NIH Collaboratory *Rethinking Clinical Trials®*

Health Care Systems Research Collaboratory

Living Textbook Grand Rounds Series
Choosing What to Measure and Making It Happen: Your Keys to Pragmatic Trial Success

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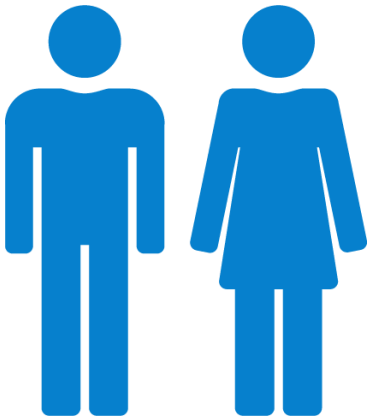
Agenda

- Devon:
  - Definitions
  - Choosing endpoints
  - Data linkage
- Rachel:
  - Patient-reported outcomes & case example
  - Using EHR Data
  - Data quality assessment
  - Recommendations
- Q&A

Endpoints and outcomes

An endpoint usually refers to an *analyzed parameter* (eg, change from baseline at 6 weeks in mean PROMIS Fatigue score)

An outcome usually refers to a *measured variable* (eg, peak volume of oxygen or PROMIS Fatigue score)



Key differences between explanatory & pragmatic trials

	EXPLANATORY	PRAGMATIC
Research question	Efficacy: Can the intervention work under the best conditions?	Effectiveness: Does the intervention work in routine practice?
Setting	Well-resourced "ideal" setting	Routine care settings including primary care, community clinics, hospitals
Participants	Highly selected	More representative with less strict eligibility criteria
Intervention design	Tests against placebo, enforcing strict protocols & adherence	Tests 2 or more real-world treatments using flexible protocols, as would be used in routine practice
Outcomes	**Often short-term surrogates or process measures; data collected outside of routine care**	**Clinically important endpoints; at least some data collected in routine care**
Relevance to practice	Indirect: Not usually designed for making decisions in real-world settings	Direct: Purposefully designed for making decisions in real-world settings

Adapted from Zwarenstein M, Treweek S, Gagnier JJ, et al. BMJ. 2008;337:a2390. doi: 10.1136/bmj.a2390. PMID: 19001484

Important things to know

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Choosing and specifying endpoints

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

Key questions for choosing endpoints

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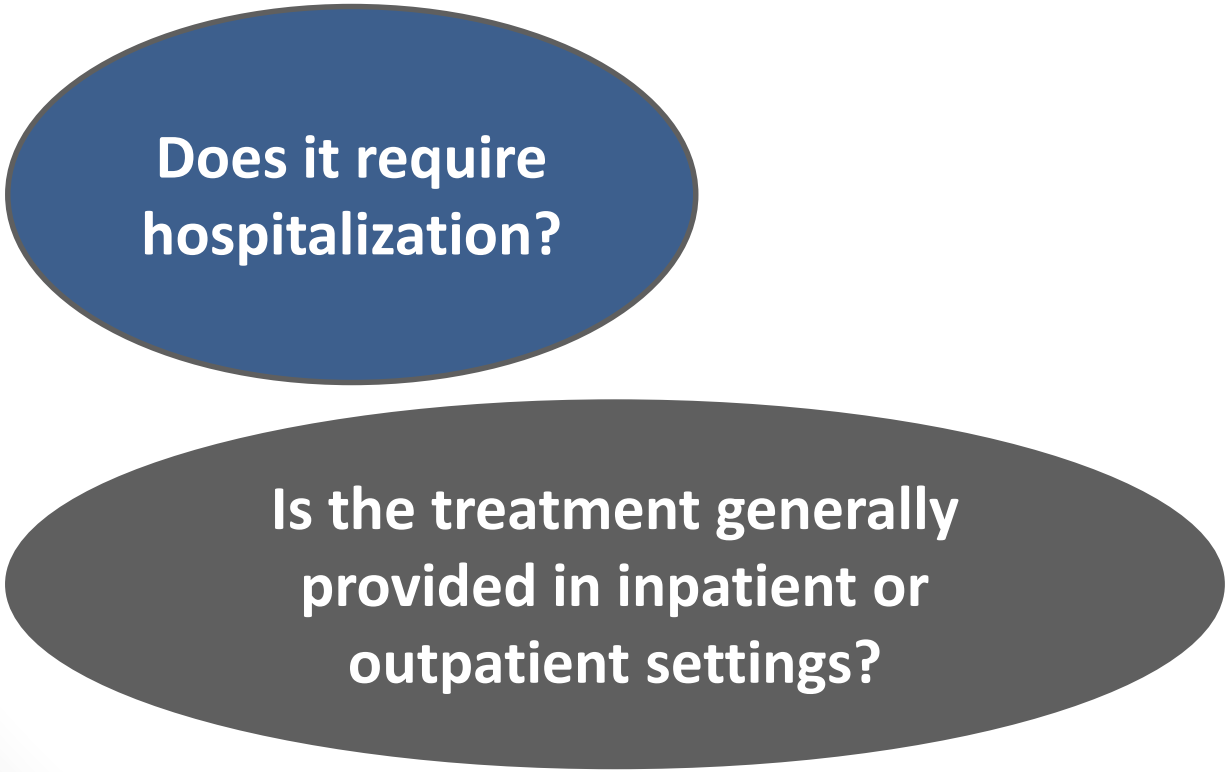

