

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

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)



- [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




Populations

- Improving outcomes for people with intellectual or developmental disabilities
- Promoting health for older adults
- Promoting healthy children and youth



Health Behaviors

- Addressing substance use
- Addressing violence and trauma



Health Conditions

- Addressing COVID-19
- Addressing rare diseases
- Improving cardiovascular health
- Improving mental and behavioral health
- Managing pain
- Preventing maternal morbidity and mortality
- Promoting sleep health

Overview

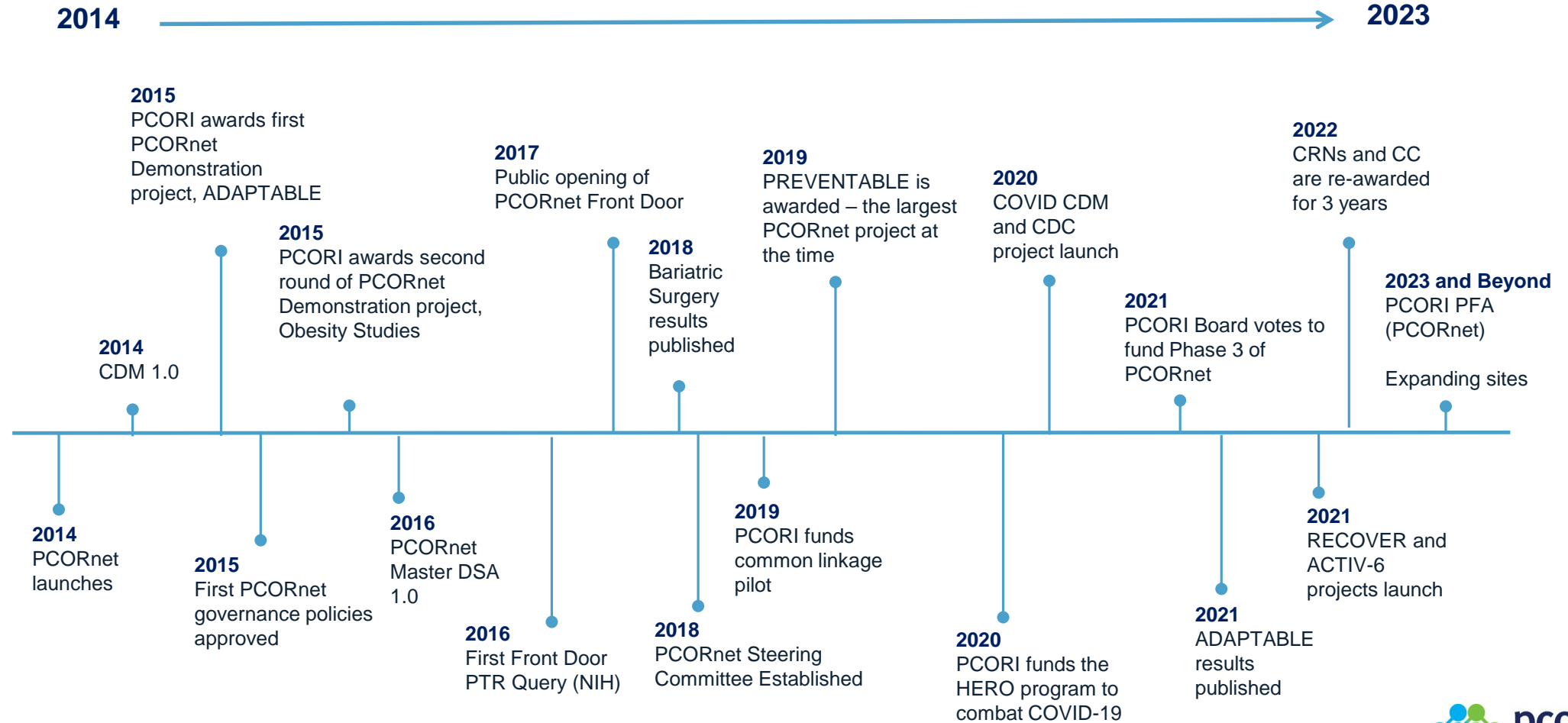


Russell Rothman, MD, MPP

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.



