PCORnet Obesity Observational Research Initiative

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Group Health Research Institute
Today

- Objectives of Initiative
- Process, leadership
- The 2 weight-related observational studies
  - Short- and Long-Term Outcomes related to Bariatric Surgery
  - Short- and Long-Term Effects of Antibiotics on Childhood Growth
- Application and requirements for CDRN participation
  - Timeline
- Q&A
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 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
Objectives:

- Support research on important unanswered questions faced by patients and their clinicians using PCORnet’s Distributed Data Research Network (DRN) and associated processes and programs.

- Formally test and evaluate the capacity of PCORnet’s data infrastructure and the functionalities of the DRN, and report on the readiness of PCORnet’s data infrastructure for observational research.

- Provide an early opportunity for clinical data research network (CDRN) and patient-powered research network (PPRN) investigators, patients, and stakeholders to organize and collaborate in a multisite study and develop an efficient, collaborative process for doing so.
Phase I of PCORnet Development

Characterize large, simple cohort to test capabilities --This is “the” Weight Cohort--

Actually 2 subpopulations:
• Children
• Adults

Patients with CDM elements

The Weight Cohort – patients who
1. have minimum CDM elements, and
2. meet additional criteria (e.g., number & types of visits, eligible years, measurement accuracy)
to do weight-based research

Specific PCORnet weight-related studies
Elements of PCORnet CDM v1.0 for Weight Cohort Test Case

Basic demographics

Visit frequency and type

Outcomes

Duh
Phase II

2 Obesity Demonstration Projects

- Patients with CDM elements
- The Weight Cohort
- Specific PCORnet weight-related studies
PCORnet CDM v2.0

**Fundamental basis**

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

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

**ENCOUNTER**
- PATID
- ENCOUNTERTIME
- SITEMID
- ADMT_DATE
- ADMT_TIME
- DISCHARGE_DATE
- DISCHARGE_TIME
- PROVIDERID
- FACILITY_LOCATION
- ENCTYPE
- FACILITYID
- DISCHARGEDisposition
- DISCHARGEStatus
- DRG
- DRG_TYPE
- ADMITTING_SOURCE

**LAB_RESULT**
- PATID
- ENCOUNTERTIME (optional)
- LAB_NAME
- SPECIMEN_SOURCE
- LAB_LOINC
- STAT
- RESULT_LOC
- LAB_DX
- LAB_TYPE
- LAB_ORDER_DATE
- SPECIMEN_DATE
- SPECIMEN_TIME
- RESULT_DATE
- RESULT_TIME
- RESULTQUAL
- RESULTNUM
- RESULTMODIFIER
- RESULTUNIT
- NORM_RANGE_LOW
- MODIFIER_LOW
- NORM_RANGE_HIGH
- MODIFIER_HIGH
- ABN_IND

**CONDITION**
- PATID
- ENCOUNTERTIME (optional)
- REPORT_DATE
- RESOLVE_DATE
- CONDITION_STATUS
- CONDITION
- CONDITION_TYPE
- CONDITION_SOURCE

**PRO_CM**
- PATID
- ENCOUNTERTIME (optional)
- CM_ITEM
- CM_LOINC
- CM_DATE
- CM_TIME
- CM_RESPONSE
- CM_METHOD
- CM_MODE
- CM_CAT

**DISPENSING**
- PATID
- RX_DATE
- NDC
- RX_SUP
- RX_AMT

**DIAGNOSIS**
- PATID
- ENCOUNTERTIME
- ENC_TYPE (replicated)
- ADMT_DATE (replicated)
- PROVIDERID (replicated)
- DX
- DX_TYPE
- DX_SOURCE
- PDX

**PROCEDURE**
- PATID
- ENCOUNTERTIME
- ENC_TYPE (replicated)
- ADMT_DATE (replicated)
- PROVIDERID (replicated)
- PX
- PX_DATE
- PX_TYPE

Data captured from processes associated with healthcare delivery

Data captured within multiple contexts: healthcare delivery, registry activity, or directly from patients
PCORnet CDM v2.0 (→ 2.1) for Demonstration Projects

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

**Data captured from processes associated with healthcare delivery**
- **ENROLLMENT**
  - PATID
  - ENR_START_DATE
  - ENR_END_DATE
  - CHART
  - ENR_BASIS

- **DISPENSING**
  - PATID
  - RX_DATE
  - NDC
  - RX_SUP
  - RX_AMT

**Data captured within multiple contexts: healthcare delivery, registry activity, or directly from patients**
- **VITAL**
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  - ENCOUNTERID (optional)
  - MEASURE_DATE
  - MEASURE_TIME
  - VITAL_SOURCE
  - HT
  - WT
  - DIASTOLIC
  - SYSTOLIC
  - ORIGINAL_BMI
  - BP_POSITION