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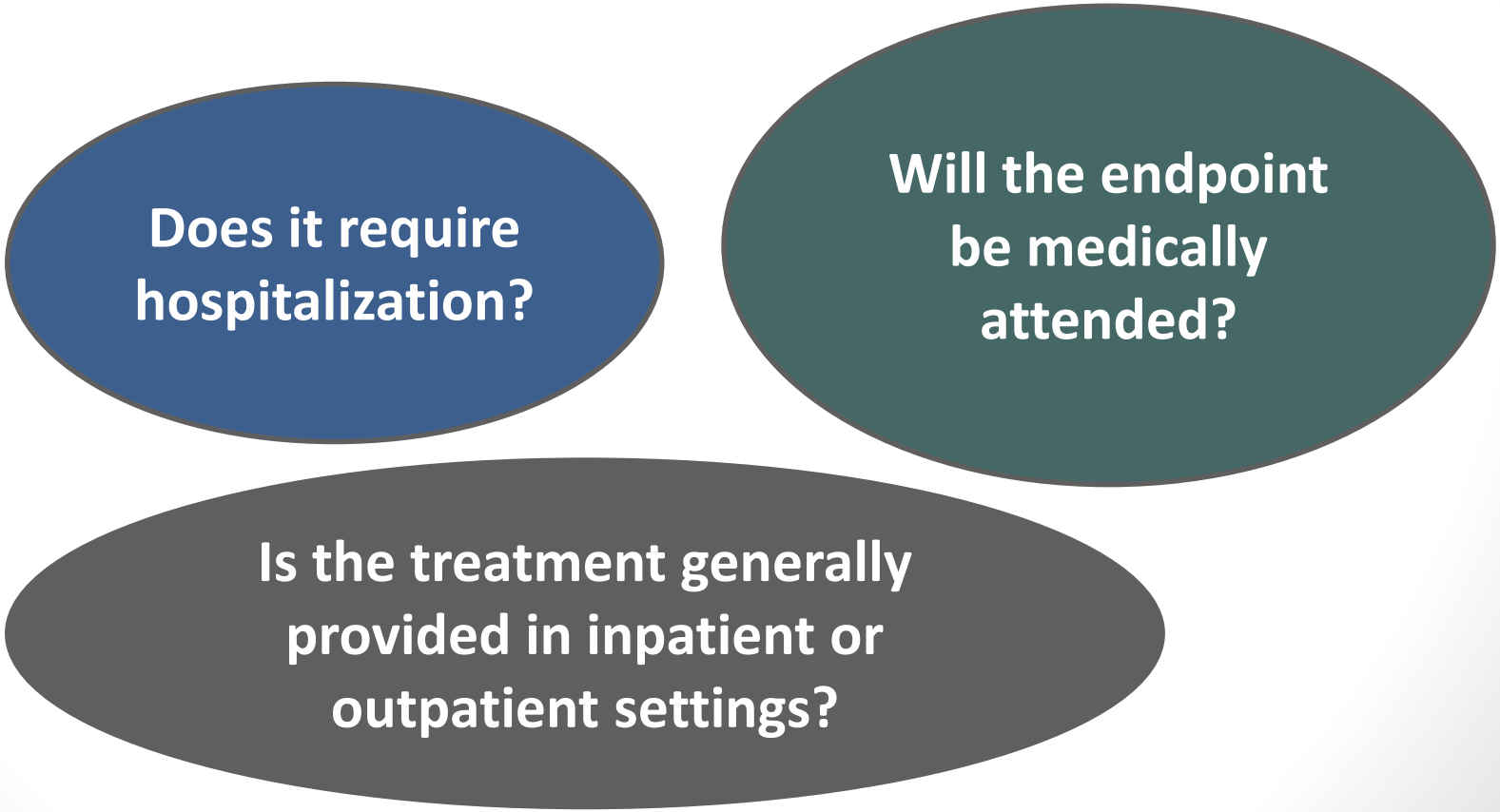

Data sources for endpoints

"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
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 (*Figure 1*)

Where is the signal?

