Pragmatic Trials Large and Small

Steps Towards a Learning Healthcare System

Data Science Course 2016

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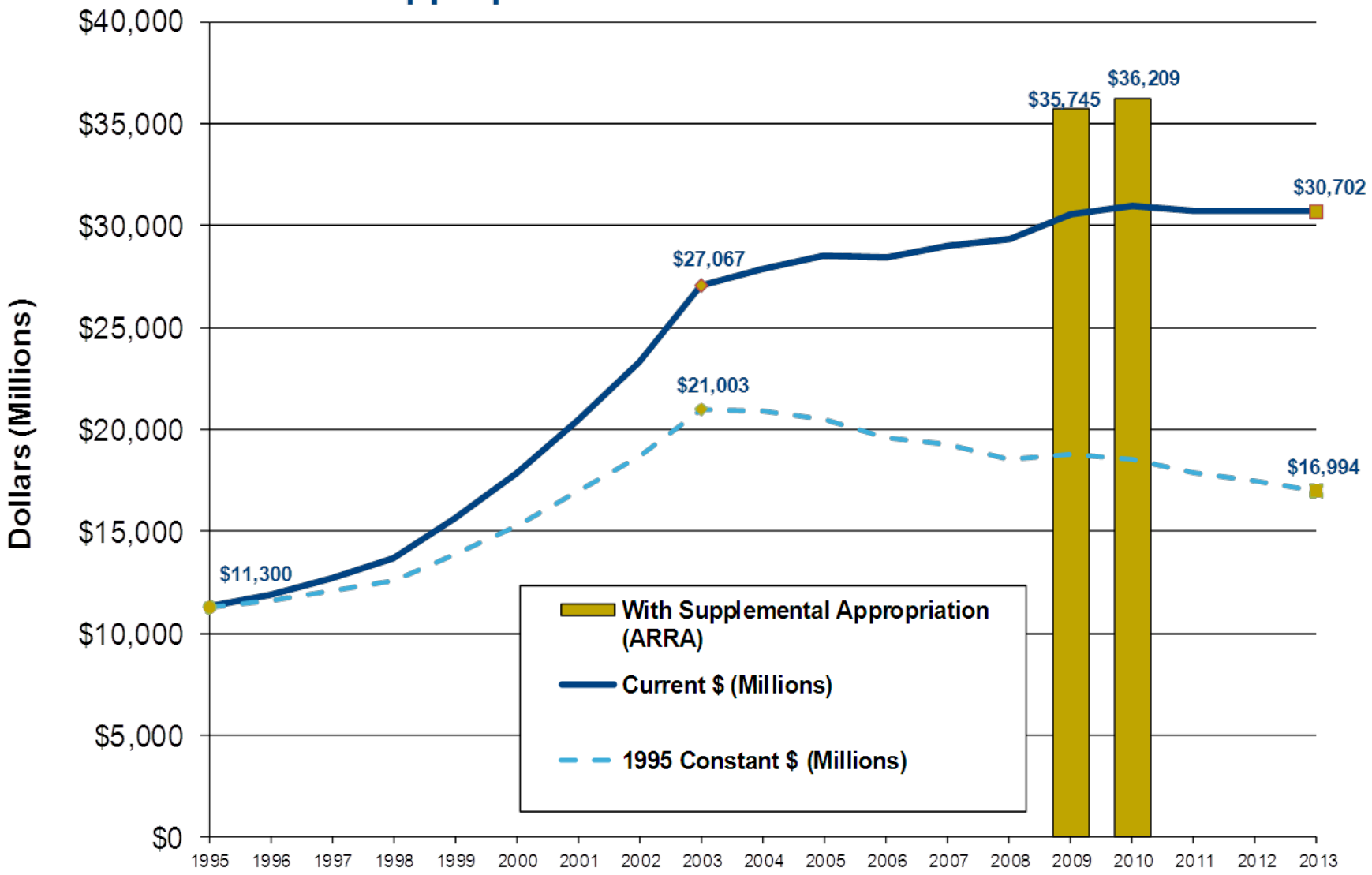
3 Related Concepts

- Pragmatic vs. Explanatory Trials
- Large Simple Trials
- Learning Healthcare System

Outline

- The Rationale
  - Make trials more efficient
  - Make trials more informative for decision-making
- The Concepts
  - Pragmatic vs. Explanatory, Large Simple Trials
  - 4 Examples: GISSI, TASTE, ADAPTABLE, VEST
- The Vision: Learning Healthcare System
  - Local efforts (UCSF CTSI)
  - National efforts and resources
- Science of using electronic health record data

NIH Appropriation in Current and Constant Dollars



FASEB
Federation of American Societies for Experimental Biology

TABLE 3-2 Breakdown of the Costs for a Large, Global Clinical Trial (14,000 patients, 300 sites)

Expense	Cost (in millions of $)
Site payments	150.0
Monitoring	90.0
Data management and statistics	12.0
Project and clinical leadership	12.0
Interactive voice response systems (IVRS) and drug distribution	10.8
Publications	.1
Total	~300

SOURCE: Califf, 2009.

From: 3, Challenges in Clinical Research

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This is crazy!

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Do randomized trials help us make decisions?

Traditional RCT design:

- Control conditions carefully
- Optimize internal validity and causal inference
- Help us learn biology

Do randomized trials help us make decisions?

Traditional RCT design:

- Control conditions carefully
- Optimize internal validity and causal inference
- Help us learn biology

These design decisions may not be optimal for informing decision-making

Do randomized trials help us make decisions?

Explanatory vs. Pragmatic Trials

- Explanatory: designed to optimize causal inference and help us learn biology

- Pragmatic: designed to help us compare effectiveness and make real-world decisions

Schwartz and Lellouch 1967 and 2009, http://www.ncbi.nlm.nih.gov/pubmed/19348976

Do randomized trials help us make decisions?

