Detecting Phenotypes Among Patients Suspected of Rare Mendelian Disorders

Kai-Wen K. Yang, BS[1], Michelle H. Nguyen, BS[1], Angie Jelin, MD[1], Masoud Rouhizadeh, PhD[1,2], Nara Sobreira, MD, PhD[1], Casey Overby Taylor, PhD[1]

[1]Johns Hopkins University SOM, Baltimore, MD; [2]University of Florida, Gainesville, FL

Our results show that it is **possible for existing tools** to detect **clinically useful phenotypes** from **clinical notes** of patients suspected of **rare Mendelian disorders**.

Background & Objective

Clinical notes captured in a patient's electronic health record (EHR) are a rich source of information for understanding disease trajectories. For patients with rare Mendelian disorders seen first by non-genetics professionals, these notes may hold hints that are informative for genetics referral and for disease diagnosis. Natural language processing (NLP) and text annotation tools have been used to extract phenotypic features from clinical text in the domain of medical genetics to accelerate genetic diagnosis.

The objective of this work was to assess the performance of four text annotation tools to identify clinically useful phenotypes from the notes of a cohort of patients suspected of congenital anomalies.

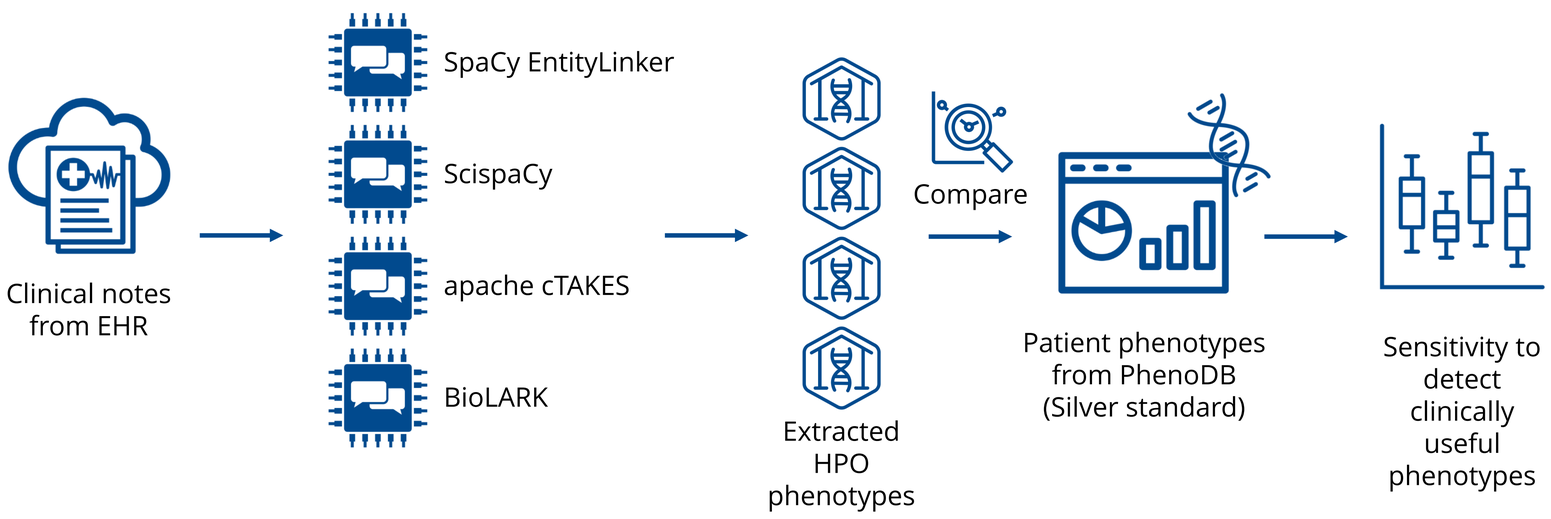

Figure 1. The workflow of the study analysis

Methods

We selected a retrospective cohort of patients suspected of rare Mendelian disorders and with a final diagnosis recorded in the Johns Hopkins Medicine (JHM) Clinical PhenoDB, a web-based platform used to store, analyze and interpret patients' genetic data[1]. Our data sources included PhenoDB and electronic health records (EHR), including patient encounter information and clinical notes. Four models were applied to nine randomly selected patients to assess the potential to identify clinically useful features from the notes of patients with congenital anomalies. Three clinical NLP models customized by the Johns Hopkins Core for Clinical Research Data Acquisition were applied to selected note types of eligible patients, including SpaCy EntityLinker[2], ScispaCy[3], and apache cTAKES[4]. We also used one Human Phenotype Ontology (HPO)[5] concept recognition (CR) tool, BioLARK[6]. For each of the four models, we followed a rule-based annotation approach, implementing HPO as the linking knowledge base. The manually entered features in PhenoDB served as a source of ground truth for this analysis. We report results for baseline extracted HPO terms and baseline + parent HPO terms. The parent terms were compiled using the python library pyHPO. Mean and SD values for sensitivity are summarized. Because PhenoDB may have some missing phenotypes, we did not calculate precision or F1 score due to lack of verified false positives. (**Figure 1.**)

