From Observational Studies to Pragmatic Clinical Trials: (Almost) A Decade of Research in PCORnet®

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Demonstrated Productivity, Increasing Maturity, and Expanding Collaborations within PCORnet

Erin Holve
Chief Research Infrastructure Officer

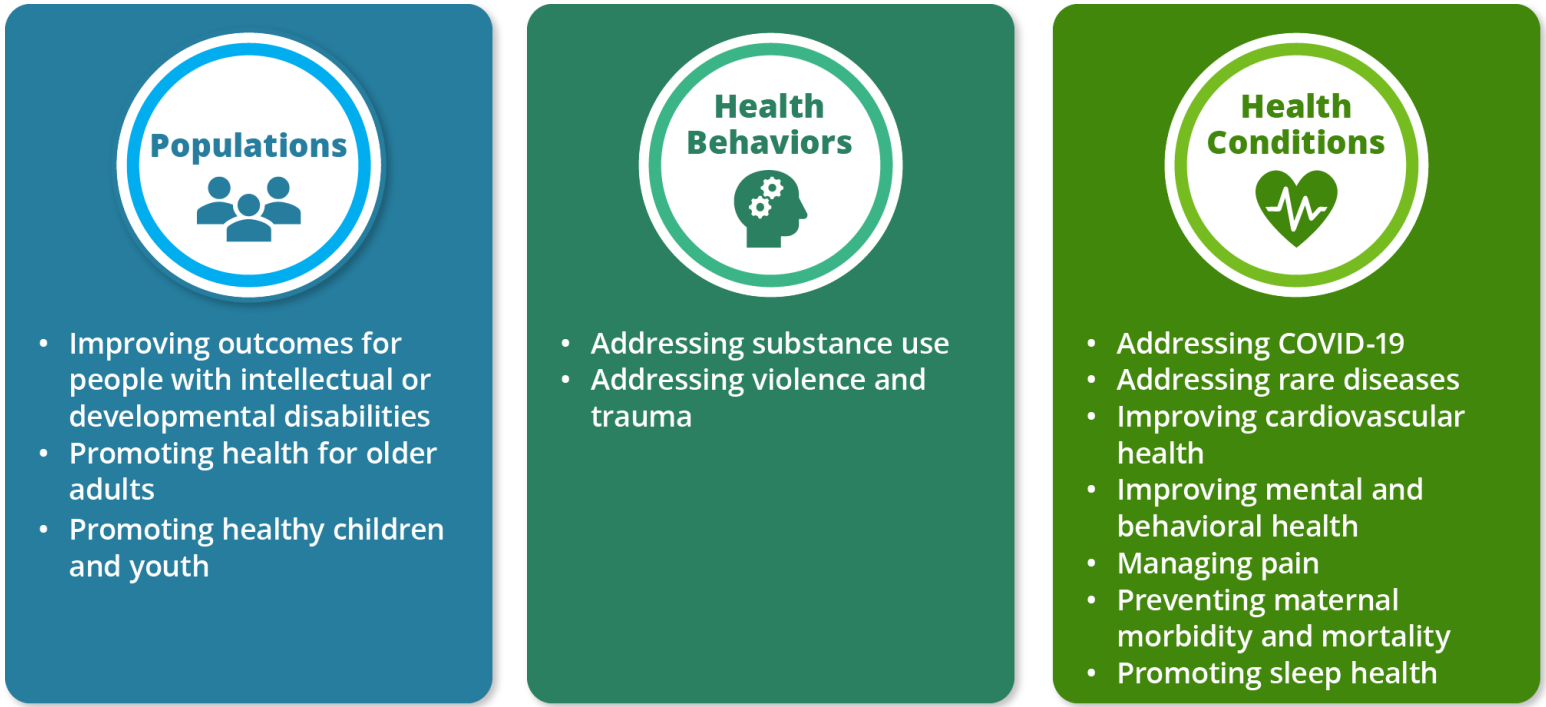
pcori
PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Patient-Centered Outcomes Research Institute
Leading Funder of CER in U.S.

- Funds studies designed to help people make better informed healthcare decisions
- Independent, nonprofit, research institute
- Leading funder of patient-centered comparative clinical effectiveness research (CER)

Powered by PCORnet®

- Broad Pragmatic Studies PCORI Funding Announcement
  - Category 3: PCORnet® Studies
- Leverage scale and national scope of PCORnet to conduct definitive studies that advance PCORI's National Priorities for Health
  - Use 2 or more Clinical Research Networks
  - Share study progress and performance metrics
  - Exchange best practices to promote continuous learning and improvement



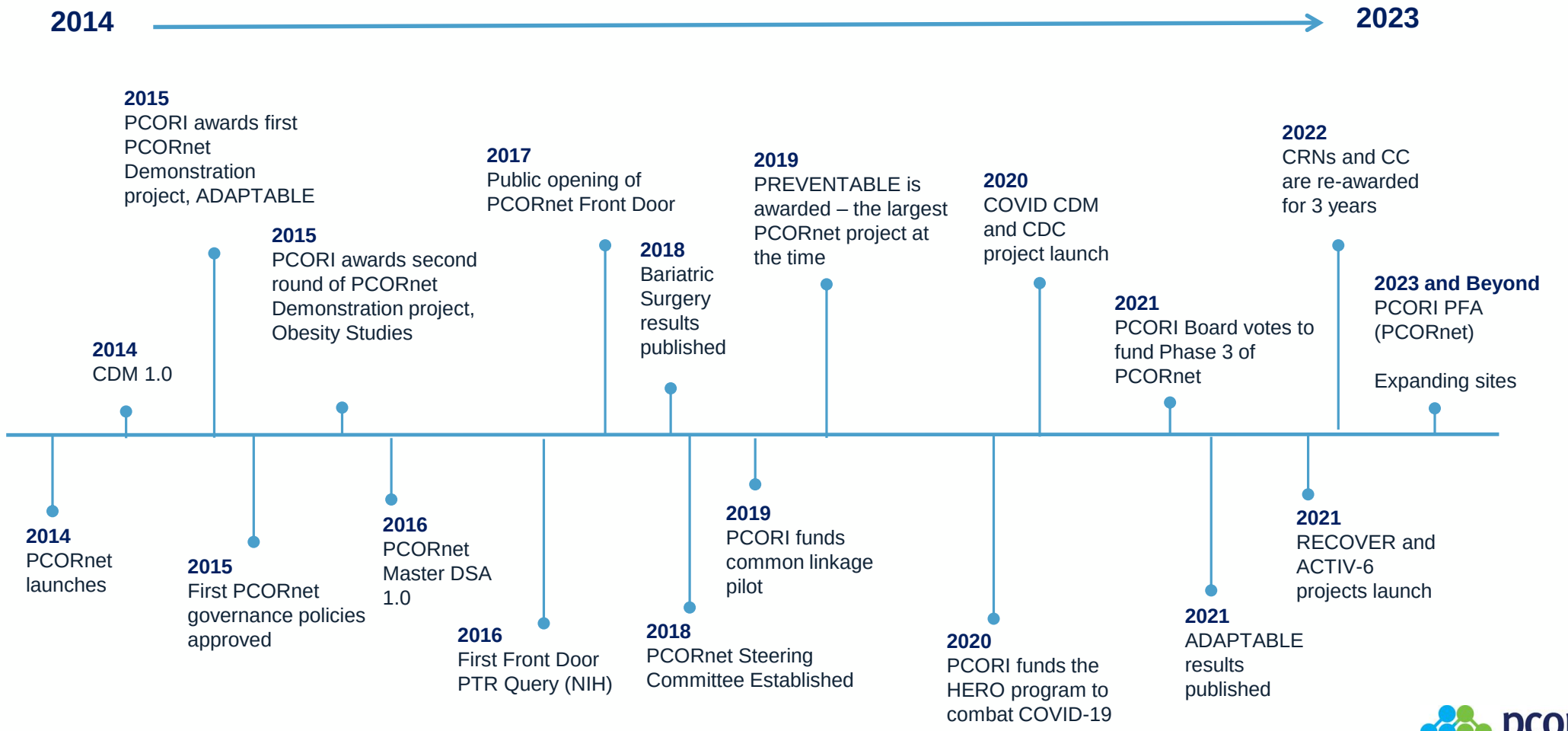
Overview

Russell Rothman, MD, MPP

Director Institute for Medicine and Public Health and Senior Vice President, Population and Public Health