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

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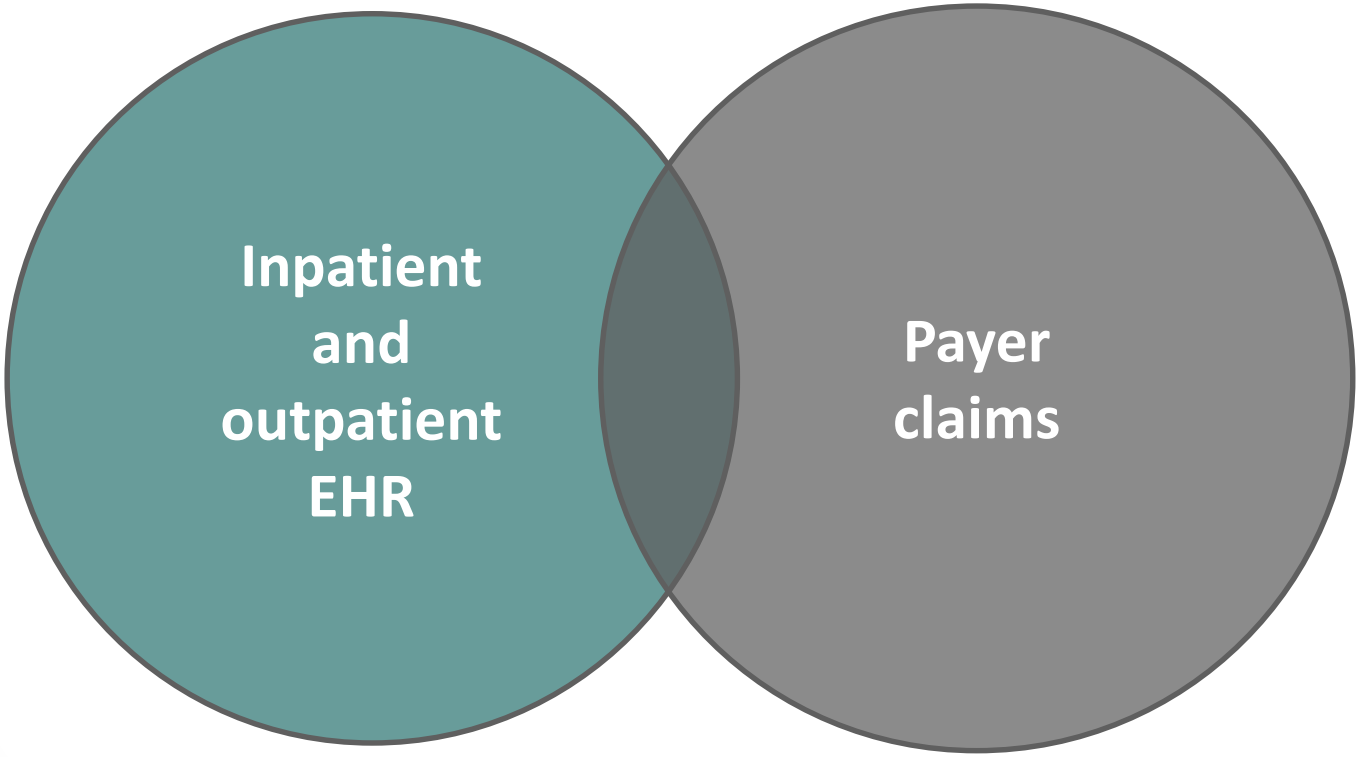

