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Specialized tools are needed when searching the web for rare disease diagnoses

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In our recent paper, we study web search as an aid in the process of diagnosing rare diseases. To answer the question of how well Google Search and PubMed perform, we created an evaluation framework with 56 diagnostic cases and made our own specialized search engine, FindZebra (findzebra.com). FindZebra uses a set of publicly available curated sources on rare diseases and an open-source information retrieval system, Indri. Our evaluation and the feedback received after the publication of our paper both show that FindZebra outperforms Google Search and PubMed. In this paper, we summarize the original findings and the response to FindZebra, discuss why Google Search is not designed for specialized tasks and outline some of the current trends in using web resources and social media for medical diagnosis.
The first is the ranking algorithm. Google Search optimizes the average retrieval performance (that is, how close to the top the chosen link appears). If a person conducting a search works within a field that generates a relatively small volume of queries, such as rare diseases, then Google’s ranking optimization might result in worse retrieval performance for this topic. For example, ranking according to page popularity may risk retrieving popular documents with only minor matches to the query. Second, if one can focus the search on websites with high quality content on the specialized topic, then one can eliminate noise coming from the overwhelming amount of irrelevant documents indexed by Google.

Can we tell which of these two reasons is the most important? Yes, because Google’s advanced search option allows the user to specify which domains to search. For FindZebra we selected ten sites with highly curated information on rare diseases that represent more than 90% of Orphanet’s list of about 7,000 rare diseases. This yields a total of 33,400 documents (see Table 1 for details). By restricting Google Search to the same domains used for FindZebra, relevant documents are retrieved in the top 20 search results in around only one-third of the cases. The ranking algorithm used in FindZebra is the one from Indri, but we can conclude that all other elements of their ranking algorithm make the overall results inferior to FindZebra for this particular task.

### Test and Feedback on FindZebra

In the following section, we discuss in more detail the setup used to test the performance of the search engines for the task of finding the correct rare disease diagnosis. We also discuss the feedback we received from users in the month after FindZebra search engine started attracting public attention and the degree to which that feedback confirms our results.

The 56 test queries used for evaluating the performance of the search engines were collected in three different ways. Five of these queries were constructed by the physician in the team, H.L.J., based upon his knowledge about the symptoms associated with specific rare diseases. For example, “Jewish boy age 16, monthly seizures, sleep deficiency, aggressive and irritable when woken, highly increased sexual appetite and hunger” corresponds to a diagnosis of Kleine Levin Syndrome. Another 25 test queries were extracted by the authors from case stories published in the *Orphanet Journal of Rare Diseases*. For example, the symptoms “six year old, girl, weight length head circumference below the third percentile, atrophic and hyperpigmented skin lesions, pointed nose, aberrant thumbs with diminished flexion, bilateral glue ears, purulent rhinitis” correspond to a diagnosis of Rothmund-Thomson Syndrome. The last 26 queries were taken from a paper by Tang and Ng from the *British Medical Journal*. These authors tailored case descriptions to web searches and then investigated how well a group of medical experts equipped with the symptom list and Google Search could identify the correct diagnosis. These latter descriptions are, in general, shorter than the rest. For example, the symptoms “acute aortic regurgitation, depression, abscess” correspond to a diagnosis of Infective Endocarditis.

Going into a bit more detail with the results of the evaluation presented in our recent study, we identify that there are five of the total 56 cases for which some version

<table>
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<th>Resource</th>
<th>Entries</th>
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<tr>
<td>Genetic and Rare Diseases Information Center (GARD) <a href="http://rarediseases.info.nih.gov/GARD">http://rarediseases.info.nih.gov/GARD</a></td>
<td>4,578</td>
</tr>
<tr>
<td>Orphanet <a href="http://www.orpha.net">http://www.orpha.net</a></td>
<td>2,967</td>
</tr>
<tr>
<td>Wikipedia <a href="http://www.wikipedia.org/">http://www.wikipedia.org/</a></td>
<td>2,239</td>
</tr>
<tr>
<td>National Organization for Rare Disorders (NORD) <a href="http://rarediseases.org">http://rarediseases.org</a></td>
<td>1,230</td>
</tr>
<tr>
<td>Madisons Foundation Rare Pediatric Disease Database <a href="http://www.madisonsfoundation.org">http://www.madisonsfoundation.org</a></td>
<td>522</td>
</tr>
<tr>
<td>About.com Rare Disease Database <a href="http://rarediseases.about.com">http://rarediseases.about.com</a></td>
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<td>Health on the Net Foundation Rare Disease Database <a href="http://www.hon.ch">http://www.hon.ch</a></td>
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</tr>
<tr>
<td>Swedish National Board of Health and Welfare <a href="http://www.socialstyrelsen.se/rarediseases">www.socialstyrelsen.se/rarediseases</a></td>
<td>114</td>
</tr>
</tbody>
</table>
of Google Search or PubMed returns relevant results and for which FindZebra does not return relevant results. Two of these cases correspond to diseases that are not present in FindZebra’s index, and four of the cases are queries from the BMJ article. Overall, we observe that Google Search handles long queries worse than FindZebra and that on shorter queries the performance of the two search engines is comparable. The two cases for which the correct diagnosis is missing from FindZebra's index point to the fact that FindZebra can be improved by including more data. In general, one can expect that multiple documents on the same disease will better capture the diversity of symptoms.