Explanatory vs. Pragmatic Trials

- Explanatory: designed to optimize causal inference and help us learn biology → laboratory conditions

- Pragmatic: designed to help us compare effectiveness and make real-world decisions → normal conditions

Schwartz and Lellouch 1967 and 2009, http://www.ncbi.nlm.nih.gov/pubmed/19348976

Explanatory vs. Pragmatic

Inclusion and Exclusion criteria

- Explanatory: ?
- Pragmatic: ?

Explanatory vs. Pragmatic

Inclusion and Exclusion criteria

- Explanatory: Carefully restricted to individuals thought likely to adhere to and respond to intervention

- Pragmatic: All-comers

Explanatory vs. Pragmatic

Intervention protocol

- Explanatory: ?
- Pragmatic: ?

Explanatory vs. Pragmatic

Intervention protocol

- Explanatory: Strict, carefully-monitored fidelity, only use experienced clinicians, avoid co-interventions

- Pragmatic: Flexible and practical

Explanatory vs. Pragmatic

Control

- Explanatory: ?
- Pragmatic: ?

Explanatory vs. Pragmatic

Control

- Explanatory: Placebo or other designed to test a specific physiologic hypothesis

- Pragmatic: Best alternative treatment or “usual care”

Explanatory vs. Pragmatic

Adherence

- Explanatory: ?
- Pragmatic: ?

Explanatory vs. Pragmatic

Adherence

- Explanatory: Run-in period to weed out non-adherers, careful monitoring, “as treated” analysis

- Pragmatic: All-comers, see what happens, imperfect adherence is part of the intervention

Explanatory vs. Pragmatic

Measurements

- Explanatory: ?
- Pragmatic: ?

Explanatory vs. Pragmatic

Measurements

- Explanatory: Measure as much as possible, try to define mechanisms

- Pragmatic: Leave participants alone as much as possible*

* Subgroup analyses still useful

Explanatory vs. Pragmatic

Primary Outcome Measurement

- Explanatory: Measure what's important for assessing physiology

- Pragmatic: Measure what's clinically apparent (easier and more important to patients?)

Explanatory vs. Pragmatic

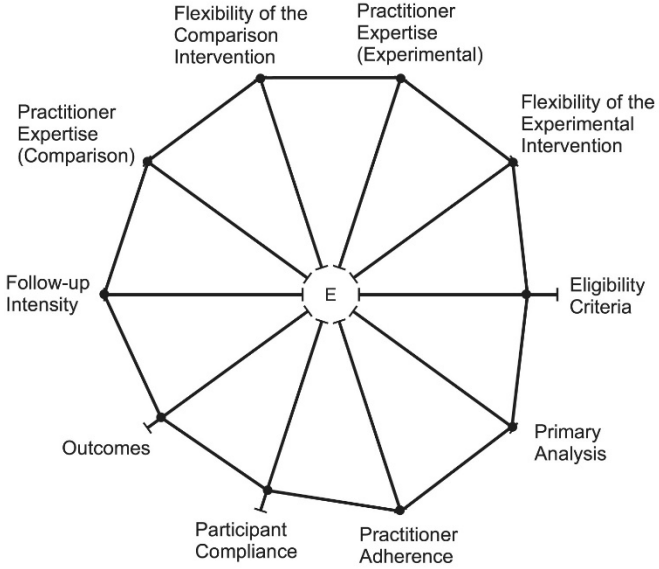
The Pragmatic-Explanatory Continuum Indicator Summary (PRECIS)

Measures pragmatism in 10 key domains

Thorpe 2009, http://www.ncbi.nlm.nih.gov/pubmed/19348971

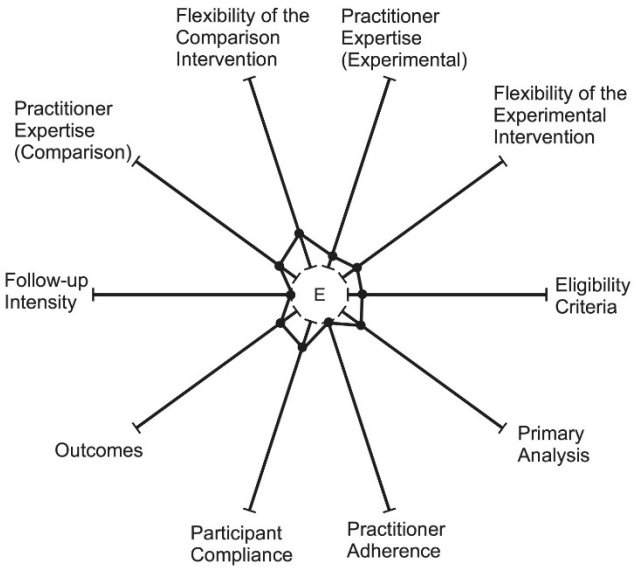
a

PRECIS summary of a randomized controlled trial of self-supervised and directly observed treatment of tuberculosis (DOT) [9]



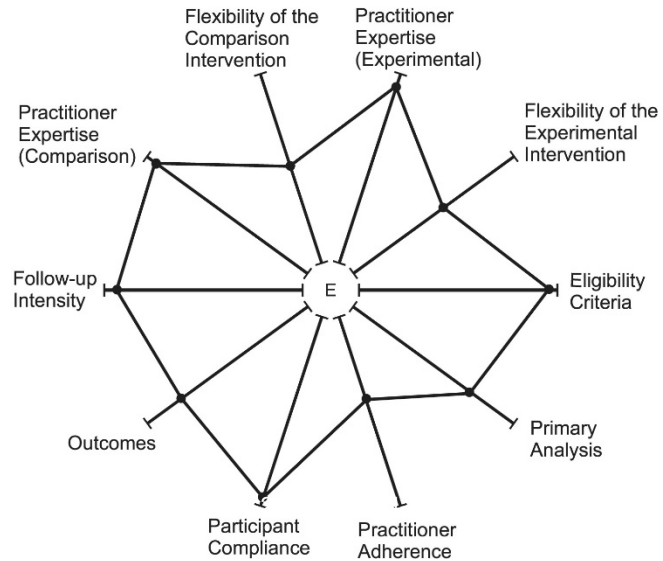
b

PRECIS summary of the North American Symptomatic Carotid Endarterectomy Trial (NASCET) of carotid endarterectomy for symptomatic patients with high-grade carotid stenosis [10]



