ADAPTABLE Recruitment and Follow-up Health Plan Research Network Engagement

Kevin Haynes, PharmD, MSCE

Adaptable

The Aspirin Study

pcornet

Follow us on Twitter @**ADAPTABLEstudy**

ClinicalTrials.gov: NCT02697916

Outline

- HealthCore/Anthem Overview
- ADAPTABLE Health Plan Engagement
  - Validation of Computable Phenotype
  - Health Plan Recruitment Activities
  - Longitudinal Outcome Ascertainment
- Next Steps in Health Plan PCORnet Pragmatic Trials

Claims
Using RWD (EHRs) to Enable Clinical Trials

Pre-Study (S1)

Protocol Design
- Characterize RWD-based outcomes & endpoints

Cohort Identification
- RWD-compatible inclusion/exclusion criteria (computable phenotype)
- Understand patient cohorts; interactions with health systems

Site Selection
- Experience using RWD to facilitate research
- Feasibility and recruitment plans

Study Setup (S1-S2)

Site Onboarding
- Translate inclusion/exclusion criteria into an EHR-based reporting program (to identify eligible patients)
- Feasibility dashboards
- Embed encounter instructions into sites' EHR systems
- Pre-consent and study-specific consent
- Model potential outcomes

Recruitment (S2)

Participant Enrollment
- Develop EHR-based screening reports – contact potential participants or identify & recruit during clinics
- Deploy provider-specific EHR alerts to identify eligible patients during care delivery
- Use of patient portals (EHR-based and stand-alone) for patient outreach and electronic consent

Study Conduct (S3)

Data Collection
- Trial-specific data capture embedded within EHR workflows
- CRFs auto-populated with data from EHRs
- Algorithms to identify RWD-based efficacy and safety outcomes
  Rules, Alerts & Checks
  - Data quality and completeness
  - Hospitalization/SAEs
  - Event rates

Participant Retention & Contact
- Use of patient portals to collect PRO's, share trial progress reports, and enhance retention

HealthCore Overview

Full Service Research Solutions

Adaptable

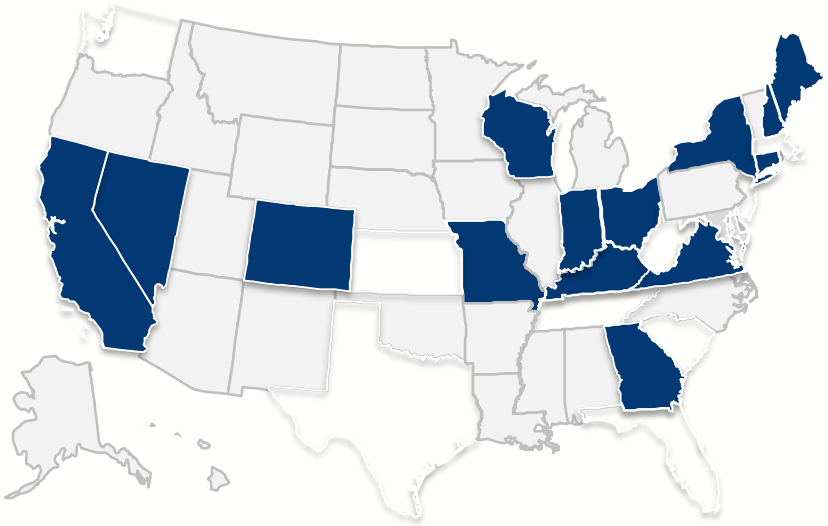
Anthem: A Health Benefits Leader

~71M
individuals served

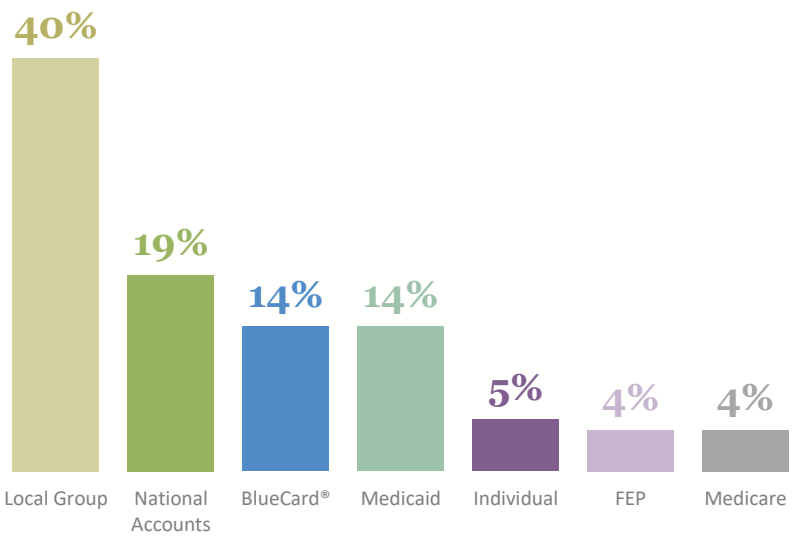
1 in 9 Americans

39.5 million
total medical members in affiliated health plans

$213 billion
benefits paid



BC or BCBS licensed commercial plans (14)



Anthem BlueCross BlueShield · Anthem BlueCross · Empire BlueCross BlueShield · Amerigroup RealSolutions in healthcare · HealthCore · CareMore It's what we do. · simply healthcare · BlueCross BlueShield of Georgia · AIM SpecialtyHealth · National Government Services · DeCare Dental

HIRE®

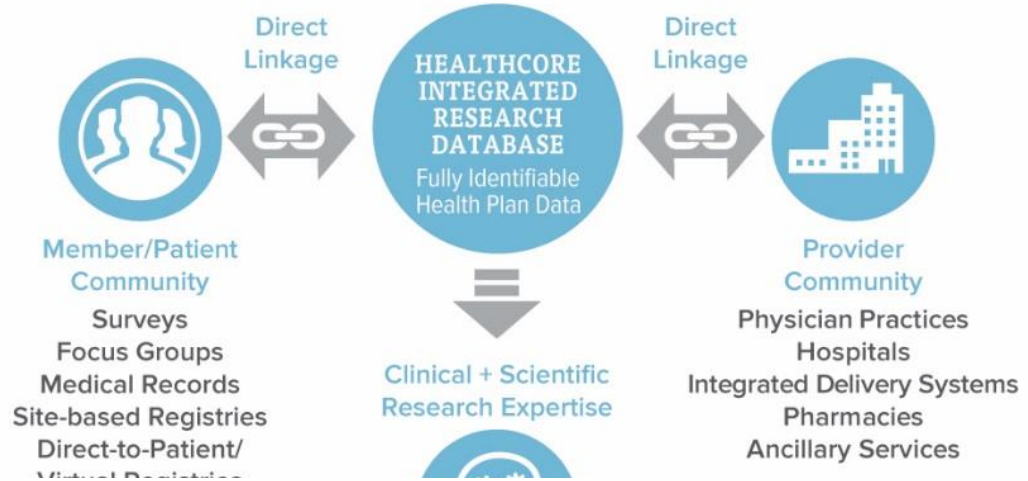
HealthCore Integrated Research Environment

