“Il ruolo dell’infermiere di ricerca”
Sessione 1 – Aggiornamento GCP

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NESSUN CONFLITTO DI INTERESSI

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

GUIDELINE FOR GOOD CLINICAL PRACTICE

E6(R3)

Final version

Adopted on 06 January 2025

Clinical trials are a fundamental part of clinical research that support the development of new medicines or uses of existing medicines. Well-designed and conducted clinical trials help answer key questions in healthcare and drug development. Their results are essential for evidence-based healthcare decisions. Trials with inadequate design and/or poorly conducted trials may place participant safety at risk, yield inadequate or unreliable results and are unethical. They waste resources and the efforts and time of investigators and participants.

Struttura complessiva e impostazione

R3 è una linea guida completamente **riorganizzata**: **12** Principi generali

Annex 1

Capitolo 1 "**IRB/IEC**"

Capitolo 2 "**Investigator**"

Capitolo 3 "**Sponsor**"

Capitolo 4 "**Data Governance Investigator and Sponsor**"

Appendice A "**Investigator Brochure**"

Appendice B "**contenuti del protocollo**"

Appendice C "**essential records**"

La prefazione esplicita l'allineamento ai concetti di **"critical to quality" di E8(R1)** e l'utilizzo di un **approccio** proporzionato **basato sul rischio**.

II. PRINCIPLES OF ICH GCP

7. **Clinical trial processes, measures and approaches should be implemented in a way that is proportionate to the risks to participants and to the importance of the data collected and that avoids unnecessary burden on participants and investigators.**

I processi dello studio dovrebbero essere **operativamente fattibili** ed **evitare complessità**, procedure e raccolte di dati **non necessarie**. Essi dovrebbero supportare i **principali obiettivi** dello studio. Lo sponsor non dovrebbe imporre **oneri superflui** ai **partecipanti** e agli **sperimentatori**.

The research burden of randomized controlled trial participation: a systematic thematic synthesis of qualitative evidence

Nivantha Naidoo [1 2], Van Thu Nguyen [1 3], Philippe Ravaud [1 2 4], Bridget Young [3], Philippe Amiel [5], Daniel Schanté [6 7], Mike Clarke [8], Isabelle Boutron [9 10]

Results: We included 45 qualitative studies that involved 1732 RCT participants. Important psychological burdens were identified at every stage of the trial process. Participants reported feeling anxiety and being afraid of "being a 'guinea pig'" and described undergoing randomization and allocation to a placebo as particularly difficult resulting in disappointment, anger, and depression. Patients' follow-up and trial closure were also responsible for a wide range of psychological, physical, and financial burdens. Furthermore, factors related to burdensome impacts and consequences were discerned. These factors involved trial information, poorly organized and too-demanding follow-up, and lack of appropriate management when the patient's participation ended. Trial participation was

Addressing the Financial Burden of Cancer Clinical Trial Participation: Longitudinal Effects of an Equity Intervention

Ryan D Nipp [1], Hang Lee [2], Emily Gorton [3], Morgan Lichtenstein [3], Salome Kuchukhidze [3], Elyse Park [4], Bruce A Chabner [3], Beverly Moy [3]

Conclusion: Cancer clinical trial participants may experience substantial financial issues, and this equity intervention demonstrates encouraging results for addressing these patients' longitudinal financial burden.

Development and Preliminary Testing of the Perceived Benefit and Burden Scales for Cancer Clinical Trial Participation

Connie M Ulrich [1], Qiuping Pearl Zhou [2], Sarah J Ratcliffe [1], Kathleen Knafl [3], Gwenyth R Wallen [4], Therese S Richmond [1], Christine Grady [4]

Affiliations + expand

PMID: 29631487 PMCID: PMC6091872 DOI: 10.1177/1556264618764730

Abstract

We developed measures of benefits and burdens of research participation in cancer clinical trials using a sequential mixed methods design with a qualitative (n = 32) and quantitative sample (n = 110) of cancer clinical trial participants. Benefit-burden items (22 for benefits, 23 for burdens) were subsequently developed and assessed through cognitive interviewing for content, clarity, and meaning. Preliminary psychometric analyses support the internal consistency reliability and construct validity of Benefit (α = .90) and Burden (α = .87) research participation scales. Item response theory models supported the discrimination ability of the items on the scales. Participants who had thoughts of dropping out had lower Benefit scale scores (p < .001) and higher Burden scores (p < .001) than those who had no thoughts of dropping out, supporting construct validity. With further psychometric testing, the scale can be used to develop appropriate interventions to address recruitment and retention of human participants in clinical research.

