UNIVERSITY OF SOUTHAMPTON

FACULTY OF ENVIRONMENTAL AND LIFE SCIENCES

School of Health Sciences

Does Rapid Mobilisation as Part of an Enhanced Recovery Pathway Improve Length of Stay, Return to Function and Patient Experience Post Primary Total Hip Replacement? A Randomised Controlled Trial

by

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ABSTRACT

Demand for total hip replacement (THR) surgery has increased over the last twelve years and continues to increase. Day zero ambulation may enable patients to recover and leave hospital quicker post-operatively, increasing efficiency and allowing services to cope with increasing demand. This thesis investigated the effectiveness of day-zero ambulation as a physiotherapeutic intervention within a UK hospital. Investigation of this topic started with a systematic review of the existing literature using a narrative synthesis. This showed that day-zero-ambulation may reduce length of stay (LOS) with resultant cost savings and speed functional recovery, without increasing incidence of post-operative complications. However, methodological limitations such as concomitant interventions mean that changes may not be confidently attributed to day-zero ambulation. Following on from this, a feasibility study was conducted which established the scientific and practical implications of conducting a randomised controlled trial.

Finally, this research included a fully-powered, single-centered, non-blinded randomised controlled trial involving 176 participants who underwent primary uncomplicated THR. Participants were randomly allocated into two groups; the intervention group attempted ambulation on the same day as surgery (n =87) and the control group attempted ambulation the day after surgery (n = 89). Apart from time of ambulation, both groups received the same post-operative management. The primary outcome was LOS, with secondary outcomes for time to physiotherapy ready for discharge, post-operative numerical pain scores, consumption of opioid and antiemetic medications, incidence of post-operative complications, time to reach functional milestones and functional independence and participant experience.

Median LOS was 3 days both in the control group (IQR 2-4) and intervention group (IQR 2-3) however, this study observed reduced LOS variation in the interquartile range between groups meaning groups were statistically significantly different ($p=0.02$). Intervention group participants were physiotherapy ready to leave hospital 19.5 hours earlier than control group participants ($p=0.00006$), achieved functional milestones significantly quicker than those in the control group, and were 2.06 (CI 1.55 to 2.74) times more likely to be functionally independent at any given time point than the control group ($p<0.0001$). There were no significant differences in the incidence of post-operative complications, post-operative pain, opioid and anti-emetic consumption and participant experience between groups. Day zero ambulation appears to improve efficiency of

recovery and speed return to functional independence without adversely affecting the incidence of post-operative complications, pain experience or overall patient experience.

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Research Thesis: Declaration of Authorship

Print name:

Mr Christopher Matthew Efford

Title of thesis:

Does Rapid Mobilisation as Part of an Enhanced Recovery Pathway Improve Length of Stay, Return to Function and Patient Experience Post Primary Total Hip Replacement? A Randomised Controlled Trial

I declare that this thesis and the work presented in it is my own and has been generated by me as the result of my own original research. I confirm that:

1. This work was done wholly or mainly while in candidature for a research degree at this University;

2. Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated;

3. Where I have consulted the published work of others, this is always clearly attributed;

4. Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;

5. I have acknowledged all main sources of help;

6. Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself;

7. None of this work has been published before submission;

Signature: Date:

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Firstly, I would like to thank my current academic supervisors Dr Dinesh Samuel and Dr Margaret Donovan-Hall for their encouragement and extremely positive guidance in steering me through the PhD process and sparking me to learn more about research. During my research, I had a complete change of supervision team, and I will ever be grateful for Dinesh and Maggie for picking up my supervision half-way through and giving me a fresh impetus to complete this thesis document.

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Definitions and Abbreviations

AE	Adverse Event
AKSS	American Knee Society Score American Knee Society Score
APR	Annual Progress Report
AR	Adverse Reaction
BD	bis die (twice daily)
CA	Competent Authority
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
CT	Computed Tomography
CTPA	Computed Tomography Pulmonary Arteriogram
DMC	Data Monitoring Committee
EC	European Commission
ERAS	Enhanced Recovery After Surgery
GAfREC	Governance Arrangements for NHS Research Ethics Committees
GDP	Gross Domestic Product
Hb	Haemoglobin
ICF	Informed Consent Form
ISRCTN	International Standard Randomised Controlled Trial Number
LOS	Length of Stay
MI	Myocardial Infarction
NHS R&D	National Health Service Research & Development
NIHR	National Institute for Health and Care Research
PAC	Pre-Assessment Clinic
Participant	An individual who takes part in a clinical trial

PI	Principle Investigator
QA	Quality Assurance
QC	Quality Control
QDS	Quater die sumendum (Four times a day)
RAPT	Risk Assessment and Prediction Tool
RBCH	Royal Bournemouth and Christchurch Hospitals
RBH	Royal Bournemouth Hospital
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SDV	Source Document Verification
SOP	Standard Operating Procedure
SSA	Site Specific Assessment
TDS	ter die sumendum (to be taken three times daily)
THA	Total Hip Arthroplasty
THR	Total Hip Replacement
TMG	Trial Management Group
TSC	Trial Steering Committee
UHD	University Hospitals Dorset

1 - Introduction

This thesis details a PhD project focussed on day-zero ambulation as a physiotherapeutic intervention following total hip replacement (THR) surgery. This introductory chapter provides some background to the key problems faced by UK elective orthopaedic services, context as to why this line of enquiry was appropriate for a PhD project, and an overview of the thesis structure.

1.1 Current problems faced in Elective Orthopaedic Services

In 2013 it was estimated that 2.12 million people in the UK were living with osteoarthritis of the hip joint, with higher prevalence in the population over the age of 45 (Arthritis Research UK 2013). Updated figures in 2019 estimated that this number to have risen to 2.76 million (Versus Arthritis 2019). Arthritis in major joints such as the hip has been shown to have significant socioeconomic impact. Recent reports in 2017 indicated that the treatment of osteoarthritis and rheumatoid arthritis incurred a direct cost of £10.2 billion and a further £2.58 billion due to an inability to work. This picture is estimated to worsen over the next decade, with cumulative costs for direct care projected to rise to £118.6 billion (Versus Arthritis 2021).

One of the most successful treatments for pain due to osteoarthritis of the hip is THR surgery. Factors, such as advancing age and obesity, have been linked with an increased need for joint replacement surgery (Harms et al. 2007) and forecasts suggest that the UK population could have 11 million more obese adults by 2030 (Wang et al. 2011) and double the number of adults over the age of 80 by 2030 (Cracknell 2010). Consequently, UK orthopaedic services can anticipate an ongoing increase in the demand for THR surgery in the future, which will make the efficiency of these services critical to maintain current clinical standards. This is a trend already seen at the Royal Bournemouth Hospital with the number of joint replacement procedures carried out increasing by 43% from 2004 to 2014 (National Joint Registry 2014).

Furthermore, the above problems have been compounded by the COVID-19 pandemic and its impact on delivering elective surgeries. For example, in 2020 less than half the expected number of joint replacements took place due to COVID-19 (Versus Arthritis 2021). Subsequently, the UK is currently experiencing the largest waiting list in a decade for elective orthopaedic

surgeries (British Orthopaedic Association 2022). This unfortunately comes at a time where UK healthcare expenditure as a percentage of gross domestic product (GDP) had seen a downward trend up until 2019 (Statista 2022), with more recent figures skewed by COVID-19 response expenditure.

Investigating ways of improving efficiency of recovery for patients undergoing THR surgery and improving clinical outcomes would provide better public value, future-proofing and patient centred quality improvements for UK orthopaedic services.

1.2 History of Enhanced Recovery and the Role of Physiotherapy with THR

Enhanced recovery after surgery (ERAS) was a concept first implemented by a group of general surgeons led by Henrik Kehlet in 1997 (Taurchini et al. 2018). This was viewed as challenging previous approaches and presented a new surgical paradigm, focussing on optimising the surgical pathway to reduce operative risk and speed patient recovery to gain the best possible outcomes. In the current understanding of ERAS, this constitutes three phases of optimisation:

- Pre-operative
- Peri-operative
- Post-operative

From conception up to the present day, there has been widespread international uptake of ERAS as a new surgical paradigm and multi-disciplinary way of working, with recognition of improved risks for the patient and faster post-operative recovery (Ibrahim et al. 2013). While first employed within a colorectal patient group, the ERAS movement spread to orthopaedic services, particularly within elective arthroplasty pathways (ERAS Society 2021). Currently, elective orthopaedic departments across the UK implement their own ERAS pathways, which can differ between hospital sites.

Within ERAS, physiotherapy intervention is a key component in assisting the patient to reach functional independence post-operatively (Wainwright et al. 2017), with a view to facilitating a safe discharge from hospital. Enacting physiotherapy treatment earlier in the patient's post-operative recovery could result in a reduction in the time the patient is required to remain in hospital following their THR. Despite promising results, other studies that have examined this concept have had various methodological flaws, which limit their transferability into practice. Also, several outcome measures which influence quality of care have not been considered in the past when researching this significant change, such as patient experience.

1.3 Researcher Background and Project Conception

The researcher has a background as a clinical specialist physiotherapist in elective orthopaedics, principally in assisting people to recover from major joint arthroplasty surgery. Working within a forward-thinking department always striving to improve service quality, the author was asked to decide if the team should implement day-zero ambulation with all patients treated by the department. However, the author felt unable to sanction this decision following informal review of the published evidence, which felt insufficient to make a proper evidence-based decision. As such, the author decided to conduct his own research and try and expand on the existing knowledge base. Consequently, this study was conceived through a desire to answer a question posed within clinical practice as to whether day-zero ambulation following THR is beneficial to the service and to the patient.

From the author's experience, within the field of elective orthopaedics, there appears to be a preponderance of published studies low in the hierarchy of evidence, which due to abundance are accepted as having reliably answered a research question. In 2010 79% of studies published in the top eight orthopaedic journals came from level III or level IV studies constituting retrospective, non-controlled or case series publications. Furthermore, only 7% of publications were classified as Level I evidence which would include RCTs and meta-analyses (Cunningham et al. 2013; Voleti et al. 2012). While there appears to have been a push by journals over the last decade to improve representation of high-level studies, a recent review suggests a gradual decrease in the proportion of high-level evidence publications within the top orthopaedic journals between 2013 and 2018 (Luksameearunothai et al. 2020). Ultimately this means services are often developed from research that is considered low level within the hierarchy of evidence.

The author experienced this phenomenon when trying to determine if adopting day-zero ambulation in practice would be a good evidence-based service change and was faced with a large volume of evidence, almost exclusively from low-level of evidence publications. This led to the aim of adding to the current empirical evidence. The author had a strong desire not to feed into the above problem and as such conducted this PhD project with a focus on producing as high-quality evidence as possible with the resources available.

The researcher was a novice in the conception, design and implementation of research and as such sought advice from the research and development department at RBCH as study sponsor and in writing the initial research proposal and research and ethics committee applications. The study was granted ethical approval and commenced the feasibility part of this study in 2015.

1.4 Project Outline

This thesis is structured in phases, outlining the different elements which combine to form this PhD project, from scoping and systematic literature review, through to RCT and discussion of the study findings.

Figure 1: Project Outline Flow Diagram

It is important to note that as part of the overarching project, the researcher also carried out a nested qualitative study examining patient experience of the intervention. The aim of this was to produce richer findings examining participant experience which can be triangulated with the findings of the fully powered RCT and published alongside quantitative findings, providing context and posing future questions for further enquiry into this intervention. Although there remains debate between purists on the merits of quantitative versus qualitative paradigms, mixed methods research has more recently been recognised as a valuable method of enquiry, with Johnson & Onwuegbuzie (2004) presenting mixed methods as a modern approach within social research, aiming to draw benefit from the strengths of both paradigms, but also reduce the weaknesses present in a single paradigm approach. Especially in healthcare research where the historical biological model of health has been overturned and prevailed by a biopsychosocial model of care (Havelka et al. 2009) both qualitative and quantitative approaches are required to examine this biopsychosocial model and continue to provide generalisability helpful for population level decision making.

The conduct of the above mentioned nested qualitative study will allow the researcher to examine both the biological and psychosocial aspects of the target intervention to present a more holistic examination of the intervention and the context surrounding it.

Despite the advantages of this mixed methods approach, the author has decided to omit this nested study from this PhD thesis. Including this piece of work would have made the project too large and complex for the current PhD write-up.

The author wished to give adequate focus on the findings of the quantitative RCT as the larger piece of work, without skimming superficially over the nested qualitative study. Despite this, the author plans to complete write-up and publication of the nested qualitative study at a later date.

1.5 Research Aims

While the research aims are discussed and refined for specificity in future chapters, this section details the research aims at the study conception.

Overarching research aim:

To investigate the multi-factorial quality of day-zero ambulation following primary THR surgery by examining in detail the existing evidence base and producing a high-quality piece of empirical research to add to the existing knowledge.

Specific Research aims:

To investigate the effect of day-zero ambulation on:

- Length of hospital stay as a measure of service efficiency
- The safety of the patient
- The speed of functional recovery of the patient
- The post-operative pain experience
- The lived experience of the patient

Overarching hypothesis:

Employing day-zero ambulation following primary uncomplicated THR improves the multifactorial quality of service delivery.

Specific hypotheses:

Employing day-zero ambulation following primary uncomplicated THR:

- Reduces length of hospital stay

- Doesn't adversely affect the safety of the patient or post-operative pain experience
- Improves the speed of functional recovery

1.6 Funding and Declarations

The author declares no competing financial interests or personal conflicts of interest that could have appeared to influence the work reported on in this thesis document.

All parts of this PhD project were conducted without any research funding throughout the duration of the work.

1.7 Thesis Outline

This PhD thesis contains seven chapters:

- In Chapter One, the context of the study has been introduced including the key problems facing elective orthopaedics in the UK, and the value of this thesis within that context.
- In Chapter Two, the existing literature will be reviewed using a systematic review methodology. This aims to evaluate the strength of the literature base and present recommendations for future research.
- In Chapter Three, the theoretical framework of this thesis will be presented. The research questions will be presented and the adoption of a quantitative research approach and RCT methodology will be justified, along with the limitations and assumptions of this approach. This chapter also deals with patient and public involvement and the specific ethical considerations of this research. The underpinning philosophy is presented in first person to reflect the individual views and philosophy of the researcher.
- In Chapter Four the feasibility study is presented, identifying pragmatic strengths and weaknesses of the research design and conduct and making recommendations for the improvement of the fully powered RCT.
- In Chapter Five the author discusses the recommendations made from the feasibility study findings and how they were translated to the fully powered study.
- In Chapter Six the fully powered RCT is presented. This includes the discussion of the interpretation of the study findings and the limitations of the chosen approach and methodology.

- In Chapter Seven the findings of all phases of this thesis are put together to discuss the implications of this PhD project's findings, the reflective journey of the researcher and recommendations for future research.

2 - Literature Review

2.1 Title

What is the multifactorial effectiveness of day-zero ambulation post-total hip replacement surgery? A systematic review.

(This chapter has been submitted for publication and is undergoing peer review at the completion of this thesis - (Efford et al. 2023))

2.2 Introduction

This chapter provides an overview of published research on day-zero ambulation as a physiotherapeutic intervention following THR. Conducting a literature review on this topic prior to embarking on empirical research was important, as while there are a large number of studies published involving this intervention, the author already had concerns from informal literature review about the methodological quality and relevance of this research body to clinical decision making in a UK orthopaedic pathway. This systematic review provides a critical appraisal of the current published literature and provides a basis for the study that comprises the focus of this thesis. Having conducted this formally instead of informally, the author could feel confident that robust methods for the identification, inclusion and exclusion of and critical appraisal of published research justified progressing to the design of an empirical research study. A systematic review of previous work in this area also served further purposes:

- Understanding of the strengths and limitations in current research – to enable design of a study to address these limitations
- To understand the context of this topic within international healthcare settings and the challenges faced.
- To identify knowledge gaps pertinent to the overarching project research aims
- To give context in refining research questions
- To determine methodologies used in previous research which may be useful in future research design.

This chapter is written following the guidance and containing all of the suggested elements for reporting systematic reviews laid out by the PRISMA checklist (Moher et al. 2009).

2.2.1 Rationale

As discussed in Chapter 1, there are many challenges facing UK elective orthopaedic services, including increasing demand, limitations in resources and finite healthcare budgets (Briggs 2015). Consequently, healthcare providers must look to pathway efficiency changes in order to maintain public value. Day-zero ambulation may be an important physiotherapeutic pathway option for improving the efficiency of these services. Reviewing the existing evidence base on this topic serves to identify the state of current knowledge, assess the strength of the evidence base and highlight areas for further investigation (Berkman et al. 2008).

Much of the research in this field focuses on length of hospital stay (Briggs 2015; GIRFT 2020). While this is an important metric in terms of service efficiency, clinical decisions also need to account for factors such as incidence of post-operative complications, patient pain experience, functional recovery and patient lived experience, which feasibly could all be influenced by day-zero ambulation.

2.2.2 Objectives

To investigate the current knowledge base of day-zero ambulation post THR as an intervention; focussed on answering the following research questions:

1. What effect does day-zero ambulation have on patient recovery in terms of?
    a. Length of hospital stay (LOS)?
    b. Financial efficiency?
2. Is day-zero ambulation safe, when considering post-operative complications and mortality?
3. What effect does day-zero ambulation have on functional recovery?
4. What effect does day-zero ambulation have on the patient's post-operative pain?
5. What is currently known about the patient's lived experience of day-zero ambulation post THR?

2.3 Methods

2.3.1 Protocol and Registration

This review was registered with PROSPERO (i.e. THE International Prospective Register of Systematic Reviews) under the reference ID 247796.

Protocol available online at:

https://www.crd.york.ac.uk/PROSPEROFILES/247796_PROTOCOL_20210408.pdf

2.3.2 Type of Review

This review was conducted as a systematic review using a narrative synthesis.

Conducting a review of available published evidence provides several advantages:

1. Combining study findings to examine the consistency of results
2. Combining and appraising results provide robustness and improved transferability of results to other settings

Furthermore, selecting a systematic collection, appraisal and synthesis method improves confidence in the review findings compared to a traditional review due to improved transparency, robustness and repeatability of the review (Glasziou et al. 2001). Indeed, Cochrane UK describe the systematic review as the cornerstone of evidence-based medicine and healthcare.

2.3.3 Eligibility Criteria

Table 2-1 Definition of search terms

Term	*Definition*
Total hip replacement	Surgical removal of the femoral head and acetabulum and replacement with a prosthetic hip joint. Not inclusive of hip resurfacing surgery.
Day zero ambulation	The patient began ambulation for the first time after THR on the same calendar day in which their surgery was completed.

2.3.3.1 Questions 1-4:

1) *What effect does day-zero ambulation have on patient recovery in terms of?*
    a. *Length of hospital stay (LOS)?*

b. Financial efficiency?

2) *Is day-zero ambulation safe, when considering post-operative complications and mortality?*
3) *What effect does day-zero ambulation have on functional recovery?*
4) *What effect does day-zero ambulation have on the patient's post-operative pain?*

Table 2-2: Literature review questions 1-4 inclusion and exclusion criteria

Inclusion/Exclusion Criteria	*Rationale*
• Published since 2005	• Enhanced recovery programmes started in colorectal in 1997 and were later adopted into orthopaedics
• Full text available in English language	• English the first language of all reviewers • No funding for translation
• Participants treated with day-zero ambulation following their THR • Participants underwent THR • Presented empirical findings relating to day-zero ambulation post THR	• To limit search findings to studies examined in the patient cohort of interest.
• Ranked as excellent or good study design as detailed in section 2.3.6	• To limit search findings to a manageable number • To capture only the highest quality evidence
• No outcome measures relevant to THR	• To exclude studies without relevant findings

2.3.3.2 Question 5: What is currently known about the patient's lived experience of day-zero ambulation post THR?

Separate eligibility criteria and a separate search strategy were used for this research question pertaining to patient experience of day zero ambulation shown in ***Table 2-3*** and ***Table 2-5*** respectively. This search was conducted independently as it was expected to yield results from both quantitative and qualitative methodologies.

Table 2-3: Literature review question 5 inclusion and exclusion criteria

Inclusion Criteria	*Rationale*
• Published since 2005 • Full text available in English language • Provided specific analysis of patient experience post total hip replacement • Participants underwent rehabilitation which included day-zero ambulation	• Enhanced recovery programmes started in colorectal in 1997 and were later adopted into orthopaedics • English the first language of all reviewers • No funding for translation
Exclusion Criteria	*Rationale*
• No outcome measures relevant to THR*	• To exclude studies without relevant findings

*Total hip replacement

2.3.4 Information Sources

The following databases were included in the search:

- MEDLINE
- CINAHL
- AMED
- EMBASE
- APA PsychInfo

These databases were selected as the principle healthcare research databases available to the researcher.

2.3.5 Search

PICO criteria were used to develop the search strategy based on the EBSCO guidance white paper (Jensen 2004) and shown below in ***Table 2-4***.

Table 2-4 - PICO criteria

PICO Domain	*Keywords*	*Search terms*
Patient, problem or population	Patients undergoing total **hip replacement**	Hip Replacement Arthroplasty THR THA
Intervention or exposure	**Day-zero ambulation**	Day zero Day 0 Fast-track Accelerated

		Day case Outpatient Ambulat* Walk* Mobilisation Mobilization
Comparison or control	Ambulating day 1 or later	
Outcome measure	All outcomes	

Search strategy used medical subject headings and text words relating to the research questions. The final search strategy was reviewed by both reviewers and an independent university librarian for completeness.

Table 2-5 shows an excerpt of the electronic search strategy used for the MEDLINE database, with the full search strategy for questions 1-4 shown in Appendix 1 and for question 5 in Appendix 3.

Table 2-5: Search terms used for Medline data search

Search Number	*Databases Searched*	*Search Terms and Limits*
S1	MEDLINE via EBSCO	(MH "Arthroplasty, Replacement, Hip") OR TI (THR OR “total hip replacement” OR THA OR “total hip arthroplasty” OR “hip joint replacement” OR "hip joint arthroplasty") OR AB (THR OR “total hip replacement” OR THA OR “total hip arthroplasty” OR “hip joint replacement” OR "hip joint arthroplasty")
S2	MEDLINE, via EBSCO	(MH “Ambulatory Surgical Procedures”) OR (MH “Ambulatory Care”) OR TI (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0") OR AB (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0")
S3	MEDLINE via EBSCO	(MH "Early Ambulation") OR TI (Ambulat* OR walk* OR mobilisation OR mobilization) OR AB (Ambulat* OR walk* OR mobilisation OR mobilization)

S4	MEDLINE via EBSCO	S1 AND S2 AND S3 **Since: 2005 Language: English**

2.3.6 Study Selection

2.3.6.1 Questions 1-4:

Two reviewers independently reviewed abstracts against the above inclusion and exclusion criteria, and full texts were obtained for all potentially relevant studies. Study type was identified using the NICE (2012) algorithm for classifying quantitative study designs shown below.