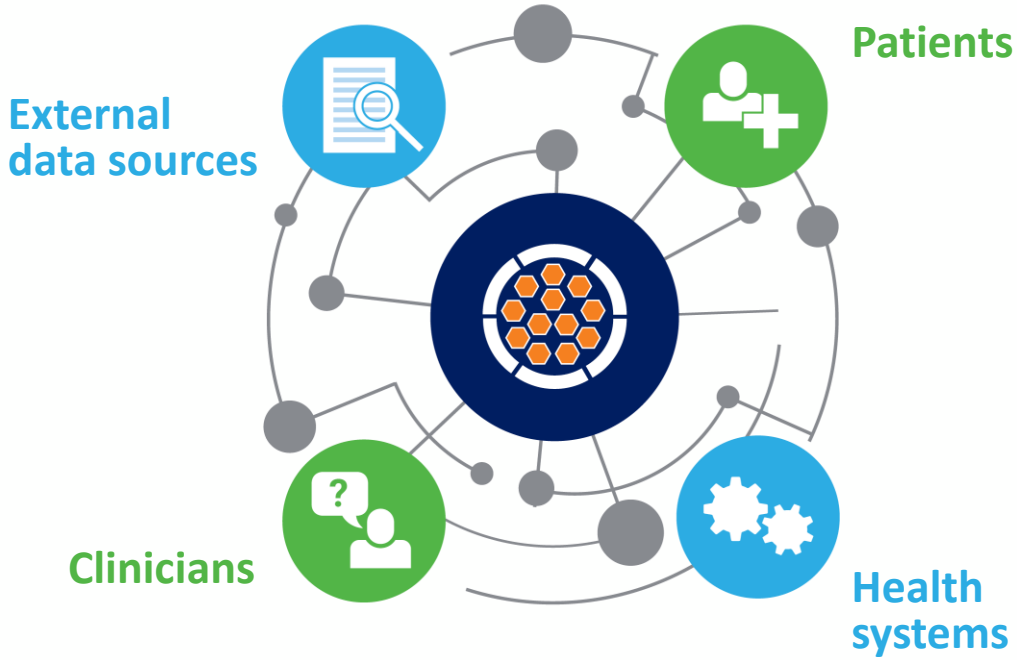
Vanderbilt University Medical Center

A Brief History of PCORnet®



A Network of networks

Patients, providers, data, and systems. In the traditional research environment, each operates in a silo. In PCORnet, they unite to form a coalition.



Patients and caregivers are integrated into all phases of PCORnet-enabled research

Data drawn from millions of EHRs with growing links to patient-reported and payor data.

PCORnet connects you to thousands of clinicians and researchers can support your effort.

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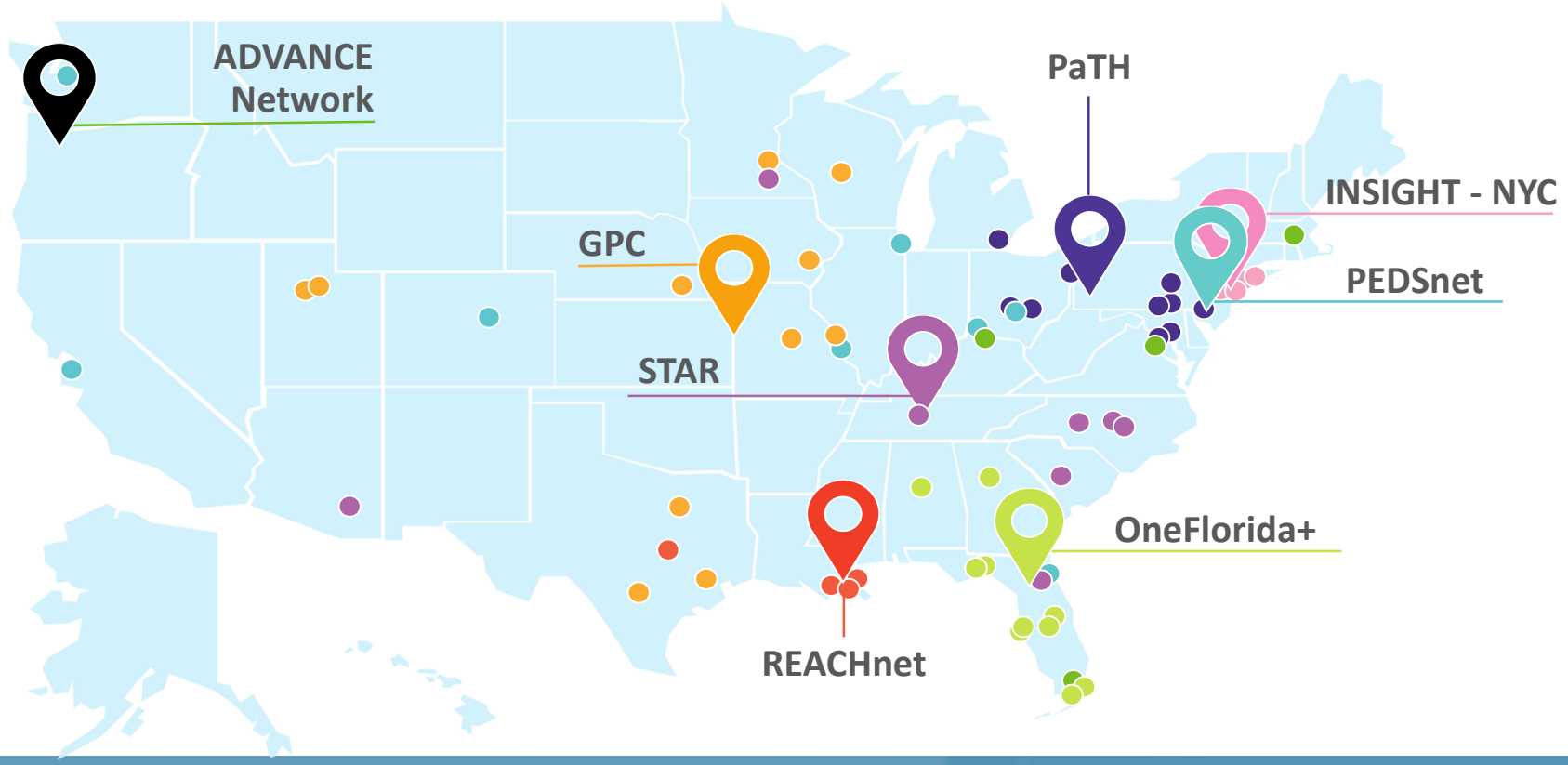
PCORnet® Clinical Research Networks (CRNs)

PCORnet networks provide nationwide coverage, and include large academic medical centers, federally qualified health centers, and specialty hospitals. PCORnet spans the breadth of health care. Over **60 health systems** and approximately **3,000 individual hospitals and clinics**. Over 30 million encounters in 2022.



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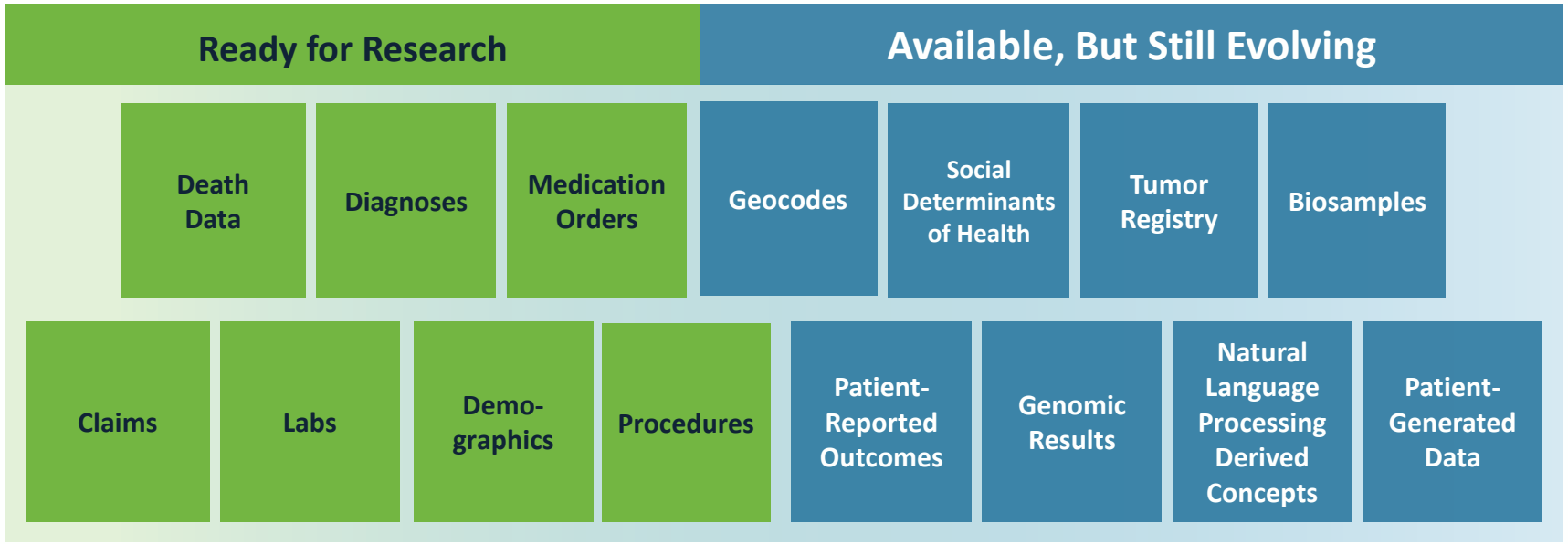
The PCORnet Common Data Model

Lots of data is great, but for it to be useful it has to be standardized across systems. The PCORnet Common Data Model standardizes data into a single language, enabling fast insights, including:



Data available from several Clinical Research Networks, in the PCORnet Common Data Model and ready for use in research.

