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Research Article

Physician barriers and dilemmas in the execution of clinical trials impacting decision-making in the DAHANCA 35 proton therapy trial for head and neck cancer

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ABSTRACT

Background: Physicians manage multiple obligations, providing best-practice treatment and patient- centred care in the standard treatment pathway while contributing to clinical trials simultaneously. These multifaceted responsibilities may introduce barriers and dilemmas to clinical trial execution, potentially impacting the clinical trial decision- making process. This study explores physicians' barriers and dilemmas in executing clinical trials and the impact on clinical trial decision-making.

Method: Qualitative semi-structured interviews were conducted with experienced oncologists. Moreover, participant observations were performed during clinical encounters involving discussions about clinical trials. The analysis followed a structured approach: (1) transcription of data, (2) inductive text coding, (3) exploration of patterns, and (4) interpretation, leading to the results. The results were discussed and validated by the study participants.

Results: The results comprise (1) a description of the clinical practice, which presents the setting of clinical trial execution; (2) results regarding physicians' barriers and dilemmas in executing clinical trials, leading to (3) the impact on clinical trial decision- making. The results involve barriers to time constraints for clinical trial tasks, dilemmas emerging from trial requirements or deviations from standard guidelines, and challenges with providing sufficient trial communication and adequate decision-making support, balancing between a paternalistic approach and respecting patient autonomy.

Conclusion: The demanding obligations of clinical practice constitute a complex setting for executing clinical trials, resulting in numerous barriers and dilemmas that impact the decision-making process in clinical trials. The study emphasises the need for tailored clinical trial decision-making interventions to facilitate supportive, informed, and non-directive clinical trial decision-making.

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Background

Physicians enrol patients in clinical trials for various reasons, including access to novel treatment with potentially better treatment outcomes than standard therapies. Moreover, physicians strive to contribute to advancing medical knowledge and developing new therapies [1].

However, clinical trial enrolment encounters structural, systemic, clinician, and patient-related barriers. Structural barriers stem from logistical and organisational aspects, including limited access to trial- or treatment facilities and inadequate time and resources for trial-related tasks [2–4]. Systemic barriers emerge from policies and guidelines involving clinical trial eligibility criteria, clinical guidelines, and bureaucratic obstacles in the trial approval process [2]. Patient barriers to clinical trials are concerns about the experimental nature of the treatment and economic issues. Additionally, the amount of medical information overwhelms some patients, impeding their ability to make informed decisions regarding clinical trial participation [2,5–7]. Physician barriers influencing clinical trial enrolment involve inadequate awareness or knowledge about available trials and concerns about trial-related risks [2,8–10].

Decision-making in healthcare has shifted from a paternalistic 'doctor knows best' attitude to increased patient involvement [11]. Patients are now considered active partners in healthcare decisions, focusing on shared decision-making between healthcare providers and patients [12,13]. However, this transformation may face challenges in clinical trial decision-making in balancing informed consent and ensuring an optimal decision that balances available options with the patient's preferences and needs [14,15].

This study aims to explore physicians' barriers and dilemmas in executing clinical trials and how these barriers and dilemmas impact the clinical trial decision-making process.

Material and methods

The study was guided by the interpretive description (ID) methodological framework. ID is a qualitative inductive method for exploring health-related phenomena [16].

Setting

The current study uses DAHANCA 35 as a host trial to explore the study's aim. It is an RCT comparing radiotherapy with photons and protons for treating laryngeal and pharyngeal cancer [17]. The clinical rationale for proton therapy (PT) is the anticipated benefit in decreasing late treatment-induced toxicity [18]. Following the Declaration of Helsinki, the RCT is conducted across six Danish cancer clinics [19]. One treatment centre in Denmark provides PT, and participants allocated to proton therapy are referred to this facility. Participants assigned to photon radiotherapy are treated at their regional hospitals.

Patients diagnosed with head and neck cancer are invited to a Multidisciplinary Team (MDT) meeting or a clinical consultation at their regional hospital. The appropriate treatment plan is determined in this meeting, and communication regarding the host RCT occurs.

Danish cancer pathways recommend a maximum of 11 days from treatment decision to treatment initiation for patients with head and neck cancer. Trial-related tasks have extended this period to 18 days in the host RCT, approved by The Danish Health Authorities.

Sampling of participants

The interview participants constitute the investigative team for the host RCT, comprising one primary investigator and six local investigators, each representing a cancer clinic. In addition to being investigators, all participants are experienced clinical oncologists actively engaged in radiotherapy and research. All seven agreed to participate in the interview.

