Enhancing the Application of Real-World Evidence in Regulatory Decision-Making

Public Conference

March 3 & 4, 2016

The Washington Plaza Hotel

The Evidence Development Spectrum: Defining Sources and Applications of Real-World Evidence

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Deputy Director, Duke-Margolis Center

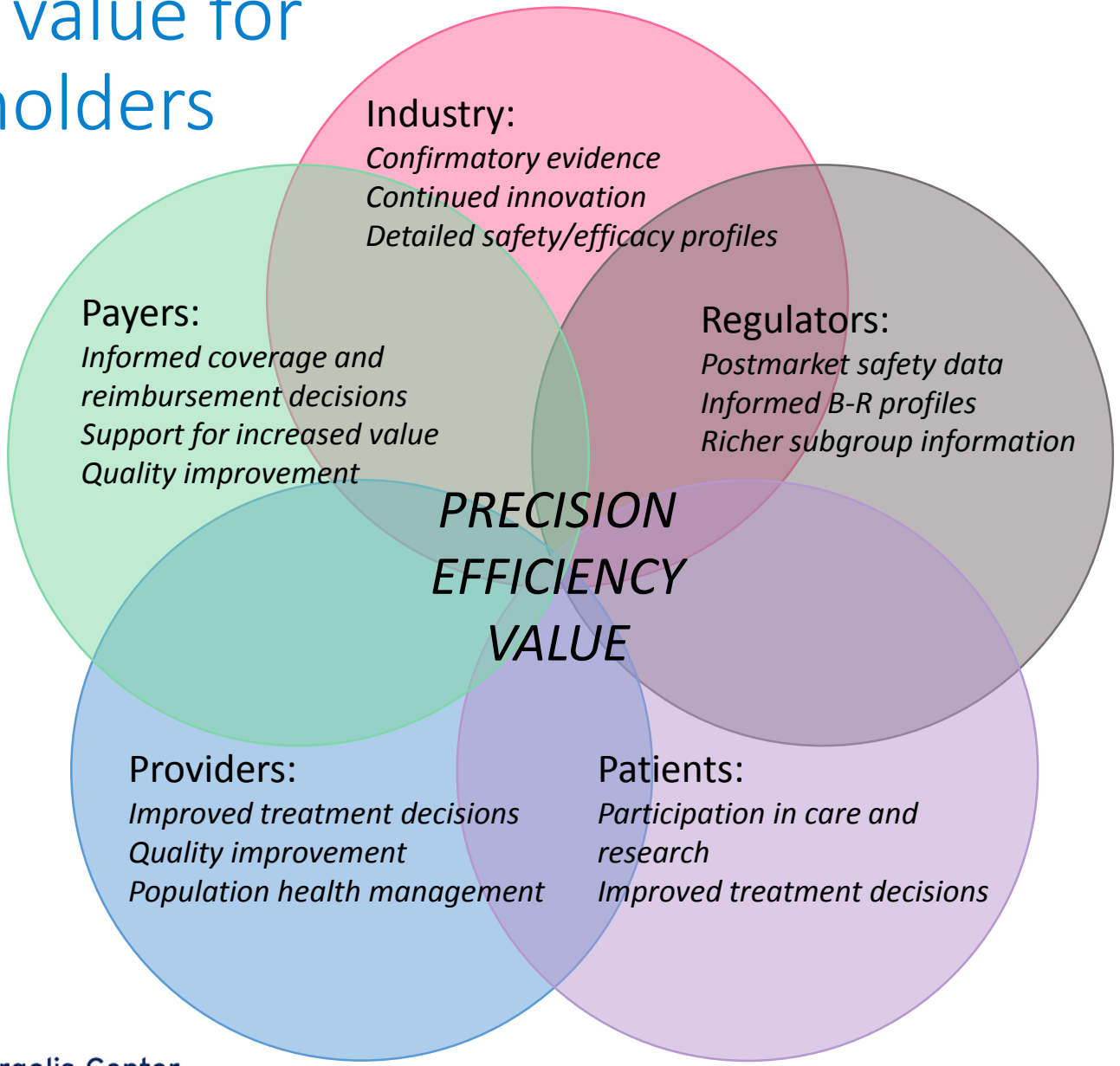
March 3, 2016

Duke UNIVERSITY | Duke-Margolis Center *for* Health Policy

What's driving the demand for Real-World Evidence?

- Nation's growing electronic health information infrastructure has enabled routine and increasingly robust collection of digital data at the point of patient care
- During a time of massive sea changes in health care, opportunities to leverage such data will only grow:
  - Drug discovery and development is longer and more costly, with growing public attention on resultant prices
  - Providers and payers are moving toward payment and reimbursement models focused on value over volume
  - Patients are more involved than ever before in their own care decisions and the push for more personalized treatments
- Learning from real-world patient experiences can support better informed health care decision-making by a range of stakeholder

RWE has value for all stakeholders

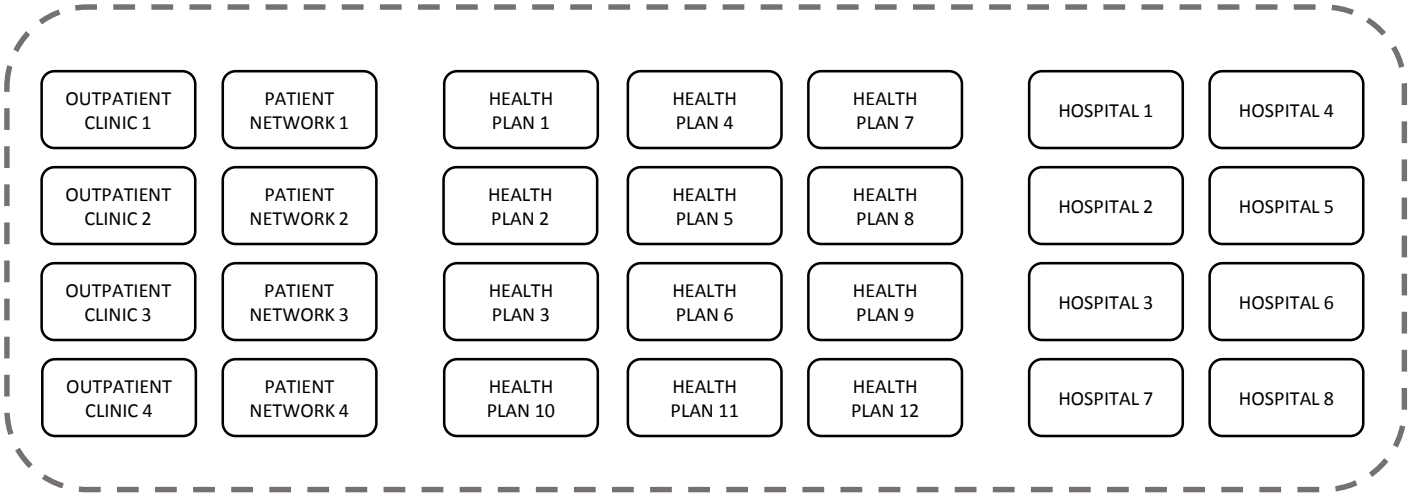


Many groups have grappled with defining RWE

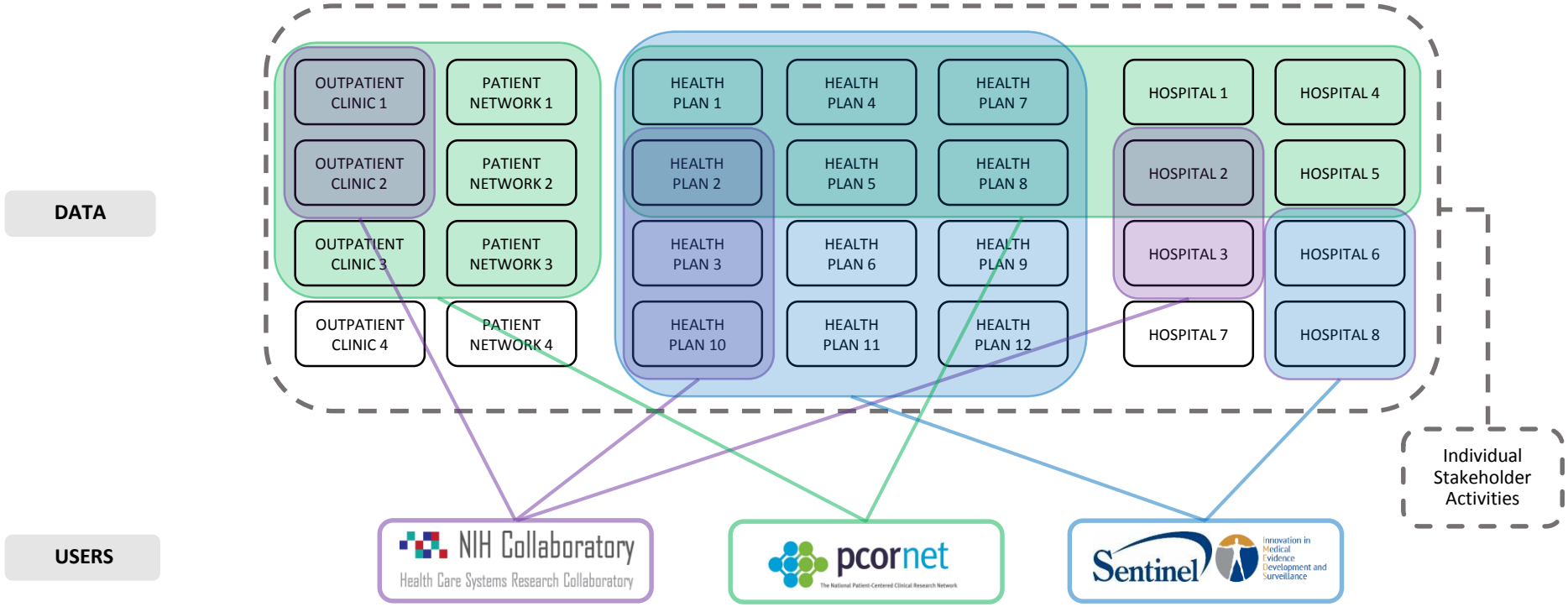
Baseline definition:

Evidence generated from data collected outside of conventional randomized controlled trials through appropriate real-world study designs and methodologies

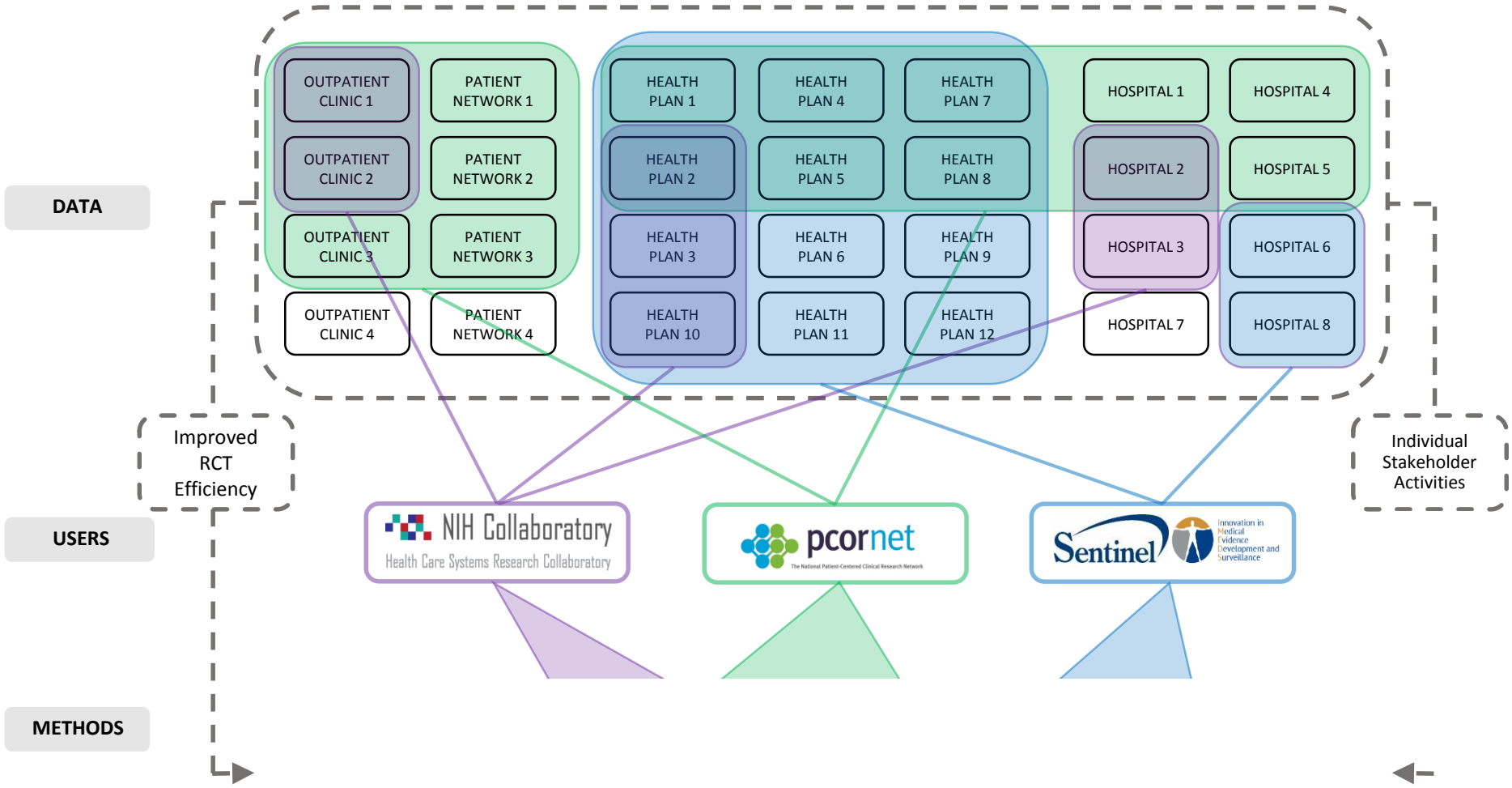
Where does real-world data come from?