II. PRINCIPLES OF ICH GCP

5. Clinical trials should be designed and conducted by qualified individuals.

Possono essere necessarie persone con **diverse competenze** e **formazioni** in **tutte le fasi** di uno studio clinico, come medici, **infermieri**, **farmacisti**, scienziati, esperti di etica, esperti di tecnologia, **coordinatori della ricerca**, monitor, auditor e biostatistici.

Gli individui coinvolti in uno studio dovrebbero essere **qualificati** tramite **istruzione**, **formazione** ed **esperienza** per svolgere i rispettivi compiti.

10. Roles and responsibilities in clinical trials should be clear and documented appropriately.

Gli accordi dovrebbero **definire** chiaramente **i ruoli**, le **attività** e le **responsabilità** per lo studio clinico ed essere adeguatamente **documentati**.

III. ANNEX 1 2. INVESTIGATOR

2.7 Participant Medical Care and Safety Reporting

2.7.1 Medical Care of Trial Participants

Un **medico** qualificato, che sia sperimentatore o sub-sperimentatore dello studio, dovrebbe avere la **responsabilità dell'assistenza medica** e delle decisioni correlate allo studio.

Altri professionisti sanitari adeguatamente **qualificati** possono **essere coinvolti** nell'**assistenza medica** dei partecipanti allo studio, in linea con le loro normali attività e in conformità ai requisiti normativi locali.

III. ANNEX 1 2. INVESTIGATOR 2.3 Responsibilities

Lo **sperimentatore** può **delegare** ad altre persone le **attività** correlate allo studio.

Lo sperimentatore mantiene la **responsabilità ultima**. Il **livello di supervisione** da parte dello sperimentatore sulle attività delegate dovrebbe dipendere dalla **natura delle attività** stesse ed essere **proporzionato** all'importanza dei dati raccolti e ai **rischi** per la **sicurezza** dei partecipanti e per **l'affidabilità** dei dati.

Lo sperimentatore dovrebbe garantire che le persone a cui ha **delegato** attività correlate allo studio siano **adeguatamente qualificate** e sufficientemente **informate** sugli aspetti pertinenti del protocollo, sui farmaci sperimentali e sulle attività di studio loro assegnate. La **formazione** relativa allo studio fornita alle persone che vi collaborano dovrebbe corrispondere a **quanto necessario** per consentire loro di svolgere le attività delegate che vanno oltre la loro formazione ed esperienza abituali.

The role of the nurse in supporting cancer clinical trials

Verna Lavender [1], Anne Croudass [2]

Affiliations + expand

PMID: 30811238 DOI: 10.12968/bjon.2019.28.4.S14

Abstract

Clinical trials are a fundamental component of high-quality care, and have been widely reported to improve care and patient outcomes. For research trials to be successful, patients need to have awareness of trials, be invited to participate, and be supported to make informed decisions about consenting to enrol in clinical trials. Some cancer nurses have been reported to be reluctant to discuss clinical trials with patients, based on their own beliefs about the perceived burden of clinical trials, while others have been reported to facilitate patient access to clinical trials by working closely with their clinical research nurse colleagues. Nursing patients enrolled in cancer clinical trials is a specialised (and often complex) area of practice. There is significant opportunity for nurses to develop their knowledge about clinical trials, for example, through reciprocal learning between clinical and research teams, which might enhance patients' experiences of, and outcomes from, clinical trials.

› Recenti Prog Med. 2020 Sep;111(9):535-538. doi: 10.1701/3421.34068.

