ADAPTABLE Recruitment and Follow-up Health Plan Research Network Engagement

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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

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[Image: Duke Clinical Research Institute logo]
HealthCore Overview

Full Service Research Solutions

- Phase II-IV Research
- Late Phase Prei/Post Approval Research
- Pragmatic Clinical Trials
- Site-Based Registries
- Direct-to-Patient Registries
- Direct Patient & Provider Outreach
- Special Populations Research & Pediatrics
- Comparative Effectiveness Research
- Health Economics & Outcomes Research
- Safety & Epidemiology Research
- Machine Learning Case Identification
- Survey-Based Research (Quantitative & Qualitative)
- Survey Instrument Development
- Medical Record Abstraction & Integration
- Health Services Research
- Digital Strategies
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

Map showing BC or BCBS licensed commercial plans (14)

- Local Group: 40%
- National Accounts: 19%
- BlueCard®: 14%
- Medicaid: 14%
- Individual: 5%
- FEP: 4%
- Medicare: 4%
HealthCore Integrated Research Environment

- Information on 66+ million individuals representing 1 in 8 Americans from multiple health plans across the U.S.
- 48+ million private U.S. commercial lives with medical and pharmacy claims, spanning 14 states from health plans dating back to 2006
- Lab results for 17+ million lives integrated with claims data
- Clinical Oncology data

HIRE®

HEALTHCORE INTEGRATED RESEARCH DATABASE
Fully Identifiable Health Plan Data

Data Environment
Extract, Transformed, and Loaded into Common Data Models

Sentinel, pcor.net
The National Patient-Centered Clinical Research Network
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

Administrative Claims Data - HIRE®
Site identification and Enrollment, Patient Recruitment using Fully Identifiable Information

Dr. Jane Doe (DRJD-001)
Patient John Smith (JS-001)

Clinical Data (EDC) & Survey Data (eCOA)
e.g. Medical History/Family History/Severity of Disease Reason for Treatment Changes, Physical Exam, Labs, Protocol Specific Assessments, Patient Reported Outcomes, Preference/Data, Provider Questionnaires

DRJD-001
JS-001

Fully Integrated Patient Data Set
Clinical, Patient Reported, Administrative Claims, Healthcare Utilization and Costs Data

Clinical Data (EDC) & Survey Data (eCOA)

Administrative Claims Data - HIRE®
Medical Claims Data:
- Health Care Resource Utilization
- Direct Medical Costs
- Pharmacy Claims Data:
  - Rx Adherence/Persistence
  - Symptomatic Medications
- Direct Pharmacy Costs

JS-001
JS-001 + Select PHI

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.

ClinicalTrials.gov: NCT02697916
ADAPTABLE Study Design

Patients with known ASCVD + ≥ 1 “enrichment factor”

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

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

ASA 81 mg QD  ASA 325 mg QD

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

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

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

Primary safety endpoint:
Hospitalization for major bleeding

† Participants without internet access will be consented and
followed via a parallel system.
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.
ADAPTABLE Inclusion Criteria – Computable Phenotype

Known ASCVD
- Prior MI
  OR
- Prior revascularization (PCI or CABG)
  OR
- Prior angiogram showing significant CAD
  OR
- History of chronic ischemic heart disease, CAD, or ASCVD

≥ 1 enrichment factor:
- Age ≥ 65 years
- Creatinine ≥ 1.5 mg/dL
- Diabetes mellitus
- Known 3-vessel CAD
- Cerebrovascular disease
- Peripheral arterial disease
- Current smoker
- Known LVEF < 50%
- Chronic systolic or diastolic heart failure
- SBP ≥ 140 (within past 12 mos)
- LDL ≥ 130 (within past 12 mos)

Electronic Patient Outreach

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
HealthCore ADAPTABLE Recruitment

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

- 148,686 Eligible Members
- 15,313 “Don-Not-Contact” lists
- 33,928 E-mail
- 104,165 Letter
- 4,720 Undeliverable E-mail

Phase 2:
- Compared two batches
- Either email/mail or brochure and 1 phone call

- 58,912 Eligible Members
- 7,135 “Don-Not-Contact” lists
- 3,289 E-mail
- 22,625 Letter
- 25,863 Brochure
- 177
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

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://thespirimstudy.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

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

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.

