NIH Collaboratory

Health Care Systems Research Collaboratory

Rethinking Clinical Trials®

Measuring Outcomes

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Essentials of Embedded Pragmatic Clinical Trials Seminar

Learning goal

Describe methods for measuring outcomes using data sources such as electronic health records (EHRs) and patient-reported outcomes (PROs)

Outline

- Definitions
- Choosing endpoints
- Possible sources of error
- Data quality assessment
- Clinical phenotypes
- Patient-reported outcomes
- Conclusions & recommendations

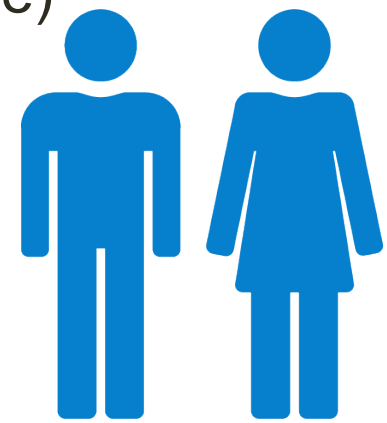
Important things to know

- 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

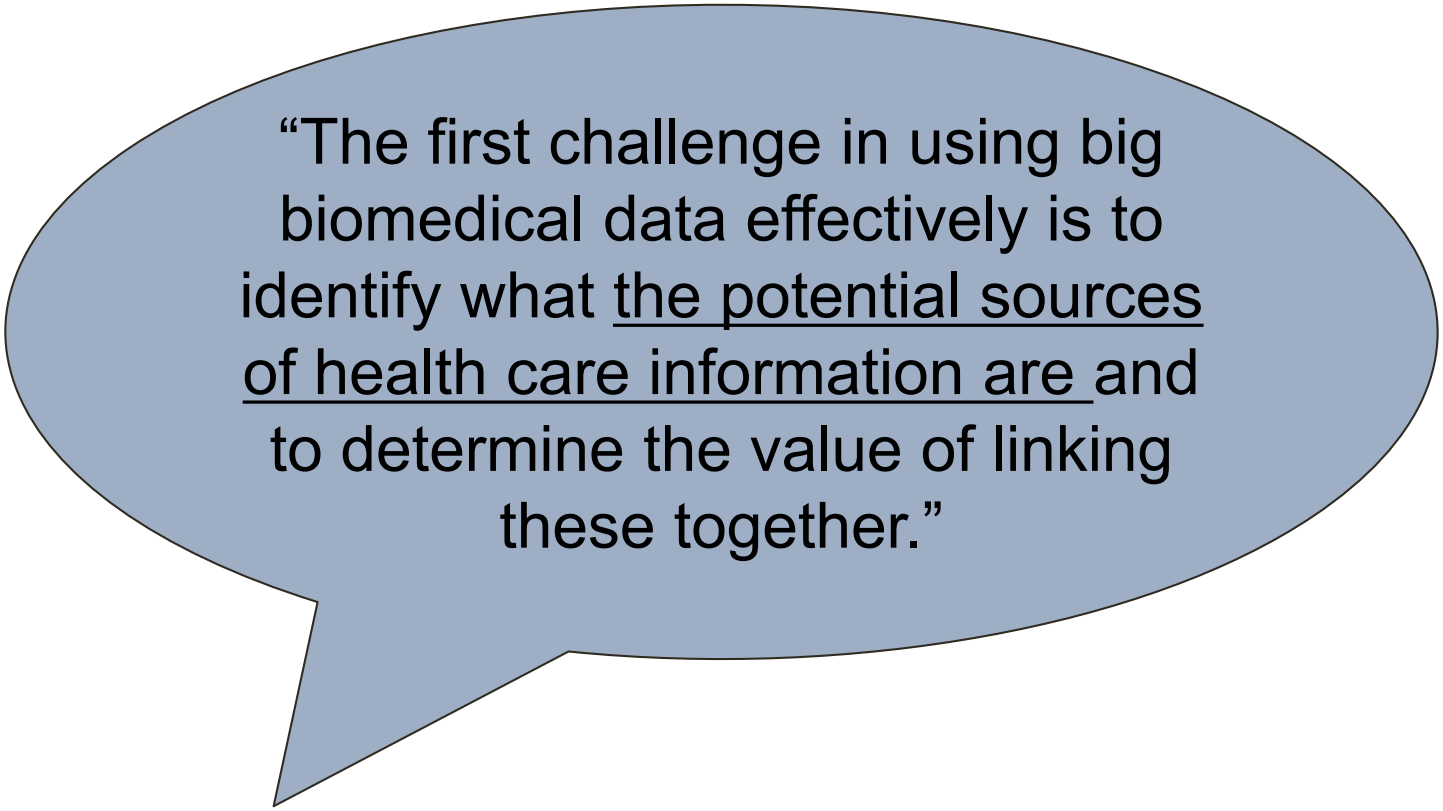
Endpoints and outcomes

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)



