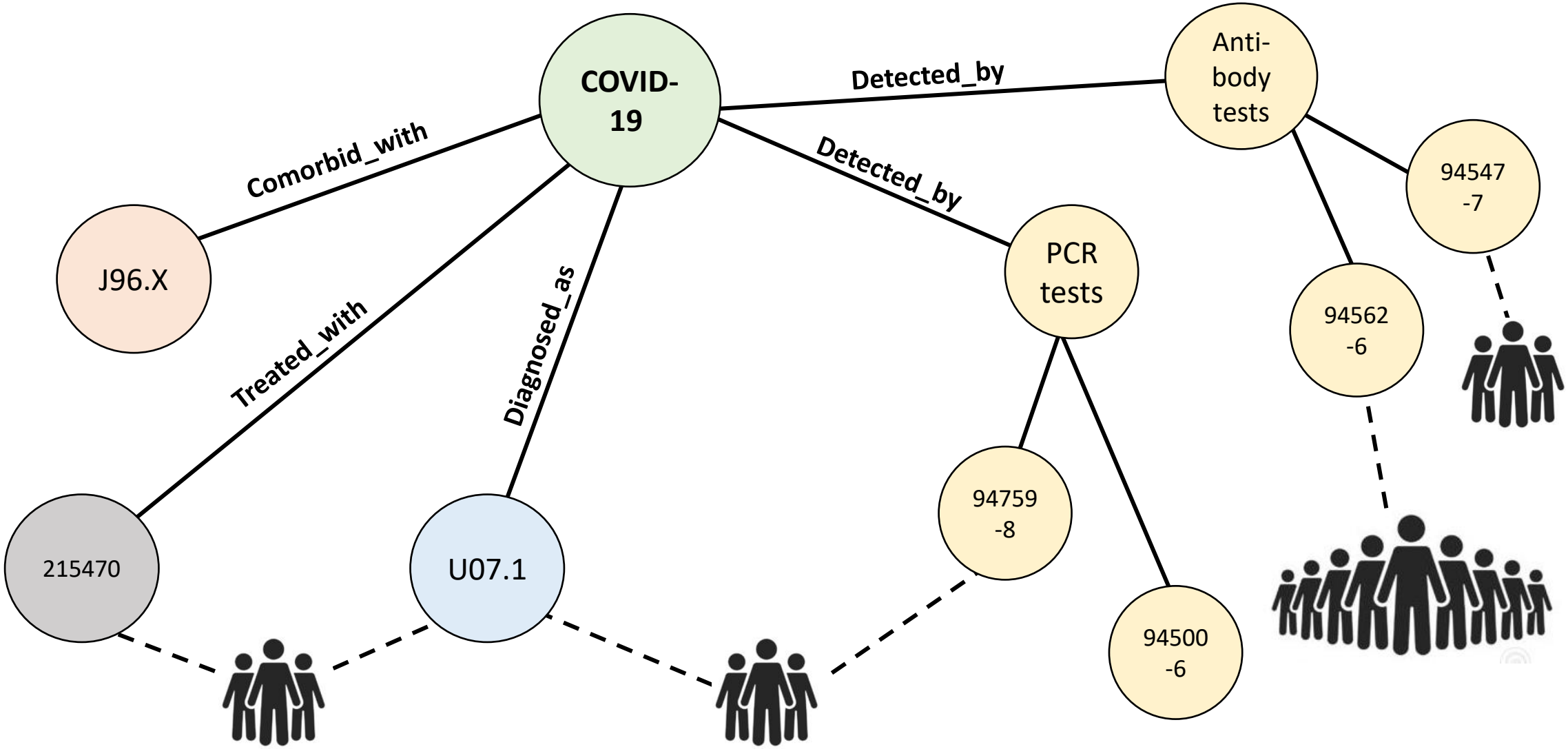
In an (ontologically) perfect world…



Reality Check

- In our non-ontologically-perfect world, a COVID-19 computable phenotype looks more like this.
- This covers all the concepts, but:
  - Must be translated into a number of different data models and dialects
  - Must be continually manually updated to stay current
- What would it take to be able to write *one* query script that:
  - Thoroughly covers all the concepts with the fewest possible codes?
  - Can be run at multiple institutions with few (or no) local changes?
  - Results in a consistently, accurately defined cohort?

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clinical ontologies

clinical ontologies

interoperable data models/technologies

Building Blocks

Literature, Current Practices, Existing Technologies

Computable Phenotyping

- *Computable phenotypes* are algorithms used to query EHR data to identify patient cohorts with conditions or events relevant to some use case.
- Important for research, but difficult to share across institutions in a machine-readable way.
- Rely heavily on standard codesets (ICD-10, LOINC, RxNorm, CPT, etc.)
- The ideal computable phenotype is shareable, data model agnostic, semantically unambiguous, machine readable, and publicly accessible.