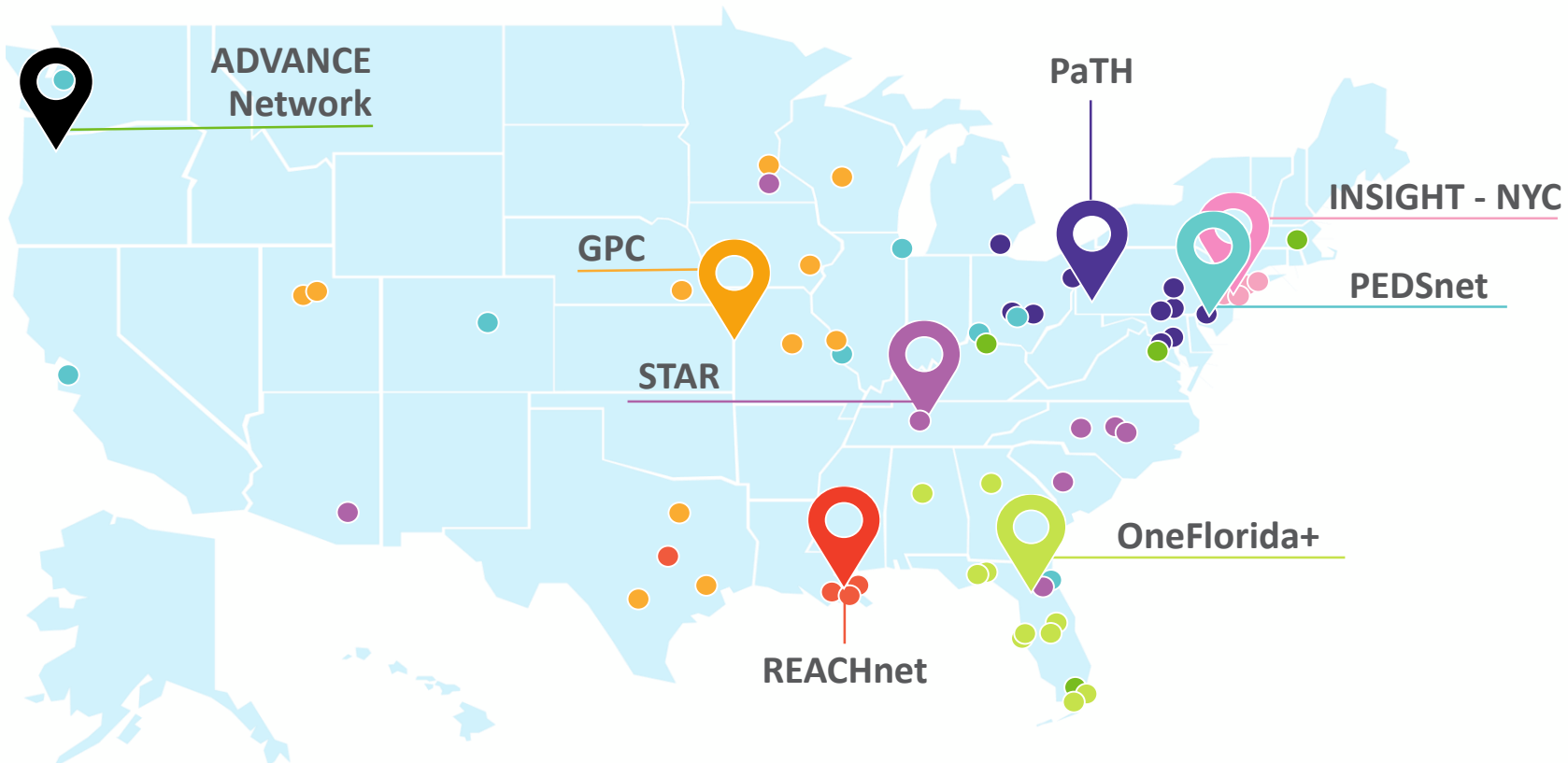
Patients and caregivers are integrated into all phases of PCORnet-enabled research

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.

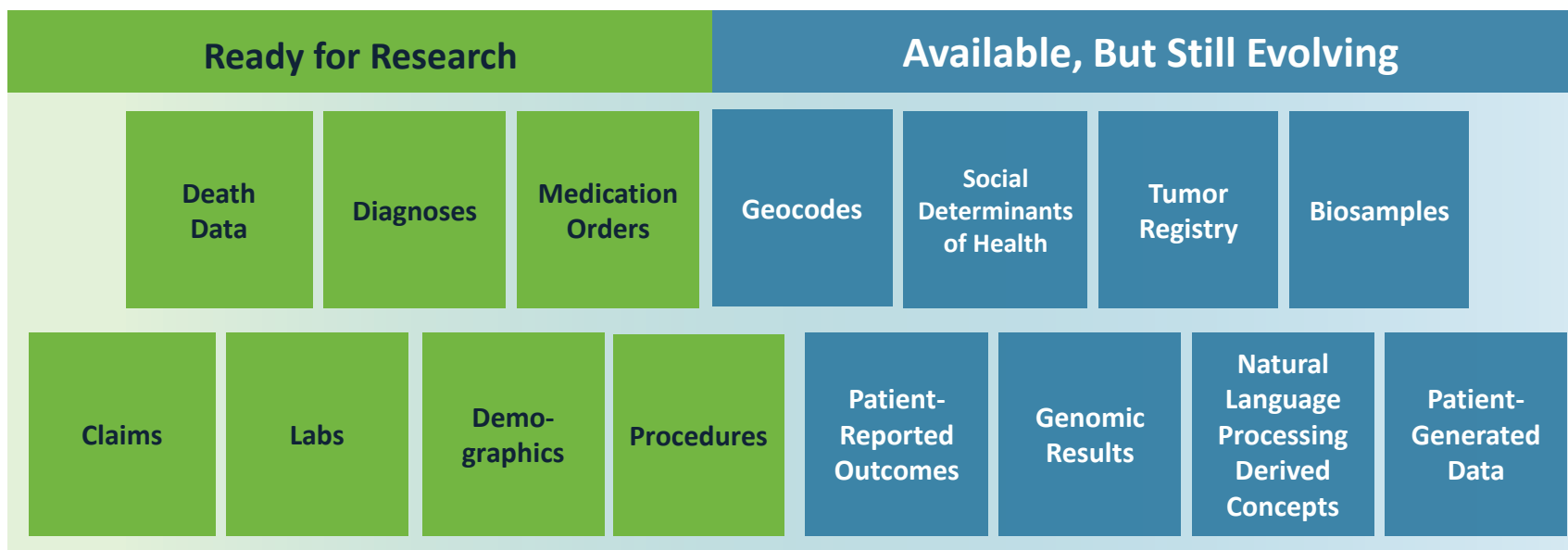
PCORnet® Clinical Research Networks (CRNs)

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.



