

# Real World Data for Clinical Research: A PCORnet Workshop with the Pharmaceutical and Biologics Industry

March 30, 2015  
9:00 AM – 5:00 PM



# Morning Agenda

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- 🕒 9:00 – Welcome
- 🕒 9:15 – Introductions and Purpose of the Workshop
- 🕒 9:30 – PCORnet in Brief
- 🕒 10:00 – Examples and Insights from the Networks
- 🕒 10:30 – Q&A on PCORnet Structure, Plans, Network Activities
- 🕒 10:45 – Break
- 🕒 11:00 – Open Discussion, Continued Q&A

# Afternoon Agenda

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- 🕒 12:00 – Lunch Presentation: PCORnet in Use for Interventional and Observational Studies
- 🕒 1:00 – Breakout Sessions
  - Randomized Trials
  - Observational Studies
- 🕒 3:00 – Break
- 🕒 3:20 – Reports from Breakout Sessions: Opportunities, Areas for Further Exploration
- 🕒 4:10 – Open Discussion
- 🕒 4:45 – Observations and Next Steps
- 🕒 5:00 – Closing Remarks and Adjournment

# PCORnet in Brief



# Enabling PCORnet Collaborations with Industry

*Rachael Fleurence, PhD*

*Program Director CER Methods and Infrastructure, PCORI*

Industry Workshops March 30&31 2015



# Overview

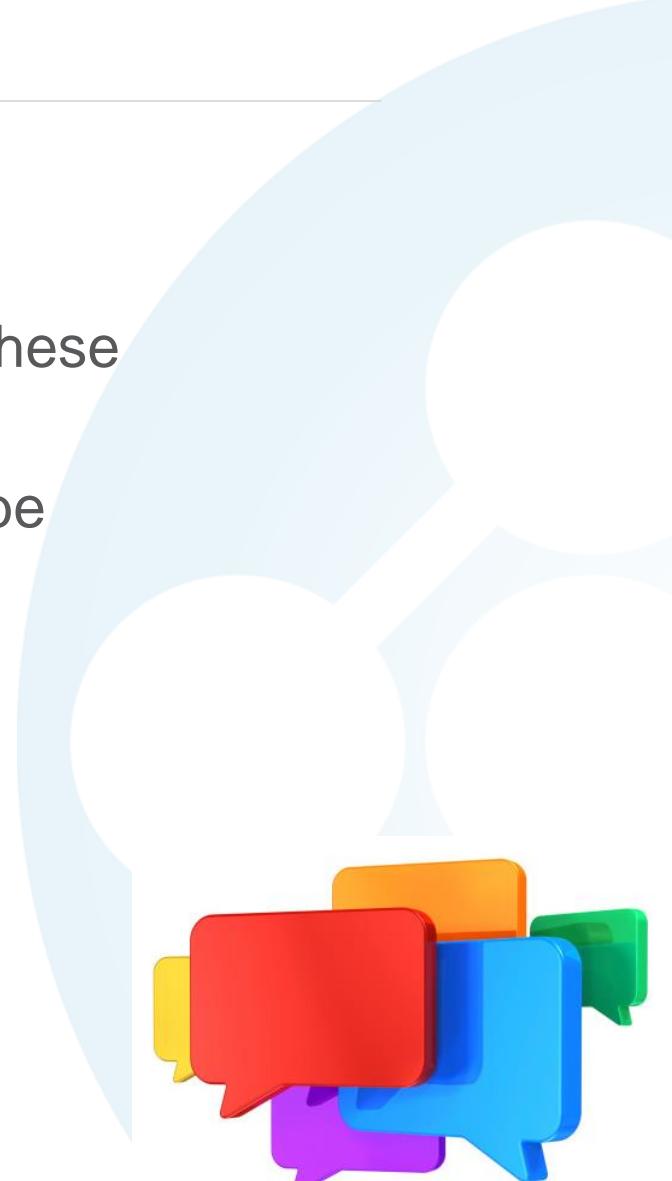
- PCORnet and Industry
- PCORnet Brief Overview
- PCORnet Emerging Operational Model
- Role and Access for External Funders
- Key Take Away Messages



# PCORnet and Industry

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- **Partnerships** with industry are critical to PCORnet's sustainability
- PCORnet is being **set up** so as to enable these partnerships to be **successful**
- Your participation and feedback today will be critical to ensure that we enable these **successful** partnerships



# Vision for PCORnet

PCORnet brings together the expertise, populations, resources, and data of its participating organizations to create a **national infrastructure** that enables more efficient, patient-centered research



“Research *Infrastructure*  
Done Differently”

# Touch points between PCORnet and industry

- Industry faces expensive and inefficient **trials** with low recruitment:
  - Large, cost-effective interventional trials leveraging electronic health data and utilizing streamlined contracting and IRB processes
- Industry needs access to increasingly large samples of **real-world data**
  - Rapid observational studies leveraging a distributed research network and a common data model
- Industry needs to respond to emerging regulatory requirements of **patient-preferences** and **patient engagement** in general
  - 18 PPRNs governed by patients
  - 11 CDRNs with patient governance
  - Patient Council involved in launching PCORnet



# Hallmarks of PCORnet's success

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1. Highly **engaged** patients, clinicians, health systems, researchers and other partners
2. A **collaborative community** supported by robust governance
3. Analysis-ready **standardized data** with strong privacy protections
4. Oversight that **protects patients**, supports the timely conduct of research, and builds trust in the research enterprise
5. Research that is **sustainably integrated** into care settings and with communities of patients

# Pivotal \$100M Infrastructure Investment



## 11 Clinical Data Research Networks (CDRNs)

System-based networks, such as integrated delivery systems, academic medical centers, federally qualified health centers,



## 18 Patient-Powered Research Networks (PPRNs)

Participants/patients working together to discover, propose, and answer relevant research questions. Building the tools to engage people more broadly in research from end to end.



## Coordinating Center

Provides technical and logistical assistance under the direction of a steering committee and PCORI program staff

# Parts of PCORnet are still under construction



# Spring 2015: Coming Into View



## PCORnet's infrastructure built to:

- To leverage rich clinical **electronic health data** linking EHR data with private and public claims data (incl. CMS)
- Support both large **observational studies** and embedded **randomized clinical trials**
- Support novel models of **participant-led research**, integrate patient-preference science, and build robust patient-participation
- Involve **patients, clinicians, and health systems** leaders in governance and use of the network

# DataMarts leveraging the CDRNs Electronic Health Data

- Each CDRN Network will have 1-10 DataMarts
- Total anticipated DataMarts: 75
- Annotated Data Dictionaries received: 62
- Software installation completed: 30
- Nine of 11 CDRNs have transformed data for at least one million individuals



# CDRNs Disease Cohorts

Organization	Common Cohort	Rare Cohort
ADVANCE	Diabetes	Co-infection with HIV and hepatitis C virus
CAPriCORN	Anemia; Asthma	Sickle cell disease; Recurrent C. Difficile colitis
Great Plains Collaborative	Breast Cancer	Amyotrophic Lateral Sclerosis (ALS)
Louisiana Clinical Data Research Network	Diabetes	Sickle Cell Disease, Rare Cancers
NYC-CDRN	Diabetes	Cystic fibrosis
Mid-South CDRN	Coronary Heart Disease (CHD)	Sickle Cell Disease (SCD)
PEDSNet	Inflammatory bowel disease	Hypoplastic left heart syndrome
PORTAL	Colorectal Cancer	Severe Congenital Heart Disease
pSCANNER	Congestive Heart Failure	Kawasaki Disease
P2ATH	Atrial Fibrillation	Idiopathic Pulmonary Fibrosis
SCIHLS	Osteoarthritis	Pulmonary arterial hypertension

# Coming Into View – Funded PCORnet Demonstration Projects

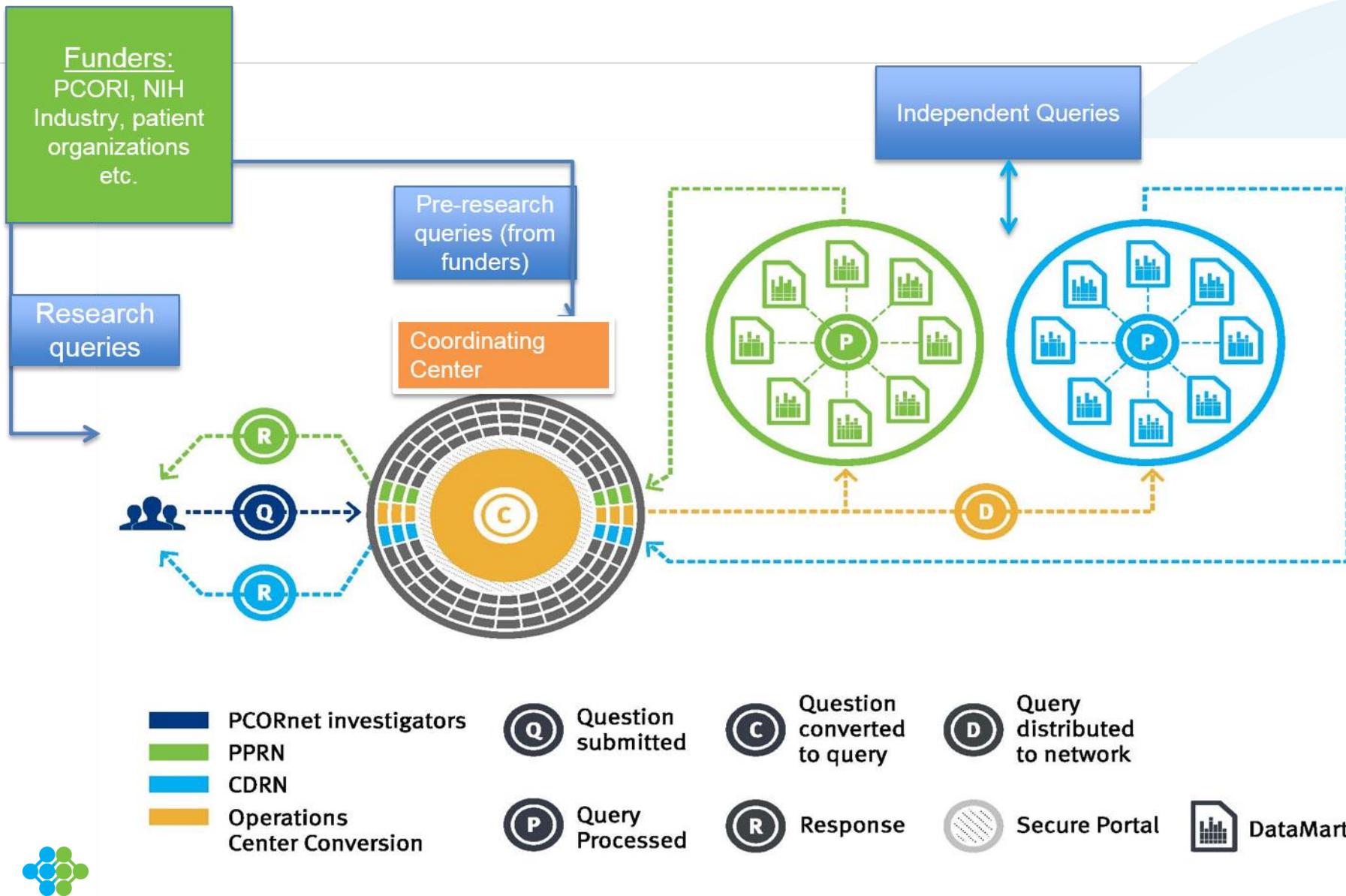
- **RCT: A Patient-centric Trial Assessing Benefits and Long-term Effectiveness (ADAPTABLE) Trial**
  - Comparative effectiveness of 81 vs 325 mg of aspirin for secondary prevention of cardiac events and serious bleeding
- **Observational CER in the Weight Cohort** – one or two large observational studies
  - Compare **bariatric surgery procedures** on weight loss, regain, and other outcomes
  - Comparative **effect of different antibiotics in children** under 2 years on BMI, patterns of growth, and rates of obesity by ages 3-5 years
- **PPRN Demonstration Projects**
  - PCORI will fund CER projects generated by patient communities of the PPRNs

# PCORnet Phase I: 2014 – 2015

	Jan	► Phase I Kick-Off, Washington DC
2014	Mar	
	May	► Common Data Model version 1.0 Released ► PCORnet Patient Council Announced ► Patient Data and Privacy Roundtable
	July	► Aspirin Clinical Trial Topic Approved by Board of Governors ► Test Queries Performed by the PCORnet Coordinating Center
	Sep	
	Nov	► Phase II RFP Released
	Dec	
2015	Jan	► Governance Policies Under Review ► Common Data Model 2.0 Released ► Aspirin Clinical Trial Review
	Apr	► Observational Weight Cohort Application Due
	May	► PPRN demos application due
	July	► Strategic planning with key funding partners
	Sep	► Phase II Begins
	Nov	► Partnerships with key external funders begin



# PCORnet uses a privacy protecting distributed data network



# PCORnet Operational Model: Key Points

## PCORnet as a National Resource and Utility

- The use of the **PCORnet Distributed Research Network (DRN)** leverages the network data organized in the **common data model**
- All networks will be contractually required in **Phase II** to participate in a minimum number of research queries using the DRN (mix between type of studies may be negotiable)
- Networks always have the right **to decline** participation in any specific study
- Networks can participate in other types of research not leveraging the **DRN**

## Planned volume of research in Phase II:

Phase II Year	Pre-Research Questions per CDRN	Observational Studies per CDRN	Clinical Trials per CDRN
Year 1	50	10	5
Year 2	100	10	5
Year 3	200	20	5

# PCORnet needs to collaborate with external funders for sustainability

⊕ **External funders** include: NIH, pharmaceutical, device, diagnostic industry, patient organizations, foundations etc.

## ⊕ **Pre-Research Queries for External Funders:**

1. The CC will be the “front door” to PCORnet and will triage requests to the Executive Steering Committee. Prioritization process is under development
2. PCORI will allocate pre-research questions to interested funders in Year 1

## ⊕ **Externally-funded studies:**

1. CDRNs and PPRNs and their investigators will be working with external funders to ensure their sustainability
2. These studies may apply for a PCORnet study designation which has some higher requirements

## ⊕ **External funders may fund studies using the PCORnet Distributed Research Network (DRN):**

1. CDRNs and PPRNs can work with external funders on queries using the DRN. The terms and conditions are described in the policies



# “PCORnet Study” Designation: Level of Requirements

Requirements for “PCORnet Study” Designation	Requirements for using PCORnet without “PCORnet study” designation	Pre-Research Queries
PCORI-funded	High Requirements	High Requirements
Externally-funded	High Requirements	Lower Requirements

# Key Take-Away Points

- ➊ Providing easy access to PCORnet to **external funders** from industry is critical to the sustainability of the network
- ➋ Understanding **industry perspectives** and constraints is critical to being able to address them in the emerging governance model
- ➌ A **concrete process**, possibly a work group, to address industry feedback in collaboration with PCORI will be essential



# Informational Slides

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# Requirements for “PCORnet study” status by type of funder

	<b>Summary of Requirements for PCORnet Study Designation</b>	<b>Summary Requirements for using PCORnet without PCORnet study designation</b>	<b>Pre-Research Queries *</b>
PCORI-funded	<p>Patient-centeredness; Patient engagement; Advisory Panels; Methodology Standards; Peer review and release of findings; Open Science; no CEA (PCORI requirements)</p> <p>A site PI is included in study for studies involving patient level data for that participating CDRN or PPRN (CDRN/PPRN requirements)</p>	Not applicable (all PCORI-funded research through PCORnet must qualify for a PCORnet study designation)	No cost-effectiveness questions Patient-centered question
Externally-funded	As above, except for loosening PCORI requirements that involve PCORI resources (e.g. peer review)	Lower requirements. Requirement for peer-review for RCTs under discussion.	No cost-effectiveness questions Patient-centered question

\*Pre-Research Query a question intended to inform the development of research questions such as assessing the feasibility of a study within the network. Pre-Research Questions can generally be executed outside an IRB

# CDRN Progress Snapshot (March 2015)

- 9 of 11 have transformed data for at least 1 million patients into the PCORnet CDM
- Progress varies with respect to completing linkage of EHR and claims data at each network, although all 11 have identified claims data sources for these linkages (e.g., CMS, Medicaid, vendors such as IMS Health)
- All CDRNs have established architecture to support distributed querying; architecture varies based on each CDRN's data governance preferences
- All CDRNs have made significant progress on their internal governance policies and data use agreements
- 6 of 11 are participating in the ADAPTABLE (aspirin) trial, and all are developing the requisite trial infrastructure, including approaches to engaging clinicians and systems
- All have 2+ significant collaborations with one or more PPRNs
- 9 of 11 have identified patients for a cohort using computable phenotypes
- 7 of 11 will have surveyed at least one of their three named cohorts by Summer 2015

## PPRN Progress Snapshot (Rare Conditions & CENA PPRN)

- 8 of 9 actively enrolling patients, 2 have achieved target enrollment
- 8 of 9 have completed governance documents
- 9 of 9 have IRB approval for the development of their network
- Data sources include patient registries (some new, some expansions of existing registries), surveys, CRFs, biospecimens
- All 9 have the ability to contact their patients about trial participation, and are working closely with patients to co-create and prioritize research questions of interest
- Data querying capabilities vary, however all should have ability to run simple queries by end of Phase I, and some will be able to run more complex queries

## PPRN Progress Snapshot (Common Conditions)

- 9 of 9 actively enrolling patients, 1 has achieved target enrollment
- 9 of 9 have IRB approval for the development of their network
- Data sources include patient registries (some new, some expansions of existing registries), surveys including patient reported outcomes, and biospecimens
- All 9 have the ability to contact their patients about trial participation, and are working closely with patients to co-create and prioritize research questions of interest
- Data querying capabilities vary, however all have ability to run simple queries, and will be able to run more complex queries over the course of Phase I & II
- 8 of 9 include clinicians as active members of the research team

# Patient Engagement in PCORnet

*Sue Sheridan, MBA, MIM, DHL*  
*Director, Patient Engagement*



# What Does Patient Engagement Look Like In PCORnet?

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- Network Partners – CDRNs and PPRNs
- Governance of PCORnet
- Future PCORnet Studies
  - Patient centeredness and patient engagement requirements

# Why Engage Patients in Infrastructure Development and Research?

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- ➊ Greater likelihood of trust and participation in research networks when patients are involved in the development and governance of research network
- ➋ Greater likelihood of uptake of research findings when patients are involved as partners in the design, conduct and dissemination of the research.

