

# Web Application To Store and Analyze Data From Clinical Trials

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## 1 Introduction

Intro about the whole project

## 2 Literature Review

Intro for Literature Review

### 2.1 Paper 1: Square<sup>2</sup> - A Web Application for Data Monitoring in Epidemiological and Clinical Studies

**Journal/Conference Rank:** Q1

**Publication Year:** 2017

**Reference:** [?]

#### 2.1.1 Summary

The paper describes a web application, Square<sup>2</sup>, which is used to monitor and evaluate data quality in complex epidemiological and clinical studies. The application is designed to handle the challenges of studies with multiple variables and examiners. It utilizes Java EE, Apache MyFaces, and PostgreSQL to manage the workflow of data monitoring, including setting up studies, handling metadata, uploading data, conducting statistical analyses, and generating quality reports. The application also incorporates a user rights and roles concept to ensure data privacy. The document discusses the development and

design of Square<sup>2</sup>, as well as its limitations and ongoing improvements. It mentions that free access to the application may be available for academic users through scientific cooperation projects. Overall, Square<sup>2</sup> improves the efficiency and accuracy of data quality monitoring in complex studies, allowing for standardized and timely generation of quality reports.

### 2.1.2 Software Architecture

The software architecture used in the paper is based on a Java EE web application called Square<sup>2</sup>. The application is deployed in Tomcat 8 and uses Java libraries such as Apache MyFaces 2 and BootsFaces for layout and style. It also utilizes the PostgreSQL database for storing all the study data and metadata [2]. The statistics backend for Square<sup>2</sup> is R, which is used for conducting statistical analyses [3a]. LaTeX is used for generating print-ready PDF reports [2]. The entire workflow of the application is managed by a GUI [2]. The application includes several in-house developed libraries such as ShipDBM for data persistence and Pwencrypt for password encryption [3b]. Overall, the architecture combines different technologies to handle data monitoring and quality evaluation in complex studies effectively. It ensures standardization, flexibility, and data protection through the incorporation of various components and frameworks.

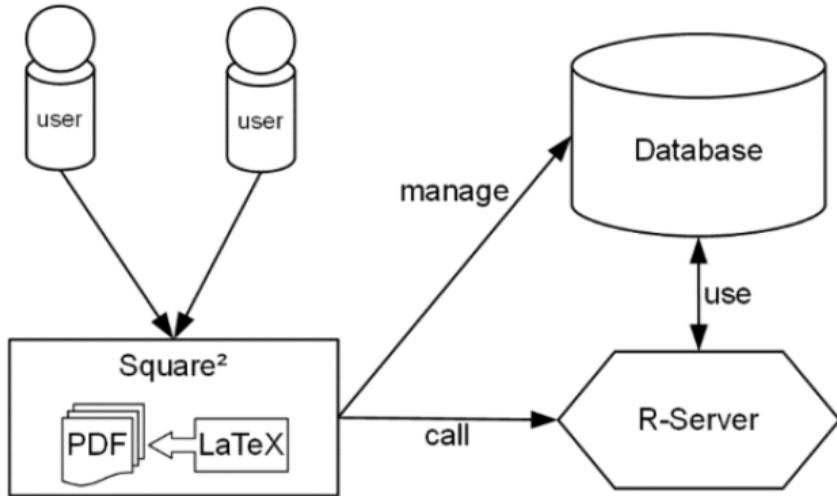


Figure 1: Software architecture diagram for Paper 1.

### 2.1.3 Data Parameters

In the paper, the following data parameters are described:

**Study structure:** This parameter defines the hierarchical elements of a study, including groups of examinations, examinations, and variables. It also includes metadata associated with the study and variables, such as variable type, plausibility limits, reference categories, missing value indicators, observer, device or center indicators, and measurement times and dates.  
**Variable sets:** Sets of variables are defined for data monitoring purposes. These sets can consist of variables from different studies, and quality officers can only create reports for variables from variable sets to which they have been

assigned. Data management: This parameter controls the upload of study data for statistical analyses. These data parameters are used within the web application, Square<sup>2</sup>, to facilitate data monitoring and evaluation in epidemiological and clinical studies.

#### **2.1.4 Datasets Used**

The paper describes the usage of a web application called Square<sup>2</sup> to monitor and evaluate data quality in epidemiological and clinical studies [1a]. The datasets used in the paper are the study data and metadata from institutions with complex and multiple studies. These datasets include information such as study variables, examiners, devices, and examination centers.

The significance of these datasets is that they enable the evaluation of data quality in complex studies, where there is a wide scope of examinations and numerous variables. This is important for ensuring the validity and accuracy of scientific inferences from epidemiological and clinical studies. The datasets help in detecting data irregularities and guiding quality management processes [1c]. They are used to evaluate the quality of collected data before conducting statistical analyses [1b]. These datasets are crucial for identifying missing values, implausible values, extreme values, and measures of reliability and validity [1c]. The Square<sup>2</sup> web application uses these datasets to manage the entire workflow of data monitoring, including setting up studies, handling metadata, uploading data, conducting statistical analyses, and generating quality reports.

#### **2.1.5 Paper Link**

Access the full paper at <https://pubmed.ncbi.nlm.nih.gov/28423853/>

### **2.2 Paper 2:Integrating Clinical Trial Data for Decision Making via Web Services**

**Journal/Conference Rank:** A\*

**Publication Year:** 2004

**Reference:** [?]

#### **2.2.1 Summary**

This document discusses the challenges faced in making decisions based on the large amount of data generated during clinical trials. It emphasizes the importance of ensuring the quality and integrity of the study data in order to assess the efficacy and safety of new medications. The cost of drug development is also highlighted, with clinical studies accounting for a significant portion of these expenses. The document proposes a solution called the Clinical Trial Console, which utilizes web services to integrate data from different clinical trial applications and provide consolidated views for decision making. The solution is designed to support various perspectives and queries on the study data, allowing different study personnel to access and view the data according to their roles. Security measures are also included to protect sensitive study data, including encryption and authentication mechanisms. The use of web services allows for seamless integration and accessibility from different geographic locations. The document mentions the potential adoption of industry standards, such as those proposed by the Clinical Data Interchange

Standards Consortium, in future research. Overall, the document focuses on the importance of integrating clinical trial data and the use of web services for decision-making in clinical studies.

### 2.2.2 Software Architecture

The software architecture used in the paper is called the Clinical Trial Console. It is a web application that utilizes web services to integrate data from different clinical trial applications and provide consolidated views for decision-making [3a]. The solution architecture consists of individual clinical trial applications that are implemented independently and usually located at different sites. A web service component is added to each application to expose the query functions. The Clinical Trial Console communicates with the applications via SOAP (Simple Object Access Protocol) messages over a secure connection. The Clinical Trial Console is implemented using Microsoft .NET framework, ASP.NET, ADO.NET, and C hash, while the web service component in each application is implemented using the respective technology corresponding to the application platform (Java web service technologies for Java platform and Microsoft technologies for Microsoft platform). The communication between the Clinical Trial Console and the clinical trial applications is done through SOAP messages, and the query results retrieved from the applications are returned in XML format wrapped in SOAP messages.

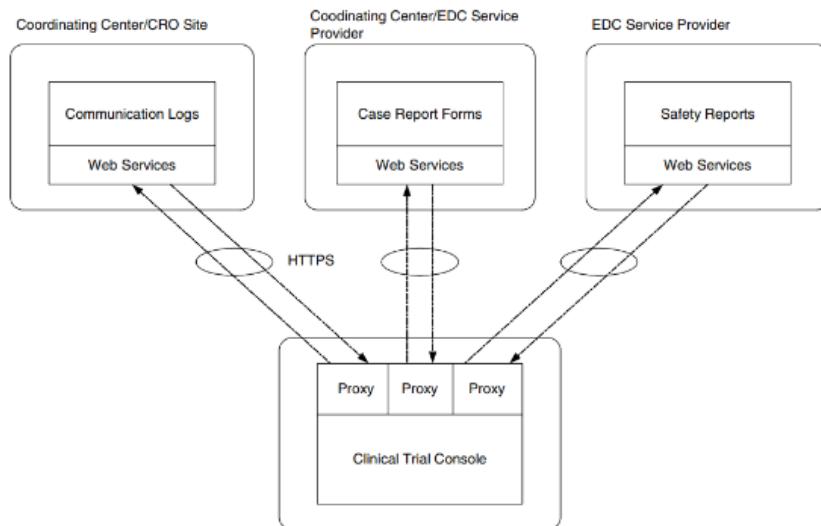


Fig.1 Solution Architecture. Each individual clinical trial application is implemented independent of each other and is usually located at different sites. A Web services component is added to each app to expose the query functions. The Clinical Trial Console retrieves data from different clinical trial applications and consolidates the multiple data sets into a single, comprehensible format

Figure 2: Software architecture diagram for Paper 2.

### 2.2.3 Data Parameters

The paper does not explicitly mention a list of data parameters used in the study. However, it discusses the challenges faced in processing and integrating data collected during clinical trials. The data mentioned in the document include patient clinical data in the

form of case report forms (CRFs) containing measurements of physiological conditions, critical adverse events, patient diaries documenting subjects' experiences, and logs of communication among study personnel [1a]. These data sources present challenges in making timely decisions due to their multiplicity and incompatible formats.

The document proposes a solution called the Clinical Trial Console, which utilizes web services to integrate data from various clinical trial applications and provide consolidated views for decision making [1b]. These consolidated views are tailored to different perspectives and queries on the study data. For example, a view of a specific subject may include clinical data, patient diary, a history of discussions among study personnel, and safety events related to the subject. The solution is designed to support different roles, such as sponsors, investigators, study coordinators, and clinical research associates, to access and view the data according to their needs.

In terms of security measures, the document mentions that the Clinical Trial Console solution should ensure the integrity and protection of sensitive study data. This includes implementing security mechanisms such as encryption and authentication to restrict access to trusted entities.

It is important to note that while the document discusses the challenges and proposed solution for integrating clinical trial data, it does not provide a comprehensive list of specific data parameters used in the paper.

#### **2.2.4 Datasets Used**

The paper discusses the datasets used in the context of clinical trials. Clinical trials involve processing large volumes of data collected from various sources and at different stages of the studies. These datasets include: Patient clinical data: This data is in the form of case report forms (CRFs) that contain measurements of study subjects' physiological conditions. This data is crucial for assessing the efficacy and safety of new medications. Critical adverse events: This data captures any adverse events experienced by the study subjects during the trial. It is important for evaluating the safety of the medications being tested. Patient diaries: These document the subjects' experiences related to a medical movement. The data collected in these diaries provides valuable insights into the subjects' perspectives on the medication's effectiveness. Logs of communication: This data captures the communication flow among study personnel, such as sponsors, investigators, study coordinators, and clinical research associates. It helps in monitoring and documenting discussions and decisions made during the trial. The significance of these datasets lies in their role in ensuring the quality, integrity, and validity of the study outcomes. Different study personnel rely on these datasets to make decisions related to the trial, such as assessing the current status of the study, evaluating specific subjects' data, and reviewing site-specific information [1b]. Proper management and integration of these datasets are crucial for prompt decision-making and cost-effective drug development.

#### **2.2.5 Paper Link**

Access the full paper at <https://pubmed.ncbi.nlm.nih.gov/17270999/>

## **2.3 Paper 3: The Internet and Clinical Trials: Background, Online Resources, Examples and Issues**

**Journal/Conference Rank:** A

**Publication Year:** 2005

**Reference:** [?]

### **2.3.1 Summary**

The paper discusses a multicenter trial of a disease management program for depression in primary care. The authors developed a web-based data management system to support the trial, which allowed study staff at participating clinics to track recruitment activities, laboratory values, and completion of assessments. The system also facilitated data entry for clinicians on patients' treatment plans and provided reminders for follow-up assessments and access to clinical notes. While the system had limitations, such as not being integrated into existing clinical records and some staff members being computer-phobic, it provided real-time access to study-related information and minimized data loss. The authors suggest future applications of web-based systems, such as offering personalized patient education and depression assessments to patients and their primary care providers.

### **2.3.2 Software Architecture**

The software architecture used in the paper is a web-based data management system. The system was developed using an Apple Power Mac G3 computer running Mac OS X as a server. It was programmed with WebObjects by Apple and the FrontBase SQL database. The system allows study staff at 18 participating clinics to access the data management system over the internet. The system supports various data management tasks such as tracking recruitment activities, laboratory values, completion of assessments, and data entry on patients' treatment plans. It also provides reminders for follow-up assessments, error-checking routines, and access to clinical notes. The system is secure, with all exchanges between the user's browser and the server being two-way encrypted to prevent tampering or data forgery. Access to the data on the server is password-protected, with different user profiles allowing access to relevant sections of the database. However, the system has limitations, such as not being integrated into existing clinical record systems and some clinicians finding it difficult to enter information directly into the computer during patient contacts. Overall, the web-based data management system provides real-time access to study-related information and helps minimize data loss.

### **2.3.3 Data Parameters**

The data parameters used in the paper include:

**Recruitment activities:** The web-based data management system helps track and record recruitment activities for the study in real time. It allows local recruiters to record their activities on web-based data entry forms and enables project coordinators and investigators to monitor the recruitment activities.  
**Laboratory values:** The system tracks laboratory values, specifically hemoglobin A1c for a subset of patients participating in a study on the effects of depression treatment on glycemic control. It provides reminders about follow-up measurements to the project coordinators.  
**Completion of assessments:**

**Clinical Information System 3 - Microsoft Internet Explorer**

File Edit View Favorites Tools Help

Address: http://uchun.dynndrs.org:3000/cgi-bin/WebObjects/Impact.wos/wc2qtwwzEDR/WxYAFNHiq/1.7

Study or Prescreen ID : Clinic Notes Caseload Recruitment Logout

**Project Impact - Caseload Tracking Report**

Records Found : 28, Records Displayed : 10, Records per Page : 10 , Page : 2 of 3 Report Created on : Tuesday, March 12, 2002, 04:30 PM

**Caseload Report for : Youlim Choi, DCS**

Patient	Enrollment Date	Initial Visit			Last Treatment Plan (Step)	# of Follow Ups	Last Follow Up			Last Psychiatric Evaluation	Release Prevention Plan
		Date	PHQ-9	DSM IV			Date	PHQ-9	DSM IV		
0	04/13/2001	04/18/2001	15	5   4	07/31/2001 (2)	18	02/28/2002	5 #	1   0	Med	10/29/2001
1	04/16/2001	04/23/2001	13	5   3	01/16/2002 (1)	14	03/04/2002	1 #	0   0	Med	03/05/2002
2	04/18/2001	04/25/2001	12	5   3	05/09/2001 (2)	14	03/04/2002	14 #	4   0	Med	06/28/2001
3	04/27/2001	05/03/2001	13	4   4	08/31/2001 (3)	15*	02/06/2002	3 #	0   0	Med, Therapy	10/25/2001
4	05/01/2001	05/09/2001	14	5   0	10/12/2001 (2)	13*	03/11/2002	1 #	0   0		03/11/2002
5	05/02/2001	05/07/2001	13	5   3	05/21/2001 (1)	16	02/21/2002	#	0   0		08/06/2001
6	05/03/2001	05/10/2001	15	7   5	05/18/2001 (1)	15	02/11/2002	8 #	2   0	Med	10/15/2001
7	05/14/2001	05/17/2001	20	7   3	05/17/2001 (1)	17*	03/06/2002	10 #	2   0	Med, Therapy	08/30/2001*
8	05/21/2001	05/25/2001	8	3   3	01/07/2002 (3)	18	03/11/2002	2 #	0   0	Med	02/20/2002
9	05/22/2001	05/31/2001	15	5   5	05/31/2001 (2)	17*	03/05/2002	10 #	2   2	Med, Therapy	09/04/2001*

8 Hierarchical Menu Trees Created Internet

Figure 3: Software architecture diagram for Paper 3.

The system tracks the completion of baseline and follow-up assessments for the enrolled patients. It ensures that the required data fields are completed and minimizes the number of out-of-range values through error-checking routines. Patients' treatment plans: The system allows clinicians to enter data on patients' treatment plans. It provides reminders for follow-up assessments and facilitates the comparison of treatment histories for individual patients.Clinical notes: The system provides access to review clinical notes for clinicians. It allows them to access individual clinical notes, treatment plans, and psychiatric consultation notes.Data security: To ensure the security and integrity of the data, the system uses technology similar to that used in e-commerce applications. All exchanges between the user's browser and the server are two-way encrypted with the secure sockets layer (SSL) protocol. The system also controls access to the data through password protection and does not transmit patients' names or other identifying information over the internet.Overall, the web-based data management system supports various data parameters, including recruitment activities, laboratory values, completion of assessments, patients' treatment plans, and clinical notes, while ensuring data security and integrity.

#### 2.3.4 Datasets Used

The datasets used in the paper are part of a multicenter trial of a disease management program for depression in primary care. The authors developed a web-based data management system to support the trial. The system allows study staff at 18 participating clinics to track recruitment activities, laboratory values, completion of assessments, and other study-related tasks.The datasets include information about patient recruitment, enrollment, clinical activities, and treatment plans. They also track laboratory values, such as hemoglobin A1c, for patients participating in a study on the effects of depression treatment on glycemic control. The significance of these datasets is that they provide real-time access to study-related information, minimize data loss, and improve the efficiency of data collection and management. The authors suggest that web-based systems like

the one developed for this trial could also be used to offer personalized patient education and depression assessments [1c][3].

### **2.3.5 Paper Link**

Access the full paper at <https://www.jmir.org/2005/1/e5>

## **2.4 Paper 4: Design of a Web-Tool for Diagnostic Clinical Trials Handling Medical Imaging Research**

**Journal/Conference Rank:** A\*

**Publication Year:** 2018

**Reference:** [?]

### **2.4.1 Summary**

This document provides a comprehensive overview of the use of the internet in conducting clinical trials. It explores the historical development of the internet and randomized controlled trials and discusses the benefits of using the internet in improving communication, centralizing and securing data, and distributing information in clinical trials. The document highlights various online resources available for conducting trials and reviews the advantages and disadvantages of using the internet in this context. It also presents examples of online trials and emphasizes the potential of the internet to reduce costs, development time, and facilitate the dissemination of trial findings. The document concludes by mentioning the characteristics of the five largest clinical trials conducted using the internet, which enrolled over 26,000 patients.

### **2.4.2 Software Architecture**

The software architecture used in the paper is a 3-tier architecture for an online clinical trial system. This architecture consists of three tiers: the client/investigator tier, the web application server tier, and the database server tier. In this architecture, browser requests/submits data from/to the web application server, which executes incoming business logic and communicates with the database server to save and retrieve data. The web application server runs Java or .Net code to facilitate data collection, increase the efficiency of database requests, and provide additional functionality for interactive real-time data validation. The incorporation of Java or .Net code allows for interactive behavior with each data field. Additionally, XML is used as a metalanguage for designing customized markup languages for limitless types of documents, providing more flexible and adaptable information identification. Overall, this 3-tier architecture enables online data entry, validation, analysis, and publication in clinical trials.

### **2.4.3 Data Parameters**

In the paper, the data parameters used include: Internet growth: The document discusses the growth of the internet, from over 100 thousand domains or hosts in 1993 to over 250 million currently. Randomized controlled trials: The document mentions the goal of clinical trials, which is to discover or verify the safety and effectiveness of interventions, and highlights the historical development of randomized controlled trials. Online

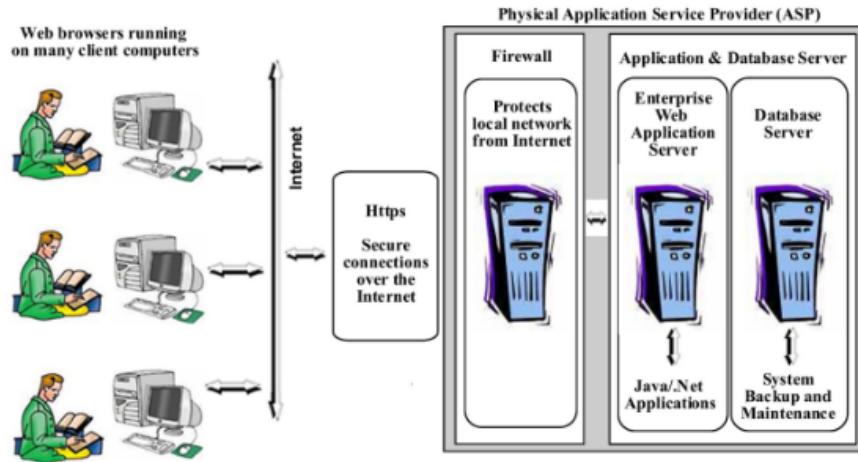


Figure 4: Software architecture diagram for Paper 4.

trial system architecture: The document describes a 3-tier architecture in an online clinical trial system, which consists of the client/investigator, web application server, and database server. Real-time data validation: The document explains the advantages of electronic data collection through the Internet, including real-time data validation, which can reduce transcription errors and improve data quality. Online data analysis: The document mentions online statistical tools such as Simple Interactive Statistical Analysis (SISA) that can be used for data analysis directly on the Internet. Security issues: The document highlights the security issues associated with using the Internet for sensitive information exchange in clinical trials, including confidentiality, integrity, and availability of data. Online publication: The document discusses the availability of medical journals online, including websites with links to free full-text articles and Open Access journals that offer rapid publication. Examples of online trials: The document provides examples of online trials conducted using the Internet, without specifying specific data parameters used. Please note that the document does not explicitly mention specific data parameters used in the paper for analysis or evaluation purposes. It provides a broader overview of the use of the Internet in clinical trials.