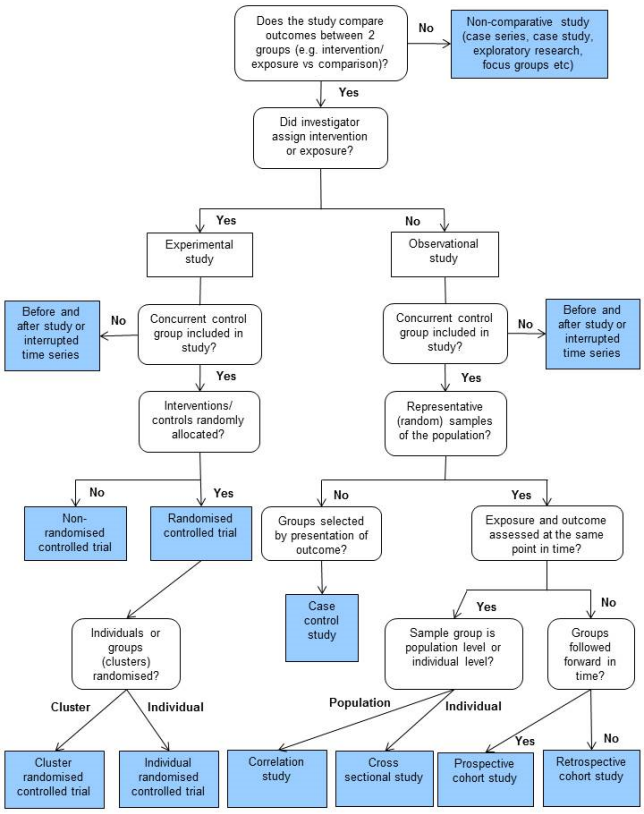


Figure 2 - NICE (2012) algorithm for classifying quantitative study types (Reproduced with permission under the NICE UK Open Content Licence)

Where the study design type was unclear from the abstract alone, the full text methodology was reviewed to determine study type. Studies were then ranked for hierarchy in evaluating efficacy of healthcare intervention according to the guidance published by Evans (2003).

	Effectiveness	Appropriateness	Feasibility
Excellent	• Systematic review • Multi-centre studies	• Systematic review • Multi-centre studies	• Systematic review • Multi-centre studies
Good	• RCT • Observational studies	• RCT • Observational studies • Interpretive studies	• RCT • Observational studies • Interpretive studies
Fair	• Uncontrolled trials with dramatic results • Before and after studies • Non-randomized controlled trials	• Descriptive studies • Focus groups	• Descriptive studies • Action research • Before and after studies • Focus groups
Poor	• Descriptive studies • Case studies • Expert opinion • Studies of poor methodological quality	• Expert opinion • Case studies • Studies of poor methodological quality	• Expert opinion • Case studies • Studies of poor methodological quality

Figure 3: Evans (2003) Hierarchy of Evidence (Reproduced with permission from John Wiley & Sons under licence number 5470840494042)

Studies that employed a design ranked as fair or poor in the effectiveness column of Figure 3 were excluded. Any exclusions were discussed and agreed and disagreements in exclusion prompted full text methodology review and inclusion /exclusion discussed and agreed between reviewers.

Following ranking, non-excluded studies were individually assessed for methodological quality by the two reviewers independently. The reporting of all elements was completed using the appropriate checklist as detailed below in ***Table 2-6***:

Table 2-6: Content checklists used by study type

Study Type	*Content Checklist*
Systematic reviews and meta-analysis studies	PRISMA checklist (Moher et al. 2009)
Randomised controlled trials	CONSORT checklist (Schulz et al. 2010)
Observational Studies	The appropriate STROBE checklist (Von-Elm et al. 2008)

In addition, overall study quality was appraised using the CASP analysis checklist (CASP 2014) shown in Appendix 6. These tools allowed the critical appraisal of each paper specific to its methodological design. Research findings and critical appraisal comments were summarised in a meta-summary table to enable structured comparison.

2.3.6.2 Question 5: What is currently known about the patient's lived experience of day-zero ambulation post THR?

Any relevant papers identified via abstract were included for full text review regardless of the study methodology due to small numbers. Quantitative papers were reviewed for quality in the same method detailed in section 2.3.6.1. All qualitative papers were appraised using the CASP checklist for qualitative research studies (CASP 2014).

2.3.7 Risk of Bias in Individual Studies

Where possible, all included studies were assessed for risk of bias in line with guidance given in the Cochrane handbook (The Cochrane Collaboration 2008).

Randomised controlled trials were assessed using the Risk of Bias (RoB) 2.0 tool (Sterne et al. 2019; Higgins et al. 2011). Studies which did not employ randomisation were assessed using the ROBINS-1 tool (Sterne et al. 2016)

Risk of bias assessments were completed individually by both reviewers. Outcomes were then discussed and agreed.

2.3.8 Risk of Bias across Studies

Risk of bias across studies was summarised for any studies that underwent RoB 2.0 or ROBINS-1 assessment using traffic light plots and weighted bar plots using the ROBvis tool (McGuinness & Higgins 2021) and presented with the study results.

2.3.9 Synthesis of Findings

Although the gold standard for the synthesis of quantitative study findings, a previous attempt by the author at meta-analysis using 8 papers examining length of stay following this intervention was flawed. While showing a concurrent direction of effect, heterogeneity testing indicated considerable heterogeneity (The Cochrane Collaboration 2008; Higgins et al. 2003). Consequently, any pooled effect size from this method cannot be considered reliable.

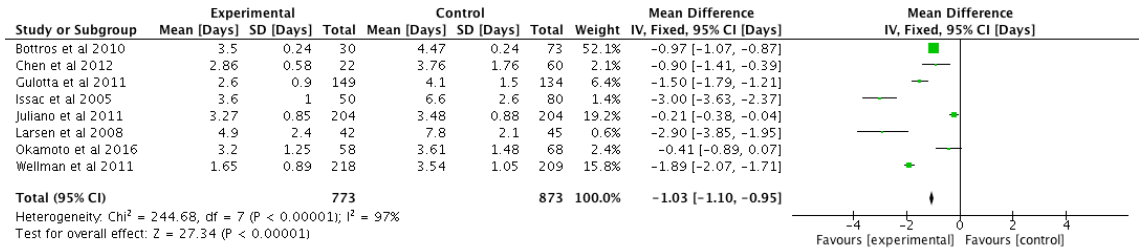


Figure 4: Previous attempted meta-analysis forest plot with heterogeneity result

As such, a narrative synthesis approach was selected for this systematic review. This method produces a synthesis of research findings, described in text following a systematic and rigorous quality appraisal of the evidence, Popay et al. (2006) have described narrative synthesis as a second-best approach when statistical meta-analysis is not appropriate.

The narrative synthesis in this review aimed to describe study findings along with similarities, differences, strengths, and weaknesses in the included studies and make interpretations about the following:

- the direction of effect – whether findings evidenced an improvement, deterioration or no change in an outcome.
- factors which may explain differences in reported effect sizes across studies
- explore the influence of heterogeneity seen across studies
- assess the robustness and quality of the available evidence to present context

For each research question, this study required a minimum of 2 included papers to create a synthesis examining this particular research question (for example, two separate papers examining the effect of day-zero ambulation on post-operative functional recovery). This threshold was set in order to target findings that go beyond and are therefore more robust compared to the already published findings of a single study. Narrative synthesis was collaboratively produced by the two reviewers, and the overall synthesis agreed.

2.4 Results

2.4.1 Study selection

After carrying out the search strategy detailed in section 2.3.5, literature search identified 162 individual articles for abstract review. 151 articles were excluded in total with reasons detailed in Figure 5 within the PRISMA flow diagram.

2.4.2 Questions 1-4

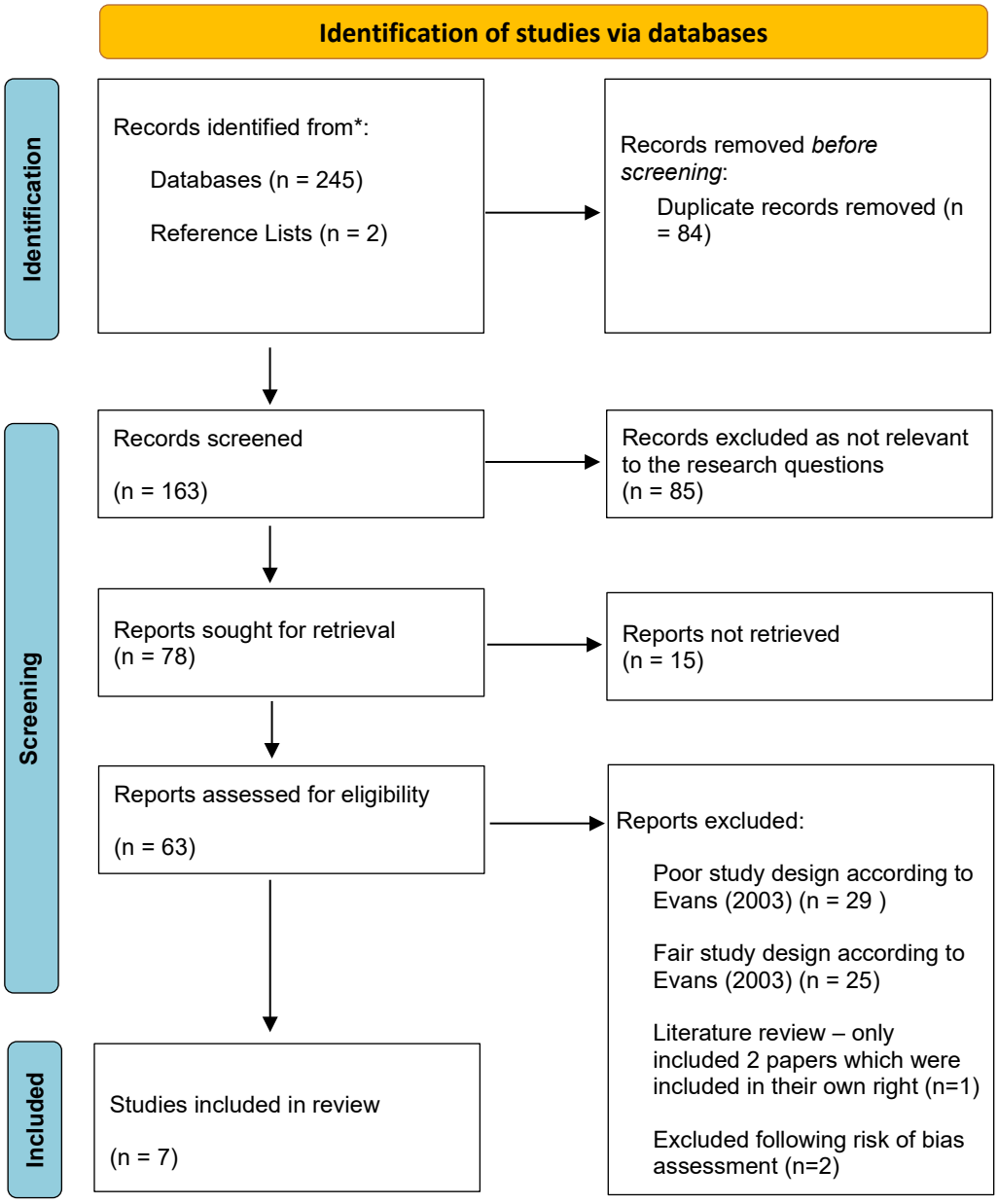


Figure 5: Literature search flow diagram

Details of excluded papers and reasons for exclusion are given in more detail as greyed out in Appendix 2. Two papers (Robbins et al. 2014; Elmoghazy et al. 2022) were excluded following risk-of-bias assessment due to critical risk of bias and high risk of bias respectively, the detail of these risk of bias assessments are shown within Appendix 4. Robbins et al. (2014)scored as critical risk of

bias for due to confounding with several important confounders neither controlled for or measured. Elmoghazy et al. (2022) scored as high risk of bias within the RoB 2.0 tool due to baseline differences between intervention groups suggesting a problem with the randomisation process. Although reported as an RCT, the decision to exclude this study was due to this study reporting significant differences in age, gender and pre-operative outcome measures which are likely to have significantly affected the reported results. This left 7 papers included for questions 1-4 of this review shown in **Table 2-7** below:

Table 2-7: Included studies

No	*Authors*	*Title*	*Study Type and (Hierarchy Rank)*
1	(K. Larsen, 2009)	Cost-effectiveness of accelerated perioperative care and rehabilitation after total hip and knee arthroplasty	Piggyback study of an RCT - Cost-utility study **(GOOD)**
2	(K. Larsen, Sørensen, et al., 2008)	Accelerated perioperative care and rehabilitation intervention for hip and knee replacement is effective: A randomized clinical trial involving 87 patients with 3 months of follow-up	Single Centre RCT **(GOOD)**
3	(Juliano et al., 2011)	Initiating Physical Therapy on the Day of Surgery Decreases Length of Stay Without Compromising Functional Outcomes Following Total Hip Arthroplasty	Cohort Study **(GOOD)**
4	(Okamoto et al., 2016)	Day-of-Surgery Mobilization Reduces the Length of Stay After Elective Hip Arthroplasty	Multi-centre RCT (**EXCELLENT)**
5	(Karim et al., 2016)	Does Accelerated Physical Therapy After Elective Primary Hip and Knee Arthroplasty Facilitate Early Discharge?	Cohort study **(GOOD)**
6	(Pollock et al., 2016)	Outpatient Total Hip Arthroplasty, Total Knee Arthroplasty, and Unicompartmental Knee Arthroplasty	Systematic Review (**EXCELLENT)**
7	Sibia et al 2016	Predictors of hospital length of stay in enhanced recovery after surgery program for primary total hip arthroplasty	Case-Control Study **(GOOD)**

Sibia et al 2016 was rated as good within the hierarchy of evidence rankings as while observational it compared outcomes from two groups, one of which represented a control group, making it more akin to a non-randomised trial than a descriptive study.

Full literature search results are shown in **Table 2-8** below with detail of yields from the range of selected databases.

Table 2-8: Literature review search results

Search Number	Databases Searched	Search Terms and Limits	Number of Results	Comments on Results
S1	MEDLINE via EBSCO	(MH "Arthroplasty, Replacement, Hip") OR TI (THR OR “total hip replacement” OR THA OR “total hip arthroplasty” OR “hip joint replacement” OR "hip joint arthroplasty") OR AB (THR OR “total hip replacement” OR THA OR “total hip arthroplasty” OR “hip joint replacement” OR "hip joint arthroplasty")	58,004	
S2	MEDLINE, via EBSCO	(MH “Ambulatory Surgical Procedures”) OR (MH “Ambulatory Care”) OR TI (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0") OR AB (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0")	1,390,383	
S3	MEDLINE via EBSCO	(MH "Early Ambulation") OR TI (Ambulat* OR walk* OR mobilisation OR mobilization) OR AB (Ambulat* OR walk* OR mobilisation OR mobilization)	256,765	
S4	MEDLINE via EBSCO	S1 AND S2 AND S3 **Since: 2005 Language: English**	489	76 Identified for abstract review.
S5	CINAHL via EBSCO	(MH "Arthroplasty, Replacement, Hip") OR TI (THR OR “total hip replacement” OR THA OR “total hip arthroplasty” OR “hip joint replacement” OR "hip joint arthroplasty") OR AB (THR OR “total hip replacement” OR THA OR “total hip arthroplasty” OR “hip joint replacement” OR "hip joint arthroplasty")	21,558	

S6	CINAHL via EBSCO	(MH “Ambulatory Surgical Procedures”) OR (MH “Ambulatory Care”) OR TI (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0") OR AB (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0")	235,536	
S7	CINAHL via EBSCO	(MH "Early Ambulation") OR TI (Ambulat* OR walk* OR mobilisation OR mobilization) OR AB (Ambulat* OR walk* OR mobilisation OR mobilization)	88,180	
S8	CINAHL via EBSCO	S5 AND S6 AND S7 **Since 2005 Language: English**	334	50 Identified for abstract review.
S9	EMBASE via OVID	hip arthroplasty/ OR hip replacement/ OR (THR or total hip replacement or THA or total hip arthroplasty or hip joint replacement or hip joint arthroplasty).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	77,972	
S10	EMBASE via OVID	outpatient/ OR outpatient care/ OR ambulatory surgery/ OR (outpatient OR ambulat* OR day case OR Rapid* OR Accelerate* OR fast-track OR fast track OR day zero OR day 0).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	1,849,052	
S11	EMBASE via OVID	mobilization/ OR (ambulat* or walk* or mobilisation or mobilization).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	446,747	

S12	EMBASE via OVID	S9 **AND** S10 **AND** S11 - **Since 2005 Language: English**	908	117 Identified for abstract review.
S13	AMED via EBSCO	TI (THR OR “total hip replacement” OR THA OR “total hip arthroplasty” OR “hip joint replacement” OR "hip joint arthroplasty") OR AB (THR OR “total hip replacement” OR THA OR “total hip arthroplasty” OR “hip joint replacement” OR "hip joint arthroplasty")	768	
S14	AMED via EBSCO	TI (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0") OR AB (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0")	10,086	
S15	AMED via EBSCO	TI (Ambulat* OR walk* OR mobilisation OR mobilization) OR AB (Ambulat* OR walk* OR mobilisation OR mobilization	15,373	
S16	AMED via EBSCO	S13 AND S14 AND S15 – Since 2005, Language: English	16	1 Identified for abstract review
S17	APA PsycInfo via EBSCO	DE "Hips" OR TI (THR OR “total hip replacement” OR THA OR “total hip arthroplasty” OR “hip joint replacement” OR "hip joint arthroplasty") OR AB (THR OR “total hip replacement” OR THA OR “total hip arthroplasty” OR “hip joint replacement” OR "hip joint arthroplasty")	1829	
S18	APA PsycInfo via EBSCO	TI (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0") OR AB (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0")	165,007	

S19	APA PsycInfo via EBSCO	TI (Ambulat* OR walk* OR mobilisation OR mobilization) OR AB (Ambulat* OR walk* OR mobilisation OR mobilization)	40,587	
S20	APA PsycInfo via EBSCO	S17 AND S18 AND S19 Since:2005, Language: English	41	1 Identified for abstract review (duplicate anyway)
Total 245 identified. 84 removed as duplicates leaving 161 for abstract review.				

2.4.3 Hierarchy of evidence rankings:

Of the 7 papers included in this literature review, 2 ranked within an excellent study design, and the remaining 5 as good.

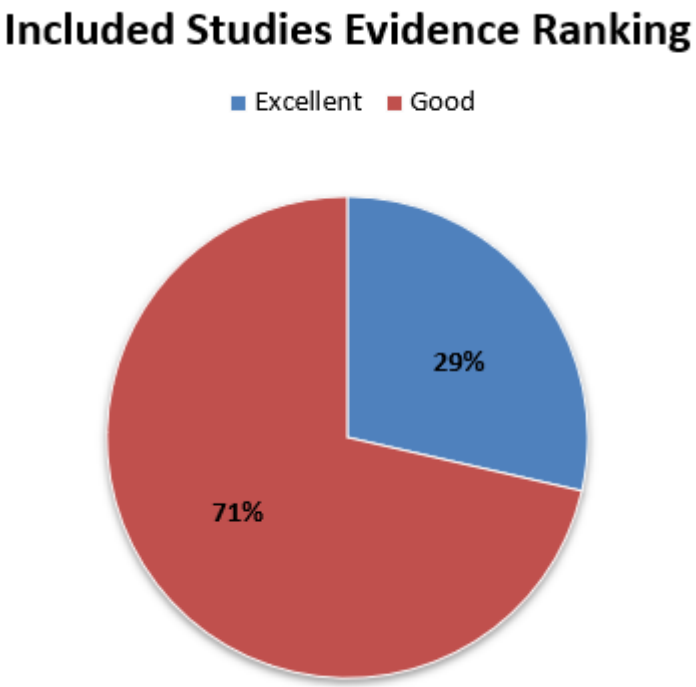


Figure 6 - Pie Chart - Included studies evidence ranking

Studies judged of excellent methodological design using the Evans (2003) classification consisted of one systematic review and one multi-centre RCT. The remaining 5 studies consisted of one single centre RCT, 2 cohort studies, one case-control study and one cost-utility study.

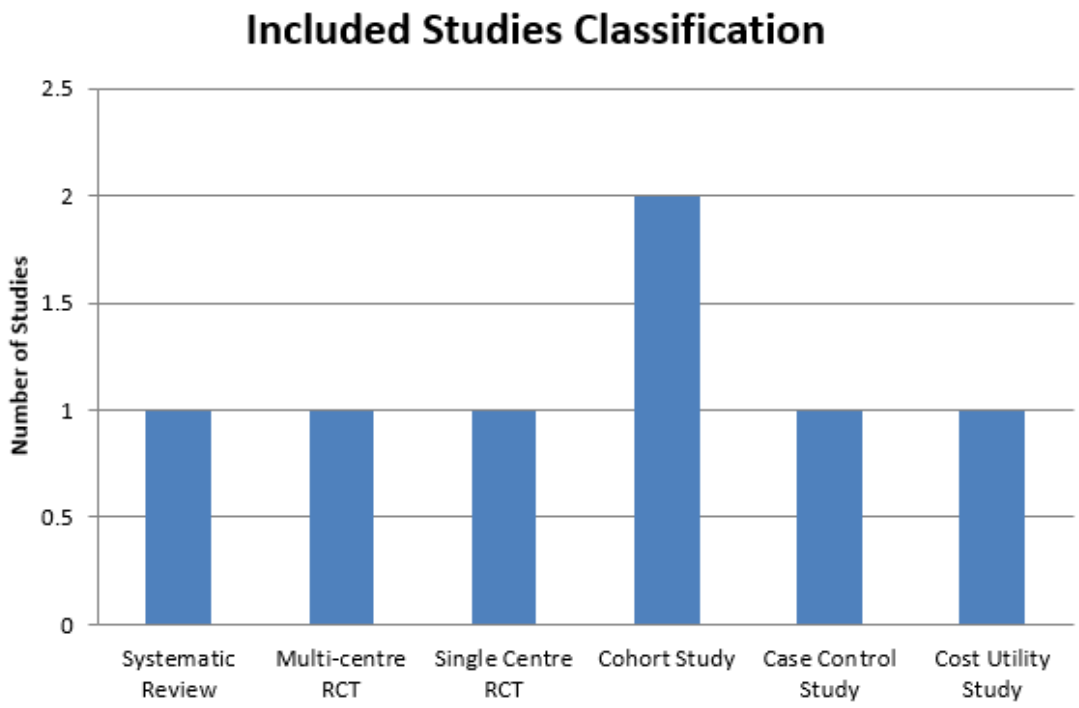


Figure 7 - Study type classifications for included studies

Study findings and appraisal of strengths and weaknesses are included in a meta-summary table in Appendix 2.