Data available at some Clinical Research Networks, may or may not be in the PCORnet Common Data Model and require additional work for use in research.

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Types of PCORnet Research

- Data-only (retrospective or prospective)
- Prospective, interventional pragmatic randomized clinical trials
- Platform trials
- Implementation science and quality improvement studies

- Projects generally characterized by:
  - Integration of patient preferences (people-centered)
  - Curated data with longitudinal outcomes and efficient integration of external data sources
  - Clinician and health system engagement
  - Administrative efficiencies and rapid study start-up

- Supports projects funded by PCORI, NIH, CDC, FDA, Foundations, Industry

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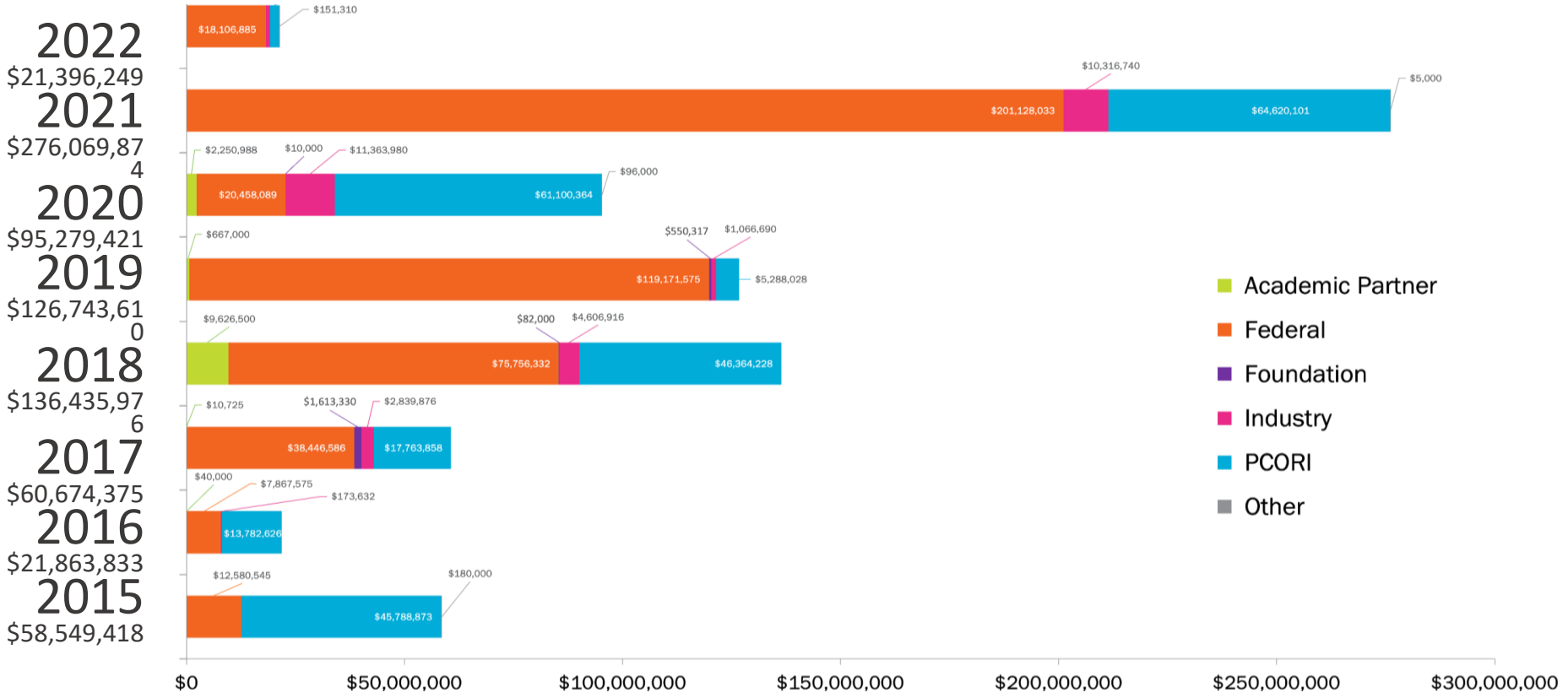
PCORnet supports nearly $800M in research projects



Includes* funded projects through January 31, 2023. N=238. Funded amount=$797,012,755.92
Includes Legacy PCORnet Network Partners

The PCORnet Front Door

The Front Door is the Access Point for PCORnet Resources & Services

Study design

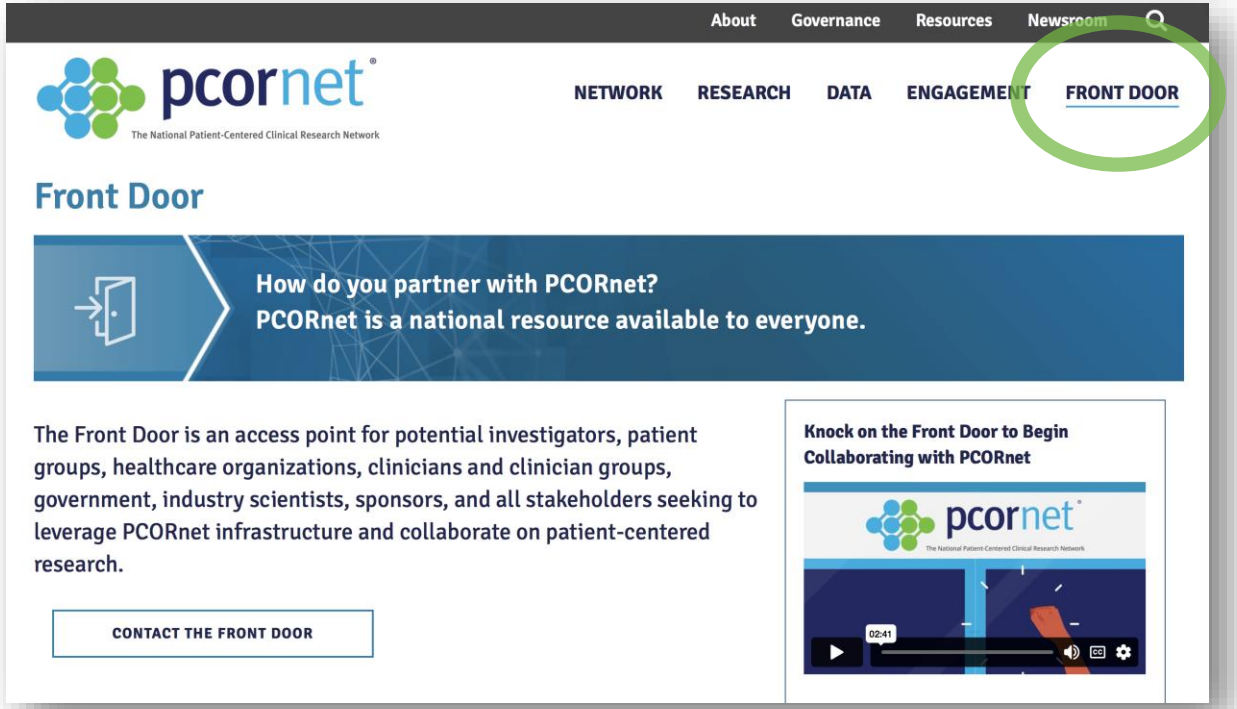
- Preliminary data for proposal feasibility, effect sizes, site identification

Connections to Network Collaborators

- Partners to co-design research and serve as study sites
- People with specific expertise

PCORnet Study Designation Support

- Deeper partnership with PCORnet provides access to best practice sharing, patient engagement, and transparent quality improvement initiatives



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Observational research in PCORnet®

Neha J. Pagidipati, MD MPH FACC
Associate Professor of Medicine
Duke Clinical Research Institute

Outline

- Review the following studies to give a sense of breadth and scope of various observational studies we have conducted within PCORnet:

  - Weight change in US adults with obesity
  - Lipoprotein (a) testing and management
  - Comparative effectiveness of empagliflozin vs. DPP4 inhibitors in patients with diabetes
  - Landscape analysis of CKD screening and management
  - Lipid testing and management in patients with ASCVD

Evaluation of weight change and cardiometabolic risk factors in a real-world population of US adults with overweight or obesity

Objective: To describe the association between weight change and cardiometabolic risk factors in a real-world population of U.S. adults with overweight or obesity

Setting: 11 PCORnet sites

Population: Adults with ≥1 encounter with BMI measurement in 2016

Evaluation of weight change and cardiometabolic risk factors in a real-world population of US adults with overweight or obesity

Results:

- 882,712 eligible individuals
- 52% maintained stable weight over 12 months; only 5% of patients lost >10% of body weight over 12 months
- Small changes in risk factors associated with 12 month weight loss were not sustained over time (likely due to weight regain)
- Both weight loss and weight gain were associated with worse clinical outcomes than weight stability

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Lp(a) testing and management

Objective: To understand testing and management patterns of Lp(a) in the U.S.