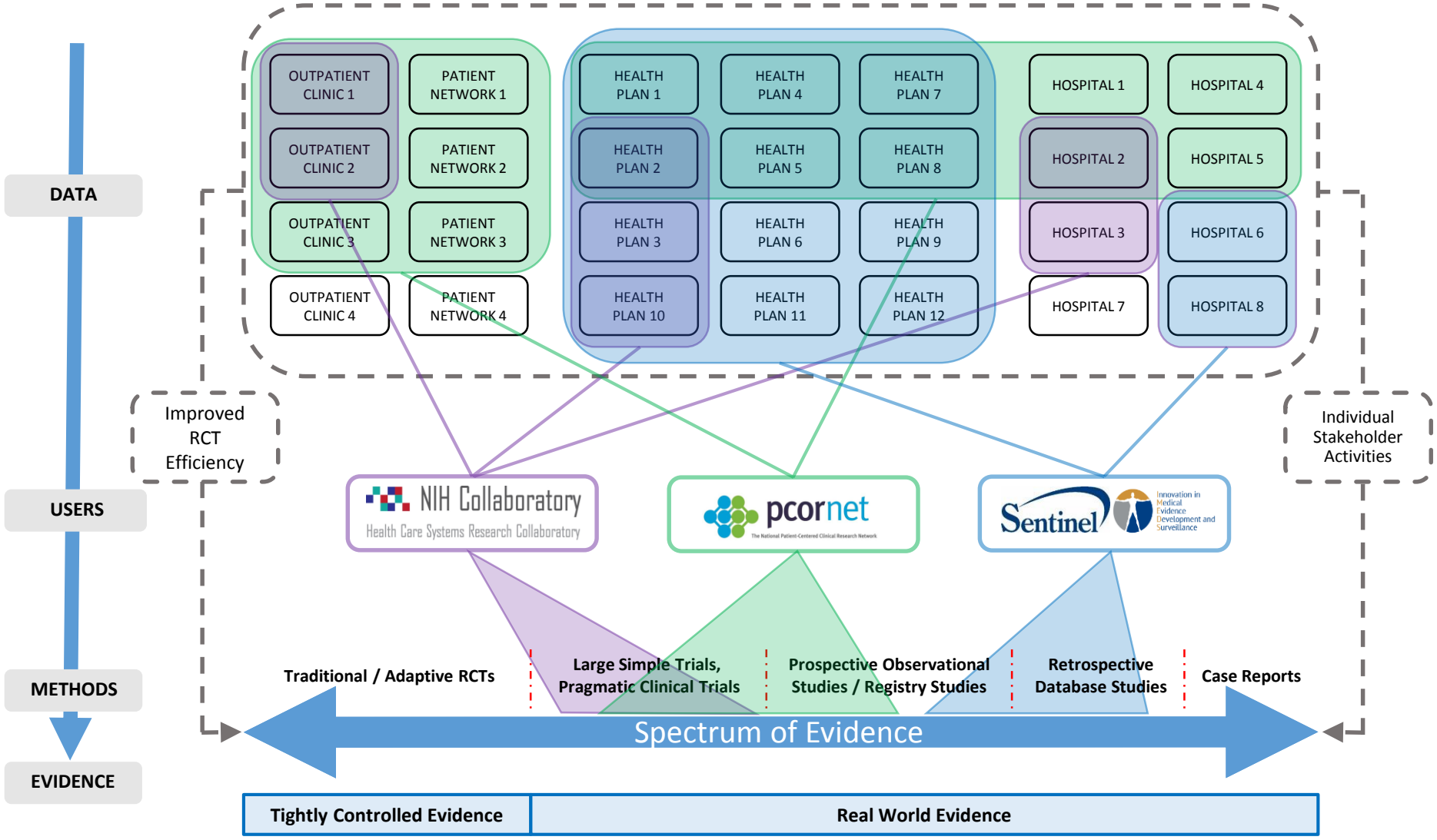
Who's using the data?



Methods applied to generate evidence from data



Applying generated RWE to decision-making



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Real-world data can support evidence development in multiple ways

- Data can be use to make traditional RCT-centered evidence development activities more efficient
  - Faster identification and recruitment of study participants, and greater retention
  - Reduced burden of data collection
  - Reduces the time and cost of RCTs
- Data can be used to generate *new RWE* to support regulatory decision-making

The use of RWE in regulatory decision-making can be enhanced

- Potential Use Cases
  - New drug approval
  - New indication
  - Label revisions
  - Postmarket commitments/ requirements
  - Phase 4 confirmatory evidence
  - Safety surveillance
- Study Design Considerations
  - Data sources
  - Study outcomes
  - Randomization in the clinical setting
  - Observational study methodologies

Efforts to improve regulatory use of RWE should bolster other uses

- An ideal infrastructure:
  - Trusted and valued by all stakeholders
  - Economically sustainable and governable
  - Adaptable, self-improving, stable, certifiable, and responsive
  - Capable of engendering a virtuous cycle of health improvement
- Potential barriers:
  - What additional incentives are needed to encourage generation of more robust and reliable RWE in the postmarket?
  - How can improvements to the connectivity and scalability of research and data collection methods help to achieve these ends?
  - Are there specific policy levers that should be pursue in order to bolster infrastructure improvements?

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Randomization in Clinical Setting New Indication

Robert Temple, MD
Deputy Center Director for Clinical Science
FDA/CDER

Duke-FDA Real World Evidence Conference
March 3, 2016

Considerations

1. Finding potential participants
2. Consent process
3. EHR entry data definitive or need for further investigator evaluation
    - Disease Present
    - Enrichment Factors
4. Need for blinding/placebo
5. Results: EMR outcomes

    Additional outcomes

No doubt many other issues

Simple – finding the patients

The most obvious use of EHR is to find candidates for a trial [Probably needs a system-wide encouragement to participate]. Should be relatively easy for marketed drug with known properties. Can screen for

- Having the disease
- Current treatment
- Perhaps severity
- Enrichment features (some)
  - Prior events
  - Lab findings (if standard, but not exotic)
  - Duration of disease

Finding the Patients

Good candidate: persistence of effect. Some have been revealed

- How long to give bisphosphonates
- Recent ticagrelor study (Pegasus)

  21,000 patient trial comparing ticagrelor 60 mg, 90 mg, and placebo (added to ASA) in patients with history of MI 1-3 years ago and at least one of: > 65, with DM, at least one other MI, evidence of multi-vessel CAD.

  Endpoint: time to CV death, MI, stroke

  HR 0.84 (0.74-0.95) p < 00043

  (no difference 60 mg vs 90 mg)

  Forest plot shows many demographic and other characteristics
- How long to use adjuvant chemotherapy

Doing the Trial

1. Still need consent
   - Interaction with investigator
   - Possibly on line

2. Probably, for maintained Rx, NEED investigators to see patients periodically; so they have to agree

Doing the Trial (cont)

3. Some (most) endpoints not routinely collected or need more precision
   - Usually, death (CV vs Other)
   - AMI (yes, no)
   - CHF function, NYHA, Minnesota exercise test
   - Wide range of others (depression scores, ADAS-Cog, etc)

   Implies need for investigator

4. For recognized, approved drugs, CAN reduce safety collection (Phase 3/4 Lite)

5. Most of the time, blinded treatments and often placebo, so need pharmacy, etc

Limitations

Enrollment: Really no problem

Use of collected data:

- Impression hides. Most of the time you're not overpowered, so a concern with using collected data

- Hard to imagine a persuasive NI study in this setting, as no prior similar experience, but maybe with very large control effect (anticoagulants for AF)
- TASTE (Thrombus aspiration in MI) possible because
  - Single treatment
  - All cause mortality IN SWEDEN

    Secondary endpoints also in registries focused on those endpoints

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RWD as basis of regulatory approval

An example in rare disease

Bill Capra, Global Head Real World Data Science Oncology, Genentech

Examples of RWD Databases

Data Sources	Characteristics	Examples
Insurance Claims	• Collected for insurance and reimbursement purposes • Often include a number of health plans • Often with >10million currently enrolled pts • Inability to validate outcome and case definition with chart	TRUVEN HEALTH ANALYTICS, JMDC, IMS LifeLink PharMetrics Plus™
Health Provider Claims	• Higher data integrity, complete knowledge of database • Ability to validate outcome and case definition with chart; possible to link with EMRs • Smaller population than insurance claims db	OPTUM™, KAISER PERMANENTE®
Registry	• Can be disease-specific or product-specific • Variable accessibility	SEER, American Academy of Ophthalmology The Eye M.D. Association
EMR	• Data collected for quality of care, performance measure, utilization, clinical research • Some include all pt records from GP, specialty care visits, medications, in-patient stays, labs, etc. Some only GP • Valuable details in unstructured data (notes)	GE Healthcare, MDV medical.data.vision, CPRD MORE DIMENSIONS TO DATA

Trends: quality & completeness are improving through technology

- *NLP + human abstraction from unstructured data*
- *Linking of insurance claims, EMR, and molecular information*

Differences between RCTs and RWD

Randomized Clinical Trials	Real World Data
Controlled setting	Real world, reflect actual practice
Academic/ research institutes	Various treatment settings, e.g. community, public, academic
Limited number of sites	Many treatment centers
Narrower inclusion criteria	Broad inclusion/ disease based
Typically shorter follow-up	Typically longer follow-up
Clinical and safety	Also real world HCRU and cost
Well established tool	Opportunity to develop new tools

Proposed setting: label expansion to rare disease

Rationale

- RCTs may not be feasible in rare disease populations.
- A confirmatory single-arm clinical trial may take years to enroll.

→ Rare diseases may be the ideal setting to assess the use of RWD for a label expansion.

Example:

Rare cancer based on combination of anatomy and biomarker alteration

Background

- Rare cancer with high mortality or morbidity and unmet need
  - Patient need – no effective treatment for patients either not responding or relapsing on standard therapy
- Experimental medication previously approved in other (larger) cancer indication(s).
  - Safety and B/R well established in initial indication
  - Safety expected to be similar in rare disease
- Biological basis for activity in rare cancer
  - E.g. Agent targets specific biomarker/pathway
- RWD may supplement prior clinical trial data
  - E.g. Phase I clinical trial data showing safety and anti-tumor activity in limited number of patients with rare cancer

Primary endpoint for rare cancer example

Real World Response from EMR

- Real world response can be abstracted from redacted physician notes and radiology reports.
  - Patient vignettes prepared for FDA.
- Small sample size (N~40-60) enables assessment of clinical relevance of treatment from patient-by-patient review.
  - Endpoint is different than clinical trial RECIST-based response.
- Creates a need for data standards - define real world response for future applications in the same disease space.

Addressing common RWD issues within rare cancer example

Data Quality & Completeness	Redacted physician notes and radiology report enable thorough assessment of treatment response.
Data Standards	Patient vignettes from limited sample size remove need to pool data .
Lack of Randomization	Lack of spontaneous response alleviates need for randomization.
Patient Privacy	Third party can de-identify when secondary data use.

Summary

Advantage of assessing RWD in a rare disease

- Opportunity to demonstrate efficacy and safety in patients with unmet medical need in setting where RCT is not feasible.
- Manageable study size enables industry and regulators in-depth review to confirm meaningful clinical activity.

Potential to build in larger populations:

- Overall survival endpoint in broader population where stable disease expected on investigational agent
- In general, data standards in specific diseases with well-defined endpoints will enable use of RWD in broader populations.
- Randomized setting where therapies with similar MOA to crossover not available – enables pragmatic design

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Study Design Considerations

Lisa M. LaVange, PhD
Director, Office of Biostatistics
OTS, CDER, FDA

Real World Evidence (RWE)
Duke-Margolis Center
March 3-4, 2016

Use of EHRs in RCTs

- Supplement case report form (CRF) data collection
  - Medical history, demographics, etc.
- More efficient than extracting/transcribing onto CRF
- Source data monitoring reduced (EHR *is* the source)
- Lack of data standards/formats
  - Difficult to expand to other clinical systems
- Variable data quality

Randomization

- Only difference between randomization groups is treatment assignment

  →observed differences attributable to drug
- Eliminates effects of confounding factors
  - if well-controlled, no differential follow-up, etc.
- Inference limited to clinical setting, studied population
  - Internal validity, but may be gained at expense of external validity

Representativeness

- Interest in drawing inference to a broader population than the one studied
- Sample survey setting
  - Probability sampling from a target population
  - Each pop. member has known, >0 chance of selection
  - Sample estimates unbiased for pop characteristics
  - Demographic, SES, health status make-up of sample reflects target population→*representativeness*
- Observational studies may have broader study populations than RCTs
  - But may not be representative of target pop of interest

Pragmatic CTs

- Randomized (RCTs and PCTs)
  - PCTs often not masked
- More meaningful (actual use) comparator
  - In contrast to RCT comparator, chosen to show superiority
- More diverse (representative?) study population
  - Diverse practices can impact study conduct, data quality
- Broader outcomes
  - Quality of life, cost effectiveness, etc.
  - Regulatory concern that these assessments impact others, e.g., safety outcomes

Interventions

- PCTs -- intervention may be adapted to clinical setting (real world)
  - In contrast to RCT, with highly standardized intervention
  - Some loss of power in PCT due to variability in delivery
- Results may be more relevant to decision-makers
  - Need to collect information about delivery
- Difficult to determine attribution (which part of intervention had impact?)
- Effect size may be reduced, but impact lessened if delivery optimized

SMARTs

- Sequential Multiple Assignment Randomized Trial
  - Personalized, dynamic treatment regimes
  - Sequence of decision points with re-randomization
- Real-world setting for treatment decisions
  - Treatment outcome determines subsequent (randomized) treatment strategy
- Statistical analysis complicated but do-able
  - Machine learning/reinforcement learning/Q learning
- FDA quandary – how to attribute effectiveness and safety (to which treatment)?