Individuals included in the participant observations comprised physicians, nurses, patients with laryngeal- or pharyngeal cancer, and caregivers sampled by convenience in the cancer clinics.

Ethical considerations

The study adheres to the Declaration of Helsinki and the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist [19,20].

Participants received written and verbal information and consented before the interviews and prior to participant observations. The participants are anonymous and referenced by using identification numbers in the interviews and observation numbers in the participant observations.

The research team had no access to the patient's medical records when conducting participant observations. Patients and caregivers were informed of the observer's role and the purpose of the observation. They verbally acknowledged the observation but were not required to complete a consent form. The Danish Data Protection Agency (record no. 1–10-72–181-20) approved the study.

Data collection

The interviews were conducted face-to-face between March 2022 and June 2022, using a semi-structured interview guide (Supplementary A) that covered participants' perspectives regarding the host RCT.

Participant observations were performed in four of the six participating cancer clinics during January and February 2023. In the remaining two clinics, no pertinent clinical encounters occurred during the scheduled observation times.

Following a structured guide (Supplementary B), participant observations occurred during clinical encounters, where physicians interacted with patients, caregivers, and the clinical team.

The researcher spent 15–20 min before and after each consultation interacting with staff and discussing the patient's case. Discussions with physicians helped the researcher (AWK) understand their thoughts on enrolling or not enrolling the patient in the RCT. Observations during encounters focused on how trial communication influenced patients' decisions regarding participation, exploring the interactions between patients and physicians and the level of support offered to patients in the decision-making process [21,22]. Comprehensive field notes were obtained throughout participant observations.

Interviews lasted approximately 30 min, and observations around one and a half hours.

Data from interviews and observations were securely stored.

Data analysis

Audio-recorded interviews and field notes from observations were transcribed and imported into NVivo 14, which supported systematic data organisation and analysis [21]. All interviews and observations were relevant for analysis.

The analysis followed four phases: data transcription, initial text coding, pattern exploration to identify categories, and interpretation leading to theme extraction. Initially, 40 codes were derived, leading to the identification of 12 categories. Three categories described clinical practice, forming one theme. The remaining nine categories delineated three themes, illustrating how barriers and dilemmas in conducting clinical trials influenced decision-making regarding enrolment (Table 1).

Two authors (AWK & ALJ) conducted simultaneous analyses, continuously comparing findings and discussing reflections to ensure consensus. The remaining authors, with extensive research and radiotherapy expertise, reviewed and discussed the analysis. A preliminary data analysis was presented to the participants during a research seminar. This member checking allowed them to validate and verify the

Table 1
The analytic process.

Inductive coding	Categories	Themes
Clinical examinations	Clinical obligations	Clinical Practice
Diagnosis/Symptoms		
Performance status		
Surgery		
Radiotherapy		
Palliative care		
Treatment effect		
Chemotherapy		
Nimorazole		
Side effects		
Nutrition		
Smoking cessation		
Dentist		
Patient state of mind (anxiety)	Patient-centred care	
Treatment- and care plan		
Patient-physician relation		
MDT	Collaboration	
Health professionals/staff		
National treatment standards		
Trial communication	Time constraints	Barriers to the Execution of Clinical Trials
Trial conduction		
Information standard treatment		
Physical/mental appearance	Patient needs	
Socioeconomic level		
Level of clinical experience	Physician competences	
Knowledge/attitude RCT		
Accelerated cancer pathway	Deviations from guidelines	Dilemmas to the Execution of Clinical Trials
Diagnosis to treatment interval		
Standard clinical workflow		
DAHANCA (network)	Research commitment	
Research agreements		
Clinical equipoise	Trial requirements	
Randomisation		
Eligibility assessment		
Paternalism/gatekeeping	Decision support	Clinical Trial Decision-Making

results, ensuring accuracy. The participants accepted the results, and no revisions were necessary.

Results

Due to the limited number of participants, characteristics are omitted for anonymity.

The presentation of results will be organised as follows: (1) A description of the clinical practice, which presents the setting for executing clinical trials; (2) two results delineating physicians' barriers and dilemmas to executing clinical trials, impacting (3) the clinical trial decision-making process (Fig. 1).

Clinical practice

MDT attendees included patients, relatives, head and neck surgeons, oncologists, and nurses. Patients appeared anxious during MDT while undergoing clinical examinations and receiving comprehensive information about their diagnosis and treatment. The surgeon and oncologist occasionally discussed using medical terminology. Patients seemed nervous when diagnosis details were discussed without their involvement.