Setting: 11 PCORnet sites

Population: Patients with either an Lp(a) test between 2015 and 2019 *or* date- and site-matched LDL-c test

Results

Lp(a) Testing Patterns

Among 11 health systems in PCORnet®

- Only 0.06% of patients per year tested for Lp(a)
- Majority of Lp(a) tests reported in mass units (80.7% in mg/dL)

Lp(a) Patient Characteristics

Compared with those with LDL-C but not Lp(a) testing, Lp(a) tested patients were more frequently

- Older (median 58 vs 54 years)
- Male (50.9% vs 44.3%)
- Secondary prevention (24.3% vs. 8.5%)
- Had multiple prior CV events (8.6% vs 2.6%)
- Tested inpatient (19.7% vs 6.9%)

Lp(a) Management

Within 3 months of Lp(a) test with elevated value:

- 14.5% initiated statin
- 1.9% initiated ezetimibe
- 0.09% initiated PCSK9i
- 0.07% initiated niacin

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Comparative effectiveness of empagliflozin vs. DPP4 inhibitors in patients with diabetes

Objective: To determine the cardiovascular and renal effectiveness and safety of empagliflozin compared with DPP4i in patients with T2D both with and without kidney disease

Setting: 20 PCORnet sites

Population: Adults with T2D (with or without kidney disease) who initiate empagliflozin vs. those who initiate DPP4i

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Comparative effectiveness of empagliflozin vs. DPP4 inhibitors in patients with diabetes

Learnings so far:

- PCORnet was essentially the only dataset we could utilize for this project
  - Need large N for smallest subgroup (patients with DKD who initiate empagliflozin)
  - Need lab data
  - Need long-term outcomes
- Methodologic issues around ascertainment of medication discontinuation and switching with EHR data

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Landscape analysis of CKD screening and management

Objective: To determine adherence to screening guidelines for DKD among patients with T2D, and to determine adherence to management guidelines for patients with DKD

Setting: 20 PCORnet sites

Population: Adults with T2D (with or without kidney disease) in the U.S.

Lipid testing and management in patients with ASCVD

Objective: To determine LDL-C and Lp(a) testing and management practices and gaps in care among patients with ASCVD in the U.S.

Setting: 6 PCORnet sites

Population: Adults with established ASCVD

Key Points

- Many different types of observational studies are possible with PCORnet
- One of the only data resources with granular clinical data, lab data, LARGE sample sizes
- Our process of working with sites to collect and refine the data have improved over time
- Collaborative academic partnership with sites is key

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Prospective Clinical Trials

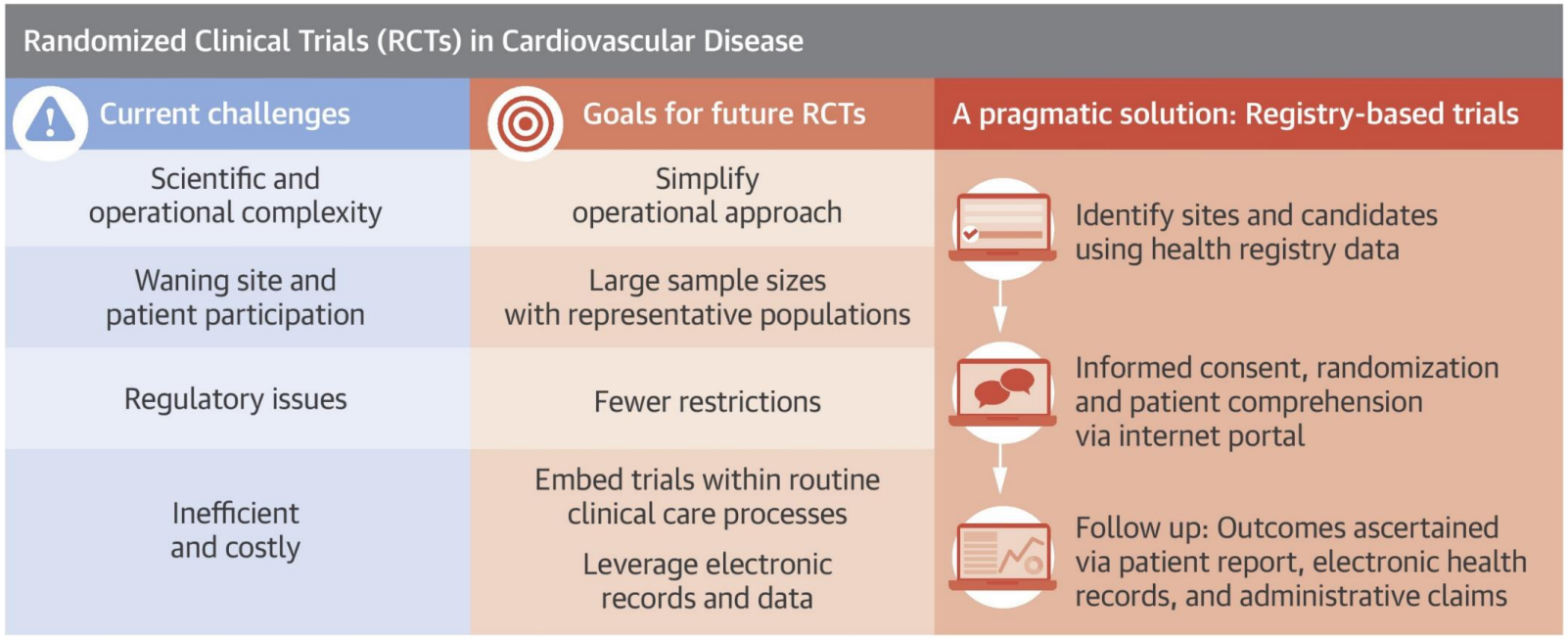
W. Schuyler Jones, MD
Associate Professor of Medicine
Duke Clinical Research Institute

JACC Journals

From: **The Changing Landscape of Randomized Clinical Trials in Cardiovascular Disease**

J Am Coll Cardiol. 2016;68(17):1898-1907. doi:10.1016/j.jacc.2016.07.781

CENTRAL ILLUSTRATION: U.S. Landscape of Randomized Clinical Trials in Cardiovascular Disease



Jones, W.S. et al. J Am Coll Cardiol. 2016;68(17):1898-907.

- Large
- Generalizable
- Efficient
  - Engage clinicians
  - Engage participants
  - Use of available data
  - Electronic consent
  - Complete ascertainment
- Patient partnered
- Results that matter

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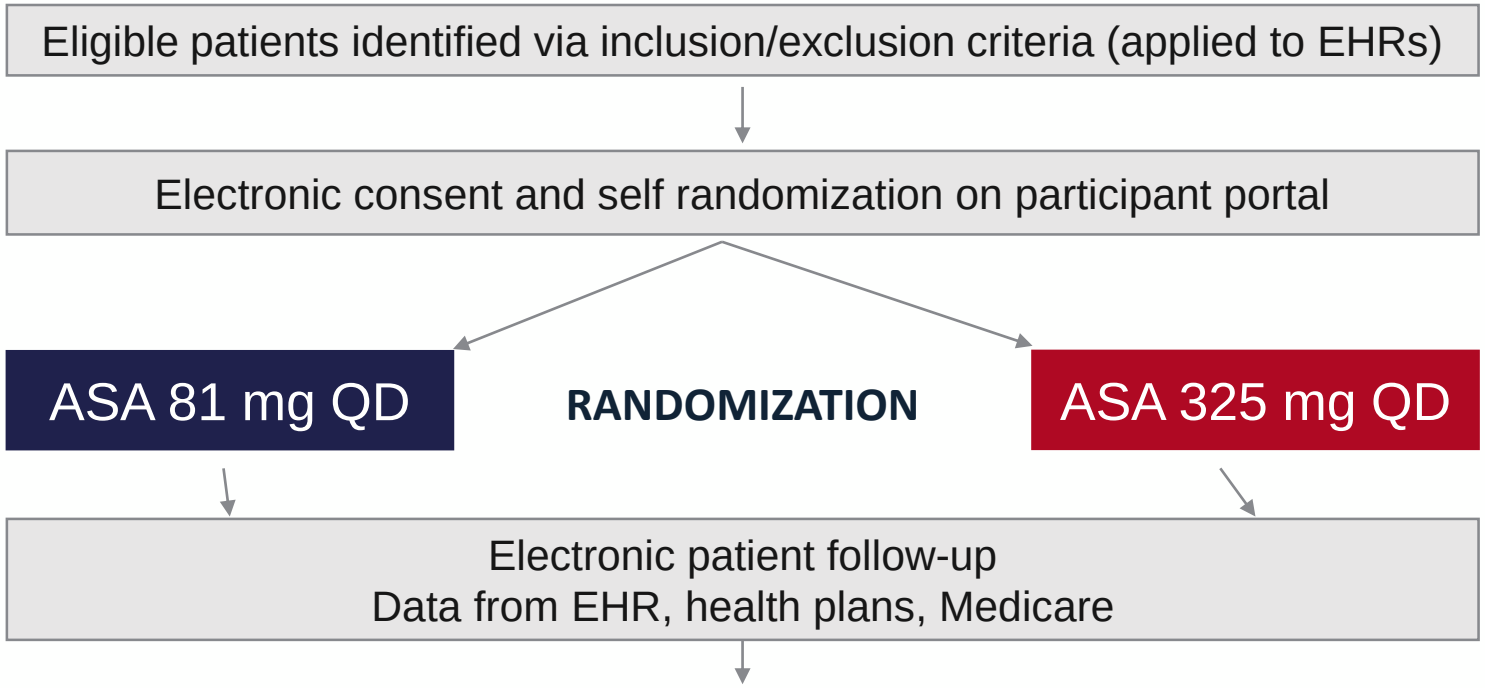
ADAPTABLE Study Design

