Introducing PCORnet: The National Patient-Centered Clinical Research Network from a Plains Perspective

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The National Patient-Centered Clinical Research Network
Acknowledgements

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Many source slides are found internally to PCORNet on the Central Desktop.  https://pcornet.centraldesktop.com

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Overview of This Talk

- **PCORnet Introduction**: A Network of Networks
- **One Clinical Data Research Network**: the Greater Plains Collaborative leveraging NIH CTSA investments
- **Data Integration to serve Comparative Effectiveness Research**
  - “Two Masters”: Trialists (Clinicians) versus Observationalists (Epidemiologists)
  - Pain Score Example
  - Data Use comparisons from sources (registry, claim, EHR)
- **ADAPTABLE aspirin pragmatic trial**: first prospective trial
Our national clinical research system is well-intentioned but flawed

- High percentage of decisions not supported by evidence*
- Health outcomes and disparities are not improving
- Current system is great except:
  - Too slow
  - Too expensive
  - Unreliable
  - Doesn’t answer questions that matter most to patients
  - Unattractive to clinicians & administrators

We are not generating the evidence we need to support the healthcare decisions that patients and their doctors have to make every day.

Both researchers and funders now recognize the value in integrating clinical research networks.

- Linking existing networks means clinical research can be conducted more effectively.
- Ensures that patients, providers, and scientists form true “communities of research”
- Creates “interoperability” – networks can share sites and data.
PCORnet embodies a “community of research” by uniting systems, patients & clinicians

11 Clinical Data Research Networks (CDRNs)

18 Patient-Powered Research Networks (PPRNs)

PCORnet: A national infrastructure for patient-centered clinical research
What will PCORnet do for research?
PCORnet’s goal

PCORnet seeks to improve the nation’s capacity to conduct clinical research by creating a large, highly representative, national patient-centered network that supports more efficient clinical trials and observational studies.
PCORnet’s vision

PCORnet will support widespread capability for the US healthcare system to learn from research, meaning that large-scale research can be conducted with greater speed and accuracy within real-world care delivery systems.
Overall objectives of PCORnet: achieving a single functional research network

- **Create** a secure national research resource that will enable teams of health researchers, patients, and their partners to work together on researching questions of shared interest.
- **Utilize** multiple rich data sources to support research, such as electronic health records, insurance claims data, and data reported directly by patients.
- **Engage** patients, clinicians & health system leaders throughout the research cycle from idea generation to implementation.
- **Support** observational and interventional research studies that compare how well different treatment options work for different people.
- **Enable** external partners to collaborate with PCORI-funded networks.
- **Sustain** PCORnet resources for a range of research activities supported by PCORI and other sponsors.
29 CDRN and PPRN awards were approved on December 17th by PCORI’s Board of Governors

This map depicts the number of PCORI-funded Patient-Powered or Clinical Data Research Networks that have coverage in each state.
CDRN Partners
Goals for Each Clinical Data Research Network (CDRN)

Create a research-ready dataset of at least 1 million patients that is:
- **Secure** and does not identify individual patients
- **Comprehensive**, using data from EHRs to describe patients’ care experience over time and in different care settings

Involve patients, clinicians, and health system leaders in all aspects of creating and running the network

Develop the ability to run a clinical trial in the participating systems that fits seamlessly into healthcare operations

Identify at least 3 cohorts of patients who have a condition in common, and who can be characterized and surveyed
CDRN highlights

• Networks of academic health centers, hospitals & clinical practices
• Networks of non-profit integrated health systems
• Networks of Federally Qualified Health Centers (FQHCs) serving low-income communities
• Networks leveraging NIH and AHRQ investments (CTSAs)
• Inclusion of Health Information Exchanges
• Wide geographical spread
• Inclusion of under-served populations
• Range from 1M covered lives to 28M
PPRN Partners

The National Patient-Centered Clinical Research Network
Goals for each Patient-Powered Research Network (PPRN)

- Establish an activated patient population with a condition of interest (Size >50 patients for rare diseases; >50,000 for common conditions)
- Collect patient-reported data for ≥80% of patients in the network
- Involve patients in network governance
- Create standardized database suitable for sharing with other network members that can be used to respond to “queries” (ideas for possible research studies)
PPRN highlights

- Participating organizations and leadership teams include patients, advocacy groups, clinicians, academic centers, practice-based research networks
- Strong understanding of patient engagement
- Significant range of conditions and diseases
- Variety in populations represented (including pediatrics; under-served populations)
- 50% are focused on rare diseases
- Varying capabilities with respect to developing research data
- Several PPRNs have capacity to work with biospecimens
The PCORnet opportunity: making a real difference for patients and their families

Until now, we have been unable to answer many of the most important questions affecting health and healthcare.