Infor
indiv
Ame
plans

48+
com
and
14 st
dating back to 2006

Lab results for **17+ million lives** integrated with claims data

Clinical **Oncology data**



Data Environment

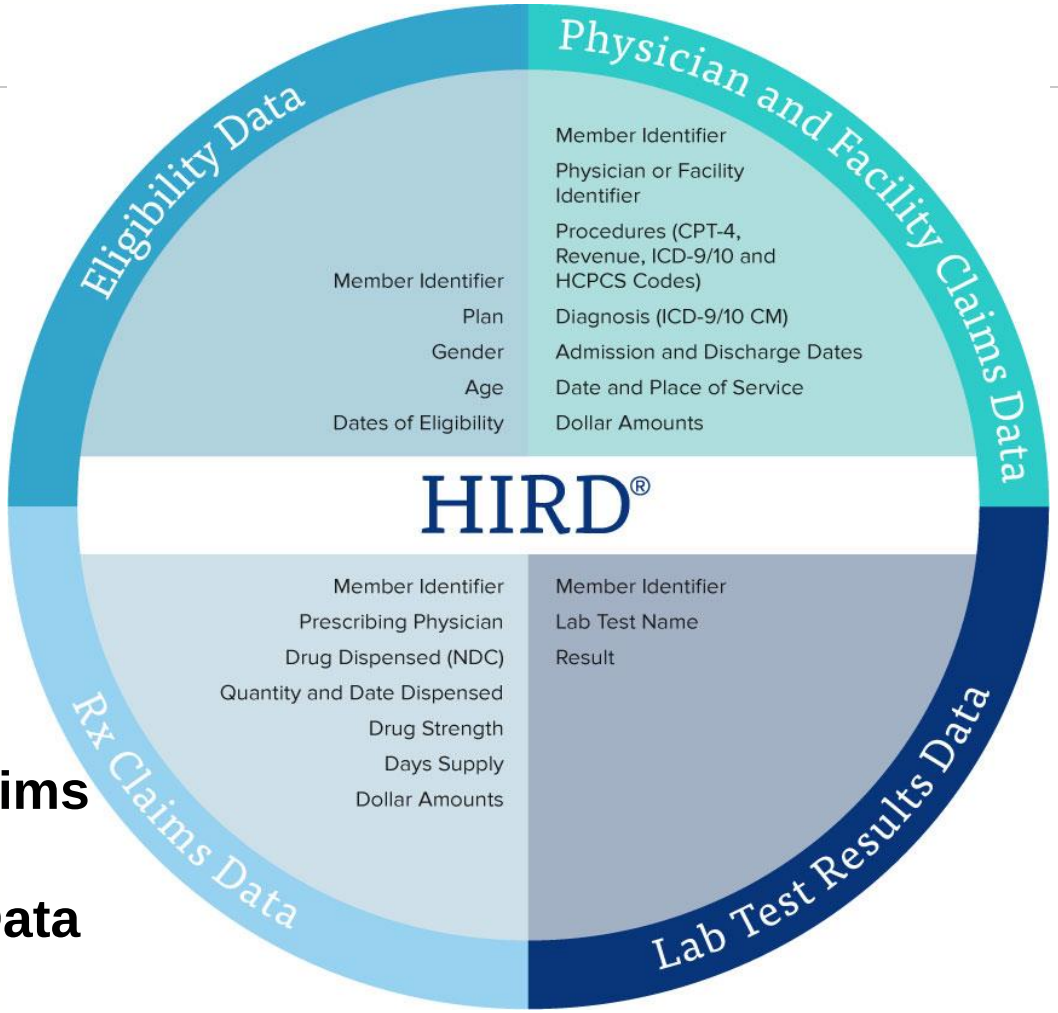
Extract, Transformed, and Loaded into Common Data Models

Sentinel

pcornet® The National Patient-Centered Clinical Research Network

Adaptable

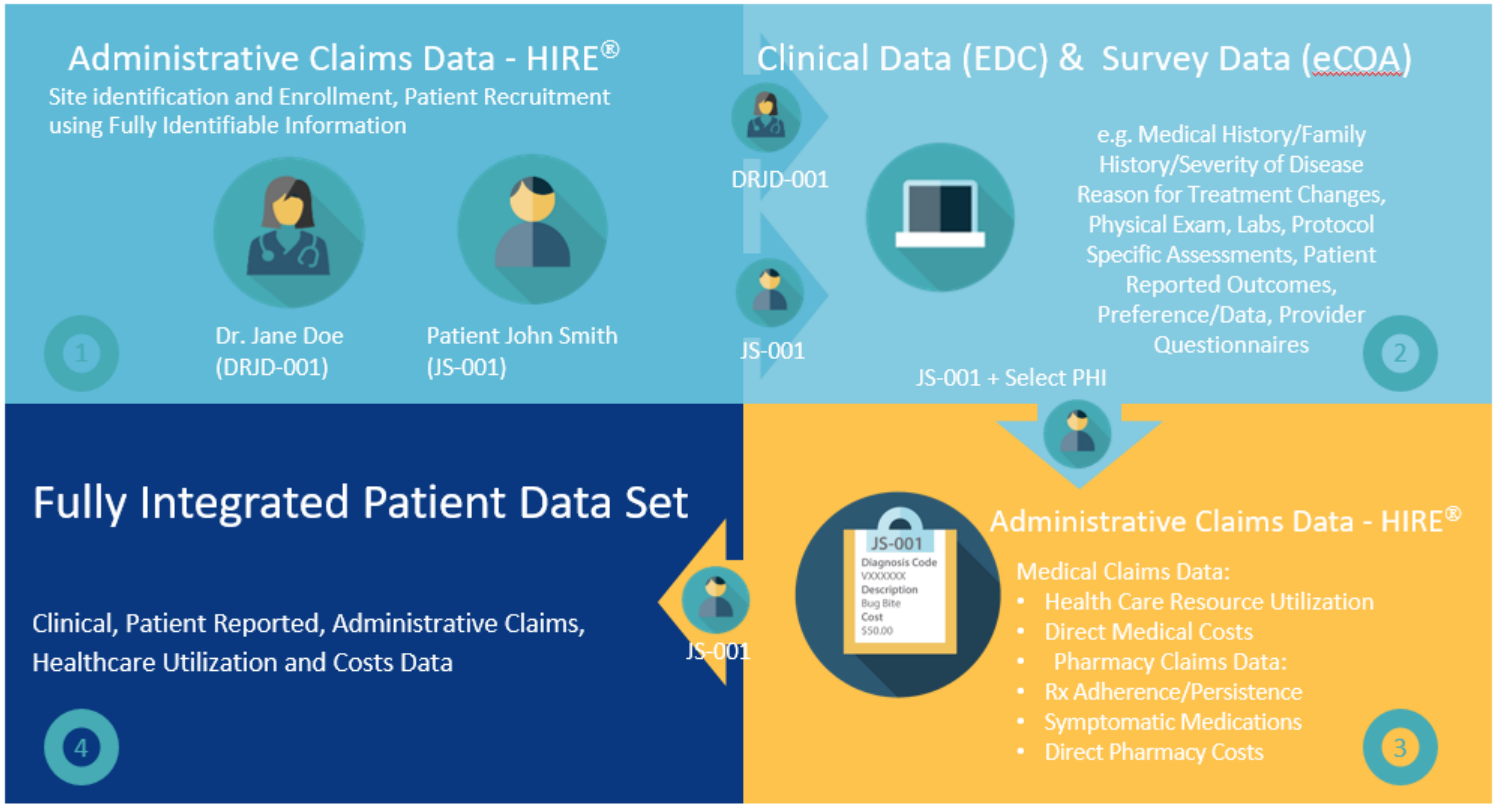
HealthCore Integrated Research Database



Four elements:

1. **Eligibility Data**
2. **Physician and Facility Claims Data**
3. **Laboratory Test Results Data**
4. **Pharmacy Claims Data**

