Towards Patient-Driven Phenotyping and Similarity for Precision Medicine

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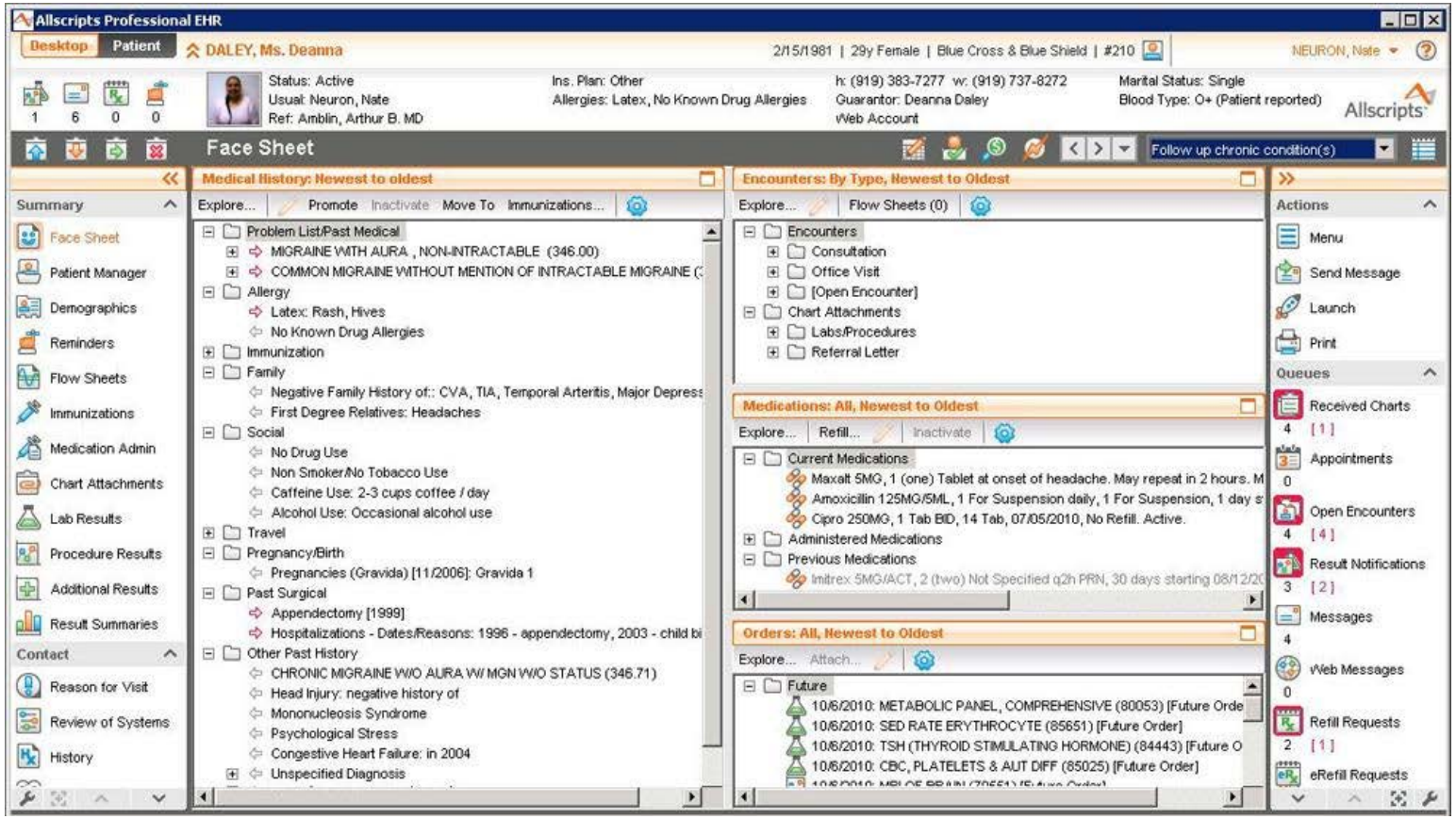
Electronic Medical Records

- Digital version of a patient's medical history:
  - Inpatient notes
  - Labs and physical exams
  - Prescribed medications
  - Diagnoses and procedures
  - Treatment plans
  - Discharge instructions



The big promise of lies in large-scale use, automatically feeding clinical research, quality improvement, and clinical phenotyping.