2.4.4 Checklists

All included studies underwent the appropriate checklist assessment, with all included studies performing satisfactorily for the expected elements of reporting. Full CONSORT, STROBE and PRISMA checklists for included studies are presented in Appendix 5

2.4.5 Risk of Bias Assessment

Five of the included studies used study designs amenable to risk of bias assessment. Larsen (2009) and Pollock et al. (2016) were not assessed as the tools available were not suitable for use with cost-utility studies or systematic reviews respectively.

Both RCTs included within this systematic review underwent risk of bias assessment using the RoB 2.0 tool. Both studies were judged overall as having low risk of bias. Elmoghazy et al. (2022) scored for high risk of bias and was excluded due to this result. This is summarised for each assessment domain within Figure 8 and Figure 9. These plots were produced using the robvis tool (McGuinness & Higgins 2021)

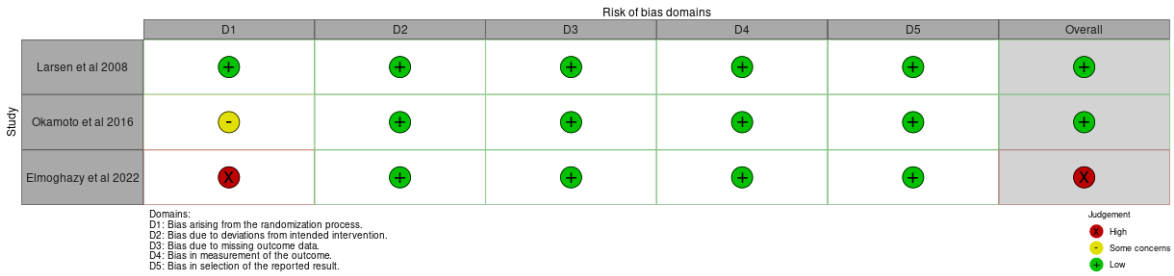


Figure 8: Risk of bias traffic light plot for included RCTs using the RoB 2.0 tool.

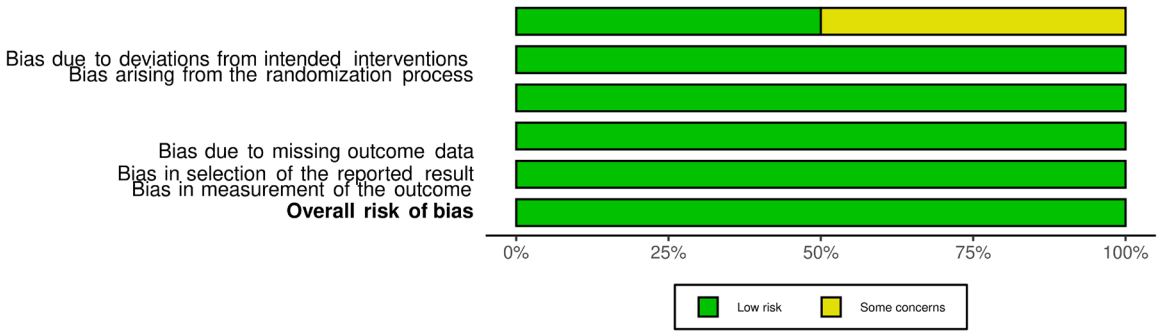


Figure 9:Risk of bias summary plot for included RCTs using the RoB 2.0 tool. (Limited to Larsen et al 2008 and Okamoto et al 2016)

Of the remaining studies assessed using the ROBINS-1 tool, Robins et al (2014) was excluded due to scoring as a critical risk of bias. Of the three studies which remained, two were determined as having a serious risk of bias and one with a moderate risk of bias. This is summarised in Figure 10 and Figure 11.

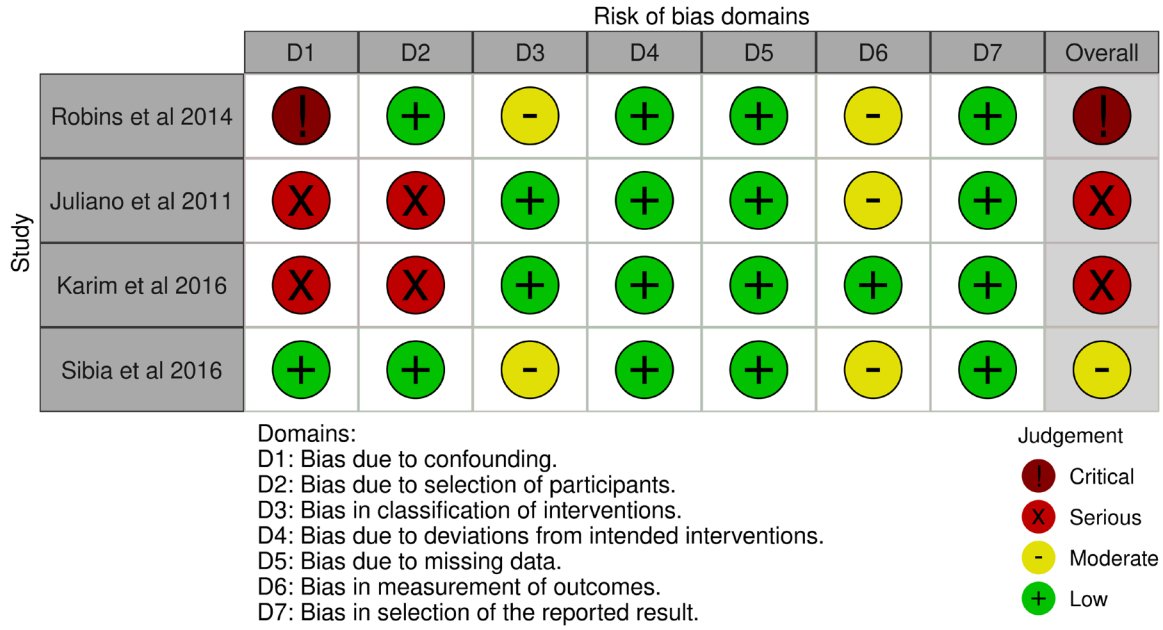


Figure 10: Risk of bias traffic light plot for included non-randomised studies using the ROBINS-1 tool.

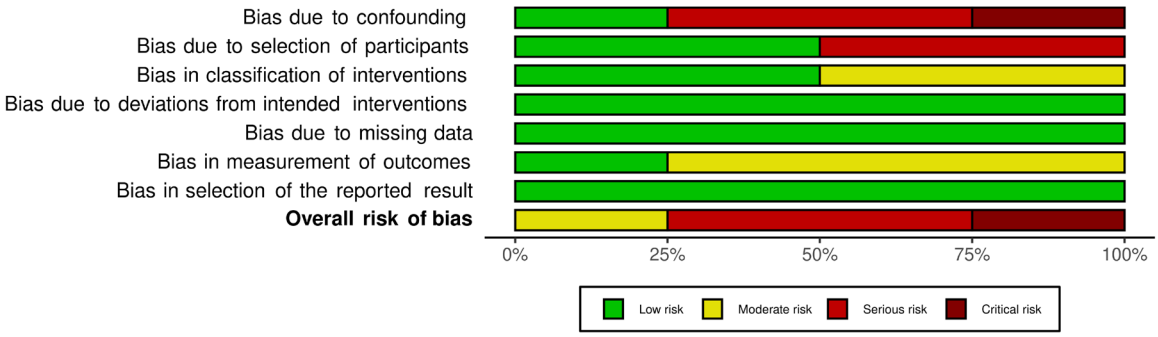


Figure 11: Risk of bias summary plot for included non-randomised studies using the ROBINS-1 tool.

Full detail of risk of bias assessments are contained within Appendix 4.

2.4.6 CASP Analysis

All seven of the included studies underwent review by two reviewers independently using the CASP analysis checklist appropriate to its design to identify strengths and weaknesses of the study. These checklists are presented in Appendix 6, and any pertinent findings from these included in the meta-summary ***Table 2-9*** below.

2.4.7 Meta-Summary Table Questions 1-4

No	*Authors*	*Study Location*	*Title*	*Study Type and (Hierarchy Rank)*	*Study Purpose*	*Sample Size*	*Outcome Measures*	*Relevant Findings*	*Specific Methodological Strengths*	*Relevant Methodological Weaknesses*
1	(K. Larsen, 2009)	Denmark	Cost-effectiveness of accelerated perioperative care and rehabilitation after total hip and knee arthroplasty	Piggyback study of an RCT - Cost-utility study **(GOOD)** Data from single centre RCT.	Compare the cost-effectiveness of a peri-operative accelerated care and rehabilitation protocol. Over the first post-operative year	N =87	Average reduction in cost QALY gain	Average cost reduction of approx. $4000 US Significant cost reduction Additional QALY gain of 0.08 Intervention significantly less costly and significantly more effective	Based on RCT data in Larsen 2008 Realistic Inc./Exc criteria	As with Larsen 2008 Pre-intervention HRQoL difference between groups
2	(K. Larsen, Sørensen, et al., 2008)	Denmark	Accelerated perioperative care and rehabilitation intervention for hip and knee replacement is effective: A randomized clinical trial	Single Centre RCT **(GOOD)**	To trial the efficacy of a 'true' accelerated surgical pathway post total joint replacement on length of stay and quality of life.	n = 87	Length of stay EQ5D Scores at 3 months	Mean length of stay reduced from 8 days to 5 days Greater gain of QoL in intervention group as measured through EQ5D - increase of an extra 0.88 on	RCT design Direct comparison between groups Realistic Inc/Exc criteria	Inclusive of THR, TKR and UKR Several other significant changes: Analgesic pathway changed Introduction of different education programme pre-op

No	*Authors*	*Study Location*	*Title*	*Study Type and (Hierarchy Rank)*	*Study Purpose*	*Sample Size*	*Outcome Measures*	*Relevant Findings*	*Specific Methodological Strengths*	*Relevant Methodological Weaknesses*
			involving 87 patients with 3 months of follow-up					EQ5D in intervention group Median length of stay reduced by 3 days		nutrition screening different anti-emetic prophylaxis Used mean to report the length of stay change - however known to be skewed data
3	(Juliano et al., 2011)	USA – New York	Initiating Physical Therapy on the Day of Surgery Decreases Length of Stay Without Compromising Functional Outcomes Following Total Hip Arthroplasty	Cohort Study **(GOOD)**	Examine whether the implementation of a new multidisciplinary clinical pathway, which began PT on the day of surgery (DOS) rather than POD1 would reduce LOS for patients undergoing THA while in the acute care setting. To assess the functional milestones achieved by these patients during the	N = 408	Length of stay Attainment of functional milestones	Reduction in LOS of 0.21 days seen in the intervention group – this reached statistical significance Control =3.48 Intervention = 3.27 Shortened LOS did not reduce the	Specific to THR High subject numbers Generic population	No co-morbidities Did not account for other non-medical factors which may have affected length of stay No randomisation Whole pathway changed not just DZM

No	*Authors*	*Study Location*	*Title*	*Study Type and (Hierarchy Rank)*	*Study Purpose*	*Sample Size*	*Outcome Measures*	*Relevant Findings*	*Specific Methodological Strengths*	*Relevant Methodological Weaknesses*
					hospital stay and whether or not the shortened length of stay resulted in patients being discharged with fewer of the milestones being reached			achievement of functional outcomes 67% of intervention group discharged in 3 days or less This was 57% in the control group		
4	(Okamoto et al., 2016)	Australia	Day-of-Surgery Mobilization Reduces the Length of Stay After Elective Hip Arthroplasty	Multi-centre RCT (**EXCELLENT)**	Determine the effect of day 0 mobilisation on time to readiness for discharge and length of stay .	N=126	Length of stay Time to readiness to discharge	Significant reduction in time to physiotherapy complete No significant differences in length of stay Significant reduction in the proportion of patients staying >72 hours	Specific to hip Only changed PT intervention RCT 3-month readmission follow-up **Good Study**	Strict inc/exc criteria Inclusive of hip resurfacing used unpaired t-test - but I would expect the data to be non-parametric No power calculation

No	*Authors*	*Study Location*	*Title*	*Study Type and (Hierarchy Rank)*	*Study Purpose*	*Sample Size*	*Outcome Measures*	*Relevant Findings*	*Specific Methodological Strengths*	*Relevant Methodological Weaknesses*
5	(Karim et al., 2016)	USA – Texas	Does Accelerated Physical Therapy After Elective Primary Hip and Knee Arthroplasty Facilitate Early Discharge?	Cohort study **(GOOD)**	To evaluate the introduction of a service change towards day 0 mobilisation.	N=116 for THR	Length of stay Distance walked on first physiotherapy session.	No significant differences in mean length of stay . Higher proportion of pts achieving discharge on day 1	Comparative study Exceeded power calculation requirements. Isolated use of day zero mobilisation as the intervention.	Inclusive of both THR and TKR. No randomisation – appears to be selective group allocation. Also changed to minimally invasive surgical technique
6	(Pollock et al., 2016)	Canada – Ontario	Outpatient Total Hip Arthroplasty, Total Knee Arthroplasty, and Unicompartmental Knee Arthroplasty	Systematic Review (**EXCELLENT)**	Review literature for the safety and feasibility of outpatient arthroplasty (THR, TKR, UKR)	17 studies included	N/A	Similar outcomes from outpatient arthroplasty in terms of complication rates and clinical outcomes but with reduced length of stay and cost savings. However – lack of high-level evidence.	Clear search and appraisal methodology Well conducted review PRISMA statement for write-up 2 x independent reviewers	Not specific to THR No RCTs included Only 4 included studies had a control group Majority of studies had a selected population – inherent selection bias

No	*Authors*	*Study Location*	*Title*	*Study Type and (Hierarchy Rank)*	*Study Purpose*	*Sample Size*	*Outcome Measures*	*Relevant Findings*	*Specific Methodological Strengths*	*Relevant Methodological Weaknesses*
7	Sibia et al 2016	USA – Maryland	Predictors of hospital length of stay in enhanced recovery after surgery program for primary total hip arthroplasty	Case-Control Study **(GOOD)**	Identify variables associated with length of stay for THAs following an ERAS protocol.	N=273 All THA	Association of pre-op patient characteristics & peri-op surgical factors on LOS Secondary outcome of hospital costs.	Old age, increased BMI, female, ASA 3 or4 and CAD associated with length of stay >2 Not ambulating Day 0 strongly correlated to longer length of stay. But 70% of patients who did not DZM had surgery after 12pm. Considering only the patients who had surgery after 12pm, not DZM increased the odds of staying >2 days.	No exclusion criteria – good external validity. Everyone followed the same ERAS pathway. No loss to follow up as retrospective	Not a proper cost analysis No power calculation length of stay Day 1 32% - 87 patients is a low number for comparison to. Not equal numbers . 43% Day 2 (n=117), 25% >2 days (n=68) Numbers small for those who had surgery after 12pm in terms of being sure of results.

Table 2-9: Meta summary table for questions 1-4

2.4.8 Length of Stay (LOS)

Four of the included studies directly presented empirical findings about length of stay (Larsen, Sørensen, et al. 2008; Juliano et al. 2011; Okamoto et al. 2016; Karim et al. 2016), this included two RCTs and two cohort studies. Findings were mixed, with the two earlier studies reporting a statistically significant reduction in length of stay, but the other two studies conducted in 2016 reported no statistically significant differences in length of stay. While the largest effect was observed in Larsen, Sørensen, et al. 2008, with a reduction of 3 days in length of stay, the other three included studies showed a much more modest or statistically insignificant reduction in length of stay. Sibia et al. 2016, while not directly measuring length of stay as an outcome, examined characteristics associated with patients staying more than a single day in hospital following THR. In this study, not ambulating on day zero was strongly associated with an increased length of stay (odds ratio 3.93, $p<0.001$), supporting the inference of a true length of stay reduction with day-zero ambulation.

Juliano et al. (2011) and Okamoto et al. (2016) isolated day-zero ambulation as the sole intervention, had high participant numbers, were specifically examining patients undergoing THR and had well representative inclusion and exclusion criteria to ensure generalizability to UK orthopaedic practice. Both studies saw a modest reduction in length of stay in the fast-track group of 0.21 days ($p=0.014$) and 0.41 days ($p=0.11$) respectively. While this is at odds with larger effect sizes seen in other studies, this may be more reliable as a representative effect size for day-zero ambulation on length of stay following THR.

2.4.9 Financial Efficiency

Only one of the included studies specifically examined the financial effect of a pathway that included day-zero ambulation. Larsen (2009) compared 45 patients treated under an accelerated rehabilitation programme, with 42 treated under standard care. Over the entire care-episode and subsequent 12-month recovery, this study observed significant reductions in the average cost-per-patient of approximately $3178 USD specific to THR (Supplementary study data).

2.4.10 Safety of Day-zero Mobilisation:

Pollock et al. (2016) was the only paper which met the inclusion and exclusion criteria for this review, which made comment on the safety of day-zero ambulation. This systematic review reported no differences in complications, revision surgeries or readmission rates in participants

who underwent day-zero ambulation as part of an outpatient arthroplasty programme. This review did not breakdown these adverse events complications into types.

2.4.11 Functional Recovery

Two studies included within this review examined an outcome measure relating to post-operative function or health related quality of life. Juliano et al. (2011) examined the achievement of functional milestones in recovery; proportions of participants who achieved independence in negotiating stairs and walking with a cane. In this study, there were no significant differences in the attainment of these milestones despite a slightly shortened length of stay within the intervention group – indicating a faster functional recovery. Larsen, Sørensen, et al. (2008) reported improved EQ5D patient reported quality of life measure (Euroqol Group 1990) in patients who had undergone day-zero ambulation, which did reach statistical significance.

This suggests a promising benefit of day-zero ambulation in speed of functional recovery and HRQoL. However, as both papers examined very different outcomes, this review cannot build more confidence in these findings beyond that which is presented within the original research papers.

2.4.12 Pain

Of the studies that reached the level of evidence to be included within this review, none examined the post-operative pain experience as part of their study aims.

2.4.13 Question 5 - The Lived Experience of Day Zero Mobilisation:

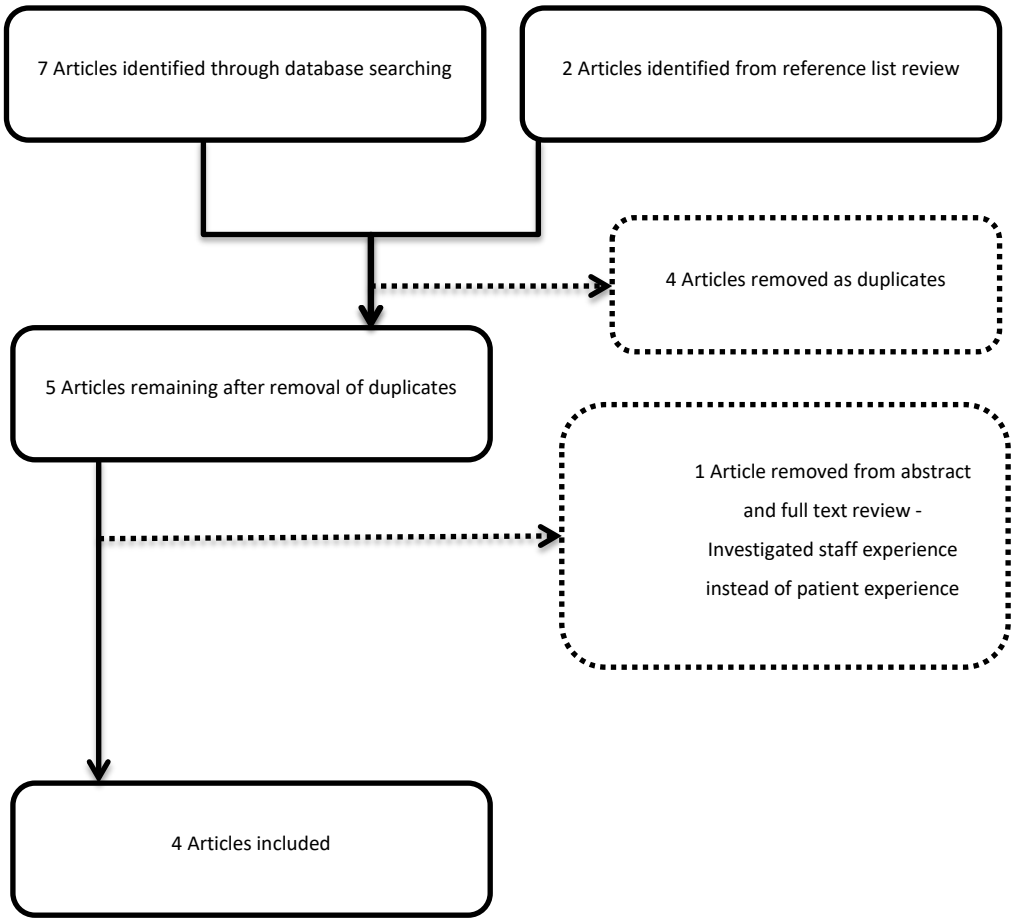


Figure 12: Question 5 Literature Search Flow Diagram

Table 2-10: Literature review question 5 search strategy and results

Search Number	Databases Searched	Search Terms and Limits	Number of Results	Comments on Results
S1	MEDLINE via EBSCO	(MH "Arthroplasty, Replacement, Hip") OR TI (THR OR "total hip replacement" OR THA OR "total hip arthroplasty" OR "hip joint replacement" OR "hip joint arthroplasty") OR AB (THR OR "total hip replacement" OR THA OR "total hip arthroplasty" OR "hip joint replacement" OR "hip joint arthroplasty")	58,004	
S2	MEDLINE via EBSCO	(MH "Ambulatory Surgical Procedures") OR (MH "Ambulatory Care") OR TI (outpatient OR ambulat* OR "day case" OR Rapid* OR Accelerate* OR "fast-track" OR "fast track" OR "day zero" OR "day 0") OR AB (outpatient OR ambulat* OR "day case" OR Rapid* OR Accelerate* OR "fast-track" OR "fast track" OR "day zero" OR "day 0")	1,390,383	
S3	MEDLINE via EBSCO	(MH "Early Ambulation") OR TI (Ambulat* OR walk* OR mobilisation OR mobilization) OR AB (Ambulat* OR walk* OR mobilisation OR mobilization)	256,765	
S4	MEDLINE via EBSCO	(MH "Qualitative Research") OR TI (qualitative OR "mixed method" OR "mixed methods" OR "focus group" OR "focus groups" OR interview* OR ethnograph* OR phenomenology* OR "grounded theory" OR "case study" OR "constant comparative" OR "constant comparison" OR "content analysis" OR "discourse analysis" OR "narrative" OR "participant observation" OR "field study" OR "field studies" OR "concept analysis") OR AB (qualitative OR "mixed method" OR "mixed methods" OR "focus group" OR "focus groups" OR interview* OR ethnograph* OR phenomenology* OR "grounded theory" OR "case study" OR "constant comparative" OR "constant comparison" OR "content analysis" OR "discourse analysis" OR "narrative" OR "participant observation" OR "field study" OR "field studies" OR "concept analysis")	651,706	
S5	MEDLINE via EBSCO	(MH "Patient Satisfaction+") OR TI (View* OR experience* OR feel* OR know* OR opinion* OR belief* OR descript* OR expectation* OR perception* OR "patient experience" OR "patient satisfaction" OR "lived experience") OR AB (View* OR experience* OR feel* OR know* OR opinion* OR belief* OR descript* OR expectation* OR perception* OR "patient experience" OR "patient satisfaction" OR "lived experience") View* OR experience* OR feel* OR know* OR opinion* OR belief* OR descript* OR expectation* OR perception* OR "patient experience" OR "patient satisfaction" OR "lived experience"	4,017,507	
S6	MEDLINE via EBSCO	S1 **AND** S2 **AND** S3 **AND** S4 **AND** S5 Limits: **Since 2005, English Language, Full Text**	8	3 Identified for abstract review
S7	CINAHL via EBSCO	(MH "Arthroplasty, Replacement, Hip") OR TI (THR OR "total hip replacement" OR THA OR "total hip arthroplasty" OR "hip joint replacement" OR "hip joint arthroplasty") OR AB (THR OR "total hip replacement" OR THA OR "total hip arthroplasty" OR "hip joint replacement" OR "hip joint arthroplasty")	21,558	
S8	CINAHL via EBSCO	(MH "Ambulatory Surgical Procedures") OR (MH "Ambulatory Care") OR TI (outpatient OR ambulat* OR "day case" OR Rapid* OR Accelerate* OR "fast-track" OR "fast track" OR "day zero" OR "day 0") OR AB (outpatient OR ambulat* OR "day case" OR Rapid* OR Accelerate* OR "fast-track" OR "fast track" OR "day	235,536	
S9	CINAHL via EBSCO	(MH "Early Ambulation") OR TI (Ambulat* OR walk* OR mobilisation OR mobilization) OR AB (Ambulat* OR walk* OR mobilisation OR mobilization)	88,180	

