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Harmonization of Measurement Codes for Concept-Oriented Lab Data Retrieval

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Abstract

Measurement concepts are essential to observational healthcare research; however, a lack of concept harmonization limits the quality of research that can be done on multisite research networks. We developed five methods that used a combination of automated, semi-automated and manual approaches for generating measurement concept sets. We validated our concept sets by calculating their frequencies in cohorts from the Columbia University Irving Medical Center (CUIMC) database. For heart transplant patients, the preoperative frequencies of basic metabolic panel concept sets, which we generated by a semi-automated approach, were greater than 99%. We also made concept sets for lumbar puncture and coagulation panels, by automated and manual methods respectively.

Keywords

Logical Observation Identifiers Names and Codes; Systematized Nomenclature of Medicine; Data Accuracy

Introduction

Laboratory measurement data are essential to observational healthcare research. Prior research efforts have focused on a symbolic representation of laboratory measurements into concept-oriented repositories such as the Medical Entities Dictionary (MED) primarily for clinical care purposes [1,2]. Today, Logical Observation Identifiers Names and Codes (LOINC) or Systematic Nomenclature of Medicine Clinical Terms (SNOMED-CT) terminologies are commonly used to represent measurement concepts within electronic health record systems. Both LOINC and SNOMED-CT have encoded clinical concepts and have categorized them into hierarchies, which can improve research analyses. However, a lack of measurement concept harmonization is a challenge for using measurement data in large scale observational research.

The concept harmonization challenges exist, in part, because of heterogeneity of laboratory tests. In the context of discussing test results, harmonization refers to the ability to compare assay results for a given biological or chemical entity, independently of how the test is run. Standardization refers to the traceability of the test result to an international system of (SI) units. That challenge can be especially difficult when the assay is for a heterogeneous compound, or an entity without a known mass. The standardization and harmonization challenges for test results are ongoing and open-ended. In the absence of solutions to these issues, there are multiple laboratory tests for the same entity, and some of those test results report different units [3-8].

Each laboratory test may have a distinct concept in large scale observational databases. For example, there are separate LOINC codes for potassium measurements that were drawn pre or post dialysis (LOINC 3039651 and 3015066, respectively). Additionally, there are separate cholesterol measurement concepts for assays that report results in mmol/L (LOINC 14647-2) or mg/dL (LOINC 2093-3). The prevalence of measurement concepts can vary across sites [7,8]. The issues with measurement concept harmonization are more pronounced in research networks that use healthcare data from multiple sites, such as PCORnet, All of Us (AoU) and the National COVID Cohort Collaborative (N3C). In those research networks, differences in coding practices across sites can lead to a lack of measurement harmonization and potential information loss.

Grouping the concepts, based on terminology hierarchies, into sets that are meaningful for large scale observational research might improve harmonization and reduce information loss. However, the existing LOINC and SNOMED-CT hierarchies include heterogeneous concepts that are difficult to harmonize, and do not include related concepts from other hierarchies. For example, the LOINC hierarchy term LP386618-5 (“Potassium|Serum or Plasma| Chemistry – non-challenged”) subsumes measurements that were drawn pre and post dialysis as well as measurements that were not drawn in relation to a dialysis session. Furthermore, that hierarchy incudes measurements that were drawn from serum or plasma but not from blood [9]. LOINC is aware of the problem of multiple codes that are closely related. In 2018, LOINC introduced a concept of LOINC groups that are a supplemental and parallel to the existing hierarchy in order to address some of these issues. For example, the secondary LOINC hierarchy group maps differing weights and measurement units. The SNOMED-CT mappings are more heterogeneous than the LOINC mappings. The SNOMED-CT code 59573005 (“Potassium measurement”) subsumes LOINC codes for potassium extracted from blood, urine, or water as well as tissue, hair or stool. Also, point measurements as well as measurements that are collected over a more extended time interval map to that term [10].

