Role and Impact of PCORnet in Precision Medicine:

Integration of Clinical and Genomic Research

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PCORI EAIN-3885

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Disclosures

- Chair, Biomedical Informatics Graduate Program, UNMC

- PI, UNMC Clinical Research Analysis Environment

- Director, GP-CTR BMI & CI Core

- Co-PI, Greater Plains Collaborative Research Network

- Chair, Emergency Care Workgroup, HL7

Objectives

- Describe evolving requirements for Clinical Research in age of precision medicine

- Introduce the Greater Plains Collaborative Research Network and PCORnet

- Discuss our effort to integrate genetic, biomarker, Anatomic Pathology and EHR data in Precision Medicine

- Look forward to next steps

Hidden agenda: Keep all the acronyms straight

THE PRECISION MEDICINE INITIATIVE

PRECISION MEDICINE   INITIATIVE   PRINCIPLES   STORIES   f y GO TO TOP
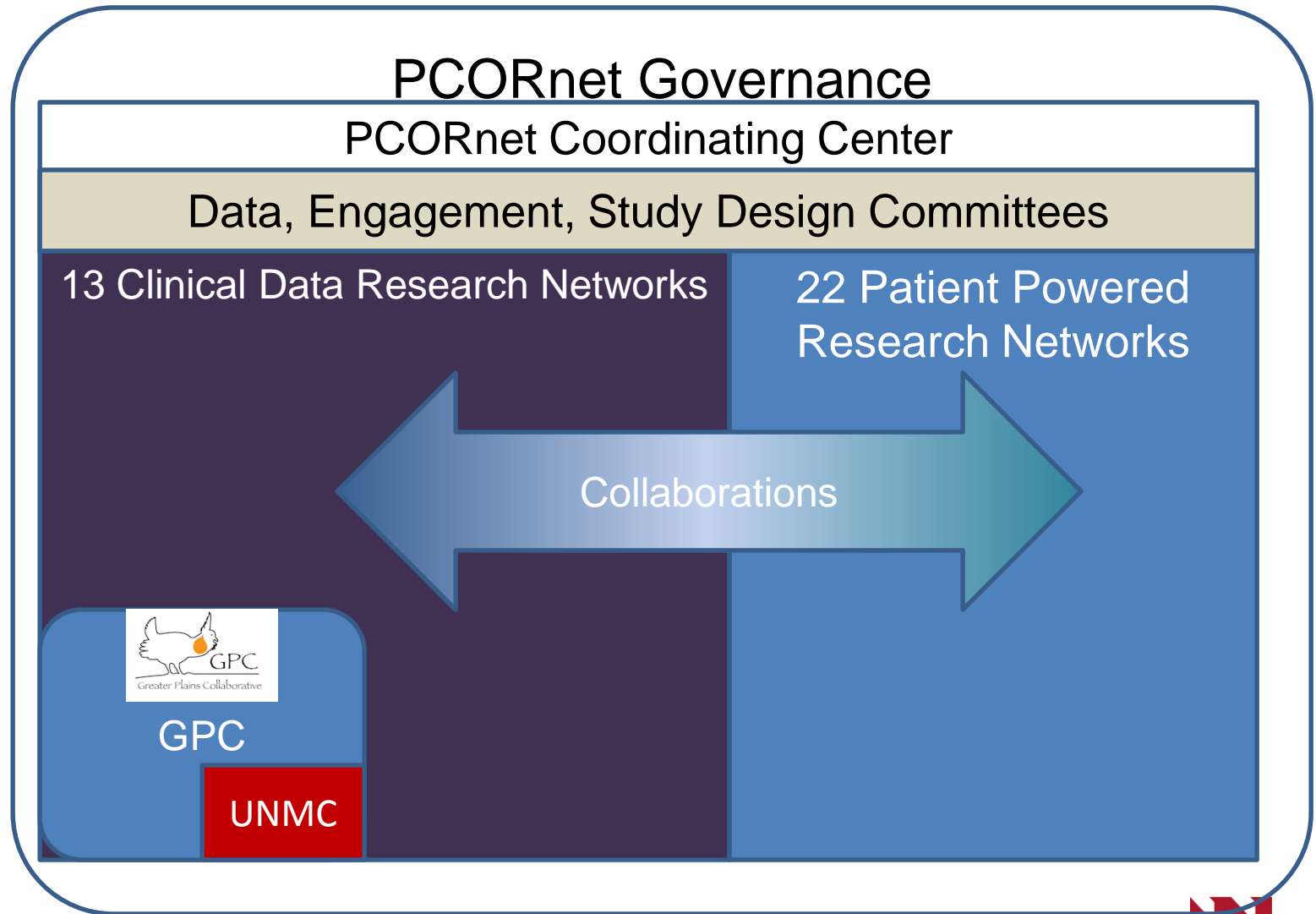
"Doctors have always recognized that every patient is unique, and doctors have always tried to tailor their treatments as best they can to individuals. You can match a blood transfusion to a blood type — that was an important discovery. What if matching a cancer cure to our genetic code was just as easy, just as standard? What if figuring out the right dose of medicine was as simple as taking our temperature?"