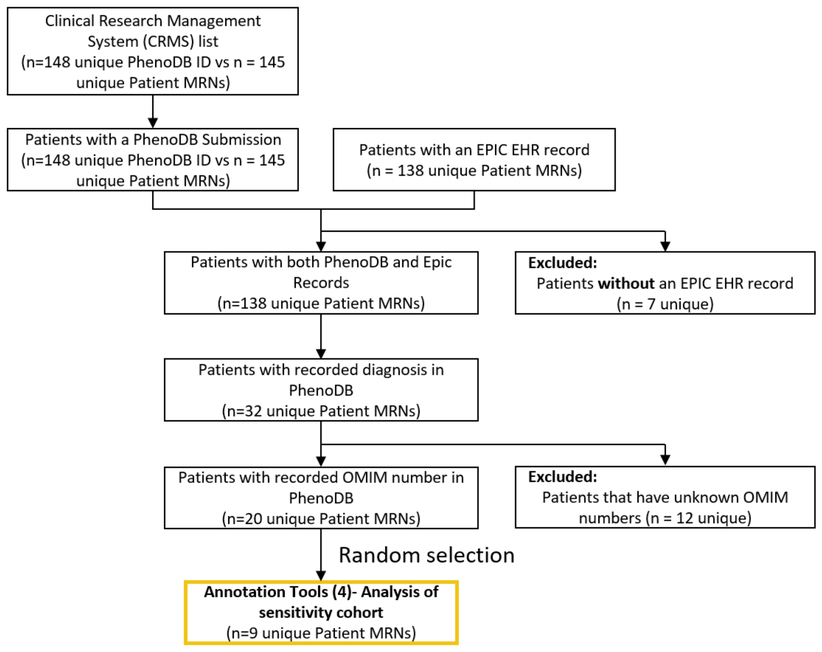

Figure 2. Cohort selection flowchart

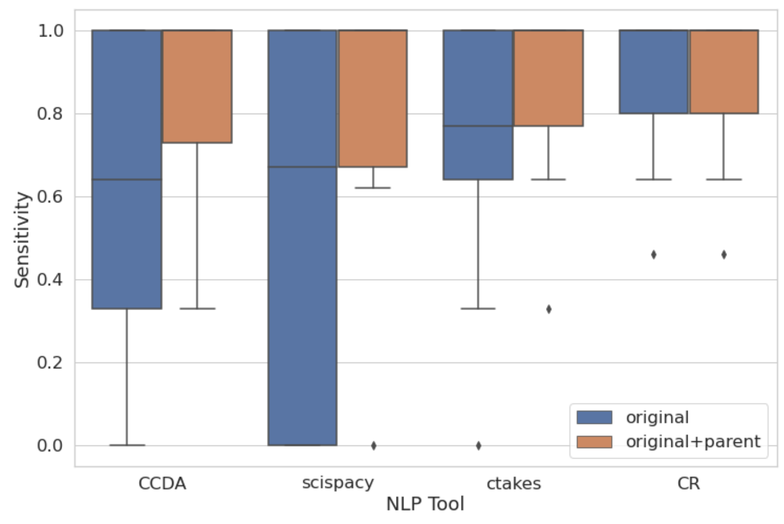

Figure 3. Results of the analysis of sensitivity

Results

Study population. The original cohort was 145 patients with a PhenoDB record. After excluding patients without an EHR record, final diagnosis recorded, and OMIM number in PhenoDB, 20 patients remained. Nine of these 20 patients were randomly selected to be included in the sensitivity analysis of the phenotype annotation tools. (**Figure 2.**)

Performance of four text annotation tools. Mean sensitivity to detect clinically useful phenotypes is the highest with CR (85.9±19.7%), followed by cTAKES (69.9±33.9%), SpaCy (59.0±40.6%), and ScispaCy (54.9±44.2%). The performance of CR stayed the same while the rest improved with parent-term inclusion (85.9±19.7%, 83.8±23.3%, 83.1±23.7%, 79.0±33.3%, respectively) (**Figure 3.**)

Discussion

Few JHM patients met the inclusion criteria for this study (20 altogether). This illustrates difficulties in establishing a final diagnosis for patients suspected of rare Mendelian disorders and further motivates studying automated strategies to assist clinicians with diagnosing patients. Our results show that it is possible for existing tools to detect clinically useful phenotypes from clinical notes of patients suspected of rare Mendelian disorders. Results from analyzing sensitivity of existing annotation tools to detect clinically useful phenotypes from patient notes were promising, with on average over 79% of the phenotypes in our ground truth dataset being detected. The best-performing tool identified 86% of the phenotypes on average. For our task to detect clinically relevant phenotypes among patients suspected of genetic conditions, out-of-the-box text annotation solutions may be sufficient, without the need for additional customization. In our case, CR performed similarly to the other customized NLP tools and required less effort to implement. Further research is needed to confirm this finding.