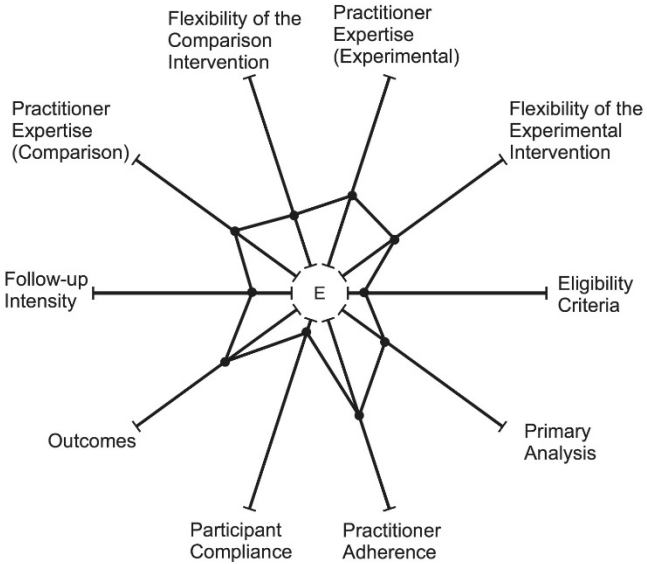
c

PRECIS summary of a randomized trial of low-dose aspirin for the prevention and treatment of pre-eclampsia (CLASP) [11]



d

PRECIS summary of a randomized trial of low-dose aspirin for the prevention of pre-eclampsia in women at high risk [12]



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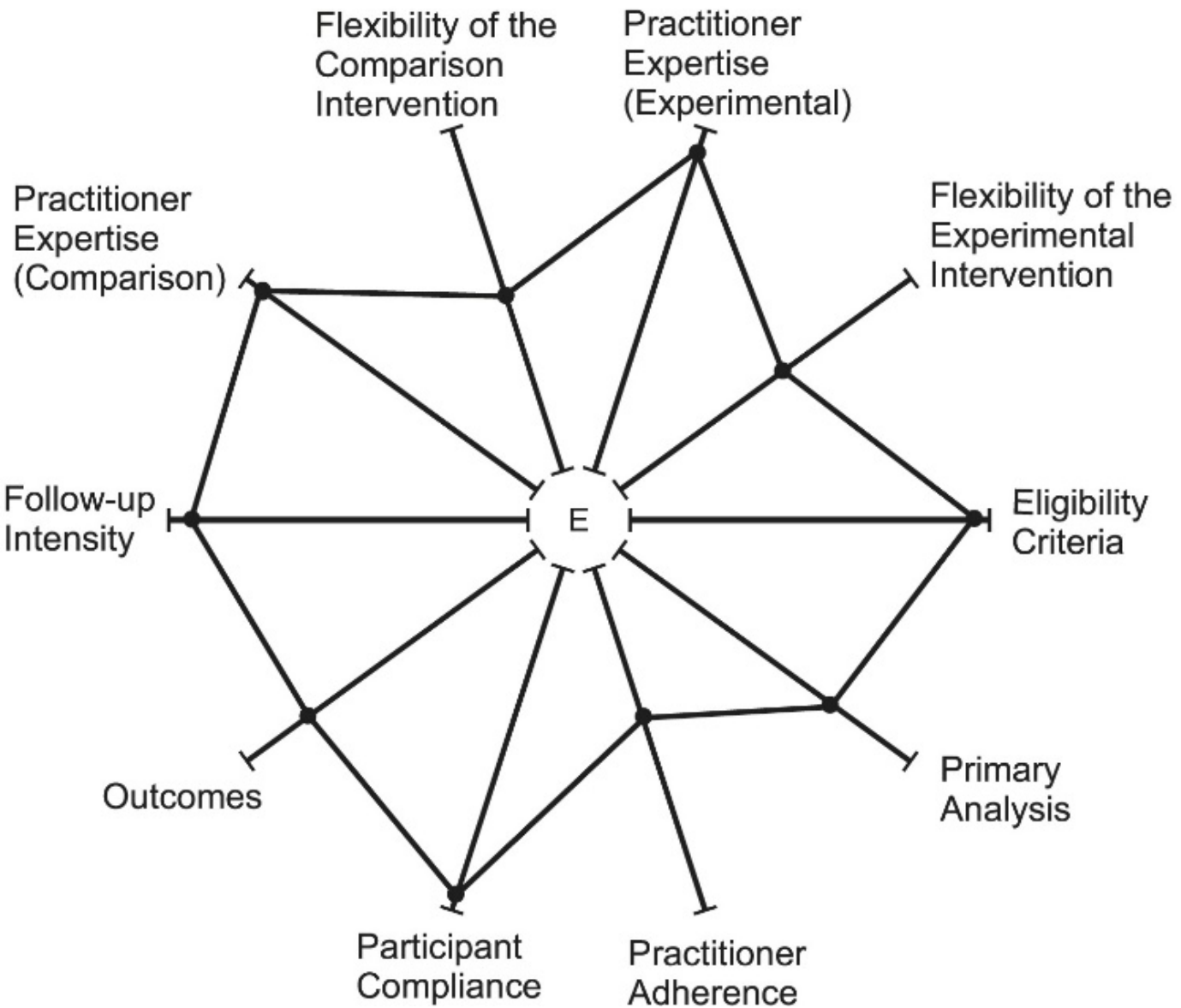

Explanatory vs. Pragmatic

- Which kind of trial is cheaper?