Complete Data Integration via Direct Linkage within the HIRE



HealthCore

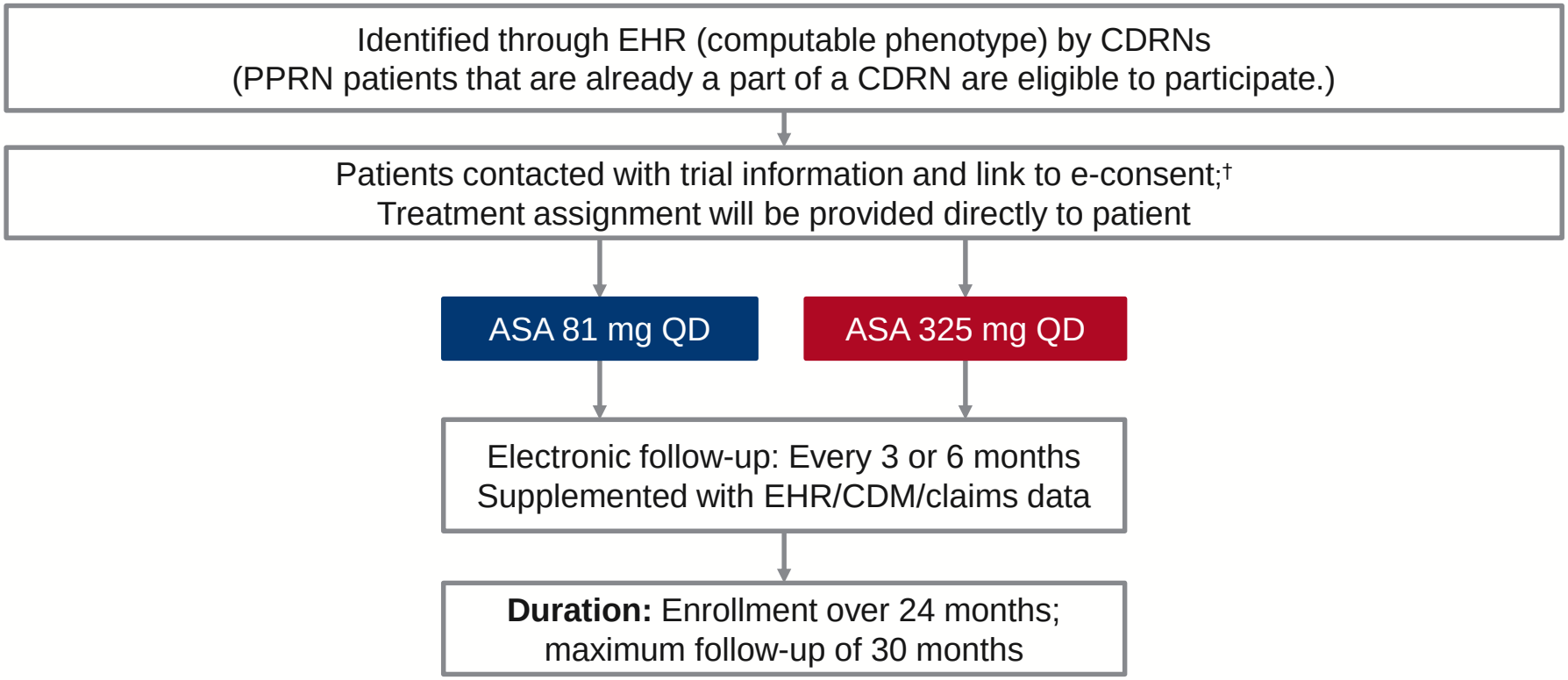
Adaptable

Principles for Conducting Pragmatic Clinical Trials in Learning Health Care Systems

- Leverage available medical data from electronic health records (EHRs) and **administrative claims** to identify eligible patients
- Ascertain endpoints as part of routine healthcare delivery and **administrative claims**
- Simplify baseline and follow-up data collection through **systematic direct patient contact** (patient-reported outcomes) and multiple data sources
- Recruit large samples of patients within healthcare systems to limit selection bias and provide more generalizable results
- ADAPTABLE is the **first large scale pragmatic** trial conducted via PCORnet in **learning health care systems**

ADAPTABLE Study Design

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

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

Adaptable

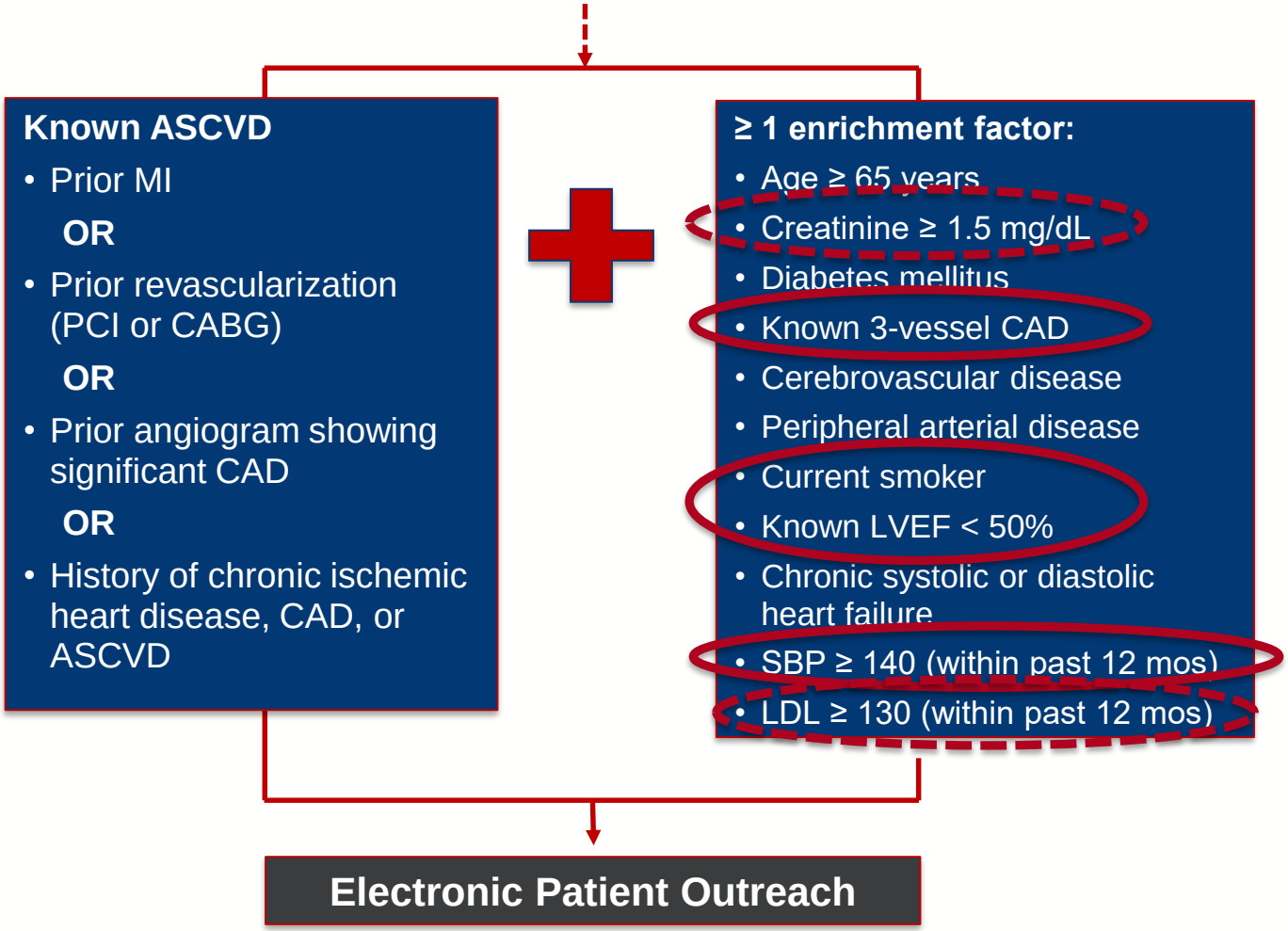
ClinicalTrials.gov: NCT02697916

Efficiencies in ADAPTABLE

- Employs system-wide screening of EHRs or **claims** using key indicators to identify patients to approach
- Eliminates data entry redundancies by obtaining information directly from EHRs or **claims** via the Common Data Model
  - **Medical History**
  - **Endpoints (rehospitalizations) and Safety Data**
  - **Labs and Medications**
- Collects longitudinal patient-reported outcomes directly from participants via the Adaptable web portal
- Eliminates costly monitoring to verify data accuracy

ClinicalTrials.gov: NCT02697916

ADAPTABLE Inclusion Criteria – Computable Phenotype



ClinicalTrials.gov: NCT02697916

Validation of a claims-based algorithm identifying eligible study ADAPTABLE subjects

