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FoPraNet-BW: An Infrastructure for Clinical Studies in Practice-Based Research Networks in the German Health System

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Abstract. General practice-based research networks have become an integral tool to gain medical knowledge from primary care in many countries. For this purpose, a scalable IT-infrastructure is presented considering the limiting peculiarities in the German health system and enabling GPs to participate in clinical studies based on their patient population. The infrastructure consists of a central study management server and local clients for each practice. It adopts to the currently limited digital connectivity of GP practices, data protection regulations for clinical data and the needs of the medical staff to manage a clinical study. The infrastructure is in production at the four university hospitals in the state of Baden-Württemberg. Until now three clinical studies with over 70 GPs and 350 Participants are successfully conducted or have been finished. Further clinical studies are in the planning stages.

Keywords. Clinical studies, health services research, primary care, digitalization

1. Introduction

General practice-based research networks (GPBRNs) are communities in which general practitioners (GPs) and researchers collaborate with the common goal of quality improvement and enabling research close to health care delivery [1]. This has been demonstrated by integrated concepts such as the PraksisNett project in Norway [2]. Conducting clinical studies in GPBRNs in the German health system must adopt to the technical, and organizational peculiarities and limitations such as self-governance, heterogeneous software tools and structural independence of GPs [3]. Integrating data from a distributed network of GP practices requires an efficient infrastructure with appropriate procedures. To answer questions relevant for public health, several projects have been launched to collect routine data from the primary care sector by accessing the

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electronic health records (EHR) from the multitude of over 130 different patient data management systems available on the German market [4]. This is an ongoing challenge with respect to quality assurance, lack of standardization and data protection regulations. In this work a novel infrastructure is presented which aims at achieving three main goals: 1) To enable a clinical trial and three observatory studies in FoPraNet-BW based on primary data from the involved GP practices; 2) To support GP-based research teams in achieving valid data processing along their clinical work and 3) To support involved stakeholders in building a sustainable GPBRN[2].

2. Methodological Approach

To our knowledge there is no generic IT infrastructure available to conduct primary data collection from GPBRNs in the German health system, beyond existing routine data. However, this is needed to meet the necessary standards of data quality for clinical studies. The infrastructure must consider the current reality of GP settings to be implementable for application and evaluation. The proposed solution has been developed in an ongoing agile development process with both researchers and GP teams involved in the GPBRN complemented by literature research, market exploration, stakeholder interviews and focus groups. Here, only a general overview of the resulting most relevant prerequisites and requirements can be given.

2.1. Relevant preconditions of GP practices in Germany

In Germany, GPs are resident doctors who are generally self-employed entrepreneurs with individual and autonomous practice management. Thus, easy to use and flexible tools which fit into a variety of environments must be created, interfering as little as possible with every day work. Doctors can select from a set of 130+ different Patient Data Management System (PDMS) which offer vendor specific data access and export interfaces. Since there are no mandatory specifications for a digital infrastructure, each practice has its own digital solution ranging from a single isolated computer with on-demand internet access to a complex and layered local area networks with servers and specific workstations. Yet, the extent of mandatory standardized sharing of medical data besides billing and order entry has been low. Even routine documentation from the EHR cannot be exported from the PDMS in a standardized way [4].

2.2. Organizing clinical studies in a GPBRN

A study in a GPBRN can be considered as multi-centric with the GP practices as study centers. To keep the number of participants for each practice manageable the number of GP practices has to be high enough to meet the studies predefined sample size which increases the number of study centers to be managed. The standard operating procedures (SOPs) must be adopted to the GPs situation (Sec 2.1.). For instance, the inclusion criteria have to be applicable to a PDMS query and a randomization method must adapt to unpredictable recruiting numbers in individual GP practices. And most important the

[2] https://www.forschungspraxennetz-bw.de/ (Website in German)

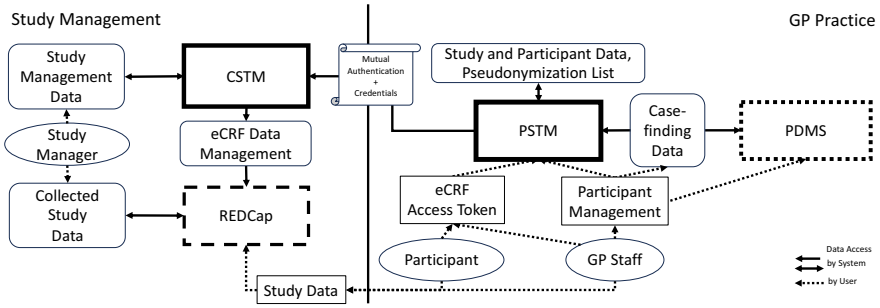

Figure 1. Overview of the principal components and main dataflows of the infrastructure.

overall progress of including participants and capturing data must be efficiently monitorable. For this purpose, electronic case report forms (eCRF) and their allocation to participants must be managed. The digital representation of SOPs must support compliance to good clinical practice for valid clinical studies. A distribution mechanism to the GP practices is needed.

2.3. Conducting clinical studies in a GP practice

A specific digital representation of an investigator site file is needed for each study in the GP practice. It provides all data entry forms and the necessary standardized documentation and information related to a clinical study. First, eligible participants must be identified by querying the PDMS based on the case finding criteria defined in the site file. This initial list is used to contact patients, and obtain their consent to participate. If a patient agrees, information and consent have to be documented. Once enrolled in the studies participants' progress must be tracked. During predefined study visits, patient data is documented. Patient-reported data must be collected as well, management of drop outs and adverse events is required. This is common for all types of clinical studies.