These cases represent fairly realistic examples of how a list of symptoms made by medical experts will look at a well-informed stage of the diagnostic process. It is doubtful that the lists of symptoms are truly blind—that is to say finalized before the final diagnoses have been reached. This means that there may be a slight bias toward emphasizing symptoms known to be associated with the disease.

Since the publication of the FindZebra paper, the search engine has received widespread attention and use. Over five weeks, from March 17th to April 21st, FindZebra delivered more than 1,000,000 diagnostic hypotheses to more than 30,000 unique visitors. Anecdotally, users appear to agree that FindZebra offers improved search results over existing alternatives. For example, one blog reports that for the query “purple urine” FindZebra suggests the likely diagnosis (Porphyrias) at rank two. In contrast, Google does not return documents relevant for the diagnosis on at least the first three pages of results. Another example is the query “osteopenia, hepatomegaly, anemia, fatigue, thrombocytopenia, nosebleed, Jewish” with Gaucher disease as the likely diagnosis. Another case study reported on the web describes the laborious process of finding the correct diagnosis. Typing in the symptoms listed in that case story, “muscle cramps, intense headaches, rapid weight gain, fatigue, edema, intolerance to heat, excessive sweating, joint pain, tingling in her hands and feet, frequent bone fractures, acid reflux, intense anxiety and panic attacks, high blood pressure, high cholesterol, high blood sugar, sleep apnea, menstrual irregularities, peripheral vision loss and double vision” results in the correct diagnosis (Cushing’s syndrome) being retrieved at rank 15 in FindZebra. Performing the same search in Google returns the web page from which the list of symptoms were taken, followed by many pages with no immediate association with the correct diagnosis.

**Using Web Search and Social Media for Diagnosis**

FindZebra provides a simple and easy-to-use interface, which streamlines the diagnostic process. Most of FindZebra’s search results include the disease name in their title, so it is easy to get an overview of the potential diagnoses. The documents are descriptions of the diseases so it is fast to get the relevant information and rule out possibilities. As with the anecdotal examples given above, Google Search often returns documents with no direct association with the specific disease, so even though the information might be there, it takes longer to extract. It is quite likely that the patient in the last example above would have been able to benefit from FindZebra. It would not take the patient long to go through the first 20 suggestions given by FindZebra, ruling out quite a few and taking a shortlist of potential diagnostic hypotheses back to her physician.

The main target users for FindZebra are general practitioners and specialists within fields where rare diseases can occur. Time is an important factor for general practitioners, which makes dealing with unusual symptoms especially challenging. General practitioners are bound to meet diseases that they will only encounter once in their career and thus are very likely to miss the correct diagnosis. It is our hope that FindZebra can facilitate the correct diagnosis. Lack of awareness about the specific diagnosis is definitely the main reason for rare diseases being mis- and late-diagnosed. For example, a study conducted by the European Organisation for Rare Diseases (EURORDIS) showed that 40% of rare disease patients were wrongly diagnosed before the correct diagnosis was given and that 25% of patients had diagnostic delays between 5 and 30 years.

Diagnosis of rare diseases is one of the prime examples of how information technology can aid physicians. They are rare, and there are many of them. The medical community will collectively have the needed experience and knowledge to deal properly with rare diseases, whereas this is not possible for an individual physician. Information technology, such as FindZebra, should enable the individual to tap into this collective knowledge. Social media also has the same potential, as exemplified by recent initiatives. Elsewhere, we will discuss the relationship between search engines and current social media approaches as potential aids for diagnosis.

FindZebra and similar systems can have a major impact over how medical diagnostic decisions are made. Certainly, these systems can be improved, and the feedback we have received so far indicates that there is a strong support from the medical community to facilitate this. Decision support (test and treatment options) is only a part of FindZebra to the degree that the indexed documents contain such information. One could definitely streamline the presentation of the decision support aspect and include an option to have prevalence as a part of the ranking algorithm. One long-term vision is to have a truly individualized system in which the physician registers each case so that queries and the final diagnosis are logged on a case-by-case basis. This is a complex task because of the need for user involvement, the possibly long time-span before diagnosis and issues surrounding patient privacy. However, it has the advantage of being unbiased (symptoms are reported before a diagnosis is reached) and is a much richer information source than using only the cases and consensuses reported in literature. Such a shared knowledge base on rare diseases would have the potential of increasing our understanding of rare diseases and greatly improving diagnostics.

**Disclosure of Potential Conflicts of Interest**

No potential conflict of interest was disclosed.
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