15,000 patients with known ASCVD + ≥ 1 “enrichment factor”



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

Primary Safety Endpoint:
Hospitalization for major bleeding

ClinicalTrials.gov: NCT02697916

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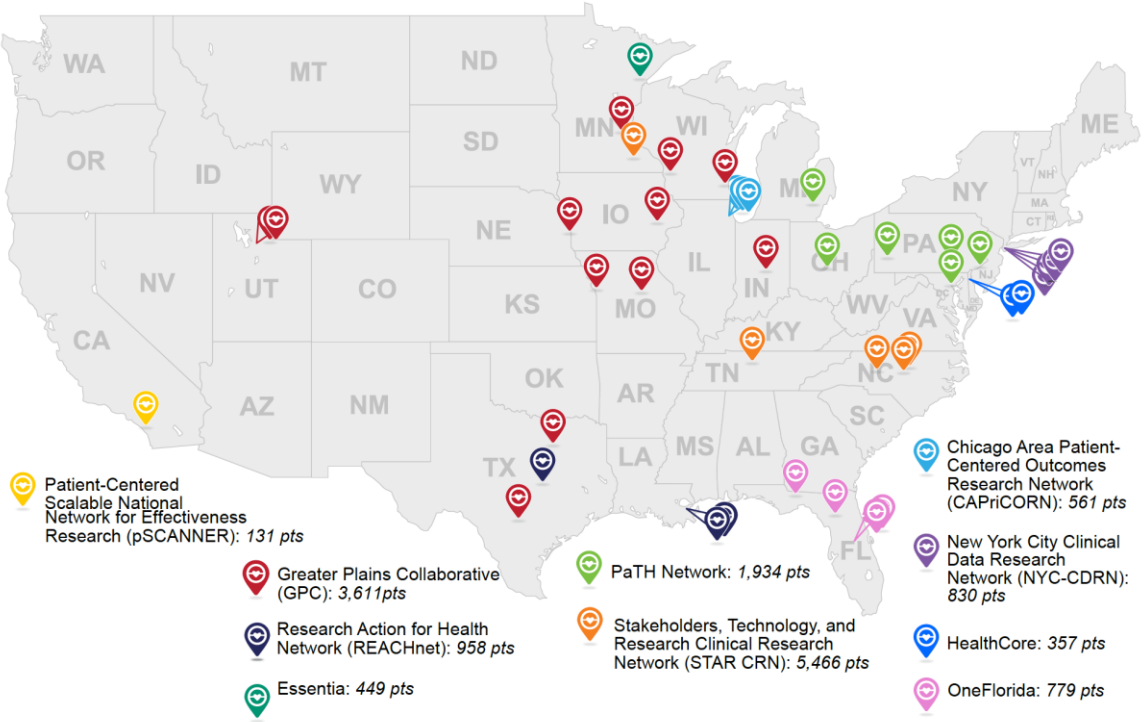
PCORnet® was under construction

2015-2016

40 Study Centers within PCORnet®



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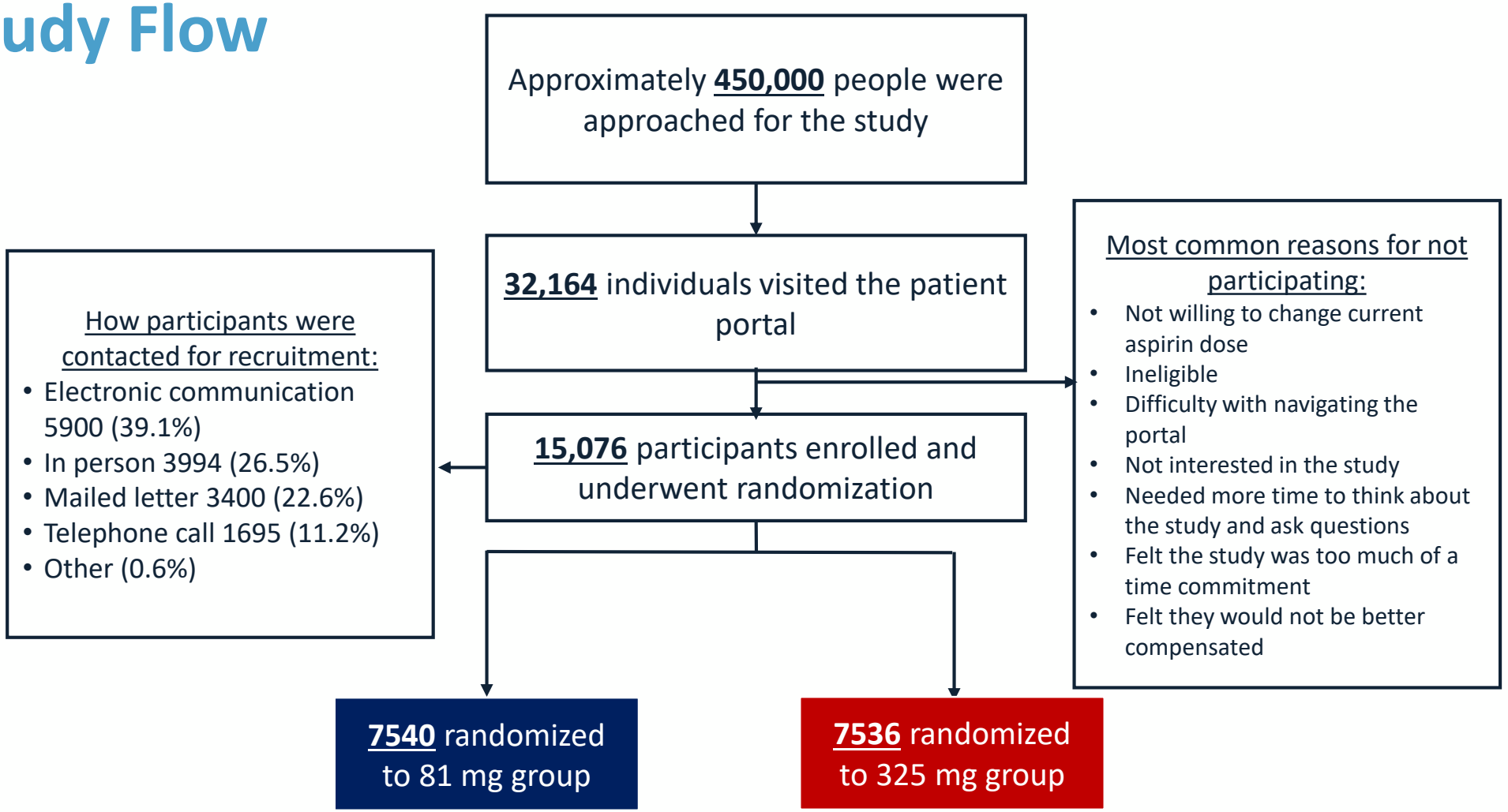
Study Flow



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Electronic Data Collection and Follow-Up

ADAPTABLE enrollee

Baseline data

Web portal follow-up
- *Randomized to 3 vs 6 mos contact*
- *Patient-reported hospitalizations*
- *Medication use*
- *Health outcomes*

DCRI call center
- *Patients who miss 2 contacts*
- *Patients without internet access*
- *Validated coding algorithms for endpoints*

PCORnet Coordinating Center follow-up
- *Via Common Data Model*
- *Validated coding algorithms for endpoints*

CMS and private health plans follow-up
- *Longitudinal health outcomes*
- *Validated coding algorithms for endpoints*