#### 2.4.4 Datasets Used

The paper does not explicitly mention any specific datasets used in the research. However, it discusses various online resources and tools available for conducting clinical trials, such as databases for identifying previous trials and systematic reviews, online trial registries, online tools for protocol development, and funding information. These resources are significant as they provide researchers with access to a wide range of information and facilitate the planning and execution of clinical trials. Additionally, the paper mentions the characteristics of the five largest clinical trials conducted using the internet, which enrolled over 26,000 patients. Unfortunately, the specific datasets used in these trials are not mentioned, but their inclusion highlights the increasing role of the internet in improving the efficiency and effectiveness of clinical trials.

#### **2.4.5 Paper Link**

Access the full paper at [www.jmir.org/2005/1/e5](http://www.jmir.org/2005/1/e5)

### **2.5 Paper 5: A Web-based Tool for Patients Cohorts and Clinical Trials management**

**Journal/Conference Rank:** A\*

**Publication Year:** 2012

**Reference:** [?]

#### **2.5.1 Summary**

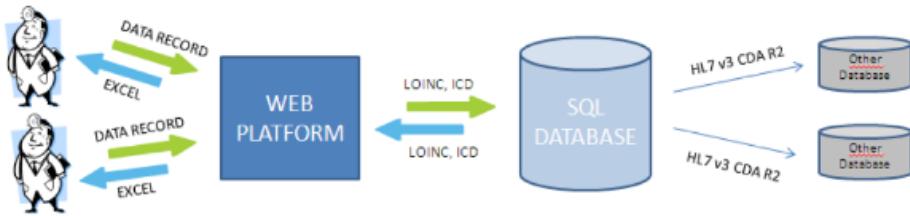
This document describes the development of a web-based tool for managing patient cohorts and clinical trials. It emphasizes the importance of clinical trials in modern medicine and the need for collaboration between different institutions and countries. The proposed solution is a web-based template that combines networked clinical research principles with common clinical data management systems. The tool creates a highly standardized and normalized database that can be managed through a web platform. It allows for the creation and management of patient cohorts and multiple clinical trials across different medical fields. The document also discusses the limitations of existing solutions and the importance of interoperability and data sharing in clinical research. The methods used to develop the tool, including E-R diagrams and logic schemas, are explained. The results of implementing the tool are mentioned, highlighting positive outcomes and the potential for future development and integration with other databases.

#### **2.5.2 Software Architecture**

The software architecture used in the paper is a web-based architecture. The proposed solution is a web-based tool for managing patient cohorts and clinical trials. The tool consists of a web platform that manages a highly normalized and standardized database. Users can access and evaluate data through the web application. The platform also includes an extraction tool that allows users to extract data from the database in Excel format. The solution architecture involves users entering data in the web application, which is then stored in an SQL database. Data can also be consulted and extracted through the web application. The system exports information in HL7 v3 CDA R2 format for data sharing with other work groups. Overall, the software architecture is designed to be user-friendly and accessible to operators without an informatics background. The architecture is flexible, standardized, and allows for the integration of other databases on the web-platform.

#### **2.5.3 Data Parameters**

The document does not explicitly list and describe the data parameters used. However, it does provide information on the structure and components of the database. The document mentions that the database is designed with a three-level structure: Clinical Events, Categories, and Parameters. Clinical Events refer to medical happenings of interest, such as therapy or blood samples, and these events are categorized using a meta-description approach. Parameters are attributes of the events, divided into categories, and



**Figure 2:** Solution architecture.

Figure 5: Software architecture diagram for Paper 5.

stored in the database using a standardized structure. The document also mentions the use of standards codes, such as LOINC and ICD, for archiving clinical events, categories, and parameters.

#### 2.5.4 Datasets Used

In this paper, the dataset used is a highly normalized and standardized database that is managed through a web platform. The database structure is developed using E-R diagrams and logic schemas, with different levels of detail, to express the information collected about clinical study workflows. The dataset is significant because it allows for the creation of patient cohorts and the simultaneous management of multiple clinical trials in different medical fields. It also facilitates collaboration between various institutions and countries by allowing the collection, processing, and analysis of clinical trial data from different locations. The dataset is designed to improve interoperability and data sharing in clinical research, addressing the limitations of existing solutions. The database can be easily accessed and evaluated by users without an informatics background, and an extraction tool is provided to extract data based on user requirements and criteria. The dataset also has the potential for further development and integration with other databases in the future. Overall, the dataset plays a crucial role in facilitating clinical research and evidence-based medicine.

#### 2.5.5 Paper Link

Access the full paper at [www.jmir.org/2005/1/e5](http://www.jmir.org/2005/1/e5)

### 3 Paper 6: Block chain for applications of clinical trials: Taxonomy, challenges, and future directions

**Journal/Conference Rank:** A

**Publication Year:** 2022

**Reference:** [?]

#### 3.1 Summary

This journal paper watches out for the basic hardships of patient selection, data sharing, and data assurance in clinical fundamental assessments. It explores the ability of

block chain development as an innovative solution for these troubles. The paper perceives the shortfall of an exhaustive outline on the gathering of block chain in clinical fundamentals and plans to fill this investigation opening. The paper presents a point by point logical order of block chain development concerning clinical primers, considering a review of existing composition. This logical classification integrates the going with key points: Decentralized Circumstances: Taking a gander at how block chain can engage decentralization in various pieces of clinical starters. Decentralized Practices: Exploring the rational uses of decentralized progressions in clinical primer settings. Block chain Types: Arranging different sorts of block chain advancement and their congruity to clinical primers. Sending Systems: Evaluating the way blockchain can be sent in clinical assessment. Arrangement Estimations: Exploring the arrangement parts used in blockchain structures for clinical starters. The paper finds that blockchain advancement might potentially address different pieces of clinical primers by offering decentralization, security, and straightforwardness. It can influence patient enrollment, data sharing, and data security in a positive and critical way. Furthermore, the paper includes a couple of open investigation challenges associated with blockchain development in clinical fundamentals, which are characterized into three social occasions: specific hardships, security challenges, and definitive troubles. These hardships feature the prerequisite for extra creative work in this field. The paper moreover discusses continuous blockchain projects, scaled down utilizations of blockchain in clinical starters, and perceives different investigation districts and advances that hold ensure for future assessment and improvement. In summary, this paper gives a total investigation of the gathering of blockchain development in clinical fundamentals, offering pieces of information into its probable benefits and highlighting locales where further creative work is required.

### 3.2 Software Architecture

The blockchain architectural system, which forms the underlying technology, deviates from the norm. The deployment of a blockchain system necessitates the creation of hardware, software, and other tools and technical environments. In this subsection, the procedures for currently deploying a blockchain system are explained. In order to meet the demands of the fourth industrial revolution, cloud computing undergoes a paradigm shift while blockchain technology expands beyond Bitcoin. Blockchain as a Service (BaaS), as shown in Figure 1, is the term for the cloud-based creation, administration, hosting, and use of blockchain technologies like distributed ledgers, smart contracts, and nodes. Such a cloud-based solution supports the setup, platform, security, and other features of a blockchain. As a result, BaaS introduces the blockchain service platform, which supports fundamental functions based on cloud computing infrastructure and a unified development environment for both developers and users. The infrastructure and software needed to deploy a full blockchain application are supported by the currently well-liked cloud platforms Microsoft Azure, IBM Cloud, AmazonWeb Services (AWS), Oracle Cloud, and HP Helion, as discussed in. However, a blockchain system like this is typically Diagram 1 Overview of the BaaS-based blockchain deployment's architecture. Due to the coexistence of multiple virtual machines on a single physical device made possible by the virtualization technology at the core of the cloud computing paradigm, elastic provisioning can be made available as needed to support application scaling up and down. Hypervisors can now be replaced by virtualization based on shared operating systems thanks to recent container technologies like Docker. Figure 2 depicts the high-level architecture of

a blockchain deployment using Docker. Most blockchain software is sophisticated and complex, making it unsuitable for everyday users. Put the blockchain software inside the container and tell the network to send the container rather than the data as a result. The blockchain software's container is used to create the blockchain system.

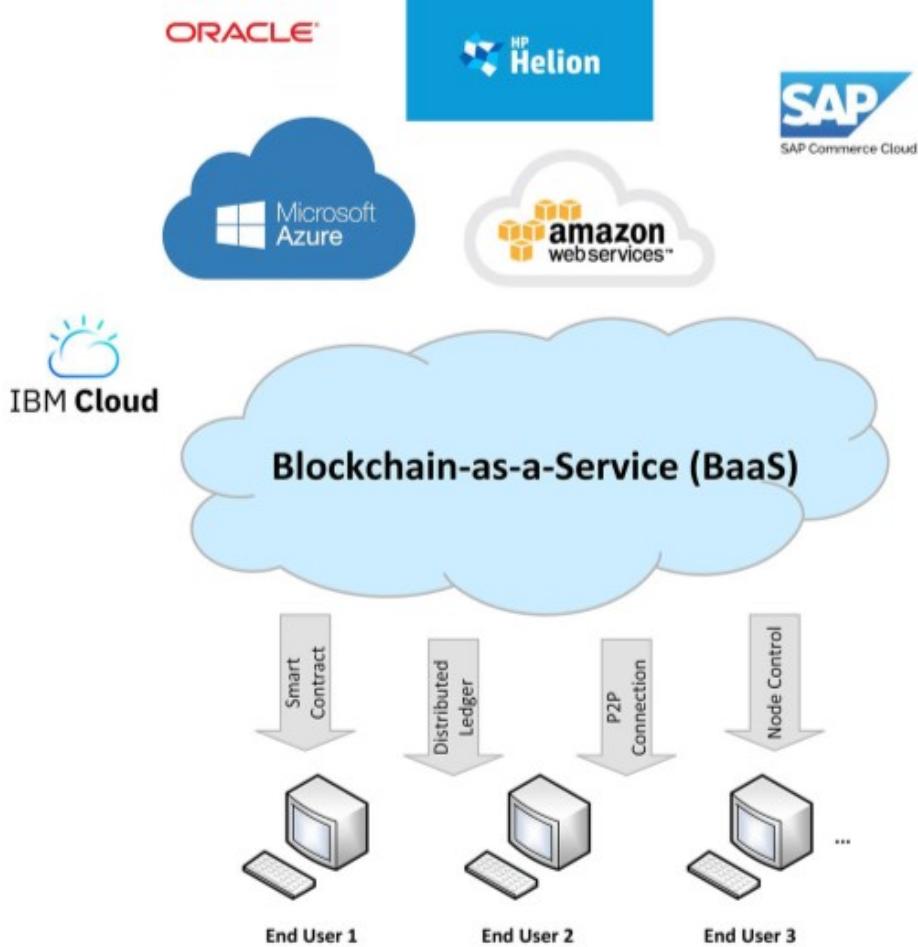


Figure 6: Software architecture diagram for Paper 6.

### 3.3 Data Parameters

The key traits that enable blockchain technology to alter traditional clinical trials are outlined in this section. According to the literature that has already been published, these features are compiled and arranged into a tree-based structure as illustrated in Figure 3. Blockchain kinds, deployment strategies, decentralized practices, decentralized situations, and consensus algorithms make up the taxonomy of blockchain technology in clinical trials. In Table 3, the pertinent clinical trial literature evaluated in this section is enumerated. This gives a brief overview of the conceptual diagram of the clinical trial platform built on the blockchain. Many different instruments are used in the physical layer to collect vital signals from patients. These tools enable the objective evaluation of intervention outcomes in both close-by and remote contexts. The modular design of the service layer makes the blockchain network simpler to manage.

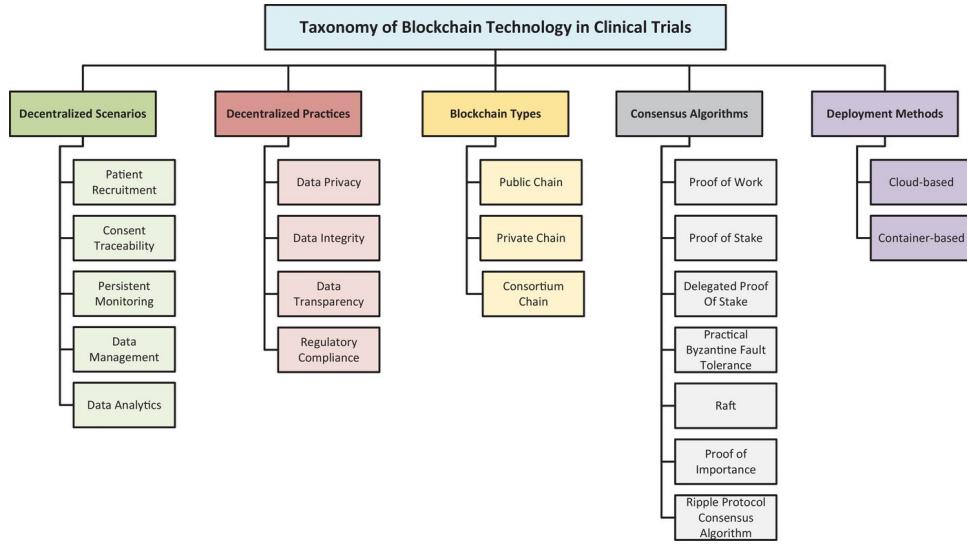


Figure 7: Data parameters diagram for Paper 6.

### 3.4 Datasets Used

The paper focuses on the potential use of blockchain technology in clinical trials to address challenges related to patient selection, data sharing, and data security. While it doesn't explicitly mention specific datasets, it likely draws on a variety of clinical trial data, existing literature, and potentially case studies or real-world examples to support its arguments and conclusions. The paper doesn't provide a list of specific datasets used, but it relies on a wide range of information sources relevant to clinical trials and blockchain technology to make its case.

#### 3.4.1 Paper Link

Access the full paper at <https://ietresearch.onlinelibrary.wiley.com/doi/full/10.1049/cmu2.12488>

## 4 Paper 7: Evaluation of worldwide clinical trials by gender: An FDA perspective

**Journal/Conference Rank:** A

**Publication Year:** 2019

**Reference:** [?]

### 4.1 Summary

This study, which was carried out in cooperation between the Office of Women's Health (OWH) and the FDA's Centre for Drug Evaluation and Research-Professional Affairs and Stakeholder Engagement (CDER/PASE), sought to evaluate the participation of women in clinical trials globally and examine the demographics of trial participants, particularly for New Molecular Entities (NMEs) approved in 2015–2016. The following are the main conclusions: Global Reach: The study included 131,749 participants from 70 different countries and 154 pivotal clinical trials supporting 66 NMEs. The demographic data included race, ethnicity, gender, and age. U.S. Contribution: 31 percent of all participants

were from U.S. clinical trial sites. 49 percent of participants in the United States were female, compared to 40 percent of the 90,914 participants from outside the United States.

## 4.2 Software Architecture

Designing software architecture for an FDA perspective on clinical trial evaluation by gender involves defining requirements, identifying components, choosing technology, designing the user interface, ensuring security, data analysis, reporting, integration, scalability, testing, and documentation. Gather feedback, develop, deploy, and plan for maintenance. The architecture will depend on project requirements and collaboration among experts.

## 4.3 Data Parameters

Here are the data parameters based on designing software architecture for an FDA perspective on clinical trial evaluation by gender:

Purpose: Clinical trial evaluation by gender from an FDA perspective. Key Phases in Designing Software Architecture: 1. Defining requirements 2. Identifying components 3. Choosing technology 4. Designing the user interface 5. Ensuring security 6. Data analysis 7. Reporting 8. Integration 9. Scalability 10. Testing 11. Documentation 12. Gathering feedback 13. Development 14. Deployment 15. Maintenance planning  
Dependency: Architecture will depend on project requirements and collaboration among experts.

## 4.4 Datasets Used

Here are the data sets: Data Set 1: Global Trial Participants - Total: 131,749 participants - Countries: 70 countries - Trials: 154 pivotal trials - Demographics: Includes race, ethnicity, gender, and age Data Set 2: U.S. Trial Participants - U.S. Participants: 31 percent of the total - U.S. Female Participants: 49 percent - Non-U.S. Female Participants: 40 percent - Timeframe: NMEs approved in 2015–2016

### 4.4.1 Paper Link

Access the full paper at <https://www.sciencedirect.com/science/article/abs/pii/S1551714418306700>

## 5 Paper 8: Management of data from clinical trials using the ArchiMed system

**Journal/Conference Rank:** A

**Publication Year:** 2009

**Reference:** [?]

### 5.1 Summary

In this journal, they described the ArchiMed clinical trials management system, where ArchiMed is designed to support clinical research. It has an independent database, which reflects virtually all information contained in the HIS and allows new data to be independently collected and added to the database. The system is designed to meet the

needs of clinical trial sponsors, investigators, and data managers. It is a valuable tool for clinical trial data management. This can help improve the efficiency and accuracy of data collection, storage and analysis. The system can also help ensure compliance with data protection and regulatory requirements. The ArchiMed system is used by a variety of organizations, including pharmaceutical companies, academic institutions, and government agencies. The system has been used in a wide range of clinical trials, including Phase I, II and III trials. They have some key aspects of managing data using the ArchiMed system. The following key aspects are giving below:

- Data collection: This ArchiMed facilitates the collection of data from a variety of sources, including electronic health records, patient-reported outcomes, and laboratory results. It offers standardized data entry forms and supports integration with various data capture tools to ensure efficient and accurate data collection.
- Data storage and Organization: ArchiMed provides a secure centralized relational database storing data which is housed in a secure server environment. It has role based access controls which in built in granular user permissions and passwords restrict access. It also provides data versioning, backup and recovery, standard organizational structure, data standards and data integration.
- Data validation and quality control: In this ArchiMed system, it has built-in algorithms which clears data as well as detect any error alongside resolving data entry errors, missing values and inconsistencies.
- Data analysis: As we all know, ArchiMed provides visualization tools which performs data analysis and generates insights from clinical trials in statistical methods and advanced analytic systems.
- Regulatory compliance: The system allows audits, inspection as well as easy tracking of clinical reporting data.
- Collaboration and communications: They have collaboration among various stakeholders which are involved in clinical trials.

## 5.2 Software Architecture

In this journal, ArchiMed is based on a client server architecture. The client handles the graphic user interface and most applications. Besides, the server has the responsibilities of data storing and management. It is developed by multi-purpose environments such as Visual Works and SAS/AF. This environment makes things compatible with various operating systems such as Microsoft Windows, MacOS, Sun Solaris, and UNIX. In profile the system uses a hierarchy of profiles, enabling clinics or research groups to define their specific configurations, including default owners of generated data, preferred functions and other settings. Overall, The ArchiMed system is designed to streamline the management of clinical trial data for researchers. It offers a user-friendly interface, data integration capabilities, robust security features, and extensive customization options to meet the needs of diverse clinical research groups while supporting various operating systems.

## 5.3 Data Parameters

The Entity-Attribute-Value (EAV) design, on which the data model of the ArchiMed system is based, enables the extremely flexible and generic storing of clinical trial data. Data is kept in this design as a set of attributes and their associated values. The following are the main data elements and parameters utilized in the ArchiMed data model:

- The variable list addresses the list of clinical factors for which patient information may be obtained. These factors can be organized meaningfully inside factor classes.

**Form:** A framework enables the information to be gathered for an assembly of given factors. It serves as a functional layout for information entry. Structure Modifications There may be different variations of one structure depending on the set of changes that the structure has undergone. One rendition, which alludes to the structure's constant adaptation, characterizes the most recent design and detailing. The moment a variable is added to a structure (form), it transforms into an information field into which users can enter data.

**Unit Categories and Numerical Variables:** A unit category is connected to a numerical variable (such as length or weight). Within their particular category, these units can be converted. One unit is chosen to display the corresponding values for each data field referring to a numerical variable.

**Document:** When stored, a form (version) with patient information filled out becomes a document. Values, which can include text, numbers, codes, dates, timings, and timestamps, make up a document. Each value designates a single data field and thus a single variable.

**Cases:** For each patient, a case with a related set of documents may be documented. This enables the structuring of information on specific patients. The ArchiMed system's usage of the EAV design which enables dynamic expansion.