[Clinical research nurse in italian centers: a mandatory figure?]

[Article in Italian]
Marzia Martucci [1], Agata Guarrera [2], Daniela Valente [3], Francesca Resente [4], Celeste Cagnazzo [5]

Affiliations + expand

PMID: 32914783 DOI: 10.1701/3421.34068

Abstract

Over the past few years, clinical research has developed considerably. To achieve adequate quality standards in its design and management, it was necessary to set up dedicated and qualified multi-professional teams, made up not only of medical personnel. This has led to the emergence of new professional roles, such as that of the research nurse (clinical research nurse, study nurse or clinical trial nurse). While in Europe this professional role is defined, in Italy it has started to assert itself only recently, with a profile linked mainly to practical rather than managerial tasks. The role is not yet recognized at institutional level and is not registered. The goal of our research was to understand how many research centers can rely on the presence of a research nurse in their staff and what was the research nurse's contribution to achieving the satisfaction of patients enrolled in clinical studies and on the work of the research team.

Cancer Clinical Trials: Implications for Oncology Nurses

Wendy S Portier [1]

Conclusion: Oncology nurses' interactions with patients entered on clinical trial and communication with the clinical research team is crucial to the successful conduct of clinical trials. The oncology nurse must work in concert with the clinical research team to protect patient safety and to produce accurate information for protocol requirements that will be used to evaluate whether a drug becomes approved or not by the US Food and Drug Administration.

Implications for nursing practice: Oncology nurses play a central role to the successful outcome of clinical research studies. Nurses must work in close collaboration with the clinical research teams for the successful completion and adherence of the clinical trial and to maintain the safety of the patient enrolled into clinical trial.

Clinical research nurse predictions of trial failure, recruitment and retention: a case for their early inclusion in trial design

Frances Shiely [1 2 3], Danielle Murphy [4 5], Seán R Millar [6]

Conclusions: CRNs are very good judges of trial recruitment and site performance issues and are a vital part of the clinical trial team. Taken with the ESP (Estimating Site Performance) study, we have made a strong case for broadening the trial team at the trial design stage. Early engagement of a broad skillset can potentially offset problems of recruitment, retention and trial failure.

Effect of a research nurse on patient enrollment in a clinical study

D J Isaacman [1], E A Reynolds

Conclusions: Addition of a shared research nurse increased recruitment of patients and demonstrated equivalent judgment of the research nurse and physician investigators regarding patient eligibility for the study. This arrangement demonstrates a practical and effective means of increasing the efficiency of ED-based clinical research.

2.8 Informed Consent of Trial Participants

Possono essere utilizzati approcci diversi (ad es. **testi, immagini, video e altri metodi interattivi**) nel **processo di consenso informato**, inclusi quelli per fornire informazioni al partecipante. Le **caratteristiche della popolazione** dello studio (ad es. partecipanti che potrebbero non avere familiarità con i sistemi informatizzati) e l'**adeguatezza del metodo** di acquisizione del consenso dovrebbero essere prese in considerazione nello sviluppo dei materiali e del processo di consenso informato.

Quando vengono utilizzati **sistemi informatizzati** per ottenere il consenso informato, ai partecipanti allo studio può essere offerta l'opzione di utilizzare un approccio **cartaceo come alternativa.**

L'acquisizione del **consenso a distanza** può essere presa in considerazione quando appropriato.

Sia che il processo di consenso informato avvenga di persona o a distanza, lo sperimentatore dovrebbe accertarsi dell'**identità del partecipante (**o del rappresentante legalmente accettabile) in conformità ai requisiti normativi applicabili.

Assent

Accordo esplicito di un minore a partecipare a uno studio clinico.

L'assenza di un'espressione di consenso o di dissenso **non** dovrebbe essere interpretata come **assenso**.

Se dei **minori** devono essere inclusi in uno studio, l'IRB/IEC dovrebbe esaminare le **informazioni** relative all'assenso tenendo conto dell'**età**, della **maturità** e dello **stato psicologico** della popolazione minorile che si intende arruolare, nonché dei requisiti normativi applicabili.