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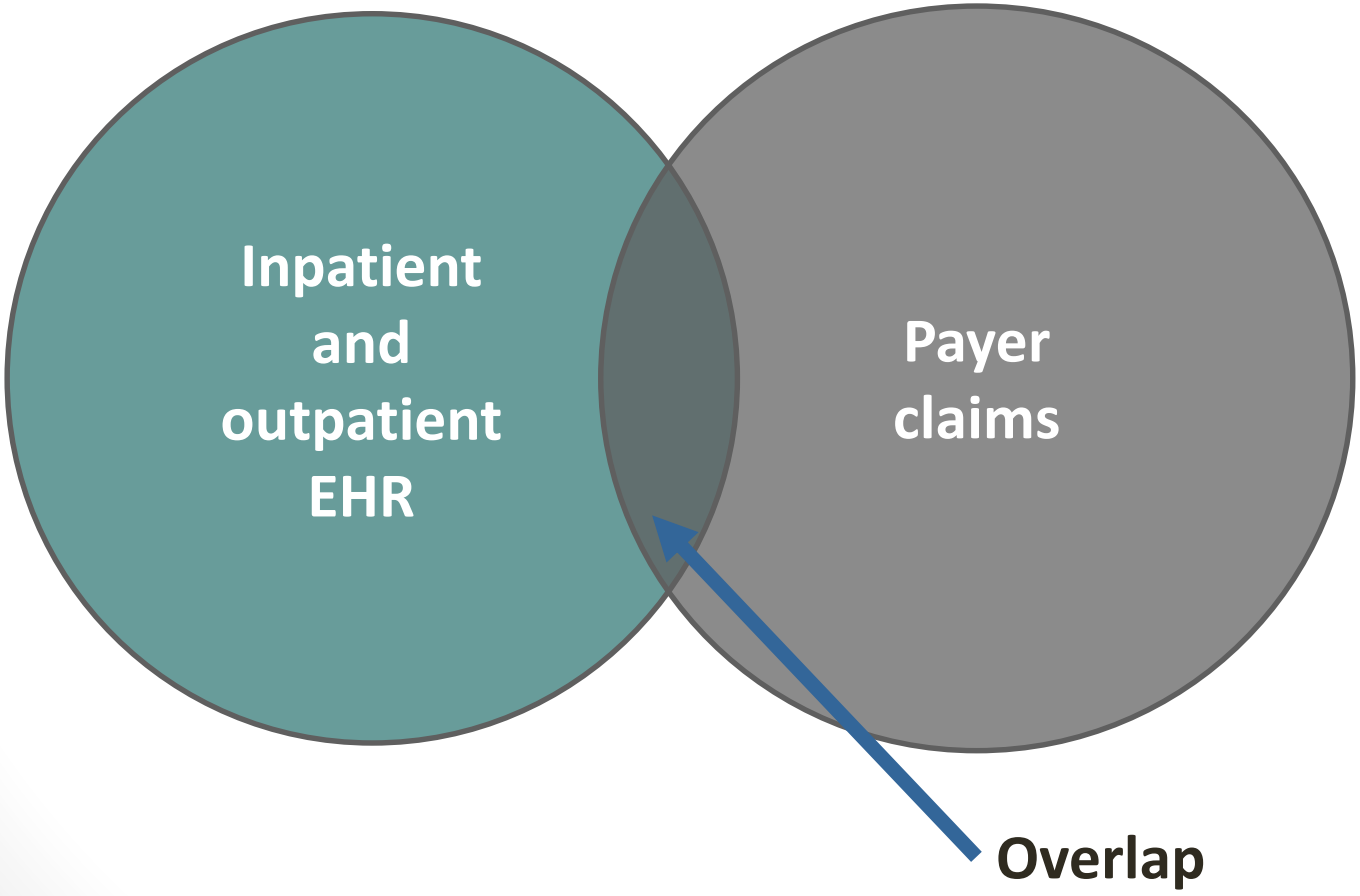
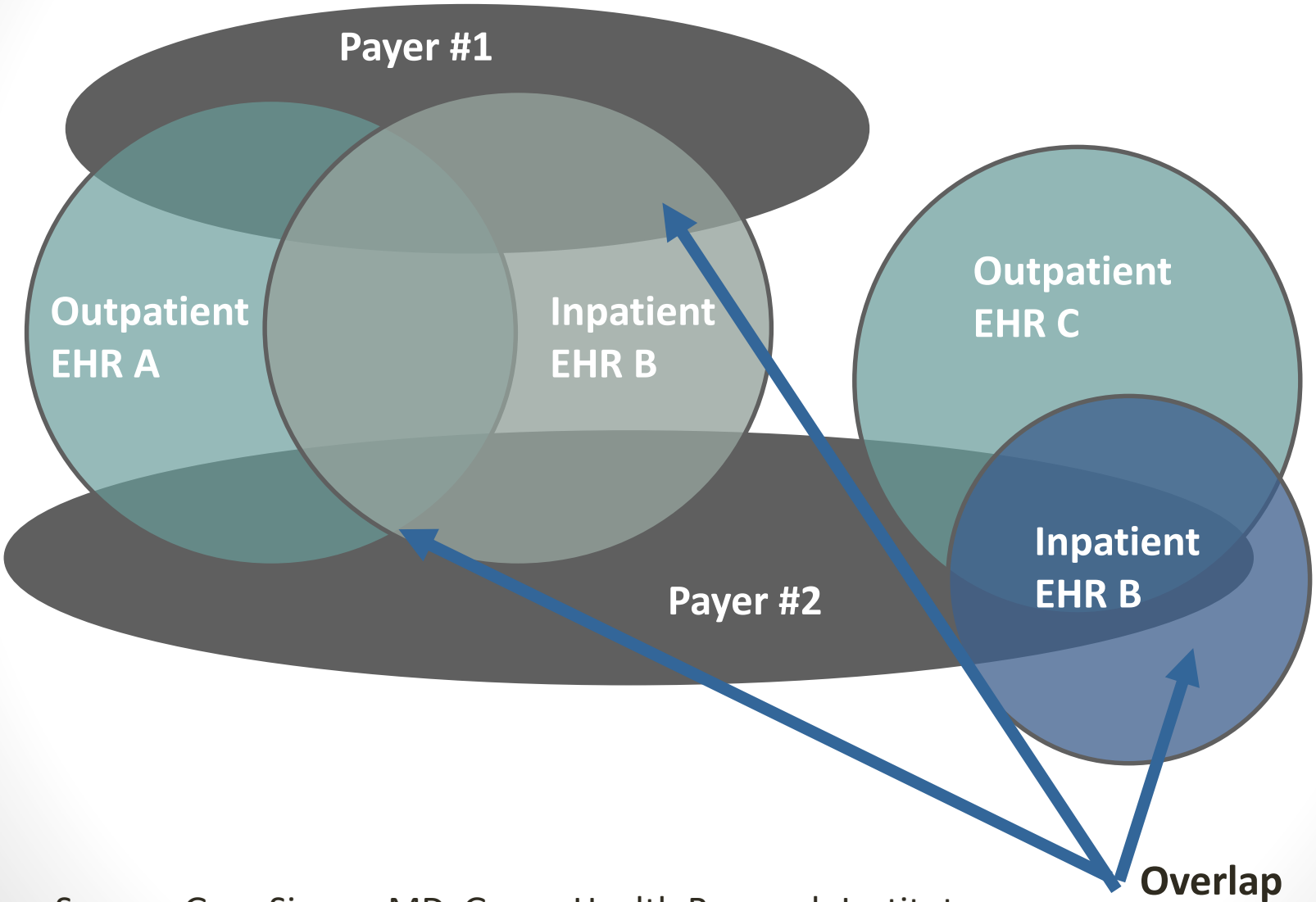


Reality is not straightforward



Source: Greg Simon, MD, Group Health Research Institute

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

Data sources for endpoints in embedded PCTs (ePCTs)