Externally Controlled Trials

- FDA rules and regulations allow use of historical controls
  - If randomization to concurrent control group not feasible or not ethical
  - Single-arm studies may be only choice (e.g., ultra-rare diseases, some oncology settings)
- Use of historical or external control group of patients
  - Allows adjustment for confounding factors
  - Outcome in control or no-treatment group not known
- Well-controlled implies a certain level of rigor
  - Pre-specification; selection of controls before outcomes are known, etc.

Externally Controlled Trials

- Importance of planning cannot be over-emphasized
  - Post-hoc external control comparisons difficult to interpret
- Availability of actual historical control patients important
  - To check for comparability to new patients (concurrent control)
  - To adjust for confounding, e.g., with propensity score methods
  - To assess variability in estimate of historical control outcome
- Without such data, single-arm study may not be appropriate
- Historical/external control group data (patient-level) can be leveraged to supplement concurrent control in RCTs
  - Increase power; useful in cases with limited populations
  - Interim analyses to assess comparability and adapt, if needed

Selected References

PCTs

- Tunis SR, Stryer DB, Clancy CM. Practical clinical trials: increasing the value of clinical research for decision making in clinical and health policy. *JAMA*, 2003.
- Schwartz D, Lellouch J. Explanatory and pragmatic attitudes in therapeutical trials. *Journal of Clinical Epidemiology*, 2009.
- Peikes D, Geonnotti K, Wang W. Using pragmatic clinical trials to test the effectiveness of patient-centered medical home models in real-world settings. AHRQ, 2013.

Selected References

Historical controls

- Pocock SJ. The combination of randomized and historical controls in clinical trials. *Journal of Chronic Diseases*, 1976.
- Viele K, Berry S, Neuenschwander B, et al. Use of historical control data for assessing treatment effects in clinical trials. *Pharmaceutical Statistics*, 2013.
- D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a nonrandomized control group. Statistics in Medicine, 1998.
- FDA Guidance for Industry: Design considerations for pivotal clinical investigations for medical devices, 2013 (Section 7.6 Non-comparative clinical outcome studies).

Selected References

SMARTs

- Zhao Y, Kosorok MR, Zeng D. Reinforcement learning design for cancer clinical trials. *Statistics in Medicine*, 2009
- Zhang, B, Tsiatis A, Laber E, Davidian M. Robust estimation of optimal dynamic treatment regimes for sequential treatment decisions, *Biometrika*, 2013.

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Duke Clinical Research Institute

Real World Evidence Development: Harnessing Randomization & The How?

March 3, 2016

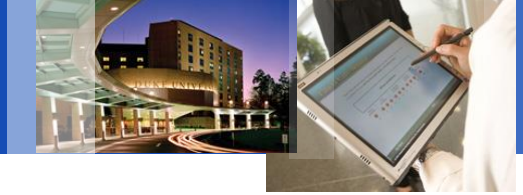
Adrian Hernandez, MD, MHS
Director, Health Services & Outcomes Research
Associate Director, DCRI

Millions

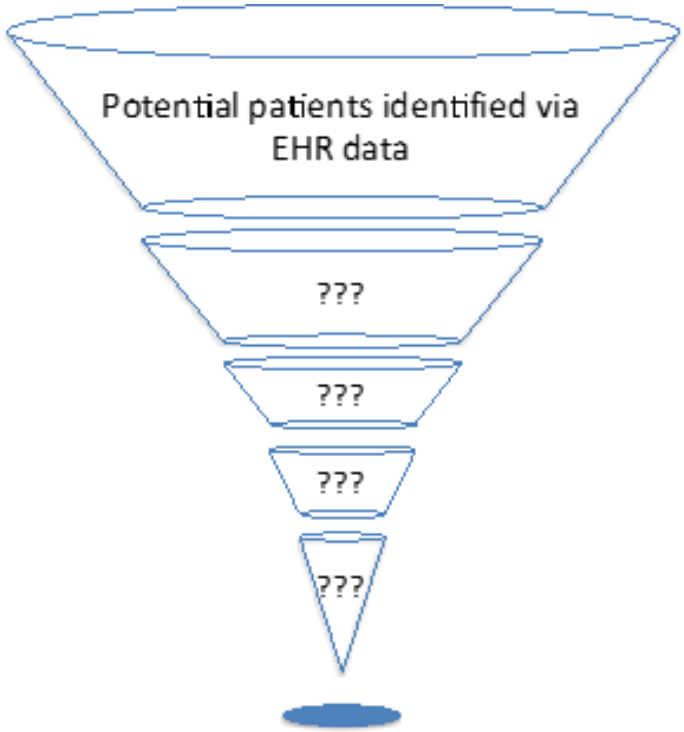
Patients **walk through the doors** of hospitals and clinics each year **with questions** about their health and their care.

?

How do we **study their experiences** to **find answers** and **create solutions** that **change care** and **improve outcomes**?

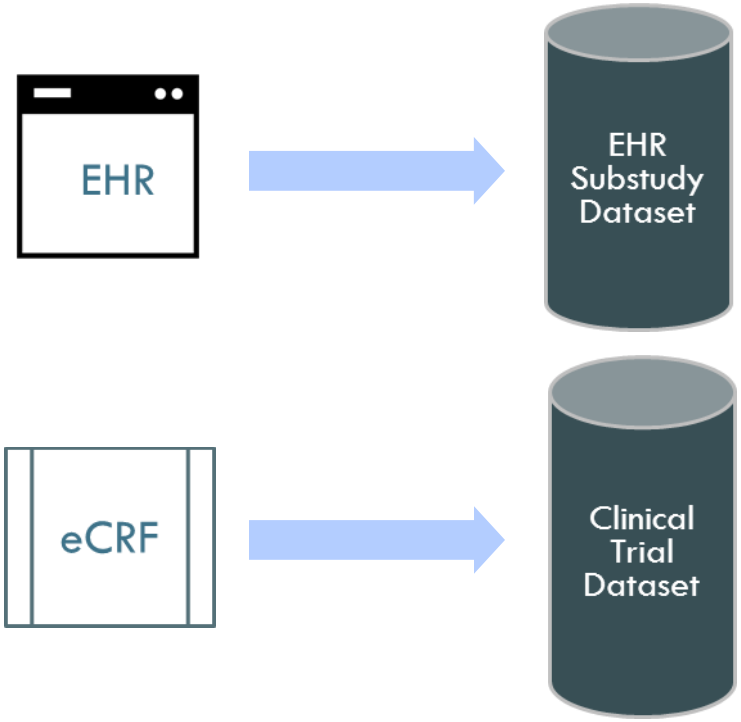


How are EHR data used to facilitate recruitment?



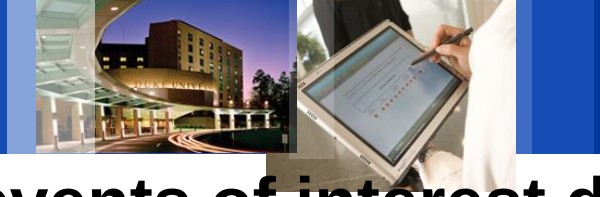
Survey/focus groups
Site-level funnel measurement
EHR-based algorithm

Can the EHR reliably provide baseline characteristics ?



What's better quality?

Direct extraction from the medical record vs. human entry?



Can the EHR (or claims) find events of interest during follow-up?

Case-finding algorithm identifies endpoints

EHR

Study Coordinator identifies endpoint events from all potential sources: patients, care providers, investigators, EHR

eCRF

What is more systematic for collecting endpoints?

Guiding Principles to Define Quality

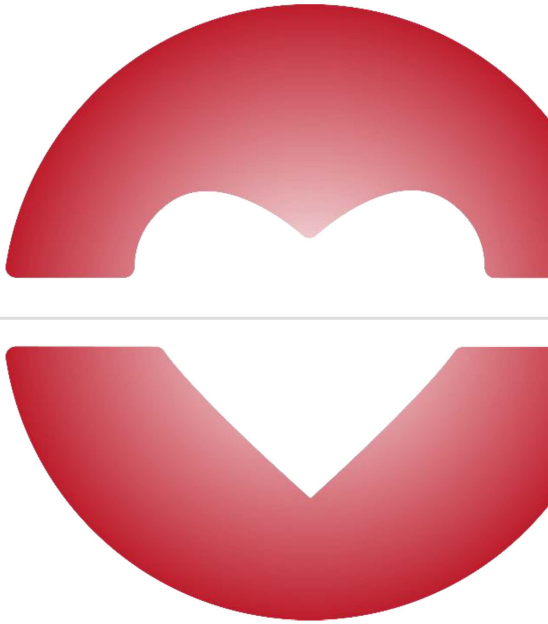
- Right Patient:
  - Have we enrolled the right participants according to the protocol with adequate consent?
- Right Intervention:
  - Did participants receive the assigned treatment and did they stay on the treatment?
- Right Primary/Secondary Outcomes:
  - Was there complete ascertainment of primary and secondary efficacy data?
- Right Safety Outcomes:
  - Was there complete ascertainment of primary and secondary safety data?
- Right Study Conduct:
  - Were there any ***major*** GCP-related issues?

QUALITY ≠ MORE

LESS = MORE

CASE EXAMPLES

ADAPTABLE Trial: What's the right dose of aspirin?

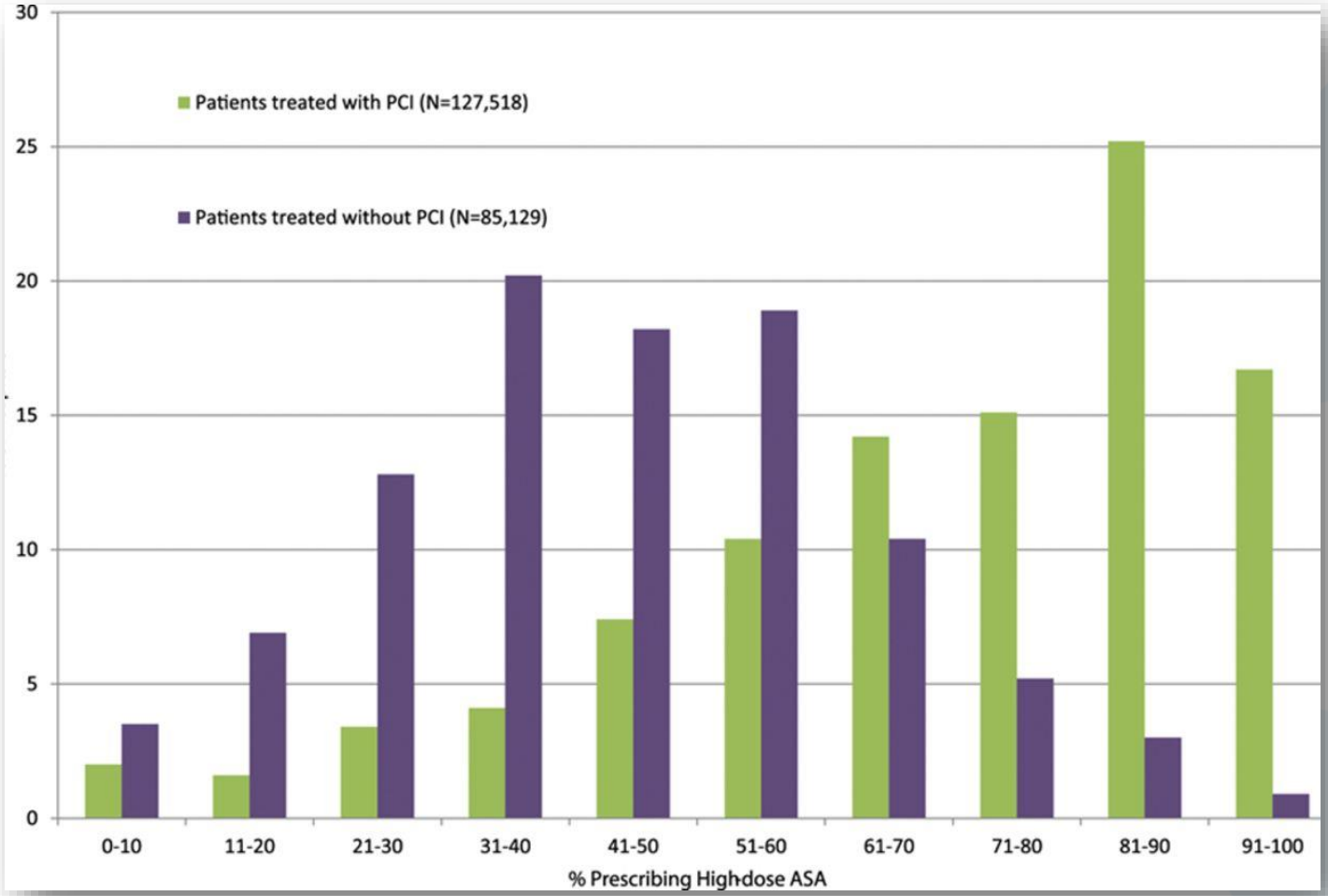


Adaptable

The Aspirin Study

pcornet

High (25 -fold) Variation Across Hospitals on Use of Aspirin by Dose



>440 US Hospitals

Hall et al. Circulation Cardiovascular Quality and Outcomes 2014

Main objectives

- To compare the effectiveness and safety of two doses of aspirin (81 mg and 325 mg) in high-risk patients with coronary artery disease
  - **Primary effectiveness endpoint:** Composite of all-cause mortality, hospitalization for MI, or hospitalization for stroke
  - **Primary safety endpoint:** Hospitalization for major bleeding
- To compare the effects of aspirin in predefined key subgroups of patients
  - Age, diabetes, sex
  - Race, P2Y12 inhibitor use
  - Chronic kidney disease
- To develop and refine the infrastructure for PCORnet to conduct multiple comparative effectiveness trials in the future

ADAPTABLE Study Design

Patients with known ASCVD + ≥ 1 "enrichment factor"*

Identified through EHR (computable phenotype) by CDRNs
(PPRN patients that are already a part of a CDRN are eligible to participate.)

