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Impacts of clinical research units on clinical research — a systematic review of empirical studies

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Abstract

Background Clinical research is essential for evidence-based decision-making in healthcare practice, but its conduct is hindered by various barriers. While previous studies suggest that clinical research units (CRUs) provide critical support and expertise for complex clinical research, their necessity for ensuring high-quality clinical research remains uncertain. The primary objective of this systematic review is to identify, assess, and summarize results of studies that empirically evaluated the impacts of CRUs on clinical research.

Methods We conducted a comprehensive search of PubMed, Embase, Web of Science, and ProQuest Dissertations and Theses Global from inception to July 2024 to identify relevant studies. Study selection, quality evaluation, and data extraction were performed independently by two reviewers, with any disagreements resolved through discussion. Data extracted from the included studies were summarized in tables, and the synthesis were guided by a realist review approach.

Results A total of 11 publications corresponding to 10 studies were included in the review. These studies involved 8 independent CRUs and 2 groups of CRUs. The settings in the CRUs operated were diverse, including general hospitals or medical centres, paediatric hospitals, professional sarcoma group, and others. The CRUs featured varied structures and staff compositions, with services tailored to the specific needs of local research teams, study types, and the availability of other research resources. The reported impacts of CRUs were consistently positive in terms of efficiency, quantity, and quality of clinical research. Following the establishment of the CRUs, the number of clinical research has increased by 5 to 23 annually.

Conclusions The implementation of CRU enhances the efficiency, quantity, and quality of clinical research through process refinement, methodological support, resource pooling, reduced researcher workload, and adherence to good clinical practice (GCP), thereby ensuring patient safety and data integrity. Future research should include rigorous comparative studies, such as randomized controlled trials (RCTs) comparing outcomes with and without CRUs, to further validate these findings.

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Keywords Clinical research, Systematic review, Empirical studies

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Background

Clinical research, particularly randomized controlled trial (RCT), is essential for evidence-based decision-making in healthcare practice. However, the conduct of clinical research is hindered by several barriers, including insufficient funding, limited time for clinicians, inadequate training in research methods, and difficulties in participant recruitment [1]. Moreover, concerns about substandard quality and research misconduct have led to increasingly complex regulatory and quality assurance requirements [2, 3]. The administrative process associated with trial activation may involve approximately 30 different activities, up to 11 different individuals, and lasts from 44 to 172 days [4].

One approach to facilitating the conduct of clinical research is the establishment of research support services within academic medical centres. Various terms have been used to describe these services for both clinical trials and nonexperimental or observational studies, despite their similar functions. In this study, we use the term "clinical research unit" (CRU) to encompass all research support services, including clinical trials support unit, clinical research unit, the centre for clinical trials, clinical trials office, and clinical research support office. It has been advocated that CRUs can improve the efficiency, quantity, and quality of clinical research by sharing well-trained and experienced research staff, providing methodological support to less experienced clinicians, offering logistic assistance to alleviate the administrative burden on busy clinicians, and ensuring the adherence to good clinical practice (GCP) guidelines. However, opinions differ on whether CRU support is essential for high-quality clinical research [5]. The structure, services provided, staff involved, and functions of existing CRUs vary significantly, and their development and implementation incur costs [6, 7], making it necessary to evaluate the impact of CRUs on clinical research.

The primary objective of this systematic review is to identify, assess, and summarize the findings of studies that have empirically evaluated the impacts of CRUs on clinical research. The primary question we aim to answer is as follows:

Does empirical evidence support the claim that CRUs improve the efficiency, quantity, and quality of clinical research?

Other questions of interest include the following:

- What are the general characteristics of the included empirical studies (e.g. country, setting, year of publication)?
- What are the main features of CRUs evaluated (e.g. types of clinical research supported, service categories, funding sources)?
- What factors influenced or determined the success or failure of CRUs?

Methods

The report of this systematic review was guided by the Preferred Reporting Items for Systematic reviews and Meta-Analyses [8]. The protocol was registered on the International Prospective Register of Systematic Reviews (CRD42024575392, PROSPERO: https://www.crd.york.ac.uk/PROSPERO/view/CRD42024575392). This study was conducted in strict accordance with the pre-registered protocol, ensuring consistency across the research design, methods, and analysis. No patients or public were involved in the design of this study.

Inclusion and exclusion criteria

CRUs provide a range of services to support the clinical research process, including scientific mentorship, protocol development, regulatory compliance, study coordination, and data management [9]. We included studies that evaluated the impacts of CRUs or similar research support services on the efficiency and outcomes of clinical research in hospitals or other academic medical centres. In this paper, clinical research studies encompass clinical trials as well as any studies that provided or analysed real-world data [10] relevant to the management of patients in clinical practice.

Outcomes of interest focused on changes in the efficiency, quantity, and quality of clinical research. Specifically, the relevant outcomes included the number of clinical studies conducted, the number of participants recruited, the quality of clinical research or compliance with GCP guidelines, the time from Institutional Review Board (IRB) submission to initiation of participant recruitment, and the rates of successful completion of clinical studies.