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

It's a balancing act

High relevance to real-world decision-making may come at the expense of trial efficiency

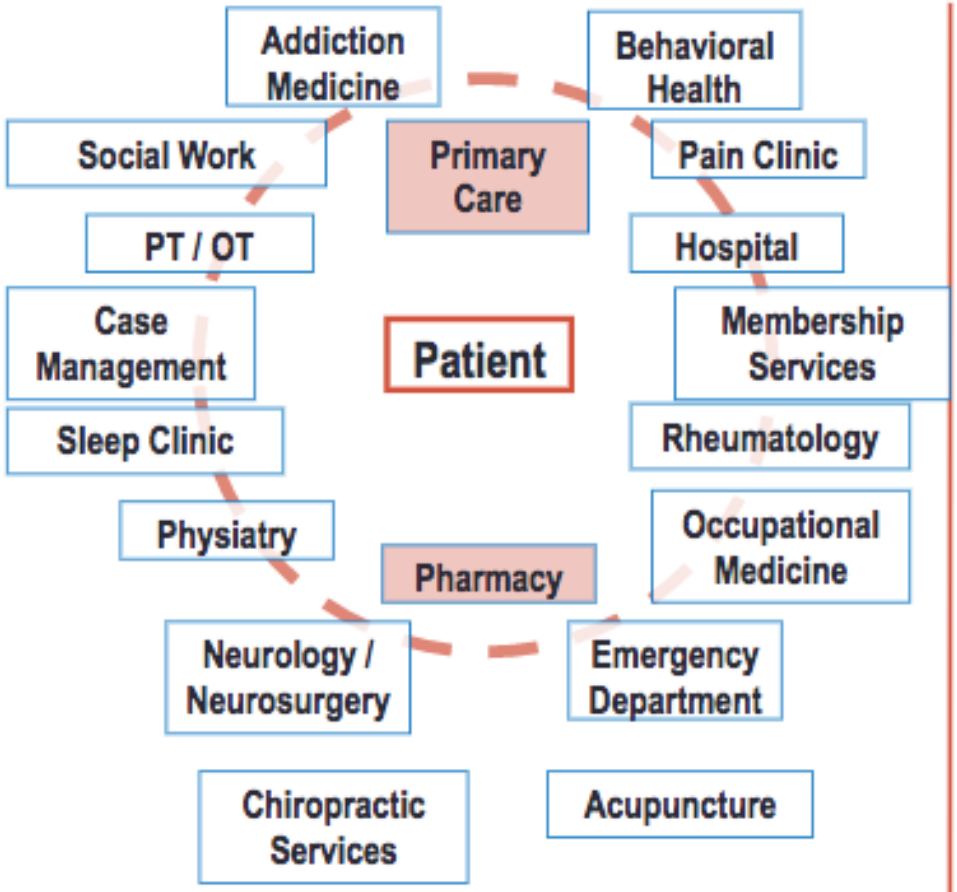
For example, a trial measuring outcomes that matter most to patients and health systems may not be able to rely exclusively on information from the EHR, and instead need to assess patient-reported outcomes, which is more expensive and less efficient

Outcomes measured via direct patient report

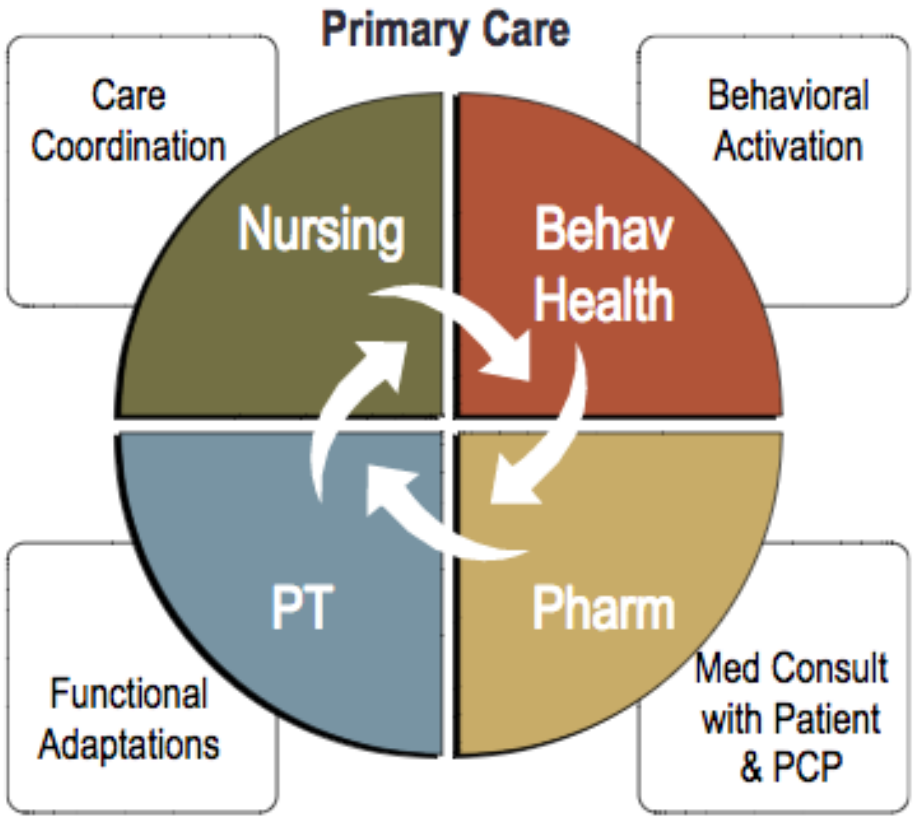
- Patient-reported outcomes (PROs) are often the best way to measure quality of life
- Challenges
  - Not routinely or consistently used in clinical care
  - Not regularly recorded in EHR

