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Organization of the data monitoring process within the framework of clinical trials

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Abstract

This article explores innovative methodologies for organizing the data monitoring process in clinical trials, with a focus on traditional, remote, and risk-based approaches, as well as the integration of digital technologies. Through a comparative analysis of monitoring models, the study highlights the advantages of combining these methods in multicenter projects to enhance data accuracy, security, and compliance with modern regulatory standards. The findings demonstrate that digitalization and centralized systems significantly improve monitoring efficiency and risk management, offering actionable recommendations for clinical researchers and project managers. The materials of the article are based on a comparison of different monitoring models. Their application in multicenter projects is being considered, and their compliance with modern regulatory requirements is being assessed. Special attention is paid to the stages of planning, execution, completion of monitoring, as well as the introduction of information technologies. The possibilities of using data management systems. The results confirm that the combination of methods using elements of digitalization helps to increase the efficiency of data analysis, and minimizes the risks that arise in the process of processing large amounts of information. Ensuring data security and adapting monitoring to the specifics of specific projects is of particular importance. This work is of interest to researchers, clinical project managers, and specialists involved in the development of digital solutions. The proposed recommendations are aimed at introducing relevant approaches that meet the requirements of modern science. Data monitoring remains an important element of clinical research. To achieve these goals, it is necessary to use methods that combine traditional practices and innovative solutions aimed at improving management and data processing technologies.

Keywords: Data monitoring; Clinical trials; Risk-based monitoring; Digital technologies; Data management systems; Analytical platforms

1. Introduction

Data control in randomized controlled trials (RCTs) plays a crucial role in ensuring the reliability and validity of clinical outcomes. This process requires strict adherence to data validation and verification protocols for accurate information processing. Its objectives include preventing systematic and random errors, upholding bioethical standards, and protecting the rights of study subjects.

The increasing volume of biomedical data necessitates the development of effective solutions for analysis and management. Enhanced regulatory requirements from oversight bodies drive the creation of strategies that optimize information processing in electronic data capture (EDC) systems. Innovative methodologies enable the rationalization of resource utilization, more efficient data management, and improved research process efficacy.

The objective of this article is to examine existing data control methodologies in clinical trials, analyze their characteristics and limitations, and formulate recommendations for their enhancement in accordance with current Good Clinical Practice (GCP) requirements.

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2. Material and methods

Scientific studies on data monitoring in clinical trials encompass diverse methodologies, including traditional on-site monitoring, remote monitoring, centralized monitoring systems, digital tools, statistical and Bayesian algorithms, and organizational frameworks.

The study by Yamada O. et al. [1] presents a comparative analysis between traditional monitoring methods and remote monitoring technologies, highlighting practical advantages such as management flexibility and cost reduction. Shen L. et al. [5] describe an EDC system that ensures prompt and accurate data monitoring. Houston L. et al. [3] examine regional peculiarities in the application of these methods.

Centralized monitoring approaches are recognized as effective management tools. Afroz M. A., Schwarber G., and Bhuiyan M. A. N. [4] emphasize their relevance during the COVID-19 pandemic when minimizing in-person contact became a priority. Olsen M. H. et al. [6] developed a model for multicenter projects focused on data integration. Love S. B. et al. [2] underline the importance of separating processes for data cleaning and centralized monitoring, requiring independent execution.

Digital technologies are evaluated in Zhang H. et al. [12], highlighting platforms that optimize data collection and processing. Shen L. et al. [5] focus on automated systems that enhance audit efficiency.

The Bayesian approach, utilizing prior probabilities for adaptive analysis, is presented by Hatayama T. and Yasui S. [7]. Anisimov V. and Austin M. [10] describe statistical methods aimed at managing participant recruitment processes and resource allocation.

Machado T. et al. [11] emphasize the role of Data Monitoring Committees (DMCs) in pediatric studies, addressing patient safety and adherence to ethical standards. Bryant K. E. et al. [8] analyze organizational challenges associated with implementing centralized models in large-scale projects.

Houston L. et al. [9] identify key data quality issues, including insufficient staff training and technical barriers.

A review of scientific literature demonstrates the advancement of data monitoring methods, particularly in the context of digitalization and process centralization. However, unresolved issues remain, such as standardizing data processing approaches, adapting methods to specific project requirements, and engaging participants in management processes.