By combining the knowledge and insights of patients, caregivers, and researchers in a revolutionary network with carefully controlled access to rich sources of health data, we will be able to respond to patients’ priorities and speed the creation of new knowledge to guide treatment on a national scale.
The Greater Plains Collaborative Partners

- KS, the University of Kansas Medical Center (KUMC)
- MO, Children’s Mercy Hospital, University of Missouri
- IA, University of Iowa Healthcare
- IN, Indiana University
- WI, the University of Wisconsin-Madison, the Medical College of Wisconsin, and Marshfield Clinic
- MN, the University of Minnesota Medical Center
- NE, the University of Nebraska Medical Center
- TX, the University of Texas Health Sciences Center at San Antonio and the University of Texas Southwestern Medical Center.
GPC Size, Goals and Structure in Phase 1

**11.8 Million Covered Lives**

- 13 hospitals, 430 clinics, 1800 primary care providers, 7600 specialists

**Establish Governance**

**Measure EHR Meaningful Use standardization and align for 3 use cases:**
- Breast Cancer
- ALS (Lou Gerhig’s Disease)
- Obesity (Pediatric Inpatient Focus)

**Develop Patient Reported Outcome Measure Methods**

**Develop Comparative Effectiveness Research Trial infrastructure embedded in EHRs**

**Enhance Patient Recruitment**

- i2b2 and REDCap technologies
The GPC held a “Boot Camp” the day before the sessions with GPC investigators to prepare the patients, patient advocates, and other community representatives in attendance to participate more fully in Cohort working group discussions.

Kim Kimminau and Cheryl Jernigan leading engagement

http://www.gpcnetwork.org/LEK2014
Interventional Informatics: “Develop the Ability to Run a Clinical Trial in Participating Systems that fits Seamlessly into Healthcare Operations”

- Example: ALS Drooling Study: identify patients, prescreen, consent, randomize drug choices from among approved drug, outcomes, monitor

- IRB Reciprocity and GPC Data Sharing Agreements

- Enhanced data integration: not all data in Epic goes into Clarity database
  - Ex: Performance Status for Cancer Center in notes smart data elements

- Build needs:
  - Add forms/flowsheets/notes/registry
  - Integrate REDCap/Consent with EMR
  - Patient Portals
  - Alerting for trial recruitment
  - Randomizing drug selection: orders

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Gross Observation:

Trialists/Clinicians Want “Their” Rich Data:

Tumor Registry Morphology, Death Index, Patient Portal Usage
More Rich Data: Cardiovascular Registry (NCDR) – Arterial Stenosis
Rich Data:

University HealthSystem Consortium Visit Details,

EMR Visit Vitals
Rich Data: REDCap Patient Reported Outcome Measures for Alzheimer's Disease Center
Observationalists (Epidemologists) Want “The” Data

Create a research-ready dataset of at least 1 million patients that is:

- “Comprehensive, using data from EHRs to describe patients’ care experience over time and in different care settings”
- “Utilize multiple rich data sources to support research, such as electronic health records, insurance claims data, and data reported directly by patients”

Execution and Governance:

- Developing relationship with external data partners (CMS, State, private insurers)
- Commercial data partners and sustainability

Figure 3.1. Comprehensive and complete data example from KUMC: heat map of percentage of proposed data elements from the HER and billing sources recorded in six month intervals surrounding the data of breast cancer diagnosis specified by the hospital tumor registry.
Comparing How Data are Organized Across Sites

http://babel.gpcnetwork.org/i2b2/webclient/

http://babel.gpcnetwork.org/i2b2/webclient/
Mapping to a Common Data Model

- **Standardizing within the GPC CDRN**
  - i2b2 a CTSA/NIH adopted technology
  - Single representation for all “facts” about a “patient” during an “encounter”
  - Software has been developed that executes against a GPC i2b2 ontology (containing CDM and additional domains such as labs, meds) to populate the CDM