- President Obama, January 30, 2015

A Vision For A National Patient-Centered Research Network
Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health
National Workshop to Advance the Use of Electronic Data in
Patient-Centered Outcomes Research
July 2, 2012

www.pcori.org/assets/2-Collins-Slides-Network.pdf

PCORnet Architecture

PCORnet Governance

PCORnet Coordinating Center

Data, Engagement, Study Design Committees

13 Clinical Data Research Networks

22 Patient Powered Research Networks

Collaborations

GPC

GPC
Greater Plains Collaborative

UNMC

PCORI

PPRNs

American BRCA Outcomes and Utilization of Testing Patient-Powered Research Network (ABOUT Network)
University of South Florida

ARthritis patient Partnership with comparative Effectiveness Researchers (AR-PoWER PPRN)
Global Healthy Living Foundation

CCFA Partners Patient Powered Research Network
Crohn's and Colitis Foundation of America

Collaborative Patient-Centered Rare Epilepsy Network (REN)
Epilepsy Foundation

Community and Patient-Partnered Centers of Excellence for Behavioral Health
University of California Los Angeles

Community-Engaged Network for All (CENA)
Genetic Alliance, Inc.

COPD Patient Powered Research Network
COPD Foundation

DuchenneConnect Registry Network
Parent Project Muscular Dystrophy

Health eHeart Alliance
University of California, San Francisco (UCSF)

ImproveCareNow: A Learning Health System for Children with Crohn's Disease and Ulcerative Colitis
Cincinnati Children's Hospital Medical Center

Interactive Autism Network
Kennedy Krieger Institute

Mood Patient-Powered Research Network
Massachusetts General Hospital

Multiple Sclerosis Patient-Powered Research Network
Accelerated Cure Project for Multiple Sclerosis

National Alzheimer's and Dementia Patient and Caregiver-Powered Research Network
Mayo Clinic

NephCure Kidney International
Arbor Research Collaborative for Health

Patients, Advocates and Rheumatology Teams Network for Research and Service (PARTNERS) Consortium
Duke University

Phelan-McDermid Syndrome Data Network
Phelan-McDermid Syndrome Foundation

PI Patient Research Connection: PI-CONNECT
Immune Deficiency Foundation

Population Research in Identity and Disparities for Equality Patient-Powered Research Network (PRIDEnet)
University of California San Francisco

Vasculitis Patient Powered Research Network
University of Pennsylvania

CDRNs

ADVANCE
Accelerating Data Value Across a National Community Health Center Network (ADVANCE)
Oregon Community Health Information Network (OCHIN)

CAPriCORN
Chicago Area Patient Centered Outcomes Research Network (CAPriCORN)
The Chicago Community Trust

GPC — Greater Plains Collaborative
Greater Plains Collaborative (GPC)
University of Kansas Medical Center

