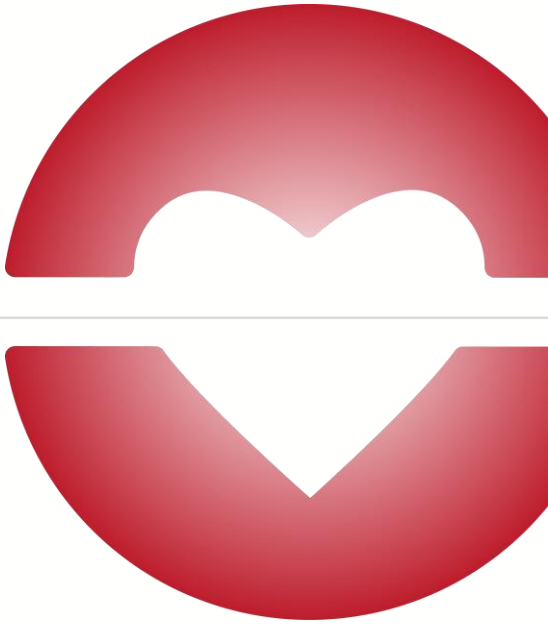
Please note that these slides were created during the earlier development phase.

Details are subject to change and should not be applied without confirmation.

PCORnet ADAPTABLE
Data Strategy Discussion



Friday, January 29, 2016

Hosted by Lesley Curtis, PhD and Schuyler Jones, MD

Facilitated by Shelley Rusincovitch and Lisa Eskenazi

pcornet

Adaptable

The Aspirin Study

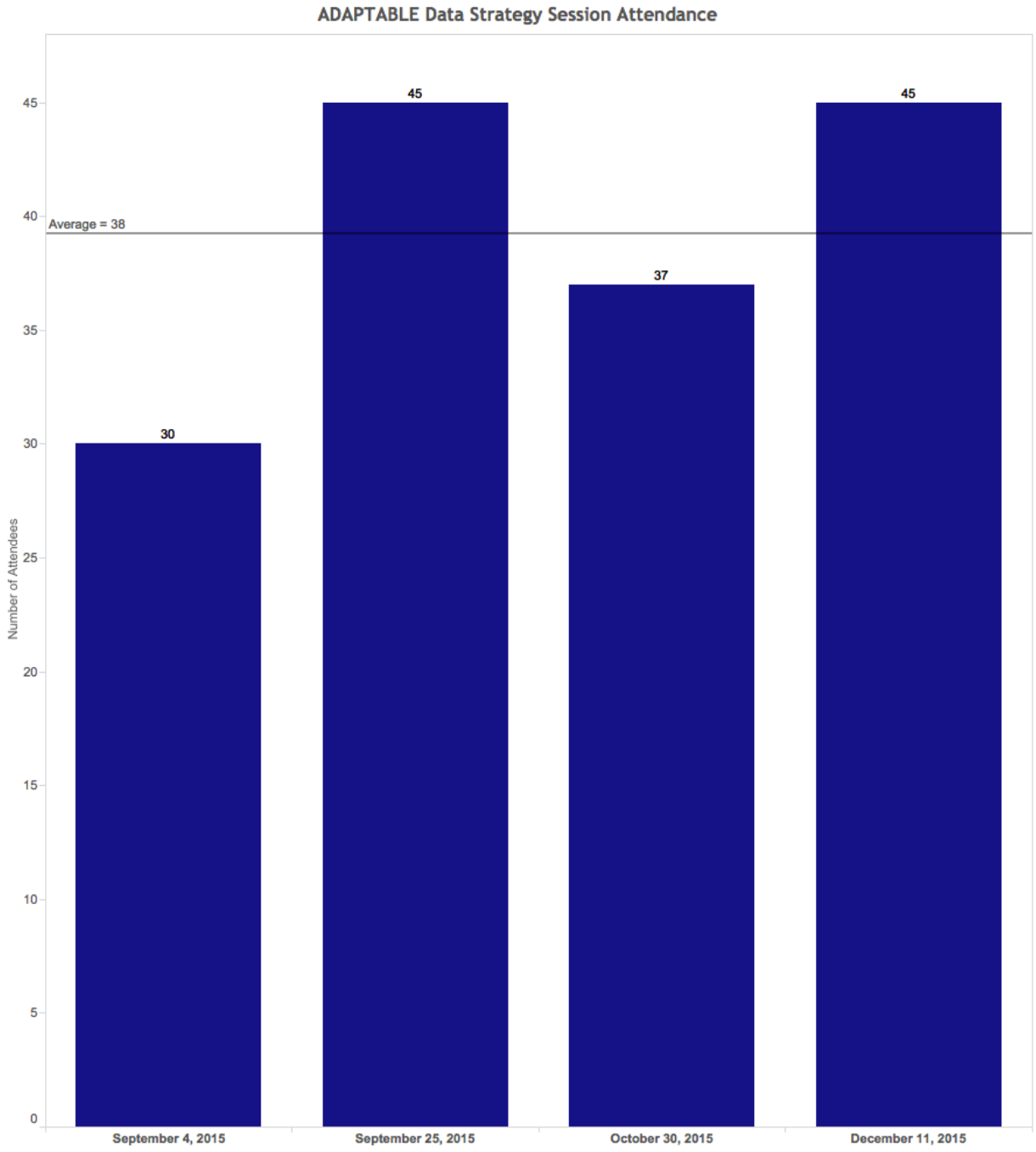
Welcome & Overview

Where to find materials from prior meetings

- Phenotype working session on **September 4, 2015**
  - Slides, recording, and summary: https://pcornet.centraldesktop.com/p/ZgAAAAAAZgS3
- Data strategy session on **September 25, 2015**
  - Slides, recording, and summary: https://pcornet.centraldesktop.com/p/ZgAAAAAAZn7T
- Data strategy session on **October 30, 2015**
  - Slides, recording, and summary: https://pcornet.imeetcentral.com/p/ZgAAAAAAaMVO
- Data strategy session on **December 11, 2015**
  - Slides, recording, and summary: https://pcornet.imeetcentral.com/p/ZgAAAAAAa76Y

Average of 38 attendees per session

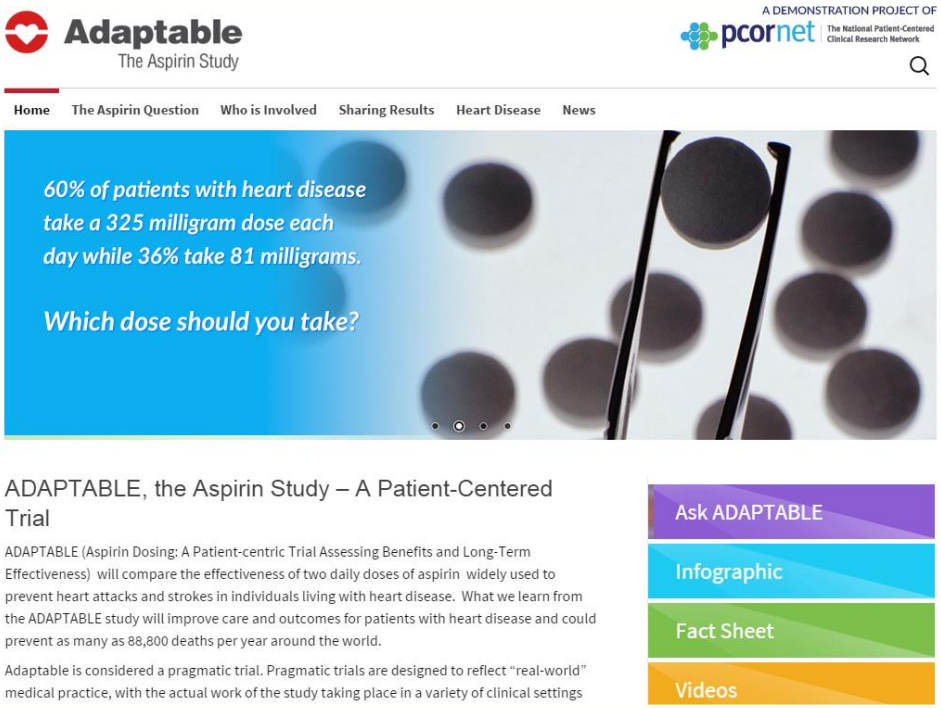
Four sessions between September - December 2015



Adaptable

The study website is now live!

- Public-facing
- Dual branded with PCORnet
- Mirrors PCORnet's visual style in order to provide a seamless experience for visitors
- Relevant content, rich media, and milestones will be shared as the study progresses



theaspirinstudy.org

CMS Linkage Pilot presentation on February 1

Why it may be of interest to this group:

- Update on the PCORnet CMS Linkage Pilot Project, including discussion of transformation of Medicare datasets into the CDM v3.0

PCORnet: DRN Operations Center Meeting (CDRNs)

February 1, 2016 from 11 am – 12 pm ET

Online Component:
https://dukemed.webex.com/dukemed/j.php?MTID=m673a55da642446e051031e5ec3813340

Call-in toll-free number (US/Canada): 1-855-244-8681

Call-in toll number (US/Canada): 1-650-479-3207

Access code: 735 866 908

ADAPTABLE podium at AMIA, March 24

Design and Architecture of a Distributed Network Pragmatic Clinical Trial: The PCORnet ADAPTABLE Study

Lesley H. Curtis, PhD[1], Shelley Rusincovitch[1], Jenny Ibarra[1], Bradley G. Hammill, DrPH[1], Laura G. Qualls[1], Debra F. Harris[1], W. Schuyler Jones, MD[1], Russell L. Rothman, MD[2], Matthew Roe, MD[1], Adrian F. Hernandez, MD[1]

[1]Duke University, Durham, North Carolina, [2]Vanderbilt University, Nashville, Tennessee

Abstract

The ADAPTABLE (Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-term Effectiveness) study will be the first randomized clinical trial to be executed within PCORnet, the National Patient-Centered Clinical Research Network. Design of the ADAPTABLE data architecture incorporates features of the Distributed Research Network, including innovative use of the PCORnet Common Data Model. The ADAPTABLE study database will amalgamate multiple data sources into an integrated data ecosystem.

Podium for March 24, 2016

Track: CRI: Clinical And Research Data Collection; Curation; Preservation; Or Sharing

Adaptable

Where to find the ADAPTABLE protocol and informed consent

- Publically posted on http://theaspirinstudy.org/
  - Direct link to the protocol: http://theaspirinstudy.org/wp-content/uploads/2015/10/ADAPTABLE-Final-Protocol-Vers-1-Oct-22-2015.pdf

Setting the stage for today's meeting

Our scope for today:

- Discuss the current status of development for the ADAPTABLE data components
- Outline considerations and areas needing further assessment

Setting the stage for today's meeting (2)

- We'll be talking today about the *current* state of development
- These details may change during the iterative design, development, and implementation of the project

Today is the last strategy-focused session!

These sessions will continue with a focus transition **from strategy to implementation.**

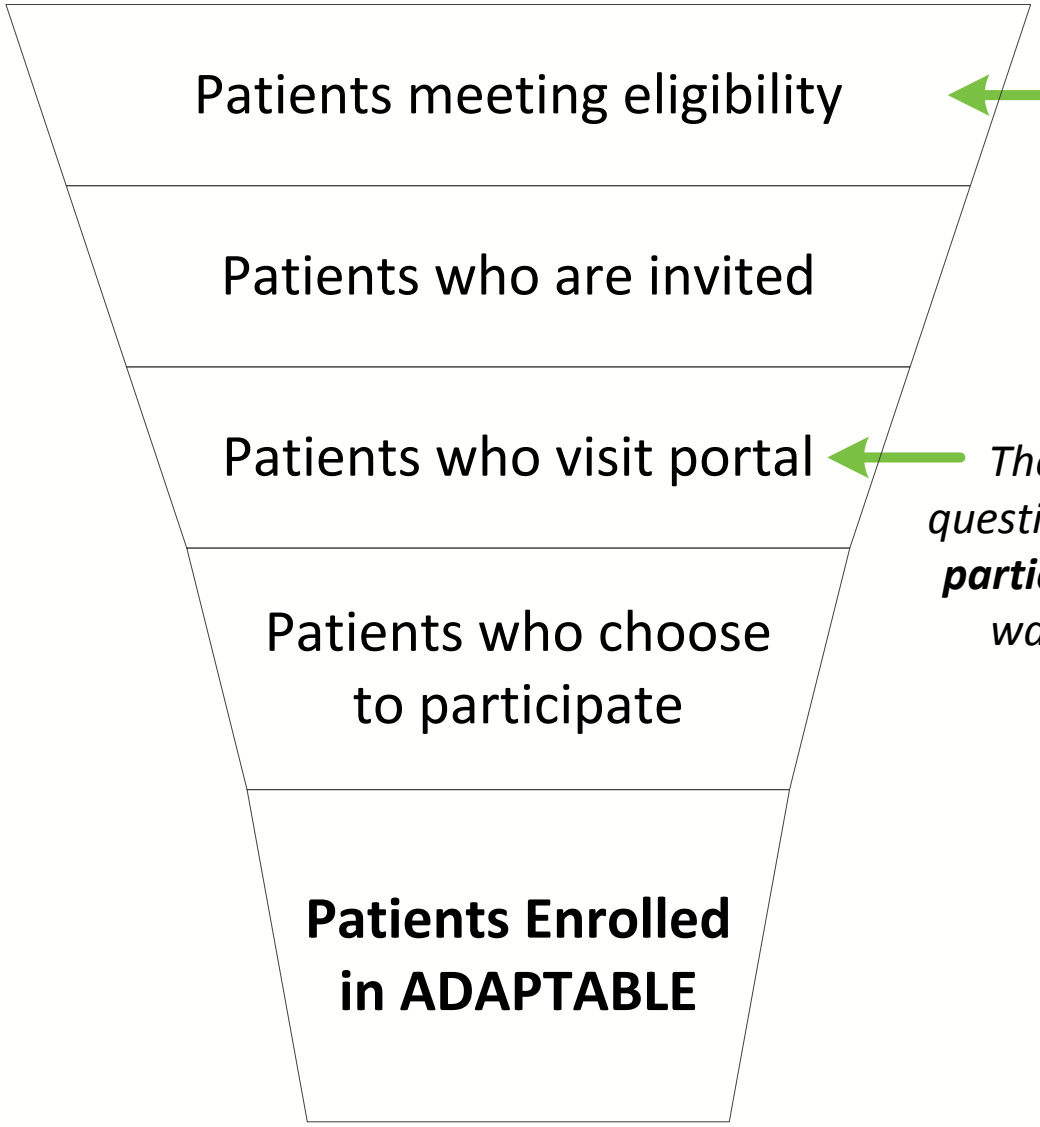
Items from December 11 session

- Question about network-acquired claims data
  - For ADAPTABLE, claims-based datamarts are entirely appropriate to include
- Generalizability for data completeness
  - Important area of assessment, especially in analysis stage

Plus, question during Dan Vreeman LOINC Best Practices session this past Wednesday (January 27)

- The CDM v3.0 common lab result categories will be used for ADAPTABLE analysis

Eligibility Phenotype Development



Managed at site and/or network level

This is where the phenotype is situated

*The patient answers a few basic questions to **check for those unsafe to participate**, but full eligibility criteria was determined at the site level*

ADAPTABLE eligibility criteria

ADAPTABLE Protocol Final Version 1.0, October 22, 2015, section III.A.1., pages 16-17 (PDF pages 20-21).