In this study, various methods were applied to analyze and develop approaches for improving data monitoring standards in clinical trials

3. Results and Discussion

Data monitoring serves as a quality control instrument to ensure protocol compliance and data integrity. Its significance increases in the context of multicenter clinical trials, complex study designs, or implementation of innovative methodologies such as adaptive trial designs.

The primary monitoring objectives include identifying protocol deviations, verifying source data accuracy, and assessing risks associated with ethical non-compliance or methodological errors [1]. This process constitutes an essential component of mandatory procedures governed by International Council for Harmonisation Good Clinical Practice (ICH GCP) guidelines. Figure 1 illustrates monitoring approaches, which are determined by study scope, methodological complexity, and resource availability.

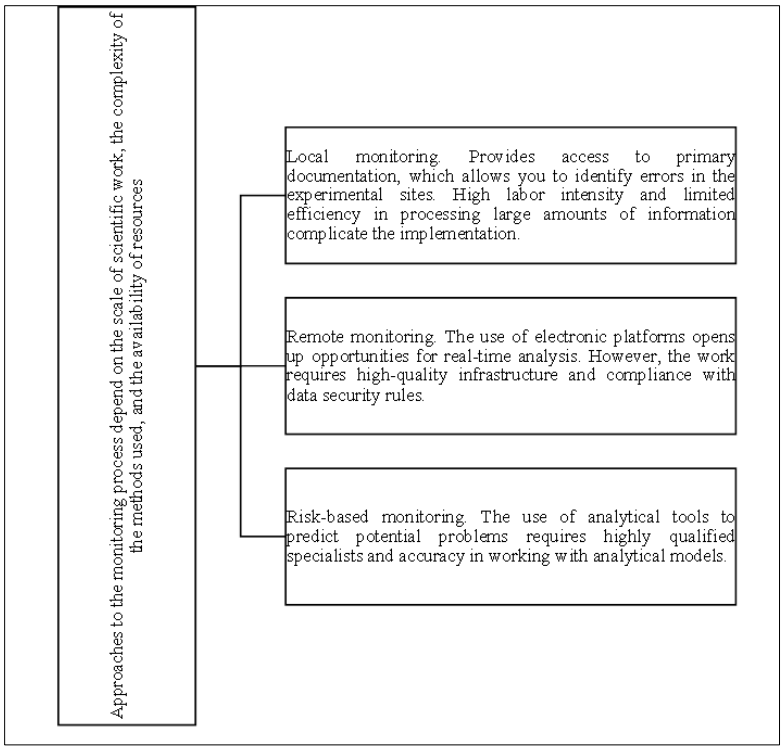

Figure 1 Approaches to the monitoring process depend on the scale of scientific work, the complexity of the methods used, and the availability of resources (compiled by the author)

Optimization frequently involves integrating multiple approaches. For operational processes, automated systems facilitate data collection, processing, and analysis, including:

- Electronic Case Report Forms (eCRFs): Standardized forms minimize data entry errors and streamline verification procedures.
- Clinical Data Management Systems (CDMS): Enable integration of data from multiple sources, centralized processing, and detection of data discrepancies.
- Statistical Analysis Systems (SAS): Used for pattern identification, large dataset processing, and risk assessment [3].

The key stages are visually represented in Figure 2.

