NIH Collaboratory

Health Care Systems Research Collaboratory

Phenotype, Data Standards, and Data Quality Core

Update, Steering Committee Meeting, February 25, 2014

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Rethinking Clinical Trials

Phenotype, Data Standards, Data Quality Core Participants

- **Monique Anderson,** Duke
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- **Alan Bauck**, Kaiser Permanente
- **Denise Cifelli**, U. Penn
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- **Jon Puro,** OCHIN
- **Tammy Reece**, Duke
- **Rachel Richesson,** Duke
- **Shelley Rusincovitch**, Duke
- **Jerry Sheehan,** National Library of Medicine (NIH)
- **Greg Simon**, Group Health
- **Michelle Smerek**, Duke

Charter

- Promote multi-disciplinary discussion and collaboration.
- Participants will share their experiences using EHR to support research in various disease domains and for various purposes.
- Identify generalizable approaches, methods, and best practices to support the widespread use of consistent, practical, and useful methods to use widely available clinical data to advance health and healthcare research.
- Suggest where tools are needed.
- Explore and advocate for cultural and policy changes related to the use of EHRs for identifying populations for research, including measures of quality and sufficiency.

Projects

- Phenotype Use Cases in Collaboratory (white paper in progress)
- Environmental Scan (on-going; phenotype sources on Collaboratory KR)
- Literature search guidelines (posted on Collaboratory KR)
- Phenotype "template"
- Phenotype validation guidelines
- Table 1 project (update yesterday)
- Data quality guidelines (three drafts circulated)
- Knowledge dissemination (ongoing)

Authoritative Sources of Phenotype Definitions

(work in progress)

Table 1: Primary Phenotype Sources

Source	*Comments*
Clinical Classifications Software (CCS), also known as AHRQ Bundles	Only based upon diagnosis codes, but very large listing of conditions; this is the basis for most early SEDI variables. http://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp
CMS Chronic Conditions Warehouse (CCW)	Only based upon diagnosis codes and procedure codes; clinical review to date has felt that inclusion logic can be overly broad. https://www.ccwdata.org/web/guest/condition-categories http://www.ncbi.nlm.nih.gov/pubmed/21649659
Mini-Sentinel	Exhaustively researched definitions, but limited number of phenotypes represented. http://www.mini-sentinel.org/assessments/diagnoses_and_medical_procedures/default.aspx
eMERGE Network and PheKB phenotypes library	Probably the most well-recognized phenotyping source at present, but limited number of phenotypes represented; should be carefully evaluated because core mission of genomic studies can result in exclusionary logic inappropriate for the SEDI population health focus. http://www.phekb.org/phenotypes http://www.ncbi.nlm.nih.gov/pubmed/21269473
Quality Net (joint effort of CMS and Joint Commission)	Separates measures between inpatient basis and outpatient basis. Go to the "specifications manual" option; the appendixes contain specific listings of ICD-9 code tables, medication tables, and CPT codes. This is one of the only CPT code groupings that we've seen so far (CPT licensure is very restrictive), but QualityNet only includes for outpatient context. https://www.qualitynet.org/
National Drug File Reference Terminology (NDF-RT)	Search on a term (eg, diabetes) using "contains" and "name/code" specifiers. The results tab for "view all" contains the "may_treat" relationship of conditions to drugs. http://nciterms.nci.nih.gov/ncitbrowser/pages/vocabulary.jsf?dictionary=National%20Drug%20File%20-%20Reference%20Terminology
Professional society guidelines	These are an important source for definitions of abnormal laboratory results and specific ranges, which are often not represented in other definitions. Examples: American Diabetes Association, National Kidney Foundation, American College of Cardiology
Major and well-recognized clinical trials and registries using EHR data to identify cohorts	Clinical and expert guidance can be important for identification of these pivotal trials; another potential technique might be to limit results to high-impact journals via a PubMed search.

Table 2: Secondary Phenotype Sources

Source	*Comments*
Joint Commission	**The CMS/Joint Summit QualityNet is generally the better source, not using the Joint Commission directly.** This organization evaluates hospital adherence with federal regulations, and publishes a specifications manual for inpatient quality measures. Appendix A.1 lists the definitions for specific conditions, mostly based upon ICD-9. A limitation is that these definitions are centered on inpatient admissions, and may not be applicable in an outpatient setting. http://www.jointcommission.org/specifications_manual_for_national_hospital_inpatient_quality_measures.aspx
World Health Organization (WHO) Global Burden of Disease	**In general, this may be useful for mental health, but probably not helpful for most clinical condition phenotypes.** The Global Burden of Disease classifications include both ICD-9 and ICD-10 diagnosis code groupings. See "cause-specific documentation" for individual conditions (eg, cerebrovascular disease, diabetes mellitus, etc). The diagnosis codes are not granular (eg, it just lists 250 for diabetes mellitus), due to global application, and the clinical conditions are very broad. May be somewhat out of date; it appears that the classifications date back to 2000; the last formal GBD update appears to have been 2004, although this is difficult to ascertain from their website. However, there are a lot of mental health classifications, which may be useful. http://www.who.int/healthinfo/global_burden_disease/data_sources_methods/en/index.html
Meaningful Use	*This area needs further research. Does MU publish specific phenotypes for disease conditions? Most documentation appears related to attestation of technical capacities, especially in stage 1, not clinical definitions.* http://www.cms.gov/Regulations-and-Guidance/Legislation/EHRIncentivePrograms/Meaningful_Use.html

Presented by Shelley Rusincovitch at Collaboratory Grand Rounds, Nov. 2013.