The advantage presented by ontologies

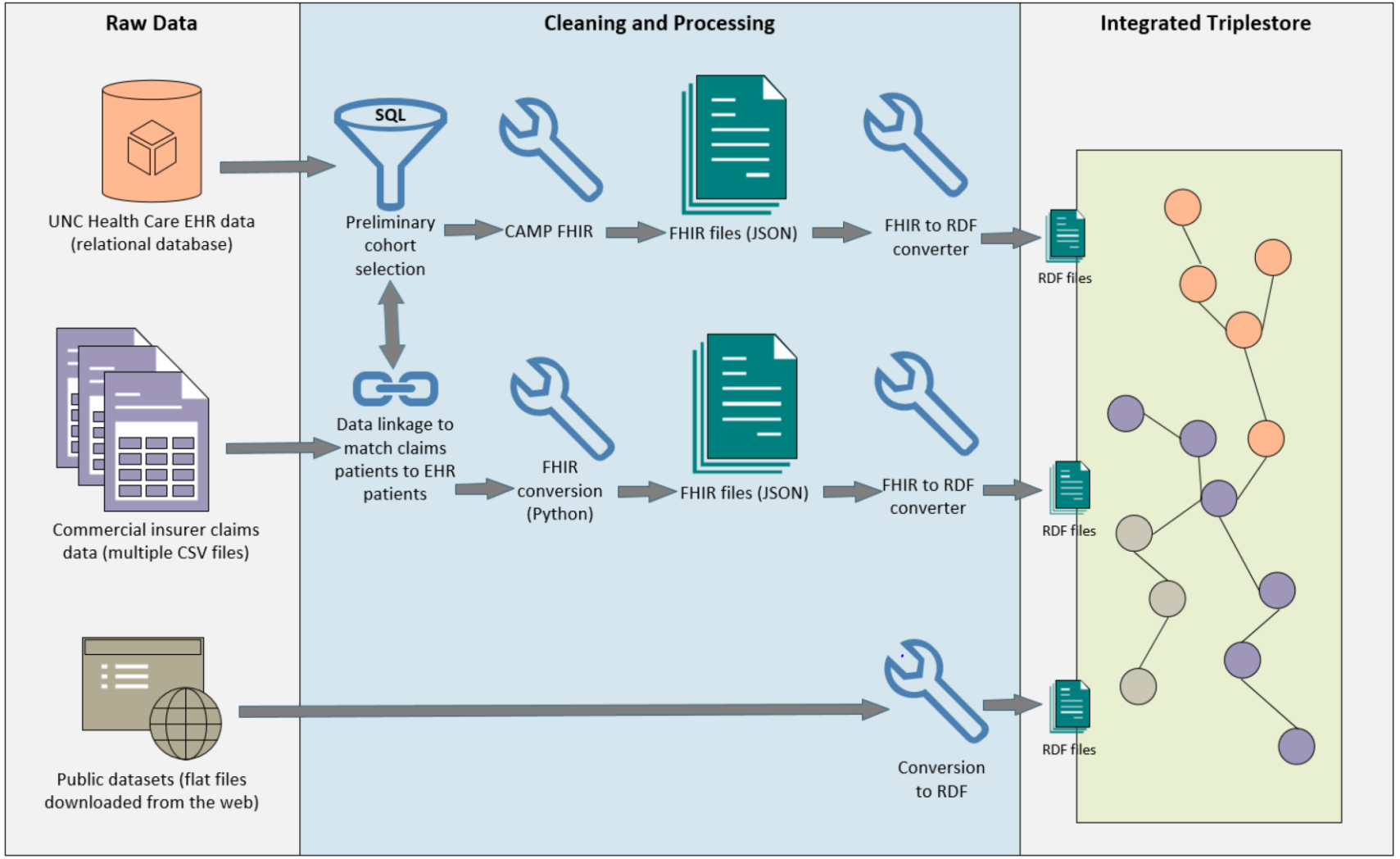
Current state: exact code matches, from all over the hierarchy