S10	CINAHL via EBSCO	(MH "Qualitative Research") OR TI (qualitative OR "mixed method" OR "mixed methods" OR "focus group" OR "focus groups" OR interview* OR ethnograph* OR phenomenology* OR "grounded theory" OR "case study" OR "constant comparative" OR "constant comparison" OR "content analysis" OR "discourse analysis" OR "narrative" OR "participant observation" OR "field study" OR "field studies" OR "concept analysis") OR AB (qualitative OR "mixed method" OR "mixed methods" OR "focus group" OR "focus groups" OR interview* OR ethnograph* OR phenomenology* OR "grounded theory" OR "case study" OR "constant comparative" OR "constant comparison" OR "content analysis" OR "discourse analysis" OR "narrative" OR "participant observation" OR "field study" OR "field studies" OR "concept analysis")	407,029	
S11	CINAHL via EBSCO	(MH "Patient Satisfaction+") OR TI (View* OR experience* OR feel* OR know* OR opinion* OR belief* OR descript* OR expectation* OR perception* OR "patient experience" OR "patient satisfaction" OR "lived experience") OR AB (View* OR experience* OR feel* OR know* OR opinion* OR belief* OR descript* OR expectation* OR perception* OR "patient experience" OR "patient satisfaction" OR "lived experience")	1,223,338	
S12	CINAHL via EBSCO	S7 **AND** S8 **AND** S9 **AND** S10 **AND** S11 Limits: **Since 2005, English Language, Full Text**	5	2 identified for abstract review
S13	EMBASE via OVID	hip arthroplasty/ OR hip replacement/ OR (THR or total hip replacement or THA or total hip arthroplasty or hip joint replacement or hip joint arthroplasty).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	77,972	
S14	EMBASE via OVID	outpatient/ OR outpatient care/ OR ambulatory surgery/ OR (outpatient OR ambulat* OR day case OR Rapid* OR Accelerate* OR fast-track OR fast track OR day zero OR day 0).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name,	1,849,052	
S15	EMBASE via OVID	mobilization/ OR (ambulat* or walk* or mobilisation or mobilization).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	446,747	
S16	EMBASE via OVID	qualitative research/ or qualitative.mp. or mixed method.mp. or mixed methods.mp. or focus group.mp. or focus groups.mp. or interview*.mp. or ethnography.mp. or ethnographic.mp. or phenomenology.mp. or phenomenological.mp. or grounded theory.mp. or case study.mp. or constant comparative.mp. or constant comparison.mp. or content analysis.mp. or discourse analysis.mp. or narrative.mp. or participant observation.mp. or field study.mp. or field studies.mp. or concept analysis.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	989,216	
S17	EMBASE via OVID	(View* or experience* or feel* or know* or opinion* or belief* or descript* or expectation* or perception* or patient experience or patient satisfaction or lived experience).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	5,767,906	
S18	EMBASE via OVID	S13 **AND** S14 **AND** S15 **AND** S16 **AND** S17 Limits: **Since 2005, English Language, Full Text**	21	2 Identified for abstract review
S19	AMED via EBSCO	TI (THR OR "total hip replacement" OR THA OR "total hip arthroplasty" OR "hip joint replacement" OR "hip joint arthroplasty") OR AB (THR OR "total hip replacement" OR THA OR "total hip arthroplasty" OR "hip joint replacement" OR "hip joint arthroplasty")	768	

S20	AMED via EBSCO	TI (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0") OR AB (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0")	10,086	
S21	AMED via EBSCO	TI (Ambulat* OR walk* OR mobilisation OR mobilization) OR AB (Ambulat* OR walk* OR mobilisation OR mobilization	15,373	
S22	AMED via EBSCO	TI (qualitative OR “mixed method” OR “mixed methods” OR “focus group” OR “focus groups” OR interview* OR ethnograph* OR phenomenology* OR “grounded theory” OR “case study” OR “constant comparative” OR “constant comparison” OR “content analysis” OR “discourse analysis” OR “narrative” OR “participant observation” OR “field study” OR “field studies” OR “concept analysis”) OR AB (qualitative OR “mixed method” OR “mixed methods” OR “focus group” OR “focus groups” OR interview* OR ethnograph* OR phenomenology* OR “grounded theory” OR “case study” OR “constant comparative” OR “constant comparison” OR “content analysis” OR “discourse analysis” OR “narrative” OR “participant observation” OR “field study” OR “field studies” OR “concept analysis”)	18,448	
S23	AMED via EBSCO	TI (View* OR experience* OR feel* OR know* OR opinion* OR belief* OR descript* OR expectation* OR perception* OR “patient experience” OR “patient satisfaction” OR “lived experience”) OR AB (View* OR experience* OR feel* OR know* OR opinion* OR belief* OR descript* OR expectation* OR perception* OR “patient experience” OR “patient satisfaction” OR “lived experience”)	57,910	
S24	AMED via EBSCO	S19 AND S20 AND S21 AND S22 AND S23. Since 2005 Language: English	0	0 Identified for abstract review
S25	APA PsycInfo via EBSCO	DE "Hips" OR TI (THR OR “total hip replacement” OR THA OR “total hip arthroplasty” OR “hip joint replacement” OR "hip joint arthroplasty") OR AB (THR OR “total hip replacement” OR THA OR “total hip arthroplasty” OR “hip joint replacement” OR "hip joint arthroplasty")	1829	
S26	APA PsycInfo via EBSCO	TI (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0") OR AB (outpatient OR ambulat* OR “day case" OR Rapid* OR Accelerate* OR “fast-track” OR “fast track” OR "day zero" OR "day 0")	165,007	
S27	APA PsycInfo via EBSCO	TI (Ambulat* OR walk* OR mobilisation OR mobilization) OR AB (Ambulat* OR walk* OR mobilisation OR mobilization)	40,587	
S28	APA PsycInfo via EBSCO	DE "Qualitative Methods" OR TI (qualitative OR “mixed method” OR “mixed methods” OR “focus group” OR “focus groups” OR interview* OR ethnograph* OR phenomenology* OR “grounded theory” OR “case study” OR “constant comparative” OR “constant comparison” OR “content analysis” OR “discourse analysis”	552,229	

		OR “narrative” OR “participant observation” OR “field study” OR “field studies” OR “concept analysis”) OR AB (qualitative OR “mixed method” OR “mixed methods” OR “focus group” OR “focus groups” OR interview* OR ethnograph* OR phenomenology* OR “grounded theory” OR “case study” OR “constant comparative” OR “constant comparison” OR “content analysis” OR “discourse analysis” OR “narrative” OR “participant observation” OR “field study” OR “field studies” OR “concept analysis”)		
S29	APA PsycInfo via EBSCO	DE "Life Experiences" OR DE "Experiences (Events)" OR TI (View* OR experience* OR feel* OR know* OR opinion* OR belief* OR descript* OR expectation* OR perception* OR “patient experience” OR “patient satisfaction” OR “lived experience”) OR AB (View* OR experience* OR feel* OR know* OR opinion* OR belief* OR descript* OR expectation* OR perception* OR “patient experience” OR “patient satisfaction” OR “lived experience”)	1,729,667	
S30	APA PsycInfo via EBSCO	S25 AND S26 AND S27 AND S28 AND S29. Since 2005 Language: English	1	0 Identified for abstract review.

In total, 9 papers were identified from search for further investigation. Of these, four were identified as duplicated. One further paper was excluded as it examined the lived experience of nursing staff rather than the patient. This left 4 papers included within this question of the review.

The four included papers are summarised in the meta-summary ***Table 2-11*** below:

Table 2-11: Literature review lived experience of day zero mobilisation meta-summary table

Paper	*Study Type*	*Findings*	*Limitations*
Husted et al. 2009	Multi-departmental audit. Examined 8 different orthopaedic departments. Produced 635 questionnaires for analysis.	No significant differences in patient satisfaction, regardless of significant differences between department's length of stay	Unclear as to how patient satisfaction was measured. Self-developed and non-validated questionnaire, but the questionnaire content not published. Minority of departments used d ay-zero ambulation Amalgamated results from THR and TKR
Specht, Kjaersgaard-Andersen & Pedersen 2015	Interpretive phenomenological study	Patient uncertainty around taking pain relief: *Fear of addiction* *Uncertainty around expected levels of pain.* *Feeling they should be in more pain before requesting extra pain relief* *The importance of nurse involvement for advice and pain management* Education/information is linked to confidence: *Providing correct informati on at the right time improves patient confidence.* *Contradictory information causes insecurity* The importance of resting time on the ward to get	Amalgamated experiences from THR and TKR. Not specifically focussed on day-zero ambulation – looked at experience across an entire enhanced recovery pathway. No discussion of thematic saturation. No discussion of the author reflexivity.

Paper	*Study Type*	*Findings*	*Limitations*
		the most from rehabilitation sessions: *Sleep or* *rest disturbances led to patients feeling unable to cope with their physiotherapy programme.*	
Berg et al. 2019	Qualitative – Inductive content analysis	Early mobilisation *Patients were mentally prepared to get up.* *However some patients had doubts as to whether it could be possible and were surprised when they were able to stand and walk.* *Early Discharge:* *Most accepting of early discharge, however, some had objections or worries*	Looked at the whole patient pathway, but did have some content directly relating to early mobilisation and early discharge. Conducted a large number of interviews (n=24) Was multi-centred to pick up a breadth of experience. Amalgamated experiences from THR and TKR. Reduced depth in each area as having to cover the entire pathway. No discussion of author influence or bracketing process.
Sjøveian & Leegaard 2017	Qualitative Descriptive semi-structured interview design	n = 12 Participants described on-going pain at rest and on movement after discharge. Several expressed they would have benefitted from more individualised advice on pain and rehabilitation prior to discharge.	Did not specifically examine day-zero ambulation – focussed on discharge after fast track surgery. Combined experiences from TKR and THR

Overall, Berg et al. (2019) was the only paper which presented findings directly related to the lived experience of day-zero ambulation as an intervention, with participants feeling mentally prepared to undertake day-zero ambulation, but describing doubts about their physical ability, and surprise when they were able to ambulate so early post-operatively.

2.5 Discussion

2.5.1 Summary of Key Findings

2.5.1.1 What effect does day-zero ambulation (DZM) have on patient recovery in terms of length of hospital stay and financial efficiency?

Length of Stay

There are indications that day-zero ambulation may reduce length of stay (Larsen, Sørensen, et al. 2008; Juliano et al. 2011; Okamoto et al. 2016; Karim et al. 2016) and consistency in the direction of effect within the wider literature beyond the inclusion of this systematic review (Berger et al. 2009; Husted, Solgaard, et al. 2010; Robbins et al. 2014; Bottros et al. 2010; Tayrose et al. 2013; Wellman et al. 2011; Chen et al. 2012; den Hertog et al. 2012; Gulotta et al. 2011; Isaac et al. 2005; Raphael et al. 2011). However, methodological heterogeneity and the lack of studies isolating and comparing day-zero ambulation as an intervention against standard care, mean that there is not enough high-quality evidence to support this as a clinical conclusion.

Across all studies, there was either a comparative reduction in length of stay or a lower length of stay than would be normally expected in standard UK care which has been evidenced at a mean of 12.3 days when examined across 151 UK hospitals (Gaughan et al. 2012). Most length of stay measures reached statistical significance, however there were two studies, including a recent RCT (Okamoto et al. 2016) and Karim et al. (2016) which did not reach statistical significance. Furthermore, different studies showed a huge variation in how much length of stay reduced following day-zero ambulation, ranging from observations in length of stay from 0.21 (Juliano et al. 2011) to 3 days (Larsen, Sørensen, et al. 2008). Within the wider literature an even greater range of change is reported with den Hertog et al. (2012), although examining TKR alone, reporting a length of stay reduction of 6.45 days. As such, amalgamation of effect size across studies is of little value. This leaves clinicians with poor confidence in the number of bed days which could be saved by employing day-zero ambulation. Reduction in length of stay is also reflected within the wider literature of studies not included within this review, with a further 16 papers showing a relative reduction in length of stay (den Hertog et al. 2012; Robbins et al. 2014; Bottros et al. 2010; Tayrose et al. 2013; Wellman et al. 2011; Husted, Lunn, et al. 2011; Banerjee 2014; Chen et al. 2012; Gulotta et al. 2011; Isaac et al. 2005; Khan et al. 2014; Malviya et al. 2011; Raphael et al. 2011; Berger et al. 2009; Husted 2012).

This suggests a majority agreement across studies that day zero-ambulation reduces length of stay. However, due to limitations in methodological heterogeneity and minimal studies

isolating day-zero ambulation as the sole intervention, attributing this change directly to day-zero ambulation as an intervention is flawed.

Financial Efficiency

Only one of the included studies specifically examined the financial effect of a pathway that included day-zero ambulation. While Larsen (2009) observed significant reductions in the average cost-per-patient of approximately $3178 USD specific to THR (Supplementary study data). Andreasen et al. (2017) also claimed a reduction in the cost of providing THR of $10,471. Their comparison, however, was made using costs from a previous 2016 publication and without a direct comparison group. This costing also did not account for the prosthetic implant costs. While these two studies indicate there could be significant financial savings by using day-zero ambulation, currently these studies are in isolation and were carried out in healthcare systems very different to UK practice. While Larsen (2009) has a strong methodology as a fully-blown cost-utility study, it was based on data from the study by Larsen, Sørensen, et al. (2008), which illustrated the greatest reduction in length of stay. Cost saving on bed days is expected to be one of the main sources of cost saving. If identical economic evaluation were carried out the studies which saw more modest reductions in length of stay, the cost-per-patient savings would also likely be much more modest.

As financial efficiency is strongly linked with length of stay, financial efficiency findings based on studies examining length of stay are inherently subject to the same limitations affecting length of stay findings. Ultimately, to employ day zero-ambulation in UK practice, most UK orthopaedic services would require reconfiguration to provide physiotherapy services over extended hours to support the additional rehabilitation. Extending services to provide physiotherapy later into the evening will cost money and justification of the spend required for this needs a more robust prediction of effect size.

2.5.1.2 Is day-zero ambulation safe, when considering post-operative complications and mortality?

Judgement on the safety of day-zero ambulation within this review is limited to one included systematic review, which ultimately was not examining day-zero ambulation as an intervention as it was exploring outpatient arthroplasty pathways. Despite this, other studies in the wider literature although not reaching the inclusion criteria of this review, presented encouragingly positive findings. In particular, seven different published studies have found no difference in post-operative complication rates between their intervention and control groups (Berger et al. 2009;

Wellman et al. 2011; Gulotta et al. 2011; Banerjee 2014; Khan et al. 2014; Klein et al. 2017; Pollock et al. 2016).

Although Pollock et al. (2016) looked at overall incidence of complications, other studies showed similar findings in specific post-operative complications. For complications directly associated with THR, multiple studies report no significant differences in incidence of DVT/PE (Berger et al. 2009; Husted, Otte, Billy B Kristensen, et al. 2010; Jorgensen et al. 2016; Klein et al. 2017), no increase in dislocation rates (Andersen et al. 2009)(Husted, Otte, Billy B. Kristensen, et al. 2010; Klein et al. 2017; Andersen et al. 2009) and no increase in risk of falls (Jorgensen & Kehlet 2013). There are also other individual studies which show positive findings such as benefits in preserving post-operative cognitive abilities (Krenk et al. 2012; Krenk et al. 2014), reduced post-operative blood transfusion rate and 30-day incidence of myocardial infarction (Khan et al. 2014).

However, there are some areas of the literature where studies do not agree and show inconsistent results. Gulotta et al. (2011) showed lower incidences of post-operative dizziness, however Jans et al. (2015) found a high rate of post-operative orthostatic intolerance (39%) which is characterised by dizziness. Similarly, Klein et al. (2017) reported no significant difference in the incidence of infection, but Amlie et al. (2016) reported a significant increase in the incidence of revision surgery within 3 months post-op due to deep infection. One study also saw an increase in the incidence rates of post-operative nausea and vomiting (Raphael et al. 2011).

When looking at readmissions, one study reported reductions in readmission rates (Robbins et al. 2014), but this study was in isolation. The majority of studies supported the results of Pollock et al. (2016) in finding no significant differences in readmission rates between groups (Jorgensen & Kehlet 2013; Husted, Otte, Billy B. Kristensen, et al. 2010; Dorr et al. 2010; Khan et al. 2014; Raphael et al. 2011; Stambough et al. 2015; Klein et al. 2017). However, it must be noted that Dorr et al only included participants under the age of 65 years, and is directly challenged by the findings of Pitter et al. (2016) who specifically examined participants over 85 years and observed a 20% increase in readmissions within a 90 day follow-up; suggesting that age is likely to be a confounding factor in readmission rates examined in research. One area where all literature appears to be in agreement is in mortality rates, with all identified studies showing no significant differences or improvements in mortality rates (Jorgensen & Kehlet 2013; Khan et al. 2014; Malviya et al. 2011; Savaridas et al. 2013; Pitter et al. 2016). However, all these studies had methodological limitations specific to the research aims of this paper and these limitations are discussed below.

Overall, there may be some potentially important safety benefits observed in the wider literature, with some benefits appearing to have lasting post-discharge advantages for mortality, and risks of morbidity. Indeed, most publications paint a positive picture. However, while in

comparison relatively few; there were some negative findings within this wider literature. While complications such as orthostatic intolerance and PONV are relatively minor. The findings in Amlie et al. (2016) suggesting an increased requirement of revision surgery due to peri-prosthetic infection and Pitter et al's. (2016) increased readmission rates in cohorts over the age of 85 years are concerning as more serious potential implications.

Overall methodological limitations mean that the proposed benefits of pathways inclusive of day-zero ambulation cannot be confidently determined solely as effects of day-zero ambulation. Indeed the systematic review by Pollock et al. (2016), as the highest quality of evidence currently available on this topic commented on the lack of high-level evidence and selection biases within their own included studies. Considering this, further research is needed in this topic area.

2.5.1.3 What effect does day-zero ambulation have on functional recovery?

Potential benefits of using day-zero ambulation as an intervention include a faster functional recovery and improved health related quality of life (Juliano et al. 2011; Larsen, Sørensen, et al. 2008). There are other published studies which didn't reach the standards demanded to be included in this review. Despite this, several support the findings of a faster functional recovery, measured across a range of different functional measures. Banerjee (2014) reported patients undergoing day-zero ambulation were able to achieve the milestone of walking three metres with a walking frame 19.5 hours earlier on average than those treated under standard care and Den Hertog et al. 2012 reported improvements in EQ5D scores, and significantly higher AKSS (Insall et al. 1989) and WOMAC (Roos et al. 1998) scores in the intervention group at 5-7 days post-operatively. However, the differences in scores between groups did not reach statistical significance at subsequent follow-ups. This suggests that the functional head-start gained through day-zero ambulation may be short in duration.

Two further studies presented promising results, with Smith et al. (2012) reporting fast-track rehabilitation resulted in earlier achievement of functional milestones, examined through ILOA scores (Shields, L J Enloe, et al. 1995) and Klapwijk et al. (2017) reporting improvements in various PROMS over the first 6 post-operative weeks, including the OHS (Dawson et al. 1996) and the HOOS-PS (Nilsdotter et al. 2003). However, both studies lacked a comparison group, inhibiting comparison of effectiveness of day-zero ambulation against standard care. Similarly Temporiti et al. (2020) found improved FIM scores in participants who underwent day-zero ambulation when measured at 3 and 7 days post-operatively compared to a non-randomised control group.

However, participants who failed day-zero ambulation were automatically excluded from the study calling into question the relevance of these findings to real life application.

All the above studies agree on a direction of effect, and no studies presented negative findings. While many of these studies did not meet the rigors for inclusion within this review, overall, there seems to be no arguments against there being functional benefit to day-zero ambulation, particularly in the early post-operative phase.

2.5.1.4 What effect does day-zero ambulation have on the patient's post-operative pain experience?

Unfortunately, no published papers which examined the effect of day-zero ambulation on post-operative pain experience reached the standards demanded for this review. Within the included studies, none included pain experience within their intended outcomes or objectives. Screened studies which did investigate pain were excluded for methodological limitations. This was often due to concomitant changes to analgesic regimens, with high probability that these extra variables could confound the study outcomes when trying to examine day-zero ambulation in isolation. As such the present review cannot provide a conclusive argument as to the effect of day-zero ambulation on post-operative pain experience.

