NIH Collaboratory Rethinking Clinical Trials®
Health Care Systems Research Collaboratory

Phenotyping in Pragmatic Clinical Trials: The MURDOCK Case Study

The Phenotypes, Data Standards, and Data Quality Core of the NIH Health Care Systems Research Collaboratory is continually surveying for efforts related to electronic health records (EHR)–based phenotyping to inform work in this area and prevent duplication of effort. This document is part of the **Learning Lab** series exploring challenges and solutions to phenotyping through case studies of clinical trials.

Case Study

The Measurement to Understand the Reclassification of Disease of Cabarrus/Kannapolis (MURDOCK) Community Registry and Biorepository collects participant-reported medical conditions, procedures, hospitalizations, and medications as well as corresponding data from EHRs. Our project is undertaking a data quality study to calculate the positive predictive value of participant-reported data compared with EHR data. Comparing the two data sources requires phenotype definitions for the 34 medical conditions as well as procedures and definitions for hospitalizations and medications. Participants are interviewed about the differences in their self-report and EHR data.

Principal Investigators

MURDOCK Study: L. Kristin Newby, MD, MHS, Duke University
Data Quality Study: Meredith Zozus, PhD, Duke University

Study Design

Prospective cohort study

Number of Sites

10 sites in Kannapolis and Cabarrus County, North Carolina, and the surrounding region (18 ZIP codes in total)

Conditions of Interest

34 medical conditions, 8 procedures, and hospitalizations

Date of First Enrollment

2009

Phenotype Development Challenge

We started drafting phenotype definitions in late fall of 2013 to directly compare participant self-reports of 34 medical conditions, procedures, hospitalizations, and medications with corresponding data from participants' EHRs. At the time, there were limited available authoritative sources of phenotype definitions. To operationalize the data quality study, we needed to classify the EHR data as confirmatory, uncertain/possibly, and no evidence in the

health record data. We started by identifying diagnosis and procedure codes, laboratory, medication, and other clinical data that would be considered by expert clinicians as confirmatory for each of the 34 medical conditions. Thus we sought consultation from specialists in each of the 34 conditions. When these were defined, they underwent clinical review by an independent clinician and exception testing over the summer of 2014. For the exception testing, a third independent clinician reviewed each phenotype definition and identified two types of scenarios for each condition: (1) where a patient may have the condition but not meet the phenotype definition or (2) where a patient who does not have the condition would meet the phenotype definition. These exceptions were used to improve phenotype definitions. The table describes several challenges that arose in our initial phenotype development and the potential solutions.

Challenge	Solution
Participant self-report was prompted by a form asking for each medical condition, "Do you have, or have you ever had, any of the following …?" with response options of yes, no, and don't know. For some of the prompts, such as kidney disease or depression, study participants may likely have different working definitions of the condition than a clinician. A participant may report kidney disease if they had kidney stones, whereas a clinician may have a more narrow definition of the concept, as in, for example, chronic kidney disease.	Initially, we wrote the phenotype definitions based on the patient's conceptualization of the condition. However, we settled on drafting phenotype definitions in line with clinical definitions and probing for known areas of difference in interview questions or EHR data. For example, patients with bipolar disorder may report depression rather than other mental disorder; there were only these two "conditions" probed. Cases where a participant self-reported depression and the EHR data contained a bipolar disorder diagnosis were tabulated separately and reported with agreement and positive predictive value results.
During phenotype development, curated collections of authoritative phenotypes became available. Some of these listed phenotype validation results or other relative quantitative comparisons of phenotype definitions. In some cases, our definition differed significantly from published definitions with high positive predictive value.	For a second iteration, we surveyed publicly available collections of phenotype definitions, indicating which contained a phenotype definition for each of the 34 medical conditions of interest. We are in the process of comparing the identified phenotype definitions with our initial definitions.
To obtain the desired 3-way classification, we have 2 phenotype definitions to write for each condition: (1) a confirmatory definition—a definition for which we can say that the EHR confirms a self-reported medical condition and (2) a suggestive	Our current approach is to write the confirmatory definition first, and to then define confirmative as a select set of some but not all of the data required for the confirmatory definition.

Challenge	Solution
definition—a definition for which we can say that the EHR contains information that suggests that a self-reported medical condition exists.	