Desired state: conceptual matches, powered by ontologies

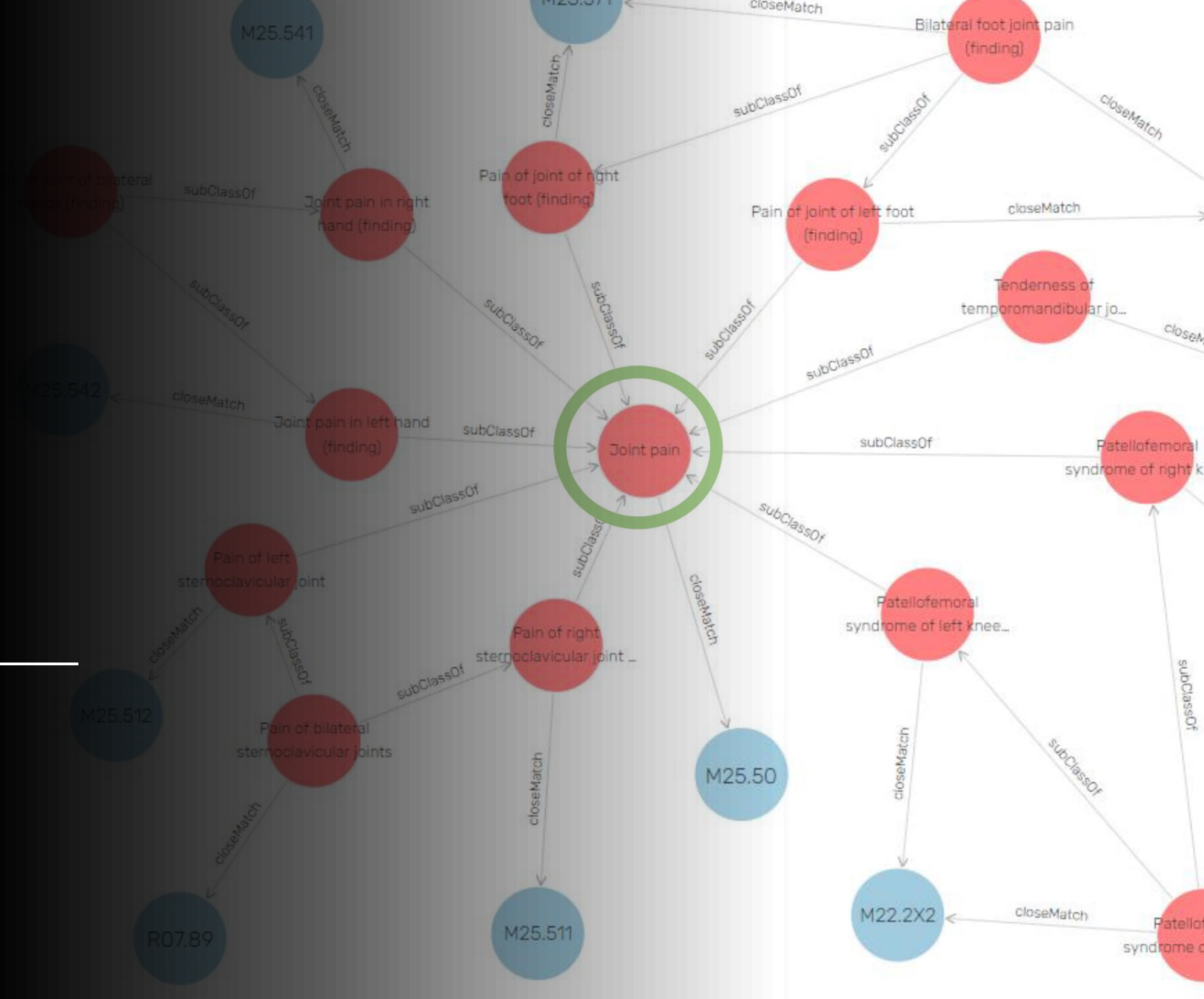
The Opioid Triplestore

Existing clinical dataset from a prior project*; a triplestore containing EHR, claims, and community-level data for post-surgical patients who were prescribed opioids.

*Collaborative project; see Acknowledgements slide for list of contributors and funding information



Experiments



Comparing Phenotype Performance: Ontology versus ICD-10-CM codeset

- Consider two computable phenotypes: (1) depression, and (2) rheumatoid arthritis.
- Objective is to compare the “coverage” of a computable phenotype defined by a list of ICD-10-CM codes (from PheKB) against a phenotype defined by a single concept (along with its child concepts) from the SNOMED or HPO ontology.
- Measuring the sensitivity and specificity of the phenotype methods is not possible in this study, as there is no way to know who the “true” cases are—we can only know which patients are identified by each phenotyping method.
- What is critical to measure, then, is the degree to which the two phenotyping methods overlap, as well as the degree to which they diverge.

Mapping SNOMED to ICD-10-CM

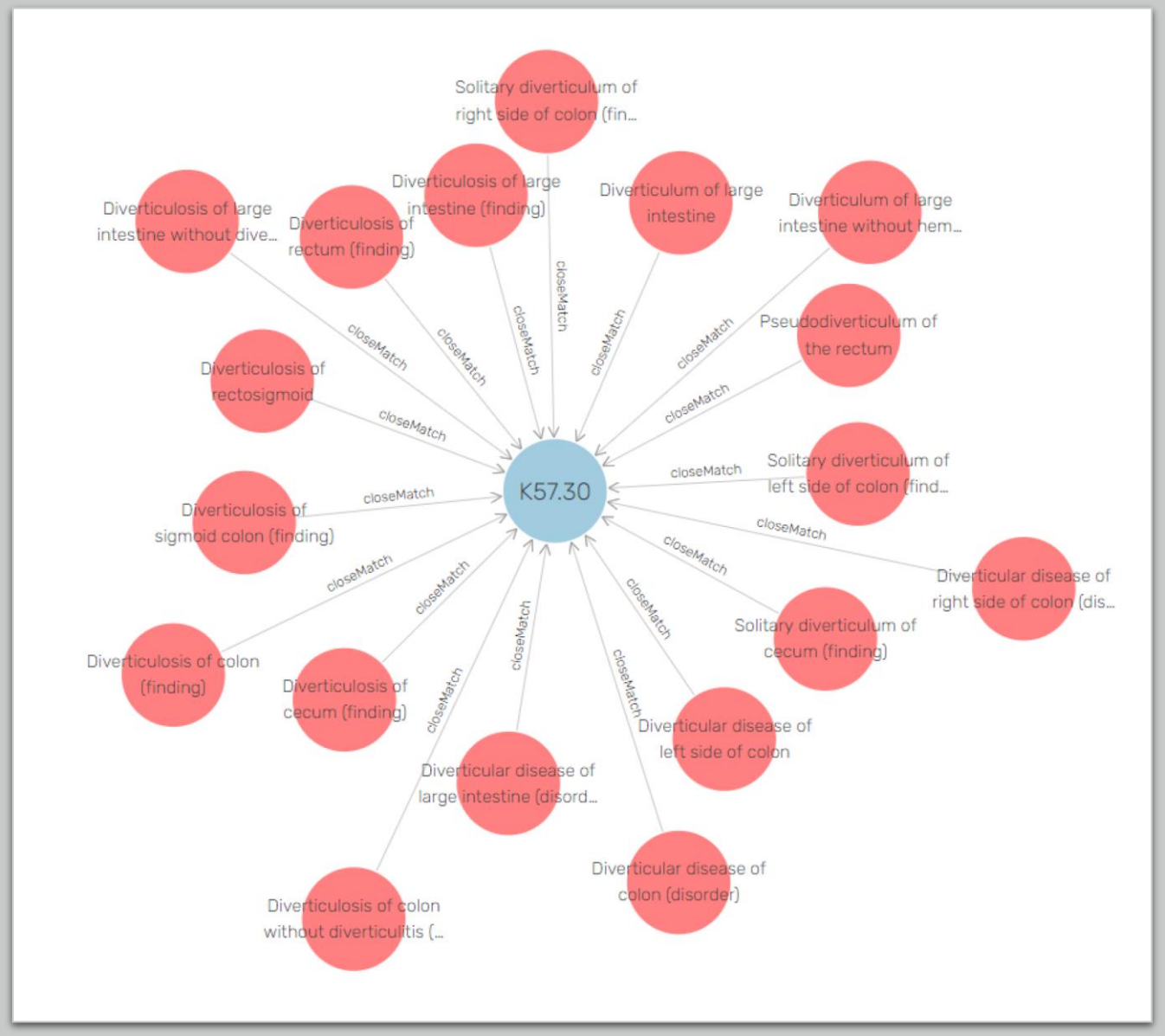
SNOMED Code	SNOMED description	Mapping Rule	Mapping Advice	ICD-10-CM code	ICD-10-CM descr.
100801000119107	Maternal tobacco use in pregnancy	IFA 107613910001 19102 | Tobacco use in mother complicating childbirth |	IF TOBACCO USE IN MOTHER COMPLICATING CHILDBIRTH CHOOSE O99.334	O99.334	Smoking (tobacco) complicating childbirth
100801000119107	Maternal tobacco use in pregnancy	OTHERWISE TRUE	ALWAYS O99.330	O99.330	Smoking (tobacco) complicating pregnancy, unspecified trimester