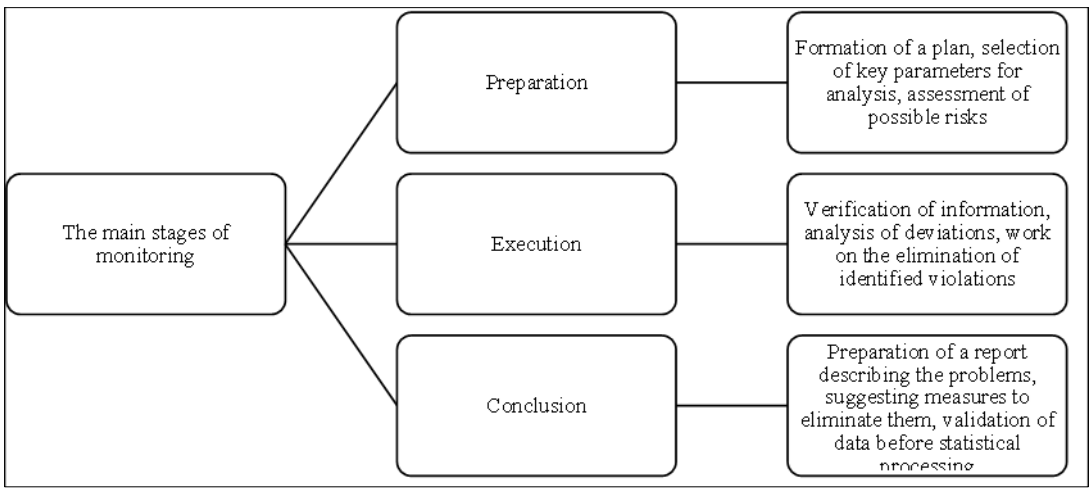

Figure 2 The main stages of monitoring (compiled by the author)

As illustrated in Figure 2, monitoring encompasses three stages, each with defined objectives. Following examination of clinical trial data monitored by Contract Research Organizations (CROs) at study sites, attention will focus on specific considerations for trials conducted in healthcare institutions. This quality control process ensures adherence to standards during data collection, analysis, and reporting in accordance with the protocol, regulatory requirements, and ICH GCP principles. Various monitoring approaches are outlined in Table 1.

Table 1 Description of Methods (compiled by the author)

Method	Description
Traditional on-site	Involves visiting research centers to analyze documentation and verify data compliance with established standards.
Centralized approach	Conducted remotely using electronic systems, enabling timely detection of deviations and assessment of overall trends.
Risk-based approach	Focuses on key aspects, reducing the volume of checks on less critical elements.

For effective data collection, study sites must facilitate open communication to ensure subjects report all adverse events (AEs) and symptoms. Observing participants' non-verbal cues and affect is essential for identifying unreported adverse events or discomfort. The Principal Investigator (PI) or Sub-Investigator should conduct structured interviews during scheduled visits, documenting findings in source documents:

- Have there been any changes in activities of daily living (ADL) since the last visit?
- Has there been any social or occupational impairment due to physical or psychological symptoms?
- Have any new symptoms or adverse events been noticed since initiating the investigational medicinal product (IMP)?
- Has the dosage regimen of any concomitant medications been modified?
- Have there been any cutaneous reactions or hypersensitivity responses post-IMP administration?
- Have there been any changes in appetite or dietary patterns?
- Have there been alterations in sleep architecture?
- Have any psychological symptoms, including anxiety, mood lability, or irritability, been experienced?
- Have any menstrual irregularities or abnormal bleeding been noticed (for female subjects)?
- Has sexual or reproductive dysfunction been experienced?
- Have any unscheduled medical interventions been required?
- Has the IMP been discontinued for any reason since the last visit? If so, please specify the rationale.
- Have any other health-related changes not previously discussed been noticed?
- Have any unexplained symptoms been experienced, regardless of perceived causality?
- How would the quality of life be assessed since study initiation?
- Have there been any significant life events requiring documentation?

Study subjects must be informed during each site visit about their obligation to report AEs and symptoms per protocol requirements. This ensures expedited safety reporting to the sponsor and enables communication of new safety findings prior to subsequent visits.

The investigator must emphasize that symptom reporting will not result in involuntary study discontinuation, but rather facilitate appropriate medical management and protocol-specified interventions.

The Columbia-Suicide Severity Rating Scale (C-SSRS) assesses subject psychological status, monitoring mental health throughout trial participation. This ensures reliable symptom reporting, particularly in trials involving life-threatening conditions or significant psychiatric impact.

The C-SSRS evaluation includes:

- Assessment of suicidal ideation, including timing
- Documentation of preparatory acts and timing
- History of suicide attempts, including interrupted or aborted attempts

For positive C-SSRS findings, subjects require psychiatric consultation for mental status examination and continued trial participation assessment.

QT/QTc interval monitoring is essential (prolongation of ventricular repolarization visible on ECG, associated with ion channel dysfunction and risk of Torsades de Pointes):

- Obtain triplicate 12-lead ECGs using calibrated equipment
- ECG interpretation requires cardiologist and PI verification with signature/date
- Document clinical significance in laboratory reports
- QTcF prolongation criteria: >500 msec or increase from baseline >60 msec requires confirmation with two additional ECGs at 2-5 minute intervals
- Complete documentation in source records required

Prior to blood sample collection, evaluation of vital signs, physical examination findings, and patient interview results must be conducted to ensure absence of acute conditions contraindicating collection.