Explanatory vs. Pragmatic

- Which kind of trial is cheaper?
  - Many "pragmatic" design features are also easier to implement
- "Large Simple Trials" – related concept that emphasizes the cost benefits
  - See JAMA Viewpoint by Eapen/Lauer/Temple
  - Strongly supported by FDA (Rob Califf→Commissioner!)

Quintiles 2011 file:///C:/Users/mpletcher/Downloads/use-large-simple-trials.pdf
Roehr 2013 http://www.ncbi.nlm.nih.gov/pubmed/23449675
Eapen 2014 http://www.ncbi.nlm.nih.gov/pubmed/24715072

Large simple pragmatic trials

- Win-win: both cheaper and better for informing real-world clinical decisions?

Example 1: GISSI

Gruppo Italiano per lo Studio della Streptochinasi nell'infarto Miocardico (GISSI) - 1986

- RCT comparing streptokinase to usual care for all-cause in-hospital mortality in acute MI
  - 11,806 randomized, 11,712 follow-up
  - 10.7% vs 13%, RR=0.81, p<.0002
  - More benefit if given earlier

Lancet 1986 http://www.ncbi.nlm.nih.gov/pubmed/2868337

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Super-simple, large, very important results

Lancet 1986 http://www.ncbi.nlm.nih.gov/pubmed/2868337

Example 2: TASTE Trial

Thrombus Aspiration in ST-Elevation Myocardial Infarction in Scandinavia (TASTE trial)

- Registry in Sweden for angiography and angioplasty already collecting outcomes
- RCT within registry patients: thrombus aspiration vs. conventional PCI
- All-cause mortality at 30 days: No difference

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Embedded "Registry Trial"

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Cost?

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Cost = $300,000 (compare with $300M)

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Watchtell 2016 http://www.ncbi.nlm.nih.gov/pubmed/26758999

Example 3: ADAPTABLE Trial

Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-Term Effectiveness (ADAPTABLE)

- RCT aspirin 325 vs. 81 mg for secondary prevention
- Demonstration trial for PCORnet
- Use electronic health records to:
  - Find patients (n=10,000)
  - Measure outcomes (MI, bleeding, death)

Johnston 2016 http://www.ncbi.nlm.nih.gov/pubmed/27423939
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Embedded in EHR, network

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Cost = ~$10 million

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Will it succeed? Is it the right model?

Johnston 2016 http://www.ncbi.nlm.nih.gov/pubmed/27423939
http://pcornet.org/

Example 4: VEST

The Vest Prevention of Early Sudden Death Trial

- RCT LifeVest (wearable defibrillator vest) vs. usual care → sudden death within the first 3 months for immediately post-MI patients with EF<35%.

https://clinicaltrials.gov/ct2/show/NCT01446965

Example 4: VEST

The Vest Prevention of Early Sudden Death Trial

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How pragmatic is it? Redesign ideas?

https://clinicaltrials.gov/ct2/show/NCT01446965

Example 4: VEST

The Vest Prevention of Early Sudden Death Trial

Subjects	EF<35%, no renal failure, nursing home, etc
Recruitment	Find post MI patients in hospital, recruit and randomize
Intervention	Wear the Lifevest as much as possible; avoid co-interventions
Control	Usual care, co-interventions carefully monitored
Adherence	Carefully monitored, per-protocol analysis planned
Outcome	Sudden death, not all-cause mortality

https://clinicaltrials.gov/ct2/show/NCT01446965

39728

V2 (Month 3): Procedure Checklist

Study ID#	Acrostic	Date Visit Commenced	Staff ID #
		Day / Month / Year	

Case Report Form# / Procedure	Please mark if done		
	Yes	No, participant refused	No, other reason (or N/A)
#93: Vital Status [NOTE: If the participant is found to be deceased, complete CRFs #93, 45, 35, and 36. If vital status cannot be ascertained (unknown), the participant is considered "lost to follow-up". Complete CRFs #93 and 45. For deceased or lost to follow-up participants, the other CRFs on this checklist do not need to be completed - Mark "No, other reason (or N/A)".]	○	○	○
#16: Medical Care Utilization	○	○	○
#17b: VEST F/U Symptoms Checklist	○	○	○
#19: F/U Medication Inventory	○	○	○
#22: LifeVest Use & Satisfaction	○	○	○
#99: Device Follow-Up	○	○	○
#33: Health Questionnaire	○	○	○
#8: Echocardiogram	○	○	○
#45: Close-Out Form (if applicable)	○	○	○

Example 4: VEST

How could VEST have been more pragmatic?

https://clinicaltrials.gov/ct2/show/NCT01446965

Example 4: VEST

How could VEST have been more pragmatic?

- VEST prescription vs. usual care → all-cause mortality using death index, no other measurements
  - No adherence monitoring except what is clinically appropriate and feasible
  - Allow co-interventions
  - No adjudication of sudden death; all-cause mortality is what counts

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Example 4: VEST

How could VEST have been more pragmatic?

Hard to give nothing...

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  - No adherence monitoring except what is clinically appropriate and feasible
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Example 4: VEST

How could VEST have been more pragmatic?

- Could we randomize patients BEFORE we approach them?
  - Find patients via EHR search and alert system
  - Randomize to:
    - A: Approach, offer and encourage LifeVest use
    - B: Don't approach at all – PURE Usual care (might use LifeVest)
  - Note: randomization occurs BEFORE consent

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Is this ethical?

https://clinicaltrials.gov/ct2/show/NCT01446965

Example 4: VEST

"Randomized Encouragement Design"

- Randomizing to encouragement to do something
  - Likely much lower adherence rates → much larger sample size needed
    - Adherence 40% vs. 10% instead of 90% vs. 3%?
  - But much easier??
  - Works best if:
    - You are collecting outcome data passively (e.g., via EHR)
    - You don't need consent before randomizing
    - The intervention could be considered "quality improvement"?