Grouping related concepts is an ongoing informatics challenge. The Value Set Authority Center (VSAC) platform created by the National Library of Medicine is another example of concept groupings that supports multiple medical domains (i.e. diagnoses, procedures, laboratory tests) [11]. However, despite these research initiatives, there remain challenges with grouping measurement concepts to support analysis on observational databases [12]. We aimed to achieve two goals with measurement concept harmonization. First, we intended to group concepts by a common biological or chemical assay. Second, we intended to validate the groups of lab tests based on their clinical use.

Methods

Workflow

We have illustrated our workflow for generating and validating concept sets in Figure 1. To summarize, we selected a laboratory measurement concept set of interest. Then, we decided which of our 5 measurement concept generation algorithms was the most appropriate and used it to make the concept set. Last, we validated the concept set.

Data Source

The Columbia University Irving Medical Center (CUIMC) data warehouse contains lab data from the early 1980s to present day. We converted our data to the Observational Medical Outcomes Partnership Common Data Model (OMOP CDM) and analyzed them in that format. We used ATLAS, which is a unified interface to enable research on top of the OMOP CDM, to obtain record counts and design cohorts.

Algorithms

We uploaded the LOINC table file, which we acquired from the official LOINC website (https://loinc.org/), into a Pandas dataframe. Each LOINC concept is composed of five or six main parts: Component or analyte (i.e. glucose), property (i.e. substance concentration, mass or volume), time aspect (i.e. momentary or timed measurement), system (i.e. urine, serum, plasma) and scale (i.e. qualitative vs. quantitative). We used semi-automated or automated algorithms to organize the LOINC terms into concept sets based on a subset of these parts [13]. For our semi-automated and automated algorithms we used a combination of the following parameters: i) component, which is the biological or chemical entity that is measured (i.e. cholesterol) ii) system, which is the kind of specimen from which the sample is drawn (i.e. serum/plasma, blood, urine, etc.) iii) time aspect, which describes the time interval over which the measurement is run (i.e. point measurement, 1 hour measurement, etc.) iv) status, which differentiates active codes that continue to be used in billing data from passive codes that were used historically v) property, which describes the kind of units reported from the measurement (i.e. mass concentration, substance concentration, etc.) vi) analyte, which is the standardized subpart of component that is independent of suffixes and vii) analyte core, which is a standardized subpart of component that is independent of suffixes or precoordinated ratios. We made a total of five algorithms. A comparison of the four automated and semi-automated algorithms is shown in Table 1.

In our first algorithm, we filtered the data frame by four parameters: component, system, time aspect and active use. We assigned a concept set identifier and named each concept set. We selected concept sets that had positive frequency counts from the CUIMC OMOP database. We created concept sets for the components of the basic metabolic panel (BMP), and complete blood count (CBC). For those concept sets, we combined the blood and serum/plasma systems and only used point measurements to create concept sets that are accurate depictions of how the laboratory tests are used in clinical practice.

In a second algorithm, we additionally filtered concepts by property. We replicated concept sets for the CBC and BMP with this algorithm and used it to make distinct concept sets for the lipid panel and liver function tests (LFTs). We also made concept sets for ordinal and continuous variables of the urinalysis (U/A) in order to make concept sets for high yield laboratory tests for a second biological fluid.

In a third algorithm, we substituted analyte for component, to create concept sets that were standardized by the biological or chemical entity that was assayed. As a use case, we used this algorithm to produce concept sets for laboratory test that were part of the lumbar puncture panel, which were high yield laboratory tests from a third biological fluid. We also replicated the BMP concept sets with this approach.

Similarly, in a fourth algorithm, we substituted analyte core for component. We used this algorithm to produce concept sets for laboratory tests that are part of the differential blood count, and often expressed as ratios.