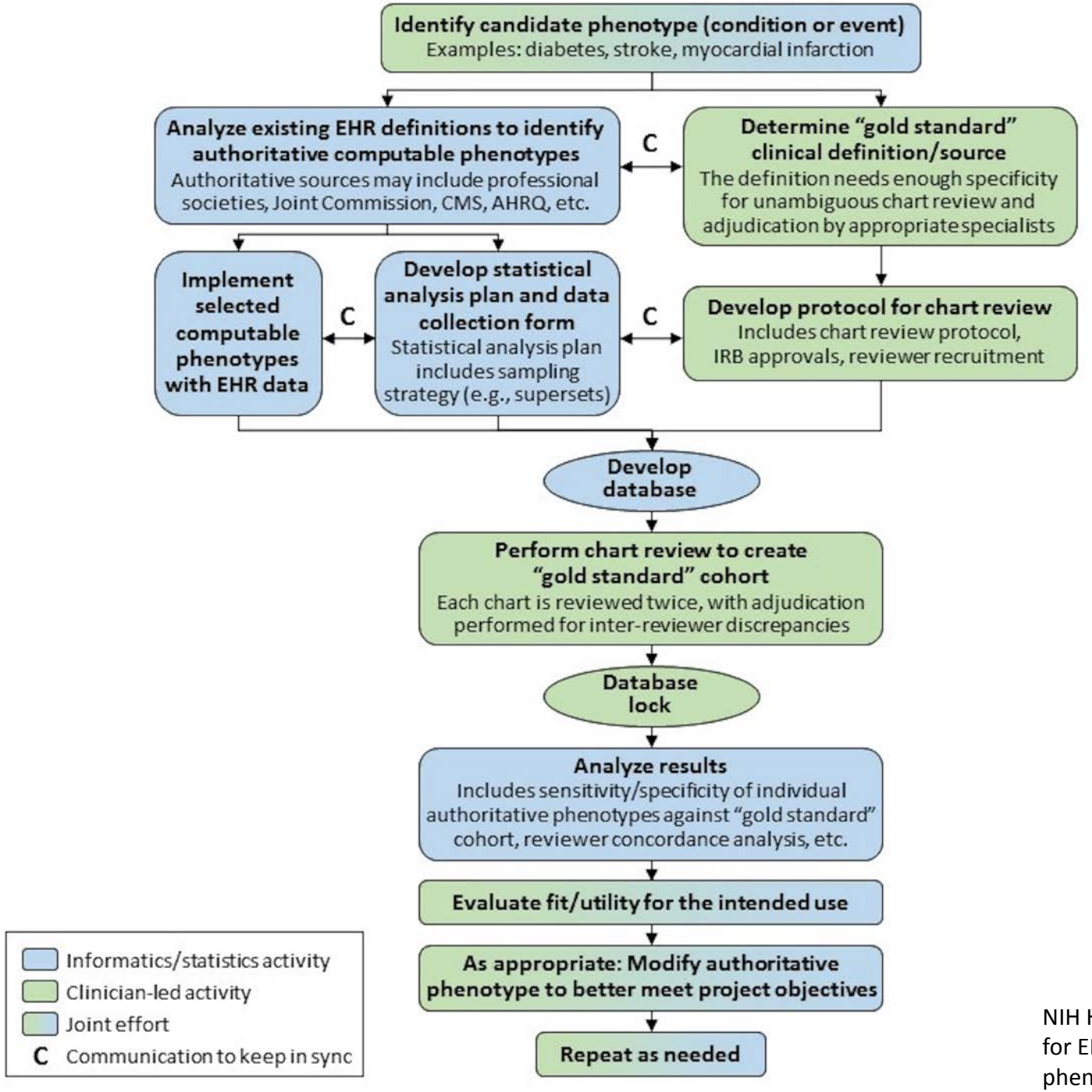
Hripcsak & Albers, *JAMIA*. 2013

Clinical Phenotyping

- **Goal**: identify cohorts of patients with specific clinical features characteristic of a disease of interest
- Typical approaches:
  - Rule-based
    + interpretable, fast to implement, good results on limited datasets
    - requires expert knowledge and multiple iterations, not easily generalizable
  - Natural language processing and text mining
    + rich data not found in other sources
    - sensitive to misspelling/bad grammar, redundancy, ambiguity
  - Machine learning
    + many standardized approaches, easy implementation, robust
    - curse of dimensionality; difficult with rare disease/small patient cohorts