Data sources for endpoints in ePCTs



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*)

Data sources for endpoints in ePCTs

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

Endpoints in ePCTs

- All research endpoints should be meaningful to providers and patients
- 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**!**

Choosing and specifying endpoints in ePCTs

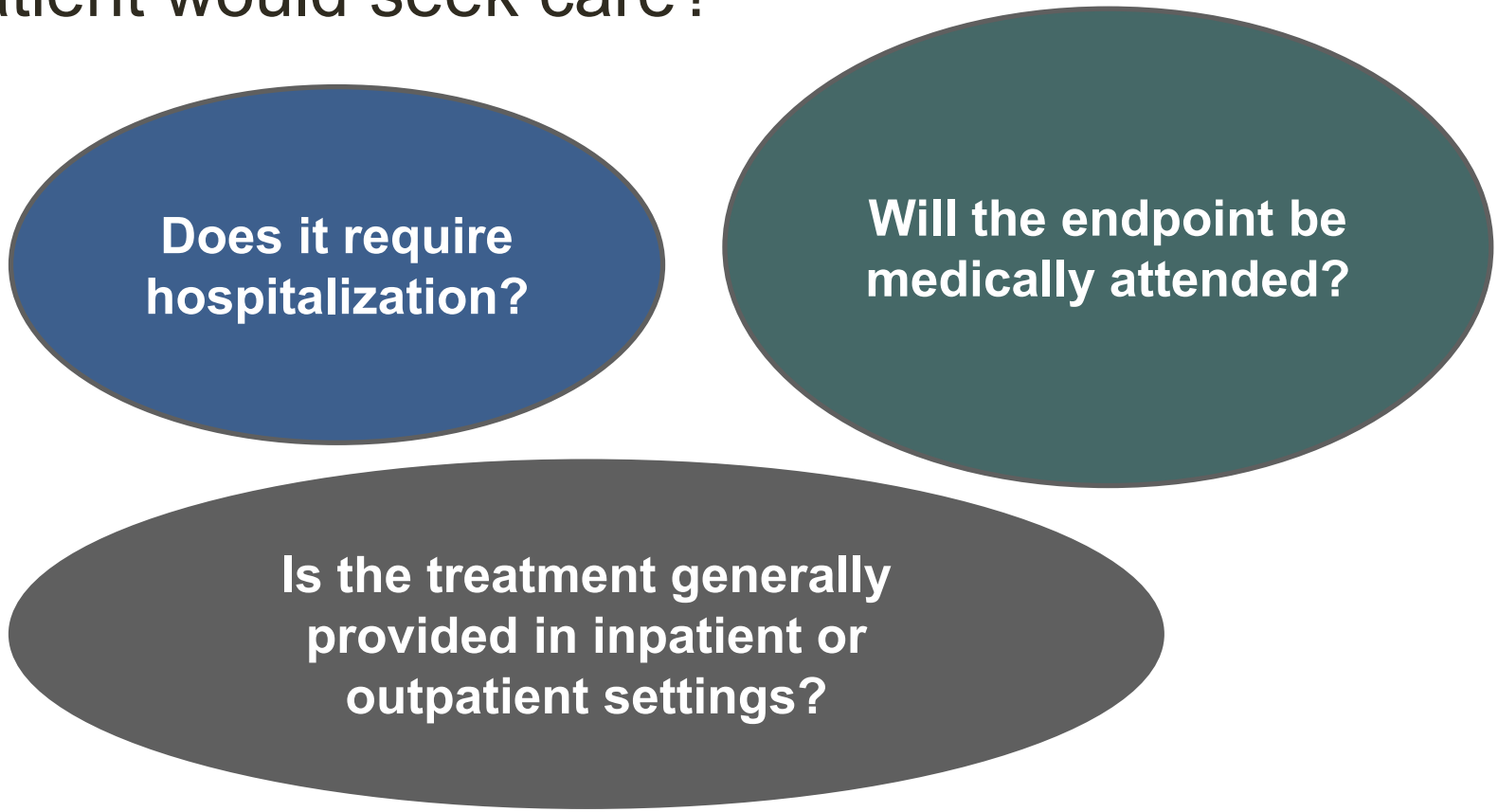
Endpoints and outcomes need to be available as part of routine care