In a fifth algorithm, we iteratively created concept sets manually in ATLAS, a web-based research platform created by the Observational Health Data Sciences and Informatics (OHDSI) network. We chose the coagulation panel concepts, because physicians use the results of the coagulation panel routinely. We performed manual string searches for coagulation panel terms in ATLAS. We used LOINC 'Long Common Name', which is used as OMOP concept names, to search for a concept. In ATLAS, we were also able to rank OMOP terms in descending order of record count frequency, and prioritized the concepts with the highest record counts. Two investigators compared the effectiveness of our five concept generating methods by making subjective assessments of which algorithms were most effective for generating different kinds of concept sets. For concepts that were not named intuitively, we created the concept sets by a manual method. That method custom picked which concepts belonged in a set, at the discretion of the investigators. One investigator was a licensed physician.

Validation

To validate our concept sets, we calculated their frequency antecedent to cohorts of interest. For example, we calculated the proportions of heart transplant patients who had a BMP ordered within 30 days antecedent to the operation. We designed the cohorts in ATLAS and performed sub characterizations with each concept set. For concept sets that yielded frequencies that were disproportionately lower than other concepts in a laboratory panel, we did a manual string search for OMOP concepts in ATLAS. This helped us identify concept sets that may not have been identified by an automated approach owing to counterintuitive naming of parameters, such as component name or

system. We then repeated the validation with a modified concept set. To validate the BMP concept sets, we calculated their 30-day preoperative frequency prior to a heart, lung, liver, kidney or solid organ transplant. We created cohorts for each kind of transplant in ATLAS using Current Procedural Terms (CPT) codes for the procedures. We performed similar validation calculations for all concept sets. CUIMC has institutional approval for use of the Observational Health Data Sciences and Informatics tools (IRB#AAAO7805) and allowed for this analysis.

Results

A representative output for our first algorithm, which filtered on component, system, time aspect and active use, is shown in Table 2. The concept set for sodium includes distinct concepts for measurements drawn from blood and from serum/plasma.

The frequencies of some concept sets improved with manual additions. For example, the preoperative frequency of the bicarbonate concept set produced by our algorithm was 50.20% (Table 3). Subsequently, we expanded the concept set with additional selection of OMOP terms, such as OMOP 3008152 ("Bicarbonate [Moles/volume] in Arterial blood"). This is an example of a semi-automated generation of a concept set. After manual selection of additional terms, the preoperative frequency of the bicarbonate concept set increased to 99.37%.

Validation data for the BMP are shown in Table 4. For the heart transplant cohort, the preoperative frequency of the BMP concepts were greater than 99%. However, the preoperative frequencies of those labs were lower in the liver, kidney and solid organ transplants. The frequencies of urea nitrogen and creatinine concept sets were lower than other concept sets in the BMP, and lowest in the kidney transplant cohort. We used the second algorithm, which also filtered on property, to create CBC and BMP concept sets. These concept sets were very similar to those produced by the first algorithm. We also used and created lipid panel, LFTs and urinalysis concept sets with this method.

We used our third algorithm, which substituted analyte for component, to make BMP and lumbar puncture panel concept sets. The BMP concept set was larger and more heterogeneous than the concept sets produced by our other approaches. For example, the potassium concept set included the potassium concepts that were drawn pre and post dialysis (LOINC 40408 "Potassium [Moles/volume] in Serum or Plasma--pre dialysis", and LOINC 20169 "Potassium [Moles/volume] in Serum or Plasma--post dialysis"), potassium measurements that were drawn after administration of vasopressin (LOINC 82161 "Potassium [Moles/volume] in Serum or Plasma--1 hour post dose vasopressin") in addition to other concepts (LOINC 18971 "Potassium [Moles/volume] in Serum or Plasma"). Therefore, manual selection of concepts would improve the concepts produced by algorithm#3. We created the cell differential panel concept sets by a fourth algorithm, which used analyte core instead of component.