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

Pain Management: Usual Care



Interdisciplinary Management Embedded in Primary Care



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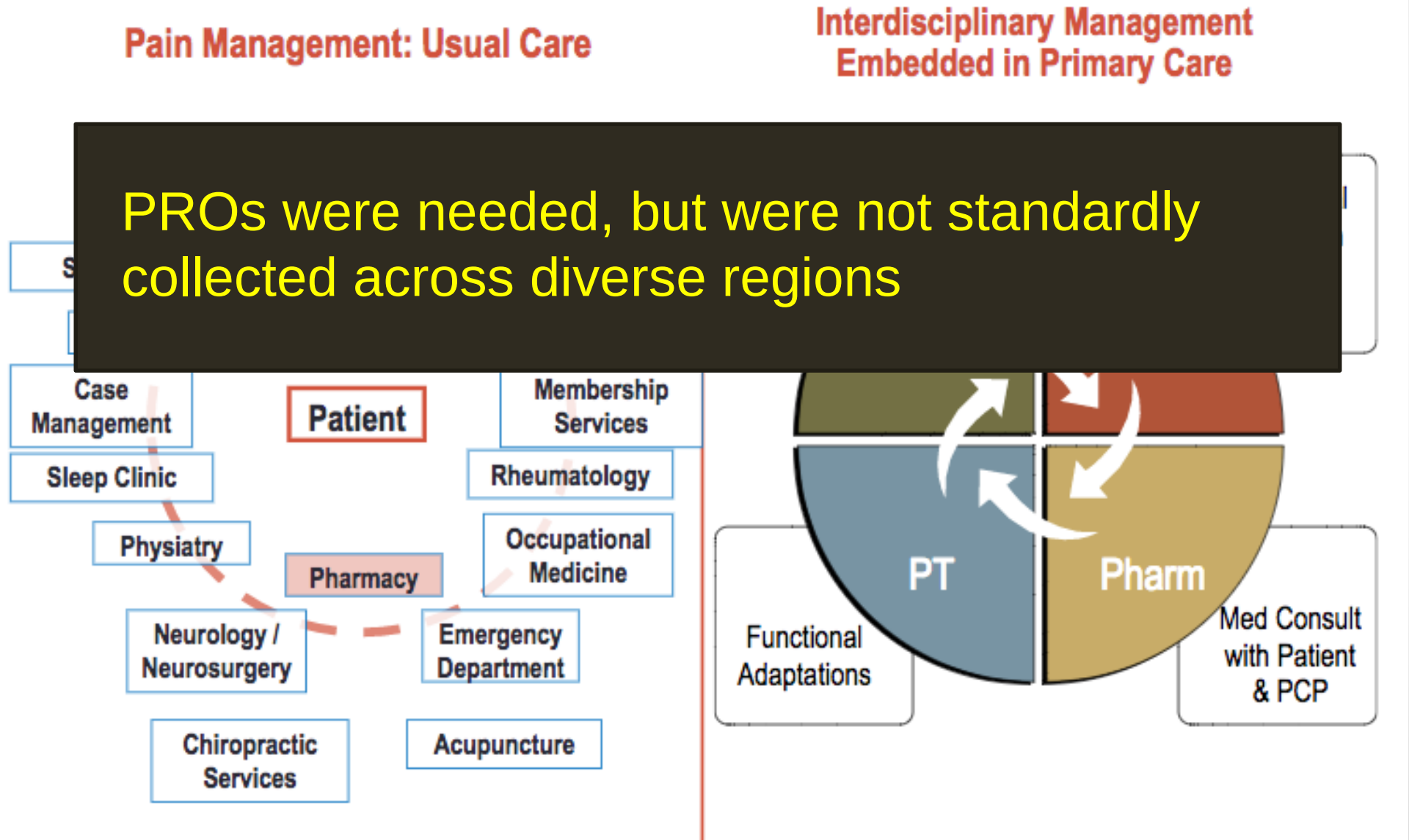