Within the wider literature three studies have shown statistically significant reductions in post-operative pain numerical rating scores in patients undergoing pathways inclusive of day-zero ambulation (Bottros et al. 2010; Raphael et al. 2011; Smith et al. 2012)and Andersen et al. (2009) reported acceptable post-operative pain scores when a multi-modal pain management strategy was used. Raphael et al. (2011) also reported significantly less opioid consumption in the fast-track group than standard care. However, den Hertog et al. (2012) contradicted this; with consumption of analgesics being higher over the first two post-operative days than standard care, although when examined at three month follow-up, analgesia consumption was significantly reduced in the intervention group.

2.5.1.5 What is currently known about the patient's lived experience of day-zero ambulation post THR?

Currently there is minimal published work specifically around the lived experience of day-zero ambulation. Berg et al.(2019) is the only study providing information directly relating to the lived experience of day-zero ambulation. It was found that patients did feel mentally prepared to

ambulate on day zero, but also had some doubts as to whether it was possible. However, this study was not designed specifically to examine the experience of day-zero ambulation and as such only dedicated a small part of its findings to this.

THR is considered an extensive life event (Gustafsson et al. 2010), and the descriptive phenomenological study by Reay et al. (2015) highlighted patient fears and challenges associated with early hospital discharge such as social isolation and frustrations with physical immobility. Introducing day-zero ambulation would undoubtedly affect the complex emotional lived experience of THR and influence patient satisfaction with their care. Therefore, further enquiry into the lived experience would be valuable in moving this field forwards.

2.5.2 Systematic Review Limitations

This section discusses the limitations specific to the methods of this systematic review.

Small Number of Included Studies

This systematic review had strict inclusion and exclusion criteria. Consequently, only a small number of studies reached the standards set for inclusion. While this approach was designed to identify and limit this review to the highest quality evidence available, it meant there was limited information across several of the research questions set at the outset of this review, in particular in the domains of functional recovery and post-operative pain.

Employing strict inclusion and exclusion criteria and rigorous risk of bias assessment served to keep the number of papers for review to a manageable number. This in turn enabled this unfunded study the use of a second reviewer without additional resources; without which, this study would not be classified as a systematic review and would have lost methodological strength. It also ensured only the highest quality of evidence was included. While there are many studies in the wider literature which include day-zero ambulation as an intervention, methodological flaws in this research base for answering these research questions are rife.

If this review had included all papers from a ‘Fair’ hierarchy of methodology as defined by (Evans 2003) this would have made another 30 papers eligible for review. This highlights how much of the research base on this topic comes from studies considered low in the hierarchy of evidence. As such, despite a relatively large number of studies including findings around patients treated within a protocol that included day-zero ambulation, there are several significant problems discussed in the next section in using the whole research base of studies to draw conclusions about day-zero ambulation as an intervention.

Limited to Studies Published in English

This systematic review was unfunded, and as such did not have the resource to commission translation services. As such, the author was unable to appraise or include any studies published in other languages.

Publication Bias

Trials with positive findings are more likely to be published, published faster and cited more often (Hopewell et al. 2009). As literature reviews rely on reviewing a published research base, limitations and biases within the publication process, must also apply to the findings of systematic reviews. Doleman et al. (2021) recommends authors of systematic reviews include search conference proceedings and other grey literature to identify unpublished studies. However, this runs the risk of introducing trials of lesser quality into the review. In practice less than 4% of systematic reviews employ this time intensive method (Doleman et al. 2017).

2.5.3 Summary of the limitations in the body of literature

This section discusses more generalised limitations within the wider body of evidence.

Concomitant Pathway Changes:

Within five of the seven included studies for examining questions 1-4, there were concomitant interventions or changes to the experimental group pathways. These changes varied between studies but included interventions that are likely to have been significant confounding factors such as changes in surgical technique, anaesthetic protocol, post-operative analgesia regime and changes in pre-operative patient education. In these cases, the reported results cannot be confidently attributed solely to day-zero ambulation.

This is a problem also reflected in the wider literature, with most of the studies published on this topic not designed to examine specifically the effectiveness of day-zero ambulation. Instead, most studies examined a combination of accelerated pathway changes for experimental group participants. Consequently, there are inherent limitations in using this literature to answer a research question specifically focussed on day-zero ambulation such as this one.

Generalising results from both THR and TKR:

Of the papers reviewed, four studies were inclusive of THR and TKR with results presented as one finding. Grouping THR and TKR together when considering the effectiveness of day-zero ambulation appears non-scientific, given the significant differences in surgical procedure with likely different pain experiences, trauma, functional challenges and rehabilitation aims.

Again, this problem is inherent in the wider published literature, where it appears that presenting conjoined findings for different types of arthroplasty is widely accepted. This approach is questionable as it may not provide specific enough findings to make robust clinical decisions for a particular arthroplasty group.

Heterogeneity:

The Cochrane Handbook (The Cochrane Collaboration 2008) breaks down causes of heterogeneity into clinical diversity or methodological diversity, of which there is evidence of both when examining this review's literature. Evidence is visible through the significant variability in control group outcomes. Using length of stay as an example, Larsen, Sørensen, et al. (2008) reported a control group length of stay of 7.8 days compared with 3.48 days in Juliano et al. (2011). Indeed, the control group with the Juliano study outperformed the intervention group length of stay of 4.9 days seen in Larsen, Sørensen, et al. (2008). This suggests a significant difference in either the population examined or the methods of control group care delivery. In addition, the above issues of amalgamating both THR and TKR results, and the use of concomitant interventions are clear potential causes of clinical diversity and methodological diversity respectively.

The attempted meta-analysis presented earlier in this chapter (Figure 4), while inclusive of some studies which were eventually excluded from this review, does provide statistical evidence that heterogeneity is inherent within this literature base and must be considered a limitation within any literature review on this topic.

Hierarchy of Evidence:

Much of the published research about day-zero ambulation following THR comes from studies using a fair or poor research design within the Evans (2003)hierarchy of evidence. Cross-sectional studies constituted 58% of the identified literature; as such, this proportion of evidence did not provide any experimental comparison with standard care. This review only identified three empirical RCTs relevant to this topic, one of which was excluded for only examining TKR. The findings of these studies were also contradicted by the third RCT (Okamoto et al. 2016). Currently, there is a lack of studies using high-end methodologies that would be most visible and meaningful to front-line clinicians.

Reporting of Means:

All the studies included within this systematic review which examined length of stay reported their findings in terms of the mean length of stay. However, the mean is vulnerable to skewing from small numbers of patients with long length of stay, something frequently seen in

orthopaedic length of stay data. This makes it a poorer measure of central tendency than the median in skewed datasets and violates the assumption of normal distribution associated with the parametric comparative testing used in these publications. McCulloch et al. (2017) recognised length of stay datasets in elective arthroplasty cohorts as skewed and recommends using the median for reporting length of stay for the above reasons.

2.6 Conclusions

From the findings synthesised within this systematic review, adopting day-zero ambulation in wider practice shows potential to reduce length of stay, reduce costs and promote faster functional recovery. There is some evidence that this may be achievable without raising the risk of serious post-operative complications. However, included studies did not provide enough strength of evidence to allay fears of increasing the risk of periprosthetic infection and readmissions in older populations which have been reported in the wider literature.

Limitations within the published literature also lower confidence about attributing these positive effects directly to day-zero ambulation. Heterogeneity in both methods and findings leave little confidence over the effect sizes that services may expect if delivering day-zero ambulation to patient populations. In addition, there is a lack of evidence focussed on how day-zero ambulation may affect post-operative pain and the patient reported experience of THR rehabilitation, meaning this review was unable to draw any conclusions in these domains.

Implementing day-zero ambulation would require some significant service redesign and staffing investment with orthopaedic physiotherapy services having to provide services later into the evening. As such physiotherapy service leaders and decision-making clinicians need future research which gives greater confidence in the effect size on length of stay and consequent financial efficiencies to justify change.

2.7 Rationale for further Research

It is clear from the findings of this systematic review that the evidence specific to day-zero ambulation as a physiotherapeutic intervention is not strong enough for orthopaedic departments to employ it as an evidence-based service change. However, there appear to be some potential benefits in service efficiency and patient centred perspectives with potential length of stay reductions and morbidity and mortality benefits.

Considering the challenges facing elective orthopaedic services, further investigation into the multi-factorial effectiveness of day-zero ambulation would give evidence as to whether this

should be widely adopted as standard practice following THR. With much of the published evidence coming from cohort and cross-sectional studies, producing future empirical evidence through RCTs that examine day-zero ambulation as an isolated intervention and report findings in terms of the median, with consequent non-parametric analysis, would contribute greatly to determining the potential of this intervention through building confidence in effect size, examining incidence of infection, readmission and effect on post-operative pain. Moreover, further research examining this lived experience using methodologies which provide a rich analysis of patient experience would aid in the multi-factorial quality assessment of day-zero ambulation, assist effective clinical decision making and may reveal factors that could be used to enhance patient experience and develop key indicators for evaluation that may have been hitherto un-recognised.

3 - Research Questions and Paradigm Selection

3.1 Introduction

This chapter discusses the philosophical underpinnings of this research project, the philosophical standpoint of the researcher and the assumptions that come with the study design selection. Following this, the researcher finalises the research questions and hypotheses to be tested with the subsequent clinical trials and. This chapter finishes by discussing the specific ethical considerations within this research and how public and patient involvement was used to influence the research methodology.

3.2 Background

When considering day-zero ambulation within a clinical context, Gray & Muir's (2001) work on evidence based healthcare decisions illustrates how any clinical decision to implement such a change is a complex decision. Within their work, they describe the adoption of a new intervention or therapy as a multi-factorial decision, requiring contemplation across several dimensions to assess the overall quality of the intervention:

- **Acceptability** – The willingness of a patient population to be treated in this way
- **Effectiveness** – The degree to which the desired health outcomes are achieved in clinical practice
- **Safety** – Determined by knowing the probability that an adverse event will occur
- **Patient Experience** – A judgement about the quality of the patient's experience, regardless of whether the patient is satisfied
- **Cost-Effectiveness** – The relationship between the outcomes of a healthcare service or intervention in context of the inputs required.
- **Appropriateness** – A judgement of the 'good v harm' relationship related to the intervention.

These dimensions fit well with the key white paper produced by Lord Darzi (2008) examining quality within the UK NHS and described quality care as safe, effective and providing a patient experience encompassing compassion, dignity and respect. Consequently, this project aimed from conception to assess the overall quality of day-zero ambulation, and generate empirical evidence designed to provide answers in each of the above dimensions of 'quality' with the expectation

that any future publications be understandable and useful to front-line clinicians. This ethos heavily informed the development of the overarching research question.

3.3 Research Question

What is the multifactorial quality of using a day-zero ambulation physiotherapy protocol for patients having undergone primary uncomplicated total hip replacement, considering efficiency, functional recovery, safety and patient experience as factors of quality?

3.4 Philosophical Underpinnings

Kawulich & Holland (2012) structure methodological choice, as a convergence of three parts. Whereby the methodological choice is guided by the researchers philosophical belies and assumptions, but also by the previous existing theory and practice in the field, and the researcher's individual values and ethics.

As such, this chapter aims to cover each of these domains to explain the underpinnings of methodology selection and justification.

3.5 Ontological Standpoint

This section is written in the first person as it represents the personal viewpoint of the author and how they are reviewing and reflecting on their theoretical stance.

As the researcher, my ontological position was developed through my own questions as a clinician approaching this problem:

1. What is the best way to treat **a population of people** undergoing THR
2. What is the best decision we can make on this **across all the people** we are trying to serve?
3. How can we **feel most confident** that we are making the right decision for this service?

Each of the questions above ask for answers which can inform healthcare decisions at a population level. This demonstrates that the requirement here was for generalisability, in turn requiring a quantitative approach.

Positivism, as the philosophy underpinning quantitative research approaches; theorises that all knowledge can be explained through systematic scientific investigation of phenomena through observation, measurement and hypothesis testing, to identify laws and principles in practice (Maltby et al. 2014; Tombs & Pugsley 2020). As such, this assumes a single, objective reality that is stable and measurable and exists whether the researcher examines it or not. This approach fits well with pure scientific domains, such as chemistry and physics and has been used to develop robust scientific laws with Newton's laws of gravity as an exemplar example (Turner 2001). However, within human healthcare science, my standpoint is of the existence of multiple levels of reality depending on which level of healthcare a researcher examines. For example, if examining the effect of strength training on a person's ability to care for themselves, this could involve the reality of what happens at a cellular level as a result of muscle strengthening, but also the individual reality of the patient who has received the treatment and whether or not they judged it as beneficial.

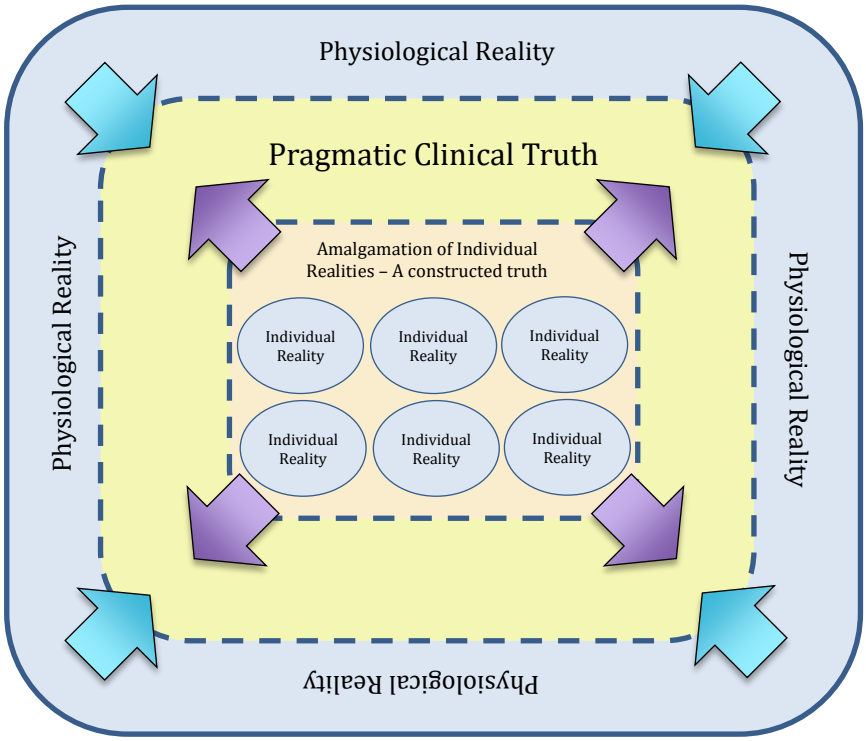


Figure 13 – Personal Researcher standpoint - healthcare intervention research philosophy (created by the student)

Figure 13 is an original diagram to show visually my belief that at an individual level, patients within a healthcare setting will construct individualised realities of intervention effectiveness based on many individual factors and self-assessments; grounded in their own experience, values, background and the resultant interpretation of their experience. This part of the above model follows the philosophy of Creswell (2013) and other interpretivists, which suggest that within

research, researchers make the best attempts at amalgamating into group-shared realities in order to provide information useful in healthcare policy and clinical decision making. I also believe there is a 'physiological reality', constituting the physiological effects of the intervention on the body. This closely links to a positivist reality but should be viewed in the post-positive vein as imperfectly measurable and have recognition that it can be influenced by the psychosocial. Indeed it is well documented that physiological effects on the body can result through psychological influence (Purves et al. 2001).

When considering healthcare intervention, I believe that both realities exist in combination, and combined, form a 'pragmatic clinical truth' which I have shown in yellow on the above diagram. Physiological changes in the body brought about by healthcare interventions change the way the body behaves and influence what we measure in practice. Simultaneously, measurements made within healthcare studies cannot be considered discrete from the influence of the patient's interpretation of them, pain numerical rating scales are a prime example. I believe that the 'pragmatic clinical truth' is a practical middle ground, able to provide generalisable answers to research questions, but recognises the complexity of human level research which inevitably intertwines with the constructed realities of individuals. As such, I believe any healthcare research must be considered on a spectrum between paradigms, unable to sit purely in either camp, but depending on the research aims, focussed at a targeted point in the spectrum.

Figure 14: Pragmatic clinical truth paradigm spectrum

In context of this research study, I believe the answer to my research question lay within the 'pragmatic clinical truth', and that as the researcher I must decide where on the spectrum between positivism and constructivism my research is best pitched to answer my question. As generalisability is a key feature of answering the above research question, pragmatically my research lends itself more towards a positivist paradigm, but I recognise the influence of individual realities on my findings.

3.6 Epistemological Standpoint

This section is written in the first person as it reflects the personal viewpoint of the author

When considering the quality of a healthcare intervention, I recognise that ultimately, a definitive and generalised result is most useful in order to allow clinical decision-making in healthcare

systems serving large numbers of people. In context of my above ontological standpoint, this involves deriving knowledge from the 'Pragmatic Clinical Truth' which can be statistically determined by probability theory, and able to predict future behaviour if replicated in clinical practice. While this lends towards a positivist approach, my epistemological stance fits most comfortably within the post-positivism paradigm (Kawulich & Holland 2012), as I recognise my inability to perfectly measure an objective truth, but that experimental research can still yield useful generalisable findings in this domain. I also recognise that parts of my research were likely to require a more constructivist standpoint, particularly in examining the patient experience component of healthcare intervention quality.

The epistemological assumptions associated with this approach are discussed below.

3.7 Axiological Stance

This section is written in the first person as it reflects the personal viewpoint of the author

Kawulich & Holland (2012) include axiology as one of the principle assumptions in a positivist paradigm. Axiology concerns the researchers own value on the different stages of the research process. Simply put, what the researcher values within their research. This can affect how researchers conduct their research and what they value within their research findings (BRM 2021).

While pure positivism assumes that all enquiries should be value-free (Kawulich & Holland 2012), I hold with a post-positivist belief that my experience of practice in this field will have instilled individual background knowledge, values and beliefs on this topic which are impossible for me to remove from my observation and interpretation of the phenomena.

3.8 Methodology Selection

In order to answer the above research question, a quantitative research methodology was selected, which fit with recommendations from Offredy & Vickers (2010):

- The project already had a clear objective of what dimensions to investigate, therefore lending to a deductive analysis approach.
- The project is attempting to establish information for or against a causal relationship related to day-zero ambulation, with specific interest in the strength and significance of the relationship.

- The useful application of the project relies on generalisation of the results to a wider population

Most of the research aims within this project target comparison between experimental and standard care across variables that are traditionally numerically measurable such as length of stay and incidences of adverse events. The anomalous variable in terms of this was patient experience, for which the researcher recognises the limitations of quantitative research in investigating this domain. Indeed, following the feasibility study in Chapter 4 the majority of the tenure of this PhD project, aimed for a mixed methods approach by also conducting a nested qualitative study investigating patient experience to supplement quantitative findings. Within the larger mixed-methods project, nested qualitative study findings were planned to be presented alongside quantitative findings to lend inductive context to the deductive analysis (Johnson & Onwuegbuzie 2004). It is the researcher opinion that when published, the qualitative and quantitative findings of this overarching project will be synergistic in generating overall conclusions on day-zero ambulation as an intervention.

However, this project grew in size and complexity, becoming too big a piece of work to write-up within a single thesis. As such, this thesis focuses on the quantitative enquiry, and the researcher plans to write-up and disseminate the results of the nested qualitative study at a later date.

3.9 Research Design

This research required an experimental, interventional design in order to compare between the intervention of day-zero ambulation and a control of standard care. As we have already seen within Chapter 2, most of the publications on this topic come from research designs that sit low in the hierarchy of evidence. It was important to the researcher that the evidence produced be of the highest quality possible within the scope of this PhD project in order to address some of these limitations and add new knowledge and confidence to the existing literature base. As such, a phase 3 randomised controlled trial (RCT)was selected as the main research design.

The decision to conduct this research as an RCT was driven by the following:

- RCTs are deemed to be the gold-standard in clinical trials
- RCTs are high within the hierarchy of research evidence (Evans 2003; Petticrew & Roberts 2003)
- Provide the strongest evidence of the treatment effect

- Aim to achieve the most rigorous minimisation of bias to provide confidence in the results
- Using an RCT will address weaknesses in the current literature
- Researcher learning as part of the PhD program
- Recognised methodology within the field and likely to be respected when published

An RCT trial design was selected for this study as most of the published evidence around day-zero mobilisation comes from observational study designs. Using an RCT design aimed to provide a higher methodological quality than currently available in the published literature based on the widely accepted hierarchy of quantitative research (Petticrew & Roberts 2003), and by minimising the potential for bias as much as possible within a quantitative paradigm. In this way, this PhD project was placed to make a unique contribution to the published evidence both through examining outcomes across all domains of intervention quality, isolating day-zero ambulation as the sole intervention, and using a gold-standard methodology.

3.10 Assumptions

There is active debate within the literature on the glorification of RCT based research as 'Gold Standard', and recent publications have spent time detailing the assumptions incumbent within RCT research and therefore its limitations (Wadhwa & Cook 2019). These modern arguments challenge the assumptions of RCTs as not always met, undermining the pedestal that RCT research is held upon.

Specific to this project, the researcher identified the following epistemological level assumptions:

- The independence of the researcher from the phenomenon being studied
- The assumption that all variables of interest are quantifiable and accurately measurable
- The assumption that measured variables accurately represent the phenomenon they are intending to – construct validity

Specific to this project, the following research design level assumptions apply:

- Reliant on sufficient sample size to ensure treatment and control conditions are functionally identical – internal validity
- That researching in a controlled environment to reduce bias doesn't annul the generalisation to results to wider healthcare settings. – External validity
- That there is no differential attrition between groups

3.10.1 Philosophical assumptions

The independence of the researcher from the studied phenomenon.

This is a key point within this PhD project, as for pragmatic reasons, the researcher was required to be part of the clinical team. Consequently, the researcher was not independent of the phenomenon examined during treatment. In this sense, an RCT methodology provides some ability to manage potential bias by employing randomisation and opportunity for allocation concealment and minimising loss to follow-up. However, the researcher recognises this doesn't resolve the assumption that in the analysis and interpretive phase of the research that the researcher remains independent.

Personal equipoise

Cook & Sheets (2011) describe it as naive to assume researcher equipoise in RCT research. The fact that the researcher has been subject to clinical experience, conducted a detailed literature review and designed the study raises the possibility of conscious and unconscious bias through preconceived thoughts on outcomes and effect-size. This is a problematic and difficult assumption to try to account for.

Again, an RCT design gives some opportunity to combat this, by preventing the researcher from selecting intervention allocation and closely defining the treatment regimens for each group with an importance on ensuring that the control group exactly reflects typical existing clinical practice.

Variables are accurately quantifiable and measurable

Any experimental research will always be limited by the accuracy within which it is able to measure a phenomenon. The researcher recognises that within healthcare there are many measurements we take which are constructed to measure phenomena that are ultimately impossible to perfectly measure and are unique to the individual patient such as intensity of pain.