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:



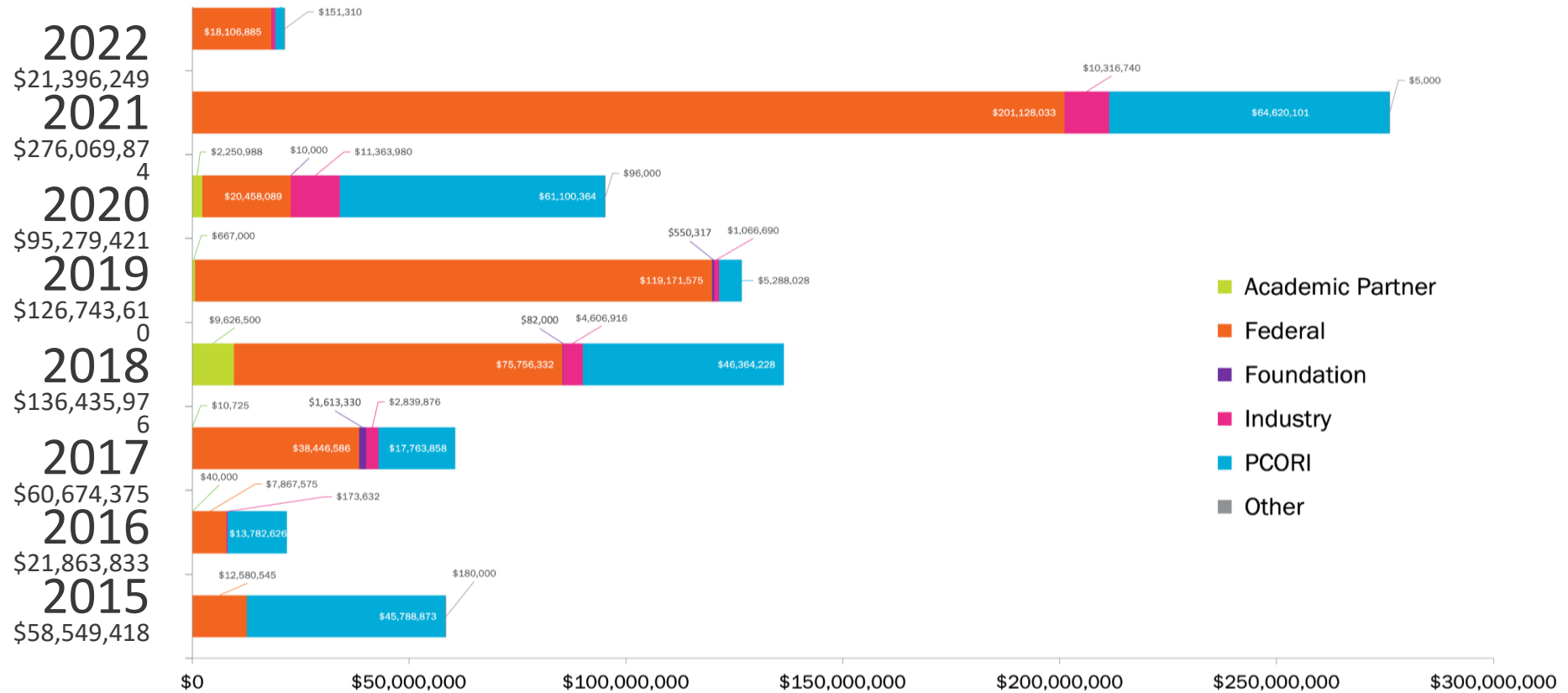
Data available from several Clinical Research Networks, in the PCORnet Common Data Model and ready for use in research.

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.

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

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

pcornet[®]
The National Patient-Centered Clinical Research Network

About Governance Resources Newsroom

NETWORK RESEARCH DATA ENGAGEMENT **FRONT DOOR**

Front Door

How do you partner with PCORnet?
PCORnet is a national resource available to everyone.

The Front Door is an access point for potential investigators, patient groups, healthcare organizations, clinicians and clinician groups, government, industry scientists, sponsors, and all stakeholders seeking to leverage PCORnet infrastructure and collaborate on patient-centered research.

[CONTACT THE FRONT DOOR](#)

Knock on the Front Door to Begin Collaborating with PCORnet

pcornet[®]
The National Patient-Centered Clinical Research Network

02:41

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

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

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

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

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

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

Prospective Clinical Trials








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

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

Randomized Clinical Trials (RCTs) in Cardiovascular Disease		
 Current challenges	 Goals for future RCTs	A pragmatic solution: Registry-based trials
Scientific and operational complexity	Simplify operational approach	 Identify sites and candidates using health registry data
Waning site and patient participation	Large sample sizes with representative populations	 Informed consent, randomization and patient comprehension via internet portal
Regulatory issues	Fewer restrictions	 Follow up: Outcomes ascertained via patient report, electronic health records, and administrative claims
Inefficient and costly	Embed trials within routine clinical care processes Leverage electronic records and data	

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

ADAPTABLE Study Design

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

Eligible patients identified via inclusion/exclusion criteria (applied to EHRs)

Electronic consent and self randomization on participant portal

ASA 81 mg QD

RANDOMIZATION

ASA 325 mg QD

Electronic patient follow-up
Data from EHR, health plans, Medicare

Primary Endpoint:

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

Primary Safety Endpoint:

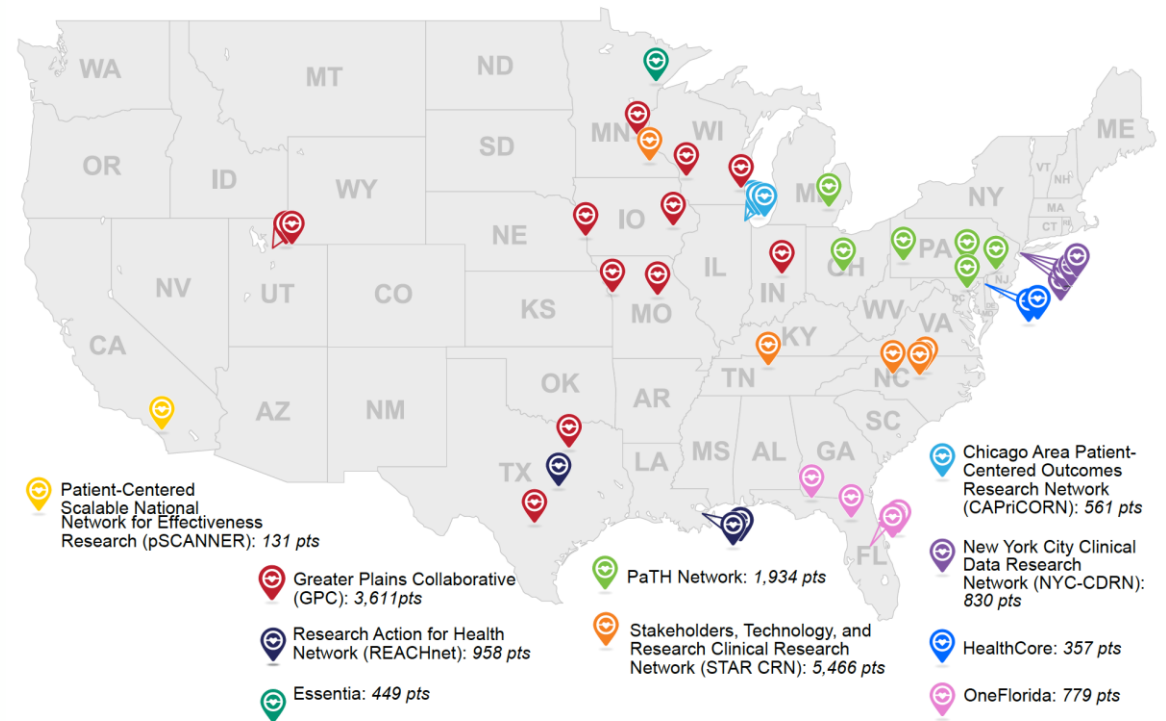
Hospitalization for major bleeding

PCORnet® was under construction

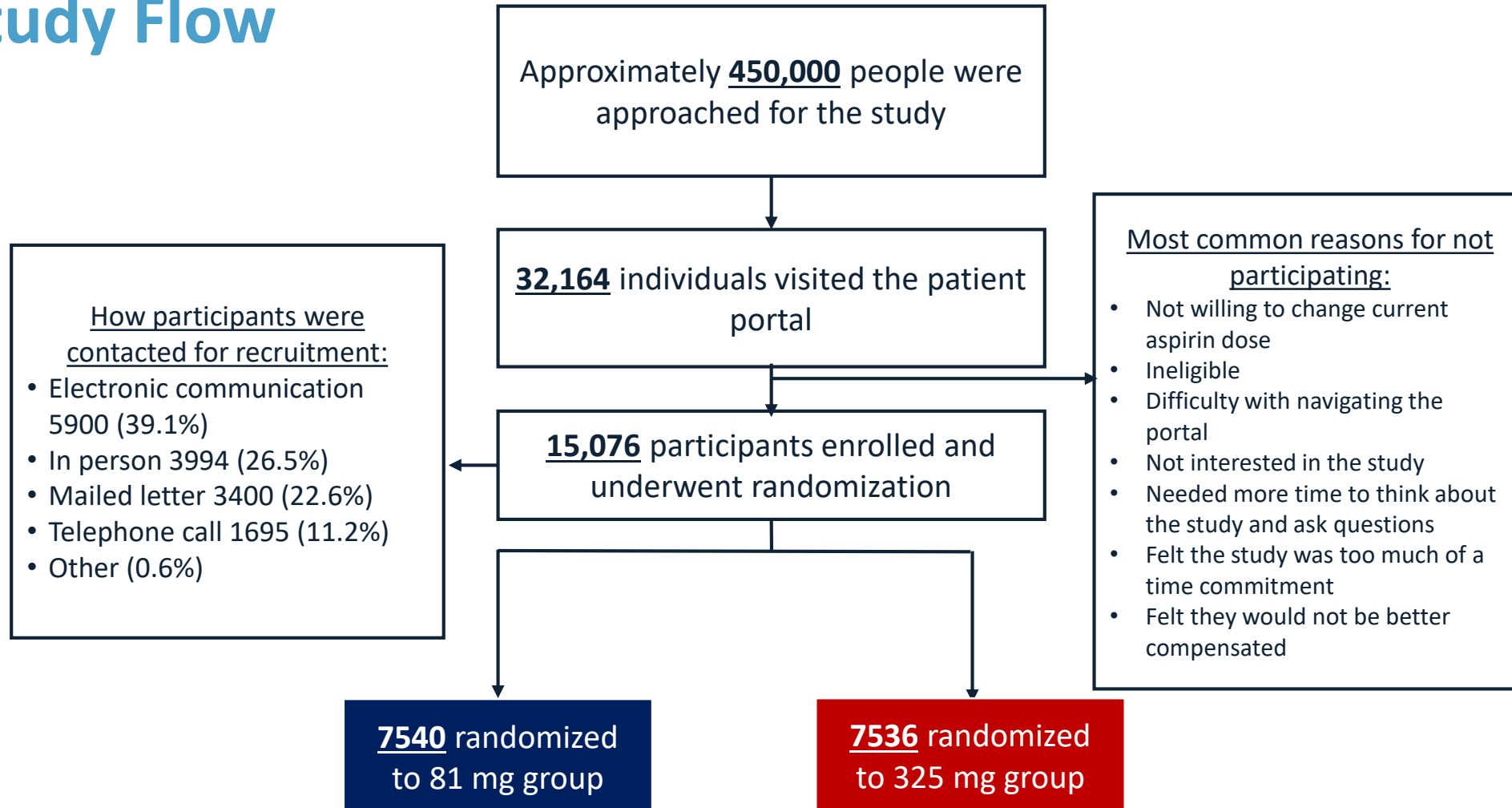


2015-2016

40 Study Centers within PCORnet®



Study Flow



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*

Death Ascertainment

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



PCORnet Coordinating Center follow-up

- *Via Common Data Model*
- *Validated coding algorithms for endpoints*



CMS and private health plans follow-up

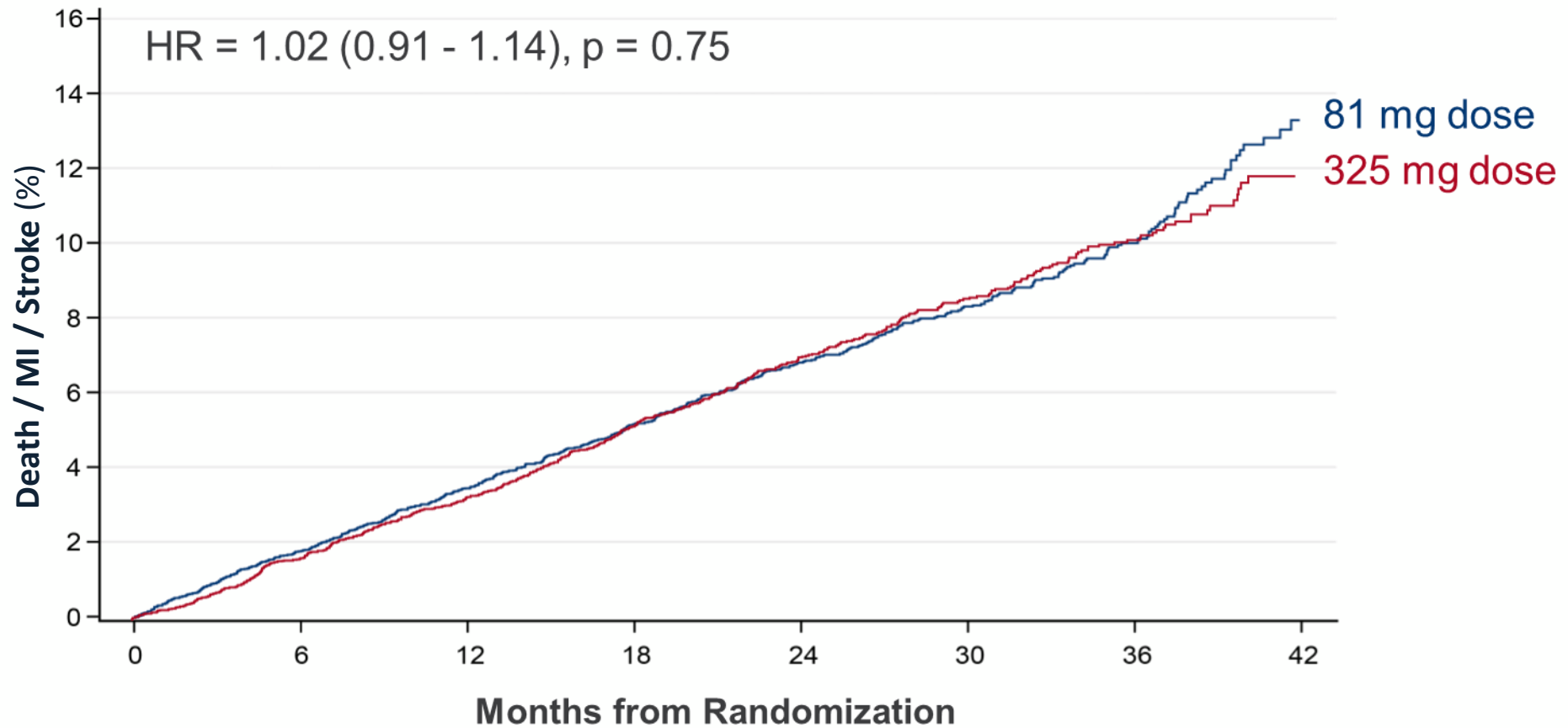
- *Longitudinal health outcomes*
- *Validated coding algorithms for endpoints*

Primary Effectiveness Endpoint

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

Caveats

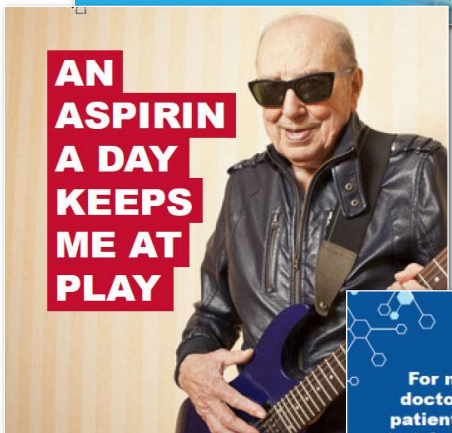
- Open label
- Dose switching



	At risk	0	6	12	18	24	30	36	42
81 mg dose	7540	7357	7177	5627	4190	2712	1558	636	
325 mg dose	7536	7297	7095	5544	4090	2613	1489	592	

Patient Engagement

Patient blogs



For more than 40 years, doctors have been telling patients with heart disease to take aspirin. Now there is a nationwide study to determine the best dose of aspirin to prevent heart attacks or strokes for these patients.

The Adaptable team of local UFHealth researchers invites you to be part of the answer.

If you are **18 years** or older, can safely take **aspirin** and have been diagnosed with **heart disease**, you may qualify.

Study enrollment and followup will be done entirely **online** or over the **phone**. You will not have to visit a clinic for the study.

