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Exploring Recruitment to Randomised Trials Within Current Clinical Care Pathways: A Qualitative Case Study

Thesis submitted in fulfilment of the requirement for the Degree of Doctor in Philosophy at Trinity College Dublin

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2024

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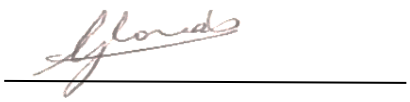

Gloria Emmanuel

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Dedication

To my beloved parents, who raised me against all odds and gave me your all, I dedicate this thesis in memory of you. You were my unwavering source of strength, inspiration, and guidance, and your love and support have been the driving force behind all my achievements. This work is a testament to the values of hard work, patience, and love that you instilled in me. I know that you are watching over me with pride and joy.

Summary

Background: Randomised clinical trials constitute a cornerstone in the establishment of evidence-based healthcare practices (Hariton & Locascio 2018). Internationally, a positive correlation exists between the degree of research activity within a national health system and improved patient outcomes (Ozdemir *et al.* 2015, Jonker *et al.* 2020). Despite this, the execution of clinical trials frequently encounters challenges, characterized by missed targets, extensions, and recruitment failures (McDonald *et al*. 2006, Briel *et al.* 2021). The PRioRiTy study, a collaborative effort between the Health Research Board-Trials Methodology Research Network (HRB-TMRN) and the James Lind Alliance (JLA) in the United Kingdom, sought to address and prioritise key methodological questions aimed at enhancing recruitment to randomised trials (Healy *et al.* 2018). This pivotal initiative yielded a curated list of the top 10 priority recruitment questions, collectively addressing uncertainties surrounding the recruitment to randomised trials. Foremost among these uncertainties, is the paucity of empirical knowledge pertaining to the coexistence of randomised trials with existing clinical care pathways and the utilisation of clinical care pathways for the recruitment of participants into trials.

Aim: To explore, understand and describe if, and how, current Clinical Care Pathways (CCPs) were being utilised for recruitment to randomised trials.

Methods: The study employed a single instrumental case study design, aligning with the goal of exploring the use of CCPs for trial recruitment. The utility of CCPs were explored through a purposive selection of seven case trials in diverse clinical care pathways that were currently recruiting within a large acute care setting in Ireland. A multiple data collection method was employed, which included document analysis of Patient Information Leaflets (PILs) and trial protocols, Non-Participant Observations of trial recruitment and semi-structured interviews (n=25) with trial recruiters (n= 23) and trial participants (n=2) in relation to these seven case trials. The study data was holistically analysed using a Reflective Thematic Analysis (RTA) approach.

Findings: The findings of this case study are thematically represented into four themes and 13 corresponding sub-themes that describes the utility of CCPs during the various phases of a trial recruitment process. The four overarching themes identified in this study were: 1) ‘CCPs as a conduit for initiating recruitment’; 2) ‘A parallel pathway approach for trial recruitment’; 3) ‘Complexities of recruitment - an issue beyond CCPs’; 4) ‘Factors affecting trial recruitment within CCPs’.

Conclusion: The case study presented the various ways in which CCPs were utilised through the different phases of trial recruitment. CCPs were commonly used during the initial phase of trial recruitment, where potential participants were identified, pre-screened for eligibility, and introduced to the trial. However, CCPs were less commonly utilised during subsequent phases of trial recruitment including informed consent, screening, and randomisation due to the advanced requirements of tasks involved in these phases. The advanced requirements included the need for specialised facilities, focussed time and attention, and adherence to strict protocol timelines. In order to address these challenges, the subsequent recruitment processes diverged onto a parallel pathway that offered a purpose-built infrastructure and focused attention to potential trial participants. Although the parallel pathway approach benefitted the overall conduct of the trial recruitment process, avenues for further optimising the utility of CCPs for trial recruitment was identified.

Key considerations for optimising the utility of CCPs for trial recruitment include expediting the development of a national healthcare records system to streamline sourcing of patient data for trial eligibility, appointment of clinician academics, securing protected research time, facilitating funding mechanisms, and enhancing the overall governance and infrastructural support. These enhancements could collectively contribute to a more streamlined and efficient trial recruitment process, addressing existing challenges and fostering a conducive environment for advancing evidence-based healthcare practices.

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Abbreviations list	
CCP	Clinical Care Pathway
CONSORT	Consolidated Standards of Reporting Trials
COVID-19	Coronavirus disease of 2019
CRO	Contract Research Organisation
EBM	Evidence-based medicine
GP	General Practitioner
IMP	Investigational Medicinal Product
JLA PSP	James Lind Alliance Priority Setting Partnership
MDT	Multi-disciplinary team
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIH	National Institutes of Health (US)
NIHR	National Institute for Health Research
NRES	National Research Ethics Service
ORRCA	Online Resource for Research in Clinical Trials
PIL	Patient / Participant Information Leaflet
PRioRiTy	Prioritising Recruitment in Randomised Trials study
QUESTS	Qualitative Research in Trials Centre
QuinteT	Qualitative Research Integrated within Trials
RCT	Randomised Controlled Trial
RN	Research Nurse
SWAT	Study Within A Trial
TMRP	Trials Methodology Research Partnership
UK	United Kingdom
UKCRC	UK Clinical Research Collaboration
USA	United States of America

Chapter 1: Introduction

1.1 Introduction to the topic

The subject of this enquiry is immersed in the field of clinical research conduct; more specifically, that of trial methodology and recruitment to randomised clinical trials (RCTs). Clinical research is an in-depth examination of the safety and efficacy of novel developments or advancements in patient care, for example in areas such as medications, medical devices, or diagnostic tests (Hulley *et al.* 2013). Hence, clinical research differs from laboratory research in that it relies on people (individuals or patients and the public) volunteering as study participants to help researchers better understand medicine and health (Hackshaw 2011, Hulley *et al.* 2013). Clinical research studies may be observational or experimental in design. Observational studies attempt to identify and describe patterns or associations in health-related data. Experimental studies, referred to as clinical trials or intervention studies in the context of clinical research, are alternatively, designed to test or intervene in individuals' lives with a novel intervention, such as a new treatment or lifestyle change, and then evaluate the effect of the intervention on health-related outcomes e.g., mortality, morbidity, disease prevention, etc. (Hackshaw 2011, Hulley *et al.* 2013). As a result, clinical trials play an important role in the provision of evidence-based healthcare.

The randomised controlled trial (RCT), a type of clinical trial, has been described as one of the most robust methods for supporting evidence-based practice because they involve a rigorous and systematic approach to testing the effectiveness of a particular intervention or treatment (Hariton & Locascio 2018). This is important for patients who may benefit from the intervention and for practitioners who want to deliver effective clinical care, as well as for researchers who want to contribute to the evidence base for improving health outcomes (Loudon 2015). The systematic approach employed in the design and implementation of RCTs is characterised by three primary characteristics. These are the inclusion of a control group of participants, also referred to as the comparator group, who do not receive the intervention being evaluated; the random assignment of participants to either the intervention or control group; and the implementation of blinding procedures, where

possible, whereby the allocation of participants to either the intervention or control group is concealed from both the trial participants and members of the research team (Hariton & Locascio 2018). The process of randomisation in the trial serves to mitigate the potential confounding effects caused by variations in both observed and unobserved natural factors between the intervention and control groups (Hariton & Locascio 2018). Therefore, randomisation aims to ensure the observed differences in the outcome could be attributed to the trial intervention rather than variations in the study population such as gender, height, or weight (Kendall 2003, Hackshaw 2011).

RCTs that specifically involve evaluating investigational medicinal products (IMPs) intended for treating illnesses before they can be used in clinical practice are further categorised into numerically denoted trial phases (Friedman *et al.* 2015, Bhide *et al.* 2018). Phase I trials involve the participation of healthy volunteers with the trial conducted to ensure that the new IMP is safe in humans and to study how the IMP is absorbed and distributed in the body. Phase II trials are known as proof of concept trials since in this trial phase, researchers investigate the therapeutic efficacy of the IMP. Phase III trials are also called confirmatory trials, which can include multi-national trial locations involving large numbers of trial participants, are conducted to confirm the effectiveness and safety of the IMP. Phase IV trials involve the ongoing collection or the collection of therapeutic data for an extended duration after the IMP has been approved for use by the relevant regulatory body, for example, the European Medicines Agency (Bhide *et al.* 2018). The purpose of Phase IV trials is to continue to monitor the effectiveness and safety of an IMP intervention.

Irrespective of the trial purpose, trial phase or medical condition involved, well-designed, conducted and reported RCTs are regarded as the gold standard for evaluating the safety and effectiveness of an intervention on healthcare outcomes and in assisting healthcare professionals to determine evidence for informed decision-making on effective treatment options (Copeland *et al.* 2016). RCTs which are poorly designed or conducted, alternatively, could result in unreliable findings and may lead to research waste (Morley & Farewell 2000, Chalmers & Glasziou 2009). One prevalent challenge in conducting RCTs is the issue of meeting trial recruitment targets as pre-determined in sample size estimates (McDonald *et al*. 2006, Silcocks & Gheorghe 2014, Fogel 2018, Briel *et al.* 2021). The research study

reported in this thesis was thus designed and implemented to facilitate exploration of recrutiment to RCTs, utilising the context of clinical care pathways in an acute care setting as a platform for exploration.

1.2 Purpose of this thesis

RCTs are typically conducted in clinical care settings, where the recruitment of trial participants is intertwined with ongoing clinical care activities (Harwood *et al.* 2011, Ozdemir *et al.* 2015). Despite the importance of this context, previous research has primarily studied recruitment to trials without considering how the existing clinical care pathways may facilitate or hinder recruitment efforts (Adams *et al.* 2015, Team *et al.* 2018). This PhD study was conducted to better understand the utility of clinical care pathways (CCPs) in facilitating recruitment to clinical trials; a trial recruitment uncertainty highlighted by the PRioRiTy study which identified a 'Top-10' list of trial recruitment uncertainties using a James Lind Alliance Priority Setting Partnership (Healy *et al*. 2018) (see section 2.7 for further details). By gaining a more comprehensive understanding of the utility of CCPs for recruitment to trials, researchers may work towards optimising trial recruitment processes alongside or embedded within clinical care provision.

1.3 Aims and objectives of the study

The aim of the study was to explore, understand and describe if, and how, current CCPs were being utilised for recruitment to RCTs in an acute healthcare setting in Ireland. Ongoing RCTs (referred to as 'trials') at the study setting were purposively selected to enable the exploration of trial recruitment within CCPs (section 5.5 provides further details).

The objectives of the study were:

i. To review the selected trials' documents to collect data on their recruitment processes.

ii. To ascertain if and how CCPs were being utilised in recruitment by observing and shadowing recruiters (research nurses, pharmacists, investigators) to these trials.
iii. To explore the experiences of using CCPs from the perspective of key stakeholders (recruiters and patients) involved in the recruitment processes associated with the selected trials.
iv. To triangulate the findings arising from objectives i-iii in describing and understanding trial recruitment including facilitators and barriers within the context of CCPs.
v. To provide scientifically sound evidence-based recommendations for how trial recruitment processes can be optimised within current CCPs.

1.4 Personal journey and motivation of this PhD

My passion for clinical research began during my time as a pharmacist in community care. During that time, I realised the crucial role of clinical trials research in drug development and the significant impact it can have on patient care. I knew that my skills could be put to use in this area, and so I pursued a Postgraduate Diploma in Clinical Research, which later led me to a career in drug safety reporting. While working at a back-end office and reviewing multiple trial documents, I realised the vastness of the research being conducted globally. This realisation sparked a desire in me to be a part of designing and conducting trials. Therefore, to acquire a deeper understanding of trials and to obtain hands-on experience in this area, I pursued an MSc in Clinical Research. It was during this time that I got the opportunity to work on a large Phase III RCT and to truly understand the conduct of clinical trials from within. Later, I became a Clinical Trials Manager managing one of Ireland's first clinical trials in humans on a cartilage regeneration product developed in Ireland. The hands-on experience I gained in setting up the trial was invaluable. However, the trial team faced significant challenges in implementing the study at the clinical sites, which resulted in delays in planned trial recruitment. These challenges could not be addressed from a clinical trial administrative perspective alone, as they were also related to the clinical care setting. Upon completing the trial, I was immediately

drawn to the scholarship offered by Trinity College Dublin (TCD) and the Health Research Board Trials Methodology Research Network (HRB-TMRN) in 2018 to pursue doctoral study in the area of trial methodology, and specifically recruitment to trials. This scholarship presented a unique opportunity for me to explore clinical trial recruitment from a care pathway perspective and gain a deeper understanding of the issues therein. By undertaking this PhD, my intention was to inform, contribute to, and advance trial conduct and scholarship in trial methodology for the benefit of both trial researchers and trial participants engaging with clinical trials in the acute care setting.

1.5 Structure of this thesis

Having introduced the study in Chapter one, the remainder of this thesis is organised with reference to the following chapters. Chapter two addresses the topic of RCTs in detail, particularly focussing on the issue of recruitment challenges in the conduct of such trials. This chapter also discusses methodological initiatives which were established or undertaken with a focus on recruitment to clinical trials. Chapter three presents a concept analysis of CCPs resulting in an operational definition of the concept by critically analysing how the concept is used or described in literature by following the principle-based concept analysis method of Penrod & Hupcey (2005). The operational definition produced from the analysis informed the planning, conduct of the PhD study. Chapter four outlines the philosophical assumptions and the methodological choice underpinning the conduct of the study. The rationale for a qualitative case study, type of case study and the rationale of choice of data collection and analysis methods are discussed.

Chapter five provides a comprehensive overview of the research methods employed in operationalising the qualitative case study. This includes a discussion of the approaches utilised to determine the sample, the procedures employed in the collection and analysis of data, and the measures implemented to enhance the overall quality of the research. Ethical considerations associated with this research study are also discussed. The thematic findings of the study are presented in Chapter six. Chapter seven discusses the results of this case study with reference to

the literature on trial recruitment that focuses on the use of CCPs. The strength and limitations of this research study are also considered. Chapter eight, the final chapter of this thesis, provides recommendations for policy and practice, as well as suggestions for future trial methodological research, based on the findings of this study.

Chapter 2: Background and Context

2.1 Introduction

This chapter begins by discussing the importance of evidence-based medicine and of RCTs. The methodological challenges concerning recruitment and the initiatives undertaken to enhance recruitment to RCTs are also discussed. The purpose of this chapter is to provide a background to subsequent chapters and to contextualise the work presented in this thesis.

2.2 Evidence-based medicine and randomised controlled trials

The term evidence-based medicine (EBM) was originally coined by the evidence-based working group at McMaster University, Canada, under the leadership of Gordon Guyatt (Guyatt *et al.* 1992). The term was subsequently defined by Sackett (1996, p 71) as: “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available clinical evidence from systematic research”. Therefore, clinicians considering EBM shift from solely relying on clinical experience for patient care to addressing clinical uncertainties through systematic searching and critical appraisal of the latest evidence, and through the conduct of clinical research to produce evidence-based recommendations (Straus *et al.* 2018).

Evidence for informing clinical practice has been ranked according to a ‘hierarchy of evidence’ (see Figure 1) based on research design types and the strength of evidence they produce (Greenhalgh 2014). Rigorously conducted RCTs and systematic reviews of RCTs have traditionally occupied the highest levels of the evidence hierarchy and are widely regarded as providing the 'best' evidence for the effectiveness of treatments or diagnostic procedures. RCTs, which aim to establish causal relationships between an intervention and outcomes, are widely regarded as the benchmark in clinical research due to their rigorous design, effectively minimising bias and controlling for confounding variables (Hulley *et al.* 2013). Furthermore, well-designed and conducted systematic reviews and meta-analyses of

RCTs are regarded as the pinnacle of all levels of evidence because they evaluate and aggregate the evidence (results) from all RCTs that address the same research question. Hence, RCTs and systematic reviews of RCTs are commonly used for policy or clinical guideline development and evidence based clinical decision making in clinical practice (Barton 2000, Robinson *et al.* 2021).

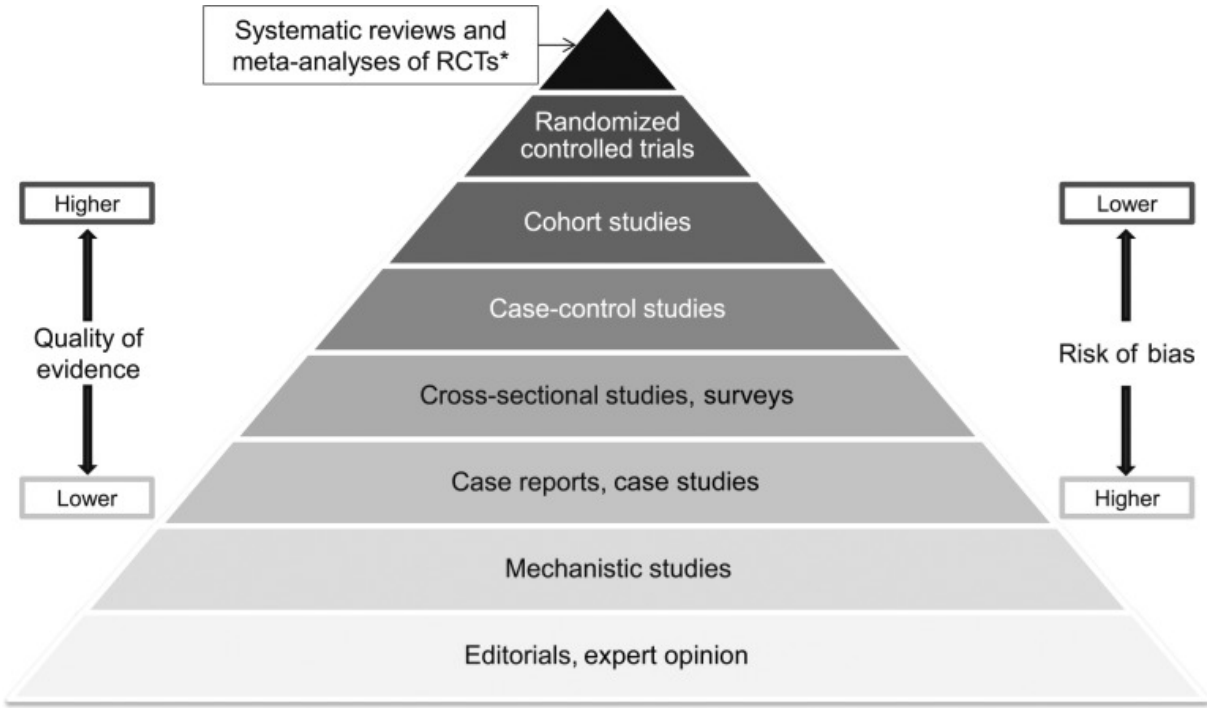

Figure 1: Hierarchy of evidence (Yetley *et al.* 2017, p. 259)

Although RCTs and systematic reviews, when rigorously conducted, provide high-level evidence for the effectiveness of interventions, they are not necessarily suitable for all clinical situations or research questions. For example, a cohort or case-control study design would be suitable for examining the association between disease and exposures (Barton 2000, Wald *et al.* 2003). Similarly, if a research question seeks to understand a particular phenomenon subjectively, such as gaining insight into experiences or understanding patient views, then a qualitative research study may be undertaken to generate the required evidence (Barton 2000, Hackshaw 2011). Acknowledging this, however, the RCT remains the ‘gold standard’ study design for generating evidence of cause and effect for the application of EBM in clinical practice (McErlean *et al.* 2023).

2.3 The emergence of trial methodology research

Trial methodology research is the scientific study of how RCTs (hereafter referred to as 'trials') are designed, conducted, and reported so that they may be optimised, and the quality of trials improved (Tudur Smith *et al.* 2014). This is important because trials, as one type of clinical research study, are used to generate the evidence for evidence-based clinical decisions in healthcare practice. A poorly designed or executed trial could provide results that are misleading or even harmful to individuals (Evans *et al.* 2011).

Researchers who undertake trial methodology research are commonly referred to as trial methodologists. Professor Doug Altman (1948- 2018), a renowned statistician and a prominent trial methodologist, is widely acknowledged for his leading role in establishing higher standards for the conduct and reporting of research in healthcare. He was a co-founder of the international Enhancing the Quality and Transparency Of health Research (EQUATOR) network (https://www.equator-network.org/) and was one of the earlier members of the Consolidated Standards of Reporting Trials (CONSORT) group, a group committed to standardising methods for researchers to report trials by providing trialists with reporting guidelines (Schulz *et al.* 2010). Altman, in one of his erstwhile publications titled '*The scandal of poor medical research'* highlighted the appalling number of research papers published in medical journals that were misleading due to methodological flaws (Altman 1994). He argued that enormous sums of money were being spent annually on research that was severely defective due to the use of improper designs, small or unrepresentative samples, or the application of inappropriate methods of analysis.

To address methodological concerns surrounding the conduct and reporting of trials, various developments have emerged as potential solutions. For example, in 2005 the International Committee of Medical Journal Editors (ICMJE) proposed comprehensive trial registration as a means of combating selective reporting of trial results. This approach prioritises full transparency in clinical trial reporting and is now a requirement for authors submitting to all ICJME member journals. Similarly, the CONSORT guidelines (1996) provide a helpful tool for authors reporting on trial results in medical journals. In a review of trial results, Hewitt *et al*. (2005) found that

authors adhering to CONSORT guidelines (1996) were more likely to clearly report on allocation concealment, that is “the technique of ensuring that implementation of the random allocation sequence occurs without knowledge of which patient will receive which treatment, as knowledge of the next assignment could influence whether a patient is included or excluded based on perceived prognosis” (Dettori 2010, p.8). By providing a detailed description of how allocation concealment was achieved, a critical element for minimising bias during randomisation, authors following CONSORT guidelines (1996) helped ensure that treatment assignment was truly random and unbiased, thereby increasing the reliability of the reported outcome results. This represents an important step forward in improving the integrity and rigor of clinical trial research.

Despite these earlier efforts, the conduct high-quality trial research continued to appear sub-optimal. Altman presenting at a conference in 2015, expressed regret that his original 1994 paper should have been titled the scandal of 'bad' medical research rather than 'poor' (Altman 2015). Altman posited that the problem was not only about using appropriate statistical methods, but a lack of understanding of the fundamental principles of scientific inquiry, coupled with a "publish or perish" (Altman 1994, p. 284) attitude that encourages researchers to publish as many research papers as possible, regardless of their quality. The continuation of sub-optimal or poor-quality trial conduct was more recently highlighted by Pirosca & colleagues (2022), who, in examining 96 Cochrane systematic reviews of RCTs across 40 Review Groups, discovered that the majority of trials (n=1013, 62%) had high risk of bias. This infers that the results from these 1013 trials were potentially inaccurate, and at best should be viewed with caution, due to flaws in how they were designed, conducted or reported.

Achieving high-quality trial results is further hindered by the challenges associated with below-par trial recruitment; one of the most cited reasons for trial failures worldwide (McDonald *et al.* 2006, Silcocks & Gheorghe 2014, Fogel 2018, Briel *et al.* 2021). Section 2.4 further discusses recruitment to trials and associated issues.

2.4 Recruitment to trials

Completing a trial successfully can be challenging, and it is often dependent on successfully recruiting a sufficient number of study participants for the trial results to be meaningful. Securing participation in trials, however, has been a perennial challenge, in particular, recruiting to sample size target within study timeframes. Inadequate recruitment has been identified as one of the greatest impediments in trial conduct with less than 50% of trials meeting recruitment targets regardless of revised timescales (McDonald *et al.* 2006). In a review of RCTs (n=151) funded by the National Institute for Health and Care Research (NIHR) in the UK between 2004 and 2016, the authors reported that just over half of the trials (56%) achieved their sample size target (Walters *et al.* 2017). This review examined a sample of single and multi-centre RCTs in several broad clinical areas, including mental health, cardiovascular, dermatology, and gastrointestinal, with most trials (n=82) being conducted in hospital settings (Walters *et al.* 2017). Results from reviews of clinical trial registries further show that only 20% of trials were informative discontinuations based on findings of efficacy, safety or futility of the trial interventions. The majority of trials were discontinued for unscientific reasons (68%) with insufficient recruitment cited as the lead reason for trial termination (57%) (Carlisle *et al.* 2015, Williams *et al.* 2015).

Evidence also suggests that recruiting participants is challenging irrespective of the population involved, type of treatment or study sponsor (Kasenda *et al.* 2014, Logan *et al.* 2017). Reports from the Institute of Medicine (2017), for example, indicate that 40% (n=221) of all the approved cancer therapy evaluation programmes closed without reaching 100% of their recruitment targets. Similarly, in a review of terminated cardiovascular studies and studies involving military personnel, 54% (n=278) and 12% (n=36) of the trials respectively experienced poor enrolment and were subsequently terminated due to issues of low recruitment (Cheng *et al.* 2010, Bernardez-Pereira *et al.* 2014, Cook & Doorenbos 2017). These findings thus highlight that sub-par recruitment remains a prominent challenge for trials irrespective of the clinical condition under study, the health topic area in which the trial is taking place, or the population involved.

Although the potential for RCTs to offer robust evidence is well recognised, challenges owing to insufficient recruitment can have significant scientific, ethical, and economic consequences (Gul & Ali 2010, Macleod *et al.* 2014, Chalmers & Glasziou 2016). The scientific implications of below-par recruitment include a reduction in the statistical power of a trial and the introduction of biased sampling, both of which compromise the trial's potential to yield statistically informative results (Copeland *et al.* 2016). Inefficient recruitment can also lead to ethical challenges because the benefits and risks of any intervention can only be fully evaluated if a trial is successfully completed. Furthermore, trials that face insurmountable barriers to completion expose human subjects to research burdens without any gains in scientific knowledge (Carlisle *et al.* 2015). Underpowered trials, caused by an inability to recruit to sample size estimates, stagnate the ability to answer critical healthcare questions, and can lead to repeatedly reinvesting and duplicating clinical investigations (Copeland *et al.* 2016). Many studies have identified that the complexity inherent in participant recruitment is often compounded by the research teams' immense workload and futile endeavours to enhance recruitment processes during trial conduct.

Trials that overrun or extend into lengthy durations beyond expected recruitment timeframes, without meeting the intended goals additionally pose a financial burden to the research enterprise resulting in missed opportunity costs that could have supported other endeavours (Williams *et al.* 2015). Furthermore, trial discontinuation due to a lack of recruitment frequently has further heightened ethical and economic concerns, as many of these trial results go unreported, and therefore represent a significant waste of valuable research resources, including of those given by individuals who have freely volunteered to participate in trials for the benefit of science and society (Kasenda *et al.* 2014, Briel *et al.* 2019, Briel *et al.* 2021). The above challenges have been reinforced by the findings of multiple studies and researchers agree that the challenges of recruiting to trials are complex and continue to be an ongoing concern to researchers (McDonald *et al.* 2006, Gul & Ali 2010, Vedelø & Lomborg 2011).

The issue of optimising trial recruitment poses an international challenge that calls for special attention across all healthcare fields and populations (McDonald *et al.*

2006, Vedelø & Lomborg 2011). Ireland, as in other countries and trial settings, faces similar challenges and experiences in optimising trial recruitment. A recent survey, for example, conducted by the Irish Pharmaceutical Healthcare Association (IPHA 2019) found that, in Ireland, it can take up to eight months for a trial to recruit its first participant following ethical approval submissions. This figure is based on 90 clinical trials across 11 therapy areas, between 2013 and 2018 (IPHA 2019). The results show that, respectively, only 53% (24 out of 45) of trials in oncology, 41% (7 out of 17) in cardiology, 25% (1 in 4) in infectious diseases, 20% (1 in 5) in respiratory diseases and 0% (0 of 8) in immunology successfully recruited to their sample targets (IPHA 2018). Trials conducted in Denmark, a country which has the same population as Ireland, although it conducts three times the number of clinical trials as Ireland, similarly can take six months to recruit its first participant (IPHA 2019). Therefore, finding practical solutions to overcome challenges to recruitment to ensure trial success and optimise the utility of trial results is a priority.

2.4.1 Understanding recruitment to trials

Recruitment is defined by the NIHR (2019) as "… the enrolment of an individual person meeting specific inclusion criteria into a research study. Each study participant who has both provided informed consent to join a study and is taking part in the study (i.e., participants who count towards the sample size of the study as set out in the study protocol), should be recorded as a participant in our NIHR Central Portfolio Management System (CPMS)." (NIHR CRN Recruitment Policy Document available at https://www.nihr.ac.uk/documents/nihr-crn-recruitment-policy-document/11347). Informed consent is a prerequisite for patients to participate in medical research. The Declaration of Helsinki (2013) by the World Medical Association lays out the ethical guidelines for human medical research and emphasises how informed permission must be given voluntarily by individuals who have the capacity to provide consent. Recruitment to trials is commonly understood as the process of enrolling patients or volunteers into trials after obtaining informed consent and ensuring they meet the eligibility requirements. However, recent methodological research indicates that recruitment to trials should not be viewed as a discrete action that occurs at a specific point in time, but rather as a complex

procedure that involves several processes spanning, for example, screening, consent, enrolment, and randomisation (Wilson *et al.* 2018, Bracken *et al.* 2019, Delaney *et al.* 2020).

When it pertains to defining trial recruitment, however, the aforementioned authors observed that there was a lack of clarity in existing literature in clearly outlining the recruiting process. The focus of Wilson ***et al.'s*** (2018) study was to develop a framework for the process of recruitment to RCTs. According to Wilson *et al.* (2018) there are four components to trial recruitment, namely Screened, Eligible, Approached and Randomised (SEAR); a framework which was proposed to help researchers monitor and improve recruitment processes. In contrast, Bracken *et al.* (2019) conducted a study to identify and review evaluations of strategies for recruiting adults over the age of 50 years to trials. According to this study, recruitment is a process that involves identifying prospective participants, assessing participant eligibility, providing participant information, and seeking consent. Whereas Delaney *et al*. (2020) undertook a three-phase analysis (theoretical, fieldwork and analysis) on the concept of trial recruitment to understand and describe the ways in which trial recruitment is understood, defined, and measured. The authors note that trial investigators are required to follow the CONSORT guidelines (Schulz *et al.* 2010), and in doing so should report on how investigators assessed participant eligibility to participate in the trial, method of randomisation, patient follow-up, outcome assessment and plan for analysis of trial results. While the CONSORT flowchart (see Figure 2) requires authors to report on the numbers of individuals assessed for eligibility, randomised and excluded (ineligible, refused to take part, or excluded for some other reason), the flowchart does not explicitly delineate all of the steps potential participants may be exposed to as they are being recruited to a trial. This has led to differences in the ways that recruitment is reported in clinical trials (Delaney *et al*. 2020).

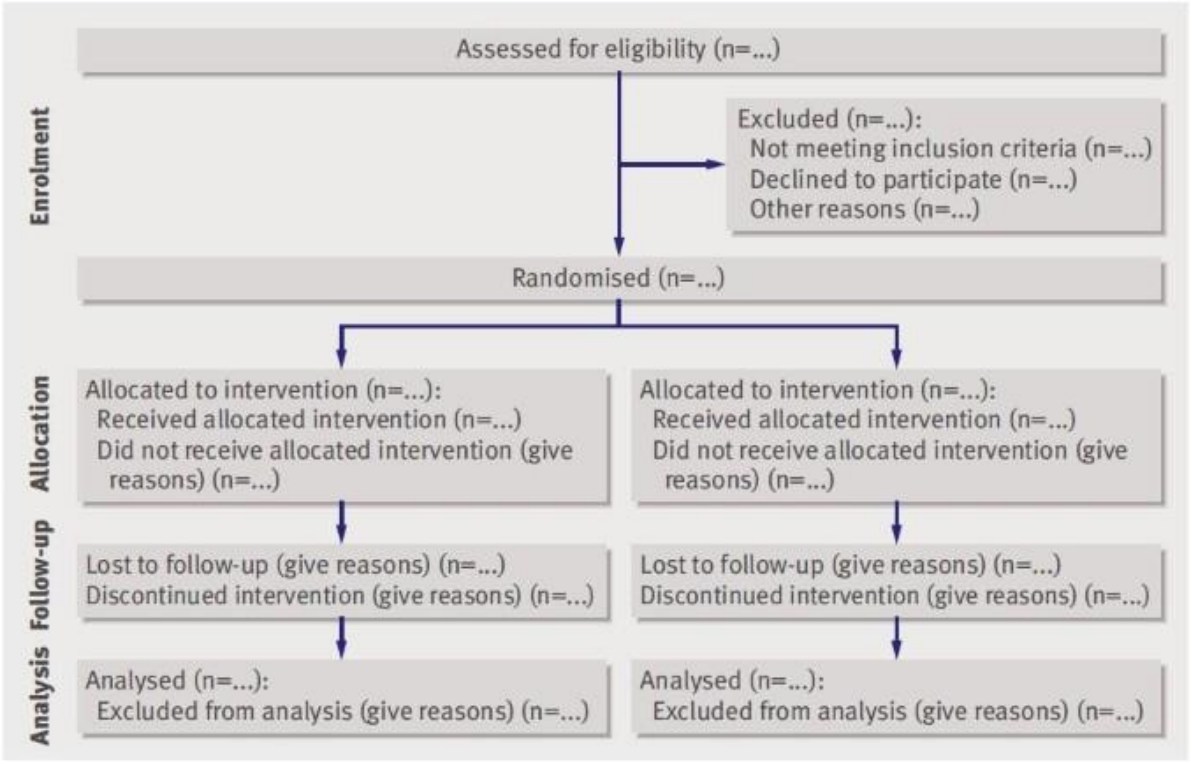

Figure 2: Flow diagram of the CONSORT recruitment process (Schulz *et al.* 2010)

While the studies by Wilson *et al.* (2018), Bracken *et al.* (2019), and Delaney *et al.* (2020) served distinct purposes, they collectively provided a comprehensive exploration or view of trial recruitment processes. Delineating the findings from these three sources revealed the following: in recruiting to trials, once the target population have been identified, trial investigators generally engage with a subset of a target population, by selecting and approaching potential participants in the setting(s) where the trial is being conducted (the study population) based on trial eligibility criteria. In doing this, trial recruiters may be described as engaging with the recruitment processes of identification, pre- or before screening, and screening based on pre-specified eligibility criteria for inclusion in a trial. As part of the CONSORT guidelines (Schulz *et al.* 2010), trial investigators are also expected to report on how potential participants are selected in order to minimise concerns about how trial participants differ from non-participants. This is done to ensure that the trial results are generalisable to the larger target population.

After eligibility is determined, subsequent recruitment processes involve informed consent and enrolment, wherein individuals who are eligible to participate in the trial make an informed decision to enrol in the trial. Once a participant enrols in the trial (gives consent and agrees to participate), the final recruitment process involves randomly allocating consenting participants to the intervention (trial or experimental arm) or control arm (existing treatment, alternative treatment, or placebo) of the trial. Therefore, based on a collective review of the research by Wilson *et al.* (2018), Bracken *et al.* (2019), and Delaney *et al.* (2020), trial recruitment, for the purposes of my research study, involves the sequential processes of: 1. Identification, 2. Screening and eligibility 3. Informed consent and enrolment, and 4. Randomisation and allocation. In this regard, the duration of recruitment for the purpose of my research study was defined as the time period from the identification of potential trial participants up to the point following participant randomisation and group allocation.

2.5 Methodological initiatives for improving trial research.

In efforts to advance trial methodological research and improve trial processes, including how trials are designed, conducted, and reported, several collaborative initiatives and networks, which not only conduct trial methodological research, but offer training and education in trial methods, have been established. For example, the UK-based Trials Methodology Research Partnership (TMRP) was established in June 2019 following funding awarded by the Medical Research Council- National Institute for Health and Care Research (MRC-NIHR) (https://www.methodologyhubs.mrc.ac.uk/about/tmrp/). The TMRP, not only brings together people, institutions and networks working in trials methodology research within the UK, but also involves those working in the field of trial methodology in Ireland and across the globe. These include members of the Health Research Board- Trials Methodology Research Network (HRB-TMRN) Ireland, Health Data Research UK (HRDUK), the UK Trial Managers' Network (UKTMN), the UK Clinical Research Collaboration (UKCRC) registered Clinical Trials Units network (UKCRC-CTU) and The Global Health Network (TGHN). Further initiatives focusing either exclusively on trial recruitment issues, or that have trial recruitment as a focus of

their broader methodological research scope also exist. Table 2.6 provides an overview of some of these.

Table 1: Overview of trial methodological research initiatives

Initiative/Network	Date established	Location	Remit/Scope
HRB-TMRN[1]	2014	University of Galway, Ireland	To strengthen the methodology and reporting of trials in health and social care in Ireland through a programme of work focussed on support, training and education, and research and innovation related to the methodology of trials. Although broad in scope, improving recruitment to trials is a core focus of the HRB-TMRN.
QuinteT[2]	Evolved since 1999 (Donovan *et al.* 2016)	University of Bristol, UK	Focuses on qualitative approaches to improving recruitment and informed consent in RCTs. The Group have developed QuinteT Recruitment Interventions (QRIs) to support ongoing host trials (currently n=40 trials) address recruitment challenges.

QUESTS[3]	2015	University of Galway, Ireland	QUESTS embedded within the HRB-TMRN was founded in 2015 at the University of Galway with the objective of maximizing the value of qualitative research in trials. The QUESTS team also provide support for conducting qualitative research in trials as well as training and education on the use of qualitative research in trials.
COMET[4]	2010	International	The COMET initiative, with their base in the University of Liverpool, UK, was established by trial methodologists and members of the general public who share a similar understanding of challenges associated with clinical trials. COMET, involving members from across the globe is focused on developing core outcome sets (COS) for use in trials and systematic reviews. A COS is a standardised set of agreed outcomes for measuring and reporting in all trials for a specific health condition or health domain (Clarke & Williamson 2016).

MRC-START[5]	2011	UK	The MRC- START initiative has three main goals: to improve the evidence base for trial recruitment, to increase recruitment rates, and to make research more accessible to the general population (Bower & Rick 2013). A main goal of the project was to create and evaluate interventions, at scale, to improve trial recruitment.
SWAT[6]	2011	Northern Ireland Network for Trials Methodology Research in collaboration with MRC HTMR and HRB TMRN	The SWAT program focuses on designing and embedding methodological research studies within 'host trials' whereby the embedded SWATs are designed to explore better ways of delivering key trial processes such as recruitment or retention of trial participants
Trial Forge[7]	2015	UK	Trial Forge is a collaborative initiative, co-ordinated by the Health Services Research Unit at the University of Aberdeen. The aim of Trial Forge is to strengthen the evidence base in decision making through all stages of a trial, that is from design stage to dissemination of findings (https://www.trialforge.org) The goal is to make incremental improvements in trial processes that will lead to significant gains across the whole trials network (Treweek *et al.* 2015).

ORRCA[8]	2016	Database maintained by UK and Ireland	The Online Resource for Research in Clinical triAls (ORRCA) database was created in order to effectively manage and organize the growing body of material on trial recruitment and retention literature (Kearney *et al.* 2018)

[1] HRB-TMRN: Health Research Board-Trials Methodology Research Network; [2] QuinteT: Qualitative Research Integrated within Trials; [3] Qualitative Research in Trials Centre; [4] Core Outcomes Measures in Effectiveness Trials; [5] The Medical Research Council (MRC) Systematic Methods for Facilitating Recruitment to Trials was an early project led by the University of Manchester (MRC-START); [6] Studies Within a Trial; [7] Trial Forge; [8] Online Resource for Research in Clinical triAls (ORRCA).

2.6 Prioritising Recruitment in Randomised Trials (The PRioRiTy study)

As previous subsections have demonstrated, the focus on recruitment to trials as a topic of research enquiry has become one of the top priorities for trial methodological research due to its criticality in the effective conduct and completion of trials. Tudur Smith *et al.* (2014) conducted an online Delphi survey involving the directors of 48 UK Clinical Research Collaborations and registered Clinical Trials Units (CTUs) to determine priority topics for methodological research in trials. The survey resulted in a consensus list of priority areas with 'Research into methods to boost recruitment in trials' achieving the highest priority, followed by 'Methods to minimise attrition' and 'Choosing appropriate outcomes to measure' (p. 1-7).

Although Tudur Smith *et al.* (2014) identified trial recruitment as a priority area requiring attention, the study did not report specific aspects related to recruitment that could or should be subject to further investigation. Recognising the importance of recruitment to the success of trials, a subsequent study, called the Prioritising Recruitment in Randomised Trials - Priority Setting Partnership (also known as the PRioRiTy study) (Healy *et al*. 2018) was undertaken to identify and prioritise the methodological uncertainties surrounding trial recruitment. The study involved two surveys with stakeholders (i.e., people who had been invited to participate in a trial

or participated in Trial Steering Committees, front line clinical and research staff who were or had been involved in recruitment to trials, people who had established expertise in designing, conducting, analysing and reporting randomised trials and people who were familiar with the trial methodology research landscape) to identify uncertainty trial recruitment questions (n=31 uncertainty questions) and to rank these. As part of the PRioRiTy study, each question was mapped to existing literature to confirm their 'uncertainty' status; that is, each of the 31 uncertainty questions were confirmed as being unanswered or 'uncertain' prior to being offered to stakeholders for ranking in the second survey. After the second survey, clinicians, researchers, research funders and members of the public who had previously taken part in a trial from Ireland and the UK came together in a James Lind Alliance - Priority Setting Partnership (JLA-PSP) to agree a 'Top-10' of these uncertainty trial recruitment questions. The HRB-TMRN, in association with the JLA oversaw the project.

The PRioRiTy-PSP culminated in a face-to-face meeting in Birmingham in December 2016, attended by 26 representatives from across the aforementioned stakeholder groups where the 'Top-10' questions on recruitment uncertainties was agreed (see Appendix 1 for these Top-10 questions). The intention in establishing this list, was to provide priority uncertainty questions that should be used to inform methodological research on trial recruitment in the future. Attendees of the JLA-PSP unanimously agreed that embedding trials as part of routine care, that is, viewing and ensuring trials as part of 'usual' care rather than an addition to it, could help to significantly address trial recruitment challenges (Healy *et al*. 2018). This resulted in the number 1 priority question: *"How can randomised trials become part of routine care and best utilise current clinical care pathways?"*

The HRB-TMRN in funding PhD scholars across the five partnership universities namely Trinity College Dublin, University College Dublin, University of Galway, University College Cork and University of Limerick, have encouraged the scholars to focus their area of study around the top-ten PRioRiTy questions. As such, PRioRiTy question one, with slight modifications, formed the basis of this PhD study; that is, to explore and understand if and how CCPs were being used in recruitment to trials, including the barriers and facilitators which may hinder or enhance the use of CCPs

for recruiting to trials, in one large healthcare setting in Ireland. In addressing PRioRiTy question one, the intent was to produce evidence to inform and advance scholarship on the topic of recruitment to trials as part of routine healthcare, and to make recommendations to enhance the conduct of future trial research.

As a step towards this, however, it was crucial to firstly establish and clarify what was meant by a CCP. To that end, to gain understanding and clarity, it was necessary to explore the literature on CCPs sufficiently in-depth especially in the context of the acute healthcare setting. After consideration and discussion with my supervisory team, a decision was taken to conduct a formal concept analysis of CCPs. A concept analysis, it was considered, would provide a structured approach to the critical analysis of CCPs, provide a deeper understanding of CCPs, and help establish an operational or theoretical definition of a CCP to inform the planning and implementation of the fieldwork phase of my PhD study. The following chapter presents the concept analysis thus conducted.

2.7 Chapter Summary

This chapter provided the background and context to the research topic that is explored in this thesis. The importance of EBM and trials, and the methodological issues that are associated with their conduct were discussed. In addition, examples of methodological initiatives established or undertaken to improve recruitment to trials have been identified and briefly described. One such initiative was the PRioRiTy study (Healy *et al*. 2018), which identified key uncertainties related to recruitment to trials. Drawing inspiration from the results of this study, this PhD research aims to explore the utility of CCPs for trial recruitment, thus addressing the number one PRioRiTy unanswered trial recruitment research question. The following chapter presents the conduct and findings of the concept analysis of CCP.

Chapter 3: A concept analysis of clinical care pathway

3.1 Introduction

This chapter presents an in-depth concept analysis of the 'clinical care pathway' in acute health care settings. The analysis was undertaken to enhance clarity on, and develop a deep understanding of, the concept of a CCP to inform the planning and conduct of the study's fieldwork phase (e.g., planning and guiding field observations, and designing the interview guide).

3.2 Choosing a concept analysis strategy

The methodological approach to undertaking a concept analysis is chosen based on the concept being analysed and the associated questions that require resolution (Meleis 2007). For example, a concept analysis could be undertaken to develop an understanding of an existing concept, clarify the concept where there is a lack of clear agreement on its meaning, or investigate a novel concept in practice that is underdeveloped with the aim of raising awareness of the new concept (Meleis 2007). Common methodological approaches for conducting a concept analysis include those developed by Wilson (1963), Walker and Avant (2005), Rogers (2000) and Penrod and Hupcey (2005). Therefore, an examination of these approaches, including their similarities and differences (see Table 2: Approaches to concept analysis methods.) was conducted to choose an appropriate methodological approach for undertaking the current concept analysis.

The origin of the methods involved in undertaking a concept can be traced back to Wilson's (1963) work, which is credited for influencing the development of all other concept analysis methods in nursing and health sciences (Beckwith *et al.* 2008, Cronin *et al.* 2013). Wilson (1936) proposed an 11-step approach to develop critical writing skills to examine concepts within their respective contexts. This method was specifically tailored for high school pupils to complete their admission examinations effectively. Although Wilson's work provided the foundation for concept analysis methods, it has faced criticism for its inclination towards prioritising critical thinking over facilitating the scientific exploration of concepts within the fields of nursing and

health sciences (Hupcey & Penrod 2005, Beckwith *et al.* 2008, Risjord 2009)**.** Subsequently, Wilson's method (1963) was adapted by Walker & Avant (1995) for use by novice researchers in nursing sciences. This adaptation resulted in an 8-step method for undertaking a concept analysis with the intention of making it easier to use. However, the simplification as Beckwith *et al* (2008) argue, lacks justification, and may not provide the necessary depth or rigor for advancing nursing theory.

Table 2: Approaches to concept analysis methods.

Wilson (1963)	**Walker & Avant (1995, 2005)**	**Rogers (2000)**	**Penrod & Hupcey (2005)**
11 step method	***8 step method***	***6 step method***	***Principle based approach***
Isolate the concept from other concepts	Select the concept	Identify a concept and associated expressions	Identify the concept and collect literature relevant to the enquiry
Choose the right concept by examining the multiple meanings associated with the concept	Determine the aims of the analysis	Select an appropriate realm for data collection	Assess the literature using criteria based on epistemological, pragmatic, linguistic, and logical principles
Construct a model case from real life that illustrates the concept	Identify all the uses of the concept that can be discovered	Collect relevant data including attributes along with surrogate terms, antecedents, and consequences	Integrate the assessments to form a theoretical understanding and description of the concept.
Construct a contrary case that does not reflect the concept	Determine the defining attributes	Analyse the data	
Construct a related case that demonstrates instances related to the concept	Construct a model case	Identify an exemplar of the concept	
Construct a borderline case that illustrates a possible instance of a concept	Construct additional cases such as borderline, related, contrary, invented, and illegitimate cases	Identify implications and propose hypotheses for further development	

Construct an invented case if examples from real life are lacking	Identify antecedents and consequences		
Identify social context in which the concept is used	Define empirical referents		
Examine underlying anxiety			
Identify the practical results			
Present the results in language			

The posited lack of rigour of Walker & Avant's (2005) method compared to Wilson's (1936) seminal work, can be attributed not only to the decreased number of steps involved but also to the modifications in the approach to case construction (Beckwith *et al.* 2008). Wilson (1963) emphasises case construction based on real-life situations relevant to the context being analysed, and from which, attributes relevant to the concept are developed. On the other hand, Walker & Avant (2005) focus on identifying attributes from broad literature sources, followed by case construction to include the identified attributes. As a result, these steps are limited to illustrations that fit the attributes rather than involving critical thinking and the analysis of a concept within its social context, (e.g., education or nursing sciences), as proposed in Wilson's (1963) original method.

Another commonly used method of concept analysis also adapted from Wilson's (1963) work is Rogers' (2000) evolutionary method of concept analysis. In this method, concepts are viewed as context-bound entities that evolve over time based on their significance, use and application. As a result, Rogers (2000) proposed an inductive approach to improve the rigour and validity of the concept analysis. Although Rogers' ideas are philosophically sound, they are not reflected in the steps proposed (Beckwith *et al.* 2008). For example, the 6-step method appears relatively similar to Walker & Avant's (2005) approach without accounting for the diversity of the concept in the methods. This is because, similar to Walker & Avant (2005), Rogers (2000) allows only a single example of a model case to explain concept evolution and thus fails to consider contextual meanings over time. By selectively

choosing specific examples from the literature, researchers may inadvertently exclude relevant literature, thereby limiting an in-depth understanding of the topic (Beckwith *et al.* 2008). Furthermore, rather than producing the attributes, surrogate terms, antecedents, and consequences as reflections of the analysed exemplar of the concept in Rogers (2000) approach, these features are gathered prior to the data analysis. Thus, the Rogers (2000) approach has encountered similar criticisms as Walker & Avant's (2005) approach, despite its strong philosophical stance (Hupcey *et al.* 1996, Hupcey & Penrod 2005, Beckwith *et al.* 2008, Beecher *et al.* 2019).

An alternative, more recently developed, method for concept analysis, is the principle-based method which was developed by Penrod and Hupcey (2005). Using this method requires the researcher to focus on evidence found in scientific literature rather than constructed cases or illustrations based on a random selection from extensive interdisciplinary literature sources that utilised the concept. Therefore, Penrod and Hupcey's (2005) method seeks to understand the concept within its context by not only necessitating the acquisition of scientific literature relevant to the investigation, but also via a thorough examination of the concept within four philosophical principles. These are the Epistemological, Pragmatic, Logical, and Linguistic principles. Evaluating literature under the epistemological principle involves assessing the extent to which an idea is defined and distinguished from other concepts. The pragmatic principle pertains to the practicality and utility of the concept, while the logical principle evaluates if the concept holds its boundaries when theoretically integrated with similar or related concepts. Finally, the linguistic principle involves analysis of the consistency in the meanings attributed to the concept in literature (Penrod & Hupcey 2005). Assessments under each principle are then integrated to form a theoretical description or operational definition of the concept (Penrod & Hupcey 2005, Beecher *et al.* 2019). This method therefore provides an in-depth exploration of the concept, resulting in a comprehensive understanding of the concept, as opposed to one based on a single model case as posited in other methods, which might be limiting (see Table 2). Furthermore, when using the principle-based approach, consideration is given to how well the concept is developed, often referred to as the maturity of the concept. Maturity implies that the concept has a clear definition, described characteristics, and delineated boundaries (Morse *et al.*1996).

In the acute health care context, the concept of CCP is broad, embracing several specialities and diverse medical conditions (Rotter 2012). Choosing a broad-based, approach for analysing the concept so that a deep understanding of and clarity on the concept could be achieved was thus needed in the current study. For this reason, the principle-based approach to concept analysis (Penrod & Hupcey 2005) appeared to be the most appropriate and logical choice. In choosing this approach, a more in-depth examination of the CCP and its complexities was facilitated, which also enabled analytically uncovering an operational definition of CCP as will now be described.

3.3 Literature search strategy

The principle-based approach to concept analysis requires the collection of evidence from scientific sources, which is then used to answer questions posed under the four broad philosophical principles (Penrod & Hupcey 2005). Therefore, a comprehensive search strategy was designed and implemented to capture the most relevant literature related to CCP.

To identify suitable search terms, a scoping search for a list of key terms related to the CCP was first undertaken, without applying date limiters, using the following four databases: Cumulative Index to Nursing and Allied Health Literature (CINAHL), Excerpta Medica Database (EMBASE), PsycINFO (database of the American Psychological Association) and PubMED (database of the National Library of Medicine). These databases were chosen because they include literature from diverse healthcare disciplines, e.g., medicine, nursing, biomedicine, healthcare, pharmacy, psychology, and allied health, within which CCPs may be used. This initial scoping search yielded approximately 28,000 citations, of which a sample of 50 papers were reviewed to ascertain and determine their keywords. After noting the keywords, and in discussion with my supervisory team, the following key terms were identified as being relevant for use in the concept analysis search strategy: *clinical care pathway, care pathway, care map, critical pathway, care protocol, care model, integrated care pathway,* and *care path*. Further, I also included search terms related

to the acute care setting, combining these with the CCP search string using the Boolean operand 'AND' given that the planned field work for my study was within an acute care setting. These terms were: *acute care, acute hospital, emergency care, critical care, acute hospital, acute medicine,* and *acute medical care*.

In addition to using the identified keywords, which were combined within each search string using 'OR', the associated Medical Subject Heading (MeSH) identified in three databases (CINAHL, Psych Info and PUBMED) and Emtree terms identified in EMBASE, were also used in the search strings. Truncations (*) towards the end of search terms were applied, where relevant, to capture all the variations of the term such as pathway, pathways, path, or paths. Similarly, truncations were applied to acute care terms to capture variations in descriptions such as acute medicine, acute medical care, acute cardiac care in hospital, and so forth. Table 3 presents the search strategy using the CINAHL database for illustrative purposes, and the results. The searches were limited to ten years (2010 to August 2020) to obtain a contemporary perspective of the concept in focus. However, even limiting the results to the last decade still returned a significant number of citations, indicating increased interest in the concept of CCP over recent years (Table 4).