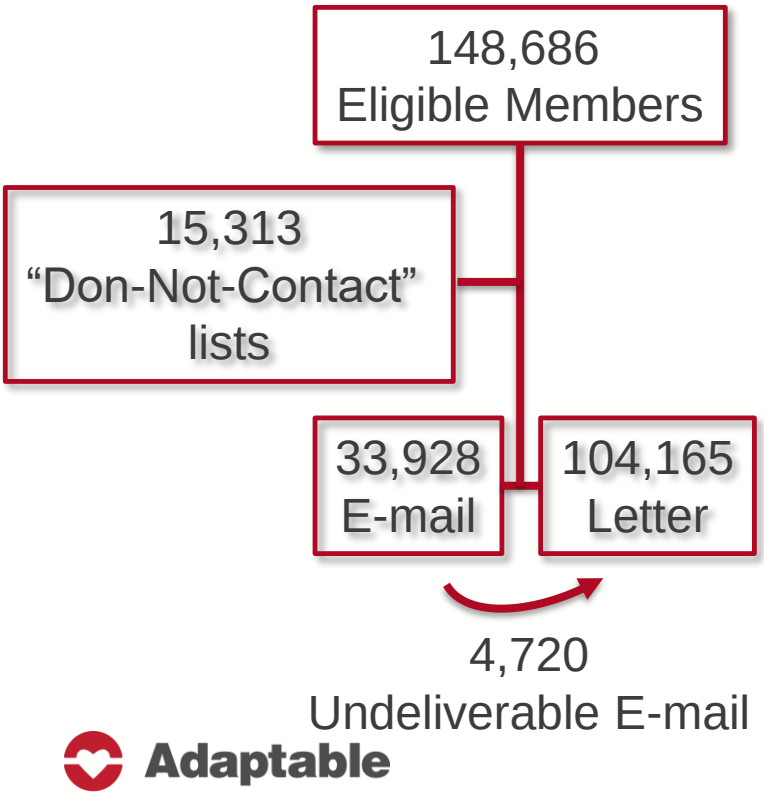
- Requested medical records from 300 potential subjects
- Reviewed 185 (62%) patient records
- PPV: 90.8% (95%CI: 85.7%, 94.6%)
- The proportion did not differ between patients identified with codes for AMI and patients identified with codes for PCI or CABG
- Of the 17 disconfirmed patients,
  - 5 had conditions excluding them from the study population (aspirin allergy or history of GI bleed)
  - 4 had records showing coronary artery disease (CAD) only
  - 8 were records from non-cardiology encounters, lacking documentation of AMI, PCI, CABG, or CAD

Contemporary Clinical Trials Communications December 2018

HealthCore ADAPTABLE Recruitment

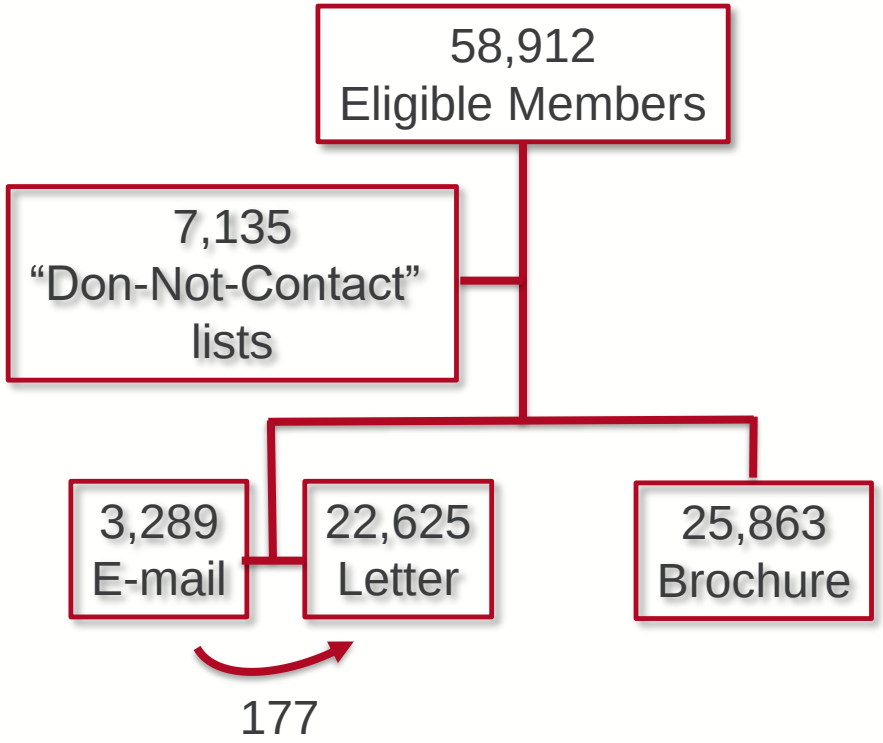
Phase 1:

- 2 batches of e-mail/mail and 1 phone call



Phase 2:

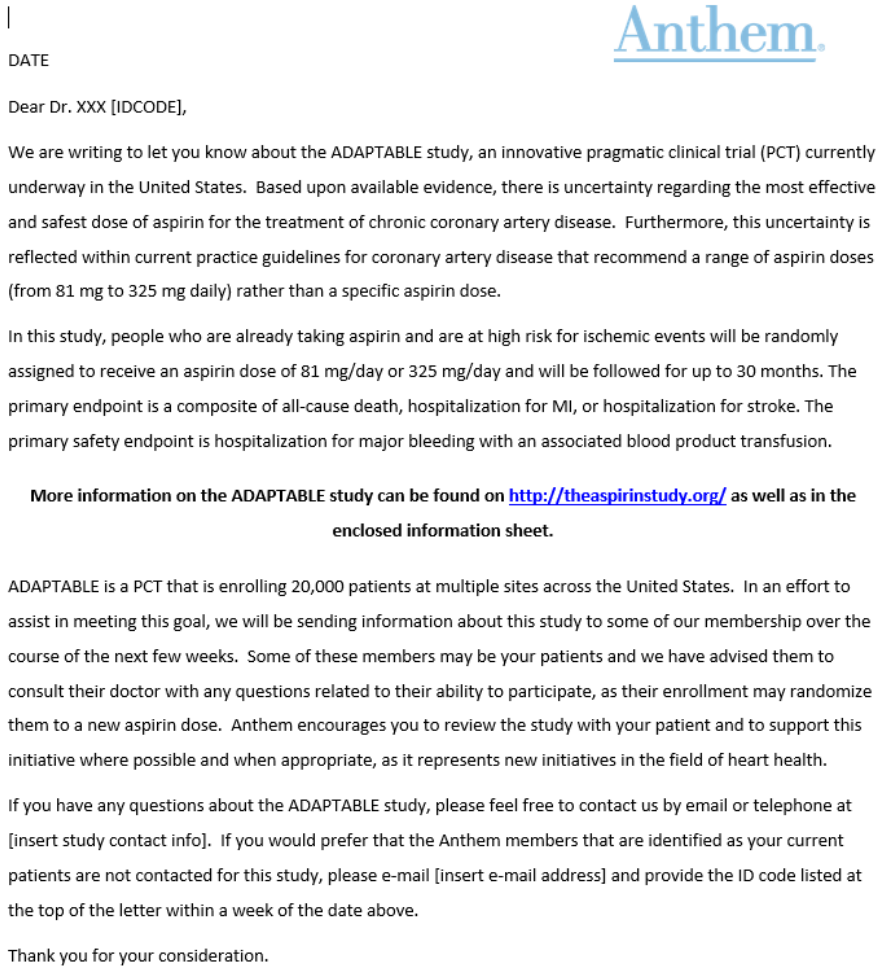
- Compared two batches
- Either email/mail or brochure and 1 phone call



Cardiologist and Primary Care Engagement

- Mailed “Grand Rounds” to inform Providers of the study

- Phase 1: 28,593
  - 6 providers declined participation resulting in 55 members excluded from outreach
- Phase 2: 5,077
  - 4 providers declined participation resulting in 22 members excluded from outreach.