Death Ascertainment

- CDM and Social Security Databases
- Alternate contacts via DCRI Call Center

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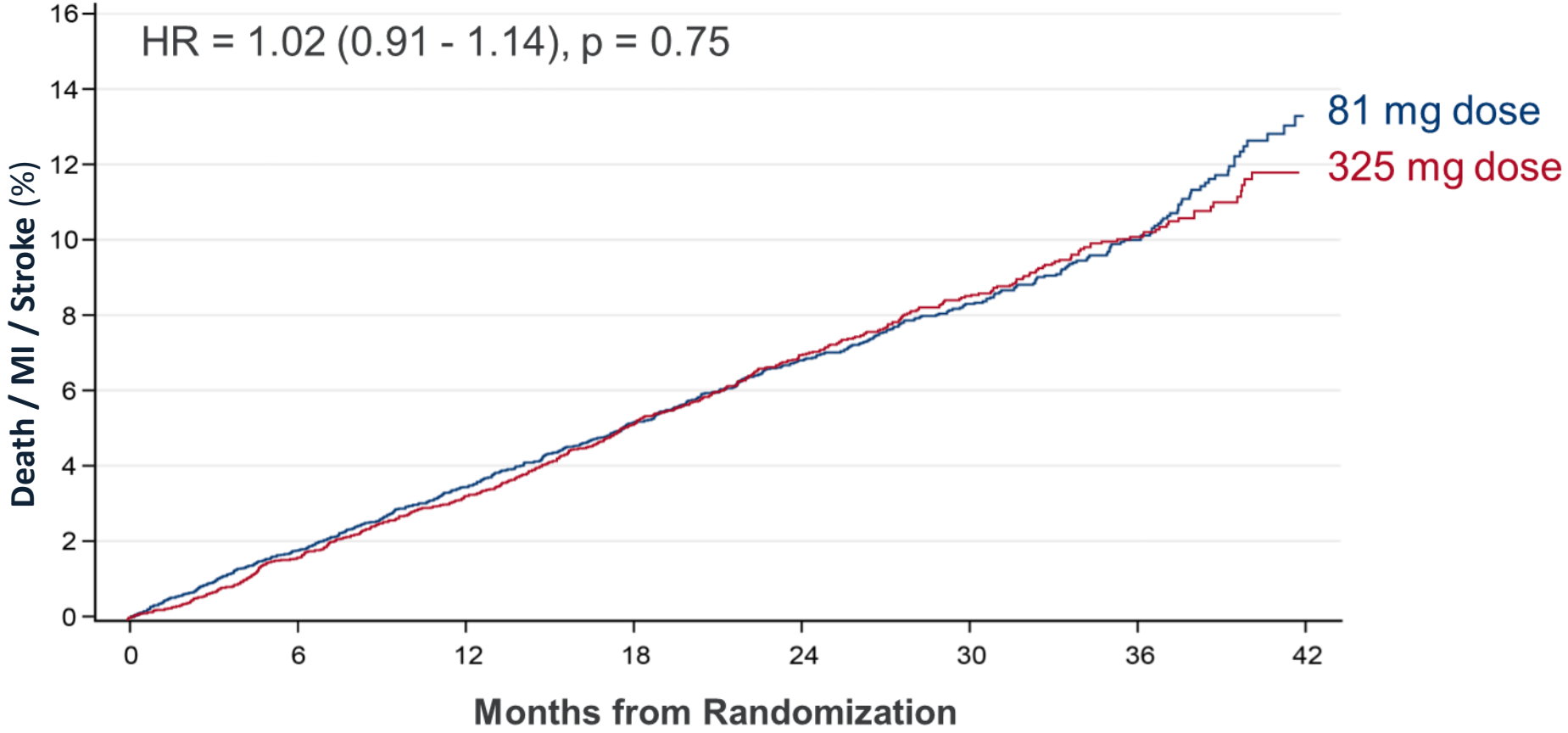
Primary Effectiveness Endpoint

(All-cause death, hospitalization for MI, or hospitalization for stroke)

Caveats
- Open label
- Dose switching



At risk								
81 mg dose	7540	7357	7177	5627	4190	2712	1558	636
325 mg dose	7536	7297	7095	5544	4090	2613	1489	592

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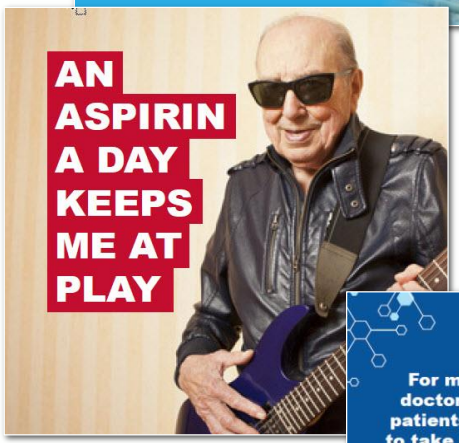
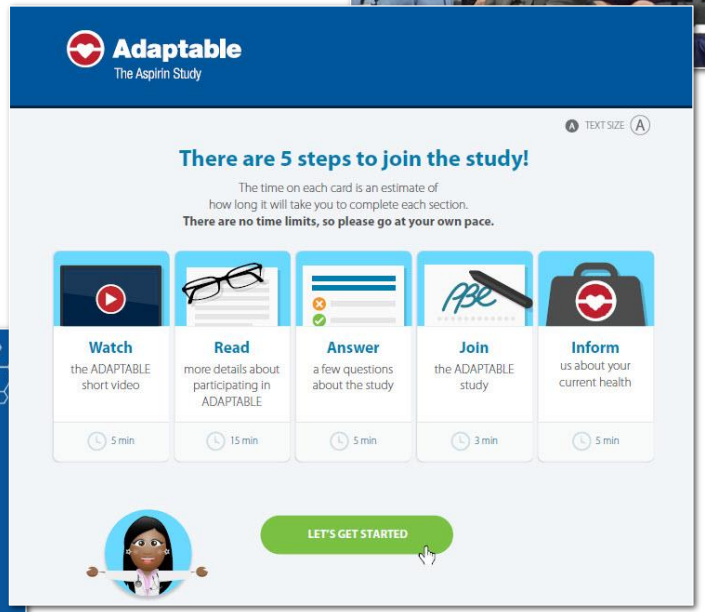
Patient Engagement

Patient blogs



Facebook Lives

Patient Engagement Pavilion



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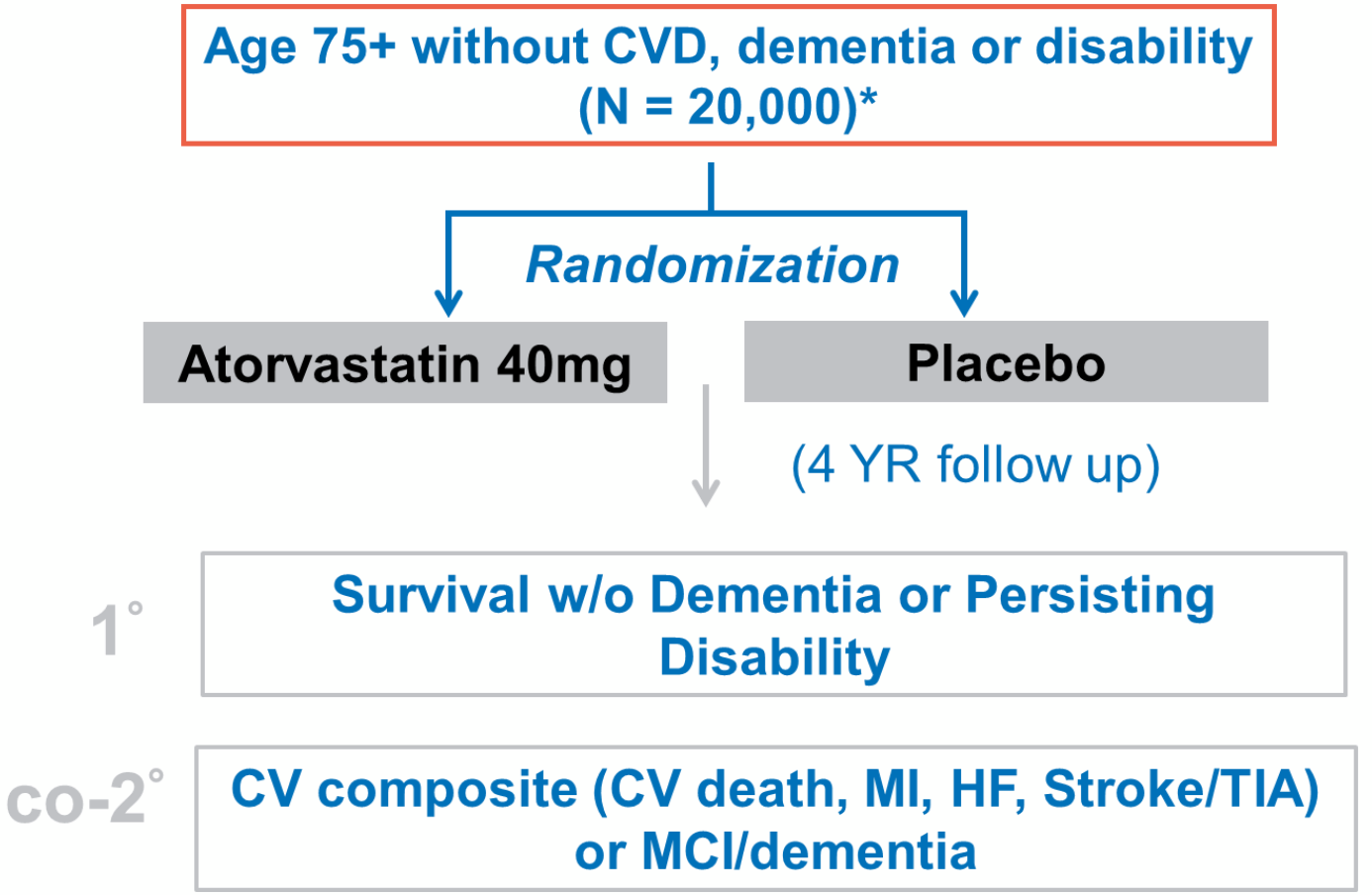
PREVENTABLE