This study design aimed to account for this by using validated measures wherever possible, and setting clear criteria for the measurement of functional milestones and length of stay.

3.10.2 Internal Validity

While internal validity is considered a principal strength of randomised controlled trials, the inclusion of randomisation alone is not enough to ensure internal validity. As such, the author gave specific thought to the following and the subsequent research presented within this thesis was designed with these dimensions in mind in order to maximise internal validity.

Properly and impartially implemented randomisation

This involved the randomisation being carried out by an independent party and included allocation concealment.

Sufficient sample size

Ensuring an a priori sample size calculation based on a feasibility study limits bias through sample-size variation.

Checking Groups are as identical as possible

This was addressed through baseline measurement and analysis of baseline data to identify any failure in randomisation to balance known confounders between groups.

Clear pre-defined methods for handling loss to follow-up and missing data

This involved using intention-to-treat analysis to prevent loss to follow-up impacting on the results

No differential attrition

This was minimised by ensuring identical time periods for intervention period, measurement period and follow-up periods.

3.10.3 External Validity

Conversely to internal validity, external validity is seen as a weakness of RCT research. Controlling for factors which threaten to confound results of the experiment detract from the applicability of the results to real life. This study aimed from conception to be a pragmatic RCT, aiming to keep the cohort and conditions in which the cohort were treated as similar to standard care in a UK hospital as possible. This was considered achievable through:

- Setting inclusion and exclusion criteria representative of a UK orthopaedic patient population, including no exclusion based on general demographic information such as age or gender.
- Conducting the study in a UK orthopaedic unit
- Ensuring the control group are treated identically to the standard care usually delivered within this unit.

3.11 Project Specific Objectives and Hypothesis

This section breaks down the research question in section 3.3 into individual objectives and hypotheses which so structured can be used for deductive testing as part of the subsequent research:

3.11.1 Primary Objective and Hypothesis:

- To evaluate the effectiveness of a rapid ambulation physiotherapy protocol in reducing the length of hospital stay, for patients having undergone primary THR.
    - Hypothesis: A rapid ambulation protocol will significantly reduce length of hospital stay following THR when compared to standard care.

3.11.2 Secondary Objectives and Hypotheses:

- To evaluate the impact of a rapid ambulation physiotherapy protocol on the patient reported experience of post-operative physiotherapy care
    - Hypothesis: That rapid ambulation will improve patient experience of post-operative physiotherapy when compared to standard care.
- To evaluate whether a rapid ambulation physiotherapy protocol will affect the time taken for patients to reach functional milestones postoperatively.
    - Hypothesis: Rapid ambulation will reduce the time taken for patients to reach functional milestones post-operatively when compared to standard care:
        - First range of movement of the new prosthetic THR.
        - First sit on the edge of the bed.
        - First transfer from bed to chair using a walking frame or appropriate walking aid.
        - First walk of greater than or equal to 5 meters using a walking frame and appropriate physiotherapy support.
        - First walk of greater than or equal to 10 meters using a walking frame pair of elbow crutches independently.
        - First walk of greater than or equal to 40 meters using a pair of elbow crutches independently.
        - First completion of a step or stairs independently using elbow crutches.
- To determine if implementing a rapid ambulation physiotherapy protocol will affect the incidence of post-operative complications.
    - Hypothesis: Rapid ambulation post-operatively will reduce the incidence of post-operative complications when compared to standard care
- To determine whether a rapid ambulation physiotherapy protocol will affect post-

operative numerically rated pain scores when attempting mobility for the first time.

- Hypothesis: Rapid ambulation post operatively will reduce the levels of pain as measured using a numerical pain rating scale reported by patients on initial mobility when compared with standard care.

3.12 Feasibility Study

As discussed earlier in this chapter and following the findings and recommendations of the systematic review conducted in Chapter 2, the researcher wished to conduct a randomised controlled trial in order to address limitations in the existing research body. Designing and conducting a large-scale randomised controlled trial is complex and challenging, with many variables and factors to consider just in relation to the aims and hypotheses above. Ensuring the study is well designed and carried out is critical to produce valid and reliable research findings. Although conducting a feasibility study is a substantial piece of work, and an added burden on top of conducting a large scale study, conducting a feasibility study is one strategy to facilitate sound study design (Cope 2015). Indeed, conducting a feasibility study is a key part of the MRC framework for the development of complex interventions (Skivington et al. 2021). This framework recommends a feasibility study should be designed and conducted to evaluate uncertainty in the research design around recruitment, data collection, participant retention, outcomes and analysis. It can also evaluate the intervention itself for delivery, acceptability, adherence, cost and capacity of the providers to deliver the intervention. As a novice researcher, there was uncertainty in most of the above domains meaning that conducting a feasibility study was the ideal structure for this project before moving on to a large-scale study. The upcoming sections discuss the ethical considerations and patient involvement in the setup and conduct of said feasibility study.

3.13 Ethics

In the context of past atrocities in research involving human subjects, the importance of gaining Research and Ethics Committee (REC) approval for conducting this study is important, not just from a legal and regulatory perspective, but also in ensuring the safety, properly informed consent and confidentiality for the participants who elected to take part.

This study was sponsored and registered as a clinical trial by the Research and Development Department at the Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust and

received favorable approval for the research presented subsequently as part of this PhD from the Hampshire B REC

ClinicalTrials.gov Identifier: NCT02428829
Research ethics committee reference: 15/SC/0018

As part of preparing this study for ethical approval, the author considered the following domains and specific ethical considerations in relation to this research:

3.13.1 Number of Participants

Ensuring the correct number of participants are recruited serves two purposes:

- Keeping the risks associated with research to the minimum number of people
- Ensuring the right number of participants required to answer the research question through statistical analysis.

Consequently, this PhD project from conception planned to conduct an a-priori sample size calculation based on pre-collected data on estimated effect-size such as from a pilot or feasibility study.

3.13.2 Safety of Participants

The hypothesised specific risks involved with undertaking day zero ambulation were:

- risk of delayed wound healing
- risk of falling when attempting to ambulate post-operatively.

It was deemed that the procedures used in standard care for the assessment of neurovascular status and muscle power prior to ambulation were enough to mitigate the risk of falling. However, it was also deemed prudent to exclude participants who underwent a nerve block as part of their surgery or who were advised not to fully weight bear post-operatively, and thereby may have an increased likelihood of motor deficit.

Risk of delayed wound healing was purely theoretical, and as such the researcher decided to measure this as part of the adverse events reporting of the research. Mechanisms were established and agreed with the study sponsor for the timely reporting of adverse events and

serious adverse events. These procedures formed part of the study protocol for both the feasibility study and fully powered RCT and are detailed in Appendix 7.

3.13.3 Informed Consent

Mechanisms to ensure that participants have had understandable information, be able to process that information and give informed consent is one of the key priorities of a REC. Within this PhD, these issues were addressed by ensuring that prospective participants were provided with the study information 1-2 weeks prior to surgery and had opportunities to ask questions of the Chief Investigator on multiple occasions. However, within this cohort, there were two principal consideration points for gaining informed consent which were challenged by the REC and needed adjustment prior to ethical approval.

Firstly, in ensuring that participants who have undergone an anaesthetic just a few hours earlier, retain the ability to consent to the experimental intervention. The research team addressed this by asking the participant to explain back to the treating clinician post-operatively which research study they had signed up to, and what the expectations of them were for the intervention. Secondly was the concern that prospective participants who had undergone a general anaesthetic as opposed to a spinal anaesthetic may be affected by a pharmacologically induced cognitive deficit for the remainder of post-operative day-zero, limiting their ability to give informed consent. As such, any prospective participants who underwent general anaesthesia were excluded.

3.13.4 Exclusion of groups

The researcher gives specific recognition and justification that inclusion and exclusion criteria used in the subsequently presented research actively excluded the following groups in **Table 3-1** below:

Table 3-1: Exclusion of groups justification

Excluded Population Groups	*Reasons*
Persons who are: Non-English speaking English illiterate Lacking mental capacity Children	To assure proper understanding of all the criteria required for informed consent in relation to this study, both at enrolment and throughout.
Persons who: Suffer intra-operative complications	To reduce the risk of harm to the participants

Have a past-medical history indicating increased risk of post-operative complications Unsuitable to undergo spinal anaesthesia	To avoid known confounding factors on research findings.
Persons who: Are participants in other research studies	To reduce the burden on participants from being asked to participate in multiple research studies To avoid the risk of concomitant research influencing the RAPID study findings and incurring bias

3.13.5 Over-researched Groups

The intended population of participants for inclusion does not constitute a group that is frequently or extensively researched on or asked to participate in research

3.13.6 Confidentiality

As all subsequently presented research was carried out within a single NHS hospital, the research team adhered to the information governance procedures agreed and routinely used within the hospital. All electronic research documentation was held within the hospital computer system accessible only by the research team. Similarly, all paper documentation was held within a locked office on the hospital site only accessible by the research team. At no point was any research documentation taken or sent off site.

3.13.7 Conflicts of Interest

The author declares no financial or non-financial conflicts of interest in relation to this research.

All research completed as part of this PhD was carried out without funding.

3.14 Patient and Public Involvement and Engagement

Patient and public involvement and engagement (PPIE) in research design and implementation has become an expectation of research funders and research ethics committees and can add some significant strengths to research design and outputs (National Institute for Health and Care Research. Centre for Engagement and Dissemination 2021). This briefing document clearly defines the different levels of public involvement in research:

- Involvement – Research being carried out with or by members of the public rather than to or about them. This can vary between advising on research design and materials, to becoming co-applicants and/or co-researchers.
- Engagement – Where information and knowledge if provided and disseminated to the public.
- Participation- Where people take part in a research study

The NIHR briefing notes also present three options for researchers to involve members of the public in research; consultation, collaboration and co-production. This PhD project selected to consult with patients through a focus group format. This is suggested through the NIHR briefing notes as a good choice for novice researchers to start with PPIE.

3.14.1 PPIE Aims

Aims for PPIE were defined before the focus group was arranged:

- Gain patient perspective of day-zero ambulation as an intervention and highlight any theorised practical challenges or risks.
- Review the outcomes proposed for the study and check they align with patient interests
- Patient with lived experience to review the participant information sheet and give constructive feedback.
- Highlight any ethical issues pertinent to the patient which hitherto had not been considered.

3.14.2 Implementation and Impact of PPIE

This PhD project used a focus group format to consult with members of the public. This was carried out prior to submitting the REC application and led to some significant changes in the study aims and protocols. The focus group was conducted with the guidance of some pre-written questions focused around the above aims (Appendix 8) in October 2014 and was arranged and chaired by the head of patient and public involvement at the Royal Bournemouth and Christchurch NHS Foundation Trust, who also collated the minutes of the meeting shown in Appendix 9.

Feedback from this focus group consultation led to the following changes to the study:

- Re-writing of the patient information sheet to provide more focus on risk and potential benefits to participants and to give more clarity that participation was voluntary.

- Inclusion of outcome measures in the interest of the patient.
- Post-operative pain scores
- Time to achievement of functional milestones
- Patient experience of the intervention
- Setting of a minimum of 4 hours recovery time prior to undertaking day-zero ambulation.

While the UK standards for Public Involvement in Research (UK Public Involvement Standards Deveopment Partnership 2019) had not been written when this PPIE was carried out, this PPIE did manage to fulfil several of the now suggested standards including involving patients at the early stages of research design, developing a clear communication plan and aims for the PPIE, valuing the opinions and feedback of the public and adopting these into the research design and participant information.

The author recognises that PPIE has been further championed since this example in 2014 and that if conducting this research study in the present day, options for collaboration and co-production would be seen to strengthen the PPIE methods selected within this PhD project. Nevertheless, this served as a pertinent learning experience for the author.

4 - Feasibility Study

4.1 Introduction

This chapter details the first phase of experimental research within this PhD which formed a feasibility study and was used to inform the methodology and sample-size within a fully powered study. As such, this chapter will discuss the theoretical and methodological flaws within this part of the study design and how this made recommendations for the development of the main study methodology. While within the published literature there is some debate on the classification of preliminary studies, this study has been classified as a feasibility study in line with the NIHR definition (National Institute for Health and Care Research 2016) and based on the conceptual framework presented by Eldridge et al. 2016:

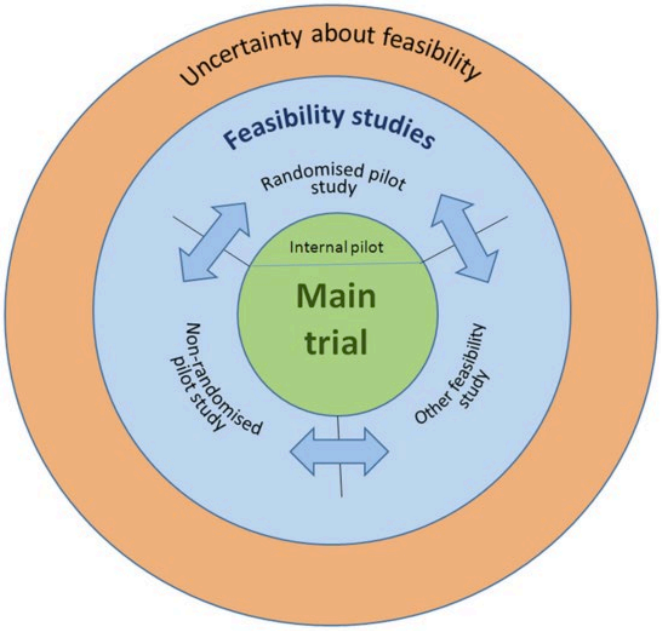


Figure 15: Feasibility study framework (Eldridge et al. 2016) (Reproduced with permission under the PLoS Terms of Use in accordance with the Creative Commons Attribution (CC BY) Licence)

There is some debate on the classification of feasibility and pilot studies with the terms occasionally used interchangeably (Cope 2015). In methodology this study does imitate the main trial. However, the outcomes from this study were designed to answer feasibility questions, led to substantial amendments to the methodology and never planned to include the feasibility data collected within a subsequent large-scale study. Consequently, classification as a feasibility study is most appropriate.

Conducting a feasibility study in the course of a research project forms a part of the Medical Research Council framework for developing complex interventions (Skivington et al. 2021) and holds many advantages in enabling the researcher to assess the adequacy of assessment techniques, the acceptability of the intervention, participant recruitment strategies, identify potential participant retention problems, assess the strength of key variable relationships, identify confounding variables, determine study resources, assess the proposed data analysis and carry out sample size calculation (Cope 2015). In addition, while not relevant as part of this unfunded project it may provide preliminary evidence to justify research funding. The author also recognises the potential drawbacks of feasibility work, which if identifying methodological inadequacies which cannot be overcome may affect the viability of research and research funding.

Finally, conducting a feasibility study was of significant interest to the author in this project. As a novice researcher this gave the opportunity to learn and develop practical skills in research design, implementation and governance before progressing to the large-scale study. The work detailed in this chapter has been published in a peer reviewed journal (Efford & Samuel 2022), with full details within the reference list for this thesis.

4.2 Feasibility Study Aims

Within this feasibility study, it should be acknowledged that the results gathered were not considered towards analysis of estimating effect size or answering the research questions detailed in section 3.12. This principle is widely advocated in the conduct of feasibility or pilot studies (Tickle-Degnen 2013; Eldridge et al. 2016; Thabane et al. 2010), with any problems identified within the feasibility methodology having the potential to contaminate main study data (Cope 2015).

Thabane et al. (2010) and Tickle-Degnen (2013) presented some guidance on the purpose of feasibility studies in preparing for phase III randomised controlled trials (RCT) and a framework for analysis of the feasibility of conducting a fully powered RCT. This breaks down feasibility analysis into 4 dimensions of process, resources, management and scientific analysis. Consequently, the feasibility study aims have been structured in this way in order to achieve the overarching aim of ensuring sound methodology, research governance mechanisms and scientific validity.

4.2.1 Process Aims

Process assessment aimed to answer feasibility questions focused on the processes involved in the delivery of the study protocol in practice. This included processes for informed consent, recruitment and retention processes and management processes. As part of this, the researcher identified the following questions which needed to be explored in order to determine feasibility and identify improvements to the study:

- What are the expected eligibility numbers?
- What are the expected recruitment rates?
- What is the expected refusal rate?
- What are the success rates for enacting a RAPID physiotherapy protocol?
- What are the expected retention rates?
- Are the inclusion and exclusion criteria appropriate?
- Were there any dangers for any patient groups?
- Do they allow appropriate recruitment?
- Are the data collection processes appropriate?
- To what degree is there missing or unusable data?
- Are there any issues with the practical burden of data collection?

In relation to these questions, the following criteria for phase III study feasibility were set:

- Ability to safely recruit and retain the entire study cohort within a 24-month period.

4.2.2 Resource Aims

Resource assessment in other forms of research may take the form of justifying financial allocation, grant proposals and determining what new materials, equipment or systems may require procurement in order to make the research a success (Tickle-Degnen 2013). For this unfunded study, resource assessment focussed on the existing human and non-human resources which would need optimisation to maximise success. This included thinking about how the small research team was able to work collaboratively as a team and within the running operations of a working hospital. As such the following questions were explored:

- Is there the resource capacity to cope with recruitment numbers?
    - Research team staffing
    - Equipment
    - Computer software
- Were communication methods appropriate?
    - Between research team and participants

    - Internally within the research team
- What were the departmental willingness and engagement to conduct the study?
- Were appropriate mechanisms in place to cope with staff sickness and annual leave periods?

4.2.3 Management Aims

Management assessment concerns the ability of the investigator to manage and deliver the planned research within the correct governance and safety mechanisms. As a novice researcher, and a very inexperienced research team, the focus on this was to consider the strengths and weaknesses of the study management for reflective learning and improvement of processes going into the main RCT. This section also needed to consider data collection and management for accuracy, and any ethical issues not previously considered which may come to light. As such, the following questions were posed for exploration:

- Were there any problems with:
    - Chief investigator study management
    - Research team and staff expertise
- Was the study data collection paperwork appropriate?
    - Was data collected and entered accurately?
    - Was there appropriate matching of participant data?
- Were any ethical issues highlighted?

4.2.4 Scientific Aims

Scientific assessment concerns the safety and acceptability of the intervention along with the validity of assessment and data analysis. As such the following questions were posed for this feasibility study:

- Were there any safety concerns with the intervention conducted?
- What are the reliability, validity and trustworthiness of the assessments methods?
- What are the descriptive statistics for interventional effect sizes and the variance in this?
- What is the level of burdensomeness of the intervention?
- Are there any unpredicted confounding factors identified?

Descriptive statistics generated from this feasibility study were also be used in the conduct of an a priori sample size calculation. This would ensure correct power is reached within the fully powered study, and also ensure that participants are not recruited unnecessarily above the study requirement.

4.2.5 Patient experience Questionnaire Specific Aims – Including Open-Ended Survey Questions

This feasibility study aimed to judge the usability of the questionnaire to produce response to individual questions relating to patient experience. This included both the validity of the survey questions, and the verification of open-ended survey questions as qualitative data elements.

Summary:

Following this framework of considerations, this feasibility study aimed to answer the following questions:

- Can the target number of participants feasibly be recruited to the main study within a time period of 24 months?
- Are good clinical practices being used in the conduct of the feasibility study and what can be done to optimise good clinical practices for the main study, inclusive of:
    - Study documentation
    - Informed consent procedures
    - Data collection methods
    - Regulatory reporting procedures
    - Research team training and expertise

4.3 Feasibility Study Design

The feasibility study was conducted as a single centre; non-blinded, parallel group randomised controlled trial of patients undergoing primary THR. With the intervention group seen by a physiotherapist to attempt walking 4-6 hours post operatively and the control group receiving standard physiotherapy in line with hospital protocol including first walking approximately 24 hours post operatively. Following the completion of this feasibility study, qualitative analysis of the feasibility study aims were assessed through a research team debrief and evaluation meeting. The above feasibility study aims were answered using a combination of collected data and qualitative research team evaluation.

4.4 Feasibility Study Diagram

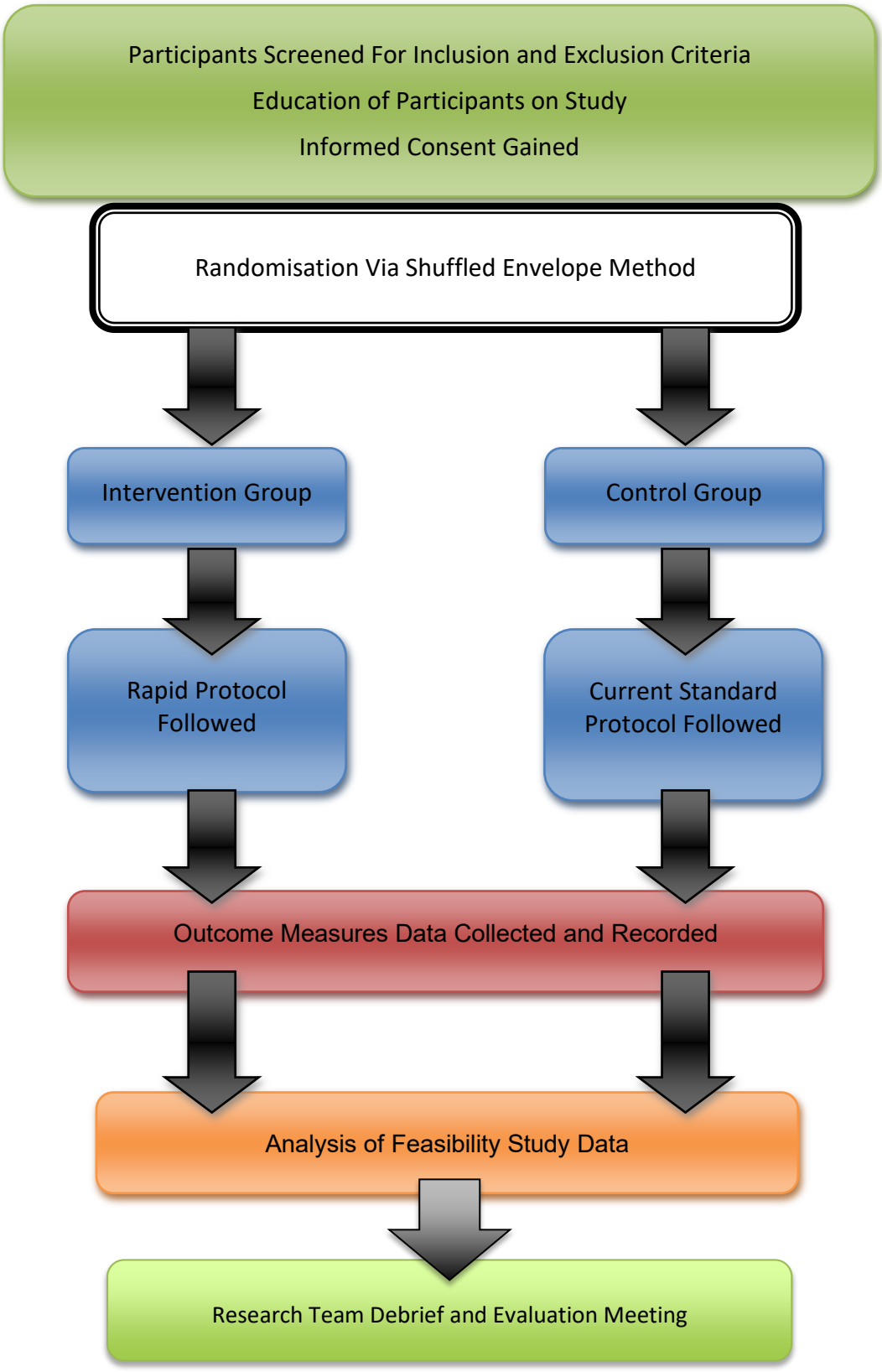


Figure 16: Feasibility study flow diagram

4.5 Study Setting and Context

This feasibility study was conducted on a single orthopaedic ward specialising in lower limb major joint replacement surgery. Within this setting an enhanced recovery protocol had been well established and included the following regimens for patients undergoing primary THR. Participants were recruited over 17 separate weeks between the dates of 16/04/2015 and 27/10/2015.