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

- **DIAGNOSIS**
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  - ENCOUNTERID
  - ENC_TYPE (replicated)
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  - PROVIDERID (replicated)
  - PX_DATE
  - PX_TYPE
  - PX

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

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  - ENCOUNTERID (optional)
  - LAB_NAME
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  - LAB_LOINC
  - STAT
  - RESULT_LOC
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  - 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

2.1: PRESCRIBING
Topic Selection

Topic generation and prioritization coordinated by the PCORnet Obesity Task Force

- Obesity TF presented to Coordinating Center, Steering Committee, CDRNs, PPRNs for feedback
- Teams of 8-10 created topic briefs for top 2
  - Submitted them to PCORI for consideration

Briefs reviewed by PCORI Advisory Panel on Disparities

PCORI Board of Governors approved development of PFA

PFA for Obesity Observational Research Initiative announced February 26, 2015
Study PIs

- CDRNs, PPRNs, and Coordinating Center nominated 16 PCORnet colleagues as potential PIs.
- Executive Committee chose 3 PIs for each study
Demonstration Project Topics—1

Short- and Long-Term Outcomes related to Bariatric Surgery

- **Research Question:** What is the comparative effectiveness of different bariatric surgical procedures—Roux-en-Y gastric bypass, sleeve gastrectomy, and adjustable gastric banding—with respect to
  - initial weight loss,
  - weight regain, and
  - occurrence of obesity-related outcomes
    - resolution of prevalent type 2 diabetes
    - incidence or recurrence of type 2 diabetes?

- **Topic Brief:**
  https://pcornet.centraldesktop.com/p/eAAAAAAAFAXXAAAAAHHFCJcE
Demonstration Project Topics—2

Short- and Long-Term Effects of Antibiotics on Childhood Growth

- Research Question: What are the comparative effects of alternative antibiotics used during the first 2 years of life on
  - Weight-related outcomes during 3rd to 5th years of life
    - body mass index and
    - risk of being overweight or obese, and
  - Growth trajectories from infancy to preschool ages?

- Topic Brief: https://pcornet.centraldesktop.com/p/eAAAAAAAFAXYAAAAAAD8h5d4
Both Projects
Evaluation of PCORnet Functionality

- Requirement to test, evaluate, and report on the readiness of PCORnet’s data infrastructure & use of the DRN
- CC to lead testing and evaluation activities, report on solutions implemented to resolve technical issues, and lead evaluation of functionality of the network
General Application Information

- Application Deadline: Wednesday, May 27\textsuperscript{th}
- Maximum Project Budget (Total Costs): $4.5M per project ($9M total)
- Maximum Project Period: 2 years
- Eligible Applicants: Phase 1 funded CDRNs, PPRNs, and CC
- Applicant Town Hall: Monday, 3/23, 12:00PM ET (Register for the webinar on the PCORI website.)
- Awards Announced: Aug./Sept. 2015
- Earliest Anticipated Start Date: Sept./Oct. 2015
Short- and Long-Term Outcomes related to Bariatric Surgery
Study PIs

David Arterburn, clinical investigator, PORTAL [lead PI]
- Bariatric surgery researcher
- Leader of several multisite bariatric studies
- Group Health Site-PI for PORTAL

Kathleen McTigue, clinical investigator, PaTH
- Obesity researcher
- Lead, PaTH Weight Cohort
- Co-chair of the Bariatric Topic Brief Team

Neely Williams, patient partner, Mid-South
- Community engagement leader
- Patient co-investigator, Mid-South
- Bariatric surgery patient
There is an ongoing major shift in bariatric procedures in the United States.

N=43,732, Michigan, Reames, JAMA 2014
# Long-term Outcomes of Bariatric Surgery

*Special Communication*

A National Institutes of Health Symposium

Anita P. Courcoulas, MD, MPH; Susan Z. Yanovski, MD; Denise Bonds, MD, MPH; Thomas L. Eggerman, MD; Mary Horlick, MD; Myrline A. Staten, MD; David E. Arterburn, MD, MPH