[This image altered to remove page break.]

1. Known atherosclerotic cardiovascular disease (ASCVD), defined by a history of prior myocardial infarction, prior coronary angiography showing ≥75% stenosis of at least one epicardial coronary vessel, or prior coronary revascularization procedures (either PCI or CABG)
2. Age ≥ 18 years
3. No known safety concerns or side effects considered to be related to aspirin, including
    a. No history of significant allergy to aspirin such as anaphylaxis, urticaria, or significant gastrointestinal intolerances
    b. No history of significant GI bleed within the past 12 months
    c. Significant bleeding disorders that preclude the use of aspirin
4. Access to the Internet. In the event that the CDRNs are notified that a cohort of patients without internet access can be included, then patient agreement will be obtained during the consent process to provide follow-up information by telephone contact with the DCRI Call Center.
5. Not currently treated with an oral anticoagulant – either warfarin or a novel anticoagulant (dabigatran, rivaroxaban, apixaban, edoxaban) – and not planned to be treated in the future with an oral anticoagulant for existing indications such as atrial fibrillation, deep venous thrombosis, or pulmonary embolism.
6. Not currently treated with ticagrelor and not planned to be treated in the future with ticagrelor.
7. Female patients who are not pregnant or nursing an infant
8. Estimated risk of a major cardiovascular event (MACE) > 8% over next 3 years as defined by the presence of at least one or more of the following enrichment factors:
    a. Age > 65 years
    b. Serum creatinine > 1.5 mg/dL
    c. Diabetes mellitus (Type 1 or Type 2)
    d. 3-vessel coronary artery disease
    e. Cerebrovascular disease and/or peripheral arterial disease
    f. Left ventricular ejection fraction (LVEF) < 50%
    g. Current cigarette smoker

Base phenotype customization is expected

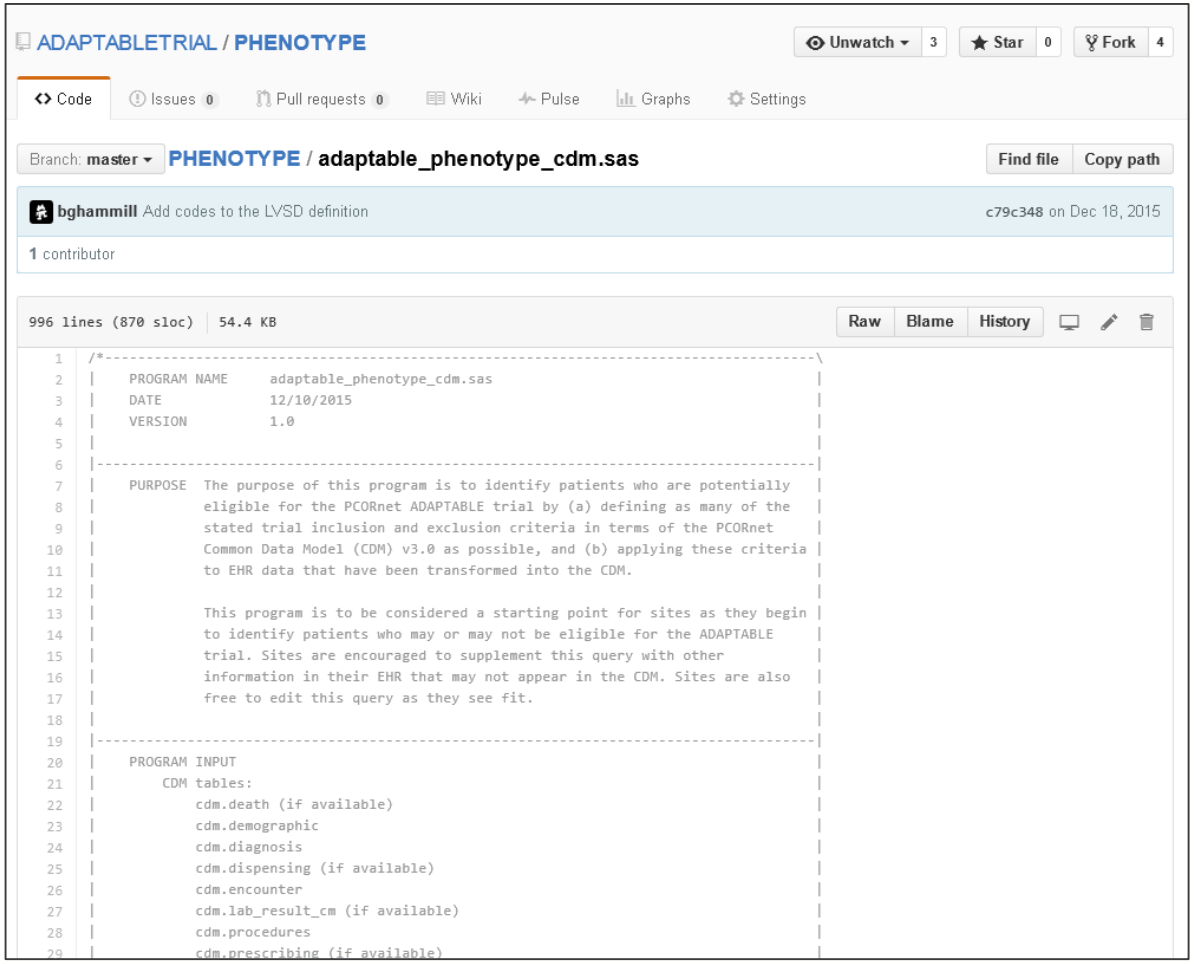
III.A.3.b. Cohort Identification

Local site investigators within the CDRNs will be asked to endorse the protocol. They will then be asked to give their permission for the CDRN, through its integrated health system members, to identify and contact potentially eligible patients. In the latter case, patients who meet criteria for secondary prevention after a cardiovascular event will be identified using search algorithms developed by the DCRI Coordinating Center (based on the trial inclusion criteria) and customized by the CDRN for their own EHR systems. Broad agreement from both cardiovascular specialists and primary care physicians will be sought. In this trial, we believe that most systems will agree that prior approval of the relevant clinician will be needed and useful since these patients will be at high-risk for death or a major disabling event. Although it is unlikely that a medical reason for ineligibility will be found, most of these patients are close to their clinicians, whose confidence in and support of the trial will be important for patient engagement, both in terms of participation as well as promoting adherence to the study medication and treatment of the inevitable clinical events.

Adaptable

ADAPTABLE Protocol Final Version 1.0, October 22, 2015, section III.A.3.b. Page 21/PDF page 25.

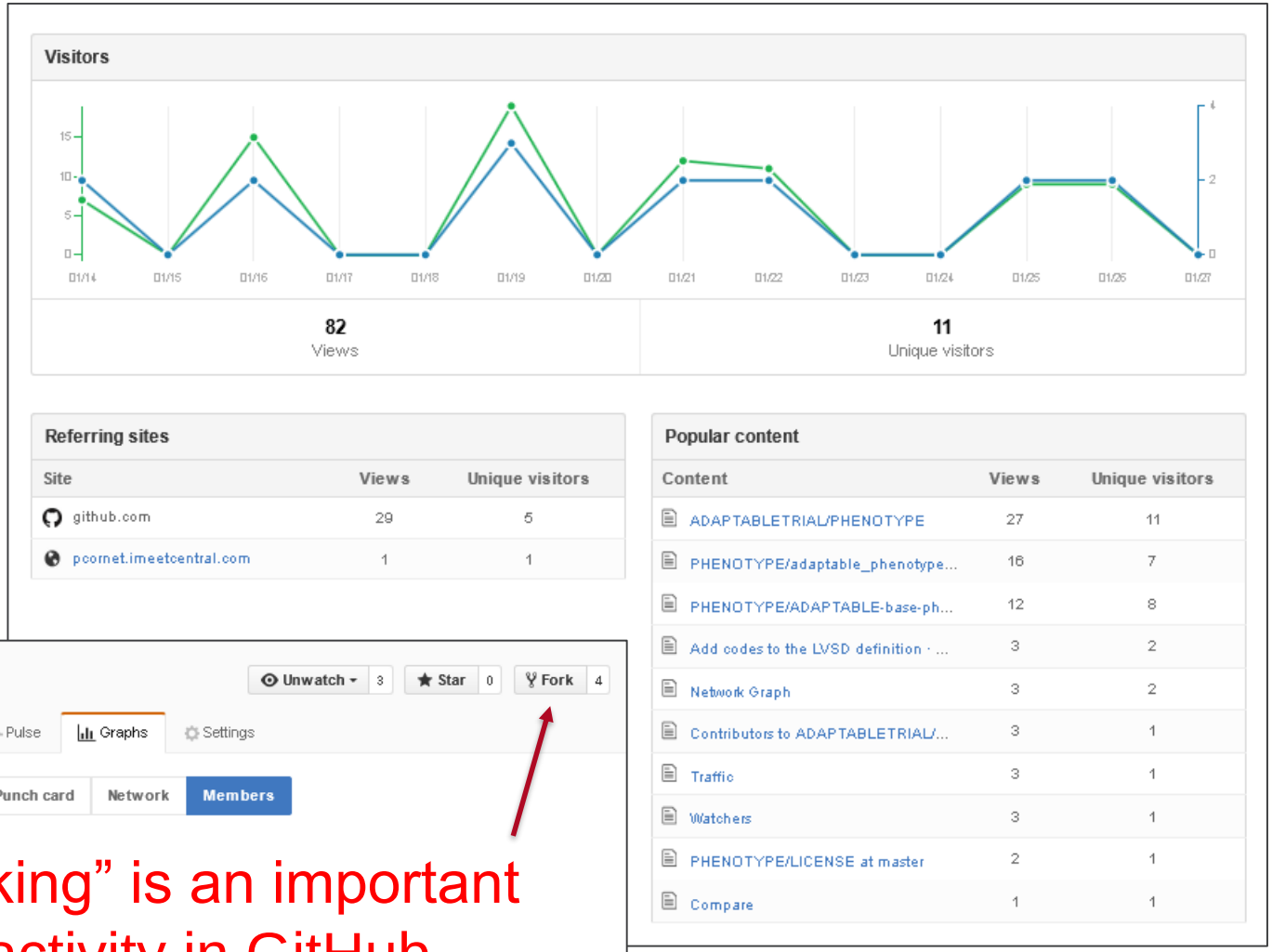
Where to find the ADAPTABLE base phenotype code on GitHub

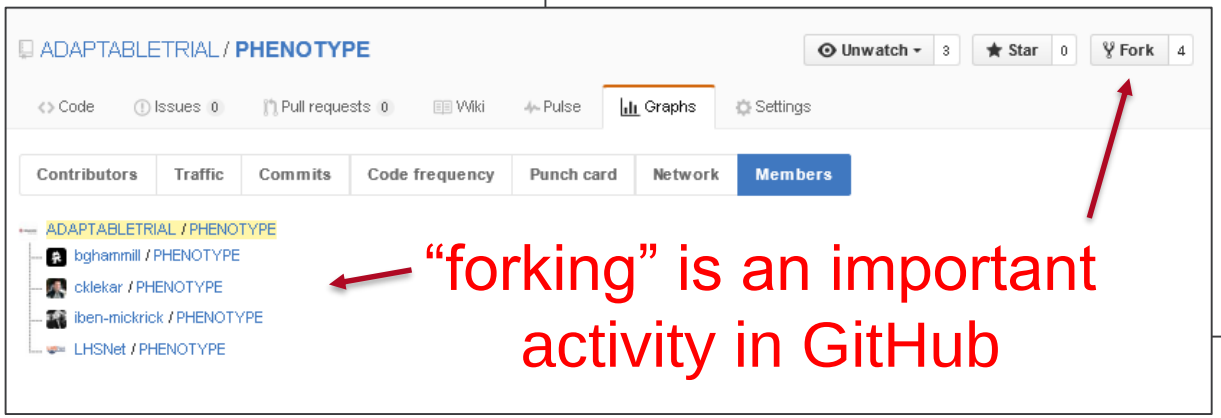


https://github.com/ADAPTABLETRIAL

Adaptable

Increasing traffic and activity on GitHub (2-week view)





Recap and Purpose Setting

- The coordinating center has completed development of the base phenotype
  - Released in December 2015
  - With appreciation to Brad Hammill!
  - https://github.com/ADAPTABLETRIAL/PHENOTYPE
- The next set of discussion questions are intended to help facilitate CDRNs sharing experiences

Discussion Questions (1 of 3)

- How are your plans shaping up for **programming and implementation** of your site's customized eligibility phenotype?
  - Are you planning to use NLP in your phenotype implementation?
  - Are you planning to run your site's phenotype in SAS, SQL, or something else?

Discussion Questions (2 of 3)

- What are your plans for **workflow of the invite**s?
  - Do you plan to automate the invitations?
  - What are your plans for activity now (prior to IRB approval)?