Pearl 1995 http://www.ncbi.nlm.nih.gov/pubmed/8963376
Hirano 2000 http://www.ncbi.nlm.nih.gov/pubmed/12933526

Example 4: VEST

- Extension of ITT thinking
- Encouragement is an "instrumental variable"

"Randomized Encouragement Design"

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Example 4: VEST

Could we have used a Randomized Encouragement Trial to study the LifeVest?

(maybe?)

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Could we have used a Randomized Encouragement Trial to study the LifeVest?

(maybe?)

Passive data collection via EHR could make pragmatic RCTs much more feasible...

Learning Healthcare System

- A healthcare system that embeds pragmatic trials throughout delivery of healthcare, and learns as it goes...

- Learning Healthcare System vision
  - Every patient should be randomized! Multiple times!
  - Continuous learning and refinement of care
  - “A/B testing” embedded in EHR
    - Google does it, why shouldn’t we?

Learning Healthcare Systems

- UCSF CTSI is funding LHS demonstration projects
  - Two projects funded:
    - Detection and alerts to avoid hypoglycemia events in the hospital
    - Using smart triggered standardized order sets in patients that may have COPD to improve quality of care + reduce readmissions and length of stay

Learning Healthcare Systems

- Steps for LHS projects
    - Identify an important health outcome that is easily measured by EHR query
    - Develop an intervention to improve it
    - Design a study to test whether it works

Learning Healthcare Systems

- Challenges for LHS projects
  - Data work is HARD
    - Outcome assessment may be easy, but also need data to identify patients, create prediction algorithm, etc
  - Intervention design is an art form
    - Alert fatigue
    - Workflow integration
    - User testing and involvement in design is critical
  - Study design is fun
    - Unit of randomization?
    - Consent required or not*?
    - IRB approval pushing boundaries

*Pletcher 2014 http://www.ncbi.nlm.nih.gov/pubmed/24615554

Learning Healthcare Systems

- Even UCSF Health is talking this up
  - Learning Healthcare System is one of UCSF Health's "True North Pillars" in a new strategic plan
- Institute for Computational Health Sciences, Atul Butte
- New cross-UC data initiative

IOM 2012 http://www.nationalacademies.org/hmd/Activities/Quality/LearningHealthCare.aspx
http://www.ncbi.nlm.nih.gov/books/NBK53494/

Learning Healthcare Systems

- Hot topic nationally
  - IOM Reports from 2007 and 2012
    - See references below
  - PCORnet: a national network with a common data model → A national Learning Healthcare System?
    - PCORI has invested $100's Millions
  - NIH CTSA Program is emphasizing EHR investments
  - NIH Collaboratory: Cutting edge, webinar series, living textbook

IOM 2007 and 2012 http://www.nationalacademies.org/hmd/Activities/Quality/LearningHealthCare.aspx
http://www.ncbi.nlm.nih.gov/books/NBK53494/
PCORnet vision http://www.ncbi.nlm.nih.gov/pubmed/23612587
NIH Collaboratory https://www.nihcollaboratory.org/Pages/default.aspx

Science of EHR data

- All of this hinges on being able to use EHR data

Science of EHR data

- Some challenges in using EHR data
  - Collected for billing and clinical use, not research
    - Example: diagnosis data (clinicians know how bad this is)
  - Data structure designed to facilitate user interface
  - Every system is different
    - EPIC vs. Cerner vs. Others
    - EPIC installations are all customized
  - Data *collection* (not just the measurement value) inherently depends on health status
    - A recipe for selection bias

Science of EHR data

- Diagnosis data
  - Sources
    - Event-based (every visit, every lab)
    - On Problem List
  - Categories are sometimes hard
    - Garbage in vs. omitted (vs. time to get it right)
  - ICD10 vs. ICD9
    - Different codes
    - Requires extreme detail

diabetes

Search

Database Lookup (F7)

ID	Name	ICD-10 Codes
256947	Diabetes mellitus arising in pregnancy	O24.419
178973	Diabetes mellitus associated with genetic syndrome	E11.69, Q99.9
178971	Diabetes mellitus associated with hormonal etiology	E11.69
508917	Diabetes mellitus associated with pancreatic disease	E11.69, K86.9
178974	Diabetes mellitus associated with receptor abnormality	E11.69
515794	Diabetes mellitus complicating pregnancy	O24.919, E11.9
321932	Diabetes mellitus complicating pregnancy, antepartum	O24.919
315433	Diabetes mellitus due to abnormal insulin	E13.9
578826	Diabetes mellitus due to cystic fibrosis	E08.9, E84.9
315422	Diabetes mellitus due to insulin receptor antibodies	E11.9
579326	Diabetes mellitus due to non-steroid drug	E09.9, T50.905A
579263	Diabetes mellitus due to non-steroid drug without complication	E09.9, T50.905A
1401294	Diabetes mellitus due to pancreatic injury	E11.69, S36.209A
443814	Diabetes mellitus due to underlying condition	E08.9
442645	Diabetes mellitus due to underlying condition with diabetic amyotrophy	E08.44
442647	Diabetes mellitus due to underlying condition with diabetic cataract	E08.36
442649	Diabetes mellitus due to underlying condition with diabetic chronic kidney disease	E08.22
442651	Diabetes mellitus due to underlying condition with diabetic dermatitis	E08.620
442653	Diabetes mellitus due to underlying condition with diabetic mononeuropathy	E08.41
442655	Diabetes mellitus due to underlying condition with diabetic nephropathy	E08.21
442657	Diabetes mellitus due to underlying condition with diabetic neuropathic arthropathy	E08.610
442659	Diabetes mellitus due to underlying condition with diabetic peripheral angiopathy with gangrene	E08.52
442661	Diabetes mellitus due to underlying condition with diabetic peripheral angiopathy without gangrene	E08.51
442663	Diabetes mellitus due to underlying condition with diabetic polyneuropathy	E08.42
442665	Diabetes mellitus due to underlying condition with foot ulcer	E08.621, L97.509
442666	Diabetes mellitus due to underlying condition with hyperglycemia	E08.65
442667	Diabetes mellitus due to underlying condition with hyperosmolarity with coma	E08.01
442668	Diabetes mellitus due to underlying condition with hyperosmolarity without nonketotic hyperglycemic-hyperosmolar coma (	E08.00
442669	Diabetes mellitus due to underlying condition with hypoglycemia with coma	E08.641
442670	Diabetes mellitus due to underlying condition with hypoglycemia without coma	E08.649
442671	Diabetes mellitus due to underlying condition with ketoacidosis with coma	E08.11
442672	Diabetes mellitus due to underlying condition with ketoacidosis without coma	E08.10
442675	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema	E08.321
442677	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy without macular edema	E08.329
442680	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema	E08.331
442682	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy without macular edema	E08.339
442684	Diabetes mellitus due to underlying condition with periodontal disease	E08.630
442687	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema	E08.351
442689	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy without macular edema	E08.359
442692	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema	E08.341
442694	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy without macular edema	E08.349
442695	Diabetes mellitus due to underlying condition without complications	E08.9
445214	Diabetes mellitus due to underlying condition with diabetic autonomic neuropathy	E08.43
445660	Diabetes mellitus due to underlying condition with diabetic neuropathy	E08.40
446860	Diabetes mellitus due to underlying condition with diabetic retinopathy without macular edema	E08.319
448524	Diabetes mellitus due to underlying condition with diabetic retinopathy with macular edema	E08.311