Table 3: Search strategy (CINAHL database)

ID	Search strings	Type of search	Citations
S1	(MH "Critical Path") OR "clinical care pathway"	MESH	2890
S2	TI ("Clinical care pathway*" OR "Care pathway*" OR "Care map*" OR "Critical pathway*" OR "Care protocol*" OR "Care model*" OR "Integrated care pathway*" OR "Care path*") OR AB ("Clinical care pathway*" OR "Care pathway*" OR "Care map*" OR "Critical pathway*" OR "Care protocol*" OR "Care model*" OR "Integrated care pathway*" OR "Care path*")	Keyword, title, abstract	11,182
S3	S1 OR S2		15,021
S4	(MH "Acute Care")	MESH	5370
S5	TI ("acute care" OR "acute hospital" OR "Emergency care" OR "Critical care" OR hospital* OR acute*) OR AB ("acute care" OR "acute hospital" OR "Emergency care" OR "Critical care" OR hospital* OR acute*)	Keyword, title, abstract	664,399
S6	S4 OR S5	-	666,277
S7	S3 AND S6	-	4,604

Table 4: Search results by databases and year limiter.

Databases	Results without limiters	Results limited to 10 years (2010-2020)
CINAHL	4604	3167
Psych Info	5799	1733
PUBMED	5340	3781
EMBASE	9003	7294

The search yielded a total of 16008 citations, which were imported into Endnote X9.2 reference management software. The results from the four databases were combined, and duplicate citations removed (n=4,560), leaving 11,448 citations. These remaining citations were imported into Covidence, a review management application (www.covidence.org) for screening. Covidence identified an additional 900 duplicates which were removed, leaving 10,546 records for screening on title and abstract. Papers were included in the concept analysis only if they fulfilled the following inclusion criteria: defined or described a CCP, in an acute care hospital setting and in an adult population. Papers describing a CCP in non-acute care settings, such as maternity, community, residential or primary care, and in child populations (<18yrs) were excluded.

To enhance the robustness of the screening process, one of my supervisors and I independently reviewed the first 50 records in Covidence. A cut-off of 80% agreement on inclusion/exclusion was deemed acceptable to continue screening singularly (Shea *et al.* 2017). The level of agreement following the dual independent screening was 88% (44 out of 50 papers), providing reassurance on the specificity of the screening process. The disagreement during this screening stage process were minor based largely on uncertainty and lack of details for conclusive decision-making regarding inclusion or exclusion. All disagreements were easily resolved through discussion and consensus. Following title and abstract screening, 1110 papers remained for full text review, following which a final dataset of 195 papers, reporting on 193 studies, were deemed eligible for inclusion in the concept analysis. Figure 3 illustrates the search and selection results.

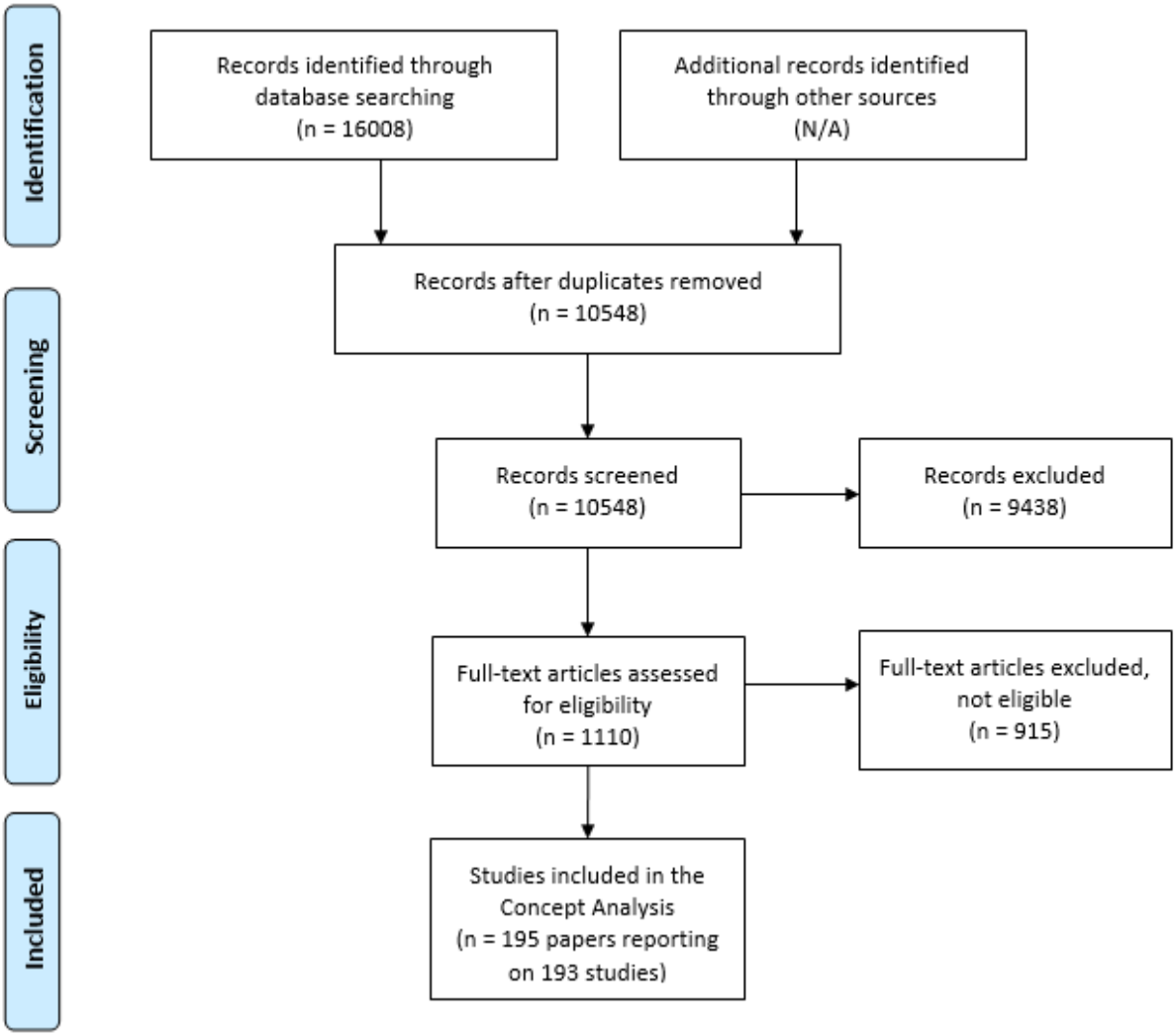

Figure 3: Search and Selection Flow Diagram

3.4 Data Extraction process

A data extraction tool (Appendix 2) was developed to aid extracting relevant data from the included papers according to the four philosophical principles that the data related to. Extracting data was guided by the questions posed in each principle, which concomitantly underpinned the analysis of the data (Penrod & Hupcey 2005). The questions posed were:

1. Epistemological principle: Is the concept well defined and well differentiated from other concepts in the literature?

2. Pragmatic principle: How useful is the concept in practice and how is it operationalised?
3. Linguistic principle: Do variations exist in how the concept is interpreted or in the use of language to describe the concept?
4. Logical principle: Are the boundaries of the concept well defined, including the concept's key characteristics and their consistency across the data?

The development of the data extraction form (DEF) adhered to established quality standards, as outlined by experienced researchers who previously employed the principle-based method for conducting a concept analysis (O'Malley *et al.* 2015, Waldon 2018, Beecher *et al.* 2019, Nevin *et al.* 2019, Smith & Mörelius 2021). These researchers recommended a series of measures to ensure the integrity of analytical depth, replicability, and transparency in the employed methods. First, a thorough read of each included article was undertaken, and the data were extracted under the questions posed by each of the four philosophical principles for each included article. Subsequently, concise summaries were generated to encapsulate the essence of the respective articles. For example, under the epistemological principle: in instances where the article presented a specific explanation or description of the concept of CCP, it was explicitly indicated as 'Yes' on the DEF (Appendix 2) and the definition or the summary description, as provided in the article, was recorded on the DEF. If the scientific article lacked a definition, description, or explanation of the concept of CCP, it was explicitly indicated as 'No' on the DEF. Furthermore, pertinent information such as the geographical location of the study, the specific healthcare discipline associated with the described CCP, the source of the article, and the research objectives were extracted and recorded on the DEF. This standardised extraction process and the structured visualisation of the data extracted from each included record via the DEF facilitated the concept analysis by enabling the data on the CCP to be collectively considered under the four principles, and the degree to which each included record contributed to this, and to which principle. It further facilitated an analytical exploration of the potential variations or similarities exhibited in the international scientific literature in relation to the concept of CCP.

The DEF was pilot tested with ten articles to ensure its suitability and was deemed 'fit for purpose' for further data extraction. The data extraction process was

challenging as some included papers contained extensive technical information related to several diseases in the acute hospital sector, including common and rare disorders of different kinds that were, at times, difficult to evaluate in terms of relevance to the concept analysis. Given the diversity of information and to reduce the risk of missing any relevant information, I initially attempted to capture every detail that potentially could have been related to the CCP. It became apparent however, that this approach was becoming unwieldy, time-consuming, and importantly, unnecessary by pulling information that went beyond the scope of the concept analysis. I overcame this challenge by returning to the explicit aims and objectives of the concept analysis, which became the guiding focus throughout the data extraction process (see Appendix 2 and 3).

3.5 Results

3.5.1 Epistemological principle

The epistemological principle investigates the nature of knowledge concerning the concept. A mature concept, according to this principle, is one that is well defined, differentiated, and clearly positioned in the body of related literature (Penrod & Hupcey 2005). Due to the dynamic nature of CCPs encompassing numerous specialties, medical conditions, and interventions, variations in how CCPs are defined might have been expected. The analysis of CCP under the epistemological principle, however, revealed that the concept of CCP is largely well-defined whereby the implicit descriptions and definitions of CCPs from the included studies appeared consistent with each other. Table 5 illustrates these definitions or descriptions as reported in a sample of 12 included studies, selected based on the variation in the speciality of care and country of origin and provides the study source types these were reported in. Although the CCPs described in the included studies relate to varying medical conditions including diabetes, depression, cancer, dementia and procedures or interventions such as bariatric surgery, stroke rehabilitation, and pain management, among others, the implicit meaning of a CCP was found to be somewhat generic in that it relates to guiding care. Similarly, while different terms are used to describe the CCP, such as care protocols, multidisciplinary care plans or

multidisciplinary pathways, care maps, critical care pathways, and Integrated Care Pathways (ICP), all CCPs appear to share common definitional elements that include guiding quality, safe, effective or standardised healthcare.

Of the 195 papers included in this concept analysis, 20 (10.3%) referred to the European Pathway Association's (EPA 2007) defining statement for a CCP. The primary function of the EPA is to offer training and educational resources on care pathway development. The EPA's influential definition developed by Vanhaecht *et al.* (2007, p.154) defines the CCP as "a complex intervention for the mutual decision making and organisation of care processes for a well-defined group of patients during a well-defined period". The CCPs underpinned by this definition were described as complex interventions because patient care involved several components that worked both independently and interdependently to ensure patient safety, satisfaction, and optimal use of resources (Schmit *et al.* 2011, Clerici *et al.* 2014, van Zelm *et al.* 2018, Bilò *et al.* 2020). Fundamentally, however, as with other definitions, implicit in the EPA's definition is that a CCP guides clinical care.

Table 5: Definitions of CCPs

Source	Country	Speciality	Definition
Rotter *et al.* (2010)	Australia and Germany	Systematic review on effect of pathways	Clinical pathways aim to link evidence to practice for specific health conditions in order to improve patient outcomes and clinical efficiency.
Agrawal *et al.* (2011)	UK	Invasive Mould disease	A successful pathway necessitates ownership of the pathway by the patient's clinical team, including radiology, microbiology, infectious disease, and respiratory physicians.
Hogan *et al.* (2011)	Ireland	Quality assurance of CCPs	CCPs have been evaluated as an effective tool for continuous quality improvement method aimed at improving patient outcomes and clinical efficiency.
Yan *et al.* (2011)	Taiwan	Cardiac catheterization procedure	The clinical pathway provides medical care guidelines that assist healthcare staff in improving job efficiency. It aids in the elimination of unnecessary tests and complications for patients and improves overall patient satisfaction.
Tastan *et al.* (2012)	Turkey	Breast cancer surgery	Clinical pathways are standard comprehensive management systems that provide specific care plans and include multidisciplinary services. They have been improved to better coordinate care by managing quality, time, and cost.
vanHoeve *et al.* (2014)	Netherlands	Breast cancer care	Care pathways are logically coherent individual care processes that patients with a specific condition go through for the duration of their care.
Vosler *et al.* (2016)	USA	Management of Epistaxis	CCPs are evidence-based protocols that are used to implement treatment guidelines and minimize variability in patient care in order to optimize outcomes and reduce costs.
AboSharkh *et al.* (2019)	Canada	Maxillofacial surgery	A CCP is a set of coordinated and standardised events, interventions, and goals for people with specific diagnosis.
Featherall *at al.* (2019)	USA	Total knee arthroplasty	Care pathways are clinical algorithms that are based on the latest evidence and allow for standardised care delivery.
Yong-Mei *et al.* (2019)	China	Endoscopic Sinus Surgery	A clinical pathway is a care plan developed by a group of hospital staff for the monitoring, treatment, rehabilitation, and nursing of a specific disease to reduce rehabilitation delays and waste of resources, and to enable clients to receive the best medical and nursing services.

Maheshwari *et al.* (2019)	USA	Colorectal surgery	Care pathways contribute to the goal of high-quality healthcare by delivering safe and effective interventions on a consistent basis.
GonzalezGarcia *et al.* (2020)	Spain	Healthcare technology	Care pathways (CPWs) are multidisciplinary care plans that detail essential care steps for patients with specific clinical problems.

The EPA (Vanhaecht *et al.* 2007), and later Kinsman *et al*. (2010), further describe five characteristics, which encapsulate the components of a CCP (Table 6).

Table 6: Components of CCPs

Defining characteristics of CCP by EPA (Vanhaecht *et al.* 2007)	**Defining constituents of CCP by Kinsman *et al*. (2010)**
• Contains an explicit statement of the goals and key elements of care based on evidence, best practice, and patients' expectations and their characteristics. • Facilitates the communication of team members, patients, and their caregivers. • Enables the coordination of care process by coordinating roles and sequencing of activities by multidisciplinary team. • Allows documentation, monitoring, and evaluation of variances and outcomes. • Identifies appropriate allocation of resources.	• Includes a multidisciplinary plan of care. • Translates evidence or guidelines into local structures. • Provides detail steps in a course of treatment or care in a plan, pathway, algorithm, guideline, protocol, or other 'inventory of actions'. • Contains timeframes or criteria-based progression. • Aims to standardise care in a specific population for a specific clinical problem, procedure, or episode of healthcare.

While both descriptions appear somewhat similar, they are not fully comprehensive on their own; the EPA (2007) definition of a CCP, for example, fails to emphasise that the goal of having CCPs is to standardise care. Contrastingly, Kinsman *et al.* (2010) overlooks the critical elements of communication and coordination among team members that are essential for the smooth functioning of CCPs (Seys *et al.* 2018, Aeyels *et al.* 2019). However, when these characteristics are examined together, they clearly communicate the implicit meanings of the definitions provided by CCPs as shown in Table 6 from an epistemological standpoint. Moreover, it was observed the definitions of CCPs were context-dependent, varying according to the clinical condition and specialisation and hence the authors seemed to have chosen a definition that they may have considered a best fit for their respective study. Despite some variations in the way CCP characteristics were described, there were more similarities than differences. For example, it was considered important that every CCP should use a structured multidisciplinary plan for standard care delivery (Kinsman *et al.* 2010, Seawright & Taylor 2011, Leonard *et al.* 2017). While the EPA's definition of CCP as a 'complex intervention for mutual decision making' (Vanhaecht *et al.* 2007), appeared prominent as it was referred to by the majority of

the authors of studies included in this concept analysis, there were other ways, however, that CCPs were described in the included literature.

CCPs were commonly described as care plans or multidisciplinary plans or guidelines that incorporated all of the anticipated elements of treatment or care provided by all the members of the multidisciplinary team for a specific type of patient group or clients (example, patients who had experienced a stroke) within a specific timeframe (Yan *et al.* 2011, Yong-Mei *et al.* 2019). Several included studies described CCPs as containing a series of clinical care activities which were not just a random series of steps but rather a well-organised logical sequence of events (Mhawej *et al.* 2020a, de Belvis *et al.* 2019c, Broussy *et al.* 2019, Baffert *et al*. 2015, Aicher *et al.* 2019). Thus, a CCP could be considered to provide, overall, the outline for a course of care, beginning with the initial evaluation of the patient and continuing through to diagnostic tests, potential side effects of treatment, referrals, and discharge planning. This aligns with CCPs being described in many of the studies included in this analysis as an "organised sequence of events" (Argulian *et al.* 2011, Iyer *et al.* 2012, Betts 2014, van Hoeve *et al.* 2014, Mhawej *et al.* 2020a).

The sequence of clinical events referred to in these CCPs were frequently presented as algorithms or care maps, which included illustrations or flow charts that visually represented the order of events that occurred (He *et al.* 2018, Cash *et al.* 2019, Bilò *et al.* 2020, Hare *et al.* 2020). Therefore, CCPs were also described in some studies as 'algorithms for clinical care' based on the latest evidence that allowed for standardised care delivery (Seawright & Taylor 2011, He *et al.* 2018, Cash *et al.* 2019, Featherall *et al.* 2019, Bilò *et al.* 2020, Hare *et al.* 2020, O'Hare *et al.* 2020). In addition to an emphasis on treatment, CCPs incorporate factors such as resource planning and utilisation to enhance efficiency in healthcare delivery. Consequently, CCPs are characterised as medical care guidelines that assist healthcare providers in enhancing job efficiency (Yan *et al.* 2011). The concept of an efficient CCP encompasses various layers of care planning, such as devising an individual's treatment or care plan, organising resources (such as personnel, equipment, and physical space), and coordinating care activities performed by both clinical and administrative staff. Therefore, CCPs incorporate various aspects of care planning

hence they were also referred to as a comprehensive management system (Yan *et al.* 2011, Tastan *et al.* 2012, Altman 2014, Yong-Mei *et al.* 2019).

Critically though, the CCPs described in all of the included studies that contributed data to this principle appeared to have the same goal, that is, to improve care quality by standardising clinical care processes. Shoemaker (1974), who provides one of the earliest definitions of a CCP, refers to it as a standardisation process. He states that a CCP "uses routines or patient protocols to standardise care, facilitate completeness of services, and evaluation of both the patient's progress and the therapeutic efficacy of the program" (Shoemaker 1974, as cited by Mhawej *et al.* 2020 p.1). Following this early definition, several studies described how CCPs were used to standardise care processes, thus giving rise to the term "standardised care pathway" (Bona *et al.* 2014, Eldridge & Apau 2015, Bradywood *et al.* 2017, Leonard *et al.* 2017, Burlet *et al.* 2018, Gehi *et al.* 2018, Bryant *et al.* 2019, Maheshwari *et al.* 2019b, Daghash *et al.* 2020).

Standardisation of care processes minimised variations and ensured better patient outcomes. This was accomplished by evaluating and updating the care processes in accordance with the most recent evidence (Seawright & Taylor 2011, Bona *et al.* 2014, Eldridg & Apau 2015, Leonard *et al.* 2017, Maheshwari *et al.* 2019, Bilò *et al.* 2020, Daghash *et al.* 2020). However, this is a complex task because it requires a dedicated multidisciplinary team that can collaborate to achieve this, and thus CCPs were also referred to as a ‘communication tool’ for mutual decision making (Fasola *et al.* 2012b, Castillo *et al.* 2015, AboSharkh *et al.* 2016, Burlet *et al.* 2018). As a result, a successful CCP necessitates a sense of ownership of the pathway by the clinical team caring for patients (Bona *et al.* 2014, Agrawal 2015). The resultant proactive multidisciplinary management ensured better care quality and thus, in some instances, a CCP was also regarded as a ‘quality improvement tool’ (Vanhaecht *et al.* 2010b, Yan *et al.* 2011, Holroyd-Leduc *et al.* 2013, Kul *et al.* 2013, Denbo *et al.* 2018, de Belvis *et al.* 2019a, Featherall *et al.* 2019).

In summary, the analysis of CCP under the epistemological principle revealed that CCPs were predominantly characterised as multidisciplinary plans, an organised sequence of events, and an evidence-driven tool that was regularly updated in

accordance with new scientific research to standardise clinical practice and enhance healthcare quality. These descriptive characteristics were not necessarily separate entities, rather they appeared as components of a CCP that work in tandem for efficient safe healthcare delivery. These descriptions were also reflected in the components of the CCP as described by the EPA (2007) and Kinsman *et al.* (2010) (Table 6), demonstrating consistency in how CCPs are described and defined across the broad ranging healthcare areas within acute clinical care. As a result, this analysis has demonstrated that the concept of CCPs can be considered epistemologically mature in the context of acute care settings.

3.5.2 Pragmatic principle

The pragmatic principle is concerned with a concept's application and usefulness within its context (Penrod & Hupcey 2005). According to Penrod and Hupcey (2005), a concept is pragmatically mature if it can demonstrate a high level of operationalisation that rings true with experience. CCPs were identified in this analysis as being widely used across healthcare disciplines with demonstrated success. The analysis revealed three stages to the application and utility of CCPs: development, implementation and evaluation.

3.5.2.1 Development of CCPs

Analysis identified that the CCPs were consistently used as a tool for managing patient care, however from a pragmatic standpoint the key drivers for CCP implementation were patient safety, variability in care and rising healthcare costs (Husni *et al.* 2010, Kul *et al.* 2013, Denbo *et al.* 2018, Feng *et al.* 2018, de Belvis *et al.* 2019b, Featherall *et al.* 2019).

Variability in care patterns, regardless of clinical speciality, appeared frequently in the studies as a reason for CCP development and use. For example, in one study, patients admitted to an emergency department with Atrial Fibrillation (AF) were co-managed by a team of cardiologists, primary care specialists, nurses and pharmacists. However, there was no guidance for a valid hospital admission for

patients who have AF, resulting in unnecessary hospital admissions and procedures (Gehi *et al.* 2018). In their study, Gehi *et al.* (2018) report how these variations in practice patterns prompted the emergency team to create a standardised CCP, which included a protocol for patient triage processes. This resulted in not only structuring the AF care process, but also increased patient safety by ensuring timely treatment (Gehi *et al.* 2018).

Similarly, Burlet *et al*. (2018), in their study described how variations in clinician referral practices for diagnostic imaging processes delayed timely interventions for those most in need, while also increasing hospital costs, wastage of resources and subjecting patients to unnecessary radiation. This necessitated the development of a standardised CCP that would allow inter-clinician decision making involving multiple specialties such as urologists, emergency physicians, gynaecologists, and general surgeons, which became extremely valuable to the entire healthcare team and their patients (Burlet *et al.* 2018). As noted epistemologically, CCPs encapsulated 'standardisation of care' in their definitions; pragmatically, the intention then in developing and operationalising a CCP was to minimise variations, enhance patient safety and reduce associated healthcare costs for optimised patient care delivery (Bona *et al.* 2014, Loftus *et al.* 2014, Eldridge & Apau 2015, Bao *et al.* 2016, Bradywood *et al.* 2017, Leonard *et al.* 2017, Burlet *et al.* 2018, Gehi *et al.* 2018, Bryant *et al.* 2019, Maheshwari *et al.* 2019b, Bergin *et al.* 2020, Daghash *et al.* 2020).

Developing CCPs involved multiple levels of planning irrespective of the condition or patient cohort for which they were intended, for example, patients with myocardial infarction or therapy for pneumonia (Schuur *et al.* 2011, Aeyels *et al.* 2018). Inherent in developing a CCP was consideration of efficient patient flow through the hospital, that is, a patient could navigate from the admissions office to the outpatient clinic, a day ward, a laboratory, a radiology department, and a nursing ward until discharge. Furthermore, in developing CCPs, logistical and operational issues, such as the capacity of professionals, equipment and space also required consideration (Schmit *et al.* 2011, Yan *et al.* 2011, Tastan *et al.* 2012, Yong-Mei *et al.* 2019, Mhawej *et al.* 2020)

Irrespective of the specific clinical care procedures or health conditions described in the included studies, the analysis identified a common approach for the development of CCPs within the acute care setting. This approach involved the active participation of a multidisciplinary team of experts responsible for patient management and a systematic approach to formulating the content of the CCP based on the latest evidence and best practices available (Seawright & Taylor 2011, AboSharkh *et al.* 2016, Elnahal *et al.* 2016, Feng *et al.* 2018, Arabacioglu *et al.* 2020). Leonard *et al.* (2017) further elaborates on developing a standardised CCP through five essential steps. These are: 1) identifying key stakeholders, 2) gaining stakeholder consensus on a standardised approach to disease management based on evidence, 3) increasing provider awareness of care paths, 4) incorporating care path tools into the electronic health record and workflow processes, and 5) securing the resources to develop, implement, and maintain care paths. While other studies included in the analysis reflected the steps proposed by Leonard *et al.* (2017), the most common steps that appeared were steps one and two, indicating that team involvement and consensus on evidence-based practices were the most important initial steps for CCP development. This could be because the later steps such as such as raising CCP awareness and incorporating CCPs into electronic medical records, as well as resource procurement, can occur only after CCP development, when CCPs are planned for implementation.

The analysis revealed that team involvement in developing a CCP was prominent. The development of a CCP for treatment of heart failure, for example, included a team of heart failure service managers, cardiology consultants, medical consultants, technicians, pathologists, cardiology ward administrators, and ward managers where the collaborative team effort and skills brought complementary knowledge and the scope of access to patient services in cardiology care (Crouchley 2012). The second apparent critical stage of CCP development involved reviewing evidence-based literature sources along with national or international care guidelines. For example, development of a CCP for Hymenoptera venom allergy (HVA) included an extensive review of literature sources for evidence-based practices for venom allergies and anaphylaxis reactions along with guidelines from the National Institute for Health and Care Excellence (NICE) and the European Academy of Allergy and Clinical Immunology (Bilò *et al.* 2020). Following this step, the content of the CCP was

finalised based on collaboration and consensus meetings (Kinsman *et al.* 2010, Van Citters *et al.* 2014, Butow *et al*. 2015, Denbo *et al.* 2018, He *et al.* 2018, Bilò *et al.* 2020). The CCPs were presented as ordered sequences of care, illustrated through flowcharts or algorithms (He *et al.* 2018, Cash *et al.* 2019, Bilò *et al.* 2020, Hare *et al.* 2020,) or described textually in care protocols (Birkhahn *et al.* 2012, Bloomer *et al.* 2015, Butterworth 2015, Brockman *et al.* 2016, Burton *et al.* 2020), which were then forwarded to hospital authorities for approval before implementation (Seys *et al.* 2018, Abo Sharkh *et al.* 2019, Bilò *et al.* 2020). In this regard, the analysis revealed that the approach to CCP development was, on the whole, systematic and consistent.

3.5.2.2 CCP Implementation

CCPs naturally vary based on their care trajectories, that is, the paths or routes that a patient takes through an acute hospital from beginning (point A) to end of the journey (point B) to meet their specific healthcare needs. Thus, CCPs can guide care over relatively short periods, for example, a few hours on a single day (Akinbobuyi 2016) through to longer periods, including several months based on the care path (Aicher *et al.* 2019). The CCPs included in this analysis involved diverse clinical care trajectories. For analytical discussion, these were broadly categorised, based on similarities in their care trajectories, into three categories: CCPs in surgical care, CCPs in non-surgical care and, CCPs during the COVID-19 pandemic and discussed here to illustrate implementation under the pragmatic principle.

3.5.2.2.1 CCPs in surgical care involving longer care trajectory

Fifty-five (28%) of the included studies reported on CCPs in surgical care. These related to multiple conditions, for example, maxillofacial reconstructive surgery (Abo Sharkh *et al.* 2019); radical prostatectomy (Abou-Haidar *et al.* 2014); vascular surgery (Aicher *et al.* 2019); head and neck surgery (Alibhai *et al.* 2017); spinal surgery (Ali *et al.* 2018) and breast reconstruction surgery (Astanehe *et al.*2018) among others. The majority of the CCPs in surgical care covered lengthy care trajectories from the initial consultation visit to discharge, and they typically included

three phases with similar goals including: the preoperative phase, intraoperative phase and the post-operative phase.

The preoperative phase generally included a diagnostic checklist of orders and procedures that patients undergo to prepare them for the operative phase. The emphasis in this step was given to discussions and meetings with patients on surgical plans, expectations, and milestones on all aspects of patient care during and after the planned surgery (Abou-Haidar *et al.* 2014, Abo Sharkh *et al.* 2019, Cash *et al.* 2019, Kaye *et al.* 2020). In the case of an unplanned emergency presentation, such as a hip fracture, appendicitis, or sporting injury, however, extensive patient discussions were avoided to expedite referral to surgery on the same day of admission (Turesson *et al.* 2012, Bona *et al.* 2014, Hotchen *et al.* 2016, Ng *et al.* 2019).

The intraoperative phase of the CCPs followed, which included the patient's surgery in the operating theatre as well as associated care events such as monitoring of blood pressure, haematocrit levels and administration of fluids or antibiotics. This was followed by a post-operative phase that included transfer to a recovery ward and the management of CCP elements such as administration of prophylactic medications, airway management, wound care, monitoring, and nutrition, culminating with a discharge and follow-up period. These surgical CCPs were therefore designed and implemented for lengthy care trajectories commencing with the first consultation visit to the last follow up visit, up to twelve months later in many studies (Tastan *et al.* 2012, Turesson *et al.* 2012, Abou-Haidar *et al.* 2014, Van Citters *et al.* 2014, Alibhai *et al.* 2017, Ali *et al.* 2018, Abo Sharkh *et al.* 2019, Cash *et al.* 2019, Kaye *et al.* 2020).

3.5.2.2.2 Non-Surgical CCPs involving shorter care trajectory

Contrastingly, non-surgical CCPs had a relatively short care trajectory since they largely focused on a single clinical setting within the hospital, such as an inpatient ward, outpatient clinic, diagnostic department, or emergency department (ED) where the journey begins and ends within the same setting. A CCP for patients with diabetes, for example, involved monitoring of glucose and insulin levels as well as

regular foot evaluations, which were managed by a diabetes specialist team in an inpatient ward. The typical length of stay was five days and was overseen by a relatively smaller clinical team consisting of a diabetes consultant, a specialist nurse, and a foot care team (Akiboye *et al.* 2020). Other examples for inpatient care CCPs, include the assessment of malnutrition by dieticians at the point of inpatient admission (Al-Zeer *et al.* 2015) or assessment and treatment for mental health needs within a short span of seventy-two hours within a psychiatric ward (Attfield *et al.* 2017).

Outpatient or ambulatory CCPs which do not include overnight hospital stays, in contrast, were designed to guide a point in time of clinical care. These CCPs were more often used in settings such as clinics or medical assessment units (Taduma-Tomàs *et al.* 2012, Akinbobuyi *et al.* 2016). Examples of health care conditions for which these CCPs were implemented included clinical risk assessments for pericardial disease for patients presenting with chest pain in an outpatient setting (Argulian *et al.* 2011), administration of pain medication for non-traumatic headaches in the ED (Clarke & Thomas 2010), a diagnostic procedure in the radiology department to detect blood clots (Bloomer *et al.* 2015), pharmacological treatment for depression and alcohol dependence (Awan *et al.* 2015), and pharmacological treatment for gastrointestinal bleeding (Franco *et al.* 2015).

Although mainly condition specific, the analysis did find that CCPs do not exist wholly in isolation, that is, in the acute setting, a patient may transition from one CCP to another; for example, a CCP guiding a clinical assessment of abdominal pain in the ED could lead to the patient being transferred to a CCP for appendicitis in a surgical unit (Crouchley 2012, Ball *et al.* 2014). Similarly, the presentation of severe epistaxis (nosebleed) required multidisciplinary management, with consultation and severity assessment taking place under the emergency CCP and later transitioning to the otolaryngology CCP (Vosler *et al.* 2016). Therefore, patients' care was frequently guided by transitioning from one CCP to another or through multiple CCPs within the same speciality at the same time (Clerici *et al.* 2014, Bao *et al.* 2016). This emphasises that, regardless of the CCP's purpose, the main intention of CCP implementation was to ensure a standardised approach across the patient care continuum.

3.5.2.2.3 CCPs during COVID-19 (coronavirus disease 2019)

The data for this analysis were collected approximately 8 months (Aug 2020) into the COVID-19 pandemic, when evidence for patient management during the pandemic was emerging. As a result, only four literature sources on the management of conditions during COVID-19 were identified in the search strategy. These studies described CCPs for head and neck cancer surgery (Butler *et al.* 2020), stroke (Frisullo *et al.* 2020), minimising COVID-19 infections (Boffa *et al.* 2020) and caring for patients with COVID-19 (Capalbo *et al.* 2020). Although the data are limited, given the enduring context of COVID-19 and the resulting impact on both patient care and healthcare provision in general (e.g., curtailing of some services), I deemed it informatively valuable to include this category of CCPs in the analysis.

While Capalbo *et al.* (2020) reported on a CCP specifically for the management of the COVID-19 condition, others reported on already developed CCPs which were modified for use during the COVID-19 pandemic. This was required because the efficient implementation of CCPs, as originally designed, was not operationally feasible during the pandemic, mainly because of the changes imposed on hospital services, including, for example, redeployment of staff, cancelling elective procedures, and restructuring of hospital areas (Boffa *et al.* 2020). Hence, it was observed that CCPs exhibited a remarkable degree of flexibility and adaptability, enabling them to remain unaffected by external circumstances, thereby continuing their functioning without interruption during the pandemic. This highlights the adaptable pragmatic utility of CCPs in the context of a pandemic. Furthermore, some of key steps taken to develop and implement CCPs during the pandemic were similar to those used in CCP development in the pre-pandemic period. Butler *et al.* (2020), for example, describe a collaborative effort between BAHNO (British Association of Head and Neck Oncologists) and ENT UK (a professional membership body representing Ear, Nose, and Throat surgery in the United Kingdom), during the pandemic, in developing guidance for hospitals for patients needing head and neck cancer surgery. This indicates, that irrespective when or for what a CCP is being developed, collaborative stakeholder involvement remains key for CCP development and implementation.

Where the COVID-19 CCPs differed to others, is that rather than being designed as a detailed series of steps in guiding patient care, the aim was to help ensure continuation of the service. In this sense, COVID-19 specific CCPs, while operationally having similar intent to all CCPs, that is to support a standardised approach to patient care, may have less depth due to the rapidity of their development in response to a global health crisis.

3.5.2.3 CCP evaluations

The analysis demonstrated that CCPs underwent ongoing evaluation following implementation through the review of existing practices, such as assessing the impact of utilising the new CCP on patient outcomes, including reduction of complications (Vanhaecht *et al.* 2010b, Kul *et al.* 2013, Bergin *et al.* 2020). CCPs were also implemented to curtail rising healthcare costs; consequently, care services, following CCP implementation, were reorganised to reduce hospital associated costs by allowing timely patient access, early hospital discharge, and avoidance of unnecessary procedures. As a result, several studies focussed on evaluating their success in reducing the duration or length of hospital stay (LOS) and associated hospital costs (Edwards *et al.* 2016, Hotchen *et al.* 2016, Vosler *et al.* 2016, Attfield *et al.* 2017, Barinaga *et al.* 2017, Abo Sharkh *et al.* 2019, Aicher *et al.* 2019). The findings from an evaluation of a CCP are then relayed back to the multidisciplinary team enabling them to review their care practices. Thus, the CCP is a dynamic entity that was routinely updated in accordance with new evidence and national practice guidelines (Yan *et al.* 2011, van Hoeve *et al.* 2014, Feng *et al.* 2018, Rathod *et al.* 2020).

CCP evaluations were conducted using a variety of methods, including pathway audits, surveys, case control studies, retrospective reviews, cohort studies, and systematic reviews (Rotter *et al.* 2010, Chung *et al.* 2012, Sheridan *et al.* 2012, Allen Liles *et al.* 2014, Birch *et al.* 2014, Bona *et al.* 2014, Aeyels *et al.* 2018, Burlet *et al.* 2018, Aeyels *et al.* 2019, Arabacioglu *et al.* 2020). The analysis revealed that the impact of CCPs on patient outcomes was consistently described as positive, including reducing complications, timely treatment, early recovery, adherence to

treatment, improved care coordination, and reduction in LOS and costs irrespective of the evaluation method(s) chosen by the authors of particular studies (see Figure 4 and Table 7) (Kinsman *et al.* 2010, Lyckner *et al.* 2010, Rotter *et al.* 2010, Lodewijckx *et al.* 2011, Vanhaecht *et al.* 2011, Yan *et al.* 2011, Denbo *et al.* 2018, Iiellis *et al.* 2018, Loots *et al.* 2018, Ovaere *et al.* 2018, Mhawej *et al.* 2020).

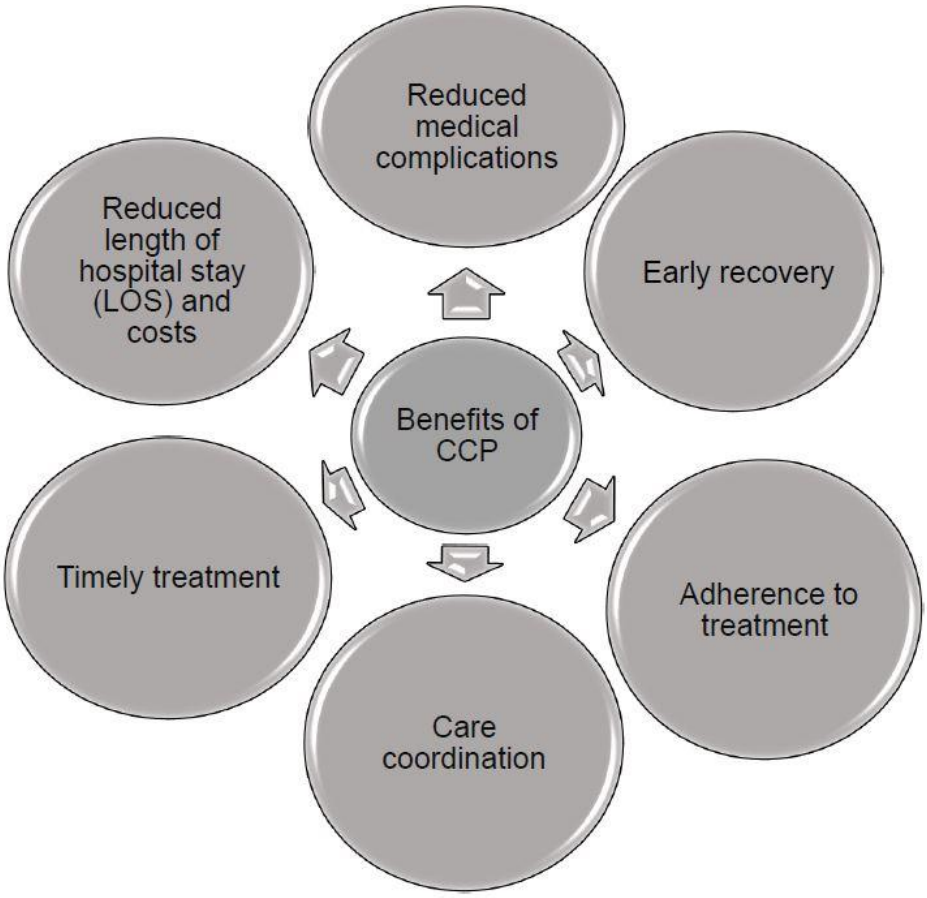

Figure 4: Benefits of CCP

Table 7: Examples of CCP evaluation studies and their outcomes

Source	Country	CCP speciality	Outcomes	Evaluation method
Rotter et al (2010)	Australia	CCP practices	Reduced LOS and complications	Systematic review
Aziz et al (2011)	Canada	Radiography	Reduced waiting time	Retrospective cohort study
Lodewijckx et al (2011)	Belgium	Respiratory diseases	Reduced LOS and readmission rates	Systematic review
Chung et al (2012)	Korea	Lumbar laminectomy	Reduced LOS and costs	Retrospective cohort study
Birch et al (2014)	Australia	Robotic prostatectomy	Increased patient satisfaction	Survey
Bona et al (2014)	Italy	Colorectal surgery	Reduced LOS and readmission rate	Prospective cohort study
Gordon & Reiter (2016)	USA	Head and neck cancer surgery	Reduced LOS and costs	Systematic review
Attfield et al (2017)	UK	Schizophrenia	Reduced LOS	Case control study
Aeyels et al (2018)	Belgium	Myocardial Infarction	Timely treatment	Pathway audit
Astanehe et al (2018)	Canada	Breast reconstruction surgery	Reduced complications and early recovery	Retrospective cohort study
Aeyels et al (2019)	Belgium	Cardiology	Improved care coordination	Model for Understanding Success in Quality (MUSIQ) scale
Akiboye et al (2020)	UK	Diabetes	Reduced LOS, mortality and readmission rates	Interrupted time series analysis

The evaluation of CCP implementation demonstrated reduced clinical complications in several studies (Husni *et al.* 2010, Vanhaecht *et al.* 2010a, Kul *et al.* 2013, van Hoeve *et al.* 2014, de Belvis *et al.* 2019a, de Belvis *et al.* 2019b, Bergin *et al.* 2020). This was because the CCP enabled a faster and easier patient flow management system in which the care was efficiently directed to the specialised care units. For example, identifying and transferring patients with ischemic stroke from the ED to specialised neurology and stroke care units reduced complications and readmission rates (de Belvis *et al.* 2019b). The context sensitive patient channelling also strengthened the multidisciplinary team involvement of ED, stroke, and neurology healthcare teams (de Belvis *et al.* 2019b).

Use of CCPs also improved care coordination and consistency of care delivered by different professionals reducing the risk of variations in clinician practice or divergent opinions (Schmit *et al.* 2011, Cumbler *et al.* 2012, Deneckere *et al.* 2012, Leigheb *et al.* 2012, Hoof *et al.* 2014). The MDTs awareness of the care processes within the respective CCPs, as well as ongoing improvements to CCPs based on evidence-based guidelines was also linked to increased adherence to CCPs that improved the quality of patient care. For example, the treatment of psychosis was improved through a CCP developed in compliance with National Institute of Health and Care Excellence (NICE) guidelines, which demonstrated improved quality of care when compared with a pre-CCP group (Rathod *et al.* 2020).

Use of CCPs was extremely beneficial to patients in reducing delays in care procedures. The earlier a diagnosis was made, the sooner the treatment began, and the period of uncertainty without a diagnosis was shortened. It was observed that patients who received timely treatments also recovered earlier (Kinsman *et al.* 2010, Lyckner *et al.* 2010, Rotter *et al.* 2010, Lodewijckx *et al.* 2011, Yan *et al.* 2011, Hotchen *et al.* 2016, Denbo *et al.* 2018, Iiellis *et al.* 2018, Loots *et al.* 2018, Ovaere *et al.* 2018, Mhawej *et al.* 2020). For example, a CCP involving faster access to diagnostic services, operating facilities, and rapid assessments, was implemented to reduce long waiting periods and avoidance of unnecessary hospitalisations for day case emergency surgeries (Hotchen *et al.* 2016). The post-evaluation of this CCP therefore revealed a shorter inpatient stay, earlier recovery, and reduced overall

costs. Use of other CCPs were also found to reduce costs, mainly by avoiding duplication of procedures such as repetition of blood tests or care procedures benefitting patients and health care professionals (Baffert *et al.* 2015, Attfield *et al.* 2017, Broussy *et al.* 2019). Pragmatically, these findings indicate that CCPs positively impact the overall quality of care while adding value for patients, clinicians, and healthcare institutions. Furthermore, as the core development and implementation processes, and evaluation outcomes for CCPs were found to be largely consistent across the included studies, the analysis revealed that CCP, as a concept, has a high level of pragmatic maturity.

3.5.3 Linguistic principle

Linguistics is a term that refers to the study of speech and language (Penrod 2005). A linguistically mature concept is consistent in its application and meaning within the scientific discipline under consideration (Penrod 2005). In this analysis, the concept of CCP was evaluated for linguistic consistency across clinical care specialities in acute care.

The term CCP appeared as a generic term used to represent a 'pathway of care' irrespective of what that pathway might be or focus on. The term, in this sense, is linguistically narrow and tight; that is, irrespective of the discipline or care condition for which a CCP is developed, it's meaning, or the understanding given to the CCP is the same. A CCP and its purpose, is thus linguistically understood as a mechanism or process through which a standardised approach to patient care is operationalised. In this analysis, 14 studies involving surgical interventions linguistically referred to CCPs as Enhanced Recovery After Surgery (ERAS) Pathways (see Table 5 for examples), emphasising the focus of the pathway as early recovery following surgeries. Interestingly, 41 other studies reporting on surgical intervention care pathways simply referred to them as CCPs or surgical pathways although they focused on early recovery by reducing hospital stay and improving patient outcomes, in a manner similar to the ERAS pathways. Regardless of whether they were referred to as ERAS or surgical CCPs, they provided standardised surgical care to streamline patient care processes from the pre-operative to post-operative stages.

Similarly, the term Integrated Care Pathway (ICP) was used by 12 included studies (see Table 5) emphasising the integration of a broad range of healthcare services across the patient continuum. However, because CCPs by definition include the integration of multidisciplinary services, Schrijvers *et al* (2012) argue that the term "integrated care" is no longer necessary since fragmented care pathways cannot exist. Therefore, although subtle differences in the terminologies used for a CCP exist, even for the same health condition (e.g., for the treatment of hip fracture, Burgers *et al.* (2014) refers to a CCP whereas Barinaga *et al.* (2017) notes an ICP), analysis demonstrates that linguistically, the meaning was the same.

CCPs were also referred to as care maps, algorithms, and evidence-based protocols in several studies included in the analysis (Rotter *et al.* 2010, Duffy *et al.* 2011, Kul *et al.* 2014, Vosler *et al.* 2016, de Belvis *et al.* 2019, Featherall *et al.* 2019, Arabacioglu *et al.* 2020). These terms, rather than describing the CCP document itself, describe adjunct tools that were developed as part of the CCP to aid in the ease of implementation of the CCP. Several CCPs, for example, included a documented protocol outlining the sequence of care processes for guidance, as well as a graphical representation, such as a care map or algorithm, for ease of reference by staff (He *et al.* 2018, Cash *et al.* 2019, Bilò *et al.* 2020, Hare *et al.* 2020). As a result, these terms are taken to mean and are understood to be components of the CCP rather than representing a CCP in its entirety.

In summary, the analysis has shown that the concept is linguistically equivalent regardless of whether the term used is CCPs, ERAS pathways, or ICPs. This is because these descriptions share ‘pathway’ as a common term, in addition to having a common linguistic meaning. As such, the concept of CCP can be considered linguistically mature.

3.5.4 The Logical principle

The logical principle focuses on the concept's boundaries, defining what is and is not part of the concept. This means to examine if the concept becomes blurred when combined with related concepts. According to Penrod and Hupcey (2005), clear

boundaries allow for the demonstration of interrelationships with related concepts without becoming lost in theory. A clear understanding of boundaries associated with the concept of CCP was critical for informing the data collecting and analysis stages of the main PhD study, in order to ensure that the research remained within its defined scope.

CCPs were frequently referred to as a 'complex intervention' (Vanhaecht *et al.* 2010a, Schmit *et al.* 2011, Hoof *et al.* 2014, Vanhaecht *et al.* 2016, Bjurling-Sjöberg *et al.* 2018, Wang *et al.* 2018, Aeyels *et al.* 2019, Bilò *et al.* 2020). This is because healthcare providers were confronted with a series of complex medical conditions, variations, and disease severities. Oncology care, for example, entails treating various cancer modalities, each of which includes cancer stages, genetic variations, laboratory variations, and so forth (Baker *et al.* 2017, Langius-Eklöf *et al.* 2017, Macleod & Radley 2017, Gessler *et al.* 2019). Complexities may also arise due to the multidisciplinary nature of care provision, necessitating the formation of a dedicated MDT capable of collaborating to make consistent patient care decisions (Fasola *et al.* 2012b, Castillo *et al.* 2015, AboSharkh *et al.* 2016, Burlet *et al.* 2018). As a result, caring for patients is a complicated task that requires a standardised approach to care delivery.

Healthcare institutions' emphasis has shifted from a service-based care delivery towards a patient centric, goal driven approach underpinned by CCPs (Leonard *et al.* 2017, Feng *et al.* 2018, Featherall *et al.* 2019). Analysis of the studies included in this concept analysis identified that the CCP approach had pre-determined targets and patient care outcomes which were regularly evaluated against linked quality indicators (see section 3.5.2.3 on CCP evaluation). CCP evaluations were conducted against a pre-existing pathway or a pathway that existed prior to the development of a CCP known as 'routine care', 'usual care' or 'pre-pathway care'. These were not specifically defined in the literature, but the studies referring to them point out that they lacked important characteristics for a standard care delivery such as absence of standard care protocols, evidence-based assessment tools and coordination of MDTs (Husni *et al.* 2010, Akinbobuyi *et al.* 2016, Baker *et al.* 2017, Gehi *et al.* 2018, Featherall *et al.* 2019, Rathod *et al.* 2020). In contrast, CCPs are evidence-based plans developed by multidisciplinary teams through collaboration and consensus

(Schmit *et al.* 2011, Deneckere *et al.* 2012, Deneckere *et al.* 2013, Aeyels *et al.* 2018, Gautam *et al.* 2018a, Gautam *et al.* 2018b), and that the evidence-based plan is carefully derived from structured clinical trials, or other robust studies, rather than from learning directly through experience gained during routine clinical practice (Baker *et al.* 2017b). Moreover, it is important to note that a CCP was not necessarily absolute, but rather subject to adaptation to align with the demands of patient care and to evidence-based guidelines for care if or as these were updated. Adaptations to a CCP frequently occurred as a result of collaborative efforts, including both clinical and administrative staff. Consequently, the boundaries were determined based on the needs of patient care, the expertise of the healthcare team, and the accessible resources within the acute care setting (Aziz *et al.* 2011, Hartjes *et al.* 2018, Abo Sharkh *et al.* 2019, Berg *et al.* 2019, Brueton & Brueton 2019, Arabacioglu *et al.* 2020). The terms ‘routine’ or ‘usual care’ pathways were also used to describe health care practices that were performed on a routine basis (Kul *et al.* 2013, Kul *et al.* 2014, Awan *et al.* 2015, Bapat *et al.* 2017). These pathways were constantly striving to improve patient outcomes by minimising disadvantages such as variation and errors in clinical practice by incorporating evidence-based guidelines, protocols, and standards that eventually became the new CCP. However, after thorough implementation, the new CCP could become the standard CCP that could be used routinely in clinical practice (Tastan *et al.* 2012, Kul *et al.* 2013, Kul *et al.* 2014, Gautam *et al.* 2018a), albeit in a documented, organised, and supported way. Therefore, with respect to logical maturity, the meaning of a CCP does not blur when viewed with related terms such as ‘routine care’ and ‘usual care’ rather CCP ‘holds its own’ as a mature concept.

3.6 Conceptual components and chapter summary

This chapter explored the concept of CCPs using a principle-based approach (Penrod & Hupcey 2005) underpinned by the four broad principles of: epistemological, pragmatic, linguistic, and logical principles to guide the analysis. Following analysis, the concept of CCP was found to be largely mature under all four of the principles.

3.6.1 Conceptual components

The conceptual components of CCP centre on the preconditions (events that precede and influence the concept), the characteristics (expressions used to describe the experience of the concept) and outcomes (the consequences of the concept) (Waldon 2018). The preconditions for development and implementation of a CCP that were identified in this analysis were variation in care practices, sub-optimum patient outcomes, and healthcare cost. The fundamental characteristics of a CCP included a documented approach for standardised care delivery, based on contemporary evidence, irrespective of medical condition or setting within the acute care hospital, involving specific intervention(s) or care events, logically and sequentially organised and delivered by all members of the MDT consistently. The outcomes of CCP use were reduced variation in care, improved care quality and improved patient outcomes.

3.6.2 Chapter Summary

A CCP under the epistemological principle was described as a standardised plan or guideline for patient care consisting of an organised documented sequence of care events. The care events are based on contemporary evidence developed through multidisciplinary collaboration and consensus; critical components for every CCP to function. The CCP, when implemented, is done so consistently by all care providers, whether that is for a brief period such as in a single point of care or extended across a care continuum depending on the CCP's goal. In doing so, improved patient outcomes were demonstrably achieved. The linguistic principle explored the language used to describe the concept as well as its consistency in meaning across

contexts. Although subtle variations in the terms describing a CCP were found, such as ICPs and ERAS pathways, their inherent meanings were consistent with that of CCP. Other terms associated with the term CCP were care maps, algorithms, and evidence-based protocols, however these were identified as components of or adjuncts to a CCP rather than representing the entirety of a CCP. In analysing if CCP as a concept can 'hold its own' when positioned alongside concepts such as 'routine care' and 'usual care', CCP was deemed logically mature, as even though the CCP, when implemented fully, could become considered usual or routine, it is done so through a documented evidence-based, organised and standardised mode.