Facebook Lives



Patient Engagement Pavilion



Adaptable
The Aspirin Study

TEXT SIZE (A)

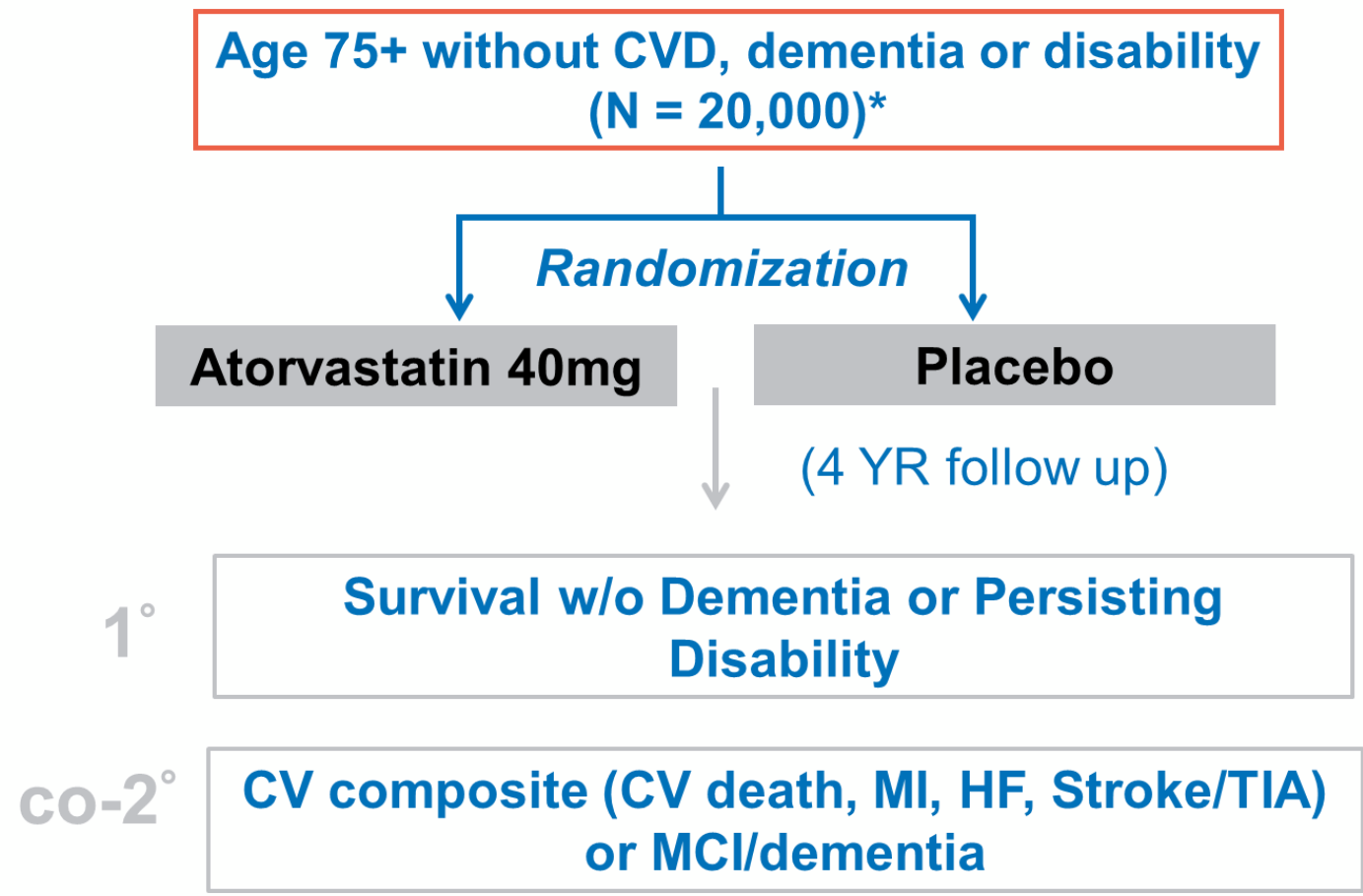
There are 5 steps to join the study!

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.

Step	Icon	Description	Time
1	Play button	Watch the ADAPTABLE short video	5 min
2	Glasses	Read more details about participating in ADAPTABLE	15 min
3	Checklist	Answer a few questions about the study	5 min
4	Stethoscope	Join the ADAPTABLE study	3 min
5	Medical bag	Inform us about your current health	5 min

LET'S GET STARTED

PREVENTABLE



* Include risk for MCI or Frailty by Computable Phenotype

Study Drug

- **High-intensity statin**

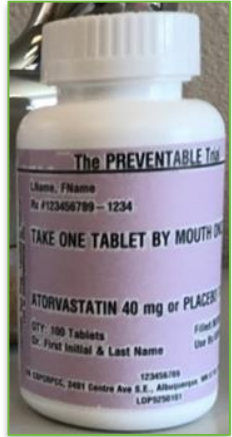
- Generic atorvastatin 40 mg (Same as STAREE Trial)¹
- No differences in safety or effectiveness were observed in Lipitor® trials among the 7% of participants aged ≥ 75 years (2,800/39,828)
- IND Exemption: “well-known drug”, used as labelled, no intention to seek label change

- **Placebo-controlled design**

- Unbiased reporting of drug-associated safety concerns/ events
- Less competing therapies in open-label no-statin arm