Rethinking Clinical Trials

Attribution: Center for Predictive Medicine

Evaluating Existing Definitions (work in progress)

Phenotype Overview: Acute Myocardial Infarction (research by Maria V. Grau-Sepulveda)

Clinical Definition Source: Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of MI[1]

Table 1: Authoritative Phenotype Comparison

Source	*Evaluation of Prevalence vs. Incidence*	*EHR Data Subject Areas*	*Phenotype Comments*	*Phenotype Encounter Basis*

AHRQ Bundles (Clinical Classifications Software)[2]	Prevalence	ICD-9 Diagnoses	• Broad definition
			• AMI diagnosis codes:
			  ○ initial episode
			  ○ subsequent episode
			  ○ unspecified episode
				Any encounter

CMS Chronic Conditions Warehouse[3]	Incidence	ICD-9 Diagnoses Encounter Basis	• Only AMI initial episode codes	Inpatient basis, first/second diagnosis code
Mini-Sentinel #1 (AMI/Anti-Diabetic Agents)[4]	Incidence	ICD-9 Diagnoses Encounter Basis Death Data	• AMI initial/unspecified episode codes	Inpatient basis, first diagnosis code Also includes death w/i one day of ED visit with ischemic disease codes
Mini-Sentinel #2 (Validation of AMI Cases)[5]	Incidence	ICD-9 Diagnoses Encounter Basis	• AMI initial/unspecified episode codes • Does not include death criteria	Inpatient basis, first diagnosis code
CMS/Joint Summits QualityNet (Yale models for AMI and HF)[6] Joint Commission identification of AMI[7]	Incidence	ICD-9 Diagnoses Encounter Basis	• AMI initial/unspecified episode codes	Inpatient basis, first diagnosis code

[1] http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/Guidelines_Univ_Def_Myocardial_Infarc_FT.pdf
[2] http://www.hcup-us.ahrq.gov/toolssoftware/ccs/AppendixASingleDX.txt
[3] https://www.ccwdata.org/cs/groups/public/documents/document/ccw_conditionreferencelist2011.pdf
[4] http://www.mini-sentinel.org/work_products/Assessments/Mini-Sentinel_AMI-and-Anti-Diabetic-Agents_Protocol.pdf
[5] http://mini-sentinel.org/work_products/Validation_HealthOutcomes/Mini-Sentinel-Validation-of-AMI-Cases.pdf
[6] https://www.qualitynet.org/dcs/BlobServer?blobkey=id&blobnocache=true&blobwhere=1228889871496&blobheader=multipart%2Foctet-stream&blobheadername1=Content-Disposition&blobheadervalue1=attachment%3Bfilename%3D2.1+AMI_4.2a.pdf&blobcol=urldata&blobtable=MungoBlobs
[7] http://www.jointcommission.org/specifications_manual_for_national_hospital_inpatient_quality_measures.aspx

Presented by Shelley Rusincovitch at Collaboratory Grand Rounds, Nov. 2013.

Attribution: Maria Grau-Sepulveda, MD, MPH

Tool: Phenotype Templates

- Metadata and supporting documentation
  - Detailed definition sufficient to reproduce in different systems
  - Metadata about developers and PURPOSE
- Validation study methods and results

Identifying Computable Phenotypes for Table 1 Project

Co-morbidities:

Table 1. Patient Demographics and Baseline Characteristics

Characteristic	No. (%) of Patients[a] Gentamicin-Collagen Sponge (n = 753)	Control (n = 749)
Patient demographics		
Age, median (IQR), y	64.2 (58.0-71.5)	64.9 (57.2-72.1)
White race	688 (91.4)	683 (91.2)
Weight, median (IQR), kg	98.0 (86.1-113.0)	98.8 (85.0-111.1)
Body mass index, median (IQR)	33.1 (30.2-37.2)	32.8 (30.0-36.2)
Body mass index >30	574 (76.2)	563 (75.2)
Male sex	530 (70.4)	530 (70.8)
Medical history		
History of hypertension	659 (87.5)	659 (88.0)
History of diabetes	493 (65.5)	513 (68.5)
Current or history of smoking	458 (60.8)	450 (60.1)
Current smoking	136 (29.7)	123 (27.3)
History of chronic obstructive pulmonary disease	117 (15.5)	107 (14.3)
History of peripheral vascular disease	105 (13.9)	89 (11.9)
Previous median sternotomy	52 (6.9)	42 (5.6)
History of TIA or stroke	77 (10.2)	81 (10.8)
History of myocardial infarction	233 (31.0)	245 (32.7)
History of congestive heart failure	89 (11.8)	90 (12.0)
History of hyperlipidemia	619 (82.2)	607 (81.0)
Steroid use ≤1 mo prior to surgery	28 (3.7)	33 (4.4)
Receiving dialysis preoperatively	4 (0.5)	2 (0.3)
Preoperative diagnostic values		
Left ventricular ejection fraction, median (IQR), %	55 (45-60)	55 (45-60)
Serum glucose, median (IQR), mg/dL	125 (101-160)	124 (103-167)
Serum hemoglobin A_{1c}, median (IQR), %	6.5 (5.9-7.6)	6.6 (5.9-7.7)
Hematocrit, median (IQR), %	39 (36-42)	39 (36-42)
Serum creatinine, median (IQR), mg/dL	1.0 (0.9-1.3)	1.0 (0.9-1.2)
Preoperative core temperature, median (IQR), °C	97.6 (97.0-98.2)	97.7 (97.0-98.2)
Preoperative hospital stay, median (IQR), d	1.0 (0-3.0)	1.0 (0-3.0)
Parsonnet risk score, median (IQR)[b]	9.0 (6.0-14.5)	9.0 (6.0-16.0)

Abbreviations: IQR, interquartile range; TIA, transient ischemic attack.
SI conversion factors: To convert creatinine to µmol/L, multiply by 88.4; glucose to mmol/L, multiply by 0.0555.
[a]Unless otherwise indicated.
[b]Theoretical range is 0 to 148; 50% in Parsonnet et al[11] had a score between 0 and 9.

Multiple phenotype definitions:

SUPREME-DM Phenotype

Definition:
Adult Durham Population patients who meet **ONE OR MORE** of the following criteria during a DukeMed encounter between 2007-2011:

- One or more instances of the specified ICD-9-CM diagnosis codes (**see table 7**) on an inpatient encounter
- OR 2 or more instances of the specified ICD-9-CM diagnosis codes (**see table 7**) on outpatient encounters on separate days
- OR 1 or more instances of active stand-alone medication (**see table 8**) reported during outpatient medication reconciliation[3]
- OR 1 or more Oral Glucose Tolerance Test (OGTT) 2-hour 75g result >= 200 mg/dl where there is NO DIAGNOSIS CODE on the same encounter indicating pregnancy (V22, V23)[4]
- OR 2 or more hemoglobin A1c results >= 6.5% on 2 different days within 730 day span
- OR 2 or more fasting glucose results >= 126 mg/dl on 2 different days within 730 day span
- OR 2 or more random glucose results >= 200 mg on 2 different days within 730 day span
- OR within a 730 day span on 2 different days:
  - Fasting glucose results >= 126 mg/dl
  - AND Random glucose results >= 200 mg
- OR within a 730 day span (can be same day):
  - Hemoglobin A1c results >= 6.5%
  - AND Fasting glucose results >= 126 mg/dl

Abnormal Lab Results

Source:
Laboratory results

Definition:
Adult Durham Population patients who meet **ONE OR MORE** of the following criteria during a DukeMed encounter between 2007-2011:

- One or more instances of hemoglobin A1c results >= 6.5%
- OR one or more fasting glucose results >= 126 mg/dl within 365 day span
- OR one or more random glucose results >= 200 mg/dl within 365 day span

Abnormal HbA1c (NCY A1c Registry Definition)

Source:
Glycated hemoglobin laboratory results

Definition:
Adult Durham Population patients who meet **ONE OR MORE** of the following criteria during a DukeMed encounter between 2007-2011:

- One or more instances of hemoglobin A1c results >= 6.5%

Data Quality Assessment Update

- Three versions have been reviewed by the Core
- Has also been shared with a PCORI data quality working group looking at frameworks for data quality assessment
- Last comments were to remove much of the background and all literature review and evidence-based rationale to appendix so that the document contained only the recommendations. This is in progress.
- Next step: Final review with Core

Dissemination

- Posters/presentations on Phenotype Template, and Methods for Development and Evaluation
- Manuscript (informatics journal) on EHR Phenotyping experience and strategies of Demonstration Projects
- Collaboratory website and part of “Living Textbook”?

Future ideas

- Standards – consensus or strategy
- ICD-10 conversion (guidance for researchers)

- Cultural change/education/creativity regarding data quality
  - Getting specific about “which” quality and how much
  - Expecting data quality assessment
    - Comparison-based, i.e., data verification or reproducibility-based, i.e., multiple analyses on data from different sources
  - Using assessment results to answer how good is good enough?
    - Practicality versus perfection - how can we help draw some lines on the balance

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