† Participants without internet access may be consented and followed via a parallel system.

Adaptable

ADAPTABLE Study Design

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↓

Patients contacted with trial information and link to e-consent;†
Treatment assignment will be provided directly to patient

↓

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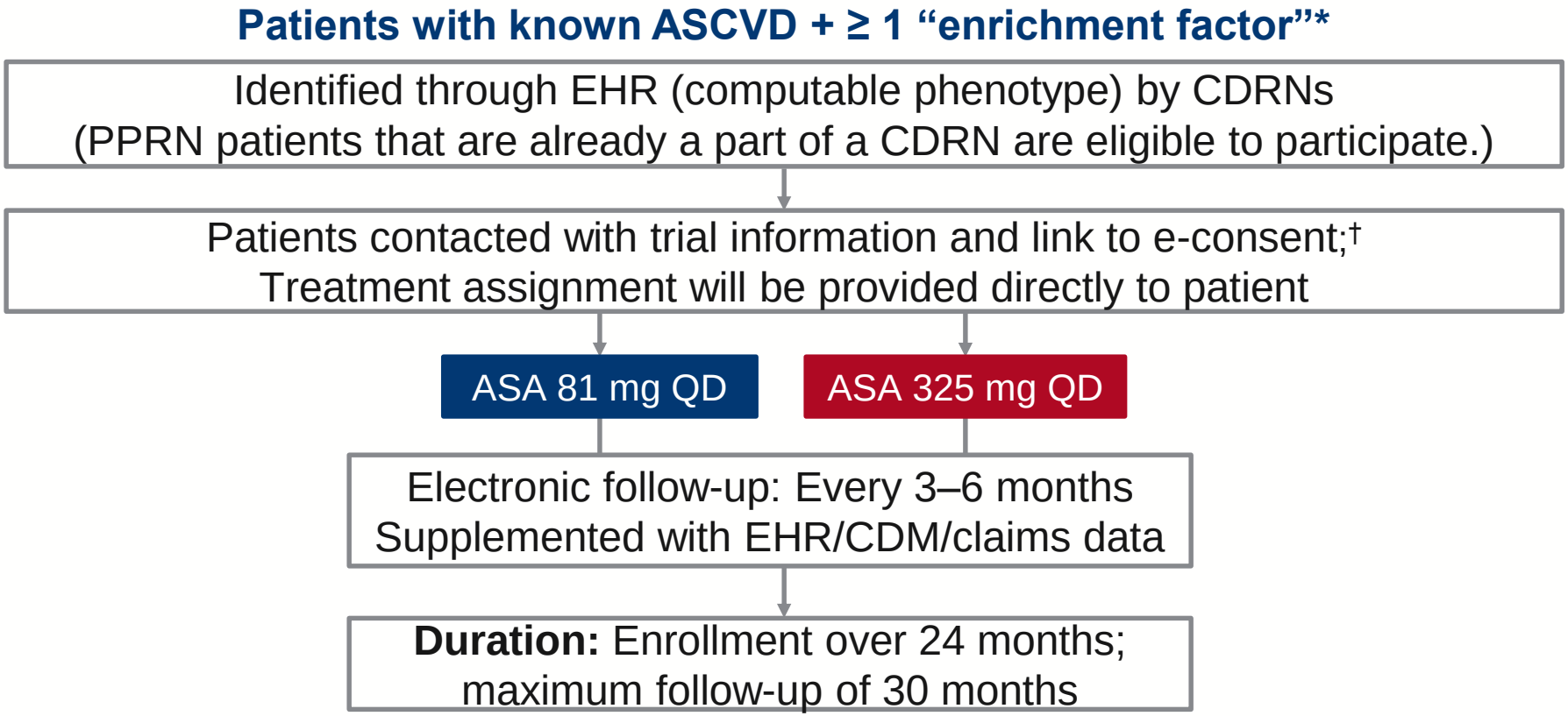
ADAPTABLE Study Design



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Treatment assignment will be provided directly to patient

ASA 81 mg QD | ASA 325 mg QD

Electronic follow-up: Every 3–6 months
Supplemented with EHR/CDM/claims data

Duration: Enrollment over 24 months;
maximum follow-up of 30 months

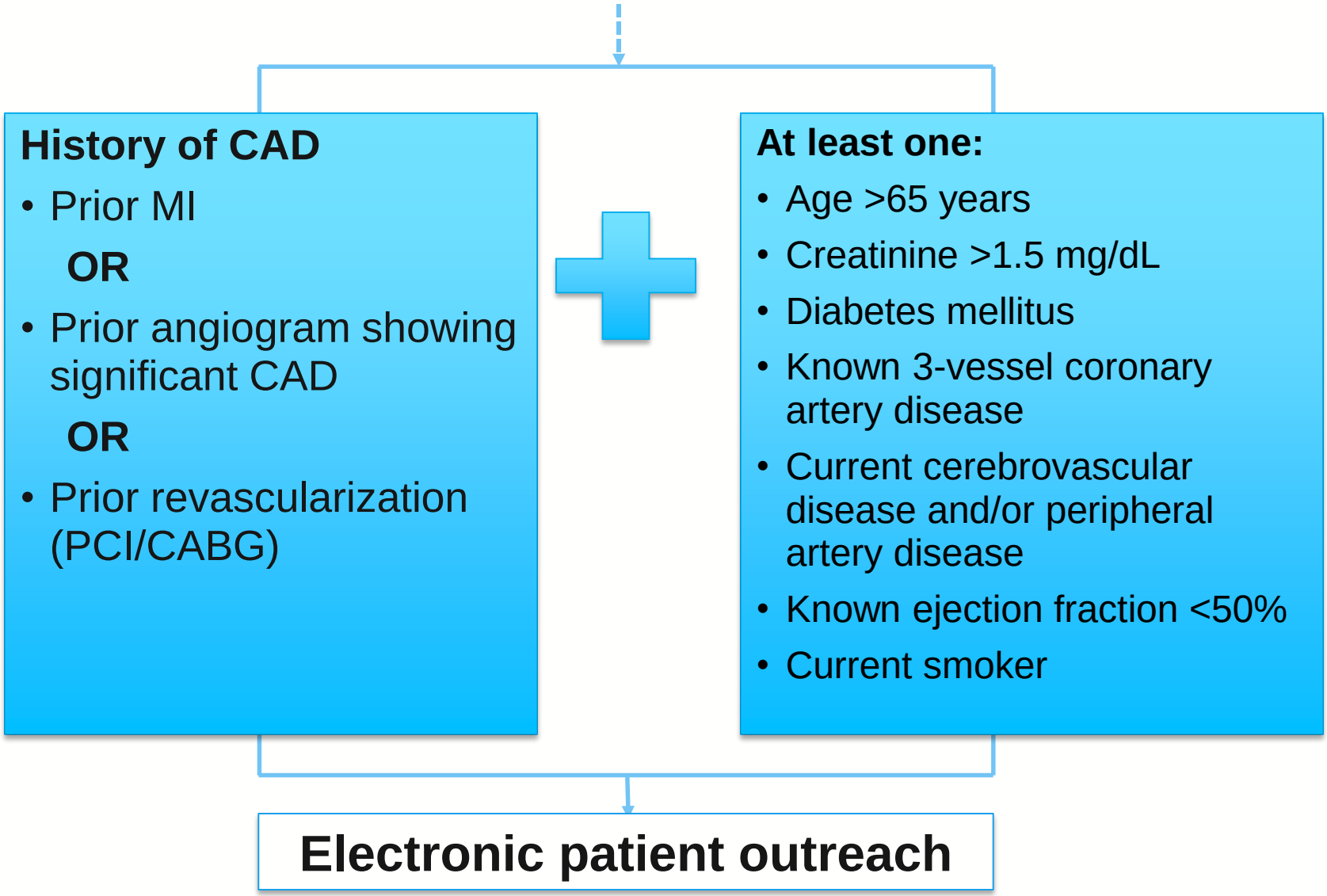
Primary endpoint:
Composite of all-cause mortality, hospitalization for MI or stroke

Primary safety endpoint:
Hospitalization for major bleeding

† *Participants without internet access may be consented and followed via a parallel system.*

Adaptable

Computable phenotype for CDRNs



Informed consent and randomization

Electronic outreach to potential participants with trial introduction and link to ADAPTABLE web portal

↓

Web-based, electronic informed consent (English & Spanish)

- Initial patient contact via web portal ➔ text and video consent
- Common consent form with selected local adaptations
- Questions to confirm patient comprehension for informed consent and eligibility for randomization after consent obtained

↓

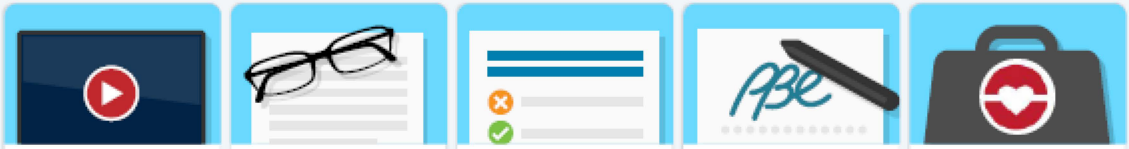
Randomization and aspirin dose assignment

Adaptable
The Aspirin Study

TEXT SIZE A

There are 5 steps to join the study!

The time on each card is an estimate of
how long it will take you to complete each section.
There are no time limits, so please go at your own pace.



Watch
the ADAPTABLE short video
5 min

Read
more details about participating in ADAPTABLE
15 min

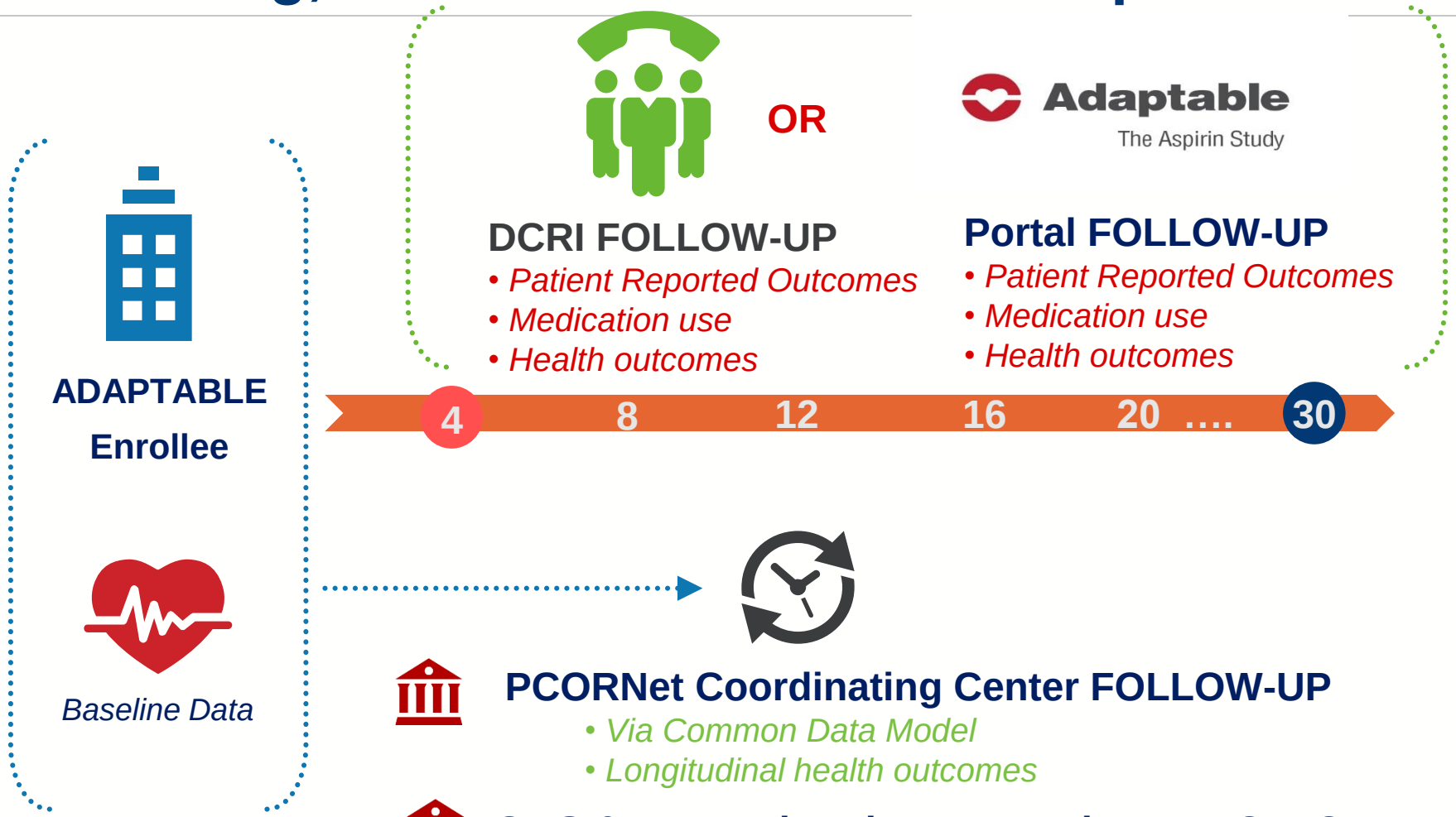
Answer
a few questions about the study
5 min