Eligible study designs included before-and-after comparisons or studies that concurrently compared CRU support with no-CRU support. We included studies that were formally or informally published in English. Studies that did not report the impacts of CRUs on clinical research, studies available only in abstract form, and studies published in languages other than English were excluded.

Literature search strategy

We conducted a comprehensive search of PubMed, Embase, Web of Science, and ProQuest Dissertations and Theses Global, from inception to July 11, 2024, to identify relevant studies. Key words used in the search included "clinical trial unit", "clinical trial support", "clinical research unit", "clinical trial office", "clinical research office*", "center for clinical trial", "clinical research

center", "clinical research centre", "research support office", "clinical research organization", "clinical research organisation", "clinical trial organization", "clinical trial organisation", "clinical research management", "clinical trial management", and "clinical trial institution" (Appendix 1). Additionally, we manually checked the references of included primary studies and performed forward and backward citation chaining of included studies.

Identified records from searching multiple databases were downloaded and managed using EndNote software.

Assessment of study eligibility

Titles and abstracts of references from multiple databases were de-duplicated and screened independently by two reviewers using ASReview (Automatic Systematic Reviews) [11]. ASReview employs an active researcher-in-the-loop machine learning algorithm to rank articles from high to low probability of eligibility for inclusion through text mining. Before using the tool for screening, its algorithm requires training with at least one relevant and one irrelevant article. To achieve this, we manually screened and pre-labelled two relevant studies and two irrelevant studies that met the inclusion criteria in ASReview. This step enabled the machine learning algorithm to effectively screen and rank similar relevant literature. The screening process for each reviewer concluded after at least 200 consecutive irrelevant references, as the likelihood of identifying additional eligible studies among the unscreened references was very low.

Two reviewers independently conducted the full-text assessment of studies that were possibly relevant according to the initial screening of titles and abstracts. Any disagreements between reviewers were resolved by discussion.

Assessment of quality of included studies

The quality of (risk of bias in) studies was assessed using the JBI Critical Appraisal Checklist for Quasi-Experimental or non-Randomised studies (Appendix 2) [12]. For studies with a before-after comparison design, the validity assessment focused on the comparability of conditions before and after the implementation of CRUs, specifically examining whether clinical research outcomes were influenced by factors other than the development of CRUs. For studies that concurrently compared clinical research performance and outcomes between centres with and without CRUs, the assessment focused on the comparability between the centres.

Data extraction methods

Data extracted from studies included study design, setting, reasons for the development of CRUs, main service categories, types of clinical research supported, structure of CRUs, the number of staff and their level of their training/experience, and changes in clinical research performance [6]. We designed and pilot-tested a data extraction spreadsheet (Appendix 3). Two independent reviewers used the data extraction sheet to obtain data from included studies. Any disagreements between reviewers were resolved through discussion or if necessary by involving a third reviewer.

Data synthesis and analysis methods

Information obtained from included studies was presented in tables and summarized descriptively. We described the general characteristics of studies, including country and type of clinical research centres. Tables were used to summarize the main characteristics of CRUs, including staffing, funding, structure, and services provided. Reported impacts of CRUs on clinical research performance were presented in a table and narratively discussed.

Similar to other complex interventions or programmes, the successful implementation of CRUs depends on the specific context and circumstances. Our evidence synthesis was guided by realist review approach [13], focusing on the justification of CRUs as a solution to recognized barriers, empirical evidence, specific context, and circumstances. Although this is not a full-scale realist synthesis, we attempted to reveal the relevant mechanisms regarding "what works for whom, in what circumstances, in what respects and how" [13].

Results

The screening of titles and abstracts identified 45 records for full-text assessment of eligibility (Fig. 1). The full-text assessment excluded 34 records for the following reasons: not related to CRU ($n=7$), not an empirical evaluation of CRUs' impacts ($n=17$), conference abstracts ($n=6$), unavailability of full text ($n=3$), and not published in English ($n=1$). We finally included 11 publications corresponding to 10 studies involving 8 independent CRUs [9, 14–20] and 2 groups of CRUs [21–23].

Quality of included studies

Results of quality assessment for the included studies are presented in Supplementary Table 1. All the included studies used a before-after comparison design without a parallel control (Q4). For a valid before-after comparison, it is crucial that any changes in the performance of clinical research were attributable to the development of CRUs without being affected by other factors (Q3), including possible simultaneous changes in investigators (Q2). However, this was clearly not the case in one study [14] and remained unclear in all other studies. Mixed judgements were observed for other quality items,