Anthem.

DATE

Dear Dr. XXX [IDCODE],

We are writing to let you know about the ADAPTABLE study, an innovative pragmatic clinical trial (PCT) currently underway in the United States. Based upon available evidence, there is uncertainty regarding the most effective and safest dose of aspirin for the treatment of chronic coronary artery disease. Furthermore, this uncertainty is reflected within current practice guidelines for coronary artery disease that recommend a range of aspirin doses (from 81 mg to 325 mg daily) rather than a specific aspirin dose.

In this study, people who are already taking aspirin and are at high risk for ischemic events will be randomly assigned to receive an aspirin dose of 81 mg/day or 325 mg/day and will be followed for up to 30 months. The primary endpoint is a composite of all-cause death, hospitalization for MI, or hospitalization for stroke. The primary safety endpoint is hospitalization for major bleeding with an associated blood product transfusion.

More information on the ADAPTABLE study can be found on http://theaspirinstudy.org/ as well as in the enclosed information sheet.

ADAPTABLE is a PCT that is enrolling 20,000 patients at multiple sites across the United States. In an effort to assist in meeting this goal, we will be sending information about this study to some of our membership over the course of the next few weeks. Some of these members may be your patients and we have advised them to consult their doctor with any questions related to their ability to participate, as their enrollment may randomize them to a new aspirin dose. Anthem encourages you to review the study with your patient and to support this initiative where possible and when appropriate, as it represents new initiatives in the field of heart health.

If you have any questions about the ADAPTABLE study, please feel free to contact us by email or telephone at [insert study contact info]. If you would prefer that the Anthem members that are identified as your current patients are not contacted for this study, please e-mail [insert e-mail address] and provide the ID code listed at the top of the letter within a week of the date above.

Thank you for your consideration.

Member Mailers

Return mail address

Please consider joining us as a team of nationwide researchers works to determine which dose, low-dose or regular strength, aspirin is better.

Adaptable
The Aspirin Study

Anthem.

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.

Adaptable

We're asking you to join a research study called ADAPTABLE.

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. You will not have to visit a clinic for the study.

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

Participants will receive compensation for their time.

Visit us online at AdaptablePatient.com/ and enter your unique code: J2XXX

For more information, or assistance enrolling, call 1-833-569-7650

Anthem.

Date

<FIRST NAME>, would you like to be part of an exciting research study?

tients with heart disease. A new study
rin for these patients. The study will
he United States with a goal of 20,000
value of studies like this in the field of
part of this important research.

"baby" aspirin (81mg) and track several
ntry and this study would like to find out

enrolling, just visit adaptablepatient.com

invite_id].
ne, with your computer or phone and not

spirin or a baby aspirin every day.
health once every 3-6 months for up to

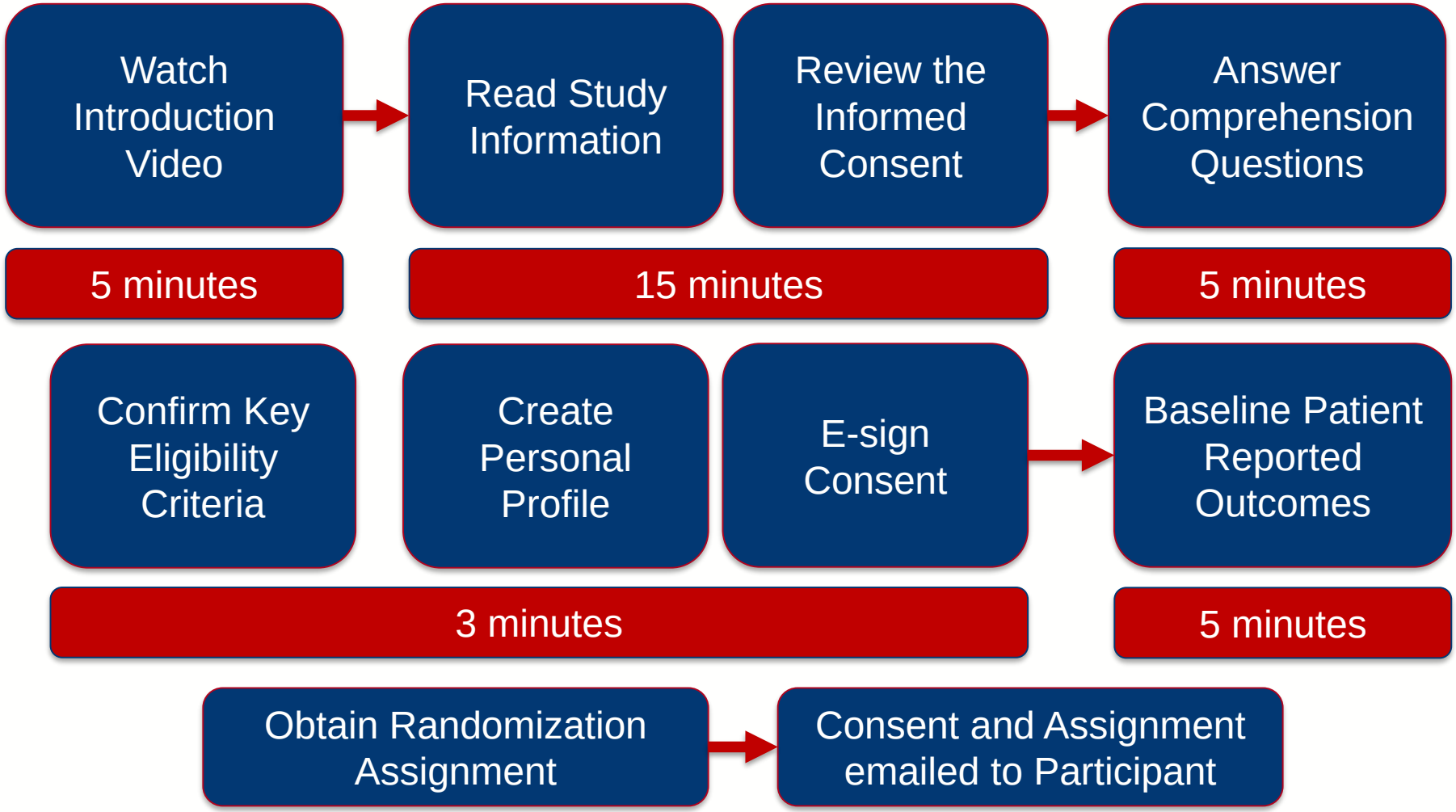
or this study, but we do encourage you to
also provided information about this study

opt to receive a $25 gift card as a thank

the study, go to:

voluntary and doesn't affect your

Web-Based Portal Work Flow



Adaptable

ClinicalTrials.gov: NCT02697916

Adaptable
The Aspirin Study

Presented in English
En Espanol

www.adaptablepatient.com

TEXT SIZE A

Let's get started!

Thank you for taking the time to find out more details about the ADAPTABLE aspirin study.
With your help, we hope to find out what is the right dose of aspirin for people with heart disease.

Got a code?

Please enter in the special code that was included in your invitation:

AX3BN

ENTER

No code? No problem!

You can still learn more about this study even if you have not been asked to participate.

CONTINUE

Already have a profile? Login

ClinicalTrials.gov: NCT02697916

Adaptable

The Aspirin Study

TEXT SIZE A

There are 5 steps to join the study!