- Acute MI
- Broken bone
- Hospitalization

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

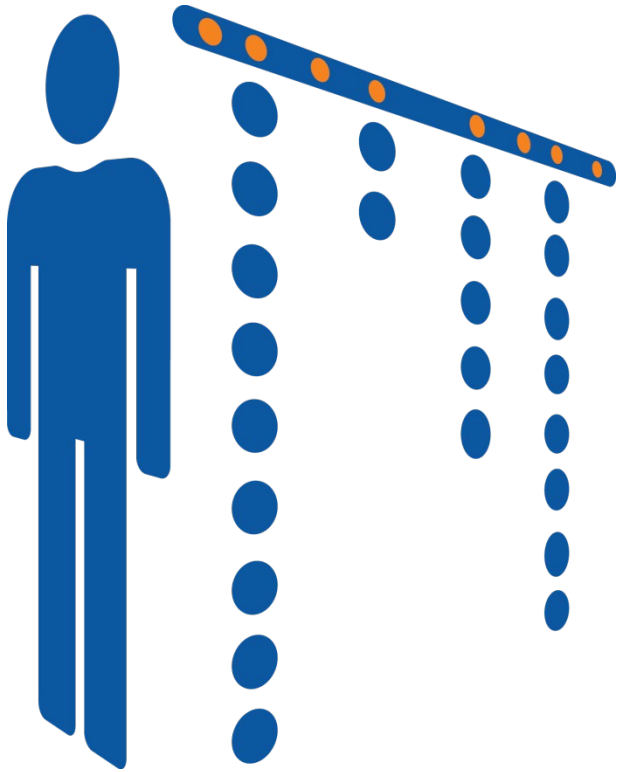
Key questions for choosing endpoints

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



Caveats when using EHR data for research (selected)