Quando un **minore** deve essere incluso come **partecipante**, dovrebbero essere fornite e discusse con lui informazioni sull'assenso adeguate all'età, come parte del processo di consenso, e **l'assenso** del minore all'arruolamento nello studio dovrebbe essere **ottenuto** quando appropriato.

Qualora, durante lo svolgimento dello studio, il minore raggiunga l'**età del consenso legale**, dovrebbe essere previsto un **processo di consenso**, in conformità ai requisiti normativi applicabili.

The importance of applying the statement of assent to children and adolescents: a qualitative study

Cristiane da Silva Varejão [1], Fátima H do Espírito Santo [2], Maria de Nazaré de Souza Ribeiro [3]

Conclusions: The Statement of Assent was important for participants understanding the study and having autonomy over their participation. As the statement strengthened the main role of children and adolescents in the research process, the conclusion was that its use in studies involving the pediatric population should be encouraged.

Operationalization of assent for research participation in pre-adolescent children: a scoping review

Florence Cayouette [1], Katie O'Hearn [2], Shira Gertsman [2 3], Kusum Menon [4 5]

Conclusion: We found significant variation in criteria used for assessment of patient capacity, delivery of information used to obtain assent and documentation of the assent process. While we acknowledge that individual children, settings and jurisdictions may require different approaches to obtaining assent, there should be agreement on important principles to be followed with resulting common guidance on assessing capacity, delivering information and documentation of the assent process for publication.

Consent and Assent in Pediatric Research

D Micah Hester [1], Skye A Miner [2]

Affiliations + expand

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Abstract

Research involving pediatric populations has important ethical and regulatory considerations. As children generally cannot consent to research, there are special protections put in place to ensure that the decisional vulnerability is protected, including parental permission and often the child's assent. Assent is an ethically important part of the research because it allows the child to participate in the process of agreeing to research, develop their autonomy, and express their values. This article explores a case where the child and parent disagree about the child's participation. In doing so, the regulatory requirements of pediatric research are outlined and the process and product of obtaining assent from a minor is described.

Interruzione o ritiro dal trial

Quando un **partecipante interrompe il trattamento**, si ritira o conclude lo studio, lo sperimentatore deve attenersi al protocollo per **evitare la perdita di dati** già raccolti. La perdita di dati può **compromettere l'affidabilità dei risultati** e portare a conclusioni errate sulla sicurezza del farmaco.

Motivazioni del ritiro anticipato

Il partecipante **non è obbligato a spiegare** le ragioni del ritiro, ma lo sperimentatore dovrebbe cercare di **comprenderle**, rispettandone i diritti. Un **colloquio** può aiutare a chiarire i motivi ed eventualmente **ridurre i ritiri,** senza influenzare indebitamente la decisione del partecipante.

Comunicazione dei risultati

Lo sperimentatore dovrebbe **informare** i partecipanti dei **risultati** dello studio e del trattamento ricevuto, quando disponibili dopo l'apertura del cieco. Tale comunicazione deve avvenire nel rispetto della preferenza del partecipante a ricevere o meno queste informazioni.

2.10 Investigational Product Management

Uso corretto del farmaco sperimentale

Lo sperimentatore o un suo delegato deve **spiegare** a ogni partecipante il **corretto uso** del farmaco sperimentale. A intervalli appropriati deve anche **verificare** che le istruzioni vengano seguite correttamente.

Fornitura e somministrazione

Il farmaco sperimentale può essere **spedito a casa del partecipante** o fornito in una sede vicina, come farmacia o centro sanitario locale. La **somministrazione** può essere effettuata dal personale del centro, dal partecipante stesso, da un caregiver o da un professionista sanitario.

Gestione del farmaco sperimentale

La gestione del farmaco deve **rispettare i requisiti normativi applicabili**. Devono essere previsti sistemi di sicurezza per garantire l'integrità del prodotto, l'uso secondo protocollo e la sicurezza dei partecipanti.