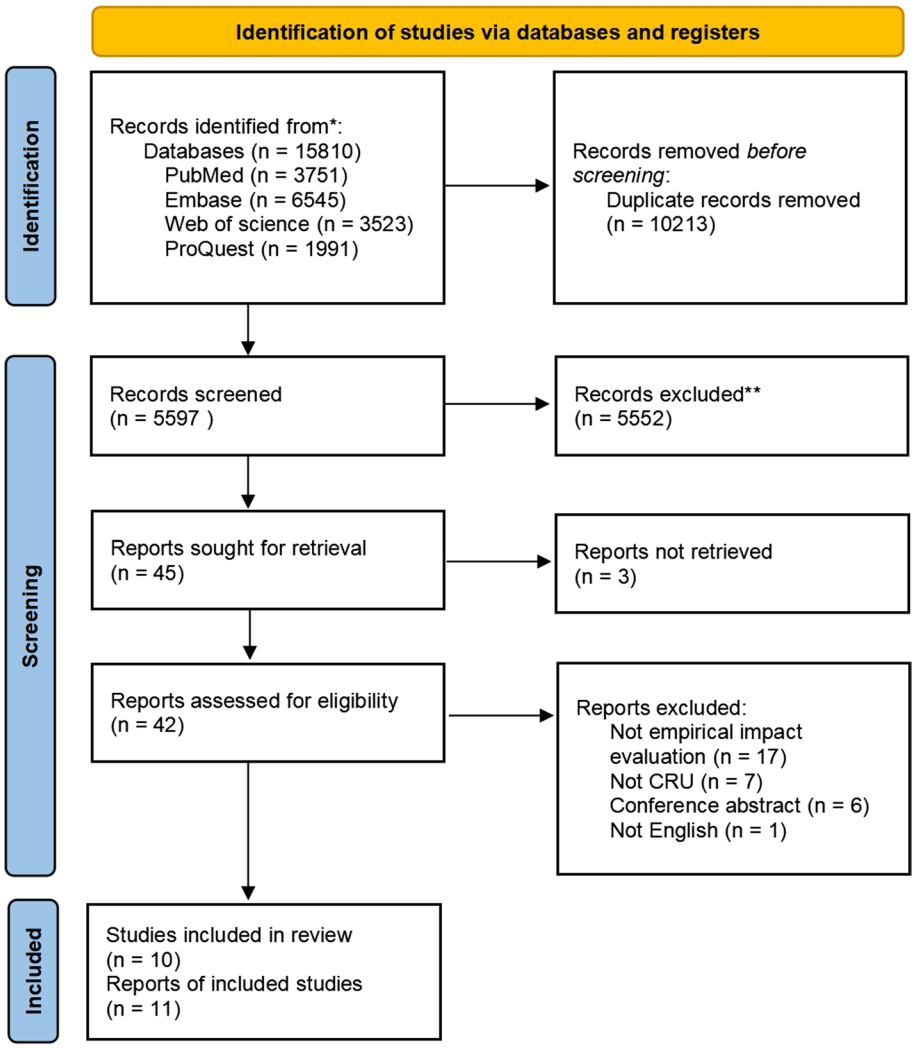

Fig. 1 Flow diagram of study selection process

including multiple measurements (Q5), follow-up completeness (Q6), and similarity and reliability of outcomes measurements (Q7, Q8). Statistical analyses of outcomes were conducted in only three studies [14, 17, 23].

The main characteristics of CRUs evaluated

The main characteristics of CRUs evaluated in the included studies are summarized in Table 1, with additional details provided in Supplementary Table 2. Of the 10 studies, 5 focused on CRUs in the United States of America (USA), 2 in Italy, and 1 each in Spain, Germany, and Switzerland. The settings in which the CRUs operated were diverse, including five general hospitals or medical centres, two paediatric hospitals, a professional sarcoma group, a department of radiology and nuclear medicine, and a department of surgery.

Rationales for the development of CRUs

The CRUs were often developed or reorganized to improve efficiency and productivity in clinical research by sharing experienced trial coordinators and other resources, often as a response to reduced fundings and a shortage of resources for clinical research (Table 1) [9, 14, 15]. Increasingly complex regulatory requirements generated the need for the CRU services to reduce burdens on clinicians [20, 21]. The development of CRUs might aim to increase the number of industry-sponsored and/or academic-initiated clinical studies [9, 16, 17, 21]. For example, the development of a CRU aimed to overcome problems of poor marketing of organization's research capabilities and to attract more industry-sponsored trials [16]. A programme of CRUs was initiated in Switzerland since 2007 focusing on the improvement of the value and quality of clinical research [22, 23].

Table 1 Main characteristics of clinical research units and their impacts on clinical research studies