# Patient Engagement in PCORnet Network Partners

## Governance

- Development of network governance structure, roles and responsibilities
- Development of procedures, bylaws and policies for the network
- Patients are partners in decision making about research priorities

## Enrollment and Diversity

- Increasing size of the network
  - Increasing the diversity of the network
  - Retention of network members

## Data Collection

- The development of data collection tools
  - Identification of Patient Reported Outcomes (PROs) for inclusion in database
  - Registry development

## Consent, Data Sharing and Privacy

- The development of consent processes and policies
  - Development of data sharing agreements

# Governance of PCORnet

- Patients engaged at Coordinating Center level and on Executive Committee of Steering Committee
- Patients engaged in PCORnet task forces and policy development
- PCORnet Patient Council, a national deliberative body of patient leaders, provides feedback and recommendations on key PCORnet policies to ensure full consideration of both the highest patient engagement standards and issues related to protection of patient privacy, consent and autonomy

▶ Patients are involved in choosing in which research studies to participate

# Patient-Centeredness and Patient and Stakeholder Engagement In PCORnet Studies

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- Patient-Centeredness:  
Does the project aim to answer questions or examine outcomes that matter to patients/caregivers?
- Patient and Stakeholder Engagement:  
Are patients/caregivers and other stakeholders involved as partners in research, as opposed to study participants?

# Elements of Patient Engagement in PCORnet Study



Planning the Study



Conducting the Study



Disseminating the Study Results



PCOR Engagement Principles

# Planning the Study

**1. PLANNING THE STUDY:** Describe how patient and stakeholder partners will participate in study planning and design.

Potential activities include:

## Potential Activities Include

- Identifying the topic and developing the research question to be studied
- Identifying the intervention or comparators to be studied
- Defining the characteristics of study participants

partners in the planning of your study, and include key guidance on study design offered by your patient and stakeholder partners.

- Discuss how the engagement of patients and other stakeholders helped to refine your study's research question, outcomes, and comparators.

### *Real-World Examples:*

- *Epilepsy study: The patients and parents of patients with epilepsy pose the question: Which anti-epileptic drugs best preserve sufficient cognition to go to work or school and to function normally, while still preventing seizures adequately?*
- *Diabetes study: Clinicians who reviewed the initial study design indicated that clinical practice is quite variable and suggested that a three-arm approach would be more appropriate for the study. The study design was revised accordingly.*

# Conducting the Study

**2. CONDUCTING THE STUDY:** Describe how patient and stakeholder partners will participate in the study conduct.

Potential activities include:

## Potential Activities Include:

- Participating in and monitoring the conduct of the project
- Assisting with the recruitment of study participants
- Assisting with data analysis

### *Real-World Examples:*

- *Chronic pain study: The informed consent document is developed with patient partners to make it understandable to study participants.*
- *Depression study: Patient advocacy groups assist with recruitment through their patient networks—the “book club” model.*

# Disseminating the Study Results

**3. DISSEMINATING THE STUDY RESULTS:** Describe how patient and stakeholder partners will be involved in plans to disseminate study findings, and ensure that findings are communicated in understandable, usable ways.

Potential activities include:

## Potential Activities Include:

- Identifying partner organizations for dissemination
- Planning dissemination efforts
- Participating in dissemination efforts, such as the authoring of manuscripts and the presentation of study findings

○ *Cardiac study: A Patient Dissemination Board is helping to craft the dissemination plan and advise the research team on how to best share study findings.*

○ *Chronic pain study: Patient partners co-author manuscripts, present at scientific and lay conferences, and share study findings through their networks.*

# The Vasculitis Patient-Powered Research Network an Example for Potential PCORnet-Industry Partnership

*Patient-Centered Outcomes Research Institute (PCORI)*

**March 30, 2015**

**Peter A. Merkel, M.D., M.P.H.**

Co-Principal Investigator,

Vasculitis Patient-Powered Research Network

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**Vasculitis is a family of rare, complex, severe/life-threatening, multi-organ system diseases that involve inflammation of blood vessels**

# The Vasculitides

## Immune Complex Small Vessel Vasculitis

*Cryoglobulinemic Vasculitis*

*IgA Vasculitis (Henoch-Schönlein)*

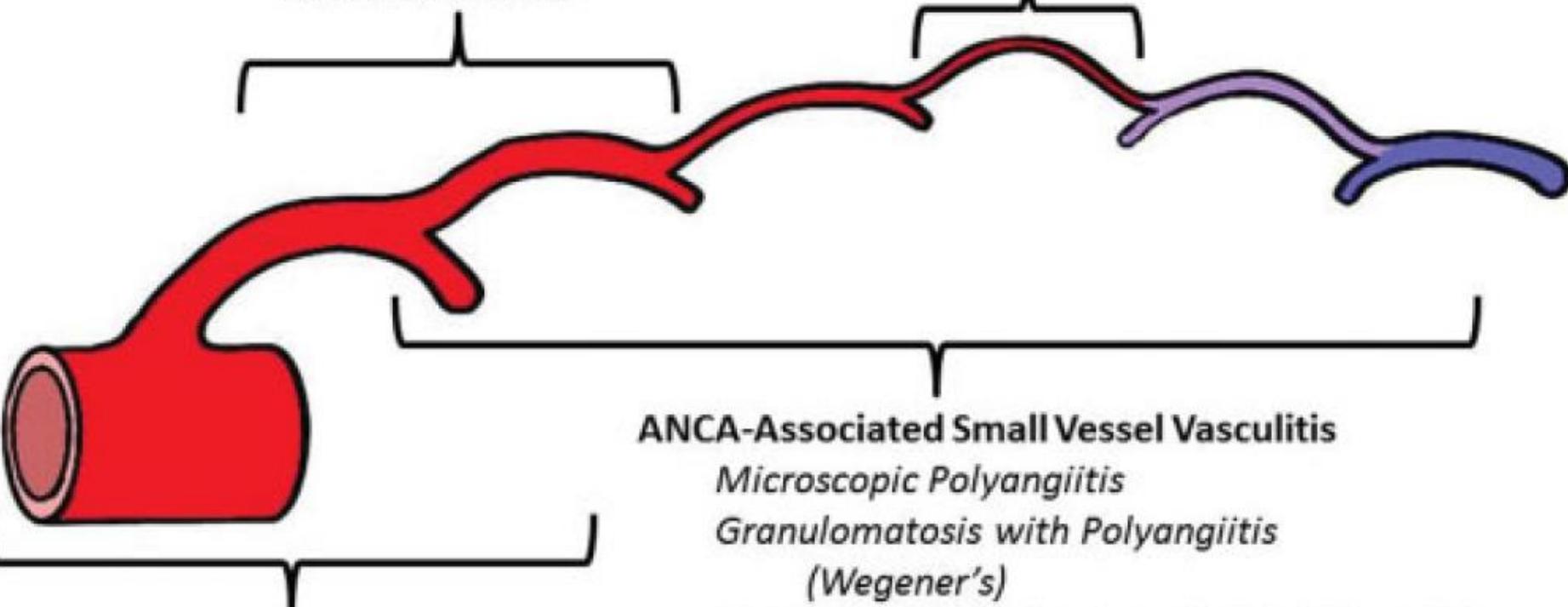
*Hypocomplementemic Urticarial Vasculitis  
(Anti-C1q Vasculitis)*

## Medium Vessel Vasculitis

*Polyarteritis Nodosa*

*Kawasaki Disease*

## Anti-GBM Disease



## Large Vessel Vasculitis

Takayasu Arteritis

Giant Cell Arteritis

*Eosinophilic Granulomatosis with Polyangiitis  
(Churg-Strauss)*

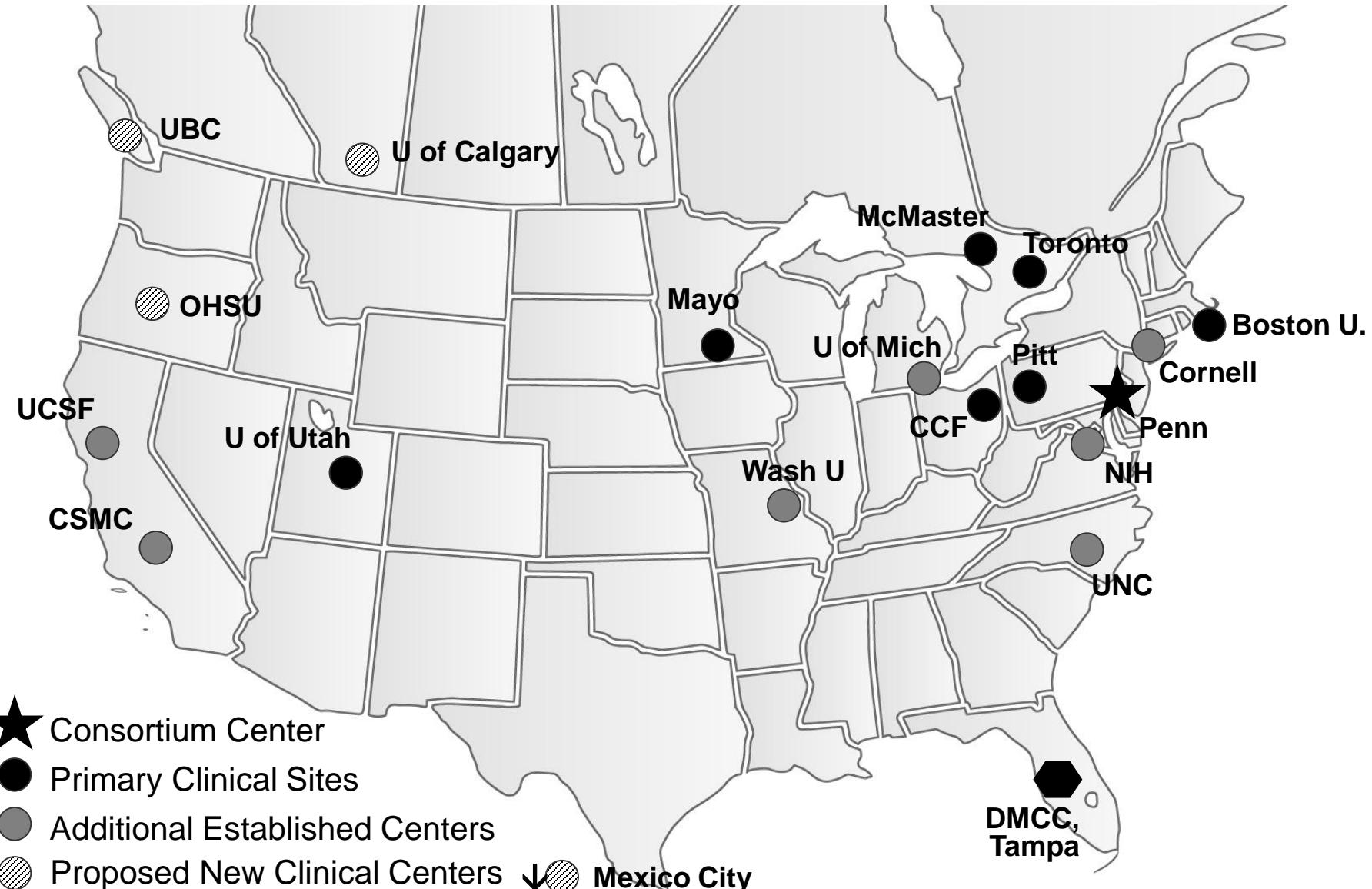
# The Vasculitis Clinical Research Consortium

**The VCRC is an international, multicenter research infrastructure for conducting clinical and translational investigation in various types of vasculitis**

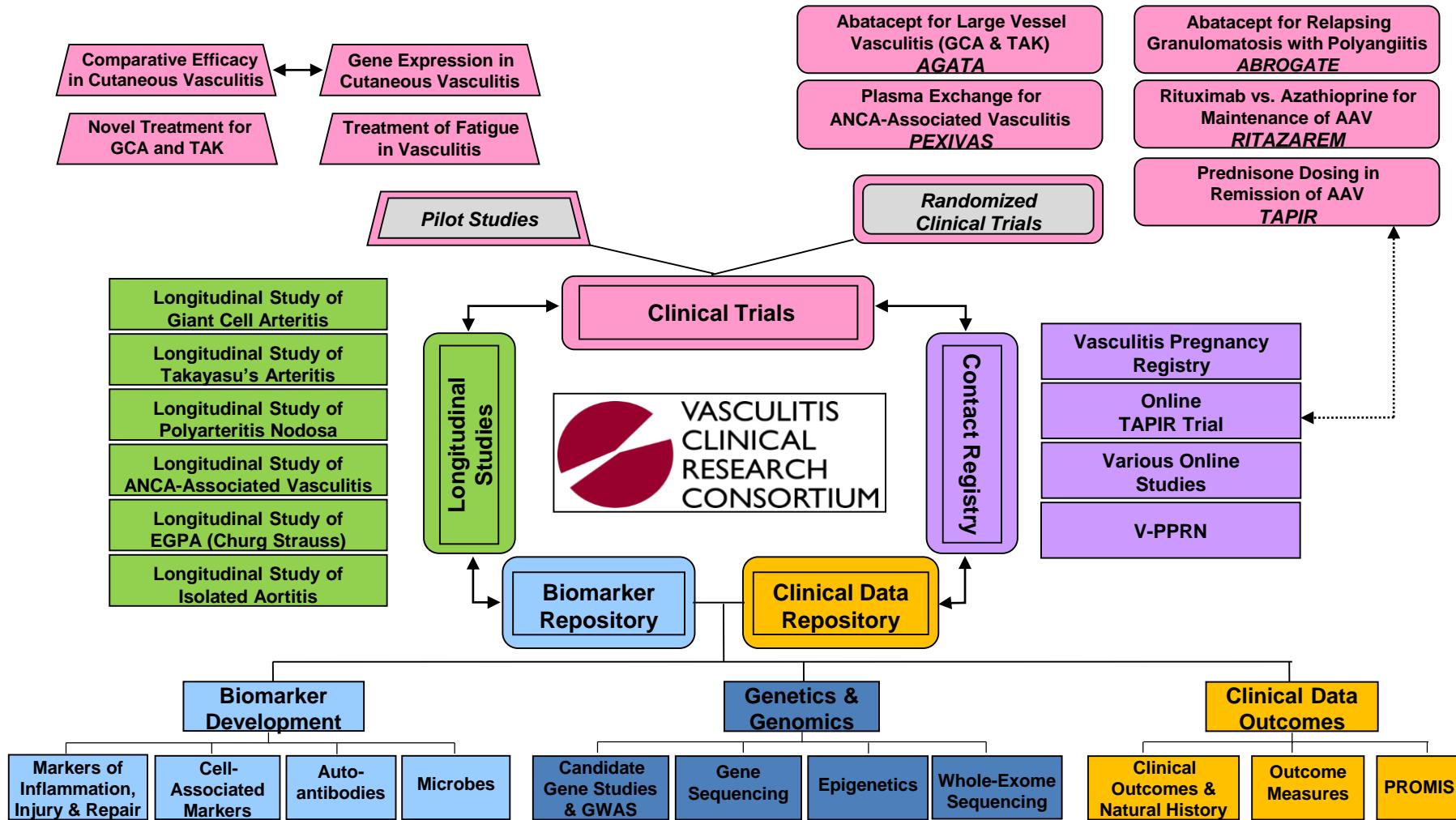
**Part of the NIH Rare Diseases Clinical Research Network**

# Vasculitis Clinical Research Consortium

## North American Clinical Sites



***Many additional VCRC partner sites in EU, Asia, Australia***

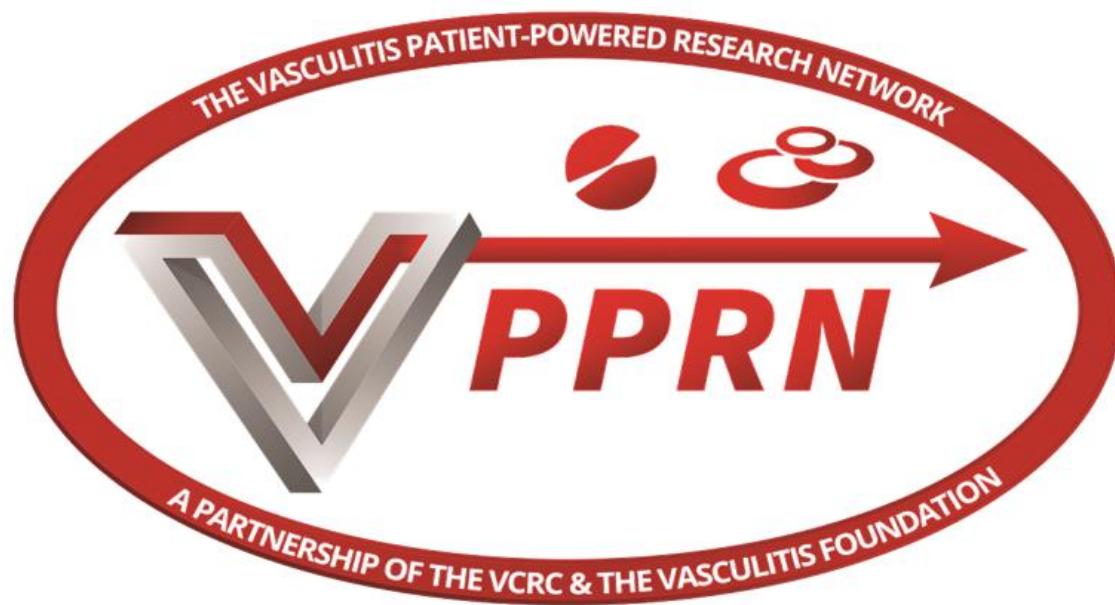
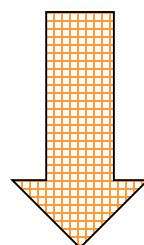


# Patient Engagement in Vasculitis Research: Evolution Over a Decade

- ◆ **Vasculitis Clinical Research Consortium & Vasculitis Foundation: >10 year partnership**
  - Support/promotion → advice/review → co-investigators → co-governance
  - Steadily accelerated
  - Promotion, recruitment, awareness
  - Steering Committee and research working groups
- ◆ **PCORI Vasculitis Outcomes Initiative: 2012--present**
  - Patients on Steering Committee and engaged in researchers
- ◆ **Vasculitis Patient-Powered Research Network: 2014**
  - Patients and physicians are co-investigators (including co-PIs)
  - Rapid growth of Network clearly due to patient engagement



VASCULITIS  
CLINICAL  
RESEARCH  
CONSORTIUM



**The Vasculitis Patient-Powered Research Network**

http://vpprnat.epi.usf.edu/

Vasculitis Patient Powered ...