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

Watch
the ADAPTABLE short video

5 min

Read
more details about participating in ADAPTABLE

15 min

Answer
a few questions about the study

5 min

Join
the ADAPTABLE study

3 min

Inform
us about your current health

5 min

LET'S GET STARTED

ClinicalTrials.gov: NCT02697916

Results of Health Plan Outreach

	Phase 1		Phase 2		Total	
	N	%	N	%	N	%
Outreached	133,373		51,777		185,150	
Portal Visit	890	0.7%	662	1.3%	1,552	0.8%
Enrollees	238	27%	119	18%	357	23%

- 8 per 1,000 outreaches resulted in portal visit interest in the study
  - Brochure group had the highest portal visit rate
- 2 per 1,000 outreaches resulted in an enrolled participant

Broad Geographic Representation

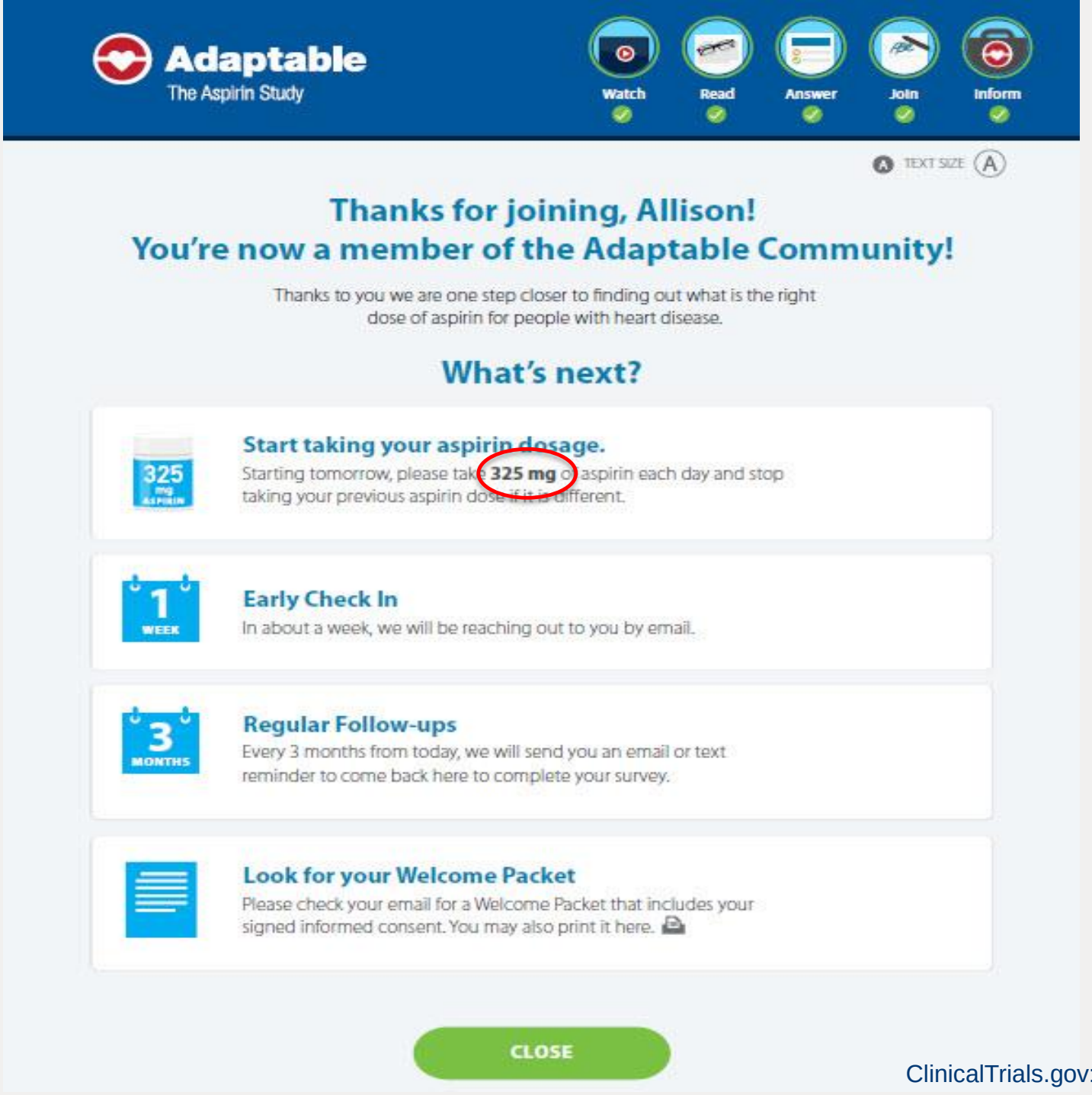
State	Freq	Percent
OH*	89	25%
CA*	42	12%
IN*	33	9%
KY	32	9%
VA	30	8%
GA	18	5%
MO*	18	5%
NY*	14	4%
WI*	14	4%
CO	14	4%
Other	42	15%

- * Indicates CRN ADAPTABLE recruiting site
- Increased diversity of nationwide recruitment
- Recruitment from non-Academic Medical Centers

Web-Based, Electronic Informed Consent

- Direct patient feedback and user testing for the development of the consent form and process as well as the comprehension questions
- Simplified common consent form with selected local adaptations
- Text and video review of the consent is completed on the web portal
- Focused questions to confirm patient comprehension for informed consent and eligibility for randomization prior to consent is obtained

ClinicalTrials.gov: NCT02697916



ClinicalTrials.gov: NCT02697916

Approach to endpoint ascertainment

- Routine queries of the PCORnet common data model (CDM) to capture and classify endpoints
  - Hospitalizations will be identified via standardized, validated coding algorithms developed centrally and applied to the CDM
- ADAPTABLE web portal will ask about possible endpoint events (hospitalizations for MI, stroke, or major bleeding) during participant contacts (every 3–6 months)
  - Patient-reported outcomes supplement the CDM-generated hospitalization data
  - Surveillance of CMS and **private health plan** data for potential “out-of-network” hospitalizations
- Death ascertainment via Social Security Administration (Medicare beneficiaries) and National Death Index

E-nabling Pragmatic Research: e-data collection and e-follow-up

N=15,000

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*

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

National Death Index (NDI) & Social Security Database

Adaptable

ClinicalTrials.gov: NCT02697916

Health Plan Engagement

662 Participants

813 Participants

737 Participants
(inclusive of 357 directly engaged)

Health Plan Authorization

By signing the health plan claims release, the enrollee understands and agrees to the following:

- I have read the contents of this form and I understand, agree, and allow my Health Plan, The ADAPTABLE Study Coordinating Center at Duke Clinical Research Institute, and my healthcare provider to use and release information about me as described above. I also understand that signing this form is of my own free will and will in no way affect the health benefits or medical care that I receive from my Health Plan or providers.

- If you withdraw consent, the ADAPTABLE Study will retain all information up to the date you withdraw your consent. Once your information is shared outside the ADAPTABLE team, it will not be traceable to you. However, the information from your records (but not you may still be protected by other privacy rules and agreements).

- If I choose not to participate in providing Health Plan information, I understand that my Health Plan will not base decisions regarding my treatment, eligibility for benefits, enrollment in a Health Plan, or payment of claims on my decision regarding study participation.

- If I choose not to participate in providing Health Plan information it will not impact my participation in the ADAPTABLE study. Additionally, I can choose to withdraw from providing Health Plan information at any time and remain in the ADAPTABLE study if I choose.

- I have the right to withdraw this approval at any time by giving written notice of my withdrawal to the ADAPTABLE study team. I understand that my withdrawing this approval will not affect any action taken before I do so. I also understand that once my information is shared outside the ADAPTABLE team, it will not be individually identifiable. Though once disclosed to the ADAPTABLE team, my data will no longer be protected by HIPAA. However, the information from my records may still be protected by other privacy rules and agreements. At my request, I will be given a copy of this form either when I sign it or while the study is ongoing. My authorization to share information is effective for the duration of the study, or until I withdraw my authorization.

