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# Design for a Modular Clinical Trial Recruitment Support System Based on FHIR and OMOP

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**Abstract.** The MIRACUM consortium is developing a Clinical Trials Recruitment Support System to support the data-driven recruitment of patients for clinical trials. The design of the prototype includes both open source solutions (OMOP CDM, Atlas) and open standards for interoperability (FHIR). The aim of the prototype is to create a patient screening list of potential participants for a clinical study. The paper shows the modular structure and functionality of the prototype building the foundation for the practical implementation of the CTRSS and, at the same time, demonstrating the use of open source solutions and standards for the development of clinical support systems.

**Keywords.** clinical trial recruitment support system, FHIR, OMOP, OHDSI, secondary use of electronic health records, automation, open standards, decision support systems

## 1. Introduction

Clinical trials are fundamental in clinical research and in evidence based medicine since they are needed to evaluate new treatment methods, the effectivity of drugs, or new diagnostic tools [1]. However, many studies fail during the recruitment phase for the following two reasons: either the minimum necessary number of patients is not reached or the recruitment process takes too much time and effort to find enough eligible patients to participate [2] [3]. One option to overcome those issues is the specific reuse of already observed data during inpatient treatment. Since the availability of digital health care data is growing rapidly it offers high potential for reuse in clinical research [4]. The idea of automated screening electronic health care data is not new. During the last ten years the number of publications on clinical trial recruitment support systems (CTRSS)

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is continuously increasing. This trend demonstrates the importance and need of such systems to allow faster and more efficient patient screening [5]. Köpcke et al. [5] pointed out the lack of standards and missing interoperability of CTRSS as well as a missing formalisation of eligibility criteria for the definition of a potential trial cohort. Thus a major goal of the MIRACUM consortium [6] is to provide a modular CTRSS based on open standards. This approach shall ensure interoperability and flexibility to connect to other systems such as study registries and hospital information systems. As one of four consortia MIRACUM is part of the German Medical Informatics Initiative (MII). The MII brings together 30 university hospitals and a number of industry partners to establish data integration centres. The aim is to provide clinical health care data from various source systems in one place to ensure to "prove their benefit for researchers, doctors and patients" [7]. To demonstrate the benefits of integrated data one use case the MIRACUM consortium is responsible for is "Alerting in care - IT support for patient recruitment". This paper illustrates how to build a CTRSS concept that consists of separate modules, can be transferred to other locations, make use of existing open source tools and benefit from open standards.

## 2. Methods

To address the topics modularity, transferability, open source tools and open standards, a heterogeneous group of computer scientists, medical information scientists, data scientists and physicians joined forces to developed the CTRSS prototype. The team evaluated how the communication between loose coupled modules of the prototype can be done based on Representational State Transfer (REST) over HTTP protocol and what is needed to represent data using the Fast Healthcare Interoperability Resources (FHIR) developed by Health Level Seven Organization (HL7) standard for data exchange. A common data model was needed to store data that gets searched for potential trial participants by the CTRSS prototype. The *Observational Health Data Sciences and Informatics* (OHDSI) organization consists of a rapidly growing worldwide community of universities to foster worldwide medical scientific community and to improve scientific research [8]. Thus they developed a common data model (CDM) *Observational Medical Outcomes Partnership* (OMOP) including a set of standardized vocabularies(e.g. SNOMED, LOINC, rxNorm, ICD10) and their translations between each other to allow researches to speak a common language when exchanging data. To validate OMOP CDM is a proper patient data storage needed by a CTRSS we installed it on a PostgreSQL database and added standardised vocabularies using the OHDSI Athena web application. Athena is a service that provides regular updates of the vocabularies to ensure utilization of the most recent vocabulary versions. In Germany a modified version of the ICD10 world health organization (WHO) vocabulary is in place to serve local billing purposes. Thus the ICD10GM vocabulary has been added as an additional vocabulary to the OMOP database based on the work done by Maier et al. [9]. In a next step the patient data based on the MII core data set were imported into OMOP. All data included in the MII core data have been mapped into the OMOP CDM successfully. Afterwards the Atlas web application was used to define cohorts based on the eligibility criteria of a clinical trial using a web interface for several clinical trials. The exchange of cohort definitions between different locations was done with the import and export capability of the Atlas

web application. All information of defined cohorts was stored in the OMOP database. Furthermore OHDSI provides a Web Application Programming Interface (API) based on REST for the OMOP CDM. The REST Web API was used to realize the access to already defined cohorts. This included the execution of cohort definitions against the OMOP database, status checks of a cohort execution and the call of a result list of patient ids for a certain cohort definition. To implement the notification of research teams about any changes on the patient screening lists, we evaluated the functionality offered by the FHIR HL7 standard. FHIR provides subscription resources that allows us to register a certain resource to act on any event such as change, create or delete. The subscription resource was configured to use a certain communication channel such as e-mail, REST post request and others.