Decentralized clinical trials (DCTs): A few ethical considerations

Carlo Petrini [1], Chiara Mannelli [1], Luciana Riva [1], Sabina Gainotti [1], Gualberto Gussoni [2]

Decentralized clinical trials (DCTs) are studies in which the need for patients to physically access hospital-based trial sites is reduced or eliminated. The CoViD-19 pandemic has caused a significant increase in DCT: a survey shows that 76% of pharmaceutical companies, device manufacturers, and Contract Research Organizations adopted decentralized techniques during the early phase of the pandemic. The implementation of DCTs relies on the use of digital tools such as e-consent, apps, wearable devices, Electronic Patient-Reported Outcomes (ePRO), telemedicine, as well as on moving trial activities to the patient's home (e.g., drug delivery) or to local healthcare settings (i.e., community-based diagnosis and care facilities). DCTs adapt to patients' routines, allow patients to participate regardless of where they live by removing logistical barriers, offer better access to the study and the investigational product, and permit the inclusion of more diverse and more representative populations. The feasibility and quality of DCTs depends on several requirements including dedicated infrastructures and staff, an adequate regulatory framework, and partnerships between research sites, patients and sponsors. The evaluation of Ethics Committees (ECs) is crucial to the process of innovating and digitalizing clinical trials: adequate assessment tools and a suitable regulatory framework are needed for evaluation by ECs. DCTs also raise issues, many of which are of considerable ethical significance. These include the implications for the relationship between patients and healthcare staff, for the social dimension of the patient, for data integrity (at the source, during transmission, in the analysis phase), for personal data protection, and for the possible risks to health and safety. Despite their considerable growth, DCTs have only received little attention from bioethicists. This paper offers a review on some ethical implications and requirements of DCTs in order to encourage further ethical reflection on this rapidly emerging field.

Decentralized Clinical Trials in the Era of Real-World Evidence: A Statistical Perspective

Jie Chen [1], Junrui Di [2], Nadia Daizadeh [3], Ying Lu [4], Hongwei Wang [5], Yuan-Li Shen [6], Jennifer Kirk [6], Frank W Rockhold [7], Herbert Pang [8], Jing Zhao [9], Weili He [5], Andrew Potter [6], Hana Lee [6]

The value of decentralized clinical trials: Inclusion, accessibility, and innovation

Girardin Jean-Louis [1 2], Azizi A Seixas [1 3]

In this Review, we explore the transformative potential of decentralized clinical trials (DCTs) in addressing the limitations of traditional randomized controlled trials (RCTs). We highlight the merits of DCTs fostering greater inclusivity, efficiency, and adaptability. We emphasize the challenges of RCTs, including limited participant diversity and logistical barriers, geographical constraints, and mistrust in research institutions, showing how DCTs are preferred in addressing these challenges by utilizing remote digital technologies and community providers to enable broader, more inclusive participation. Furthermore, we underscore the potential of DCTs for democratizing clinical research. We also stress the importance of addressing unresolved challenges, including data security and privacy, remote patient monitoring, and regulatory variations. Research is needed to devise standardized protocols to streamline DCT processes, explore its long-term impacts on patient outcomes, and overcome challenges through equitable stakeholder engagement.

Abstract

There has been a growing trend that activities relating to clinical trials take place at locations other than traditional trial sites (hence decentralized clinical trials or DCTs), some of which are at settings of real-world clinical practice. Although there are numerous benefits of DCTs, this also brings some implications on a number of issues relating to the design, conduct, and analysis of DCTs. The Real-World Evidence Scientific Working Group of the American Statistical Association Biopharmaceutical Section has been reviewing the field of DCTs and provides in this paper considerations for decentralized trials from a statistical perspective. This paper first discusses selected critical decentralized elements that may have statistical implications on the trial and then summarizes regulatory guidance, framework, and initiatives on DCTs. More discussions are presented by focusing on the design (including construction of estimand), implementation, statistical analysis plan (including missing data handling), and reporting of safety events. Some additional considerations (e.g., ethical considerations, technology infrastructure, study oversight, data security and privacy, and regulatory compliance) are also briefly discussed. This paper is intended to provide statistical considerations for decentralized trials of medical products to support regulatory decision-making.