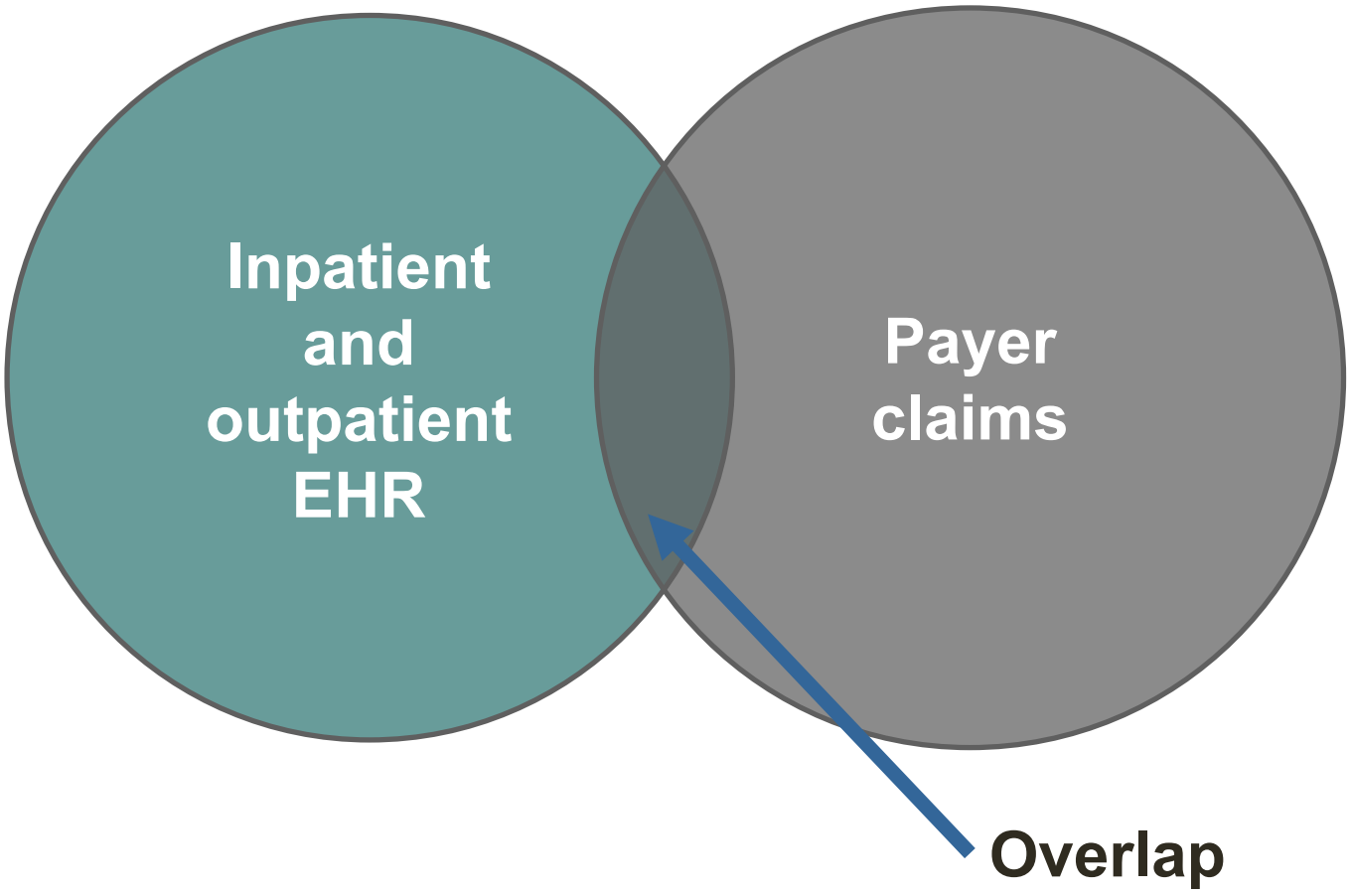
EHRs often do not tell a complete story



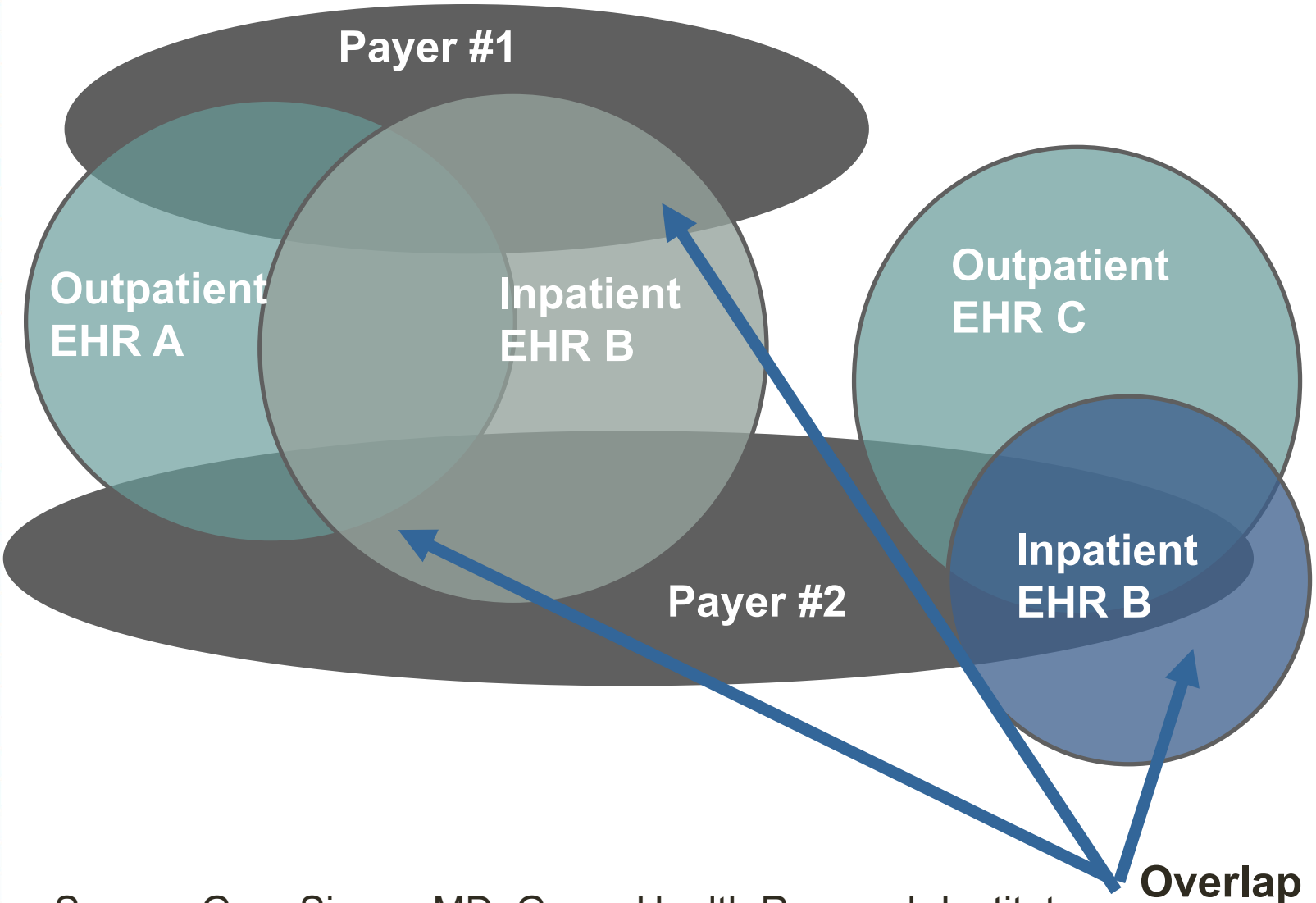
Source: Hersh WR et al. Med Care 2013;51:S30-S37