3.7 Application of the concept analysis to trial recruitment within CCPs and theoretical definition

This concept analysis aimed to clarify the meaning of the concept of CCP and understand the use of this concept for the purposes of fieldwork in this research study examining the use of CCPs in the recruitment of clinical trials. The analysis was successful in achieving a detailed and comprehensive understanding of CCPs where CCPs were clearly understood as a conduit through which standard care is delivered. However, there was no literature found that discussed the relationship between CCPs and clinical trials, specifically with regard to trial recruitment making it challenging to draw conclusions about the use of CCPs for trial recruitment. This further highlights that the potential of CCPs for trial recruitment has not been adequately explored in the scientific literature, making this PhD research novel.

Although there is a lack of data related to trial recruitment in the concept analysis, valuable information was obtained regarding what exactly constitutes a CCP that guided the data collection and analysis stages of the PhD study. Through the concept analysis, it was found that a CCP is not limited to specific clinical care guidelines or established care plans but encompasses the entire trajectory of care provided by a multidisciplinary team of healthcare professionals. The CCP also includes a path consisting of a series of healthcare activities or events such as admission procedures, consultation visits, laboratory examinations, delivery of

treatment or intervention, and the availability of services and resources within the setting. It was also noted that CCPs evolve over time, and changes may occur in the services provided within CCPs, as evident by the recent COVID-19 pandemic. The concept analysis also revealed that the activities and procedures of CCPs during the pandemic were similar to pre-pandemic periods however, CCPs were rapidly adapted (e.g., change in navigation within the hospital setting and using personal protective equipment) to ensure continuation of clinical care for those critically in need. These findings became important information as the data collection for this PhD study occurred during the pandemic period.

Applying the concept analysis of CCP to this PhD study also meant that clinical trials had to take place in a clinical setting where clinical care activities were occurring in order to examine the utility of CCPs for trial recruitment. This means that all patients were to be provided with standard medical care regardless of whether they decided to participate in a clinical trial. As a result, when selecting the case trials, I ensured that they occurred in the chosen clinical setting or CCP, such as neurology care pathway or cancer care pathway where standard care was being administered.

Further, to evaluate the utility of CCPs during trial recruitment, it was necessary to determine whether the CCP's key components were being used. The concept analysis identified four key components of CCPs: the availability of standard clinical care, the involvement of the multidisciplinary team in routine clinical care, the usefulness of standard care documentation (medical notes/charts), and availability and use of resources for clinical care delivery (see Table 6). The data analysis was driven by the theoretical definition of CCP constructed following the concept analysis reported herein and determination of whether CCP components were used during various trial recruitment phases, starting with identifying potential trial participants and continuing until randomisation.

Drawing on the findings of the concept analysis, the following theoretical definition, was identified and operationalised in the fieldwork research phase of my study (as reported in Chapters 4 and 5) where the use of CCPs in clinical trial recruitment in the acute care setting was explored:

> A CCP is a standard approach to clinical care based on documented evidence-based care events or interventions, for specific medical conditions involving short or long-term care trajectories, delivered by a multidisciplinary team of healthcare professionals in a clinical setting.

Having developed a clear understanding of the concept of CCP and by devising a theoretical definition that could be operationalised during the conduct of my study, the following chapter discusses the PhD research methodology.

Chapter 4: Methodology

4.1 Introduction

This chapter provides an overview of research paradigms, an explanation and justification for the chosen paradigm (constructivism) underpinning this study, and details of the selected research methodology (case study). In addition, the chapter will discuss how constructivism and the single instrumental case study methodology shaped the study. The choice of and procedures for data collection and data analysis, and the rationale for these associated components are also discussed.

4.2 Research Aim and Objectives

The aim of the study was to explore, understand and describe if and how current CCPs were being utilised for recruitment to randomised clinical trials in an acute healthcare setting in Ireland. The operational definition for the CCP which was used in the study was developed from the concept analysis reported in Chapter 3 (see section 3.6.2). To address the study aim, seven trials that were recruiting in the research setting during the field work phase of the study (February – July 2021) were purposively selected to explore recruitment within associated CCPs (see methods section 5.5 for the process of selecting and a description of these trials).

The objectives of the study were:

i. To review the selected trials' documents to collect data on their recruitment processes.
ii. To ascertain if and how CCPs were being utilised in recruitment by observing and shadowing recruiters (research nurses, pharmacists, investigators) to these trials.
iii. To explore the experiences of using CCPs from the perspective of key stakeholders (recruiters and patients) involved in the recruitment processes associated with the selected trials.
iv. To triangulate the findings from objectives i-iii in describing and understanding trial recruitment including facilitators and barriers within the context of CCPs.

v. To provide scientifically sound evidence-based recommendations for how trial recruitment processes can be optimised within current CCPs.

4.3 Research paradigm

Disclosing ontological, epistemological and methodological positions at the outset of scientific inquiry is important as these shape the way the researcher sees and acts in the world (Chilisa & Kawulich 2012). These positions permeate every phase of the investigative process, from the choice of the phenomenon of interest to the composition of the final report (Denzin & Lincoln 2011). A research paradigm, or 'worldview' (Creswell 2014, p.6) encompasses the epistemological, ontological and methodological premises, defined as a 'basic set of beliefs that guides action' (Guba, 1990, p.17). Ontology is described as a way of knowing the truth or reality that leads to the epistemological assumption of the different ways of knowing what we know. These philosophical positions influence how we know what we know, how we perceive reality, and how we examine (methodology) the research questions we pose (Lincoln & Guba 1994, Hanson *et al.* 2005). Therefore, it is important for researchers to recognise and articulate their position about worldviews or socio-political contexts that may have influenced their research project (Tashakkori & Newmab 2010). Common worldviews associated with research enquiries and their dominant features, as described by Creswell (2011) are presented in Table 8.

Table 8: Creswell's four worldviews (2011, p.6)

Positivism	**Transformative**	**Pragmatism**	**Constructivism**
Determination	Political	Consequences of actions	Understanding
Reductionism	Power and justice oriented	Problem-centred	Multiple participant meanings
Empirical observation and measurement	Collaborative	Pluralistic	Social and historical construction
Theory verification	Change-oriented	Real-world practice oriented	Theory generation

Positivist inquiry, underpinned by positivist thinking, uses the traditional method of scientific investigation (Philips & Burbules 2000). Positivists believe in realist ontology and objectivist epistemology wherein positivist researchers believe in a single reality which is examined based on the researchers' assumptions (Krauss 2005) using quantitative measurements, such as in experiments and surveys (Chilisa & Kawulich 2012). The transformative worldview, alternatively, is embraced by scholars who advocate and address issues relating to those who are marginalised, discriminated against and who face social inequality. This worldview is held by critical theorists, participatory action researchers, marxists, and feminists, among others (Creswell 2014). The pragmatic view commonly adopted by mixed methods researchers, holds greater importance for the consequences of inquiry than to the process of research (Hanson *et al.* 2005, Creswell & Plano Clark 2011). As such, pragmatic researchers will often draw on both quantitative and qualitative approaches in addressing research aims (Creswell 2014). The fourth worldview described by Creswell (2011) is that of constructivism. Considering the nature of my research question and aim, with a focus on exploration, understanding and description, derived from the 'meanings' of multiple stakeholders and sources, the constructivist paradigm presents a natural philosophical underpinning for the research inquiry reported in this thesis, as will now be demonstrated.

Constructivists believe that reality is constructed collectively between participants and researchers as opposed to being discovered by the individual researcher as in experimental research (Creswell 2014). Constructivism is based on a relativist ontology and a subjectivist epistemology, meaning that there are multiple realities to the situation or research problem and realities are often constructed by individuals who seek interpretation of the world where they 'live and work' (Creswell 2014). As the aim of my research was to understand the use of CCPs for recruitment to trials, engagement with study recruiters and trial participants who have first-hand (real world) experience of trial recruitment in a healthcare setting that undertakes trials was required. Engagement was required at the personal level so that understandings of trial recruitment within CCPs could be constructed by interpreting participant experience and perceptions (Denzin & Lincoln 2011). Adopting a constructivist approach to guide my study, facilitated an exploration of multiple and unique factors

that affect trial recruitment within current CCPs from the perspectives of those directly involved or associated with this phenomenon.

4.4 The theory and choice of constructivism

The history of constructivism can be traced back to the philosophers of the eighteenth-century, namely Giambattista Vico (1668-1744) and Immanuel Kant (1724-1804). However, the theory of constructivism is more associated with the Swiss psychologist Jean Piaget (1896–1980) who developed an influential theory on cognitive development in the field of education (Piaget 1971). Founders of related educational theory believed that knowledge was transmitted from one generation to the another based on teachers' presentation of information, which is retrieved by the learner, thereby improving comprehension (Alanazi 2016). Piaget (1971), alternatively, asserted that students construct new knowledge based on their prior experience and knowledge influenced by their social environments; accordingly, learning is achieved by constructing knowledge from personal experiences. This implies that learners actively derive meaning while listening to or observing the teacher who supports the learning environment (Piaget 1971). According to Piaget (1971), human learning is conceptualised as an internal process that occurs within individuals, impacted by their interactions with ideas and experiences, rather than solely being shaped by external factors such as individuals around them.

The constructivist theory was endorsed and expanded by several proponents in the literature. Lev Vygotsky (1896-1934), for example, developed the theory of the 'Zone of Proximal Development' which highlighted the importance of socio-cultural learning; where a learner progresses to a higher level of understanding, or a new zone, based on support obtained from knowledgeable individuals. Jerome Bruner (1978) expanded on Vygotsky's theory to develop the principle of educational scaffolding, in which students require active support from teachers who act as a scaffold that gradually detaches as they acquire new skills and gain independence. Hmelo-Silver *et al's* (2004) theory on social constructivism focussed on the advantages of problem-based learning that enhances competitive learning and communication skills. Subsequently, Thomas and Brown (2011) expanded on the concept of problem-based learning by emphasising the importance of learning

through practical application and establishing social relationships among learners. While these theories may be descriptively diverse, they all fundamentally emphasise that learning happens through socio-cultural interactions and experience (Piaget & Inhelder 2008, Thomas & Brown 2011).

The constructivist theory, originating in the field of education, has undergone significant expansion beyond its initial influence on cognitive development. It has been applied in various disciplines such as history, sociology, education, psychology, and health sciences, enabling an increased understanding of social concepts, hidden implications, and cultural disparities (Yilmaz, 2008). For example, constructivism in sociology, called social constructivism, is influenced by the works of Peter Berger & Thomas Luckmann (1966) who coined the term social construction where people interacting with each other in a society create mental interpretations of each other's behaviour. Constructivism in psychology was adapted from Piaget's (1971) learning theory elaborating on the human mind's active response in creating knowledge and understanding realities (Balbi 2008). Ernst Glaserfeld (1917- 2010), an eminent philosopher and psychologist who pioneered the theory of radical constructivism, claimed that the human mind did not transport knowledge from one mind to the other, rather knowledge and understanding were created based on each individual's subjective interpretation and experience (Terhart 2003). While the theory of constructivism was influential and robust, a contemporary, constructivism-influenced view of philosophy emerged. Jean Piaget's student, Seymour Papert (1928 - 2016), developed the modern theory of 'constructionism' to build on the Piaget's (1971) learning theory. He argued that students gain knowledge by creating physical artefacts or practicing a skill that was experienced through tangible objects or project-based activities. In other words, constructionism emphasised teaching methods and visible objects used for instruction rather than their learning and cognitive processes or interactive experiences (Papert & Harel 1991).

As apparent from the illustrations above, the theory of constructivism, followed by constructionism, has several models of explanation provided by numerous scholars in the fields of education and social sciences. However, researchers in the field of health sciences use the terms 'constructivism' and 'constructionism' interchangeably to mean that truth or reality is constructed as a result of social interaction, as

opposed to the belief that there is an objective reality that must be discovered (Green and Thorogood 2004, Alanazi 2016). In choosing the appropriate terminology for this qualitative case study, however, a further exploration of how both terms were used in qualitative inquiry revealed differences for the use of one terminology over the other. For example, Crotty (1998) describes constructionism as making meaning out of lived human experiences inspired by the work of Merleau-Ponty & Heidegger (1976) in phenomenology. Glaser & Strauss (1997) associated constructionism with grounded theory, whereas Kathy Charmaz (2012), a contemporary author of grounded theory methodology, describes constructivism as a broader term encompassing the concept of constructionism. Social constructionism is also adopted by those interested in anthropology, culture, society and aspects of human behaviour such as attitudes and personalities (Crotty 1998, Galbin 2014).

In relation to, pioneers in qualitative case study research, Merriam and Stake, were guided by the philosophical underpinning of constructivism believing that knowledge is constructed rather than discovered (Stake 1995, Merriam 2001). Therefore, Merriam (2001) and Stake (1995) appear to perceive qualitative case study researchers as interpreters, and gatherers of interpretations, which requires these researchers to provide their rendition or construction of knowledge acquired through their investigation. As an emerging qualitative case study researcher, this perspective influenced the use of ‘constructivism’ as my philosophical positioning in the current study. Furthermore, my adoption of the philosophical position of constructivism further aligned with the pioneers of constructivist theory namely Piaget (1971), Lev Vygotsky (1980) and Yvonna Lincoln (2013), who place emphasis on existing knowledge and experience, social context and interaction, and understanding through interpretation. Thus, constructivism was the philosophical underpinning of this research study and was influential in shaping the research process from determining the aim of the study through to the analysis and interpretation of the experiences of those involved in trial recruitment activities within CCPs in an acute clinical care setting.

4.5 The research approach

Although a researcher's ontological and epistemological leanings can naturally influence their chosen approach to scientific inquiry, the research approach needs to be selected based on appropriateness in terms of what works best in answering the research question (Denzin & Lincoln 2011). Two traditional and well-known research approaches are quantitative and qualitative research, although mixed methods research, a third approach, has become established as a distinct research methodology (Denzin & Lincoln 2011). Choosing the appropriate approach for a research study to address a research question, lies in the differential characteristics and their implications that distinguish these approaches from one another (Guba & Lincoln 1985). For example, quantitative studies are concerned with answering questions related to quantity, that is how much, how many or to what extent, such as estimating prevalence, proportions, correlations, and associations. Quantitative studies are thus founded on positivistic philosophies, with the goal of predicting, controlling, or confirming a hypothesis using inanimate instruments such as tests, experiments, surveys, and questionnaires, and the results are frequently presented in precise numerical or statistical figures (deductive methods) (Creswell & Poth 2016). Large samples and tightly controlled conditions are required to ensure that the results produced can be generalised or replicated in similar settings (Denzin & Lincoln 2011, Creswell & Poth 2016).

In contrast, qualitative studies focus on the nature or quality of phenomena by asking how or why questions to obtain a deeper understanding of the richness and complexities of social worlds such as eliciting a better understanding of issues in healthcare from the participants' perspectives (Guba & Lincoln 1985). Therefore, qualitative inquiry is interpretive or naturalistic, focusing on meanings in context and requiring a sensitive data collection instrument to capture the underlying data on the phenomenon of interest (Guba & Lincoln 1985). Therefore, the researcher becomes the ideal instrument for data collection as he/she can sensitively respond to contexts and can flexibly use techniques such as probing, clarifying and summarising or being sensitive to nonverbal aspects during interviewing, observing and analysing activities (Merriam 2001). Qualitative studies are therefore designed to build knowledge or theory inductively with the help of a smaller sample. In qualitative studies, the focus

is not on producing a statistical generalisable result, instead, the researcher is focussed on gaining understandings, deeper insights and explanations or interpretations of phenomena, which are conceptually or theoretically transferable to other situations (Pope & Mays 2020). For this reason, the researcher, in carrying out a qualitative study, purposefully selects a sample from which the most can be learned (Pope & Mays 2020).

According to the findings of the PRioRiTy study, there is a lack of knowledge regarding how recruitment to trials occurs alongside or within CCPs (Healy *et al.* 2018). Therefore, I held the view that employing a qualitative research approach was suitable for developing an in-depth understanding of unexplored perspectives and novel insights that are underrepresented in existing scholarly investigations. Furthermore, Hennessy *et al.* (2018) emphasised the significance of qualitative methodologies being integral (as opposed to add-ons) in answering the priority recruitment questions identified in the PRioRiTy study. Moreover, qualitative methodologies have been useful in addressing the underlying complexities and challenges of trial recruitment that quantitative methodologies do not easily address (O'Cathain *et al.* 2013). For example, changes made to communicating recruitment information based on the findings from a qualitative study resulted in increased patient recruitment in a prostate cancer trial (Donovan 2002). In another example, Dormandy *et al.* (2008) interviewed general practitioners to better understand the factors that facilitate recruiting and retaining general practices for clinical trials. Similarly, Kohara & Inoue (2010) conducted qualitative research to learn about patients' decision-making processes for participating or declining to participate in clinical trials.

Considering the exploratory nature of this research, which aimed to gain deeper insights into the phenomenon of trial recruitment within CCPs, a qualitative approach was identified as most appropriate rather than a quantitative approach. This is because qualitative investigation would allow for a deeper understanding of a physically occurring process (recruitment to trials) in its real-life context (CCPs) from the perspective of trial researchers in an acute care hospital (a natural setting). In this regard, by adopting a qualitative methodology, a holistic understanding of the

complex processes of trial recruitment that occur alongside clinical care could be attained (Casey & Houghton 2010, Crowe *et al.* 2011, Melo 2018).

4.6 Qualitative case study methodology

Various qualitative methodologies or designs are used to understand social phenomena, with the choice of design often based on the aim or purpose of the research. Phenomenology, for example, is generally chosen when a researcher wishes to specifically explore people's lived experiences (Wojnar & Swanson 2007). An ethnographic approach is frequently used to investigate the cultural aspects of a group whereby the researcher becomes immersed in or becomes a member of that group for an extended period of time (Goodson & Vassar 2011). A grounded theory approach, alternatively, is used when the purpose of the study is to uncover or develop a theory based on the narratives of those taking part in the study. Narrative studies, contrastingly, generally involve oral histories and interpretive biographies to explore and gain understanding of the phenomenon under investigation (Denzin & Lincoln 2011, Algozzine & Hancock 2017). In considering case study research, another approach to qualitative inquiry, Yin (2014) and Thomas (2021) state that a case study would be suitable when a researcher is asking 'how' or 'why' questions where the intent is to explore how or why something is happening by looking at the case from many angles. This appeared to align with the current study whereby I wished to investigate 'how' CCPs within an acute care hospital were used for recruitment to trials and where the perspectives and experiences of the activities that occur in relation to trial recruitment (phenomenon of interest) cannot be controlled or manipulated.

While case study is primarily described as a type of qualitative research method (Stake 1995, Merriam 2001, Baxter & Jack 2008, Starman 2013, Thomas 2021), it may also employ quantitative measures or a combination of quantitative and qualitative approaches. The approach developed by Yin (2012) and Eisenhardt (1989) are two instances of this type of case study, where the goal is to build a testable and logically consistent theory from the case (positivistic position). Given the variations in approaches to case studies, Stake (2005) believes that a case study is

not a methodological choice, but it is a choice of what is to be studied. This means that a case study can take any philosophical stance or use any methodology while remaining focused on the phenomenon of interest (the case); a case is further described as a bounded system that draws attention to it as an object of study rather than a process and is thus described as "a bridge across paradigms" (Luck *et al.* 2006, p.103).

4.6.1 Characteristics of a case study

While the methodology employed for conducting case studies is not constrained to a single method or research paradigm, a qualitative case study is distinguished by its unique characteristics. One of the distinctive characteristics that guides a case study is its singularity enabling a researcher to capture the complexities of a single unit of analysis or the object of study (the case) bounded by space and time (Stake 1995, Merriam 2001). Case study, according to Stake (1995, p.xi), is “the study of the particularity and complexity of a single case, coming to understand its activity within important circumstances”. Merriam (2001) also states that the single most distinguishing feature of a case study is the delimitation of the case, or the object of the study, where a case can be a single person, a program, or a group. Thomas (2021) further describes a case as being concentrated on one thing in detail and Yin (2014) describes a case as a unit of inquiry. As a result, the focus of a case study is its singularity, which means it is concentrated on one phenomenon that is examined in detail with an interest in its uniqueness and completeness.

Case study proponents further argue that a simple examination of the phenomenon of interest, such as a person or process, does not constitute a case study; a case must be a case of something (Starman 2013, Thomas 2021). This means, for a case to exist, a characteristic unit must be identified that provides some explanation to a larger phenomenon of interest; the unit itself has no meaning. Wieviorka (1992) views the characteristic unit, also known as the object of study, as an analytical lens or frame through which a phenomenon of interest is investigated. As a result, each case study has two parts: the phenomenon of interest (case study object) observed

within an analytical frame (case study subject); a case is not complete unless both parts are present (Luck *et al.* 2006, Starman 2013, Thomas 2021).

Thomas (2021) demonstrates the subject and object of a case by illustrating a case study of a quiet child, where the phenomenon of quiet children serves as the case study object. In order to explore the case, the author selects a quiet child, Amelia (case study subject), who is studied during set timeframes of her school hours (case study binding). This means that simply describing Amelia and her characteristics does not constitute a case; rather, Amelia is a case of a quiet child, and investigating Amelia provides insight and understanding of quiet children. As a result, the case study object (phenomenon of interest) and the subject (for example, a person) are always linked, with the subject viewed through the analytical frame of the study's object. This means that a case study subject is chosen according to the desired characteristics (binding) that explain the object of study.

As such, another important characteristic of a case study is its boundedness. Merriam (2001) claims that if the phenomenon of interest is not bounded, it is not a case. Case boundaries, according to Thomas (2021), are like edges placed around the case; they are the direction and extent of the research. Merriam (2001) describes them as fencing in and fencing out of what is to be studied. By fencing in, researchers are setting boundaries and narrowing down the scope of their study to specific elements or phenomena that are relevant to their research questions. On the other hand, fencing out refers to the deliberate exclusion of certain aspects or elements that are not considered relevant or important to the research objectives (Merriam 2001, p.27).

According to Stake (2005), one of the most important steps is binding a case with its context, which eventually becomes part of the focus of inquiry. This means that binding a case allows researchers to stay focused on the case's objectives rather than attempting to answer several broad questions for a single case, ensuring the study remains reasonable in scope (Baxter & Jack 2008). Further, Stake (1995), Creswell (2003) and Yin (2003), suggest that a case could be bounded by time, space, event or activity that assists in limiting data collection where the boundaries are set through the description of the locality, group, process or institution. Stake

(1995) describes binding a case as an integrated system that is specific, recognisable, and purposive, focused on the object of the study. Further, a case is bounded by studying the case within a particular context, such as an economic or social context which is significant to the understandings of the case (Miles & Huberman 1994, Stake 2005).

A case study is also differentiated as an in-depth examination of a 'contemporary phenomenon' occurring in a 'real-life context' using 'multiple sources of evidence' (Robson 1993 p.52, Yin 2014 p. 16). A case is thus described as contemporary in the sense that it is happening now within its real-life context, where the researcher goes to where the phenomenon is happening. This is required to capture the contextual factors associated with the case, such as factors and relationships that may affect the phenomenon. This bringing out of factors occurs through multiple sources; for example, by talking about the activities involved (by conducting interviews), collecting documents, and observing individuals connected with the case in context (Merriam 2001). A synopsis of the key characteristics of a case study and how they are applicable to the current study are presented in Table 9.

Table 9: Case study characteristics and application to this study

Case study characteristics	How it applies to this study
Singularity	This case study was interested in a single issue, namely the phenomenon of recruitment to trials occurring in the context of CCPs.
A case consists of an object and a subject of study	To study the phenomenon of recruitment in the context of CCPs (case study object), recruiting RCTs were purposively chosen (case study subject).
A case is a bounded system	This case is bounded by location, time and activity, that is the case is limited to one research active acute care setting with ongoing recruitment to RCTs examined within a calendar year time frame.
A case is studied within a context	The phenomenon of trial recruitment is studied within the context of CCPs.

Research is undertaken in a real-life contemporary context where the researcher has little or no control over the events	The phenomenon of trial recruitment was studied from the perspective of study participants/stakeholders involved in the trial by selecting trials with ongoing recruitment without the researcher controlling the trial recruitment encounters at the setting or the meaning people ascribed to their experiences.
Case study is preferred when 'how' or 'why' questions are posed	This research sought to understand how CCPs were being utilised when recruiting participants to trials.
Relies on multiple sources of evidence	A case study aims to illuminate a reader by delving into the phenomenon of interest in depth from multiple angles or using multiple sources of information. In this study, the phenomenon of recruitment was examined through data collected in interviews, through observations and via trial-related documents to obtain a thorough, contemporaneous and holistic view of trial recruitment within the context of CCPs.

In addition to the distinctive characteristics (presented in Table 9), case studies are particularly valuable in exploring and understanding complex day to day processes in healthcare practice and research (Casey & Houghton 2010, Brogan *et al.* 2019). This has been demonstrated by Sheikh *et al.* (2009) who employed case study to explore the reasons for under recruitment of minority ethnic people to asthma trials within a healthcare practice in the UK. Similarly, Robertson *et al.* (2010) used a case study to understand the challenges in the implementation and use of electronic health records in acute healthcare settings. Recently, Wyatt *et al.* (2021) used a case study to examine the impact of COVID-19 on clinical research which led to widescale adaptions to research practice within the National Health Service (NHS) in the UK. For example, research staff were redeployed, leading to a faster setup and delivery of COVID-19-related research. Additionally, the consent process for research was digitalised, further streamlining the process. These changes were important in helping the NHS respond to the pandemic and continue conducting critical research.

The complex healthcare processes operating within particular contexts often require studying of experiences and relationships of people within healthcare settings (Merriam 2001, Gilson *et al.* 2012, Thomas 2021). In the current study, however, the influence and use of CCPs was the context and also part of the focus of inquiry whereby trial recruitment processes were examined through the experiences of those involved in recruitment. As this subsection demonstrates, case studies allow for comprehensive investigations using multiple data collection methods for an holistic understanding of complex healthcare processes and the people involved. In the current study observations, analysis of trial documents and interviews to capture experiences, were used to achieve this end.

4.7 Case study design

Case studies are distinguished into three types: intrinsic, instrumental and collective cases (Stake 1995, Merriam 2001, Thomas 2021). A case becomes an intrinsic case when it is unique or atypical, and the researcher seeks to understand what distinguishes this one case from similar others. In an intrinsic case study, a case is chosen not to learn about other cases or a general problem, but because of an intrinsic interest to learn about the case itself (Stake 1995). In contrast, an instrumental case is chosen when the purpose is to understand a general phenomenon in a specific context, where the chosen case becomes instrumental in understanding the phenomenon of interest (Stake 1995, Thomas 2021). Collective cases are similar to instrumental cases, with the exception that the researcher may chose a number of single instrumental cases to allow comparisons or replications of findings across cases in an attempt to produce a generalisable theory and may incorporate quantitative methods such as those proposed by Yin (2014) and Eisenhardt (1989). In the current study, the seven chosen trials within an acute care setting became instrumental for enlightening the process of recruiting participants within the context of CCPs and how the CCPs facilitated recruitment to the trials, including barriers and challenges. Hence, this case study represents an instrumental case that sheds light on an issue that is poorly understood within the field of trials methodology research.

A case study is focussed on a single phenomenon analysed in depth yet may incorporate qualitative and qualitative approaches (Stake 2005). Therefore, it was necessary to determine and draw on the relevant case study expert(s) for guiding this inquiry. Yin (2014) and Eisenhardt (1989) use a positivistic approach to case study research, emphasising hypothesis testing and theory building. Judgement about the quality of research is based on four measures in this perspective on case study, which are similar to those used in quantitative inquiry, namely construct validity, internal validity, external validity, and reliability. In contrast to Yin (2014) and Eisenhardt (1989); Merriam (2001), Stake (1995) and Thomas (2021) argue that every contribution by case study researchers depends on a clear understanding of knowledge and reality. According to these authors, qualitative case studies are guided by constructivist philosophies (as is the case in this study) because most contemporary researchers believe that knowledge is constructed, rather than discovered, through a holistic examination from multiple perspectives. As a result, the definitions of case study (see Table 10) offered by Stake (1995), Merriam (2001), and Thomas (2011) informed the manner in which this case study was conducted.

Table 10: Definitions of case study research

Stake (1995)	'Case study is the study of the particularity and complexity of a single case, coming to understand its activity within important circumstances' (p.xi)
Merriam (2001)	'Case studies are intensive descriptions and analyses of a single unit or bounded system such as an individual, program, event, group, intervention, or community' (p.19)
Thomas (2011)	'Case studies are analyses of persons, events… or other systems which are studied holistically by one or more methods. The case that is the subject of the inquiry will be an instance of a class of phenomena that provides an analytical frame- an object- within which the study is conducted and which the case illuminates and explicates.' (p. 23)

As this case study sought to gain in-depth understandings rather than testing or confirming existing theories, qualitative case study experts, namely Stake (1995), Merriam (2001) and Thomas (2021) were drawn on for methodological guidance in

the design and conduct of the study. All three authors emphasise the importance of studying a single case or phenomenon of interest in a holistic manner (see definitions in Table 10), specifying documents, interviews, and observation as common sources of data. In this sense, the methodological guidance provided by these experts including the philosophical paradigm of constructivism aligned appropriately with my inquiry focus. The application and components of the single instrumental case study to the study conducted are presented in Figure 5.

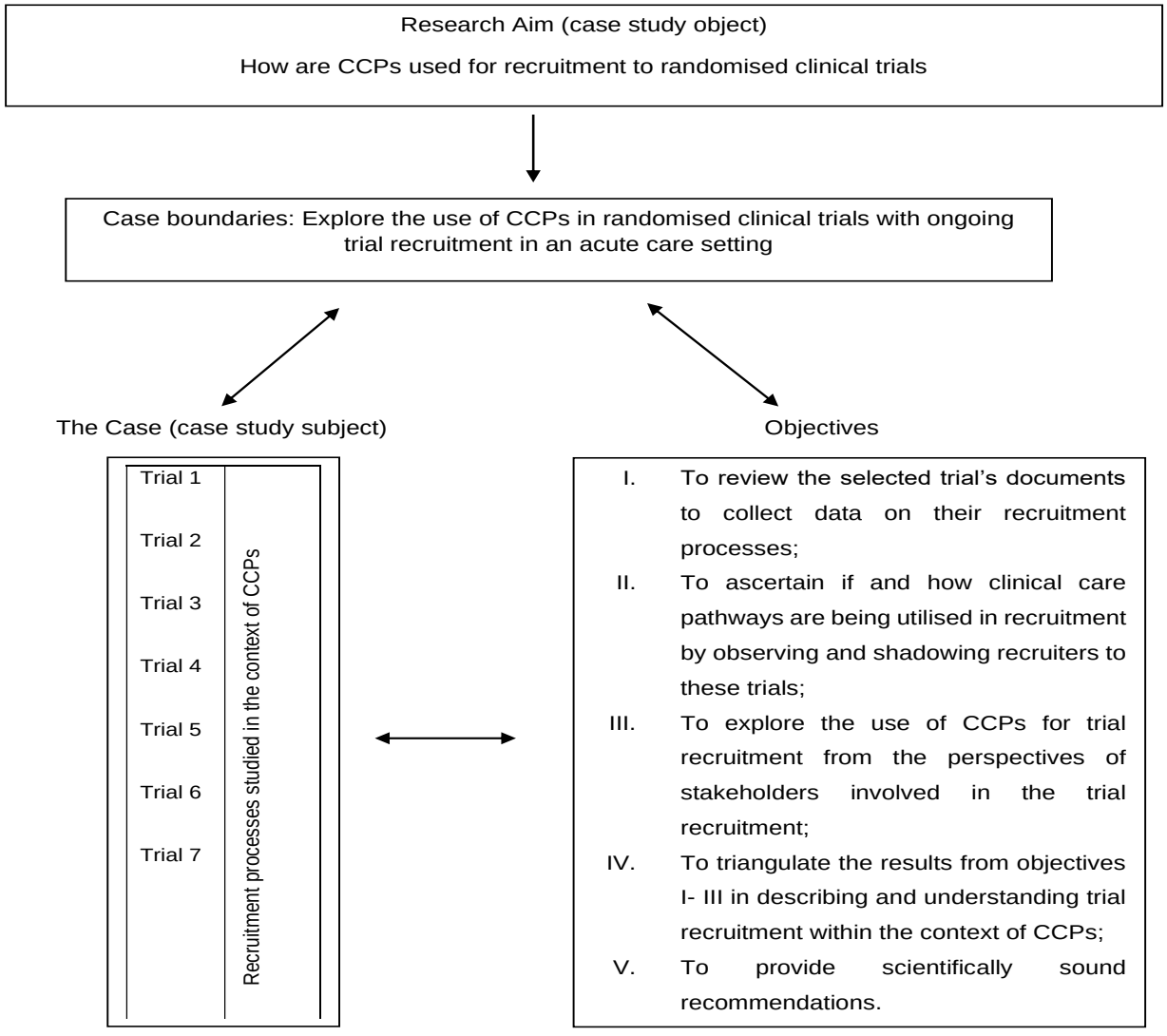

Figure 5: Application of the components of this instrumental case study

As illustrated in Figure 5, the ‘case’ represents the chosen subject for study, in this instance the seven selected RCTS become the subject of this investigation, with each trial’s recruitment processes contributing to an understanding of how trials use CCPs for recruitment in acute health services (the context). Each of the chosen trials rest within a distinct healthcare speciality which included upper gastro-enterology, lower gastro-enterology, oncology, neurology, cardiology, critical care and genito-urinary care with each speciality having their own specific healthcare and research staff (e.g., practising consultants who were also trial principal investigators, doctors as co-investigators, clinical nurse specialists and research nurses). Despite the diversity of trials resting within different care specialties, this study was focussed on a single or rather a common phenomenon, across all the included trials, that is the utility of CCPs during trial recruitment. As a result, an in-depth understanding of the phenomenon of interest (case study object) was obtained, that is coming to understand the extent of the use of CCPs, and their facilitators and its barriers for trial recruitment within a clinical acute care setting.

4.8 Data Collection in case study research

The nature of case study inquiry, and the pursuit of understandings, requires in-depth data, based on thick explanations and interpretations which are substantially rich and generally include multiple sources of information such as observations, interviews, archival records, reports, documentation, audio-visual data and physical objects (Baxter & Jack 2008). The major strength of a case study is the opportunity to use multiple sources of evidence to address a broader contextual issue through converging lines of inquiry whereby the conclusion is drawn from different sources of corroborating data (Merriam 2001, Baxter & Jack 2008, Thomas 2021).

The appropriate approach to data collection in a given study is chosen based on the aim of the research, the philosophical paradigm, and the underpinning methodology (Crotty 2003). The data were collected in this study using semi-structured interviews, document analysis and observations as appropriate methods to both case study inquiry and in addressing the aim and objectives of the study. The use of multiple

data collection methods allowed for triangulation, which assisted in comparing data to determine if it corroborated (Patton 2002, Creswell 2003), and in providing breadth in comprehending the data. Triangulation is the use of two or more methods to investigate the same phenomenon (Denzin & Lincoln 1998, Holloway & Wheeler 2010). For the current study, the use of multiple sources of evidence increased the depth of the case study (Luck *et al.* 2006), which increased the confidence in and credibility of the research findings and conclusions (Guba & Lincoln 1985, Merriam 2001, Thomas 2021). Furthermore, using all three data collection methods has been praised for helping uncover any inherent biases that the researcher may have been unaware of during the study's conduct (Thurmond 2001), especially when the phenomenon is examined by a single researcher.

As my research was principally concerned with learning about and understanding the utility of CCPs from those involved in trial recruitment, one-to-one interviews presented a critical method for collecting pertinent data. Alternative interview methods, such as focus groups, were carefully considered, but evidence has shown that such groups may lack anonymity and outlying opinions may be suppressed owing to group dynamics and strong personalities dominating discussions (Polit & Beck 2012, Nyumba *et al.* 2018). Thus, focus groups would not have fully addressed the research objectives, as they had the potential to obscure an in-depth understanding of the unique and common features of recruitment processes taking place within the trial recruiters respective care specialities as well as patients receiving care in these care specialities. Collecting data from the selected trials' documents and using observations were also important to understand the recruitment processes. This is because they provided information on the planned trial processes (e.g., through their protocols and participant information leaflets) and facilitated me to collect data in the real world setting as an observer. As I was not directly involved in recruitment activities, it would have been difficult to report comprehensively on recruitment processes based solely on either interviews, observations or trial documents (Clarke 2009). Thus, multiple data collection methods were required in exploring my topic of interest. Herein lies a particular strength of choosing case study methodology, as it flexibly allows for the application of a diverse range of research methods (Casey & Houghton 2010, Carolan *et al.* 2016).

4.8.1 Semi-structured interviews

Interviews are often conducted to acquire new information. Dexter defines interviews as a ‘conversation with a purpose’ (Dexter 1970, p.136). Interviews are conducted for several reasons such as journalistic interviews to report events, therapeutic interviews to improve critical healthcare conditions or research interviews that seek to produce new knowledge (Kvale & Brinkmann 2009). Kvale and Brinkmann (2009) explain that a research interview involves a professional inter-action or an inter-change of views between the two or more people in conversation. The research interview is therefore a systematic guided conversation between the interviewer and the interviewee where, based on the data attained, new knowledge can be constructed (Merriam 2001, Kvale & Brinkmann 2009).

Interviews can be structured, semi-structured or unstructured (Merriam 2001, Robson 2011). Structured interviews are similar to conducting an oral form of surveys or questionaries where the rigid pre-determined questions limit access to the participants’ perspectives and understandings of a phenomenon of interest. Semi-structured interviews are rather open-ended and less structured, where the interviewer uses an interview guide or schedule consisting of questions flexibly worded and applied to guide questioning and discussions during the interview (Silverman 2021). Neither the exact wording nor the order of questions are completely determined ahead of the interview thereby allowing the researcher to deviate from the interview guide based on emergent ideas on the topic (Kvale & Brinkmann 2009) or in response to the narratives that unfold as the interview progresses. Unstructured interviews are similar to conversations in that they are mostly exploratory and contain fewer predetermined questions or none at all (Wengraf 2001, Silverman 2021). This interviewing technique may be useful for gathering information about a particular topic to formulate questions for subsequent interviews. While unstructured interviews cover topics in greater depth, it takes experienced qualitative researchers to handle the degree of flexibility demanded by unstructured interviews, and novice researchers risk becoming lost or overwhelmed if disconnected data of divergent viewpoints emerges (Merriam 2001).

In considering my interview approach, I also determined that unstructured interviews were rarely used in previous literature exploring trial recruitment experiences (Featherston & Donovan 1998, Jackson *et al.* 2010, Hamilton *et al.* 2013, Harrop *et al.* 2016, Horwood *et al.* 2016, Hughes-Morley *et al.* 2016). Therefore, the use of individual semi-structured interviews was chosen to address objective iii of this case study.

Merriam (2001, p.74) suggests that a semi-structured interview is *'guided by a list of questions or issues to be explored'* while being flexible with the order of questions or the choice of words used Yin (2014) suggests that the researcher conducting a case study interview, needs to consider two elements; i) a conversation that meets the needs of the research, while ii) simultaneously remaining open to and inviting the interviewees to express their opinions and insights.

To gather the interview data, the experiences and opinions of study participants from different professional backgrounds, or who had different roles in the selected trials, as well as patients as potential trial participants was required. As such, adapting interview questions to account for the differences was necessary to ensure that sufficient in-depth, rich data, were collected (Denzin & Lincoln 2000, Ryan *et al.* 2009). Semi-structured interviews, which offer a flexible approach to questioning (Merriam 2001, Kvale & Brinkmann 2009, Charmaz & Belgrave 2012), provided the opportunity for interview participants to elaborate on the issues posed and bring new issues or views into the conversation that might otherwise have been overlooked, especially in the early stages of the fieldwork. Additionally, in choosing and using semi-structured interviewing, I was able to explore immediately any new issues that emerged as the interviews progressed using 'prompt questions' and to adapt questioning on emergent issues in interviews with subsequent participants (Merriam 2001, Charmaz & Belgrave 2012).

4.8.2 Observations

Observations of trial recruitment within the CCPs were conducted to complement data collection and analysis (see chapter 5 section 5.6 on priority of data sources in this study). Observations were a valuable source of evidence as the case study was

taking place as recruitment to the selected trials was occurring (Stake 1995, Merriam 2001, Yin 2014, Thomas 2021). While interviews facilitated discussion about the experiences of the use of CCPs during recruitment, observations were an advantageous additional data source as they allowed me to directly see and understand what people were doing (Becker & Geer 1957) and how the recruitment process worked in the real-life setting. This method of data collection, with observations recorded on a purposively developed observation sheet (Appendix 4) offered real-world first-hand encounters on recruitment processes to enhance the information obtained through interviews. Observations also helped me to gain further insight into a rarely studied phenomenon (Merriam, 2001). While interview data mainly added to the understanding of the phenomenon of interest, observations were an integral piece of the puzzle because they allowed me to also record details of routine everyday tasks and their contexts which were important to the study but that did not necessarily arise during the interviews (Green & Thorogood 2009). Merriam (2001) presents a guide for case study researchers in planning what can be observed in the field, and this guided observations in this study. The observations that I recorded in the observation chart used in the study (Appendix 4) were held securely by myself, with extracts used to inform data analysis. Merriam's (2001) guide included observations, and making notes of:

1. The *physical setting*: Observing and capturing the context and physical environment of where recruitment happened.
2. The *participants*: Observing and describing participants in the scene and the characteristics of the recruiter (e.g., principal investigator or research nurse, etc.).
3. *Activities and Interactions*: Observing and describing the activities that took place during recruitment. Any typical or unusual activities were specifically documented.
4. *Conversation*: Observing the conversation surrounding recruitment and noting points or aspects of importance to recruitment around this.
5. *Subtle factors*: Observing and noting any subtle factors such as nonverbal communications or descriptions of the physical space, for example, whether a clinic/clinical area was busy or quiet.

6. *Your own behaviour*: As I was part of the scene, I noted my thoughts at the time of observation, or any potential influence that I thought I might have brought to the setting.

These six categories of observational data were carefully recorded within hours of the observations as endorsed by Polit & Beck (2012). This supported an understanding of what was happening, making it possible to verify and add understanding to the interview narratives when later triangulating the data. Simultaneously, observations also provided the knowledge and context for specific behaviours and incidents that were used as reference points for subsequent interviews as suggested by Stake (1995) and Merriam (2001).

It was also important to consider the relationship of the observer within the case setting while collecting observational data. As proposed by Gold (1958), a researcher can position themselves in any one of four possible instances; that is as a complete participant where the researcher is part of the activity being observed to a complete observer being a spectator hidden from the group that is observed, with participant as observer and observer as participant in-between (Figure 6).

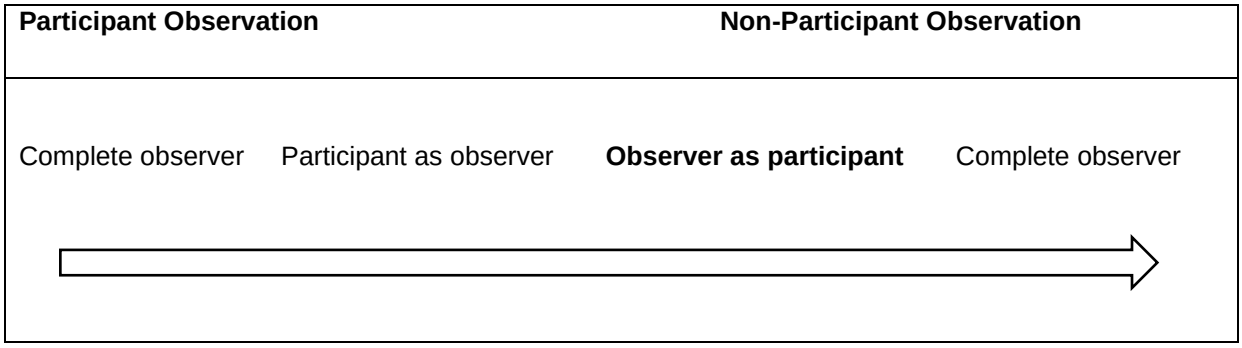

Figure 6: Spectrum of qualitative observation Gold (1958)

In a ‘complete observer’ role, the researcher observes phenomena concealing one’s observer role while being an active member of the group or setting being observed, whereas in the ‘participant as observer’ role the researcher maintains active participation in the activities of the group without concealing one’s identity as an observer. In non-participant observation, the researcher could assume the ‘observer as participant’ role where the researcher’s intent of observation is known to the

group and the researcher is not an active participant in the activities of the group being observed. Adler & Adler (1994, p.380) describe this as a “peripheral membership role” differentiating from the active membership role described in participant observation. The role of a complete observer is where the researcher is not involved in any of the activities of the group being observed and where one's observer role is completely hidden from those being observed.

Gold’s (1958) observational spectrum provided a structure to inform my choice of observational role. When applied to data collection in this case study, the ‘observer as a participant’ role (highlighted in bold in Figure 6) was assumed. This was because the intended goal was to observe how trial recruiters, who were healthcare staff, recruited participants so that I could understand how CCPs enabled the recruitment process and what factors, if any within the CCP hindered recruitment without actively participating in recruitment or concealing my identity as a researcher. This was consistent with Gold’s (1958) typology where I was a silent observer in the clinical setting allowing me to spend time with those in observation without becoming part of the culture/setting or its processes (Gold 1958).

4.8.3 Document analysis

In collecting document data, data is systematically extracted from existing printed or electronic resources, relevant to the study purpose. The information can be used exclusively in answering a research question or as part of a wider qualitative study (Corbin & Strauss 2008, Green & Thorogood 2009). Like other analytical approaches in qualitative research, document analysis requires constant review, evaluation and interpretation of the data to obtain empirical knowledge and understanding of the phenomenon under study (Corbin & Strauss 2008, Green & Thorogood 2009).

Document analysis is frequently used in case study research along with observations and interviews to corroborate, expand and triangulate the data from all sources collectively (Merriam 2001, Bowen 2009). By using multiple sources of data in case study research, the researcher reduces the potential for biases that could exist if a single method of data collection was used. In this way, ‘*a confluence of evidence that breeds credibility’* is provided (Eisner, 1991, p. 110). According to Merriam (2001),

documents of all types can assist the researcher in uncovering meaning, developing understanding, and discovering insights relevant to the research problem. Moreover, the documents can be consulted as many times as needed without any formalities or alterations in behaviour such as those encountered when interacting with human beings (Merriam 2001).

Document analysis acted as a complementary method in addition to the interviews and observations in this study as the documents analysed were produced for the purposes of planning and guiding the conduct of the trials selected for this case study. They provided valuable insights for understanding details about the trials and their procedures before entering the research field. The information in the documents had the potential to trigger important questions that I could ask in an interview or in making observations. Furthermore, once extracted, the information from the documents was analysed to verify findings from the other sources of data collection thereby complementing the interviews and observations in an interactive and iterative process. The convergence of evidence from the different sources was used to increase the credibility of the findings obtained (Lincoln & Guba 1985). In this study, electronic trial documents namely the clinical trial's protocols and patient information leaflets were accessed as sources of information for document analysis (Stake 1995, Merriam 2001, Thomas 2021). The process of accessing these documents and the methods used in extracting and analysing the related data is described in chapter 5, section 5.6.1.

4.9 Common qualitative approaches to data analysis in case studies

A qualitative case study can be analysed in several ways and there is no one method that works for all qualitative data analysis (Barbour 2001). The analytical approach chosen is often informed by the purpose of the research as well as the researcher's theoretical perspective and use of an inductive or deductive reasoning method (Baxter & Jack 2008). Common data analysis techniques within case study research involve content analysis, discourse analysis, framework analysis, grounded theory analysis, and more recently reflexive thematic analysis (Merriam 2001,

Brogan *et al.* 2019, Braun & Clarke 2021). Content analysis is used by researchers to examine the content within the qualitative dataset, such as frequency of words or themes, and to methodically organise and quantify textual data in order to make sense of it (Moriarty *et al.* 2007, López *et al.* 2012, Bjornsdottir & Ceci 2022, Im *et al.* 2022). However, this approach was not appropriate because I was not interested in frequency counting or occurrences of words or themes; rather this research was focussed on developing an in-depth understanding of if and how CCPs were used for recruitment to trials.

Another popular method of data analysis used in case studies within health sciences is framework analysis, a method that was originally developed by Ritchie and Spencer (1994) for evidence-based policy making (Ritchie & Spencer 2002, Wells *et al.* 2012, Ward *et al.* 2013). Framework analysis has previously been used in case studies to evaluate clinical practices and to inform the future development of guidelines for clinical practice (Simons *et al.* 2007, Wells *et al.* 2012, Lalor *et al.* 2013, Wang *et al.* 2018). For example, a national study, using case study and framework analysis, was conducted to evaluate specialist and advanced practice roles on clinical outcomes within the Irish health service (Lalor *et al.* 2013). Framework analysis is a robust technique that is applied to research that has specific questions, pre-designed sample and a priori issues (Srivastava & Thomson 2009). However, while this approach is widely used to inform policy and practice, the approach involves fragmenting data, which are sifted and charted in the form of participant summaries into a matrix in accordance with the key issues that need to be addressed. This approach like content analysis is less exploratory since it provides a structured approach to data analysis by moving away from original data earlier, hence it is also referred to as a codebook approach to analysis (Braun & Clarke 2021).

Discourse analysis examines the use of language in written texts or in a conversation, such as an interview or focus group, in order to determine the underlying meanings of communication (Hodges *et al.* 2008, Madden *et al.* 2016, Saldert *et al.* 2018, Byrne *et al.* 2021). A narrative analysis on the other hand is concerned with understanding human experiences through the study of participant stories (Riessman 2005). The researcher, using narrative analysis, makes sure to

faithfully communicate the first-hand accounts of experiences while also emphasising the ways on how these stories are constructed. This method is used to capture unique accounts of people's lives in the form of autobiography, life history, interviews, or written materials such as letters and journals (Clandinin & Connelly 1994). However, both these methods of analyses were deemed unsuitable for this case study, as this study's purpose was not focussed on analysing conversations or in providing an extended account of people's lives.

Constant comparative analysis is another qualitative analytical method commonly used in Ground Theory research, a design that was developed by Glaser and Strauss (1967) for their study on the awareness of dying. This method of analysis is focused on the generation of theory by limiting any predetermined hypothesis or theoretical understandings, resulting in a theory that is fully data driven. Theoretical sampling is employed which involves the process of generating theory or hypothesis from the initial set of data collected (Suddaby 2006, Chapman *et al.* 2015, Roux-Levy *et al.* 2022, Stagg *et al.* 2022). The theory established from the initial data analysis directs the researcher to areas that need further investigation. For example, in a grounded theory study conducted by Noble & Mitchell (2016), in-depth interviews with patients living with heart failure revealed systematic issues in general practice. Based on this initial analysis the researcher then chose to interview general practitioners (GPs) to gather further evidence to support or dispute patient opinions (Noble & Mitchell 2016). This approach follows a cyclical process of data collection and analysis by making constant comparisons of excerpts of data until a meaningful theory is complete (Suddaby 2006). The current case study was not focused on building a substantive theory as in the Grounded Theory approach, Rather the intended focus was exploring a well-defined case meaning that the data collection was purposive and hence consisted of a pre-defined sample that was only related to the case under investigation. Thus, Grounded Theory approach for analysis was not suitable for this case study.

Several case study researchers have employed thematic analysis (TA) (Emily *et al.* 2022, Maddy *et al.* 2022) inspired by the guidance offered by Braun and Clarke (2006). Recently, the authors have renamed their approach as 'Reflexive Thematic Analysis' (RTA) in which the researcher's position and reflections are considered an

integral part of data analysis. RTA is described as ‘a journey of exploration and discovery’ (Braun & Clarke 2022, p. xxvii), which is in line with the purpose of this case study in exploring the utility of CCPs in recruiting participants to trials.

Braun and Clarke (2022) also emphasise that RTA is a distinctive approach, standing apart from other qualitative approaches like content analysis, framework analysis, discourse analysis, and constant comparative analysis, as discussed above. This means that while TA has been flexible in incorporating existing theory or frameworks known as a codebook approach, the current RTA approach is different, as it focuses solely on a reflexive approach to analysis by looking for patterns across the dataset to construct meanings and understandings of the phenomenon of interest based on researcher’s reflection and interpretation of the data (Braun & Clarke 2021). The researcher’s subjectivity is an integral part of the analysis hence adds value to the research process. This method is also compatible with the constructivist orientation of case study research, in which the researcher is an integral part of the analysis where knowledge is co-constructed based on researcher reflections, participant interactions, field observations, and trial documents (Stake 1995, Merriam 2001, Thomas 2021).

In addition, the concept of data saturation does not align with RTA nor with case study rather this case study is guided by the concept of information power, meaning that power based on information the sample holds rather than determining saturation based on frequency of similar occurrences within the data (Malterud *et al.* 2016, Braun *et al.* 2019, Thomas 2021). Braun and Clarke (2022) argue that the concept of saturation is adequate for other forms of qualitative research such as in grounded theory where a theoretical saturation is used to ensure no new insights emerge and that all relevant conceptual categories have been examined and explored before any further data is collected. On the contrary, RTA is consistent with the purposive approach used in this case study where the analysis is focused on the holistic examination of the case. This is because the case is not specifically seeking to represent a sample of a wider population, rather it is about a deliberate choice, a selection from which the researcher could understand and gain insight on the phenomenon of interest. In this study therefore, using an illustrative case of seven ongoing randomised trials (case study subject), data obtained about each of these

trials becomes a nested unit of analysis within a wider case. This means that the patterns or themes from the nested units (trials) collectively informed the interpretations of this analysis in understanding the ways in which CCPs were used for trial recruitment within an acute care setting (the wider case) (Merriam 2001, Thomas 2021) (see Figure 7).