**VPPRN**

Vasculitis Patient-Powered Research Network  
A partnership of the Vasculitis Clinical Research Consortium and the Vasculitis Foundation



You are not a data point.  
Your experiences are valuable.  
Patient experience and participation is what powers research with the V-PPRN.

Who We Are   What's Involved   Blueprint for Innovative Research   FAQ   Privacy   Login

We are patients, researchers, clinicians, advocates, and family members all working to improve healthcare for patients with vasculitis through high-quality clinical research.

Become part of our Research > [Join The Network!](#)

http://vpprnat.epi.usf.edu/blueprint.htm

Blueprint for Innovative Res... X

**VPPRN**

Vasculitis Patient-Powered Research Network  
A partnership of the Vasculitis Clinical Research Consortium and the Vasculitis Foundation

Home   Who We Are   What's Involved   Blueprint for Innovative Research   FAQ   Privacy   Login

Blueprint for Innovative Research

What we are collecting

Why we are collecting data from patients

Patient-Powered Research

How to join

Back to top

## Blueprint for Innovative Research

### The Challenges

 All types of vasculitis are **rare diseases** making it difficult to find enough patients for research studies.

 Patients are spread out geographically.

 It is hard to get health information from physicians to researchers.

 Getting the attention of funding agencies for research is hard.

### The Solutions

 Enroll patients and collect data on-line to break down geographic barriers.

 Involve patients so that health information is easily shared with researchers.

 Work within PCORnet so the V-PPRN will have a much larger pool of patients and data and can collect electronic health records.

 Build a strong, vibrant Network and we will get funders' attention.

[Join](#)[Login](#)[FAQs](#)[Contact Us](#)

# Agreement to Participate in the Vasculitis Patient-Powered Research Network (V-PPRN)

The V-PPRN seeks to **transform how clinical research in vasculitis is conducted** by directly engaging patients, investigators, care providers, and health systems to develop research methods to electronically collect health records and patient-reported data on a large number of patients with various forms of vasculitis. The goal of the V-PPRN research program is to conduct high-quality studies that will improve the care and the health of patients with vasculitis by exploring research questions that matter most to patients and advance medical knowledge about vasculitis.

**When you join the V-PPRN, you will be asked to...**  
(“You” means you, your child or the person for whom you are providing care)

## Tell us about yourself



- Provide information about yourself, your diagnosis and treatment, and how vasculitis impacts your life.

## Agree to let us contact you



- We plan to give you opportunities to participate in studies that may lead to improved care and outcomes for patients with vasculitis.
- By joining the V-PPRN, you will automatically be enrolled in the [Vasculitis Clinical Research Consortium \(VCRC\) Patient Contact Registry](#) which connects patients with opportunities to participate in clinical research trials and experts in vasculitis.

## Check-In



- We will need you to periodically update your information so that we have your latest data and contact information.

## Stick Around



- Participation is completely voluntary and you may choose to withdraw at any time. We hope that you choose to stay an active participant in the research to help improve care for people with vasculitis.

## The V-PPRN will...

### Respect Your Privacy



- The information you provide us will be kept confidential and secure to the extent permitted by law. The V-PPRN will never sell, rent, or lease your contact information. Please see the V-PPRN [privacy policy](#) for additional information.
- The V-PPRN follows all federal, state, and local guidelines regarding patient protection, including HIPAA.

### Keep You Informed



- We will give you feedback and share what we learn about vasculitis. All the information you provide may help us learn more about vasculitis.
- We will also keep you informed about new research opportunities that arise within the Network.

### Make Participation Easy



- Updates may be entered directly by you or, with your permission, directly from your healthcare provider.
- There are no costs or any unanticipated risks associated with participation in the V-PPRN.

I confirm that I am at least 18 years of age and I live in the United States (including US territories and commonwealths).

[Accept](#)[Decline](#)

By clicking "Accept" you consent to participate in the V-PPRN.  
By clicking "Decline" you do not consent to participate but wish to help in another way.

Questions? [Contact](#) the V-PPRN Network Manager  
Kalen Young, V-PPRN Network Manager

# VCRC-V-PPRN-NIAMS DSMB

- NIAMS recognized need for Consortium-specific DSMB with expertise in vasculitis and independence from investigators
- The NIAMS-VCRC-V-PPRN DSMB oversees all projects
  - Efficient review and approval of new studies given familiarity with diseases and investigators
  - Shorter start-up since DSMB formed and processes in place
  - Independence well maintained
  - Institute retains control/oversight
- Model for Rare Diseases Research
  - High level of satisfaction by program officials, DSMB members, and investigators
  - Acceptance and appreciation by industry/funders

# IRB of Record Within the V-PPRN

- The University of Pennsylvania has a progressive IRB willing to take the lead as the IRB of Record
- NIH and PCORI *strongly* urges this to happen
- Currently in place in three VCRC clinical trials conducted in collaboration with industry
- V-PPRN-Penn has substantial experience with this process

# VCRC & V-PPRN Protocols

Clinical Cohorts and Biospecimens Repository: Biomarker Studies	
02	Longitudinal Protocol for GCA
03	Longitudinal Protocol for TAK
04	Longitudinal Protocol for PAN
05	Longitudinal Protocol for GPA/MPA
06	Longitudinal Protocol for EGPA
06	<i>Longitudinal Protocol for IA (proposed)</i>
10	Genetic Repository (One-Time DNA)
Outcome Measures	
15	Imaging Protocol for MRI and PET in TAK
	OMERACT Vasculitis Working Group
	Validation of PROMIS in Vasculitis
	Development of an AAV-Specific PRO
	International Classification of Function

Clinical Trials	
22	Pilot Study: Abatacept in Mild GPA
23	RCT: Abatacept for GCA/TAK (AGATA)
24	RCT: Plasma Exchange for AAV (PEXIVAS)
25	RCT: Rituximab vs. Azathioprine for AAV (RITAZAREM)
26	RCT: Tapering of Prednisone in GPA (TAPIR)
27	<i>RCT: Abatacept for Mild/Mod GPA (ABROGATE)</i>
	<i>Several others under development</i>
Contact Registry/V-PPRN Studies	
31	Reproductive Health in Vasculitis
32	<i>Vasculitis Pregnancy Registry (V-PREG)</i>
33	Vasculitis Illness Perception Study (VIP)
34	Vasculitis Educational Needs Study
35	<i>Vasculitis Diagnostic Confirmation Study</i>
36	<i>Work Disability Survey (VascWorks)</i>
37	<i>Validation of PROMIS in Vasculitis</i>

# **The V-PPRN/PCORnet Greatly Expands the Reach and Capabilities of the VCRC-VF Partnership**

# THE V-PPRN IS RESEARCH-READY

## THE V-PPRN IS ABLE TO CONDUCT THE FOLLOWING:



**Comparative  
Effectiveness  
Research**



**Cross-Sectional  
&  
Longitudinal  
Studies**



**Randomized  
Clinical Trials**

# How PPRNs Add to Industry-Partnered Clinical Studies

- **Access to a large number of patients with target condition**
  - Wide geographic catchment—well beyond usual centers
  - Rapid/efficient ability to select patients with specific criteria
- **Capacity for collection of extensive clinical data for CER and RCTs**
  - Links to CDRNs and electronic health records (EHR)
  - On-line portals to collect PROs and other types of data
- **Established & organized collaborators**
  - Immediate/inherent patient “buy-in” and collaboration
  - Imbedded group of expert investigators, data managers
- **Ability to leverage PCORnet infrastructure and PPRN resources**
  - Established use of single/central IRBs, DSMBs, data coordination
- **Flexibility**
  - Opportunities for novel designs of RCTs
    - e.g.: screen/collect data on-line with treatment at selected CTSA sites

# GRANT/FUNDING SUPPORT



National Institute of  
Arthritis and Musculoskeletal  
and Skin Diseases



National Center  
for Advancing  
Translational Sciences



Genentech/Roche

Bristol-Myers Squibb

TerumoBCT



National Heart, Lung,  
and Blood Institute



National Institute for  
Health Research



AMERICAN COLLEGE  
OF RHEUMATOLOGY  
EDUCATION • TREATMENT • RESEARCH

Arthritis  
Research UK

eular  
european league against rheumatism



# Questions/Comments



# PCORI/Industry Workshop

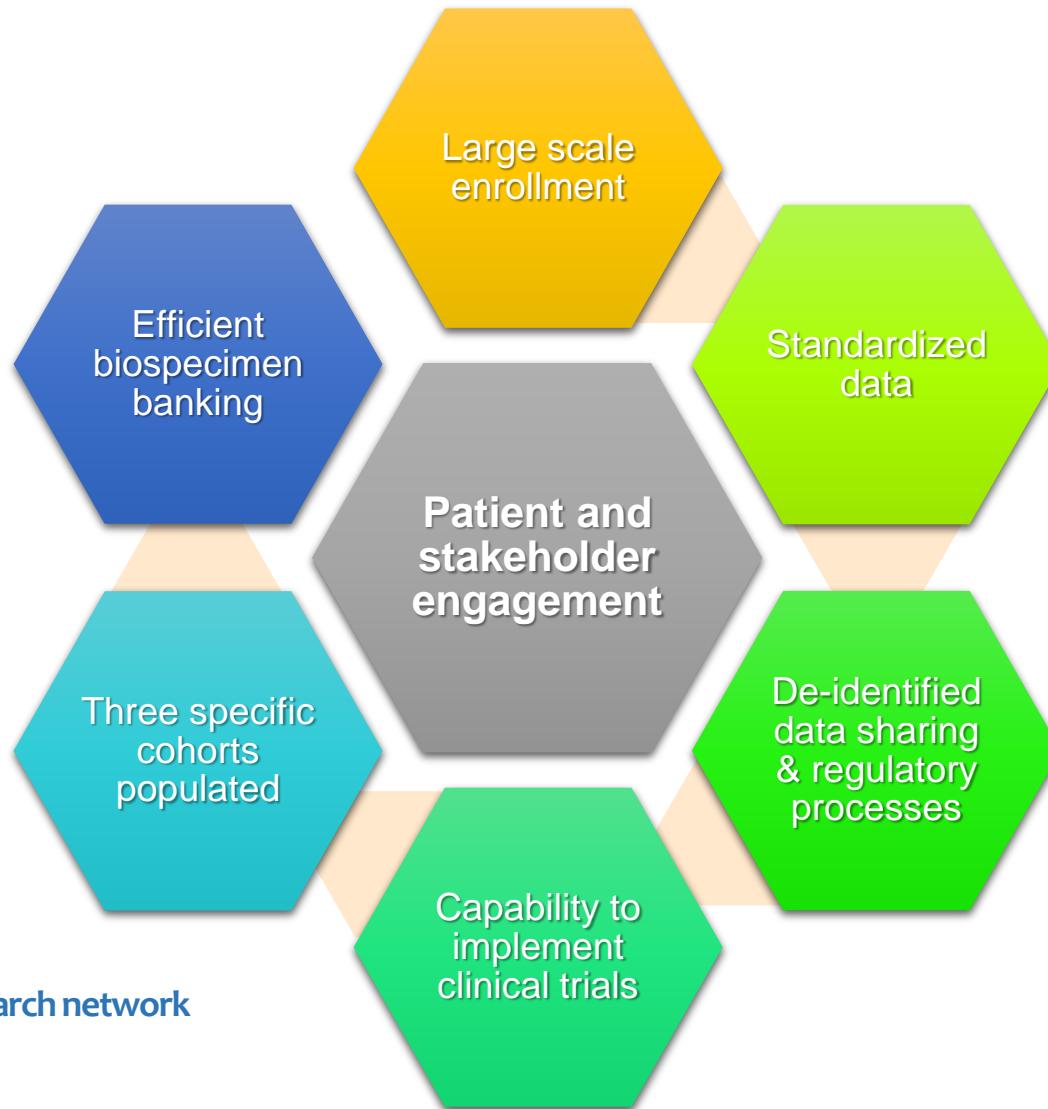
March 30 – March 31, 2015

**Russell Rothman MD MPP**

Professor, Internal Medicine, Pediatrics, Health Policy  
Director, Vanderbilt Center for Health Services Research  
PI, Mid-South CDRN  
Vanderbilt University



# Key Milestones for Phase I



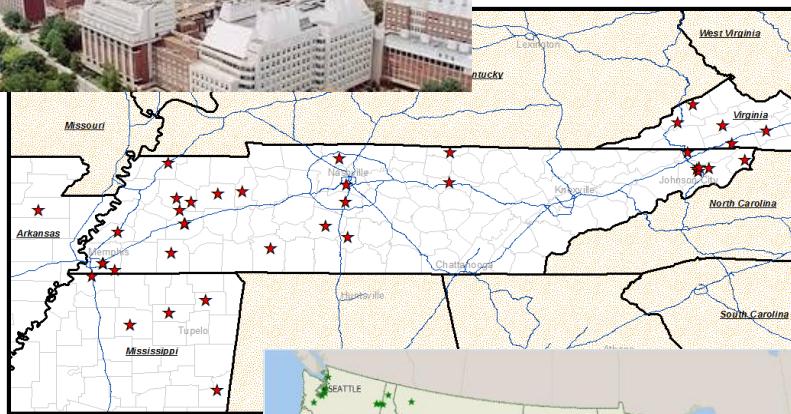
# Our Mission

- Support comparative effectiveness and pragmatic research that is robust, efficient, and impactful.

# Mid-South CDRN Has Local & National Reach



Vanderbilt Medical Center: hospitals,  
>100 clinics engaging 2 million patients



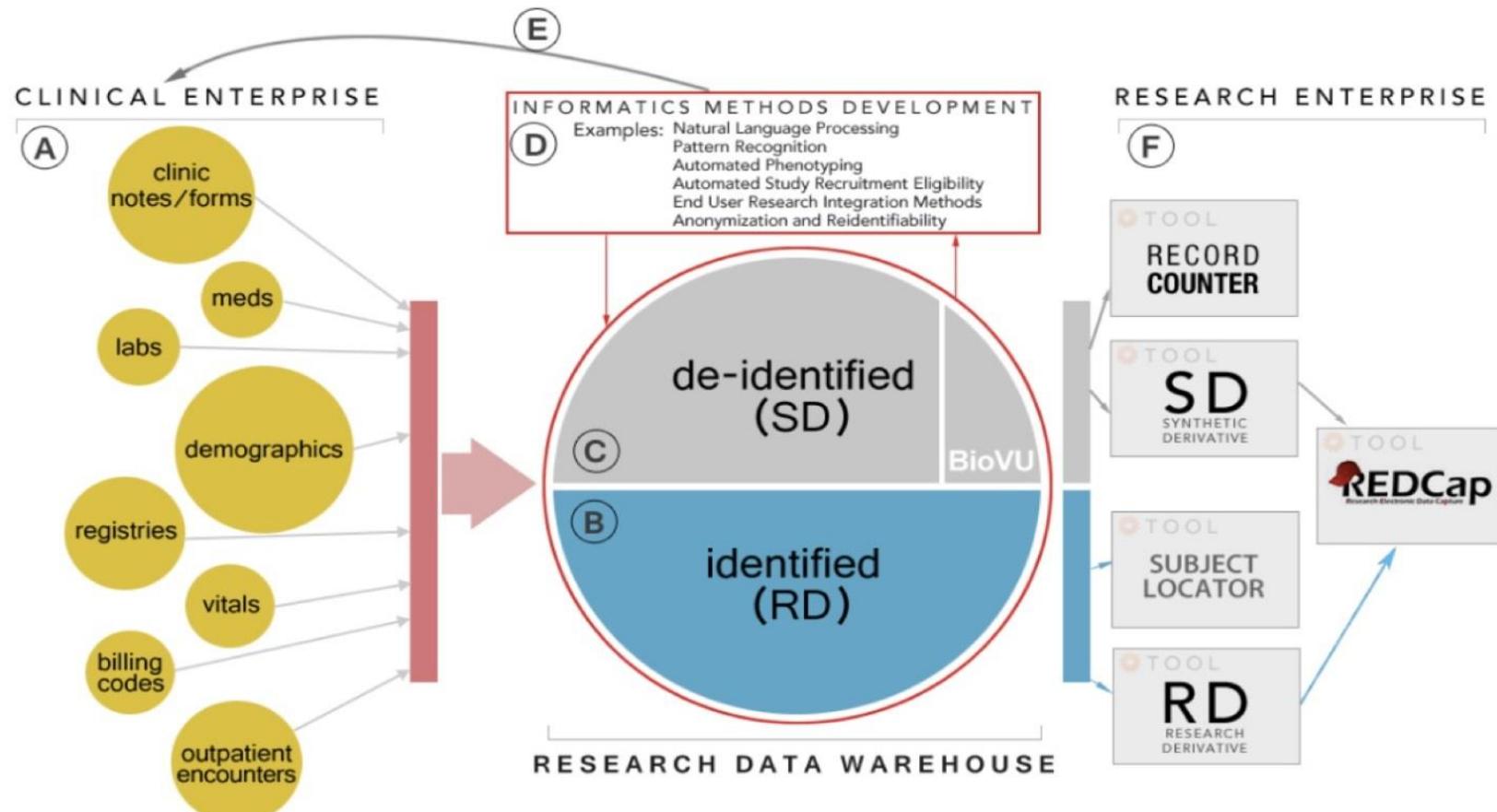
VHAN: 7 health systems, 34+  
hospitals, 350+ clinics  
engaging >3 million patients



