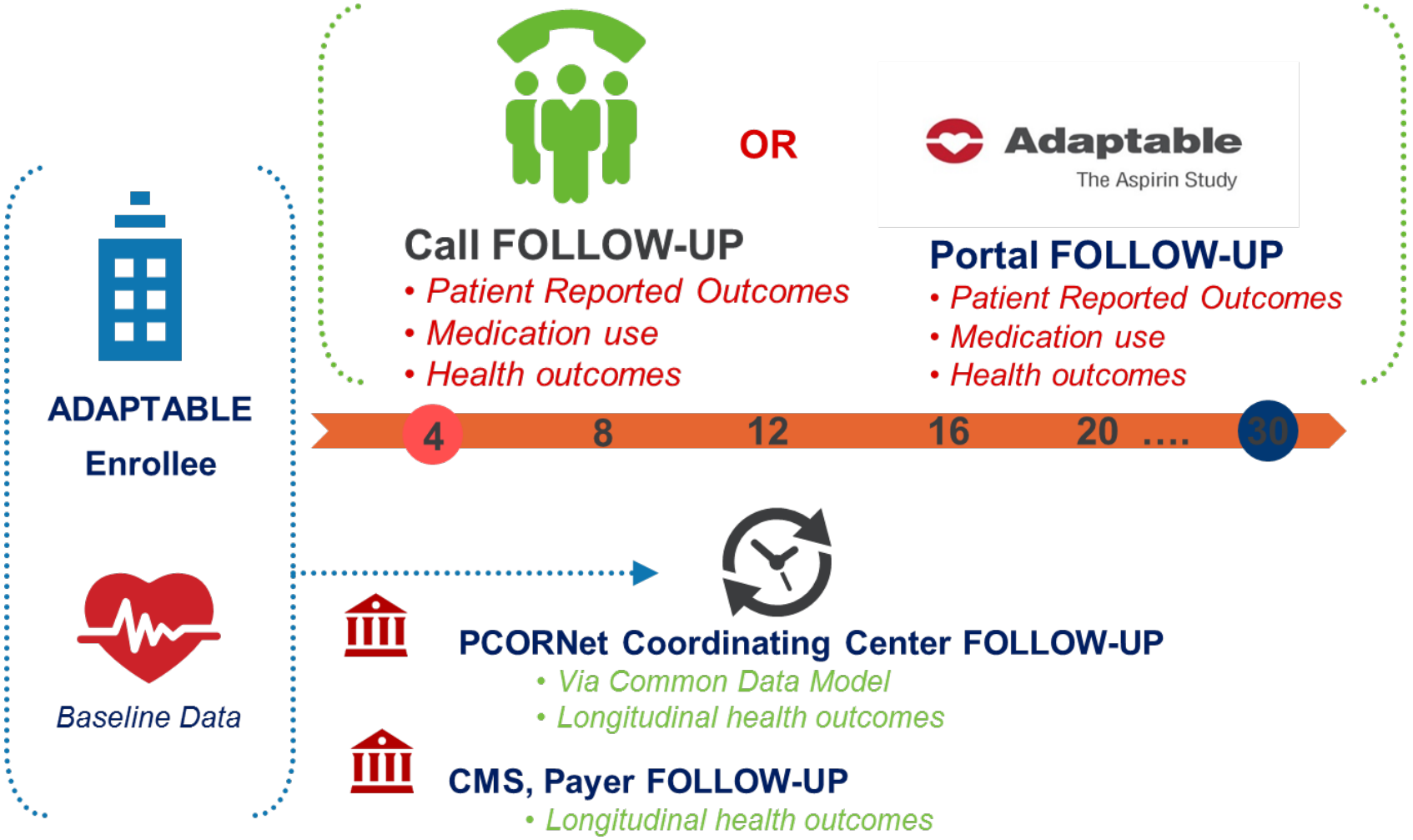


Source: Hersh WR et al. Med Care 2013;51:S30-S37.