PORTAL
Kaiser Permanente & Strategic Partners Patient Outcomes Research To Advance Learning (PORTAL) Network
Kaiser Foundation Research Institute

REACHnet — Research Action for Health Network
Research Action for Health Network (REACHnet)
Louisiana Public Health Institute (LPHI)

mid-south clinical data research network
Mid-South CDRN
Vanderbilt University

pcornet

PEDSnet — A Pediatric Learning Health System
National PEDSnet: A Pediatric Learning Health System
The Children's Hospital of Philadelphia

NYC-CDRN — New York City Clinical Data Research Network
New York City Clinical Data Research Network (NYC-CDRN)
Weill Medical College of Cornell University

OneFlorida Clinical Research Consortium
OneFlorida Clinical Data Research Network
University of Florida

LHSNet — LEARN . STUDY . TRANSLATE . DISSEMINATE — www.lhsnet.org
Patient-Centered Network of Learning Health Systems (LHSNet)
Mayo Clinic

pSCANNER
Patient-oriented SCAlable National Network for Effectiveness Research (pSCANNER)
University of California, San Diego (UCSD)

PaTH Network — patient empowered research
PaTH: Towards a Learning Health System
University of Pittsburgh

SCILHS
Scalable Collaborative Infrastructure for a Learning Healthcare System (SCILHS)
Harvard University

PCORnet Common Data Model

CONDITION v2.0

A condition represents a patient's diagnosed and self-reported health conditions and diseases. The patient's medical history and current state may both be represented.

DEATH v3.0

Reported mortality information for patients.

DEATH_CAUSE v3.0

The individual causes associated with a reported death.

DEMOGRAPHIC v1.0

Demographics record the direct attributes of individual patients.

DIAGNOSIS v1.0

Diagnosis codes indicate the results of diagnostic processes and medical coding within healthcare delivery.

DISPENSING v2.0

Outpatient pharmacy dispensing, such as prescriptions filled through a neighborhood pharmacy with a claim paid by an insurer. Outpatient dispensing is not commonly captured within healthcare systems.

ENROLLMENT v1.0

Enrollment is a concept that defines a period of time during which all medically-attended events are expected to be observed. This concept is often insurance-based, but other methods of defining enrollment are possible.

ENCOUNTER v1.0

Encounters are interactions between patients and providers within the context of healthcare delivery.

HARVEST v3.0

Attributes associated with the specific PCORnet datamart implementation

LAB_RESULT_CM v2.0

Laboratory result Common Measures (CM) use specific types of quantitative and qualitative measurements from blood and other body specimens. These standardized measures are defined in the same way across all PCORnet networks.

PCORNET_TRIAL v3.0

Patients who are enrolled in PCORnet clinical trials.

PRESCRIBING v3.0

Provider orders for medication dispensing and/or administration.