4.5.1 Operative Care

All inpatient care took place within a single specialist orthopaedic unit including participant surgery and post-operative recovery. This unit has been using ERAS pathways for more than 8 years. All participants underwent uncomplicated, unilateral primary total hip replacement using a posterolateral approach, and using a cemented femoral component (Zimmer CPT trilogy Hip System (Zimmer.Inc 2006)) and uncemented acetabular component. Due to the operative approach, a 3-month period of standard posterolateral approach hip precautions were advised and taught to each participant as part of standard care:

Participants were advised to avoid:

- Internal or external rotation at the hip joint
- Hip flexion beyond 90 degrees
- Hip adduction

4.5.2 Standardised Anaesthetic

All participants were treated under a standardised anaesthetic and postoperative analgesic pathway (Shown in Appendix 10)

During the pre-operative phase this involved:

- Pre-operative paracetamol (1g QDS) - If not already taken regularly and not contraindicated

During the peri-operative phase:

- Spinal anaesthetic using intrathecal diamorphine 0.25-0.4mg
- Sedation using a target-controlled infusion of Propofol
- Insertion of a urinary catheter
- Systemically delivered tranexamic acid 15mg/kg
- One dose of intravenous Diclofenac 75mg

- Intraoperative antibiotic prophylaxis with one off doses of:
    - Cefuroxime – 1.5g
    - Gentamicin – 80mg

This is in line with guidance provided in the Oxford handbook of Anaesthesia for primary uncomplicated total hip replacement (Allman & Wilson 2012) and BNF guidance on antibiotic surgical prophylaxis (BNF 2017)

4.5.3 Standardised Post Operative Analgesia

All participants were also treated using a standardised post-operative analgesic pathway summarised in ***Table 4-1***, also detailed in Appendix 10.

This involved both a standardised analgesia regime, and an escalation ladder of analgesia as required.

On the standard element of the pathway, all participants were treated with the following post-operative medications unless otherwise contraindicated:

Table 4-1: Feasibility study standardised analgesia regimen

	Dose	*Frequency*
Paracetamol	1g	QDS
Ibuprofen	400mg	TDS
Omeprazole	20mg	OD
Ondansetron	4mg	TDS
Magnesium Hydroxide	20ml	BD

The following medications were then used as required:

Oramorph	10-30mg	Up to 4 Hourly
Cyclizine	25mg	Up to TDS
Chlorphenamine	10mg	Up to TDS

OD = Once per day, BD = twice per day, TDS = three times per day, QDS = four times per day.

4.5.4 Standardised Post-Operative Rehabilitation

Post-operative physiotherapy was carried out in line with guidance in Appendix 11 for the respective groups. Standardised care applicable to both groups ensured that all participants were seen for two physiotherapy sessions per day, once in the morning and once in the afternoon. Where possible they saw the same physiotherapist throughout their stay. Standardised bed exercises and advanced exercises are detailed in Appendix 12

4.5.5 Post-Operative Medical Care

Post-operative medical care was completed using standardised care policies for blood transfusion, thromboprophylaxis and dealing with venous thrombo-embolisms.

Blood Transfusion:

Standardised decision making for delivering blood transfusion were based on nationally accepted standards (NICE 2015) with patients undergoing a routine post-operative full blood count blood test. Thresholds were a haemoglobin result of less than 70g/l, or less than 80g/l in patients who have a background of cardiovascular disease (See Appendix 13). This full blood count test including haemoglobin was carried out routinely at 24 hours post-operatively.

Thromboprophylaxis

Post-operatively, patients were treated using a standardised thromboprophylaxis protocol (Appendix 14) This involved subcutaneous injection of 5000 units of Daltaparin once daily for a period of 35 days post-operatively. Any patients who were diagnosed with a VTE were treated with a dose of 200 units/kg of Daltaparin once daily subcutaneously for at least 5 days or until their international normalised ratio (INR) was above 2 for at least 24 hours. This is in line with national guidance from NICE (National Institute for Health and Care Excellence 2015) .

4.6 Study Population

Participants were considered eligible for screening if they were booked to undergo a primary and unilateral total hip replacement.

4.7 Inclusion Criteria

Table 4-2: Feasibility study inclusion criteria and rationale

Inclusion Criteria	*Rationale*
Any Age	To keep the recruited sample representative of a UK elective THR population.
Able to give informed written consent	To ensure proper compliance with informed consent procedures.
Returned from theatre > 4 hours Primary unilateral THR No intraoperative complications Post-operative weightbearing status: Fully weight bearing Weight bearing as tolerated	To reduce risk of harm to the participants by ensuring that spinal anaesthetics have resolved. To ensure that research findings are not confounded by including surgeries with more complex and restrictive rehabilitation protocols.
Adequate home support to facilitate early discharge	To ensure research findings are not confounded by delayed discharges due to social delays.

4.8 Exclusion Criteria

Table 4-3: Feasibility study exclusion criteria

Exclusion Criteria	*Rationale*

No current or historical serious co-morbidities in particular: Cerebro-Vascular Accident Myocardial Infarction Pulmonary Embolism (PE) Deep Vein Thrombosis (DVT) Diabetes Mellitus (DM) Significant intra or post-operative wound ooze Poor pre-morbid mobility/level of function Clinical signs of DVT or PE Altered Weight-Bearing status Repair to abductor muscle complex Peripheral nerve block as part of anaesthetic	To reduce risk of harm to the participants by ensuring that participants are not at high risk of cardiovascular complications. To ensure that research findings are not confounded by: including surgeries with more complex and restrictive rehabilitation protocols common post-operative complications more likely due to past medical factors.
Inflammatory Arthritis Developmental dysplasia of the hip Concomitant procedure at time of THR Participation in any other research trials	To ensure research findings are not confounded by existing medical conditions likely to affect recovery or by other experimental research.

4.9 Outcome measures

4.9.1 Primary Endpoint – Length of Stay

Primary outcome was length of stay following surgery, measured to the nearest day. This was calculated from the date of the operation to the date the patient was discharged from hospital. Within this patient group, length of stay is considered, the most important component in the consumption of hospital resources, a significant point of comparison between hospitals and countries, a key performance indicator used by hospital management teams and a key efficiency measure within the NHS (Kulinskaya et al. 2005).

4.9.2 Secondary Endpoints

Time to Physiotherapy Complete:

Calculated in post-operative hours from the time returned to the ward from theatre, to the point the participant was deemed to have achieved all inpatient physiotherapy goals for hospital discharge.

Functional Milestones:
Measured in number of hours post-operatively:

The time that the patient returned to the ward following their operation was recorded.

1) First movement of the new prosthetic hip joint.
2) First sit on the edge of the bed.
3) First transfer from bed to chair using a walking frame or appropriate walking aid.
4) First walk of greater than or equal to 5 meters using a walking frame and appropriate physiotherapy support.
5) First walk of greater than or equal to 10 meters using a walking frame or pair of elbow crutches independently.
6) First walk of greater than or equal to 40 meters using a pair of elbow crutches independently.
7) First completion of a step or stairs independently using elbow crutches.

The date and time that participants completed the above milestones as recorded by the member of the physiotherapy team. From this the time taken to reach the milestone was calculated.

The above functional milestones were selected for the following reasons:

- To be representative of accepted physical criteria for post-operative discharge. Enloe et al. 1996 described survey results of physiotherapists agreeing a consensus of patients being able to walk 100 feet (30m) and managing steps/stairs as respective of their own social history prior to physiotherapist sanctioned discharge.
- Callaghan et al. 2007 noted that physiotherapy care post THR should reflect progressive gait treatment – a trait that is reflected in the above milestones.
- Will highlight any differences between groups in speed of functional recovery, a suspected effect of day-zero ambulation through current literature.

Incidence of Post-Operative Complications:
The number of patients who experienced a post-operative complication was recorded and the nature of the complication was selected from a list of categories:

- Post-operative orthostatic hypotension
    - Defined as a reduction in systolic blood pressure of >20mmHg and with symptoms of postural hypotension
- Syncope
- Deep Vein Thrombosis

    - As confirmed by radiological imaging
- Pulmonary Embolism
    - As confirmed by CT pulmonary angiogram
- Excessive wound ooze
    - This constitutes any wound ooze that escapes the operative site wound dressing.
- Post-operative Respiratory Tract Infection
    - As confirmed by medical diagnosis
- Blood Transfusion Required and delivered
    - Determined once the patient has received ≥ 1 unit of blood transfusion.
- MI
    - Confirmed via ECG and troponin blood test and medical diagnosis.
- CVA
    - Confirmed by radiological imaging and medical diagnosis
- Bowel Obstruction
    - Confirmed by radiological imaging and medical diagnosis
- Other – (Open-ended section for details)

This data was collected throughout hospital admission up until discharge.

Pain on Day 0 and Day 1 Physiotherapy:
This was collected as a patient reported pain numerical rating score (PNRS), with the patient asked to rate their pain level from 0-10.

PNRS was selected for pain measurement for the following reasons:

- A familiar pain outcome measure using routinely in the clinical setting proposed for the study
- Well-evidenced validity and reliability (Jensen & McFarland 1993; Herr et al. 2004; Bijur et al. 2003; Ferreira-Valente et al. 2011)

PNRS was collected in the following instances both on day 0 and day 1:

- **Pain at rest**
- **Pain on joint ROM**
- **Pain on Walking (if applicable)**

Patient Experience:

Assessed with a specific patient experience questionnaire (Appendix 15), where participants were asked to rate their experience between 0 and 10 (0 representing the worst and 10 the best experience). Questions 1, 3 and 4 were adopted from the CQC inpatient survey 2013 (Care Quality Commission 2013).

Although un-validated, this method has been devised due to a lack of validated patient experience measures specific to an orthopaedic patient group (Jones et al. 2014). Each question was considered in isolation and no cumulative score calculated from the obtained scores. The two comments box questions within the questionnaire, aimed to give opportunity for improved depth of participant comments. Structure of scaled questions with open comments boxes were chosen according to Lees' (2011) recommendations on designing patient satisfaction surveys.

4.10 Participant Selection

4.10.1 Randomisation Method

Randomisation was carried out by the study sponsor, using a non-stratified, computer generated, block randomisation method. Participants were randomised on a 1:1 ratio into either 'standard post-operative physiotherapy' or 'rapid ambulation physiotherapy' groups. Group allocation was then determined by the research team sequentially opening the appropriate envelope during participant enrolment.

4.11 Study Physiotherapy Treatment Regimens

4.11.1 Control Group

Participants randomised to the 'standard post-operative physiotherapy' group were treated using the physiotherapy treatment protocol detailed in Appendix 11

4.11.2 Intervention Group

Participants randomised to the 'RAPID post-operative physiotherapy' group were treated using the physiotherapy treatment protocol detailed in Appendix 11

4.12 Schedule of Assessment

Table 4-4: Feasibility study schedule of assessment

Time Period / ***Outcome***	*Surgery*	*Post-Op*	*Mobilising*	*Post-Op Stay*	*On Discharge*

Length of stay			✓
Time to Physiotherapy Complete		✓	✓
Patient Satisfaction Questionnaire			✓
Functional Milestones	✓	✓	✓
Post-Op Complications	✓	✓	
Pain Numerical Rating Scores	✓	✓	

4.13 Statistical Analysis Methodology

4.13.1 Descriptive Statistics

All quantitative data were analysed for normality of distribution, this was to enable the author to determine the most appropriate measure of central tendency. Data are presented separately for the RAPID and Control groups, with the mean, median and their respective standard deviations or interquartile ranges.

4.13.2 Comparison of Groups

In line with advice from Tickle-Degnen 2013; and Thabane et al. 2010, it is acknowledged that this feasibility study was not powered appropriately to assess for statistical significance. Comparison testing is included for reader interest and not as an attempt to confirm or deny the null hypotheses.

4.13.3 Sample Size Calculation

Sample size calculations for the fully powered study were completed following advice from a statistician and using the software package G*Power 3.1 (Franz Faul 2007; Faul et al. 2009). A value of 0.05 was used for the α-error and a value of 0.10 for the β-error as within convention for a clinical trial (Banerjee et al. 2009; Machin et al. 2009).

4.14 Qualitative Analysis

4.14.1 Feasibility Study Evaluation

Aside from the empirical participant collected data, the process aims, resource aims and management aims for the feasibility study were assessed through the analysis of research team evaluation and debriefing following the completion of the study. The following structures were used to promote thinking during this evaluation:

- Research team formal debrief and evaluation meeting
- A strengths, weaknesses, opportunities and threats analysis was completed by the chief investigator following the completion of the feasibility study relating to the conduct and management of the study.
- A self-evaluation of the chief investigator was completed using the Vitae researcher development framework (CRAC 2011).

4.14.2 Open-Ended Survey Questions

Open-ended questions within the participant experience questionnaire will form the collected qualitative data for this feasibility study. Due to limited depth of information provided within these written answers to specific questions, this data was not expected to reach thematic saturation. However, the following stages were taken for analysis with the intention of identifying any common themes even from this small dataset:

1. Comments from the open-ended questions 5 and 6 within the participant experience questionnaire were transcribed into NVivo 11 (QSR International Pty Ltd 2015).
2. The researcher read the comments in their entirety to gain familiarity with the data.
3. Data were coded according to recurrent phrases or topics

Basic themes uncovered were not used to generate ultimate findings within this study, but are instead presented as recommendations for enquiry within the fully powered study.

4.15 Results

4.15.1 Process Aims

4.15.1.1 Eligibility and Recruitment:

The feasibility study ran for a period of 26 weeks, with recruitment over 18 weeks. 78 potential participants were screened between the dates of 16/04/2015 and 27/10/2015. 79% of those participants were eligible according to the study inclusion/exclusion criteria (n=62).

The observed recruitment rate was 44%. Reasons for exclusion are detailed in **Table 4-5**.

Table 4-5: Reasons for non-recruitment of screened participants

Exclusion Reasons	***n***	***%***
Patient Opted Out	10	12.8%
Inclusion / Exclusion Criteria	16	20%
PIS not received*	10	12.5%
Late back from Theatre	8	10%
Total	44	55%

*PIS = Participant information sheet

This saw a total enrolment of 34 participants. This equates to a recruitment rate of 1.9 participants per week. However, during the first 10 weeks, one of the significant problems encountered was a number of potential participants not receiving the PIS. This resulted in a recruitment rate of 1.5 participants per week.

Over the last 8 weeks of recruitment, the research team posted the PIS packs out to all potential participants instead of providing them at a pre-operative education class. This improved the recruitment rate to 2.4 participants per week.

This recruitment rate of 2.4 would predict a recruitment potential maximum of 249 participants in a 24-month period.

4.15.1.2 Success of Day 0 Mobilisation

17 participants were randomised to the RAPID group and therefore attempted day-zero ambulation. 12 participants (71%) were successful in walking on the same day as their operation.

This left 5 participants (29%) who did not achieve walking on day zero. All five of these participants either managed to sit over the edge of the bed or stand, therefore completing more than their counterparts in the control group. Four of these RAPID group participants didn't walk due to symptoms of orthostatic hypotension and a resultant clinician decision not to continue for safety, and one RAPID participant did not mobilise due to severe post-operative nausea and vomiting.

Within the control group, 14 participants (82%) were able to achieve walking on post-operative day one, and three participants (18%) didn't achieve walking on post-operative day 1. Two of these participants didn’t achieve walking due to symptoms of orthostatic hypotension, and one due to a concern over a potential pulmonary embolism, which was later, confirmed by radiology.

4.15.1.3 Retention Rates

There were no dropouts observed within this feasibility study.

4.15.1.4 Inclusion/Exclusion Criteria

16 potential participants were excluded due to not meeting the inclusion/exclusion criteria, the details of these are shown in **Table 4-6** below:

Table 4-6: Participants excluded due to Inclusion/Exclusion criteria

Exclusion Criteria	*Number Excluded Due to This*	*Percentage of Total Screened*
History of MI	3	3.8%
History of DM	7	9.0%
History of CVA	3	3.8%
Intra-Operative Complications	3	3.8%
History of DVT	1	1.2%

Caption: One participant met both MI and DM Exclusion criteria

The most common cause for exclusion was a co-morbidity of diabetes mellitus constituting 9% of exclusions. Both the inclusion and exclusion criteria appeared to allow an acceptable rate of recruitment and safety and did not need adjustment.

4.15.1.5 Data Collection

There were no reported issues with the burden of data collection for the participants or for the researchers (Appendix 16) – Debrief minutes

4.15.1.6 Missing Data

There were no missing data within any of the outcome measures.

4.15.2 Resource Aims

In order to answer the feasibility study questions relating to resource and management aims, a debriefing meeting of the research team was completed to discuss the conduct of the feasibility study. The minutes of this meeting are presented in Appendix 16.

Is there the resource capacity to cope with recruitment numbers?

There was appropriate research team staffing for all elements of the data collection and treatment of the participants. However, having only a single person trained to gain informed consent was a limitation of this feasibility study.

This study resulted in no specific changes in equipment requirements from standard care, meaning that current equipment provision was sufficient.

Collected data were collated and retained within an excel spreadsheet. This was satisfactory for the numbers recruited within this feasibility study. However, this did mean discontinuity between different aspects of the study paperwork and duplication of data entry, for example within the PIS log, screening log and enrolment logs, increasing the burden of data entry.

Were communication methods appropriate between research team and participants?

Communication with participants exceeded ethical requirements, providing multiple points of contact and opportunities to ask questions prior to giving informed consent. The research team also commented that all participants appeared well informed throughout the course of their involvement in the study.

Within the senior members of the research team there were no concerns with communication, however, with rotational staff surrounding the research team it was suggested they would benefit from education on the study very early into their 6-month rotation.

What were the departmental willingness and engagement to conduct the study?

Departmental engagement and willingness was excellent with support across the nursing and medical team.

Were appropriate mechanisms in place to cope with staff sickness and annual leave periods?

The size of the research team and number of physiotherapists who underwent protocol training was sufficient to allow the study to continue even through periods of absence of some team members. However, the feasibility study did not have mechanisms in place to deal with absence of the CI.

4.15.3 Management Aims

4.15.3.1 Evaluation of Chief Investigator Study Management

Self-analysis of research management was completed using the Researcher Development Framework and is shown within a meta-table as Appendix 17. This was then summarised within two research SWOT analyses, one examining the CI's research management skills in general, and the second focussing on the management of the feasibility study specifically (Appendix 18 and Appendix 19).

Chief Investigator Skills (Appendix 18)

In summary this self-analysis highlighted the CI as a novice researcher, in particular with minimal experience in the following areas:

- Working outside of a quantitative paradigm
- Publication and dissemination of research

Were adverse events dealt with properly?

There were 2 serious adverse events reported – both within the control group and dealt with appropriately and to the satisfaction of the sponsor.

4.15.3.2 Research Team and Staff Expertise:

There were no concerns with research team roles or expertise with all roles carried out within a strict delegation log. There were no concerns raised by members of the research team.

4.15.3.3 Data Management

There were no inaccuracies of data entry or problems with the matching of patient data.

4.15.3.4 Any ethical issues highlighted

There were no new ethical issues brought to light which had not previously been considered during research and ethics committee review.

4.15.4 Scientific Aims

4.15.4.1 Intervention Safety Concerns

There were no safety concerns raised related to the RAPID mobilisation protocol, with no adverse events occurring during any intervention sessions.

4.15.4.2 Reliability, Validity and Trustworthiness of the assessment methods?

Validity, reliability and trustworthiness considerations are presented for each outcome measure in **Tables 4-7 to 11** below:

Table 4-7: Length of stay reliability, validity and trustworthiness assessment methods

Length of Hospital Stay	
Validity	Good validity – time stamp measure
Reliability	Data collected from the hospital computer system accurate to the nearest minute
Trustworthiness	Relies on theatre and ward staff completing time stamps on the hospital computer system accurately. Easily recalled and checked on screen for data entry error

Table 4-8: Time to PT complete reliability, validity and trustworthiness assessment methods

Time to Physiotherapy Complete	
Validity	Good validity – time stamp measure
Reliability	Good reliability - Data documented by the treating physiotherapist immediately following completion of the physiotherapy session – accurate to the nearest 30 minutes.
Trustworthiness	Relies on the judgement of the individual physiotherapist to interpret the suitability of the patient's physical ability to cope following discharge – this is guided by set discharge criteria.

Table 4-9: Functional milestones; reliability, validity and trustworthiness assessment methods

Functional Milestones	
Validity	Good validity – time stamp measure
Reliability	Date and time documented by the treating physiotherapist immediately following completion of the physiotherapy session.
Trustworthiness	Relies on the observation of the treating physiotherapist, some milestones may be completed concurrently with others within the same physiotherapy session.

Table 4-10: Post-operative complications reliability, validity and trustworthiness assessment methods

Post-Operative Complications	
Validity	Data collected to encompassing all adverse events, but limited to the inpatient admission period.
Reliability	Data collected from the hospital computer system accurate to the nearest minute
Trustworthiness	Relies on theatre and ward staff completing time stamps on the hospital computer system accurately. Easily recalled and checked to screen for data entry error

Table 4-11: PNRS reliability, validity and trustworthiness assessment methods

Pain Numerical Rating Scores	
Validity	Published excellent validity in non-specific populations (Herr et al. 2004)
Reliability	Published excellent reliability and consistency in non-specific populations (Herr et al. 2004)
Trustworthiness	Relies on the treating physiotherapist asking the patient for scores at the appropriate times and entering onto the study paperwork accurately.