Longitudinal data linkage

- To fully capture *all* care—complete longitudinal data—linking research & insurance claims data is often necessary
- Without explicit consent, getting longitudinal data from an insurance carrier can be an insurmountable hurdle, both technically and legally

Enabling pragmatic research: escreening, eenrollment & efollow-up



Choosing and specifying endpoints in ePCTs

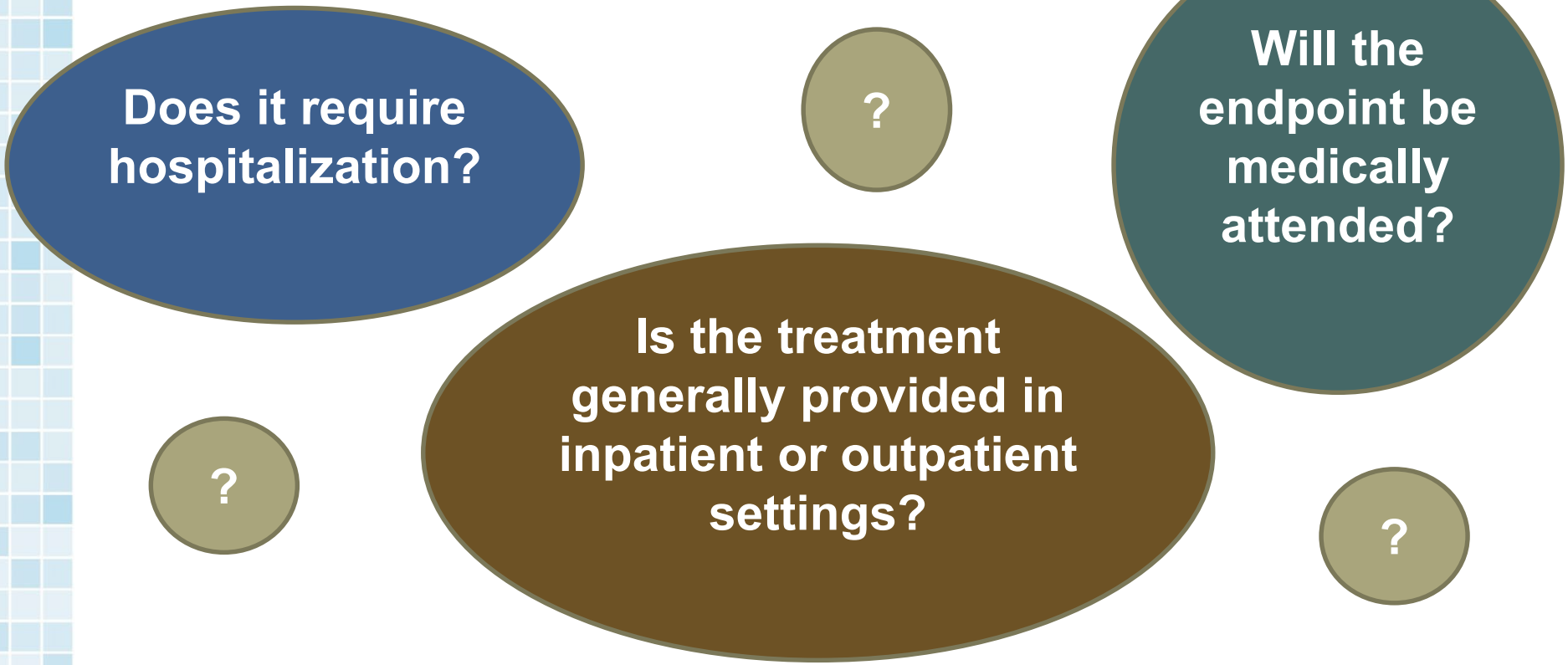
- Endpoints and outcomes need to be available as part of routine care

- Acute MI
- Broken bone
- Hospitalization

- Suicide attempts
- Gout flares
- Silent MI
- Early miscarriage

Key questions for choosing endpoints

Is the outcome medically significant such that a patient would seek care?

