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User-Centred Development of a Diagnosis Support System for Rare Diseases

Jannik SCHAAF[a,1], Martin SEDLMAYR[b], Brita SEDLMAYR[b] and Holger STORF[a]

[a] *Institute for Medical Informatics, Goethe University Frankfurt, University Hospital Frankfurt, Frankfurt, Germany*
[b] *Institute for Medical Informatics and Biometry, Carl Gustav Carus Faculty of Medicine, Technical University of Dresden, Dresden, Germany*

Abstract. The diagnosis of rare diseases is often challenging for physicians, but can be supported by Clinical Decision Support Systems. The MIRACUM consortia, which includes ten university hospitals in Germany, develops a Clinical Decision Support System to support the diagnosis of patients with rare diseases. The users are involved in different phases using a user-centred design process. This publication has the objective to summarize the results of all studies performed in context of the requirements elicitation and to derive concrete requirements for the development of the system. Several studies were performed for requirements elicitation: a cross-sectional survey, expert interviews and a focus group. Participants were experts in rare diseases of the MIRACUM locations. 32 requirements were derived and implemented in a prototype. The prototype allows similarity analyses as a decision support functionality by comparing patients without a diagnosis to patients with a rare disease. In the final evaluation, the prototype was rated with a good usability. Since the system is limited in its functionality, further work and improvements are necessary to make it ready for clinical usage.

Keywords. Rare Diseases, Clinical Decision Support, Undiagnosed Patients

1. Introduction

Patients with rare diseases (RDs) are often suffering from late, unclear or wrong diagnoses [1]. This is caused due to lack of expertise and few available experts. Since a RD is defined as no more than 5 out of 10000 people are affected and more than 7000 RDs exist, not every physician can know every RD [1]. Due to these issues, it is useful to combine clinical routine data and improve research and healthcare of RDs [2]. The MIRACUM (Medical Informatics in Research and Care in University Medicine) consortium of the Medical Informatics Initiative (MI-I) in Germany decided to develop a Clinical Decision Support System (CDSS) for RDs using shared clinical data of ten 10 university hospitals in one of its use cases [3]. According to Sutton et al., a CDSS is defined as a software that improves health care by enhancing medical decisions through targeted clinical knowledge, patient information, and other health information [4].

[1] Corresponding Author, Jannik Schaaf, Medical Informatics Group, University Hospital Frankfurt, Theodor-Stern-Kai 7, 60590 Frankfurt am Main, Germany; E-mail: jannik.schaaf@kgu.de

The CDSS developed in MIRACUM, which is called DISERDIS (Diagnosis Support for Rare Diseases), will compare an undiagnosed case with previously diagnosed cases of RDs. Due to the similarity to other diagnosed patient cases, the attending physician receives a hint to a diagnosis for the undiagnosed patient.

In the past, various CDSS for RDs have been developed and published [5, 6]. While the focus of these systems is on functionality, according to the results of a scoping-review, the requirements and needs of users in current CDSS for RDs are insufficiently considered [6]. Most existing studies on CDSS for RDs focus mainly on performance and accuracy in terms of diagnostic recognition. Furthermore, the integration of the systems into the clinical workflow as well as usability, which describes whether a system can be used with a high task efficiency and user satisfaction, is also crucial for user acceptance [7, 8]. Therefore, user requirements should be collected and documented as comprehensively as possible in the development process of those systems [9].

In the past, we have conducted several studies on the requirements elicitation of DISERDIS [6, 10-12]. In this paper, we summarize the results of these studies and derive concrete requirements on this basis. Thereby, we focus on the concrete decision support component, its functionality and the user-interface.

2. Methods

For the development of the CDSS, we followed a user-centred design process (UCD) according to ISO 9241-210:2019 “Ergonomics of human-system interaction - Part 210: Human-centred design for interactive systems”. The UCD actively involves future users of software in the development process to ensure that all times needs and objectives of the users, their tasks as well as their working environment are considered [13].