PRO_CM v2.0

Patient-Reported Outcome (PRO) Common Measures (CM) are standardized measures that are defined in the same way across all PCORnet networks. Each measure is recorded at the individual item level: an individual question/statement, paired with its standardized response options.
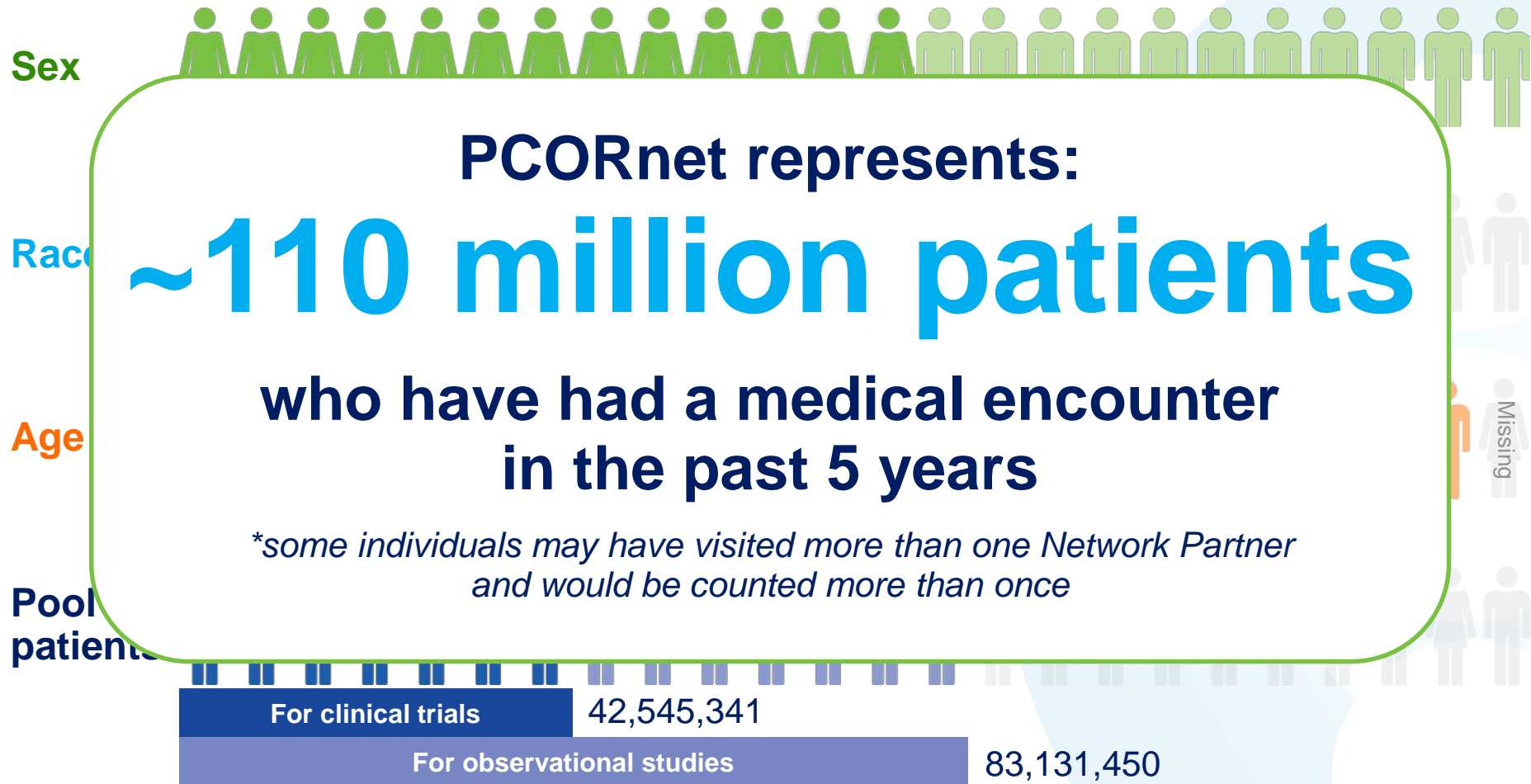
PROCEDURES v1.0

Procedure codes indicate the discreet medical interventions and diagnostic testing, such as surgical procedures, administered within healthcare delivery.

VITAL v1.0

Vital signs (such as height, weight, and blood pressure) directly measure an individual's current state of attributes.

Resulting in a national evidence system with unparalleled research readiness

Sex

Race

Age

Pool patients

PCORnet represents:

~110 million patients

who have had a medical encounter in the past 5 years

some individuals may have visited more than one Network Partner and would be counted more than once

Missing

For clinical trials   42,545,341

For observational studies   83,131,450

pcornet®

Greater Plains Collaborative

University of Kansas Medical Center (KUMC)