Context-dependent mapping

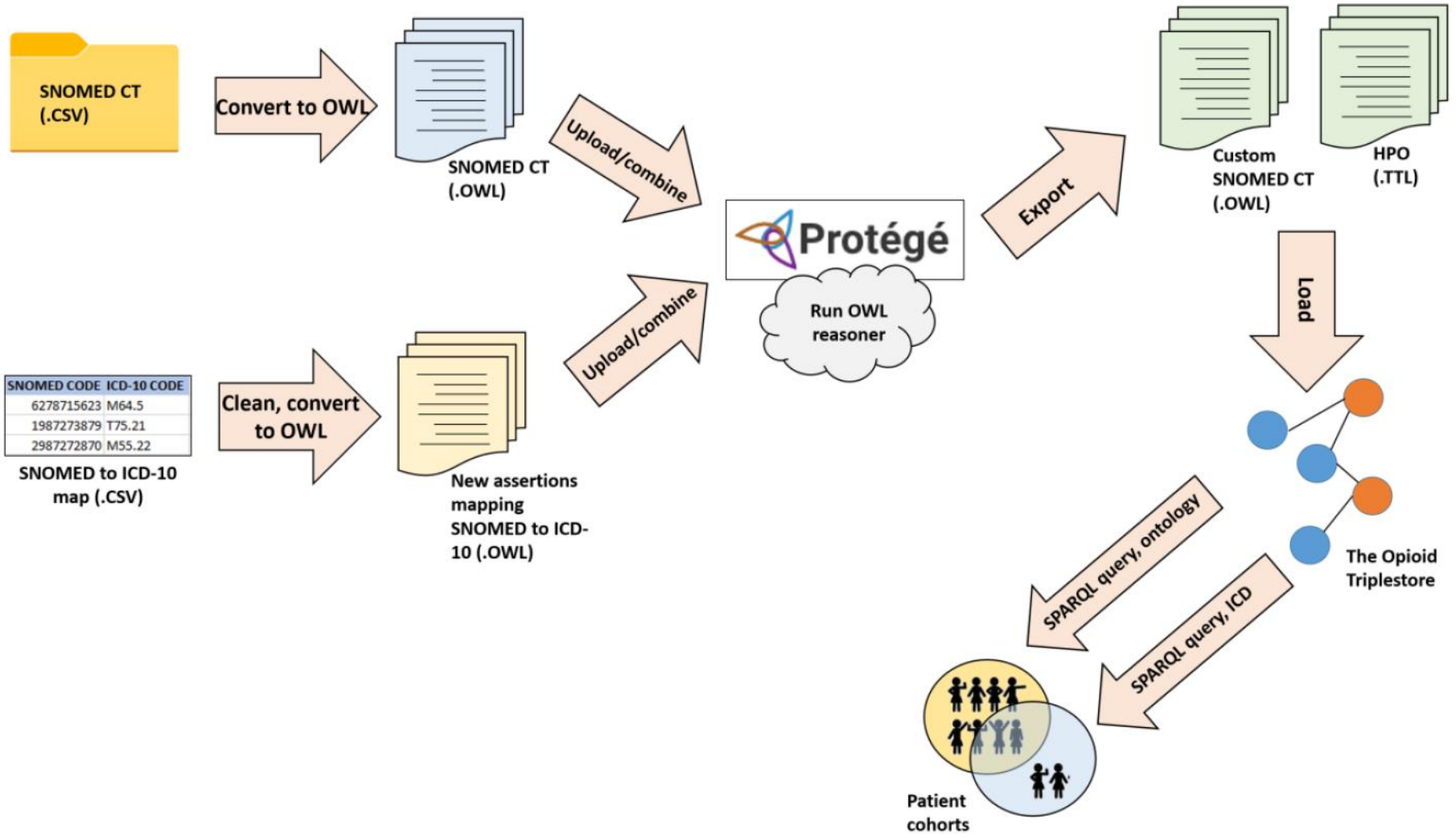
SNOMED CT Code	SNOMED CT description	Mapping Advice	ICD-10-CM code	ICD-10-CM description
10298002	Victim, motorcycle rider in vehicular AND/OR traffic accident	ALWAYS V29.9XX? | EPISODE OF CARE INFORMATION NEEDED | THIS IS AN EXTERNAL CAUSE CODE FOR USE IN A SECONDARY POSITION	V29.9XX?	Motorcycle rider (driver) (passenger) injured in unspecified traffic accident, episode of care unspecified