2.1 Requirements analysis

At the beginning, a scoping review was performed to identify influencing factors for the development of the CDSS [6]. We investigated, which CDSS for RDs are available for diagnosis support, which data and functionalities they use and if data integration is performed automatically [6]. In the next step, a cross-sectional survey [10] and expert interviews [11] were performed to investigate what are relevant organizational conditions for the operation of DISERDIS, what the appropriate user group is and which data are necessary to enable diagnosis support. For each study, we invited eight experts in RDs who are physicians at the rare diseases centres (RDCs) at the university hospitals. Each of them have a completed medical degree and specialist qualification in human medicine. RDCs are specialized in the diagnosis and treatment of RDs and available at eight MIRACUM locations [11]. Furthermore, a focus group was performed to discuss how the results provided by the CDSS for diagnosis support should be visualized to the user. There, we invited the RDs experts as well as scientists in medical informatics [12]. After these steps, we defined the requirements based on the results of these studies and separated them to functional and organizational conditions. Additionally, we have defined non-functional requirements as quality aspects such as efficiency or maintainability according to ISO/IEC 9126:2001 ”Software engineering - Product quality - Part 1: Quality model” [14].

2.2 Conception and implementation of the CDSS

In the next project phase, a data set for diagnosis support was defined, as well as a concrete software-function which uses the data set and enables diagnosis support. Finally, a concrete software-architecture was specified on the basis of which the CDSS was subsequently implemented.

The data set was developed based on an existing data set, used in the Frankfurt Rare Diseases Centre at University Hospital Frankfurt for undiagnosed patients. The data set contains information about gender and age, prior diagnosis, symptoms and family history. We used the ICD-10 (International Classification of Diseases and Related Health Problems) to describe diagnosis data and the Human Phenotype Ontology (HPO) for symptoms [15]. For each data category, a similarity sub-function was created to measure similarity between a pair of patients with a result between 0 (not similar) and 1 (similar). The sub-functions were summarized in one function using the arithmetic mean.

The CDSS was implemented using Microsoft ASP. NET Core framework. The database includes a common data model with OMOP-CDM (Observational Medical Outcomes Partnership Common Data Model) to describe data at each MIRACUM location uniformly [16]. The communication of DISERDIS between its software-components is performed with FHIR (Fast Healthcare Interoperability Resources) [17].

2.3 Evaluation

After the development of DISERDIS, a thinking aloud test was performed to evaluate the design and quality of the system so far. Eight RDs experts (as in the previous studies) were invited to use the CDSS and were asked to say out loud what they think about the system while using it. Thereby, a questionnaire was used to assess the System Usability Scale (SUS), which measures usability of a system on a scale from 0 to 100 [12].

3. Results

3.1 Requirements analysis

As a result of the requirements analysis phase, we identified 32 requirements in total, whereas 11 functional requirements are shown in Table 1.

Table 1. Requirements to DISERDIS based on requirements analysis studies

No.	Description
1	The CDSS should offer an analysis and comparison possibility of genetic and/or phenotypic data.
2	The CDSS should not be tailored to one specific disease or disease group.
3	The CDSS should enable data entry via forms, upload or Data transfer via REST API.
4	The CDSS should be usable online.
5	The CDSS should enable the possibility to rank patient cases according to urgency.
6	The CDSS should enable the possibility to deposit information for case discussions.
7	The CDSS should present the overview of similar patients via scatterplot and table overview. Percentages for the similarities should be provided.
8	The CDSS should enable the selection of certain criteria to customize the similarity analysis. Furthermore, missing values should be considered.
9	The CDSS should enable an overview of the similar patients over time with a timeline.
10	The CDSS should enable a comparison of similarity values between patients.
11	The CDSS should enable an overview of the progression of various medical parameters for a similar patient.