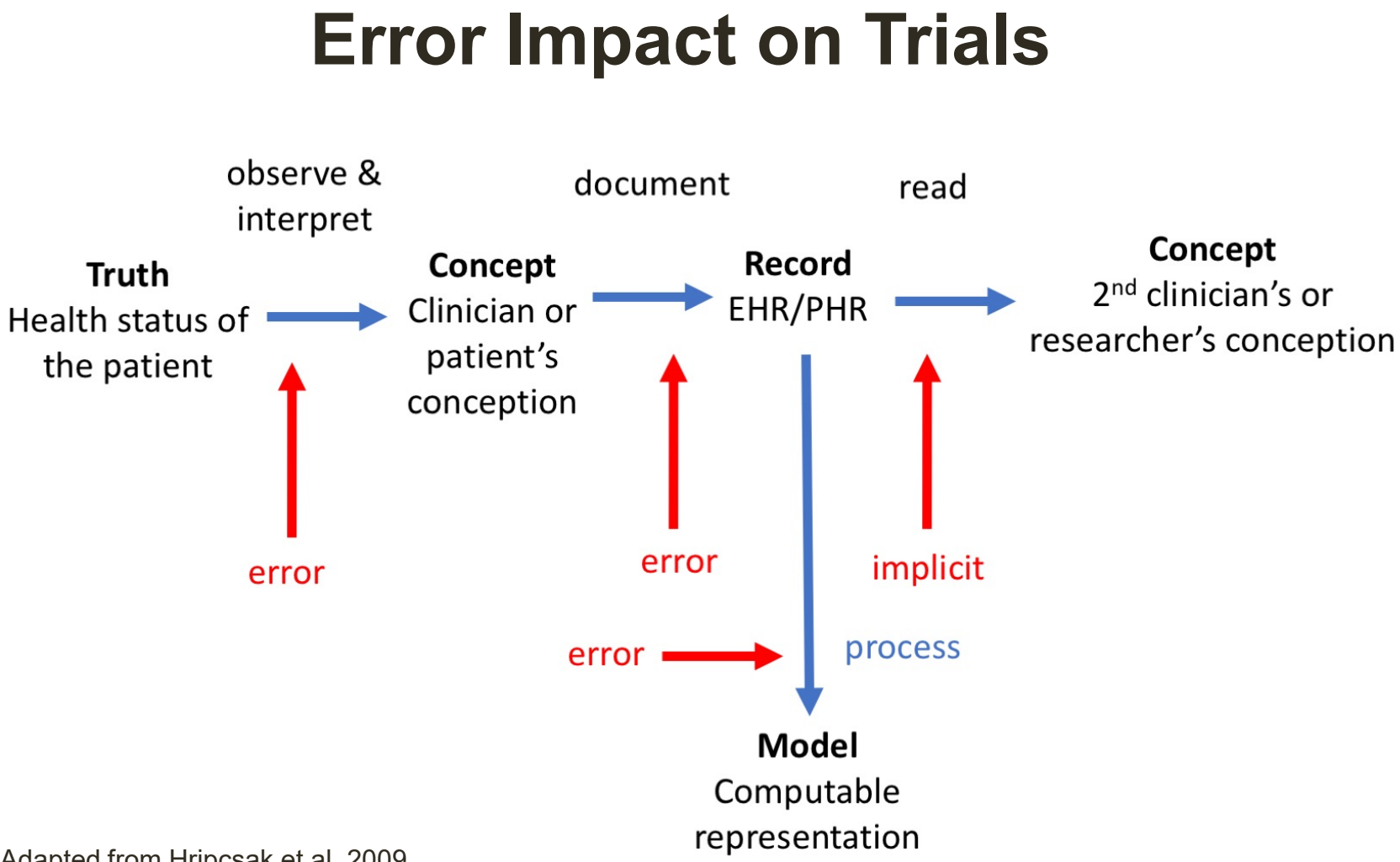


Endpoints in ePCTs

- Endpoints should be meaningful to providers and patients
  - MACE vs myocardial infarction
  - Good example of a blood test vs a clinical event
- More pragmatic endpoints …
  - Matter to providers and patients
  - Are captured reliably as part of routine clinical care
  - Do not require central adjudication
  - Are shorter-term in nature

Choosing an endpoint that is not captured reliably as part of routine clinical care or impedes the clinical workflow is not pragmatic!