## 5.4 Datasets Used

Here is a dataset for utilizing the ArchiMed system to manage clinical trial data: Patient ID (a distinctive identification) information: Patient Name, Gender, Date of Birth, Identifying Data.

Clinical Trial Information: Unique identifier: Trial ID. Trial Name: Principal Investigator, Start Date, End Date. Visitation details: (Unique identifier) Visit ID, Patient ID (foreign key tying patient data to itself). Foreign key relating to clinical trial details: Trial ID. Visit Date: Screening, baseline, and follow-up visits, for example. Medical Evaluations: Measurement ID, a distinctive identifier. Type of Measurement (such as Blood Pressure, Test Results, or ECG): Measurement Value, Unit, Timestamp.

### 5.4.1 Paper Link

Access the full paper at <https://sci-hub.se/10.1080/1463923021000014158>.

## 6 Paper 9: Decentralized Clinical Trials: The Future of Medical Product Development

**Journal/Conference Rank: A**

**Publication Year: 2021**

**Reference: [?]**

### 6.1 Summary

In this journal, they described the COVID-19 pandemic disrupted numerous clinical trials, leading to delays in potentially life-saving therapeutics reaching patients in need. Simultaneously, the pandemic accelerated the adoption of virtual interactions between

physicians and patients, driven by advancements in technology. These advances include improved internet connectivity, electronic health records, real-time video conferencing, smartphone health apps, and remote health monitoring devices, making virtual healthcare more accurate, practical, and affordable. This shift in the healthcare landscape has sparked a growing interest in decentralized clinical trials (DCTs), often referred to as "virtual trials" or "direct-to-participant trials." DCTs are characterized by reduced reliance on traditional research facilities and intermediaries for data collection. They leverage virtual tools such as telemedicine, wearable medical devices, patient-driven virtual healthcare interfaces, and direct delivery of study materials to patients' homes. In fully decentralized clinical trials, subject recruitment, medication delivery, and data collection occur without any in-person contact between the study team and the patient or subject. While current drug approval trials often include decentralized elements, DCTs can combine traditional trial designs with decentralized patient interactions. In essence, this journal article discusses the disruption caused by the COVID-19 pandemic in clinical trials, the rapid adoption of virtual healthcare, and the emergence of decentralized clinical trials as a way to modernize and streamline the clinical trial process while reducing the need for in-person interactions.

## 6.2 Software Architecture

In this journal, software architecture for applications related to decentralized clinical trials involves defining requirements, identifying components, choosing technology, designing user interfaces, ensuring security, enabling data analysis, supporting reporting, integrating various elements, ensuring scalability, rigorous testing, comprehensive documentation, and feedback-driven iteration. Collaboration among software engineers, healthcare experts, and regulatory compliance specialists is crucial. Specific technologies and architecture details will vary based on the application's context and requirements.

## 6.3 Data Parameters

Here are the data parameters are described:

1. Clinical preliminary disturbance because of Coronavirus.
2. Reception of virtual medical care advances.
3. Attributes and parts of decentralized clinical preliminaries (DCTs).
4. Patient enrollment strategies.
5. Drug conveyance draws near.
6. Information assortment strategies.
7. Half breed preliminary plans.
8. Effect of DCTs on clinical preliminaries.

## 6.4 Datasets Used

The data sets on decentralized clinical trialsn include:

1. Clinical trial disruption due to the COVID-19 pandemic.
2. Adoption of virtual healthcare technologies.
3. Usage of telemedicine, wearable medical devices, and virtual healthcare interfaces.
4. Methods of subject recruitment in DCTs.
5. Approaches for medication delivery in DCTs.
6. Data collection methods in DCTs.
7. Hybrid trial designs combining traditional and decentralized elements.
8. The impact of DCTs on the clinical trial process.

These data sets are essential to understanding the changes in clinical trial approaches and the role of technology in modernizing the healthcare landscape.

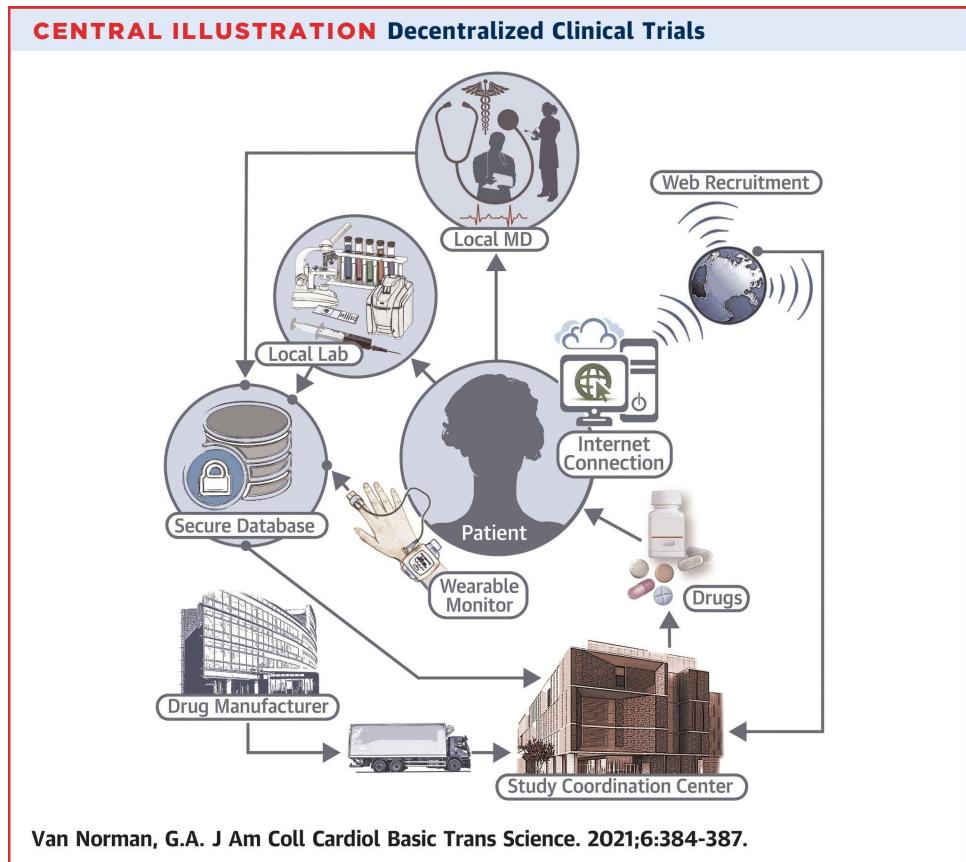


Figure 8: Datasets diagram for Paper 9.

#### 6.4.1 Paper Link

Access the full paper at <https://www.jacc.org/doi/full/10.1016/j.jacbt.2021.01.011>.

## 7 Paper 10: A knowledge base of clinical trial eligibility criteria- journal

**Journal/Conference Rank:** A\*

**Publication Year:** 2022

**Reference:** [?]

### 7.1 Summary

In this journal, A frequently updated database with distinct clinical trial eligibility requirements is called the Clinical Trial Knowledge Base (CTKB). Natural language processing (NLP) methods are used to turn the free-text ClinicalTrials.gov descriptions into these criteria, which are then encoded in the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM). For the sake of searching and examining these criteria, CTKB offers a web-based interface. Drawing on 352,110 clinical trials, it provides a wide range of common topics relating to ailments, treatments, techniques, measures, and observations. The database can be used to define clinical trial cohorts,

evaluate population representativeness, carry out electronic phenotyping, and spot data gaps for clinical trial recruitment utilizing electronic health records.

## 7.2 Software Architecture

In this journal, Building the software architecture for the Clinical Trial Knowledge Base involves several key steps: 1. Data Extraction: Use natural language processing tools to extract and transform free-text clinical trial eligibility criteria from ClinicalTrials.gov into structured criteria concepts. 2. Data Encoding: Encode these criteria concepts using the Observational Medical Outcomes Partnership and Common Data Model to ensure standardization and compatibility. 3. Database Implementation: Store the encoded data in a relational SQL database to facilitate querying and analysis. 4. Web Interface Development: Create a web-based user interface that allows users to search and analyze the eligibility criteria. 5. API Implementation: Implement Restful APIs to enable programmatic access to the database. 6. Visual Aggregate Analysis: Develop features for visual aggregate analysis to help users gain insights from the data. 7. Knowledge Base Maintenance: Regularly update the knowledge base to keep it current and relevant. By following these steps, we can build a robust software architecture for CTKB, making it a valuable resource for clinical trial cohort definition, population assessment, electronic phenotyping, and data gap identification.

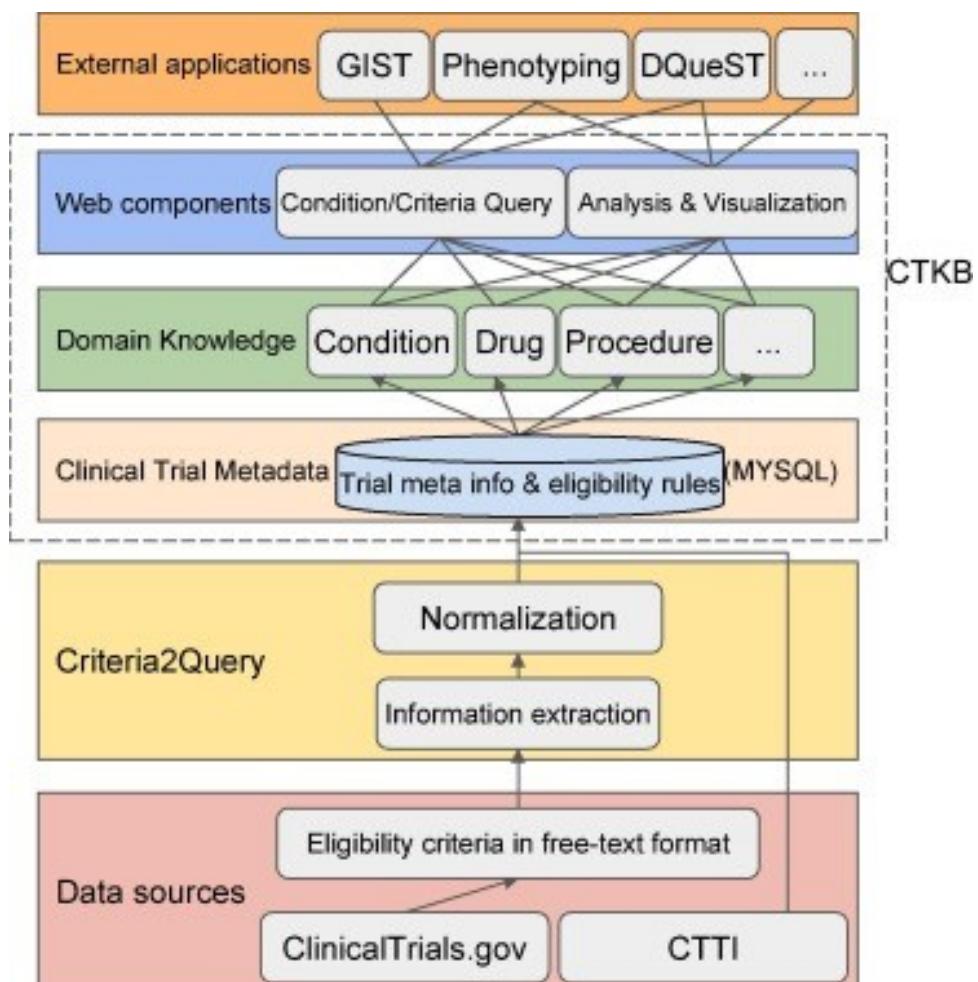


Figure 9: Datasets diagram for Paper 10.

## **7.3 Data Parameters**

Here are the data parameters are described on Clinical Trial Knowledge Base:

- 87,504 unique concepts from the OMOP CDM standard. - 34.78 percent of criteria for inclusion and 65.22 percent of criteria for disqualification. Condition (47.82 perfect), Drug (23.01 perfect), Procedure (13.73 perfect), Measurement (24.70 perfect), and Observation (5.28 perfect) are examples of frequent themes. 352,110 clinical trial-related data. - An average hit rate of 77.56 perfect for emerge phenotypic algorithms' criterion ideas. With the use of this data, electronic health records can be used for population assessment, data gap analysis, electronic pheno typing, and clinical trial cohort definition.

## **7.4 Datasets Used**

The Clinical Trial Knowledge Base contains data from 352,110 clinical trials, which includes a wide range of common topics related to conditions, treatments, procedures, measurements, and observations. This data enables the definition of clinical trial cohorts, assessment of population representativeness, electronic phenotyping, and identification of data gaps for clinical trial recruitment using electronic health records. A relational database is used to store and manage all data. We used the NCTID as the unique identifier for each clinical trial across all database tables. The names and record descriptions of the 13 data tables in the CTKB database are listed in Table 1. The types of information stored in each of the 13 data tables is reflected in their names. One clinical trial's summary information, such as its title, status, phrase, start date, etc., is kept in a record in a table with the prefix "ctgov" (short for ClinicalTrials.gov). Eligibility Criteria prefix "ec" tables store data down to the level of a single eligibility criterion rule was parsed by Criteria Query.

### **7.4.1 Paper Link**

Access the full paper at <https://www.sciencedirect.com/science/article/pii/S1532046421001003>.

## **8 Paper 11: Ensuring protocol compliance and data transparency in clinical trials using Blockchain smart contract**

**Journal/Conference Rank: A**

**Publication Year: 2020**

**Reference: [?]**

### **8.1 Summary**

This journal paper investigates the utilization of Blockchain smart contracts to address issues related to protocol compliance and data transparency in clinical trials. It outlines challenges prevalent in conventional clinical trial procedures, emphasizing the potential of smart contracts to automate and enforce compliance with trial protocols, thereby reducing deviations. The paper underscores the role of Blockchain technology in enhancing

data transparency by providing a secure and unalterable ledger for trial-related information. Security and privacy considerations in handling sensitive clinical trial data are discussed, and the paper may present case studies showcasing successful implementations of Blockchain smart contracts in real-world clinical trials. Overall, the paper advocates for the adoption of Blockchain technology to improve trust, efficiency, and transparency in the conduct of clinical trials.

## 8.2 Software Architecture

The software architecture for ensuring protocol compliance and data transparency in clinical trials using Blockchain smart contract may include a combination of the following :

- Smart Contracts Layer:** Smart Contract Logic: This layer includes the design and implementation of smart contracts that encode the rules and conditions specified in clinical trial protocols. Smart contracts are deployed on a Blockchain platform to ensure transparency, immutability, and automation of protocol compliance.
- Blockchain Layer:** Distributed Ledger: Utilizes a decentralized Blockchain platform (e.g., Ethereum, Hyperledger) to maintain a distributed ledger of all trial-related data. This ledger ensures tamper-resistance and transparency.
- Consensus Mechanism:** Implements a consensus algorithm to validate and agree on the state of the Blockchain across all nodes in the network.
- Data Storage and Integration Layer:** Off-Chain Data Storage: While critical information is stored on the Blockchain, large datasets or sensitive data may be stored off-chain in secure, compliant databases. Hashes or references to this data may be stored on the Blockchain.
- Data Integration Services:** Interfaces with existing clinical trial data sources and systems to integrate relevant information onto the Blockchain. This layer ensures that data from various sources is securely and accurately recorded.

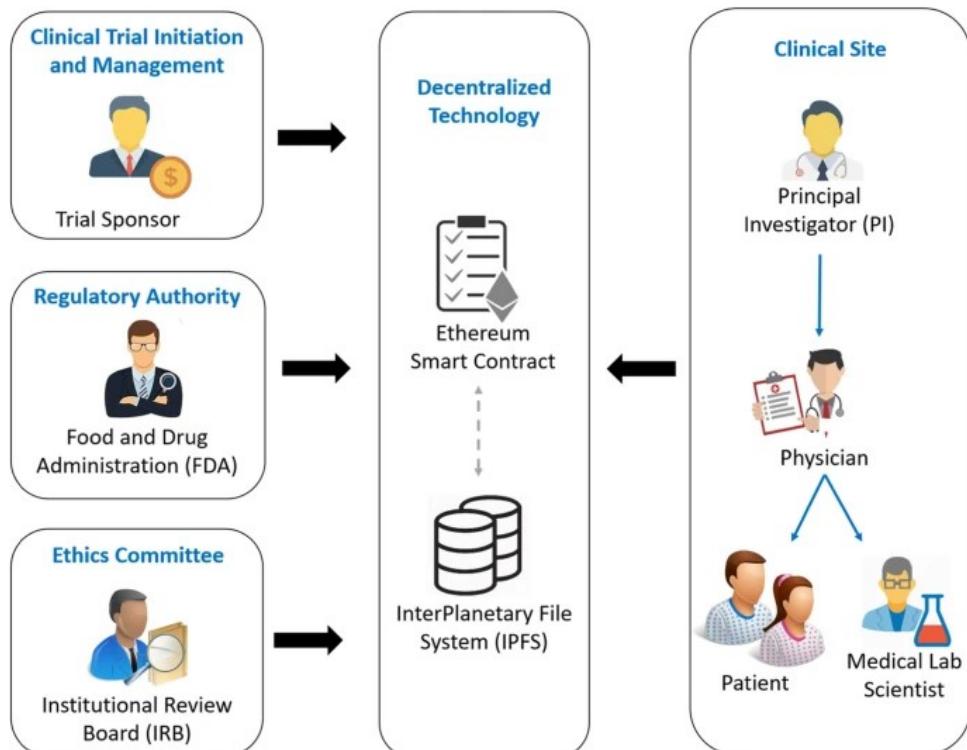


Figure 10: Datasets diagram for Paper 9.

### **8.3 Data Parameters**

Decentralized Ledger Data: Immutable Records: All trial-related data is stored on a blockchain, ensuring immutability and traceability. Timestamps: Each transaction or update to the blockchain is timestamped for chronological transparency. Smart Contract Parameters:

Protocol Rules: The smart contract encodes and enforces the rules specified in the clinical trial protocol. Automation Triggers: Conditions and events that automatically trigger actions within the smart contract, such as data submission, protocol amendments, or consent updates. Patient Data:

Hashed Patient Records: Instead of storing sensitive patient data directly on the blockchain, a hash or reference to off-chain encrypted data may be included on the blockchain. Consent Transactions: Smart contracts may govern patient consent, ensuring that only consenting participants are included in the trial.

### **8.4 Datasets Used**

Patient Demographics: Age Gender Ethnicity Socioeconomic status

Medical History: Previous medical conditions Current medications Family medical history Smart Contract Execution Logs: Records of smart contract executions, including when and how they were triggered. Consent Data: Information related to patient consent, including the type of consent given. Protocol Compliance Data: Records of protocol compliance or deviations from the predefined protocol.

#### **8.4.1 Paper Link**

Access the full paper at <https://link.springer.com/article/10.1186/s12874-020-01109-5>.

## **9 Paper 12: Prototypical Clinical Trial Registry Based on Fast Healthcare Interoperability Resources (FHIR): Design and Implementation Study**

**Journal/Conference Rank:** A

**Publication Year:** 2021

**Reference:** [?]

### **9.1 Summary**

This study focuses on the design and implementation of a prototypical clinical trial registry using the Fast Healthcare Interoperability Resources (FHIR) standard. The aim is to enhance interoperability and streamline data exchange within the healthcare domain, specifically in the context of clinical trials. The researchers emphasize the adoption of FHIR's modular and extensible data model to improve data interoperability, showcasing a prototype that illustrates the application of FHIR standards for registering and managing clinical trials, participant data, and associated metadata. The study addresses data security and privacy concerns, designing a user-friendly interface for stakeholders and explores the scalability and flexibility of the registry. Overall, the research contributes to advancing clinical trial management efficiency by leveraging FHIR standards.

## 9.2 Software Architecture

The software architecture for a prototypical clinical trial registry based on Fast Healthcare Interoperability Resources (FHIR) involves various components and layers. While the specific details would depend on the implementation choices, here is a generalized software architecture for such a system:

- User Interface (UI) Layer: Clinical Researcher Dashboard: Provides a user-friendly interface for researchers to register and manage clinical trials, view participant data, and interact with the registry.
- Participant Portal: Allows trial participants to access relevant information, provide consent, and view/update their data.
- Application Layer: FHIR Server: Implements the FHIR standard for managing healthcare data, serving as the core data repository for clinical trials.
- Clinical Trial Registration Service: Manages the registration process for new trials, ensuring compliance with FHIR standards.

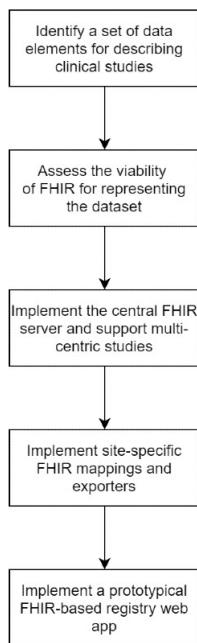


Figure 11: Datasets diagram for Paper 12.