Children's Mercy Hospital

University of Iowa Healthcare

University of Wisconsin-Madison,

Medical College of Wisconsin

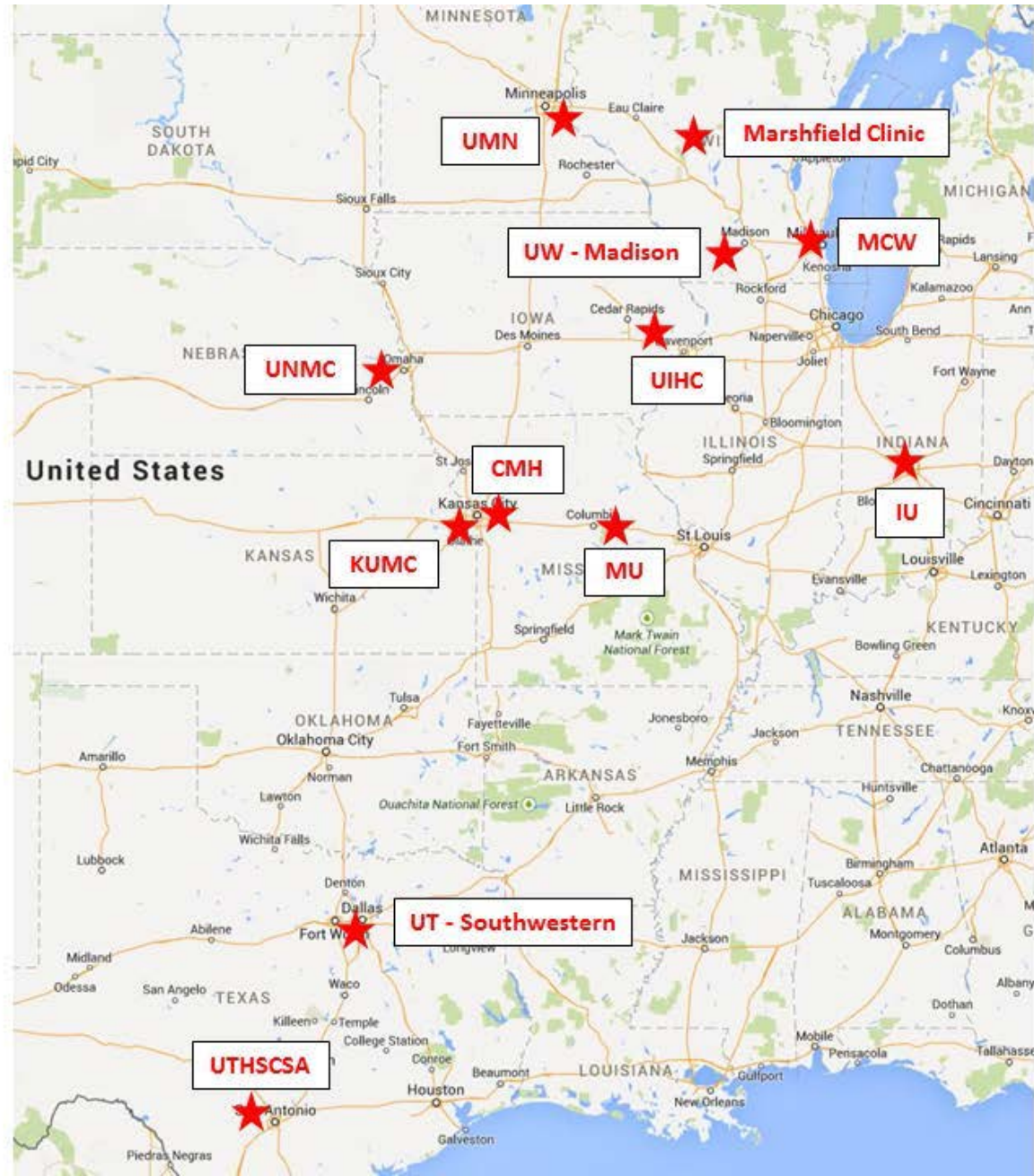Marshfield Clinic

University of Minnesota Medical Center

University of Nebraska Medical Center

University of Texas Health Sciences Center at San Antonio

University of Texas Southwestern Medical Center

University of Indiana

University of Missouri

GPC CDRN:

- Rich **clinical data** stored in *standardized* format on **~10 Million patients**.