Author, country	Setting	Reasons for CRU development	CRU service categories	Maintenance funding	Types of studies	Reported impacts of CRU
Abzug (2001) [14], USA	Children's Hospital of Denver, University of Colorado School of Medicine	A centralized clinical trials office (CTO) was established to facilitate faculty productivity in clinical research in 1997	• Protocol development • Budget negotiation/management • Regulatory documentation • IRB submission • Identification of trial site • Coordination of ancillary services • Participant recruitment • Study nursing • Case record form maintenance • Data management	Use of the CTO was voluntary and paid for on a fee-for-service basis	Mainly industry-sponsored studies	• Increased the number of studies • Increased revenues
Allen (2013) [15], USA	The Center for Clinical and Translational Research (CCTR), Virginia Commonwealth University (VCU)	Two separate clinical research units were combined to create a new clinical research services (CRS), to reduce duplicated or conflicting services, and to decrease costs through shared leadership and administration	• Budget negotiation/planning • IRB and regulatory documents • Coordinator support • Nursing/dietary/laboratory support	Fee for services such as nursing support and project coordination	Both NIH- and industry-sponsored studies	• Improve efficiency • Increased revenue • Reduced costs
Croghan (2015) [9], USA	Mayo Clinical Department of Medicine (DOM)	In 2006–2009, a Clinical Research Office (CRO) was developed to share knowledge and expensive resources within an institution. In 2014, CTU was established to support investigators who lacked research resources but had funding available	• Scientific mentorship • Protocol development • Regulatory documentation • Study coordination • Data management • Innovative leading-edge programmes	Funded through a fee-for-service model. Funding is sourced from internal support rather than external awards	Industry- and investigator-sponsored clinical trials	• Reduced research costs • Improved budget feasibility
Marchesi (2017) [21], Italy	The Italian Sarcoma Group (ISG), a nonprofit group of professionals	The increased regulatory requirements, the chance to increase the number of trials with other cooperative groups, and an interest from industry in supporting clinical research, generating the need of an internal service for research management	• Protocol development • Budget plan/negotiation • IRB submission • Database management • Monitoring activities • Regulatory/safety management • Educational/administrative management	Fundraising activities of the group and by the internal overheads derived from previous supported studies	Interventional and observational clinical studies. A total of 52% were industry-sponsored	• Increased the number of studies • Increased revenues • Decreased time required

Table 1 (continued)

Author, country	Setting	Reasons for CRU development	CRU service categories	Maintenance funding	Types of studies	Reported impacts of CRU
Paller (2002) [16], USA	Academic Health Centre (AHC), University of Minnesota	In late 1997, a research service organization (RSO) was established to facilitate industry access to university's resources and to provide faculty with support services for their research projects	• Initial contact point for industry • Marketing for the AHC's research community • Protocol review • Contract negotiation • Budget assistance • IRB submission • Regulatory documents • Coordinator support	Revenues were generated by direct costs and other costs funded by the AHC	Industry-sponsored trials	• Decreased time required • Increased the number of studies • Avoided waste of time on unsuitable studies
Penadés-Blasco (2022) [17], Spain	Radiology and Nuclear Medicine Departments, La Fe University and Polytechnic Hospital	A Medical Imaging Clinical Trials Unit (MICTU) was created in 2016 to be involved in clinical trials and to generate resources to foster internal continuous education and research	• Documentation required for trial initiation • Scheduling • Image acquisition and report • Completion of the tasks • Closing the clinical trial	Charged 5–15% added cost with specific tasks or specific and more complex imaging protocols	89% were industry-sponsored	• Increased the number of studies • Increased research revenues • Improved collaborations
Pontrelli (2021) [18], Italy	A large paediatric trial centre, the Bambino Gesù Children's Hospital in Rome	Additional to CTUs' non-clinical support, the Investigational Clinical Centre (ICC) was established in 2010 to provide support on clinical management of enrolled patients	• Clinical management of patients • AEs and SAEs report • Randomization • Blinded drug administration and compliance • Study coordinators support • Organize visits procedures • Complete case report forms (CRFs) • Monitoring visits	Not described	Many were industry-sponsored	• Increased the number of studies • Reduced the number of failed trials • Improved participant recruitment
Seiler (2006) [19], Germany	Department of Surgery at the University of Heidelberg	In 10/2001, the Centre for Clinical Studies was established to make clinical studies more organized and standardized within the Department of Surgery	• Study protocol • Clinical reporting file • Operative manual • Patient's insurance and medication • Recruitment • Informed consent	Not described	50% were industry-sponsored trials	• Increased number of studies • Improved participant recruitment

Table 1 (continued)

Author, country	Setting	Reasons for CRU development	CRU service categories	Maintenance funding	Types of studies	Reported impacts of CRU
Snyder (2016) [20], USA	Duke University School of Medicine	The Duke Office of Clinical Research was formed in 2012 to help clinical investigators navigate the complex research environment and operationalize research ideas	• Protocol review • Study start-up • Electronic health record • Outreach and mentorship	Initial consultation was subsidized by the School of Medicine. Direct effort costs were charged to studies	22% were industry-sponsored, 22% NIH sponsored, and 39% internal studies	• Decreased time required • Increased the number of studies • Improved participant recruitment • Improved satisfaction with investigators
von Niederhausern, (2015 [22]; 2018 [23]), Switzerland	Five Swiss University Hospitals and St Gallen Cantonal Hospital	Since 2007, a programme to establish clinical trial units as centres of competence was initiated to improve the quality of Swiss clinical research	• Clinical research protocols • Methodological and statistical support • IRB submission • Regulatory documentations • Logistical support • Recruitment of participants • Technical support • Access to investigator networks • Training and education	Initially cofinanced by affiliated institutions and then generated own revenue through charges for service provision	>70% were of academic origin, 60% were interventional trials, and 40% belonged to other types of studies	• Improved quality of protocols • Perceived positive impacts on study quality

AEs adverse events,
AHC academic health centre,
CCTR the centre for clinical and translational research,
CRFs case report forms,
CRO clinical research office,
CRS clinical research services,
CRU clinical research unit,
CTO clinical trials office,
DOM Department of Medicine,
ICC the investigational clinical centre,
IRB Institutional Review Board,
ISG the Italian Sarcoma Group,
MICTU, medical imaging clinical trials unit,
NIH National Institutes of Health,
RSO research service organization,
SAEs serious adverse events,
VCU Virginia Commonwealth University

Details on the processes for the CRU development are summarized in Supplementary Table 2. CRUs were often developed through a step-by-step approach after evaluating problems and factors that affected efficiency, quantity, and quality of clinical research [9, 14, 15, 20–23]. It was important to justify the CRUs' establishment and ensure that the services provided by CRUs are needed to facilitate the clinical research.