3. Realizing the Infrastructure

3.1. Components and interoperation

The infrastructure consists of three main components (Fig. 1): A REDCap server for eCRF management and data collection, and the central study manager (CSTM) with associated practice study manager (PSTM) instances. All information on the study structure and its processes can be configured on the CSTM (Sec 2.2.). The PSTM retrieves local data and enables case finding and study execution in practices (Sec 2.3.). To cope with different export formats from the PDMS (Sec 2.1.) a generic mapping tool is provided for standardized imports. Information on participants is only posted to the CSTM if necessary. The connection between PSTM and CSTM is based on RESTful-APIs via the Internet and secured via multi factor authentication by X.509 certificates and credentials. Consequently, practices do not require direct access to REDCap besides

access tokens to individual study specific eCRFs and therefore no separate REDCap account or training is needed. CSTM and PSTM are accessible via web browser.

Table 1. Overview of current studies. Data from 27.03.2024

Studies	Type	Start	End	Partici -pants	Persons in Case Finding	eCRFs submitted
Induct	RCT	07/23	11/24	141	683	3338
BEBOP PMR	observational	11/23	02/24	170	546	2371
BEBOP Depression	observational	02/24	04/24	146	5057	508

3.2. Pseudonymization of participants

Due to data protection regulations concerning health and personalized data, pseudonymization is required to protect the participants' identity. Pseudonyms are generated by the CSTM, and assigned to a participant within the PSTM after consent has been given. This ensures that only the GP's office retains knowledge of the participants' identities in the local pseudonymization list. However, errors or implausibilities of the study data can be addressed by utilizing the pseudonym.

3.3. eCRF Data Management

Data capturing is realized in GP practices by presenting the correct eCRF according to the individual study progress of each participant to the GP-based research team. To achieve this, the CSTM keeps track of the processing status of each eCRF assigned to each pseudonym. This ensures that participants or practices get access and notifications only to required forms according to the SOPs, streamlining data capture and maintaining accuracy throughout the study duration. Individual access tokens and processing periods for each participant can be exported by the GP staff via the PSTM as a PDF-Document and thus transferred directly to the patient. Study managers can centrally monitor progress across all GP practices.

4. Results

The entire setup has been approved by data protection officers and a legal expertise. CSTM and PSTM are implemented as python/Django Webserver using PostgreSQL Databases. The CSTM and REDCap Server are operated at the Reutlingen University computing center. The PSTM has been installed in the 70 participating GP practices via remote access. GP practices in the GPBRN have been recruited, accredited and qualified by the four general medicine university locations in the state of Baden-Württemberg, Tübingen (TÜ), Freiburg (FR), Heidelberg (HD), Ulm (UL). By now three studies have been implemented on the infrastructure (Tab. 1.). Induct is a two-arm randomized controlled trial (RCT) to examine intermittent fasting. BEBOP Depression and BEBOP PMR are observational studies. BEBOP Heart Failure is currently configured. The workload for each GP practice research team is an average of less than three participants per study. The high number of 3338 eCRFs for 141 participants in Induct corresponds to the complex assessments and patient diaries. 5057 patients during case finding in one month and only 146 participants in BEBOP Depression indicate a low consent rate which

has to be evaluated. The teams reported that after an initial learning curve, the solution with progress tracking and context-specific eCRF being presented is helpful while patient export solutions from the PMDS in case finding must be improved. Based on feedback from the users, the infrastructure is considered useful.

5. Discussion

The results illustrate the feasibility of conducting multicentric clinical studies within a GP practice setting. The PMR study has surpassed its initially projected patient enrollment target, highlighting the potential of a distributed approach to eligibility-based patient identification in the GPs office. This is demonstrated by the significant number of individuals listed in the case finding for the depression study shortly after it started, but with a low enrolment rate. The real-time supervision of study data enables the study managers to respond quickly to unforeseen developments. The generic concept allows for efficient configuration of new studies and with growing experience GP practices increase their processing rate. Together with ongoing support by the collaborating universities, user feedback and ongoing evaluation of the GPBRN, factors that facilitate the sustainability of the GPBRN are derived. The infrastructure will be continually developed in the agile process, contributing to a sustainable digital infrastructure.

Declarations

All Studies conducted or planned on the infrastructure are registered at the German Clinical Trials Register, DRKS00031928 (Induct), DRKS00032715 (BEBOP PMR), DRKS00033568 (BEBOP Depression), DRKS00033582 (BEBOP-HI, Heart Failure). Conflict of Interest: The authors declare that there is no conflict of interest. Acknowledgments: This work was funded by the Federal Ministry of Education (Grant No. 01GK1904A-D). In addition to the authors, the FoPraNet-BW project-group consists of Lorena Braun(TÜ), Christina Buchta(TÜ), Hannah Marie Haumann(TÜ), Stefanie Joos(TÜ), Andy Maun(FR), Attila Altiner(HD), Annika Baldauf(HD), Anna Molle(HD), Sandra Schramm(HD), Anne Barzel(UL), Sybille Beck(UL) and Gudrun Hübner(UL).

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