We created concept sets for the coagulation panel by a fifth algorithm, which was a manual generation of concept sets. This approach was necessary because the nomenclature of concepts for the coagulation panel were not intuitive. Specifically, prothrombin time (PT), activated partial thromboplastin time (aPTT) and international normalized ratio (INR) were not listed in the names of the LOINC concepts (Table 5). Therefore, manual selection with OMOP terms was effective for coagulation panel concept sets. Our subjective assessment of which algorithms are most effective for making different kinds of concept sets is summarized in Table 6. For the basic metabolic panel, we used a semi-automated approach because the concepts were named intuitively but were heterogeneous. First, we organized the concepts by automation. Then we either added or removed concepts to optimize their validation metrics. The lumbar puncture panel concept sets were homogenous and intuitive. Therefore, an automated method was effective for making those concept sets. Manual methods were most effective for the coagulation panel concept sets, which were not named intuitively and were difficult to automate.

***Figure 1**: Workflow for generating concept sets.*

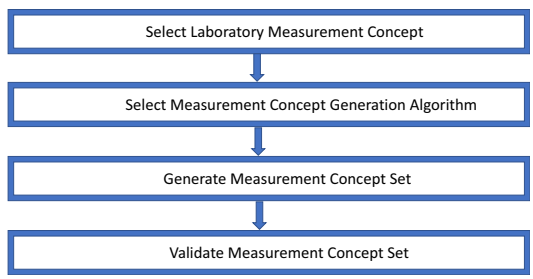

***Table 1**: Summary of the automated and semi-automated concept set generation algorithms. Y = Yes; N=No.*

LOINC Parameters	**Algorithm#1**	**Algorithm#2**	**Algorithm#3**	**Algorithm#4**
Analyte?	Component	Component	Analyte	Analyte Core
System?	Y	Y	Y	Y
Time Aspect?	Y	Y	Y	Y
Active?	Y	Y	Y	Y
Property?	N	Y	Y	Y

***Table 2:** Sample concept set for sodium in serum, blood or plasma. A total of 4 parameters were used in this algorithm (Component, Time Aspect, System, Active). LOINC NUM, LOINC number; TA, Time Aspect; SYS, System; CS ID, Concept Set Identifier; Pt, Point measurement*

LOINC NUM	COMPONENT	TA	SYS	Name	CS ID	DESCRIPTION
2947-0	Sodium	Pt	Bld	Sodium [Moles/volume] in Blood	6	Sodium in Serum, Plasma or Blood (point

						measure-ment)
2951-2	So-dium	Pt	Ser/Plas	Sodium [Moles/volume] in Se-rum or Plasma	6	Sodium in Serum, Plasma or Blood (point measure-ment)

Table 3: *Preoperative counts and frequencies of basic metabolic panel labs 30 days prior to a heart transplant. All data were acquired from the Columbia University Irving Medical Center database. Preop lab, Preoperative laboratory entities.*

30 Day Preop Lab	Heart Transplant (n=1,263)
Sodium in Serum, Plasma or Blood	1,261 (99.84%)
Potassium in Serum, Plasma or Blood	1,261 (99.84%)
Chloride in Serum, Plasma or Blood	1,261 (99.84%)
Bicarbonate in Serum, Plasma or Blood	**634 (50.20%)**
Urea Nitrogen in Serum, Plasma or Blood	1,260 (99.76%)
Creatinine in Serum, Plasma or Blood	1,261 (99.84%)
Glucose in Serum, Plasma or Blood	1,261 (99.84%)

Table 4: *Preoperative counts and frequencies of basic metabolic panel labs 30 days prior to heart, liver, kidney and solid organ transplants. All data were acquired from the Columbia University Irving Medical Center database. Preop Labs, Preoperative laboratory entities.*

Preop Labs (30 days)	Heart Trans-plant (n=1,263)	Liver Transplant (n=1,843)	Kidney Trans-plant (n=3,489)	Solid Organ Trans-plant (n=9,238)
Sodium	1,261 (99.84%)	1,823 (98.91%)	3,139 (89.97%)	8,532 (92.36%)
Potas-sium	1,261 (99.84%)	1,823 (98.91%)	3,139 (89.97%)	8,532 (92.36%)
Chloride	1,261 (99.84%)	1,823 (98.91%)	3,129 (89.68%)	8,513 (92.15%)
Bicar-bonate	1,255 (99.37%)	1,810 (98.21%)	3,060 (87.70%)	8,330 (90.17%)
Urea Ni-trogen	1,260 (99.76%)	1,821 (98.81%)	2,907 (83.32%)	8,203 (88.79%)
Creati-nine	1,261 (99.84%	1,823 (98.91%)	2,907 (83.32%)	8,216 (88.94%)
Glucose	1,261 (99.84%	1,824 (98.97%)	3,137(89.91%)	8,525(92.28%)