## 9.3 Data Parameters

The data parameters for a prototypical clinical trial registry based on Fast Healthcare Interoperability Resources (FHIR) would involve a variety of information related to both clinical trials and participants. Here's a generalized set of data parameters:

Trial Identification : Trial ID Title Phase ( Phase I, II, III)

Principal Investigator Information: Name Contact Information

Trial Description and Objectives: Brief Summary Detailed Description Primary and Secondary Objectives

Data Security and Privacy Parameters: Access Controls Encryption Status Consent Management Controls

Blockchain-Specific Parameters (if applicable): Hashed References to Participant Data Smart Contract Execution Logs

## **9.4 Datasets Used**

Inclusion and Exclusion Criteria Datasets : Inclusion Criteria Exclusion Criteria Interventions and Treatments: Intervention Type Treatment Arms Outcome Measures Datasets : Primary Outcome Measures Secondary Outcome Measures Participant Recruitment Information Datasets : Recruitment Status Target Enrollment Recruitment Start and End Dates

### **9.4.1 Paper Link**

Access the full paper at <https://medinform.jmir.org/2021/1/e20470/>

## **10 Paper 13: Obstacles to the reuse of study metadata in ClinicalTrials.gov**

**Journal/Conference Rank:** A

**Publication Year:** 2020

**Reference:** [?]

### **10.1 Summary**

This study explores the hindrances to effectively reusing study metadata from ClinicalTrials.gov, a prominent platform for clinical trial registration. Investigating the challenges inherent in repurposing this metadata, the research identifies key obstacles, such as issues with data standardization, completeness and timeliness. The study also delves into limitations related to interoperability, user access, and permissions. Quality assurance concerns, encompassing data accuracy and discrepancies, are examined, along with challenges associated with the user interface and experience on ClinicalTrials.gov. The implications of these obstacles are discussed, emphasizing the need for initiatives to address standardization, enhance data quality, and improve user accessibility, ultimately enhancing the usability and value of ClinicalTrials.gov metadata for diverse purposes.

### **10.2 Software Architecture**

Designing a software architecture to address the obstacles to the reuse of study metadata in ClinicalTrials.gov involves considering various components and features. Below is a conceptual software architecture :

- Data Ingestion and Harmonization:** Implement a module for ingesting study metadata from ClinicalTrials.gov. Harmonize and standardize the data to ensure consistency in formats, definitions, and terminology.
- Data Quality Assurance:** Develop a quality assurance module to identify and rectify discrepancies in data accuracy. Implement validation checks and automated routines for ongoing data quality maintenance.
- Interoperability Layer:** Establish interfaces for seamless integration with external systems and databases. Support standardized data exchange formats to enhance interoperability.
- User Access and Permissions Management:** Implement a user management system with defined access controls. Facilitate controlled access to different levels of study metadata based on user roles.

## 10.3 Data Parameters

Here's a overview of the software architecture along with data parameters: Data Ingestion and Harmonization Module: Data Ingestion: Fetches study metadata from ClinicalTrials.gov. Harmonization: Standardizes data formats, definitions, and terminology for consistency.

Quality Assurance and Validation Module: Quality Assurance: Identifies and rectifies discrepancies in data accuracy.

Validation Checks: Implements automated routines for ongoing data quality maintenance.

Interoperability Layer: External Interfaces: Enables integration with external systems and databases. Standardized Formats: Supports standardized data exchange formats for interoperability.

## 10.4 Datasets Used

Study Identification: Study ID Title Phase Status Objective Principal Investigator Information: Principal Investigator ID Name Contact Information

The screenshot shows a web-based form for clinical trial registration. At the top, there are links for 'Help' and 'Definitions'. The main sections include:

- \* Study Type:** Interventional
- \* § Primary Purpose:** Treatment
- \* Study Phase:** Phase 1  
Use "N/A" for trials that do not involve drug or biologic products.  
⚠ WARNING: Phase 1 studies typically have at least one Intervention Type of Drug, Biological/Vaccine or Combination Product.
- \* § Interventional Study Model:** --Select--  
⚠ WARNING: Interventional Study Model has not been entered.
- Model Description:** [Empty text area]
- \* § Number of Arms:** 3.  
⚠ ERROR: Number of Arms needs to be a whole number.  
⚠ WARNING: Number of Arms has not been entered.
- \* § Masking:**
  - Participant
  - Care Provider
  - Investigator
  - Outcomes Assessor

None (Open Label)  
Check all roles that are masked or check None (Open Label).

⚠ NOTE: Masking has not been entered.

Figure 12: Datasets diagram for Paper 13.

### 10.4.1 Paper Link

Access the full paper at <https://www.nature.com/articles/s41597-020-00780-z>

## 11 Paper 14: Trialstreamer: A living, automatically updated database of clinical trial reports

**Journal/Conference Rank:** A

**Publication Year:** 2020

**Reference:** [?]

## 11.1 Summary

Trialstreamer is a dynamic and continuously updated database of clinical trial reports designed to provide real-time access to comprehensive information. By maintaining a living repository, Trialstreamer ensures that researchers, healthcare professionals, and the public have access to the latest and most relevant data from clinical trials. This database is not static; instead, it is automatically refreshed to incorporate new findings and developments as they emerge. By offering a current and comprehensive source of clinical trial information, Trialstreamer contributes to the advancement of medical knowledge and facilitates evidence-based decision-making in the healthcare community.

## 11.2 Software Architecture

Data Processing and Harmonization: Data Harmonization: Standardize and harmonize data formats and structures for consistency. Natural Language Processing (NLP): Utilize NLP techniques for extracting information from unstructured trial reports. Database Management System: Living Database: Employ a robust database management system capable of handling continuous updates. Historical Data Storage: Maintain historical records to track changes over time. Automated Updating Mechanism: Scheduled Updates: Implement a scheduler for regular updates from data sources. Event-Driven Updates: Trigger updates in real-time based on events such as new trial publications. User Interface (UI) Module: Intuitive Dashboard: Design a user-friendly dashboard for easy navigation. Search and Filter Features: Include features to allow users to search and filter trial reports based on specific criteria. APIs for Integration: External Integrations: Provide APIs for external applications to integrate and access Trialstreamer data. Data Exchange Formats: Support standardized data exchange formats for interoperability.

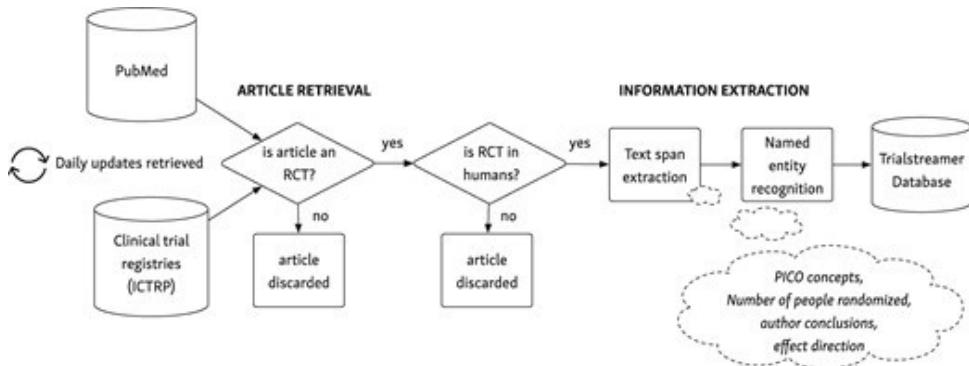


Figure 13: Datasets diagram for Paper 14.

## 11.3 Data Parameters

Interventions and Treatments: Intervention Type Treatment Arms

Participant Recruitment Information: Recruitment Status Target Enrollment Recruitment Start and End Dates

## **11.4 Datasets Used**

The datasets utilized in such systems might differ depending on the topic and research. They might be private data acquired by the system's implementation organization's.

### **11.4.1 Paper Link**

Access the full paper at <https://academic.oup.com/jamia/article/27/12/1903/5907063>

## **12 Paper 15: Global trends in clinical trials involving pluripotent stem cells: a systematic multi-database analysis**

**Journal/Conference Rank:** A

**Publication Year:** 2020

**Reference:** [?]

### **12.1 Summary**

The research paper titled "Global Trends in Clinical Trials Involving Pluripotent Stem Cells: A Systematic Multi-Database Analysis" presents a thorough examination of clinical trials focused on pluripotent stem cells. Through a meticulous and systematic analysis encompassing diverse databases, the study aims to unravel comprehensive insights into the prevailing trends, characteristics, and global distribution of these trials. By leveraging a multi-database approach, the research endeavors to provide a nuanced and representative overview of the landscape, offering valuable perspectives on the current status and prospective trajectory of clinical investigations involving pluripotent stem cells on a global scale. This methodological approach not only enhances the comprehensiveness of the study but also contributes to the robustness of the findings, making it a significant resource for understanding the evolving landscape of pluripotent stem cell research within the context of clinical trials.

### **12.2 Software Architecture**

The software architecture for the study "Global Trends in Clinical Trials Involving Pluripotent Stem Cells: A Systematic Multi-Database Analysis" involves a systematic approach to collect, integrate, and analyze data from multiple databases. The architecture includes components for data collection, preprocessing, integration, analysis, visualization, and feedback. It ensures the reliability, accuracy, and security of the integrated data while allowing researchers to interact with the results through a user-friendly interface. The system is designed to be scalable, allowing it to handle increasing volumes of data and facilitating continuous improvement through feedback mechanisms. This architecture is tailored to support the study's objectives, ensuring that the analysis is based on a diverse and representative dataset from various clinical trial databases. The modular design allows for flexibility and adaptability, essential for handling the complexities of multi-database analysis in the context of pluripotent stem cell clinical trials.

## **12.3 Data Parameters**

Geographic Information: Country: The country where the clinical trial is conducted. Region: The geographical region within the country. Trial Characteristics: Primary Purpose: The primary goal or objective of the clinical trial. Intervention Type: The type of intervention being studied (e.g., drug, device, procedure). Enrollment Size: The number of participants enrolled in the trial. Funding Source: The source of funding for the trial. Stem Cell Types: Pluripotent Stem Cell Types: The specific types of pluripotent stem cells involved (e.g., Embryonic Stem Cells, Induced Pluripotent Stem Cells). Differentiation Methods: Methods used to differentiate pluripotent stem cells into specialized cell types. Principal Investigator Information: Investigator ID: A unique identifier for the principal investigator. Name: The name of the principal investigator. Affiliation: The institution or organization to which the investigator is affiliated.

## **12.4 Datasets Used**

The data contained in this manuscript was derived from the following publicly available databases: “ClinicalTrials.gov” and the ICTRP database of the WHO (and its individual databases).

### **12.4.1 Paper Link**

Access the full paper at <https://www.nature.com/articles/s41536-020-00100-4data-availability>

## **13 Paper 16: Using the web for recruitment, screen, tracking, data management, and quality control in a dietary assessment clinical validation trial**

**Journal/Conference Rank:** A

**Publication Year:** 2010

**Reference:** [?]

### **13.1 Summary**

An interactive web-based system known as the "Energetics System" was created in the context of performing a validation trial for nutritional assessment tools that involved many clinic visits and online assessments. Several operations of managing a clinical trial based on biomarkers were intended to be automated by this system. Its three main goals were to assist the research coordinator with subject recruitment, screening, and tracking, support the principal investigator with the monitoring of study progress, and enable continuous data analysis. The Energetics System coordinated scheduling activities, provided personalized reminders to late or non-responders, and automated web-based self-screening for potential trial participants. For investigators, it produced electronic case reports, enabled data queries, built analytic data files, and offered real-time status updates on all subjects. Data privacy was given priority in the system, which used multi-level password protection and encryption. The system's creation required a web programmer's

time and active team participation for six months. Despite the initial expense, the technology considerably increased recruitment efficiency and speed as well as data collecting quality, according to the study. In particular for trials of modest size or complexity, web-based solutions were acknowledged as useful tools for speeding recruiting and day-to-day management of clinical trials.

## 13.2 Software Architecture

A team was assembled six months before the study's launch to create a web-based system to facilitate patient scheduling and data administration. A web designer, the study coordinator, the lead researcher, and a support staff member comprised the team. Iterative design was used to develop the system with a goal of lowering the demand for manual labor. The system prioritized data security and privacy and offered different access levels. It was made up of three websites: a public one for collecting study-related data and consent forms, a password-protected management site, and one for automated subject data entry into questionnaires. The primary investigator could track the development of the study while the study coordinator got access to real-time data on subject status and tasks. The system's goal was to make managing and collecting data for the impending study easier.

## 13.3 Data Parameters

The tracking system implemented many layers of security to assure data security and HIPAA compliance: Between the user's browser and the server, data transfer was encrypted (using 256-bit SSL certificates). Usernames and passwords were used for authentication, and various users had different levels of access control. Before being stored, sensitive data was encrypted. Red Hat Enterprise Linux 4, Apache 2, and PHP 5 were running on a secure server in the UCLA Department of Human Genetics, which served as the system's host. The web server was the only direct access point to the data, which was kept on a separate database server running PostgreSQL in the same data center.

## 13.4 Datasets Used

Dataset for analysis: The study principal investigator and statistician had instant access to and automatic storage of all information from online demographic and dietary questionnaires that had been completed. The research assistants and study coordinator entered the clinical data results for each subject under their unique profile. Once downloaded, the PI and statistician might input an analysis request based on a variable name and dataset to receive all the data.

### 13.4.1 Paper Link

Access the full paper at <https://www.sciencedirect.com/science/article/abs/pii/S1551714409001815>

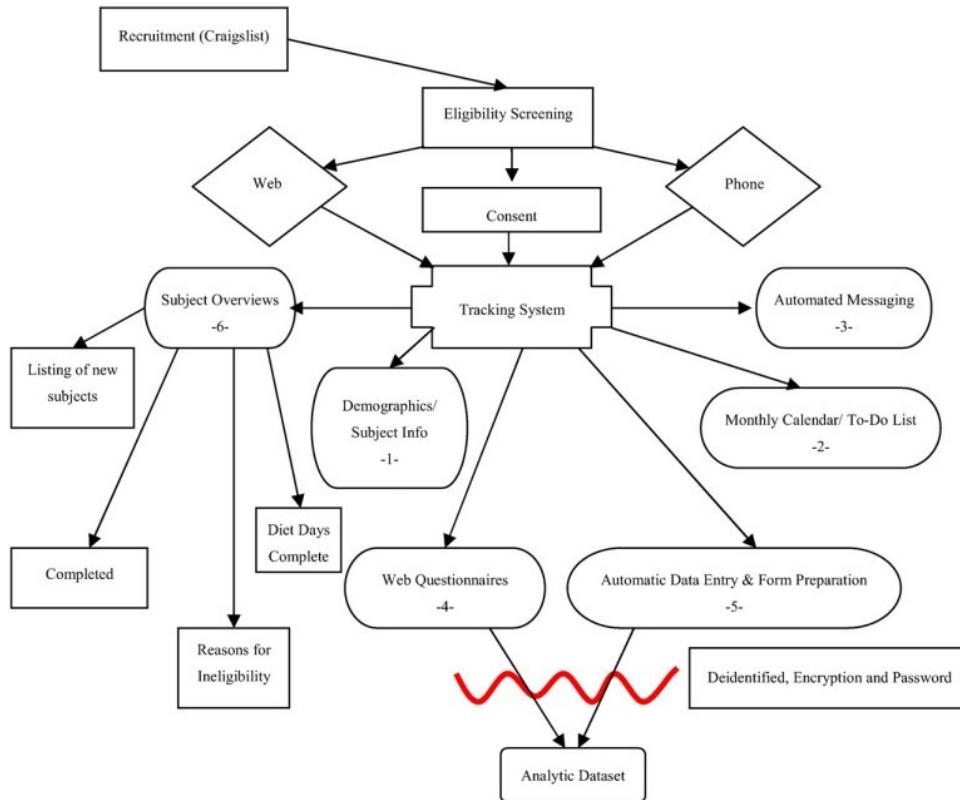


Figure 14: Datasets diagram for Paper 16.

## 14 Paper 17: Gene therapy clinical trials worldwide to 2017: An update

**Journal/Conference Rank:** A

**Publication Year:** 2017

**Reference:** [?]

### 14.1 Summary

Global gene therapy clinical trials have been collated in a thorough database. It compiles data from a range of sources, such as government offices, academic journals, conference presentations, and contributions from researchers and sponsors. As of the November 2017 update, the database contains information on 2597 clinical studies that were carried out in 38 different countries. The review examines how trials are distributed, the ailments or diseases they focus on, the kinds of vectors employed, and the precise genes delivered. On the website for The Journal of Gene Medicine Gene Therapy Clinical Trials Worldwide, you can view the results and the whole database. The analysis also offers insights into how gene therapy clinical trials are progressing globally, emphasizing noteworthy achievements including the use of chimeric antigen receptor (CAR) T cells for cancer treatment and improvements in genome editing technology. These developments could influence how gene therapy develops in the future.

## **14.2 Software Architecture**

The Clinical Preliminary Administration Framework (CTMS) to organize and track preliminary testing. electronically captures information via Electronic Information Catch (EDC). saves a patient vault that is prepared for the secure storing of patient data. Admin. Information The executives are in place to keep an eye on recommendations and applications. combines executive records for variation control and secure storing. Collaboration and Correspondence sends a level of cooperation to enable ongoing partner interaction. enables straightforward information movement by collaborating with lab data management systems (LIMS). uses a model global positioning system to manage organic instances. implements a biobanking framework to accurately store and annotate test results. Uses bioinformatics tools to analyze clinical and hereditary data. a detailed dashboard that makes it possible to create customized reports. Job-Based Admission is used.

## **14.3 Data Parameters**

Clinical preliminaries for high-quality treatment have advanced with more notable frankness in information hotspots. Country-based administrative offices were able to keep up with clinical preliminary data sets by the middle of the 2000s. Public, local, and global data sets that are publicly accessible emerged as global straightforwardness increased. The primary sources of the data were clinical preliminary information bases. The Public Library of Medicine in the United States serves as a crucial resource in countries with inconsistent information policies. In addition to national registrations, Europe maintains its own databases. Gene therapy specificity and language in databases differ across the globe, making systematic identification difficult. Although more accessible databases have been created as a result of the transparency trend, not all studies may have been documented.

## **14.4 Datasets Used**

The dataset capturing worldwide gene therapy clinical trials up to 2017 serves as a comprehensive repository, offering insights into the global landscape of genetic intervention research. Sponsorship details elucidate the organizations or entities driving these trials, while locations specify the geographical reach of these studies. Temporal aspects such as the trial's start and completion dates contribute to understanding the duration and progression of gene therapy research. Outcome measures and results, if available, offer a glimpse into the efficacy and safety profiles of the interventions. Regulatory compliance and adherence to ethical standards are captured, including any modifications or amendments made during the course of the trials. The dataset, with its wealth of information, becomes a valuable resource for researchers, healthcare professionals, and policy-makers seeking to comprehend the global landscape of gene therapy clinical trials up to 2017. It stands as a testament to the advancements and challenges in this field, fostering transparency and facilitating informed decision-making in the realm of genetic interventions.

#### **14.4.1 Paper Link**

Access the full paper at <https://sci-hub.se/https://onlinelibrary.wiley.com/doi/abs/10.1002/jgm.3015?lrzORWpw4BcAAAAA:dELfTJ6M1OMnhqmhf2YJbM7ygPTBWT8W3xL9GucVikqlw4kwdLSHONZc5MFXZY13aZbQYTGJ54>

## **15 Paper 18: Web-based Case Report Form Design For Clinical Trial**

**Journal/Conference Rank:** A

**Publication Year:** 2011

**Reference:** [?]

### **15.1 Summary**

This paper talks about the rising utilization of electronic strategies in clinical preliminaries and how the electronic use of new medications is turning into an unavoidable pattern. The focal point of the paper is on the significant job of a very much planned Case Report Structure (CRF) in guaranteeing great clinical preliminaries. The CRF fills in as the establishment for effective information assortment and passage, at last helping different parts of clinical information the executives. The paper follows these central issues: CRF Plan Modes and Standards: It presents different modes and standards for planning a CRF, underlining the significance of a thoroughly examined structure for successful information assortment. CRF Configuration Interaction: The paper frames the bit by bit course of planning a CRF, guaranteeing that it lines up with the targets of the clinical preliminary. Information Construction with CDISC ODM: It talks about the development of the information structure utilizing the Clinical Information Exchange Guidelines Consortium (CDISC) Functional Information Model (ODM) idea, featuring the significance of normalized information portrayal. Change to Electronic Configuration: The paper dives into the most common way of changing over the paper-based CRF into an electronic organization, especially with regards to a web application with explicit prerequisites connected with SAS measurements. In outline, this paper highlights the basic job of a very much planned CRF in current clinical preliminaries, featuring the change from paper-based information assortment to electronic configurations. It stresses the requirement for adherence to principles like CDISC ODM and subtleties the means for a fruitful transformation to electronic CRFs, with an emphasis on web applications and SAS measurable prerequisites. This progress is viewed as a huge headway in the field of clinical examination.