- Reciprocal **IRB** Agreement (now SMART IRB)

- **Data Sharing Agreement**

- Capacity to conduct **trials embedded in clinical settings**

- **Complete set of Policies and Procedures**

- **Engagement** of **patients**, clinicians and health systems in governance and use of the network

- **"Front Door"** portal for engaging researchers

- Biobank sharing agreement

UNMC Initiatives

UNMC Clinical Research Analysis Environment (CRANE)

- i2b2 based de-identified, patient level data aggregation system for clinical & translational research.
- Integrates EHR, Registry, HIE, Death Index, CMS Claims data, patient reported outcomes, encoded pathology data, biomarker data, Genomic data
  - J. McClay & Clinical Informatics Team
  - UNMC Research IT OFfice

UNMC Health eStandards Project (BD2K U01)

- International collaboration to extend and coordinate computable phenotypic data linked with genomic data
- Extend SNOMED-CT & LOINC standardized encoding to include anatomic pathology, biomarker, and genetic marker data for inclusion in EHR
  - WS Campbell, JR Campbell, J McClay,

UNMC Health eStandards Project

GPC & SCILHS Common Data Model

- Joint project between UNMC, GPC member sites and Harvard i2b2 developers.

NIH BD2K Grant

- Extends EHR data to include anatomic pathology, protein marker and genomic data.

Deploying ONC Natinal Standards in Support of Metadata for Big Data Research Warehouse Management of Repurposed Laboratory, Pathology & Patient Findings Data from the EHR

University of Nebraska Medical Center
Principal Investigator: Scott Campbell
Grant Number: U01 HG009455
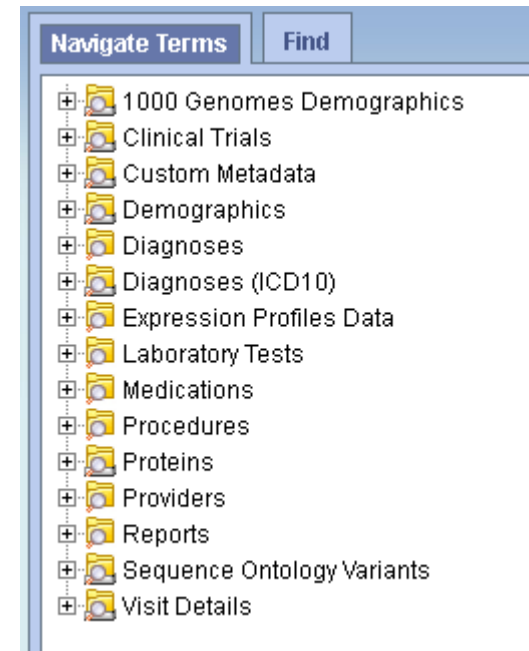
Limitations of ONC terminologies for Human Genomics

Research community
- ➤ HUGO; Human Gene Nomenclature Committee
- ➤ UniProt; Ensemble; Cosmic
- ➤ NCBO: OMIM; Orphanet; Protein Ontology

Clinical community
- ➤ SNOMED CT:
  - – No concept model for subcellular anatomy or molecular structure
  - – No concept model for Observable entity or molecular basis of disease in Clinical findings
  - – Little content, all primitives
- ➤ LOINC 2.54:
  - – 1275 PCR; 1406 MOLGEN; 116 FISH; 1502 CELL MARKERS
  - – Concept model inadequate to fully define what is being result
  - – Provides only tag-level interoperability of molecular data

➤ **No meaningful bridge joining genetic scientific findings with clinical concept models**

UNMC: Project for structured encoding of Pathologist cancer reports

➢ Objective: Detailed structured reporting of all anatomic and molecular pathology observations for all CAP synoptic cancer worksheets (82 types of malignancies)

➢ Proposal: Analyze detailed semantics of CAP worksheets; apply harmonized concept model to develop terminology requirements; deploy as real-time structured reporting from COPATH system interfaced to tissue biobank and EPIC