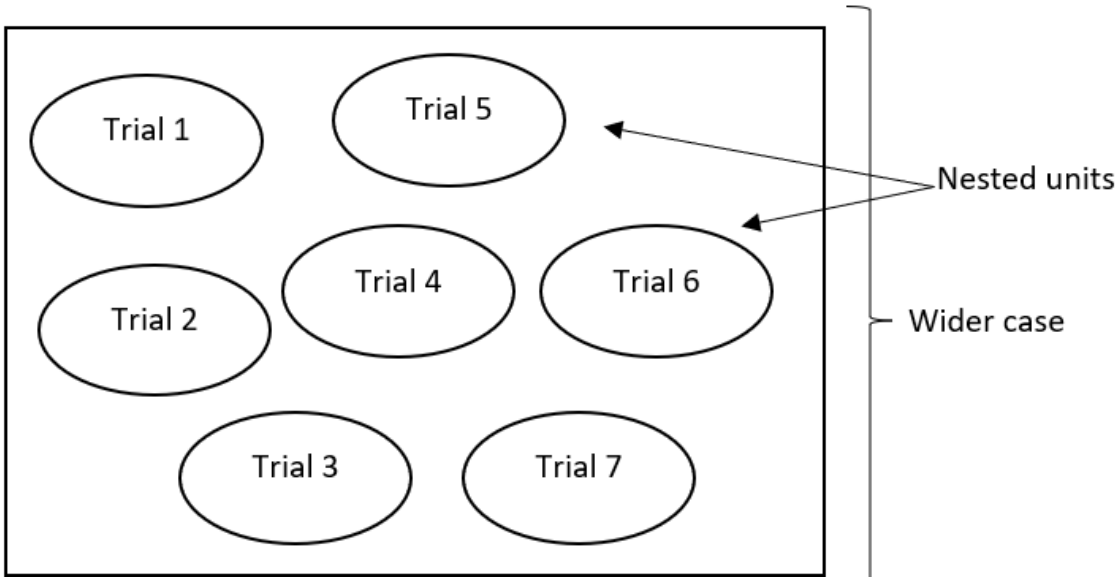

Figure 7: Nested units within a single case adapted from Thomas (2021, p.192)

As a result, RTA provides a comprehensive method for data analysis of a single bounded system (the case). Identifying patterns or themes within the data without introducing predetermined assumptions, a priori codes or frameworks contributes to the exploratory nature of this case study. This method is also aligned with the philosophical orientation of constructivism, assisting the researcher in generating findings that are reflective of the study data. Another benefit of employing RTA is that it is an easily accessible yet robust approach that assists novice researchers who are undertaking the journey of analysing qualitative data through the availability of trainings, webinars, textbooks, and online resources (Campbell *et al.* 2021).

4.10 Chapter Summary

This chapter identified and justified the philosophical underpinnings guiding this study and the rationale for choosing qualitative case study to address the research aim and objectives. It further included a discussion on the choice of methods for data collection, including the conduct of interviews, observations and collection of documents and demonstrated their alignment with qualitative case study. Finally, the choice of RTA as the method for analysing the case study was discussed. This chapter also provided the methodological backdrop to the following chapter, which discusses the conduct of the study and the operationalisation of the methods used to achieve the research aim and objectives.

Chapter 5: Methods

5.1 Introduction

This chapter describes how the research design and case study method, as described in Chapter 4, was operationalised in the study. The selection of the case study setting, the process of selecting the case study subject (case trials), the recruitment of study participants, the process of collecting the documents and the conduct of observations are described and discussed. How the data were analysed, ethical considerations related to the study, and ensuring rigor in the case study are also discussed.

5.2 Case study setting

The case study setting was a large, urban, acute care teaching hospital with a bed capacity of just over 1000. The hospital provides a wide range of healthcare speciality services such as emergency, inpatient, outpatient, surgical, medical, laboratory, and diagnostic care services. In addition, the hospital is supported by a clinical research facility that supports clinical research activities alongside delivering essential healthcare services. The clinical research facility supports over one hundred clinical research studies within the hospital, including observational studies, non-randomised controlled studies, and RCTs, for a wide range of medical conditions. This setting was purposefully chosen for the current study because it offered an opportunity to access and gather an information rich case, fulfilling the requirement for an instrumental case, i.e., an exemplar where the phenomenon of recruitment is occurring within the context of CCPs. As a result, the case was bound to the single setting (space), which implies that case trials ongoing in the study site were chosen, and not trials that were supported by the research facility that were outside of the chosen setting. Choosing the case trials within the context of CCPs was important for exploring how CCPs were being used for recruitment to trials. The chosen setting also provided me with ample opportunity to explore if and how trial recruitment processes occurred alongside the delivery of clinical care. The case was also time-bound, meaning that the selected case trials were open to recruitment

during the data collection period. This was to gather a contemporaneous perspective of trial recruitment occurring alongside clinical care within the context of CCPs.

5.3 Preparatory phase- determining the availability, accessibility and feasibility of potential case trials

Authors writing about case study research propose that the selection of a case study subject should be based on the availability, accessibility and feasibility of the potential cases that will answer the research question (Merriam 2001, Yin 2014, Thomas 2021). Therefore, an early initial meeting was held with both the Director and the trials operations manager of the research facility, located at the study site, in October 2019 to discuss and ensure the suitability of the site for the purposes of my study. This included determining that the study setting was actively recruiting to RCTs on a consistent basis (i.e., to determine availability of trials). I also discussed at this meeting that, to fulfil the study objectives, I would require access to trial documents and would need to interview staff and patients involved in recruitment processes as well as make observations on recruitment processes within the case study setting. This discussion was important to enable me to determine accessibility to trials and the feasibility of conducting the study at this clinical setting. These early discussions established quickly that the chosen site provided an ideal setting for which the study could take place, as i) it was an acute care setting, ii) with CCPs across multiple care specialities, and iii) was research active with RCTs as well as other research studies ongoing at the time. During this meeting, as discussions about how the study might be operationalised at the site progressed, the trials operations manager agreed to act as the gatekeeper for distributing the study information to the staff involved in trial recruitment. The logistical aspects of how data collection would occur at the site were also discussed. For example, we discussed considerations pertaining to accessing trial documents associated with recruitment (patient information leaflets (PILs) and protocols); undertaking observations in the hospital setting where recruitment to trials was taking place and holding study interviews in a private meeting room within the research facility. The preparatory phase spanned from October 2019 to January 2020, and was considered an integral part of the research process as it established an early understanding of the numbers and types of trials that were ongoing at the time of the

study and helped build rapport and develop relationships with members of the research facility. These were critical to the success of the later stages of the project (e.g., distribution of the study information, access via the trial PIs to selected trials' documents, introductions to the Director of research facility and others in gaining access to the site to conduct observations, and so forth).

5.4 Impact of COVID-19 pandemic on this PhD research

As preparatory plans for data collection (see section 5.3) were in place and ethical approval was granted in March 2020 (see section 5.10 on ethical approval), the plans for data collection were interrupted due to the COVID-19 pandemic. In order to minimise the contamination due to the virus, Ireland, like other countries around the world, imposed restrictions for travel and social distancing. This further led to a nationwide lockdown where only the most essential services were available. As a result, all research activities, including clinical trials, were ceased in the clinical care setting. No immediate alternatives to the study plans were possible as both the clinical care and clinical trial recruitment had to occur simultaneously to answer the PhD research question. I was able to resume preparations for data collection in January 2021 following the amendment of ethical approval for inclusion of remote interviews, easing of nationwide travelling restrictions and resumption of clinical trial recruitment related activities in the clinical care setting (see section 8.6 for a personal reflection on the pandemic).

Overall, this led to a ten-month delay in starting the field work phase of this study. The ongoing pandemic era posed several challenges, such as reduced feasibility to conduct non-participant observations, as only socially distanced observations were possible. Hence, it was possible to observe only a few recruitment-related activities over two days. Despite patients returning to the clinical care setting for their routine clinical care services, the availability of patient-clinician interactions was minimal, resulting in fewer patient study participants available for participating in for the interview component of this PhD study. On a positive note, due to less patient in-flow to the clinics, the availability and active participation of the majority of consultants,

doctors, and nurses sharing their real-life experiences of being involved in clinical care and trial recruitment has been immensely advantageous to this PhD study.

5.5 Sampling

As the study was an instrumental case study, one or more case study units, that is, the case trials, were required so that the utility of CCPs for trial recruitment could be explored. Sampling in case studies occurs at two levels. In this study, the first level involved the selection of case(s), i.e., the selection of case trials within CCPs and from which recruitment could be studied. The second level involved the selection of participants, documents, and observations i.e., determining the trial documents to be collected, trial recruitment activities to be observed, and the selection of participants to be interviewed (Merriam 2001, Brown 2008).

Sampling methods can be broadly categorised into probability and nonprobability sampling methods (Merriam 2001, Bowen 2005). The main differences between these sampling methods relates to whether all individuals in the sample population have an equal chance (probability sampling) or not (non-probability sampling) of being selected to participate in the study (Pace 2021). Table 11 illustrates some different sampling techniques according to probability and non-probability methods (Pace 2021, p.3)

Table 11: Examples of Probability and Non-probability Sampling Techniques (Pace 2021, p.3)

Probability Sampling	**Non-Probability Sampling**
Simple random sampling (SRS)	Purposive Sampling
Systematic sampling	Convenience Sampling
Stratified sampling	Quota Sampling
Cluster sampling	Snowball Sampling

Random sampling, the most common form of probability sampling, allows researchers to generalise the findings of the study to the population from which it was drawn (Curtis 2000, Mtisi 2022). This is because the sample size is usually

large, based on mathematical sample size estimates, and importantly, selecting the sample is free from human bias and subjectivity as the study sample is selected using a 'by chance' technique (e.g., random number generator, coin tossing) (Taherdoost 2016; Higgins *et al.* 2023). Since generalisation in statistical sense was not the goal of this research study, probability sampling, such as random sampling, was not a justifiable choice for this case study. Since this case study was seeking a deeper understanding of the utility of CCPs for trial recruitment, I needed to select a sample of information rich cases, i.e., case trials from which issues central to the purpose of the study could be studied (Patton 2015); hence a nonprobability sampling technique appeared more appropriate; more specifically purposive sampling. Purposive sampling involves identifying and selecting individuals (and case trials in the context of the case study) deliberately because it is known that they are able to provide information on the phenomenon under study (Taherdoost 2016).

Some researchers argue that purposive sampling could be prone to researcher biases as sample selection is guided by subjective or generalised assumptions, and thus, generate findings that support pre-conceived notions (Sharma 2017, Bhardwaj 2019). To minimise the risk of researcher bias in this study, I first determined selection and inclusion criteria as follows:

i. The case trials occurred only within the case study setting.
ii. All the case trials were RCTS. This was because the research question was based on the recruitment issues associated with RCT, trial design. As a result, all non-randomised trials, and other studies such as observational studies or cohort studies, were excluded.
iii. The case trials were aligned with a specific speciality CCP where standard clinical care was simultaneously being delivered to patients regardless of whether patients in the CCP were, or were not, taking part in the trial.
iv. All the case trials were actively recruiting participants. This meant that participants were recently recruited into the trials (within 3 months of starting data collection) or that the trials remained open to recruit new participants during the data collection phase of my study (February- July 2021).

To ascertain the availability of potential case trials, I organised a virtual meeting (January 2021) attended by both the Director of the research facility and the trials

operations manager to identify RCTs that were undergoing recruitment at that time, and to assist me as gatekeepers to progress the field work phase of my study. At this meeting, seven randomised trials were identified as open to recruitment, and these trials became the potential case trials for inclusion in the case study. I chose to include all seven RCT's that were open for recruitment, as each trial focused on a different clinical care specialty, thus potentially enabling me to gather rich data about trial recruitment across diverse CCPs. Further, choosing actively recruiting trials, was paramount to capturing a contemporary perspective of how CCPs were being used for recruitment. This also meant that I could gather recent experiences of trial recruitment from interviewees who were involved in the recruitment processes of these trials, as well as obtain opportunities to conduct observations on recruitment as it was occurring within the case setting.

The second level of sampling involved collection of data sources which were confined to the chosen case trials, in other words this formed the bounded system (Merriam 2001, Stake 2005) from which the investigation on the utility of CCPs for trial recruitment was carried out. The biases in the second level of sampling were minimised by: the development of a detailed interview guide for participant interviews, development of an observation chart for non-participant observations and drawing on information on trial recruitment activities from clinical trial documents and PILs for document analysis prior to collecting the observation and interview data, with the intention that this source data would help guide the collection of data during observation and interview (i.e., having knowledge of trial specific recruitment processes and in developing the interview guide). The second level of sampling also involved choosing an appropriate sample size for this case study as discussed in the following section.

5.6 Sample size

It is widely acknowledged that there is no precise means of determining the sample size in qualitative case studies (Curtis *et al.* 2000, Ishak & Abu Bakar 2014, Mtisi 2022). The question of the optimal number of case units to select, specifically in terms of the number of interviews to conduct, documents to be analysed, or observations to be made, is addressed by numerous authors with the opinion that, it

depends on the question that is being posed in a case study (Merriam 2001, Baker & Edwards 2012, Patton 2015, Saunders & Townsend 2016, Thomas 2021). The existing body of case study literature, however, suggests that researchers should select a limited number of sample or case units that are highly relevant to the research topic (Curtis *et al.* 2000). By doing so, researchers can obtain an in-depth understanding of the phenomenon of interest by examining a wide range of features within the case units (Thomas 2021). This approach prioritises the richness of data over statistical representativeness typically associated with larger sample sizes (Ishak & Abu Bakar 2014, Njie & Asimiran 2014). Therefore, the sample size considerations for this study depended upon the aim of the study, the philosophical position underpinning the study, heterogeneity of the study participants, the availability of time, resources and potential participants, and advice from experts in the field of qualitative research and case study research (Adler & Adler 2012, Patton 2015, Bryman 2016, Saunders & Townsend 2016, Thomas 2021).

Interviews are commonly used as one of the major sources of data in qualitative case studies taking precedence as the primary source of data, while other documents and observations play a supporting role in providing an in depth understanding of the case. While multiple sources of data are commonly used in case studies, it is common that a single method, usually qualitative interviews become the primary source of data, while the second or third sources of data supplement the data obtained in the primary data (Bowen 2009, Jamshed 2014). In this case study, the use of semi-structured interviews took precedence over documents and observations as the primary source of data whereas the documents and observations were used as secondary sources or supplementary sources of data to enhance the contextual understanding of the data collected in the primary source. Hence, a detailed sample size strategy was employed which is discussed below.

Document analysis involved the collection of the trial protocols and PILs of all seven case trials. These data sources provided information on the recruitment procedures involved in the trials as well as providing a contextual understanding of trial activities taking place in the clinical setting. However, advance planning for the number of observations to be conducted from each trial was not possible due to the COVID-19

pandemic restrictions that were in place at the time of data collection; hence observations were solely based on the feasibility of conducting a socially distanced observation. Ultimately, due to COVID-19 only two non-participant observation episodes were feasible. These were conducted on two separate days for 4 hours on 11 March 2021 and for five hours on 23 March 2021. Therefore, data from observations and documents were used to supplement the interview data in obtaining a holistic perspective on the utility of CCPs for trial recruitment.

In considering a sample size strategy for interviews in qualitative research, the concept of saturation is a common recommendation (Merriam 2001, Mason 2010, Lincoln *et al*. 2011, Patton 2015, Saunders & Townsend 2016). This means that the sample of interview participants are determined based on saturation of data, wherein the researcher stops conducting further interviews when no new information is emerging or arising from interviewees, as the number of interviews increasingly progresses, or when redundancy of information occurs when interviews are continued (Merriam 2001, Lincoln *et al.* 2011). However, there is no common understanding within qualitative literature that demonstrates at what point saturation could possibly occur to guide novice researchers in estimating a sample size for interviews prior to commencing field work.

On examining previous qualitative research studies, it was found that the time points where saturation was indicated varied; for example, Guest *et al.* (2006) suggested a sample size of six interviews to achieve data saturation, whereas Alder & Adler (2012) report data saturation between twelve and sixty interviews. In another study whereas Brannen (2012) included 260 interviews to reach data saturation. Further, Guest *et al.* (2006) notes that data saturation could be relevant only for a homogenous sample, meaning that participants taking part in interviews should be of similar characteristics or of similar backgrounds in discussing the phenomenon under study. This also assumes a certain degree of structure within interviews where a similar set of questions are asked of all participants involved in the study. However, this case study, while involving a homogenous group in that they were all involved in trial recruitment processes, concurrently involved a heterogenous population, that is, consultants and doctors, trial principal investigators, research nurses, clinical nurses, pharmacists, research assistants, trial coordinators and trial participants who held

different roles in trial recruitment processes and in clinical care setting. For this reason, slight modifications to interview questions were needed based on the role of the participants involved in trial recruitment activity (see Appendix 5 and 6 for the interview guides).

Further, considering the sample size for interviews, Mason's (2010) recommendation of an appropriate sample size of 30 participants for qualitative interviews, which the author made after studying 560 PhD theses in the UK (England and Wales) was appealing for the purpose of my research study. A similar investigation by Saunders & Townsend (2016) found a mean sample size of 32 for qualitative journal articles in workplace and organisational research using semi-structured interviews as a data collection method. These studies thus became important in determining a provisional sample size in my study; that is, based on the average numbers of interviews of 30-32, as recommended by Mason (2010) and Saunders & Townsend (2016) the target number of interviews, involving one interview per participant, for the case study, was set at an average of 30. This number allowed me to plan for approximately four to five interviews from each of the seven case trials; three to four with those undertaking trial recruitment and at least one or two with patients who had been recruited into each of the case trials. Determining the approximate sample size prior to commencing the interviews, avoided sample size determination based solely on data saturation, and critically, met the ethical approval requirement of providing an expected sample size for interviews for the site Research Ethics Committee. In the actual execution of the study, I obtained a sample of 25 individual interviews with an average of 3.5 interviews per case trial; this sample was deemed sufficient in generating an information rich case on the phenomena studied. This was in line with the important observations made by Miles & Hubermann (1994) and Patton (1994) who note that the insights and meaningfulness generated from qualitative studies have more to do to do with information-richness of the selected cases and the analytical capabilities of the researcher rather than with the sample size.

Further, in line with the data analysis strategy adopted for this study, the concept of information power (Malterud *et al.* 2016) and adequacy of data (Vasileiou *et al.* 2018) seemed appropriate over the concept of data saturation which follows an iterative data gathering and analytical process. The reason for this is that, if I had solely relied

on data saturation as the basis for determining the sample size, it would have required me to simultaneously sample, collect data, and analyse it in the field in order to ascertain data saturation (Baker & Edwards 2012, Bryman 2012, Bonde 2013).This is in contrast to having these processes carried out sequentially and as independent stages of the research process, which, due to time constraints in collecting and interpreting the data within a relatively short data collection time period, and in the context of an ongoing pandemic, would have been challenging. As a result, rather than relying on saturation, this case study was conducted based on the concept of ‘information power', which means that the study sample was based on the relevance and quality of the information the sample would provide, rather than information saturation. This decision was also supported by the uniqueness and novelty of exploring trial recruitment within CCPs, a phenomenon that had, heretofore, not been explored in the context of trial methodology research and trial recruitment in an acute healthcare setting.

5.6.1 Gaining access to the case trials

To gain access to the case trials, the gatekeepers introduced the study and its purposes to the Principal Investigators (PIs) of the seven case trials via email (see Appendix 7 for email information). The Participant Information Leaflet (PIL) and consent forms were also forwarded on this email for further information. The email advised that information sessions about the trial would be arranged where I would be available to discuss the study further and answer questions. To arrange the information sessions, a doodle poll for suggestions of date and time for holding a virtual information session was circulated by the gatekeeper. As per the availability of the PIs, two information sessions were arranged, with the zoom invitation link for these sessions circulated to the PIs by the trials operation manager gatekeeper. The first information session was held on the 9th February 2021 attended by three PIs and the second session was held on the 11th February 2021 attended by two PIs.

The information sessions provided the PIs with the opportunity to become more familiar with the purpose of this study and clarify questions related to why collecting multiple sources of data for the case study was required. The PIs signed the consent form (Appendix 8) on the same day following the information session providing

permission to include the chosen trial in the study as well providing permission to access the trials' protocols and PILs for document analysis. Two trial PIs who were not available to attend the virtual information session, later contacted me for further information via emails and, after providing the required clarifications, they also gave consent to include the trials in the case study. These signed consent forms were emailed to me on 16 March 2021 and 14 April 2021 respectively.

During the information sessions with the PIs, the feasibility of conducting non-participant observations was also discussed. As a result, two PIs linked me with the lead research nurses of their trial team who informed me of scheduled recruitment processes in the following month (March 2021), and for which observations might be feasible. I was also notified at the information sessions that conducting socially distanced observations for all of the trials would not be feasible. The feasibility of conducting non-participant observations was also clarified via email communication from the two PIs who were not available to attend the information session. Of these two trials, the feasibility of conducting observation was confirmed for one trial, and I was linked with the lead research nurse of the trial by the PI, who would then inform me when a recruitment activity was scheduled.

Likewise, a plan for conducting interviews was also discussed and any questions regarding the conduct of same were clarified. The study information was shared by the PIs with their respective trial teams, followed by a formal invitation email forwarded to the team members by the gatekeeper, inviting them to participate in an interview. The process of accessing the case trials and the collection of data is represented in Figure 8 below. Fostering a collegial, honest, and non-threatening relationship with the gatekeepers and PIs, and assuring them that as little disruption as possible would be made during the data collection process influenced the strategies for gaining access to the case trials. This supports evidence referring to the process of managing one's identity and image, as well as convincing stakeholders that the researcher is not a threat in terms of gaining access (Waddington 1994).

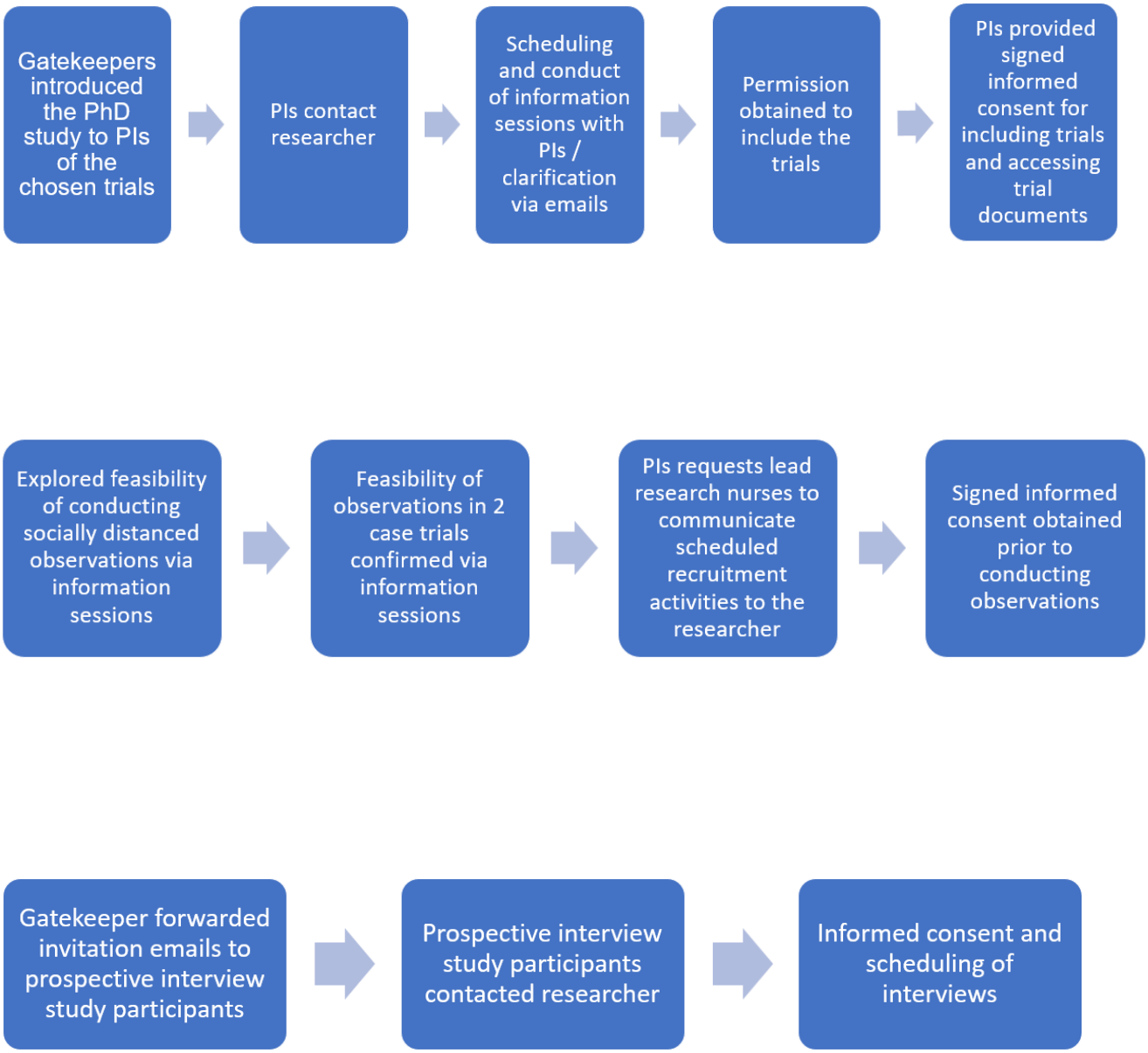

Figure 8: Processes involved in accessing case trial data and interviewee participants.

5.7 Data collection

5.7.1 Documents

Documents were an important source of information for understanding the recruitment processes involved in each trial and the context of the CCP to which each trial was aligned. As a result, clinical trial protocols and PILs were identified as key data sources for document analysis. Following written informed consent provided by the trial PI (as described in section 5.6.1 above), the trial documents were received from each PI as password-protected files by email. The trial documents were reviewed to make note of aspects related to standard care delivered as part of a CCP such as nature of the disease and the normal course of CCP care plans and the recruitment processes involved in the trial.

Obtaining documentation ahead of the interviews and thus having the opportunity to engage with trial documentation made me familiar with the procedures involved in the clinical trials, allowing me to ask pertinent questions during interviews such as probing deeper on a specific recruitment process, such an activity involved in a screening visit relevant to each trial and its CCP. For example, some trials required lengthy screening visits (up to 45 days) to determine if participants were eligible to take part in the trials.

Reviewing trial document data enabled me to explore the utility of the CCPs for the conduct of these screening procedures and to further explore this aspect of trial recruitment during interviews and observations. As a result, during interviews, clarification on recruitment processes was sought, including where and how recruitment processes occurred within the CCP, as well as who was involved in conduct of the tasks involved in recruitment. Furthermore, knowing the trial recruitment processes prior to interviewing allowed me to focus the interview discussions on recruitment specifically, whilst avoiding discussions that were less relevant to the study’s research question.

5.7.2 Non- Participant Observations

As the pandemic was ongoing during the time of data collection. only socially distanced observation was possible. This meant that I had to maintain two meters distance away from staff and follow hospital guidelines on wearing face coverings and hand sanitisation procedures throughout the observations. Due to these protective regulations, a socially distanced observation was potentially possible for three trials only (T1, T2, T3). The remaining four trials (T4, T5, T6 and T7) involved vulnerable or very ill patients, hence it was not possible to conduct observations in these trials for ethical and safety reasons. However, during the data collection time period, opportunities to observe trial recruitment was available only for two trials (T1 and T2). Hence only two separate observation visits to the clinical site were made, involving four hours on 11th March 2021 and five hours of observation on 23rd March 2021 for trials T1 and T2, respectively in the clinical setting. These observations included observations of the clinical care setting (1 hour), pre-screening (2 hours) and informed consent processes (1 hour) for T1. For T2, the preparation involved in laboratory assessments (1 hour), screening procedures (3.5 hours) and the process of documentation of patient participation in case report forms (0.5 hours) were observed. Although written informed consent from the PIs of T1 and T2 for including the scheduled recruitment processes as a source of observation for this case study were received in advance of planned observations, the PIs of these trials further sought verbal consent from both staff members and patients who were present in clinical setting before the planned observational sessions. During the observation period, I engaged in shadowing the recruiters while they engaged in the activities of trial recruitment processes.

The majority of the observation sessions did not involve patients in the setting except on two occasions, namely an informed consent process and a screening process. It was clarified for the staff conducting recruitment that the focus of my observation was to capture the utility of CCPs as and when the recruitment process occurred rather than evaluating the recruiters' trial recruitment conduct. Establishing this awareness was important to ensure that the recruiters felt comfortable with my presence in their clinical setting. I also stepped away from the clinical area to the waiting area during clinician-patient interactions, or while patients engaged in clinical

procedures as part of the screening process. This decision was made as the specific interactions or procedures involved were not relevant to the purpose of this study. Hence the observations were limited to shadowing the recruiters and documenting the utilisation of CCPs during the recruitment process.

The observations included making descriptive notes on how CCPs were used in T1 and T2 recruitment processes. The observations were recorded on a purpose-designed observation sheet (Appendix 4), which included the start and end time of the observation, the recruitment process of the trial, the physical setting and location where recruitment was taking place, and activities and interactions that were relevant for the case study, for example the activity of pre-screening or randomisation. Observations were non-participant (as described in section 4.8.2) whereby I made note of relevant information on the observation chart during the observation, with further detailed notes and associated reflections captured, in a personal reflective diary, later on the same day following the actual observation period. These observational data were subsequently used as supplementary data, to the interviews, to deepen the understanding of the phenomenon of recruitment within CCPs.

5.7.3 Interviews

5.7.3.1 The Pilot Interviews

Interviews are one of the most commonly employed methods for data collection in qualitative research, enabling the researcher to understand the research phenomenon through the interviewee's account (Gill *et al.* 2008, Kvale & Brinkmann 2009, Majid *et al.* 2017). In contrast to a quantitative study, the researcher is the primary instrument of data generation (Merriam 2001). Moreover, individual interviews are widely recognised as a suitable strategy for obtaining rich and detailed information from persons experiencing the phenomenon of interest (Merriam 2001, DeJonckheere & Vaughn 2019). However, being a novice qualitative researcher, I needed to gain practice in interviewing techniques, for example, maintaining a conversational tone, pacing the interview so it was comfortable to each interviewee and ensuring that the questions and responses fitted the objectives of the actual study (Hennink *et al.* 2011, DeJonckheere & Vaughn 2019). For this reason, I

undertook five pilot interviews to prepare for and help me optimise interview data collection in the study. These pilot interviews took place via the zoom communication platform between April and May 2021.

Hennink *et al.* (2011) suggest that the participants invited to take part in a pilot interview should be of similar characteristics, in as much as possible, to the study interview participants. As participants in this case study held diverse roles and responsibilities for trial recruitment processes, and in different areas of healthcare practice, I decided to conduct the pilot interviews to gain experience of interviewing people from various healthcare backgrounds, as well as practising and perfecting my comfort with the interview technique and using the interview guide. Therefore, three pilot interviews were conducted with clinicians who were also experienced qualitative researchers, who acted as a PI, junior doctor, and research nurse, respectively; two additional interviews were conducted with a former clinical trials coordinator and a healthcare user who acted as a patient. Reflection on my experience of the pilot interviews and debriefing with my supervisors identified a need to modify questions based on the interviewee's role and responsibility in the trial (see Interview guides used for pilot interviews in Appendix 5 and actual interviews in Appendix 6). As a result, by the end of the fifth pilot interview, I had become familiar and comfortable with the interview process, from warming up, introducing the research, asking questions, and wrapping up, and I was able to freely immerse myself in the conversation by overcoming the need to constantly look at the interview guide during the interviews. This led to my enhanced competency and dexterity in the conduct of the research studies within the context of the main study.

5.7.3.2 Case study Interview process

I initially intended to conduct semi-structured face-to-face interviews in the hospital setting, but due to COVID-19 restrictions on physical distancing, the option of one-to-one virtual or telephone interviews were also provided to the participants (see section 5.10 for information on ethical approval and amendments to progress with online data collection). Being in the pandemic era, the use of Voice over Internet Protocol (VoIP) services such as Zoom and Microsoft teams and telephone services

became a widely accepted method for qualitative researchers across the globe (Archibald *et al.* 2019, Lupton 2021, Self 2021). Additionally, conducting the pilot interviews remotely (via VoIP and telephone) increased my confidence in using these technologies for research purposes with actual study participants. In contrast to the challenges faced when conducting in-person interviews during the pandemic, where visual cues may be hindered by using masks and face shields, remote interviews enabled me to actively interact with the participants without needing facial coverings or concerns about maintaining social distance. However, it was not possible to observe the visual cues and reactions of four study participants who chose to have their interview via telephone.

To invite a potential participant to take part in an interview, invitations were distributed to trial members of the seven case trial teams, by the gatekeeper, with a request for a potential participant to contact me directly if they were interested in taking part in an interview (see Appendix 9). As the majority of the trials' team members, and thus potential study participants, in addition to having trial recruitment responsibilities, had busy clinical roles in the acute care setting, interviews were scheduled in advance with flexibility to fit the participant's schedule. It was also emphasised, when arranging an interview, that the study details would be explained again on the day of the interview. At the beginning of the interview each participant was thanked for their time and commitment followed by a brief introduction, and descriptions of the purpose of the study. Verbal consent was obtained before the interview in addition to receiving a signed informed consent form (Appendix 8) as a password protected document through email communication before each interview took place. The participants also were aware of the purpose of digital recording of the interview conversation and consent for recording the interview was obtained before starting the formal interview. In addition, the interview guide was adapted for each interview to include details on the specific recruitment processes informed by document review and observations (see Appendix 6 for interview guides). For example, observations highlighted challenges that clinicians faced during screening in T1. To gain further insight and understanding of these challenges from the perspectives of recruiters, and using notes taken during observations, these challenges were discussed and probed further during interviews with interviewees who were involved in T1. As the focus of this case study was on the utility of CCPs

for trial recruitment, a focus, however, on probing about the utility and application of CCPs in trial recruitment was maintained throughout all interviews.

During interviews, I adopted a relaxed approach reassuring the participants that the interviews were reflective accounts of their individual experiences and that there were no right or wrong answers. Researchers are considered as instruments of data collection in qualitative research (Merriam 2001, Wa-Mbaleka 2020). As I was the only person collecting interview data, this ensured a consistent approach in the conduct of interviews (Merriam 2001) and minimised variability in executing the interviews. It was also observed that having a relaxed researcher approach, the participants were able to disclose information without any pressure; they had the opportunity to qualify their answers and explain in depth the underlying meanings of their responses (Polit & Hungler 2004). As a result, the participants spontaneously raised issues on their own, with participants revealing more and expanding on information as their respective interview progressed. This further indicated that the participants were at ease and relaxed while taking part in an interview. To ensure accuracy and strengthen the credibility of the study, a member checking process was employed after each interview. This involved recapping the interview with each participant and providing a summary of the discussion by reflecting on the notes taken during the interview. This allowed for any unintended errors to be rectified and enhanced the clarity of understanding regarding the clinical and recruitment procedures. By doing so, both myself as the interviewer and the participant were able to reach an agreement on the final content of the interview, ultimately resulting in more accurate and reliable data.

The interviews were planned to accommodate the participants' preferred availability times, ensuring their convenience and comfort. The interviews were conducted between May 2021 and July 2021, mostly during the daytime between 9 am and 6 pm. However, two interviews were scheduled earlier in the day at 7.30 am and 8 am, respectively, in consideration of the participants' busy schedules. Twenty-five interviews were ultimately held (see below for further information) ranging in duration from 25 minutes to 62 minutes, with a total interview time of 15 hours and 28 mins. After each interview, the digital recordings of the interviews were uploaded to TCD's OneDrive which is a secure file hosting service that was operated by Microsoft as

part of its web version of Office. Once the voice data files were uploaded, the original file on the digital recorder was deleted. Each uploaded file was assigned a study ID that included the trial code as well as the participant role code for example, Trial 1, Nurse 2 and so forth. I personally transcribed 13 of the recordings verbatim and utilised a transcription service approved by the university to transcribe the remaining 12 interviews. This decision was made due to time constraints. The digital recordings were deleted after the transcripts were checked for accuracy, and anonymity was ensured by removing any participant identifying data and replacing it with pseudonyms. Section 5.10.3 provides further details on data protection and secure handling of data in the study.

5.7.4 Benefit of using multiple methods in a single instrumental case study

The benefit of using multiple sources to inform this research is that it facilitated obtaining a more holistic perspective of the phenomenon under investigation than would have occurred from obtaining information from a single source only, such as interviews only. The use of document analysis and observations enhanced the interview experience given the novelty of the topic within the trials methodology field. The use of multiple sources led to the identification of key findings mainly related to activities involved in pre-screening and screening as important recruitment phases that take place within CCP, which otherwise would have gone unnoticed. Therefore, the use of multiple methods of data collection provided a holistic understanding of the uncertain issue of if and how trial recruitment occurs alongside CCPs. Table 12 provides a brief description of each type of data source and its influence in the subsequent data collection.

Table 12: Application of multiple methods in single instrumental case study

Data source	**Influence and use of the data collection method**
Document Analysis *Type of source:* *Secondary source*	Analysis of clinical trial protocols and trial PILs were used to understand the specific recruitment related activities that were planned to take place from the time of identifying potential trial participants until randomisation in the seven case trials included in

	this PhD study. The documents also provided information relating to whether the procedures were normally conducted as part of clinical care, or the procedures were an addition to clinical care. This was valuable information to further explore the utility of CCPs during the observations and interviews.
Observations *Type of source:* *Secondary source*	The in-person experiences of non-participant observations enhanced my understanding of where and how the recruitment activity took place within the CCP. This included the setting where the recruitment activity occurred and who was involved in recruitment activity (such as research nurses, consultants, or clinical nurses). The observations proved to be particularly useful in gathering new insights, especially in relation to pre-screening and screening activities of trial recruitment, which were not indicated in the trial documents nor identified in previous literature. The challenges faced by staff while undertaking pre-screening activities, as noted during the observations, then became important exploration points during the interviews.
Interviews *Type of source:* *Primary source*	Interviews took place towards the end of the data collection process following document analysis and observations. Interviews were the primary source of data collection that informed the exploration of the research question. The observations and document analysis supplemented the interview data providing a holistic experience of data collection and analysis. For example, instead of asking a generic question on how screening was conducted within CCPs to all of the participants, I was able to gather the specific list of screening procedures and direct the specific questions to the trial team related (such as clinical nurse or pharmacist) who would be performing them. The challenges related to recruitment noted during the observations were also explored in detail during the interviews. The information gathered from documents and observations led to the development of informed interview questions, which in turn enabled a deeper understanding of the activities involved in trial recruitment from a holistic perspective.

5.8 Data analysis: The application of Reflexive Thematic Analysis (RTA)

As described in section 4.9, RTA (Braun & Clarke 2022) was applied for the analysis of data in this case study. According to Campbell *et al.* (2021), RTA is becoming increasingly popular in qualitative health sciences research. This method of data analysis was expanded from long standing version of TA (Braun & Clarke 2006). RTA is a flexible method of data analysis and is described as being a 'fully qualitative' (Braun & Clarke 2022, pg.7) approach embracing researcher subjectivity. According to Braun & Clarke (2022), the researcher and their subjectivity serve as instruments that can be consciously and actively used. The application of RTA meant that my prior knowledge of recruitment to trials research, formed by education and training, as well as my prior experience working as a clinical research associate and as a clinical trials manager, could add value to this research study. This means that while the findings were wholly driven by the addressing the study aim via data obtained, my prior knowledge and experiences of trials would have helped me in exploring and making sense of the data. The following section demonstrates the application of the six phases of RTA described by Braun & Clarke (2022) to the case study.

Phase 1: Familiarising myself with the dataset.

The first phase of RTA involves becoming and being immersed in the data to ensure depth of familiarity with it, followed by taking notes on initial thoughts while actively engaging with the dataset. The dataset for analysis was derived collectively from the interviews, observations and trial documents, with separate source data concurrently reviewed and compared to gain a holistic understanding of the phenomenon of recruitment within the context of CCPs. Familiarisation with the interview data was achieved by repeated listening to the audio-recordings for transcription and by verifying transcripts against the audio-recordings to rectify any errors. The transcription period involved being fully immersed with the data to carefully take note of all the inflections, pauses and breaks as well as adding clarifications to reflect the correct meaning of the study data (Clarke & Braun 2013). This process also involved

making notes of initial thoughts and reflections about the interview data in terms of the research phenomenon.

The observational data which was recorded on an observational chart during field work was also transferred to a Microsoft word format to enable coding of data. As observations were restricted due to the pandemic, the interviews were the primary source of data and were supplemented by observation and trial documents to enhance the understanding of the case. This approach is common in qualitative case studies where one data collection method takes prominence as the primary source and other sources offer a supporting role in acquiring a deeper understanding of the case (Bowen 2009). For example, Harris (1995) conducted a study on planning a learning programme for which the researcher primarily relied on interviews which were regarded as the primary data source; documents enhanced the understanding of the planning process which was categorised as a secondary source; the observations were included as a tertiary source as they minimally informed the case. For example, the description of an informed consent process in the document, the observation in a real life setting and the personal experience of the stakeholder in combination gave a deeper understanding of the same process i.e., a description of the same instance guided by multiple sources increasing the trustworthiness of the data study.

Further, it is important to note the supplementary use of documents in this study. This was because documents were not specifically generated for the purpose of this research study, rather they were intended for the conduct of the clinical trial. This means that the documents lacked real-life experiences of using CCPs for recruitment and they also contained information beyond what was necessary such as procedures involved until the completion of a trial including pharmacological properties, and the safety profile of the interventional medicine, as well as handling and storage instructions. As a result, the familiarisation phase with documents involved comprehending clinical information and identifying information relevant to the purpose of this case study. Documents were used as supporting material in this case study, which entailed segregating pertinent information aligned with the research purpose which were later coded thematically in a similar manner to observational and interview data (Bowen 2009, Morgan 2022).

Familiarising myself with the data also involved meticulously removing identifying information from all data sources, such as names of people involved in the trial, name of the trial or location for confidentiality reasons. The name of the specific disease conditions involving the trial investigations were also removed in order to avoid indirect cues identifying the study participants involved in this case study. For example, if the trial sponsor's name was provided, it was deleted and [sponsor] was added to the document; similarly, participants' names were substituted by the person's role. As a result, the familiarisation process included deleting all identifying information from the data.

Familiarisation also involved being familiar with the trial recruitment processes, understanding information regarding the current CCP associated with the disease condition and then drawing an understanding of if and how CCPs were utilised for recruitment to the trials. This process took time and was iterative whereby it involved reading and re-reading the entire dataset numerous times. During this early phase, I took note of trends in the data by documenting the potential meanings, patterns and my assumptions of the data while also making reflexive notes on my thoughts and feelings in relation to the dataset. Exemplar illustrations of notes taken during data familiarisation are provided in Box 1 below. Some of these early notes subsequently informed final interpretations.

Box 1: Example of phase one familiarisation notes

It is difficult to say if CCPs were used for trial recruitment because stakeholders spent several weeks in T1 and T3 in pre-screening and screening procedures without finding patients who met the trial eligibility criteria. So, in a sense, CCPs were utilised from perspective of using time and resources, as well as conducting tests and examinations, but they were unsuccessful in recruiting patients to the trials due to the stringent protocol criteria.

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I see consistency of issues, thoughts, and opinions across the data. However, only the interviewees who were experienced in clinical practice like the consultants, provided insights on the higher-level issues such as of governance and regulations affecting CCPs. In contrast, nurses and coordinators discussed the challenges involved in the day-to-day activities of the trials elaborately. This has been a benefit in understanding the challenges of using CCPs for recruitment from all the different angles.

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Some study participants insisted that CCPs do not exist once the patients decide to join the trial, that trials are not part of the standard care or that they are unusual to what a patient is routinely receiving and therefore is different from CCP. These statements have caused me to be perplexed for some time. I need to keep reminding myself that CCPs are not only about treatment or cure, but it includes a whole trajectory of care events. It is important for me to constantly refer to the definition of CCP to conduct a comprehensive analysis.

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I additionally performed two rounds of proofreading to ensure that no identifiable information was accidentally present in any of the data sources, such as names of people, institutions, or sponsors. Following this step, I moved to the next phase of data coding. However, the familiarisation process continued throughout the data analysis process, as I noted any new ideas, assumptions or confusions during each phase of the analysis.

Phase 2: Coding

The second phase consisted of generating initial codes, which are labels attached to segments of data that seemed potentially relevant to the research study. Codes were the fundamental building blocks of this analysis, serving as the basis for theme development in later phases of the RTA. Qualitative researchers use manual methods of coding such as coding onto the sides of printed transcripts or by using Computer-assisted qualitative data analysis software (CAQDAS) (Trainor & Bundon 2021, Braun & Clarke 2022). CAQDAS has been developed to aid in the handling, storage, and manipulation of data in studies (Bringer *et al.* 2004, MacMillan & Koenig 2004, Silverman 2010). QSR NVivo version R1 was selected as the CAQDAS for this study because it aided in data management (Bringer *et al.* 2004, Bazeley 2007, Bazeley & Jackson 2013), facilitated a clear data analysis process, and provided a consistent overview of data (Richards & Richards 1994, Morrison & Moir 1998). According to Fielding and Lee (1998), qualitative researchers 'want tools that support analysis while leaving the analyst (researcher) firmly in charge' (p. 167). Therefore, I decided to use QSR NVivo version R1 (henceforth referred to as NVivo) so that I could effectively organise and analyse large amounts of data from interviews, information on recruitment from trial documents, and observation field notes in a single location.

The coding process was led organically by the data (inductive approach) i.e., labelling information based on content of the data rather than pre-existing codes or categories. I found the initial coding process to be time-consuming, requiring an average of 6 hours per transcript and taking approximately four weeks to complete

this coding phase with respect to the entire dataset, but this allowed for a thorough early engagement with and understanding of the data. During this phase, further familiarisation was achieved by recording noteworthy insights or thoughts that emerged as I was actively engaged with the data. Recording notes or comments about a specific phrase or content was achieved by making annotations to the segment of the data being reviewed for coding. The use of NVivo software application helped me to link the annotations to the specific data by automatically highlighting the annotated content in blue as the annotation was being recorded on the software (see Appendix 11 for an example).

During this phase, I completed initial coding of the 25 interview transcripts, 14 files of trial documents and four files of field note observations which together resulted in 371 codes. Each code was assigned a description using the functions of NVivo (see examples in Appendix 12 and Appendix 13) where necessary so that the meaning of the code label was not lost or forgotten as the process advanced. Braun & Clarke (2022) describe that it is common that the coding process could be of different levels, where a researcher could initially code semantically capturing descriptive meanings of the text, while later moving to a higher level of coding, referred to as latent coding, where the implicit meanings of the text are captured. Likewise, during this process, many of my initial codes were subsequently changed as the interpretation of the data deepened.

Thus, the coding process moved from an initial semantic coding (descriptive coding) that captured the surface meaning of the data that closely aligned with the participant's language and meaning to latent codes (researcher-driven conceptual codes) capturing the implicit meanings of data based on my interpretation of the data. For example, the code 'struggling often' was initially used to label participant statements that described the constant struggles of conducting trial recruitment. This label was later modified to 'burden of clinical care' to capture a deeper analytical meaning as my understanding of the data deepened. The modification allowed the new code to evolve from the participant's precise language to capturing the underlying reason behind the struggles of conducting trial recruitment alongside clinical care.

I continued to review the codes as I progressed through the analysis and where necessary further coding was conducted to minimise duplication having codes that had the same meaning. For instance, during coding, I created two codes, namely ‘dedicated time’ and ‘protected time’. Subsequently, the codes pertaining to dedicated time were merged under the category of protected time. I also eliminated irrelevant codes that did not clearly align with the research purpose. For example, codes such as 'altruism' and 'research philosophy' were excluded from the analysis, as they did not contribute to the intended purpose of the study. Hence, a total of 326 codes were finalised from the initial group of 371 codes, which would later be grouped for developing themes in the next phase.

Phase 3: Generating themes.

The third phase began soon after all the data were initially coded. The focus during this phase shifted from analysing individual data items to interpreting aggregated meanings or patterns of similar meanings across the dataset, wherein the patterns of data could be underpinned by a central organising concept or shared meanings known as themes (Braun & Clarke 2017) (see example of patterns of coding in Appendix 14). During this phase the codes were reviewed and analysed to see whether codes could be combined based on shared meanings so that they formed a theme or sub-theme. However, I was also conscious that the themes and sub-themes needed to capture aspects related to the research question (Braun & Clarke 2013). Therefore, the development of themes did not occur as a passive process where the themes were waiting in the data to be found, rather I actively created the themes during the analytical process (Braun & Clarke 2019). During this phase, I realised that theme development was much more than organising codes into topic summaries, for example I had initially organised all the codes involving the challenges of using CCPs as ‘barriers to the utility of CCPs’ without considering any meaningful connections between the codes; this theme was later developed under different themes. Having the research aim of this study and the operational definition of CCP (as noted in Chapter 3) in front of my desk throughout the analysis process acted as a guide as I repeatedly returned to these as touchpoints in determining what was relevant in the development of potential themes or clusters of patterned meanings (Terry *et al.* 2017).

Phase 4: Developing and reviewing themes.

This phase required recursive review and refining of initial themes (Braun & Clarke 2020). Based on the review of initial themes, a brief description of each of the overarching themes was developed. For example, the first theme was named ‘CCPs as a conduit for initiating the recruitment process’ and a corresponding description for this theme was constructed as: ‘This theme discusses different ways of utilising CCPs during the initial phases of the trial recruitment process’. These short descriptions helped me understand the core meaning of each theme, while distinguishing it from other themes. In addition to adding clear descriptions for themes, the recursive review of themes also enabled restructuring of themes and sub-themes in line with the aim of this study. For example, one of the sub-themes initially referred to as 'protocol related barriers' was developed into a broader theme entitled ‘complexities of the recruitment process and the utility of CCPs’. This redeveloped theme encompassed the perspectives of all participants regarding the challenges associated with the utility of CCPs, which arose from the complex nature of trial recruitment processes. As a result, this phase involved developing at the time under-developed themes and collating or discarding any themes or subthemes that lacked sufficient data to support them as an independent or prominent standalone theme (Braun & Clarke 2006). During this phase, I also used visual tools such as drawings, mind maps and paper post-it notes to visualise the relationships between the sub-themes and themes (see Figure 9 below and further examples in Appendix 15 and 16). Developing the thematic structure and nomenclature of themes and sub-themes was thus an ongoing iterative process, and the changes to the names of the themes continued through the final stages of the analysis.

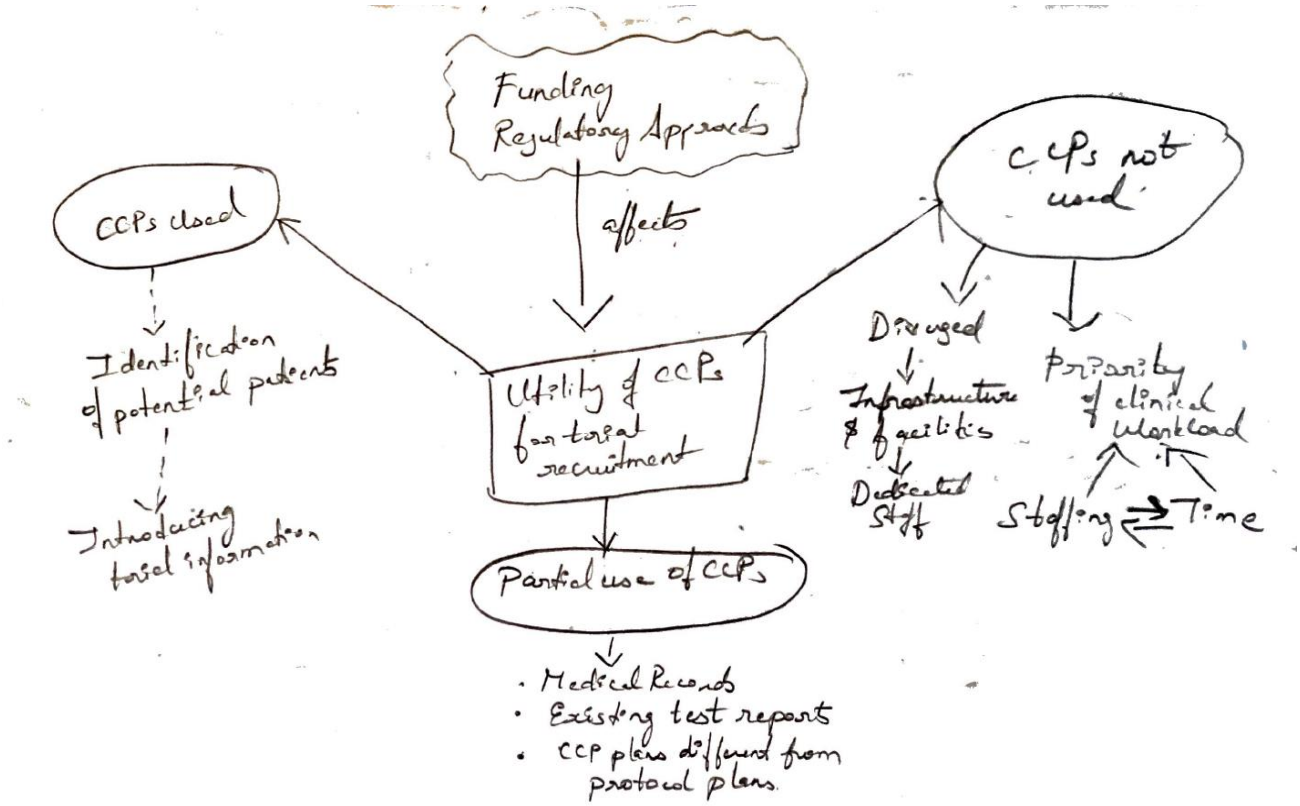

Figure 9: Example of a mind map

Phase 5: Refining, defining, and naming themes.