Name (printed)	(Signature)	(Date)

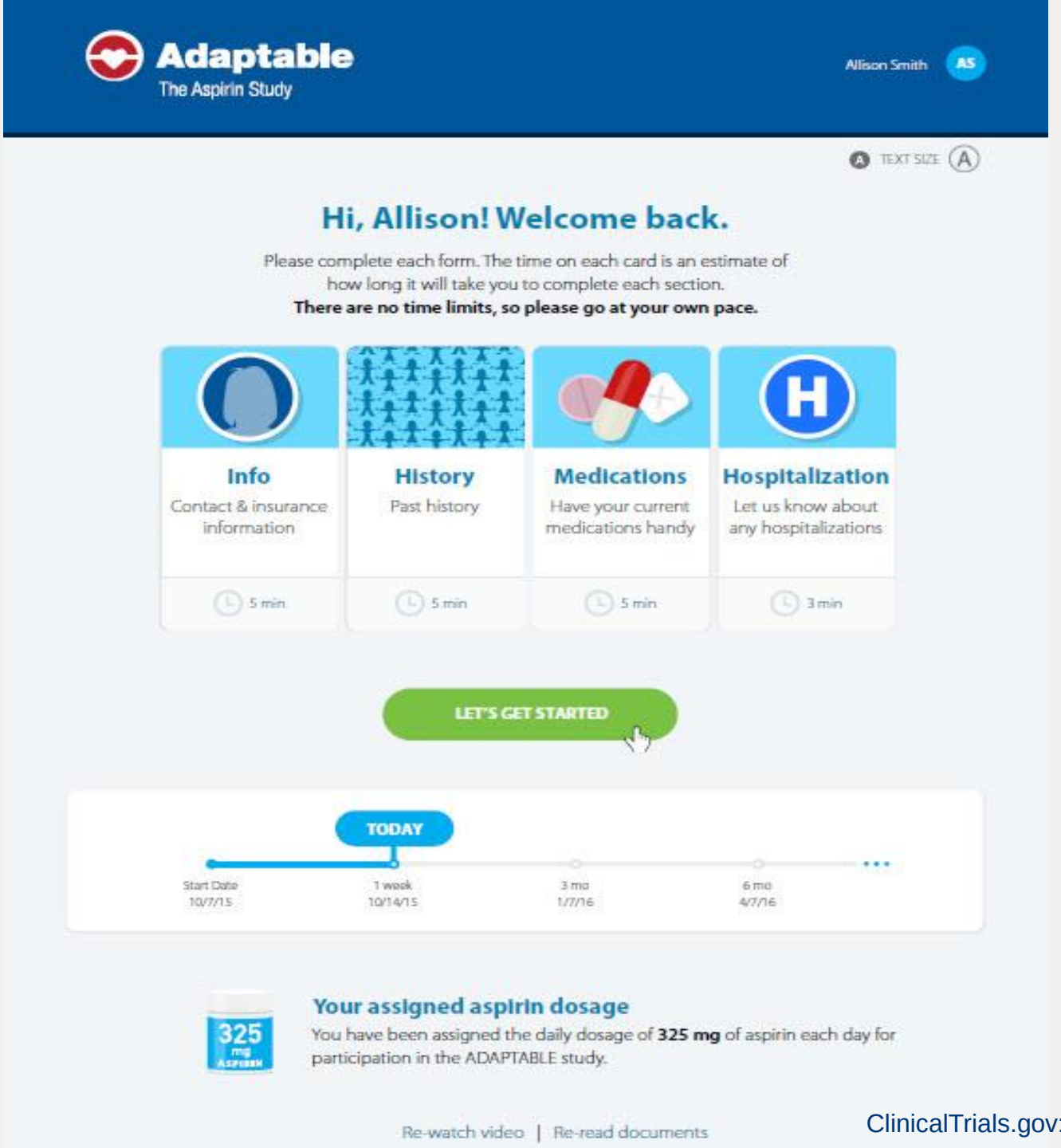
Signing the release is voluntary and will not impact any healthcare services.

You can withdraw your authorization at any time.

Not releasing your health plan data will not impact your health plan benefits or services

Not releasing your health plan data will not impact your decision to participate in the study

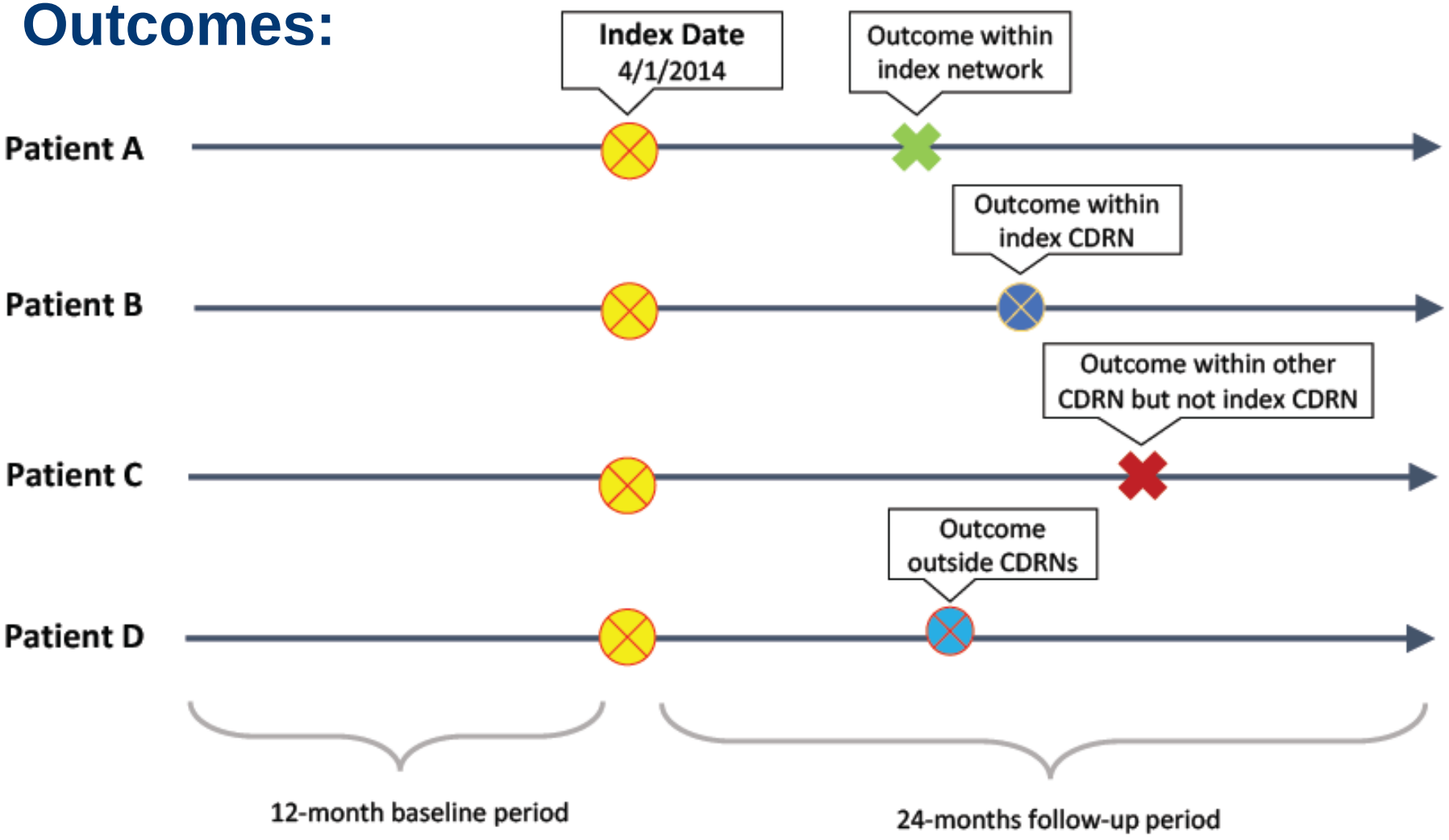
The privacy of your health plan data will be preserved