Data is a surrogate for clinical phenomena



Adapted from Hripcsak et al. 2009

Key questions for using EHR data

What is the phenomenon you are trying to identify or measure?

What are the sources of error?

?

How can an you assess and reduce that error?

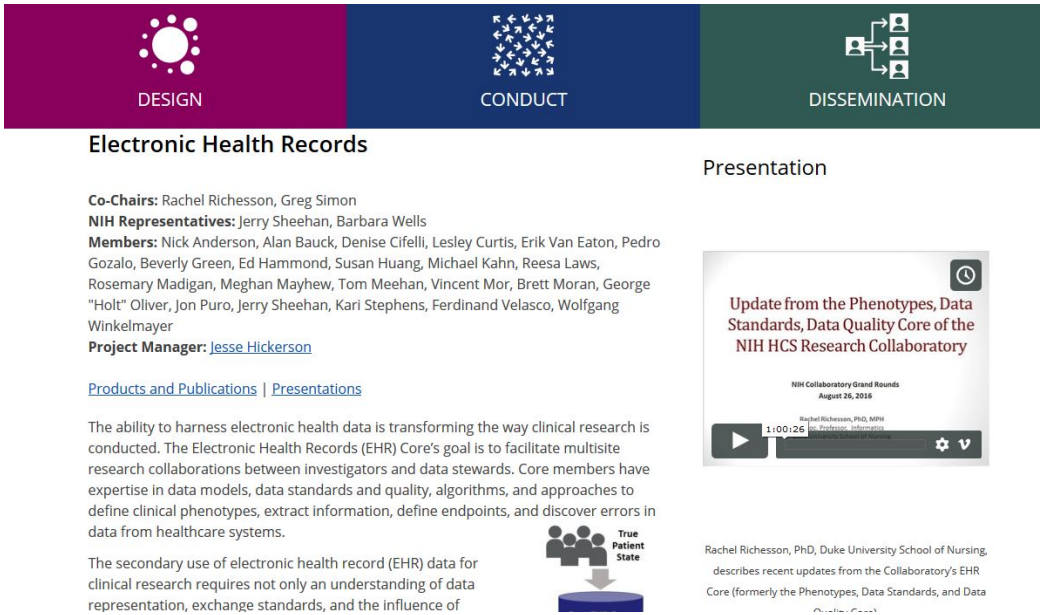
In what type of health care activity, event, documentation or data value could a "signal" be detected?

?

?

Data quality assessment

- Identify variation between populations at different sites or study groups
- Recommend formal assessment of accuracy, completeness & consistency for key data
- Data quality should be described, reported & informed by workflows