Join
the ADAPTABLE study
3 min

Inform
us about your current health
5 min

LET'S GET STARTED

Enabling Pragmatic Research: eScreening, eEnrollment and eFollowup



Adaptable

Traditional trials vs. ADAPTABLE

	Traditional	ADAPTABLE
Incl/Excl criteria reviewed	Sample via CRA visit	Common Data Model
Representative cohort	Narrow	Broad
Consent	Facilitated	Patient-directed
Comprehension tested	No	Yes
Format	Paper	e-consent
Data collection	Patient-reported Site-recorded	Patient-reported CDM
Source documents	Only seen by site	Received via CDM
Endpoint adjudication	Yes	CDM, EHR data
Patient involvement	Participants only	Protocol design, committee, analyses, dissemination

INfluenza **V**accine to **E**ffectively **S**top Cardio**T**horacic **E**vents and **D**ecompensated heart failure **(INVESTED)**

Orly Vardeny, PharmD, MS
Associate Professor of Pharmacy and Medicine
Unversity of Wisconsin

CCC Co PI

Scott D. Solomon, MD
Professor of Medicine
Harvard Medical School
Brigham and Women's Hospital

CCC Co PI

KyungMann Kim, PhD
Professor of Biostatistics
University of Wisconsin

DCC PI

BWH BRIGHAM AND WOMEN'S HOSPITAL

HARVARD MEDICAL SCHOOL

UNIVERSITY OF TORONTO

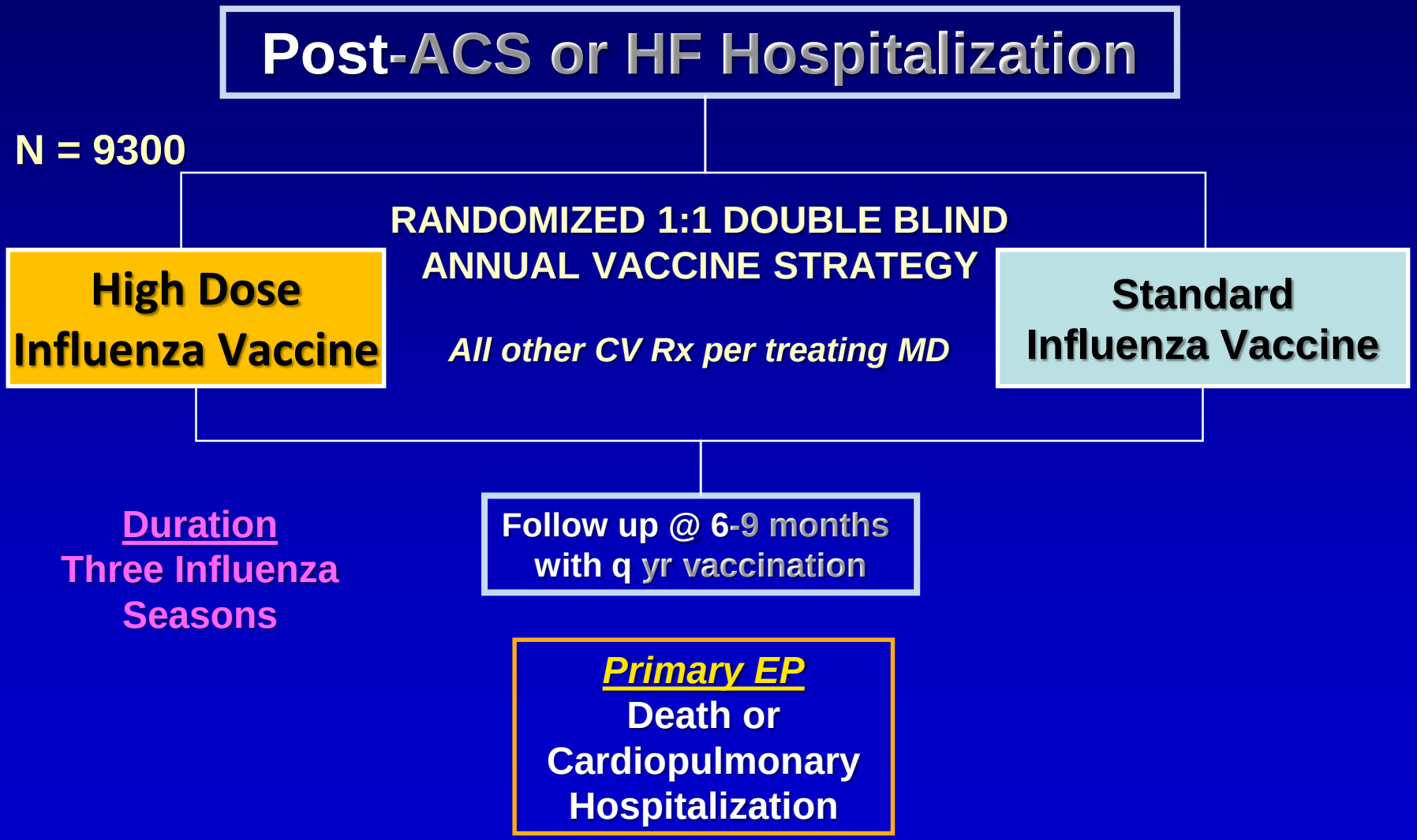
THE UNIVERSITY of WISCONSIN MADISON

Impact of Influenza - United States

- Approximately 36,000 influenza-associated deaths during each influenza season
- Over 200,000 influenza-related excess hospitalizations
- Greater number of hospitalizations and higher mortality during seasons when influenza type A (H3N2) viruses predominate
- ACIP does not preferentially recommend one influenza vaccine over another

Thompson et al JAMA. 2003;289:179 186
Thompson et al JAMA. 2004;292:1333 1340

INfluenza Vaccine to Effectively Stop CardioThoracic Events and Decompensated Heart Failure in Patients with CVD (INVESTED)



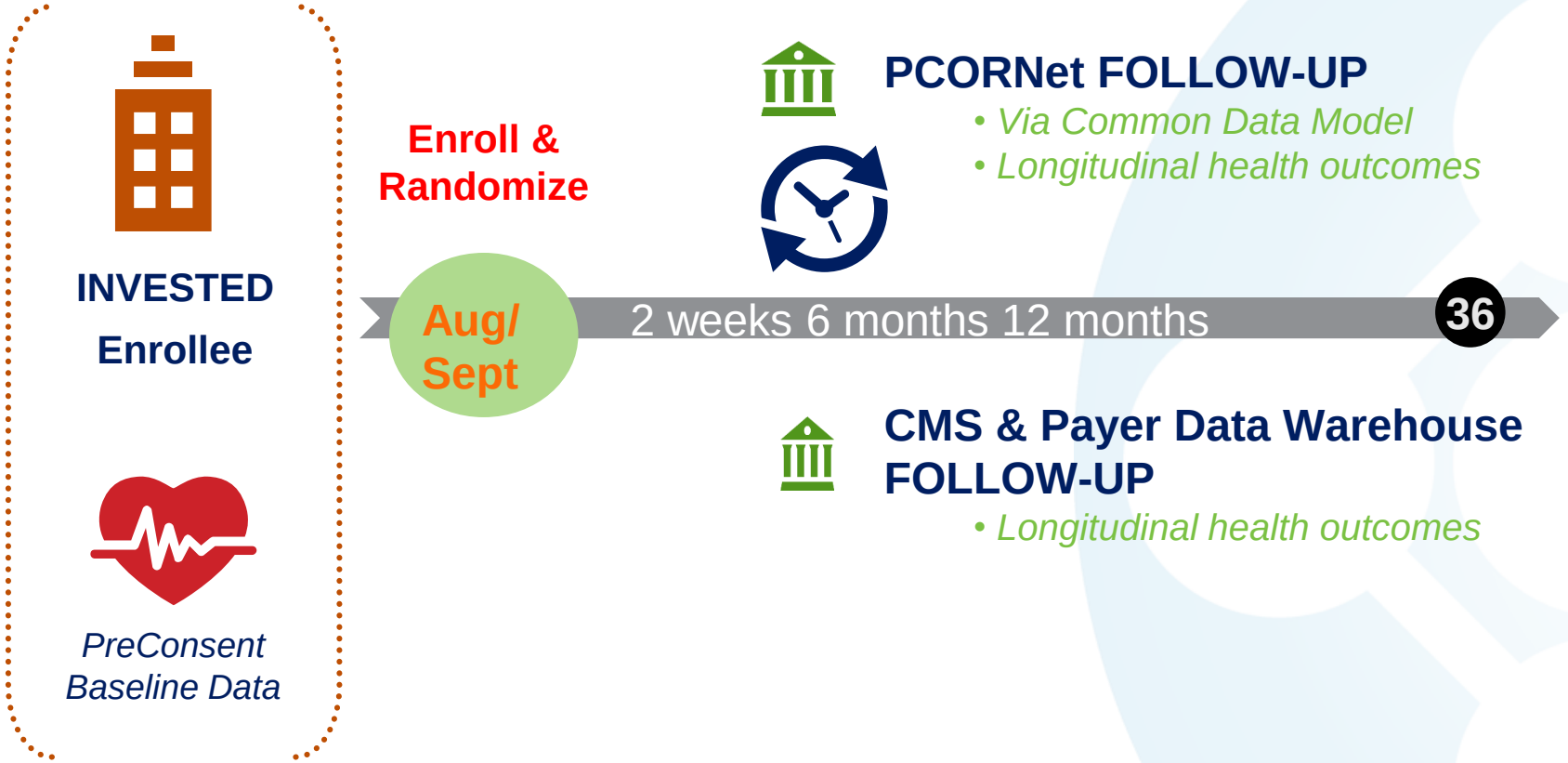
Recruitment Strategy

- Recruitment window is limited to August/September prior to influenza season
- Electronic health records to e-identify eligible participants
  - Heart failure hospitalizations or clinic follow-up
  - Acute coronary syndrome hospitalizations
- Pre-schedule randomization appointments
  - Randomization clinic

Event Ascertainment and Assessment

- Combination of novel and traditional ascertainment
- **EMR assessment of hospitalizations where feasible;**
- End of season phone follow-up by local study coordinators, and in person at subsequent year baseline visit
  - Simple Discharge summaries for hospitalizations will be acquired for event categorization

Enabling Pragmatic Research for INVESTED: eScreening and eFollowup



Conclusions

- Multiple Opportunities & Interests for Real-World Evidence Development
  - Through Pragmatic Trials Leveraging E.M.R
- What Matters?
  - Objective/Purpose
  - Study Design
  - Enrolling the Right Patient
  - Capturing the Right Outcomes
  - Quality by Design (Pre-specify plans)