## Table 3. Deficiencies in Knowledge of Long-term Bariatric Surgery Outcomes

<table>
<thead>
<tr>
<th>Area of Knowledge Gap</th>
<th>Issues and Problems</th>
<th>Potential Study Designs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of surgical complications</td>
<td>Standards for completeness of follow-up and management of missing data are needed</td>
<td>Comparative safety of surgical procedures; analyses of EMR databases</td>
</tr>
<tr>
<td>Predictors of surgical outcomes</td>
<td>Very little data available to inform which patient should undergo which procedure</td>
<td>Comparative outcomes of surgical procedures; analyses of EMR databases</td>
</tr>
<tr>
<td>Overall mortality/survival</td>
<td>Data from observational trials only</td>
<td>Long-term observational and RCTs; analyses of EMR databases</td>
</tr>
<tr>
<td>T2DM remission</td>
<td>Little data on durability of remission</td>
<td>Long-term observational and RCTs; analyses of EMR databases</td>
</tr>
<tr>
<td>T2DM microvascular complications</td>
<td>No data on long-term microvascular disease</td>
<td>Long-term observational and RCTs; analyses of EMR databases</td>
</tr>
<tr>
<td>Cardiovascular events (stroke and myocardial infarction)</td>
<td>Data from 2 observational studies only</td>
<td>Long-term observational and RCTs; analyses of EMR databases</td>
</tr>
<tr>
<td>Mental health outcomes including suicidality, alcohol, substance abuse, and other risk-taking behaviors</td>
<td>Comprehensive, long-term data lacking for most mental health outcomes</td>
<td>Long-term studies with focus on mental health outcomes; analyses of EMR databases</td>
</tr>
<tr>
<td>Cancer</td>
<td>Data from 2 observational studies only</td>
<td>Long-term studies with accurate cancer incidence; analyses of EMR databases</td>
</tr>
<tr>
<td>Reproductive outcomes</td>
<td>Very little data available</td>
<td>Shorter- and longer-term observational studies; analyses of EMR databases</td>
</tr>
<tr>
<td>Cost and health care use</td>
<td>Lack of data with standard reporting of cost and use outcomes</td>
<td>Shorter- and longer-term data with cost and health care use; analyses of EMR databases outcomes in surgical vs control groups</td>
</tr>
</tbody>
</table>

Published online October 1, 2014.
PCORnet Bariatric Study: Draft Aims

Aim 1: To what extent does weight loss and weight regain differ across bariatric surgical procedures (Roux-en-Y gastric bypass, sleeve gastrectomy, and adjustable gastric banding) at 1, 3, and 5 years?
   - Sub Aim: explore heterogeneity by race/ethnicity, pre-op BMI, age

Aim 2: To what extent does bariatric surgery lead to improvements in diabetes risk at 1, 3, and 5 years?
   - Rate of remission from diabetes (A1C <6.5%, off DM medications)
   - Rate of relapse of diabetes following initial remission
   - Rate of incident diabetes among those without it at baseline

Aim 3: What is the frequency of adverse events following different bariatric surgical procedures at 1, 3, and 5 years?
   - Severe adverse events, including hospitalization, re-operations
   - Mortality
Possible PPRN-focused Secondary Aim

PCORI will consider up to one Secondary Aim that engages patients from PPRN communities through surveys, interviews, focus groups, or other appropriate methods to:

• elicit patient preferences around the risks and benefits of the study treatments, and/or
• collect relevant patient-reported outcomes (PROs) meaningful to patients living with obesity.
Short- and Long-Term Effects of Antibiotics on Childhood Growth
Study PIs

- Matt Gillman, clinical investigator, Obesity Task Force
  - Professor and Director of the Obesity Prevention Program in the Department of Population Medicine (HMS/HPHCI)
  - Research focuses on early life prevention of chronic disease
  - Lead, PCORnet Obesity Task Force

- Chris Forrest, clinical investigator, PEDSnet
  - Pediatrician at The Children’s Hospital of Philadelphia
  - Academic investigator in childhood obesity research for the Healthy Weight Program
  - PI, PEDSnet CDRN

- Douglas Lunsford, patient partner, PEDSnet
  - Parent Member, Nationwide Children’s Hospital Healthy Weight Program
  - Patient/Caregiver Member, PEDSnet
Antibiotics cause weight gain in RCT of ~300 Navy recruits

Haight and Pierce, J Nutr 1955;56: 151
MRI images reveal far greater amounts of abdominal fat (in red) in mice exposed to low-dose of penicillin and fed a high-fat diet as opposed to mice fed only a high-fat diet (image on left).
Pathways in microbe-induced obesity

Early infancy antibiotic exposure associated with subsequent increases in body mass
Cohort with primary data collection

Adjusted for birth weight, maternal parity, race, social class, education, parental BMI, first trimester smoking, breastfeeding, timing of introduction of complementary foods, TV time, time in car, dietary patterns at 38 m, sleep at 7 years.