Required seventh digit mapping

Mapping SNOMED to ICD-10-CM

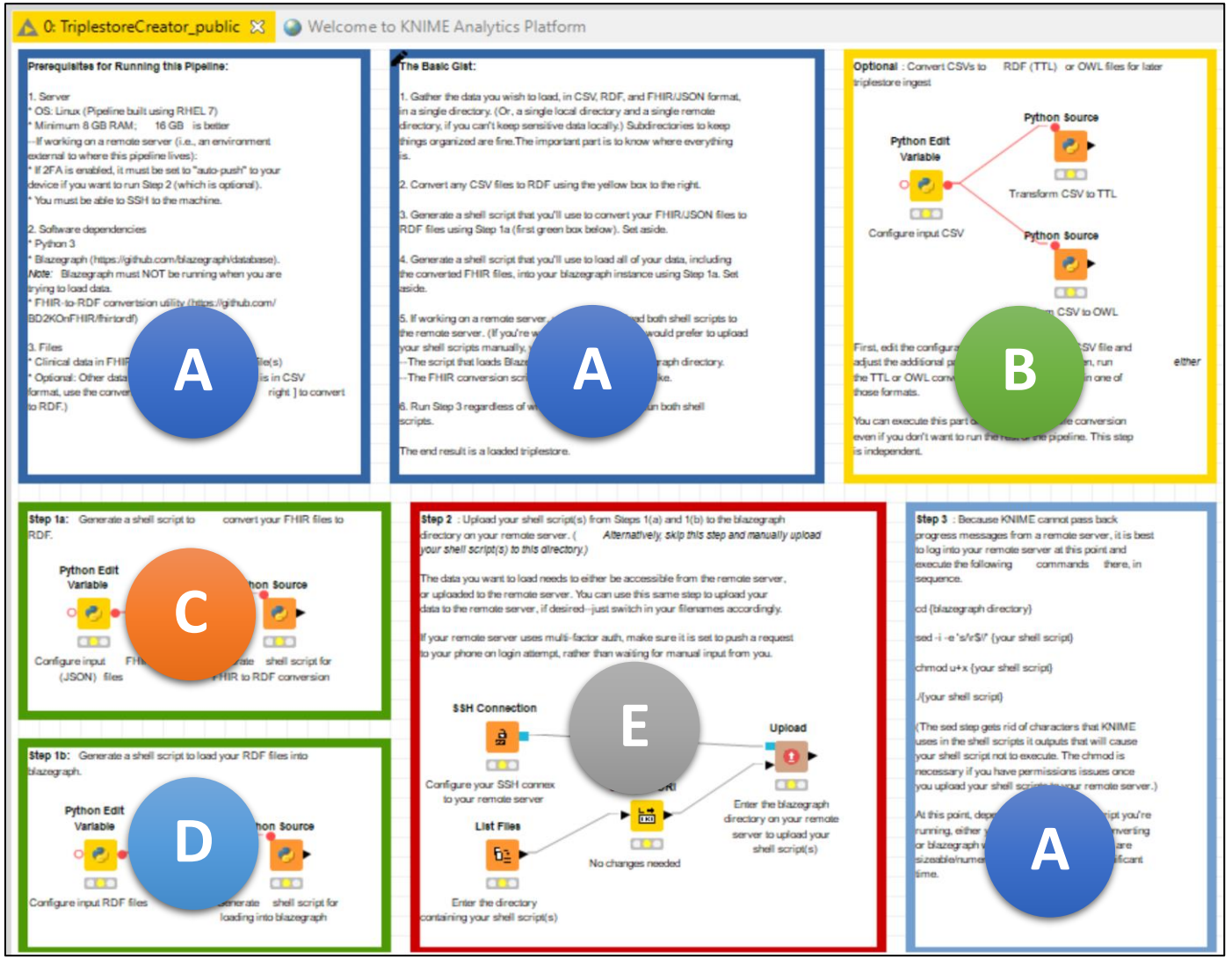


Transformation Pipeline



Implementing the Pipeline in KNIME

A. Documentation
B. CSV to RDF/OWL converter
C. FHIR to RDF converter
D. Triplestore loader
E. Data mover (optional)



Pipeline available for download at https://github.com/empfff/clinical-tripleizer

Experimental Steps (Each Phenotype)