- **Standardizing Data across the Nation**
  - Leverage FDA Sentinel Data Model, its analysis methods, and framework

- **Accessing the data**
  - Within the GPC: query using i2b2/babel; request de-identified or limited data sets; data delivery in REDCap and database files
  - Across PCORnet: query using Distributed Research Network and PopMedNet; execute data quality programs; execute detailed SAS analysis methods for observational studies
PCORnet Common Data Model, Original v1.0

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

**Fundamental basis**

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

Data captured from processes associated with healthcare delivery

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

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

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

Data captured from healthcare delivery, direct encounter basis

**PROCEDURE**
- PATID
- ENCOUNTERID
- ENC_TYPE (replicated)
- ADMIT_DATE (replicated)
- PROVIDERID (replicated)
- PX
- PX_TYPE

Data captured within multiple contexts: healthcare delivery, registry activity, or directly from patients
### PCORnet Common Data Model, Draft v2.0 Modifications

#### 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
- PATID
- RX_DATE
- NDC
- RX_SUP
- RX_AMT

Data captured from processes associated with healthcare delivery

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

#### CONDITION
- PATID
- ENCOUNTERID (optional)
- REPORT_DATE
- RESOLVE_DATE
- CONDITION_STATUS
- CONDITION
- CONDITION_TYPE
- CONDITION_SOURCE

#### DIAGNOSIS
- PATID
- ENCOUNTERID
- ENC_TYPE (replicated)
- ADMIT_DATE (replicated)
- PROVIDERID (replicated)

#### PROCEDURE
- PATID
- ENCOUNTERID
- ENC_TYPE (replicated)
- ADMIT_DATE (replicated)
- PROVIDERID (replicated)

#### ENCLUSTER
- PATID
- ENCOUNTERID
- SITEID
- ADMIT_DATE
- ADMIT_TIME
- DISCHARGE_DATE
- DISCHARGE_TIME
- PROVIDERID
- FACILITY_LOCATION
- ENC_TYPE
- FACILITYID
- DISCHARGE_DISPOSITION
- DISCHARGE_STATUS
- DRG
- DRG_TYPE
- ADMITTING_SOURCE

#### LAB_CM_RESULT
- PATID
- ENCOUNTERID (optional)
- LAB_NAME
- SPECIMEN_SOURCE
- LAB_LOINC
- STAT
- 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
- MODIFIER_LOW
- NORM_RANGE_HIGH
- MODIFIER_HIGH
- ABN_IND

#### PRO_CM
- PATID
- ENCOUNTERID (optional)
- CM_ITEM
- CM_LOINC
- CM_DATE
- CM_TIME
- CM_RESPONSE
- CM_METHOD
- CM_MODE
- CM_CAT

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

New to v2.0
Phase 2 and v3.0: Five New Tables Proposed

<table>
<thead>
<tr>
<th>DEMOGRAPHIC</th>
<th>PATID</th>
<th>BIRTH_DATE</th>
<th>BIRTH_TIME</th>
<th>SEX</th>
<th>HISPANIC</th>
<th>RACE</th>
<th>BIOBANK_FLAG</th>
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<td><strong>Fundamental basis</strong></td>
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<th>NDC</th>
<th>RX_SUP</th>
<th>RX_AMT</th>
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<th>ENCOUNTERID (optional)</th>
<th></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>DEATH_CONDITION</th>
<th>PATID</th>
<th>ENCOUNTERID (optional)</th>
<th></th>
</tr>
</thead>
</table>

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

Data captured from healthcare delivery, direct encounter basis

New to v3.0

Associations with PCORnet clinical trials

PCORNET_TRIAL

HARVEST

Process-related data
GPC Ontologies -> PCORnet Common Data Model (CDM)

GPC Progress

- All sites have counts on Babel
  - Study population – 8.4M
- Annotated data dictionaries have been completed by all sites
- Software has been developed that executes against a GPC i2b2 ontology (containing CDM and additional domains such as labs, meds) to populate the CDM

Examples on the road to data standardization

- Specification for CDM is billing diagnosis (vs. clinical encounter diagnosis); we can supply both
- Enrollment; may have “micro” enrollments per condition (eg. Admission; Cancer); defining encounters also challenging
Russ’ GPC mindset:
Serve both Customers

Integrating sources sets up “quality/fitness” comparisons
- Meds: home list, inpatient order vs Rx, barcode med admin, claim, fill event
- Diagnosis: problem list, reason for test, procedure bill, claim, tumor registry
- i2b2 Ontology alignment for QC across CDRN and with other i2b2 CDRNs SCILHS

National level intersection
- Shared CDM ETL Harmonization (next slides)
- PCORnet Coordinating Center developing
Observations on Pain and Data Standards

- Millions of data points, painstakingly observed by clinical professionals...just sitting there in electronic medical records.