All clinically significant laboratory deviations require re-evaluation at a local laboratory to exclude pre-analytical variables during sample collection.

Unscheduled visits must be conducted for clinically significant laboratory findings, with weekly result monitoring until stabilization.

Unscheduled visits or telephone follow-up must continue until urgent issues resolve, with comprehensive source documentation.

The Common Terminology Criteria for Adverse Events (CTCAE v5.0) should be used for adverse event classification and reporting. For toxicities not listed, grades 1-4 correspond to mild, moderate, severe, and life-threatening conditions.

Initial IMP administration must occur in an intensive care unit (ICU) or emergency department for monitoring of infusion-related reactions. Required monitoring parameters:

- Vital signs
- Peripheral oxygen saturation (SpO2)
- Temperature measurements
- Skin, eye, and throat examinations
- Hypersensitivity reactions (occurring within 24 hours post-infusion: flushing, rash, pyrexia, rigors, dyspnea, or anaphylaxis)

Management of acute infusion-related events (AIRE):

Grade 1-2 AIRE:

- Pause infusion
- Upon symptom resolution, consider prophylaxis and reduced infusion rate

Grade 3-4 AIRE:

- Discontinue infusion
- Permanently cease administration

All clinically significant deviations or abnormal results must be documented in medical records. Adverse events require EDC entry within 5 business days. Serious adverse events (SAEs) require immediate PI notification via SAE form and EDC entry within 24 hours.

For detection of treatment toxicity, convene investigator and clinical research department head meeting to evaluate benefit-risk ratio and continuation criteria. Decisions require immediate sponsor notification and communication to all study stakeholders.

Provide subjects with medication logs to document concomitant medications between visits. Reinforce requirement for investigator consultation prior to medication use and remind subjects to bring logs to each visit.

During each site visit, investigators must emphasize contraceptive requirements and obtain subject confirmation, documenting these discussions in source records.

- Contraceptive methods for both female and male subjects must be documented in source documentation
- Urine human chorionic gonadotropin (hCG) testing must be performed at each visit for women of childbearing potential (WOCBP)
- The following are not considered acceptable methods of contraception: periodic abstinence, coitus interruptus, spermicides alone, and lactational amenorrhea method (LAM)

Regarding data evaluation criteria, the following parameters are applied:

Data Completeness. This parameter measures the extent of required field completion. Assessment uses the following formula:

$$P = \left(\frac{N_f}{N_t}\right) \times 100\% \ldots\ldots\ldots\ldots\ldots (1)$$

Where:

- N_f: Number of completed fields.
- N_t: Total number of fields.
- P: Completeness percentage.

Data Accuracy. This parameter is defined by source data verification (SDV) concordance. The accuracy percentage A is determined using:

$$A = \left(\frac{N_c}{N_v}\right) \times 100\% \ldots\ldots.(2)$$

Where:

- N_c: Number of entries deemed correct (valid, meeting criteria).
- N_v: Total number of reviewed entries (all analyzed records).
- A: Percentage of accurate entries in the reviewed dataset [7,11].

Thus, data monitoring serves as a tool to ensure compliance with standards and the accuracy of obtained results

4. Conclusion

Various approaches, including traditional on-site monitoring, remote monitoring, risk-based monitoring (RBM), and implementation of digital technologies, present opportunities for optimizing monitoring processes. Methodology selection depends on study-specific characteristics, data volume, and available resources.

Implementation of clinical data management systems (CDMS) enhances information processing efficiency, reduces transcription errors, and increases overall quality metrics. However, significant challenges persist regarding methodology adaptation to different trial designs, ensuring data confidentiality, and maintaining regulatory compliance. Issues related to integration of traditional and digital monitoring tools emphasize the need for technological advancement and optimization of existing solutions.

The findings of this study demonstrate that employing a comprehensive monitoring strategy that integrates traditional and innovative methodologies ensures robust quality control, regulatory compliance with international standards, and improved study outcomes.

Compliance with ethical standards

Disclosure of conflict of interest

There is no conflict of interest to be disclosed.

Statement of informed consent

Inform consent was obtained from each respondent in this study.

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