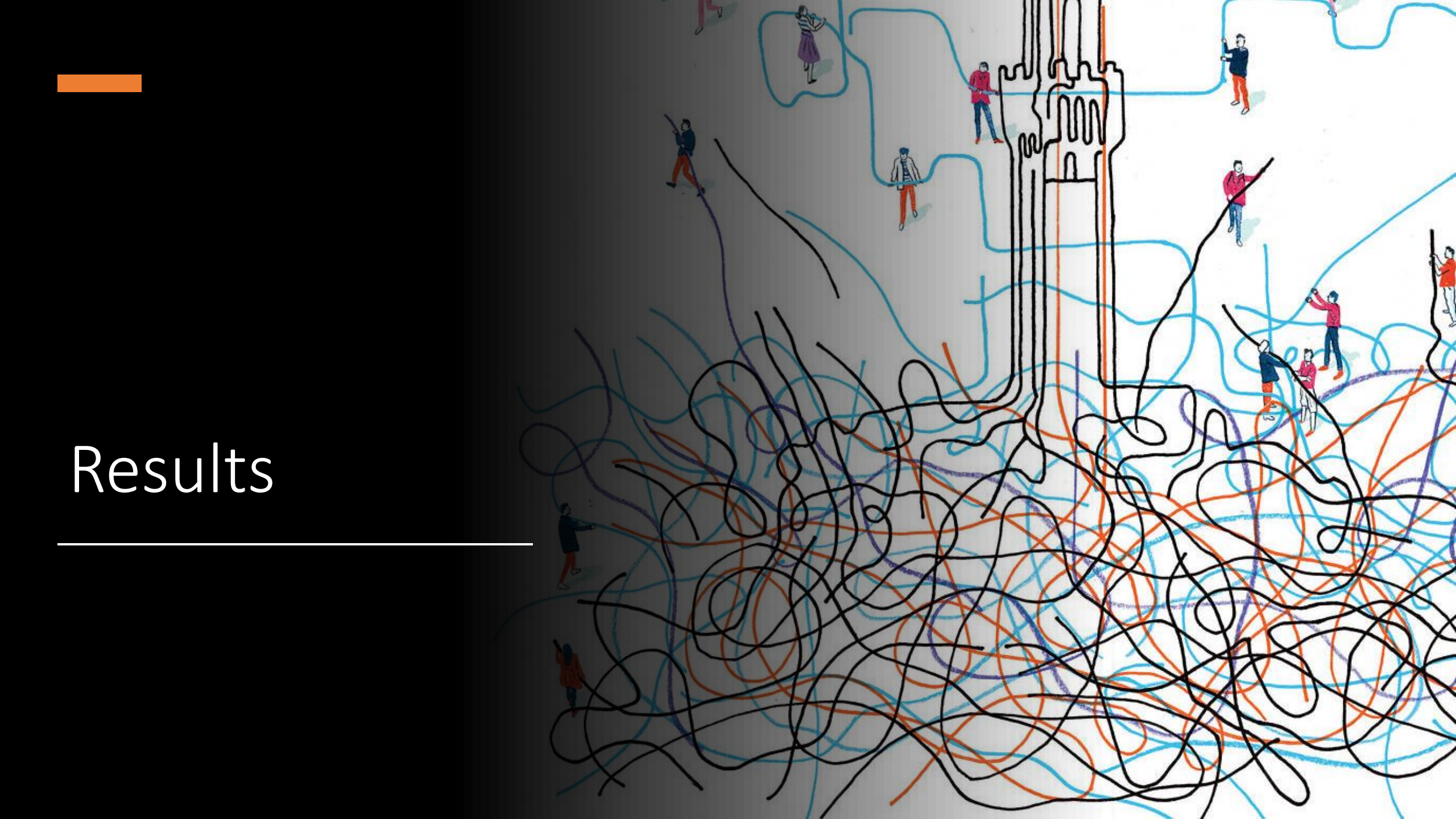
1. Execute a SPARQL query in the Opioid Triplestore using the ICD-10-CM codeset from the PheKB phenotype to identify matching patients.
2. Execute a SPARQL query in the Opioid Triplestore using a single ontology concept (SNOMED or HPO*), as well as any child nodes, to identify matching patients.

```
?snomednode skos:closeMatch ?icdnode .
?snomedsubnode rdfs:subClassOf* ?snomednode .
?snomedsubnode skos:closeMatch ?icdsubnode .
```

3. Compare the ICD-10-CM codes in the subgraphs defined by #1 and #2.
4. Compare the patients captured in the subgraphs defined by #1 and #2

*Because HPO maps to SNOMED, though the queries differed, the results were the same.

Results



Depression

- In general, SNOMED/HPO is picks up more patients than the PheKB phenotype, with a broader definition of "depression."
- SNOMED/HPO codeset included all but one of the PheKB codes (F43.21, adjustment disorder), and added more.
- SNOMED/HPO includes several bipolar codes; PheKB phenotype specifically excludes them.
- SNOMED/HPO graph contains two "problem codes": T81.89X (complications from procedure) and B94.9 (sequelae of unspecified disease).