Discussion Questions (3 of 3)

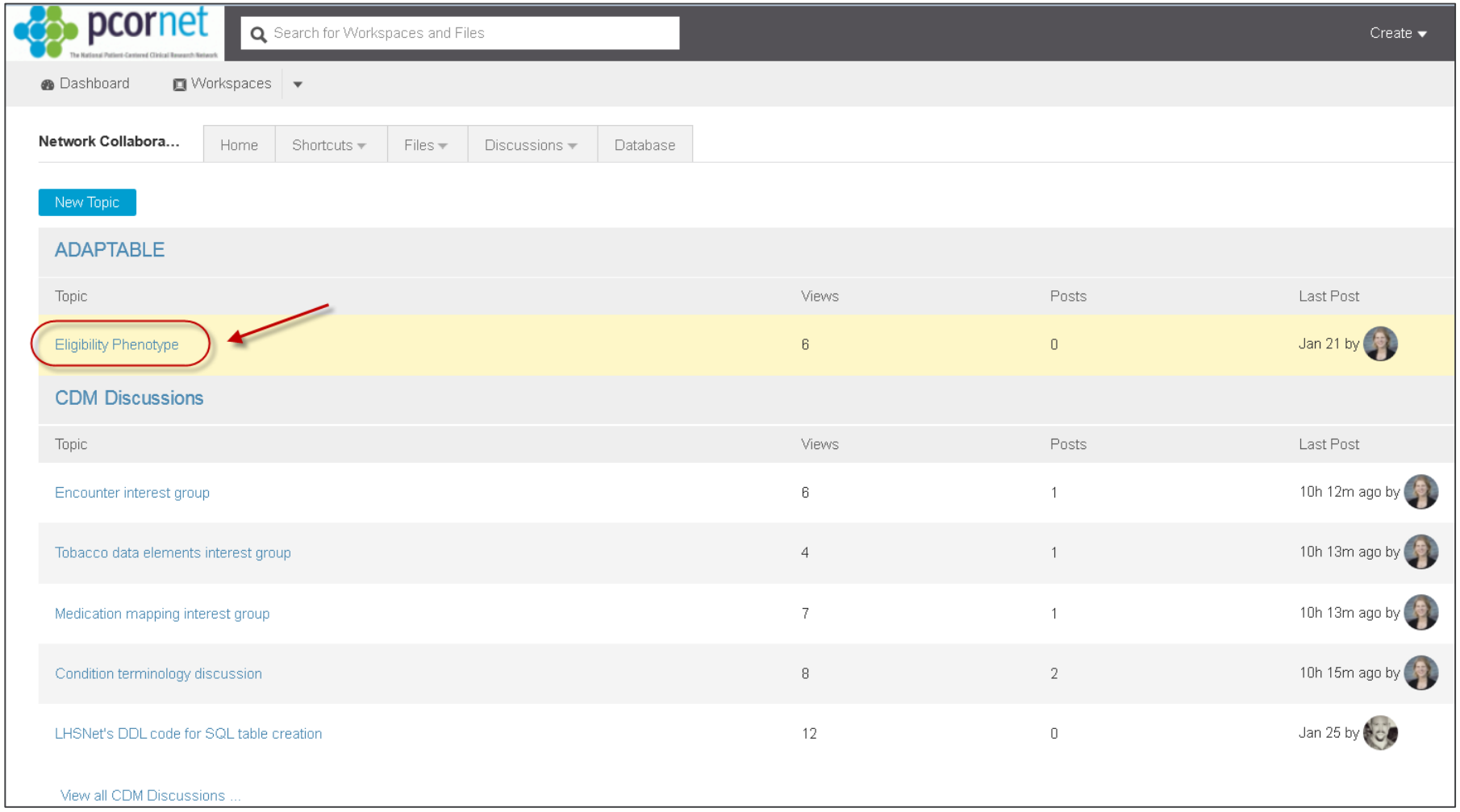
- Are you interested in **collaborations with other CDRNs**?
  - One CDRN is interested in creating SQL code from the base phenotype posted on GitHub, and opportunities for sharing code – does this interest your network?
  - Do you have other areas of development where you'd like to ask to connect with others?

Logistics of collaboration: a few potential options

- Collaborative space on iMeetCentral (within PCORnet-authenticated space)
- GitHub
  - Both public-facing repositories and private repositories
- Institution-hosted solutions, such as protected Box.com sharing
- Many other options exist!

Collaborative space on iMeetCentral:

https://pcornet.imeetcentral.com/p/ZgAAAAAVfoecwAAAAABihp



Patient Portal Development

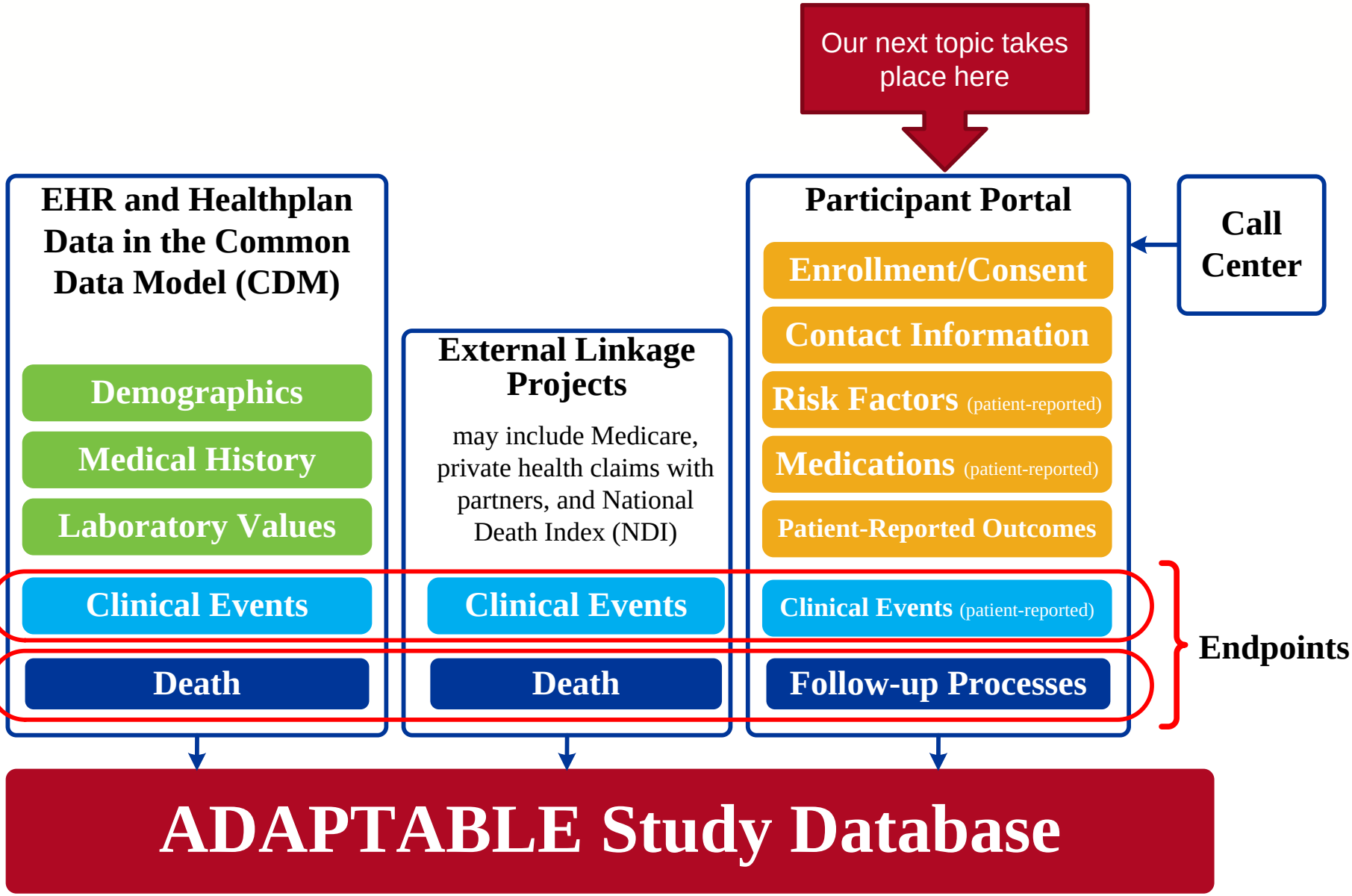


Figure 1. The ADAPTABLE study database will amalgamate multiple data sources in an integrated ecosystem.

Walk-through of portal development

Discussion and questions

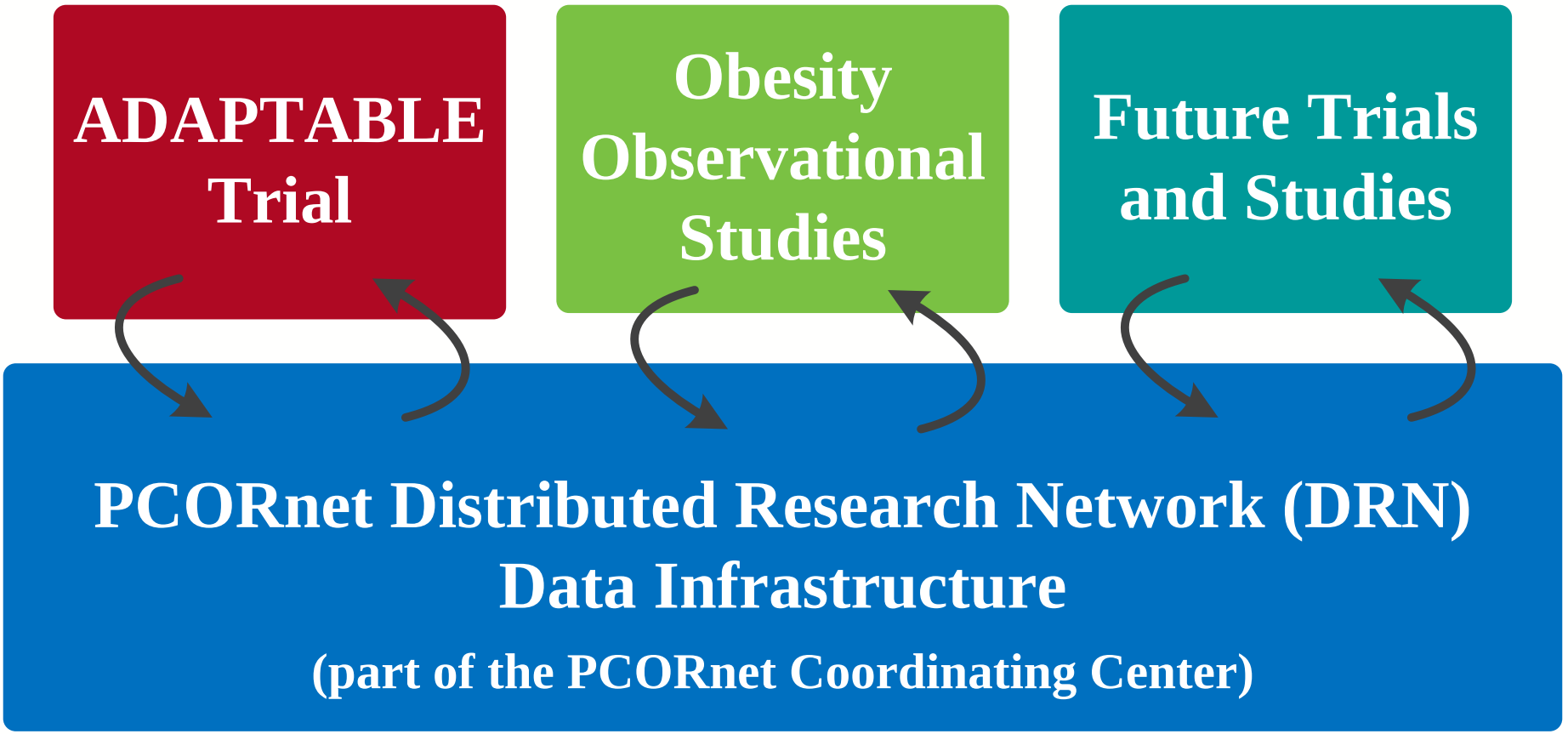
Next steps

- Materials from this meeting to be shared
  - We post updates on the DRNOC blog: https://pcornet.centraldesktop.com/drnoc-workgroups/blog/
- Contracting, site operations, and startup
  - Biweekly CDRN Calls, Mondays at 2 PM

Supplemental Slides: Reference

Abbreviations

- CDM = Common Data Model (http://pcornet.org/resource-center/pcornet-common-data-model/)
- DCRI = Duke Clinical Research Institute, the ADAPTABLE Coordinating Center
- DRN = Distributed Research Network
- DSMB = Data and Safety Monitoring Board
- DSSNI = Data Standards, Security, and Network Infrastructure
- LTFU = Lost to Follow-up
- RDBMS = Relational Database Management System (for example, Oracle, SQL Server, PostgreSQL, MySQL)



The ADAPTABLE trial is based upon the foundation of the PCORnet DRN data infrastructure. PCORnet trials and studies form a continuous cycle of improvement in data infrastructure development.