Phase 5 entailed further defining and refining each theme. Braun & Clarke (2013) advise the use of “catchy” (p.258) and thoughtful names that are reflective of the aim of the study. I found this process heuristically useful, i.e., the themes developed provided the correct interpretation of the data supporting them while also maintaining a relationship with the aim of this research study. Further, refining the theme names was based on the analytical perspective of the data displaying its importance rather than simply describing the data (Braun & Clarke 2013). For example, in the context of discussing recruitment procedures that occurred outside of CCPs, the theme was named ‘parallel pathway approach’. This name was considered appropriate as it effectively encapsulated the essence of the narratives within the theme, meaning it highlighted the conduct of some recruitment processes occurring parallel to CCPs. At this stage I started to note that all themes came together to form a clear narrative that was consistent with the dataset and related to the study's

research aim. Following any necessary modifications to the theme names, I began deciding on data extracts from the many data items under each theme to provide clear exemplars during the writing up of the findings chapter. The data excerpts were chosen to present a vivid and persuasive account of the arguments advanced by the corresponding theme. Extracts from multiple data sources were used to inform a theme, to demonstrate its cohesiveness.

Phase 6: Writing up.

The writing process was interwoven into the entire analytical process, and as with previous phases, a recursive approach to writing was used, therefore this phase cannot be referred to as the final phase because it did not occur solely towards the end of the analysis (Braun & Clarke 2012). As the codes and themes evolved throughout the analysis, so did the write-up and the changes were documented in my reflexive journal (see Appendix 17 for example reflections note during analysis) which was maintained over the entire duration of this research study. The outcome of this phase, in the context of the study, constituted the findings chapter, complete and proofread in creating a coherent, logical and non-repetitive account of the story of the data from within and across the themes (Braun & Clarke 2006). During this phase, I gave myself a timeframe of six weeks to ensure that my findings chapter presented sufficient detail to comprehensively illustrate the complex story of how CCPs were used for trial recruitment in a logical and concise manner. I also established the order in which the themes were reported so that a logical connection between the themes was maintained. The themes were also deemed to be internally consistent based on the evidence from the data associated with them. In other words, the themes could communicate information on their own even if they were separated from other themes (Braun & Clarke 2012).

Two models, namely the ‘gap model’ or the 'argument model' are described for phase 6 of RTA (Braun & Clarke, 2022 p. 120). The 'gap model' is based on the notion that gaps owing to a lack of research in the field can be resolved. According to Braun and Clarke (2022), such analysis is inconsistent with a qualitative approach and represents a positivist-empirical idea of truth seeking. The other model supported by the authors is the ‘argument model,’ which belongs to the philosophy of

constructivism, whereby the researcher embarks on an exploratory journey rather than searching for certain solutions to bridge specific gaps in the literature. The themes are contextualised in the 'argument model' to create a 'rich tapestry of understanding' (Braun & Clarke 2022 p. 120). I found that in using this approach in the current study, it aided the intensive and holistic analysis of the use of CCPs during trial recruitment within a single case study setting.

5.9 Rigour in qualitative case study research

Ensuring the methodological quality of qualitative research holds considerable importance in ascertaining the truthfulness of individual experiences and guaranteeing the reliable accurate portrayal of participants' viewpoints and opinions (Bradshaw *et al.* 2017). It is important to note that the criteria for evaluating the quality of qualitative investigations should be different from those employed in quantitative studies, which prioritise methodological validity and reliability (Creswell 2014). Therefore, the idea of trustworthiness is applied to qualitative research in establishing methodological rigor, ensuring that study credibility, transferability, dependability, and confirmability are upheld and visible (Lincoln & Guba 1985, Houghton *et al.* 2013, Bradshaw *et al.* 2017).

5.9.1 Credibility

Credibility is a fundamental component of establishing trustworthiness in qualitative research. According to Lincoln and Guba (1985), to establish the credibility of research findings, it is imperative to assess and analyse the obtained data from study participants in a manner that yields a credible interpretation. Different techniques were employed to improve the credibility of this research. The utilisation of triangulation is a notable practice in the establishment of credibility (Polit & Beck, 2020) where multiple sources of data are used in case study research (Yin 2018, Thomas 2021). This study's data collection methods were triangulated by drawing on data from individual interviews, observations and by reviewing trial documents. A further form of triangulation involved gathering multiple perspectives on the same phenomenon i.e., exploring the utility of CCPs during recruitment from participants who had different and, at times dual roles (clinical and trial recruitment

responsibilities). Knafl & Breitmayer (1991) argue that the utilisation of multiple sources of evidence to establish consistency can increase trustworthiness in the credibility of study findings. The use of triangulation enhanced the credibility of findings in this study because the findings were informed by the collation of data from three sources. The collation of data obtained from multiple data sources is posited as minimising the potential for errors or biases during the analysis process (Johnson *et al.* 2020).

Peer debriefing is a technique that has been identified in the literature as a means of strengthening the credibility of qualitative research (Johnson *et al.* 2020). Peer debriefing is a process that involves sharing and discussing study findings, interpretations, and methodological approaches with experienced individuals such as research supervisors or experienced colleagues (Lincoln & Guba 1985, Nowell *et al.* 2017). Therefore, I sought verification for the data collection methods and reviewing of analysis process, such as discussing the coding process and reviewing themes developed from my supervisors who have extensive experience in qualitative research. The utilisation of peer debriefing served to facilitate a more profound examination of my analytical thinking, hence enhancing the overall trustworthiness of the study's findings. The credibility and trustworthiness of this study were further increased by maintaining a reflective journal (Appendix 17), which allowed me to reflect on the research study's strengths, weaknesses, and my feelings during the various stages of this research study. It also allowed me to document my assumptions as well as investigate and reflect on any potential biases. Throughout the data collection and analysis stages, constantly reflecting and clarifying, using my journal to document my reflections, aided in establishing an understanding of the current use of CCPs for trial recruitment.

5.9.2 Transferability

When conducting qualitative research, it is important to consider the transferability of findings to other contexts or populations (Leininger 1994, Stenfors *et al.* 2020). The goal is to determine the extent to which the knowledge gained from a study can be applied and transferred to similar settings. While this study did not aim to generalise its findings, it did provide a thick description of the research context, methods, and

participant quotes to aid in the potential transferability of the findings to similar clinical care settings where trial recruitment is conducted (Stake 1995, Graneheim & Lundman 2004, Dawson 2009). By presenting a detailed account of the study's context, setting, and participant characteristics, the reader can make an informed decision about the applicability of the research findings to other similar contexts (Graneheim & Lundman 2004).

5.9.3 Dependability

In qualitative research, dependability refers to the consistency and reliability of the findings. It refers to the degree to which the results may be relied on and replicated (Forero *et al.* 2018). Dependability in qualitative research is attained by rigorous and transparent research practises that ensure the reliability and consistency of data collection, analysis, and interpretation (Johnson *et al*. 2020). Dependability was ensured by maintaining an audit trial of the analysis process by using the qualitative data analysis software, NVivo (version R1). With the help of search functions in the software I was able to thoroughly examine and locate all references included within each code. The NVivo software not only helped with managing and organising the study data but also allowed me to keep an audit trail of the entire research process. This was preferable to paper-based methods since I could immediately retrieve all codes linked to a theme, as well as annotations and memos linked to the data that led to decision-making at different stages of the analysis. I was also able to export the work completed during each phase of the data analysis to share and update my work with my supervisors. To optimise study dependability, I used a reflective journal to document details regarding all research activities conducted, along with personal thoughts on the research experience, facilitated the evaluation of the extent to which the study's findings were firmly founded in the collected data. This practice contributed to enhancing the dependability of the research.

5.9.4 Confirmability

Confirmability refers to the extent to which the findings of this study can be confirmed or verified by others (Houghton *et al.* 2013). Confirmability within the research process was enhanced through choosing the appropriate data collection tools and study methodology and ensuring fidelity to them when implementing the research

process. For example, according to case study researchers, the role of triangulation by using multiple sources of data and establishing a chain of evidence throughout data collection has been highlighted as promoting confirmability (Houghton *et al.* 2013, Yin 2018, Thomas 2021). Confirmability was also maintained by keeping pertinent records that formed an audit trail to reflect various stages of the study and how each decision was made. To support this, the NVivo data analysis software was used to provide a record of decisions made during the analysis phase of the research, and it produced a codebook that demonstrated each stage of the analysis (see Appendix 18) Additionally, meetings with my supervisors were held to check the ongoing interpretation of the data and confirm that the data analysis reflected the participants' accounts. It is worth noting that Shenton (2004) highlights the role of supervisors in confirming the data interpretation and thereby enhancing research trustworthiness.

5.10 Ethical approval and considerations

An application for ethical approval to conduct the study was submitted in October 2019 to the Research Ethics Committee (REC) of the hospital site and subsequently granted approval in March 2020. The onset of the global pandemic however, necessitated alterations to the originally planned study methods, namely the method for data collection, which was originally planned to be in person, but required an option for conducting the interviews online due to requirement for social distancing. An amendment to the REC requesting approval to conduct interviews remotely (via Zoom) and via telephone, as well as face-to-face/in person, where and when possible, was submitted in September 2020, and approved in November 2020 (See Appendix 19 and Appendix 20 for, Ethical and Data Protection Officer approval letters).

Given my past experiences of working in research trials, and from undertaking training on Good Clinical Practice Guidelines 2016, Data Protection guidelines 1988, General Data Protection Guidelines 2018 and the TCD policy on Good Research Practice (2021), I was very aware of the need to uphold ethical principles in research and was sensitive to those that required consideration for this case study. Therefore,

the rights and welfare of participants were prioritised over those of this study at all times. Ethical issues related to the recruitment of participants for interviews, conducting the interviews, and carrying out the observations as part of data collection involved consideration of the following:

5.10.1 Autonomy and Informed Consent

The principle of autonomy seeks to uphold the participants' right to make choices, as outlined by Artal & Rubenfeld (2017). This principle encompasses the right to self-determination and the right to full disclosure which was addressed in this study through the process of obtaining informed consent. Informed consent is an ethical consideration that ensures participants are fully aware of the nature of the research study, including the benefits and risks, and are free to consent or decline research participation (Beauchamp & Childress 2019). As such, obtaining informed consent from all of the participants was central to the conduct of the study. Recognising the importance of participants not being coerced to participate in this study, both the PIL and the consent forms (Appendix 8) clearly articulated that participation was voluntary and that the participants retained the right to withdraw up to the point of data analysis, when the data were combined prohibiting disaggregation. Hence, the invitation to the study was made through the gatekeeper (see section 5.6.1) where both the recruiter participants and patient participants were invited to contact the researcher to indicate their potential interest in participating in interviews. A separate consent from the PIs of the case trials was obtained to procure the PILs and protocols of the selected trials for document analysis. With regard to the observations involving recruitment to trials T1 and T2 a prior written consent was also obtained from the PIs of these trials before entering the clinical setting for observation. A verbal consent was also obtained from personnel (e.g., nurses and patients) who were situated in the clinical setting where the observations were taking place (see further details in section 5.7.2).

5.10.2 Beneficence

Beneficence implies avoiding or minimising undue harm while doing good by maximising the positive outcomes of research for participants involved and society as a whole (Polit & Beck 2014). In this study, there was no direct benefit to those

taking part other than advancing the knowledge of how CCPs were currently being used for recruitment including their barriers and facilitators for the benefit of future trialists conducting recruitment within CCPs. The majority of the study participants were trial recruiters who were actively involved in the conduct of recruitment activities and were genuinely interested in the advancement of trial methodology scholarship and knowledge for the benefit of society. Similarly, the patient volunteers were eager to share their experiences of how they found out about the trial, and their experience of being recruited. Moreover, this research particularly being less sensitive, that is, not involving personal issues or painful life experiences such as bereavement (Dickson-Swift *et al.* 2007), was deemed low risk in terms of the potential to cause harm or emotional distress to participants. As a result, the interviews were generally calm and non-distressing because the conversation was solely focused on the recruiting processes and the utility of CCPs. None of the participants who took part in the interviews requested that their interview should be paused or stopped. This noted, the welfare of all participants was prioritised throughout the duration of this study and a process approach to ensuring ongoing consent (e.g., okay to continue as an interview progresses) was adopted throughout the interviews (Klykken 2022).

5.10.3 Confidentiality and anonymity

The principle of confidentiality includes the researcher's responsibility to uphold the dignity and autonomy of human participants by safeguarding any information obtained from or disclosed by them (Bos 2020). The PIL and consent forms (Appendix 8) explicitly stated that the identity of the participants would remain confidential at all times, where their experiences would be collated and presented with those of other participants. The confidentiality of data, as a priority in this study, was achieved by assigning a code to each participant, thereby making the data pseudo anonymous. To ensure participant confidentiality, pseudonyms were assigned to all people, places or institutions mentioned in the transcripts, and no personal identifiers were included in my field notes of observations or interview transcripts. The collection of the trial documents occurred electronically due to the restrictions on social contact at the time of collecting these; electronic transfer however, involved password protecting all transferred files with the password sent

separately. The trial documents did not contain any personal identifying data, and only contained information about the trial design, including recruitment processes, and other trial conduct details. All interviews were audio-recorded using a digital voice recorder to enable transcription and analysis. A professional transcriber approved by the university who is obliged by the data confidentiality agreements, transcribed 45 % of the interviews and securely transferred the password protected transcripts through the TCD one drive.

To further maintain confidentiality, participants' identities were not linked to personal responses. I also avoided using the names of the trials included in this study so as to prevent the risk of identifying the participants linked to the trials. All interview and observation data, the trial documents and the participant consent forms were stored on my secure TCD's One Drive application space accessible via my TCD secure username and password. After confirming the accuracy of the transcripts, I deleted the audio recordings and destroyed permanently any identifiers that linked an individual's data to the transcripts. Thus, the data was anonymised as it could not be linked back to any of the original sources. Lastly, when reporting the study findings and choosing illustrative quotes to support them (Chapter 6), every effort was made to make sure that selected quotes did not risk identifying individuals or the trials in which they were involved.

5.11 Chapter Summary

This case study, based within the constructivist paradigm, explored the utility of CCPs for recruitment to RCTs by purposively choosing actively recruiting trials within the case setting. This chapter described the case study setting, sampling strategies, and the decision-making process for selecting included case trials. The methods for collecting data through documents, observations, and interviews were also described. Finally, issues concerning the analysis of the study data, efforts to ensure study rigor and ethical considerations pertinent to this study were discussed. Having elucidated the conduct of the study, the following chapter presents the study findings.

Chapter 6: Findings

6.1 Introduction

This chapter presents the findings of the study. The first section describes the characteristics of the seven case trials (Trial 1 to Trial 7) and the characteristics of the study participants involved in these case trials. In the second section, the findings of the case study are presented with reference to four prominent themes and 13 sub-themes.

6.2 Characteristics of the case trials

The seven selected case trials (hereafter referred to as T1 to T7 to maintain trial, researcher and participant confidentiality) were all aligned with a discrete CCP within the hospital. These CCPs were a: Lower gastrointestinal care pathway (T1), Cardiology care pathway (T2), Upper gastrointestinal care pathway (T3), Critical care pathway (T4), Neurology care pathway (T5), Genito-urinary care pathway (T6) and Cancer care pathway (T7) (see Table 13 for characteristics of the case trials).

Table 13: Characteristics of the case trials

Characteristics of the case trials			
Case trials	CCP	Type of trial	Sponsor
Trial 1 (T1)	Lower gastro-intestinal care pathway	Phase IIB International multicentre trial	Pharma company
Trial 2 (T2)	Cardiology care pathway	Phase III International multicentre trial	Pharma company
Trial 3 (T3)	Upper gastro-intestinal care pathway	Phase IV Irish (national) multicentre trial	Academic institution
Trial 4 (T4)	Critical care pathway	Phase II Irish (national) multicentre trial	Academic institution
Trial 5 (T5)	Neurology care pathway	Phase I International multicentre trial	Pharma company
Trial 6 (T6)	Genito-urinary care pathway	Phase IIIB International multicentre trial	Pharma company
Trial 7 (T7)	Cancer care pathway	Phase III International multicentre trial	Pharma company

All seven trials involved an evaluation of novel drugs compared to placebo or to the existing standard treatment; in trials T1, T2, T4, and T7, the focus was on treating or preventing certain illnesses from deteriorating. Trials T3 and T6 focused on intervention efficacy and the quality of life of patients undergoing treatments. Trials T1, T2, T5, T6, and T7 were large pharmaceutical clinical trials that took place at multinational locations (from 20 to 500 clinical settings worldwide). The sample size targets for these trials, across the compliment of trial settings, ranged from 90 participants to 1580 participants. Trials T3 and T4 were multisite academic clinical trials led by consultants within Ireland. Six national clinical settings, in total, were involved in these two trials. The total sample size target for these trials was 176 participants. The planned duration of the seven case trials ranged from 12 to 18 months, with trial participant numbers being pooled from across multiple clinical sites rather than from a single clinical setting.

The recruitment process for each case trial was conducted within the corresponding clinical care specialty, in accordance with distinct trial aims and objectives. The trials ranged in complexity from phase I where little was known about the intervention or treatment to phase IV trials involving trials of existing standard of care therapies. While the trials were diverse in terms of the complexities of scientific investigation and their aligned clinical care specialities were different, the case trials all had one thing in common: they were all RCTs of IMPs or medicines and they were all open to recruitment in the clinical setting at the time of this study.

6.3 Characteristics of the study participants

The gatekeeper of this study reported that 30 email invitations were distributed to members of the seven case trial teams. Of these 23 participants involved in recruitment responded to the invitation indicating their interest and willingness to take part in an interview. As presented in Table 14 (participant characteristics) below, 11 participants (consultants, doctors, and a nurse) had dual roles, which meant they had a full-time clinical role while also undertaking trial recruitment responsibilities. A further, 12 participants were part of the trial team who were

appointed for dedicated trial-specific roles including trial recruitment. Further, recruitment of patient study participants occurred through the discretion of the gatekeeper via the PIs, based on their abilities to partake in interviews. This meant that patients who were very ill were not invited to take part in this study, and only those deemed suitable by a PI were provided with study information via the gatekeeper. As a result, only two patients who were receiving care in a CCP were invited (see Appendix 10 for letter of invite) to share their experiences of being recruited to a trial; both of whom contacted me expressing an interest, following which interviews with them were scheduled.

Table 14: Characteristics of the study participants

Characteristics of the Study Participants		
Principal Investigators (PI)	7	PIs were consultants who held dual clinical and teaching roles. They had between 15 and 20 years of experience in providing care across the seven trial CCPs.
Co-Investigators (Co-PI)	3	The co-investigators included one junior doctor and two senior speciality doctors who worked with their consultants in three different clinical care specialities
Nurses	8	The majority of nurses (n=7) were clinical trial nurses who had dedicated roles for trials research except for one nurse who worked clinically within a CCP as well as having an active role in assisting research nurses to recruit patients into trials
Pharmacists	2	The research pharmacists were involved in some recruitment procedures such as in randomisation, blinding or unblinding as well as dispensing and management of clinical trial drugs.
Trial co-ordinators	2	Trial co-ordinators engaged in the planning, set-up and conduct of recruitment to the case trials.

Research assistant (RA)	1	The research assistant was involved in taking patient samples such as blood or tissue fluid in determining trial eligibility and captured trial data on the trial database.
Patients (PN)	2	Patients were adult men who were recently recruited into two different case trials.

6.4 Case study findings

The following section presents the findings of the case study. As noted in Chapter 5, the interview data predominantly supported the findings of this study, while the data obtained via observations and documents enhanced or reinforced the thematic findings identified further to the analysis of participants' narratives. To provide a comprehensive depiction of accounts that support the thematic findings, direct participant quotations are included in italics when presenting the findings. To preserve the confidentiality of the participants, and their affiliated clinical specialisations, the names of the trials were substituted with anonymous descriptions enclosed in parentheses. The results of the case study are presented with reference to four prominent themes and 13 sub-themes. Figure 10 illustrates these themes with the main themes presented on the left and the sub-themes illustrated on the right of the Figure 10. In analysing and writing up the findings, I also remained cognisant in drawing guidance from the definition of CCP, as determined in the concept analysis (Chapter 3, section 3.6.2).

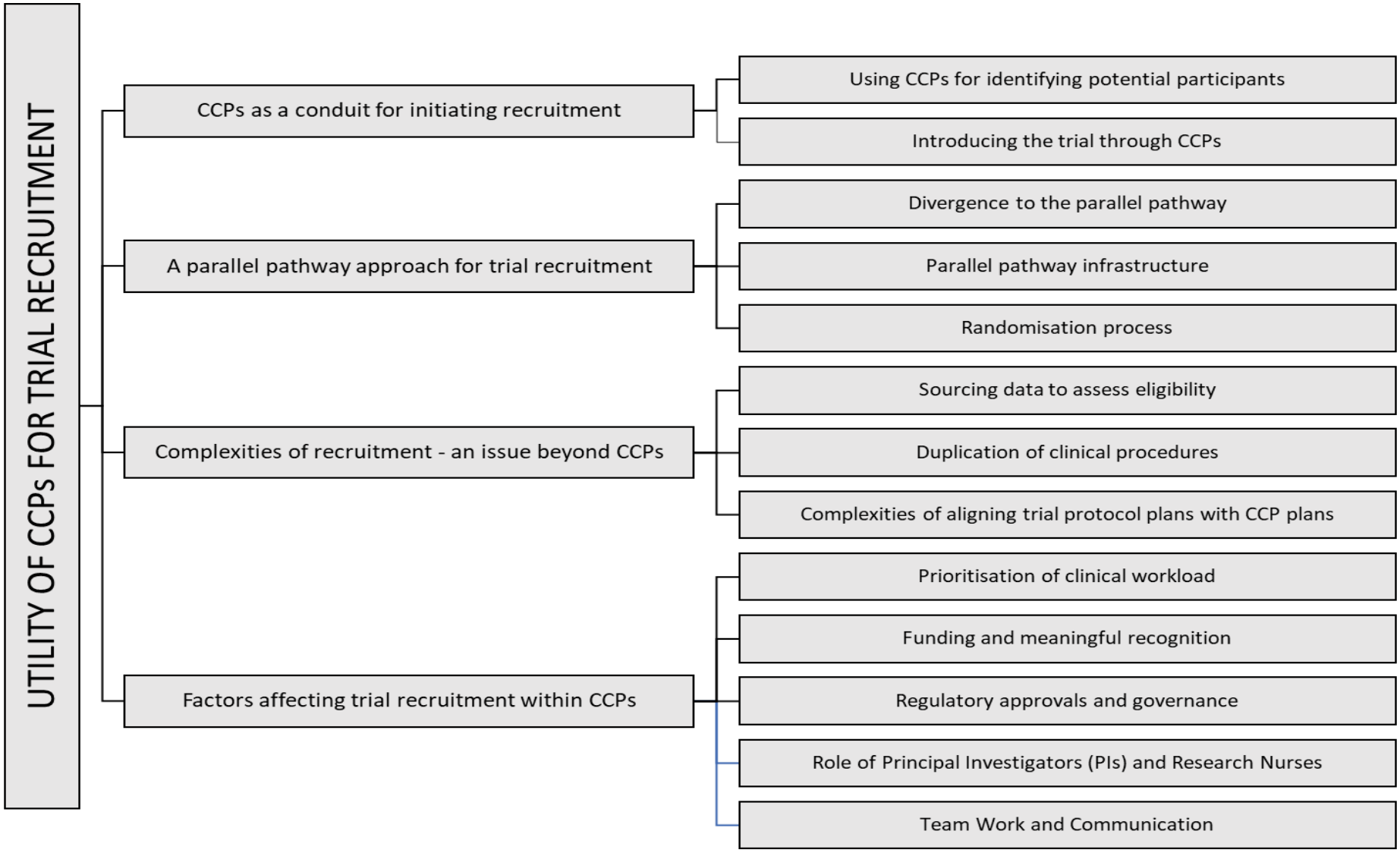

Figure 10: Overview of thematic findings illustrating the utility of CCPs for trial recruitment.

The process of recruiting participants for trials was perceived as a complex endeavour encompassing several processes aimed at selecting eligible individuals for inclusion in a trial. The study data examined across all case trials suggested that the trial recruitment process occurred through six sequential phases beginning from 1) Identification phase, 2) Pre-screening phase 3) Trial introduction phase 4) Informed consent phase, 5) Screening phase and 6) Randomisation phase. Completion of the randomisation phase allowed potential participants to be recruited into the respective trial. This somewhat aligns with the definition of 'trial recruitment' and its inherent phases as identified in the review of related literature in the Background Chapter of this thesis (Chapter 2, section 2.5, notably, 1. Identification, 2. Screening and eligibility 3. Informed consent and enrolment, and 4. Randomisation and allocation), albeit with subtle differences, in particular the temporality on where screening and informed consent are positioned. These differences, which are revisited to inform discussion in Chapter 7 (the Discussion chapter) service to highlight, that while some phases of trial recruitment are understood or viewed in fairly similar ways, differences in terminology and temporality still exist. The following section elaborates if and how CCPs were being used for trial recruitment in the context of the six phases as identified in this study.

6.5 Theme 1 – CCPs as a conduit for initiating recruitment.

This theme addresses the utility of CCPs for patient identification, pre-screening, and delivery of clinical trial information. This theme encompasses two subthemes entitled 'Using CCPs for identifying potential participants', and 'Introducing the trial through CCPs'.

6.5.1 Sub-theme1.1: Using CCPs for identifying potential participants.

CCPs were found to be conducive to enabling healthcare professionals, including doctors and nurses, to identify potential trial participants as part of their clinical care activities as CCPs provided access to a diverse group of patients who received various healthcare services. Many of the study participants who were recruiting to trials stated that they would have an approximate idea of patients who might be

suitable to take part in a planned trial even before recruitment to the planned trial was initiated, that is an awareness of patients who may be potentially suitable as trial participants began during formal trial initiation procedures, for example, as regulatory approvals for trial initiation were being sought by trial sponsors. This also meant that identifying potential trial participants occurred mainly through familiarity with patients as part of routine clinical care encounters. As one interviewee illustrates:

> *"We have a rough idea how many of them* [patients have the disease]*, how many of them are Irish, how many of them are in their* [age group]*, how many of them are women…" (Interview, consultant 4).*

Some study participants elaborated by adding that the identification of potential trial participants was also facilitated by the availability of a large cohort of patients receiving care within their respective CCPs. Therefore, having an established cohort of patients receiving care through CCPs was considered an important factor in supporting the identification of potential trial patients as per the requirements of a trial protocol, and thus in facilitating recruitment.

> *"We recruit because we have large numbers of patients coming through our clinics. So, this links with the care pathway because our care pathway says, that people with, you know,* [name of the] *conditions should have access to a* [name of the clinical specialty] *… " (Interview, Consultant 5)*

> *"…there would be a lot of people who would be suitable for the trial, that may not be that difficult because again we have very large clinic, a number of times a week. So, there's a huge flow of patients through the clinics so your opportunity to find somebody who might fit a particular trial is actually quite good." (Interview, Doctor 2)*

The analysis of the interview data further revealed that identifying potential trial participants in the case trials always occurred within CCPs by the consultants and nurses who had overlapping responsibilities for recruiting trial participants and providing clinical care. This finding was consistent across all case trials in this study and was supported through the narratives of the dedicated research nurse participants who stated that they were not involved in the activities of CCPs. This indicated that the identification process was not viewed as being separate from the

CCP, nor did it require additional research staff to perform tasks related to identifying potential trial participants during the early phase of participant identification for trials.

> *"The consultant and the Sub-PI would identify the patients and we wouldn't, we didn't cold call them, we only approached them at their outpatient appointments for selection* [i.e., only after the PI links in with research nurse]*". (Interview, research nurse 4)*

> *"The PI is the consultant who is caring for these patients, and* [name of the PI] *has direct oversight of the patients, so* [name of the PI] *is the gate keeper to identifying the patients…" (Interview, research nurse 6)*

Some recruiter study participants emphasised, however, that identifying patients through current CCPs involving specialised disease areas required the input from clinical staff (doctors and nurses) who were routinely caring for them. This was because the clinical staff were familiar with the disease area as opposed to research nurses and trial coordinators who were delegated for specific trial tasks within the recruitment phase of the trial and beyond. Therefore, most of the study participants conveyed that it was rather easy for CCP staff (doctors and nurses involved in clinical care) to identify potential trial patients through CCPs because they were involved in caring for the patients and were thus familiar with the patient cohort. As a result, the findings suggest that knowing the patient cohort through direct clinical experience and the familiarity with the disease condition served as supportive conduits for the initial identification of potential trial participants via CCPs.

> *"It's quite a specialised area and also our clinical nurse specialists are also very familiar with our patients, we tend to know, you know, like we don't tend to search a list and try and identify a list of patients who might be eligible. We just tend to be aware of patients who have very active disease who might be eligible because we just kind of, we don't have a formal registry, but we know patients who are very active who might be eligible". (Interview consultant 3)*

> *"They* [CCP team involving doctors and specialist nurses] *get to know the patients very, very well. So, they are, you know, a key part to the care pathway, they know whether you're sick or whether you're not sick". (Interview, doctor,2)*

Some research nurse participants described how having the pre-screening process take place in CCPs was beneficial owing to the competence of CCP clinical care staff in knowing patients who had a required diagnosis that deemed them eligible to participate in a specific trial and in developing lists of pre-screened potential trial participants. Developing pre-screen lists was described as one of the time-consuming activities associated with trial recruitment, conducted by doctors and nurses alongside their routine clinical care responsibilities (Interview, research nurse 2).

The findings suggested that delays in screening patient records to determine potential participant eligibility may have impacted trial recruitment targets; however, there was insufficient data to fully support this view. Despite the pre-screening activity being described as a time-consuming process, it is important to note, however, that study participants suggested that it would be beneficial for pre-screening to take place within CCPs by clinical care staff working within the CCPs as these staff possessed the clinical expertise of understanding the health care parameters required to fulfil pre-specified trial eligibility criteria.

> *"… but I think the fact that they* [referring to doctors and nurses in CCP] *know the patient. Because they know the disease area more than the research nurses can be knowing, but I think for them, they know more of the disease. So, the fact that they pre-screen those patients is good, you know". (Interview, research nurse 1)*

> *"The doctor and the clinical nurse specialist working together in the* [name of the clinical specialty] *looked through a patient's medical chart who was scheduled for clinical appointment with the doctor later in the afternoon. They meticulously looked through the medical chart and discussed if the patient's health-related parameters matched with trial protocol's inclusion and exclusion criteria. Following the pre-screening activity, a note was made on the patient's medical chart as a reminder to introduce the trial at the time of the clinical consultation.". (Field note, Observation 3)*

Familiarity with the patient cohort and clinical expertise of staff working in CCPs were thus noticed as common factors enabling CCPs to act as conduits for the phases of patient identification and pre-screening as part of trial recruitment. Further, the recruitment process then transitioned to the next phase, whereby patients who were

pre-screened as potentially eligible were introduced to the trial during clinical care encounters within CCPs.

6.5.2 Sub-theme1.2: Introducing the trial through CCPs.

The analysis of interview data supported by data from field observations (field observation 2 and 3) showed that the information about trials was largely introduced to patients within their CCPs during their regular consultations based upon the possibilities of a patient being eligible as identified in a pre-screening phase. In this sense, the point of delivery of care through CCPs was also the point of delivery of trial information' that is, patients were provided with trial information because they were deemed potentially eligible to take part in the trial. Hence, CCPs served as a conduit through which the information about a trial was communicated to patients receiving clinical care services.

> *"I see the patients in the outpatient clinic and discuss everything* [regarding the trial] *… and they go off with the information* [to have a think]*". (Interview, consultant 7)*

> *"…the principal investigator is the one who will obviously discuss the trial with them* [referring to patients]*, they would be given information about it* [the trial] *and the information about* [the existing] *standard of care". (Interview, research nurse 8)*

This finding was also supported by the patient participants who expressed that they were introduced to the trials they subsequently took part in when receiving care within the respective CCPs.

> *"Yeah, I would normally attend the* [name of specialty] *clinic with the* [name of the consultant] *… And it was yeah, and it was* [name of the consultant] *who actually asked me about doing the trial that's how I heard about it". (Interview, Patient,1)*

> *"I was having a conversation with* [name of the clinical nurse specialist] *and she mentioned to me that they were doing this trial". (Interview, Patient 2)*

However, in one of case trials, the delivery of trial information occurred slightly differently due to the critical nature of the clinical condition of interest in this trial. Hence the information about this trial and discussions around participation were communicated to the patient's next of kin by the consultant caring for the patient in the CCP.

> *"And then because with COVID there's no visitors. So, then the* [name of the consultant] *would ring the next of kin, explain the trial and ask if they're happy for their family member to be involved." (Interview, research nurse 4)*

Therefore, the majority of potential trial participants or, when necessary, the named next of kin of potential trial participants became aware of the existence of the trial based on the notification received during their clinical care encounters occurring as part of CCPs. In all of the case trials, trial information was provided by doctors and nurses who had overlapping clinical care and trial recruitment or trial conduct responsibilities. This means that the primary mechanism for introducing trial information to potential trial participants was through conversations with doctors and nurses working in CCPs. Hence, the analysis revealed that CCPs were being used to facilitate recruitment by identifying potential trial participants and pre-screening them against trial protocol criteria; constituting one component of recruitment, that is identification. As a result, clinical care provision within a CCP overlapped with that of initial recruitment processes, albeit integral for trial recruitment whereby CCPs serve as a conduit for identification, pre-screening, and in introducing the trial information to potential trial participants.

6.6 Theme 2 - A parallel pathway approach for trial recruitment.

Although the clinical trial processes required as part of trial recruitment differed from the usual standard care activities carried out in CCPs, some of the recruitment procedures took place within CCPs, as illustrated in Theme 1. Many other trial recruitment activities, diverged from CCPs; that is, they occurred outside of standard CCPs in parallel rather than within them. The divergence of trial recruitment occurred particularly when a need arose for trial recruiters to facilitate or engage in detailed discussions with potential trial participants about a trial so as to assist them in making an informed decision and give consent, or not, to participate in a trial. The

divergence of trial recruitment activities from CCPs is reflected in this theme of ‘A parallel pathway approach for trial recruitment’. Three sub-themes were identified in this theme: ‘Divergence to the parallel pathway’, ‘Parallel pathway infrastructure’, and 'Randomisation process’.

6.6.1 Subtheme 2.1: Divergence to the parallel pathway

Participants described how the responsibility for some recruitment procedures diverged soon after the patients were notified of the availability of the trial. Once patients expressed an interest in taking part in the respective trial, they were transferred to professional trial staff, usually dedicated research nurses, to have detailed discussions about the trial. These professional trial staff, although clinically qualified, were working in a dedicated research facility away from the CCPs within the hospital setting. This meant that some activities related to trial recruitment had their own pathway which occurred parallel to the delivery of care within the CCPs.

> *“So, I introduce the trial to the patient* [during consultation] *and then what we do is we take their information and details, and we give that to our clinical trial team of which I’m also the PI, and the clinical trial team, the clinical trial co-ordinators, then they make contact with the patient and offer the patient detailed information on the trial.” (Interview, consultant 5)*

> *“…and then usually there would be a follow up call from the research nurse then asking the patient do they want to come in and formally meet about the clinical trial, which they often would do with one of our research nurses and sometimes with one of the clinicians in the research facility”. (Interview, consultant 3)*

The majority of the study participants expressed in their narratives that patients were not in the CCP during the informed consent process. They were instead moved out of their routine care environment to a parallel trial pathway wherein a divergence occurred. If they were proceeding with the trial, they would only follow a parallel pathway from this point of recruitment phase until the completion of trial recruitment procedures.

> *"...at that point* [referring to informed consent process] *they're not in their care pathway, their care pathway is in* [name of care specialty], *this is the real separation of the care pathway from the clinical trial pathway". (Interview, doctor 1).*

> *"And you know I don't really envisage any return to the care pathway* [following the identification and delivery of trial information]*. I think that's a bifurcation, we're very lucky the clinical trials nurses take that off and do it..." (Interview, consultant 7)*

During interviews, participants provided some explanations as to why the informed consent process took place outside of CCPs. Many study participants expressed that the existing clinical care facilities were entirely occupied by clinical care services, which posed difficulties in securing clinic rooms for trial discussions within the busy clinical setting. This implies that the present infrastructure and facilities, although conducive to clinical care services, can present difficulties in accommodating informed consent discussions due to the existing demands of delivering clinical care. Hence, there occurred an issue of obtaining dedicated space for the conduct of informed consent discussions, as part of trial recruitment, within the existing CCPs.

> *"We have like the physical infrastructure here, you know, there are good facilities in so far … but again, the reality of managing those* [patient] *numbers, like every clinic room, every clinic space depending on the clinic, are always used by people seeing patients… We obviously have our own rooms where we see people. So, there wouldn't, you know, you couldn't necessarily consistently at least, you couldn't dedicate a room for trial discussion or research discussion. I mean you could probably find a corner but quite often I'd say it would be taken over by other uses". (Interview, doctor 2)*

> *"But opportunistically seeing them, checking all criteria, discussing, giving a PIL or a consent form, something like that, all within the space you have with the numbers we see in clinic is challenging certainly, yeah." (Interview, consultant 3)*

Further, due to the complex nature of the case trials, doctors and dedicated research nurses had to engage in detailed discussions with patients prior to formal screening to determine their eligibility and to discuss with patients their willingness and their ability to take part in a trial. The consultant study participants emphasized the

importance of having a thorough discussion, particularly with patients with frail conditions, and those responsible for caring for ill family members, to assess their ability to participate in the trial (Interview, consultants 2 and 5).

Some of the investigator study participants noted that the in-depth discussions required for informed consent could not have been possible in the midst of a busy clinical setting due to the need for focused attention and time to assist the patient in making a fully informed decision about participating in the trial. Therefore, the informed consent discussions took place in the dedicated research facility where dedicated trial recruiters (doctors and research nurses) could devote focussed time and attention to patients requiring assistance in comprehending the trial information and making a fully informed decision on whether to consent to take part in a trial, or not. Further, the informed consent process, in some trials, involved more than discussing the nature of the trial. It also entailed discussing the requirement for patients to successfully pass certain trial screening processes in order to participate, regardless of their willingness and written consent to be involved in the trial (Field note, observation 2).

> *"Now that can happen in the middle of a clinical arena, so for instance if you do* [name of the trial] *it occurs in the* [specialty] *care unit, but the nature of informed consent and the time that you give suggests that they should be taken a bit out of their pathway brought to a special area and dealt with there. It's not ideal that you can consent someone in the middle of a six-bed ward in the middle of a busy clinical arena it's not always a good idea." (Interview, consultant 2)*

> *"But the doctor just assured him* [the patient] *and told him it was because you have* [name of condition]*, like people his age shouldn't feel like they won't contribute anything to the research. So, after he was, he took longer actually that was the longest consultation because you know for the older population they take time, you have to really explain to them, and they appreciate the doctor sitting down and talking to them for as long as they need... and explain to them everything and yeah, once they are happy, they are happy to be inputted* [consent to take part in the trial]*". (Interview, research nurse 2)*

Following the informed consent process, potential trial participants, in some of the case trials, underwent a screening phase to determine the eligibility to take part in

the trials. The screening process, for associated trials, like the informed consent process was also carried out separately to the CCPs, in contrast to the pre-screening phase, which for all included case trials, occurred within the respective CCPs. This was because the formal screening process to determine eligibility for some trials involved a series of clinical assessments such as blood tests, ultrasound examinations, invasive procedures, research specific questionnaires, or pregnancy testing, for example. Additional facilities and dedicated trials' team members were needed to attend to some procedures that were a requirement of that trial's recruitment, for example diagnostic tests, or lengthy eligibility screening procedures. As a result, many of the study participants described how moving potential trial participants to a dedicated research setting, albeit still within the grounds of the acute care setting, supported the requirements for some recruitment procedures thereby rendering recruitment to trials easier to complete.

> *"Because naturally any of those clinic visits* [involving screening procedures*] are multiple times longer than they would on a routine visit. You would need dedicated space. … the checks that we'd need to do for a trial are obviously far more in-depth than a routine clinic. So, you almost need extra space to do that and a dedicated side team to do that. There's definitely no way the normal clinic team would be able to dedicate that much time, certainly not". (Interview, consultant 6)*

Moreover, the screening phase was noted as a laborious process in almost all case trials, which took an average of five to six weeks to complete, with the exception of one trial where the screening procedures took less than a day due to the nature of the trial and the clinical condition involved (Document analysis, trial protocols). Most of the study participants described that the realities of completing the screening visits, alongside the clinical care processes of the CCPs, were challenging, therefore the screening activities involved in recruitment to some trials were conducted parallel to CCPs and within a dedicated research facility with the assistance of a dedicated team of research staff.

> *"The screening period will last for approximately 6 weeks. You will be asked to attend a screening visit, and you may need to come to the study centre more than once for this visit. The purpose of the screening visit is to check whether the study is right for you. During the screening period, various assessments will be performed." (Excerpt from Patient Information Leaflet 5)*

> *"So, none of it actually is happening, so like the pre-screening, insofar as seeing if somebody is eligible, would happen in the routine clinical care. But as soon as the individual said "yes, I'm interested and I want to take part, book me in for a screening visit", let's say that was all done in the research facility. So, none of that, and then all their care going forward would be separate in the research facility, they won't be attending* [their routine CCP] *per se during the study period." (Interview, doctor 2)*

Thus, many of the potential trial participants were transitioned to a research facility for undergoing screening for trial eligibility from where they had been receiving standard care. Some research nurse participants pointed out that the screening procedures involved in the trial were completely different from what was routinely performed as part of standard clinical care and that this was the main reason the patients came to the research facility.

> *"No, no* [not dependent on CCPs for screening assessments]*. No, we wouldn't because the fact that they have like the bloods you have to take and they go to a central lab, … and then the questionnaire is based on the trial, they don't do these questionnaires in the hospital, these are just based on disease area. And then they are like, the* [name of the test 1] *also goes to a central lab like when you* [the research nurses] *take the* [name of the test 1] *and the* [name of the test 2] *you have to send them to a central lab* [i.e., not the existing CCP for evaluation]*." (Interview, research nurse 2)*

On the contrary, some other research nurse participants described that the screening procedures completed as part of the trial were similar to procedures completed as part of standard care, such as assessing patients' general wellbeing, including vital sign monitoring, or having blood tests performed, yet the screening process for taking part in a trial, was still considered to be a separate activity from care activities that took place in CCPs, and, as such, took place in parallel to clinical care in a dedicated research facility.

> *"So, it will still be the same process as the normal one* [referring to investigations to determine eligibility such as blood tests and biopsies] *but if you are part of the clinical trials then your care pathway will be the clinical trials pathway." (Interview, nurse 1)*

Contrary to screening procedures in six of the case trials, in one of the case trials, due to the criticality of the potential trial participants health condition, trial screening rather than being carried out in the research facility; research nurses went to the care setting to complete the eligibility checks so as to complete the screening procedures. This screening, however, was still completed in parallel to the existing care that was provided by the clinical care team. Hence, regardless of where the screening process was conducted it was always trained research staff who performed trial screening tasks and processes.

> *"… the bedside nurse would take those bloods [routine standard of care bloods] and send them off to the hospital lab and then you would have the research specific bloods as well taken by the research nurses… And I suppose the blood bottles, so it's very specific in research, they're different sizes. They're not the usual standard of care blood bottles that phlebotomists would use so they wouldn't be familiar with maybe the time points that are needed. They're shipped to an external lab. They're processed here but they're tested in an external lab". (Interview, research nurse 5)*

Additionally, some study participants emphasised the importance of conducting screening procedures in a parallel pathway. They argued that if patients were required to follow the CCP route, there would be significant delays in completing required assessments to determine trial eligibility, thereby hindering timely recruitment (potentially) and the overall recruitment process.

> *"So, to benefit increasing recruitment or availability of trials as being an available resource for recruiting into trials we have to step outside of it* [the CCP]*. So, you couldn't have a backlog of patients waiting to go see their research nurse for example. So, I think you would have to dedicate specific staff to it as opposed to adding it on to what other people are doing, purely from a patient flow point of view." (Interview, doctor 2)*

> *"It is because these tests* [referring to screening] *are pre-booked, as in weeks and weeks ago, because they need to be done urgently compared to the usual ones…" (Interview, nurse 3)*

Overall, the analysis of data revealed that the screening procedures frequently occurred outside of CCPs due to several factors. Firstly, the screening procedures were conducted with the assistance of research staff from the research facility rather than clinical care staff involved in routine CCPs. Additionally, in the majority of case trials, the procedures involved in screening were specific to the trial, that is, they were not required as part of standard care and hence required trained research staff to perform the tasks related to certain screening processes. Secondly, conducting trial screening in a parallel pathway increased the likelihood of adhering to the required protocol timelines for completing the screening procedures. Hence, the scope of CCP interactions were limited in relation to the screening of potential trial participants during trial recruitment.

As evidenced above the screening operations per se, such as conducting tests, performing scans, and collecting blood and body fluids in accordance with protocol criteria, were mostly carried out in a parallel pathway. However, the reports of these tests were uploaded to a sponsor-specific database, and tissue samples were delivered to designated central laboratories for examination (Document analysis of protocols, observation 5 of screening visit). The trial sponsor team, who were a pharmaceutical company, or an academic institution located outside of the CCPs, frequently decided whether a potential trial participant was then eligible for trial participation. This means that PI's (consultants and doctors) who previously made decisions about the course of clinical care based on CCP evaluations were dependent on the sponsors who confirmed the eligibility of potential trial participants.

In this regard, both consultants and nurse study participants, like patients, expressed, that on occasions, they could only wait in expectation of a result that confirmed, or not, whether a patient would be able to participate in the respective trial. This was further demonstrated in a comment made by one of the nurse study participants, who stated that the grading of the disease as determined by the CCP was expected to match the protocol criteria, but sponsors on reviewing the reports may return a lower grade for the disease, rendering the patient ineligible for the trial (Interview, nurse 4). As a result, there was no intersection with the current CCPs or the parallel pathway towards the end of the screening phase, as patient eligibility, in some cases, was determined independently of the care pathways.

And then that [screening evaluations] *gets sent to the sponsor for them to verify whether the patient meets the inclusion exclusion criteria. The next step is that we get the results back and they* [sponsor] *clear us that the patient meets the criteria based off the* [name of the procedure] *report. (Interview, research nurse 3)*

So, [name of the consultant PI] *will be informed [by the pharma company] if the patients are eligible and the CNS's will be told as well… (Interview, research nurse 1)*

6.6.2 Subtheme 2.2: Parallel pathway infrastructure

The majority of study participants described how the availability of a dedicated research facility compensated for the lack of infrastructure and resources needed to conduct some recruitment procedures within CCPs. Many study participants were of the view that the utility of a parallel infrastructure was not only for the trials represented in this study but that this occurred for all trials in the study setting. As a result, the participants described how having a separate parallel pathway infrastructure provided far more benefits for some trial recruitment processes (described below) than trying to recruit to a trial in a CCP alone.

Both recruiter and patient study participants expressed that certain recruitment procedures, such as informed consent discussions and screening procedures, were improved when conducted in the research facility because they removed the processes from the busy CCP environment to an environment where greater infrastructural support and dedicated time for recruitment were available. In this sense, the availability of the research facility for recruitment was considered advantageous for enhancing recruitment to trials, when compared to that of a CCP environment alone. Many of the investigator study participants observed that relocating the recruitment procedures from a current CCP setting to a specialised research facility was the sole viable approach for enhancing recruitment efficacy.

"I think there is a big advantage in having [the name of the clinicians] *see patients who are involved in clinical trials in the clinical research facility where there's more time and a more structured environment to recruit and to follow up patients" (Interview, consultant 3)*

"We're moving from our day care unit, which is a crowded, busy service delivery area to the research facility which is not, you know… if we're actually going to increase our recruitment the only way to do it is to be efficient with our team and to have separate clinics." (Interview, consultant 7)

The patient participants in the study, as well as some of the recruiter participants, recounted how they found the research facility setting peaceful and streamlined compared to attending care in a CCP. This benefitted patients in that, by attending the research facility, they described having timely appointments and screening assessments.

"I think the difference is that in the other place [routine CCP] *it was busy and packed and queues and everyone was sitting and then it just like everyone would be sitting and waiting." (Interview, patient 1)*

"When we moved to the research facility the patients were really happy, you see their waiting period, I'd say reduced by at least by 2 to 3 hours, they didn't have to wait anymore you know... We gave them the time slot, and they came in and saw the PI [Principal Investigator] *and they were out". (Interview, nurse 7)*

Furthermore, one of the patient study participants expressed that the research facility environment was perceived as less stressful due to expedited access to medical care compared to the care within the routine CCP he was attending. Additionally, being in a specialised care speciality CCP as patients, meant being unable to conceal their illness from acquaintances who may also be present in the same setting. As a result, some patients appreciated the additional level of privacy afforded by attending the dedicated research facility, albeit this relocation was associated with potentially taking part or taking part in a trial, compared to attending care in a CCP.

> *"And it just being in that environment* [the patient's routine CCP] *with people who are scared and nervous and worried about their result and then the embarrassment of seeing people you know and with it being* [a specialty healthcare clinic]*. Thinking Oh God! there is someone I know or this.. it's that type of a feeling that I get personally anyway; with here* [the research facility]*, I really like it because it's not* [a specialty health clinic]*. I could be here for anything, so it was just a lot more, I was a lot more at ease like I was just walking into a general hospital rather than it being just like that". (Interview, patient 1)*

The analysis of the interviews and the trial protocols further revealed that patients, as potential trial participants, required focused care and medical attention as per the requirements of the trial protocols. This care may have involved a requirement to have detailed tests and examinations as part of screening procedures to ascertaining eligibility for the trial. Hence the trial team worked in parallel to CCP teams in ensuring timely completion of necessary recruitment-related assessments while simultaneously providing the required care to these patients. As a result, potential trial participants received closer medical care and supervision than they may otherwise have received had they continued being cared for in the respective CCPs. Additionally, when patients were transferred to a parallel trial pathway, their medical care was mainly provided by their trial team. This had the added benefit of decreasing the workload for the clinical team working exclusively in the CCP, as the number of patients needing care in the CCP was reduced.

> *"One of the big things that they get is the understanding they are going to get very focused clinical care and have a phone number they can ring up and a contact point that is immediately accessible" (Interview, consultant 2)*

> *"It benefits the patient from the fact that they might be able to get in contact with me* [research nurse] *faster than they would be trying to get in contact with the CNSs* [their routine care nurse]*…And it makes their life* [nurses in routine CCP] *slightly easier because they have less patients to look after then because that patients' care transitions over to the research nurse that's looking after them." (Interview, research nurse 3)*

Despite the existence of a parallel pathway for the purpose of recruiting patients for clinical trials, the provision of standard treatment to patients within their aligned CCPs remained uninterrupted in the event of emergencies. In certain instances,

patients may have been transferred to the parallel trial pathway for recruitment processes, but subsequently were not interested or declined to take part in the trial, and as such, would return to receiving their care within the respective CCP. Therefore, many of the investigator study participants also emphasised the significance of accessibility to the CCP care team as part of the patient care journey, regardless of a potential participant's decision to participate, or not, in a clinical trial. This means that while patients as potential trial participants moved to a parallel pathway for the purposes of trial recruitment, they were also part of CCPs for receiving standard care, indicating that trial recruitment pathways (CCPs or the parallel pathway) maintained connections as required during the recruitment process.

> *"For instance, you know* [name of the case trial] *patient got admitted on the weekend with* [an emergency condition] *but he gets immediate attention both from the clinical team and the study team. You can't conduct clinical research without a rapidly accessible clinical team". (Interview, consultant 2).*

> *"And then at that stage some patients will proceed and if so, they proceed then, and we can see them through the clinical research facility for their screening and baseline visit etc. And if they do not wish to proceed, you know, at that stage then they would return back into our normal clinic." (Interview, consultant 3)*

6.6.3 Subtheme 2.3: Randomisation process

After confirming the eligibility of the patients to participate in a trial, the recruitment process required a randomisation procedure to allocate trial treatments and enable patients to receive interventions and clinical care accordingly. Following randomisation, patients became trial participants and began receiving care from their assigned trial team. Most of the participants in this study described the randomisation process as the most straightforward and least time-consuming aspect of the entire recruitment process, and many expressed satisfactions with the way it was currently implemented. For example, one of the study participants stated:

"I mean it's very quick, it's very straightforward, it's that online portal. We haven't had any issues with not being able to randomise people as it happens" (Interview, doctor 2).