> Physician: *"We're talking a bit over your head, but it's because we're discussing whether there are one or two suspicious lymph nodes"*.
> Patient: *"That's okay, but it makes me nervous"*.
> (OBS6)

During MDT, physicians established relationships with each patient while delivering tailored treatment recommendations aligned with nationally established standards.

> Physician: *"I considered giving you chemotherapy, but I'd prefer not to because of the nerve damage in your feet."*
> Patient: *"I don't know what to say because I want the best treatment. I have children and grandchildren who want to keep me around."*
> Physician: *"The best treatment is the one you can tolerate."*
> (OBS4)

Such treatment modifications required physicians to react appropriately while continuously communicating with patients, ensuring their understanding of the treatment implications.

Barriers to the execution of clinical trials

In addition to treatment decisions during MDT, patients were invited to consider participating in the host RCT. They were informed about the trial and received written patient information. Trial communications lasted approximately 5–10 min and occurred towards the end of the meeting. Physicians indicated that trial communication occasionally caused delays in clinical practice, emphasising the necessity of prioritising time between clinical practice and trials.

> *"When the standard treatment information is delivered, you have five to ten minutes to discuss relevant trials with the patient. This usually takes longer, and at times, it causes delays for me."*
> (ID4)

Physicians described patients as overwhelmed during MDT due to emotional distress. Thus, physicians found it challenging to balance sufficient information regarding the standard treatment pathway while simultaneously assessing the optimal timing and amount of clinical trial information within the time constraints of the meeting.

> Patient: *"I received more information than I typically get in two months. No more now, or else my head will explode."*
> (OBS5)

The conciseness and timing of trial-related communication varied among physicians across levels of expertise and engagement in the host RCT.

> *"It also matters which of us doctors have spoken with the patient and how knowledgeable one is about the trial"*.
> (ID1)

Lack of clinical experience and awareness of clinical trials impacted the quality of clinical trial communication.

Dilemmas to the execution of clinical trials

Physicians served comprehensive responsibilities by administering clinical duties within the standard treatment pathway, performing clinical trial tasks, and participating in research teams. The physicians expressed a solid commitment and responsibility to research.

> *"We are all deeply involved in research and very committed to these agreements."*
> (ID6)

Physicians aimed to uphold agreements in research teams and clinical trial contracts. However, some indicated conflicts between trial-specific agreements and clinical practice obligations. As an example, the Danish Cancer Pathway recommend a maximum of 11 days from the