100 loaded. More to load.

Accept

Cancel

Science of EHR data

- Medications data
  - Also coded, but it works better
  - But many sources
    - Prescribing event
    - Dispensing in facility
    - Dispensing at pharmacy
    - Med List
  - How do you define what a patient is actually taking?
    - Med list (hard to find, not necessarily updated, single snapshot)
    - Start date easier than end date?
    - “Medication possession ratio”, etc
      - Requires pharmacy claims!

Dovepress
open access to scientific and medical research
Risk Management and Healthcare Policy
Dove Medical Press | This Article | Suscribe | Submit a Manuscript | Search | Follow

PMC full text: Risk Manag Healthc Policy. 2014; 7: 35–44.
Published online 2014 Feb 20. doi: 10.2147/RMHP.S19801

Table 1

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3934668/

Methods of measuring adherence

Methods	Data source	Definition
Indirect measurements used in research and administrative settings		
MPR*	Pharmacy claims	= (total days supplied)/(number of days between the first and last refills)
PDC*	Pharmacy claims	= (total days supplied)/(number of days in refill interval)
Indirect measurements used in patient care settings		
Self-report	Patient	Patient recalls medications taken in response to care team query
Questionnaire	Provider	Use of validated tool for adherence markers
Pill counting	Provider	Staff member reviews patient supply for doses remaining
Dose counting device	Device	Device includes electronic or manual counter that tracks doses released
Electronic-prescribing	PBM interface	Reports transmitted from a pharmacy benefit manager to provider usually via EMR link
Direct measurement		
Direct observation	Provider	Patient receives and takes medication at health care facility
Drug levels and markers	Laboratory	Patient blood or urine sample tested

Note:

*Generally not used in direct patient care.

PDC, proportion of days covered; PBM, pharmacy benefit manager; EMR, electronic medical records.

Science of EHR data

- Laboratory data
  - Oldest and cleanest?
    - STOR data going back decades...
  - Units, normal ranges, comparability are often questionable

Slide from Mini-Sentinel and PCORnet
(courtesy of Lesley Curtis)

- 34 different result units for HbA1c

- 68 different result units for platelets

*Glycosylated hemoglobin (HbA1c) original result units**

%	%T.HGB	% TL HGB	% HGB
HEMOGLOBIN	%T.Hgb	% OF TOTAL	PERCENT
U	%T.Hgb	% of Hgb	Percent
%HB	% NGSP	% of total	HbA1c%
% OF T	%NGSP	%THb	%HbA1c
%AIC	% TOTAL HGB	%NGSP	% A1C
MG/DL	G/DL	mmol/mol†	Blank
% A1C	% A1c	%Hb	g/dL
NULL	%THb		

Platelet count original result units‡

Blank	FL	TH/UL	X10(3)
%	K/CMM	THOU/CMM	1000/UL
/100 W	k/cmm	thou/cmm	X10(3)/MCL
/CMM	K/CU MM	thou/mm3	X10(3)/UL
CMM	K/CUMM	THOU/UL	X10(6)/MCL
10 3 L	K/MCL	THOUS/CU.MM	X10*9/L
10X3UL	K/mcL	THOUS/MCL	X10E3/UL
10^3/UL	K/UL	THOU/mcL	X1000
10*3/uL	k/uL	THOUS/UL	X10X3
10?3/uL	KU/L	Thou/uL	X10^3/UL
10E3/uL	K/MM3	THOUSA	x10
10e3/uL	K/mm3	THOUSAND	X10?3/ul
10e9/L	LB	THOUSAND/UL	X10E3/UL
E9/L	PLATELET CO	U	X10E3
BIL/L	T/CMM	X 10-3/UL	K/A?L
bil/L	TH/MM3	X 10(3)/UL	K/B5L
CU MM	th/mm3	X10 3	

Source: Electronic clinical laboratory test results data tables : lessons from Mini Sentinel
MarshaA.Raebel1,,KevinHaynes,Tiffany S. Woodworth, Gwyn Saylor, Elizabeth Cavagnaro , Kara O. Coughlin, Lesley H. Curtis, Mark G. Weiner, Patrick Archdeacon and Jeffrey S. Brown

Science of EHR data

- Other numeric data...2 examples
  - Blood pressure
    - Context important?
    - In Emergency Dept vs. clinic, clinician-reported vs. dinamap, which arm, etc
    - Often need the “metadata”
  - Ejection fraction
    - Radiology/Cardiology reports – structured free text?
    - Code at UCSF – extracts from ~100 sources!
    - (thanks to Alvin Rajkomar)

Science of EHR data

- Hospitalization and death data
  - Diagnosis data coded more carefully?
  - Useful...but not complete?
    - People use different hospitals
    - People die out of hospital
    - Closed system data better than open
      - Kaiser vs. UCSF
    - Claims data helps a LOT for this...but hard to get?