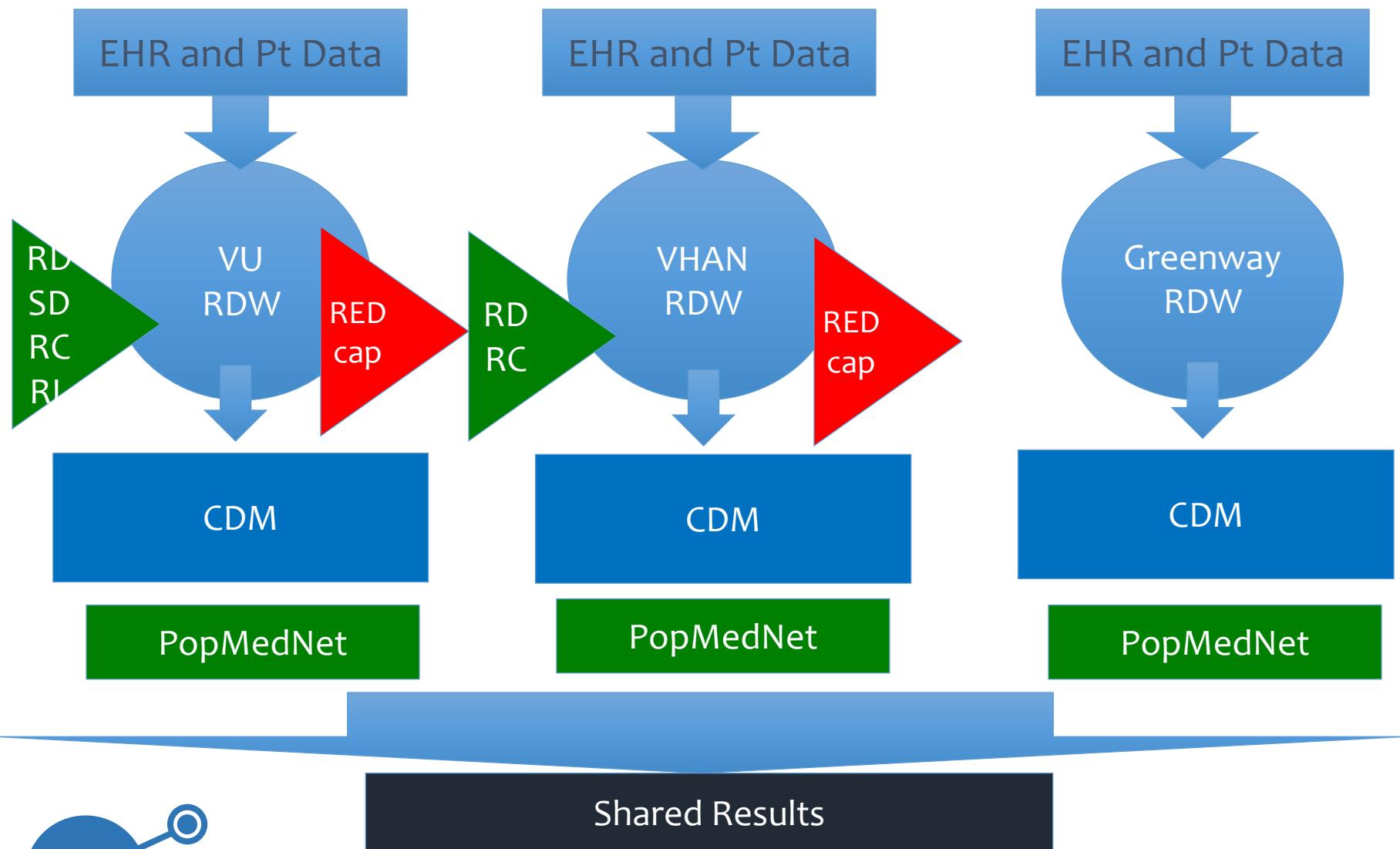
Greenway: 1600 clinics  
engaging 14 million  
patients



# Vanderbilt Data & Research Tools



# Data Aggregation Across CDRN



# Additional Linkage for “Complete” Data

Linkage to TN State Health Data (hospitalizations, birth/death data)

Linkage to TennCare Data

Linkage to CMS Data ( Virtual Research Data Center, RESDAC, CMMI data)

Linkage to Vanderbilt Health Plan (Aetna) health data (claims and PBM data)

Surescripts

Linkage to VU Home Health Data

Linkage to Nursing Home data

# Novel Informatics Tools

- Tools for quickly running queries and analyzing electronic health data
- Tools for identifying and contacting patients
- New electronic consent process
- Expanded survey tools for collection of patient reported outcomes (via web/mobile platforms, automated phone, etc.)
- Integration of PROMIS measures into REDCAP
- Electronic payment processes for study participation
- Potential integration of patient survey data into the EHR for clinical use
- Expansion of clinical decision support tools



# Current Cohorts

- Weight Cohort
  - Electronic cohort of >300,000 at VUMC
  - Identifying cohort at Greenway
  - Surveyed 4800 patients to date
- CHD Cohort
  - Electronic cohort of >30,000 at VUMC
  - Surveyed 800 patients to date
- Sickle Cell Cohort
  - Identified ~ 400 families in TN
  - Surveyed > 40 families

Collaborations with St. Judes, Cincinnati, Northwestern

# Obesity Cohort

## PCORI Pre-screening

What is your first name?

What is your last name?

What is your date of birth?

In the past 5 years, have you received treatment at a Vanderbilt health clinic or hospital?

SCREENER: Which study are you screening for?

**Determine Eligibility**

Email blast to >10,000 Vanderbilt patients with over 30% response rate!



### Patient Centered Outcomes Research

Vanderbilt University Medical Center is conducting research to help understand what factors influence decisions you make about your health. We invite you to take part in this survey because you have received care at Vanderbilt or other affiliated medical centers.

This survey includes questions about:

- Your background
- Your health habits
- Your willingness to participate in certain types of research studies in the future

Your participation in this survey is totally voluntary. If you choose not to participate, it will not affect your health care or opportunity to participate in future research. Your responses will be kept private. With your permission, we may contact you about future studies you may be interested in. If you participate, we would like to collect some information from your medical chart, such as your height, weight, blood pressure, lab test results, and other health information now and in the future.

There is very little risk involved in this survey. The main risk is that some questions may make you feel uncomfortable. You may choose not to answer any of the questions.

The survey will take about 15-20 minutes and you will receive \$10 for your time and participation. If you have any questions or comments regarding the survey, feel free to contact:

David Crenshaw, Study Coordinator  
[HealthyWeightStudy@Vanderbilt.edu](mailto:HealthyWeightStudy@Vanderbilt.edu)  
(615) 343-1765

Thank you!

Date of Birth  month  day  year

By checking this box and entering my birthdate, I agree to participate in this survey and I give permission to have the research team link my answers to my health information that is stored electronically by my doctor

By checking this box, I am refusing to participate in this survey.

**Start Survey**

# Stakeholder Engagement

- Stakeholders at Oversight Committee
- Stakeholder Advisory Council meeting
- Community Engagement Studios
- Stakeholder Surveys



A network of hospitals, specialty medical practices and primary care practices throughout the Southeast.

**MID-SOUTH CLINICAL DATA RESEARCH Network**

The Mid-South Clinical Data Research Network (CDRN) is a network of hospitals, specialty and primary care practices throughout the Southeast. The Mid-South CDRN is devoted to improving the health of communities by advancing knowledge and improving the delivery and outcomes of patient-centered outcomes research (PCOR) to facilitate more effective and efficient health care research that could quickly advance knowledge about best health care practices to improve patient health. PCORnet includes a total of 31 CDRNs, 18 Patient-Powered Research Networks (PPRNs), and a National Coordinating Center representing clinical practices and patient organizations around the country.

The Mid-South CDRN will include hospitals and clinics associated with:

- o Nashville General Hospital at Meharry and Matthew Walker Comprehensive Health Center
- o The Vanderbilt Health Affiliate Network (VIAN)
- o Greenway PrimeRESEARCH Network

The Mid-South CDRN is overseen by an Operations Council led by Principal Investigator Russell Rothman MD, MPP, a primary care provider and researcher at Vanderbilt. The CDRN is advisory to an Oversight Committee and Stakeholder Engagement Board that includes providers and patients from across the VIAN.

**Benefits to Participating:**

- Support for any VIAN priorities for pragmatic or comparative effectiveness research
- Collection and feedback on relevant patient/clinic/system data for quality and performance improvement
- Expansion of patient reported data (ex. satisfaction, adherence)
- Development of clinical decision support tools to improve delivery at the point of care
- Participation in pragmatic studies to improve care delivery and quality (federal, industry funding)
- Meet educational and regulatory requirements related to quality and performance improvement
- Direct financial support to providers/practices for participation in studies
- Scholarship and publications

**Opportunities for provider/practice involvement:**

- Provide input via the Stakeholder Advisory Board or participate in a Community Engagement Studio
- Share clinical and operational data
- Share identifiable clinical data to recruit patients for participation in studies
- Choose participation in intervention studies on a case-by-case basis
- Suggest topics and help prioritize research areas

**Role of participating hospitals/clinics:**

- Assist health care researchers on development of protocols, research designs, and incentives that fit with community-based practice settings
- Select which studies fit best with their practice and patients
- Assist in identifying and doing targeted outreach to patients who might be eligible for selected studies
- Provide needed space to research study staff when applicable

**The CDRN plans to promote the following types of studies:**

- Comparative effectiveness of clinical interventions
- Pragmatic clinical trials
- Dissemination of evidence-based practices
- Practice or hospital improvement
- Patient communication, decision-making, and patient reported outcomes studies
- Observational trials that identify and follow patients for long periods of time

**Contact Information:**

- Program Contact: Melissa Barford, MBA, [melissa\\_barford@vanderbilt.edu](mailto:melissa_barford@vanderbilt.edu)
- Clinical Contact: Russell Rothman, MD, MPP, [russell.rothman@vanderbilt.edu](mailto:russell.rothman@vanderbilt.edu)
- Informatics Contact: Jason Grant, [jason\\_f.grant@vanderbilt.edu](mailto:jason_f.grant@vanderbilt.edu)

**Greenway Clinical Data Research Network**

Greenway Provider Conference, Dallas, TX,  
September 2014

# Process for accessing resources

<https://midsouthcdrn.mc.vanderbilt.edu/>



ABOUT   TOOLS   COLLABORATE   PARTICIPATE   RESULTS

Welcome to the  
Mid-South Clinical  
Data Research  
Network

ABOUT

COLLABORATE



The Southern US has the highest rates of obesity, diabetes, cardiovascular disease, and significant rates of health disparities. The **Mid-South Clinical Data Research Network (CDRN)** centered at **Vanderbilt University (VU)** focuses on health systems in the Southern United States, but will include the capacity to reach a national population.



# Services Provided

- Development and validation of computable phenotypes
- Prep-to-research and simple queries of CDM
- Observational research of de-identified data
- Observational research of identifiable data
- CER and Pragmatic interventions at patient or system (clinic, hospital, etc) level
- Informatics, IRB, Regulatory support
- Access to patients and sites in CDRN



# Collaborations

- Over 30 collaborations to date
  - Local investigator initiated grants
    - PCORI pragmatic trials x 4
    - NIH and AHRQ Grants
    - CDC grant (Autism)
  - Academic centers
    - UAB (EDGE Trial)
    - Duke (Transform Trial)
    - Wisconsin/Harvard (Flu Vaccine Study)
  - Industry
    - Diabetes trials
    - PPRNS (CCFA, AR-POWER, SAP-CON, Health eHeart, ABOUT, Vasculitis)
  - PCORI funded trials in Coronary Heart Disease and Obesity

# Rapid Queries for “Pre-Research”

SD RecordCounter

Search Results

Criteria Search Criteria

Demographics ICD9 Codes CPT Codes Medications

Drag to add Medication Criteria

Include records where:

- Contains ICD code in group 556-Ulcerative colitis 6175

Remove Group Exclude Group

Group Count: 6175

AND Include records where:

- Contains Medication '6 MP' 1915
- OR Contains Medication 'azathioprine' 9026

Remove Group Exclude Group

Group Count: 10493

**Result Set Total: 1660**

This number may be rounded up or down. It may not perfectly match individual counts.

Female 780

Male 750

Unknown 10

More charts ...

**Results by Gender, Age and Race**

Gender	Age	Race	Population
Female	< 2	African Amer	115
	2-5	Asian	23
	6-12	Caucasian	1441
	13-18	Hispanic	25
	19-44	Native Amer	3
	45-64	Other	3
	65 >	Unknown	48
Male	< 2	African Amer	115
	2-5	Asian	23
	6-12	Caucasian	1441
	13-18	Hispanic	25
	19-44	Native Amer	3
	45-64	Other	3
	65 >	Unknown	48
Unknown			10

Population Totals (Female: 855, Male: 798, Unknown: 7)

African Amer (115) Asian (23) Caucasian (1441) Hispanic (25) Native Amer (3)  
Other (3) Unknown (48)

**BioVU Samples Filter:**

- None
- Include All BioVU Samples
- Include Non-Compromised Samples

Some BioVU samples can be compromised due to disease related changes in the blood. Genotyping results may be affected.

**Shippable Samples:**

- Include only samples available for external assays

Some BioVU samples cannot be tested outside of Vanderbilt.

mid-south clinical data research network

# Observational Research

- Identify patients electronically
- Perform analyses based on robust electronic data
- Contact patients for survey or cohort studies through electronic means, face-to-face, or phone.
- Novel tools for data collection (mobile tools, patient portal, etc)

# Intervention Studies

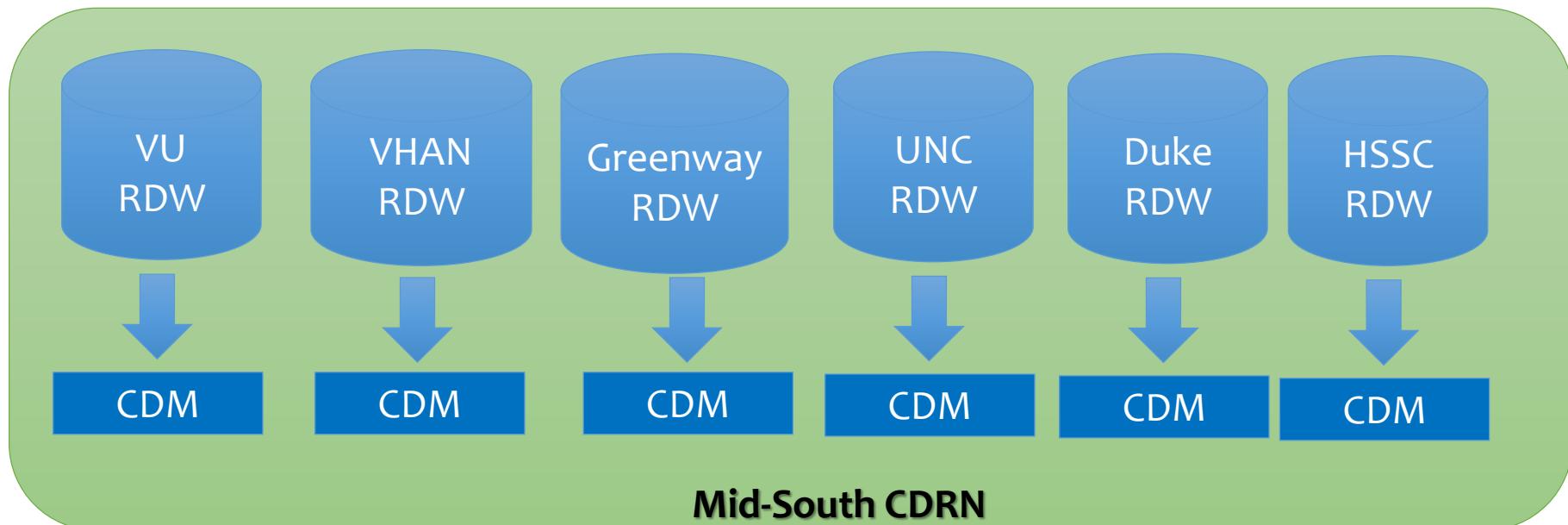
- Rapid identification of eligible patients
- Electronic consent processes
- Studies embedded into clinical care (inpatient and/or outpatient)
- Can track long-term outcomes through patient surveys and extraction of electronic data

# Advantages of PCORnet Research

- Access to robust electronic health record data and claims data
- Informatics tools to rapidly identify, contact, recruit, and survey patients
- Ability to embed research into clinical care
- Ability to collect long-term outcomes
- Rapid research at modest costs