Depression, continued

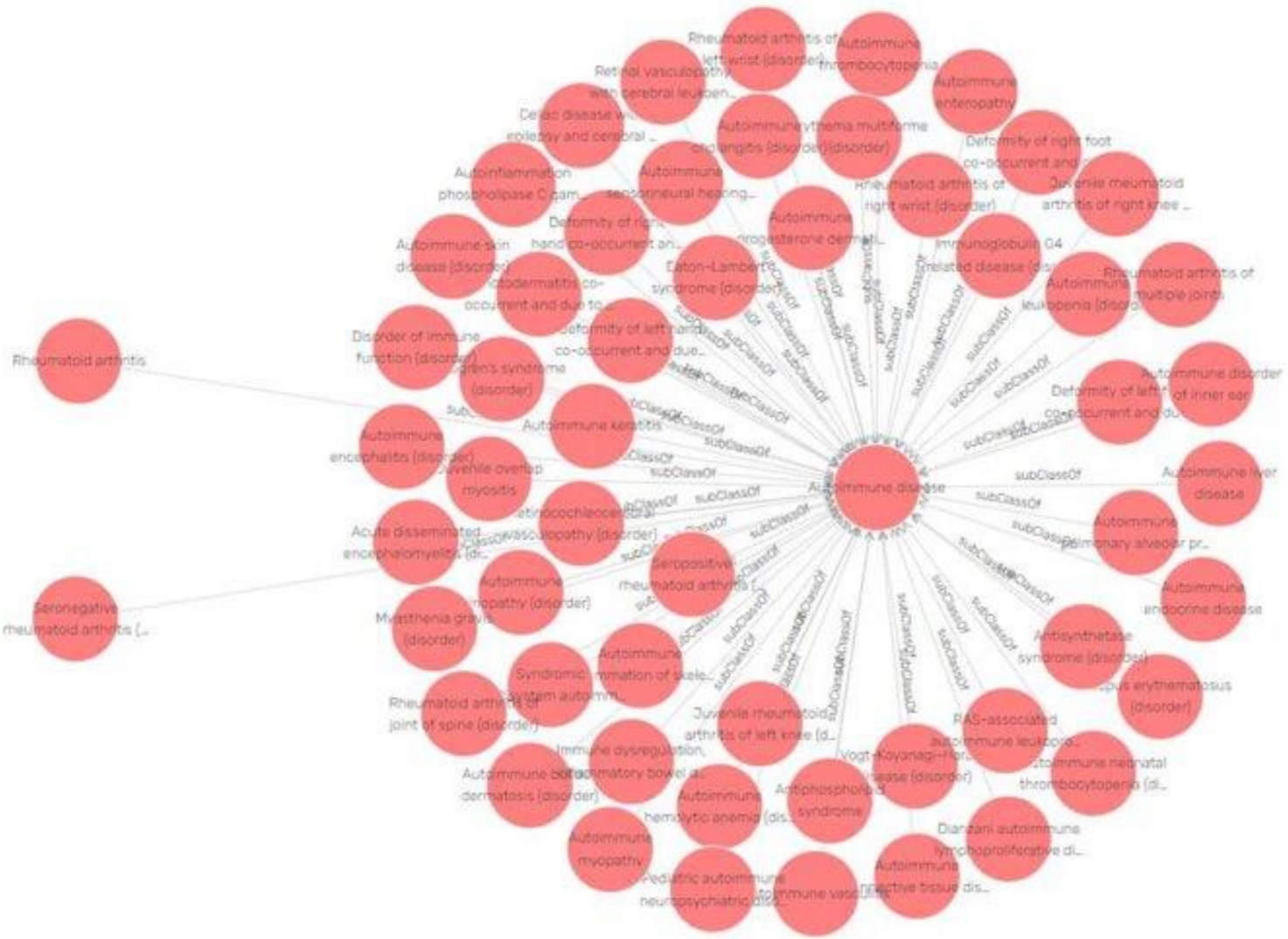
Table 2. Overlaps and differences between the cohorts defined by the PheKB and SNOMED/HPO depression queries against the Opioid Triplestore

Query	# patients found	# patients found by this query *only*	# patients found by both queries
PheKB	1,739	35	1,704
SNOMED/HPO	2,029	325	1,704