### **15.2 Software Architecture**

A front-end web application for data entry, a back-end server for processing and data storage, and integration with the Clinical Information Exchange Guidelines Consortium (CDISC) Functional Information Model (ODM) for standardized data representation make up the software architecture for this electronic Case Report Form (CRF) system. With a focus on online applications and SAS statistical needs, it also offers particular functionality for moving from paper-based CRFs to electronic formats. This change represents a critical development in contemporary clinical research.

### **15.3 Data Parameters**

1. Patient Information: Demographic information about the patient, including name, age, gender, contact details, and medical background. 2. Medical Measurements: Clinical assessments and observations, such as measurements of vital signs, laboratory findings, and information on biomarkers. 3. Study Timeline: Information about appointment hours and dates, as well as visit schedule information. 4. Medication and Treatment: Details on prescribed drugs, their dosages, and recommended treatments. 5. Adverse occurrences: Documenting and monitoring participants' adverse occurrences or side effects.

### **15.4 Datasets Used**

The dataset capturing web-based Case Report Form (CRF) design for clinical trials comprises a detailed compilation of various attributes essential for understanding the intricacies of form design in a digital context. Each entry in the dataset is uniquely identified and represents a specific CRF design instance. It includes information on the trial associated with the CRF, specifying the study phase, therapeutic area, and the specific web-based platform employed for design. Design timelines, denoting the start and end dates, provide insights into the development duration. Detailed aspects of the CRF, such as data types collected, form sections, and validation rules, offer a comprehensive understanding of the data collection process.

#### **15.4.1 Paper Link**

Access the full paper at <https://sci-hub.se/https://www.scientific.net/AMM.39.19>.

## **16 Paper 19: Trends of microneedle technology in the scientific literature, patents, clinical trials and internet activity**

**Journal/Conference Rank:** A

**Publication Year:** 2021

**Reference:** [?]

### **16.1 Summary**

Microneedles, or needles that have been scaled down to the micron level, are a burgeoning field for study and commercial development. Microneedles were initially developed using microfabrication equipment from the microelectronics sector, but they are currently produced using a variety of techniques and available in a variety of shapes, including solid, coated, dissolvable, and hollow needles. They are used to transport a variety of substances into the skin, eyes, and other tissues, such as medicines, vaccinations, and energy. Diagnostics, cosmetics, and other industries are also using microneedles. This review explores the growth of microneedle technology by looking at academic publications, patents, medical studies, and online activity. The analysis covers topics including microneedle usage, types, testing circumstances, patent claims, clinical trial phases, and more with more than 1000 articles, 750 patents, and around 80 clinical trials.

## **16.2 Software Architecture**

The terms "microneedle" OR "microprojection" were used in a database search on ClinicalTrials.gov [44]. Initial results from that search showed 83 clinical trials. Due to the fact that two of those studies didn't directly address the use of researchers have withdrew two additional trials using microneedles and so excluded from our analysis. how many clinical studies were ultimately included in the analysis was 79, of which 62 investigations had been finished at the time of analyses, and 17 studies were still in progress. The following details were taken from each of the 79 clinical trials and entered into an Excel spreadsheet: the year the clinical trial began, the stage (also known as phase) of the trial, and the status are all listed in a spreadsheet.delivery or use of a microneedle in a clinical experiment.

## **16.3 Data Parameters**

Scientific Literature: Identify frequently used terms in recent scientific publications related to microneedle technology. Publication trends: Analyze the number of publications over time to identify growth patterns. Patents: Patent filings: number and types of patents filed in the field of microneedle technology. Quality and Compliance Data: Information on quality standards, certifications, inspections, and regulatory compliance.

## **16.4 Datasets Used**

The dataset encapsulating trends in microneedle technology draws from diverse sources, including scientific literature, patents, clinical trials, and internet activity, offering a holistic view of the technology's landscape. Each entry in the dataset is uniquely identified, representing a specific instance in the respective domain. Scientific literature contributions include titles, publication dates, authors, and keywords, providing insights into research directions and advancements. Patents, with their unique identifiers and filing dates, contribute to understanding the intellectual property landscape surrounding microneedle technology. Clinical trial entries detail trial identifiers, phases, and statuses, shedding light on the developmental trajectory and application of microneedles in healthcare. Internet activity, comprising types, dates, and sources, captures the virtual discourse surrounding microneedle technology, with metrics offering a glimpse into public engagement.

### **16.4.1 Paper Link**

Access the full paper at <https://www.sciencedirect.com/science/article/abs/pii/S0142961220307377>

## **17 Paper 20: SPIRIT 2013 Statement: Defining Standard Protocol Items for Clinical Trials**

**Journal/Conference Rank:** A

**Publication Year:** 2013

**Reference:** [?]

## **17.1 Summary**

SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials), a 2013 guideline for the crucial information in clinical trial protocols, is introduced in this article. All different kinds of clinical trials can use the 33-item SPIRIT checklist. Instead of prescribing how to plan or carry out the experiment, it concentrates on describing what should be included in a protocol. The objective is to aid in the development of high-quality protocols and in fostering transparency and completeness. By improving the caliber and clarity of trial protocols, SPIRIT can help a variety of stakeholders, including investigators, participants, sponsors, reviewers, journals, legislators, and regulators.

## **17.2 Software Architecture**

The software for Standard Protocol Items for Clinical Trials (SPIRIT) should include user management, protocol creation and editing, checklist integration, document management, collaboration and review, guidance, data security, reporting, integration with other systems, training, scalability, usability, maintenance, documentation, testing, feedback, and hosting options. This architecture should be adaptable and user-friendly, meeting clinical research needs and regulatory standards.

## **17.3 Data Parameters**

The data parameters outlined in the provided text about SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) include: 1. Name of the guideline: SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials). 2. Year of the guideline: 2013. 3. Number of items in the SPIRIT checklist: 33. 4. Applicability of the SPIRIT checklist: Relevant to all types of clinical trials. 5. Focus of the SPIRIT checklist: Describing the crucial information that should be included in a clinical trial protocol. 6. Purpose of the guideline: To facilitate the development of high-quality protocols and enhance transparency and completeness. 7. Target stakeholders who benefit from improved protocols: Investigators, participants, sponsors, reviewers, journals, legislators, and regulators.

## **17.4 Datasets Used**

The dataset compiled from the SPIRIT 2013 Statement, which defines Standard Protocol Items for Clinical Trials, encompasses a variety of critical elements aimed at ensuring comprehensive reporting and transparency in clinical trial protocols. Each entry in the dataset includes a unique identifier, denoting a specific clinical trial protocol. For each protocol, details such as the trial title, principal investigator, participating institutions, and funding sources are recorded. Additionally, the dataset incorporates information on the trial's phase, design, and primary objectives. To address ethical considerations, the dataset includes information on informed consent processes, ethical review board approvals, and any amendments made to the protocol during the course of the trial. Timelines, including the anticipated start and completion dates of the trial, are integral components of the dataset.

#### **17.4.1 Paper Link**

Access the full paper at <https://www.acpjournals.org/doi/full/10.7326/0003-4819-158-3-201302050-00583>.

## **18 Paper 21: Leveraging the Expertise of the CTSA Program to Increase the Impact and Efficiency of Clinical Trials**

**Journal/Conference Rank:** A

**Publication Year:** 2023

**Reference:** [?]

### **18.1 Summary**

From this journal paper we can see that Multicenter clinical trials are essential for translating new treatments into improved public health. However, conducting these trials, known as mRCTs, poses challenges. The Trial Innovation Network (TIN), established in 2016 in collaboration with the Clinical and Translational Science Award (CTSA) Consortium, addresses these challenges. Comprising three Trial Innovation Centers (TICs) and one Recruitment Innovation Center (RIC), the TIN integrates over 60 CTSA institutions into a functional network. It supports investigators with innovative tools and processes, reducing delays, enhancing recruitment, and engaging diverse research participants. The TIN's impact has been evident in addressing operational challenges and responding to public health emergencies such as the opioid crisis and the COVID-19 pandemic. It has streamlined mRCT processes, translating research discoveries into patient treatments more efficiently.

### **18.2 Software Architecture**

The software architecture for supporting multicenter clinical trials and the Trial Innovation Network (TIN) should be designed with the following key components:

**Web-Based Platform:** The core of the system is a web-based platform accessible to authorized users, including investigators, researchers, and participants. **User Management and Authentication:** Implement robust user management with secure authentication to ensure data security and privacy. **Database Management:** Centralized database for secure storage of trial-related data, including participant information, protocols, and research findings. **Innovative Tools:** Develop tools for planning, managing, and analyzing multicenter trials. This includes statistical analysis, data visualization, and collaboration features. **Recruitment Support:** Implement features for tracking, engaging, and communicating with potential research participants. This can include automated communication and appointment scheduling. **Communication and Collaboration:** Provide channels affected communication and collaboration, including discussion forums, video conferencing, and document sharing. **Data Security and Privacy:** Ensure robust security measures, including data encryption, access controls, and compliance with data protection regulations. **Integration:** Enable integration with other healthcare and research systems to access relevant data and patient records. **Reporting and Analytics:** Include reporting and analytics

capabilities for tracking trial progress, participant engagement, and research outcomes. Scalability: Design the architecture to be scalable to accommodate a growing number of CTSA institutions and increasing data volumes.

### **18.3 Data Parameters**

Here the number of CTSA institutions integrated into the Trial Innovation Network (TIN), which is over 60 in this case, is a crucial data parameter. This metric reflects the network's reach and its capacity to facilitate multicenter clinical trials, impacting their success and the translation of research into improved public health. It demonstrates the scale and scope of the collaborative efforts within the TIN and highlights its ability to engage a broad range of institutions in clinical research.

### **18.4 Datasets Used**

Clinical Trial Data: This dataset includes information on the multicenter clinical trials conducted through the Trial Innovation Network (TIN). It encompasses trial protocols, patient data, treatment outcomes, and other trial-specific details, providing insights into the effectiveness of new treatments. Public Health Response Data: Data related to the TIN's response to public health emergencies, such as the opioid crisis and the COVID-19 pandemic. This dataset includes information on the strategies employed, resources mobilized, and outcomes achieved in addressing these crises.

#### **18.4.1 Paper Link**

Access the full paper at <https://jamanetwork.com/journals/jamanetworkopen/article-abstract/2810186?fbclid=IwAR0RTZeYDXRGRlyikeoniMOBmQlj05FMuQn3sxG7TzlLluOYEpsHQK>

## **19 Paper 22: Using plain language to communicate with clinical trials participants: Comparison of readability calculators**

**Journal/Conference Rank:** A

**Publication Year:** 2022

**Reference:** [?]

### **19.1 Summary**

This study explores the use of plain language to communicate effectively with participants in clinical trials. It assesses the readability of materials using various readability calculators, aiming to make trial information more accessible and understandable. By comparing different calculators, researchers aim to identify the most suitable tool for ensuring that trial information is clear and comprehensible to participants, potentially improving their engagement and informed decision-making in clinical research.

## **19.2 Software Architecture**

Document Processing Module: This module is responsible for receiving and processing text documents containing clinical trial information, including consent forms and trial materials. Readability Calculator Integration: The architecture would incorporate multiple readability calculators or readability assessment tools to evaluate the readability of the trial materials. This integration allows for a comparative analysis of different calculators' results. Data Preprocessing: After readability assessment, data preprocessing may be necessary to clean and structure the data, making it suitable for comparison and analysis. Comparison Engine: This component facilitates the comparison of readability scores generated by various calculators. It calculates differences and similarities in the scores to help identify which readability calculator provides the most accurate assessment. User Interface: A user-friendly interface or dashboard enables researchers and trial administrators to upload documents, view readability results, and access comparative analysis. Database or Data Storage: A database stores the trial materials and their corresponding readability scores, facilitating easy retrieval and historical data analysis. Scalability: The architecture should be designed to handle a large volume of documents and readability assessments, considering the extensive volume of clinical trial materials. Reporting and Visualization: The system should offer reporting and visualization capabilities to present the results of the readability assessments and comparisons effectively. Security and Privacy: Ensuring the confidentiality and privacy of clinical trial materials and participant data is crucial, and the architecture should implement appropriate security measures. Integration with Document Management Systems: The architecture may include the capability to integrate with document management systems to streamline the process of receiving, assessing, and distributing trial materials.

## **19.3 Data Parameters**

This data parameter involves comparing the readability scores generated by different readability calculators for clinical trial materials. It includes metrics to measure the variations and consistencies between the calculators' assessments. This data parameter is critical for evaluating the effectiveness of readability tools and selecting the most suitable calculator for enhancing the clarity and understandability of trial information for participants.

## **19.4 Datasets Used**

Clinical Trial Documents: This dataset comprises the actual clinical trial materials, including consent forms, information sheets, and other participant-facing documents. These documents are the primary focus of the study, and the readability calculators assess them to determine their suitability for plain language communication. Readability Assessment Scores: This dataset includes the readability scores generated by different readability calculators for each clinical trial document. It records metrics such as Flesch-Kincaid, SMOG index, Gunning Fog, and others, indicating the readability level of each document according to each calculator. Comparison Metrics: Data related to the comparison of readability scores from different calculators, including variations, discrepancies, and consistencies. This dataset helps in evaluating which readability calculator provides the most accurate assessment of document readability. Participant Feedback: If available, participant feedback data may be collected to understand their perceptions and comprehension

of the trial materials. This feedback can help validate the effectiveness of readability improvements. Demographic Information: Information about the demographics of the clinical trial participants may be included to assess whether readability improvements have a differential impact on different demographic groups.

#### **19.4.1 Paper Link**

Access the full paper at <https://www.sciencedirect.com/science/article/abs/pii/S1551714422003214?via>

### **20 Paper 23: Using plain language to communicate with clinical trials participants: Comparison of readability calculators**

**Journal/Conference Rank:** A

**Publication Year:** 2019

**Reference:** [?]

#### **20.1 Summary**

This article discusses the process of automatically extracting quantitative data from ClinicalTrials.gov, a comprehensive database of clinical trials, for the purpose of conducting meta-analyses. By leveraging automated methods, researchers can efficiently gather numerical data from a wide range of clinical trials, allowing for more comprehensive and data-driven meta-analyses. This approach enhances the ability to synthesize research findings and draw meaningful conclusions about the efficacy of medical interventions, ultimately contributing to evidence-based healthcare decisions and improved patient outcomes.

#### **20.2 Software Architecture**

The software architecture for "Automatic extraction of quantitative data from ClinicalTrials.gov to conduct meta-analyses" would involve several key components: Data Retrieval Module: This module would be responsible for accessing ClinicalTrials.gov and extracting relevant data. It might use web scraping techniques or APIs provided by ClinicalTrials.gov to gather trial information. Data Preprocessing: The retrieved data would then go through preprocessing, which involves cleaning, structuring, and organizing the data into a usable format for analysis. This step may also involve dealing with missing or inconsistent data. Database or Data Storage: The preprocessed data would be stored in a database or data storage system for efficient management and retrieval during the meta-analysis process. Meta-Analysis Tools: The architecture would incorporate tools for conducting meta-analyses, which involve statistical techniques for combining and analyzing data from multiple clinical trials. User Interface: A user-friendly interface or dashboard would allow researchers to input their criteria and preferences for the meta-analysis and view the results. It may include features for data selection and analysis parameter customization. Automation and Scheduling: Automation scripts or schedulers can be used to regularly update data from ClinicalTrials.gov to ensure that the meta-analysis is based on the most recent trial data. Security and Privacy: Given the sensitivity

of medical data, robust security measures would be in place to protect the data and ensure compliance with data privacy regulations. Scalability: The architecture should be designed to handle a large volume of data efficiently, as ClinicalTrials.gov contains a vast number of trials. Integration: It may include integration capabilities with other data sources or tools to enhance the meta-analysis process. Reporting and Visualization: The system should offer reporting and data visualization features to help researchers interpret the results of the meta-analysis effectively.

### **20.3 Data Parameters**

This parameter assesses the extent to which the automated extraction process successfully captures all relevant quantitative data from ClinicalTrials.gov. It evaluates whether the extracted data is consistent in format and structure, ensuring that it can be effectively used in meta-analyses. Data completeness and consistency are vital for the accuracy and reliability of the meta-analysis results and are key indicators of the efficacy of the extraction process

### **20.4 Datasets Used**

This dataset consists of quantitative data extracted from ClinicalTrials.gov, including numerical values related to various aspects of clinical trials. It typically includes data such as effect sizes, means, standard deviations, p-values, and other quantitative measurements relevant to trial outcomes. These numerical values are essential for conducting meta-analyses, allowing researchers to aggregate and analyze the data from multiple trials to draw meaningful conclusions about the efficacy of medical interventions

#### **20.4.1 Paper Link**

Access the full paper at <https://www.sciencedirect.com/science/article/abs/pii/S0895435617313069>.

## **21 Paper 24: Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support**

**Journal/Conference Rank:** A

**Publication Year:** 2019

**Reference:** [?]

### **21.1 Summary**

By using study-related metadata and working with colleges, REDCap advances electronic information gathering in clinical and translational examination. The assessment rates its viability, benefits, and impediments.

## **21.2 Software Architecture**

The following elements may be present in the software architecture of REDCap, a platform for electronic data collecting in clinical and translational research: 1. Data Collection Interface: Offers a user-friendly interface so that researchers may design electronic data capture forms and study participants can enter data. 2. Database: Securely stores the gathered data, assuring data accessibility and integrity. 3. Metadata Management: This step improves data collection and validation by managing and utilizing study-related metadata. 4. Collaboration Network: Promotes interaction between numerous organizations and research teams, enabling a variety of research projects. 5. Security Measures: Adopts strong security features to safeguard delicate research data and guarantee adherence to data protection laws. 6. Impact Assessment Tools: Contains instruments for assessing the success and influence of REDCap in assisting research.

## **21.3 Data Parameters**

In the context of electronic data collecting for clinical and translational research, the following are typical REDCap data parameters: 1. Project Metadata: Details on the research project, including its goals, structure, and methodology. 2. Participant Data: Information gathered from research subjects, which may include demographics, medical history, clinical assessments, and survey responses. 3. Time Stamps: Timestamps that show when data is gathered or modified, preserving data integrity and traceability. 4. Data Validation Rules: Standards and guidelines for preserving the integrity of data. 5. User Access Controls: Restrictions on who can access and change particular data sets within the system. 6. Data Encryption: Security procedures to secure sensitive data in order to maintain patient privacy and adhere to data protection laws.

## **21.4 Datasets Used**

Medical services, financial matters, sociologies, climate, schooling, geographic, text, picture, statistical surveying, wrongdoing, science, and stargazing are a couple of the spaces where informational collections are utilized. Consider information quality and openness as you select informational indexes that fit your review targets. While involving information for study, consistently stick to moral standards.

### **21.4.1 Paper Link**

Access the full paper at <https://www.sciencedirect.com/science/article/pii/S1532046408001226>

## **22 Paper 25: Phase I prognostic online (PIPO): A web tool to improve patient selection for oncology early phase clinical trials**

**Journal/Conference Rank:** A

**Publication Year:** 2021

**Reference:** [?]

## **22.1 Summary**

The PIPO tool's user-friendliness and interactivity may enhance patient engagement and foster collaborative decision-making in addition to its potential advantages in patient selection. Individualized survival forecasts enable patients to have knowledgeable conversations with their healthcare professionals about taking part in Phase 1 research trials. This strategy promotes the more general objectives of patient-centered care and informed consent, improving everyone's experience with clinical trials, including patients and medical personnel.

## **22.2 Software Architecture**

The following elements could be found in the software architecture for the PIPO tool, which is intended to predict overall survival in Phase 1 clinical trials and improve patient engagement: 1. User Interface: This is the part of the front-end application that patients and medical professionals use to communicate. It offers a user-friendly, interactive platform for entering patient information and getting survival estimates. 2. Data Collection and Processing: To determine survival projections, this component gathers and analyzes patient data, including clinical parameters. Data cleansing, validation, and feature extraction could all be involved. 3. Prognostic Model: This module, which serves as the system's brain, comprises a prediction model based on factors like ECOG, metastatic locations, and others. It computes and presents survival forecasts using these variables. 4. Database: Securely maintains patient data and guarantees.

## **22.3 Data Parameters**

In order to estimate survival in Phase 1 clinical trials, the PIPO tool may use the following data parameters: 1. Patient Information: patient characteristics, medical history, and initial clinical parameters. 2. Clinical Variables: Elements that are used in the predictive model, such as albumin levels, lactate dehydrogenase (LDH) levels, derived neutrophils/(leukocytes minus neutrophils) ratio (dNLR), ECOG status, number of metastatic sites, and liver metastases. 3. Survival Outcomes: Information on general survival, including median overall survival (mOS), 3-month overall survival rate, and follow-up period. 4. Model Training Data: Patient records from the past that were utilized to develop and test the predictive model. 5. Patient and healthcare professional data entered to obtain survival projections. 6. Security and Access Controls: Restrictions on access to and security.