** Include risk for MCI or Frailty by Computable Phenotype*

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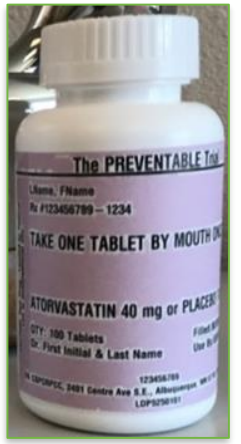
Study Drug



- **High-intensity statin**
  - Generic atorvastatin 40 mg (Same as STAREE Trial)1
  - No differences in safety or effectiveness were observed in Lipitor® trials among the 7% of participants aged ≥75 years (2,800/39,828)
  - IND Exemption: “well-known drug”, used as labelled, no intention to seek label change
- **Placebo-controlled design**
  - Unbiased reporting of drug-associated safety concerns/ events
  - Less competing therapies in open-label no-statin arm
- **Home Delivery**
  - VA Cooperative Studies Pharmacy

UNITED STATES POSTAL SERVICE®

[1] NCT02099123 https://www.staree.org.au/.

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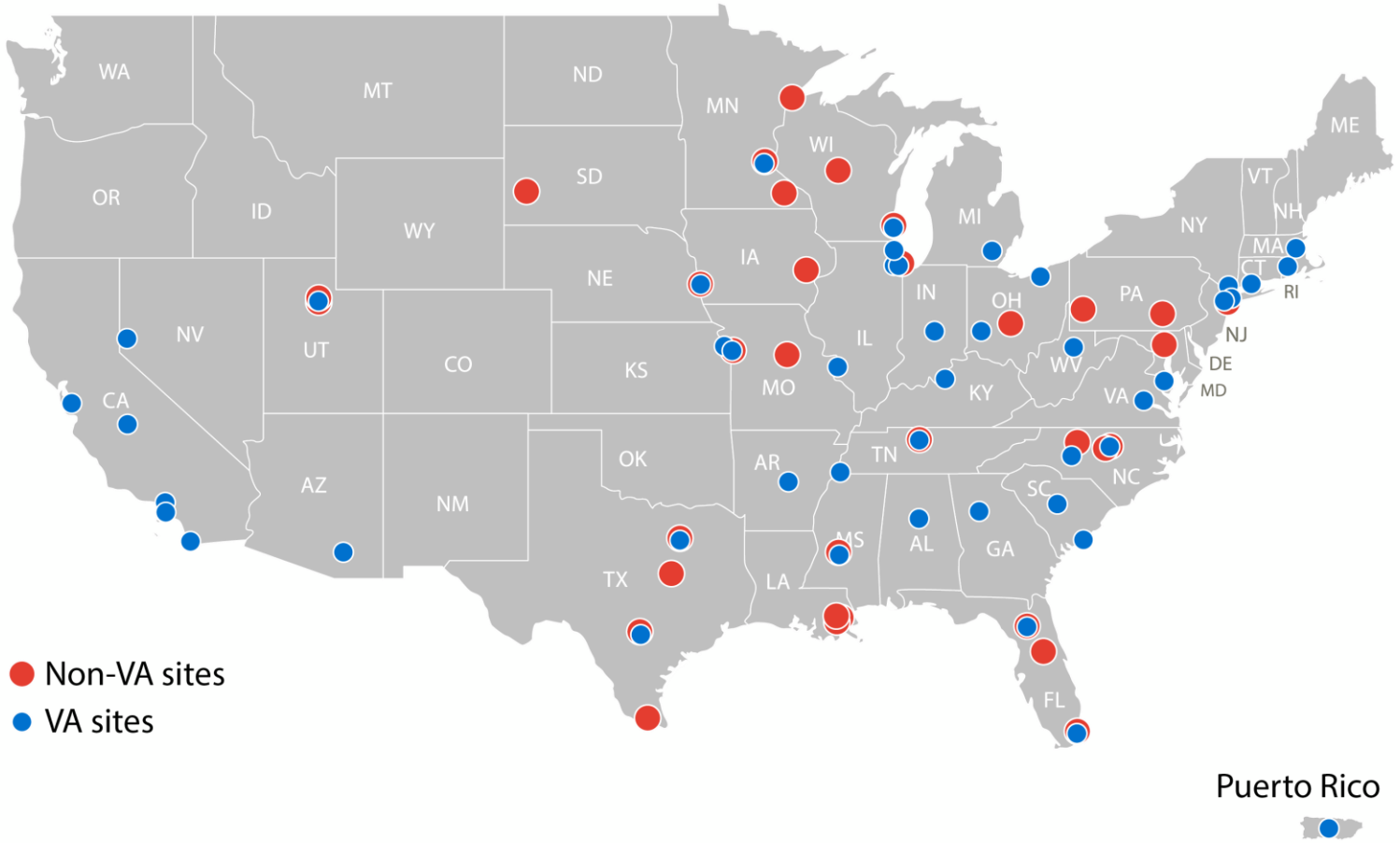
Study Sites

Approximately 90 sites from PCORnet (non-VA) and BVARI (VA) will participate.



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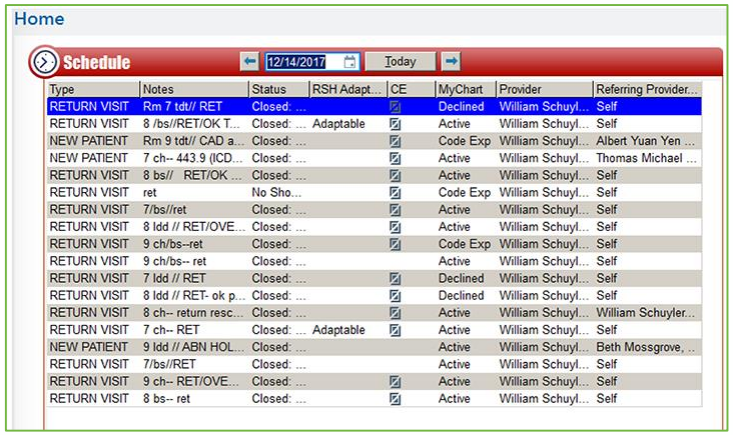
Recruitment Takes Teamwork

Clinical Team
PI(s) + CRC(s)

Informatics Team
CDRN/CDM



Type	Notes	Status	RSH Adapt...	CE	MyChart	Provider	Referring Provider...
RETURN VISIT	Rm 7 tdt// RET	Closed: ...			Declined	William Schuyl...	Self
RETURN VISIT	8 /bs//RET/OK T...	Closed: ...	Adaptable		Active	William Schuyl...	Self
NEW PATIENT	Rm 9 tdt// CAD a...	Closed: ...			Code Exp	William Schuyl...	Albert Yuan Yen ...
NEW PATIENT	7 ch-- 443.9 (ICD...	Closed: ...			Active	William Schuyl...	Thomas Michael ...
RETURN VISIT	8 bs// RET/OK ...	Closed: ...			Active	William Schuyl...	Self
RETURN VISIT	ret	No Sho...			Code Exp	William Schuyl...	Self
RETURN VISIT	7/bs//ret	Closed: ...			Active	William Schuyl...	Self
RETURN VISIT	8 ldd // RET/OVE...	Closed: ...			Active	William Schuyl...	Self
RETURN VISIT	9 ch/bs--ret	Closed: ...			Code Exp	William Schuyl...	Self
RETURN VISIT	9 ch/bs-- ret	Closed: ...			Active	William Schuyl...	Self
RETURN VISIT	7 ldd // RET	Closed: ...			Declined	William Schuyl...	Self
RETURN VISIT	8 ldd // RET- ok p...	Closed: ...			Declined	William Schuyl...	Self
RETURN VISIT	8 ch-- return resc...	Closed: ...			Active	William Schuyl...	William Schuyler...
RETURN VISIT	7 ch-- RET	Closed: ...	Adaptable		Active	William Schuyl...	Self
NEW PATIENT	9 ldd // ABN HOL...	Closed: ...			Active	William Schuyl...	Beth Mossgrove, ...
RETURN VISIT	7/bs//RET	Closed: ...			Active	William Schuyl...	Self
RETURN VISIT	9 ch-- RET/OVE...	Closed: ...			Active	William Schuyl...	Self
RETURN VISIT	8 bs-- ret	Closed: ...			Active	William Schuyl...	Self