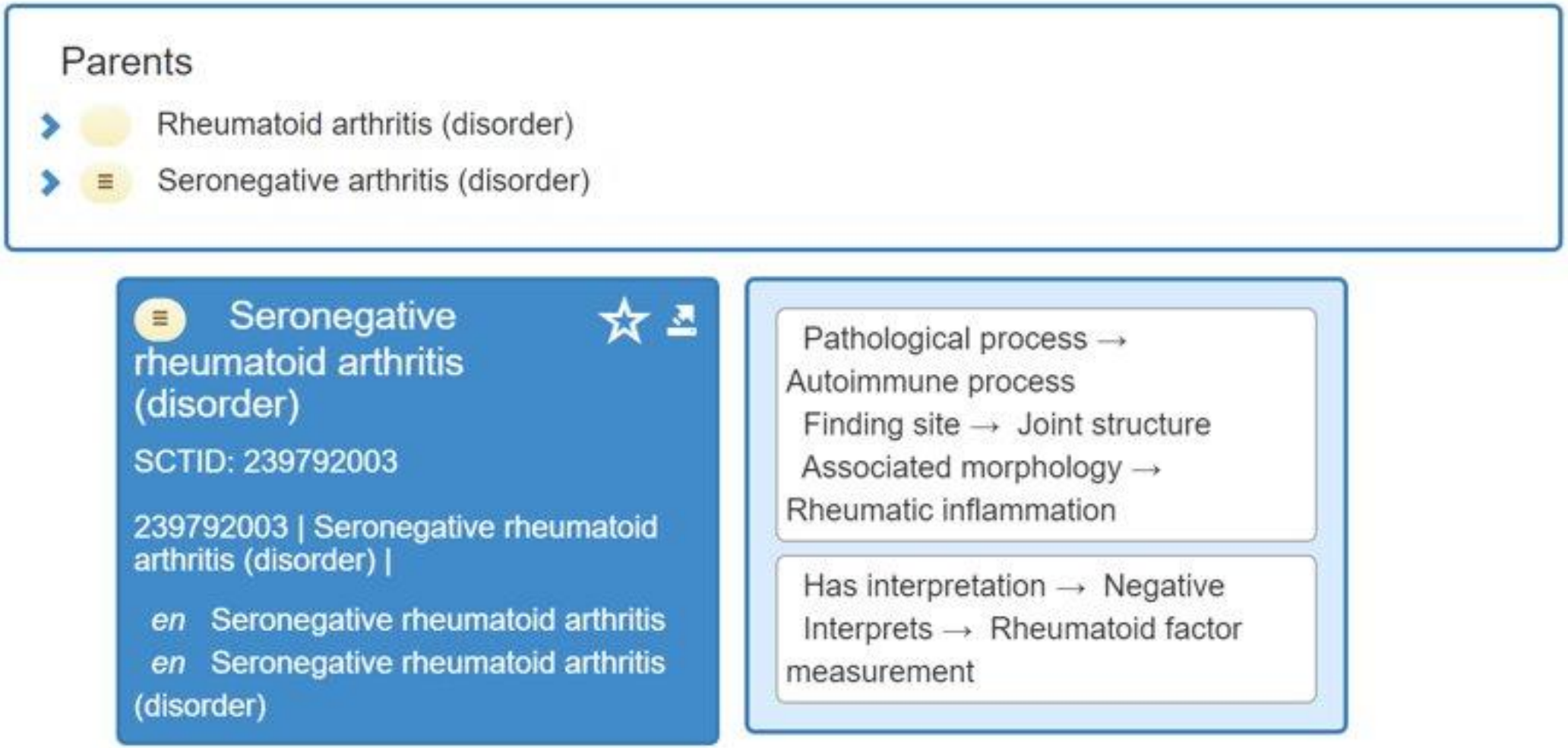
Of the "problem codes," B94.9 did not match with any actual patients in the Opioid triplestore. T81.89X? would have matched 47 more patients if the ? had been treated as a wildcard.

Rheumatoid Arthritis

- Very different from depression cohort results; SNOMED/HPO was missing several valid codes in the M05*/M06* ranges. (Missing knees, hips, wrists, and ankles!)
- Investigation revealed an issue with a subClassOf relationship in SNOMED, which has since been corrected!



SNOMED Correction (9/20 edition)



Rheumatoid Arthritis, continued

- SNOMED/HPO graph also contains two "problem codes": H20.10 (chronic iridocyclitis) and M25.80 (other specified joint disorders). Only the latter matched patients in the triplestore.

Table 6. Overlaps and differences between the cohorts defined by the PheKB and SNOMED/HPO queries

Query	# patients found	# patients found by this query *only*	# patients found by both queries
PheKB	166	30	136
SNOMED/HPO	142	6	136

Discussion & Conclusion

Ontologies as a Remedy for Semantic Ambiguity

Research Question 1: Can clinical ontologies (specifically SNOMED CT and the Human Phenotype Ontology) offer a less semantically ambiguous mechanism to perform computable phenotyping than reimbursement-focused terminologies (specifically ICD-10-CM)?

- ICD-10-CM serves an important purpose. As it is unlikely for its hierarchy to be modified, SNOMED/HPO provide a valuable augmentation, if not an alternative.
- The superset of "Google-able" or already known ICD-10-CM codes and those in the SNOMED/HPO subgraph may be a good starting point for researchers trying to choose the right codes for their phenotype.
- Using the superset fills in gaps in both SNOMED and ICD-10-CM.
- I would argue that allowing researchers to keep or pitch codes from a longer list is preferrable to not providing the choice.

Semantic Web as a Driver of Interoperability

Research Question 2: Does the use of semantic web technologies and standards (e.g., Resource Description Framework (RDF), triplestores, the Web Ontology Language) in tandem with ontologies improve the interoperability prospects of computable phenotypes and the underlying clinical data?

The infrastructure for this project addressed three interoperability challenges:

- **Challenge**: Inconsistent data models
- **Addressed By**: FHIR, RDF

- **Challenge**: Differing coding practices
- **Addressed By**: Ontologies

- **Challenge**: Integration with non-EHR data
- **Addressed By:** RDF

Limitations

- ICD-10-CM presents a bit of a catch-22—if it is the only diagnosis code type that will ever be attached to a patient, any phenotype method will eventually need to connect to ICD-10-CM. ("You're only as good as your worst ICD-10-CM code.")
- Our two phenotypes performed very differently. If I ran two more, I suspect they would each have their own idiosyncracies. This is a common issue in phenotyping studies.

Acknowledgments

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- Dr. John Preisser
- Rujin Wang
- Kellie Walters
- Dr. Matt Nielsen

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Thank you!