However, in the context of analysing the utility of CCPs in the randomisation process, it was found that randomisation, as a trial recruitment process, diverged from the CCPs in all seven case trials. The reason for this was that randomisation was consistently conducted by qualified and trained research staff located at the research facility as an independent process within the parallel pathway. The delegated research staff used specific electronic databases as assigned by the trial sponsor (trial protocol and observation data) to capture all of the screening results in order to facilitate the automation of the randomisation procedure through an electronic database.

"In this trial, patients will be centrally randomised and assigned in a 1:1:1 ratio to one of the three treatment arms of the double-blind treatment phase… Patients who are considered qualified for entry into the treatment phase of the trial, i.e. patients who meet all enrolment criteria at screening, will be randomised via the eCRF [electronic Case Report Form]*". (Protocol, Trial 1)*

"We don't randomise, I mean that's all done electronically. If it's a double-blind placebo control trial that's done, you know, the clinical trial co-ordinator and the clinical trial nurses complete that, and the clinical trial physicians will oversee that." (Interview, consultant 5)

There was, however, one case trial in which randomisation occurred remotely in the sponsor institution located outside of the clinical care setting. This indicates that neither the existing CCPs nor the designated staff from the research facility working parallel to CCPs were involved in the randomisation procedure.

"We email over information to [name of the sponsor] and then they complete the randomisation themselves. So, we just email them over the study number because we assign a study number, they just want to know the gender of the patient, their ethnicity and we send that and their date of birth. So, we send that over and then they randomise and then we get an email back to say what, the patient been randomised for…." (Interview, research nurse 3)

As a result, in the context of CCP utility for recruitment, the randomisation process was the least complicated and quickest when compared to other recruitment processes, and one which did not involve site staff (recruiters or clinical care staff). The majority of the case trials used a computer-generated automation method for randomisation and the allocation of trial treatments, which was usually executed by trained research staff or trial sponsors outside of CCP settings. As a result, randomisation was viewed as a separate procedure that occurred in parallel to CCPs rather than as part of CCPs. Moreover, patients were not required to visit the clinical care setting for the randomisation process, and those who continued to choose to participate in the trial were considered recruited and began receiving trial interventions following the randomisation process.

6.7 Theme 3- Complexities of recruitment - an issue beyond CCPs

The thematic analysis demonstrated that the utility of CCPs were conducive to initiating the trial (theme 1), and in places where the utility of CCPs were constrained, the trial recruitment processes moved to a parallel pathway as discussed in theme 2. Despite the availability of a parallel infrastructure, and dedicated research staff, most study participants experienced a number of challenges in recruiting identified potential trial participants. The issues encountered were not a result of the inherent limitations of CCPs or the parallel pathway but rather, were owing to the complexities of recruitment processes that were beyond the scope of CCPs. The theme, Complexities of recruitment - an issue beyond CCPs is further reflected in three subthemes, namely: 'Sourcing data to assess eligibility', 'Duplication of clinical procedures', and 'Complexities of aligning trial protocol plans and CCP plans'.

6.7.1 Subtheme 3.1: Sourcing data to assess eligibility.

Many of the study participants voiced how assessing potential patient eligibility for trials using the medical data recorded within the CCPs was extremely challenging. This was because the trial protocol-required information, particularly concerning patient demographics and information on past medical history, tended to be more

detailed than that which was generally recorded in medical records in CCPs. As a result, while the existing medical records system offered a gateway to recruitment, it was limited to partial utility in fulfilling the requirements for determining potential patient eligibility.

> *"The screening visit yes, you're writing down a more detailed* [information] *as the sponsors ask for more, we are writing down Male, Caucasian… but if it's through routine care they don't write down as much because it's not necessary…You know, but in the trial what they expect you to know is the day, the month and the year and frequency of medications that does not cross over into routine care. So, the expectations of the sponsor for information on the patient, it's not a reality because sometimes it just doesn't exist." (Interview, research nurse 3)*

The study participants encountered significant obstacles in obtaining the necessary data required for recruitment purposes due to the absence of detailed information and medical history sufficient to meet trial requirements within the CCPs medical records. This prompted them to explore alternative methods of establishing eligibility based on the protocol criteria of the trial. As an example, one of the study participants stated:

"so the only way we could do it was to pull *[meaning retrieve]* everybody on *[name of the medication]* through the pharmacy scripts and then we evaluated to see whether they were suitable for recruitment." (Interview, consultant 6)

Thus, the study participants from some of the case trials described having to go beyond the CCPs to capture required information for patients interested in joining trials, for example, having to seek previous medical information from the patients' General Practitioners (GPs) or from external hospitals and clinics that patients previously attended, in order to procure the detailed medical history of patients to determine their eligibility to potentially take part in a trial. The data showed that assessing eligibility, although initiated through CCPs was subsequently, where necessary, taken over by dedicated research staff who often had to go beyond the CCPs to source data for assessing trial eligibility following patient consent (document analysis, PILs and interviews). This resulted in unanticipated delays in identifying potentially suitable participants for further trial screening and trial enrolment.

"So getting like past medical history and all past hospitalisations, all this was a big challenge! So, what I had to do is on behalf of, like [name of the consultant]*, the PI allowed me to contact the GPs as well as the clinics where they used to attend just to ask about more, about the medical history and all that so, that was a huge challenge. Because that's part of the inclusion/ exclusion criteria because you can't really recruit these patients if you don't have all of the past history." (Interview, research nurse 2)*

"We have no access to that information [medical history] *… So, for example we had a patient; we were very keen on putting her on the trial as soon as possible because she was unwell and she [was] still an in-patient. But then, she was* [originally] *a patient in an external hospital, so we don't have access to all the information. And then we're like, oh! can she go on the trial, or can she not go on the trial? So that doesn't always work great." (Interview, research nurse 7)*

6.7.2 Subtheme3.2: Duplication of clinical procedures

Most study participants described the need for conducting clinical procedures or diagnostic evaluations during the screening phase of trial recruitment. In some trials, at least some of the tests and evaluations required as part of determining eligibility were duplicated in the parallel pathway even though these tests were completed as part of CCP care. This meant that these evaluation reports in determining a diagnosis or in grading a disease could have been used for the purposes of determining eligibility for trial participation. However, some of the study participants reported that many patients as potential trial participants who underwent the process of recruitment, had to have at least some diagnostic procedures repeated only because the procedures and results of these did not align with timelines required by the trial protocol for the respective diagnostic evaluations. This meant that the utility of CCPs was limited on some occasions due to the strict protocol criteria rather than because CCPs could not have facilitated the screening procedures as part of determining the eligibility of potential trial patients.

"The only thing is for the trial you might be asking them [patients] *to have another* [name of the diagnostic procedure] *done when they kind of are already having one from a month ago, not that they really need it, but we need one within a certain period of time. So, you could be asking somebody to get one done because you need it as part of the trial, that*

will never change unless the sponsors decide otherwise." (Interview, nurse 3)

"I suppose we would always try, so if a patient is out by one or two days, we'll always negotiate with the sponsor to say well 'do we really need to repeat this?' Its twenty-nine days as opposed to twenty-eight, but they are very strict on their protocols". (Interview, nurse 7)

Therefore, the findings with respect to duplication of clinical procedures across the case trials show that the assessments performed as part of routine CCPs did not always align with the same assessments as part of trial recruitment processes because some trials were constrained by strict time windows as detailed in their protocols leading to duplication of clinical procedures in most of the trials. This Duplication of clinical procedures to confirm eligibility of potential patients were noted as another reason of delays occurring within the trial recruitment process.

"Ultrasound is mandatory and should comprise examination of …Time window: initial examination 2 weeks before until 1 week after screening visit." (Document analysis, Protocol 3)

6.7.3 Subtheme 3.3: Complexities of aligning trial protocol plans with CCPs plans

The goal of a CCP was essentially focused on delivering optimal care to every individual, including providing treatments for their respective diseases. However, the study data indicated that many patients who were potentially eligible were unable to participate as they were already receiving standard care treatments prescribed as part of CCPs care plans. The study participants in recruiting capacity consistently found it challenging to find potential trial participants who were part of CCPs but not receiving standard treatments restricted by the trial protocol. This highlights one of the complexities of the determining eligibility as outlined by the trial protocols.

"The big discriminator in the exclusion criteria were the limitations in the previously allowed [standard of care treatments], that [the patients] could only have been allowed only one [type of medication] for treatment. So that cut through a huge number of patients, so we had approximately [a large number of] people on [the treatment that was allowed by the trial] on

our books total, but a huge number of them naturally will have been on previous other [medication] regimens." (Interview, doctor 2)

"So yeah, mainly looking at the protocol, and making sure, like you know, inclusion and exclusion criteria wise if they meet all the criteria. Usually, they [patients] *go on* [name of the standard treatment] *for like a longer period of time but for this trial, you know we have the concomitant medication section* [that excludes this standard treatment]*, so she* [the patient] *couldn't be on that drug and so couldn't go on the trial just because of that." (Interview, nurse 8)*

On the contrary, some doctor study participants described that some patients who were deemed eligible at the pre-screening phase, specifically those patients who were not receiving standard treatments were also excluded from trial participation. This was because many of these patients attending CCPs presented with severe medical conditions that required immediate access to standard treatments provided through CCPs. As a result of receiving standard treatment within CCPs, patients who were previously pre-screened as potentially eligible trial participants were no longer eligible to participate in the trial by virtue of receiving or progressing through standard clinical care.

"But for [name of the life-threatening condition]*, you know you have to get the patient in, and you have to treat them [immediately] so, you can't hang around. And if you do hang around you actually bias the study."(Interview, consultant 7)*

Thus, the findings indicate that access to a recruiting trial was not always possible; especially for patients who needed to receive immediate care while being cared for within the context CCPs. This was because of the lengthy screening procedures (about 4-5 weeks in most of trials as per the trial protocol data) involved in confirming the eligibility for trial participation. Therefore, the requirement for patients to undergo a lengthy trial screening phase and time it took to receive confirmation from trial sponsors that a patient was deemed eligible to take part in a trial, rendered many patients with progressive medical conditions ineligible to take part in that trial. Ultimately, the time delays in obtaining screening results from sponsor organisations would have compromised the timely provision of necessary medical care to patients.

Consultants, in the best interests of patient care often, thus, had to prioritise standard CCP care, and forfeit the opportunities for trial recruitment.

> *"Once you begin Screening, up to 35 days could be required for your study doctor to receive lab test results and determine whether you are eligible to participate." (Document analysis, trial protocol 3).*

> *"I've missed a number of patients* [who could have been recruited] *… you know, if you've got* [name of the life threatening condition] *and if you're putting somebody on a trial, you've got a number of weeks to do that … because of the difficulty in getting screening results back from company* [on time]*..."(Interview, consultant 6)*

Hence, the findings indicate that reducing the complexity related to determining eligibility, especially during the screening phase of trial recruitment could benefit increased trial participation. The data suggested that alignment of screening procedures to the immediate needs of patient care could possibly have facilitated the recruitment of patients through CCPs rather than patients missing the opportunity to participate in a trial. This could have been achieved by aligning the screening procedures specified in trial protocols with the existing procedures within CCPs where possible, such as the provision of test results in a fast-track manner to match the immediate requirements of patient's clinical care treatments.

Further, the research nurse participants highlighted that if the logistics of implementing recruitment plans in a clinical setting with routine clinical workloads had been considered during the design phase, the screening process could have been less burdensome for both staff delivering care and patients receiving care through CCPs. For example, one nurse study participant voiced that the execution of screening procedures within a clinical setting took longer than the predicted timelines provided by the trial protocol. Therefore, by aligning activities involved in trial recruitment to the requirements of patient care as well as from the perspective of staff delivering care within a CCP setting, the efficacy of recruiting to trials within CCPs, could have been enhanced.

> *"I had challenges with the protocol (laughs)! … so that was a big challenge-because the amount of time they give it…to do all your assessments… so really the patient had to stay here very long, the way the protocol was!* [challenging to implement] *but that's my opinion but I think sometimes they do protocols of which they don't realise the amount of work that happens in the clinical setting." (Interview, research nurse 2)*

The majority of study participants unanimously agreed on the importance of planning in relation to how the trial recruitment plan would be implemented in a real-world context of CCPs, with patient care taking priority, so that both care delivery and a trial may coexist within a CCP setting. In this sense, aligning the trial recruitment procedures with existing care plans of CCPs so as to prevent adding to the burden of delivery of care while simultaneously supporting the recruitment process could better facilitate recruitment of patients through CCPs.

> *"So, before we invite patients to participate in trials,* [trial designers need to think] *what are the barriers to have patients engage in the trial and what are the burdens that we impose on patients to engage in trials that we could mitigate to help people enter trials to a greater extent. So that's to do with trial protocol design." (Interview, consultant 5)*

> *"And I think maybe, I think if, you know, maybe the pharmaceutical industry … is a little more thoughtful about what the inclusion and exclusion criteria for their studies are. And maybe I think if* [they used] *newer technologies which are coming on stream …rather than to have patients go through multiple* [name of the invasive procedures] *and things like that. I think they would be factors that will help as well in encouraging patients to take part in clinical trials." (Interview, consultant 3)*

According to some study participants, in order for CCPs to be effective in recruiting participants for clinical trials, the trial protocol design should align with existing CCP practices as much as possible. To achieve this, trialists or trial designers may need to reduce the complexities involved in determining trial eligibility by having less restrictive eligibility criteria and aligning the screening procedures with CCPs as closely as possible. However, trial protocol designers must balance this need with maintaining the quality of the trial design. In doing so, they can increase recruitment through CCPs while maintaining the integrity of the trial design.

6.8 Theme 4 - Factors affecting trial recruitment within CCPs

The narratives provided by the study participants across all seven case trials indicated that there were common factors affecting trial recruitment in its entirety, from identification through to randomisation. Many of these factors were inherent to CCPs such as CCPs services being overburdened with the provision of clinical care, therefore staff having clinical care responsibilities as their primary focus within CCPs could not work efficiently in recruiting to trials as well. Factors affecting trial recruitment within CCPs are discussed in the following subthemes: 'Prioritisation of clinical workload', 'Funding and meaningful recognition', 'Regulatory approvals and governance of CCPs', 'Role of Principal Investigators and Research Nurses' and 'Teamwork and communication'.

6.8.1 Subtheme 4.1 Prioritisation of clinical workload

The narratives provided by the participants in this study highlighted how the clinical care services provided through CCPs were oversubscribed, or in other words, in high demand. As a result, the study found that recruitment to trials was often delayed due to the competing demands of clinical services. Staff who had previously planned to perform recruitment activities often had to change their plans to prioritise clinical work. Additionally, many doctor study participants pointed out that the demands placed on Irish clinical care settings were higher than those in other countries. This view was held partly due to the lower doctor-to-patient ratios in Ireland, which made it extremely challenging to conduct trial recruitment activities alongside clinical care within CCPs.

> *"Most of the time* [my colleague] *was the only one doing it* [screening patient records]*, because we're very busy here so instead of me doing the clinical trials, I would be doing the normal clinic…" (Interview, nurse 1)*

> *"I have a very intense clinical service and therefore it's a struggle to get the appropriate time* [for trials recruitment]*. We have twenty-five per million population* [doctors within a care speciality] *in Ireland, in Sweden*

it's seventy-five per million. So, we are doing three times as much work on the clinical side so it's a bit hard to shake off." (Interview, consultant 2)

In addition, the doctor study participants noted that managing a high volume of patients was not the only challenge they faced. They also had to prioritise addressing the urgent needs of patients with complex medical conditions. These complexities included handling emergency cases, planning for additional procedures, and referring patients to different specialties. As a result, these study participants emphasised that their responsibility to provide care and make difficult decisions often resulted in overlooking potentially eligible participants who were receiving care from them.

"… And then, so on [this day of the week] *I spend my entire day in the day unit and during that day I will start a number of patients on* [the required] *treatments. And I just hope I'll remember that every time a patient comes in, this person could be part of a clinical trial." (Interview, consultant 8)*

"There's such a service demand in the Irish health service and we're so understaffed at most hospitals … and therefore people appointed are just the people who can deliver the service. Like it is tacitly in it at the moment that you should do [trials] *research but most, a lot of people are just so busy with clinical work." (Interview, consultant 3)*

Owing to the challenges of conducting trial recruitment during a busy clinical service, many of the investigator study participants voiced that one of the main challenges faced when trying to use CCPs for trial recruitment was the lack of protected time for research for doctors and nurses primarily involved in the provision of day-to-day clinical care. The study participants explained that most of the processes involved in trial recruitment were also time-consuming such as evaluating patient records to determine potential eligibility. Thus, the absence of protected time for research within a busy clinical environment meant that the clinical care providers with dual responsibilities for trial recruitment had to try to fit the latter around their clinical care activities. Consequently, most of the study participants who also held clinical care responsibilities perceived the activity of trial recruitment as an additional task to their existing clinical workload rather than as part of it.

"…but even in our department we don't have anyone.... anyone with protected time for research. So, and this is you know, a pity… and time is you know, key in research because we know that research involves a lot of time. So, I think that this is the main barrier in research." (Interview, consultant 4)

"… the volume of things to be done is too much. So, there's no protected time. This is an add on to everybody's fulltime work." (Interview, consultant 6)

The interview data from research nurse study participants concurred with that of investigator study participants, whereby providing doctors with protected research time would encourage more doctors to participate in trials, which could benefit trial recruitment initiatives across the diverse CCPs.

So, they've got their normal job let's say and then they take on research on top of that. So, if they had dedicated research time you might have more doctors being interested in doing research. And you'd have more engagements then and with more engagements then, hopefully more recruitment. (Interview, research nurse 3)

I suppose the busyness of the place and you know lots of services are stretched as it is and research is not, there's no dedicated time to research which I think is a massive issue. (Interview, research nurse 7)

Additionally, the interview data showed that the majority of investigator study participants were clinician academics and doctors in training programs, which meant that they had to balance both clinical and research responsibilities as part of their work contracts. Many of these participants expressed that there were no conflicts between the dual roles they played i.e., being an investigator of the trial while being a consultant or a doctor in clinical practice, however the conflict was with the time set apart for the dual responsibilities. This emphasises the need for a structured and supportive approach to allocating research time, especially for doctors involved in trial recruitment who also carry clinical care responsibilities within CCPs.

"… it's part of our professional training and ambition to do that [trials research]*, it's in my contract to engage with further education, training and research so I don't think there's a conflict there. There's a conflict in terms of lack of time put aside for that." (Interview, consultant 2)*

" …we're supposed to have, you know, as it goes, half a day a week of dedicated research time. But the reality is you don't ever really get that because you know, you just have so many inpatient commitments, clinical commitments or otherwise. It just generally doesn't happen. So, you know, realistically, you know, any of the trainees who are supposed to get it, but we don't, and that's across hospital wide." (Interview, doctor 2)

During the interviews, one of the consultant study participants suggested, as a potential solution to the challenge of insufficient research time, to increase the number of academic clinician appointments (Interview, consultant 5). However, the participant noted that healthcare governing bodies tend to prioritise appointing individuals who can provide clinical services. The participant suggested that exploring ways to balance the need for clinical services with the importance of research could lead to a more effective and sustainable solution.

The above issue was further reflected by nurse study participants who stated that they could not recruit participants to trials without having more doctors delegated to activities involved in trial recruitment. However, doctors could not be delegated the tasks involved in trial recruitment unless they had up to date training and clinical experience for undertaking these tasks as evidenced by majority of the data sources in this study. Thus, having more doctors who are trained in the conduct of clinical research and /or having more academic clinicians delegated to supporting trials would benefit the completion of recruitment related activities. This would potentially minimise missing opportunities for trial recruitment as can occur when investigators, for example PIs, who have a primary responsibility in the conduct of a trial, are otherwise busy with clinical care activities.

"We need more investigators [referring to doctors] *on this study because if you're doing the* [clinical procedure] *you need to be on the delegation log for the* [clinical procedure]*. And* [the doctor] *may not be available on that day to do the* [clinical procedure] *and we sometimes have a very short window of opportunity to get the* [clinical procedure] *in to determine the patient's eligibility." (Interview, research nurse 3)*

"I think it could help [recruitment] *perhaps if more doctors were involved in the trial. It was just mainly one PI* [referring to consultant] *and one doctor... So, if that consultant wasn't in that day, I couldn't recruit the patient." (Interview, research nurse 4)*

6.8.2 Subtheme 4.2 Funding and meaningful recognition

According to the majority of the study participants, clinical trials are considered to play a crucial role in advancing patient care. Despite this belief, an important limitation identified by the study participants in conducting trials in conjunction with the activities of CCPs was the suggested dearth of financial resources allocated for trials by healthcare governing bodies. Therefore, the availability of funding was recognised as one of the prerequisites to enable the implementation of trial recruitment processes within CCPs.

"…this is something that we're acutely aware of, that the [the governing body] *doesn't have a resource either to fund this type of integrated research in clinical care. And the hospitals are also quite reluctant." (Interview, Consultant 5)*

"But the budgetary envelope doesn't include a clinical research pathway and that's one of the problems. And then when we're asked to do care pathways, there isn't any mechanism within that care pathway programme to incorporate or embed research…" (Interview, Consultant 4)

Most of the consultant study participants also emphasised the significance of having dedicated trials staff working in conjunction with the staff involved in routine clinical care for the efficient execution of trial tasks along with care activities within the CCPs. However, the lack of funding was described as a big disadvantage for most consultants acting as PIs, for without sufficient funding, they could not secure the services of dedicated research staff.

"…where in order for you to be able to tender for a trial, you have to be able to show that you have the staff in order for you to do it. But if you don't have the money to do the trial, you don't have the staff" (Interview, consultant 3).

Lack of funding was also related to not having a meaningful reward or recognition for staff involved in trials research. Some consultant participants were of the opinion that many of their colleagues who were doctors and nurses involved in fulltime service as part of CCPs were reluctant to participate in trials research as they found it less rewarding, mainly because the trial related activities involve a lot of time, training and resources beyond the requirements of CCPs clinical care activities. It was also perceived that being involved in research only increased workload burden, while affording minimal benefits to the individual trying hard to balance the workload of routine care activities within CCPs. As a result, some of the consultants proposed that in order to make trial recruitment within CCPs sustainable, some form of reward or recognition were desirable.

"And there's no incentive to do it [trials research] *really because there's no budget and people don't really get rewarded for doing it." (Interview, Consultant 5)*

"…but again what is the benefit for nurse to do research? so, I think that you know, just to say, well done, or it's good for the patient; I don't think that this is enough. I think that you know the human being needs to get a reward, and that reward has to be something, and I don't think that it's always to have a name in a manuscript. I think that they need something else and something else could be having some time or having something like [funding their training] *or* [purchasing new equipment] *etc." (Interview, Consultant 4)*

Contrastingly, a few study participants held opposing views in relation to providing any form of recognition or rewards. Some study participants considered that it was a moral obligation to contribute to improve patient care and that any form of reward could generate ethical concerns.

"We incentivise the juniors [doctors] *and get them put on papers more. That would be their reward. I don't think financial rewards for patients or recruiters is a good idea, but I think that occurs in some types of phase II*

studies [in another country] *that renumerate patients. That's ethically quite challenging and sometimes you end up recruiting the wrong type of patients." (Interview, consultant 2)*

According to the analysis of the interview data, the majority of the study participants believed that there was a need to recognise staff with some form of reward to enhance the work related to trial recruitment alongside activities involved in CCPs, such as having additional resources of time, space, or equipment rather than monetary rewards. However, it is crucial to ensure that the rewards offered are ethical and do not compromise the integrity of the trial and patient care.

6.8.3 Subtheme 4.3: Regulatory approvals and governance

Initiating recruitment to trials involving medicines requires approval from the national regulatory authority, in addition to the site research ethics committee. In the current study, recruitment to the trials involving medications, as part of respective CCPs, was described as being impeded by slow or delayed regulatory approval, for example up to 16 months in one trial (Interview, consultant 3). Many of the participants commented on this issue and expressed their disappointment especially when these delays impacted directly on initiating trial start-up and recruitment. More critically, however, was the perceived impact of these delays on the CCP team's reputation, especially in the context of multicentre or international clinical trials, where it was suggested that regulatory delays could render the CCP and trial setting as a questionable suitable location for collaborative trial activity, and risked trial initiation and conduct.

".. we are very slow on ethics committee approvals that's a bit of a problem. I think we suffered international damage because of that … pharma companies have a less enthusiastic attitude to including Ireland in European centres particularly because of the ethics committee slowness to approve." (Interview, consultant 2)

"Because we have such a long period of time then in getting the trial approved…our relationship with industry is not very good…Ireland is much slower than most other countries [for initiating recruitment]. I think we're at the tail end." (Interview, consultant 4)

Some study participants attributed the delays in approval with the regulatory body's lack of understanding of trial related treatments, especially in CCPs that involve niche therapeutic areas, or in CCPs involving patient care for rare medical illnesses.

> *"So, the expertise within the* [names of the regulatory bodies] *was minimal, their understanding of our problems was minimal, and it was just, you know."* (Interview, consultant 7)

> *"We nearly lost this trial, where the* [regulatory bodies] *just put up so many barriers that the company walked away … And I happened to know the medical person who was involved in the trial, I managed to get him to pull the trial back in."* (Interview consultant 5)

The majority of the consultant study participants noted the challenges in having to follow lengthy regulatory approval processes, that it was suggested resulted in the study site having a poor reputation for recruitment when compared to other clinical sites undertaking recruitment for the same trials. Furthermore, some nurse study participants added that the delays in initiating recruitment not only led to a poor reputation, but also resulted in missed opportunities for recruitment as the potential patients for trials completed their treatment and were discharged from their CCPs while waiting for regulatory approvals to be obtained. This eventually meant that CCPs were under-utilised for recruitment as the recruitment targets were being met by other clinical sites before the study site was in a position to start recruiting patients.

> *"Because we were late coming on as a site. Had we started in January we would've had loads* [of patients] *but there wasn't that many patients anymore …And by the time we started* [the trial]*, they* [other clinical locations] *had already recruited…So, there was only a few left to go, yea…" (Interview, research nurse 4)*

This suggests, for CCPs to be utilised efficiently in recruiting trial patients, the aligned trials need to be supported by a regulatory system that enable timely trial initiation and recruitment according to a trial's prespecified timeline. This is especially important for trials that are part of an international network of trials, whereby Ireland

may have fewer trial sites available to for recruitment compared to other (larger) countries across Europe or internationally that may offer larger numbers of trial sites.

Many of the consultant study participants recognised the importance of improving trial recruitment within existing CCPs. Nevertheless, study participants argued that the healthcare governing bodies were predominantly prioritising the provision of healthcare services. Many study participants were of the view that healthcare governing bodies need to initiate efforts to integrate research activities into the provision of care for trial recruitment to take place within CCPs. This implies that CCPs were primarily viewed as pathways for delivering care rather than a medium for conducting research alongside the delivery of clinical care.

> *"So historically, it's kind of considered as all clinical services as one thing, certainly in Ireland, and research is a separate thing and they're kind of siloed. So, I think kind of, you know, making it a core principle that they are both part of the same paradigm of excellence in patient care. I think that's an important thing to establish … Now obviously at a higher level, the* [healthcare governing body] *needs to support that" (Interview, consultant 3)*

> *"..research drives good clinical care and good clinical care should incorporate research. That's absolutely true, but in Ireland the clinical care trajectory as funded by the* [healthcare governing body] *and recognised by the* [the same healthcare governing body]*, doesn't really incorporate clinical research. There's no mechanism to include that in how we deliver clinical care." (Interview, consultant 5)*

As a result, the participants of this study described how, in fully utilising CCPs for trial recruitment, clinical care settings must have a research culture embedded within them. This implies that while the governing structure of the CCP and the existing trials were distinct, it was important to recognise the need for embedding a research culture within CCPs. Having a research culture allows many more clinicians to engage in activities such as conducting trials or recruiting participants for trials, all with the overarching goal of generating evidence for enhancing patient care. As a result, the participants in this study suggested that addressing this culture at a higher level, such as at the national level, rather than addressing it mainly at the level of

healthcare service delivery through CCPs, would be more effective in recognising trials research as a component of providing excellent patient care within CCPs.

> *"I think the bottom-up approach at each individual hospital level is good, that that's* [research is] *embedded but there is also a top-down element in that the* [healthcare governing bodies] *are positioned towards embedding research... So, you know, pushing money into research projects does deliver but I think it's going to deliver much more effectively if, you know, hospital groupings are positioned and have an embedded research culture, if that makes sense." (Interview, consultant 3)*

6.8.4 Subtheme 4.4: Role of Principal Investigators (PIs) and research nurses

In each of the case trials, the PIs who were also consultants working in a CCP oversaw the whole trial recruitment process at the clinical study setting. Data from interviews revealed that the PI's leadership was one of the main enabling factors influencing the trial recruitment process. Many of the nurse study participants across the case trials stated that having PI's who were engaged in the trial recruitment process as well as having good leadership attributes such as having strong relationships within the clinical care setting, aided the recruitment processes.

> *"…but it's definitely works well* [trials recruitment process] *it's very much led I think by the principal investigators, what their relationship is with other disciplines, departments, also what education they give around it, how they let people know about what trials they have, things like that." (Interview, research nurse 5)*

> *"So, we've always been very driven for clinical trials here. To be honest we don't have a massive, we have never had a huge portfolio but anybody that has run the clinical trials* [referring to Investigators] *have been very interested in them. So, there has been a huge buy-in obviously from the investigators, so they drive a lot of it." (Interview, research nurse 7)*

According to some nurse study participants, the PI's spent a significant amount of time preparing their trial team for the recruitment process. These nurse study participants highlighted how the PI's took the time to clarify the responsibilities associated with the trials as well as plan for trial recruitment processes within

the CCP. The nurses also described how the initial preparatory meetings with their PIs and their support during the recruiting phase were highly beneficial in enabling them to carry out the recruitment processes.

> *"The PI had a proper meeting with us even before we started the clinical trial* [recruitment] *within the* [clinical specialty]*… we agreed on the day we work on trials* [recruitment] *..the* [name of the PI] *discussed what* [the PI] *wants and how* [the PI] *wants it to be done, and if we are willing to do it ." (Interview, research nurse 1)*

> *"It's really, really smooth* [referring to the trial recruitment process]*. It is because* [the research nurse] *and I* [clinical nurse] *are in sync and* [the consultant PI] *is in sync with us, what* [the PI] *really wants, you know. I think that is one great factor, that the PI knows the stuff, what is the clinical trial, because* [the PI] *guides us as well on what we need to do." (Interview, clinical nurse 2)*

Conversely, many investigator study participants commended the research nurses for their consistent support, with one investigator attributing the success of the recruitment process to the research nurses by stating, *"we recruit only because nurses have our back" (Interview, consultant 1).* Hence, the research nurse's position was not perceived solely as one of executing delegated trial responsibilities, but rather as individuals who assumed ownership of the trial's recruitment process, because the nurses went above and beyond the delegated responsibilities to ensure the processes were conducted as required by the trial protocols.

> *"I think our research nurses are core there and they basically are very good at interrogating a potential patient's background as to whether or not they meet inclusion criteria, and they're very efficient at driving any other kind of investigations that might be needed to clarify their eligibility. And I think they drive a lot of that which I think, you know, speeds up the confirmation of eligibility of a patient and also increased communication and shortens the time to a patient maybe being informed if they're not eligible… "(Interview, consultant 3)*

> *"…the key resource in delivering the trial is the research nurse … and with dedicated nurses it becomes easier to do it* [the trial]*, you know."(Interview, consultant 2)*

The research nurses were noted to have taken ownership of the recruitment processes in many ways. They were responsible for scheduling screening assessments according to the trial protocols. However, some nurses decided to additionally conduct quality checks (QC) with their colleagues to verify the accuracy of the scheduled screening procedures. This demonstrates their commitment to meticulous work, even when steps like performing a QC was not obligatory.

> *"…when I was planning how the* [screening] *visit was going to be. Like the* [number of] *hours and looking at this to be done at this time, and this time, and I'm looking through the protocol I had to give another research nurse to actually QC* [quality checks] *and see if I've missed out anything. Because there could be something I'm not seeing, which is very important." (Interview, research nurse 5)*

> *"…there was a team of CNS's and also there was another nurse there in the ultrasound department. So, because they are the ones who are going to assist the doctor when they're* [completing an invasive procedure]*. But I kind of go ahead of time and tell the nurse this is how they* [referring to sponsors] *want the* [name of the procedure] *to be done, sometimes I tell the doctor as well. I just kind of took up the form and showed how they* [sponsors] *needed* it"*. (Interview, research nurse 4)*

Furthermore, the research nurse participants demonstrated a comprehensive understanding of the difficulties faced by clinical staff when carrying out recruitment-related tasks, particularly in screening patients, alongside their currently demanding clinical responsibilities. One of the research nurse participants stated:

> *"And then the other thing is, they might miss out on small things…it could be, I understand they are busy, they can't be having it all…" (Interview, research nurse 1).*

Hence, many research nurse participants expressed their recognition and understanding of the diverse demands of clinical care within the busy clinical setting. The proactive involvement of research nurses in taking ownership of the recruitment processes played a crucial role during the screening phase of trial recruitment as it not only facilitated the timely completion of scheduled procedures during the screening phase but also ensured their accurate execution i.e., minimising errors, thereby enhancing the overall success of the trial recruitment process.

6.8.5 Subtheme 4.5: Teamwork and communication

According to the perspectives of the study participants, the recruitment processes through the span of the trials were deemed successful due to the seamless coordination between the clinical care staff with overlapping responsibilities to trials and dedicated research staff working synchronously within the clinical care setting.

> *"That the PI, the sub-PI and the research coordinator and the CRA* [clinical research associate]*, they always should be in sync with each other, you know, because one lapse or a gap within these four, it will be a very bad clinical trial." (Interview, nurse 2)*

> *"And then the link, I suppose the relationship and the communication between myself, the Sub-PI and the consultant worked really, really well because we could link in together." (Interview, research nurse 6)*

The study participants therefore shared instances where they mutually supported their team members to ensure completion of activities involving trial recruitment. In this example below, one of the clinical nurses mentioned that the responsibility of assigned trial related tasks was taken over by research nurses working on the same trial team so that the tasks involved in recruitment were completed on time.

> *"It works well with* [the name of the trial]*, if I cannot do something as planned, …,* [the research nurse] *is always doing things for me, which is basically a shared responsibility. The* [research nurse] *would really be giving a hand in doing that for me." (Interview, nurse 1)*

The dedicated research nurses had expertise in overseeing and running the trials as per the required trial standards however they were not always equipped with the expertise on the operational aspects of CCPs nor did they have an in-depth knowledge about the specific disease condition. Therefore, the research nurses, who were delegated the responsibility for trial recruitment tasks, collaborated with the clinical care nurses and doctors in the aligned CCPs during trial recruitment. This allowed the utilisation of the clinical expertise of the multi-disciplinary staff members involved in CCPs. For example, they explained the clinical condition to the research nurses for better determination of patient eligibility, and also assisted in managing the operational requirements, such as booking scans for screening visits.

"So, the nurse specialist [in the CCP] *is the one who actually organises it* [booking the scans for screening visit]*, because they know, because they work with these patients all the time… yeah, it's good to have them helping, because sometimes without having the CNS's, it's kind of difficult you know. Getting the charts, and they help big time, you know, …" (Interview, research nurse 3)*

"Sometimes you wouldn't [know all the details of the disease]*, what do you call it, for me having the* [understanding the specific detail of the disease] *I wasn't sure are they two different* [names for the condition]*? You know, you have to input this information as well* [on the electronic case report form to confirm eligibility checks]*, so that, yeah….And having access to medical personnel* [from a CCP] *helped, otherwise sometimes, you know, you'll have to delay this* [screening] *process until we can clear all these doubts." (Interview, research nurse 6)*

Many study participants noted that a key aspect facilitating trial recruitment in the case trials was the regular communication of ongoing trials to the clinical care staff who were part of the corresponding CCPs within the specific care speciality. The study participants revealed several instances where clinical care staff who were not involved delegated trial responsibilities notified the members of the trial team of patients who could be potential trial participants. This was because the clinical staff were aware of that a trial was open to recruitment within their department through regular communications mechanisms that existed within the CCPs.

"So, I do my rounds and I identify the patients and sometimes the [clinical care] *nurses before I come, they say oh there is a patient with* [the condition] *in bed number X. And then rather than myself, like I may miss that patient, they are telling me because they know that I am doing this* [the trial]*." (Interview, consultant 4)*

"….if they [referring to doctors] *knew that a trial was going on, and even if they're not directly involved, they would call whoever they know in the* [name of the trial]*. Like if one of the doctors see somebody* [see the patient in the clinic]*, they call them* [trial team] *and say, "oh I think I have somebody there". They could come down and opportunistically then meet that person." (Interview, doctor 2)*

On the contrary, one of the study participants observed that insufficient communication regarding the trials available for recruiting could hinder the recruitment process. The participant was of the perspective that spreading awareness of ongoing trials amongst consultants working in the same clinical speciality could potentially facilitate referral of patients to relevant trials. The participant also highlighted the importance of having proactive communication among colleagues, including consultants, doctors, and nurses involved in routine clinical care to harness the potential of trials recruitment within the clinical care setting.

> *"Because if you have five consultants working on one disease area, and there's only one consultant out of the five that's research active, the other four consultants are still seeing the same type of patient cohort, but they may not be referring those patients because they don't know about the study* [trial]*. So, they need awareness and communication amongst all clinical staff about the clinical trials within the field they work in. Because, if that's not the case and that's problematic then for recruitment."*
> *(Interview, research nurse 7)*

The data from this study indicates that improving communication and spreading awareness of the inclusion and exclusion criteria for participating in trials open to recruitment among all staff members within the CCP ensured that suitable patients were referred to a relevant clinical trial. As a result, communication of trial information within the aligned CCPs was identified as an effective strategy for enhancing trial recruitment within CCPs.

6.9 Chapter Summary

The findings of this study demonstrated consistency of data concerning the utility of CCPs for trial recruitment obtained from all seven case trials, despite their varying differences in type of trial and the associated CCPs. The analysis of data indicated that CCPs functioned as conduits for initiating trial recruitment by enabling the identification of trial participants when CCPs provided clinical services to large patient cohorts, accessing potential trial eligibility and in introducing the trial information to potential trial participants. The utility of CCPs was found to be diminished from the time of conducting informed consent discussions wherein the

potential trial participants diverged from CCPs to a parallel pathway that supported the requirements of conducting trials as laid out by trial protocols. However, links with existing CCPs existed through the patient care journey such as when emergency care through standard care was required from a CCP. While the parallel pathway met most of the infrastructural needs of the trials, complexities occurring due to requirements of a trial made it extremely challenging to maximise the potential for CCP utility to support trial recruitment, sometimes even leading to missed recruitment opportunities. Finally, factors inherent to CCPs, such as the existing burden of clinical care, funding issues, and regulatory approval delays, appeared to hinder trial recruitment processes, whereas the role of PIs and research nurses, as well as the presence of teamwork and communication, were considered as enabling factors across all phases of trial recruitment. Having presented the thematic findings in this chapter, the next chapter will discuss the findings in the context of existing literature.

Chapter 7: Discussion

7.1 Introduction

This chapter provides a critical discussion of the thematic findings of this study and their implications with reference to extant literature, and the utility of CCPs for trial recruitment and the advancement of trials methodological research. Hence the findings are discussed in the context of the definition of CCPs developed in Chapter 3 and the meaning of trial recruitment as identified in the findings (Chapter 6; that is the phases of recruitment), and that of the definition of trials recruitment as established in Chapter 2. As has been demonstrated, trial recruitment is a complex process involving several phases from the identification phase through to a randomisation phase, that is, recruitment does not occur as one singular activity nor at a single point in time, hence the utility of CCPs is discussed by considering the various phases involved in trial recruitment.

7.2 CCPs as a conduit for initiating recruitment

The current case study demonstrated that the initial stage in commencing recruitment was to identify prospective trial participants and pre-screen their healthcare data to check for those that were likely to meet the inclusion criteria for a trial (see section 6.5.1). The identification of patients for the trials, in this study, were facilitated by the consultants and nurses who normally provided clinical care to a particular group of patients with specific disease conditions via the CCPs in the clinical setting. This implies that even before the trial was formally initiated for conducting recruitment, consultants and nurses who were involved in the activities of CCPs found that they were able to identify patients as potential trial participants. This was primarily due to the fact that their clinics offered care to large groups of patients. As such, consultants and nurses possessed a thorough understanding of the patient cohort as they were significantly involved in their care, which directly facilitated the process of identifying potential trial participants. Consequently, the identification process was perceived as a synergistic occurrence that transpired naturally within the established CCPs.

When evaluating the patient identification process in relation to the theoretical definition of CCP, and subsequently operationalised in this study (as outlined in Chapter 3), it was noted that the identification process was perceived as an integral part of CCPs i.e., as an event taking place within it rather than occurring separately. This can be explained specifically due to the relationship that exists between patient identification (as a recruitment process) and the delivery of patient care in the following manner. Firstly, patient identification was attributed to the large number of patients encountered during clinical care events within their respective CCPs. Secondly, the clinical care team's (consultants, doctors and nurses) close proximity to patients through the process of care delivery facilitated a deeper understanding of the patient cohort and their medical conditions. Therefore, the clinical care team in this case study reported no challenges in identifying patients as potential trial participants. Additionally, it was observed that the identification process was predominantly conducted by healthcare professionals involved in clinical care events i.e., consultants, doctors and nurses working within CCPs. Thus, from the perspective of CCP utility for trial recruitment, CCPs were well-utilised throughout the identification process, which was the initial phase of trial recruitment in this case study.

This finding is reflected, albeit conversely, in the findings of Hamlet *et al.* (2017), Clement *et al.* (2019), and Strong *et al.* (2023) who encountered difficulties in identifying suitable participants due to the comparatively lower cohort of patients accessing clinical care services through their respective studies' CCPs. This means that the consultants working within CCPs were aware that their patients' disease condition was slightly different from the criteria required for trial participation due to their proximities in providing clinical care to their patients. According to these studies, the trial team's awareness of their limited patient population made them link in with services that included larger flow of patients to overcome the challenges involved in identifying suitable patients for their trial. This underscores the importance of ensuring that CCPs have patient population or an established patient cohort suitable to the trial focus prior to initiating recruitment to facilitate the identification process as an initial step in trial recruitment. Ensuring sufficient potentially eligible participants prior to initiating trials can avoid the issues of insufficient recruitment, for example, if clinicians are already aware that there are fewer number of patients accessing the

clinical care services through CCPs, then alternative methods of recruitment could be employed because the demands of a trial are such that it needs the right patient (based on the trial criteria) at the right time (at the time of recruitment).

While the findings under Theme 1 resonated with issues of identifying potential trial participant in the literature, such as the need for an established cohort and an experienced clinician team supporting the identification process; the current body of literature lacks clarity on the utility of CCPs for initiating patient identification and pre-screening. This is because many of the authors of studies on trial recruitment discussed the issues surrounding recruitment in its entirety, rather than pertaining to particular trial phases such as patient identification (Team *et al.* 2018, Isaksson *et al.* 2019, Phelps *et al.* 2019, Realpe *et al.* 2021). Moreover, the literature presents some ambiguities in describing the identification process. According to some study reports, identifying potential participants could either mean selection, pre-screening, or screening (Wilson *et al.* 2018, Benedict *et al.* 2019, Beskow *et al.* 2019). For example, Higgins *et al.* (2018) and Wilson *et al.* (2018) described the process of identification as the process of screening for eligibility to enrol trial participants, whereas others have described identification for trial participation as the characterisation of patient data through the use of electronic databases, in accordance with the trial criteria (Hanson *et al.* 2014, Augustinov & Duftschmid 2019, Beskow *et al.* 2019, Peel *et al.* 2019). Other researchers used internet based social media campaigns as an initial step towards identification of potential trial participants (Benedict *et al.* 2019, Herbell 2019). Typically, the task of identifying patients in the above referenced studies were carried out by researchers rather than members of a clinical care team with the aim of finding suitable participants for the trial (Cauley *et al.* 2015, Benedict *et al.* 2019, Herbell 2019, Lai & Afseth 2019). This probably suggests that there was a lack of convergence with CCPs in the studies that described the identification process, as the research team frequently obtained patient data from sources outside of a patient's CCP in order to identify potential trial participants (Hanson *et al.* 2014, Augustinov & Duftschmid 2019, Beskow *et al.* 2019, Peel *et al.* 2019).

Similar to this case study, however, the identification process in some research studies was facilitated by the clinical care team’s familiarity with the particular patient

cohort receiving clinical care as part of their CCPs, rather than through purposeful database searches to identify potential patients (Aruchuna *et al.* 2019, Pessoa-Amorim *et al.* 2021). Nevertheless, there is a lack of clarity regarding the involvement of CCPs in the identification phase of trial recruitment in many studies (Higgins *et al.* 2018, Aruchuna *et al.* 2019, Laaksonen *et al.* 2021, McElvaney *et al.* 2022). This ambiguity arises from the fact that existing literature on recruitment does not explicitly classify or clearly define the identification and pre-screening process as an initial stage in trial recruitment (Schulz *et al.* 2010, Wilson *et al.* 2018, Delaney *et al.* 2020). In contrast to the aforementioned studies, the current case study addresses the ambiguity surrounding the identification phase of trial recruitment. This study demonstrated how CCPs can act as a conduit by possessing an established patient cohort and having a well-experienced clinical team that can competently handle both the responsibilities of clinical care and an early phase of trial recruitment.

Following the process of identification and pre-screening in this case study, the clinical care team introduced the availability of the trial selectively to those patients who fulfilled the criteria during the pre-screening phase i.e., by verifying the characteristics against the requirements of the trial protocol (see section 6.5.2). This meant that the clinical care team introduced the trial only to those patients who had a likelihood of meeting the inclusion and exclusion criteria for trial participation. This was corroborated by patient participants in this study who stated that they received trial information during their routine consultation visits within CCPs. Therefore, with respect to the utility of CCPs in this study, the point of delivery of care through CCPs was also the point of delivery of trial information. In this sense, CCPs served as an intersecting point for clinical care delivery and the communication of trial information. This means that the consultant caring for the patient at this point often assumes a dual role as PI of a trial; a role which was found to support trial recruitment while upholding the best interest of patients as a primary focus of concern.

In contrast to the findings of this case study, the literature indicates that some researchers conducting trial recruitment chose to send invitation letters or electronic emails to targeted mass populations in order to notify patients about trials that are open to recruitment rather than the patient care team delivering the trial information

as part of delivering clinical care services within CCPs (Cauley *et al.* 2015, Cooke *et al.* 2015, Benedict *et al.* 2019). Minimum interaction in such studies with the patient's CCP for trial recruitment, was thus highlighted, as identification, pre-screening and delivery of trial information occurred separately to the activities and events involved in CCPs. However, majority of the studies discussing the conduct of trials recruitment did not report if the patients received the trial information while being part of clinical care or if the trial information was introduced outside of the patients' CCP (Adams *et al.* 2015a, Henshall *et al.* 2018, Team *et al.* 2018, Phelps *et al.* 2019, McDermott *et al.* 2021, Realpe *et al.* 2021, Wharton-Smith *et al.* 2021, Morberg Jämterud & Sandgren 2022, Qu *et al.* 2022, Strong *et al.* 2023). Therefore, this indicates that there is a paucity of literature in understanding regarding how patients are introduced to clinical trials within their CCPs.

7.3 Parallel pathway approach for trial recruitment

According to the findings of this case study, some recruitment processes occurred outside of CCPs, which means that they occurred concurrently or in parallel within the same hospital setting but did not overlap with the clinical care activities of a CCP. Instead, activities related to trial recruitment were separated from CCP events and procedures due to inherent differences in the purposes of the CCP and trial recruitment. Patient care, therefore, transitioned to a dedicated trial team within a research facility different from where patients received CCP care. As per the definition of CCPs informing this case study, there was no interaction with a patient's standard of care trajectories in such circumstances unless there was a need for emergency care, hence trial recruitment including the informed consent phase, the screening phase and the randomisation phase occurred in parallel to CCPs.

In most of the trials in this case study, the informed consent process included scheduling detailed discussions with potential participants about their suitability or availability to participate in trials, as well as providing clarification on trial-related questions. Due to constraints of finding a free clinical space for holding informed consent discussions, staff frequently brought patients out of CCPs to a dedicated space separate from the busy clinical care setting thereby transitioning to a parallel

pathway within the clinical care setting for trial recruitment. Being in a parallel pathway also facilitated focused attention on the potential trial participants, providing them with sufficient time and space to comprehend trial information including the trial treatments that could be involved or participation commitments, thus better assisting them in making an informed decision regarding their participation. Comparing the findings of this case study with the existing literature, it was found that there is a wide body of literature presenting various challenges involving the process of informed decision making in trials such as comprehension of the patient information leaflets (Gillies & Entwistle 2012, O'Sullivan *et al.* 2020), lack of informed decision-making in populations who may be considered vulnerable (Anderson *et al.* 2019, Eisenhauer *et al.* 2019), patient perspectives on informed decision making (Gobat *et al.* 2019) as well as challenges occurring due to attitudes and perspectives of recruiters delivering, or patients receiving, trial information (Ferguson 2002, Occa & Morgan 2018, Farrar *et al.* 2022). However, it was unclear if and how CCPs were being used for the informed consent process in these research studies or if informed consent occurred in parallel to the activities involved in CCPs. This could be because the purpose of the above-mentioned studies was different from this study.

However, as evidenced by data obtained in this case study, detailed discussions were essential when sick patients as potential trial participants were dealing with complex trial information that they were not familiar with, and how they required the support of doctors and nurses in comprehending the trial information. Having these detailed discussions with potential participants was noted as an important factor in enabling the patient-decision making around trial participation. This could be true for trials involving similar complexities occurring elsewhere, that informed consent process could occur if the staff involved in recruitment can facilitate detailed conversations with patients either within the CCPs or in parallel to CCPs, although having informed consent discussion in a parallel pathway was found to be of benefit in this case study. On the contrary, studies that do not facilitate detailed discussions, may miss out on trial recruitment opportunities (Sood *et al.* 2009, Cartmell *et al.* 2016).

After completing the informed consent process, a crucial step in enrolling participants for trials was to assess the eligibility of potential patients. The determination of trial

eligibility in this case study took place in two distinct phases. The first phase, known as pre-screening, involved the clinical team assessing eligibility based on data obtained from the medical records of existing patients through CCPs. The second phase of the screening process occurred only after the patients were approached through an informed consent process. The screening process for the case trial was mostly complex and involved multiple visits by potential participants to the clinical setting. During these visits, the patients underwent various health evaluations, including specific laboratory and diagnostic tests required for specific trials. As a result, a parallel pathway incorporating a dedicated trial team supported the activities necessary for screening, which frequently took place outside of a patient's CCP within a dedicated research facility. When viewing the screening process with respect to operationalising the theoretical definition of CCPs, the procedures involved in screening were not part of a normal patient care trajectory i.e., potential participants came to a dedicated research facility and were cared for by a team dedicated to the trial under the supervision of the consultant, who also served as the PI of the trial. Therefore, the procedures involved in the screening phase of recruitment were clearly distinct from a standard patient care trajectory within CCPs.

Reviewing the existing literature on trial recruitment, it becomes evident that there needs to be a more comprehensive understanding of the nature of a trial screening phase. The literature predominantly emphasises screening as an eligibility assessment conducted solely before the informed consent phase rather than recognising it as an ongoing process that extends beyond the informed consent phase (Wilson *et al.* 2018, Bracken *et al.* 2019, Delaney *et al.* 2020). The reporting of recruitment in trials, as represented by the CONSORT guideline (Schulz *et al.* 2010), necessitates trialists to provide information on four distinct stages of recruitment: screening, consent, randomisation, and allocation. However, as indicated in CONSORT guideline (Schulz *et al.* 2010), the screening phase is conducted only before the consent period and does not occur after that. While the CONSORT (Schulz *et al.* 2010) requires trialists to report the number of participants who were eligible and not eligible to take part in trials, it does not provide for a clear definition of the screening process itself. In their study, Wilson *et al.* (2019) proposed an analytical framework referred to as the SEAR (Screened, Eligible, Approached, and Randomised) framework, which aims to enhance comprehension and documentation

of the various steps associated with recruitment to trials. According to the SEAR framework (Wilson *et al.* 2018), screening is the first important component of trial recruitment, which was defined as a process of identifying potential participants for trial inclusion whereas the second process of eligibility was defined as a process of assessment against the trial protocol criteria. As a result, the SEAR framework (Wilson *et al.* 2018) did not appear to compliment the recruitment processes identified in the current case study. This is because the potential participants were not randomised soon after they were approached, rather a formal screening process was initiated in a parallel pathway. Other authors are of similar opinion that both the CONSORT framework (Schulz *et al.* 2010) and the SEAR framework (Wilson *et al.* 2018) lack explicit definitions of the screening process, leading to ambiguities in the manner in which the screening process is reported in academic literature (Elm *et al.* 2014, McDermott *et al.* 2021). This suggests that future researchers should document the recruitment procedures employed in their trials and identify the specific phase of recruitment that posed the most significant challenges or successes. This information can assist trialists in developing strategies and solutions to enhance the efficacy of recruitment in trials.