CRU structure, staff, and costs

The CRUs had different structures and categories of staff, depending on the local circumstances, types of clinical studies, and services required. The crucial position in CRUs was the medical or scientific director with extensive experiences in clinical research and related methodology. Other staff personnel included statisticians, clinical trial coordinators, research assistants, nursing staff, information technology specialists, and administrative personnel (Supplementary Table 2).

Although the initial financial support is required to develop CRUs, most established CRUs were completely or partially funded through a fee-for-service model. In certain cases, the establishment or reorganization of CRUs can lead to reduced costs in clinical research and/or increased revenues from studies sponsored externally.

CRU service categories

Services provided by CRUs depended on the need of local research teams, types of studies, and availability of research resources. Protocol development was a service provided by most CRUs, particularly for investigator-initiated studies (Table 1). Budget negotiations or assistance was a key CRU service for industry-sponsored studies [14–16, 21]. Other common services included IRB submission, regulatory documentation, data management, participant recruitment, monitoring activities, training, and education (Table 1). Although most services provided by CRUs were non-clinical, a CRU may also provide clinical support and the direct management of patients [18].

Impact of CRUs on clinical research

Reported impacts of CRUs on clinical research were summarized in Table 1, and more details are available in Supplementary Table 2.

Seven of the 10 studies reported that the number of clinical studies was increased after the establishment of CRUs [14, 16–21]. For example, Abzug et al. (2001) [14] reported that the number of studies receiving CRU support was only two when the CRU was just established in 1997, and it increased to 72 in 2000. In a study by Marchesi et al. (2017) [21], the number of studies conducted after the implementation of the CRU increased from 9 in 2013 to 25 in 2016. Similarly, Pontrelli et al. (2021) [18] found that the number of active trials supported by the CRU increased from 18 in 2010 to 104 in 2020.

Four studies reported higher revenues from clinical studies funded by industry or other agencies [14, 15, 17, 21], and two studies reported reduced research costs or improved efficiency [9, 15]. Croghan et al. [9] provided several real scenarios showing how CRU services could reduce costs by sharing research resources. In a study by Allen et al. [15], a new CRU was formed by combining two separate research support units, resulting in reduced costs, improved efficiency, and increased revenues recovered from clinical trials. CRU services significantly shortened the time required to complete regulatory, ethical approval, budget negotiation, and other administrative procedures before participant recruitment [16, 20, 21].

The impacts of CRUs on the quality of clinical research were demonstrated by reduced unfeasible or failed studies [16] [18], improved participant recruitment [18–20], and perceived positive impacts on research quality by stakeholders of clinical research [23]. Although CRUs provide a range of valuable services, one study [23] suggests that their support for publications is relatively low compared to other services, but this is not related to their core service provision.

Discussion

Services offered by CRUs were heterogeneous in the included studies. According to a survey in 2009, clinical trials offices (CTOs) in the USA performed 14 or more activities including contract negotiations, sponsor recruitment protocol development, budget development and approval, developing billing grids, costs analysis, defining standard of care, patient recruitment and scheduling, approving charges, education and training, and compliance [7]. A survey of 15 CRUs in different countries in 2020 reported that essential services by CRUs were quality management, monitoring and project management, regulatory and legal affairs, education and training, and data management [6]. Depending on the main services provided, core staff of CRUs included senior medical trialists or clinical research directors, statisticians, people with expertise of data management, finances, and project coordinators [24]. Although CRUs were usually established to facilitate the conduct of clinical trials, some CRUs also provided services to support observational studies, particularly investigator-initiated studies. Observational cohort studies will help the conduct of experimental trials through participant recruitment, improving research experience of clinicians, and encourage clinicians more research active.

Even though the CRUs evaluated in this systematic review were heterogeneous in settings, types of studies, and services provided, the reported impacts of CRUs were consistently positive in terms of efficiency, quantity, and quality of clinical research. It is important to understand the underlying mechanisms, that is, how and why, and in what context, that the CRUs positively facilitate clinical studies in practice.

Plausible mechanisms for CRUs to facilitate clinical research

CRUs and efficiency in clinical research

The conduct of clinical research involves substantial costs, requires significant time investment, and carries a considerable risk of failure. Because resources available for clinical research are always limited, improving its efficiency has consistently remained a primary focus to avoid or reduce waste in research [25, 26]. Efficiencies in clinical research can be classified into four categories: operational efficiency, scientific efficiency, statistical efficiency, and economic efficiency [26, 27]. A study in the UK by Duley et al. (2018) [28] found that the main inefficiencies between grant award and recruitment of first participants included obtaining R&D approvals, contracts, and other approvals. They also identified that the main inefficiencies between the recruitment of first participants to publication of results were due to failure to meet recruitment targets, inadequate data management, and preparation and submission for publication [28].