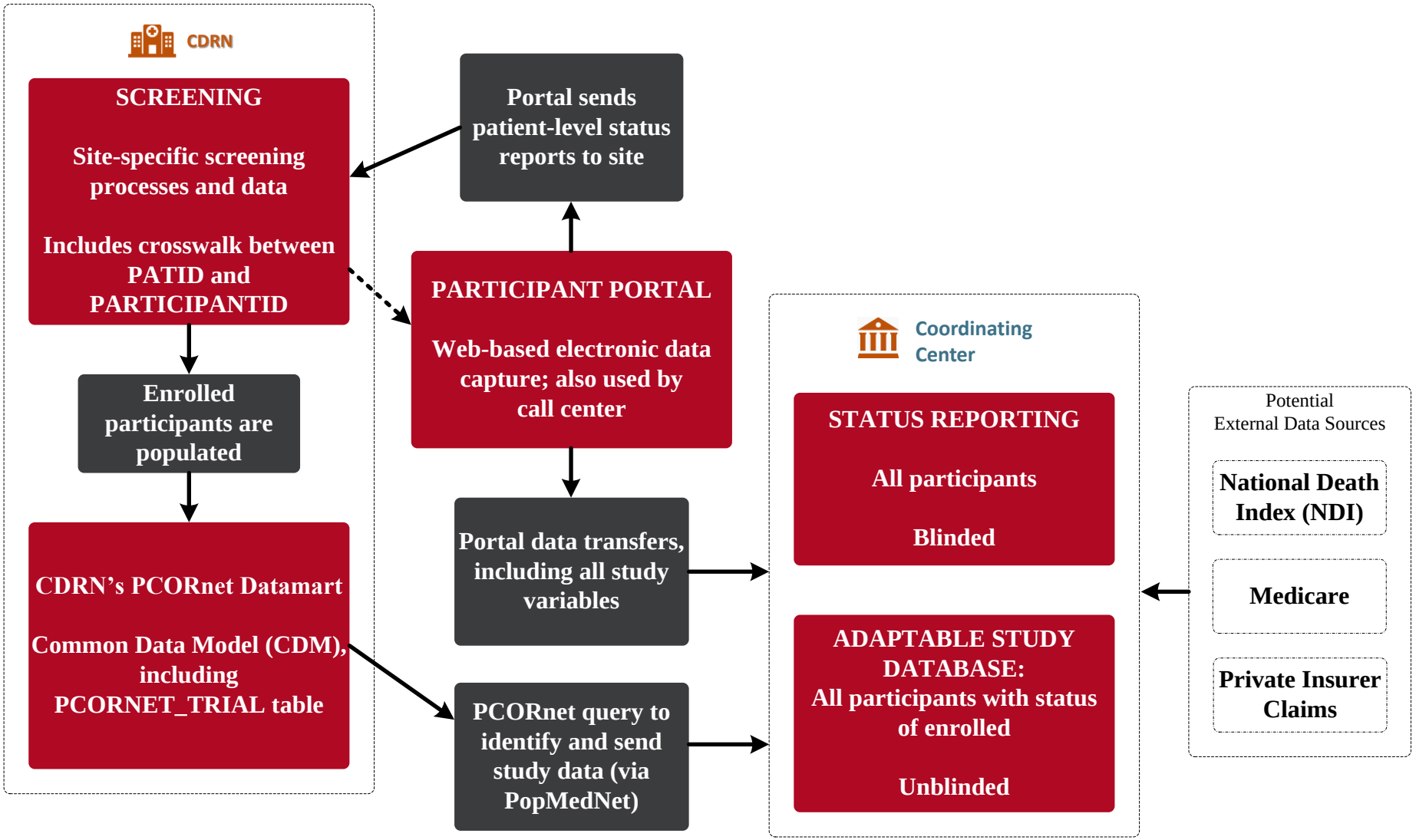


Figure 2. Data flows for the ADAPTABLE trial. Data stores are indicated in red, and data exchange processes are indicated in gray.

PCORnet Common Data Model v3.0

New to v3.0

DEMOGRAPHIC
- **PATID**
- BIRTH_DATE
- BIRTH_TIME
- SEX
- HISPANIC
- RACE
- BIOBANK_FLAG

Fundamental basis

ENROLLMENT
- **PATID**
- **ENR_START_DATE**
- ENR_END_DATE
- CHART
- **ENR_BASIS**

DISPENSING
- **DISPENSINGID**
- **PATID**
- PRESCRIBINGID (optional)
- **DISPENSE_DATE**
- **NDC**
- DISPENSE_SUP
- DISPENSE_AMT

DEATH
- **PATID**
- **DEATH_DATE**
- DEATH_DATE_IMPUTE
- **DEATH_SOURCE**
- DEATH_MATCH_CONFIDENCE

DEATH_CONDITION
- **PATID**
- **DEATH_CAUSE**
- **DEATH_CAUSE_CODE**
- **DEATH_CAUSE_TYPE**
- **DEATH_CAUSE_SOURCE**
- DEATH_CAUSE_CONFIDENCE

Data captured from processes associated with healthcare delivery

VITAL
- **VITALID**
- **PATID**
- ENCOUNTERID (optional)
- **MEASURE_DATE**
- MEASURE_TIME
- **VITAL_SOURCE**
- HT
- WT
- DIASTOLIC
- SYSTOLIC
- ORIGINAL_BMI
- BP_POSITION
- SMOKING
- TOBACCO
- TOBACCO_TYPE

CONDITION
- **CONDITIONID**
- **PATID**
- ENCOUNTERID (optional)
- REPORT_DATE
- RESOLVE_DATE
- ONSET_DATE
- CONDITION_STATUS
- **CONDITION**
- **CONDITION_TYPE**
- **CONDITION_SOURCE**

PRO_CM
- **PRO_CM_ID**
- **PATID**
- ENCOUNTERID (optional)
- **PRO_ITEM**
- PRO_LOINC
- **PRO_DATE**
- PRO_TIME
- **PRO_RESPONSE**
- PRO_METHOD
- PRO_MODE
- PRO_CAT

Data captured within multiple contexts: healthcare delivery, registry activity, or directly from patients

ENCOUNTER
- **ENCOUNTERID**
- **PATID**
- **ADMIT_DATE**
- ADMIT_TIME
- DISCHARGE_DATE
- DISCHARGE_TIME
- PROVIDERID
- FACILITY_LOCATION
- **ENC_TYPE**
- FACILITYID
- DISCHARGE_DISPOSITION
- DISCHARGE_STATUS
- DRG
- DRG_TYPE
- ADMITTING_SOURCE

DIAGNOSIS
- **DIAGNOSISID**
- **PATID**
- **ENCOUNTERID**
- *ENC_TYPE (replicated)*
- *ADMIT_DATE (replicated)*
- *PROVIDERID (replicated)*
- **DX**
- **DX_TYPE**
- **DX_SOURCE**
- PDX

PROCEDURES
- **PROCEDURESID**
- **PATID**
- **ENCOUNTERID**
- *ENC_TYPE (replicated)*
- *ADMIT_DATE (replicated)*
- *PROVIDERID (replicated)*
- PX_DATE
- **PX**
- **PX_TYPE**
- PX_SOURCE

LAB_RESULT_CM
- **LAB_RESULT_CM_ID**
- **PATID**
- ENCOUNTERID (optional)
- LAB_NAME
- SPECIMEN_SOURCE
- LAB_LOINC
- PRIORITY
- RESULT_LOC
- LAB_PX
- LAB_PX_TYPE
- LAB_ORDER_DATE
- SPECIMEN_DATE
- SPECIMEN_TIME
- **RESULT_DATE**
- RESULT_TIME
- RESULT_QUAL
- RESULT_NUM
- RESULT_MODIFIER
- RESULT_UNIT
- NORM_RANGE_LOW
- NORM_MODIFIER_LOW
- NORM_RANGE_HIGH
- NORM_MODIFIER_HIGH
- ABN_IND

PRESCRIBING
- **PRESCRIBINGID**
- **PATID**
- ENCOUNTERID (optional)
- RX_PROVIDERID
- RX_ORDER_DATE
- RX_ORDER_TIME
- RX_START_DATE
- RX_END_DATE
- RX_QUANTITY
- RX_REFILLS
- RX_DAYS_SUPPLY
- RX_FREQUENCY
- RX_BASIS
- RXNORM_CUI

Data captured from healthcare delivery, direct encounter basis

PCORNET_TRIAL
- **PATID**
- **TRIALID**
- **PARTICIPANTID**
- TRIAL_SITEID
- TRIAL_ENROLL_DATE
- TRIAL_END_DATE
- TRIAL_WITHDRAW_DATE
- TRIAL_INVITE_CODE

Associations with PCORnet clinical trials

HARVEST
- **NETWORKID**
- NETWORK_NAME
- **DATAMARTID**
- DATAMART_NAME
- DATAMART_PLATFORM
- CDM_VERSION
- DATAMART_CLAIMS
- DATAMART_EHR
- BIRTH_DATE_MGMT
- ENR_START_DATE_MGMT
- ENR_END_DATE_MGMT
- ADMIT_DATE_MGMT
- DISCHARGE_DATE_MGMT
- PX_DATE_MGMT
- RX_ORDER_DATE_MGMT
- RX_START_DATE_MGMT
- RX_END_DATE_MGMT
- DISPENSE_DATE_MGMT
- LAB_ORDER_DATE_MGMT
- SPECIMEN_DATE_MGMT
- RESULT_DATE_MGMT
- MEASURE_DATE_MGMT
- ONSET_DATE_MGMT
- REPORT_DATE_MGMT
- RESOLVE_DATE_MGMT
- PRO_DATE_MGMT
- REFRESH_DEMOGRAPHIC_DATE
- REFRESH_ENROLLMENT_DATE
- REFRESH_ENCOUNTER_DATE
- REFRESH_DIAGNOSIS_DATE
- REFRESH_PROCEDURES_DATE
- REFRESH_VITAL_DATE
- REFRESH_DISPENSING_DATE
- REFRESH_LAB_RESULT_CM_DATE
- REFRESH_CONDITION_DATE
- REFRESH_PRO_CM_DATE
- REFRESH_PRESCRIBING_DATE
- REFRESH_PCORNET_TRIAL_DATE
- REFRESH_DEATH_DATE
- REFRESH_DEATH_CAUSE_DATE

Process-related data

http://www.pcornet.org/resource-center/pcornet-common-data-model/

Bold font indicates fields that cannot be null due to primary key definitions or record-level constraints.

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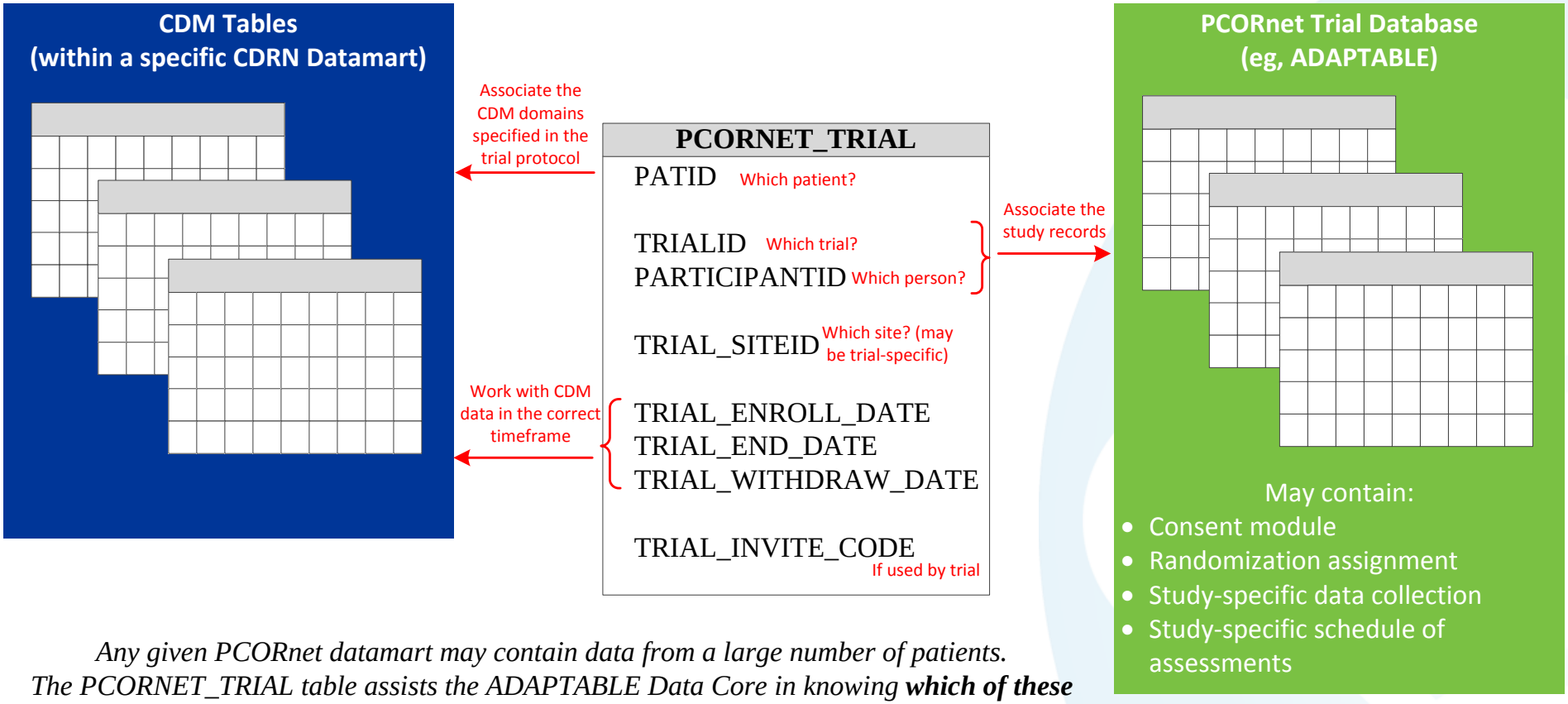
The PCORnet CDM lives at
http://pcornet.org/pcornet-common-data-model/

The PCORNET_TRIAL table serves as a connector and filter for CDM data within the parameters of a given trial protocol:



Any given PCORnet datamart may contain data from a large number of patients. The PCORNET_TRIAL table assists the ADAPTABLE Data Core in knowing ***which of these patients have consented and been enrolled*** *in the ADAPTABLE trial for querying purposes.*