In contrast to the above frameworks, identification, pre-screening, and screening were identified further to the analysis of the data in this study as distinct processes occurring within and in parallel to CCPs. Although there were ambiguities in the descriptions of screening in the literature, the findings of this case study were similar with those of some studies that reported screening process occurring in two phases, namely the pre-screening phase and the second phase involving more intensive screening after an informed consent phase (Higgins *et al.* 2018, Bracken *et al.* 2019, McDermott *et al.* 2021, Strong *et al.* 2023). The first phase of pre-screening, in the current study, occurred through the review of hospital notes or routine consultations indicating the use of CCPs; however, it was unclear whether CCPs were used in the second phase of determining eligibility through a formal screening process in those other studies, how long the screening phase lasted, or if there were any specific challenges they faced during this phase (Higgins *et al.* 2018, Bracken *et al.* 2019, McDermott *et al.* 2021, Strong *et al.* 2023).

According to the findings of this case study, the conduct of screening was one of the most time-consuming endeavours (up to 45 days) wherein recruiter study participants found it extremely challenging to manage the sophisticated tasks involved in conducting screening evaluations alongside the responsibilities of clinical care within CCPs. It was found that most of the screening procedures, in the case trials, required additional facilities, space and resources, trained research staff to conduct trial-specific tests and evaluations, and provision of focussed care to potential participants undergoing screening, therefore making it challenging to utilise CCPs during the screening phase of trial recruitment. The separation of the screening phase to a parallel pathway seemed to benefit trial recruitment overall, as screening procedures and visits could be scheduled on time without delays. Therefore, this case study has highlighted the need for a separate infrastructure from that of CCPs for undertaking efficient recruitment at the point of screening. These findings align with the work of Cimino & Braun (2021), who underscored the pivotal role of well-developed parallel infrastructural support for the successful execution of trial recruitment.

Randomisation and allocation were the final steps involved in the recruitment process of the case trials. Randomisation serves as the cornerstone of trials, wherein participants are randomly assigned to one or more groups where participants are allocated to the intervention being tested or a comparison, control, or alternative treatments group (Kendall 2003). In this study, the randomisation process was completed by delegated research staff whereby they completed the process remotely through an electronic database, with an exception in one trial where randomisation occurred outside of the clinical care setting, where neither CCPs nor the parallel pathways were utilised.

Reviewing the literature with respect to the utility of CCPs, the randomisation process, however, seemed to counter the use of CCPs where in a standard CCP, the clinical care team decide on the appropriate treatment option during their care trajectory, whereas for the purposes of trial recruitment, the treatment options were concealed from the clinical care team, dedicated research staff and patients in minimising bias (Kendall 2003, Akobeng 2005). This however meant that CCPs were not necessary for the randomisation and allocation phase of trial recruitment. There

was common agreement, however, that randomisation and allocation was the concluding phase of recruitment to trials (Moher *et al.* 2010, Wilson *et al.* 2018, Delaney *et al.* 2020, Wharton-Smith *et al.* 2021). Similar to the finding in this study, most researchers used computer assisted techniques for completion of randomisation and allocation, hence minimising the requirement of CCPs for this phase of trial recruitment (Kendall 2003, Akobeng 2005, Suresh 2011). Thus, the data from this case study and the literature shows that randomisation in trials is mainly automated, does not require using CCPs nor are challenges in executing randomisation posed.

7.4 Complexities of trial recruitment- an issue beyond CCPs

One of the primary challenges encountered in the process of recruiting participants for the case trials was the limited availability of necessary patient information within CCPs as required by the trial protocols. The findings from this study suggested that the lack of sufficient healthcare data occurred not due to poor documentation practices within CCPs, rather it was primarily due to the extensive information required of trial protocols about potential participants, which exceeded that which would usually be documented as part of clinical care delivery.

The evaluation of the issue of inadequate patient data for trial recruitment, with respect to the definition of CCP, indicated that the definition of CCP was limited to clinical care processes that occur throughout a patient's care journey, with a lesser emphasis given to the documentation processes within the various aspects of patient care. This implied that healthcare data in the form of patient records were generated by the clinical care team during clinical care provided through the CCP (Kinsman *et al.* 2010, Argulian *et al.* 2011, Leonard *et al.* 2017). Examples of such records include handwritten clinical notes, referral letters, and documentation of laboratory results (Argulian *et al.* 2011, Attfield *et al.* 2017). Therefore, while a relationship existed between the documentation of medical and healthcare data and CCPs, the activity of record keeping was limited to the care events that patients received within CCPs. As a result, the medical information required by the trial protocols was not

always available because it was not necessary for the delivery of clinical care within the CCP.

Aligning to the findings of this case study, literature suggests that recruiters often had to go beyond the data recorded within their CCPs to determine eligibility of the potential trial participants (Clement *et al.* 2019, Briel *et al.* 2021). The challenge of finding information for the purposes of trial recruitment with the patient medical records system was described as “searching for a needle in a haystack” (Hanson *et al.* 2014, p. 1025). Therefore, numerous researchers have opted for alternate approaches to address the constraints associated with patient medical records through CCPs (Hanson *et al.* 2014, Benedict *et al.* 2019, Herbell 2019, Murphy *et al.* 2021). The literature shows that trial recruiters frequently employed a combination of methods such as use of medical records data and social media in order to ascertain patient eligibility (Hanson *et al.* 2014, Benedict *et al.* 2019, Herbell 2019). Due to the constraints of obtaining data through patient records some authors have placed greater emphasis on utilising research databases rather than patient medical records to ascertain the eligibility of potential trial participants (Laaksonen *et al.* 2021, Murphy *et al.* 2021). Whereas other authors report the use of research databases, or the use of electronic patient records yielded any data to determine patient’s eligibility therefore acting as one of the key barriers to trial recruitment (Cauley *et al.* 2015, Clement *et al.* 2019, Briel *et al.* 2021).

The above literature, therefore, suggests, that accessing patient medical records were viewed as one of the many strategies used to determine patient eligibility for trial recruitment alongside other strategies including the use of disease registries, referrals from external hospitals, conducting medical or nursing rounds, organising information sessions with patients and advertisements (Cauley *et al.* 2015, Cooke *et al.* 2015, Tan *et al.* 2015). Some authors suggest, however, that despite the use of multiple methods of determining eligibility, the use of patient medical records or electronic medical records was regarded as one of easiest and cost-effective methods compared to other strategies involved in determining patient eligibility available to healthcare professionals (Effoe *et al.* 2016, Feldmeth *et al.* 2019, Jolly *et al.* 2019). Considering the utility of existing medical records, some authors argue that a nationwide interconnected electronic health record system could be a viable

solution to determine patient eligibility and reduce delays by eliminating the arduous manual task of collecting data from various clinical sites to confirm eligibility (De Moor *et al.*2015, Augustinov & Duftschmid 2019). Healthcare regulatory authorities in Ireland have recognised the importance of implementing a national Electronic Health Record (EHR) system as an essential capability for the future delivery of healthcare services (https://www.ehealthireland.ie/). Currently, Ireland is in the process of implementing a nationwide EHR system as part of the National Development Plan (2018-2027). Consolidating patient care data into a comprehensive national record would improve both the provision of patient care and the recruitment of participants for clinical trials.

Another complexity of utilising CCPs during the recruitment process was the lack of alignment with protocol plans and CCP plans. The findings of this case study indicate that the utility of CCPs in some instances were limited not because CCPs were not conducive to recruitment, but rather because the trial protocol designers primarily focussed on the scientific aspects of the trial rather than implementation of the trials within the CCPs. Similar to this finding, researchers investigating reasons for recruitment failures highlighted a lack of alignment with the trial protocol and clinical care procedures as one the factors contributing to the inefficiencies of trial recruitment (Briel *et al.* 2021, Le Boutillier *et al.* 2022). This aligns with the findings in this study, whereby, for example, it was found that the time required to obtain screening results took longer when patients with serious medical conditions needed immediate access to clinical care. This indicates a lack of alignment between recruitment and the requirements of patient care within CCPs. There are ongoing efforts by trial methodologists to help trial protocol designers plan aspects of trials including recruitment, conduct and analysis; however, the literature suggests that it would be beneficial to consider recruitment in individual phases (i.e., from identification to randomisation) in assisting healthcare professionals and researchers to design recruitment, and its associated phases, that better align with clinical care (Loudon *et al.* 2015, Norton *et al.* 2021). Ultimately, this could lead to improved recruitment rates, greater patient engagement, and more successful clinical trials.

7.5 Factors affecting trial recruitment within CCPs

In addition to the challenges encountered due to the complexities of trial protocol design with trial recruitment, the study's findings also highlighted the challenges that exist within CCPs that impeded the efficient conduct of recruitment phases. These issues were related to challenges in balancing the workload of clinical care delivery as part of CCPs and activities involved in trial recruitment. Specifically, these challenges were exacerbated by the reported availability of trained and experienced clinical care staff, particularly consultants and doctors, who reported being unable to oversee trial recruitment activities due to the extant demands of their clinical care workloads. This finding was consistent with previous studies that discussed the challenges to trial recruitment occurring in various clinical care settings as will now be explored (Adams *et al.* 2015b, Alemayehu *et al.* 2018, Team *et al.* 2018, Clement *et al.* 2019, Briel *et al.* 2021, Qu *et al.* 2022).

The existing literature substantiates that many clinicians, namely doctors and nurses, who were involved in the duties of clinical care, experienced a sense of being overburdened with their regular clinical care responsibilities (Team *et al.* 2018, Qu *et al.* 2022). Consequently, they consistently had to allocate extra time to fulfil the requirements associated with the recruitment of participants for clinical trials (Team *et al.* 2018, Qu *et al.* 2022). Consistent with the results of this case study, researchers often emphasised the importance of increasing the number of clinical staff who can assist with the responsibilities of clinical care to reduce clinical workload so as to be able to allocate more time to activities related to trial recruitment (Adams *et al.* 2015b, Alemayehu *et al.* 2018). Furthermore, researchers have emphasised that the endeavour to increase research efforts would only be effective if doctors are allocated dedicated time to engage in research activities, such as trial recruitment. Such authors assert that the provision of dedicated time to all clinicians will also increase the number of clinicians engaged in trial research, while providing support to their colleagues involved in recruiting trial participants (Fletcher *et al.* 2012, Mahase 2019, Team & Weller 2019).

In addition, the findings of this case study showed that the availability of investigators at the clinical setting played a crucial role in trial recruitment. The research nurse

participants voiced that the limited number of investigators in a trial hindered the recruitment process, even if potentially eligible participants were available. Therefore, this study highlighted the importance of having an adequate number of investigators to ensure successful trial recruitment. As a suggestion to improve the trial recruitment, some investigator study participants suggested that the health services need to focus on appointing more clinician academics. These are health care professionals who have a joint appointment in both delivering clinical care and pursuing a research career. By increasing the number of clinician academics, there would be a larger workforce of investigators involved in clinical trials, which could potentially improve recruitment rates. The importance of clinician-academics in advancing clinical research and enhancing patient outcomes is widely recognized in the literature (Joseph & Dohan 2009, Hall *et al*. 2017). Similar to the current case study, many authors have advocated for the inclusion of more clinician academics to augment research activities alongside clinical care delivery (Joseph & Dohan 2009, Fletcher *et al.* 2012, Hall *et al.* 2017)

According to the findings of this case study, inadequate funding was identified as one of the key factors affecting recruitment to clinical trials within CCPs. The study participants emphasised that without sufficient funding to support staff time and training needs, it is unlikely that trials can be efficiently conducted. Hence, funding was considered crucial for the successful execution of trials recruitment within CCPs. Similar to the current study, the issue of inadequate funding was identified by others as one of key reasons affecting trial recruitment (Briel *et al.* 2016, Briel *et al*. 2021, Howard-Jones & Webb 2021). As an example, a systematic review conducted by Briel *et al.* (2016), identified 28 reasons for recruitment failures, which were categorised into four themes. Among these themes, lack of funding emerged as a significant factor that led to the discontinuation of trials. This highlights the importance of adequate funding for the successful execution of clinical trials. Previous literature has also highlighted the importance of adequate funding and dedicated staff for successful recruitment to clinical trials (Campbell *et al.* 2007, Briel *et al.* 2016, Peckham *et al.* 2018). Clinical sites that received sufficient funding support and had dedicated staff to support the clinical teams in recruitment activities, were found to have better recruitment outcomes compared to those with insufficient funding (Campbell *et al.* 2007, Peckham *et al.* 2018). Therefore, increased funding

levels for staff time, training and equipment involved in trials research would help overcome resource constraints and increase the likelihood of successful recruitment for future trials.

In contrast to the preceding factors influencing trial recruitment, the lengthy regulatory approval process was a significant barrier to trial recruitment, which prevented PIs from initiating trials within the CCPs. According to the study participants in this study, delays in the approval procedure resulted in missed opportunities for patient enrolment, whereas other clinical sites were accredited as having met the trial's recruitment targets quicker. There was suggestion in the data that this issue can harm the clinical site's reputation, which could make the clinical site unappealing for large multicentre clinical trials. However, none of the study participants in this case study, nor the authors in the wider literature criticised the regulatory measures, rather they valued the checks and controls involved in patient safety (Dilts *et al.* 2010, De Feo *et al.* 2015, Fox *et al.* 2017, Leddy *et al.* 2020). According to the Irish Pharmaceutical Healthcare Association (IPHA) (2019), Ireland has been recognised as a prominent site for multinational trials. However, it has been observed that regulatory approvals in Ireland can experience delays of up to eight months, which was comparatively longer than the timelines observed in other international clinical locations (IPHA, 2019). Similarly, in a qualitative study conducted in Ireland by Leddy *et al.* (2020), participants highlighted delays in regulatory approvals as a significant factor impeding the timely recruitment of participants in clinical studies. Nevertheless, continuous endeavours are being made to address the obstacles associated with the delays in regulatory system in Ireland such as the setup of the National Research Ethics Committee (NREC) in March 2020, which may help overcome some of the shortfalls associated with regulatory approvals (NREC 2022).

Recruiting participants for clinical trials is a complex process that occurs through different phases, some of which are carried out within CCPs or in parallel within the same clinical care setting. Nevertheless, this case study data suggests that there were common enabling factors that influenced the successful trial recruitment. One of the key enabling factors for the successful conduct of the recruitment process was attributed to the strong leadership exhibited by principal investigators (PIs), who also

served as consultants in a specialised field of clinical care in this study. The PIs provided assistance, oversight, and direction to both the clinical care staff and research staff in carrying out their respective duties. The literature consistently acknowledges the vital role of PI leadership in the success of recruitment efforts (Blazeby 2012, Team *et al.* 2018, Isaksson *et al.* 2019, Team & Weller 2019, Farrar *et al.* 2022). For example, Blazey (2012) underscores the significant contributions of PIs, who not only successfully design and lead trials in surgery but also actively engage in trial leadership. Their responsibilities included patient recruitment, vigilant monitoring of the recruitment process, and fostering collaboration with various disciplines, including clinical trials methodology. This active involvement established an integrated culture of clinical research within surgical practice and yielded high-quality evidence crucial for informed decision-making and the enhancement of patient care and outcomes. Similarly, Peckham and colleagues (2018) reaffirmed the indispensable role of PIs in the success of clinical trials. Their study emphasised that trials performed exceptionally well when led by investigators with the capacity to influence other clinicians and promote trial engagement. Notably, PIs played a key role in positively impacting recruitment by effectively communicating the trial's importance and benefits to potential participants, thereby increasing interest and willingness to participate. This implies that the active involvement of an experienced PIs plays a crucial role in facilitating the process of recruiting trial participants.

This acknowledged, the investigator study participants of this case study acknowledged the significant and crucial contribution of research nurses in various aspects of trial recruitment and beyond. This recognition was primarily attributed to the research nurses' unwavering dedication and commitment to the trial-related activities. Additionally, the research nurses demonstrated a strong sense of ownership, supporting their colleagues with overlapping responsibilities. This support took the form of acting as informants or guides in conducting procedures according to the required trial protocol requirements and assuming responsibilities from busy clinical nurses during the recruitment process as noted in this case study. The vital role of research nurses in trial recruitment is widely recognised in academic literature; as such, many researchers contend that the absence of research nurses would render recruitment to trials unfeasible (Langley *et al.* 2000, Campbell *et al.* 2007, Team *et al.* 2018, Isaksson *et al.* 2019, Briel *et al.* 2021, McDermott *et al.*

2021, Qu *et al.* 2022). McDermott *et al*. (2021) emphasise the pivotal role of research nurses in a trial focused on comparing treatments for chronic rhinosinusitis. The success of the trial, according to the authors, was intricately linked to the enthusiasm and advanced planning demonstrated by research nurses, along with their expertise in conveying trial information to patients. Similarly, Qu *et al.* (2022) assert that experienced research nurses within a trial team serve as facilitators for a trial's successful implementation. Their support to PIs extends to assisting in patient identification and recruitment, thereby underscoring the collaborative and essential nature of their role. Recognising the significance of research nurses in the landscape of clinical trials, a study conducted by Shiely *et al.* (2023) aimed to investigate whether research nurses could serve as predictors of trial performance by assessing trial protocols (n=18). In this endeavour, research nurses were tasked with making judgments on various trial parameters, including trial status, recruitment success, on-time recruitment, and participant retention. The results revealed noteworthy predictive capabilities, with research nurses accurately predicting trial status 48% of the time, successful recruitment 74% of the time, on-time recruitment 70% of the time, and participant retention 52% of the time. This study suggests that involving research nurses early in the trial design stage can potentially offset problems of recruitment, retention, and trial failure. The involvement of research nurses can lead to a clearer and more implementable trial protocol, which is crucial for successful trial recruitment.

In this case study, teamwork and communication have been recognised as factors enhancing trial recruitment through every stage of the recruiting process. The integration of recruitment into the standard care CCP implemented through regular reminders, and structured educational sessions are examples of teamwork strategies used to encourage a collaborative culture within the clinical care setting. Additionally, the clinical care staff and research staff needed to coordinate and work as a team to complete tasks involved in recruitment either simultaneously or sequentially for the successful completion of recruitment procedures. It is widely acknowledged in literature that teamwork and communication enhance trial recruitment (Catt *et al.* 2005, Jenkins *et al.* 2013, Strong *et al.* 2016, Team *et al.* 2018, Briel *et al.* 2021, McDermott *et al.* 2021, Realpe *et al.* 2021). The study conducted by Strong *et al.* (2016) attributes the success of recruitment to the collective ownership of the trial

team rather than any or some individuals in the team. The authors additionally proposed the implementation of weekly interdisciplinary team meetings between the clinical and research teams to reduce professional barriers and increase engagement among healthcare professionals.

7.6 Strengths and Limitations of the Study

This study provides a novel investigation into the utility of CCPs in an acute care setting for recruitment to trials. In order to conduct a rigorous inquiry, it was necessary to establish a clear understanding and clarity of what a CCP entails. This involved developing a theoretical definition of CCP, which could be then operationalised in the study, via a concept analysis (Chapter 3). This is considered a strength of the study as the established definition was used as a guide during data collection and analysis, thereby ensuring fidelity to the purpose of this study.

The inclusion of data from seven trials conducted in various clinical care specialities is a further strength of this study. This is because, consistent with instrumental case study methodology, it synthesises information from trials including various clinical therapies, sponsored by different entities, and employing diverse methods. However, as all the case trials analysed in this case study were derived from a single clinical care setting involving trials of IMPs, one could consequently argue that the extent of the transferability of the findings are to trials of IMPs, which be considered as a limitation of this study. Previous research, however, has examined the utilisation of various data sources in trials; and these investigations too have primarily focused on a single large trial or trials conducted within a particular clinical specialisation such as cancer care (Donovan *et al.* 2002, Howard *et al.* 2009, Paramasivan *et al.* 2011, Shilling *et al.* 2011, Hamilton *et al.* 2013, Warnock *et al.* 2019, Byrne *et al.* 2020, McDermott *et al.* 2021). This study identified that although variations existed in the case trials, the issues surrounding the utility of CCPs for trial recruitment were common. Hence, the findings derived from this study can be deemed relevant for the purpose of designing or evaluating the use of CCPs during the recruitment process for future trials.

One of the key strengths of this study lies in its use of a case study methodology wherein multiple sources of data were used for analysis and corroboration (Merriam 2001, Baxter & Jack 2008, Starman 2013, Thomas 2021). While interviews served as the primary source of information for answering the research question (Bowen 2009, Jamshed 2014), the inclusion of document analysis and observations further enhanced the understanding of the contexts (Mtisi 2022) in which the case trials were taking place, including the disease area, current treatment plans, and the recruitment processes involved in each trial. As a result, I have gained a comprehensive understanding of the utility of CCPs for recruitment processes in the context of these trials while conducting interviews with study participants. This meant that I was able to ask relevant questions based on the trial and the aligned CCPs to gather information on if and how CCPs were being used for recruitment in each of the case trials. Nevertheless, a notable limitation of this study was the limited availability of observational data, which only comprised the examination of recruiting activities in two trials over a span of two days. This limitation arose as a consequence of the ongoing pandemic situation at the time of data collection, which necessitated the modification of the collection of observational data to what was feasible at the time.

However, a notable limitation of this study was the limited availability of patient study participants for interviews. Despite there being two patient study participants only, their insights were invaluable in understanding the utility of CCPs from a healthcare user/patient perspective in contrast to clinician's perspective. In particular, the data provided by these participants offered a detailed and nuanced understanding of the differences between receiving care within a CCP and when in a parallel pathway that was specific to activities related to recruitment. The limited number of patient participants supports the need for future studies to include additional patient participants to gain a more focused understanding of the experiences and needs of patients in relation to the research phenomenon This is important as the participation of patients is essential for the trial's progression, and their experiences of the recruitment process can potentially influence their decision-making on whether or not to take part in the trial. Similarly, there were limitations in the availability of observational data, which examined recruiting activities in two trials over two days. Both of these limitations arose as a consequence of the ongoing pandemic situation

at the time of data collection, (see section 5.4 for impact of COVID-19) which necessitated the modification of the collection of data to what was feasible at the time.

Despite the limitation outlined above, I believe that based on the approach of sample sufficiency and information power (Malterud *et al.* 2016) adopted for this study, a sample of 25 interviews, trial documents from 7 trials, and a period of 9 hours of observations was sufficient to fulfil the aim of the study. The data from the multiple sources were triangulated to inform exploration and understanding of the utility of CCPs during trial recruitment (Thomas 2021). Further, the study participants included various stakeholder types who were consultants, doctors, clinical nurses, research nurses, pharmacists, and trial coordinators. Hence, the utility of CCPs for recruitment was informed by the diversity of perspectives and the diversity of sources, meaning the phenomenon under examination was viewed from different angles rather than from a single one (Thomas 2021). The use of a triangulation approach enhanced the confirmability of findings of this study because the findings were informed by the collation of data from a variety of sources and perspectives (Merriam 2001, Thomas 2021).

The study's choice of RTA (Braun & Clarke 2022) for data analysis is a notable strength, as it allowed for an iterative inductive process that built on the findings. While researcher subjectivity can be viewed as a limitation in some forms of qualitative research (Riley *et al.* 2003), the RTA method (Braun & Clarke 2022) leverages it as a strength. Therefore, transparency was achieved by openly communicating my positionality and reflections during the analysis. Additionally, NVivo software (version R1) was used to organise, code, and facilitate analysis of the large amount of data collected, in a well-organised and transparent manner.

7.7 Chapter Summary

This chapter discussed the findings derived from the case study. The research findings were also discussed in the context of previous literature relating to

recruitment-related issues; however, it was not entirely clear from previous studies whether CCPs were being used or for what phase(s) of recruitment they were being used for. For this reason, the study reported in this thesis is one of the seminal efforts in understanding the contexts in which trial recruitment occurs, i.e., the utility of CCPs. Based on the findings identified in this case study, the next and final Chapter of this thesis, Chapter 8, provides practice and research recommendations, and concludes the thesis.

Chapter 8: Recommendations and conclusion to thesis

8.1 Introduction

The findings identified and discussed in this study, albeit unique in their own right, contribute to the existing body of literature on trial recruitment by enhancing the understanding of the extant utility of CCPs for trial recruitment. This study makes a valuable contribution to the field of trials methodological research by offering a novel perspective on the challenges of recruitment and the use of CCPs. Further, the findings from this study re-emphasise that trial recruitment is a complex process occurring through various phases from identification through to randomisation. Therefore, researchers should aim to identify and address specific challenges occurring in each phase rather than trying to tackle the issue of recruitment as a whole. This approach can help improve the efficiency of trial recruitment in its entirety. Hence, based on the findings of this study and discussion of the findings within the context of the broader literature, this chapter now presents recommendations for practice, as well as recommendations for future methodological research. The chapter also presents a conclusion to this thesis.

8.2 Recommendations for practice relating to how CCPs can be enhanced to facilitate trial recruitment

- Based on the findings of this PhD, the optimal moments for recruitment occur during the trial initiation process. This includes the identification of potential trial participants, pre-screening, and the introduction of the trial to potential participants. The pre-screening phase, in particular, was identified as one of the most critical moments that aligns with the CCP that leads to successful recruitment. Therefore, it is recommended that the CCP provides an ideal platform for pre-screening and the use of CCPs should be maximised for this critical recruitment process.

- For a successful completion of pre-screening activity, it is recommended that the depth of patient information captured by the ongoing implementation of a robust Electronic Healthcare Records (EHR) system is developed. This will allow for better characterisation of patients receiving care through CCPs, which can facilitate the efficient assessment of assessment of eligibility for trial participation by way of cross matching inclusion and exclusion criteria required by trial protocols.

- It is recommended that trial protocol designers reduce the complexities of trial protocol criteria by developing realistic eligibility criteria matched to existing CCPs where possible. Trial protocol designers should endeavour to make screening procedures simple and easy to implement by aligning screening procedures with that of standard care and limiting unnecessary or redundant tasks that create additional workload for clinicians.

- To complete recruitment related activities in a timely manner, it is recommended that researchers are supported with dedicated research nurses, funding and a dedicated infrastructure which are considered pivotal to the smooth running of recruitment activities.

- It is recommended that protected time is provided to consultants, doctors, and clinical nurses for the conduct of trial recruitment. However, it will require discussion among trialists, clinicians, and hospital management at the local level to determine how this can be facilitated. Further strategies to assist local level plans could be facilitated by national healthcare governing bodies.

- It is recommended that hospital management and healthcare governing bodies consider ways to implement measures to appoint and retain adequate clinician-academics. This will ensure that there are sufficient staff with the required competencies, who can contribute to research while also providing alongside clinical care services.

- In order to comprehensively integrate research into clinical practice, it is recommended that trial-related material be disseminated to multi-disciplinary

teams (MDTs) through concise training sessions or email correspondence. This will increase awareness among clinical care staff of the availability of trials open to recruitment, and in turn, increase the potential for successful trial recruitment. Additionally, it is imperative to provide continual educational sessions to trial teams to keep them up-to-date with current knowledge pertaining to disease areas and novel trial approaches. This will help optimise patient care services through both clinical care and clinical research.

- It is recommended that a supportive regulatory system be put in place to meet the demands of trial recruitment in the context of CCPs to enhance the reputation of Ireland as an attractive location for research. This will ensure that recruitment processes are initiated within the clinical setting as per anticipated timelines. By doing so, it will enhance the opportunities for Ireland to become a preferred location for multinational clinical trials.

8.3 Recommendations for future methodological research

- It is recommended that facilitators and barriers to trial recruitment specific to the phase of recruitment and the contexts in which they are occurring are reported in future publications as this would advance our knowledge on specific issues associated with recruitment and how CCPs facilitate trial recruitment processes. It is recommended that further methodological work including qualitative and mixed methods research is carried out to better understand trial recruitment phases from patient identification to randomisation and ascertain if and how CCPs were being used in different clinical care settings.

- There is a need for a repository of research including resultant evidence relating to recruitment occurring within the context of CCPs as the term ‘Clinical Care Pathways’ is rarely used within trial recruitment literature; hence it is challenging for researchers to source information on how researchers use CCPs to enhance trial recruitment. Therefore, it is recommended that a research domain titled ‘utility of clinical care pathways for recruitment’ is included as one of the research

domains in the trials methodology research database ORRCA (Online Resource for Research in Clinical triAls).

- This research study gathered perspectives from individuals who were directly involved in trial recruitment procedures. However, to enhance the integration of clinical trials within CCPs it is crucial also to gain insights from frontline clinical care staff who are not involved in clinical trials. This approach would enable a more comprehensive understanding of how both clinical care and clinical trial activities are perceived and why certain individuals may not participate in trial research. Such information may help promote greater participation in clinical trials and improve the overall efficiency of utilising CCPs for trial recruitment. Thus, it is recommended that further qualitative research with clinical healthcare staff working in trial active areas of the hospital is undertaken to explore and understand their views and experiences, including barriers and facilitators, to trial recruitment.

- The findings of this study have highlighted that pre-screening and screening activities are the most time-consuming aspects of trial recruitment phases. As such, it is imperative to conduct an in-depth investigation to quantify the amount of time and resources researchers devote to these activities and identify targeted solutions for delays occurring during these phases of trial recruitment. By doing so, researchers can reduce the overall burden of pre-screening and screening activities and streamline the recruitment process, ultimately improving trial recruitment efficiency by reducing delays to patient recruitment.

- The investigator study participants reported no difficulties in identifying suitable patients for the case trials. According to investigators, patients were selected from a pre-existing cohort of individuals who were already receiving care through CCPs. More research, an evaluation of best practices into the methods of identifying patients for the pre-screening phase may yield additional insights into how best to identify potential participants for clinical trial recruitment.

8.4 Dissemination plans

The dissemination of research findings is crucial for scientific progress and for the advancement in the field of clinical trial methodology. The dissemination of my doctoral research has been initiated and is presently ongoing. As part of the plan for dissemination, the following research outputs from my PhD have been presented:

- Oral Presentation titled ‘Embedding trials in routine healthcare’ at the 4th HRB-TMRN Trial Methodology Symposium, Methodological Innovations in randomised trials, Salthill Hotel, Dublin, October 11th, 2018.
- Poster presentation titled ‘A qualitative Case study exploring recruitment to randomised trials within clinical care pathways’ on May 13th, 2019, marking the International Clinical Trials Day at Dublin hosted by Health Research Board Clinical Research Coordination Ireland (HRB CRCI) (currently HRB-National Clinical Trials Office (NTCO). The theme of the event was 'Enabling Ireland as a Clinical Research Leader'.
- Oral Presentation titled ‘Exploring recruitment to randomised trials within current clinical care pathways: An overview’ at the Trials Methodology Research Partnership (TMRP) Trial Conduct Working Group (UK and Ireland) meeting on 27th April 2021.
- Awarded Bursary from European Institute of Innovation and Technology (EIT) Health – UK & Ireland to participate in the School of Nursing and Midwifery Trinity Health and Education Conference in March 2020 in response to abstract on the summary of service that will be developed as part of this PhD research.
- Research presentation on the topic of this PhD titled ‘Exploring recruitment to randomised clinical trials within current clinical care pathways’ on Research Support Education Days (RSED) in the TCD School of Nursing and Midwifery annually from 2019- 2023.

Plans for future dissemination activity include:

- Plan to meet health care professionals and clinical research staff that supported this study at a monthly research journal club meeting in April 2024.

- Planned Poster presentation on the findings of this PhD titled ‘Enhancing Recruitment to Randomised Trials: The Role of Clinical Care Pathways’ at the Annual International Clinical Trials Day (ICTD) hosted by HRB-NTCO in Dublin on 9th May 2024.
- Publication of a research manuscript in HRB Open Research titled ‘Using clinical care pathways for trial recruitment: findings from a qualitative case study’ in August 2024
- Planned Oral presentation on the findings of this PhD titled ‘Enhancing Recruitment to Randomised Trials: The Role of Clinical Care Pathways’ at the 7th International Clinical Trials Methodology Conference, Edinburgh, UK, 30th September – 3rd October 2024.
- A publication in the Contemporary Clinical Trials journal on the ‘Importance of Trials Methodology Research and ongoing methodological initiatives’ planned for October 2024.
- A publication in the International Journal of Qualitative Methods titled ‘Application of reflexive thematic analysis in a single instrumental case study’ planned for December 2024.
- A publication in the PLOS One journal titled ‘The Concept Analysis of Clinical Care Pathways using the Penrod and Hupcey method’ planned for February 2025.
- Planned Oral or Poster presentation on the findings of this PhD titled ‘Enhancing Recruitment to Randomised Trials: The Role of Clinical Care Pathways’ at the Annual International Society for clinical trials meeting in May 2025.

8.5 Conclusion to thesis

This research study set out to address the top unanswered methodological research question as determined by the PRioRiTy study (Healy *et al.* 2018) with slight modifications to explore and understand if and how CCPs were being used for recruitment to RCTs. This issue was recognised as one of most important uncertainties for trial recruitment by stakeholders who involved PIs, researchers, funders, nurses, clinicians, and members of the public. However, there was a lack of

evidence of the use of CCPs for trial recruitment in previous literature. As a result, this study aimed to discover whether CCPs were being utilised for trial recruitment and, if so, how they were being used. To address the study aim, first, a concept analysis based on Penrod & Hupcey's (2005) method was completed to understand the meaning of CCPs and to construct a theoretical definition of CCP for operational use in the study.

The findings of this study, which employed a qualitative case study methodology, demonstrate that the utility of CCPs converged and diverged throughout the stages of the recruitment period. CCPs were used during the initial phases of recruitment namely for identification, pre-screening and for introducing the trial information to potential trial participants. However, a divergence from CCPs was identified from the informed consent process onwards because patients were no longer within the CCP. Instead, they attended a dedicated research facility and encountered designated trials personnel who took responsibility for trial recruitment under the leadership of a consultant PI who had dual responsibilities of clinical care and trial conduct.

These findings were represented under four themes. The first theme, 'CCPs as a conduit for initiating recruitment', delved into how CCPs acted as a conduit during the initial phases of recruitment. The second theme, 'A parallel pathway approach for trial recruitment', discussed how trial recruitment processes diverged from CCPs from the timepoint of holding informed consent discussions. The third theme, 'Complexities of recruitment - an issue beyond CCPs', highlighted the challenges in the optimal utilisation of CCPs, while sourcing eligibility data, duplicating clinical procedures, and aligning protocol plans with CCP plans. Finally, the fourth theme, 'Factors affecting trial recruitment within CCPs', highlighted factors hindering trial recruitment, such as the prioritisation of clinical workload, lack of funding and recognition, and regulatory and governance issues. This theme also highlighted key factors enabling recruitment, including PI leadership, committed research nurses, teamwork, and communication.

The discussion of the findings was conducted in the context of existing literature, the meaning of recruitment (Chapter 2) and the definition of the concept of CCPs (Chapter 3). Nevertheless, it has been observed that the trial recruitment processes described in the literature need more clarity. Many researchers tend to address the

topic of recruitment as a whole rather than focusing on specific phases of recruitment. Consequently, it becomes difficult to determine whether CCPs were being utilised in studies that discuss recruitment issues. Therefore, drawing from the understandings obtained from this case study, recommendations for practice and recommendations for further methodological research were provided. The key factors to optimise the utility of CCPs for trial recruitment in clinical practice include accelerating the establishment of a nationwide healthcare records system to streamline the acquisition of patient data for trial eligibility, increasing the appointment of clinician academics and ensuring protected research time for PIs and clinical nurses. Further, facilitating funding mechanisms and enhancing the overall governance and infrastructural supports are vital for the sustainability of trials recruiting within CCPs.

In conclusion, this doctoral work has demonstrated that CCPs can be used for trial initiation, while subsequent trial recruitment phases diverge from CCPs to a parallel pathway from the point of informed consent. The divergence to a parallel pathway was viewed as improving the recruitment process, in which the trial team had focused attention on trial patients, as evidenced by a purpose-built infrastructure, focused care away from the busy clinical care environment, and timely completion of eligibility assessments as required by the trial protocols.

8.6 Personal Reflection

"In the midst of chaos, there is also opportunity"- Sun-Tzu, The Art of War.

Embarking on a PhD journey is a monumental undertaking, even in the best of circumstances. It demands an unwavering commitment, navigating personal and professional challenges that are, at times, beyond one's control. For me, this odyssey was uniquely shaped by the unforeseen challenges brought forth by the global pandemic, transforming an already arduous journey into a saga of resilience and adaptation.

In March 2020, following the acquisition of necessary permissions, including ethical approval, a surge in the number of cases of the Corona Virus Disease 2019 (COVID-19) occurred in Ireland. As a result, many of the routine health care services were de-prioritised or cancelled, for example cancellations of elective surgical procedures and screening services including cancer and infectious diseases. Government rules on travel restrictions additionally prevented some patients from attending their routine clinical appointments. The utilisation of CCPs was further reduced due to nationwide public health emergency measures which led to clinic closures, lockdowns, stay at home orders, and quarantine requirements. This impact of COVID-19 on service access and provision are widely acknowledged. For example, according to a systematic review by Moynihan *et al.* (2021), global utilisation of healthcare services was reduced by one-third during the pandemic when compared to pre-pandemic periods. The situation at the case study setting was similar, where staff and resources were allocated to essential services that focused on minimising mortality during the healthcare crisis.

This change in prioritisation of healthcare also directly impacted the conduct of clinical research leading to a significant drop in recruitment to clinical trials where some trials were paused, and no new trials were started. This diminished the availability of participants being recruited to clinical trials at the case study setting. The research staff in the hospital were also working remotely to minimise the spread of COVID-19 virus and clinical studies were limited to only those critical for patients' health such as ongoing oncology treatment or studies involving novel interventions for combating COVID-19 infections. To progress my study, two activities needed to occur at the clinical setting: clinical care delivery and clinical trial conduct. However, due to the pandemic, there was a change in the way care was delivered, with some patients able to have consultations remotely (for example, via telephone consultation) to obtain assessments or refill prescriptions. Patients who were taking medications as part of a clinical trial had the option of obtaining them by a mail delivery service. We were on the brink of a socially isolated world in which normal interactions in real-life settings suddenly disappeared. It was also difficult to predict if clinical care and clinical trial activities would resemble pre-pandemic periods when life returned to normal. Moreover, the restrictions and lockdowns continued throughout 2020 due to the emergence of second and third waves of COVID-19

infections. This led to a ten-month delay in accessing the case study setting and impacted the accessibility and feasibility of the selection of the case study subject (randomised trials), including attending the site for observational data collection.

In December 2020, the COVID-19 vaccine became available in Ireland, and a mass immunisation campaign commenced. This boosted the confidence and safety of healthcare professionals and patients, allowing the clinical setting care systems and processes to gradually return to normal with staff and patients concurrently adhering to personal protection guidance (e.g., hand sanitation and wearing protective face coverings) and social distancing where feasible. This eventually improved the prospects of the availability of case trials within the study setting in 2021.

As the world edged towards normalcy, I found myself at the heart of the clinical setting, collecting data that would shape the narrative of my PhD study. I purposively included all trials (n=7) open to recruitment in my study, a decision influenced by their relevance to my research focus and the urgency imposed by the lingering uncertainty due to the pandemic. The selected trials played a crucial role in providing meaningful insights aligned with the core objectives of my PhD. The resilience of frontline workers and the willingness of busy healthcare professionals and patients to contribute to my research in the midst of their demanding lives left an indelible mark on my journey. The timing of data collection coincided with a profound personal transition, as I embraced the role of mothering my second baby. Balancing the demands of a newborn and a toddler with the pressures of completing a PhD in its final year was a delicate dance, but one that sculpted a more resilient version of myself.

The undertaking of a qualitative research study was a transformative experience, where I evolved being a novice qualitative researcher to honing qualitative research skills through a series of intensive training sessions. These training sessions included attending a two-day course on qualitative data analysis software training provided by experienced NVivo consultants, a Qualitative Research method training course from University College London, and webinars by authors of reflexive thematic analysis conducted by Virginia Braun and Victoria Clarke, hosted by Sage Publishing to name a few.

During the data analysis phase, I immersed myself in the wealth of collected data. As I delved deeper into the data, my preconceived assumptions underwent a metamorphosis. What initially seemed like distinct trials and diverse disease areas faded into a common thread—the utility of CCPs. The richness of the data revealed shared challenges across trials, transcending their individual differences. This experience was a revelation of what true immersion in data felt like, and it completely reshaped my perspective. It paved the way for a meaningful exploration of the utility of CCPs.

In retrospect, my PhD journey, amplified by the challenges of a global crisis, has been a testament to resilience, adaptability, and the unwavering spirit of discovery. As I navigate the final stretches, I carry with me not just the academic insights but a profound appreciation for the human spirit that propels research forward, even in the face of adversity.

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Appendices

Appendix 1: Priority Study and the top ten questions

Question 1
How can randomised trials become part of routine care and best utilise current clinical care pathways?
Question 2
What information should trialists communicate to members of the public who are being invited to take part in a randomised trial in order to improve recruitment to the trial?
Question 3
Does patient/public involvement in planning a randomised trial improve recruitment?
Question 4
What are the best approaches for designing and delivering information to members of the public who are invited to take part in a randomised trial?
Question 5
What are the barriers and enablers for clinicians/ healthcare professionals in helping conduct randomised trials?
Question 6
What are the key motivators influencing members of the public's decisions to take part in a randomised trial?
Question 7
What are the best approaches to ensure inclusion and participation of under-represented or vulnerable groups in randomised trials?
Question 8
What are the best ways to predict recruitment rates to a randomised trial and what impact do such predictions have on recruitment?
Question 9
What are the best approaches to optimise the informed consent process when recruiting participants to randomised trials?
Question 10
What are the advantages and disadvantages to using technology during the recruitment process?
#trialmethodology
http://priorityresearch.ie
James Lind Alliance
Priority Setting Partnerships
Health Research Board
TMRN
PRioRiTy
Prioritising Recruitment in Randomised Trials

Appendix 2: Data Extraction Form

Reference	Title	Year	Journal/conference abstract	Discipline/Disease area	Country	Aim/objective of the study	Epistemological principle (definitions or descriptions)	
							Is the concept clearly defined?	Is it well differentiated from other concepts?

Pragmatic Principle(how its operationalised)		Linguistic principle		Logical priniciple		Notes
Is it useful for clinical pratice	Is it useful for research	Is the concept used consistently and appropriately within the context?	Quant measures/Qual measures	Does the concept hold its **boundaries**?	Has it been theoretically integrated with other concepts?	

Appendix 3: Example from the Data extraction form

Reference	Title	Year	Journal/conference abstract	Discipline/Disease area	Country	Aim/objective of the study
Abou-Haidar *et al* (2014)	**Enhanced recovery pathway for radical prostatectomy: Implementation and evaluation in a universal healthcare system**	2014	Canadian Urological Association Journal	Oncology/Prostate cancer	Canada	The objective of this study was to describe the creation and implementation of the pathway and estimate the impact of its introduction on LOS, morbidity, and readmissions.

Epistemological principle(definitions or descriptions)		Pragmatic Principle(how its operationalised)	
Is the concept clearly defined?	Is it well differentiated from other concepts?	Is it useful for clinical pratice?	Is it useful for research?
Yes. Enhanced recovery after surgery pathways (ERPs) are tools that have been implemented globally to provide evidence-based decision-making guidelines. The goal is to reduce variability in patient care while maintaining quality. Pathways also make it easier to evaluate outcomes, monitor standards and costs, and improve teamwork by involving all members of the multidisciplinary team.	Yes	Yes. The pathway was focussed on goals for early recovery such as improved nutrition, early removal of drains, better pain management and to align expectations between patients, nurses and surgeons through education. The development of each step of the pathway involved teamwork with clinical experts who reviewed best practices on each step of patient care. The pathway served as education material, a standard medical order and nursing plan for each day of hospital stay.	MDT consists of- The multidisciplinary ERP group included surgeons, anesthesiologists, nurses, nutritionists, physiotherapists, pharmacists, and a medical librarian to help with literature searches for pathway development.

Linguistic principle		Logical priniciple		Notes
Is the concept used consistently and appropriately within the context?	Quant measures/Qual measures	Does the concept hold its boundaries?	Has it been theoretically integrated with other concepts?	
The clinical care pathway (CCP) is called the Enhanced Recovery Pathway(ERP). The ERP was also referred to as the care plan mulitple times in the paper.The care plan was used as an alterantive phrase and maintined its meaning throughout the paper.	Quantitative Retrospective chart analysis of patients undergoing RP before and after implementation of Enhanced recovery pathway.	Yes. CCP also called ERP i.e enhanced recovery pathway.	No. The concept maintains its boundaries.	Study similar to other surgical CCPs. Uses ERAS pathway that consists of surgical procedure from preop to post op. Focuses outcome reduction in LOS.

Appendix 4: Observation Chart

Observation Chart	
Date: Location: Clinical Trial Name:	Start time: Finish Time:
Observations Physical setting: Participants: Activities and Interactions: Conversations: Subtle factors: Researcher's behaviour:	

Reflections and Interpretations

Observation chart – Example

Observation Chart	
Date: 10 March 2021	Start time: 8. 45 am
Location: [redacted] department	Finish time: 9. 45 am
Clinical Trial Name: T1	

Observations on setting prior to informed consent process

Observations included the physical setting in detail.

Participants: PI and clinical nurse

Activities and Interactions: Brief introductions

Conversations: Brief introductions

Subtle factors: Very friendly staff. PI seemed overwhelmed with tasks yet was very accommodating. I was informed that more than 80 percent of patients are returning to their routine care after a long pause due to Covid restrictions from the following week and that I was lucky to be in the setting because it was still very quiet, very few people. I would have seen a different scene had this observation visit occurred next month.

Researcher's behaviour: Thrilled and excited for the opportunity, using all my senses to capture every moment in full, however the place was very quiet. It was a long wait, the scheduled time for observation has passed. I kept journalling my thoughts as I was at the setting.

Physical setting: Explained in detail below.

I reached the [redacted] department about 15 minutes early to the scheduled observation. I was here to observe the informed consent process of potential trial participants with prior permissions from PI. It was the very first time I was here, yet I had no difficulty in figuring out the department as the navigation signs to the department were all clearly displayed. However, everybody including myself looked very strange as we seemed to have very less interactions; I did not know anyone there and we were all covered up with masks and face shields making it even difficult to recognise if anyone looked happy or sad. I couldn't recognise anyone's facial reactions. No one seemed to care.

I entered the reception area and a waiting area with about 20 seats however, due to social distancing rules in place the chairs were marked with social distancing tapes allowing fewer seats to be occupied. All the floors, doors, glass shields at the reception counters were all marked with markings related to safety and navigation routes. Hand sanitizers were available at all entrances and use of mandatory face coverings were in place. I was wearing an FFP2 mask and a face shield for added protection and I also made sure to keep my hands sanitised every often. I felt being suffocated wearing them constantly, however this soon became normal for me.

The waiting area was prepared for a socially distanced seating. It was a rather quiet location, very well-lit and ventilated, neat and organised. There was no one at the setting except for the receptionist at the desk and myself so I didn't have to wait to introduce myself and inform them why I was there. The receptionist guided me then to the PI's consultation suite. I quickly exchanged greetings with the PI, as the PI seemed very busy as the PI was preparing for another meeting before the scheduled patient consultations, so the PI introduced me to the clinical nurse who was at the desk doing some routine

work. I introduced myself to the nurse and explained the purpose of my observation, which was to gather an in depth understanding of how recruitment processes took place at the clinical setting and that I didn't need any personal or trial specific data, I also made it clear that the focus on my observation was not on the specific individuals recruiting patients or potential patients but rather the recruitment process that took place in the setting. The nurse was also very accommodating and helpful. I was instructed to come back to the setting in 30 mins when the nurse would start work related to the trial. I went back to the waiting area where I made some personal reflections and expectations for the day.

Appendix 5: Interview guide used for pilot interviews.

Introduction:

- Welcome and Introductions
- Go through participant information leaflet to ensure participant's understanding of research
- Clarify any questions
- Obtain written consent and permission to audio record conversation

Interview with trial recruiters (Investigators, Research Nurses or Research Coordinators)

Researcher:

Could you explain the trial recruitment process within your routine CCP? Please give me as much detail as possible as all information is valuable.

Participant response

Questions and prompts for further clarification:

- Does your care pathway provide sufficient support for timely recruitment to clinical trials? Could you tell me more about…
- Could you give me more details on recruitment challenges you've had?
- Do you think these challenges can be overcome?
- What do you think can be improved?
- Do you want to add anything more?

Interview with trial participants/patients

Researcher:

Would you like to share your experience of accessing this clinical trial while you are receiving your routine clinical care here?

Participant response

Questions and prompts for further clarification:

- What within the clinical care has helped you to take part in the clinical trial?
- Do you find any challenges?
- Do you have any suggestions for improvement?
- Do you have any suggestions for using other approaches to make future patients/ participants aware of the opportunity to participate in clinical trials?
- Do you want to add anything more?

Appendix 6: Interview guide for study participants

Interview Guide

Step 1: Introductions (clarify confidentiality, anonymity, permission for recording o be obtained)

Step 2: Broad warm up questions linked to my specific aims and objectives

Step 3: Dive deeper, probes, follow ups, demonstrate understanding and sensitivity to responses

Step 4: Wrap up and closing: gradual return to daily conversation and thanking participants for their time

Topics to be covered for each interview/ question to be framed based on relevance and role of the participant

- Introduction of role within clinical care/clinical trial
- Brief description of CCP involved
- Use of CCP for recruitment explored (from identification to randomisation)
- Facilitators and barriers for each step in the recruitment process above to be explored
- Other facilitators and challenges to recruitment to RCTs within CCPs
- Suggestions/ perspectives on what needs to change so trials can be closely aligned within current CCPs.

Sample Interview questions to understand the CCP involved

- To set the context for this interview, could you please describe your role as a healthcare provider (as an cancer nurse for example) and the care setting in which you work (cancer care setting)?
- How are patients diagnosed with X disease condition normally cared for? / What is the usual care pathway for these individuals?
- Where in the CCP is trial introduced to the patient (example, at the point of diagnosis of the disease, during surgery, advanced disease stage etc)

Sample questions to understand the use of CCPs for recruitment processes

- How are trial participants for the X clinical trial identified? Could you please provide me with an example of the selection process? (gather facilitators and barriers for this step)
- could you tell me about how you approach individuals to take part in the trial – that is, where in their pathway do you provide the trial information? (gather facilitators and barriers)
- Is it possible that making a decision to take part in the trial could depend on who provides the information within the setting to potential participants, what are your thoughts?
- What are the screening procedures involved in the trial; where in the care pathway do they take place? (gather facilitators and barriers)
- Where does randomisation process take place; how is this completed (facilitators and barriers)
- Have you ever thought that clinical care procedures could have been bit more closely aligned to trial procedures so that there is no overlap of procedures?
- What do you think are the important factors that have supported the recruitment within your CCP? Or in other words what had worked out really well within the pathway that helped recruiting participants?
- What are the challenges you've had in recruiting participants within your care pathway?
- What do you think could be done better to improve recruitment process in your clinical care setting?
- Is there anything else you would like to add?
- Do you have any questions for me?
- Could I come back to you if I have more questions or need further clarifications?

Closing : Thank the participant, switch off the recording

Patient Interviews

Interviews with patients are conducted to gather their perspectives on receiving clinical care and being invited to participate in a trial.

Interview questions

(Introductions, clarifications and obtain consent before interview as previous)

- You've been treated for condition x in clinic y; could you explain what your treatment normally involves? (Probes: where, how, duration, setting such as a busy clinic etc). This is to gather views on normal CCP.
- You were invited to take part in the 'x' trial, could you take me through of how you came to know about the trial.. (gather further probes on positive and negative experiences and their expectations)
- Could you take me through how you decided to take part in the study (previous studies show that people make decisions to take part based on who provides them the information ex- consultant in the clinic vs nurse vs a poster in waiting room etc) (further probes on positives and negatives and expectations)
- Could you tell me if you needed to have tests and procedures to determine if you could be part of the trial?....and if so, what did this involve and how did you feel about this (Go through screening process as per steps involved in the trial protocol- some trials have extensive screening procedures that last for several weeks before they know they could take part or not and some happen within a few days) (Gather positives, negatives, motivators and expectations)
- Gather views on decision to stay in trial despite the possibility of not getting the study medication (randomisation process). What motivates you to be part of the trial despite knowing that you have a 50-50 chance of getting the study medication or the standard treatment.
- What do you think could help future patients receiving clinical care participate in clinical trials?

Conclusion : Clarifications, thank the participant and off the recording.

Appendix 7: Email letter to Principal Investigators of the trials

Dear xxx

My name is Gloria Emmanuel, I am one of the HRB-TMRN trials methodology PhD scholars exploring the topic of how current clinical care pathways are being used for recruitment to randomised trials. This is a qualitative case study which I am currently undertaking for the purpose of my PhD at the School of Nursing and Midwifery at Trinity College Dublin. Prior to undertaking this PhD, I was working as a Clinical Trials Manager, assisting Investigators manage clinical trials projects from start to finish.

Recent evidence suggests that there has been a lack of research on how clinical trials can co-exist with current clinical care pathways. This study is particularly relevant given the efforts of trial methodologists to address under-recruitment to trials, a common problem that is currently causing uncertainty. Overall, this research aims to shed light on this issue and provide insights that can help improve the effectiveness of clinical trials.