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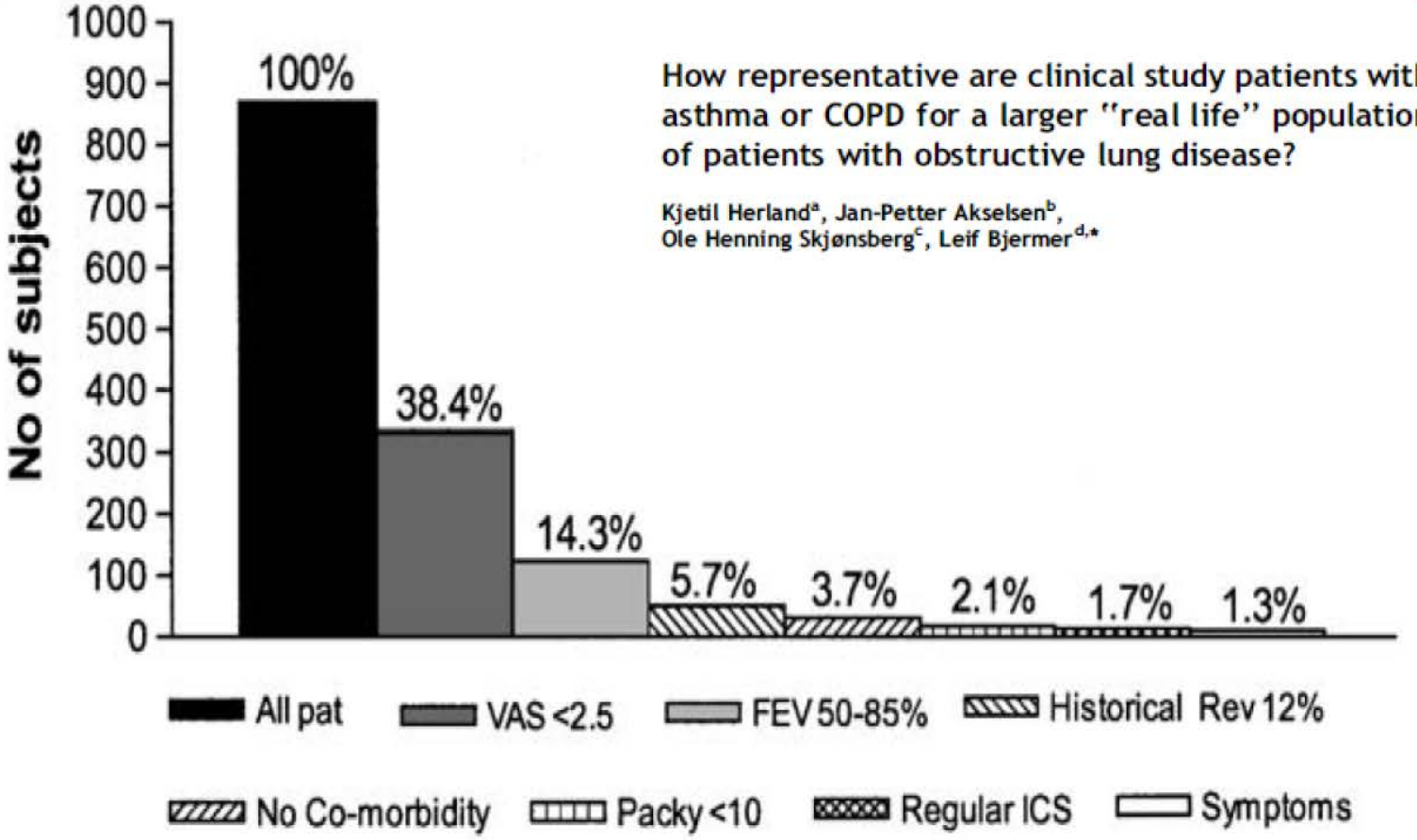
Salford Lung Studies

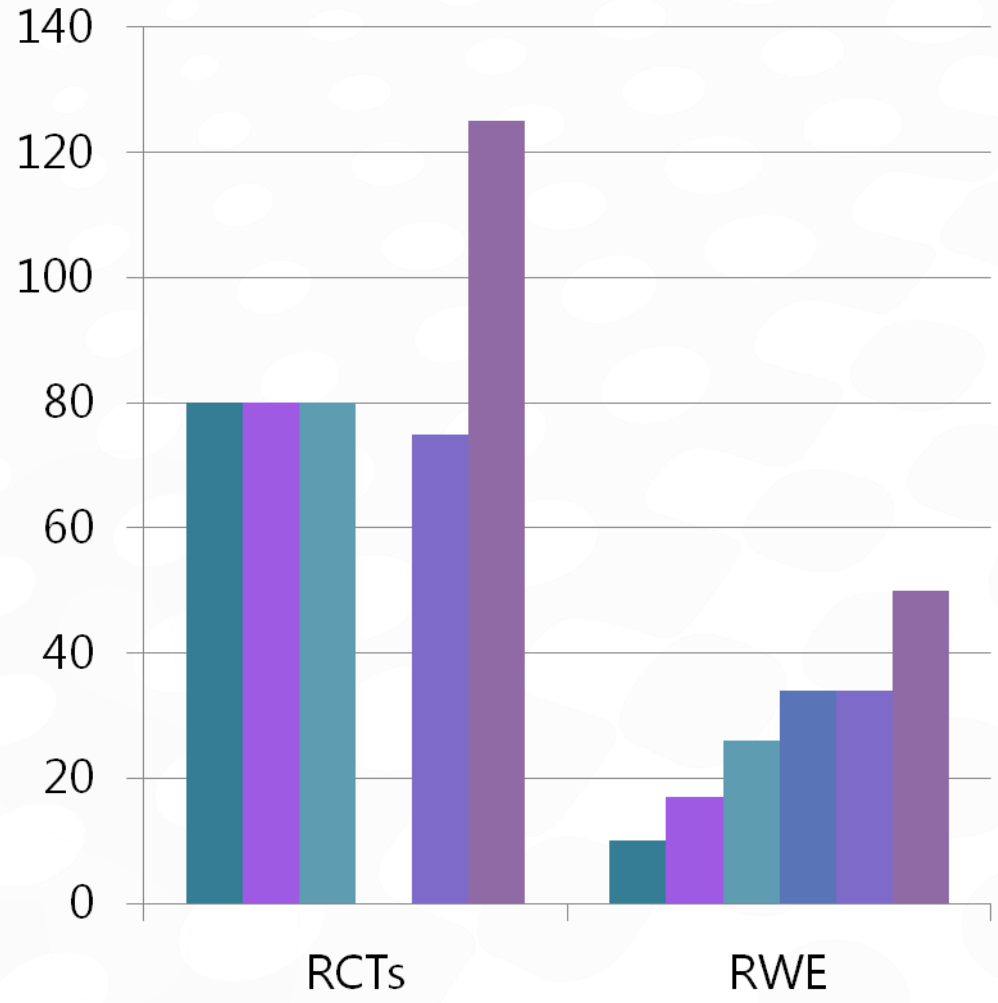
- We are running a late phase pRCT in Salford UK and surrounding areas
- Over 7200 patients are monitored in near real-time for safety and outcomes using linked electronic records
- Results expected later this year

Do RCTs represent the 'Real World'?



Herland K et al. Respir Med 2005; 99: 11–19.

% Adherence to Medications in Respiratory Studies



RCTs

Bateman, ED et al. Am J Respir Crit Care Med Vol 170. p836–844. 2004

Busse, W et al. J Allergy Clin Immunology. Vol 121.6.p1407–1414. 2008

Vestbo, J et al. Thorax Vol 64:939-943. 2009

Papi, A et al. Eur Respir J Vol 29: p 682–689. 2007

RWE studies

Breekveldt-Postma NS et al. Pharmacoepidemiology and drug safety. Vol17: 411–422. 2008

Janson, C et al. Eur Respir J Vol 26. 1047–1055. 2005

Adams, RJ et al. J Allergy Clin immunology. Vol 110.1. 58-64. 2002

Stallberg B et al. Respiratory Medicine Vol 97. 835–843. 2003

de Marco R et al. Int Arch Allergy Immunol Vol138:225–234. 2005

Corrigan, C. Primary Care Respiratory Journal Vol 20(1): 13-14. 2011

Salford Lung Study Ambition

Study is as near to "real world" as possible using a pre-license medicine

- **embrace heterogeneity of patient population**
- **normalise the patient experience as much as possible**
- **pragmatic – "usual care" in each arm**
- **relevant endpoints collected**

Maintain Scientific Rigour

- **Interventional**
- **Randomised**
- **Controlled**

Challenges and Solutions

- **How to recruit patients?**
  - **"all comers"**
  - **broad inclusion criteria**
  - **pragmatic diagnostic criteria**
  - **few exclusions**
- **How to ensure "normal" care of patients during the study?**
  - **minimal study procedures**
  - **normal prescribing and dispensing practices**
- **How to monitor patients without carrying out frequent reviews?**
  - **minimize "Hawthorne" effect**
  - **ensure patient safety**
  - **ensure robust collection of end points**

- **Recruit patients through primary care**
- **Study drug accessed through "high street" community pharmacy network**
- **No additional review**
- **No change to "care as usual"**
- **Integrated electronic patient record (EMR) with real-time access ensures that data is complete wherever and whenever patient accesses healthcare**

Study outline for COPD

Primary endpoint: Moderate/severe exacerbation (defined by oral steroid (and/or antibiotic use) +/- hospitalisations)
Secondary endpoints: Serious Pneumonias, Healthcare utilisation, COPD Assessment Test (CAT)

2800 patients

- **Patients in primary care, aged 40+**
- **GP diagnosis of COPD**
- **Taking ICS,LABA,LAMA alone or in combination**
- **Exacerbation in last 3 years**
- **Consented**

