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Web-Based Multi-Site Feasibility Questionnaire Tool

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Abstract. The design of clinical trial (CT) study protocols, currently supported by clinicians, is often a slow and cumbersome process. The Electronic Health Records for Clinical Research (EHR4CR) project supports the design of study protocols through a multi-site patient count cohort system. However, there is still a need to improve the process step in which the clinicians are involved. This research aims to enhance the EHR4CR platform with a tool to support the contact of CT sponsors with clinical investigators to obtain their input regarding feasibility data for the CT protocol design. From a list of requirements, a technical architecture that responds to the needs of feasibility assessments was modelled. With this architecture as a basis, a system that allows users to generate, send, fill out and visualise results of feasibility questionnaires across clinical sites was developed and integrated within the EHR4CR platform. The resulting system improves the current methods by providing direct contact to clinical investigators, facilitating the creation and answer of feasibility questionnaires for CTs.

Keywords. Clinical Trials as Topic, Feasibility studies, Questionnaires.

1. Introduction

Clinical trials (CTs) play an essential role in the design and development of new medication and therapeutic procedures. The initial deadlines for these CTs are often delayed and their budget increases due to several reasons such as recruitment rates not met and costly protocol amendments [1]. A good CT protocol design has been proven to be an effective solution to avoid such amendments [2].

A CT protocol ideally contains all required data to carry out CTs such as timelines, budget, targeted clinical sites, a list of eligibility criteria (EC) and the potential number of patients that fit to that EC and could participate in the CT per clinical site.

The first list of EC is usually created based on similar studies and historical records data with respect to the study requirements. Once these have been selected, the study draft along with a country feasibility questionnaire is then shared and distributed to a large number of clinical investigators to assess its feasibility and obtain a preliminary feedback about the number of patients who could participate in that particular study at each targeted country. The contacted investigators use different methods to assess the protocol feasibility and provide a first estimate of potential number of patients that are seen at their respective institutions and fit to the study EC, usually these estimations are based on the clinicians' experience. In a second round of interviews, clinical investigators are asked about the number of patients that they would commit to enrol in

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the determined CT through a site feasibility questionnaire. In the vast majority of cases, the method to answer this questionnaire includes a manual review of patients and historical records. Very few most advanced institutions offer the investigators the ability to request the local medical informatics team to query the hospital database to return these numbers. This process is highly fragmented, resource intensive and often takes several weeks to months to complete [3]. There is a rising awareness of the importance of electronic health records for the clinical research; however, none of the current systems in place covers the whole lifecycle of a clinical trial [4].

In the year 2010, the Innovative Medicines Initiative started a public-private initiative: the Electronic Health Records for Clinical Research (EHR4CR) project[1]. The EHR4CR project runs over four years and aims to support the CT steps of clinical protocol feasibility (PF), patient identification and recruitment, clinical trial execution and adverse event reporting [5]. Initially, the PF system included a patient count cohort system that could eventually semi-automatise the country selection phase of clinical trials by providing the number of potential eligible patients that could participate in a clinical trial due to their matching EC. Even with such a system in place, there would still be a need for consensus between the clinicians and the research institutions about the commitment of patients to be enrolled and other information such as clinician experience or current resources. These questions need to be answered directly by the research responsible at the clinical sites. The EHR4CR PF system requirements did not include this use case initially and the project team has been working on fulfilling this gap as follows: The nine European Federation of Pharmaceutical Industries and Associations (EFPIA) partners participating in the EHR4CR project were asked to provide examples of both country and site feasibility questionnaires, together with the original templates that they use to build new questionnaires (in case they use one). These questionnaires were analysed and the following information was extracted: the general structure, the different sections and the kind of questions they include (free text, checkboxes, etc.). The results from the analysis show that feasibility questionnaires are rather simple, containing between 22 and 100 questions per questionnaire with five different types of questions: free text, multiple choice (radio button and check boxes), numbers, free text tables and dates. This analysis (under publication review) set the baseline requirements for a multi-site feasibility questionnaire system.

Our research aims to develop and integrate within the EHR4CR PF system a tool that supports the current needs of feasibility questionnaire creation, distribution and collection of results. This tool should be based on the requirements extracted from the feasibility questionnaire analysis.

2. Methods

A team of two developers and two coordinators designed and built the technological platform, making sure it is compliant with the existing EHR4CR system and the requirements previously set.