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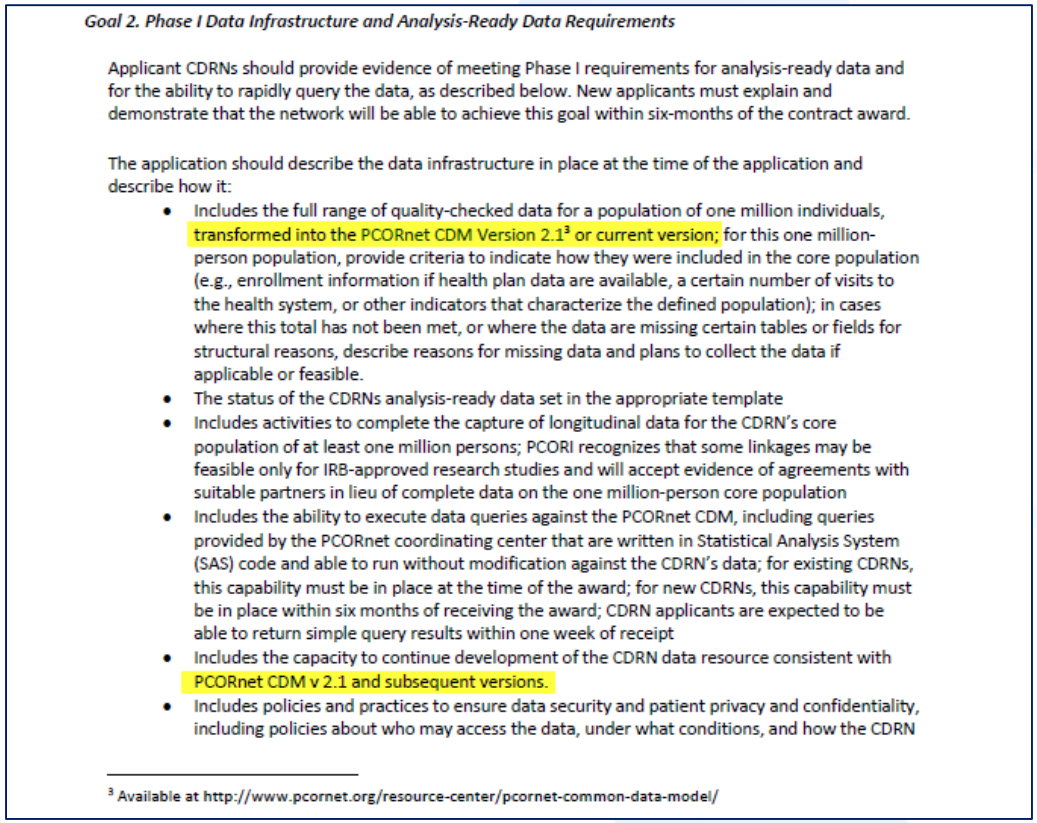
Small modifications from the slide used with the CDM v3.0 Stakeholder meetings on April 28 and 29, 2015. The CDM v3.0 was released on June 1, 2015.

Implementation of v3.0

- v3.0 expected to be in place at beginning of Phase II, per PFA
- Phase II expectations for CDM versioning are in development, and not part of this current discussion

Page 13 of the Phase II PFA (highlight added) www.pcori.org/sites/default/files/PCORI-PFA-CDRN.pdf

Slide from CDM v3.0 Stakeholder meetings on April 28 and 29, 2015.



Goal 2. Phase I Data Infrastructure and Analysis-Ready Data Requirements

Applicant CDRNs should provide evidence of meeting Phase I requirements for analysis-ready data and for the ability to rapidly query the data, as described below. New applicants must explain and demonstrate that the network will be able to achieve this goal within six-months of the contract award.

The application should describe the data infrastructure in place at the time of the application and describe how it:

- Includes the full range of quality-checked data for a population of one million individuals, transformed into the PCORnet CDM Version 2.1[3] or current version; for this one million-person population, provide criteria to indicate how they were included in the core population (e.g., enrollment information if health plan data are available, a certain number of visits to the health system, or other indicators that characterize the defined population); in cases where this total has not been met, or where the data are missing certain tables or fields for structural reasons, describe reasons for missing data and plans to collect the data if applicable or feasible.
- The status of the CDRNs analysis-ready data set in the appropriate template
- Includes activities to complete the capture of longitudinal data for the CDRN's core population of at least one million persons; PCORI recognizes that some linkages may be feasible only for IRB-approved research studies and will accept evidence of agreements with suitable partners in lieu of complete data on the one million-person core population
- Includes the ability to execute data queries against the PCORnet CDM, including queries provided by the PCORnet coordinating center that are written in Statistical Analysis System (SAS) code and able to run without modification against the CDRN's data; for existing CDRNs, this capability must be in place at the time of the award; for new CDRNs, this capability must be in place within six months of receiving the award; CDRN applicants are expected to be able to return simple query results within one week of receipt
- Includes the capacity to continue development of the CDRN data resource consistent with PCORnet CDM v 2.1 and subsequent versions.
- Includes policies and practices to ensure data security and patient privacy and confidentiality, including policies about who may access the data, under what conditions, and how the CDRN

[3] Available at http://www.pcornet.org/resource-center/pcornet-common-data-model/

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Supplemental Slides: Selected sets from prior sessions

Data Sharing in ADAPTABLE

(slides from December 11 session)

Language from ADAPTABLE Consent

6. We will get some information from other places. Taking part in ADAPTABLE does not require any special study visits or trips to your doctor. But to be sure we get a complete picture of your health:

   - We will get certain information from your medical records. Examples include information about your health problems, health care visits, hospital stays, medical procedures, and lab results. In some cases, we might need you to sign a form saying it is okay for us to get the information we need for the study.
   - We will ask for the last 4 digits of your Social Security number and health insurance ID numbers. We need these to check other sources (such as health insurance claims) for information about your health.

   We will get these kinds of information from time to time for as long as you are in the study.

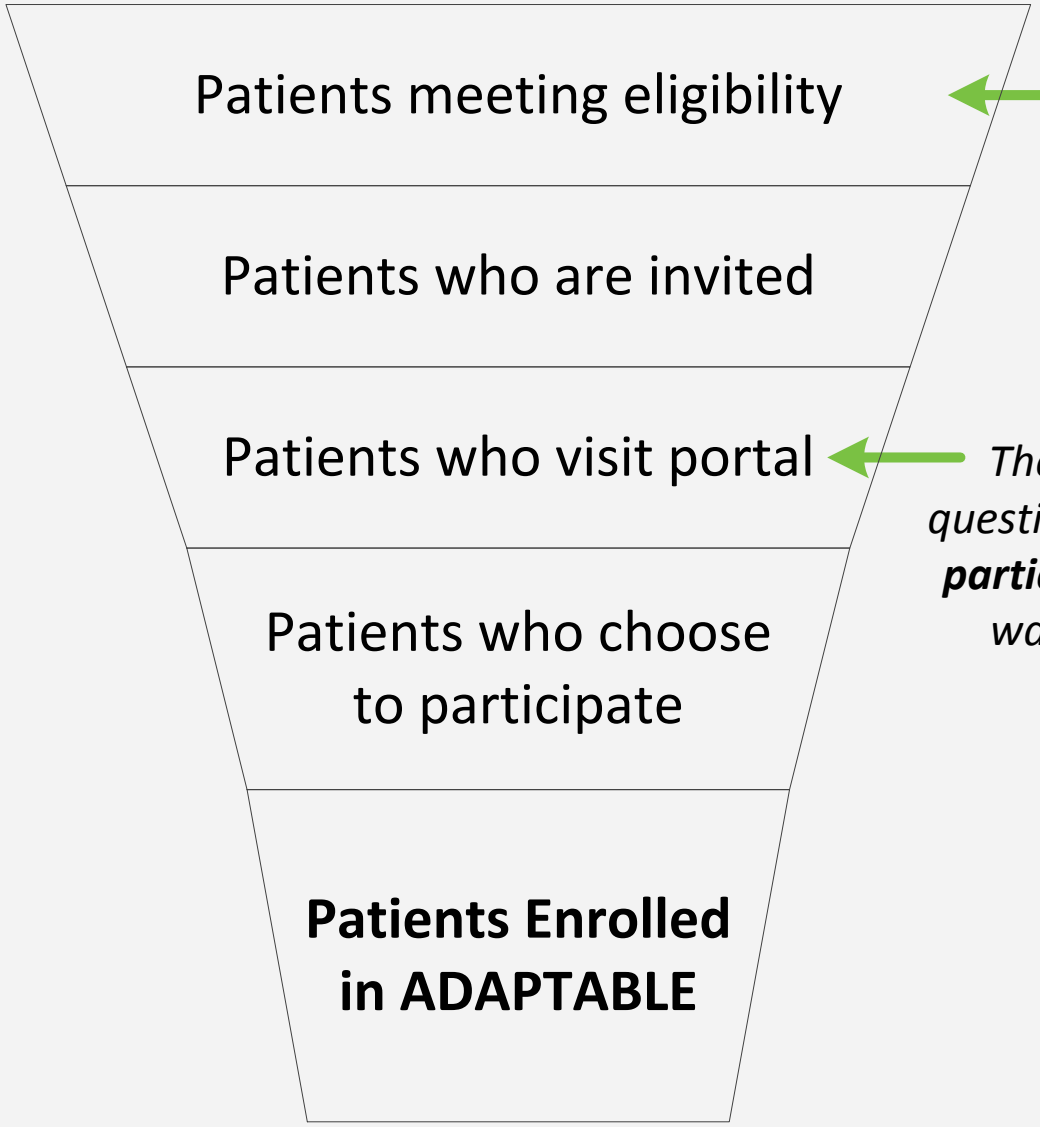
ADAPTABLE Consent, Final Version 1.0, October 22, 2015. Page 2.
http://www.pcornet.org/wp-content/uploads/2015/04/ADAPTABLE-Consent-Form_2015-10-22-FINAL.pdf

Two areas of consideration

- **External linkage projects for ADAPTABLE** (which may include Medicare, private health claims with partners, and National Death Index) will be managed by the Coordinating Center
  - Patient-level linkage between ADAPTABLE patients and these external sources will also be performed by the Coordinating Center
- Transmitting information about **subject recruitment status** is a different process and will be covered in operational updates.

Review of Phenotype Context

(slides from December 11 session)



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    c. Significant bleeding disorders that preclude the use of aspirin
4. Access to the Internet. In the event that the CDRNs are notified that a cohort of patients without internet access can be included, then patient agreement will be obtained during the consent process to provide follow-up information by telephone contact with the DCRI Call Center.
5. Not currently treated with an oral anticoagulant – either warfarin or a novel anticoagulant (dabigatran, rivaroxaban, apixaban, edoxaban) – and not planned to be treated in the future with an oral anticoagulant for existing indications such as atrial fibrillation, deep venous thrombosis, or pulmonary embolism.
6. Not currently treated with ticagrelor and not planned to be treated in the future with ticagrelor.
7. Female patients who are not pregnant or nursing an infant
8. Estimated risk of a major cardiovascular event (MACE) > 8% over next 3 years as defined by the presence of at least one or more of the following enrichment factors:
    a. Age > 65 years
    b. Serum creatinine > 1.5 mg/dL
    c. Diabetes mellitus (Type 1 or Type 2)
    d. 3-vessel coronary artery disease
    e. Cerebrovascular disease and/or peripheral arterial disease
    f. Left ventricular ejection fraction (LVEF) < 50%
    g. Current cigarette smoker

Ticagrelor criterion was added as a result of protocol comment cycle

Adaptable

ADAPTABLE eligibility criteria contain both inclusions and exclusions

There will be no exclusions for any upper age limit, comorbid conditions, or concomitant medications other than oral anticoagulants and ticagrelor that are used at the time of randomization, or are planned to be used during the study follow-up.

Simple, inclusive eligibility criteria will make enrollment easier, and will render study results more generalizable to a broader population of patients. We will exclude pregnant or lactating women (because of concern for the fetus or child), patients taking oral anticoagulants or likely to require an oral anticoagulant during trial follow-up (because of complex drug interactions and a projected excessive risk of bleeding), and patients at relatively low risk for cardiovascular events (ie, no enrichment factor because of the large number of outcomes needed to detect a clinically meaningful difference with the available sample size).

ADAPTABLE Protocol Final Version 1.0, October 22, 2015, section III.A.1., page 17 (PDF page 21).

Screening and recruitment development

- Sites and/or networks are heterogeneous, and expected to have different processes for identifying, contacting, and inviting potential trial participants
  - "Base phenotype" (to be developed by ADAPTABLE CC) **will be modified by individual sites to best suit their processes**

Base phenotype customization is expected

III.A.3.b. Cohort Identification

Local site investigators within the CDRNs will be asked to endorse the protocol. They will then be asked to give their permission for the CDRN, through its integrated health system members, to identify and contact potentially eligible patients. In the latter case, patients who meet criteria for secondary prevention after a cardiovascular event will be identified using search algorithms developed by the DCRI Coordinating Center (based on the trial inclusion criteria) and customized by the CDRN for their own EHR systems. Broad agreement from both cardiovascular specialists and primary care physicians will be sought. In this trial, we believe that most systems will agree that prior approval of the relevant clinician will be needed and useful since these patients will be at high-risk for death or a major disabling event. Although it is unlikely that a medical reason for ineligibility will be found, most of these patients are close to their clinicians, whose confidence in and support of the trial will be important for patient engagement, both in terms of participation as well as promoting adherence to the study medication and treatment of the inevitable clinical events.

ADAPTABLE Protocol Final Version 1.0, October 22, 2015, section III.A.3.b. Page 21/PDF page 25.

In summary:

The ADAPTABLE eligibility phenotype will not be executed by the Coordinating Center.

Each network will run their phenotype at the local level, against their **own data sources**, and **using logic that best fits** their local **workflows and governance** for potential participant identification.