PheKB

eMERGE Network
electronic medical records & genomics

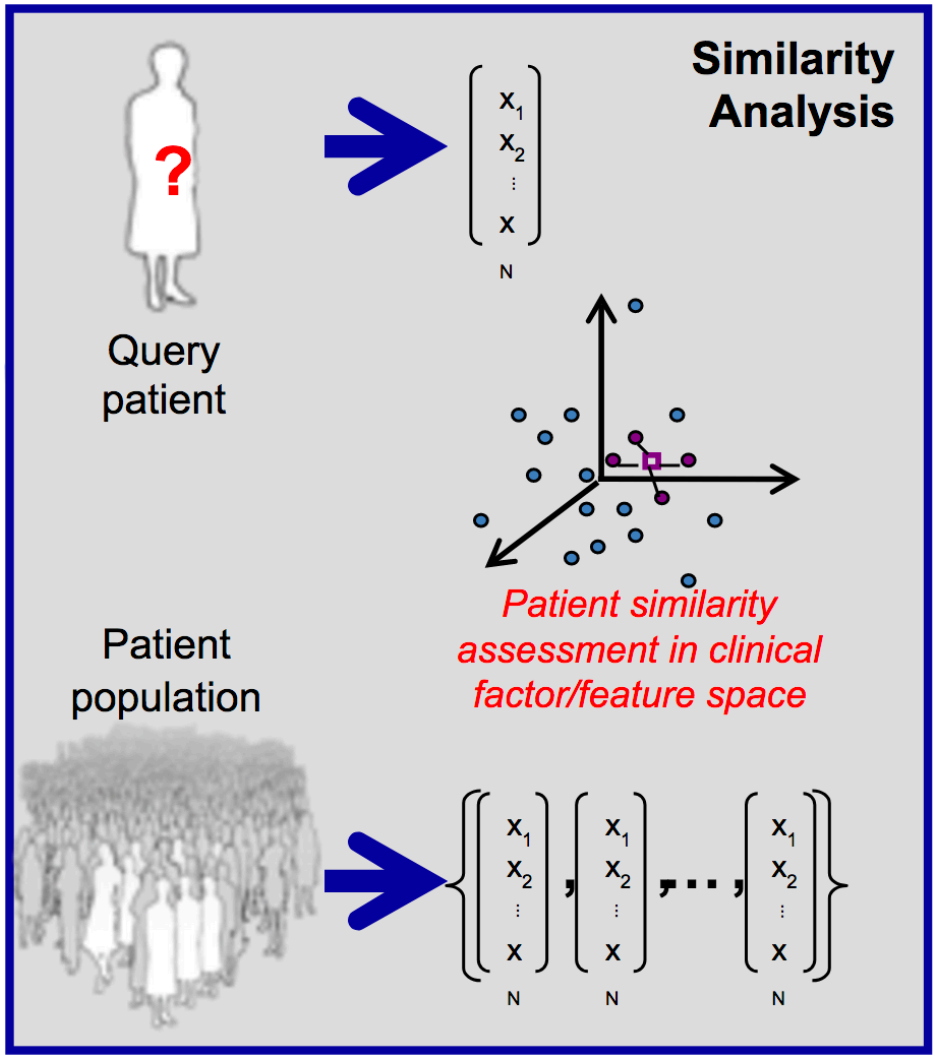


NIH Health Care Systems Research Collaboratory. Tools for EHR-based phenotyping. Type 2 diabetes mellitus phenotype definitions (Version 1.0). 2014.

Motivation

- Traditional approaches are good at providing information on the ”average patient”
- What evidence can physicians use when trying to treat a patient whose symptoms deviate from average?

- **Patient Similarity**: derive insights from patients that are similar to an index patient to provide personalized predictions[1]
- Diagnostic cohort identification
    - Drug repurposing
    - Identify and tailor treatment recommendations



[1]*Sharafoddini et al. JMIR Med Inform. 2017*

Approach

1. Similarity function
   - Data-driven; automatic
   - Pediatric data - OMOP CDM v5
2. Clustering
   - Similarity function-driven
3. Cluster identification/labeling
   - Clinical terminologies/value sets
   - Biomedical Knowledgebase
   - Literature
4. Evaluation
   - Compare to PheKB clusters
   - Verify algorithm reproducibility across data warehouses

Labs
Medications
Diagnoses
Demographics

MRN	Labs	Diagnosis	Medication
12345	Abs Cd4+ T Lymp: 1093 cells/mm^3	Age-related macular degeneration	0.05 ML Ranibizumab 10 Mg/ML injection