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.

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
Web-Based Portal Work Flow

1. **Watch Introduction Video** - 5 minutes
2. **Read Study Information** - 15 minutes
3. **Review the Informed Consent** - 5 minutes
4. **Answer Comprehension Questions** - 5 minutes
5. **Confirm Key Eligibility Criteria** - 3 minutes
6. **Create Personal Profile**
7. **E-sign Consent**
8. **Obtain Randomization Assignment**
9. **Baseline Patient Reported Outcomes** - 5 minutes
10. **Consent and Assignment emailed to Participant**

ClinicalTrials.gov: NCT02697916
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.

Already have a profile? Login
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

Read more details about participating in ADAPTABLE

Answer a few questions about the study

Join the ADAPTABLE study

Inform us about your current health

LET'S GET STARTED
## Results of Health Plan Outreach

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<th>Phase 2</th>
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<tr>
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<td>N</td>
<td>%</td>
<td>N</td>
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<tr>
<td>Outreached</td>
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<tr>
<td>Portal Visit</td>
<td>890</td>
<td>0.7%</td>
<td>662</td>
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<tr>
<td>Enrollees</td>
<td>238</td>
<td>27%</td>
<td>119</td>
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</table>

- 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

<table>
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<th>State</th>
<th>Freq</th>
<th>Percent</th>
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</thead>
<tbody>
<tr>
<td>OH*</td>
<td>89</td>
<td>25%</td>
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<tr>
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<td>33</td>
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<tr>
<td>CO</td>
<td>14</td>
<td>4%</td>
</tr>
<tr>
<td>Other</td>
<td>42</td>
<td>15%</td>
</tr>
</tbody>
</table>

* 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
Thanks for joining, Allison!
You’re now a member of the Adaptable Community!

Thanks to you we are one step closer to finding out what is the right dose of aspirin for people with heart disease.

What’s next?

Start taking your aspirin dosage.
Starting tomorrow, please take 325 mg of aspirin each day and stop taking your previous aspirin dose if it is different.

Early Check In
In about a week, we will be reaching out to you by email.

Regular Follow-ups
Every 3 months from today, we will send you an email or text reminder to come back here to complete your survey.

Look for your Welcome Packet
Please check your email for a Welcome Packet that includes your signed informed consent. You may also print it here.
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-enabling 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

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

DCRI call center
- Patients who miss 2 contacts
- Patients without internet access

Death ascertainment
- National Death Index (NDI) & Social Security Database

ClinicalTrials.gov: NCT02697916
Health Plan Engagement

Practice Research Network
662 Participants

HealthCore
737 Participants
(inclusive of 357 directly engaged)

PRACnet
662 Participants

Healthagen
813 Participants
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.

Signature
(Date)
Hi, Allison! Welcome back.

Please complete each form. 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.

Info
Contact & insurance information
5 min

History
Past history
5 min

Medications
Have your current medications handy
5 min

Hospitalization
Let us know about any hospitalizations
3 min

Let’s get started

Your assigned aspirin dosage
You have been assigned the daily dosage of 325 mg of aspirin each day for participation in the ADAPTABLE study.
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:

- **Index Date 4/1/2014**
- **Outcome within index network**
- **Outcome within index CDRN**
- **Outcome within other CDRN but not index CDRN**
- **Outcome outside CDRNs**

**Patient A**

**Patient B**

**Patient C**

**Patient D**

12-month baseline period

24-months follow-up period
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

Clin Trials. 2019 May 13
Example Participant

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