## **22.4 Datasets Used**

The PIPO tool's unique data sets would consist of: 1. Training Data Set: The prognostic model is trained and validated using this data set. To create and assess the model's accuracy, it comprises historical patient data, including clinical parameters and survival results. 2. Validation Data Set: This set is used to evaluate the model's performance independently of the training data. It contains patient information that was not used to train the model. 3. Patient Data: This data set includes information about specific patients, such as demographics and clinical factors needed to determine survival projections. As patients and healthcare professionals utilize the tool, it is gathered in real-time.

4. Model Parameters: Information used to set up and fine-tune the prediction model, including coefficients, thresholds, and parameters unique to the algorithm.

#### **22.4.1 Paper Link**

Access the full paper at <https://www.sciencedirect.com/science/article/pii/S0959804921003889>

### **22.5 Paper 26: An interactive retrieval system for clinical trial studies with context-dependent protocol elements**

**Journal/Conference Rank:** Q1

**Publication Year:** 2020

**Reference:** []

### **22.6 Summary**

The paper discusses the increasing cost of clinical trials and the importance of well-established protocols for their success. It highlights the challenges of poor study design, leading to increased costs and inefficiencies. The demand for computerized systems to aid in protocol development is emphasized. The advantages of using such systems, particularly those with a database system and advanced information retrieval method, are outlined. The text reviews existing approaches, including expert guidelines and computerized systems, categorizing the latter into database and automated systems. It notes limitations in current clinical trial databases and introduces a new system, Clinical Trial Protocol Database System (CLIPS), designed to enable semantic searches for core content, filterable semantic features, and frame structures within clinical trial protocols. The system utilizes a text mining pipeline and a graph-based querying system to enhance search accuracy and overcome limitations of existing databases.

### **22.7 Software Architecture**

The Clinical Trial Protocol Database System (CLIPS) is a sophisticated platform designed for the efficient retrieval and exploration of clinical trial protocols. Utilizing data from the Aggregate Analysis of ClinicalTrials.gov (AACT), the database employs a relational structure with key-value attributes, focusing on five key elements - design, subject, variables, statistical issues, and descriptions. The schema is crafted for streamlined management and searchability of clinical trial protocol structures. Semantic features are generated through Named Entity Recognition (NER) tools for phenotypes, genes, and chemical compounds, leveraging the Unified Medical Language System (UMLS) for disease phenotypic types and ChemSpot/ChemSpider for chemical compound entities. The web application, developed using Node.js and d3.js, features intuitive interfaces for protocol sequence design, structure visualization, and information retrieval. Query refinement is facilitated through a graph-based interface and semantic filtering connected to a REST NER API. Technical validation involves assessing the semantic filters' performance against a gold standard set from clinicaltrials.gov, employing metrics such as precision, recall, and F1-Score. CLIPS aims to simplify clinical trial retrieval and design, providing a dedicated interface for creating, sharing, and developing clinical trial protocols. The

system employs tools and frameworks like Metamap, Moara, and ChemSpot for text mining, gene annotation using Moara, and web development tools. User interaction involves four stages, including setting protocol order and structure, defining search functions, and accessing detailed protocol information. Performance metrics are employed for ongoing evaluation, using clinicaltrials.gov data for technical validation.

## 22.8 Data Parameters

The development of the Clinical Trial Protocol Database System (CLIPS) relies on crucial data parameters encompassing diverse aspects. Drawing from the Aggregate Analysis of ClinicalTrials.gov (AACT), the database incorporates 184,634 clinical trial protocols organized into a relational table with key-value attributes. The structural elements, including design, subject, variables, statistical issues, and descriptions, form the basis of the database schema crafted for efficient protocol structure management and retrieval. Semantic feature generation involves recognizing 15 disease phenotypic types, identifying chemical compounds with tools like ChemSpot, and normalizing genes using Moara. The web application, built on a Node.js backend and d3.js for visualization, offers interfaces like a drag-and-drop protocol sequence design and a collapsible tree diagram for structure visualization. Validation metrics such as precision, recall, and F1-Score are applied to a gold standard set compiled from clinicaltrials.gov, covering 25 conditional categories and specifically 353 distinct protocols in the "Cancers and Other Neoplasms" category. Users interact with the system through four stages, including setting protocol order and designing structure via a drag-and-drop interface, highlighting the system's user-friendly design. These comprehensive data parameters encapsulate the foundational elements driving the development and functionality of the CLIPS system.

## 22.9 Datasets Used

The cornerstone dataset for the development of the Clinical Trial Protocol Database System (CLIPS) is the Aggregate Analysis of ClinicalTrials.gov (AACT). Released on March 27, 2015, AACT serves as a robust repository of clinical trial information, encompassing trial design, subject details, variables, statistical aspects, and overall trial descriptions. A total of 184,634 clinical trial protocols were extracted from the AACT database, covering diverse facets such as design, subject eligibility, variables, statistical analysis plans, and general trial descriptions. For validation, a gold standard set was compiled from clinicaltrials.gov, initially focusing on the "Cancers and Other Neoplasms" category, which represents 44.74 percent of the total protocol set. The gold standard set includes 82,584 distinct protocols corresponding to 520 disease conditions, and an expanded set comprises 289,956 distinct protocols for 6,172 disease conditions. Semantic feature generation involves utilizing the Unified Medical Language System (UMLS) for disease phenotypic features, ChemSpot for chemical compounds, and Moara for gene recognition and normalization. These datasets play a fundamental role in shaping and evaluating the functionality of the CLIPS system, providing essential clinical trial information and disease conditions for database creation and retrieval system development. The AACT dataset, with its comprehensive clinical trial data from ClinicalTrials.gov, serves as a vital foundation for the project.

### **22.9.1 Paper Link**

Access the full paper at <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0238290>

## **22.10 Paper 27:Security Issues for Web-based Applications: Issues and solutions for the safe transfer of Clinical Trials data over the Internet**

**Journal/Conference Rank:** Q1

**Publication Year:** 2020

**Reference:** []

## **22.11 Summary**

This paper discusses the crucial aspect of security in web-based applications, focusing on the example of the iBiomatics Portal developed by SAS. The authors emphasize the need for addressing security concerns from the initial stages of application design. The paper covers three fundamental areas of security: hardware, development language and tools, and the application itself. The hardware section emphasizes the importance of firewalls in restricting unauthorized access to a network. It explains the role of firewalls in port and IP filtering and highlights the significance of secure socket connections for encrypting data transferred over the Internet. The discussion on development language underscores the choice of Java for the iBiomatics Portal, highlighting Java's inherent security features. The paper explains how Java enforces access restrictions, preventing unauthorized access to local resources, and contrasts it with other technologies like ActiveX. The final section delves into application-level security, addressing questions related to user access, data sharing, and specific security requirements. It details the implementation of user authentication, object security, and functionality restrictions within the iBiomatics Portal. The authors also highlight considerations for complying with industry regulations, such as 21 CFR Part 11, which impact user authentication and data access. Overall, the paper provides insights into building a secure web-based application, covering hardware, development language, and application-specific security measures, using the iBiomatics Portal as a case study.

## **22.12 Software Architecture**

The paper sheds light on the security aspects of the iBiomatics Portal, a web-based application developed by a SAS company. Although the comprehensive software architecture is not explicitly detailed, the paper provides insights into several critical elements. Notably, the iBiomatics Portal is built on Java 2 Enterprise Edition (J2EE), emphasizing its suitability for web-based applications and security, leveraging Java's inherent features. The architecture suggests a database-driven model for user authentication, with user and password information stored centrally. Secure communication is ensured through HTTPS configuration on the web server, complemented by a firewall to control access and connections between the web server and the internal network. The paper underscores diverse security measures, encompassing user authentication, object security, and functionality restrictions, indicative of a layered security architecture. Furthermore, client-side implementation is hinted at through Java applets, with a focus on restricting access to local

resources. Notably, compliance with industry regulations, such as 21 CFR Part 11, shapes considerations for user authentication, password management, and data access controls. While a detailed architectural diagram is absent, the paper provides a comprehensive overview of key elements contributing to the iBiomatics Portal's software architecture, with a strong emphasis on security and regulatory compliance.

## **22.13 Data Parameters**

The paper discusses various data parameters integral to the security architecture of the iBiomatics Portal. These parameters encompass user and password information, stored in a database table accessed by both the web server and the application. The centralization of user authentication data suggests a database-driven approach, ensuring a unified and secure repository for sensitive information. Additionally, the paper emphasizes the secure transfer of data over the Internet, highlighting the use of HTTPS for communication between the web browser and the server. The consideration for industry-specific regulations, particularly 21 CFR Part 11, further underscores the importance of data parameters related to user identification, password management, and access controls. While the paper does not delve into intricate details, it provides a conceptual framework for understanding how data parameters are managed within the iBiomatics Portal, aligning with principles of security and regulatory compliance.

## **22.14 Datasets Used**

The paper does not explicitly detail the specific datasets used in the context of the iBiomatics Portal. However, it broadly discusses the application's purpose, which involves the warehousing, analysis, and review of biomedical data. The term "biomedical data" implies diverse datasets related to medical and biological information. These datasets could potentially include clinical trial data, patient records, genomic data, or other biomedical information crucial for research and analysis. The focus on security measures within the iBiomatics Portal suggests a handling of sensitive and confidential datasets, adhering to industry regulations such as 21 CFR Part 11. While the paper does not delve into the specifics of datasets, it implies the utilization of diverse and sensitive biomedical data within the iBiomatics Portal, necessitating robust security measures and compliance with regulatory standards.

### **22.14.1 Paper Link**

Access the full paper at [https://www.lexjansen.com/pharmasug/2001/Proceed/eBusiness/eb07\\_fagan.pdf](https://www.lexjansen.com/pharmasug/2001/Proceed/eBusiness/eb07_fagan.pdf)

## **22.15 Paper 28: Computational framework to support integration of biomolecular and clinical data within a translational approach**

**Journal/Conference Rank:** Q1

**Publication Year:** 2018

**Reference:** []

## **22.16 Summary**

The paper outlines the challenges in Translational Medicine, focusing on bridging the gap between basic research and clinical applications, emphasizing the diversity of data types involved. It highlights the need for a generic and flexible model due to the heterogeneity of clinical and molecular data. The paper discusses existing computational platforms in translational science, such as Slim-Prim, STRIDE, and I2B2, pointing out their limitations in handling biomolecular data integration. It introduces the proposed framework, IPTTrans, built on the Chado model, a versatile genomic data model. The framework includes a Clinical Module designed for flexible representation of clinical and socio-demographic data using an Entity-Attribute-Value (EAV) model. The paper introduces a migration methodology to adapt legacy clinical databases to the Chado model and proposes ontological mapping using the Translational Medicine Ontology (TMO) with mappings to the ACGT Master Ontology as a common reference. The framework's four levels include data storage, semantic representation with ontologies, application modules, and a web interface using the Catalyst MVC Framework. The paper concludes by presenting a use case involving the integration of oncogenomic data, demonstrating the platform's potential for diverse applications in translational medicine.

## **22.17 Software Architecture**

The proposed software architecture, as outlined in the paper, introduces a comprehensive framework named IPTTrans for Translational Medicine. The architecture consists of four levels: data, semantic, application, and web interface. At the data level, the Chado model is employed as the basic genomic data model, with a novel Clinical Module designed for the flexible representation of clinical and socio-demographic information using an Entity-Attribute-Value (EAV) model. The semantic level involves the use of ontologies, including the Translational Medicine Ontology (TMO) with mappings to the ACGT Master Ontology, acting as a common reference for integrating clinical data. The application level encompasses modules written in Perl, facilitating the management of clinical databases, ontologies, and the data integration process. The web interface level utilizes the Catalyst Model-View-Controller (MVC) Framework to create an interactive tool called IPTTrans. The framework supports the migration of legacy clinical databases to the Chado model and enables data integration, allowing users to query and analyze integrated clinical and biomolecular information seamlessly. The proposed architecture demonstrates flexibility, generality, and potential applications in translational medicine, offering a systematic approach to address the challenges of diverse data types and their integration in biomedical research.

## **22.18 Data Parameters**

The data parameters within the proposed framework encompass various levels of information critical to translational medicine research. These parameters are systematically organized and stored in the Chado model, with a focus on the newly introduced Clinical Module designed for flexible data representation. The patient table within the module serves as a primary repository for patient-specific data, while the patientprop table stores stable clinical or socio-demographic information. Clinical or socio-demographic types, such as age, weight, and tumor characteristics, are defined by ontologies stored in the Controlled Vocabulary Module. The csd (clinic-social data) table is a central component,

providing a flexible structure to capture diverse clinical or socio-demographic information related to patients. The csdprop table stores patient-independent information, ensuring a comprehensive and standardized representation of clinical data. Additionally, the csd relationship table accommodates complex relationships between different clinical parameters. Overall, these data parameters form a robust foundation for capturing and managing the heterogeneous information integral to translational medicine studies, ensuring data consistency, flexibility, and interoperability.

## 22.19 Datasets Used

The proposed platform for translational medicine integrates diverse datasets essential for comprehensive research initiatives. The datasets employed in this framework encompass both clinical and biomolecular information, creating a unified and standardized repository. Clinical datasets, including patient-specific details, are structured using the Chado model, particularly within the newly introduced Clinical Module. These datasets cover a spectrum of socio-demographic and clinical parameters, such as patient profiles, medical history, and treatment information. On the biomolecular side, the framework incorporates datasets derived from advanced omics technologies, such as microarray gene expression data, microRNA data, and nucleotide sequence data. The integration of these datasets is facilitated by ontological mappings, ensuring semantic consistency and enabling cross-disciplinary analysis. The platform's versatility allows researchers to seamlessly navigate and analyze interconnected datasets, fostering a holistic understanding of translational medicine phenomena by bridging the gap between clinical and molecular information. .

### 22.19.1 Paper Link

Access the full paper at <https://rdcu.be/dsVwp>

## 22.20 Paper 29: Electronic Clinical Trial Protocol Distribution via the World-Wide Web: A Prototype for Reducing Costs and Errors, Improving Accrual, and Saving Trees

**Journal/Conference Rank:** Q1

**Publication Year:** 1997

**Reference:** []

## 22.21 Summary

The Physicians Research Network (PRN) was developed as a web-based solution to address the inefficiencies of traditional paper-based clinical trial operations. The system aimed to improve the distribution of trial protocols and increase community physician awareness of available trials. Tested at the Medical University of South Carolina's Hollings Cancer Center and two community oncology practices, PRN successfully eliminated the need for hardcopies of protocols, reduced photocopying by 59 percent, and saved 1.0 full-time equivalents (FTE). Although 1.0 FTE was required to manage PRN, the system proved to be secure, reliable, and favored by users. The implementation marked a shift toward a paperless and user-friendly method for distributing protocols, reducing errors, and addressing delays in the clinical trial process. The success of PRN

in protocol distribution prompted plans for further expansion to encompass other aspects of clinical trial operations, emphasizing its potential as a comprehensive automation tool for the field.

## **22.22 Software Architecture**

The software architecture of the Physicians Research Network (PRN) is characterized by a web-based system designed to enhance the efficiency of clinical trial operations. PRN relies on open standards and platform-independent technologies, employing a server architecture equipped with robust backup, monitoring, and alarm systems. The system operates as a protocol distribution platform, eliminating the need for hardcopies and maintaining a centralized, fully hyperlinked copy of each protocol in HTML format. The loading process involves the conversion of paper-based protocols through document scanning and Optical Character Recognition (OCR), and support for electronic protocols is emphasized. PRN incorporates various indices for categorizing protocols and facilitates user-friendly access through assigned access codes, training in web-browsing software, and stringent security measures. The architecture prioritizes simplicity and automation, utilizing basic HTML coding and automated maintenance tasks to minimize the need for specialized technical expertise. While the detailed technical aspects are not explicitly provided, the system's emphasis on web-based distribution, security, and user accessibility reflects a comprehensive and adaptable software architecture tailored for clinical trial management.

## **22.23 Data Parameters**

The data parameters of the Physicians Research Network (PRN) encompass a range of critical elements in the clinical trial management system. The system relies on a database of protocols represented in HyperText Markup Language (HTML) format, allowing for a centralized and fully hyperlinked repository of trial information. The loading process involves converting paper-based protocols into electronic form through document scanning and Optical Character Recognition (OCR), emphasizing accuracy in data transfer. Security measures, including user access codes and location-based restrictions, ensure the integrity and confidentiality of the stored information. Various indices, such as disease-oriented, source-based, and searchable full-text indices, are employed to categorize and organize the protocols, facilitating efficient retrieval. The data parameters also encompass information about protocol updates, which are processed promptly to maintain the system's currency. While the text does not delve into the technical intricacies of the database management system, the emphasis on maintaining accurate, up-to-date, and well-organized trial information highlights the importance of robust data parameters within the PRN architecture.

## **22.24 Datasets Used**

The specific datasets used in the context of the Physicians Research Network (PRN) are not explicitly detailed in the provided text. However, it mentions the loading of active oncology protocols, encompassing local, industry, and group trials, into the PRN system. These datasets likely include a variety of information such as trial protocols, eligibility criteria, updates, and associated documentation. The loading process involves

the conversion of these datasets from their original paper sources into HyperText Markup Language (HTML) format for web-based accessibility. The emphasis on accuracy in data transfer, as well as the subsequent maintenance of protocols and updates, underscores the importance of reliable datasets within the PRN framework. While the paper doesn't delve into specific datasets or their contents, it implies a focus on oncology trials and the necessary information for managing and disseminating clinical trial protocols effectively.

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#### **22.24.1 Paper Link**

Access the full paper at <https://academic.oup.com/jamia/article/4/1/25/747257>

### **22.25 Paper 30: Managing Clinical Trials Data with a SAS-Based Web Portal**

**Journal/Conference Rank:** Q1

**Publication Year:** 2010

**Reference:** []

### **22.26 Summary**

The Siteman Clinical Information Portal (SCIP) was developed to address the challenges of efficiently collecting electronic data from numerous small clinical trials at the A. J. Siteman Cancer Center. SCIP is a web-based system customized from a suite of browser-based form design tools, facilitating the creation and management of data collection instruments by nonprogrammers. The core tool set includes a form-writing engine driven by a simple database model containing form and item metadata. SCIP supports web-based data entry and editing, offering features such as an audit trail, patient and protocol management tools, and client-side validation rules. The system's design allows for the creation of a library of frequently used items, reducing the effort required for implementing forms. SCIP employs a note tab-based portal model to control access to forms, providing customization for each user. The portal also supports access to other web-based resources, such as electronic versions of protocols. SCIP operates under SAS/IntrNet® on a Linux server. The development of SCIP arose from the need to streamline data management procedures for the high volume of clinical studies conducted at the SCC, replacing manual and disparate data recording methods. The system effectively addresses the challenges posed by the diverse nature of clinical trials, offering a cost-effective and user-friendly solution for data collection and management. The implementation of SCIP enhances efficiency and supports the SCC's commitment to advancing cancer research.

### **22.27 Software Architecture**

The software architecture of the Siteman Clinical Information Portal (SCIP) is a web-based system customized to efficiently collect electronic data from numerous small clinical trials at the A. J. Siteman Cancer Center. SCIP utilizes a suite of browser-based form design tools, featuring a form-writing engine at its core, driven by a simple model of databases containing both form and item metadata. This architecture enables non-programmers to create and manage data collection instruments. The system supports

web-based data entry and editing, providing essential features like an audit trail, patient and protocol management tools, and client-side validation rules. SCIP allows the establishment of a library of frequently used items, streamlining the implementation of forms. Access to forms is controlled through a note tab-based portal model, offering access controls and interface customization for each user. Operating under SAS/IntrNet® on a Linux server, SCIP not only addresses the challenges of diverse clinical trials but also supports access to other web-based resources, exemplifying an architecture designed for efficiency, adaptability, and user accessibility in the clinical research domain.

## **22.28 Data Parameters**

The software architecture of the Siteman Clinical Information Portal (SCIP) is a web-based system customized to efficiently collect electronic data from numerous small clinical trials at the A. J. Siteman Cancer Center. SCIP utilizes a suite of browser-based form design tools, featuring a form-writing engine at its core, driven by a simple model of databases containing both form and item metadata. This architecture enables non-programmers to create and manage data collection instruments. The system supports web-based data entry and editing, providing essential features like an audit trail, patient and protocol management tools, and client-side validation rules. SCIP allows the establishment of a library of frequently used items, streamlining the implementation of forms. Access to forms is controlled through a note tab-based portal model, offering access controls and interface customization for each user. Operating under SAS/IntrNet® on a Linux server, SCIP not only addresses the challenges of diverse clinical trials but also supports access to other web-based resources, exemplifying an architecture designed for efficiency, adaptability, and user accessibility in the clinical research domain.