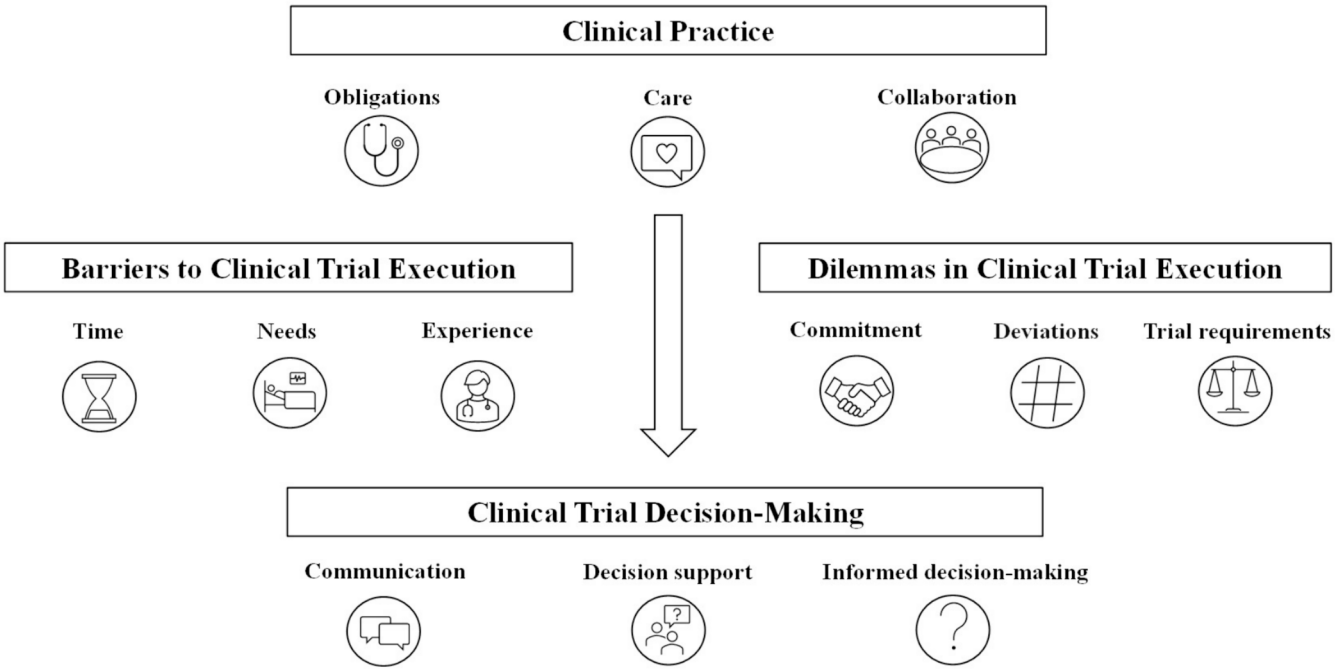

Fig. 1. Clinical practice presents a complex setting, leading to barriers and dilemmas in executing clinical trials, impacting the clinical trial decision-making process.

MDT to treatment initiation for patients with head and neck cancer. Due to additional tasks in the host-RCT, this duration was extended by seven days in case patients were randomised to PT. Data highlighted a need for more consensus among physicians regarding this postponement of treatment.

> *"I don't think the extra seven days matter much, but it's contrary to our usual approach of adhering to the cancer pathway."*
> (ID2)
> *"Sometimes, I find it difficult to tell patients that these extra days don't matter because research shows that even weeks can impact the stage of the disease."*
> (ID5)

Generally, physicians expressed that a seven-day postponement of radiotherapy would rarely affect the disease stage. However, conveying this exception to patients prioritising immediate treatment posed a communication challenge. Additionally, some physicians found deviating from national cancer treatment guidelines unethical.

Eligibility assessment in the host-RCT was a requirement before randomisation. This assessment was performed by comparing treatment plans with photon and proton radiotherapy, and patients were eligible for the host RCT if this comparison detected a theoretical advantage of PT. Consequently, patients were informed about PT's potential benefits before randomisation. Hence, some patients may have preferred allocation to PT.

> *"Some patients are disappointed to be randomised to photon treatment knowing that proton treatment might be a better treatment for them"*.
> (ID6)

A randomised design and the principle of clinical equipoise are essential requirements in clinical trials. However, these principles occasionally gave rise to dilemmas when communicating them to patients in the host RCT. It seemed challenging for physicians to balance the information regarding the presumed advantages and disadvantages of participating in the host RCT or receiving standard radiotherapy.

Insufficient clinical trial decision-making

The clinical practice constituted a complex setting for the execution of clinical trials, leading to barriers and dilemmas that impacted the decision-making process regarding participation.

Physicians encountered situations where patients needed further understanding of trial-related information but could not accommodate this need due to limited time in clinical practice, which may have hindered patients' ability to make a sufficient decision about participation.

> *"We provide verbal trial information as time permits during the consultation, and they receive written patient information. However, I'm doubtful about how much of the information they understand"*.
> (ID1)

Time constraints, lack of experience, patient needs, deviations from standard pathways, and trial requirements affected physicians' ability to provide adequate clinical trial decision-making support. On the one hand, they expressed concerns about interfering with patients' decisions because they feared influencing autonomous choices based on the patients' needs.

> "*I provide trial information and answer questions, but I don't want to influence their decision."*
> (ID7)

On the other hand, participant observation revealed instances in which physicians refrained from offering patients participation in the host RCT. Such a paternalistic approach denied patients the opportunity for autonomous decision-making regarding participation.

> Physician*: "I felt it was too much for this elderly woman to be introduced to the trial and have to deal with the decision."*
> (OBS1)

A consideration period is a requirement before clinical trial decision-making. However, some patients have made intuitive decisions regarding trial participation during MDT.

> *"Some patients even refuse to be informed about the trial, and others decide whether or not to participate already during the consultation. I*

inform patients that they can think about it for a few days, but most decide within an hour."
(ID4)

Recently diagnosed cancer patients often experience anxiety and stress. These circumstances may compromise their cognitive capacity for reflective decision-making, leading to intuitive decisions driven primarily by emotions rather than informed considerations when deciding on clinical trial participation.

Discussion

The study explored the complex setting for clinical trial execution within clinical practice, identifying physicians' barriers and dilemmas regarding clinical trials and their impact on decision-making regarding enrolment. The results were consistent across the six cancer clinics.

Clinical discussions during MDT occasionally appeared without involving the patient. Patient involvement requires physicians to possess communication competencies, which is a cornerstone of patient-centred care [22]. Similar to this study, the literature describes challenges in MDT discussions when physicians have differing opinions on treatments. This complicates conveying treatment opportunities to patients, hindering their ability to be involved in decision-making [23,24].