Case example: PPACT

- 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

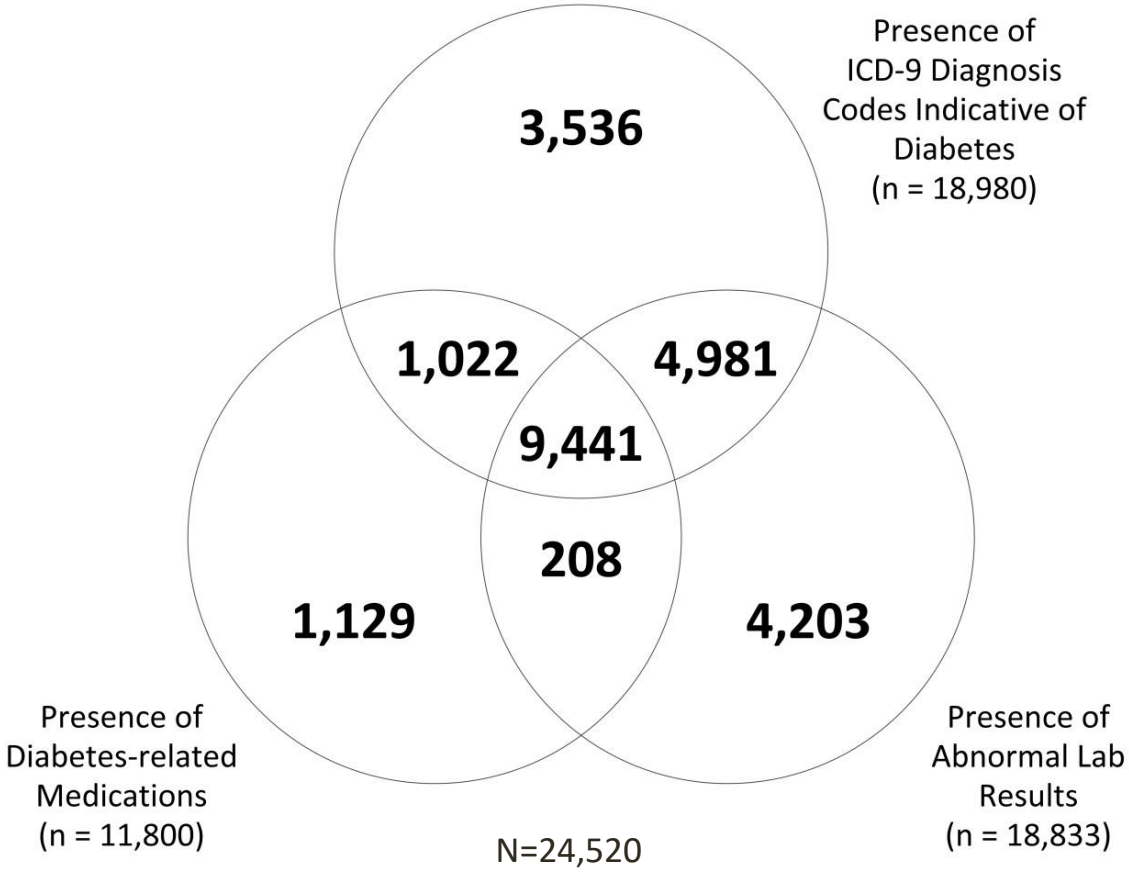
Defining outcomes with EHR data

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

A comparison of phenotype definitions for diabetes mellitus

Richesson R et al. J Am Med Inform Assoc, Volume 20, Issue e2, 1 December 2013, Pages e319–e326; doi.org/10.1136/amiajnl-2013-001952 *(Figure 1 and Table 1)*

Different definitions yield different cohorts



Research and applications

A comparison of phenotype definitions for diabetes mellitus

"Computable" phenotype definition

Diabetes defined as[1]:

ICD-9 codes

- one inpatient discharge diagnosis (ICD-9-CM 250.x, 357.2, 366.41, 362.01-362.07)

or any combination of two of the following events occurring within 24 months of each other:

Lab codes

- A1C ≥ 6.5% (48 mmol/mol)
- fasting plasma glucose ≥ 126 mg/dl (7.0 mmol/L)
- random plasma glucose ≥ 200 mg/dl (11.1 mmol/L)
- 2-h 75-g OGTT ≥ 200 mg/dl
- outpatient diagnosis code (same codes as inpatient)
- anti-hyperglycemic medication dispense (see details below)
- NDC in associated list
- **…etc., etc…**

Medication codes

1. Nichols GA, Desai J, Elston Lafata J, et al. Construction of a Multisite DataLink Using Electronic Health Records for the Identification, Surveillance, Prevention, and Management of Diabetes Mellitus: The SUPREME-DM Project. Prev Chronic Dis. 2012;9:110311.

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ICD-9 codes

Lab

Medi
co

pcornet The National Patient-Centered Clinical Research Network

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PheKB a knowledgebase for discovering phenotypes from electronic medical records