MRN	Age	Gender	Race
12345	14.0	Male	White

Patients | **Clinical Concepts**

Male != Female | White == White | $1 - \frac{(|14 - 30|)}{20}$

0.0 | 1.0 | 0.20

Concept Normalization

LOINC: | SNOM

gender, race, age | conditions, labs, medications

Patient_similarity = [0.0 + 1.0 + 0.2 + 0.389 + 0.456 + 0.027]

MxN matrix

ce conditions labs meds

ce conditions labs meds

stors

$\frac{1}{5} = 0.2$

$sim(t_1, t_2) = -log_2 \frac{|T(t_1) \cap T(t_2)|}{|T(t_1) \cup T(t_2)|}$

81423003

86555001

277869007

190909002

57676002

0.02 0.01 0.08 0.13 0.13 0.13 0.01 0.04 0.07 0.04 0.02 0.01 0.02 0.02

1.0 + 0.13 + 0.07 = 1.193

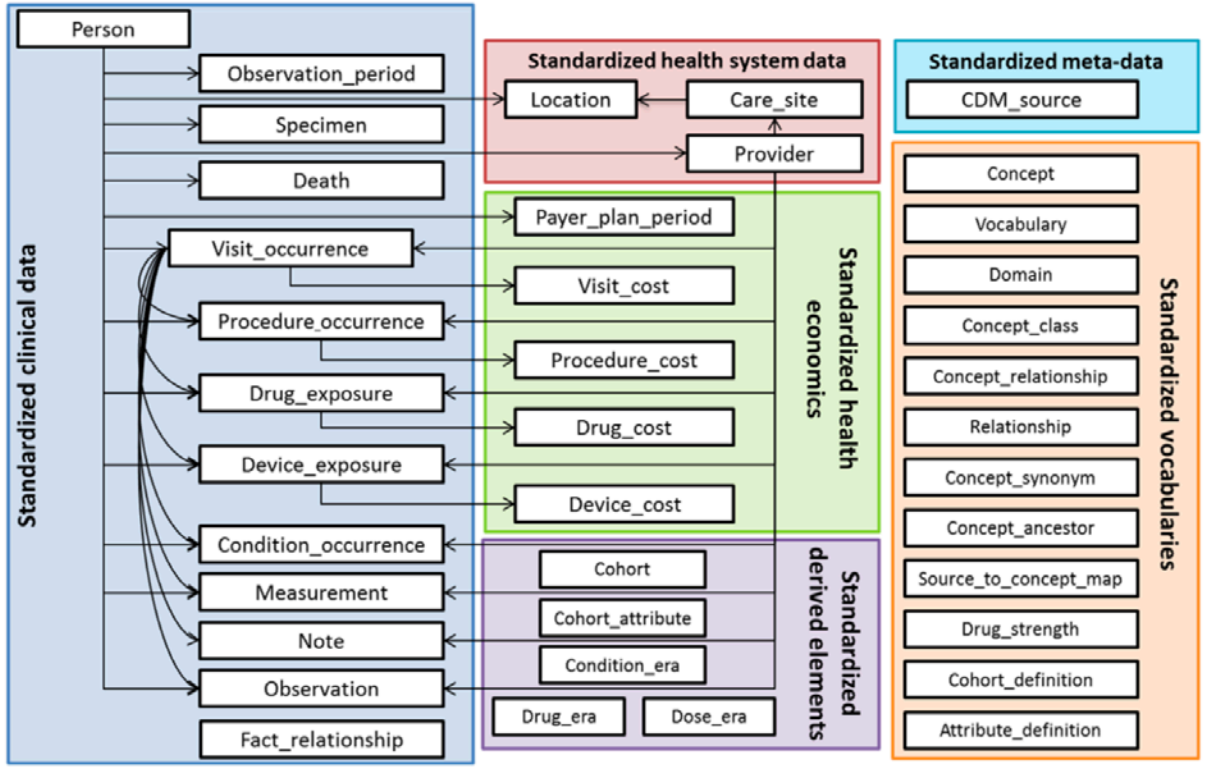
1.0 + 0.13 + 0.02 = 1.144

$(1.193 + 1.144)x \frac{1}{3+3} = 0.389$

[1]Batet et al. *J Biomed Inform.* 2011; [2]Azuaje et al. *Proc ISMB'2005 SIG. 2005*