## 3. Results

The CTRSS prototype consists of separate modules based on an architecture proposed by Trinczek et. al. [10]. Each module targets a small set of similar features and is implemented as a REST based micro-service with well-defined service boundaries. All module interfaces have a properly documented API. As shown in Figure 1 the prototype CTRSS is composed of the following five modules:

- patient data module
- Atlas web application
- query module
- notification module
- screening list module

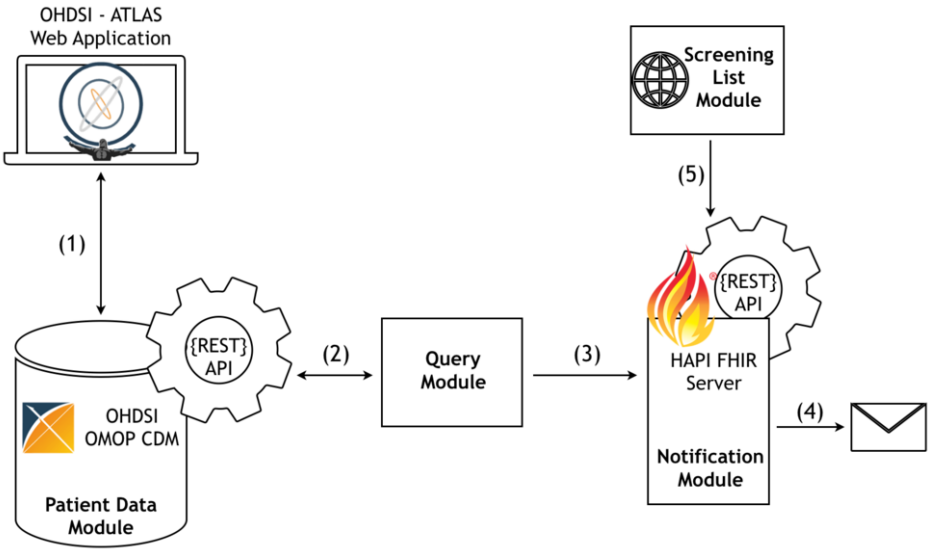


**Figure 1.** Architecture of the CTRSS

The process of creating a patient screening list consists of the following five main steps:

1. cohort definition using the ATLAS web application
2. generation of a cohort and retrieval of its contents from the OMOP database done by the query module
3. generation or update of the screening list with retrieved patients as a FHIR list-resource done by the query module
4. notification based on any event on a FHIR list-resource done by the notification module
5. screening list module receives new or changed screening lists

The patient data module is based on the OMOP CDM (version 5) and it stores all observational data of a patient. In the first step the Atlas web application is being used for cohort definition. On successful cohort definition an unique identifier of the defined cohort is returned. All cohort definitions built with Atlas can be exported to other locations. The query module is a custom implementation using REST calls to send and retrieve data. In step two the query module generates the patient list using the cohort identifier that is handed over after cohort definition with Atlas. Based on a defined scheduling or on notification when patient data changes, the query module runs a REST POST query against the OMOP Web API to generate the list of potential trial participants in the database. The query module uses another REST call to check the current status of a cohort generation. After successful cohort creation the query module retrieves the patient list. In step three the list of patients for a particular trial is sent using a FHIR list-resource that contains all patient ids. There has been a subscription resource created for the list-resource that sends e-mail messages to recipients when a list of patient ids gets created or changed on the FHIR server. The patient screening list module is a custom web application that reads the list-resources data from the FHIR server. It displays all potential patients for a trial of interest based on the cohort id. The screening list module is implemented as a web application based on HTML 5 and the java script framework Vue.js.