# Questions

# Distributed Data Model

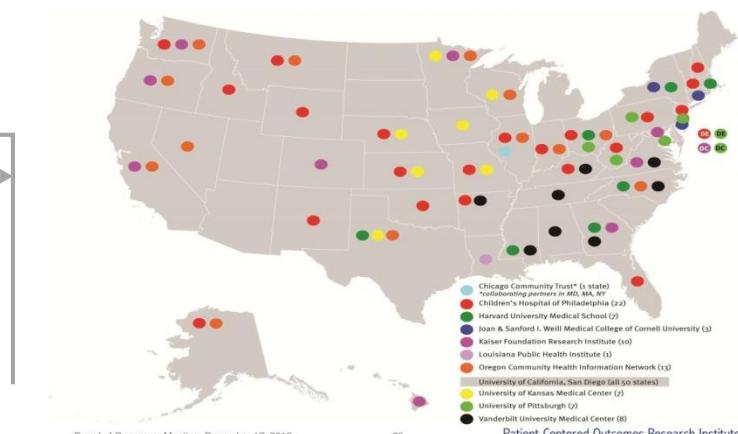


1. Queries and  
Analytic Software  
Packages from  
PCORI

2. CDRN returns  
Counts and  
Aggregate resulting  
data

PopMedNet

PCORNet



# Q&A on PCORnet Structure, Plans, and Network Activities



# Break



## Open Discussion, Continued Q&A



# PCORnet's Demonstration Projects

*Rich Platt, MD, MSc, PCORnet Executive Committee*

*Adrian Hernandez, MD, MHS, PCORnet Executive Committee*



# PCORnet's goal



Conduct widely generalizable observational and interventional research quickly and at low cost

# Guiding principle: Make research easier

- Analysis ready data
  - Standard format
  - Harmonized definitions
  - Quality checked in advance
- Reusable analysis tools
- Efficient clinical trial enrollment and follow up mechanisms
- Simple, pragmatic studies integrated into routine care
- Administrative simplicity

# Goal of demonstration observational and interventional studies

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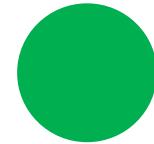
- Address questions important to patients and clinicians that require multi-site evaluation
- Facilitate collaboration between PCORnet's networks
- Guide further development of PCORnet policies, procedures, infrastructure
- Evaluate the readiness of PCORnet's data and networking capabilities
- Assess PCORnet's privacy protecting data infrastructure and analysis capabilities
- Develop efficient methods for identifying potential clinical trial participants, reaching out to them, enrolling, and obtaining follow up
- Assess end-to-end functionality, from protocol development through implementation, analysis, and reporting

# Observational Studies in PCORnet's Weight Cohort



The National Patient-Centered Clinical Research Network

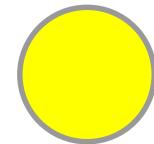
# PCORnet's weight cohort



Entire PCORnet  
CDRN population



The Weight Cohort:  
Weight and  
height/length  
measurements

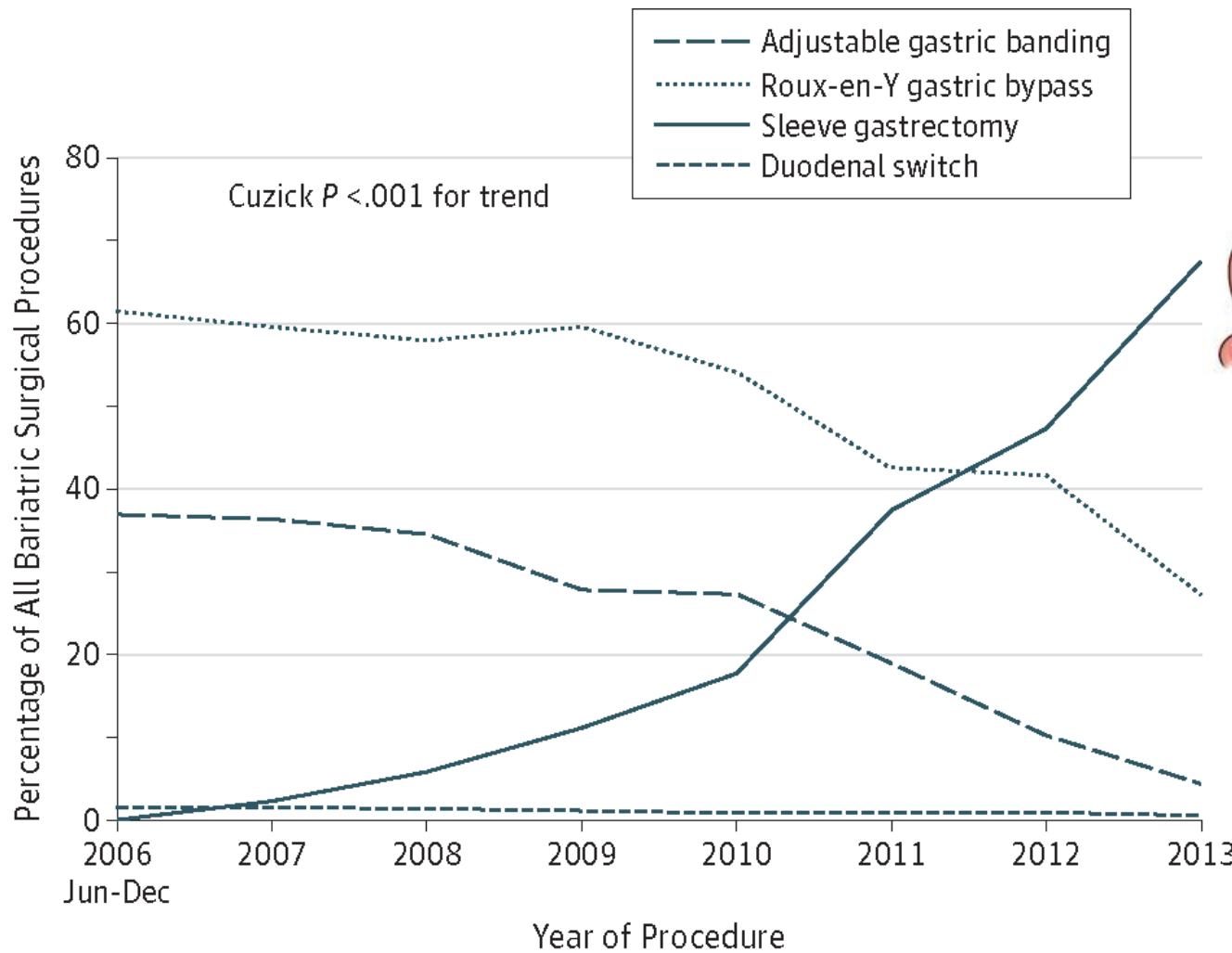


Weight-related  
studies

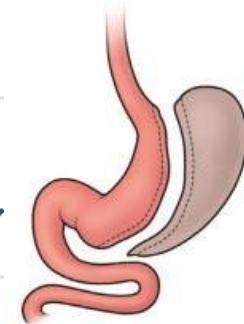
# Short- and Long-Term Outcomes related to Bariatric Surgery



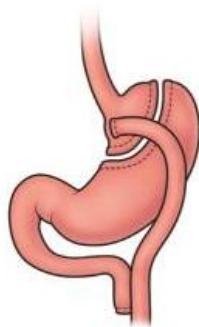
# There is an ongoing major shift in bariatric procedures in the United States



Vertical Sleeve  
Gastrectomy  
(VSG)



Roux-en-Y  
Gastric Bypass  
(RYGB)



Adjustable  
Gastric Band  
(AGB)



# Outcomes of Bariatric Surgery (in development)

## Compare three bariatric surgical procedures

- Roux-en-Y gastric bypass
- Sleeve gastrectomy
- Adjustable gastric banding

## Outcomes under consideration:

- Weight loss and regain
- Obesity-related outcomes
  - Resolution of type 2 diabetes
  - Incidence or recurrence of type 2 diabetes
- Adverse outcomes: hospitalization, reoperation, death

# Potential Secondary Aim

---

- Engage patient communities through surveys, interviews, focus groups, etc. to
  - Elicit patient preferences around the risks and benefits of the study treatments
  - Collect patient-reported outcomes meaningful to patients with obesity

# Principal Investigators

● David Arterburn, clinical investigator [lead PI]

- Bariatric surgery researcher



● Kathleen McTigue, clinical investigator

- Obesity researcher

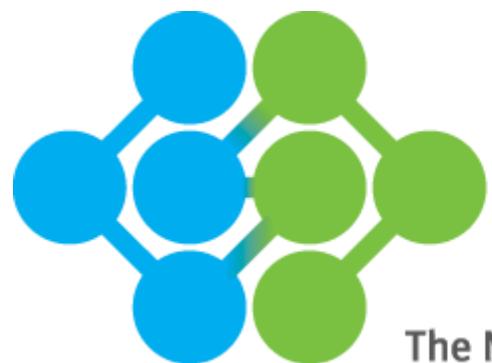


● Neely Williams, patient investigator

- Community engagement leader
- Bariatric surgery patient



# Short- and Long-Term Effects of Antibiotics on Childhood Growth

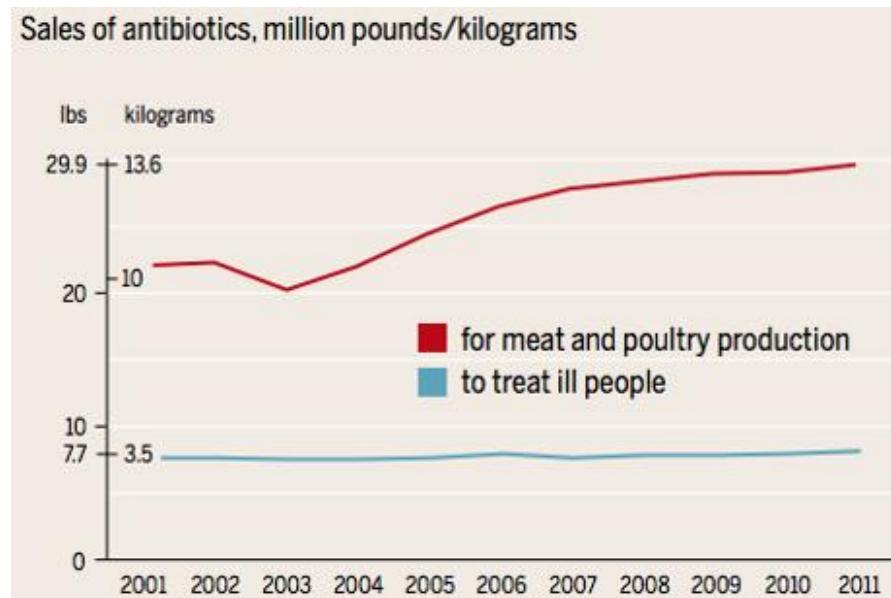


**pcornet**

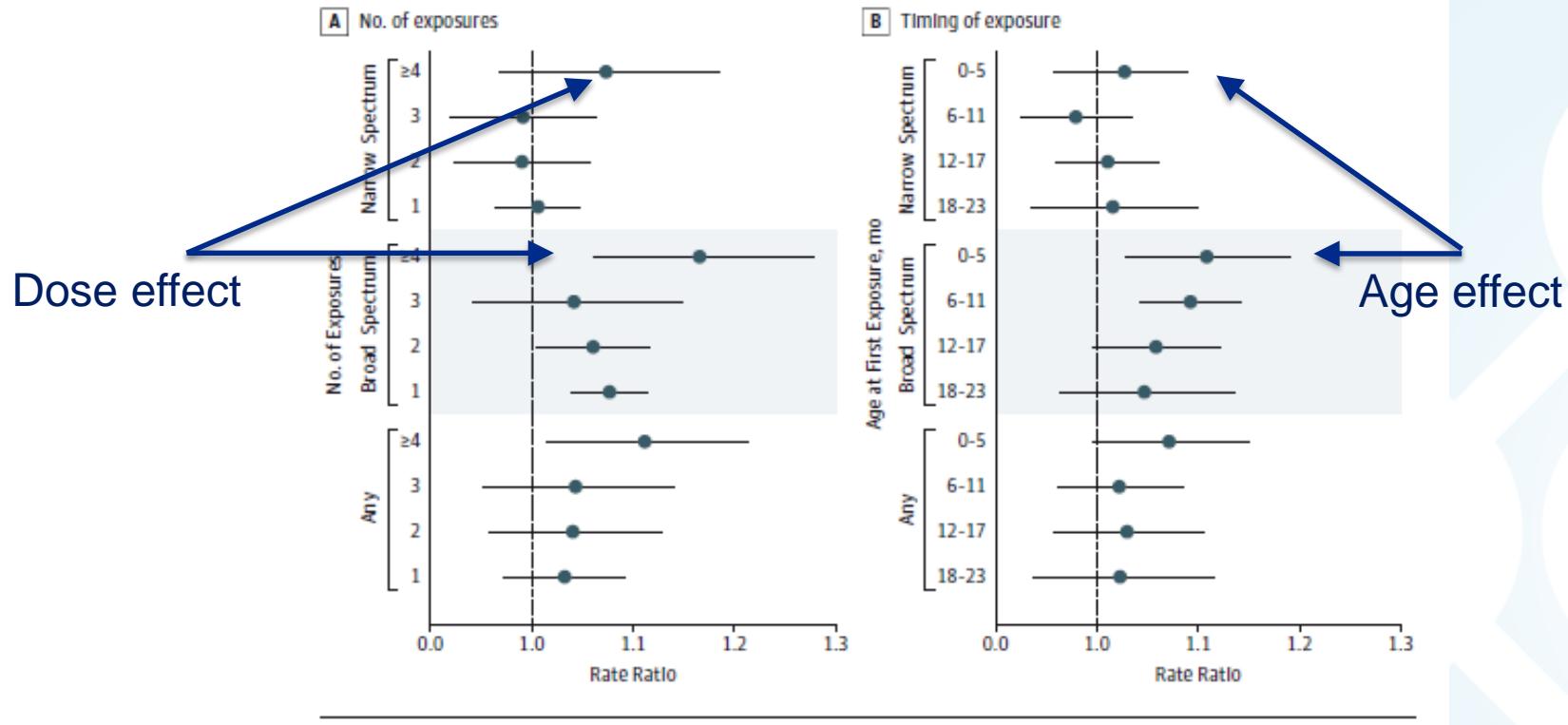
The National Patient-Centered Clinical Research Network



Sales of antibiotics, million pounds/kilograms



# Association of Antibiotics in Infancy with Early Childhood Obesity



Bailey et al., *JAMA Pediatr.* doi:10.1001/jamapediatrics.2014.1539;  
N ~ 65.000 primary care visits

# Short- and Long-Term Effects of Antibiotics on Childhood Growth

---

- Compare different antibiotics used during the first 2 years of life
- Outcomes
  - Weight-related outcomes during 3<sup>rd</sup> to 5<sup>th</sup> years of life
    - Body mass index and
    - Risk of being overweight or obese
  - Growth trajectories through preschool ages

# Antibiotic Use and Childhood Obesity: Unresolved Issues (in development)

- ⌚ Is there a sensitive exposure age? If yes, does it matter
  - How large the exposure is (#doses)?
  - Broad v. narrow spectrum?
  - Class of antibiotic?
- ⌚ Timing of outcome?
  - Early v. late
  - Growth trajectories could help
- ⌚ Is there potentiation by chronic steroid use?
- ⌚ How much does confounding play a role in observed effects?
- ⌚ To what extent will information about this association change practice?