Phenotype Feedback Cycle

(slides from December 11 session)

Feedback cycle for base phenotype specification

- Feedback cycle November 3-20
- **89 discreet comments received from 6 networks**
  - With many thanks!
- Comments classified into 16 thematic categories, responses added, and posted:
  - https://pcornet.imeetcentral.com/adaptabletrial/file/43196859/

16 thematic categories

Tag
AGE
ALLERGY
AUTHORITATIVE_SOURCE
BLEED
COHORT_BASIS
ENRICHMENT
FUTURE_TX
GLOBAL
LOOK_BACK
MEDS
MI
MORTALITY
NET_ACCESS
PREGNANCY
SITE_PLANNING
SMOKING

Enrichment factors (eligibility #8)

1. Known atherosclerotic cardiovascular disease (ASCVD), defined by a history of prior myocardial infarction, prior coronary angiography showing ≥75% stenosis of at least one epicardial coronary vessel, or prior coronary revascularization procedures (either PCI or CABG)
2. Age ≥ 18 years
3. No known safety concerns or side effects considered to be related to aspirin, including
   a. No history of significant allergy to aspirin such as anaphylaxis, urticaria, or significant gastrointestinal intolerances
   b. No history of significant GI bleed within the past 12 months
   c. Significant bleeding disorders that preclude the use of aspirin
4. Access to the Internet. In the event that the CDRNs are notified that a cohort of patients without internet access can be included, then patient agreement will be obtained during the consent process to provide follow-up information by telephone contact with the DCRI Call Center.
5. Not currently treated with an oral anticoagulant – either warfarin or a novel anticoagulant (dabigatran, rivaroxaban, apixaban, edoxaban) – and not planned to be treated in the future with an oral anticoagulant for existing indications such as atrial fibrillation, deep venous thrombosis, or pulmonary embolism.
6. Not currently treated with ticagrelor and not planned to be treated in the future with ticagrelor.
7. Female patients who are not pregnant or nursing an infant
8. Estimated risk of a major cardiovascular event (MACE) > 8% over next 3 years as defined by the presence of at least one or more of the following enrichment factors:
   a. Age > 65 years
   b. Serum creatinine > 1.5 mg/dL
   c. Diabetes mellitus (Type 1 or Type 2)
   d. 3-vessel coronary artery disease
   e. Cerebrovascular disease and/or peripheral arterial disease
   f. Left ventricular ejection fraction (LVEF) < 50%
   g. Current cigarette smoker

Only "**one or more**" enrichment factor is required

8. Estimated risk of a major cardiovascular event (MACE) > 8% over next 3 years as defined by the presence of at least one or more of the following enrichment factors:
   a. Age > 65 years OR
   b. Serum creatinine > 1.5 mg/dL OR
   c. Diabetes mellitus (Type 1 or Type 2) OR
   d. 3-vessel coronary artery disease OR
   e. Cerebrovascular disease and/or peripheral arterial disease OR
   f. Left ventricular ejection fraction (LVEF) < 50% OR
   g. Current cigarette smoker

Some networks expressed concern about reliability of certain factors in their data (such as current smoking status).

However, the "one or more" requirement means that **sites have discretion** about which enrichment factor(s) to implement.

Adaptable

Overlap with baseline CRF

In the portal, the potential participant will answer a few basic questions to check for those unsafe to participate.

The basic questions are expected to include:

1. Aspirin allergy
2. History of severe bleeding
3. Oral anticoagulant use
4. Pregnancy

1. Known atherosclerotic cardiovascular disease (ASCVD), defined by a history of prior myocardial infarction, prior coronary angiography showing ≥75% stenosis of at least one epicardial coronary vessel, or prior coronary revascularization procedures (either PCI or CABG)
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3. No known safety concerns or side effects considered to be related to aspirin, including
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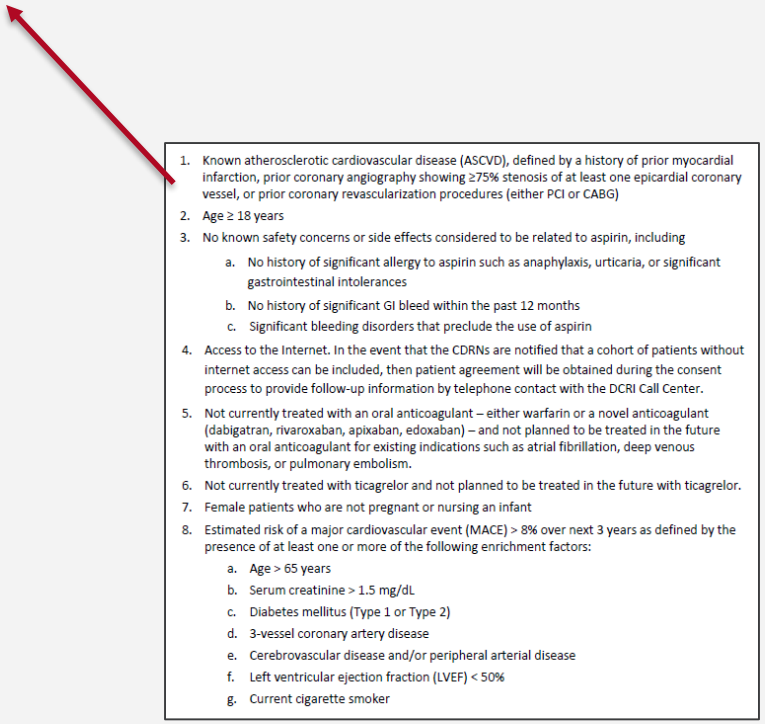
    a. Age > 65 years
    b. Serum creatinine > 1.5 mg/dL
    c. Diabetes mellitus (Type 1 or Type 2)
    d. 3-vessel coronary artery disease
    e. Cerebrovascular disease and/or peripheral arterial disease
    f. Left ventricular ejection fraction (LVEF) < 50%
    g. Current cigarette smoker

Adaptable

Known Atherosclerotic Cardiovascular Disease

1. Known atherosclerotic cardiovascular disease (ASCVD), defined by a history of prior myocardial infarction, prior coronary angiography showing ≥75% stenosis of at least one epicardial coronary vessel, or prior coronary revascularization procedures (either PCI or CABG)



1. Known atherosclerotic cardiovascular disease (ASCVD), defined by a history of prior myocardial infarction, prior coronary angiography showing ≥75% stenosis of at least one epicardial coronary vessel, or prior coronary revascularization procedures (either PCI or CABG)
2. Age ≥ 18 years
3. No known safety concerns or side effects considered to be related to aspirin, including
    a. No history of significant allergy to aspirin such as anaphylaxis, urticaria, or significant gastrointestinal intolerances
    b. No history of significant GI bleed within the past 12 months
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    c. Diabetes mellitus (Type 1 or Type 2)
    d. 3-vessel coronary artery disease
    e. Cerebrovascular disease and/or peripheral arterial disease
    f. Left ventricular ejection fraction (LVEF) < 50%
    g. Current cigarette smoker

Other important areas (1 of 2)

- Cohort basis, including consideration of “loyalty cohorts”
- Practices of date obfuscation within a datamart (such as shifting all birth dates by a random number of days)
- Concern for reliability of smoking data (enrichment factor)

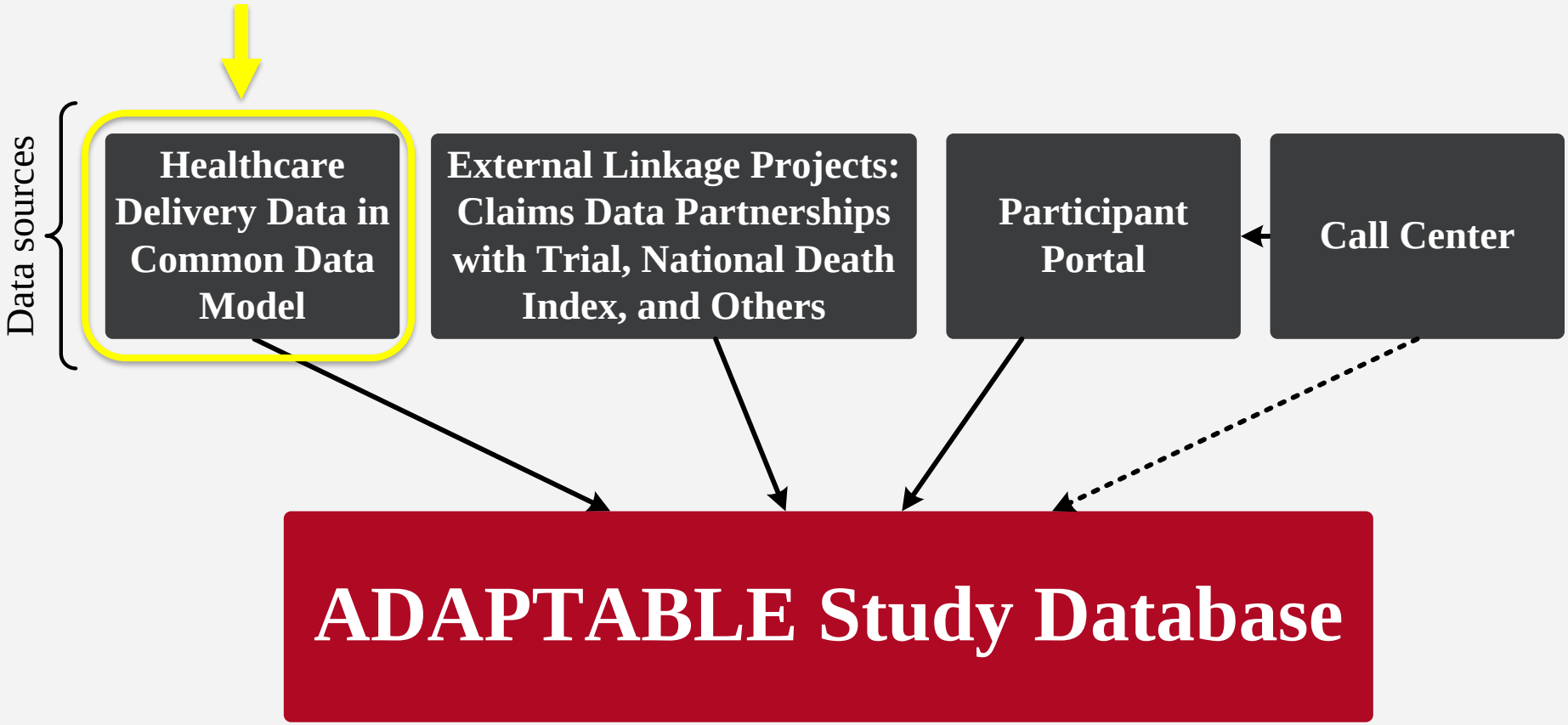
Other important areas (2 of 2)

- Does the presence of an e-mail address serves as a proxy measure for Internet access
- Confirmation of future treatment issue
- Global: Development processes

ADAPTABLE RDBMS and SAS Platform Basis

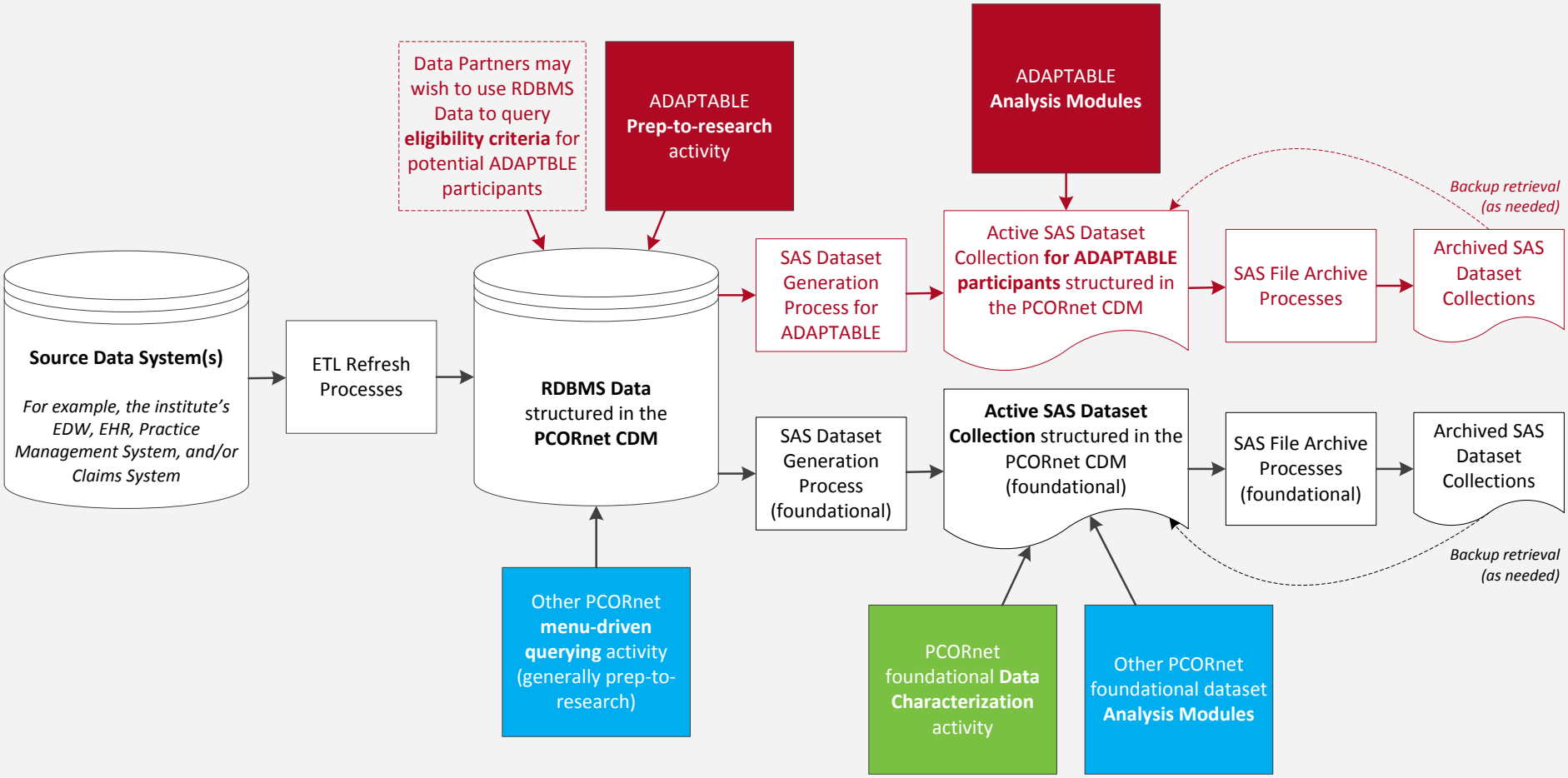
(slides from October 30 session)

Modules of the data landscape amalgamate into the study database



Recommended setup* for ADAPTABLE data partners - DRAFT

* Please note that data partners are known to be heterogeneous in their technical configurations and processes.