I am reaching out to request your support to conduct this study. I have been in contact with [name of the gatekeepers] who have been assisting me in identifying randomised trials open to recruitment. The data collection methods include accessing trial protocols and patient information leaflet to gather recruitment specific information from the trials, conduct nonparticipant observations of activities involved in the recruitment to the trial and conduct interviews with staff recruiting to the trial and patients undergoing recruitment. For further information, please find attached the information sheet and consent form for this study.

I would like to assure you that I do not require any confidential details of the trial for the purposes of my PhD, and the xxx trial is just one of seven trials selected for my study. It would serve as one of the illustrative examples to learn about the utility of clinical care pathways for participant recruitment to these trials and specifically learn about their use, i.e., if they facilitate or hinder trial recruitment activities at [name of the hospital].

If you would be happy for me to include the [name of the trial] for my PhD study, please let me know by emailing me on gemmanue@tcd.ie. I am planning to organise a brief information session for clarifying any aspects of this study following your response to this message.

Thank you for considering my request. If you have any questions or concerns, please do not hesitate to reach out to me.

Kind regards,
Gloria Emmanuel

Appendix 8: Participant Information Leaflet and Consent Forms

PARTICIPANT INFORMATION LEAFLET

An exploration of recruitment to randomised trials within current clinical care pathways

Lead Researcher: Ms. Gloria Emmanuel
School of Nursing & Midwifery
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24 D'olier Street, Dublin 2

Academic Supervisors: Prof Valerie Smith
Prof in Midwifery/Director of Undergraduate Teaching & Learning
School of Nursing & Midwifery
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Prof Martina Hennessy
Assoc Professor of Consultant Medical Education,
School of Medicine
Trinity College Dublin

Dr. Louise Daly
Associate Professor/Head of Discipline for General Nursing
School of Nursing & Midwifery
Trinity College Dublin
24 D'olier Street, Dublin 2

You are being invited to take part in a research study which is being carried out as part of a doctoral study, through the Clinical Research Facility [redacted] Please read the information provided in this leaflet carefully to understand why the research is being done and what it will involve. Please ask any questions you may have about the information provided. Take enough time to decide whether or not you wish to take part in this study.

PART 1 – THE STUDY

Why is this study being done?

Doing research is very important in healthcare as it helps discover better ways to treat people, and to improve how we care for people who are experiencing ill health. People (patients) are often invited to take part in research studies, a process called 'recruitment', when they go to a hospital for treatment; however, in many studies fewer people join the study than is needed, or it can take much longer than expected to recruit enough people into the study. There can be many reasons for this, but sometimes, the reason is not known. Therefore, an understanding of barriers and facilitators to recruitment within usual care is required to make recommendations for change. Improved recruitment helps to deliver efficient clinical trials, thus enhancing the potential for better treatments to reach patients more quickly.

Why am I being asked to take part?

You are invited to take part in this study as you are currently undertaking, recruiting to or taking part in a research study that is a clinical trial.

Do I have to take part? What happens if I say no? Can I withdraw?

Participation in this study is voluntary. If you are a patient a decision not to take part in this study will not affect your medical care. You can change your mind about taking part in the study and opt out at any time even if the study has started. You don't have to give a reason for not taking part or for opting out. If you wish to opt out, please contact Gloria Emmanuel on [redacted] or email at gemmanue@tcd.ie.

How will the study be carried out?

If you decide to take part in the study, I will arrange an interview with a time that is convenient to you. During the interview I will ask you to share your views and experiences of trial recruitment/being recruited to a trial as part of usual clinical care. In addition to the interview I will be making notes of observations related to trial recruitment as well as analysing clinical trial documents such as the study protocol, patient information leaflets and advertisements related to the clinical trial. The interviews will be recorded and transcribed (written on paper). You can receive a paper copy of the transcribed interview by checking the box in the form below. This study is not interested in any healthcare data or any personal details (other than name and contact so as to arrange an interview) of any of the participants, and this information will not be collected as part of the study.

Are there any benefits to me or others if I take part in the study?

By taking part in this study you will help increase understanding on the barriers and facilitators of recruitment as part of care in the hospital setting which will help make recommendations for improving recruitment to trials in the future.

Are there any risks to me or others if I take part in the study?

There are no physical risks or psychological stress to any of the participants in this study.

Will I be told the outcome of the study?

The findings of this study will be published in medical journals and presented at research conferences. You will be provided with the summary of results.

PART 2 – DATA PROTECTION

What information about me (personal data) will be used as part of this study? Will my medical records be accessed?

Your personal data or medical record data is not required and will not be accessed. Information about your participation in this study will be associated by using an identification code and therefore your identity will always remain confidential. Your identity will not appear in any of the results that will be published.

What will happen my personal data?

The information obtained from the interview will not identify you and the original digital recording of the transcript will be erased once the accuracy has been confirmed by you.

Who will access and use my personal data as part of this study?

Only the lead researcher and her research supervisor will have access to your data

Will my personal data be kept confidential? How will my data be kept safe?

All information regarding the participation in this study will be kept strictly confidential. No personal details are required and a number instead of your name will be used to store audio recordings and transcripts. The audio recordings will be deleted once transcription is complete and accuracy has been confirmed. All data collected will be stored in an encrypted password protected device and will always be securely stored in a locked cabinet.

What is the lawful basis to use my personal data?

Only minimum personal data such as your name and contact details are required so that the lead researcher can contact you for verification of transcripts.

What are my rights?

You have the following rights

- Right to access data held: A copy of the interview will be provided after transcription is complete
- Right to restrict the use of the data held: You can withdraw from the study up to any time before the publication of results

- Right to correct inaccuracies: You have the right to correct inaccuracies in the interview transcript
- Right to have information deleted: Your information will be deleted if you chose to withdraw from the study.

PART 3 – COSTS, FUNDING & APPROVAL

Will it cost me anything if I agree to take part?

There are no costs associated with participation in this study.

Who is funding this study? Will the results study be used for commercial purposes?

This is an academic research study funded by the Wellcome-Trust HRB Clinical Research Facility [redacted] and Health Research Board - Trials Methodology Research Network (HRB-TMRN). The results of this study will help researchers to conduct clinical trials more efficiently in Ireland. There are no commercial sponsors or pharmaceutical companies involved in this study.

Has this study been approved by a research ethics committee?

This study is currently being reviewed by the [redacted] (REC). This research study will progress only after a full ethics committee approval is granted.

Where can I get further information?

You can contact Ms. Gloria Emmanuel at [redacted] or email at gemmanue@tcd.ie for any further information or queries in relation to this study.
If you like to speak to my research supervisor please contact Professor Valerie Smith on 01-8964031 or email smithv1@tcd.ie.

Will I be contacted again?

You will not be contacted for further research following the participation in this study. Informal interviews from your own perspective will provide valuable information on how people take part in research studies, leading to a better understanding of how we can improve the way we do research. If you are willing to participate, please contact Ms. Gloria Emmanuel on [redacted] or email at gemmanue@tcd.ie with a day and time that suits you. Thank you for taking time to read the information on this study.

Consent Forms for study participant

CONSENT FORM

An exploration of recruitment to randomised trials within current clinical care pathways

To be completed by the **PARTICIPANT**:

I have read and understood the information leaflet.	YES □	NO □
I have had the opportunity to discuss the study, ask questions about the study and I have received satisfactory answers to all my questions.	YES □	NO □
I have received enough information about this study.	YES □	NO □
I understand that I am free to withdraw from the study at any time without giving a reason and this will not affect my future medical care.	YES □	NO □
I understand that I will be receive an opportunity to review the interview transcripts to confirm accuracy	YES □	NO □
I understand that my participation is anonymous and that no personal details will be reported in any of the publications.	YES □	NO □
I give my free and voluntary consent to participate in this research study	YES □	NO □

I wish to have a copy of my | YES □ | NO □ | interview

Send copy of interview to

_____

Participant's Name (Block Capitals):	
Participant's Signature:	
Date:	

To be completed by the **RESEARCHER**:

I have fully explained the purpose and nature (including benefits and risks) of this study to the participant in a way that he/she could understand. I have invited him/her to ask questions on any aspect of the study.	YES □	NO □
I confirm that I have given a copy of the information leaflet and consent form to the participant.	YES □	NO □

Researcher's Name (Block Capitals):	
Researcher's Title & Qualifications:	

Researcher's Signature:	
Date:	

Consent Forms for PI

CONSENT FORM

An exploration of recruitment to randomised trials within current clinical care pathways

To be completed by the **PRINCIPAL INVESTIGATOR**:

As the PI of the _____ (enter trial name) clinical trial I give permission for the student researcher to include my clinical trial for the investigation on clinical trial recruitment.	YES □	NO □
I give permission for the student researcher to access the clinical trial documents such as the study protocol, patient information leaflet to analyse the recruitment process within the clinical care pathway.	YES □	NO □
I give permission to the student researcher to make observations on recruitment to the trial.	YES □	NO □

PI Name (Block Capitals):	
PI's Signature:	
Date:	
Researcher's Name (Block Capitals):	
Researcher's Signature:	
Date:	

Appendix 9: Email to prospective interview study participants

Dear xxx,
I hope this message finds you well. My name is Gloria Emmanuel, and I am one of the HRB-TMRN trials methodology PhD scholars. I am currently conducting a qualitative case study on how current clinical care pathways are being used for recruitment to randomised trials, for the purpose of my PhD at the School of Nursing and Midwifery at Trinity College Dublin.
I would like to invite you to take part in an interview to share your perspective about how the clinical care pathways are used /helping in the recruitment of xxx trial. I have received permission from your Principal Investigator, who would have informed you about this study. Please find attached the information sheet and consent form for this study. The interviews can be facilitated via zoom, telephone or face to face based on your convenience. If you choose to participate, please contact me by email at gemmanue@tcd.ie or phone xxxx and I am happy to answer any questions you may have. We can then schedule the interview at a time most convenient to you.

Thank you again for your time and consideration and I look forward to hearing from you.

Kind Regards,
Gloria Emmanuel

Appendix 10: Email to prospective patient participants

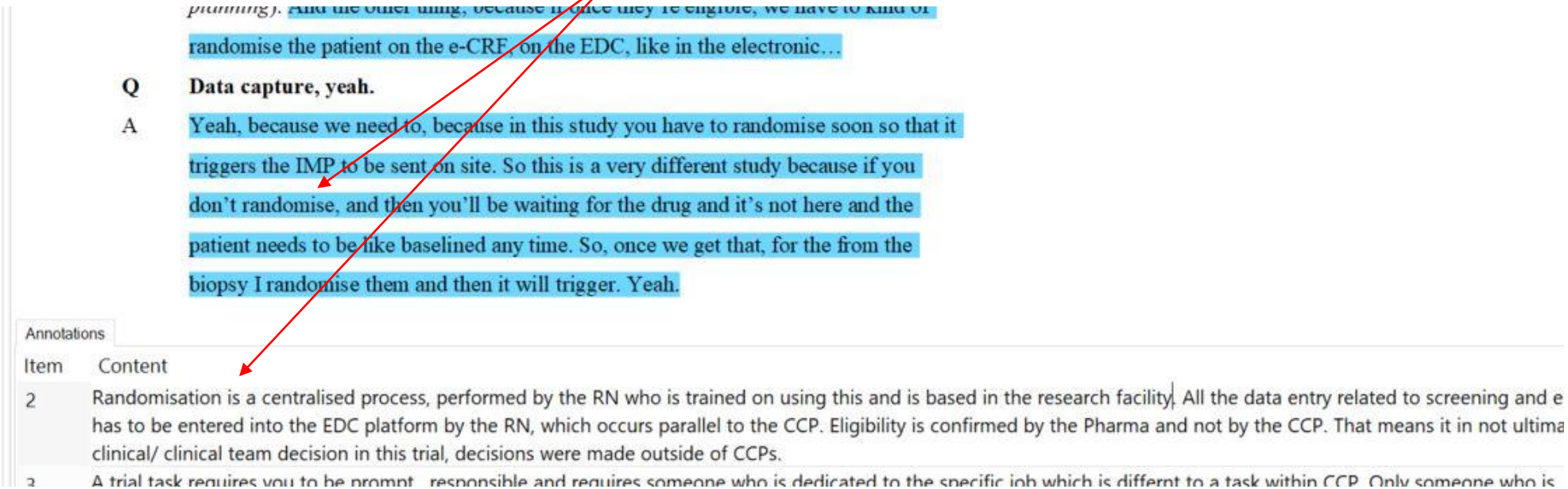
I hope this message finds you well. My name is Gloria Emmanuel, and I am one of the HRB-TMRN trials methodology PhD scholars. I am currently conducting a qualitative case study on how current clinical care pathways are being used for recruitment to randomised trials, for the purpose of my PhD at the School of Nursing and Midwifery at Trinity College Dublin.
You might already be aware of this PhD study as informed by your consultant [Dr. xxx] and I would like to invite you to take part in an interview to share your perspective on how you find being recruited into the xxx trial while receiving care as a patient in this xxx hospital. Please find attached the information sheet and consent form for this study.

The interviews can be facilitated via zoom, telephone or face to face based on your convenience. If you choose to participate, please contact me by email at gemmanue@tcd.ie or phone xxxx and I am happy to answer any questions you may have. We can then schedule the interview at a time most convenient to you.

Thank you again for your time and consideration and I look forward to hearing from you.
Kind Regards,
Gloria Emmanuel

Appendix 11: Example of annotation

Annotation of transcript linked with observations, coding assumptions and researcher's thoughts and ideas contributing to the holistic view of participants' perspective.



planning). And the other thing, because if once they're eligible, we have to kind of

randomise the patient on the e-CRF, on the EDC, like in the electronic…

Q **Data capture, yeah.**

A Yeah, because we need to, because in this study you have to randomise soon so that it triggers the IMP to be sent on site. So this is a very different study because if you don't randomise, and then you'll be waiting for the drug and it's not here and the patient needs to be like baselined any time. So, once we get that, for the from the biopsy I randomise them and then it will trigger. Yeah.

Annotations

Item	Content
2	Randomisation is a centralised process, performed by the RN who is trained on using this and is based in the research facility. All the data entry related to screening and e has to be entered into the EDC platform by the RN, which occurs parallel to the CCP. Eligibility is confirmed by the Pharma and not by the CCP. That means it in not ultima clinical/ clinical team decision in this trial, decisions were made outside of CCPs.
3	A trial task requires you to be prompt , responsible and requires someone who is dedicated to the specific job which is differnt to a task within CCP. Only someone who is

Appendix 12: Systematic data coding

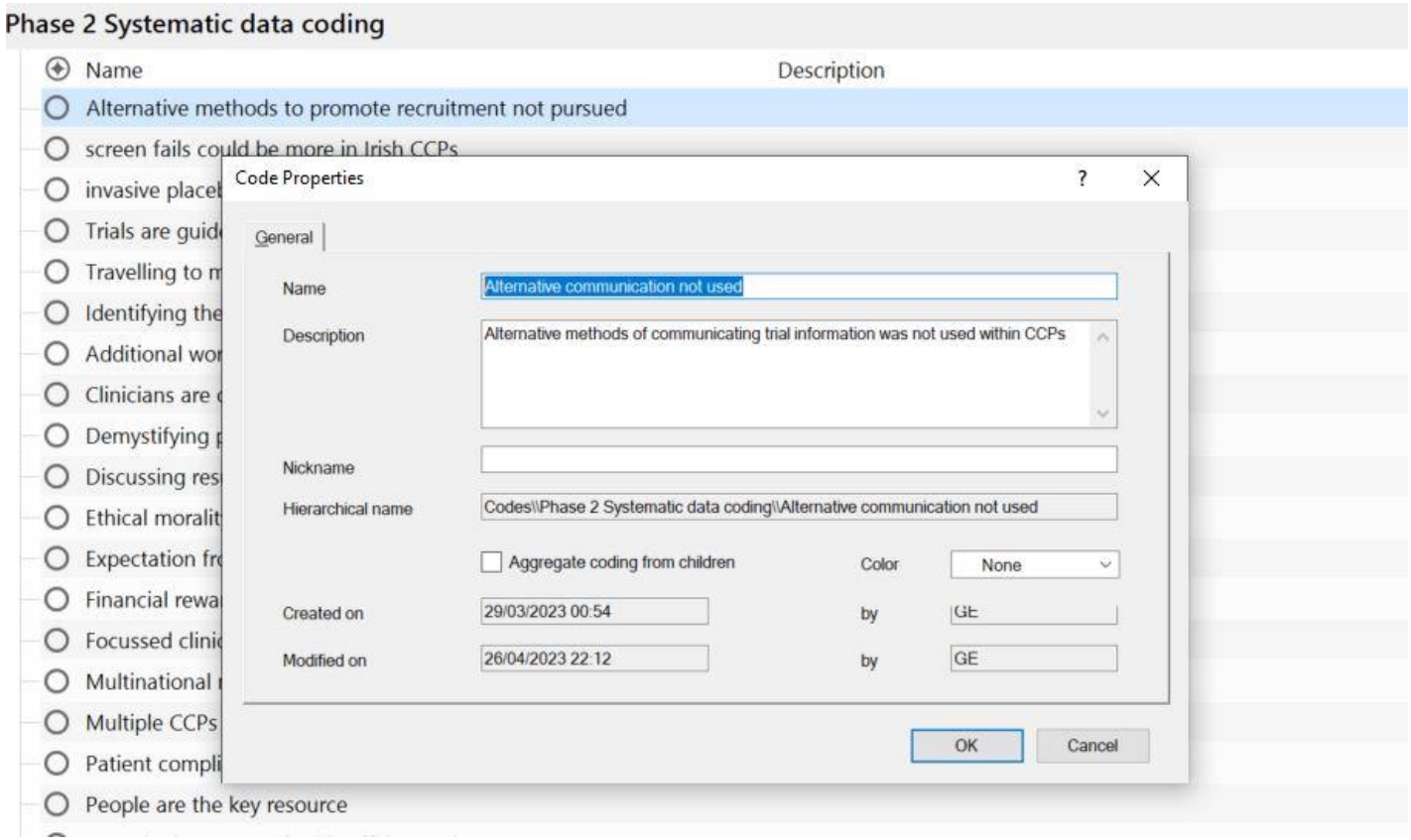
Codes

Code Description

Phase 2 Systematic data coding

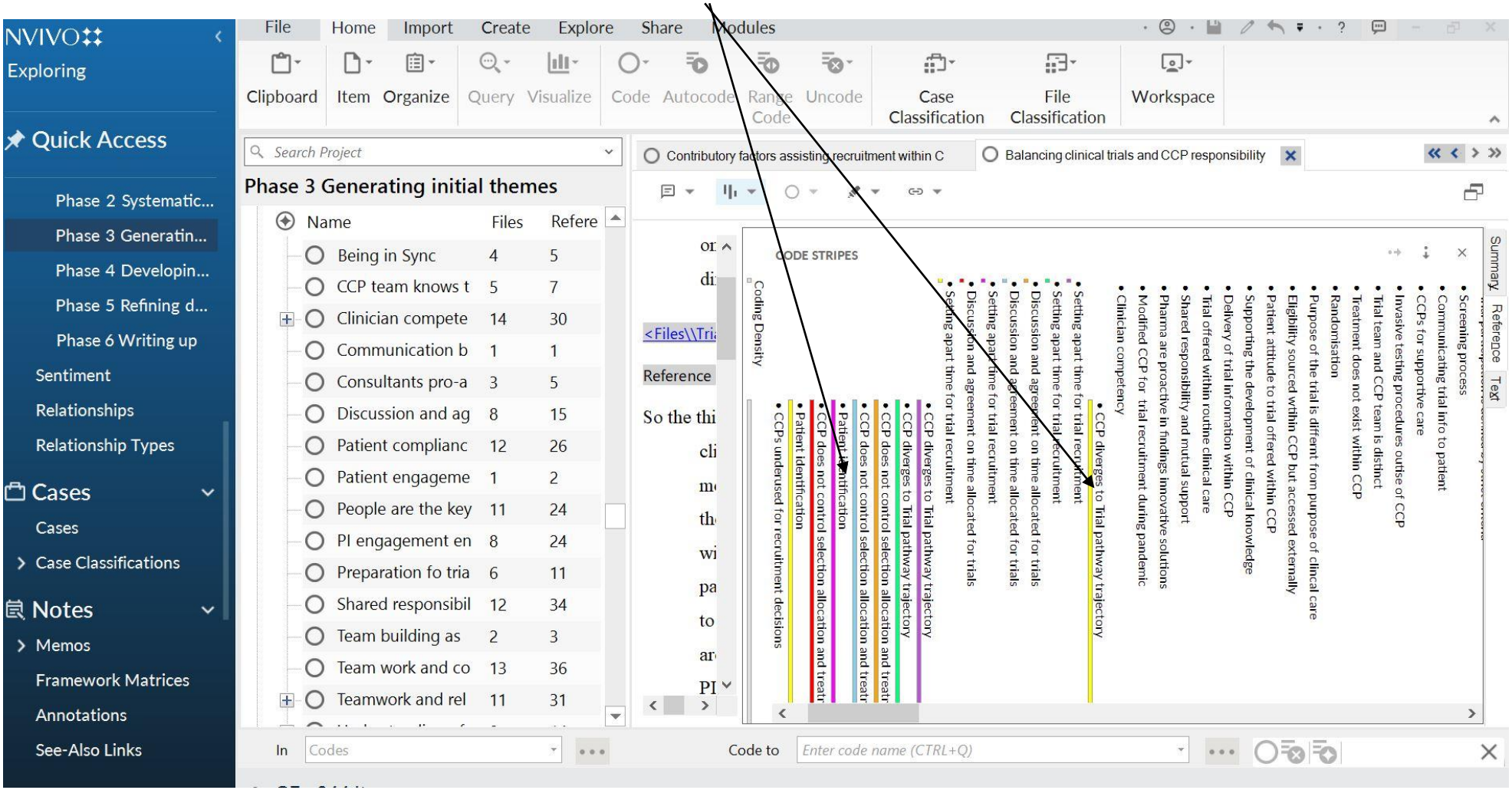
Name	Description	Files	References
Meeting time requirements	Trials have to meet strict time requirements for screening related procedures	4	8
Good funding model	Trial with a good funding model works well	3	5
Modified CCP for trial recruitment during pandemic	Trial recruitment was not affected due to pandemic.	11	24
IMP management outside of CCP	Trial pharmacist manages IMP and hence is not involved in routine CCP care	9	18
Trial pathways reduce burden of caregiving	Trial pathways take over caring of patients from CCP	7	19
Awareness	This code relates to how trial stakeholders become aware of clinical trials	7	20
Being in Sync	This code means that there was agreement and co-ordination between CCP and research te	4	5
Niche clinical area	This code means that because the clinical area niche they have small patient population	2	6
Beyond a clinical hospital	The vision of becoming a clinical academic centre that considers research and routine care	5	6
Increased care and attention	The level of care and attention for trial patient is more than conventional care through CCPs	5	7
Ability to attract trials	The ability of CCPs to attract trials into the setting.	8	15
CCPs for supportive care	Texts related to CCPs where supportive treatment was offered to manage the medical condi	10	17
standard treatments a barrier	Text coded for being excluded of trials beacuse of receiving another type of standard care	3	4
CCP lacks space	Text coded around lack of space within routine CCP for trial activities.	6	11
Privacy and confidentiality	Taking part in trials offered them better privacy ad confidentiality	6	10
Sponsor decision	Sponsor makes final decision on trials recruitment	7	24
Aspirations to take part in the trial	Aspiration by patients to be part of the trial	6	14
RNs are supported by CCP staff	RNs found help by CCP nurses and PI support very valuable mainly in understanding the dis	11	26
Research nurses execute majority of tasks	RNs execute majority of day to day trial tasks.	9	15
Bystander	RNs cannot involve in routine care activities	4	5
Value of Research nurses in recruitment	RNs are applauded for skillls and knowledge regarding trials	5	9
No rewards for research	References stating lack of being recognised or rewarded for doing trials research	7	21
Bad Reputation	References related to bad reputation of conducting trials in Ireland	3	6
Trial processes need to be prompt and efficient	Recruitment processess need to take place quickly and without any delays as this ensures ti	11	30
CCPs underused for recruitment decisions	Recruitment decisions of selecting a participant, randomisation and allocation to treatemnts	10	16
Trial termination	Recruitment cannot take place if trial is terminated based on sponsor decision or regulatory	12	27
CCP diverges to Trial pathway trajectory	Quotes capturing the separation of trials from the routine CCPs	18	50
Trial Protocols inconsiderate about CCP	Protocol designers do not consider practicalities of clinical work in the setting.	10	27
Patient identification	PI needs to know their patients well	21	64

Appendix 13: Example of coding

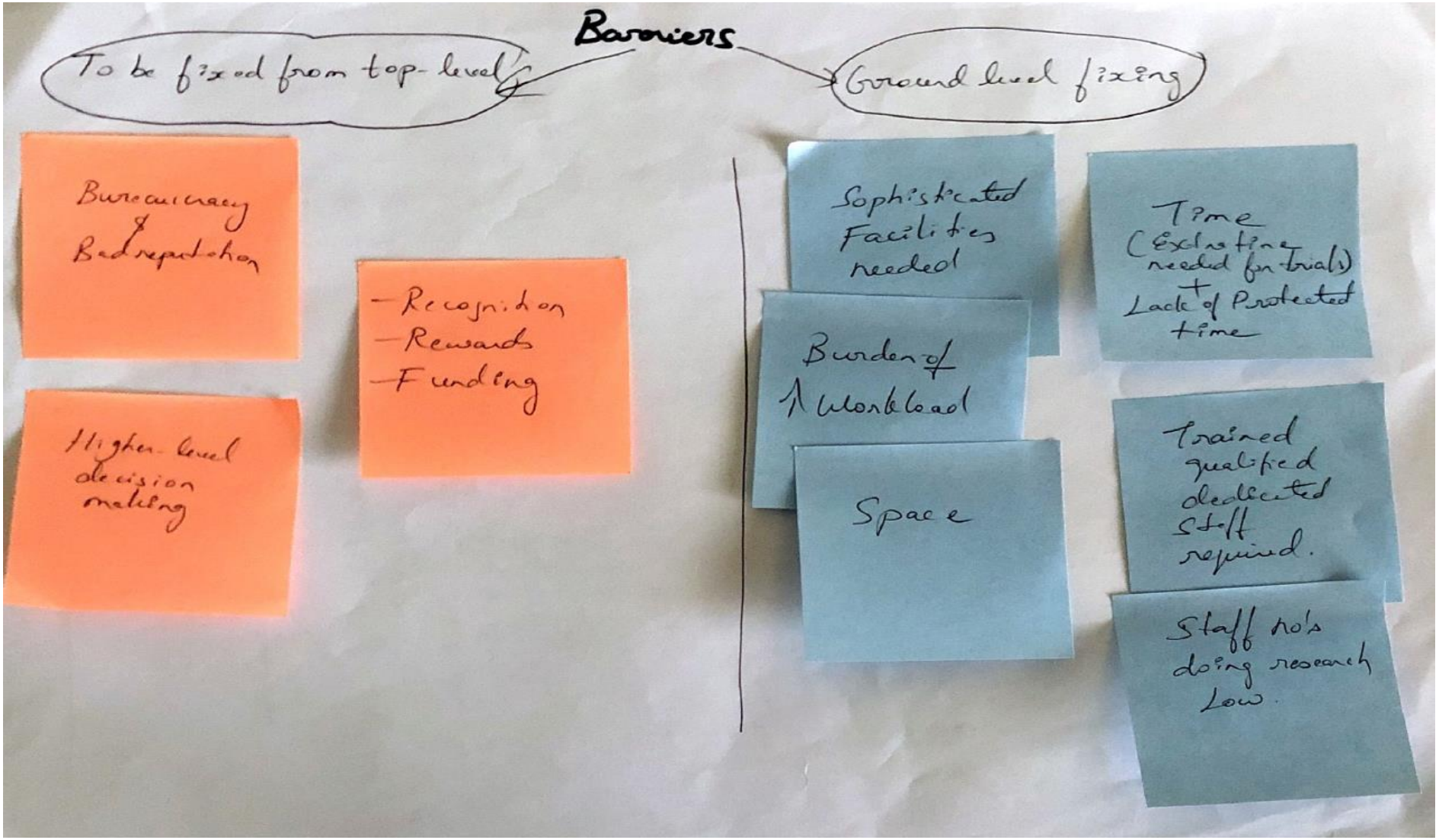


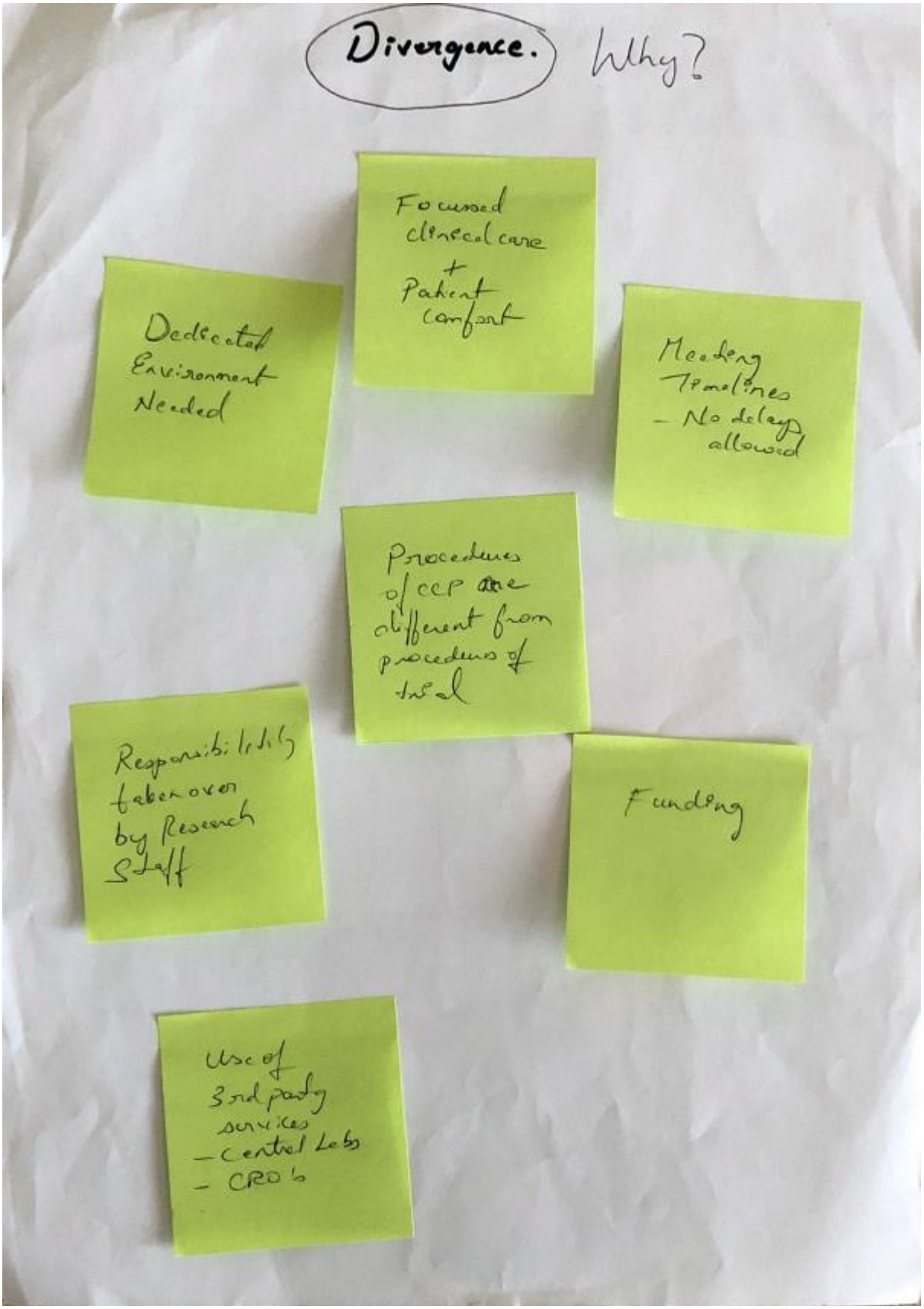
Appendix 14:Example of coding stripes

Phase 3 showing the density of coded content helping in identifying initial themes

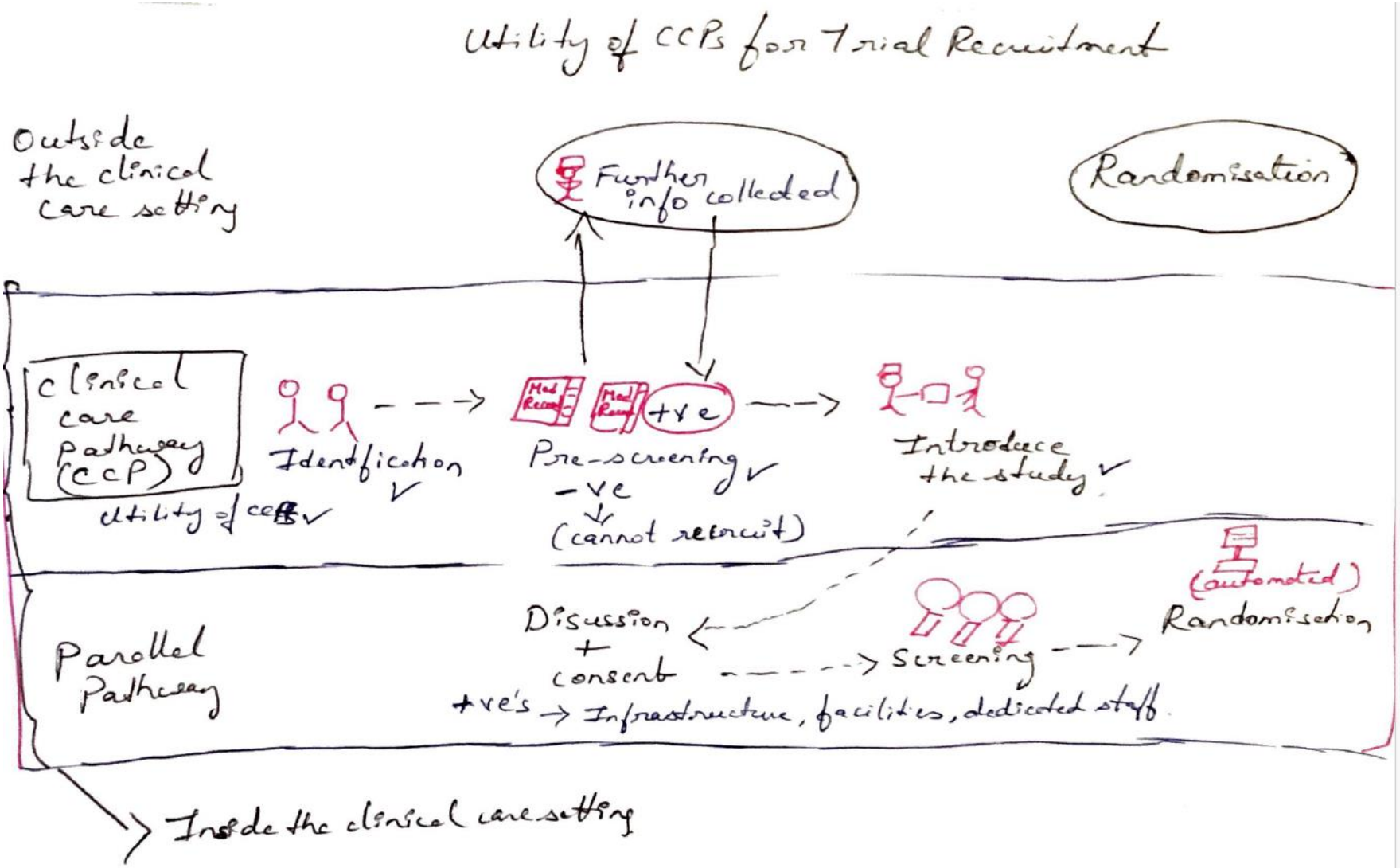


Appendix 15: Theme generation using post-it notes.




Divergence.
Why?
Focused clinical care + Patient comfort
Dedicated Environment Needed
Meeting Timelines - No delays allowed
Procedures of CCP are different from procedures of trial
Responsibilities taken over by Research Staff
Funding
Use of 3rd party services - Central Labs - CRO's

Appendix 16: Example of visual drawings



Appendix 17: Reflections during data collection and analysis

Reflections before the Pilot Interview

22 April 2021

Before the first pilot interview, I was quite nervous. I felt a little out of my head at first, but after the first few questions, I relaxed a little. It was 45 minutes long but felt much shorter. I understand the introduction is too long and will need to revise it. The person answered all of the questions correctly and in great detail.

Reflective thoughts during data collection

9 February 2021

I had a wonderful information session with the PIs today. I never ever imagined it would go on so well, they were all on board and I am really happy that they understand this study. I've always struggled to make people understand what my PhD is about to those not involved in clinical research. But now I feel home.

11 March 2021

I am extremely enthusiastic, full of excitement coming onsite for the observation. The place looks deserted. There are self-check machines everywhere, asking patients Covid related questions on every floor. Social distancing in standing, sitting, literally everywhere. Everyone is on masks and PPE, no one knows if they even have a smile. Strange world, strange times. However, the PI was lovely and welcomed me into the clinical setting and asked me to position myself towards corner of the room to make socially distanced observation for the informed consent procedure. It was a great start!

6 April 2021

I wonder why is consent and screening all mentioned on the same day of patient visit for determining eligibility in the protocol. Are they not separate processes that take place one after the other? I've to explore about this more during the interviews.

6 May 2021

I had two interviews today and am excited to get things started. Participants were extremely genuine in their responses. There was minimal questioning required, and I didn't feel the need to clarify my questions, so the interview went really well.

02 June 2021

It seems strange that lack of training of staff or lack of knowledge of trials did not come up as issues in the interviews so far rather a lot of them resonate issues of funding, crazy working hours and decrease in work life balance. I wonder what the key message is about for this study.

4 June 2021

I can only imagine how busy this PI was, but he was very kind to reschedule the interview a third time now. I was quite conscious of stealing his valuable time. I felt it was probably more necessary for patient care than for an interview with a PhD student. However, this gives me reassurance that this study is vital; people participate because they recognise the importance of research like this!

11 June 2021

I was really impressed with this nurse who came prepared for the interview and even brought the trial documents for us to discuss. Despite receiving notifications on her phone, she remained dedicated to the discussion, even when I told her she could take a break or leave early. In fact, she spent a whole hour during her lunch break just for this study. I'm not sure how to thank her enough for her generosity and dedication. I truly appreciate the time and effort she has taken to make it a fruitful interview.

Reflective thoughts during data analysis

10 January 2022

Listening to the whole interview makes me think the trials and clinical care are separate, they do not interact. And this lends me thinking... well, is there any worth asking my research question in the first place? It came out as the most important

question in the priority study. Yet, now putting myself in the shoes of the PI, I can only see them as separate things that never meet. Sure, they do have frustrations on how the system works, and I feel their pain too. I've been there!

07 February 2022

Two of the interview participants commented CCPs don't exist, yes, it's very confusing they said don't exist when they are in being recruited from the CCP! Is it because there is no defined treatment for the condition or patients get removed from the CCP while attending the trial? Could they have they associated CCPs with the treatment for cure of the disease or better management? Remember my CCP definition doesn't say that it needs to have definitive treatment. No, it doesn't say that! Maybe I should have clarified the meaning of CCP a little better during the interview, obviously I did not realise this then!

11 April 2022

Reading requirements for the study from protocol T5 -This note brings another example to my mind from previous trial I worked on; that we had signed up to a trial based on PI expertise and patient pool however, we were unaware of all the facilities that we needed to have like laboratory requirements, pharmacy requirements and hence the trial had to be closed at the site. In a way trials can be dependent on the existing CCPs if they have the required infrastructure, if not they cannot conduct the trial even if we have the right patient! All this shows why a parallel pathway in this study adds on so much value to the conduct of all the trials in this study.

14 August 2022

More than naming it as clinician competency, I think it is to think on behalf of the patient and doing what is right, not to work in favour of recruitment rather thinking what works best for the patient. Patient interest is at heart of decision making. Competency is not just being based of looking at the recruitment criteria and selecting patients based of that but it's about knowing your patients well. Someone who is not involved in routine patient care may not necessarily feel that for patients.

15 May 2023

Yes, there is additional documentation for trials, and all this is different to routine work. Does it mean trials are separated from CCPs because of this? But my question is how were the CCPs enabling the recruiters perform all this additional work?

Appendix 18 NVivo Codebook

Exploring recruitment to randomised trials within current clinical care pathways

Codes\\Phase 5 Refining defining and naming themes

Name	Description
CCP resourcing issues affecting trial recruitment	Inadequate resources and facilities within CCPs affect trial recruitment activities.
Having protected time	
Inadequate funding	
Infrastructure and facilities	
Recognition and rewards	
Shortage of dedicated research staff	

Name	Description
Shortage of experienced doctors doing research	
CCPs as a conduit for initiating trials	This theme describes how CCPs were used for initiating recruitment to trials
CCP have desired patient pool	
CCP in alignment with trials	Descriptions where standard of care and care offered as part of trial are in alignment
CCP team awareness helps identification	
CCP team knows their patients well	
CCP team knows their patients better than trial nurses	
CCP used when trial compares standard therapies	
CCPs do not interact with trials	
Communicating trial info to patient	How do patients become aware of trial
creating disease registries	

Name	Description
RN not part of identification process	
Routine care nurses help in identification	
Delivering trial information	
EPR as a source of identification	
Identification and pre-screening overlap	
Identification process is similar across trials	
Identifying the disease is identifying potential trial candidate	
Investigator identifies patients	
Multiple CCPs were used for trial recruitment	
Patient cohort	

Name	Description
Patient identification	PIs knows their patients well
Patient rounds make identification easy	
Patients finding trial information through CCPs	
PI as the key person for identifying patients	
PI competency	
Awareness of patient cohort before initiation	
Pre-existing databases within CCPs assist in identification	
Pre-screening takes place within CCPs	Informal process of looking through patient records
Raising awareness of trial within CCPs	
Research integration	
Screening patient records	

Name	Description
Trials as part of CCP care in cancer trials	
Trials grounded in CCPs leads to professional gains	Trials that are not solely focussed on product development are helpful for clinicians with experience and education and provides slightly better embedding within CCPs.
Use of electronic patient records	
Complexities of trial recruitment and the utility of CCPs	Trial recruitment activities cannot be progressed via CCPs due to the complexities of the procedures involved in the trial recruitment processes.
Aligning clinical care with recruitment	
Duplication of procedures	
Meeting recruitment timelines	
Sourcing patient data for eligibility	
Using standard care treatments	
Governance and regulations	Issues related to governance, delays due to regulatory approvals affecting recruitment through CCPs
Delays in regulatory approvals	
Need of embedding a research culture	
Parallel pathway approach to trial recruitment	Trial recruitment activities occur in parallel to CCPs than within them in the clinical care setting

Name	Description
CCP diverges to Trial pathway trajectory	
Benefits of being in trial pathway	
Dedicated trials team	
Recruitment is trial team activity	
Research staff supporting busy clinicians (CCP)	
Research team drives trials, not CCP	
RN taking ownership and responsibility	
Trial responsibilities are different and require dedicated trials personnel	
Trial team to be competent	Expertise and skills; for planning trial activities as per timelines

Name	Description
Trials pathway includes delegated staff	
Value of Research nurses in recruitment	RNs are applauded for skills and knowledge regarding trials
Focussed clinical care in trials pathway	
Perception of trials as part of care pathway	
Sophisticated and high quality care in trials	
Trial pathway offers better clinical care	
Trial patients require extra special attention	
Trials offer superior quality care and	Better outcomes for all those who participate in trials whether in treatment or placebo arms linked to the high quality of care provided to the patient compared to CCP

Name	Description
better outcomes	
Patients are comfortable with the trial pathway over CCP	
Privacy and confidentiality	Taking part in trials offered them better privacy and confidentiality
Screening in parallel pathway is non biased	
Trial pathways reduce burden of caregiving	Trial pathways take over caring of patients from CCP
CCPs diverge from delivery of trials information (soon after identification)	
Delivery of trial information is by a dedicated research nurse	
Potential trial participant lists are handed over to research nurses	

Name	Description
clinical care works in close proximity to trials	Normal clinical care continues to occur and trials team have to work in tandem with clinical team to make right clinical decisions
RNs are supported by CCP staff	RNs found help by CCP nurses and PI support very valuable mainly in understanding the disease area and the patients
Trial pathway and CCP overlap	
Trials are dependent on existing CCPs	If CCPs do not have resources, facilities, staff, equipment, room, bed space among others they cannot happen
Trial procedures coincide with clinical care procedures	
Consent process	Consent process diverged to parallel pathway
Consent involves additional permissions	Consent involves more than just consenting to partake in trials, its about granting a whole range of permissions on using their tissue samples, accessing their medical records, transferring their data to third parties.
Consent process is separate to CCP	
consent process is straight forward	
Consent process takes place within the normal clinical setting	
Delivering the trial information	

Name	Description
Facilitating the consent process is time consuming	
Obtaining signed informed consent	
reducing the burden on CCPs	
Role of consultant PI is important during consent	
screening and consent overlap	
Willingness to comply with study procedures	
Dedicated research infrastructure a boon for recruitment within CCPs	This code relates to how a dedicated infrastructure benefits trials recruitment within CCPs.
CCP are short staffed hence are supported by RNs	
Research facility a supportive tool	
Research facility facilitates majority of trials work	
Research facility is well	

Name	Description
resourced	
Research facility offers infrastructure needed to run trials	Infrastructure offered by research facility - Rooms, consultation suites, patient beds, inpatient trial care
Dedicated trials co-ordinator	
Frequency of visits and procedures	
Logistics for doing trial do not exist in CCP	
Randomisation	Is centrally performed
challenges	
Inputting extensive information into sponsor database that's not the norm	
Is electronically performed through a centralised database	
patient view on randomisation	
Performed by dedicated research nurses	
Randomisation is fair with centralised model	

Name	Description
Randomisation is performed by the sponsor (academic trials)	
Randomisation is performed on site by designated pharmacist	
Reasons for divergence	
CCP does not control selection allocation and treatments of trial intervention	
Eligibility sourced within CCP but accessed externally	
CCP staff do not engage in trials research	
CCP nurses do not do research	
External lab	
Trials pharmacy not intertwined within CCP	
CCPs diverge in the absence of effective standard therapies	Patients are in only to be part of the trial not standard care

Name	Description
CCPs do not offer treatment	
Research as care option	No distinction is seen between trials or clinical care
Trial pathway begins where CCP ends	
Commitment to trials on scheduled visits	
Meeting time requirements	Trials must meet strict time requirements for screening related procedures
No delays in trial pathway	All procedures happen on time with ease
Divergence from CCP when procedures are trials specific	Trial specific procedures are different from that of std of care
Trial processes need to be prompt and efficient	Recruitment processes need to take place quickly and without any delays as this ensures timely response like delivery of IMP to site etc. A controlled mechanism but needs efficient staff to handle procedures on time.
Trials are guided by trial protocols not by CCP	
Trials are on their	

Name	Description
own pathway as they are different	
Purpose of the trial is different from purpose of clinical care	
Invasive testing procedures outside of CCP	
Treatment does not exist within CCP	No effective treatment exists within the CCP
Trial team and CCP team is distinct	
Trials require additional work and commitments	

Name	Description
Divergence when a dedicated environment is required	
Referrals to trial pathways from external CCPs	
Research investment comes outside of CCPs	
Research infrastructure is funded by HRB	
Trials research work on parallel pathway	
Trials research runs on a separate funding pathway	

Appendix 19: Ethics approval letters

[redacted] Research Ethics
Committee Secretariat email:
[redacted]
Ms Gloria Emmanuel,
Trinity College Dublin,
D'olier Street,
Dublin 2

015th January 2020

REF: An Exploration of Recruitment to Randomised Trials within Current Clinical Care Pathways: A Qualitative Case Study

REC: 2020-01 Chairman's Action (02)
(Please quote reference on all correspondence)

Date of Valid Submission to REC: 30.10.2019
Date of Ethical Review: 13.01.2020
Research and Innovation Number: **PLEASE SUBMIT**

Dear Ms Emmanuel,

The Chairman, [redacted], on behalf of the Research Ethics Committee, has reviewed correspondence you submitted to the [redacted] and approved this research subject to a number of clarifications:

- Section A3 (b): there must be a PI for the study, this usually a clinical lead or supervisor however the applicant can be PI if they have relevant experience. Please state who the PI is.
- Please clarify the number of patients to be interviewed
- Who is the gate-keeper?
- Usually pseudonymised codes are stored at site and not on personal laptops. The onus is on the researcher to ensure the data is secure. Please ensure a DPIA is submitted to the research and innovation office for approval.
- Add version number and dates to foot of PIL and CF

Documents Reviewed:

- SAF, dated 30.10.2019
- PIL and CF

Applicants must submit an annual report for ongoing projects and an end of project report upon completion of the study. It is the responsibility of the researcher/research team to ensure all aspects of the study are executed

in compliance with the General Data Protection regulation (GDPR), Health Research Regulations and the Data Protection Act 2018. ***Additionally, please note for documents submitted for GDPR purposes that the REC and the Chair are not confirming that your documents are GDPR compliant, they are approving the document from an ethical perspective.***

Yours sincerely,

[redacted]

REC Officer – [redacted]

[redacted] Research Ethics Committee

[redacted] Research and Ethics Committee operates in compliance with and is constituted in accordance with the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004 & ICH GCP guidelines.

[redacted] esearch Ethics Committee Secretariat [redacted] Reference: 2020-02 List 7 – Response to Comments (21)
email [redacted]

Ms Gloria Emmanuel,
[redacted] Hospital,
[redacted]

09th March 2020

REF: An Exploration of Recruitment to Randomised Trials within Current Clinical Care Pathways: A Qualitative Case Study

REC: 2020-02 List 7 – Response to Comments (21)
(Please quote reference on all correspondence)

Date of Valid Submission to REC: 17.02.2020
Date of Ethical Review: 21.02.2020

Dear Ms Emmanuel,

The Chairman, Prof. [redacted] on behalf of the Research Ethics Committee, has reviewed the Response to the Committees comments you submitted to the [redacted] REC and has given **FULL** approval for this study to proceed in [redacted]

The following documents were reviewed:

- Response to Comments, dated 17.02.2020

Please note that ethical approval for this study is only active under the following conditions:

- ✓ *Applicants must submit an annual report for ongoing projects.*
- ✓ *Applicants must submit an end of study declaration/end of study report upon completion of the study.*
- ✓ *All adverse events must be reported to the* [redacted].
- ✓ *All changes (minor and substantial) to documentation/study must be submitted to the* [redacted] *zing the amendment request form and the changes must be tracked/highlighted clearly. Approval from the* [redacted] *is required before implementation of the changes.*

It is the responsibility of the researcher/research team to ensure all aspects of the study are executed in compliance with the General Data Protection regulation (GDPR), Health Research Regulations and the Data Protection Act 2018.

Yours sincerely,

[redacted]

REC Officer – [redacted]
[redacted] Research Ethics Committee

The [redacted] Research and Ethics Committee operates in compliance with and is constituted in accordance with the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004 & ICH GCP guidelines.

[redacted] Ethics Committee Secretariat
email: [redacted]

[redacted] eference: 2020-11 List 43 – Amendment (25)

Ms Gloria Emmanuel
[redacted] Hospital,
[redacted]

30th November 2020

REF: An Exploration of Recruitment to Randomised Trails within Current Clinical Care Pathways: A Qualitative Case Study

REC: 2020-11 List 43 – Amendment (25)
(Please quote reference on all correspondence)

Date of Valid Submission to REC: 30.09.2020
Date of Ethical Review: 06.11.2020

Dear Ms Emmanuel,

The Chairman, Prof. [redacted] on behalf of the Research Ethics Committee, has reviewed the amendment you submitted to the [redacted] for the above named study and has given **FULL APPROVAL** for this amendment.

The following documents were reviewed:

- *Amendment Request Form*

Please note that ethical approval for this study is only active under the following conditions:

1. *Applicants must submit an annual report for ongoing projects.*
2. *Applicants must submit an end of study declaration/end of study report upon completion of the study.*
3. *All adverse events must be reported to the J[redacted]*
4. *All changes (minor and substantial) to documentation/study must be submitted to the [redacted] using the amendment request form and the changes must be tracked/highlighted clearly. Approval from the [redacted] required before implementation of the changes.*

It is the responsibility of the researcher/research team to ensure all aspects of the study are executed in compliance with the General Data Protection regulation (GDPR), Health Research Regulations and the Data Protection Act 2018.

Yours sincerely,
[redacted]

REC Officer [redacted]
[redacted] Research Ethics Committee

Th[redacted] Research and Ethics Committee operates in compliance with and is constituted in accordance with the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004 & ICH GCP guidelines.

Appendix 20: DPIA Approval

Gloria Emmanuel <gemmanue@tcd.ie>

RE: R&I 6095 - Exploring recruitment to randomised trials within current clinical care pathways: A qualitative case study

4 messages

Research & Innovation <research@[redacted]> 20 March 2020 at 11:04
To: Gloria Emmanuel <gemmanue@tcd.ie>

Hi Gloria,

Did the Ethics come through for this project?

The DPIA has been approved by the DPO.

Kind regards,

[redacted]