Evaluation

- Children's Hospital of Colorado EHR data
  - De-identified (COMIRB # 15-0445)
- PEDSnet OMOP version 5
  - Concepts normalized to standardized terminologies
- Test Case – 2 groups (N = 20)
  - Huntington's Chorea (ICD-9-CM 333.4)
  - Cystic Fibrosis (ICD-9-CM 722.0)



Google BigQuery

```
SELECT
person_id,
condition_source_value,
COUNT(condition_source_value) AS count
FROM omop5deid.condition_occurrence
WHERE condition_source_value LIKE '333.4 %'
GROUP BY person_id, condition_source_value
ORDER BY count DESC
LIMIT 10
;
```

Row	person_id	condition_source_value	count
1	151130	333.4 | Huntington's chorea	125
2	322136	333.4 | Huntington's chorea	47
3	456778	333.4 | Huntington's chorea	21
4	65447	333.4 | Huntington's chorea	19
5	53666	333.4 | Huntington's chorea	16
6	434388	333.4 | Huntington's chorea	15

Huntington's Chorea

- Fatal disorder caused by breakdown of nerve cells in the brain
- 30,000 Americans have been diagnosed
- Symptoms include:
  - Personality, mood changes
  - Unsteadiness, poor coordination
- Diagnoses ($\bar{x}$ = 320.2; unique = 334)
- Laboratory tests ($\bar{x}$ = 114.1, unique = 119)
- Medications ($\bar{x}$ = 1528.7, unique = 177)

Hdsa.org/what-is-hd/

Row	co_person_id	OMOP_concept	SNOMED_code	source_code	count
1	151130	374341	58756001	333.4 | Huntington's chorea	125
2	151130	435642	29164008	784.5 | Other speech disturbance	59
3	151130	441277	25766007	315.32 | Mixed receptive-expressive language disorder	57
4	151130	441417	281016006	781.3 | Lack of coordination	40
5	151130	440086	192127007	314.00 | Attention deficit disorder without mention of hyperactivity	38
6	151130	440374	191736004	300.3 | Obsessive-compulsive disorders	22
7	151130	442077	197480006	300.00 | Anxiety state, unspecified	17
8	151130	436077	248290002	315.9 | Unspecified delay in development	17
9	151130	438409	406506008	314.9 | Unspecified hyperkinetic syndrome	16
10	151130	436073	69322001	298.9 | Unspecified psychosis	16
11	151130	379782	5158005	307.23 | Tourette's disorder	14