## Potential Secondary Aim

---

- Investigate attitudes of pediatric clinicians and parents of infants/toddlers regarding
  - Potential impact of information about obesity risk on antibiotic prescribing
  - How the risk of obesity compares with other potential risks to individuals (e.g., allergy) or society (e.g., resistance) in relation to antibiotic decision-making

# Principal Investigators

## Matt Gillman, clinical investigator, lead PI

- Research focus on early life prevention of chronic disease
- Lead, PCORnet Obesity Task Force



## Chris Forrest, clinical investigator

- Academic investigator in childhood obesity research for the Healthy Weight Program



## Douglas Lunsford, patient investigator

- Parent Member, Nationwide Children's Hospital Healthy Weight Program



# Guiding principle: Make research easier

- Analysis ready data
  - Standard format
  - Harmonized definitions
  - Quality checked in advance
- Reusable analysis tools
- Administrative simplicity
- Simple, pragmatic studies integrated into routine care

# Requirements for Network Participation in Observational Studies

---

- Work with a single IRB of record (1 per project)
- Complete contracting and data use agreements quickly
- Have analysis ready data (Common Data Model v2.1)\*
- Use PCORnet's networking querying capabilities\*
- Execute supplied QC and analytical programs (SAS) without modification\*
- Share relevant data and documentation

\* *Clinical data research networks*

# Requirements for Network Participation in Observational Studies

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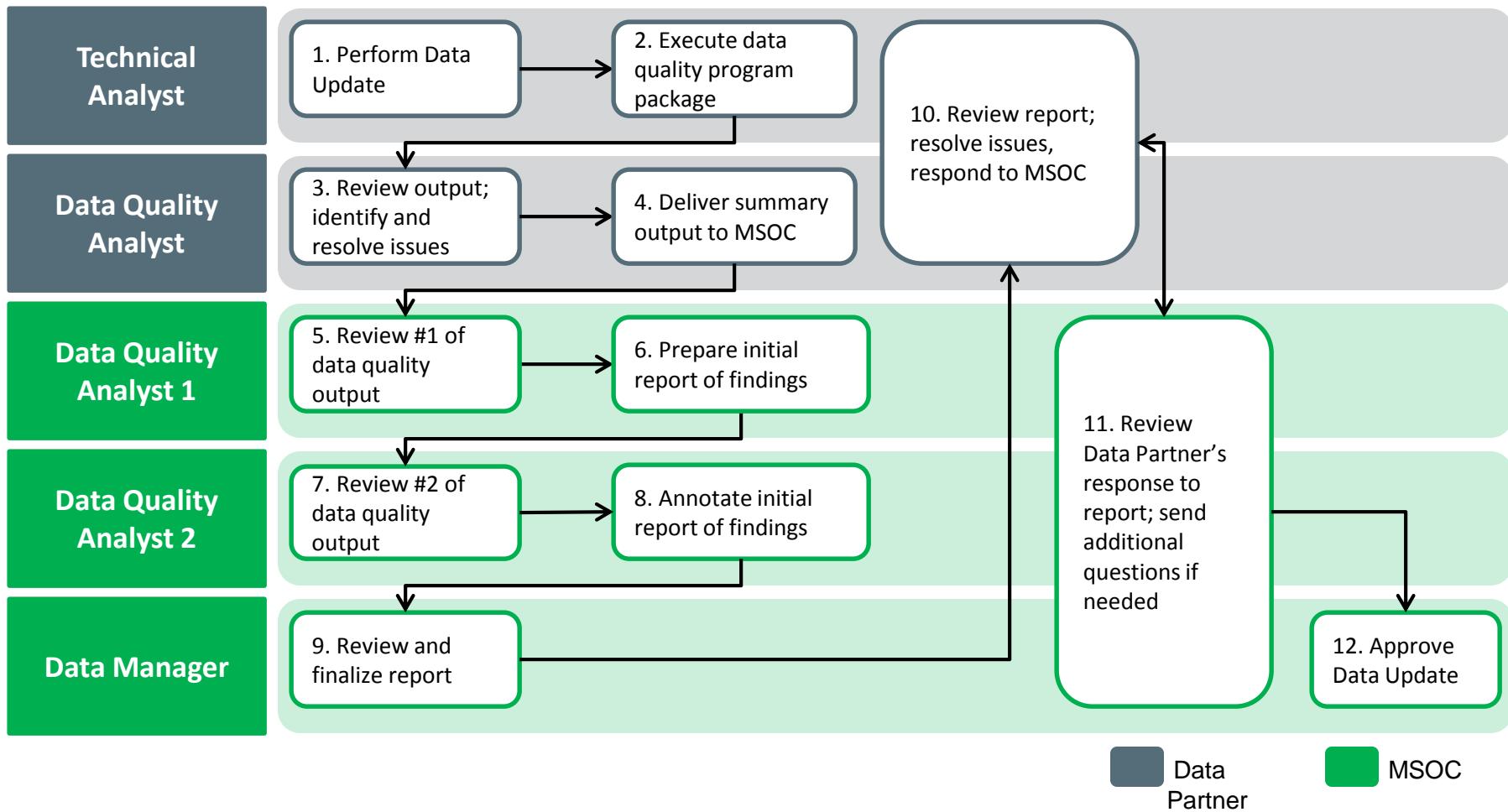
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\* *Clinical data research networks*

# PCORnet Common Data Model v2.1

<b>DEMOGRAPHIC</b> <ul style="list-style-type: none"> <li>PATID</li> <li>BIRTH_DATE</li> <li>BIRTH_TIME</li> <li>SEX</li> <li>HISPANIC</li> <li>RACE</li> <li>BIOBANK_FLAG</li> </ul> <p>Fundamental basis</p>	<b>VITAL</b> <ul style="list-style-type: none"> <li>PATID</li> <li>ENCOUNTERID (optional)</li> <li>MEASURE_DATE</li> <li>MEASURE_TIME</li> <li>VITAL_SOURCE</li> <li>HT</li> <li>WT</li> <li>DIASTOLIC</li> <li>SYSTOLIC</li> <li>ORIGINAL_BMI</li> <li>BP_POSITION</li> </ul>	<b>ENCOUNTER</b> <ul style="list-style-type: none"> <li>PATID</li> <li>ENCOUNTERID</li> <li>SITEID</li> <li>ADMIT_DATE</li> <li>ADMIT_TIME</li> <li>DISCHARGE_DATE</li> <li>DISCHARGE_TIME</li> <li>PROVIDERID</li> <li>FACILITY_LOCATION</li> <li>ENC_TYPE</li> <li>FACILITYID</li> <li>DISCHARGE_DISPOSITION</li> <li>DISCHARGE_STATUS</li> <li>DRG</li> <li>DRG_TYPE</li> <li>ADMITTING_SOURCE</li> </ul>	<b>LAB_RESULT</b> <ul style="list-style-type: none"> <li>PATID</li> <li>ENCOUNTERID (optional)</li> <li>LAB_NAME</li> <li>SPECIMEN_SOURCE</li> <li>LAB_LOINC</li> <li>STAT</li> <li>RESULT_LOC</li> <li>LAB_PX</li> <li>LAB_PX_TYPE</li> <li>LAB_ORDER_DATE</li> <li>SPECIMEN_DATE</li> <li>SPECIMEN_TIME</li> <li>RESULT_DATE</li> <li>RESULT_TIME</li> <li>RESULT_QUAL</li> <li>RESULT_NUM</li> <li>RESULT_MODIFIER</li> <li>RESULT_UNIT</li> <li>NORM_RANGE_LOW</li> <li>MODIFIER_LOW</li> <li>NORM_RANGE_HIGH</li> <li>MODIFIER_HIGH</li> <li>ABN_IND</li> </ul>
<b>ENROLLMENT</b> <ul style="list-style-type: none"> <li>PATID</li> <li>ENR_START_DATE</li> <li>ENR_END_DATE</li> <li>CHART</li> <li>ENR BASIS</li> </ul>	<b>CONDITION</b> <ul style="list-style-type: none"> <li>PATID</li> <li>ENCOUNTERID (optional)</li> <li>REPORT_DATE</li> <li>RESOLVE_DATE</li> <li>CONDITION_STATUS</li> <li>CONDITION</li> <li>CONDITION_TYPE</li> <li>CONDITION_SOURCE</li> </ul>	<b>DIAGNOSIS</b> <ul style="list-style-type: none"> <li>PATID</li> <li>ENCOUNTERID</li> <li>ENC_TYPE (<i>replicated</i>)</li> <li>ADMIT_DATE (<i>replicated</i>)</li> <li>PROVIDERID (<i>replicated</i>)</li> <li>DX</li> <li>DX_TYPE</li> <li>DX_SOURCE</li> <li>PDX</li> </ul>	<b>PROCEDURE</b> <ul style="list-style-type: none"> <li>PATID</li> <li>ENCOUNTERID</li> <li>ENC_TYPE (<i>replicated</i>)</li> <li>ADMIT_DATE (<i>replicated</i>)</li> <li>PROVIDERID (<i>replicated</i>)</li> <li>PX_DATE</li> <li>PX</li> <li>PX_TYPE</li> </ul>
<b>DISPENSING</b> <ul style="list-style-type: none"> <li>PATID</li> <li>RX_DATE</li> <li>NDC</li> <li>RX_SUP</li> <li>RX_AMT</li> </ul>	<b>PRO_CM</b> <ul style="list-style-type: none"> <li>PATID</li> <li>ENCOUNTERID (optional)</li> <li>CM_ITEM</li> <li>CM_LOINC</li> <li>CM_DATE</li> <li>CM_TIME</li> <li>CM_RESPONSE</li> <li>CM_METHOD</li> <li>CM_MODE</li> <li>CM_CAT</li> </ul>		<p>Data captured from healthcare delivery, direct encounter</p>

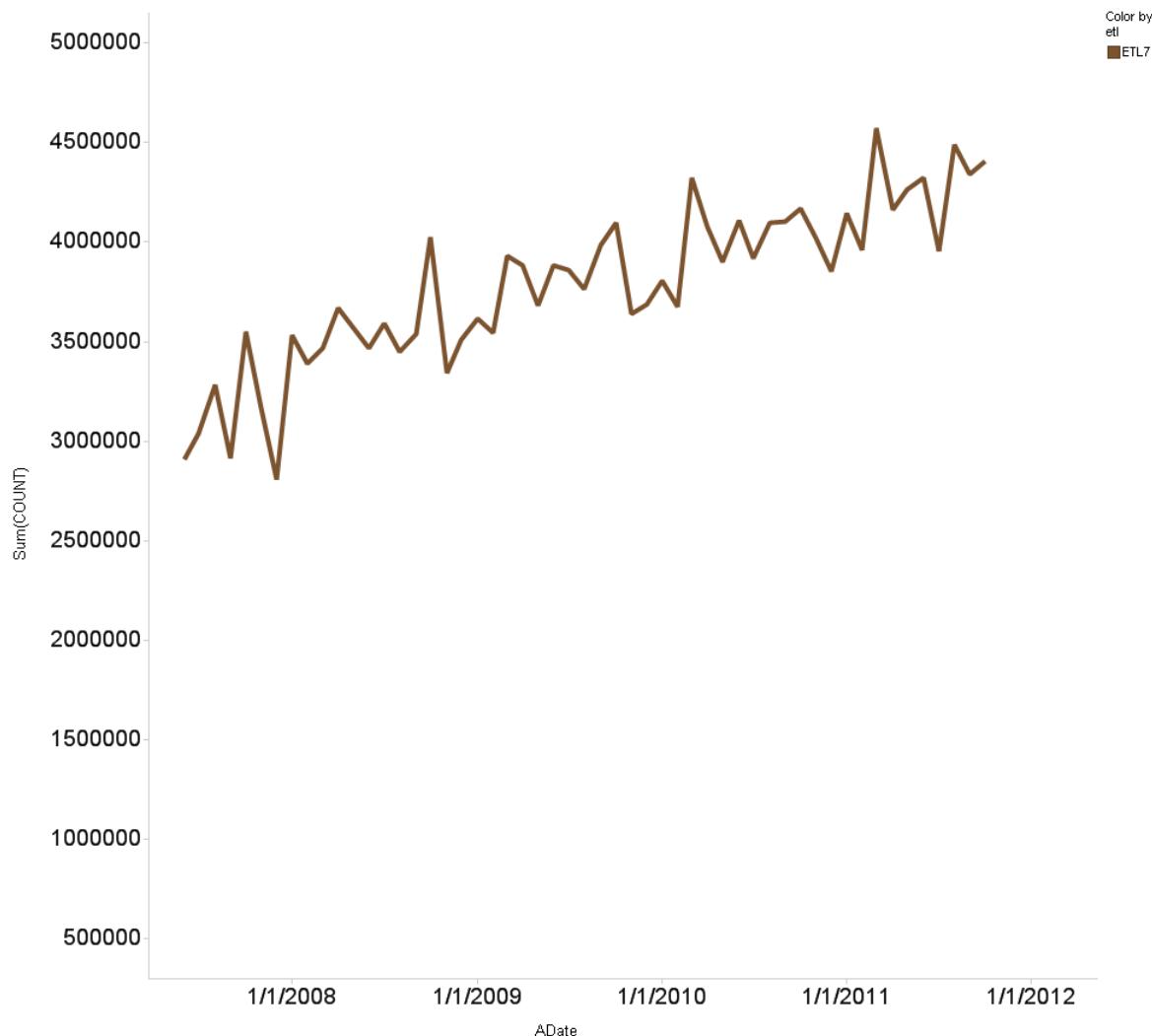
# Data Quality Assurance review process



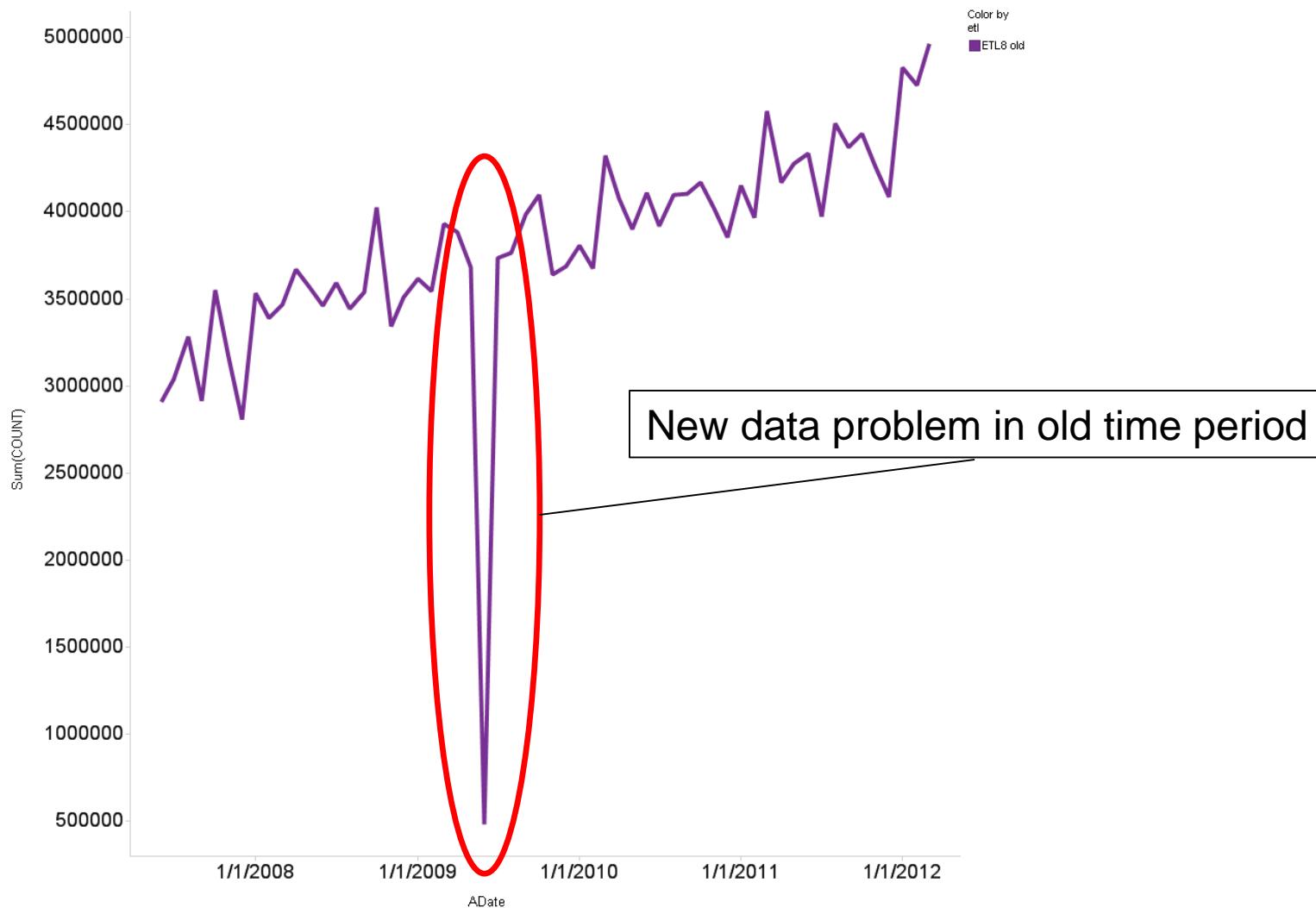
# Glycosylated hemoglobin (HbA1c) units

%	%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 <sup>†</sup>	Blank
% A1C	% A1c	%Hb	g/dL
NULL	%THb		

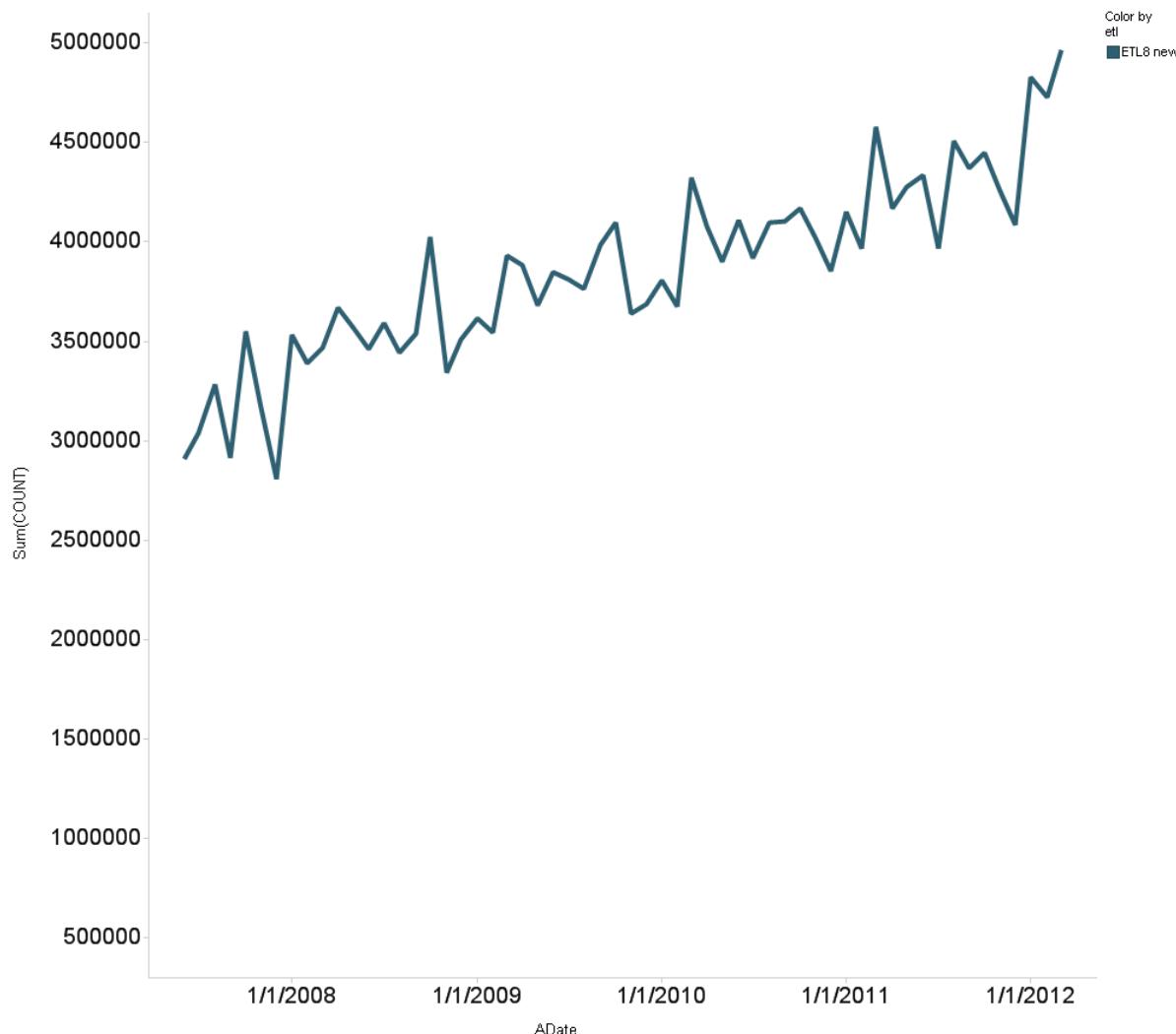
# Data Visualization: After 7<sup>th</sup> refresh, partner A