3.2 Conception and implementation

3.2.1 Similarity function

According to requirement 1 and 2 (see Table 1), a decision support function which performs similarity of patients was defined. The similarity function primarily should use phenotypic data and should be independent of a specific RD or disease group. A specific requirement for the similarity function was the consideration of missing values (requirement no. 8). Therefore, sub-functions were defined which allow to calculate the similarity between patients only on selected data of interest (e.g., only diagnoses and symptoms) and to ignore a specific data-category, if not available. In summary, the following sub-functions were created:

The similarity of age was calculated according to Gottlieb et al. and yields a value between 0 and 1 [18]. The gender similarity is indicated by the attributes 'Male' or 'Female'. Therefore, the similarity is always 0 or 1. The similarity of symptoms was defined according to Robinson et al., using the (HPO) [14]. According to the data set, the information on family history includes the question about the blood relationship of a patient's parents. The following values can be entered: 'Yes, confirmed', 'Yes, suspected', 'No, confirmed' and 'No, suspected'. Two groups are formed. Group A contains positive results (Yes, confirmed | Yes, suspected) and group B negative results (No, confirmed | No, suspected). If two values to be compared are within the respective groups, the similarity is 0.5. If the two values are the same or not, the similarity is 1 or 0. The similarity of diagnosis was calculated using the Vector Space Model (VSM) according to Garcelon et al. [19]. The similarity of two terms, is defined as the similarity of the context of the terms that occur in the terms. The resulting matrix of the VSM consists of binary values that indicate the presence or absence of a word or term in a text. For similarity calculation, we used the text designations of ICD-10 codes.

3.2.2 Software-Architecture

In the following, the process of similarity analysis in the CDSS and the components are described (see Figure 1).

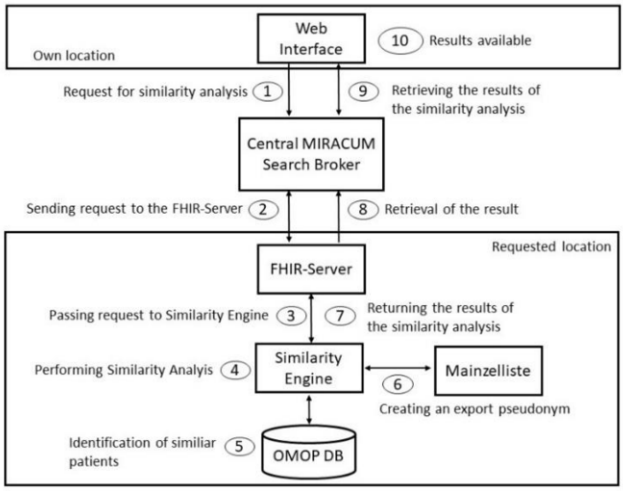

Figure 1: Software-architecture of DISERDIS

The data between MIRACUM sites will be exchanged using an interoperable and open standard (FHIR). Furthermore, this enables automatic transfer from different software systems via the use of a REST API (e.g. from electronic health records, requirement 3). The web interface, which provides the user interface for DISERDIS, sends the request to perform a similarity analysis to the MIRACUM search broker (step 1). The search broker is a central component for distributing the search requests to the MIRACUM sites. The search queries are forwarded by the search broker to the FHIR servers at the sites, which pass the query to the similarity engine for similarity analysis (steps 2 and 3). At each site, the similarity engine compares the existing patient data stored in the OMOP-RD repository, which is available at each MIRACUM site (steps 4 and 5). For each similar patient, a pseudonym is created using the Mainzelliste pseudonymization tool (step 6) [20]. The result is then forwarded back from the similarity engine to the FHIR server (step 7). In this process, the search broker makes the results of the FHIR server available for retrieval (step 8). The web interface regularly asks the search broker whether the results of the sites are already available and retrieves them if necessary (steps 9 and 10).