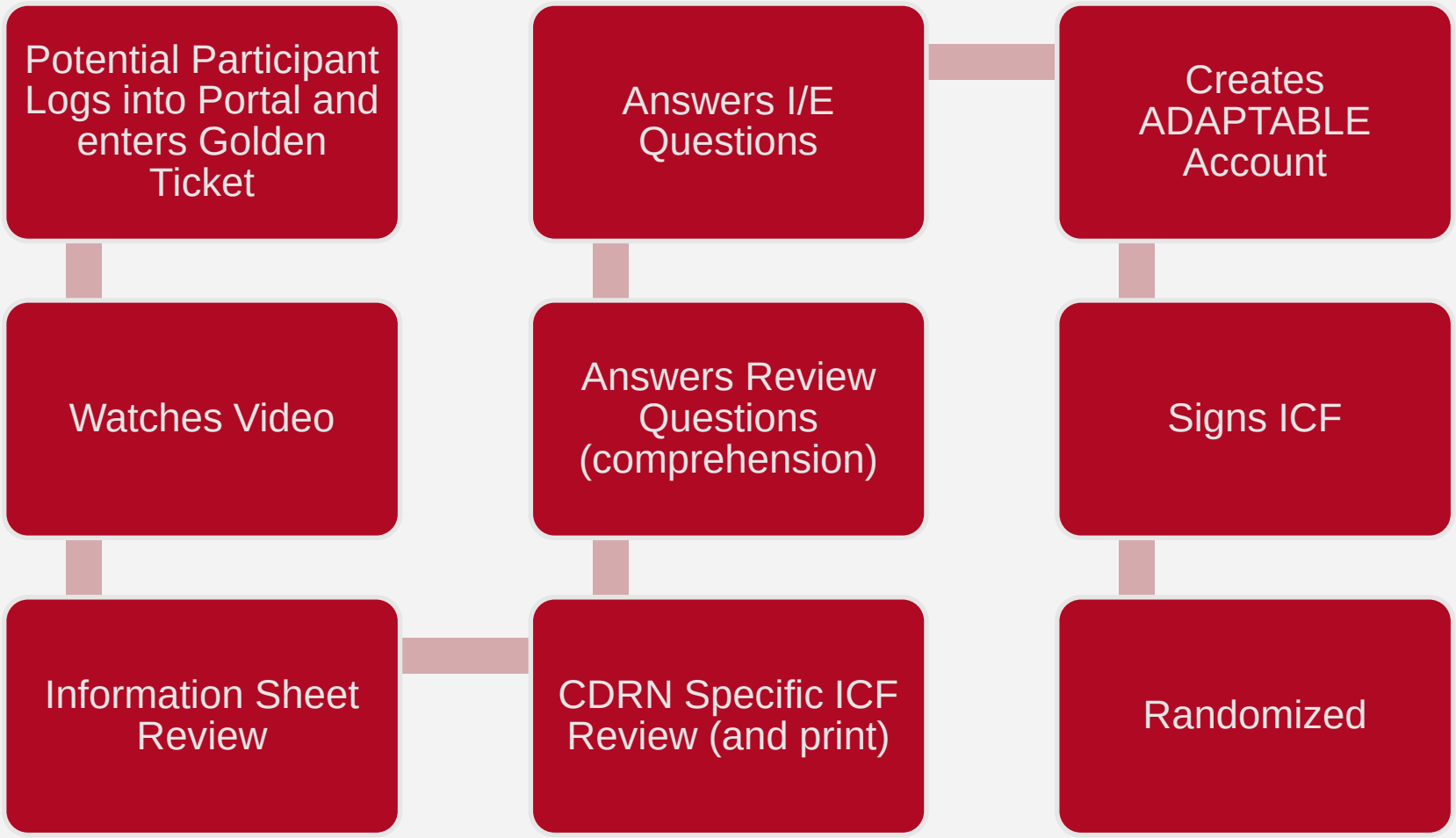


Adaptable

Data Flow Development between Patient Portal and Sites

(slides from October 30 session)

Steps to Randomize Participants



CDRN Responsibilities

- CDRNs request “Golden Ticket” codes through Mytrus
- CDRNs invite potential participants and provide each a “Golden Ticket”
- CDRNs track “Golden Ticket” assignments
- Mytrus provides “Golden Ticket” status for those entered into Mytrus
- CDRNs reconcile “Golden Ticket” to patient identifiers
- CDRNs update PCORNET_TRIAL (including the PARTICIPANTID and TRIAL_INVITE_CODE)

Golden Ticket

Mytrus Subject ID

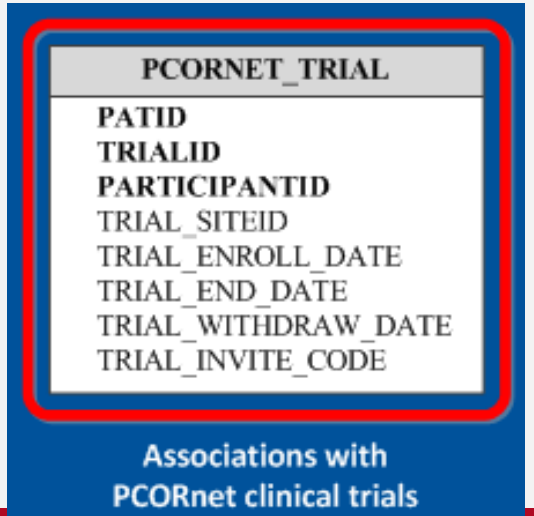
Adaptable

Participant Identifiers

ID	Origin	Trigger	Description
Golden Ticket	Mytrus	CDRNs request through Mytrus	CDRNs request as bulk and receive download that can be used for mail merges
Mytrus Subject ID	Mytrus	Upon randomization	Unique system generated study number assigned at randomization and sequential
PATID	PCORNET CDM	Present in the CDM	The unique subject identifier in the PCORNET CDM that CDRNs populate in PCORNET_TRIAL
PARTICIPANTID	PCORNET_TRIAL	CDRN Populates	The ADAPTABLE randomized participant identifier that links the Mytrus randomized participants to the PCORNET CDM
TRIAL_INVITE_CODE	PCORNET_TRIAL	CDRN Populates	The ADAPTABLE invited participant identifier captured in PCORNET_TRIAL

Mytrus Reports

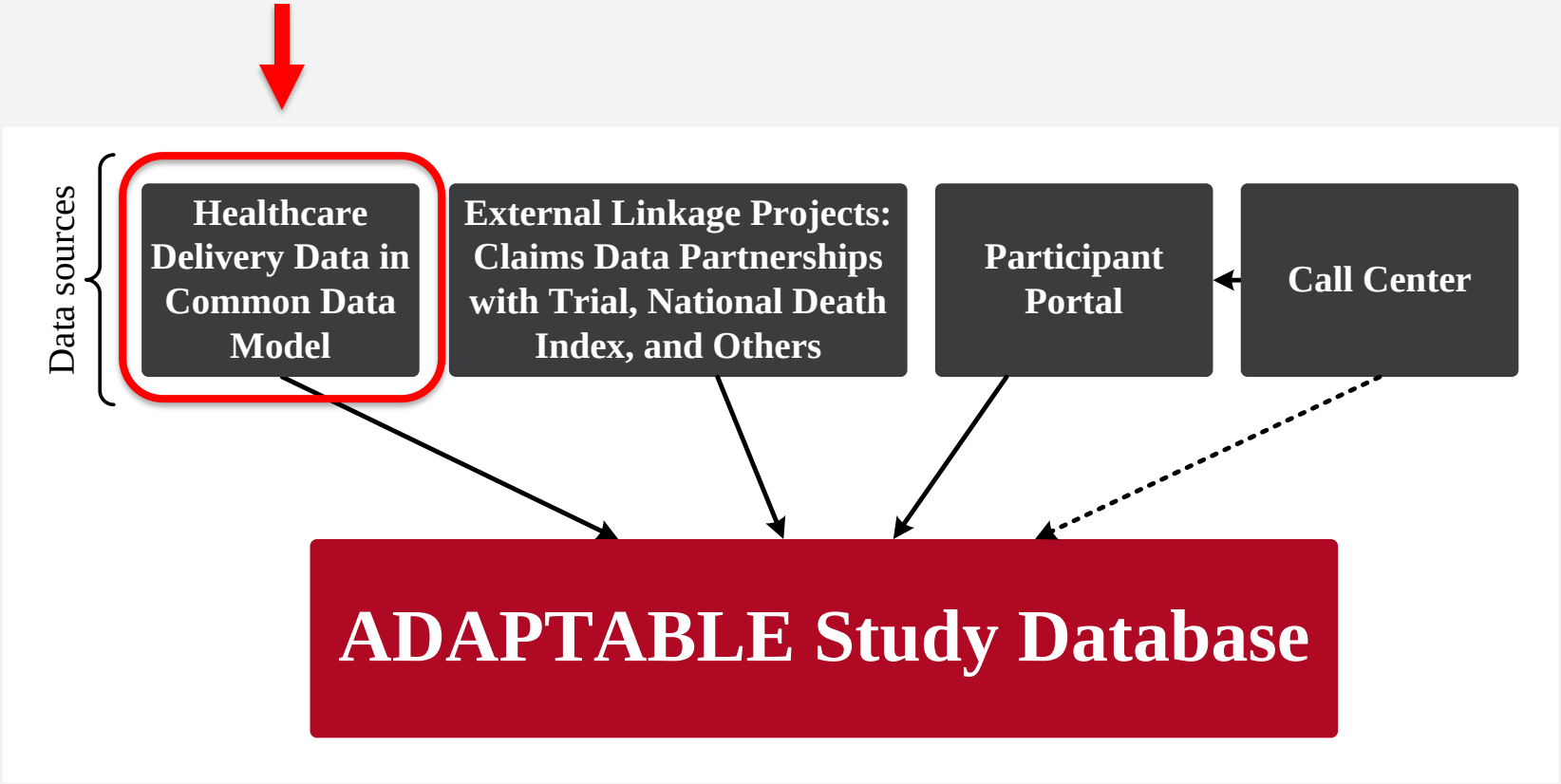
- Entered “Golden Ticket” Codes
- I/E Dropped Out *(aggregate)*
- Completed Account Creation
- Signed Consent
- Randomized
- Key Participant Identifiers (e.g. Name, DOB, Gender, Race)
- Other fields needed for PCORNET_TRIAL



Drilling Down into Individual Modules

(slides from September 25 session)

Module #1: CDRN CDM data



#1: CDM development notes

- The ADAPTABLE trial will use CDM v3.0
- ADAPTABLE trial DRN activity will be performed in SAS
- DRN OC data characterization processes will be the primary mechanism for determining datamart “analysis-ready” state
- ADAPTABLE Site PIs will receive request to confirm ADAPTABLE datamart concordance with ADAPTABLE clinical sites

Why are “sites” different from “datamarts”?

Working definitions:

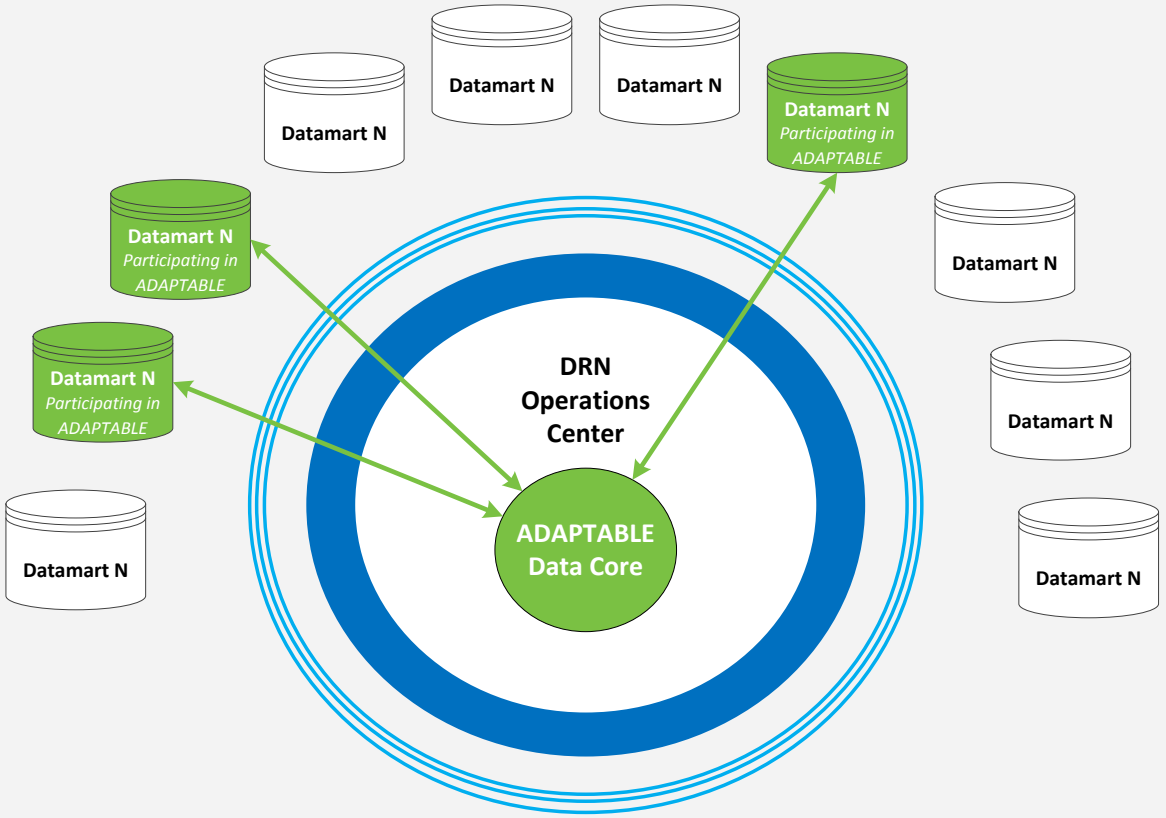
Sites = **Organization of people** for clinical and patient-facing purposes.

Datamarts = **Organization of data** for distributed querying activity.