## **22.29 Datasets Used**

The data parameters within the implementation of the Siteman Clinical Information Portal (SCIP) are intricately designed to centralize information for individuals working on clinical trials at the A. J. Siteman Cancer Center (SCC). At the core of SCIP lies a dynamic form-writing engine capable of generating forms for Clinical Research Associates (CRAs) to enter participant information. The collected data is stored in a standard SAS dataset on the server, facilitating subsequent analyses and reports. SCIP supports the development of a question library, allowing the creation of standardized items for use across multiple studies. Metadata, including response options, requirements, and keywords, is associated with each question, streamlining the form creation process. The web-based interface enables developers to aggregate questions into forms, promoting efficiency and reuse across studies. SCIP further provides tools for CRAs to visualize and track the status of data entry for each participant, along with generating various reports to monitor study progress. The heart of SCIP's architecture is the creation of a question library, aligning with efforts to develop model forms in collaboration with the Clinical Trials Office, Biostatistics Core, and investigators. The question library draws inspiration from the Common Data Element (CDE) project, aiming to standardize and simplify data collection for clinical trials. SCIP employs robust security measures, implementing SSL encryption, password management, and access controls to safeguard sensitive participant information and adhere to privacy regulations, including HIPAA. The system supports user authentication against a local SAS encrypted dataset or an LDAP server, providing

flexibility and integration with other applications. Additionally, SCIP's security features include log monitoring, customizable reports, and automatic logout for inactivity, ensuring a secure and compliant environment for clinical trial data management.

### **22.29.1 Paper Link**

Access the full paper at <https://citeseerx.ist.psu.edu/document?repid=rep1type=pdfdoi=509f0ee98f44f>

## **23 Paper 31: Square<sup>2</sup> - Using digital technologies in clinical trials: Current and future applications**

**Journal/Conference Rank:**

**Publication Year:** 2021

**Reference:** [?]

### **23.1 Summary**

Clinical trials only occasionally used digital technologies in 2015, and there wasn't much advice accessible. But the use of cellphones and digital health devices has significantly increased during the past five years. This paper provides an update on the subject by highlighting numerous use of technology in clinical trials for diverse medical diseases. Digital technology integration in clinical trials now takes many different forms, from using real-world information like electronic health records for recruiting to adding artificial intelligence into diagnostic tools. Notably, some clinical studies can now be carried out fully online, negating the necessity for face-to-face communication. Numerous investigations and studies have demonstrated how these digital strategies can improve clinical trial planning and execution. Even though there are still issues, the field has made encouraging progress, and these difficulties can be surmounted with appropriate preparation.

### **23.2 Software Architecture**

Clinical trials are essential for producing data, but they are frequently expensive, complicated, and time-consuming. Digital technologies present prospects for cost savings, procedure simplification, and a lighter load for clinical trials. The utilization of various digital technologies in clinical trial phases like recruitment, participant consent, delivery of the intervention, data collection, and data management is covered in this study. The authors give examples from recent research that illustrate both totally virtual trials and those integrating digital and conventional methods, spanning a wide spectrum of health issues.

Clinical trials face significant issues with participant recruitment and retention, with participant recruitment frequently leading to delays and study failures. Less than 10 percentage of patients in the United States participate in clinical trials, and rates are even lower for some demographic groups, according to the paper. Digital recruiting and retention strategies are covered, including websites and social media, which can assist in spreading knowledge of trials and finding new volunteers. Further study is necessary, though, to determine how beneficial these tools are. Additionally, messaging and direct emails, have been utilized with various degrees of success, underscoring the necessity for

careful thought and planning in this area. database-screening technologies and other recruitment and retention strategies, like SMS

### **23.3 Data Parameters**

With regard to obtaining appropriate informed consent for electronic materials and protecting participant privacy and confidentiality while using digital technology, the use of digital tools in clinical research raises major ethical, legal, and human subjects problems. These obstacles and constraints demand careful management and thought. Recently, a guide proposing suggestions to address data quality and privacy issues in this context was created by the Clinical Trials Transformation Initiative (CTTI). Eagleson and colleagues have examined the ethical and privacy considerations related to using digital technologies in clinical research, and McKay and colleagues did a systematic review on the efficacy and quality of mobile technology data. These resources offer insightful advice to handle these important problems.

### **23.4 Datasets Used**

Clinical research participant privacy and confidentiality are urgently at risk, particularly in light of recent controversies involving the abuse of social media data. Many mobile applications used for research have ambiguous privacy policies or employ words that are hard to grasp. Furthermore, user data sharing practices are frequently not made clear in app privacy agreements. App privacy and data sharing policies should be carefully reviewed by researchers conducting Randomized Controlled Trials (RCTs) employing apps, and participants should be made aware of these policies during the consent process. Guidance for data protection has improved, and recommendations for security measures against external hazards have been made. Through the cooperation of various stakeholders, including potential participants whose opinions may differ from those of researchers, ethical standards and best practices are being formed. Surprisingly, some social network users do not consider account monitoring for RCT recruitment to be a violation of their privacy. With an emphasis on data protection and administration, the Clinical Trials Transformation Initiative (CTTI) makes suggestions for employing mobile technologies in clinical trials. Blockchain technology is seen as an effective way to improve data security.

The Clinical Data Interchange Standards Consortium (CDISC) has developed requirements for data format in research that regulatory organizations like the FDA have approved. When using data from Electronic Health Records (EHRs) and Real-World Data (RWD) sources, uptake has been sluggish in the research community, posing issues with data quality, validity, security, and privacy. Some suggest implementing CDISC standards to boost the quality of the data coming from EHRs. In conclusion, there are many resources and suggestions available to solve these issues when using digital tools in clinical research, including ensuring data privacy, promoting data interoperability, and strengthening data standards.

## **24 Paper 32: Electronic Data Capture for Registries and Clinical Trials in Orthopaedic Surgery: Jatin Shah BAMS, PDCR, Dimple Rajgor MSc, Shreyasee Pradhan MSc, Mariana McCready BS, Amrapali Zaveri MSc, Ricardo Pietrobon MD, PhD, MBA**

**Journal/Conference Rank:** A

**Publication Year:** 2010

**Reference:** [?]

### **24.1 Summary**

**Summary:** Orthopedic surgeons often collect and analyze clinical data to practice evidence-based medicine, but they face limitations with traditional methods like spreadsheets and offline databases. These methods lack flexibility, security, workflow support, and the ability to generate standardized and interoperable data. Additionally, they often lack structured planning, leading to unachieved goals. This study aims to address these issues by providing an overview of Electronic Data Capture (EDC) systems, their types, pros and cons, and commonly used EDC platforms and features. It also outlines the steps involved in designing a clinical study using DADOS P, an open-source EDC system. international levels, but their adoption at an individual level is lacking. There is a wide Orthopaedic surgeons interested in deploying EDC systems may be confused by the current trend of institutional and national adoption of EDC systems, which includes a variety of features, benefits and drawbacks, and business models. The goal is for orthopedic surgeons to collect data alongside their clinical activities to answer clinical questions and participate in studies effectively. To achieve this, they should adopt a simple, user-friendly, and robust EDC system. Making an informed choice involves a balanced evaluation of available EDC options, aligning them with specific goals and requirements.

### **24.2 Software Architecture**

To lay out a powerful programming engineering for Electronic Information Catch (EDC) frameworks in clinical information assortment, follow these key stages:

1. Assessment: Start by understanding your particular information assortment and examination needs while perceiving the constraints of existing strategies.
2. Research EDC Systems: Investigate the accessible EDC frameworks, surveying their sorts, highlights, benefits, and weaknesses. Pick a framework that lines up with your targets.
3. Plan and Plan: Foster a very much organized execution plan for the picked EDC framework. This includes characterizing work processes, making information assortment frames, and executing safety efforts.
4. Easy to use Interface: Guarantee the EDC framework flaunts an easy to understand interface that muscular specialists can explore effortlessly.
5. Testing: Thoroughly test the product to recognize and amend any issues or bugs. Check that it sticks to the predefined prerequisites.

6. Documentation: Give thorough documentation to direct clients on viable usage of the EDC framework.

7. Deployment: Carry out the EDC framework inside the clinical climate, guaranteeing availability to muscular specialists.

8. Information Collection: Flawlessly gather clinical information close by ordinary exercises, ensuring information normalization and interoperability.

9. Information Analysis: Utilize the EDC framework for productive information investigation, empowering the responding to of clinical inquiries really.

10. Cooperation in Studies: Influence the framework to work with commitment in clinical examinations and exploration.

Generally, the goal is to embrace a clear, easy to understand, and strong EDC framework that upgrades the course of information assortment and examination, all while lining up with your particular objectives and necessities.

**Data Parameters:** Data Parameters for Electronic Data Capture (EDC) Systems in Clinical Data Management:

1. Data Handling: EDC systems aim to streamline data entry, data cleaning, and related activities. Ensuring data accuracy and minimizing errors introduced by multiple individuals during data handling is crucial.

2. Single Point Access: If resources allow, it's preferable to use single point access systems or all-in-one suites that offer comprehensive data capture, management, analysis, and report generation. Examples include Oracle Clinical and InForm.

3. Data Security: Data security is a paramount concern. EDC systems should ideally comply with 21 Code of Federal Regulations (CFR) chapter 11 and Health Insurance Portability and Accountability Act (HIPAA). Data should be stored in encrypted and password-protected servers. Web access should use secure internet protocols. Changes in the database should be tracked through an audit trail.

4. Data Backup and Recovery: A robust data backup and recovery strategy should include redundant backup solutions, remote backup through mirror servers, and tape-based backup. This ensures data integrity and availability.

5. Standards Support: EDC systems should support data interchange standards to facilitate the merging and analysis of data from different studies and sources.

These parameters are essential for the effective and secure management of clinical data using EDC systems. They address issues related to data quality, security, backup, and interoperability, ensuring that EDC systems can be used to make informed decisions in clinical research and practice.

## 24.3 Datasets Used

The provided text outlines key steps for developing software architecture for Electronic Data Capture (EDC) systems in clinical data gathering. It does not, however, list the data sets or sources used in this procedure. The architectural procedures to develop EDC systems are the main focus instead.

### 24.3.1 Paper Link

Access the full paper at <https://link.springer.com/article/10.1007/s11999-010-1469-3> <https://scihub.ee/10.1007/s11999-010-1469-3> <https://www.jmir.org/2005/1/e5>.

## **25 Paper 33: Design of a Web-Tool for Diagnostic Clinical Trials Handling Medical Imaging Research**

**Journal/Conference Rank:**

**Publication Year:** 2018

**Reference:** [?]

### **25.1 Summary**

## **26 Paper 34: African Journal of Pharmacy and Pharmacology Full Length Research Paper Assessment of pharmacy professionals' knowledge and practice on the management and dispensing of investigational drugs in clinical trials**

**Journal/Conference Rank:** A

**Publication Year:** 2010

**Reference:** [?]

### **26.1 Summary**

A study in Burkina Faso (January-June 2018) assessed pharmacy professionals' knowledge in clinical trial drug management. Among 30 participants, only 26 percent had clinical trial training, and 54percent had no trial experience. Less than half knew the pharmaceutical file, and knowledge on prescription validation and treatment delivery varied (60-76percent). Overall, knowledge was considered average. Challenges include inadequate training and regulatory frameworks. The study emphasizes the need for continuous staff training and regulatory improvements to enhance clinical trial quality and competitiveness.

### **26.2 Software Architecture**

Software Architecture for Clinical Trial Pharmacy Assessment: 1. User module: Authentication, secure login for pharmacy professionals, questionnaire management, administering surveys and collecting responses. 2. Training and Knowledge Module: Content Repository, Storage for training materials, Training Scheduler, Scheduling and tracking sessions, Assessment Integration, Measuring knowledge levels and providing immediate feedback. 3. Practice Evaluation Module: Case Studies, Simulated scenarios for practical evaluation, Observation Tracking, Assessing real-world practices, Feedback and Reporting, Detailed reports on observed practices. 4. Data Analytics and Reporting: Analytics Engine: Processing data for insights, Visualization Tools, Charts for easy interpretation, Custom Reports, Tailored reports for stakeholders. 5. Regulatory Compliance Module: Updates and Alerts, Keeping professionals informed, Documentation Repository, Storage for guidelines. 6. Communication and Collaboration: Messaging System, Facilitating

communication, Discussion Forums, Sharing best practices and experiences. 7. Security and Compliance: Data Encryption, Ensuring information security, Audit Trail, Logging actions for accountability, This concise architecture addresses data collection, training, assessment, and communication, enhancing the knowledge and practices of pharmacy professionals in clinical trial drug management.

## 26.3 Data Parameters

Authentication: Username, Password Demographics: Name, Position Training History: Courses taken, Dates Participation History: Clinical trials involved, Dates Knowledge Assessment: Scores, Responses Practice Evaluation: Observations, Responses Communication: Messages, Forum Posts

## 26.4 Datasets Used

User - ID, Name, Position, Training, Engagement Questionnaire: - ID, Question, Answers Training:- Course ID, Materials, Timetable Assessment: - ID, Date, Scores Practice: - ID, Date, Observations Regulatory: - Update ID, Text, Timestamp Documentation - Document ID, Name, Content, Upload Date Observation - ID, Date, Observations Security: - Log Action, Timestamp, and ID

### 26.4.1 Paper Link

Access the full paper at [https://www.researchgate.net/publication/372044626\\_African\\_Journal\\_of\\_Pharmaceutical\\_Science\\_Paper\\_35\\_Risk-Based\\_Monitoring\\_in\\_Clinical\\_Trials\\_Past,\\_Present,\\_and\\_Future](https://www.researchgate.net/publication/372044626_African_Journal_of_Pharmaceutical_Science_Paper_35_Risk-Based_Monitoring_in_Clinical_Trials_Past,_Present,_and_Future)

**Journal/Conference Rank:** A

**Publication Year:** 2010

**Reference:** [?]

## 26.5 Summary

In this report, the Association of Clinical Research Organizations (ACRO) performed a landscape survey among its member organizations to examine the level of Risk-Based Monitoring (RBM) adoption in the clinical trial sector. The survey included 6,513 clinical studies that were still active at the end of 2019. Among the key results are: Components of RBM: Key risk indicators (KRIs), centralized monitoring, off-site/remote monitoring, reduced source data verification (SDV), and reduced source document review (SDR) were all used in 22 percent of the trials assessed. Implementation Rates: Implementation rates for particular RBM components ranged from 8percent to 19percent. Centralized monitoring was the most often deployed component, while decreased SDR was the least usually implemented. Impact of COVID-19: Additional data collected during the COVID-19 pandemic showed a significant shift from on-site to off-site/remote-site monitoring. Despite this shift, there was little or no reduction in monitoring effectiveness, as similar numbers of non-COVID-related protocol deviations were detected. Monitoring Effectiveness During Pandemic: The majority of monitoring visits were initially on-site in February 2020, but by April, an even higher percentage were off-site, corresponding with the first peak of the pandemic. Opportunity for RBM Uptake: Both pre- and mid-pandemic data emphasize the need to promote the adoption of RBM. The shift toward greater RBM uptake during the pandemic presents an opportunity for continued adoption in a

post-pandemic environment. The overall conclusion is that RBM is a powerful tool for enhancing patient safety and data integrity in clinical trials. The survey results highlight the variability in RBM implementation rates and the positive impact of RBM during the COVID-19 pandemic, providing valuable insights for promoting the continued adoption of RBM in the future. In this report, the Association of Clinical Research Organizations (ACRO) performed a landscape survey among its member organizations to examine the level of Risk-Based Monitoring (RBM) adoption in the clinical trial sector. The survey included 6,513 clinical studies that were still active at the end of 2019. Among the key results are: Components of RBM: Key risk indicators (KRIs), centralized monitoring, off-site/remote monitoring, reduced source data verification (SDV), and reduced source document review (SDR) were all used in 22 percent of the trials assessed. Implementation Rates: Implementation rates for particular RBM components ranged from 8 percent to 19 percent. Centralized monitoring was the most often deployed component, while decreased SDR was the least usually implemented. Impact of COVID-19: Additional data collected during the COVID-19 pandemic showed a significant shift from on-site to off-site/remote-site monitoring. Despite this shift, there was little or no reduction in monitoring effectiveness, as similar numbers of non-COVID-related protocol deviations were detected. Monitoring Effectiveness During Pandemic: The majority of monitoring visits were initially on-site in February 2020, but by April, an even higher percentage were off-site, corresponding with the first peak of the pandemic. Opportunity for RBM Uptake: Both pre- and mid-pandemic data emphasize the need to promote the adoption of RBM. The shift toward greater RBM uptake during the pandemic presents an opportunity for continued adoption in a post-pandemic environment.

## 26.6 Software Architecture

Designing a software architecture for Risk-Based Monitoring (RBM) in clinical trials involves considering various components to ensure efficiency, data integrity, and patient safety. Here's a simplified software architecture for RBM in clinical trials:

- Frontend Application: User Interface (UI):** Allows users to interact with the system. Provides dashboards for real-time monitoring of clinical trials. Enables access to reports, analytics, and key risk indicators.
- Backend Services:**
  - User Management:** Manages user roles and permissions. Authentication and authorization for different stakeholders (e.g., monitors, investigators, sponsors).
  - Trial Configuration:** Configures trial-specific parameters and risk assessment criteria. Defines Key Risk Indicators (KRIs) and monitoring strategies.
  - Monitoring Strategy Engine:** Determines the monitoring strategy based on trial parameters and risk assessment. Handles the logic for when to use centralized monitoring, remote-site monitoring, etc.
  - Data Processing:** Integrates with clinical trial databases and data sources. Processes and analyzes trial data to identify potential risks. Generates alerts and notifications based on predefined risk thresholds.
  - Reporting and Analytics:** Generates reports on trial progress, risk trends, and monitoring effectiveness. Provides analytics tools for in-depth analysis of trial data.

## 26.7 Data Parameters

This article gives us the results of a landscape survey on risk-based monitoring (RBM) implementation in clinical trials. Based on that, here are some data parameters that can be derived:

- Total Number of Clinical Trials (as of the end of 2019):** The total number of

clinical trials surveyed in 2019 is 6,513. RBM Implementation Rates: Overall RBM implementation rate: 22 percent of the surveyed trials included at least one of the five RBM components. Implementation rates for individual RBM components: Ranged from 8RBM Components: Key Risk Indicators (KRIs) Centralized Monitoring Off-site/Remote-site Monitoring Reduced Source Data Verification (SDV) Reduced Source Document Review (SDR) Impact of COVID-19 on Trial Monitoring: Percentage of monitoring visits that were on-site in February 2020. Percentage of monitoring visits that were off-site in April 2020 (during the first peak of the pandemic). Comparison of on-site vs. off-site monitoring effectiveness. Number of non-COVID-related protocol deviations detected from February through June. Implementation Rates During the Pandemic: How the implementation rates of RBM components changed during the COVID-19 pandemic. Any notable shifts in the adoption of RBM during the pandemic. Post-Pandemic Environment: Opportunities for greater RBM uptake in a post-pandemic environment. Considerations for promoting the adoption of RBM based on the experiences during the pandemic.

## 26.8 Datasets Used

Initial cross-functional risk assessment Ongoing cross-functional risk assessment QTLs (Quality Tolerance Limits) KRIs (Key Risk Indicators) Centralized monitoring Off-site/remote-site monitoring Reduced SDV (Source Data Verification) Reduced SDR (Source Document Review)

### 26.8.1 Paper Link

Access the full paper at [https://www.researchgate.net/publication/351204326\\_Risk-Based\\_Monitoring\\_in\\_Clinical\\_Trials](https://www.researchgate.net/publication/351204326_Risk-Based_Monitoring_in_Clinical_Trials)  
sectionPaper 36: Risk Management in Clinical Trials: Assessment of Current Practices  
at Portuguese Clinical Trial Sites **Journal/Conference Rank:** A  
**Publication Year:** 2010  
**Reference:** [?]

## 26.9 Summary

This cross-sectional study aimed to assess the implementation of risk management activities in Portuguese clinical trial sites. Conducted through a non-validated questionnaire, the survey revealed that 57.0 percent of sites reported using a systematic risk management tool. However, only 19.6 percent described having a standard tool for systematically analyzing risks at the site level. The majority of sites (87.0 percent) expressed willingness to adopt a risk management tool tailored to their operational needs. Lack of knowledge about risk management was identified as the primary obstacle to implementation. The study suggests that, while clinical trial sites recognize the importance of risk management, there is a current lack of experience with these methodologies, hindering widespread adoption. The development of a tailored risk management tool is proposed to address this gap in the management of trial-related operations.