3.2.3 Implementation

Regarding requirement no. 4, a web application was implemented (shown in Figure 2). The menu of DISERDIS consists a left navigation bar and four navigation boxes in the middle of the application. There, the user can see (front the left to the right in Figure 2), how many undiagnosed patients are available, the date of the last case discussion and similarity analysis and how many urgent patients are available. According to the requirements no. 5 and 6, patients can be prioritized from “low” to “high”. Interdisciplinary case discussions, which are conducted in the RDCs, can be created with a date of the meeting and the patients to be discussed. DISERDIS also offers a patient overview and to enter patients manually in a form (requirement no. 3).

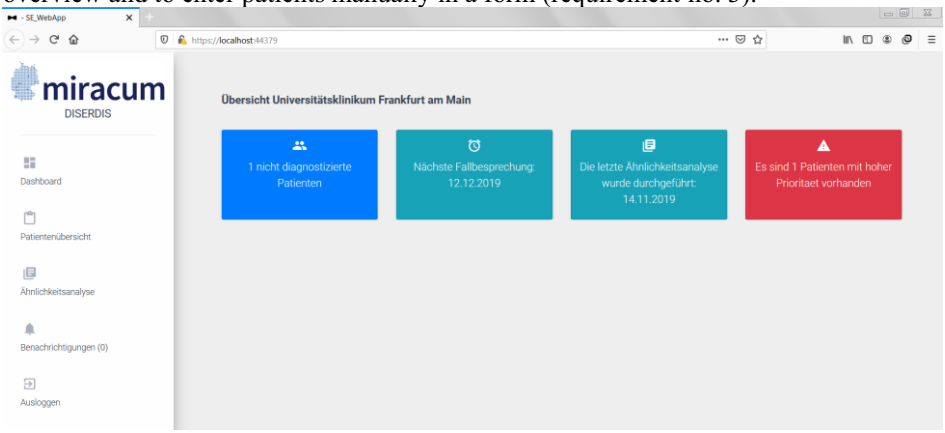

Figure 2: Web application of DISERDIS

Furthermore, a similarity analysis can be performed, which is accessible via the left navigation bar. There, it is possible to select several MIRACUM locations. After the similarity analysis, the user receives a notification as soon as the results are available. The user gets an overview of the results as shown in Figure 3. It is possible, to select between four different panels to show more details of the similarity analysis.

In panel 1, it is possible to get an overview of the similar patients in a table overview and a scatterplot (requirement no. 7). A similar patient can be selected and the data of

this similar patient can be viewed in the other panels. In panel 2, it is possible to see a direct comparison of similarity values. There, a percentage is shown, i.e. how high the similarity in a certain data-category is (requirement no. 10).

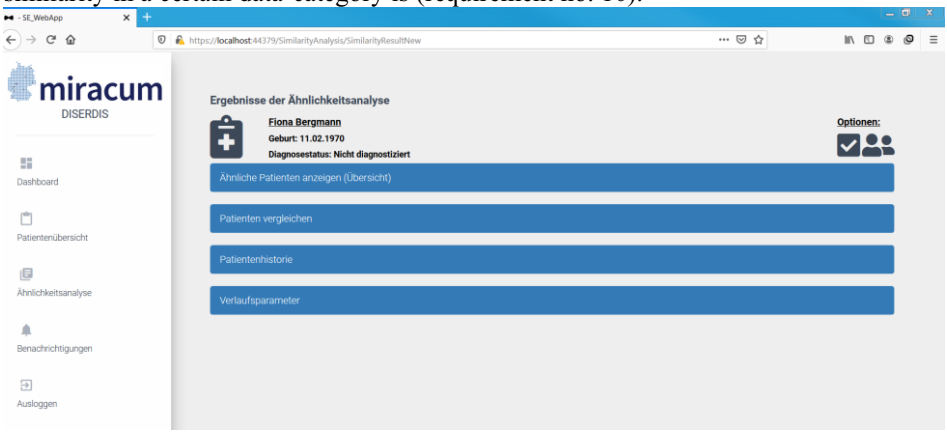

Figure 3: Panel overview

Furthermore, in the third panel, which is shown in Figure 4, the user can see an overview of the patient history of the selected similar patient regarding diagnosis and symptoms (requirement no. 9). Each time stamp can be clicked, and further information like the date of the symptom occurred, symptom name and symptom expression are shown.