Trasande et al, IJO 2013; 37:16–23; ALSPAC study; N ~11,000
Association of Antibiotics in Infancy with Early Childhood Obesity
Cohort drawn from EMR data (PEDSnet)

Antibiotic Use and Childhood Obesity: Unresolved Issues

- Is there truly a sensitive exposure age? If there is, does it matter
  - How large the exposure is (#doses)?
  - Broad v. narrow spectrum?
  - Class of antibiotic?
- Timing of outcome?
  - Early v. late
  - Growth trajectories could help
- Is there potentiation by chronic steroid use?
- How much does confounding play a role in observed effects?
- To what extent will information about this association change practice?
Antibiotic Use and Excess Weight Gain: Aims/Hypotheses

To examine the extent to which antibiotics *prescribed* in early childhood are associated with excess weight gain through preschool age

- Larger effects with earlier age of prescription; largest effect for 1st months of life?
- Dose-response, ie, larger effects with more doses?
- Larger effects with broad v. narrow spectrum? Different classes?
- Effects potentiated by long-term corticosteroid use?
- Effect modification by child sex, clinical condition?
- How much attenuation by adjustment for factors related to reasons for prescription?
PCORnet Advantages

- Standardized measures across CDRNs
- Large N allows
  - Concurrent stratification by #doses and age
  - Stratification by practice, provider, family characteristics
  - Potentiation by steroids
  - Growth trajectories
  - Sib-pair analyses
  - Other confounding structures
Secondary Aim: Among pediatric clinicians and parents of infants/toddlers, use surveys or qualitative methods to explore

- The extent to which information on obesity risk will change decision-making on antibiotic prescribing
- How the risk of obesity compares with other potential risks to individuals (e.g., allergy) or society (e.g., resistance) in relation to antibiotic decision-making
- How clinicians and parents weigh (short-term) potential benefit v. (long-term) risk in these decisions
- Sub aim: Engage parents from PPRN communities to
  • elicit clinician and parent preferences around the risks and benefits of antibiotic prescribing
Questions?
Extra Slides
Bariatric Study
Inclusion/Exclusion Criteria

Inclusion criteria

- Adults and children, age 13-79 years
- ICD/CPT procedure code for a primary bariatric surgical procedure, excluding reoperation
- Adults:
  - At least 1 adult height measure ever
  - At least 1 pre-op weight within 1 year
  - At least 2 post op weights within 1 year
- Children:
  - Height and weight measured on the same day for pre- and post-op BMI measures

Exclusion criteria

- CPT code for re-operation
Bariatric Study
Data Requirements

Aim 1
- Must identify patients who had bariatric surgery using ICD/CPT codes
  - With 1+ BMIs in 12 m before procedure
  - With 2+ BMIs in follow-up
  - Demographic, comorbidity, and smoking data

Aim 2
- Track diabetes status among patients with and without diabetes at baseline
  - 1+ HbA1c measures before surgery
  - Diabetes medication ordering and/or dispensing data
  - Demographic, comorbidity, and smoking data

Aim 3
- Must identify major adverse events outside index hospital stay
  - Data from both EMR and claims, for hospitalizations, reoperations, re-intervention
  - Link to National Death Index or other State Death Index
  - Demographic, comorbidity, and smoking data
Antibiotics Study
Inclusion Criteria

- Weight cohort criteria (2+ measures of length/height and weight in time window), plus
  - Primary care visits in 1st 5 years of life
  - At least 1 in each of several age groups
- Medication prescription data in 1st 2 years of life
- Consider expanding time window for exposure and outcome
Antibiotics Study
Measurement/Analysis

Exposures
- Outpatient prescriptions for antibiotics
- Need to define
  - New Rx, eg 14-day antibiotic-free interval
  - Medication episodes
- Challenge to define start/stop/dose
  - Parents stop med when symptoms abate
  - In kids, “dispensed” is volume; “sig” not in databases

Outcomes
- Opportunity to examine trajectories of weight, length/height, BMI
- Individual-level analyses (v. data queries)

Flexing anti-confounding muscles
- Obtain as much individual covariate data as possible via CDM
- Innovative approaches
  - Sib-pair analyses
  - Alternative meds or outcomes with different confounding structure
Requirements for CDRN Participation

- Willing and able to work with a single IRB of record (1 IRB per project)
- Able to sign necessary paper work and dedicate allocated effort upon project initiation (~Sept./Oct. 2015)
- Data transformed into PCORnet CDM v2.1
- Able to use PCORnet’s DRN and associated querying capabilities
- Able to run SAS software programs provided by the CC without modification
- Have relevant data elements to conduct the projects
- Share relevant data and appropriate documentation upon request