Our systematic review revealed that the establishment of CRUs can improve efficiencies in clinical research, which may be due to the following plausible mechanisms. First, CRU staff are well-versed in operational procedures and possess extensive experiences, with dedicating time to research projects in preparing and submitting necessary documents for obtaining R&D, ethics, and other approvals. CRU staff are familiar with operational procedures, of extensive experiences and dedicated time on research projects, in preparation and submission of documents required to obtain R&D, and ethical and other approvals. Initiating a clinical trial is a multifaceted and time-intensive process that encompasses approximately 30 distinct activities and up to 11 individuals, taking between 44 and 172 days [4]. The support of CRUs can enhance the efficiency of the activation process and reduce the time required for participant recruitment, compared to individuals who lack familiarity with the intricate procedures, possess limited experience, and are not guaranteed with sufficient time. Secondly, scientific efficiencies can be enhanced through methodological support from CRUs, ensuring that study protocols are more scientifically and statistically rigorous. Well-designed clinical studies are more likely to be successful in providing scientifically valid data for evidence-based medicine. Thirdly, multiple different clinical studies can be simultaneously supported by the same CRU staff when certain CRU services were required only for a short period of time during cycles of research projects. By sharing research resources through a centralized CRU services, research teams only need to pay the services required and can save costs on hiring full-time researchers for short-term tasks.

Impacts of CRUs on quantity of clinical research

The most noticeable impact of establishing CRUs is increased numbers of clinical studies. Mechanisms for increased quantity of clinical studies after implementing CRUs are different depending on types of clinical research and specific contexts. For industry-sponsored trials, the increase in quantity of studies is likely primarily due to centres with established CRU infrastructure for participant recruitment being preferred clinical trial sites [29, 30]. For investigator-initiated studies, methodological support from CRUs will enable more clinicians who have limited research experience to initiate clinical studies. In addition, CRU services will alleviate non-clinical burdens on clinicians with research experiences and enable them to have time on more clinical studies. The improvement in research efficiency will save time, money, and other research resources so that more clinical studies can be conducted.

Impacts of CRUs on quality of clinical research

The quality of clinical studies may be defined or measured in various ways [31]. A comprehensive framework involves six dimensions for clinical research quality, including protection of patient safety, relevance of study questions, minimization of bias (internal validity), precision, transparency and access to data, and generalizability of study results (external validity) [32]. Additionally, a complete cycle of clinical studies consists of the following successive stages: conception of research questions, planning and feasibility, conduct, analysis and interpretation, and reporting and knowledge translation [32].

Underlying mechanisms for quality improvement in clinical research with support from CRUs may involve better designed protocols and the involvement of CRU staff who are well-trained and of experiences in GCP compliances. For investigator-initiated research, an important service provided by CRUs is assisting clinicians to clarify research questions and confirm that the research question is relevant and has not been satisfactorily answered by existing or ongoing studies. Once a research question has been identified, CRU staff with expertise in research methodology can assist clinicians in determining an appropriate study design and developing

a feasible study protocol. A well-designed study protocol will ensure the protection of patient safety, adequate sample size, and high internal and external quality. For all types of clinical studies, CRU staff who have experiences in GCP compliance may monitor the research conduct to prevent or reduce the breach of study protocols and to ensure the validity of data collection. The successful completion of a clinical study according to its protocol may ultimately be an important research quality issue, and CRUs' support may reduce the early termination of clinical studies due to inadequate participant enrolment.

Global disparities in clinical research

Clinical research is beneficial in advancing medical knowledge and evidence-based medicine, and patients enrolled in clinical trials, on average, have better clinical outcomes than those who did not participate in trials [33]. Existing RCTs concerned mainly about conditions affecting high-income countries, and research priorities may not be optimized to reduce the global burden of disease [34]. A study found that only 5% of all RCTs registered from 2010 to 2019 were set in South Asia and only 2% were set in sub-Saharan African countries [25]. To address the mismatch in clinical trial efforts and disease burden globally, the establishment of CRUs in low-income and middle-income countries could be a solution. Although all the studies included in our systematic review reported impacts of CRUs in high-income North America and European countries, the plausible mechanisms for CRUs to facilitate clinical research appear to be applicable in low- and middle-income settings as well. In fact, CRUs have been established in some low-income and middle-income countries. For example, 4 of the 15 CRUs in an international survey were not from high-income regions [6]. In low-income and middle-income countries, more CRUs need to be established, and their impacts on clinical research should be empirically evaluated. To expand CRU research in low-income and middle-income countries (LMICs), we suggest implementing strategies such as establishing international collaborative networks, increasing funding support, providing training and education, and promoting policy advocacy.