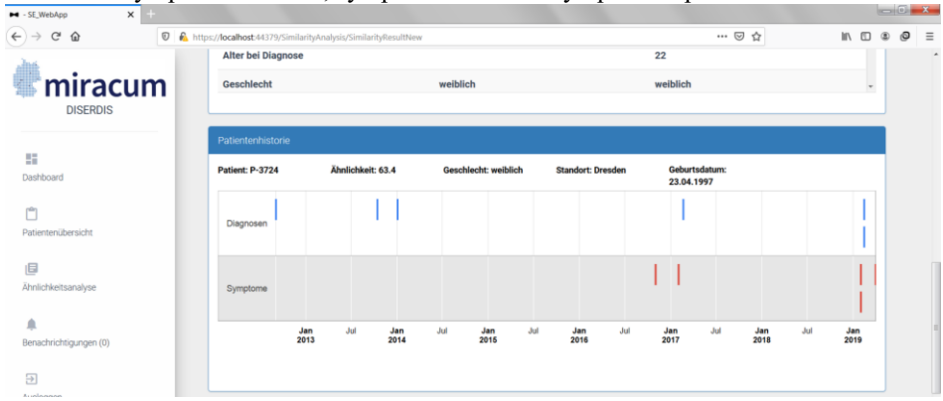

Figure 4: Overview of patient history

In the last panel, a progression of various medical parameters is assessable, if the available data allow an assessment of the course of the symptoms of a patient (requirement no. 11).

3.3 Evaluation

The CDSS achieved a SUS score of 73.21, which can be interpreted as a “good” usability according to Bangor et al. [21]. In addition, all study participants stated that they could imagine using the system in the future. However, the study participants also noted possible improvements, such as a more transparent presentation of the similarity comparisons, e.g. it should be clear which symptoms were classified as similar [22].

4. Discussion

In this paper, we present the development of a CDSS according to a UCD that focuses on user needs. In particular, we described the decision support component, its functionality and user-interface developed according to the user requirements. In context of the UCD, various methods were used. However, it is possible to use other methods, which differ in terms of the effort required, whether they produce qualitative or quantitative results, and in which phase of the UCD they are used [23].

In terms of the implementation of the software architecture and the available functionality, the CDSS is currently still limited. The similarity analysis can only be formed locally on its own dataset. Similarity analysis at the other MIRACUM sites is currently not possible because the MIRACUM search broker is still under development. However, the architecture has been designed in such a way that the distributed analyses can be carried out in the future. Within the software architecture, the decision was made to use FHIR for data exchange, as FHIR is used within the MI-I.

Nevertheless, regarding usability and user-acceptance, the evaluation showed that concerning to the SUS a good usability was achieved. Furthermore, most of the study participants stated that they could imagine using the system in the future. It can therefore be assumed that UCD is an important prerequisite of CDSS development to ensure usability and future acceptance of such systems. In order to prepare DISERDIS for real use in the clinic, further steps are necessary, e.g. a review regarding the medical device regulation, the integration of the search-broker to perform the similarity analysis on all MIRACUM sites, but also the validation and accuracy of the similarity analysis algorithm.

5. Conclusion

In this publication, we presented requirements for the development of a CDSS for RDs, which were implemented within a UCD and described the decision support functionality as well as the user-interface of the system. As a result, a prototype CDSS was developed that allows the similarity analysis of RDs patients to support the diagnosis of RDs. However, further work is necessary to refine the CDSS regarding usability, check the accuracy of the decision support function and to scale-out from local dataset using MIRACUM search broker.

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