Where is the signal?

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



Reality is not straightforward

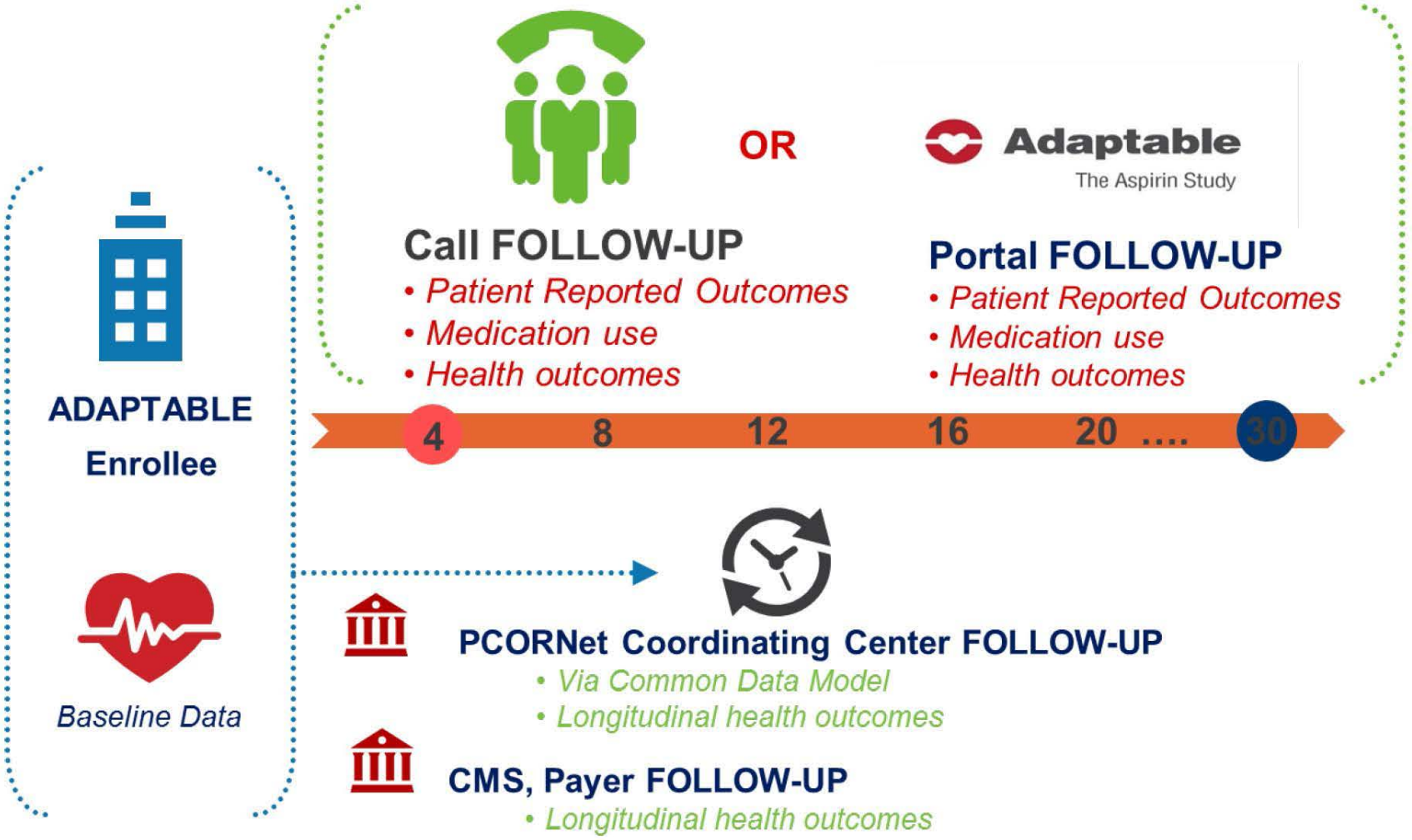


Source: Greg Simon, MD, Group Health Research Institute

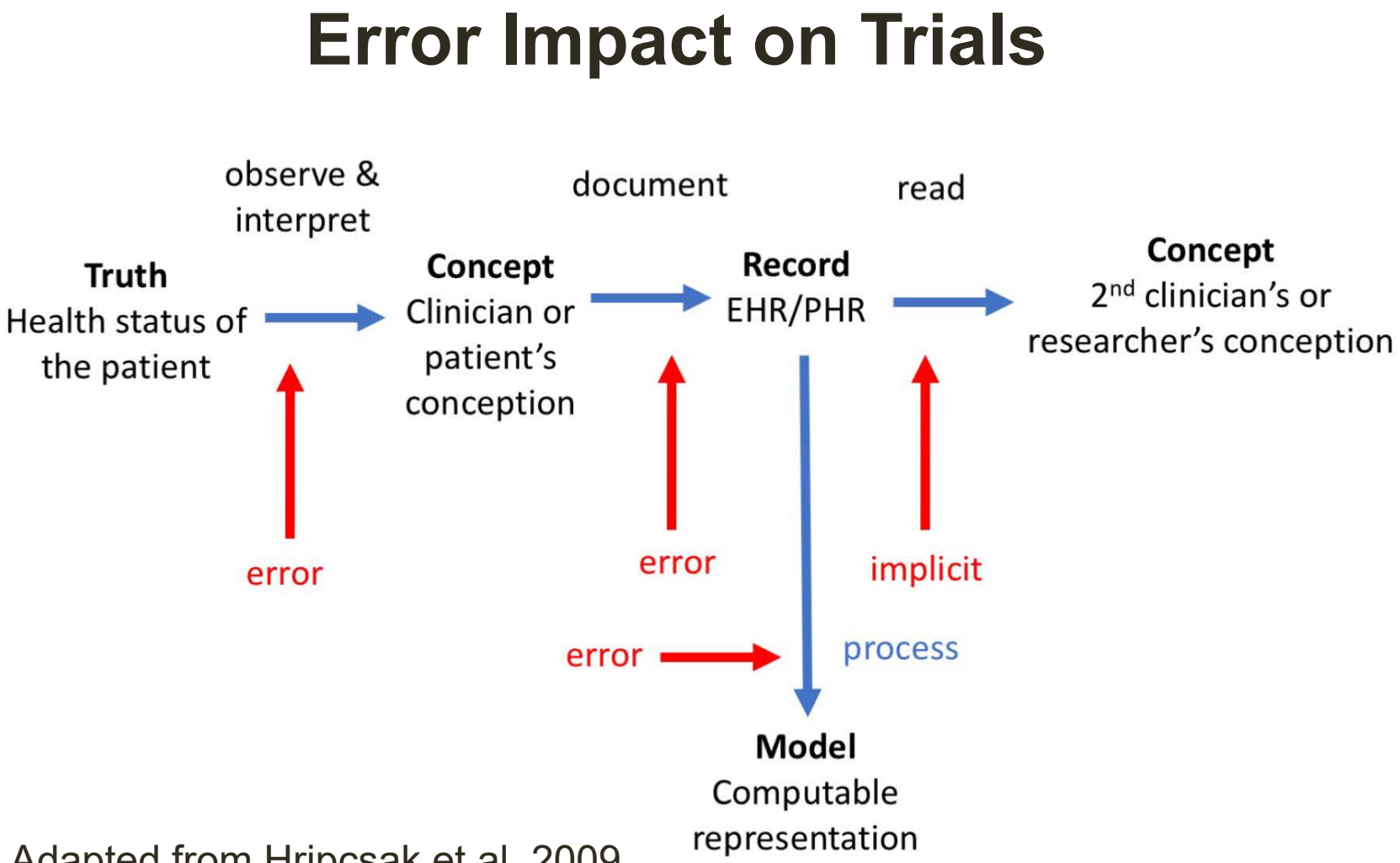
Longitudinal data linkage

- 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