Strengths

To the best of our knowledge, our study is the first to conduct a systematic review investigating the impact of CRUs on clinical research. Moreover, our evidence synthesis was guided by a realist review approach, focusing on the justification of CRUs as a solution to recognized barriers, empirical evidence, and specific contexts and circumstances. Through this approach, we explored the impact of CRUs on clinical research and uncovered the underlying mechanisms through which CRUs influence the quality, quantity, and efficiency of clinical research. This provides a novel and comprehensive understanding of the effects brought by CRUs, contributing new evidence to the existing literature.

Limitations

This systematic review has several limitations. First, the included studies may represent a biased sample of CRUs, as they primarily focus on those with positive impacts on clinical research, potentially indicating publication bias. Second, the higher prevalence of CRUs in high-income countries may reflect regional disparities but could also stem from our restriction to English-language studies, which may introduce bias and limit the generalizability of our findings. Third, only three studies included statistical comparisons, restricting the availability of robust quantitative data for assessing CRU impact. Finally, ethical approval was reported in only one of the included articles, with the remaining studies lacking such documentation, which represents an additional limitation.

Conclusions

The structure of and services provided by clinical research units were determined by specific settings, availability of research resources, types of clinical studies, and support required. Academic institutions, hospital leaders, and policymakers should pay close attention to the importance of CRUs, as empirical evidence confirmed that the implementation of clinical research units can improve efficiencies, quantity, and/or quality of clinical research. The positive findings from this systematic review could be explained by plausible underlying mechanisms. The improvement in efficiency is attributed to process optimization, methodological support, and resource sharing. The increase in quantity is driven by industry sponsorship preferences and the alleviation of researchers' burdens. Quality assurance relies on compliance with GCP, ensuring patient safety and data reliability. These mechanisms work synergistically to comprehensively enhance the level of clinical research. Future studies should conduct rigorous comparative research, such as randomized controlled trials (RCTs) comparing outcomes with and without CRUs or before-and-after studies within institutions, to further investigate the specific mechanisms through which CRUs enhance efficiency and provide methodological support. Additionally, more research is needed in LMICs to better understand the impact of CRUs in these settings.

Abbreviations

CRU	Clinical research unit
RCT	Randomized controlled trial
CTU	Clinical trials unit
GCP	Good clinical practice
IRB	Institutional Review Board

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

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Authors' contributions
FJS, conceived and designed the study.
FW and FJS, wrote the main manuscript text.
FW and XW, collected and analysed the data and prepared figures and table.
EML and YLC provided critical revisions and contributed to the interpretation of the results.
All authors reviewed and approved the final manuscript.

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Declarations

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Competing interests
The authors declare that they have no competing interests.

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References

1. Djurisic S, Rath A, Gaber S, Garattini S, Bertele V, Ngwabyt SN, Hivert V, Neugebauer EAM, Laville M, Hiesmayr M, et al. Barriers to the conduct of randomised clinical trials within all disease areas. Trials. 2017;18(1):360.
2. Seife C. Research misconduct identified by the US Food and Drug Administration: out of sight, out of mind, out of the peer-reviewed literature. JAMA Intern Med. 2015;175(4):567–77.
3. Woodhead M. 80% of China's clinical trial data are fraudulent, investigation finds. BMJ. 2016;355: i5396.
4. Martinez DA, Tsalatsanis A, Yalcin A, Zayas-Castro JL, Djulbegovic B. Activating clinical trials: a process improvement approach. Trials. 2016;17(1):106.
5. Gohel MS, Chetter I. Are clinical trials units essential for a successful trial? BMJ. 2015;350: h2823.
6. Hoffmann JM, Blümle A, Grossmann R, Yau H, Lang B, Bradbury C. Toward a global harmonization of service infrastructure in academic clinical trial units: an international survey. Front Med (Lausanne). 2023;10:1252352.
7. Rubin E, Lazar D. Clinical trials offices: What's new in research administration. Issue Briefs Assoc Acad Heal Centers. 2009;24:1–24.
8. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372: n71.
9. Croghan IT, Viker SD, Limper AH, Evans TK, Cornell AR, Ebbert JO, Gertz MA. Developing a clinical trial unit to advance research in an academic institution. Contemp Clin Trials. 2015;45(Pt B):270–6.
10. Liu J, Barrett JS, Leonardi ET, Lee L, Roychoudhury S, Chen Y, Trifillis P. Natural history and real-world data in rare diseases: applications, limitations, and future perspectives. J Clin Pharmacol. 2022;62 Suppl 2(Suppl 2):S38-s55.
11. van de Schoot R, de Bruin J, Schram R, Zahedi P, de Boer J, Weijdema F, Kramer B, Huijts M, Hoogerwerf M, Ferdinands G, et al. An open source machine learning framework for efficient and transparent systematic reviews. Nature Machine Intelligence. 2021;3(2):125–33.
12. Checklist for quasi-experimental studies (non-randomized experimental studies) critical appraisal tools for use in JBI Systematic reviews. https://jbi.global/sites/default/files/2019-05/JBI_Quasi-Experimental_Appraisal_Tool2017_0.pdf.
13. Pawson R, Greenhalgh T, Harvey G, Walshe K. Realist review–a new method of systematic review designed for complex policy interventions. J Health Serv Res Policy. 2005;10(Suppl 1):21–34.
14. Abzug MJ, Esterl EA. Establishment of a clinical trials office at a children's hospital. Pediatrics. 2001;108(5):1129–34.
15. Allen D, Ripley E, Coe A, Clore J. Reorganizing the general clinical research center to improve the clinical and translational research enterprise. Eval Health Prof. 2013;36(4):492–504.
16. Paller MS, Hostetler L, Dykhuis DA. Clinical trials at AHCs: the perspective of an academic clinical trials office. Acad Med. 2002;77(12 Pt 1):1201–6.
17. Penadés-Blasco A, Ginés-Cárdenas S, Ten-Esteve A, Arques PB, Llobera JMS, Consuelo DV, Martí-Bonmatí L. Medical imaging clinical trials unit: a professional need. Eur J Radiol. 2022;146: 110099.
18. Pontrelli G, Ciabattini M, De Crescenzo F, Biondi I, Cocchiola R, Copponi G, Frillici C, Molinari F, Rocchi F, Simonetti A, et al. The investigational clinical center: a clinical-supportive and patient-centered trial unit model. Ten years of experience through normal and pandemic times of a large pediatric trial center in Italy. Ital J Pediatr. 2021;47(1):156.
19. Seiler CM, Wente MN, Diener MK, Fröhlich BE, Büchler MW, Knaebel HP. Center for clinical studies in a surgical department–an approach for more evidence-based medicine. Contemp Clin Trials. 2006;27(3):211–4.
20. Snyder DC, Brouwer RN, Ennis CL, Spangler LL, Ainsworth TL, Budinger S, Mullen C, Hawley J, Uhlenbrauck G, Stacy M. Retooling institutional support infrastructure for clinical research. Contemp Clin Trials. 2016;48:139–45.
21. Marchesi E, Cagnazzo C, Quattrini I, Leopardi MP, Villa C, Grignani G, D'Ambrosio L, Stacchiotti S, Casali PG, Picci P. How a clinical trial unit can improve independent clinical research in rare tumors: the Italian Sarcoma Group experience. Clin Sarcoma Res. 2017;7:4.
22. von Niederhäusern B, Fabbro T, Pauli-Magnus C. The role of clinical trial units in investigator- and industry-initiated research projects. Swiss Med Wkly. 2015;145: w14161.
23. von Niederhäusern B, Magnin A, Pauli-Magnus C. The impact of clinical trial units on the value of clinical research in Switzerland. Swiss Med Wkly. 2018;148: w14615.
24. Gluud C, Sørensen TI. Organisation of a clinical trial unit–a proposal. Fundam Clin Pharmacol. 1998;12(3):298–305.