CMS.gov Centers for Medicare & Medicaid Services

NIH Value Set Authority Center U.S. National Library of Medicine

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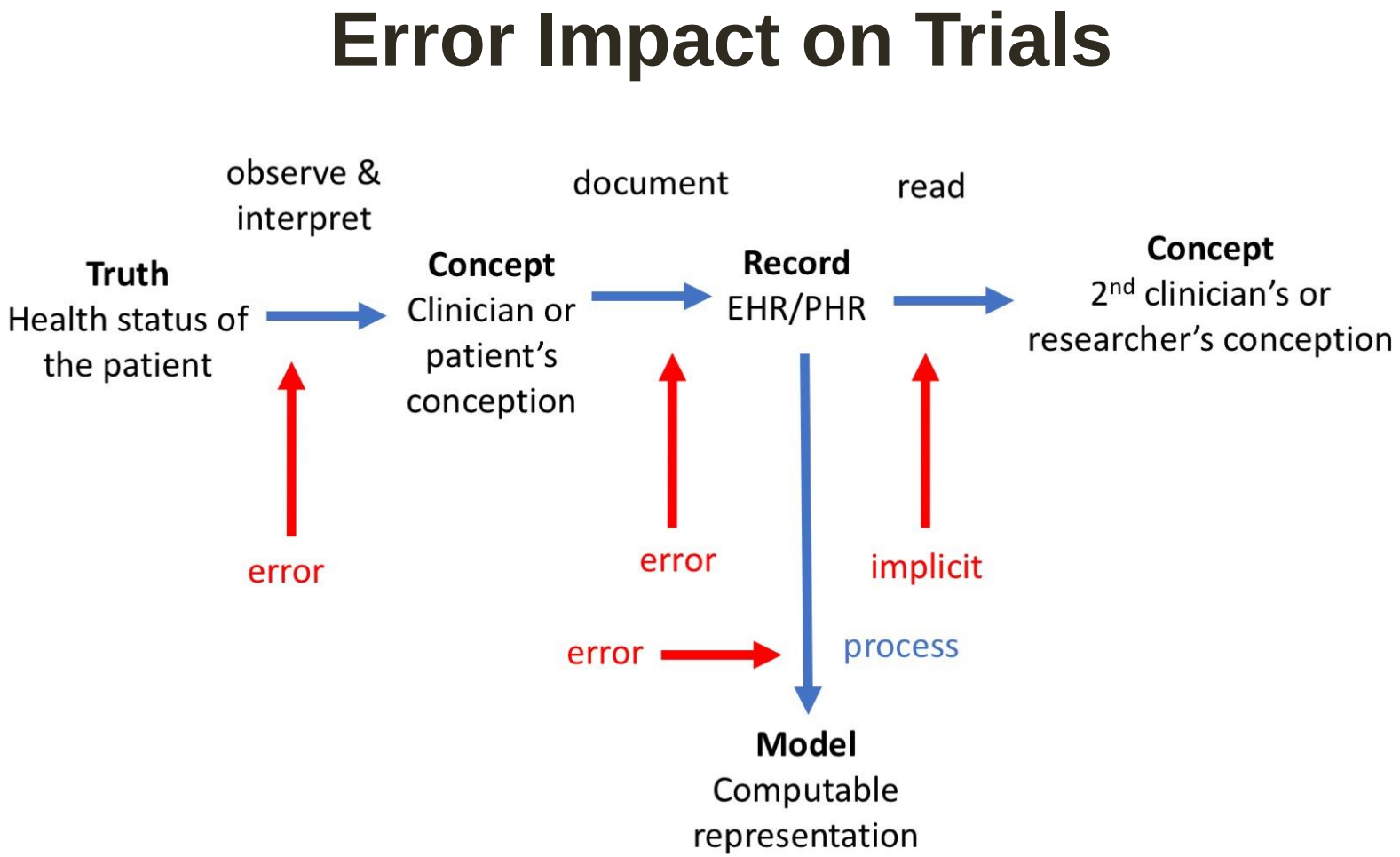
Data is a surrogate for clinical phenomena



Adapted from Hripcsak et al. 2009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Data quality assessment

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

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Assessing Data Quality for Healthcare Systems Data Used in Clinical Research

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- 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

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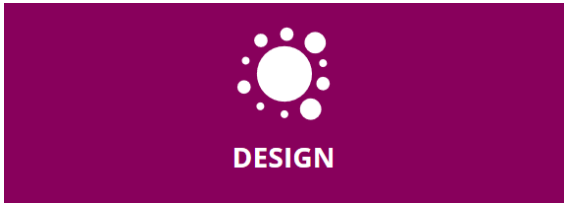
- Budget for data and systems experts at each site (… and then double it!)
- Clearly define endpoints and outcomes for transparency and reproducibility
- Develop a robust data quality assessment plan to improve value of data and to detect and address data issues

In the Living Textbook

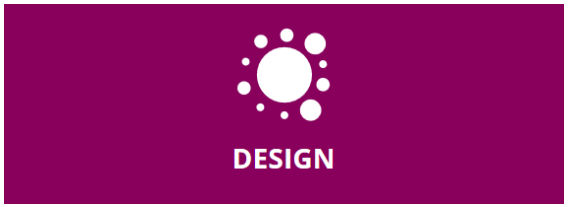


Choosing and Specifying Endpoints and Outcomes

- Introduction
- Meaningful Endpoints
- Outcomes Measured via the Electronic Health Record
- Using Death as an Endpoint
- Inpatient Endpoints in Pragmatic Clinical Trials
- Outcomes Measured via Direct Patient Report
- Outcomes Measured via Mobile Devices
- Additional Resources
- FAQ

Visit this chapter: Choosing and Specifying Endpoints and Outcomes

More in the Living Textbook



Using Electronic Health Record Data

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- Data as a Surrogate for Clinical Phenomena
- Developing and Refining the Research Questions
- Specific Uses for EHR Data in PCTs
- Identifying the Study Population and Assessing Baseline Prognostic Characteristics
- Implementing and Monitoring the Delivery of an Intervention
- Assessing Outcomes
- The Research Question Drives the Data Requirements
- Additional Resources

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Questions and Discussion