ADAPTABLE Outcomes Study

- **Objective:** To demonstrate the value of claims data in improving the capture of end points in longitudinal pragmatic clinical trials.
- **Design:** Retrospective observational cohort study on an overlapping population of PCORnet CDRNs and HCARN members
  - those who received cardiac treatment at any PCORnet network partner within 2 years prior to index date were included
  - Follow-up period (04/01/2014 – 03/30/2016)
  - Assessed for ADAPTABLE study outcomes

Outcomes:



Adaptable

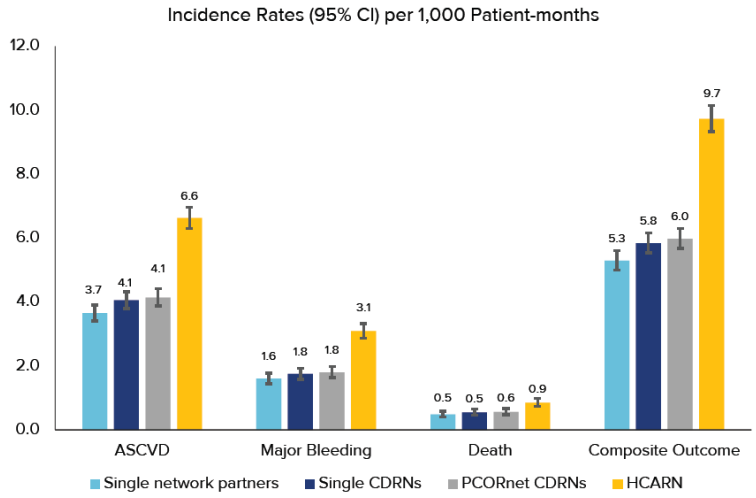
Incidence Rates of Outcome Events from Single Network Partners, Single CRNs, PCORnet CRNs and HCARN Respectively

- Out of **884,311** HCARN members identified as ADAPTABLE eligible, **11,101** overlapped with PCORnet CRN network partners

1,521
hospitalizations for ASCVD
571 (37.5%)
occurred outside CRNs

710
hospitalizations for major bleeding
296 (41.7%)
occurred outside CRNs

196
deaths at hospital
67 (34.2%)
occurred outside CRNs



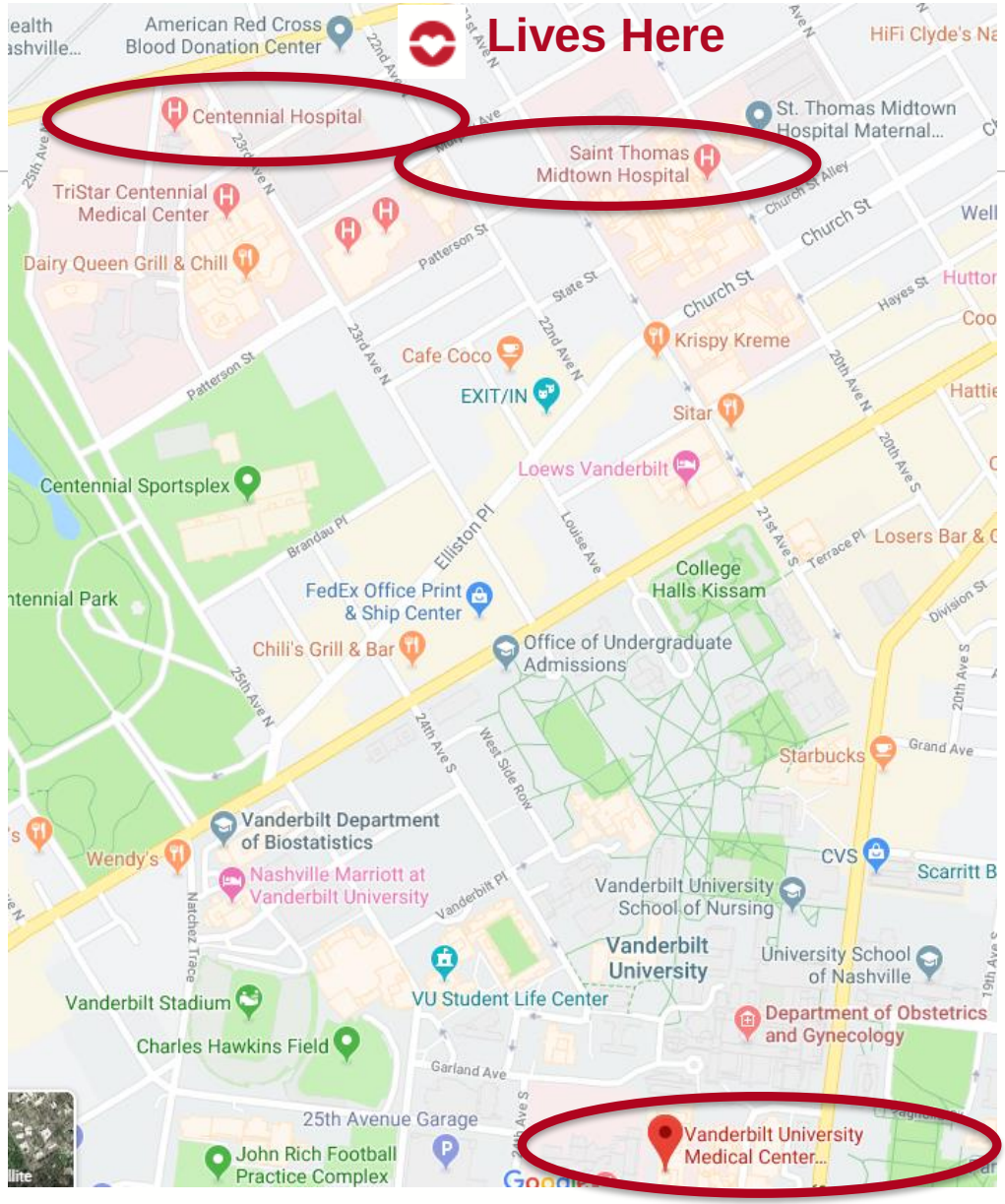
*Composite outcome includes hospitalization for ASCVD, major bleeding or death.
Abbreviation: ASCVD=atherosclerotic cardiovascular disease; MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft.

Clin Trials. 2019 May 13

Adaptable

Example Participant

- Vanderbilt ADAPTABLE patient
- Has an outcome at Centennial or St. Thomas
- Claims can capture the outcomes across health care delivery systems



Adaptable

Summary of Health Plan Data in Pragmatic Trials

- Reliably identify participants eligible for pragmatic clinical trials
- Valuable addition to participant recruitment efforts for large pragmatic clinical trials
- Provides a longitudinal electronic approach to endpoint ascertainment
- Patient engagement is a key attribute to facilitate health plan outreach

ClinicalTrials.gov: NCT02697916

www.pcornet.org

pcornet The National Patient-Centered Clinical Research Network

PATIENT-CENTRIC DATA-DRIVEN THE NETWORK IMPACT WORK WITH PCORNET CONTACT

A Network of Research Networks

PCORnet is a tightly integrated partnership of 9 large Clinical Research Networks, 2 Health Plan Research Networks, a Coordinating Center, and a Central Office. PCORnet represents a diverse set of patients and institutions, ranging from cutting-edge academic medical centers to local community health clinics caring for the nation's most vulnerable patients.

Shared Common Data Model

PCORnet's Common Data Model incorporates locally-stored data from millions of patients who receive care in the Network's health care systems in a standardized, high-quality format.

Research Expertise

PCORnet is made up of the nation's leading clinical researchers whose collective knowledge and experiences enable the Network to support a wide range of research.

Robust Infrastructure

PCORnet offers efficiencies in research capabilities through its streamlined research processes, Network reach, and identically formatted data sets at each site, with sophisticated analytic capabilities.

Learn more about ADAPTABLE

- Visit our website **http://theaspirinstudy.org**
- Follow us on Twitter @**ADAPTABLEstudy**
- Join the conversation **#ADAPTABLEstudy, #PCORnet, #PCT**