- Have variety of clinical workflow indicators (Emergency Room, hospital, ambulatory), medication exposure, mortality, co-morbidities.
Sample Query: Pain Over 7, Emergency Room Acuity Data Available, Opioids
Perils of non-revenue generating documentation

...at other sites, flowsheets are used differently

http://hyperboleandahalf.blogspot.com/2010/02/boyfriend-doesnt-have-ebola-probably.html
Towards Standardizing Clinical Measurements led by Nebraska for the GPC using LOINC

https://loinc.org/ Logical Observation Identifiers Names and Codes
Closing Observations on Data Use

How can data help recruit patients to breast cancer trials with greater accuracy and timeliness?

How do we understand integrated data’s ability to provide a complete picture of care for observational studies?
What’s the earliest indicator of breast cancer in integrated data?

E.g., tumor registrar abstracts based on radiologist mammogram interpretation preceding discrete diagnosis code.
Data’s ‘Fit for Use’ depends on need and how its captured

- While registrars pick up the first indication of breast cancer, they abstract up to a year after diagnosis.

- Health Systems changes are reflected in EHR data:
  - Did we add new breast cancer physicians or did a revenue cycle go live in Fall 2013 generate a bump up in diagnoses codes?
  - Which omniscient being knows this at your institution?
How does the picture come together across sites? Pretty good tumor registry consistency with shared HERON ETL code!

- EHR and Tumor Registry Data across sites
Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-term Effectiveness (ADAPTABLE) Trial

PCORnet’s First Pragmatic Clinical Trial
Case Scenario

- Saul had chest pain while working and was taken to the emergency room where he learned he was having a heart attack.
- Saul’s doctors told him that plaque was building up in his arteries.
- Upon discharge from the hospital Saul was advised to take 325mg of aspirin each day.
- Saul compared notes with another friend who said his doctor has him on a baby aspirin because it causes less bleeding and bruising.
- Saul is confused about what dose he should take. He does a lot of work outdoors and carpentry. He is worried about bleeding while working but doesn’t want another heart attack either.
- Saul now wonders what he should do.
Aspirin: A “wonder” drug

- Proven clinical benefit in reducing ischemic vascular events
- Cost effective
- Benefit with combination antiplatelet therapies
- But there are issues:
  - Emerging evidence for dose modifiers (ASA resistance, genetics, P2Y12 inhibitors)
  - Equal efficacy across patients?
  - Intolerance

Most effective dose uncertain
Main Objectives of ADAPTABLE Trial

To compare the effectiveness and safety of two doses of aspirin (81 mg and 325 mg) in high-risk patients with coronary artery disease.

- **Primary Effectiveness Endpoint:** Composite of all-cause mortality, nonfatal MI, nonfatal stroke
- **Primary Safety Endpoint:** Major bleeding complications

To compare the effects of aspirin in subgroups of patients:
- Women vs men
- Older vs younger
- Racial and ethnic minorities
- Diabetics
- Chronic kidney disease (CKD)

To develop and refine the infrastructure for PCORnet to conduct multiple comparative effectiveness trials in the future
ADAPTABLE
Screening, Enrollment & Data Flow

SCREENING*
Site-specific screening processes and data
Includes crosswalk between PATID and STUDYID

ENROLLED participants are populated in CDM STUDY table

CDRN's PCORnet Datamart**
Common Data Model (CDM), including STUDY table

PARTICIPANT PORTAL
Web-based electronic data capture; also used by call center

Portal sends patient-level status reports to site

Portal data transfers, including all study variables

PCORnet query to identify and send study data (via PopMedNet)

STATUS REPORTING***
All participants
Blinded

ADAPTABLE STUDY DATABASE
Participants with status of ENROLLED
Unblinded

Potential External Data Sources
- National Death Index (NDI)
- CMS
- Sentinel

Coordinating Center
Atherosclerotic CV disease is a major cause of death and disability. Getting the dose of aspirin right could save up to tens of thousands of lives or heart attacks in the US alone annually (or prevent thousands major bleeding episodes).