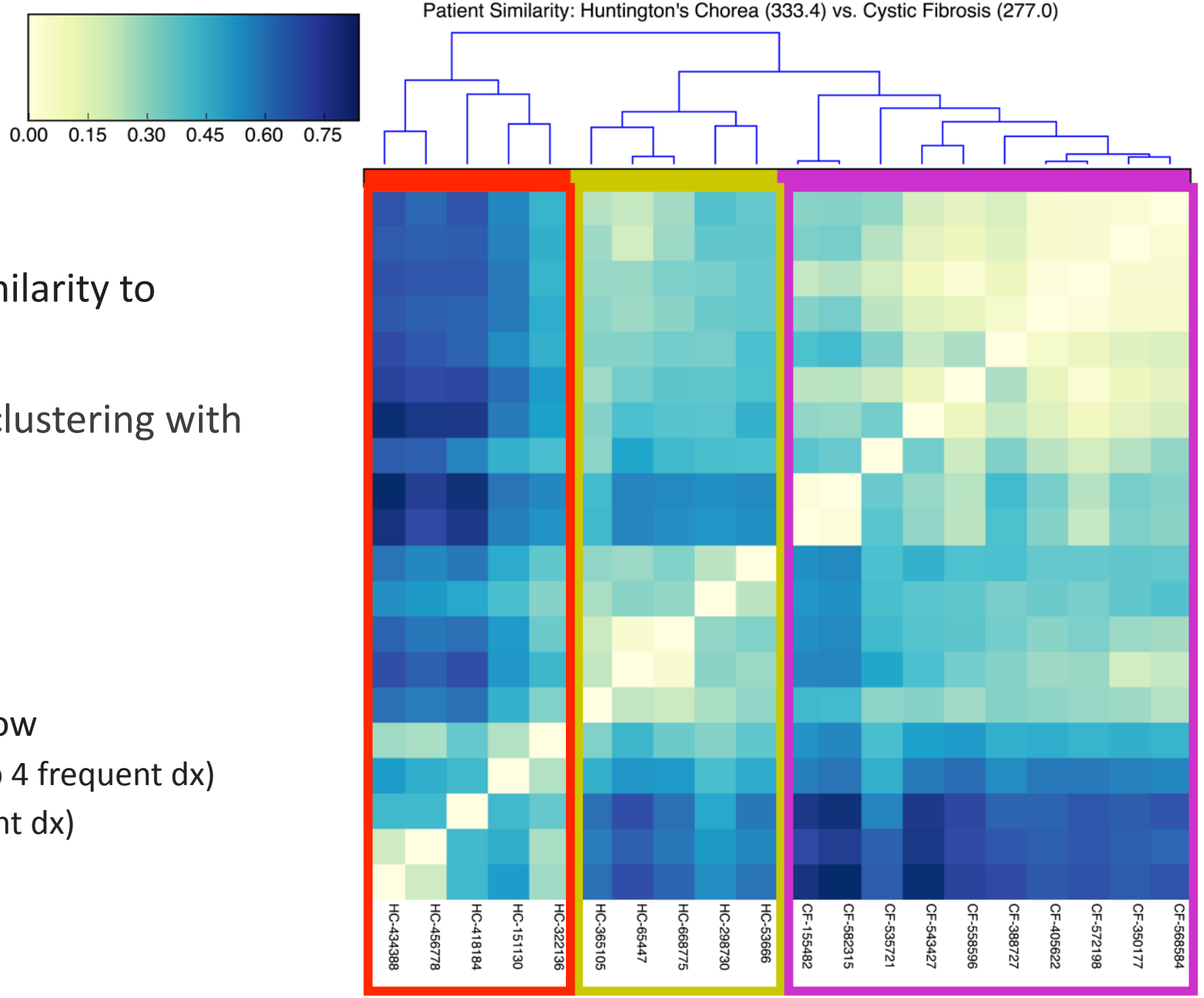
Cystic Fibrosis

- Genetic disease that causes mucus buildup resulting in persistent lung infection and difficulty breathing
- >30,000 people diagnosed worldwide
- Symptoms include:
  - Coughing, wheezing, frequent lung infections
  - Poor growth, male infertility
- Diagnoses ($\bar{x}$ = 982.5, unique = 447)
- Laboratory tests ($\bar{x}$ = 3104.4, unique = 124)
- Medications ($\bar{x}$ = 3120.3, unique = 392)

https://www.cff.org/What-is-CF/About-Cystic-Fibrosis/

Row	co_person_id	OMOP_concept	SNOMED_code	source_code	count
1	388727	434615	81423003	277.00 | Cystic fibrosis without mention of meconium ileus	538
2	388727	254320	86555001	277.02 | Cystic fibrosis with pulmonary manifestations	406
3	388727	378253	25064002	784.0 | Headache	352
4	388727	442077	197480006	300.00 | Anxiety state, unspecified	343
5	388727	194325	190909002	277.03 | Cystic fibrosis with gastrointestinal manifestations	272
6	388727	436096	82423001	338.29 | Other chronic pain	215
7	388727	4174281	277869007	031.0 | Pulmonary diseases due to other mycobacteria	194
8	388727	377889	15188001	389.9 | Unspecified hearing loss	182
9	388727	77074	57676002	719.40 | Pain in joint, site unspecified	150
10	388727	317009	195967001	493.90 | Asthma, unspecified type, unspecified	111
11	388727	4032376	108305003	V57.1 | Care involving other physical therapy	95

Clustering



- Convert pairwise patient similarity to distance matrix
- Agglomerative hierarchical clustering with complete linkage
- 3 Clusters
  - Cystic Fibrosis
  - Huntington's Chorea – red
  - Huntington's Chorea – yellow
    - Pulmonary fibrosis (3; top 4 frequent dx)
    - Asthma (2; top 10 frequent dx)

Conclusions

- Developed a patient similarity algorithm
  - Data-driven
  - Composite semantic similarity for heterogeneous data types
  - Adjust weights to customize by use case
  - Promising initial proof of concept with pediatric EHR is promising
- Limitations
  - Small test group, need to scale to larger groups
  - Limited evaluation
  - Several unmapped Generic Product Identifiers
- Future Work
  - Explore alternative semantic similarity algorithms
  - Optimize algorithm
  - Develop machine learning approach to determine patient similarity attribute weights

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