Data is a surrogate for clinical phenomena



Adapted from Hripcsak et al. 2009

Data quality assessment

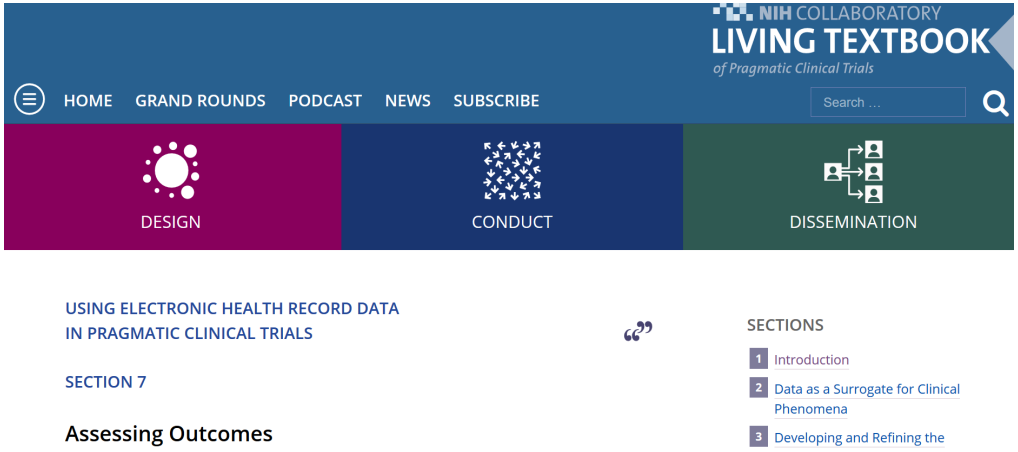
- Identify variation between populations at different sites or study groups
- Recommend formal assessment of accuracy, completeness and consistency for key data