- Existing CDRNs have different network typologies (ie, different configurations for their datamarts)
  - One datamart may include more than one site
- Sites participating in ADAPTABLE will likely be smaller components of larger networks

ADAPTABLE Distributed Querying

- Not all PCORnet datamarts will receive ADAPTABLE queries
- Only analysis-ready datamarts will populate the ADAPTABLE study database
- ADAPTABLE queries will be performed in SAS

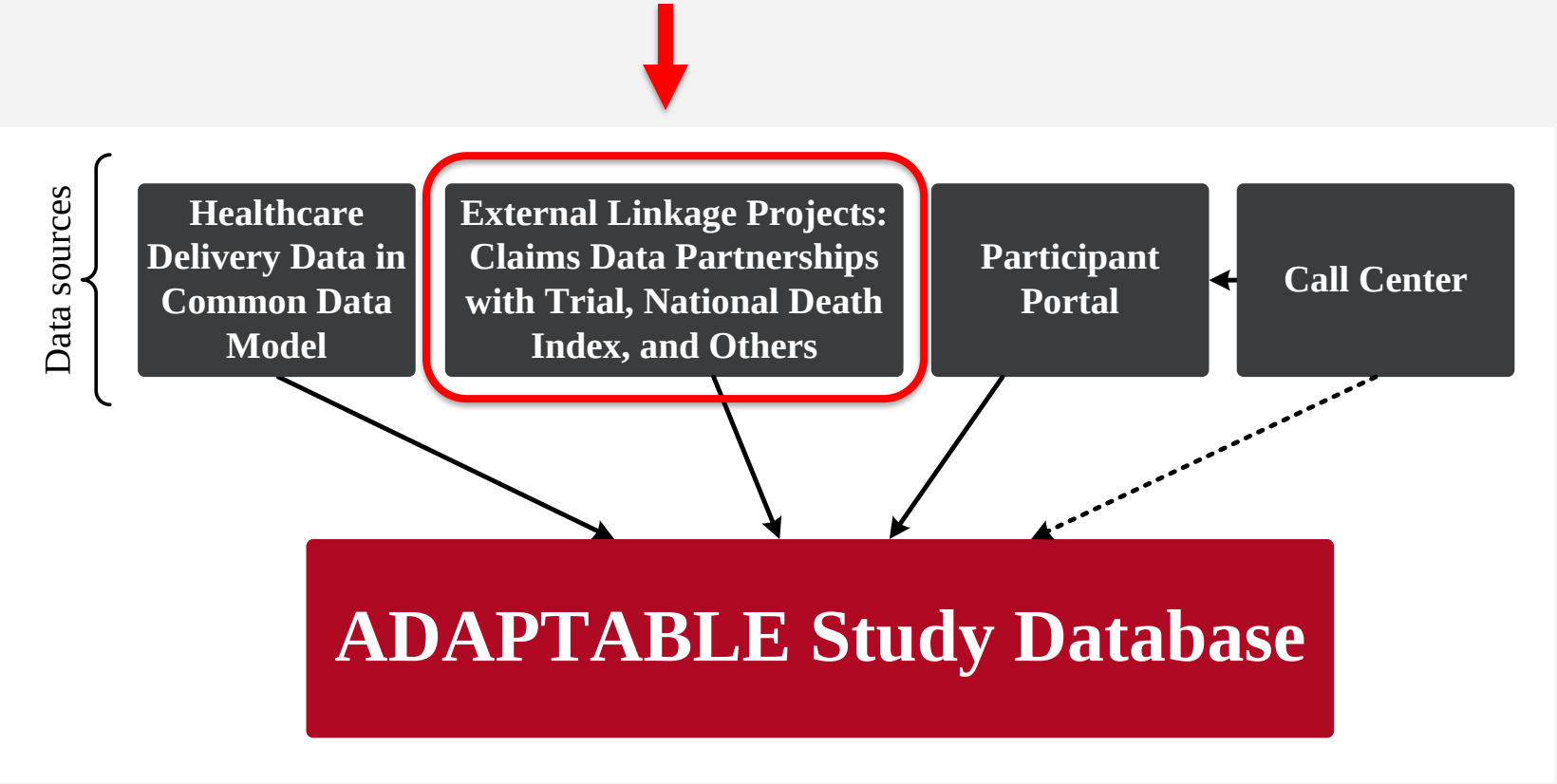


DRN Query Tool with Secure Portal (PopMedNet)

Network topology is used to direct ADAPTABLE queries to ADAPTABLE-participating datamarts

Adaptable

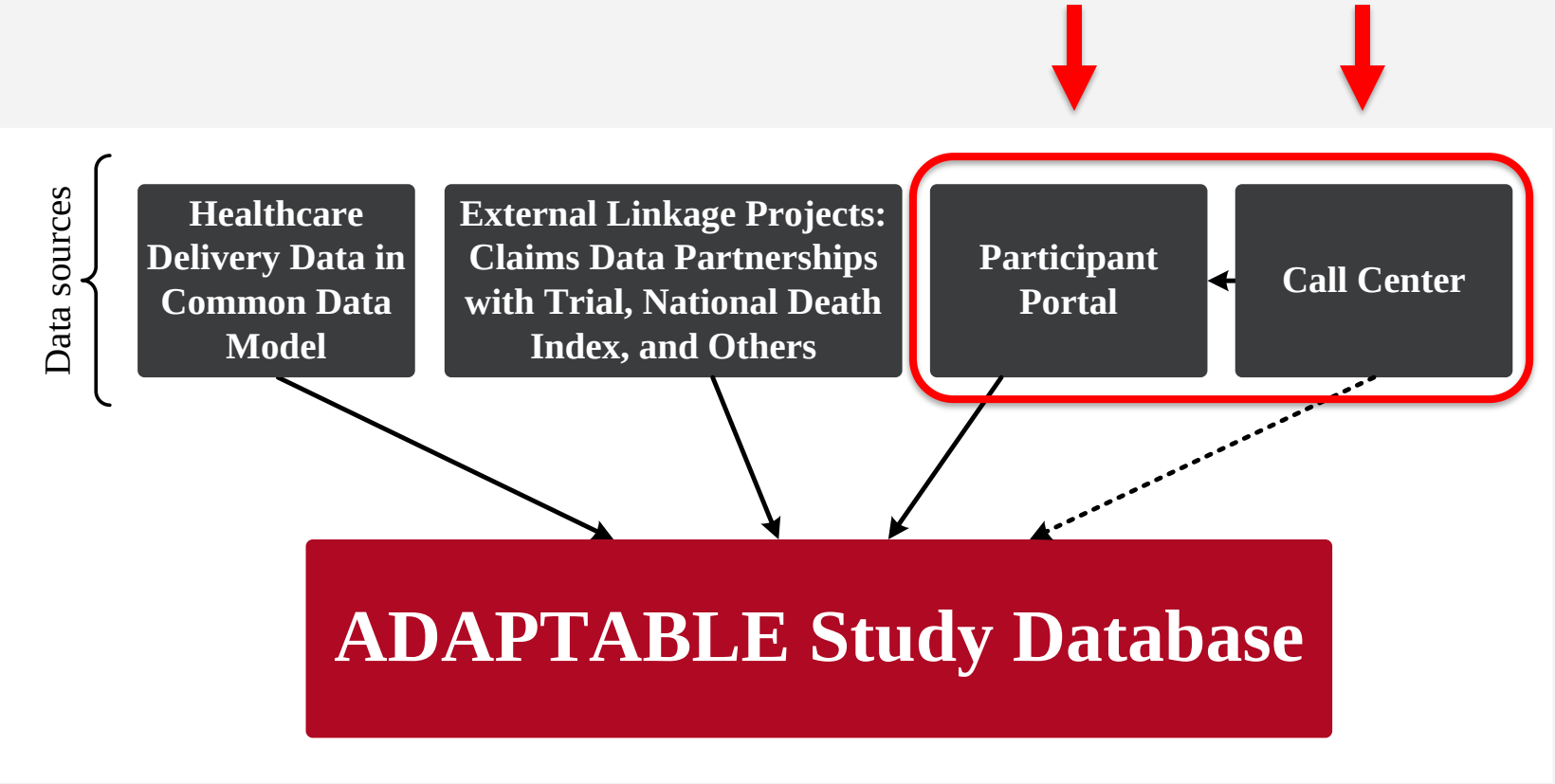
Module #2: External Linkage Projects



#2: External Linkage development notes

- Current pilot projects with GPC's Kansas University Med Ctr and Mid-South's Vanderbilt
  - Important work for developing efficient processes
- All ADAPTABLE sites will be expected to contribute patient-level identifiers for external linkage
  - These identifiers will not be exposed through the CDM; instead this will be a separate process
  - Exact details will be based upon experiences with the pilot projects

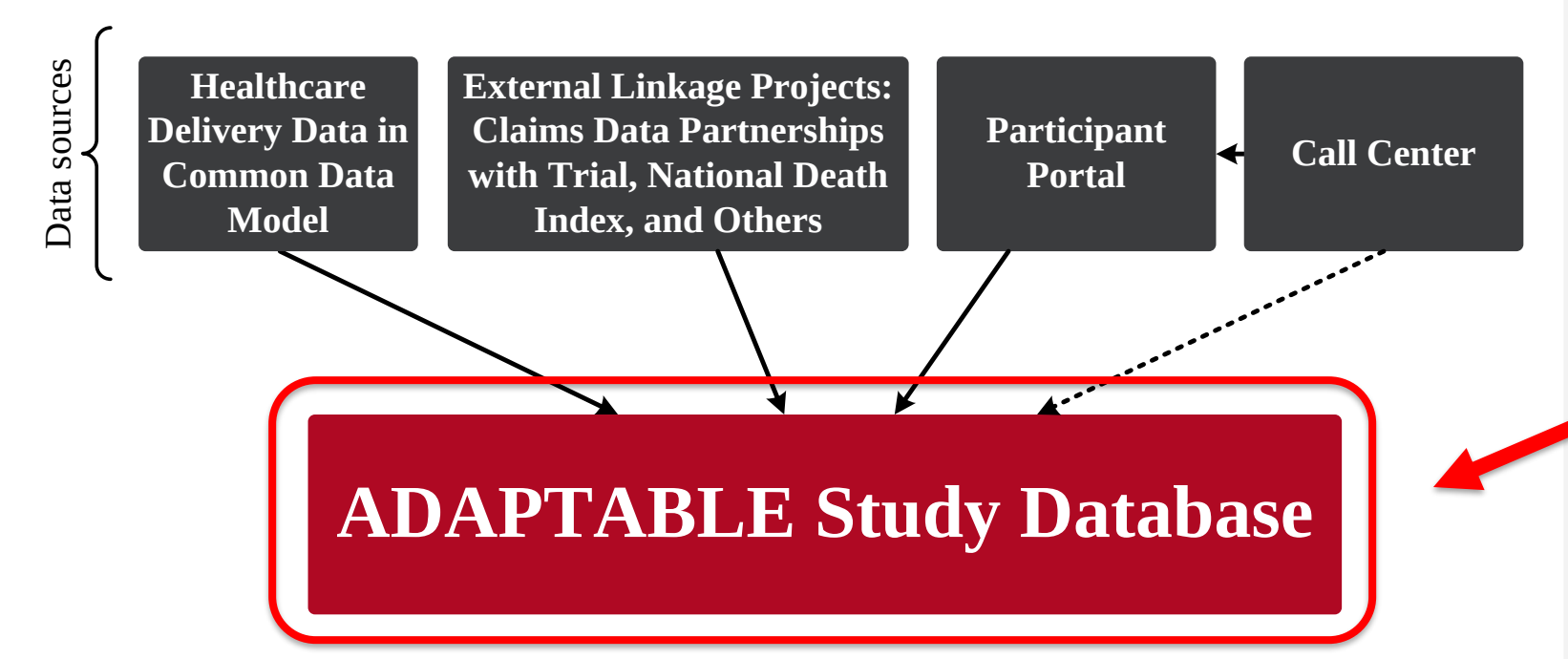
Module #3: Participant Portal and Call Center



#3: Portal and Call Center development notes

- The Participant Portal is direct patient self-report; sites are not expected to enter clinical data
- The Call Center will use the Participant Portal for follow-up of non-respondents
  - Therefore, data collection design for the Portal is consistent
- Development is underway

Module #4: Study Database



#4: Study Database development notes

- Important determinations in protocol for endpoint definitions, hierarchy of data sources, and planned analyses
- Data Safety & Monitoring Board (DSMB) reports and reviews are important process

Phenotyping Objectives and Criteria

(slides from September 4 session)

Open Discussion: Process Related

- Broadly, how has your network considered the **use of EHR data for potential participant identification** with ADAPTABLE?
- What can we all learn from your experiences from generating **prep to research** metrics for ADAPTABLE?
- What can we all learn from your experiences and lessons learned from **other projects**?

A lesson learned

- It may be helpful to consider how results will be triaged or filtered
- Techniques for filtering down thousands (or tens of thousands) of results may benefit from non-clinical elements
- May also assist in responsiveness to enrollment foci and targeted recruitment groups

Ideas for non-clinical data elements

- Are they a “current” patient? Do they receive their routine care here?
  - If not an explicit flag in the system, are there potential indirect indicators?
    - For example: do they live in this state?
    - When was their last encounter?
    - When is their next scheduled appointment?

Ideas for non-clinical data elements (2)

- How are they receiving their care?
  - Does the patient have a PCP?
  - Specialty care association?
  - Registry flag?
- Are they alive?
  - If mortality data are known to be incomplete, can last encounter data be helpful?

Open Discussion: Phenotype Criteria

- What **clinical** data domains and elements do you feel are most important for your ADAPTABLE phenotyping?
- What components of the ADAPTABLE **inclusion/exclusion criteria** may be difficult to translate for your network?
- What **non-clinical** data domains and elements do you feel may be important for your processes?

Possible Considerations

- Potential data sources may include:
  - Data transformed to CDM
  - Other non-CDM sources
- Logistics may include:
  - Latency of source data
  - Frequency of refreshes
  - Tracking previously contacted patients, including those who decline

Open Discussion: Phenotype Logistics

- What logistics do you think will be most important for your processes? Some examples may include:
  - Selection of **potential data sources**
  - Considering **structured** data elements vs. **unstructured/narrative** content
  - **Latency** considerations of source data and also associated **refreshes** and **transformation** processes