Randomised

New Rx open label

Visit 2
Routine respiratory review
Device instruction
CAT

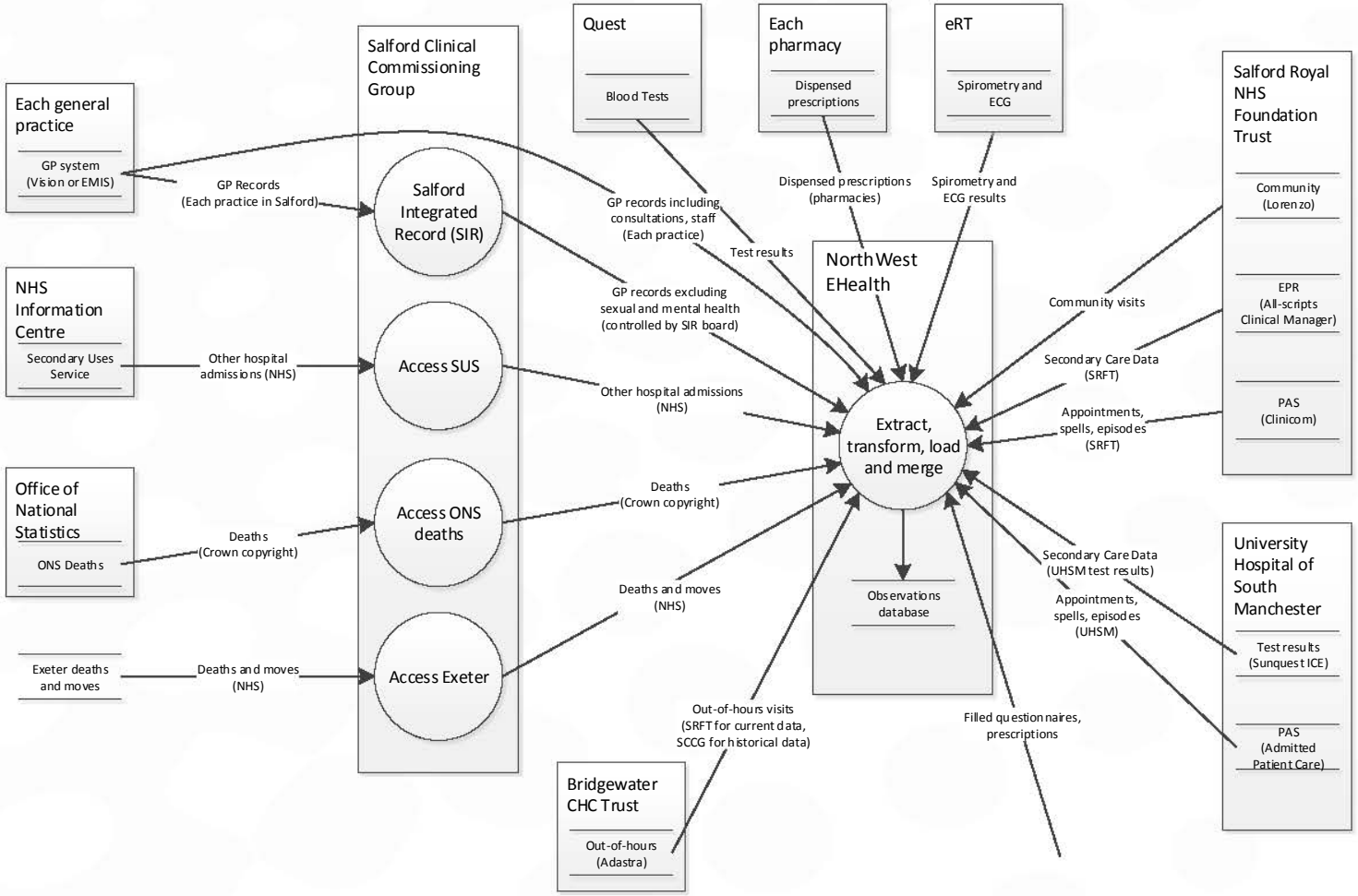
12 months of normal care

Visit 6
Routine respiratory review
CAT

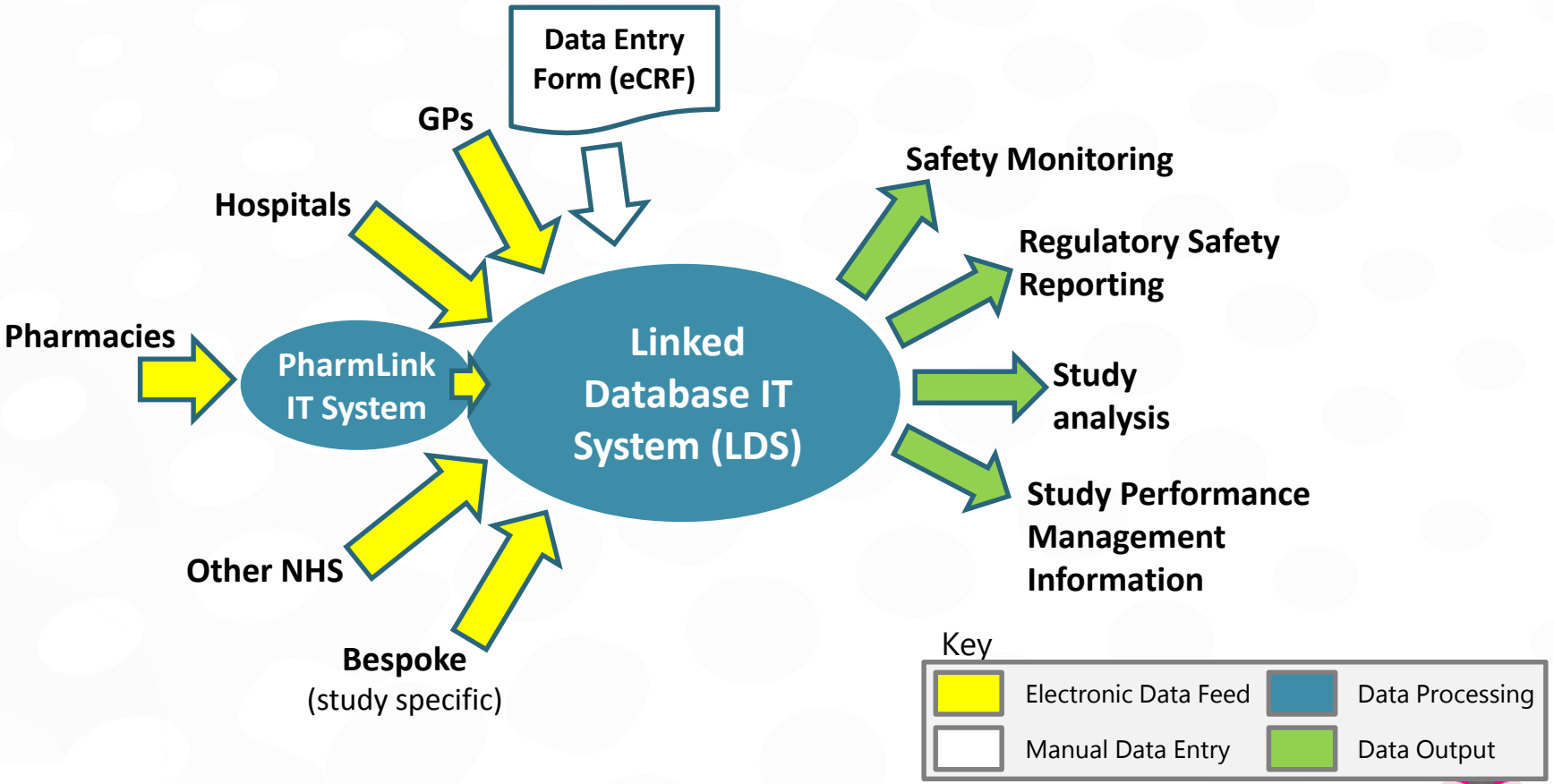
Existing maintenance Rx, ICS, LABA,LAMA

Constant real-time data collection of all HC interventions/safety monitoring

Linked database system: integration



Turning Patient EMR Data Into Study Information



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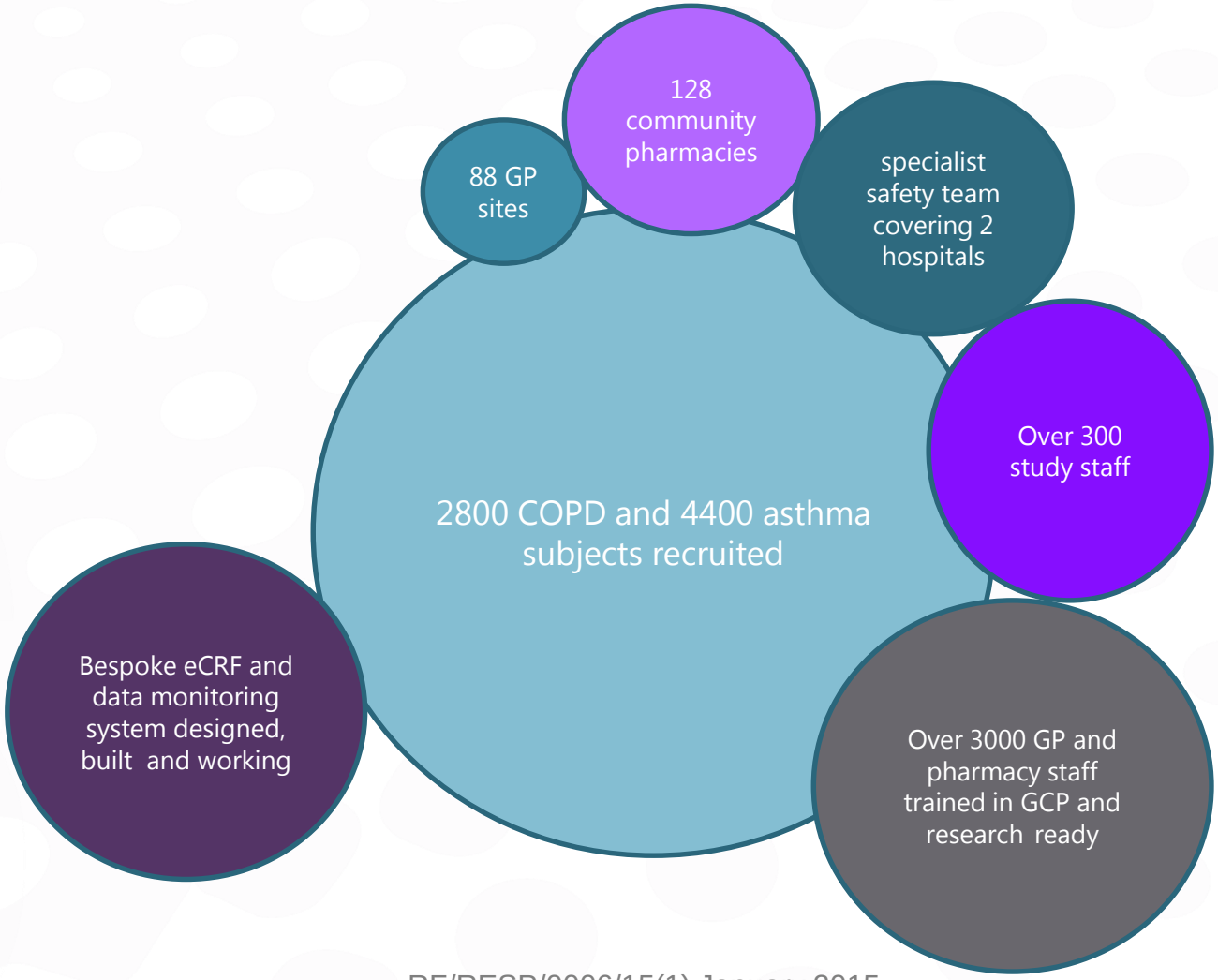
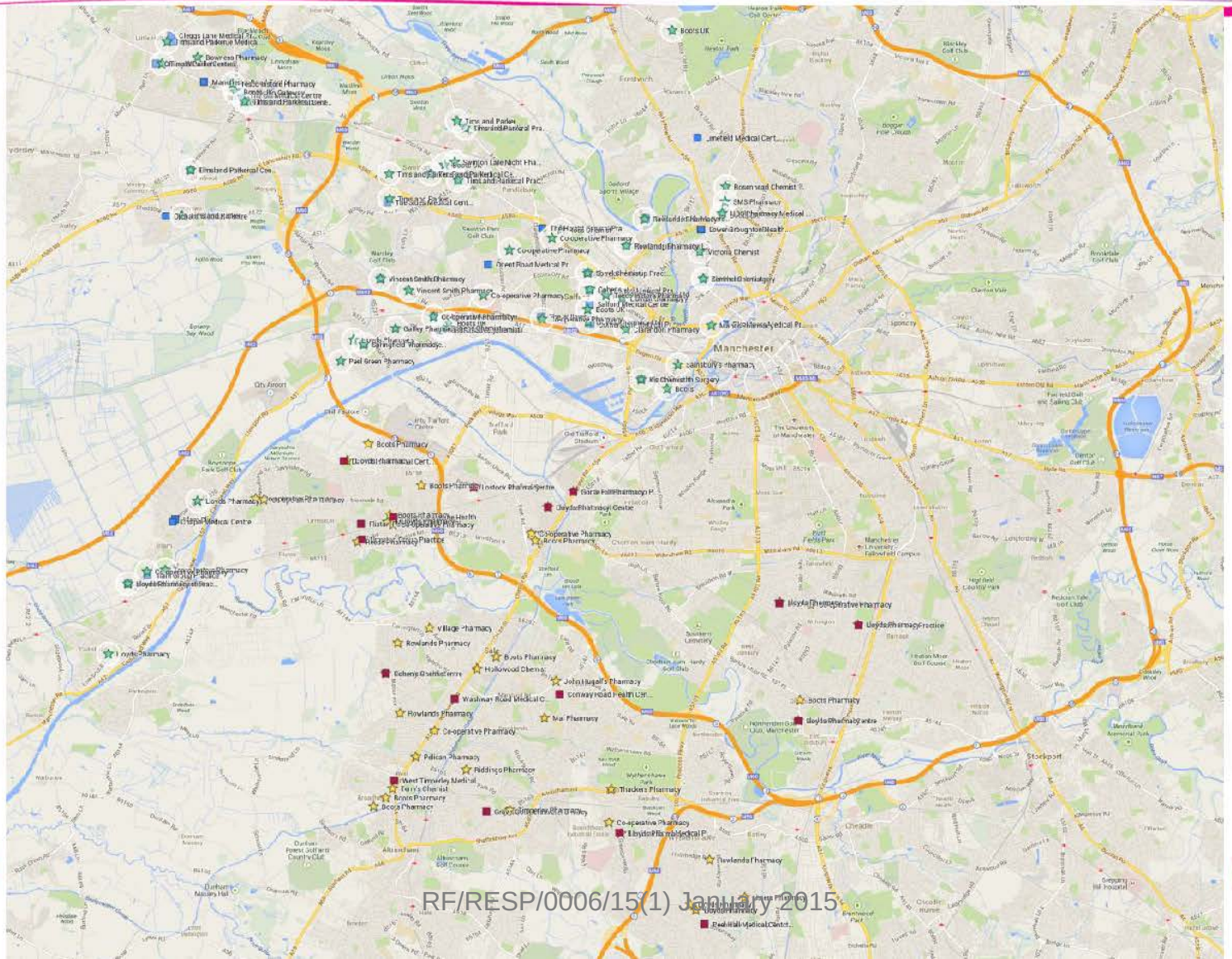
Salford Lung Study