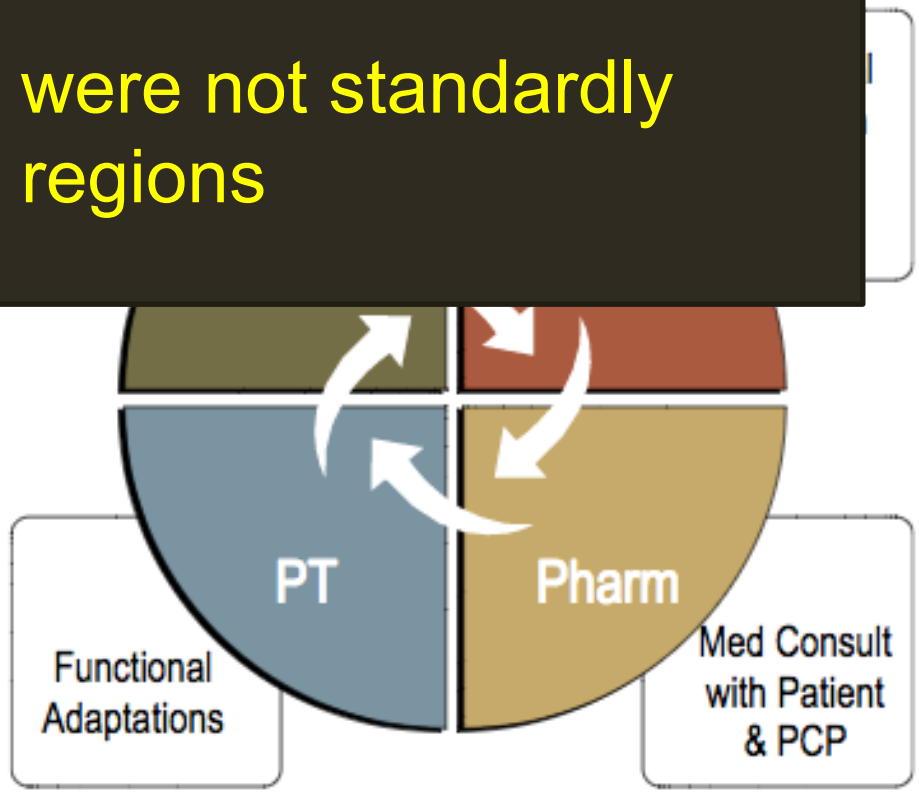


Case example: Collaborative Care for Chronic Pain in Primary Care (PPACT)

Pain Management: Usual Care

Interdisciplinary Management Embedded in Primary Care

PROs were needed, but were not standardly collected across diverse regions



Case example: PPACT

- Project leadership worked with national Kaiser to create buy-in for a common instrument
- Local IT built it within each region
- A multi-tiered approach supplemented the clinically collected PRO data at 3, 6, 9,12 months
- A follow-up phone call by research staff was necessary to maximize data collection at each time point

Outcomes measured via direct patient report

- Patient-reported outcomes (PROs) often best way to measure quality-of-life
- Challenges
  - Not routinely & consistently used in clinical care
  - Not regularly recorded in EHR
- Need mechanism to collect PROs

Mobile devices

- Smartphones, tablet computers, and portable, implantable, or wearable medical devices (mHealth)
  - Some mHealth devices transmit data to a data warehouse every night
  - Largely considered imperfect measures
- Patient-facing mobile phone apps can be used in PCT for passive or active surveillance