➢ Tooling: Nebraska Lexicon© extension namespace; SNOWOWL authoring platform; SNOMED CT International + US Extension + Observables Technology preview; ELK 0.4.1 DL classifier

➢ Penciled into IHTSDO workplan for 2017

UNMC: Project for structured encoding of Pathologist cancer reports

➢ Objective: Detailed structured reporting of all anatomic and molecular pathology observations for all CAP synoptic cancer worksheets (82 types of malignancies)

➢ Proposal: Analyze detailed semantics of CAP

+ Specimen Length (if applicable)
+ Specify: ___ cm

Tumor Site (select all that apply) (
___ Cecum
___ Right (ascending) colon
___ Hepatic flexure
___ Transverse colon
___ Splenic flexure
___ Left (descending) colon
___ Sigmoid colon
___ Rectosigmoid
___ Rectum
___ Ileocecal valve
___ Colon, not otherwise specified
___ Cannot be determined (see Comm

+ *NRAS* Mutational Analysis (Note C)
+ ___ No mutation detected
+ ___ Mutation identified (select all that apply)
    + Codon 12
    + ___ Gly12Asp (GGT>GAT)
    + ___ Gly12Val (GGT>GTT)
    + ___ Gly12Cys (GGT>TGT)
    + ___ Gly12Ser (GGT>AGT)
    + ___ Gly12Ala (GGT>GCT)
    + ___ Gly12Arg (GGT>CGT)
    + ___ Codon 12 mutation, not otherwise specified
    + ___ Other codon 12 mutation (specify): _____
    + Codon 13
    + ___ Specific codon 13 mutation (specify): _____
    + ___ Codon 13 mutation, not otherwise specified
    + Codon 61
    + ___ Gln61Lys (CAA>AAA)
    + ___ Gln61Arg (CAA>CGA)
    + ___ Codon 61 mutation, not otherwise specified
    + ___ Other codon 61 mutation (specify): _____
    + ___ Other codon (specify): _____
+ ___ Cannot be determined (explain): _____

+ *BRAF* Expression (by immunohistochemistry) (Note B)
+ ___ Positive cytoplasmic expression
+ ___ Negative for cytoplasmic expression

Precision Medicine Terminology Use Cases

➢ Health maintenance alert for BRCA1 or BRCA2 positive patients

➢ Retrieve all melanoma tissue specimens which had BRAF gene testing

➢ Alert cardiologist for CYP2C19 low metabolizer patients prior to angioplasty to adjust clopidogrel dosing

➢ Which patient with cystic fibrosis should be treated with Ivacaftor at $300,000 per year?