Lessons Learned

- Our results show that it is possible for existing tools to detect clinically useful phenotypes from clinical notes of patients suspected of rare Mendelian disorders.
- Few patients had an OMIM diagnosis assigned in PhenoDB or in the EHR, highlighting the existence of diagnostic odysseys of patients with rare genetic diseases.
- While PhenoDB was a first step toward having ground truth for clinically relevant phenotypes, more work is needed to enable comprehensive evaluation of NLP performance in this domain area.

References

1. Wohler, E., Martin, R., Griffith, S., et al. (2021). PhenoDB, GeneMatcher and VariantMatcher, tools for analysis and sharing of sequence data. Orphanet Journal of Rare Diseases, 16(1), 365.
2. Honnibal M, Montani I. spaCy 2: Natural language understanding with Bloom embeddings, convolutional neural networks and incremental parsing. 2017.
3. Neumann, M., King, D., Beltagy, I., & Ammar, W. (2019). ScispaCy: Fast and Robust Models for Biomedical Natural Language Processing. Proceedings of the 18th BioNLP Workshop and Shared Task, 319–327.
4. Savova, Guergana; Masanz, James; Ogren, Philip; et al. 2010. Mayo Clinic Clinical Text Analysis and Knowledge Extraction System (cTAKES): architecture, component evaluation and applications. JAMIA 2010;17:507-513 doi:10.1136/jamia.2009.001560
5. Robinson, P. N., Köhler, S., Bauer, S., et al. (2008). The Human Phenotype Ontology: A tool for annotating and analyzing human hereditary disease. American Journal of Human Genetics, 83(5), 610–615. PubMed.
6. Groza, T., Köhler, S., Doelken, S., et al. (2015). Automatic concept recognition using the human phenotype ontology reference and test suite corpora. Database: The Journal of Biological Databases and Curation, 2015, bav005

JOHNS HOPKINS MEDICINE

INSTITUTE for COMPUTATIONAL MEDICINE