- Data quality should be described, reported and informed by workflows

Resources

Electronic Health Records Core

Assessing Outcomes

From the *Living Textbook of Pragmatic Clinical Trials*
www.rethinkingclinicaltrials.org

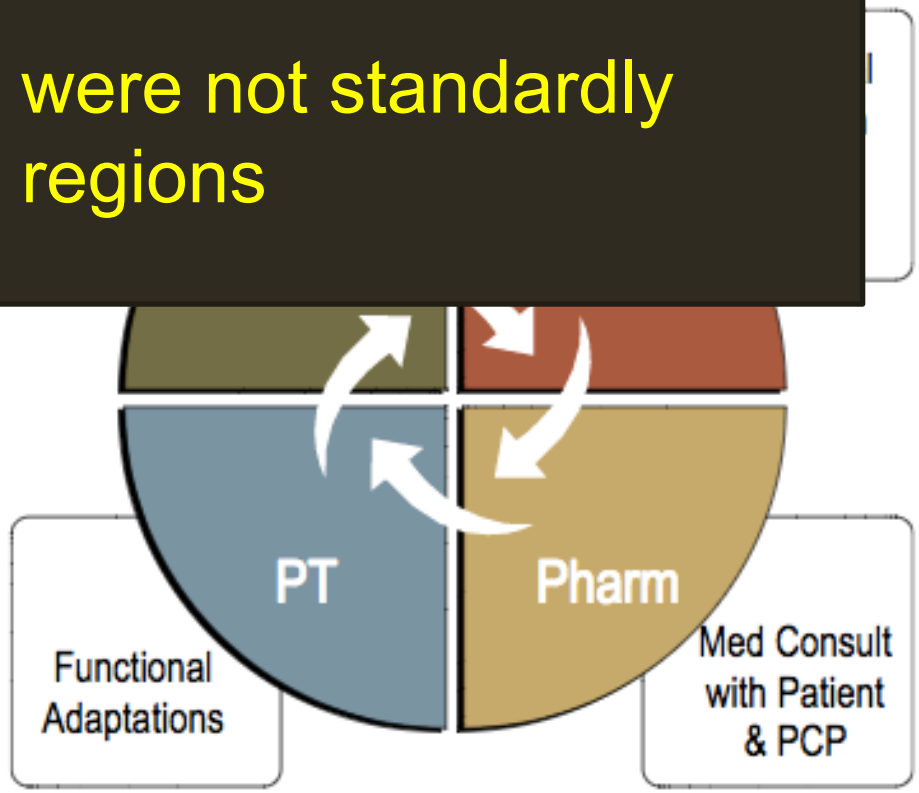


Case example: Collaborative Care for Chronic Pain in Primary Care (PPACT)