Science of EHR data

- Text data from written notes
  - Progress notes, discharge summary, nurses notes, etc
  - Extremely important information...but hard to “mine”!
  - Whole science of natural language processing
    - Find concepts (e.g., heart attack, myocardial infarction, MI)
    - Identify “negation” language (e.g., “No ___”, “rule out”, “r/o”)

Science of EHR data

- Other special data types
  - EKG signals
  - Imaging files

Science of EHR data

- Computable phenotype concept
  - Coding of data can define useful research measurements
    - Diabetes (diagnosis + meds + FASTING blood sugar level?)
    - Hypertension (uncontrolled, treated, resistant, etc)
    - Hospitalization for myocardial infarction (Diagnosis + EKG + NLP?)
  - NEVER perfect
    - Validation by chart review, etc...
    - Variations in CP's will provide different tradeoffs in terms of sensitivity and specificity (depends on research study needs)

Science of EHR data

- Data Models
  - Take source data and modify
    - Simplified data model (combining sources, etc), easier to use
    - Common data model for use across institutions
      - Allows multi-site studies
      - Allows crowd-sourced computable phenotype development
  - "Extract-Transform-Load" - ETL
    - Requires data manipulation, joining, concatenating datasets
    - Decisions!
    - Information loss at every step

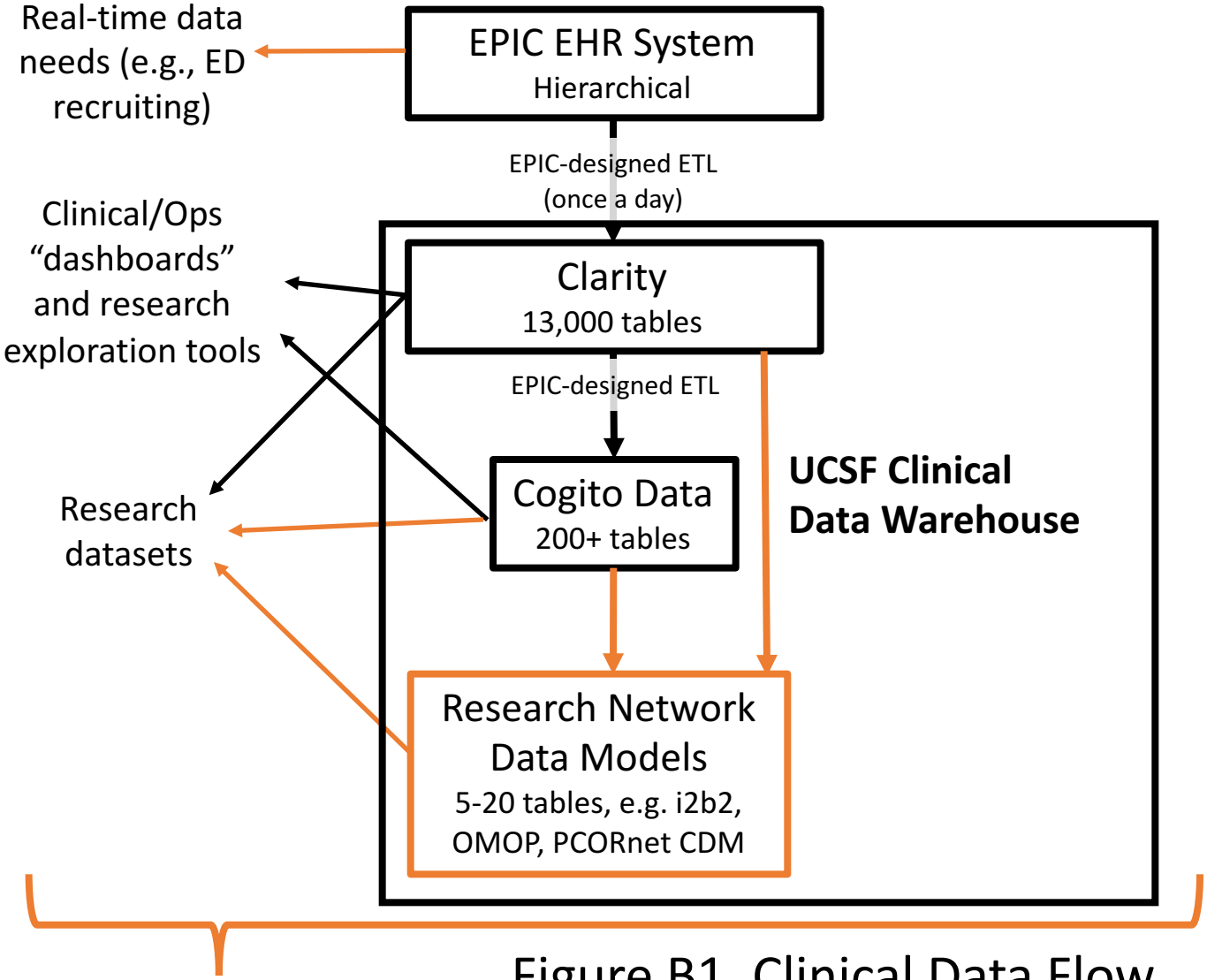

Figure B1. Clinical Data Flow, Transformation, and Usage in our EPIC-based EHR, with planned enhancements

Science of EHR data

- Some important UCSF-supported data models to know about:
  - Caboodle (AKA Cogito, Star, “Constellation”)
    - EPIC product, simplification of APEX data
    - UCSF has de-identified flat files for many Caboodle tables!
  - OMOP (hosted by OHDSI)
    - Open source community effort
    - http://www.ohdsi.org/ http://omop.org/ http://cdmqueries.omop.org/
    - Competes with i2b2 https://www.i2b2.org/about/intro.html
  - PCORnet Common Data Model
    - National network funded to do EHR work http://www.pcornet.org/pcornet-common-data-model/
    - http://www.pcornet.org/wp-content/uploads/2014/07/2015-07-29-PCORnet-Common-Data-Model-v3dot0-RELEASE.pdf