- **Home Delivery**

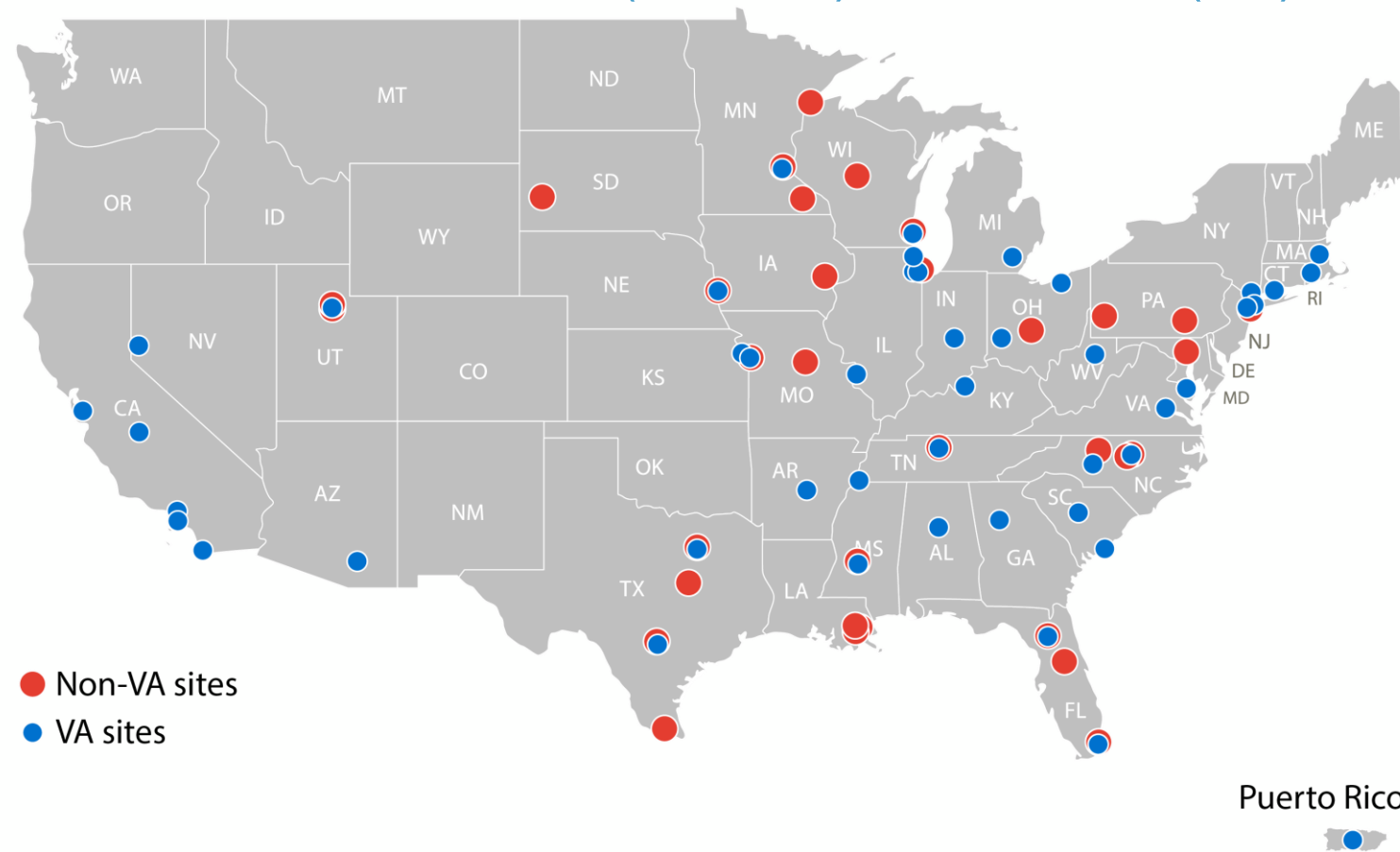
- VA Cooperative Studies Pharmacy



¹ NCT02099123 <https://www.staree.org.au/>.

Study Sites

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



Recruitment Takes Teamwork



Clinical Team
PI(s) + CRC(s)



Informatics Team
CDRN/CDM

Home

Schedule 12/14/2017 Today

Type	Notes	Status	RSH Adapt...	CE	MyChart	Provider	Referring Provider...
RETURN VISIT	Rm 7 tdt// RET	Closed			Declined	William Schuy...	Self
RETURN VISIT	8 /bs//RET/OK T...	Closed	Adaptable		Active	William Schuy...	Self
NEW PATIENT	Rm 9 tdt// CAD a...	Closed			Code Exp	William Schuy...	Albert Yuan Yen ...
NEW PATIENT	7 ch-- 443 9 (ICD...	Closed			Active	William Schuy...	Thomas Michael ...
RETURN VISIT	8 bs// RET/OK ...	Closed			Active	William Schuy...	Self
RETURN VISIT	ret	No Sho...			Code Exp	William Schuy...	Self
RETURN VISIT	7bs//ret	Closed			Active	William Schuy...	Self
RETURN VISIT	8 ldd // RET/OVE...	Closed			Active	William Schuy...	Self
RETURN VISIT	9 ch/bs--ret	Closed			Code Exp	William Schuy...	Self
RETURN VISIT	9 ch/bs--ret	Closed			Active	William Schuy...	Self
RETURN VISIT	7 ldd // RET	Closed			Declined	William Schuy...	Self
RETURN VISIT	8 ldd // RET-ok p...	Closed			Declined	William Schuy...	Self
RETURN VISIT	8 ch-- return resc...	Closed			Active	William Schuy...	William Schuyler...
RETURN VISIT	7 ch-- RET	Closed	Adaptable		Active	William Schuy...	Self
NEW PATIENT	9 ldd // ABN HOL...	Closed			Active	William Schuy...	Beth Mossgrove...
RETURN VISIT	7bs//RET	Closed			Active	William Schuy...	Self
RETURN VISIT	9 ch-- RET/OVE...	Closed			Active	William Schuy...	Self
RETURN VISIT	8 bs--ret	Closed			Active	William Schuy...	Self

EHR
Programming

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

One of the Largest Studies In Adults 75 Years or Older

The purpose of the PREVENTABLE research study is to learn if taking a statin could help older adults live well for longer by preventing dementia, disability, or heart disease. A statin is a commonly used drug to lower cholesterol.