The current study identified a discrepancy between standard and trial guidelines, specifically the extension of time before treatment, as a dilemma. Generally, physicians did not consider the seven-day delay of radiotherapy a risk of compromising clinical outcomes [25]. However, it caused a dilemma due to patients' anxiety about disease progression, requiring additional communication regarding the clinical impact of treatment delay.

Another dilemma identified was a trial requirement for eligibility assessment. Only patients with a theoretical benefit of proton therapy were relevant for randomisation in the host RCT. Communicating the principle of clinical equipoise to patients became more complicated when this selection was performed, as shown in a prior study that identified it as a source of uncertainty for patients regarding clinical trial participation [7].

Prior studies emphasise that clinical information overload can influence patients' ability to make informed decisions [7,9,10]. Information overload presents a challenge in this study, as clinical trial details must be conveyed alongside extensive diagnosis and standard treatment information. Thus, it is crucial to keep the information concise yet sufficient during MDT, supplemented by relevant written material for patients to review at home between consultations [14,26].

The current study identified that physicians occasionally abstained from offering patients clinical trial participation based on subjective clinical judgment that extend beyond the exclusion criteria. Although the intent is to provide optimal patient treatment, this approach risks a paternalistic bias, potentially denying patients the opportunity for autonomous decision-making and resulting in clinical trial gatekeeping [27,28]. The current study identified an ethical dilemma for physicians in determining the appropriate level of engagement in the clinical trial decision-making process. Shared decision-making in trials presents challenges, with physicians managing both clinical and research responsibilities potentially favouring specific options, thus introducing bias in the decision-making process. This issue has also been noted in prior studies [14,26,29–31]. To address this issue, training physicians in decision coaching to facilitate non-directive communication during clinical trial discussions could be relevant [32]. Other appropriate interventions include patient decision aids tailored to clinical trials or videos explaining the clinical trial to patients [14,33]. Moreover, patient and public involvement in research can be performed to improve enrollment, which is relevant, in particular, if it involves individuals with firsthand experience of the disease and treatment [34].

This study is based on seven interviews and seven participant observations. While this sample size is acknowledged as a limitation, further data collection could have provided additional perspectives and nuances to the results. Nonetheless, the collected data offers diverse perspectives to address the research questions adequately [35,36]. Another limitation is the potential for the lead author, who is responsible for data collection, to have preconceptions about clinical trials and radiotherapy. To mitigate this, the author conducted the analysis and continuously discussed preliminary findings with a co-author (ALJ) from a different clinical field, broadening the perspective.

One strength of the study lies in its diverse setting, with data collected from six cancer clinics. Additionally, combining data from interviews and participant observations contributes to a comprehensive understanding of the research questions.

Although the study was limited to radiotherapy for head and neck cancer, the findings may have general applicability beyond the specific setting and be relevant to various clinical practice settings and clinical trials. The decision-making setting in the host RCT is comparable to the standard process used for informed consent in clinical trials conducted in other settings [32].

Conclusion

Clinical practice, involving clinical obligations, patient-centred care and collaboration, presents a complex setting for clinical trial execution. This study identified time constraints, patient needs, and physicians' lack of experience as barriers to clinical trial execution. Furthermore, deviations between clinical practice and trials, trial requirements such as the eligibility and randomisation procedure, and the concept of clinical equipoise contributed to dilemmas in executing clinical trials. These barriers and dilemmas impacted clinical trial decision-making due to inadequacies in the trial communication between patients and physicians, lack of support in the decision-making process regarding clinical trial participation, and patients' tendency to intuitive decision-making.

The clinical implications involve an identified need for improved resources if the execution of clinical trials is to be better incorporated into clinical practice. The findings highlight the necessity for interventions that support clinical trial decision-making. Based on the results of the current study, the authors developed and are currently feasibility testing a clinical trial decision-making intervention. The intervention involves a clinical trial patient decision aid and a clinical trial communication approach to enhance informed decision-making.

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Declaration of Generative AI and AI-assisted technologies in the writing process

ChatGPT was used to improve language and readability during the preparation of this work. After using this tool, the authors reviewed and edited the content as needed and takes full responsibility for the publication's content.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data supporting the results in the current study are available upon request by contacting the corresponding author.

Disclosure statements.

The authors report that there are no competing interests to declare.

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All the contributions mentioned above were essential; this study would not have been possible without them.

The lead author (AWK) conducted interviews and participant observations. She is a Ph.D. student with prior experience and training in qualitative research methods. Furthermore, she possesses experience as a registered nurse, a radiation therapist, and a clinical trial nurse.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tipsro.2024.100259.

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