25. Park JJH, Grais RF, Taljaard M, Nakimuli-Mpungu E, Jehan F, Nachega JB, Ford N, Xavier D, Kengne AP, Ashorn P, et al. Urgently seeking efficiency and sustainability of clinical trials in global health. Lancet Glob Health. 2021;9(5):e681–90.
26. Kelly D, Spreafico A, Siu LL. Increasing operational and scientific efficiency in clinical trials. Br J Cancer. 2020;123(8):1207–8.
27. Xie CX, De Simoni A, Eldridge S, Pinnock H, Relton C. Development of a conceptual framework for defining trial efficiency. PLoS One. 2024;19(5): e0304187.
28. Duley L, Gillman A, Duggan M, Belson S, Knox J, McDonald A, Rawcliffe C, Simon J, Sprosen T, Watson J, et al. What are the main inefficiencies in trial conduct: a survey of UKCRC registered clinical trials units in the UK. Trials. 2018;19(1):15.
29. Baer AR, Bridges KD, O'Dwyer M, Ostroff J, Yasko J. Clinical research site infrastructure and efficiency. J Oncol Pract. 2010;6(5):249–52.
30. Dombernowsky T, Haedersdal M, Lassen U, Thomsen SF. Criteria for site selection in industry-sponsored clinical trials: a survey among decision-makers in biopharmaceutical companies and clinical research organizations. Trials. 2019;20(1):708.
31. von Niederhäusern B, Schandelmaier S, Mi Bonde M, Brunner N, Hemkens LG, Rutquist M, Bhatnagar N, Guyatt GH, Pauli-Magnus C, Briel M. Towards the development of a comprehensive framework: qualitative systematic survey of definitions of clinical research quality. PLoS One. 2017;12(7): e0180635.
32. von Niederhäusern B, Guyatt GH, Briel M, Pauli-Magnus C. Academic response to improving value and reducing waste: a comprehensive framework for INcreasing QUality In patient-oriented academic clinical REsearch (INQUIRE). PLoS Med. 2018;15(6): e1002580.
33. Bouzalmate-Hajjaj A, Massó Guijarro P, Khan KS, Bueno-Cavanillas A, Cano-Ibáñez N. Benefits of participation in clinical trials: an umbrella review. Int J Environ Res Public Health. 2022;19(22):15368.
34. Marshall IJ, L'Esperance V, Marshall R, Thomas J, Noel-Storr A, Soboczenski F, Nye B, Nenkova A, Wallace BC. State of the evidence: a survey of global disparities in clinical trials. BMJ Glob Health. 2021;6(1):e004145.

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