Conclusion

- Described Greater Plains Collaborative Research Network and PCORnet

- Demonstrated Pathway from Clinical Research to Precision medicine

- Discussed our effort to integrate genetic, biomarker, Anatomic Pathology and EHR data in Precision Medicine
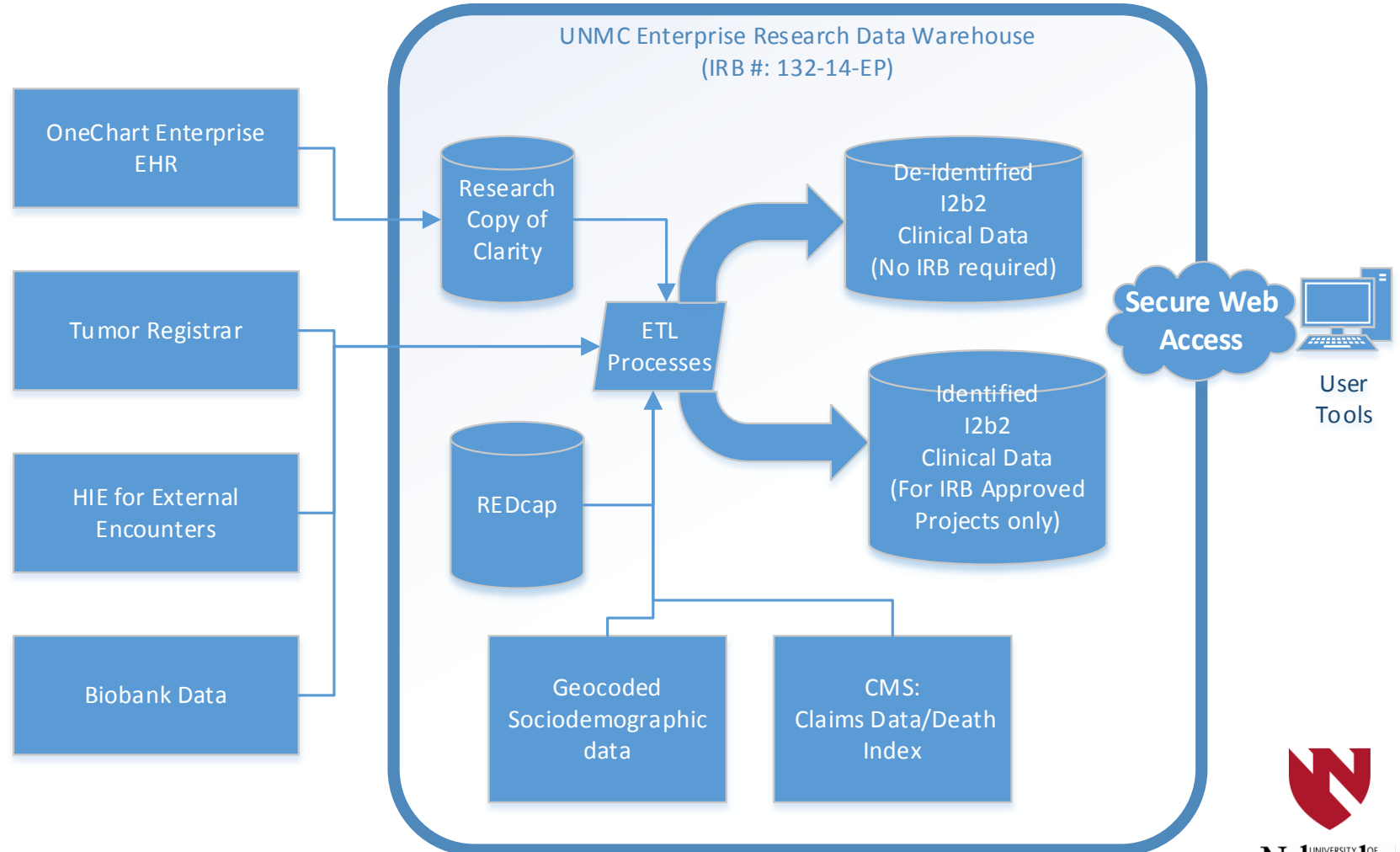
GP-CTR email: gpctr@unmc.edu

Thank You

James McClay, MD
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Molecular Pathology Data Collection, EMR storage and Biorepository Storage Model. UNMC System example

Data generation

Data analysis

Clinical Data Usage and Storage

Ion Torrent Datastore

Data:

.BAM files
.VCF (raw) files
Coverage data
Frequency
Quality score
Gene ID's
Variant type
Allele data

Metadata:
Specimen type
Specimen source
variant caller s/w
hg#

Specimen

Sequencing
(Ion Torrent)

Pathologist
Assessment

Genom-
Oncology

Final Report

VCF (called)

EHR

Secondary Use:
Basic Researcher

Secondary Use:
Clinical Users:
Prospective CDSS
Patient Identification

Basic Researcher

Biorepository
NE CARES

Data Flow/Format
HL7 2.x (FHIR?)
OBR-4|50 gene panel^LOINC^LN
OBX-4|variant detected in BRAF locus^observable code^LN|
OBX-5|**NM_004333.4(BRAF):c.1799T>A (p.Val600Glu)**

W. Scott Campbell, PhD
UNMC, February 10, 2017