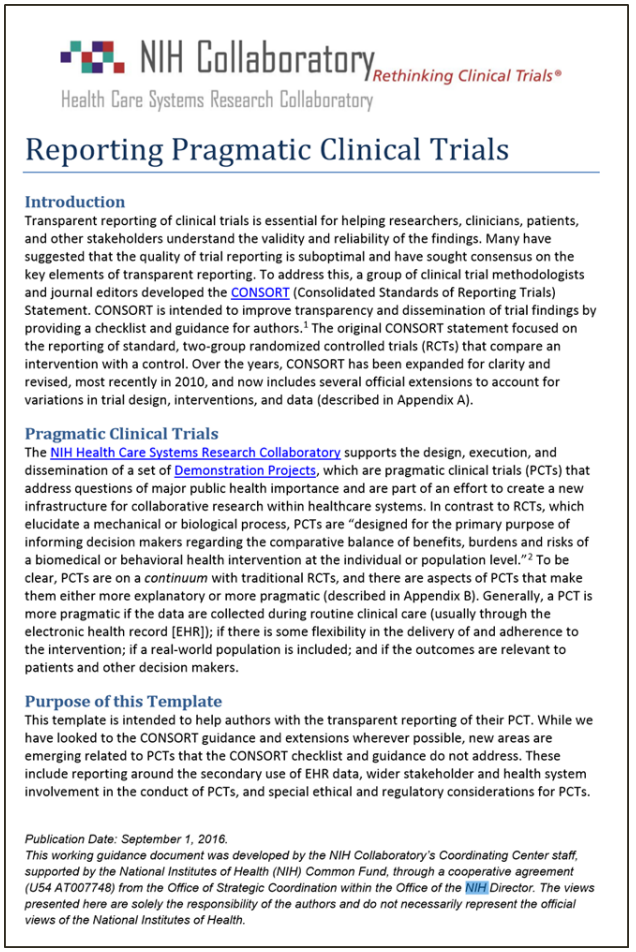
Administration

AHRQ Challenge to Focus on PROs in EHRs

According to a Federal Register notice on December 26, 2017, AHRQ is going to develop user-friendly technical tools to collect and integrate patient-reported outcome data in electronic health records or other health information technology products. AHRQ says that "the limited inclusion of PRO data in electronic health records (EHRs) and other health information technology (IT) solutions reduces the understanding and use of the patient's perspective in research and clinical care… Moreover, standards do not exist for collecting and integrating PRO data into health IT systems, thereby limiting the ability to easily share these data across health systems for research or other purposes including quality improvement." Mark your calendars, as AHRQ has targeted the Fall of 2018 for these challenges.

Consider the reporting guidelines when choosing outcomes

- Clearly define primary & secondary outcome measures
- Report methods used to enhance the quality of measurements
- Explain how selected outcomes & length of follow-up are important to stakeholders



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Reporting Pragmatic Clinical Trials

Introduction

Transparent reporting of clinical trials is essential for helping researchers, clinicians, patients, and other stakeholders understand the validity and reliability of the findings. Many have suggested that the quality of trial reporting is suboptimal and have sought consensus on the key elements of transparent reporting. To address this, a group of clinical trial methodologists and journal editors developed the CONSORT (Consolidated Standards of Reporting Trials) Statement. CONSORT is intended to improve transparency and dissemination of trial findings by providing a checklist and guidance for authors.[1] The original CONSORT statement focused on the reporting of standard, two-group randomized controlled trials (RCTs) that compare an intervention with a control. Over the years, CONSORT has been expanded for clarity and revised, most recently in 2010, and now includes several official extensions to account for variations in trial design, interventions, and data (described in Appendix A).

Pragmatic Clinical Trials

The NIH Health Care Systems Research Collaboratory supports the design, execution, and dissemination of a set of Demonstration Projects, which are pragmatic clinical trials (PCTs) that address questions of major public health importance and are part of an effort to create a new infrastructure for collaborative research within healthcare systems. In contrast to RCTs, which elucidate a mechanical or biological process, PCTs are "designed for the primary purpose of informing decision makers regarding the comparative balance of benefits, burdens and risks of a biomedical or behavioral health intervention at the individual or population level."[2] To be clear, PCTs are on a *continuum* with traditional RCTs, and there are aspects of PCTs that make them either more explanatory or more pragmatic (described in Appendix B). Generally, a PCT is more pragmatic if the data are collected during routine clinical care (usually through the electronic health record [EHR]); if there is some flexibility in the delivery of and adherence to the intervention; if a real-world population is included; and if the outcomes are relevant to patients and other decision makers.

Purpose of this Template

This template is intended to help authors with the transparent reporting of their PCT. While we have looked to the CONSORT guidance and extensions wherever possible, new areas are emerging related to PCTs that the CONSORT checklist and guidance do not address. These include reporting around the secondary use of EHR data, wider stakeholder and health system involvement in the conduct of PCTs, and special ethical and regulatory considerations for PCTs.

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Defining outcomes with clinical phenotypes

"Differences across phenotype definitions can potentially affect their application in healthcare organizations and the subsequent interpretation of data."