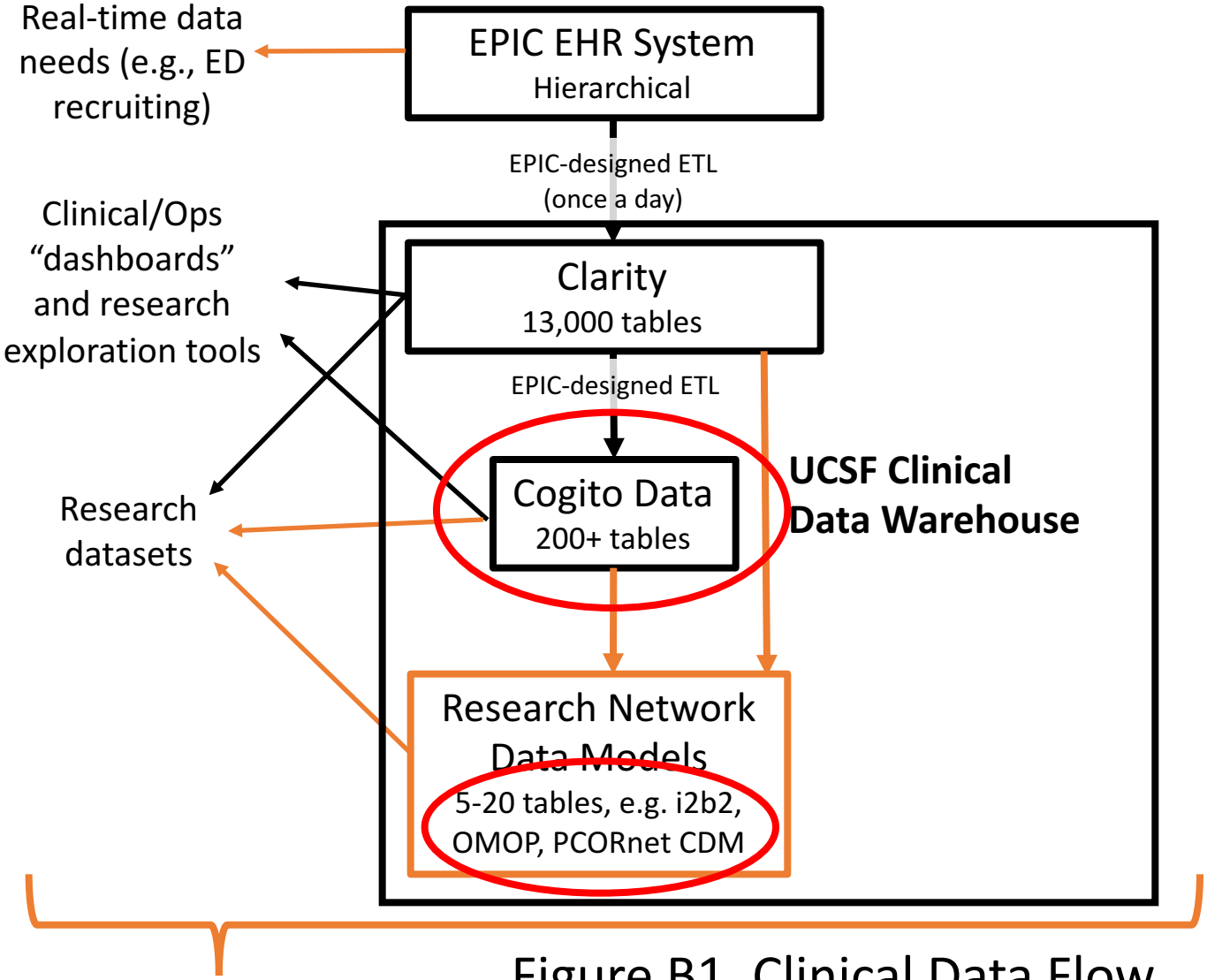

Figure B1. Clinical Data Flow, Transformation, and Usage in our EPIC-based EHR, with planned enhancements

Science of EHR data

- “Big data” approaches to EHR data
  - Define computable phenotype and use prediction tools
    - Neural networks, etc
    - Let’s just sic Google on it...?
  - Unsupervised – will it work?
    - Do we use Clarity 10,000 tables or Caboodle 200 or OMOP 20?
    - NLP?
    - Maybe if we choose the right problem?

Science of EHR data

- Accessing UCSF APEX data
  - Consultations from CTSI
    - https://accelerate.ucsf.edu/consult
  - Going directly to UCSF IT (AKA Academic Research Systems = ARS)
    - https://it.ucsf.edu/services/clinical-data-research-consultations-formerly-threds-and-idr-data-extraction-service

Take Home Points

- Potential win-win of large, simple, pragmatic trials
  - Cheaper, and more relevant for decision-making
- Learning healthcare system concept
  - Embedding trials in healthcare delivery
  - UCSF efforts
- Using electronic health record data
  - Critical for LHS vision, but hard!
  - Active area of development at UCSF
  - Resources available; some now and more coming soon

Take Home Points

Questions?

- Potential win-win of large, simple, pragmatic trials
  - Cheaper, and more relevant for decision-making
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Extra slides to follow

Learning Healthcare Systems

- Quality Improvement Research
  - QI vs. Research: OVERLAP, not spectrum/dichotomy
  - Too many projects try to avoid IRB approval
    - Better to use good research methods (e.g., randomization)
    - Waiver/modification of consent is often justifiable to IRBs

- Randomized Quality Improvement Trial*
  - A special beast
  - Equipoise not relevant?
  - Encouragement design especially reasonable?

*Pletcher 2014 http://www.ncbi.nlm.nih.gov/pubmed/24615554