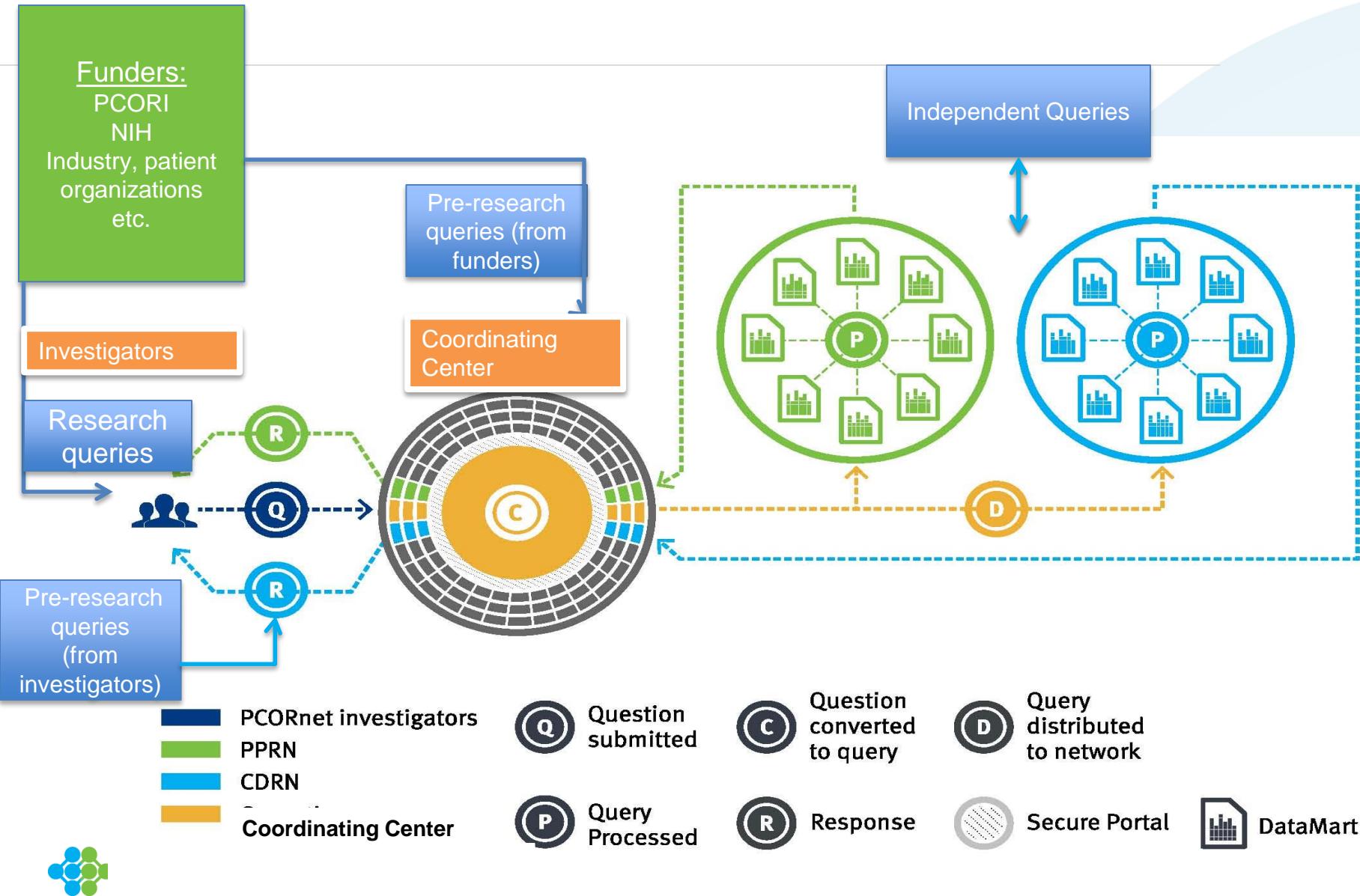
# Data Visualization: After 8<sup>th</sup> refresh, partner A

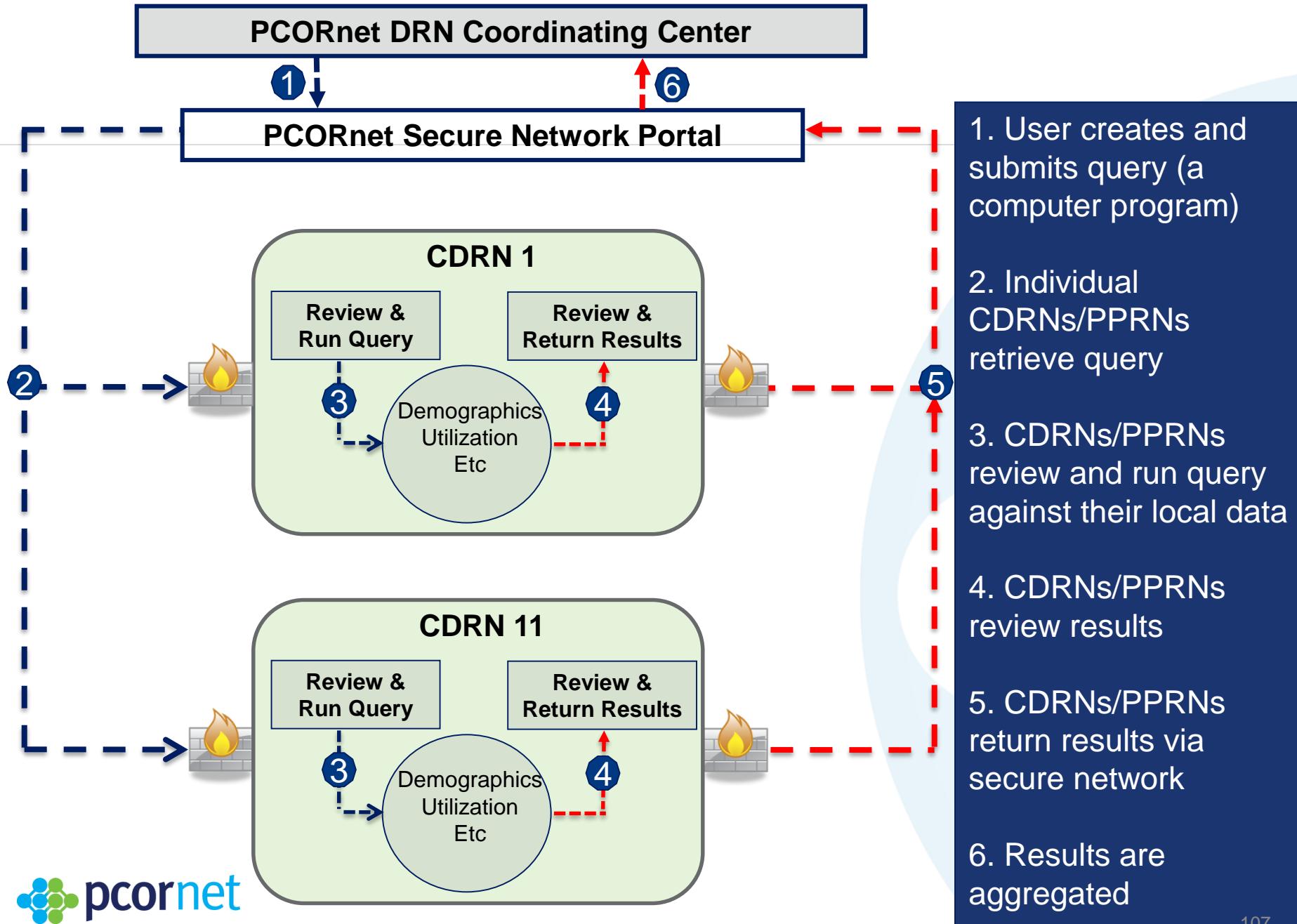


# Data Visualization: After 8<sup>th</sup> refresh fixed



# PCORnet Operational Model





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

*PCORnet's First Proposed Pragmatic Clinical Trial*



# What if a choice made over the counter prevented...



19,000 Deaths & Heart Attacks  
Or  
Prevented Thousands of Bleeds  
Annually in the United States



# Aspirin: A “wonder” drug

- ➊ Proven clinical benefit in reducing ischemic vascular events
- ➋ Cost effective
- ➌ Benefit with combination antiplatelet therapies
- ➍ But there are issues:
  - Emerging evidence for dose modifiers (ASA resistance, genetics, P2Y12 inhibitors)
  - Equal efficacy across patients?
  - Intolerance

**Most effective dose uncertain**



# Risks of aspirin therapy

## ADVERSE REACTIONS

### MMR VACCINE

SERIOUS ALLERGIC  
REACTION  
LESS THAN 1 OUT OF  
1 MILLION DOSES

### ASPIRIN

INTRACEREBRAL  
HEMORRHAGE  
12 EVENTS PER  
10,000 PEOPLE

MEASLES OUTBREAK

102 CASES REPORTED IN 14 STATES

CNN

9:27 PM ET

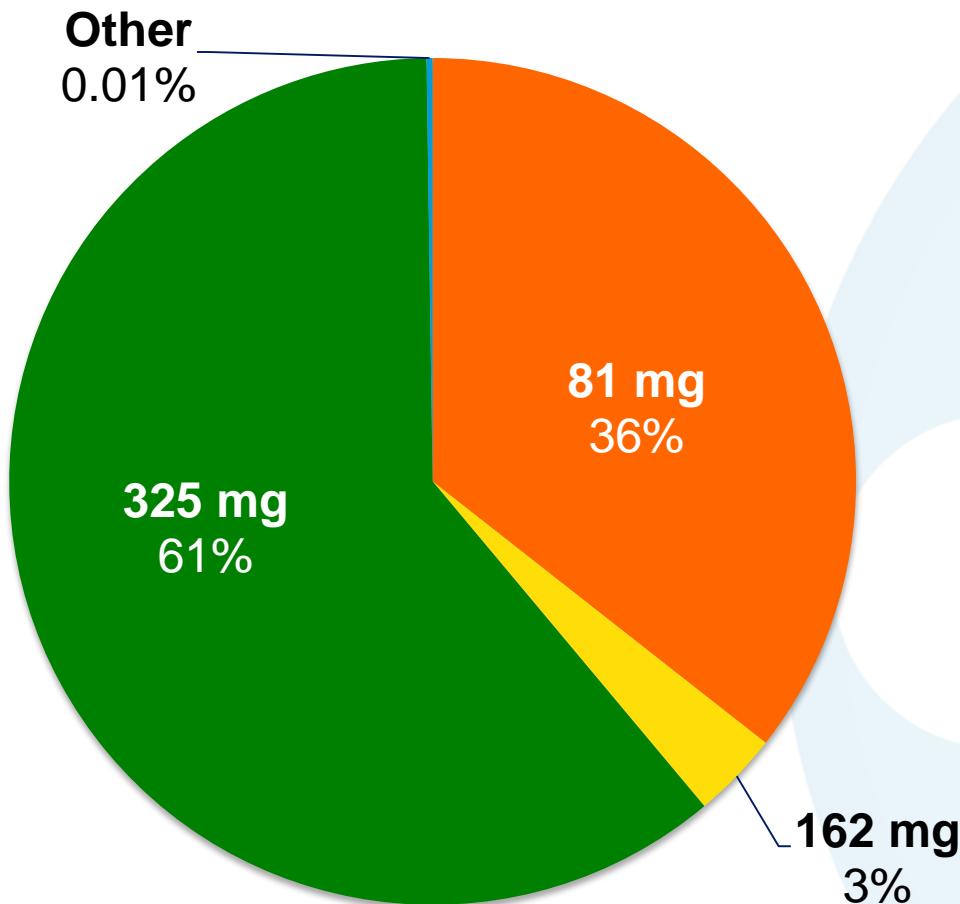
AC360°

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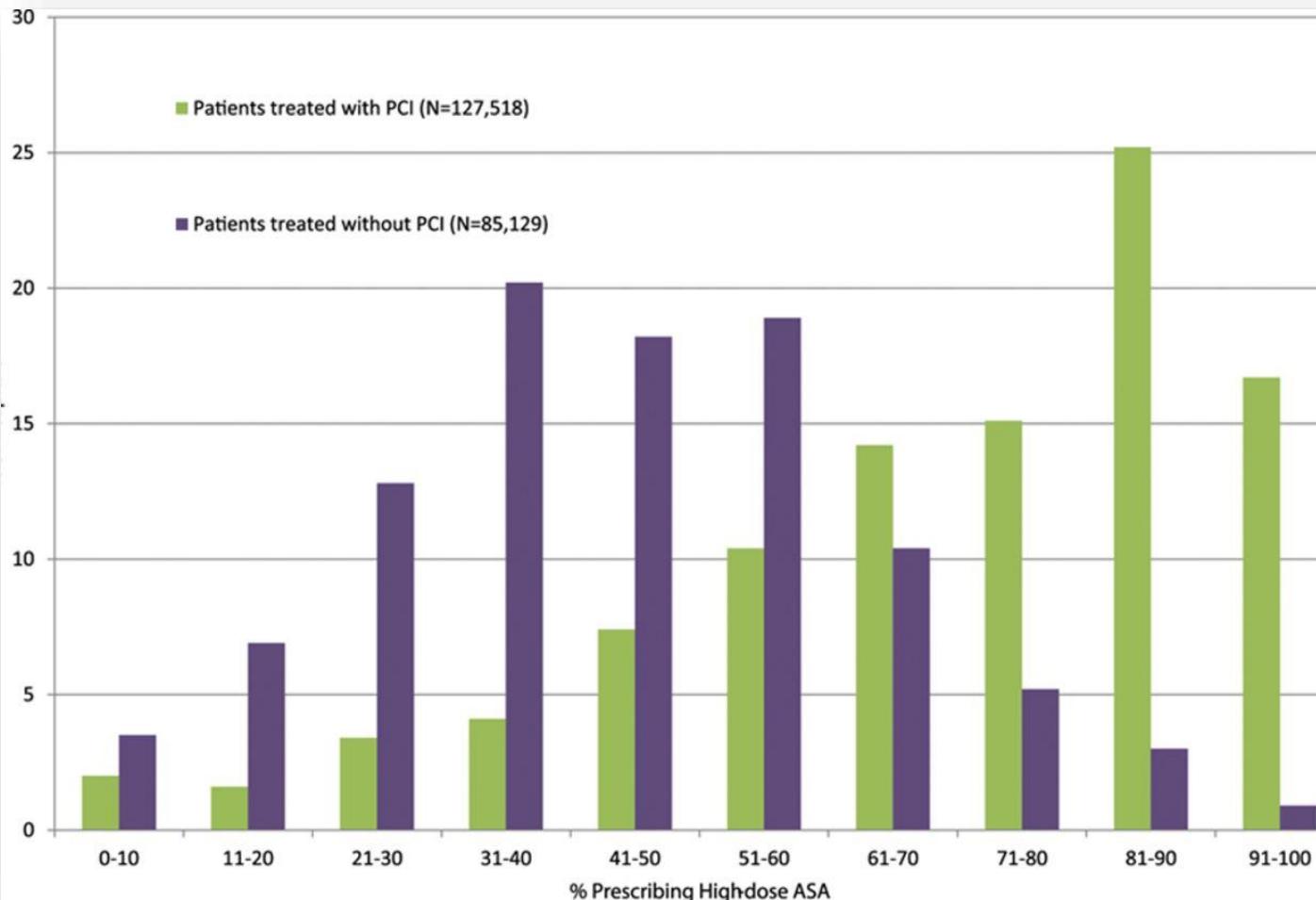
# Aspirin Dosing: Equipoise?