## 26.10 Software Architecture

User Interface (UI): Features may include risk assessment forms, tools for systematic analysis, and options for tailoring risk management strategies. Database: A centralized

database stores information related to clinical trials, risk assessments, and risk management activities. Risk Analysis Engine: It performs risk assessments based on predefined criteria, helps in identifying potential risks, and provides insights into effective risk management strategies. Tailoring Module: Users can define and modify risk assessment criteria, risk categories, and preferred risk mitigation actions. Knowledge Base: A knowledge base stores resources, guidelines, and best practices related to risk management in clinical trials. Notification and Alert System: The system should include notifications and alerts to inform users about upcoming risk assessments, changes in risk status, and recommended risk management actions. Authentication and Authorization: User roles and permissions are defined to control access to different functionalities.

## 26.11 Data Parameters

Demographic Information: Site ID or code, Location or region of the clinical trial site. Obstacles to Implementation: Reasons for not implementing risk management tools, Identification of the primary obstacles hindering implementation. Knowledge about Risk Management: Assessment of the level of knowledge about risk management among clinical trial sites. Proposed Solutions: Identification of proposed solutions or interventions to address the lack of experience with risk management methodologies, Suggestions for the development of a tailored risk management tool.

## 26.12 Datasets Used

Clinical Trial Sites: SiteID — SiteName — Location — TotalTrials 101 — ABC Hospital — Lisbon — 20 102 — XYZ Clinic — Porto — 15 103 — Medical Center — Coimbra — 25 Risk Management Tool Usage: SiteID — Tool Used — Standard Tool — Custom Tool 101 — Yes — No — Yes 102 — No — No — Yes 103 — Yes — Yes — No

### 26.12.1 Paper Link

Access the full paper at [https://www.researchgate.net/publication/375380553\\_RiskManagementinClinicalTrials](https://www.researchgate.net/publication/375380553_RiskManagementinClinicalTrials)  
sectionPaper 37: Employing Computers for the Recruitment into Clinical Trials: A Comprehensive Systematic Review  
**Journal/Conference Rank:** A  
**Publication Year:** 2010  
**Reference:** [?]

## 26.13 Summary

Clinical trial recruitment support systems (CTRSS) facilitate the evaluation of new medical interventions. A review of 101 papers on 79 systems revealed three dominant types. Newer systems involve patients directly, emphasizing workflow integration over complex algorithms. Recent literature suggests improved patient recruitment and efficiency. The authors propose a checklist for standardized reporting in future CTRSS research.

## 26.14 Software Architecture

1. User Interface: - Patient and Provider Interfaces
2. Data Management: - Clinical Data Repository - Patient Data Input
3. Workflow Integration:- Workflow Engine - Event

Monitoring 4. Reasoning Algorithm:- Eligibility Assessment Algorithm 5. Communication: - Notification System 6. Reporting and Analytics: - Reporting Engine - Analytics Module 7. Security: - Authentication and Authorization - Data Encryption 8. Integration Interfaces: - EHR Integration- External Systems Interface 9. Patient Engagement:- Patient Education- Feedback System 10. Compliance:- Regulatory Checker- Audit Trail

## 26.15 Data Parameters

1. User Data: - ID, Type, Name, Credentials 2. Clinical Data: - Patient ID, History, Eligibility 3. Workflow Data: - Events, Triggers 4. Reasoning Algorithm: - Criteria, Results 5. Communication Data - Content, Recipients 6. Reporting and Analytics: - Metrics, Insights 7. Security Data: - Logs, Encryption Status 8. Integration Interfaces: - EHR, External Systems 9. Patient Engagement Data: -Content, Feedback 10. Compliance Data: - Compliance Status, Audit Trail

## 26.16 Datasets Used

1. Publication Metadata: - Title, Authors, Publication Date, Journal 2. Research Methodology Data: - Inclusion Criteria, Search Strategy, Study Selection Stats 3. Characteristics of Included Studies: - Title, Authors, Trial Type, Recruitment Tools 4. Effectiveness Metrics: - Success Rates, Impact on Enrollment, Comparison Data 5. Features and Limitations of Tools: - Tool Features, Implementation Challenges 6. Patient Demographics: - Participant Demographics, Comparisons 7. Technology Adoption Trends: - Adoption Trends, Regional Variances 8. Challenges and Solutions: - Common Challenges, Innovative Solutions 9. Outcome Measures: - Assessed Outcomes, Outcome Variations 10. Recommendations and Future Directions: - Review Recommendations, Identified Gaps

### 26.16.1 Paper Link

Access the full paper at <https://sci-hub.se/https://www.jacc.org/doi/abs/10.1016/j.jchf.2019.12.010>  
sectionPaper 38: Natriuretic Peptides as Inclusion Criteria in Clinical Trials **Journal/Conference Rank:** A

**Publication Year:** 2010

**Reference:** [?]

## 26.17 Summary

This study explores the utilisation of B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) as inclusion criteria in heart failure (HF) clinical trials. Among 3,446 identified HF trials, 365 (10.6percent) incorporated either BNP or NT-proBNP as inclusion criteria. The research reveals significant variations in the choice of natriuretic peptide and cutoff values across trials, with 43 percent using both, 33 percent using only NT-proBNP, and 24percent using only BNP. Trials using both peptides generally showed higher cardiovascular event rates and concentrations for study entry. The paper discusses best practices, and uncertainties in specific patient populations, and emphasises the importance of documenting such criteria in ClinicalTrials.gov for future research efforts.

## **26.18 Software Architecture**

The specific data parameters for the "Natriuretic Peptides as Inclusion Criteria in Clinical Trials" project would depend on the detailed requirements and goals of the project. However, here are some potential data parameters that could be relevant to such a clinical trial:

1. Patient Information: - Patient demographics (age, gender, ethnicity). - Medical history, including pre-existing conditions. - Vital signs and other relevant health indicators.
2. Natriuretic Peptide Data: - B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentrations. - Measurement units and methods used for natriuretic peptide assessment. - Cutoff values for inclusion/exclusion criteria.
3. Clinical Trial Protocol: - Trial start and end dates. - Inclusion and exclusion criteria. - Randomization details (if applicable).
4. Intervention and Treatment Data: - Details of the treatment or intervention being tested. - Dosage, frequency, and duration of treatment.
5. Outcome Measures: - Primary and secondary endpoints. - Criteria for assessing treatment efficacy. - Adverse events and safety data.
6. Site and Investigator Information: - Information about the clinical trial sites. - Principal investigator details.
7. Ethical and Regulatory Documentation: - Informed consent forms. - Ethical approval documentation. - Regulatory compliance records.
8. Data Monitoring and Quality Assurance: - Mechanisms for data monitoring and quality control. - Data validation rules and checks.
9. Interoperability Data: - Standards and protocols for interoperability with external healthcare systems. - Data exchange formats.
10. Patient Consent and Privacy: - Documentation of patient consent. - Measures taken to ensure patient data privacy.

## **26.19 Data Parameters**

The data parameters for the "Natriuretic Peptides as Inclusion Criteria in Clinical Trials" project include:

1. Patient Information: Demographics, medical history, and vital signs.
2. Natriuretic Peptide Data: BNP and NT-proBNP concentrations, cutoff values.
3. Clinical Trial Protocol: Start/end dates, inclusion/exclusion criteria, randomization.
4. Intervention and Treatment Data: Treatment details, dosage, and duration.
5. Outcome Measures: Primary/secondary endpoints, safety data.
6. Site and Investigator Information: Trial site details, principal investigator.
7. Ethical and Regulatory Documentation: Informed consent, ethical approval, and regulatory compliance.
8. Data Monitoring and Quality Assurance: Monitoring mechanisms, and data validation.
9. Interoperability Data: Standards for interoperability, data exchange formats.
10. Patient Consent and Privacy: Consent documentation, privacy measures.

## **26.20 Datasets Used**

1. Heart Failure Patient Data: - Demographics, clinical history, medication, and lab results.
2. Clinical Trial Data: - Trial details, interventions, criteria, and outcomes.
3. Natriuretic Peptide Data: - BNP/NT-proBNP levels, variations, and correlations.
4. Multi-Center Trial Data: - Regional differences in trial outcomes.
5. Longitudinal Data: - Patient follow-up, changes over time, and long-term outcomes.
6. Genomic and Biomarker Data: - Genetic info, heart failure biomarkers, and treatment response factors.
7. Real-World Data: - Electronic health record-based outcomes, comparing trials with real-world results.
8. Patient Reported Outcomes (PRO) Data: - Symptoms, quality of life, and PROs linked to natriuretic peptides.
9. Coexisting Conditions Data:- Impact of

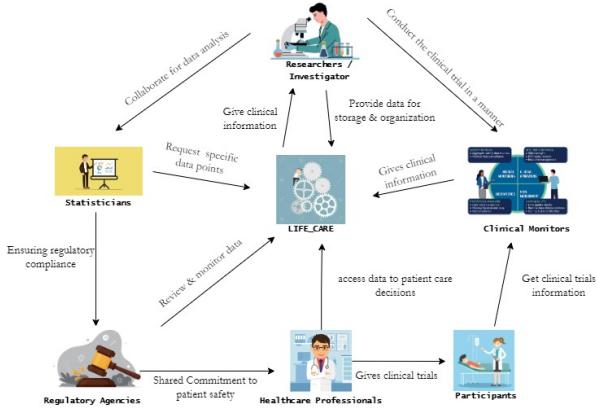


Figure 15: As is rich picture of the existing system

other conditions on heart failure treatment. 10. Patient Compliance Data: - Medication adherence, appointment attendance, and correlations with natriuretic peptides.

### 26.20.1 Paper Link

Access the full paper at <https://www.jmir.org/2014/7/e161/>

## 27 System Design

Write about the System Design:- Rich Picture, ERD, Relation Schema, Normalized Schema, Data Dictionary. Intro about what is below:

### 27.1 Rich Picture

Elements in the As-Is Rich Picture:

Clinical Monitors: Represented as individuals or symbols monitoring and overseeing clinical activities. Interacting with researchers, healthcare professionals, and the system. Collecting and reviewing data from the participants. Researchers: Shown engaged in research-related activities. Collaborating with clinical monitors and healthcare professionals. Analyzing data and generating insights. Regulatory Agencies: Depicted as external entities overseeing compliance and regulatory aspects. Interacting with clinical monitors and receiving necessary documentation. Healthcare Professionals: Represented in various roles such as doctors, nurses, and support staff. Involved in participant care, data collection, and collaborating with researchers. Participants: Depicted as individuals taking part in clinical trials or research studies. Engaging with healthcare professionals, providing data, and undergoing interventions. System: Illustrated as a central entity connecting various components. Representing the technological infrastructure facilitating data storage, retrieval, and analysis. Connecting users for efficient communication and information flow. Demographers: Shown as specialists in demographic data. Collaborating with researchers for demographic analysis and reporting.

Creating a rich picture for a proposed system involving clinical monitors, researchers, regulatory agencies, healthcare professionals, participants, system, and demographers is a visual representation that aims to capture the essence and complexity of the system. It includes various elements and relationships among stakeholders. Here's a description of the

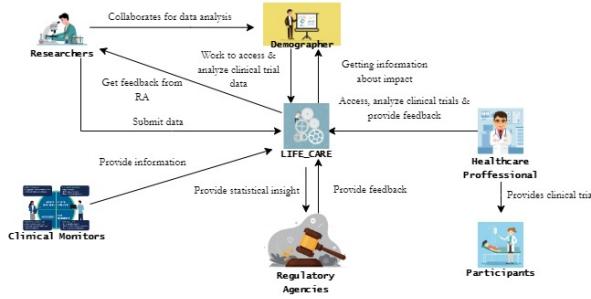


Figure 16: To be rich picture of proposed system

rich picture: The core of the picture represents the proposed system, with interconnected components and modules that facilitate data collection, analysis, and collaboration. Depict clinical monitors reviewing data and ensuring compliance with protocols. Visualize their interactions with the system, monitoring dashboards, and communication channels. How researchers involved in data analysis, hypothesis testing, and study design. Illustrate collaboration tools, data repositories, and research-related modules within the system. Include symbols or representations of regulatory bodies overseeing compliance. Connect them to the system through compliance modules and data submission channels. Visualize healthcare professionals accessing relevant patient data, contributing insights, and receiving updates. Emphasize the integration of the system with healthcare workflows. Represent participants contributing data and feedback. Highlight participant engagement tools, data entry points, and privacy/security measures. Illustrate demographers studying population data trends. Connect them to demographic analysis tools and data visualization components. Use arrows to show the flow of information and communication between stakeholders and the system. Differentiate between feedback loops, data exchange, and notifications.

## 27.2 ERD

This ERD captures the relationships between the Clinical Monitor and other key entities in the clinical monitoring process, including research sites, study protocols, participants, and visit reports. It reflects the associations and interactions that clinical monitors have within the broader clinical research context. Note that this is a simplified representation, and additional details or entities may be included based on the specific requirements of the clinical monitoring system.

## 27.3 Relation Schema

Add Image and describe it thoroughly.

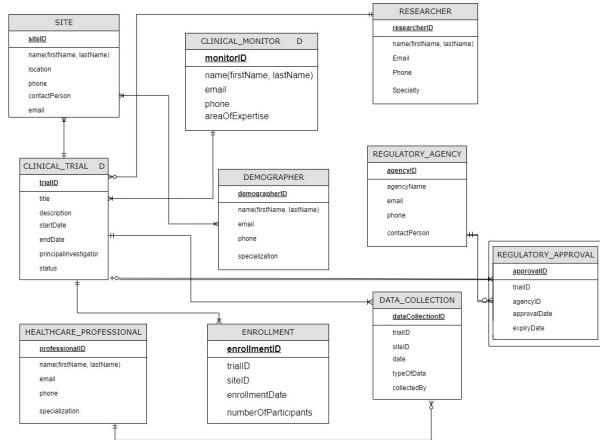


Figure 17: ERD

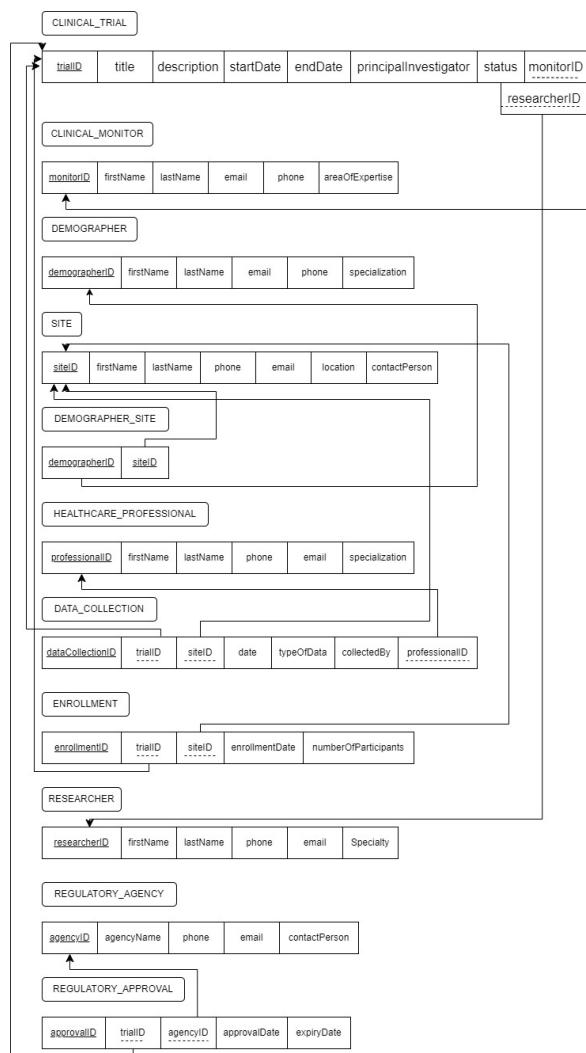


Figure 18: Relation schema

s1	s2	s3	s4	v1	v2	v3	p1	p2	p3
p4	p5	d1	d2	d3	d4	r1	r2	r3	r4
r5	u1	u2	u3	e1	e2	e3			

Table 1: 1NF

s1	s2	s3	s4	v1	v2	v3	p1	p2	p3
p4	p5	d1	d2	d3	d4	r1	r2	r3	r4
r5	u1	u2	u3	e1	e2	e3			

Table 2: 1NF

## 27.4 Normalized Schema / Normalization

Add Image and describe it thoroughly.

Study (s)	studyId (s1) , title (s2) , startDate (s3) , endDate (s4)
Visit (v)	visitId (v1) , visitDate (v2) , purpose (v3)
Patient (p)	patientId (p1) , fName (p2) , lName (p3) , gender (p4) , contactInfo (p5) , studyId (p6)
DataPoint (d) (p)	dataPoint (d1) , varName (d2) , varValue (d3) , dataType (d4) , visitId (v1) , patientId (p1)
Researcher(r)	researcherId (r1) , fName (r2) , lName (r3) , contactInfo (r4) , credentials (r5)
User(u)	userId (u1) , userName (u2) , password (u3) , researcherId (r1) , roleId (e1)
Role(e)	roleId (e1) , roleName (e2) , description (e3)
s	s1, s2, s3
v	v1, v2, v3
p	p1, p2, p3, p4, p5, s1
d	d1, d2, d3, d4, v1
r	r1, r2, r3 ,r4, r5
u	u1, u2, u3, r1, e1
e	e1, e2, e3

## 27.5 Data Dictionary

Add Image and describe it thoroughly.

# 28 Methodology and Implementation

## 28.1 Which framework and softwares are being used

Make a better subsection title describe it thoroughly.

## 28.2 Interface Design and Implementation

Add image of the interfaces and describe them thoroughly with it's purpose and functionality.

### 28.2.1 Dashboard

Add image of dashboard and describe and write a tentative SQL query for it's execution.

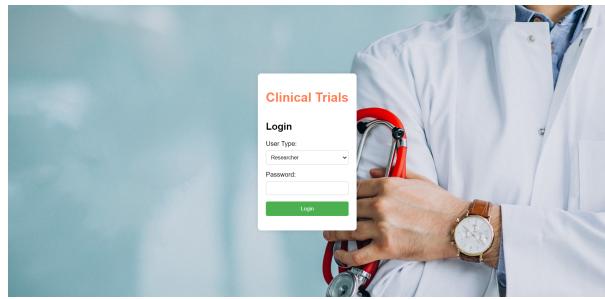


Figure 19: Login Page

**Feedback Page**

**Give Your Feedback**

Name:

Email:

Feedback:

**Submit Feedback**

**View Feedback**  
No feedback available yet.

© 2023 Feedback Page. All rights reserved.

Figure 20: Feedback Page

**Healthcare Professional - Patient Information**

<b>Patient Information</b>	<b>Patient Details</b> Patient ID: 12345 Name: John Doe Date of Birth: January 1, 1980	<b>Edit / Add Patient Information</b>
		First Name: <input type="text"/> John
		Last Name: <input type="text"/> Doe
		Date of Birth: <input type="text"/> 01-Jan-1980
		Diagnosis: <input type="text"/> Condition X
		Treatment: <input type="text"/> Medication ABC
		Admission Date: <input type="text"/> 01-Jan-2023
		<b>Save Changes</b>

Figure 21: Healthcare professional

**Regulatory Agency Feedback**

**Graph Analysis**

**Regulatory Feedback Form**

Comments:

Approval Status:  Approved

**Submit Feedback**

Figure 22: Regulatory Agencies

**Researcher - Clinical Trial Form Creator**

<b>Clinical Trial Form Creation</b>	<b>Form Details</b> Form Title: <input type="text"/> Form Description: <input type="text"/>	<b>Add Form Fields</b> Field Type: <input type="dropdown"/> Text Field Name: <input type="text"/>
		<b>Save Form Details</b>

© 2023 Researcher. All rights reserved.

Figure 23: Researcher

Clinical Monitor - Patient Information

Patient Information  
Enter Patient Information

First Name:

Last Name:

Date of Birth:  dd-mm-yyyy

Diagnosis:

Treatment:

Admission Date:  dd-mm-yyyy

Figure 24: Clinical Monitor

## 29 Result Analysis

Describe the analysis you've got.

## 30 Conclusion and Future Work

The landscape of web applications for storing and analyzing clinical trial data reflects common themes of data security, integration, cloud-based solutions, standardization, and real-time monitoring. Differences arise in the targeted specialties, regulatory compliance, data volume, analytical methods, and patient engagement. Notable trends include AI and machine learning integration, mobile accessibility, data visualization, patient-centric approaches, and collaborative data sharing. Gaps in the literature include long-term data management, ethical and regulatory challenges, data quality assurance, patient recruitment and retention, and interoperability. Future research will involve developing a patient-centric web application for rare disease clinical trials, emphasizing patient engagement, data standardization, AI-driven analytics, privacy, and long-term data management, while addressing ethical and regulatory considerations, ultimately contributing to advancements in this field.

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