COSA CAMBIA DAVVERO?

- **Struttura della linea guida:** R3 è completamente riorganizzata con 12 principi generali.
- **Approccio proportionate risk-based:** i processi devono essere proporzionati ai rischi e agli obiettivi critici dello studio.
- **Critical to Quality (E8 R1)**: qualità progettata fin dall'inizio dello studio, evitando procedure e dati superflui.
- **Competenze multidisciplinari:** riconosciuto il ruolo di più figure. Ruoli e responsabilità: devono essere definiti e documentati chiaramente tra sponsor e sperimentatori.
- **Consenso informato:** introdotti eConsent, consenso a distanza con verifica identità e opzione cartacea.
- **Assenso minori**: richiesto assenso esplicito, con gestione del passaggio alla maggiore età durante lo studio.
- **Ritiro dal trial**: va evitata la perdita di dati e lo sperimentatore deve comprendere le ragioni senza influenzare la decisione.
- **Restituzione risultati:** lo sperimentatore deve informare i partecipanti sui risultati e sul trattamento ricevuto.
- **Farmaco sperimentale (IP):** può essere spedito o dispensato vicino al paziente, con somministrazione anche da caregiver o professionisti locali.

Il ruolo del infermiere di ricerca

Observational Study > Pediatr Blood Cancer. 2025 Oct;72(10):e31900. doi: 10.1002/pbc.31900. Epub 2025 Jul 9.

Clinical Trial Nurses in Centers of the Italian Association of Pediatric Hematology and Oncology (AIEOP): A Multicenter Observational Study

Matteo Amicucci [1 2], Francesca Resente [3 4], Manuela Mampieri [1], Valeria Facciolo [3 4], Moreno Crotti Partel [5], Anna Bergadano [3 4], Debora Botta [6], Marta Canesi [7], Immacolata Dall'Oglio [8], Martina Piazzalunga [7]

Affiliations + expand

PMID: 40635181 DOI: 10.1002/pbc.31900

Abstract

Purpose: To describe numbers and activities carried out by clinical trial nurses (CTNs) present in the centers of the Italian Association of Pediatric Hematology and Oncology (AIEOP).

Materials and methods: Descriptive observational multicenter study based on data collected via electronic questionnaire.

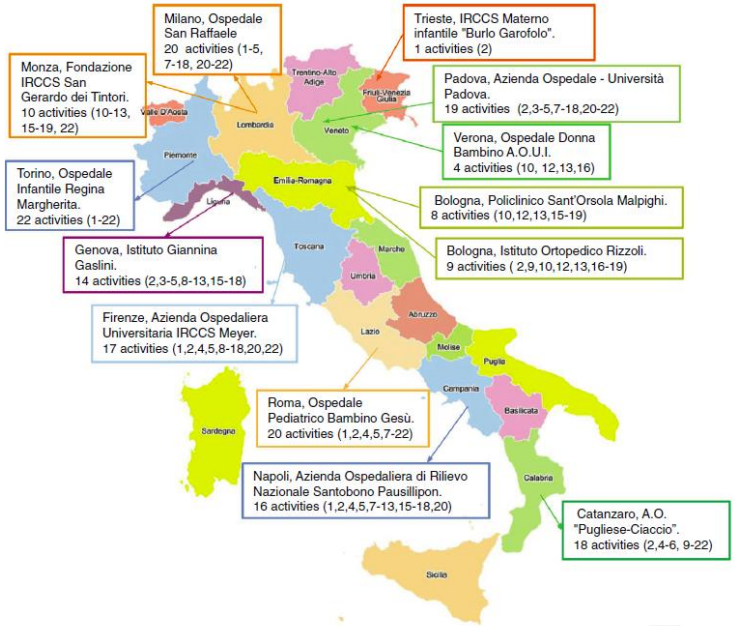

FIGURE 1 | Description of the activities carried out by the CTNs in the AIEOP centers.

GRAZIE PER L'ATTENZIONE