- And multiple times that number globally

The ADAPTABLE Research Community & Adaptors will be pioneers working together

- To solve the challenge and demonstrate the value of a reusable infrastructure
- Launch a new era for pragmatic clinical trials to answer questions with high impact on population health
Closing Phase 1 Thoughts

- PCORnet: a network of networks
  - Clinical Data Research Networks – broad populations to serve all patient populations and investigators
  - Patient Powered Research Networks - focused on specific conditions

- Support for both observational and prospective, pragmatic research

- ADAPTABLE and other early trials test network capacity, governance, and prioritize approaches

- Pain Scores illustrate the spectrum from site or sub-network data availability to national interoperability
Phase 2 Focus Area Highlights

- Vast ambitious project and proposal to address what is needed
- Can read proposal at http://www.gpcnetwork.org/

- A Taste of Topics:
  - Structure for Greater Patient Engagement and Sustainability
  - Collaborator Database
  - More comprehensive and complete data (more flavors; 24/7)
  - Support richer types of trials and studies
Modify Structure based on Learning and Challenges

- Health Systems Advisory Council
- Clinical and Translational Science Advisory Council
- Patient Advisory Council
- Governance Council
  - GPC Leadership
  - Project Management Office
- CDRN Infrastructure
  - Data Partners
    - PCORnet Distributed Research Network
    - GPC Infrastructure Core
- FUNCTIONS
  - Research Opportunity Assessment
  - Sustainability and Pricing
  - Data Request Oversight
  - Administration/Contracting
- Collaborator Engagement
  - Clinicians
  - Investigators
  - Patients
- FUNCTIONS
  - Standards
  - Software Engineering
  - QA/QC Analytics
  - Intervenional Informatics
  - Data Security
  - Study Design
  - Research Question Prioritization
  - IRB/Ethics
  - Biospecimens
  - Recruitment
Collaborator Database

Help us connect to investigators and patients/PPRNs

CTSA Investigators
- Curated by Sites’ CTSA
- required Annual Report
- Area of Specialty: “Oncology”
- “ERACommons”
- MyBibliography link

ABIGYEAR Research Opportunity Request Form
- Contact info, “ERACommons”
- Proposal, funding status
- Areas of Collaboration needed

REDCap Data Collection and Database

Health System Lead Clinicians
- Curated by Sites
- Clinicians’ Services and Divisions
- Linkable to providers in hubs’ data repositories to determine highest volume clinicians for eligible population

Request and Retrieve Matching Investigators and Collaborators

NIH NCBI Services
- PubMed citations
- Manuscript Submissions
- Awards

Patient Collaborator Sign Up Form
- Area of Interest: “Cancer”
- email address
- not a “subject”

Research Opportunity Assessment Team
- Oversee concierge activities
- Monitor Investigators and Collaborators matches
- Organized in coordination with NCATS, CTSA PIs, and TICs

External Investigator

Patient/Family Member
Better Data

- New Sources of Data
- Linked to Other groups Data
Richer Studies and Trials Supported

- **Observational** (Level 1)
- **Observational with Patient Reported Outcomes** (Level 2)
- **Cluster Randomized** (Level 3)
- **Individually Randomized** (Level 4)

**Note:** Randomized trial designs naturally exploit data collection methods employed by observational studies.

- Pragmatic EHR alerts for recruitment; extracting EHR alert effectiveness
- Patient Reported Outcome Measures from EHR Portal: Health System Engagement
- Patient Reported Outcome Measures from REDCap Survey
- Supplemental Abstraction via Case Report Forms (REDCap)

- Pragmatic dynamic EHR (flowsheets, NLP note concepts, medication history), registry, and novel data collection
- Pragmatic core EHR (diagnoses, labs, medical dispensing) billing/claims data collection

Informatics Interventions Require Heightened Clinician and Health System Engagement
References

 équipé GPC Proposal:

equipé PCORNNet:  http://pcornet.org

equipé GPC: http://www.gpcnetwork.org

equipé GPC Development: http://informatics.gpcnetwork.org

equipé PCORI: http://www.pcori.org/funding-opportunities/pcornet-national-patient-centered-clinical-research-network/

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