## 4. Discussion

The CTRSS prototype is based on separate modules that consist of a strong encapsulation to hide the details of the implementation that ensure a loose coupling between each other and thus addresses the lack of missing interoperability [11]. Our approach provides great advantages in terms of technology heterogeneity, resilience, scalability, deployment efficiency, composability, and optimization for replacement as stated by Sam Newman [12]. Hence compared to monolithic software, the modular CTRSS prototype introduced by us allows to accelerate development cycles, reduce deployment efforts, and provide improved scalability. Development teams can exchange single modules without affecting others as long as the interfaces are the same and thus flexibility of the whole system increases. Additionally the scaling of each module can be done based on performance requirements individually instead of scaling the whole prototype. As stated by Köpcke et. al. [5] ”many CTRSS are designed to fit the existing infrastructure of a clinical care provider or the particularities of a trial” and therefore most existing CTRSS are limited to local environments and conditions that cannot be transferred to other locations nor adapted to trials with different characteristics. Our CTRSS prototype was built to over-

come those limitations as it is a transferable solution that can be used across different locations. Additionally the usage of FHIR for the exchange of electronic healthcare data using web technologies enables the prototype to be extended and connected to many other health care systems. In the future the prototype can be extended to send back notification on new potential trial participants to existing health information systems (HIS). With the OMOP CDM the used patient data is transformed into a standardized format that allows scientists to search for potential participants at multiple locations national wide and with the option for extension to an international level in future projects. The usage of OHDSI Atlas allows scientists to share defined cohorts with others. This extends the range of coverage when searching for potential participants and thus increases the chance to meet set expectations in terms of number of participants. Our prototype is currently limited in terms of usage and result reporting. Therefore no results on the success of patient recruitment can be provided. The exchange of data between different locations has to be done in a next step. The test and deployment of the prototype within the MIRACUM consortium including reporting of the results and outcomes needs to be addressed in follow-up publication as suggested by Köpcke et. al. [5].

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## References

[1] Backmann M. What's in a gold standard? In defence of randomised controlled trials. Medicine, Health Care and Philosophy. 2017 apr;20(4):513–523.
[2] Ohmann C, Kuchinke W. Meeting the Challenges of Patient Recruitment. International Journal of Pharmaceutical Medicine. 2007;21(4):263–270.
[3] Sully BGO, Julious SA, Nicholl J. A reinvestigation of recruitment to randomised, controlled, multicenter trials: a review of trials funded by two UK funding agencies. Trials. 2013;14(1):166.
[4] Meystre SM, Lovis C, Bürkle T, Tognola G, Budrionis A, Lehmann CU. Clinical Data Reuse or Secondary Use: Current Status and Potential Future Progress. Yearbook of Medical Informatics. 2017;26(01):38–52.
[5] Köpcke F, Prokosch HU. Employing Computers for the Recruitment into Clinical Trials: A Comprehensive Systematic Review. Journal of Medical Internet Research. 2014 jul;16(7):e161.
[6] Prokosch HU, Acker T, Bernarding J, Binder H, Boeker M, Boerries M, et al. MIRACUM: Medical Informatics in Research and Care in University Medicine. Methods of Information in Medicine. 2018 jul;57(S 01):e82–e91.
[7] Gehring S, Eulenfeld R. German Medical Informatics Initiative: Unlocking Data for Research and Health Care. Methods of Information in Medicine. 2018 jul;57(S 01):e46–e49.
[8] Sciences OHD, Informatics. OHDSI The Book of. Independently published; 2019.
[9] Maier C, Lang L, Storf H, Vormstein P, Bieber R, Bernarding J, et al. Towards Implementation of OMOP in a German University Hospital Consortium. Applied Clinical Informatics. 2018 jan;09(01):054–061.
[10] Trinczek B, Köpcke F, Leusch T, Majeed RW, Schreiweis B, Wenk J, et al. Design and multicentric Implementation of a generic Software Architecture for Patient Recruitment Systems re-using existing HIS tools and Routine Patient Data. Applied Clinical Informatics. 2014;05(01):264–283.
[11] Krafzig D. Enterprise SOA: Service-Oriented Architecture Best Practices. Prentice Hall; 2004.
[12] Newman S. Building Microservices: Designing Fine-Grained Systems. O'Reilly Media; 2015.