The development of the system was divided into four phases: First a project plan was established containing timelines, distribution of the workload and risk planning, together with a first draft of the software architecture. The architecture was modelled using Unified Model Language 2.0 [6] diagrams. In total, three class diagrams and five

[1] www.ehr4cr.eu

sequence diagrams were created. The diagrams included all tiers of a classical Model-View-Control architecture and the functionality from both legacy and future systems, starting from a blank page due to the lack of legacy system documentation.

In the second phase, a notification system was integrated within the existing EHR4CR PF system functionality. The notification system should inform the clinical investigators via e-Mail about the existence of an un-answered feasibility questionnaire addressed to them in the EHR4CR system. This task helped the developers to familiarize with the legacy code and served as training for the upcoming tasks.

In the third phase, the prototype of the PF questionnaire system was developed and integrated in the existing system. Besides, the tool developed was both manually and automatically tested (using unit tests).

In the last phase, the code and the different functionality were tested by two users not previously involved in the development and the final documentation was written.

The current EHR4CR technological platform is based on a central web instance called central workbench (CWB) based on Java code and the Play framework[1]. The CWB allows the creation of feasibility and recruitment studies. Both of these features share the same communication services: encrypted SOAP messages sent through Java Messaging Services (JMS).

Messages coming from the central workbench are stored in an active Message Queue (MQ), which is polled regularly by endpoints at the clinical sites. The endpoints polling the MQ have their own graphic interface called local workbench (LWB) based as well on Java code.

3. Results

The feasibility questionnaire tool developed is based on the EHR4CR system and its communication protocols. The feasibility questionnaires are created in the CWB as follows: Initially the user logs into the CWB using his credentials and then he/she can access the Feasibility Questionnaire tab (PFQ). In the PFQ dashboard, users can see their feasibility questionnaires and the status of them. To create a new feasibility questionnaire, users need to provide the name and a description of the questionnaire. In a second screen, they can generate the different questions using an intuitive interface (see Figure 1). The current types of questions allowed are: multiple choice, single choice and free text. More types of questions are under development and will be available in the next version of the software.

Once the questionnaire is saved, users are able to select the candidate clinical sites and send the questionnaire to them (see Figure 2). When a user sends a questionnaire, this is sent to the clinical sites previously selected, the responses will be then gathered by the CWB that was used to create the questionnaire. The messages containing the questionnaires are encapsulated in SOAP messages and then sent via JMS to an active MQ. Each one of the sites polls its own MQ checking periodically for incoming feasibility questionnaires.

[1] https://www.playframework.com/

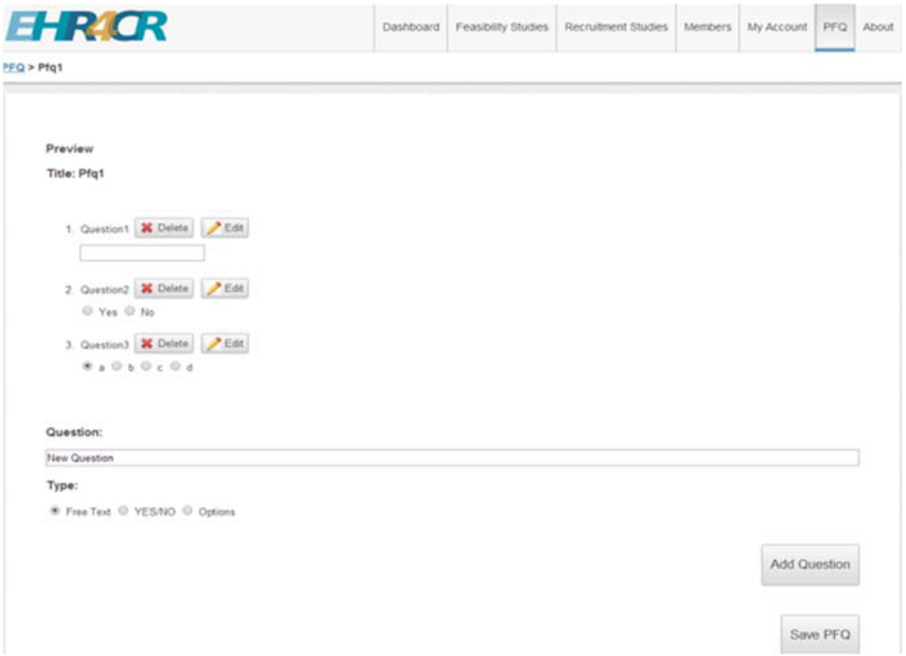

Figure 1. Creation of a feasibility questionnaire: selection of type and order of questions, and the option to edit or delete the questions and the questionnaire.