# Distribution of aspirin dosing at discharge



# High (25 -fold) Variation Across Hospitals on Use of High Dose (325mg) Aspirin



>440 US  
Hospitals

# Main objectives of the ADAPTABLE Trial

- 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, nonfatal MI, nonfatal stroke
  - **Primary Safety Endpoint:** Major bleeding complications
- To compare the effects of aspirin in subgroups of patients:
  - Women vs men
  - Older vs younger
  - Racial and ethnic minorities vs. whites
  - Diabetics vs. nondiabetics
  - Chronic kidney disease (CKD) vs. not
  - Internet users vs. not
  - P2Y12 inhibitor users vs. not
- To develop and refine the infrastructure for PCORnet to conduct multiple comparative effectiveness trials in the future

# ADAPTABLE Leadership

- Robert Harrington, clinical investigator [Study Chair]
  - Cardiovascular trialist
- Russell Rothman, clinical investigator [Study Co-Chair]
  - Health services researcher
- Matthew Roe, clinical investigator [CC PI]
  - Cardiovascular trialist
- Sana Al-Khatib, clinical investigator [CC-PI]
  - Cardiovascular health services researcher
- Bray Patrick-Lake, patient investigator
  - Community engagement leader
  - ADAPTORs leader



# Study design

Patients with known coronary artery disease (MI, or CAD or Revasc) +  $\geq 1$  “enrichment factor”\*\*

Identified through EHR/direct pt. consenting in clinics and hospitals through CDRNs/PPRNs (PPRN pts. would need to connect through a CDRN to participate)

Pts. contacted electronically with trial information and eConsent; treatment assignment will be provided directly to patient

ASA 81 mg QD

ASA 325 mg QD

Electronic F/U Q 4 months;  
supplemented with EHR/CDM/claims data

**Duration:** Enrollment over 24 months;  
maximum f/u of 30 months

**Primary Endpoint:** Composite of all-cause mortality,  
nonfatal MI, nonfatal stroke

**Primary Safety Endpoint:** Major bleeding complications

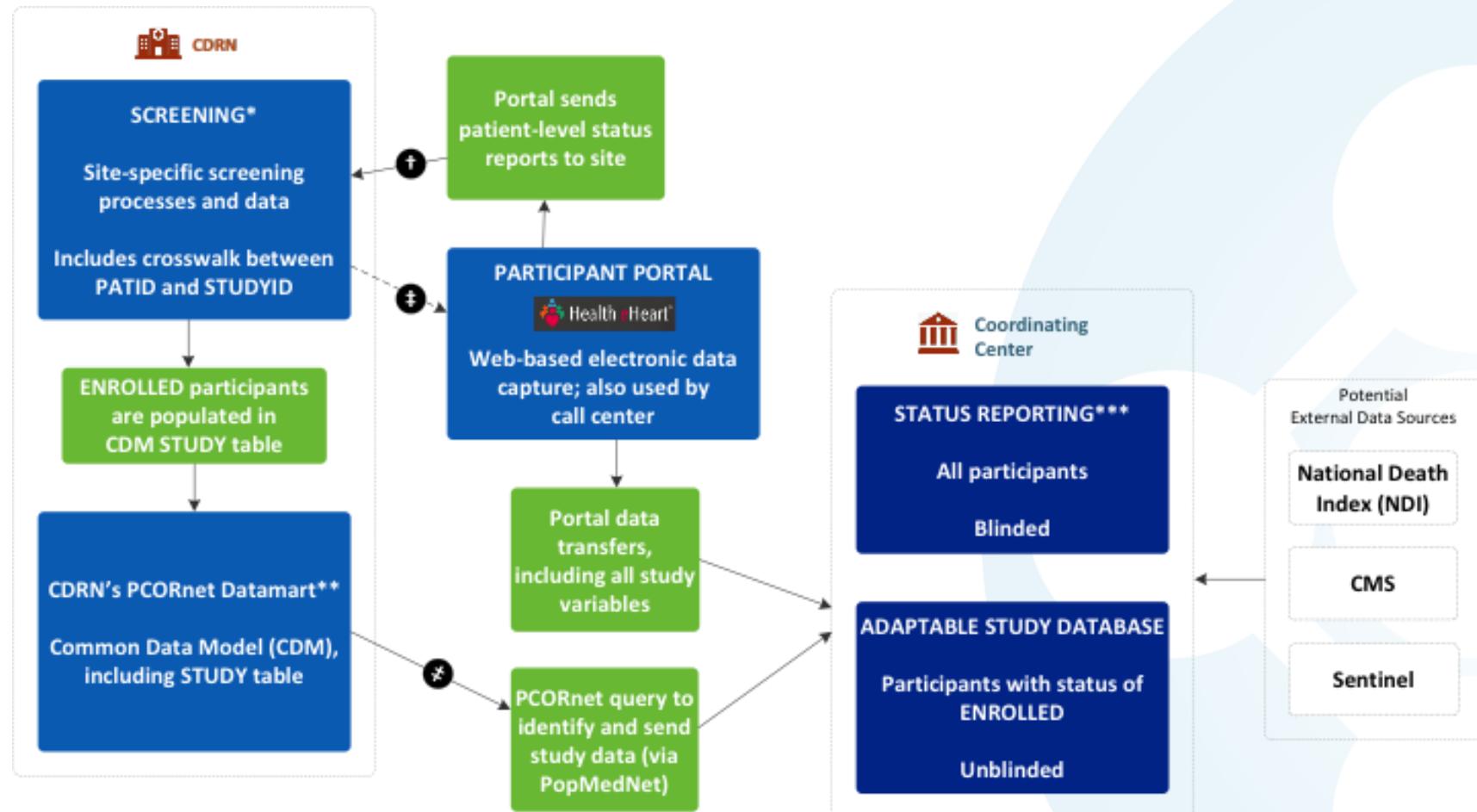
## \*Enrichment factors

- age  $> 65$  years
- creatinine  $> 1.5$
- diabetes
- known 3-vessel coronary artery disease
- current cerebro-vascular disease and/or peripheral artery disease,
- known ejection fraction  $< 50\%$
- current smoker

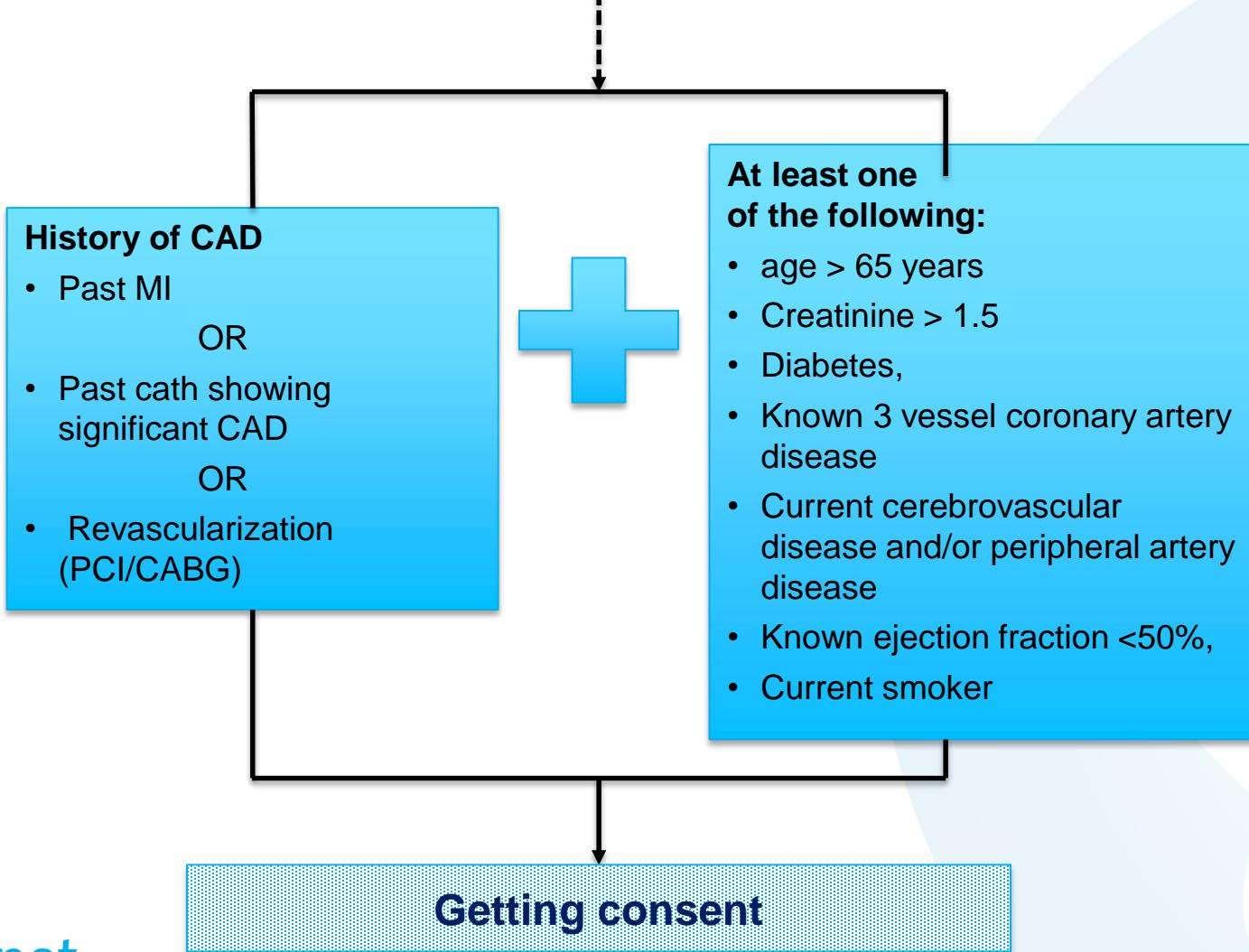
# Trial Logistics: Leveraging PCORnet Infrastructure



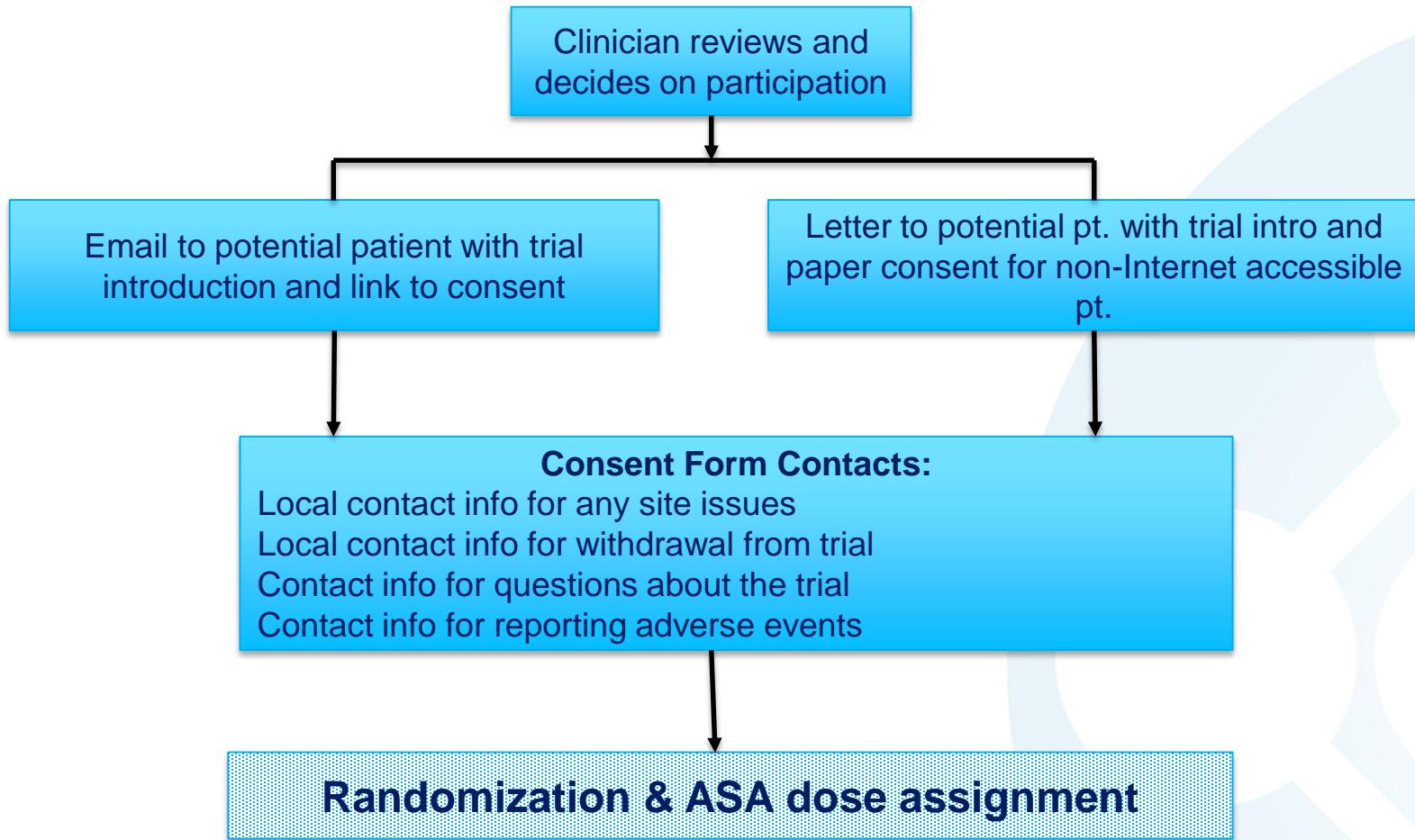
# Screening, Enrollment & Data Flow



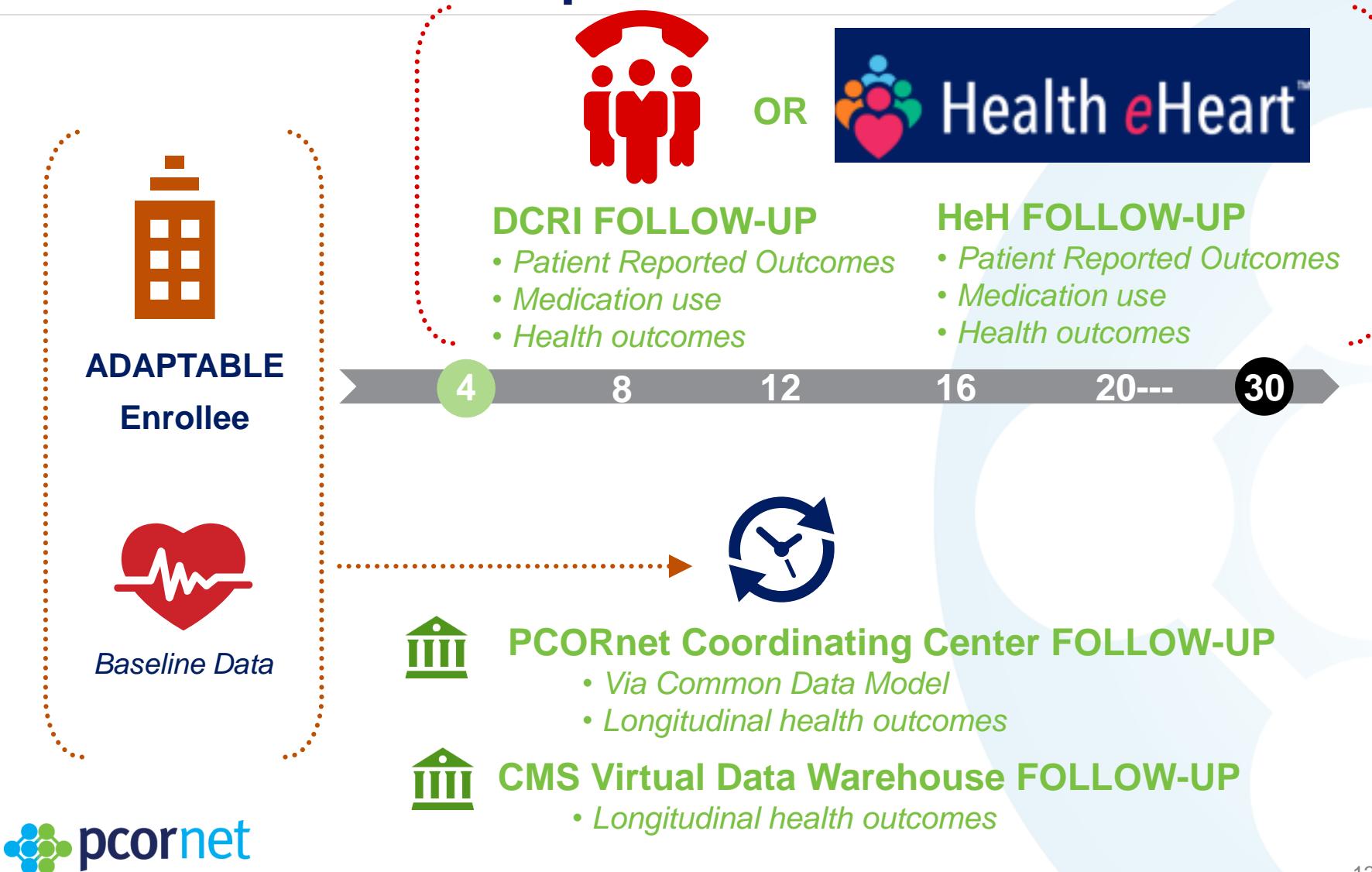
# Computable phenotype



# Getting Informed Consent



# Centralized follow-up



# Meeting Objectives of PCORnet: ADAPTABLE Achieving a single functional research network

- Create** infrastructure, tools, and policies to support rapid, efficient comparative effectiveness research
- Utilize** multiple electronic health records, insurance claims data, data reported directly by patients, and other data sources
- Engage** patients, clinicians, and health system leaders throughout

# Summary

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- ➊ Atherosclerotic CV disease is a major cause of death and disability.
- ➋ Getting the dose of aspirin right could save up to **tens of thousands of lives or heart attacks** in the US alone annually (or prevent **thousands** major bleeding episodes).
  - And multiple times that number globally
- ➌ The ADAPTABLE Research Community & “ADAPTORS” will be pioneers working together
  - To solve the challenge and demonstrate the value of a reusable infrastructure
  - Launch a new era for pragmatic clinical trials to answer questions with high impact on population health

# PCORnet's advantages

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- ➊ Many networks – large pool of engaged participants, patients, practice settings, investigators
- ➋ Robust distributed data network capable of supporting a wide array of observational and interventional studies
- ➌ Ability to supplement routinely collected electronic health data with patient reported information
- ➍ Reusable clinical trial infrastructure
- ➎ Administrative simplicity:
  - Single IRB of record for each demonstration study
  - Uniform contracting mechanism
  - Centralized data collection and follow-up

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# Questions?



# Reports from Breakout Sessions: Opportunities, Areas for Further Exploration



# Open Discussion



# Observations and Next Steps



# Closing Remarks and Adjournment