EHR Programming

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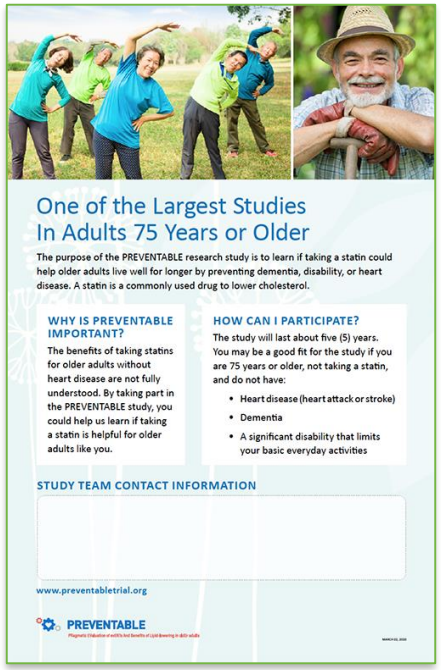
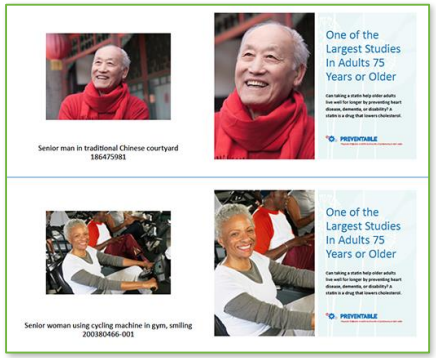
Recruitment Materials

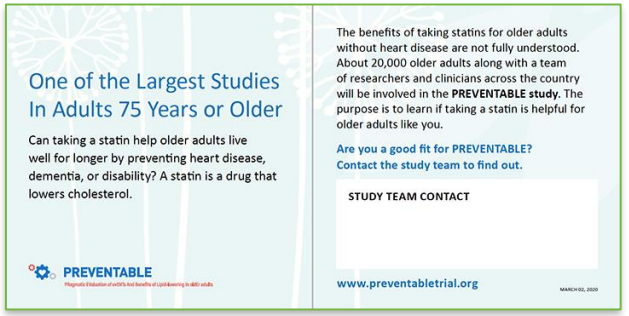
Materials

- Poster
- Flyer
- Curated images
- Brochures
- Wallet card
- Participant recruitment letter
- MyChart message
- Library of images to customize templates

Site access through study website







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Endpoint Ascertainment

Use multiple sources for endpoint ascertainment

PRIMARY ENDPOINT
MCI/dementia, disability

Call Center
+
Hawthorne Effect
(if triggered)

KEY SECONDARY ENDPOINTS:
CV outcomes
(MI, UA, stroke, HF hosp)

CDM (datamarts)
EHR queries
CMS queries

DEATH:
(cause-specific)

National Death Index
Site death narrative

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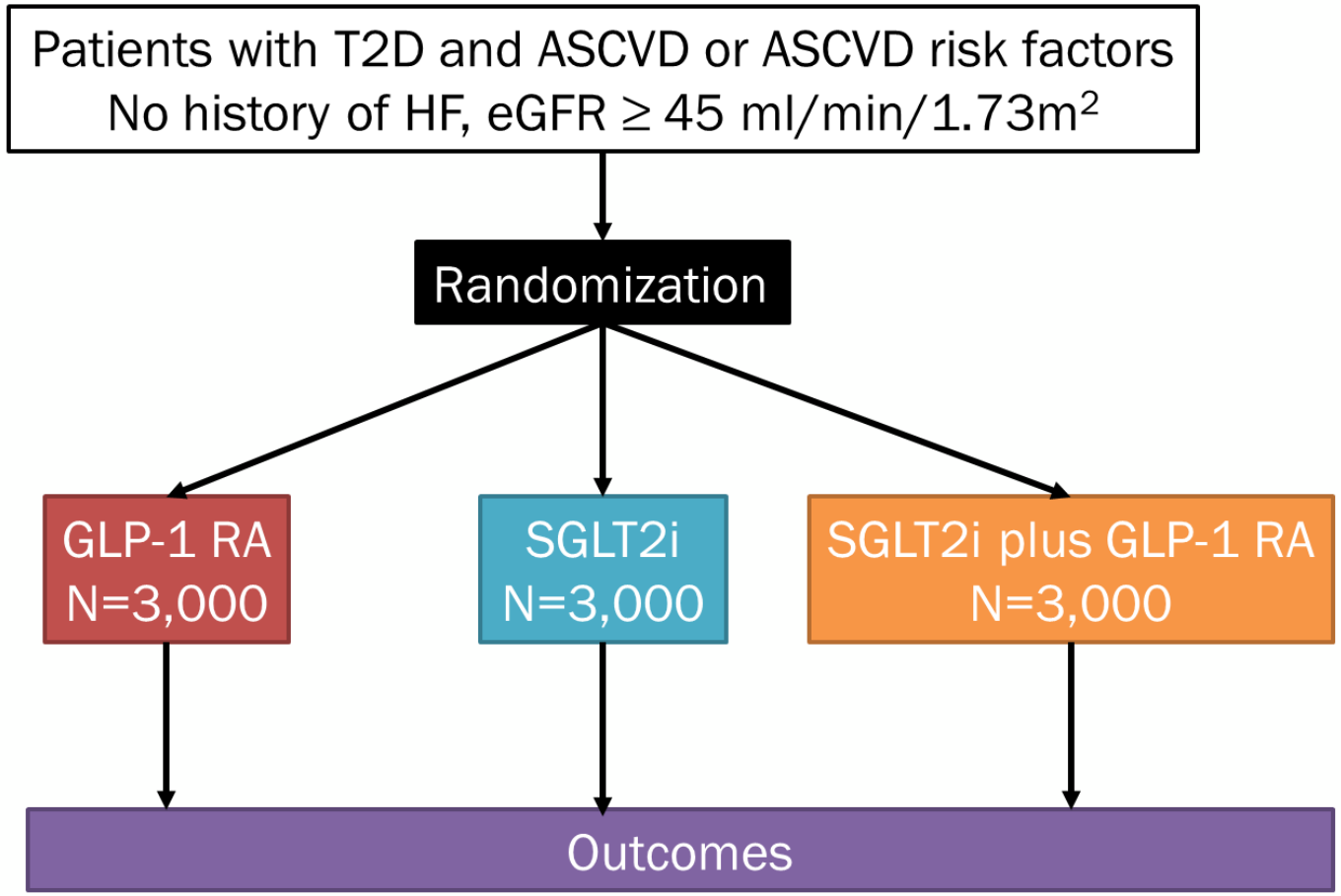
PRECIDENT D: Study Design



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Intervention

- **Random allocation to SGLT2i, GLP-1 RA, or the combination**

- **Site investigator will write a prescription for whichever drug in the assigned class is covered by the patient's benefit plan and help start the participant on medication**

- **Allowed members of each class:**
  - **SGLT2i: empagliflozin, dapagliflozin, or canagliflozin**
  - **GLP-1 RA: dulaglutide, liraglutide, semaglutide (SC or PO)**

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Primary Visit Coverage

Payer	Plan	Sponsor Code	Group Number	Group Name
MEDICARE	MEDICARE A AND B		NO GRP	

Primary Visit Coverage Subscriber

Secondary Visit Coverage

Payer	Plan	Sponsor Code	Group Number	Group Name
UNITED HEALTHCARE CONTRACT	AARP MEDICARE SUPPLEMENT		PLAN	united

After Visit Medications

		Name	Dose	Freque...	Dis...	Ref	End D...	Formulary	Copay	Coverage
		semaglutide 0.25 mg or 0.5mg (OZ...		Weekly			S+30	Preferred L...	Retail: T3/5	Quantity Li...
		semaglutide 1 mg/dose (OZEMPIC)...	1 mg	Weekly	1.5...		S+30	Unknown		

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Thank you.

Work with PCORnet.

Visit us at www.pcornet.org
to get the relationship started.