Once a questionnaire is received at a site, the user(s) with permission to respond to feasibility questionnaires receive an email (if configured) and/or see a notification in their LWB. The notification system is based on javaMail and can be configured within the LWB.

The LWB is based on a similar dashboard as the CWB where users can see their feasibility questionnaires and the status of them. When a user selects an unanswered questionnaire, an initial screen will be shown containing the name and description of the study. In a second screen, the different questions can be answered (see Figure 3).

When the clinical investigator has completed and submitted a questionnaire, the results can be visualised in both central and local workbenches.

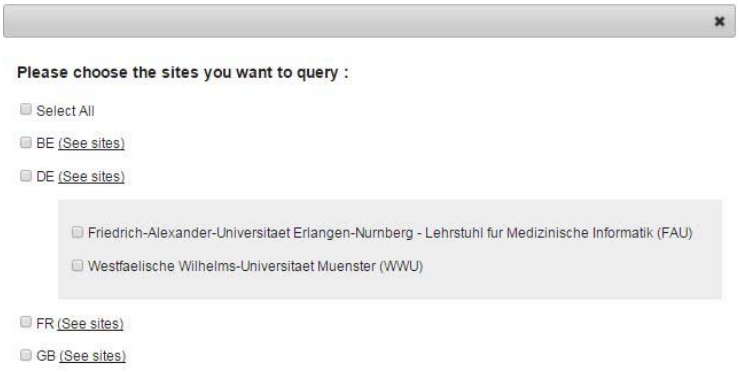

Figure 2. Selection of clinical sites per country. User can select one, several or all sites and/or countries.

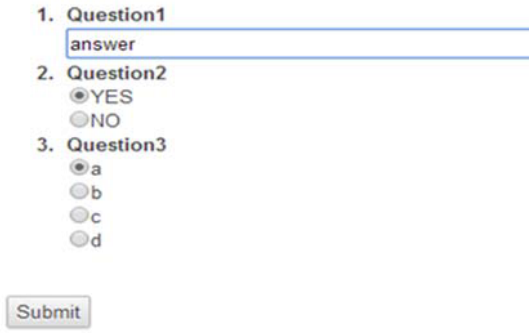

Figure 3. Visualization of the PFQ answering tool. Users can answer and submit their active feasibility questionnaires. Responses will be saved and can always be visualised.

4. Discussion

The results show that it was possible to implement an electronic questionnaire administration, distribution and response system that is integrated into the EHR4CR platform and re-uses both its code base and look and feel. Simple questionnaires, directly addressed to the clinicians at potential trial sites, can be created, distributed to chosen sites and answered using the developed tool and the EHR4CR communication services. These features allow sponsors to manage their documents and responses about patient counts and local resources within the same overall task of gathering information about potential trial sites, involving the utilisation of a single system. Such a solution might accelerate the management and provision of information and lessen the burden of utilizing several tools within the same process.

The current implementation only allows questions of certain types. Additionally, the questionnaires collected and analysed might not cover the whole possible range in feasibility surveys. Hence, a user who would want to use the system as is, might experience the limits of the current implementation. However, the types of questions chosen to be implemented are based on input provided by the intended users of this system, which increases the likelihood of being representative. Besides, the software architecture enables a relatively easy extension of question types.

Other electronic survey tools, such as LimeSurvey [7] or SurveyMonkey [8], already support more question types. Besides, there are systems as the Efficient Patient Recruitment for Innovative Clinical Trials of Existing Drugs to other Indications Authoring Tool [9], that provide an electronic web-based system to support the collection of feasibility data. Hence, a decision between using such existing tools and implementing a new survey tool can be made. The usage of such tools would lead back to the problem of utilizing several systems for related needs, since these tools are not integrated into an already existing clinical trial support platform (such as the EHR4CR) and hence not able to run EC queries and automatically obtain potentially eligible patient counts.

Since this study aimed to develop a prototype, features such as additional question types, sharing question and questionnaire templates across trials, fast inclusion of most used questions and re-using questionnaires as templates for new ones might be added in the future. A thorough usability evaluation of the system is yet needed.

5. Conclusions

Based on the analysis from several feasibility questionnaires, a protocol feasibility questionnaire tool has been developed and tested and it is now integrated within the EHR4CR PF system. With this, the EHR4CR PF system can cover the phases of country and site feasibility, saving time, effort and resources for the design of study protocols.

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