WHY IS PREVENTABLE IMPORTANT?
The benefits of taking statins for older adults without heart disease are not fully understood. By taking part in the PREVENTABLE study, you could help us learn if taking a statin is helpful for older adults like you.

HOW CAN I PARTICIPATE?
The study will last about five (5) years. You may be a good fit for the study if you are 75 years or older, not taking a statin, and do not have:

- Heart disease (heart attack or stroke)
- Dementia
- A significant disability that limits your basic everyday activities

STUDY TEAM CONTACT INFORMATION

www.preventabletrial.org

PREVENTABLE
Prevention of dementia, disability and heart disease in older adults

One of the Largest Studies In Adults 75 Years or Older

Senior man in traditional Chinese courtyard
186475981

One of the Largest Studies In Adults 75 Years or Older

Senior woman using cycling machine in gym, smiling
200380466 001

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FIND OUT MORE...

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FIND OUT MORE...

[Mailing Address]

One of the Largest Studies In Adults 75 Years or Older

Can taking a statin help older adults live well for longer by preventing heart disease, dementia, or disability? A statin is a drug that lowers cholesterol.

The benefits of taking statins for older adults without heart disease are not fully understood. About 20,000 older adults along with a team of researchers and clinicians across the country will be involved in the PREVENTABLE study. The purpose is to learn if taking a statin is helpful for older adults like you.

Are you a good fit for PREVENTABLE? Contact the study team to find out.

STUDY TEAM CONTACT

www.preventabletrial.org

PREVENTABLE
Prevention of dementia, disability and heart disease in older adults

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)



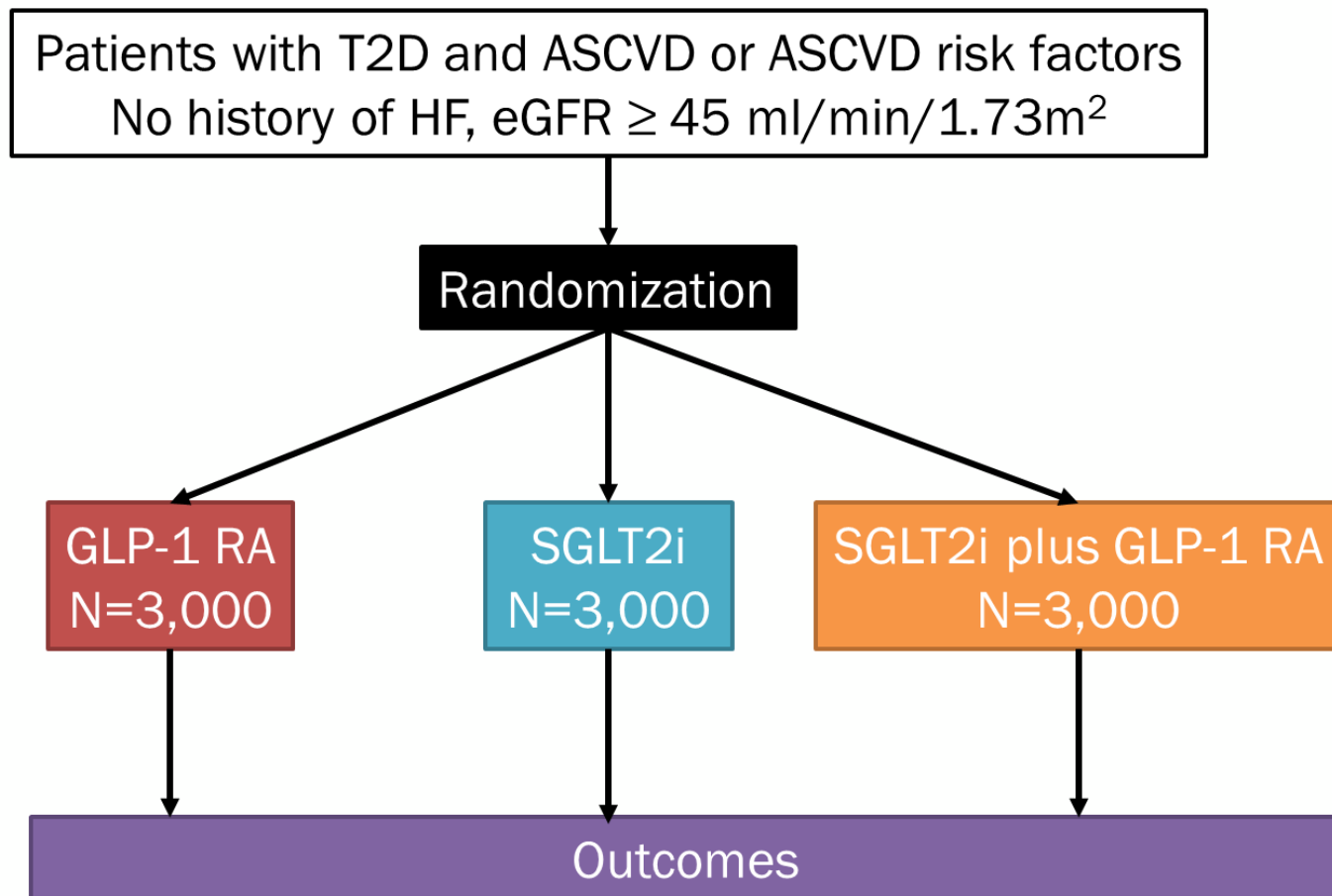
CDM (datamarts)
EHR queries
CMS queries

DEATH:
(cause-specific)



National Death Index
Site death narrative

PRECIDENT D: Study Design



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)

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	Frequ...	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		

Thank you.



Work with PCORnet.

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