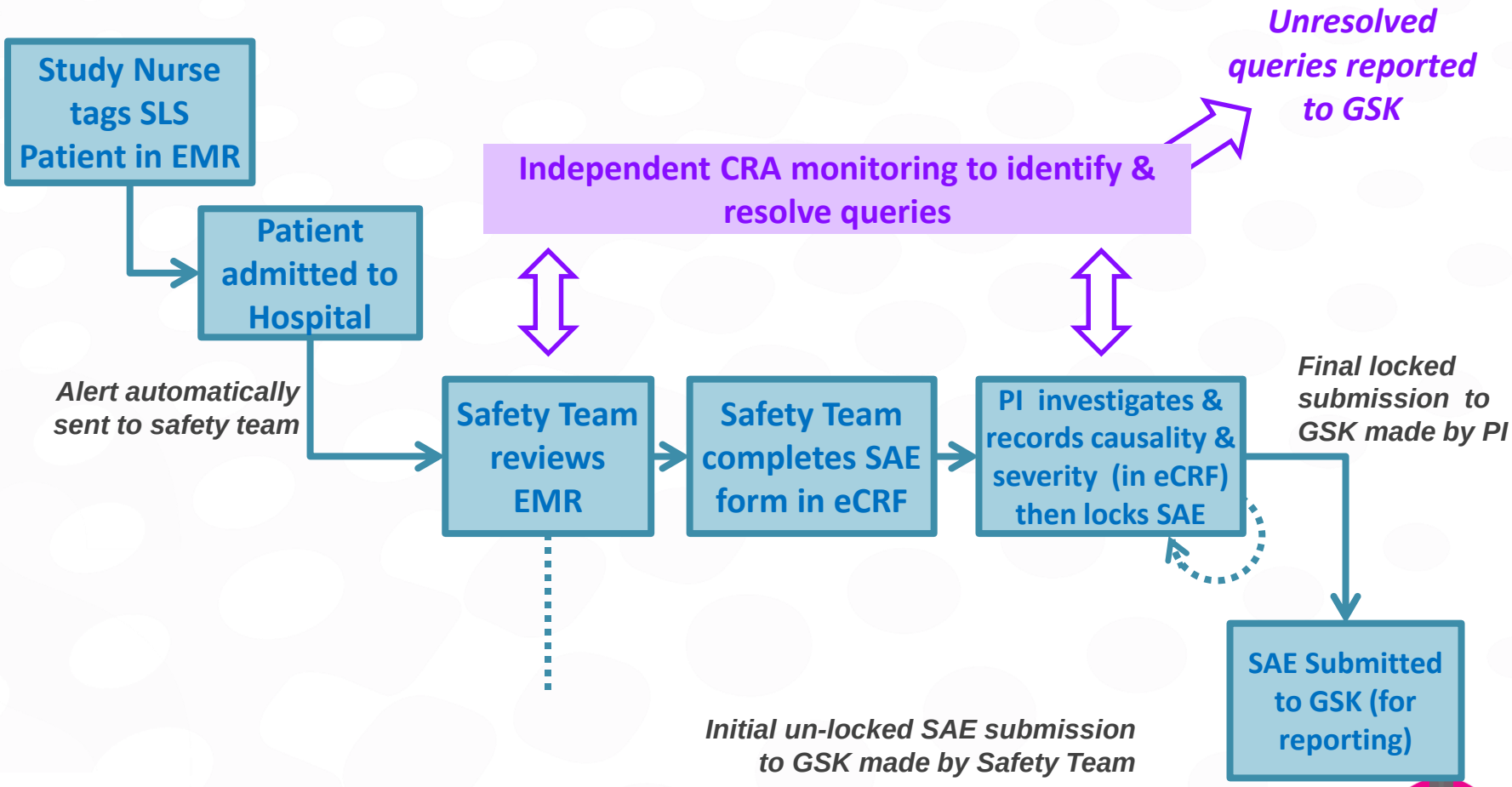
Scale of the Project



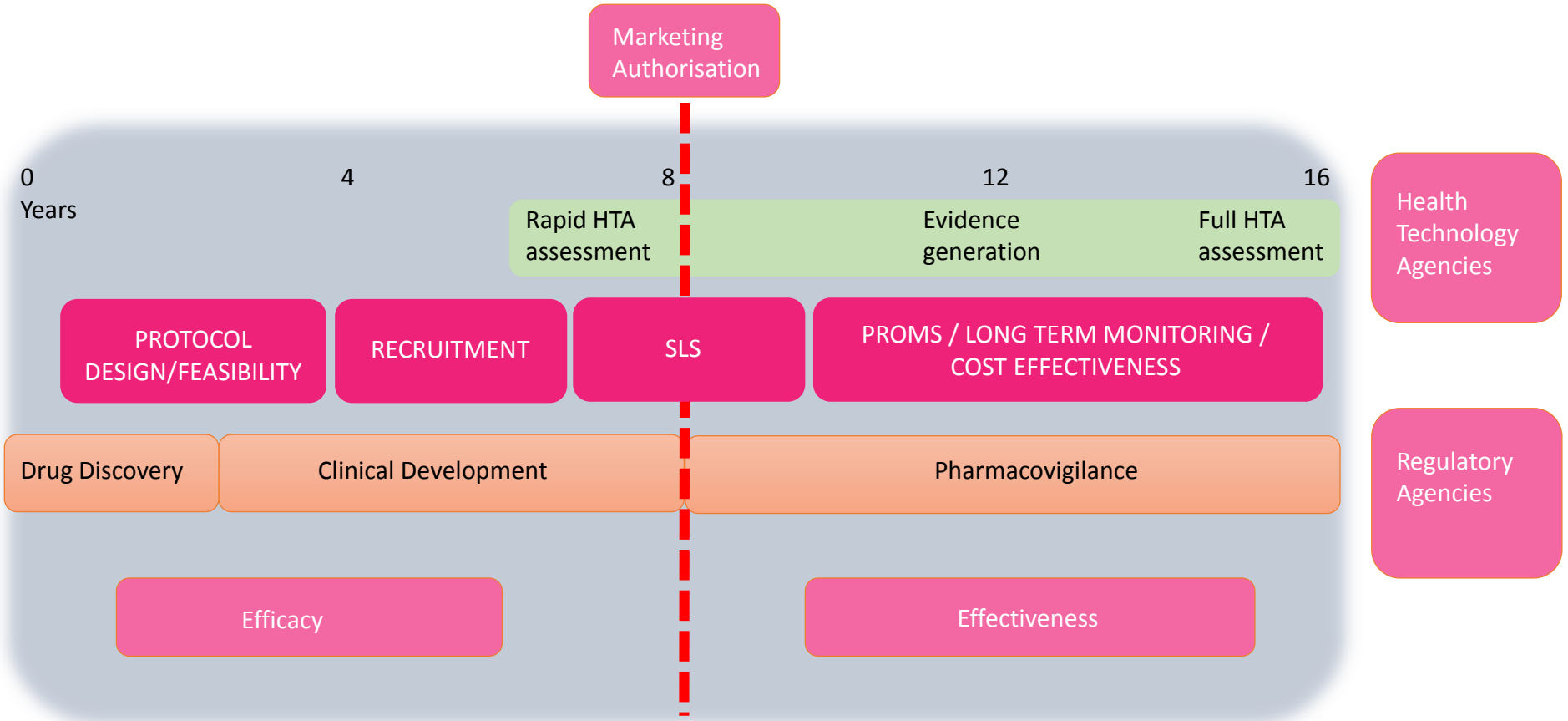
Retail Pharmacies linked to system



Serious Adverse Event (SAE) Reporting Process



Now


Marketing Authorisation
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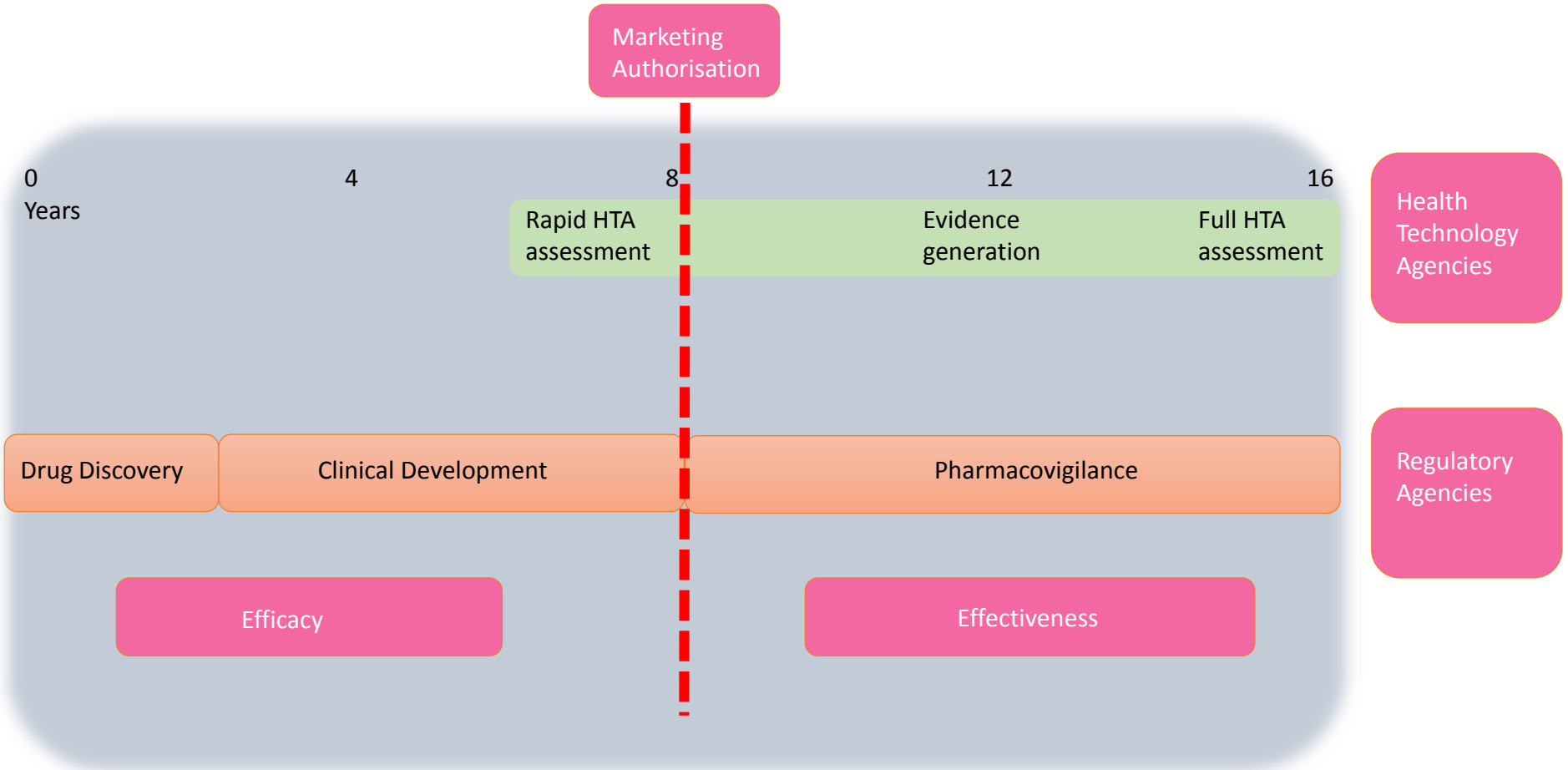
Years
4
8
12
16
Rapid HTA assessment
Evidence generation
Full HTA assessment
Health Technology Agencies
PROTOCOL DESIGN/FEASIBILITY
RECRUITMENT
SLS
PROMS / LONG TERM MONITORING / COST EFFECTIVENESS
Drug Discovery
Clinical Development
Pharmacovigilance
Regulatory Agencies
Efficacy
Effectiveness

The future?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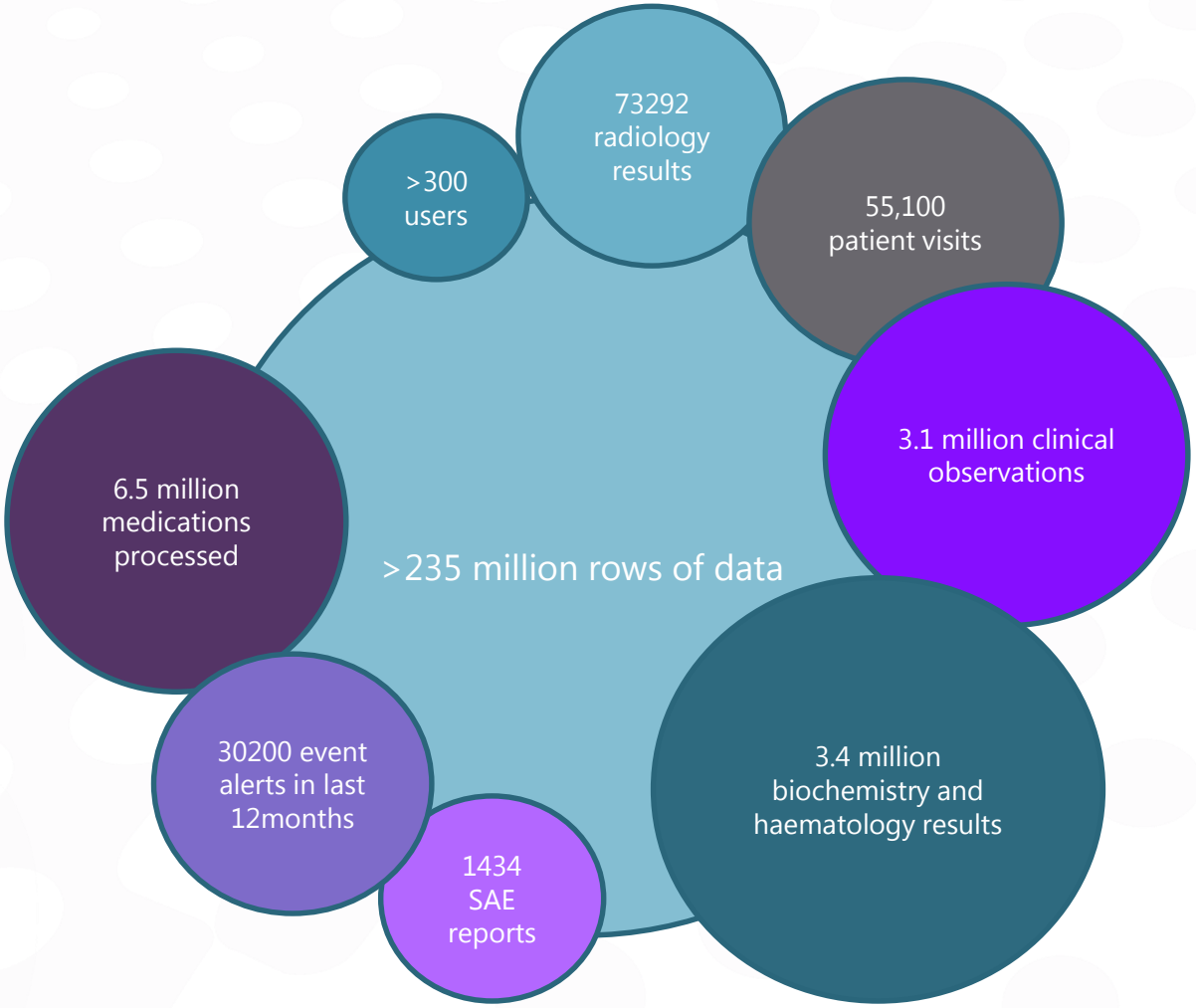
Drug Discovery
Clinical Development
Pharmacovigilance
Regulatory Agencies
Efficacy
Effectiveness

Summary

- **The Salford Lung Study is the first of its type**
- **Maintains scientific rigour**
  - **randomised**
  - **active control**
  - **robust primary endpoint**
- **It is a hybrid of RCT and real-world**
- **Offers ability to create flexible trial design based on stage of development – from something resembling a standard RCT to something more like an observational study**
- **It provides valuable information about how to conduct real-world studies in future**

Electronic Clinical Monitoring



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