A comparison of phenotype definitions for diabetes mellitus
(See Figure 1 and Table 1)

Rachel L Richesson, Shelley A Rusincovitch, Douglas Wixted, Bryan C Batch, Mark N Feinglos, Marie Lynn Miranda, W Ed Hammond, Robert M Califf, Susan E Spratt

J Am Med Inform Assoc, Volume 20, Issue e2, 1 December 2013, Pages e319–e326; doi.org/10.1136/amiajnl-2013-001952

Phenotypes

Group - Any -

Include Methods ICD 10 Codes

Exclude Methods

Mine Only - Any -

Apply

Title	Groups	Institutions	Data and Methods	Status
Atrial Fibrillation - Demonstration Project	Vanderbilt - SD/RD Group	Vanderbilt University	CPT Codes, ICD 9 Codes, Natural Language Processing	Final
Cardiac Conduction (QRS)	eMERGE Phenotype WG	Vanderbilt University	CPT Codes, ICD 9 Codes, Laboratories, Medications, Natural Language Processing	Final
Cataracts	eMERGE Phenotype WG	Marshfield Clinic Research Foundation	CPT Codes, ICD 9 Codes, Medications, Natural Language Processing	Final
Clopidogrel Poor Metabolizers	Denny's Group at Vandy, VESPA - Vanderbilt Electronic Systems for Pharmacogenomic Assessment		CPT Codes, ICD 9 Codes, Laboratories, Medications, Natural Language Processing	Final
Crohn's Disease - Demonstration Project	Vanderbilt - SD/RD Group	Vanderbilt University	ICD 9 Codes, Medications, Natural Language Processing	Final
Dementia	eMERGE Phenotype WG	Group Health Cooperative	ICD 9 Codes, Medications	Final
Diabetic Retinopathy	eMERGE Phenotype WG	Marshfield Clinic Research Foundation	CPT Codes, ICD 9 Codes, Medications, Natural Language Processing	Final
Drug Induced Liver Injury	eMERGE Phenotype WG	Columbia University	ICD 9 Codes, Laboratories, Medications, Natural	Final

Most Recent Phenotypes

- Severe Early Childhood Obesity
- Warfarin dose/response
- Drug Induced Liver Injury
- Clopidogrel Poor Metabolizers
- Rheumatoid Arthritis - Demonstration Project

Perspective

JAMIA
A SCHOLARLY JOURNAL OF INFORMATICS IN HEALTH AND BIOMEDICINE

Pragmatic (trial) informatics: a perspective from the NIH Health Care Systems Research Collaboratory

Rachel L Richesson,[1,2] Beverly B Green,[3] Reesa Laws,[4] Jon Puro,[5] Michael G Kahn,[6] Alan Bauck,[4] Michelle Smerek,[7] Erik G Van Eaton,[8] Meredith Zozus,[9] W Ed Hammond,[2] Kari A Stephens,[10] and Greg E Simon[3]

- Competition for IT resources
- Need to optimize clinical data for research
- Only small proportion of research in EHRs

- Need to capture intervention or control activities
- Including standard of care
- Need to enable learning & research activities into EHR functions

https://academic.oup.com/jamia/article/24/5/996/3069877/ Pragmatic-trial-informatics-a-perspective-from-the

Important things to know

- Endpoints and outcomes should be meaningful to providers and patients
- Endpoints and outcomes should be relatively easy to collect (ie, pragmatic)
- Researchers do not control the design or data collected in EHR systems
- Good practices for using clinical data in PCTs are based upon scientific principles

Very important …

- The data available from the EHR may be convenient & pragmatic, but might not actually drive clinical practice or policy if used as endpoints
- Need to make sure that the endpoint that IS conveniently available will also be accepted as one that will be influential for stakeholders when the PCT results are disseminated
- “Plan with Implementation in Mind” (Topic 3)

Important things to do

- Ask questions that the data will support and design trials to minimize new data collection
- Engage EHR and data experts when defining endpoints and outcomes
- Budget for data and systems experts at each site (… and then double it)
- Develop a robust data quality assessment plan to improve value of data and to detect and address data issues

1. *What is your primary endpoint?*
2. *Is that endpoint sufficiently informative for your stakeholders?*
3. *What challenges do you anticipate in trying to ascertain that endpoint?*
4. *How might you address those challenges?*

2 min

5 min