Table 5: *Concept names for activated partial thromboplastin time (aPTT) in the Observational Medical Outcomes Partnership (OMOP) and Logical Observation Identifiers Names and Codes (LOINC) ontologies. aPTT, activated partial thromboplastin time.*

Concept Set	OMOP Name (OMOP ID)	LOINC Component Name (LOINC Code)
aPTT	aPTT in Platelet poor plasma by Co-agulation assay (3018677)	Coagulation surface induced (14979-9)
aPTT	aPTT in Platelet poor plasma by Co-agulation assay -- 2nd specimen (3004144)	Coagulation surface induced^2nd speci-men (13058-3)
aPTT	aPTT.factor substi-tution in Platelet poor plasma by Co-agulation assay -- immediately after addition of normal plasma (3010589)	Coagulation surface induced.factor sub-stitution^immedi-ately after addition of normal plasma (5946-9)

Table 6: *Subjective assessment of which algorithms are most effective for different laboratory panels.*

Examples	Method	Terms
Basic Metabolic Panel	Semi-automated	Heterogeneous
Lumbar Puncture	Automated	Homogeneous
Coagulation Panel	Manual	Non-intuitive

Discussion

We created measurement concept sets from different systems, synchronized concepts by time interval of collection and restricted to codes that were not deprecated, as indicated by LOINC. We also demonstrated methods for harmonizing similar concepts with standardized definitions of chemical or biological species. We grouped our concepts into the panels that are ordered by clinicians in order to identify inaccurate concepts since the components of the panel should occur in similar frequencies.

We showed that for some panels, automated and semi-automated methods were effective for generating concept sets. However, for panels that used concepts that were not named intuitively, as was this case with coagulation panel concept sets, manual selection was more effective. The reliance of user input may limit the scalability of our methods. Furthermore, a manual

design of concept sets may introduce bias. However, that bias can be overcome by using objective metrics such as the prevalence of each concept in the database when creating the grouping.

By cross referencing our LOINC concept codes with OMOP codes, we have enabled our concept sets to be used in a large scale observational research network such as the Observational Health Data Sciences and Informatics (OHDSI) network. Our measurement concept sets can help with heuristic based phenotyping on observational databases.

Some limitations of our analysis were that we used data from a single medical center. We performed the analysis on a subset of cohorts for validation. In addition to validating the concepts, that validation process can help identify data quality issues, such as underutilized concepts. However, the validation data helps improve the objectivity of the analysis.

Our method can be replicated on other databases and scaled to a larger range of measurements. We intend to perform a replication study on other sites in the OHDSI network to improve the external validity of our concept sets, and the scalability of our process. In international context, integration of LOINC-coded and non-LOINC coded terminology (such as the Nomenclature for Properties and Units (NPU), which is used in Nordic countries) in a value set is important in order for studies to execute reliably in international context.

Differences in coding practices across multiple sites within the OHDSI network can lead to information loss for measurements. The most popular code for a given biological or chemical assay may vary across sites. Therefore, concept sets that include a comprehensive set of measurement codes may perform consistently across databases in the OHDSI network and reduce information loss. Furthermore, those concept sets should be related in order to minimize heterogeneity in the data. Our research efforts may enable measurement data to be used reliably and consistently in network studies.

Conclusions

We created measurement concept sets for use in the Observational Health Data Sciences and Informatics (OHDSI) network by a combination of semi-automated, automated and manual methods. Our concept sets were validated on a database from our institution. Continued research on multiple databases is warranted.

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