Diagnosis Support for Rare Diseases Using Phenotypic Profiles

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Abstract. The common occurrence of characteristic symptoms can be used to infer diagnoses. The aim of this study is to show how syndrome similarity analysis using given phenotypic profiles can help in the diagnosis of rare diseases. HPO was used to map syndromes and phenotypic profiles. The system architecture described is planned to be implemented in a clinical decision support system for unclear diseases.

Keywords. Clinical Decision Support, Rare Disease, Syndrome

1. Introduction

The common occurrence of certain characteristic symptoms, also known as a syndrome, can be used to infer diagnoses. The diagnoses give affected individuals and their families access to resources, prognosis, and available treatments. There is an increasing use of expert systems to support syndrome diagnosis, including computer databases and analytic software, but also human expert and online services [1].

The aim of this study is to show how syndrome similarity analysis using given phenotypic profiles containing observable characteristics can help diagnose rare diseases (RD). This study describes a feasible system architecture to be used as an interoperable module of a case-based clinical decision support system (CDSS) for unclear diseases.

2. Methods

First, such a system must capture symptoms in a standardized form ensuring accurate similarity analysis. One ontology that covers a wide range of bioinformatics resources for human disease analysis, especially RDs, is the Human Phenotype Ontology (HPO) [2]. Complete phenotypic profiles on RDs can be accessed via Monarch [3] or HPO [2].

The selection of the similarity algorithm is crucial for the quality of the analysis. For HPO, there is the Python library *pyhpo* [4], which is open source and offers the possibility to define and compare different symptom sets. This functionality enables the module to compare syndromes of a new patient with given phenotypic profiles of RDs.

The usage of the HL7 data exchange standard FHIR ensures interoperability.

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3. Results

Figure 1 shows a system architecture that determines the similarity of the syndrome of a new patient case with the phenotypic profiles of given RDs. In addition to the calculated percentage similarity, further information such as the indication of identical, similar, or missing symptoms to the different phenotypic profiles is conceivable as an output.
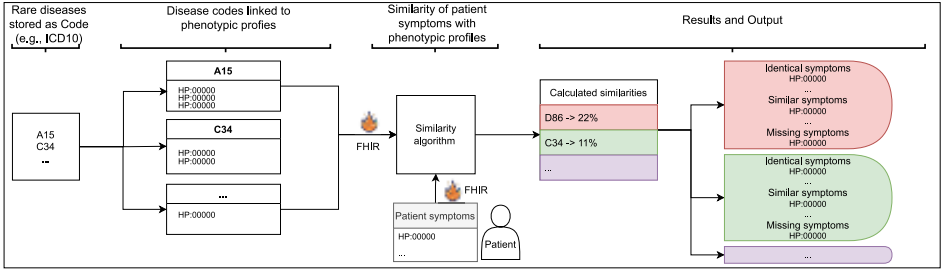
Figure 1. System architecture of an interoperable module providing disease prognosis based on a syndrome.

4. Discussion

The applied similarity algorithm works similarly to the *Phenomizer* [5], a clinical diagnostic web application that uses semantic similarity searches in ontologies, which however has no API. This study shows such an algorithm in conjunction with FHIR.

The advantage of an interoperable module over an isolated web-based platform is the cross-system operability and the possibility of a combined analysis of symptoms along with additional characteristics such as demographic data or laboratory tests to accumulate distinctive information and make an accurate differential diagnosis.

5. Conclusion

To validate the feasibility, the next step is to implement the described system architecture as an interoperable module into SATURN [6], a project funded by the German Federal Ministry of Health which aims to develop a CDSS for patients with unclear diseases.

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