Pain Management: Usual Care

Interdisciplinary Management Embedded in Primary Care

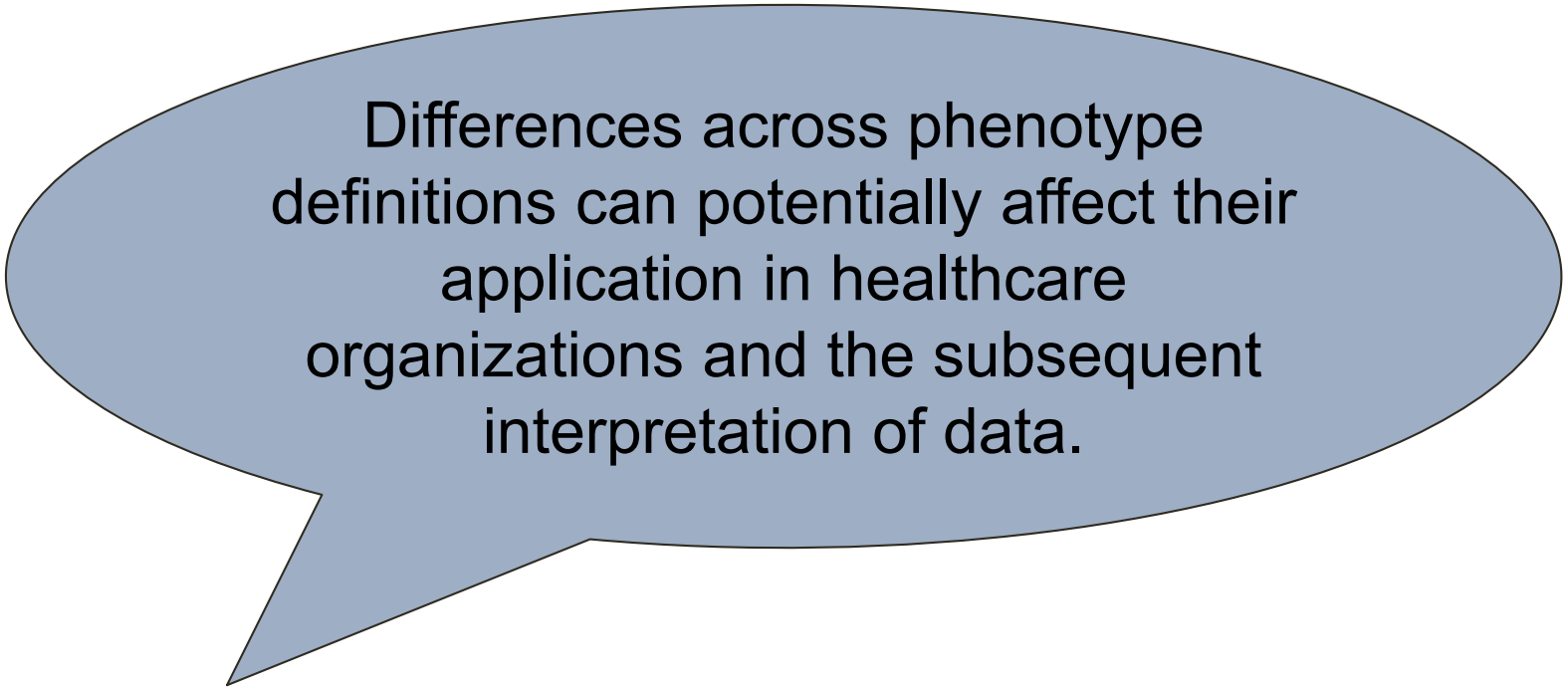
PROs were needed, but were not standardly collected across diverse regions



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

Defining outcomes with clinical phenotypes



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)*

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

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
- Need a 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 ePCTs for passive or active surveillance

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

Concluding Points

- The data available from the EHR may be convenient and 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