	Easily reviewed within patient notes for documented scores. May be confounded by the degree of pharmacological pain management the patient has received.

4.15.4.3 Descriptive Statistics for Interventional Effect Sizes and Variance

Baseline Group Characteristics

Table 4-12: Group baseline characteristics

	Control	*Rapid*	*Comparison*
Age (Years)	66.7	67.4	0.7
Gender	30% Male	35% Male	5%
Number on Theatre List	2.03	1.90	-0.13

As shown in **Table 4-12**, no statistical comparison testing was carried out for baseline characteristics in line with the aims of this feasibility study and limited numbers of participants. However, on observation there appeared to be no difference between groups at baseline comparison.

4.15.4.4 Testing for Normality

Peat & Barton 2014 advocate using a summary of several indicators for normality of distribution in the decision making process of determining distribution. As such, the feasibility study variables were reviewed in this manner and the findings summarised in Table 4-15: Milestones summary of whether analyses indicate normal distribution.

Relationship Between the Mean and Median:

Mean and median values were assessed for proximity by expressing the difference between the mean and median as a percentage of the mean. A small percentage difference indicates a likely normal distribution, with a large difference indicating non-normality.

Skewness, Kurtosis and Critical Values:

Table 4-13: Skewness, kurtosis and critical values meta-summary table: Values indicating normal distribution highlighted in green, moderate skewness highlighted in orange and values indicating non-normal distribution highlighted in red.

Variable	Group	Skewness (Std. Error)	Critical Value	Kurtosis (Std. Error)	Critical Value
Length of stay	Control	3.663	6.99	14.645	14.44
	Rapid	0.935	1.61	-0.017	-0.02
Time to PT Complete	Control	2.926	5.58	10.586	9.91
	Rapid	0.168	0.29	0.973 (1.121)	0.87
Time to First ROM	Control	4.329 (0.524)	8.26	18.818 (1.014)	18.56
	Rapid	1.038 (0.580)	1.79	1.085 (1.121)	0.97
Time to First SOEOB	Control	2.392 (0.524)	4.56	10.129 (1.014)	9.99
	Rapid	0.651 (0.580)	1.12	-0.120 (1.121)	0.11
Time to First T/F	Control	2.282 (0.524)	4.35	8.021 (1.014)	7.91
	Rapid	1.612 (0.580)	2.70	1.273 (1.121)	1.14
Time to First Walk >5m	Control	1.666 (0.524)	3.18	3.973 (1.014)	3.92
	Rapid	0.408 (0.580)	0.70	-0.504 (1.121)	-0.45
Time to First Walk >10m	Control	0.662 (0.524)	1.26	2.004 (1.014)	1.98
	Rapid	0.650 (0.580)	1.12	1.267 (1.121)	1.13
Time to First Walk >40m	Control	1.118 (0.524)	2.10	1.094 (1.014)	1.08
	Rapid	-0.405 (0.580)	-0.70	-0.425 (1.121)	-0.38
Time to First Stairs	Control	2.911 (0.524)	5.56	10.503 (1.014)	10.36
	Rapid	0.106 (0.580)	0.18	0.261 (1.121)	0.23

ROM = Range of motion, SOEOB = sit on edge of bed, T/F = transfer to the bedside chair. Values indicating normal distribution highlighted in green, moderate skewness highlighted in orange and non-normal distribution highlighted in red.

When summarised, the skewness, kurtosis and their respective critical values suggest that almost all control group data appears to be non-normally distributed. They also suggest that most of the RAPID group data appears to be normally distributed except for the time to first transfer variable.

Statistical Testing for Normality:

Table 4-14: Statistical testing for normality results

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Group	Statistic	df	Sig.	Statistic	df	Sig.
Hours to PT Complete	Control	.258	19	.002	.673	19	.000
	RAPID	.215	15	.061	.932	15	.288
Days to PT Complete	Control	.259	19	.002	.673	19	.000
	RAPID	.216	15	.058	.932	15	.292
Length of stay (Days)	Control	.330	19	.000	.523	19	.000
	RAPID	.213	15	.066	.875	15	.040
Time to First ROM	Control	.484	19	.000	.294	19	.000
	RAPID	.142	15	.200*	.918	15	.181
Time to First SOEOB	Control	.410	19	.000	.579	19	.000
	RAPID	.130	15	.200*	.948	15	.492
Time to First TF	Control	.330	19	.000	.735	19	.000
	RAPID	.418	15	.000	.640	15	.000
Time to First Walk >5m	Control	.295	19	.000	.826	19	.003
	RAPID	.198	15	.116	.887	15	.060
Time to First Walk >10m	Control	.241	19	.005	.907	19	.065
	RAPID	.251	15	.012	.820	15	.007
Time to First Walk >40m	Control	.271	19	.001	.863	19	.011
	RAPID	.269	15	.005	.886	15	.057
Time to First Stairs	Control	.256	19	.002	.676	19	.000
	RAPID	.186	15	.172	.942	15	.414

*. This is a lower bound of the true significance.
a. Lilliefors Significance Correction

ROM = Range of motion, SOEOB = sit on edge of bed, T/F = transfer to the bedside chair

Plots:

All plots were inspected and assessed for normality of distribution using the following guidance from Pete and Barton 2014:

Histograms: Reviewed for the approximation of a bell-shaped normal distribution curve and for any gaps within the dataset.

Q-Q Plot: Reviewed and considered how close points fell to the expected normal distribution line.

Detrended Q-Q Plot: Observed for spread of points above and below the normal line, and for the siting of the horizontal normal line in the middle of the plot.

Box Plots: The length of the whiskers to be within 1.5 times the spread of the inter-quartile range. These plots were also used to identify outliers and extreme values.

<u>Length of stay: -</u>Control Group:

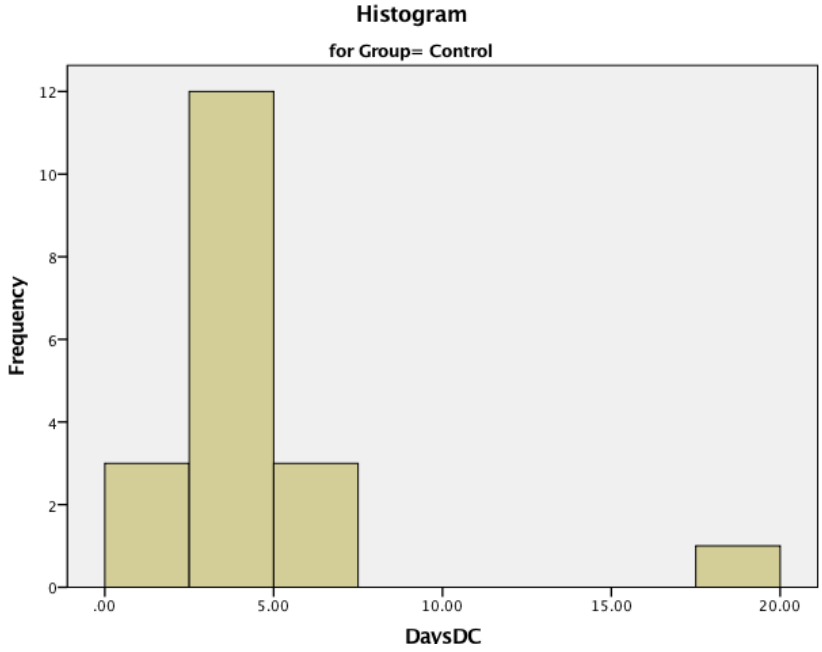


Figure 17: Assessment for normality: Length of stay Histogram Control Group

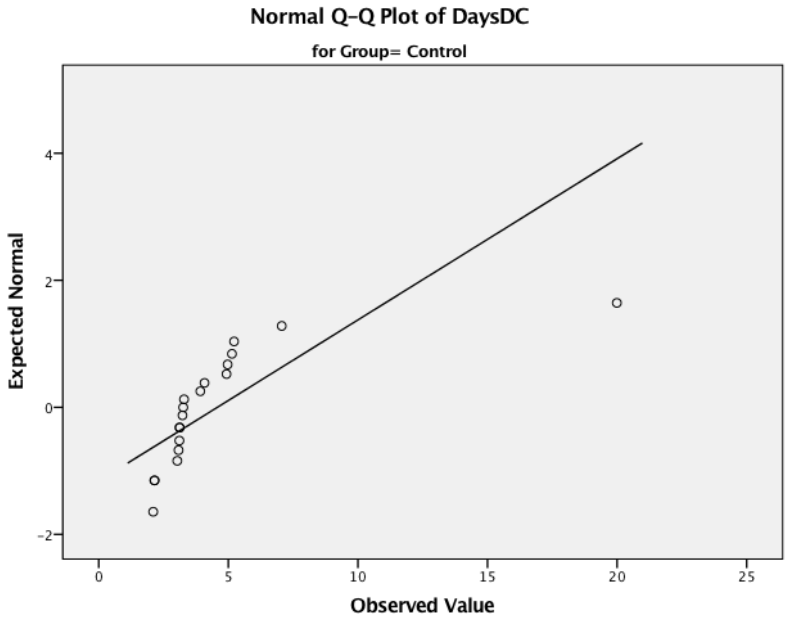


Figure 18: Assessment for normality length of stay Normal Q-Q Plot – Control Group

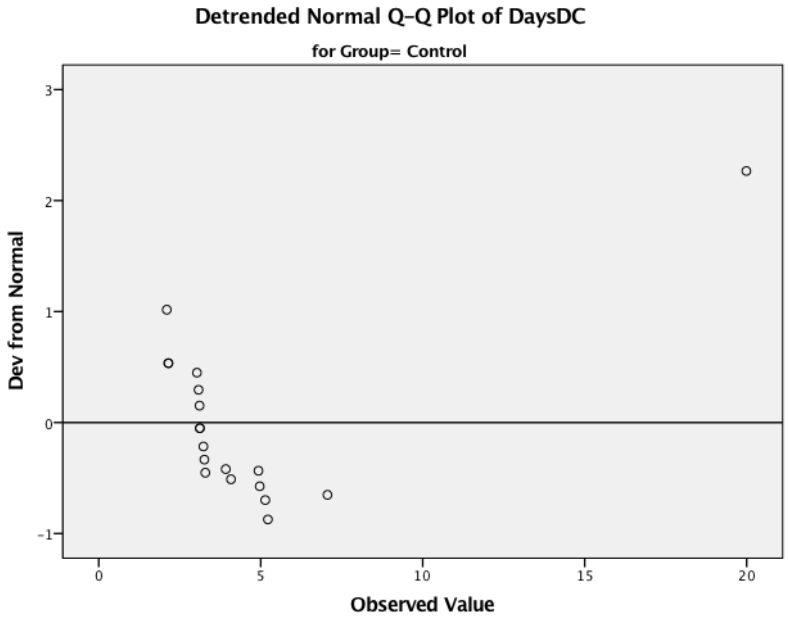


Figure 19: Assessment for Normality: length of stay Detrended Q-Q Plot Control Group

Length of stay - Rapid Group:

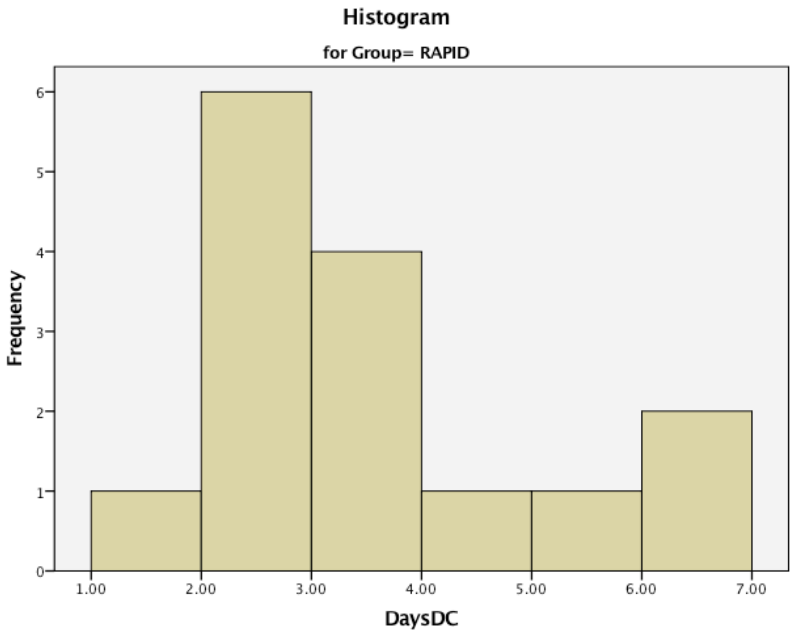


Figure 20: Assessment for normality: length of stay Histogram Rapid Group

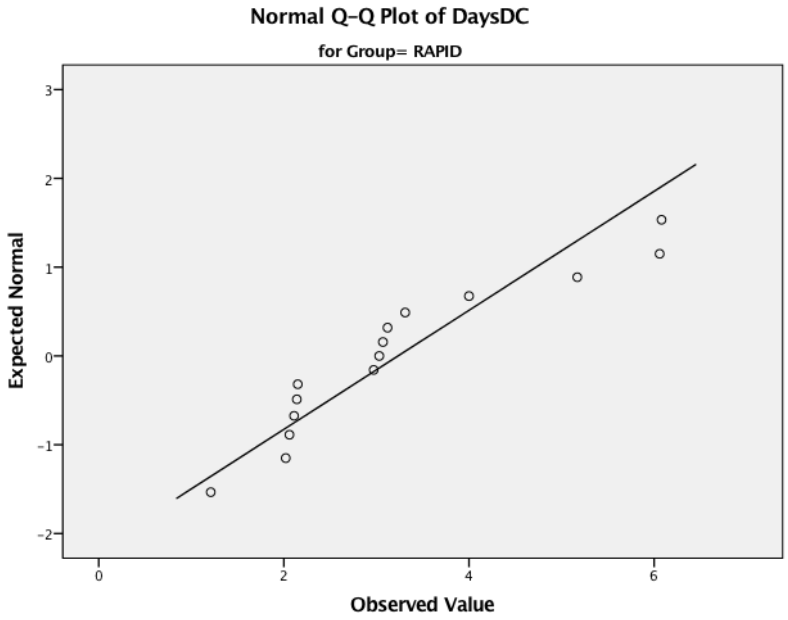


Figure 21: Assessment for normality: length of stay Normal Q-Q Plot Rapid Group

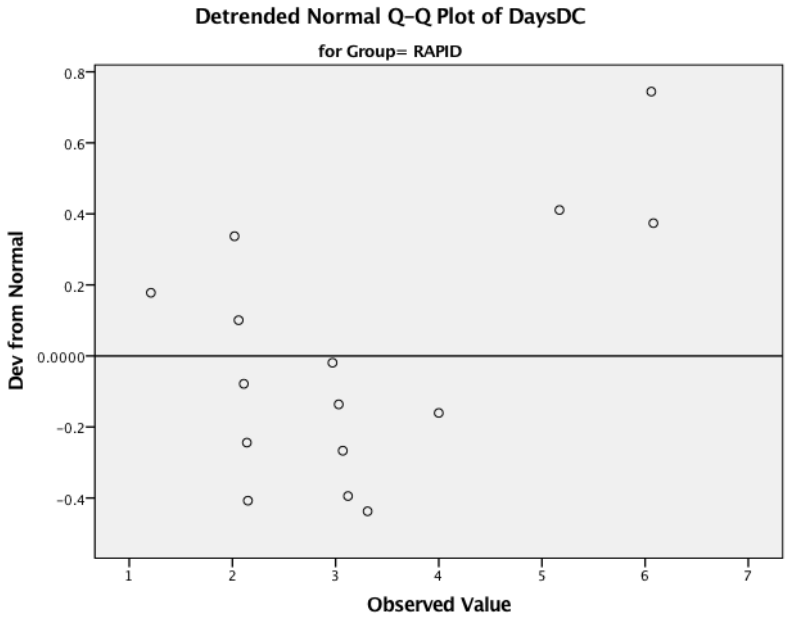


Figure 22: Assessment for normality: length of stay Detrended Q-Q Plot Rapid Group

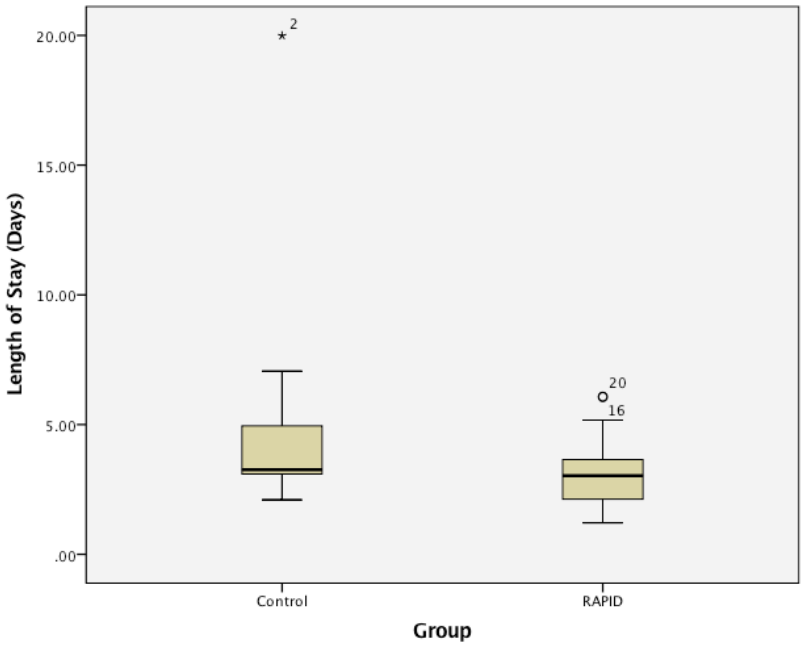


Figure 23: Assessment for normality length of stay box plot

The above figures give an example of the plots produced for length of stay data. Similar plots were produced for each outcome variable and assessed using the same above guidance.

Table 4-15: Milestones summary of whether analyses indicate normal distribution

Variable	Mean to Median Relationship		Mean ± SD – Good Approximation?		Skewness and Kurtosis		Critical Values		Shapiro-Wilk Test		Plots		Overall Decision
	Control	Rapid	Control	Rapid	Control	Rapid	Control	Rapid	Control	Rapid	Control	Rapid	Distribution
Length of stay (Days)	11.7%	0.0%	No	Yes	No	Yes	No	Yes	No	No	No	No	Non-normal
Time to PT Complete	11.6%	1.7%	No	Yes	No	Yes	No	Yes	No	Yes	No	No	Non-normal
Time to First ROM	34.8%	4.0%	No	Yes	No	Yes	No	Yes	No	Yes	No	No	Non-normal
Time to First SOEOB	0.2%	0.0%	No	Yes	No	Yes	No	Yes	No	Yes	No	No	Non-normal
Time to First T/F	4.1%	58.6%	No	No	No	Yes	No	No	No	No	No	No	Non-normal
Time to First Walk >5m	9.2%	9.6%	No	No	No	Yes	No	Yes	No	Yes	No	No	Non-normal
Time to First Walk >10m	13.3%	11.3%	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	No	Non-normal
Time to First Walk >40m	12.4%	11.4%	No	Yes	Yes	Yes	No	Yes	No	Yes	No	No	Non-normal
Time to First Stairs	12.7%	2.6%	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	Non-Normal

ROM = Range of motion, SOEOB = sit on edge of bed, T/F = transfer to the bedside chair

4.15.4.5 Identification of Outliers

Outliers were identified using the box plots and Mahalanobis distances calculated:

Mahalanobis distance calculations were then used to identify any multivariate outliers across the 9 variables examined. Mahalanobis distance values were then evaluated using critical values of chi-squared to nine degrees of freedom relating to the number of variables. P-values less than 0.001 were deemed as multivariate outliers. Through this method, three data points were identified as multivariate outliers.

These identified outliers were then assessed for potential reasons as to why the outlier occurred. None of these outliers could be put down to erroneous data collection or handling but were all genuine values. All three outliers were related to post-operative complications delaying recovery and skewing time to functional milestones to the right.

4.15.4.6 Dealing with Outliers

Given that all outliers were determined genuine values, it was appropriate to retain these values within the dataset as they reflect variation within the data that would be expected within a fully powered study.

Consideration was given to the option of transforming the data toward normality, with the aim of allowing parametric comparison testing. All amenable variables were trialled as transformed into base 10 logarithmic values and the dataset in this form reconsidered for normality of distribution using statistical testing detailed in ***Table 4-16***:

Table 4-16: Statistical testing for normality of transformed data

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Group	Statistic	df	Sig.	Statistic	df	Sig.
Log_{10}DaysDC	Control	.201	19	.041	.824	19	.003
	RAPID	.156	15	.200*	.941	15	.396
Log_{10}DaysPTComp	Control	.167	19	.170	.902	19	.053
	RAPID	.262	15	.007	.882	15	.051
Log_{10}HoursFirstROM	Control	.346	19	.000	.440	19	.000
	RAPID	.127	15	.200*	.948	15	.500
Log_{10}HoursFirstSOEOB	Control	.427	19	.000	.585	19	.000
	RAPID	.133	15	.200*	.964	15	.756

Log_{10}HoursFirst TF	Control	.292	19	.000	.766	19	.000
	RAPID	.378	15	.000	.712	15	.000
Log_{10}HoursFirst Walk5m	Control	.267	19	.001	.833	19	.004
	RAPID	.266	15	.006	.821	15	.007
Log_{10}HoursFirst Walk10m	Control	.233	19	.008	.783	19	.001
	RAPID	.304	15	.001	.821	15	.007
Log_{10}HoursFirst Walk40m	Control	.199	19	.046	.915	19	.093
	RAPID	.315	15	.000	.819	15	.006
Log_{10}HoursFirst Stairs	Control	.171	19	.147	.905	19	.060
	RAPID	.252	15	.011	.885	15	.056

*. This is a lower bound of the true significance.
a. Lilliefors Significance Correction

ROM = Range of motion, SOEOB = sit on edge of bed, T/F = transfer to the bedside chair

Statistical testing for normality with the Shaprio-Wilk test indicated that some variables expressed within a logarithmic scale just met the p >0.05 threshold for normal distribution. However, these values were very close to the threshold for normality, and the majority of variables remained non-normally distributed. Consequently, it was decided to retain all outliers, use the non-transformed dataset and use non-parametric comparison testing to account for this.

4.15.4.7 Length of Hospital Stay

Length of stay within the RAPID group was observed as a median of 1 day shorter than observed within the control group, as expected within a feasibility study this did not reach statistical significance (p=0.096).

Time to Physiotherapy Complete to Leave Hospital

Time to physiotherapy complete also indicated a clinically significant median difference with this milestone being reached just over one day quicker in the RAPID group than the control group. In this instance the results were indicated to be statistically significant (p=0.015)

4.15.4.8 Achieving Functional Milestones

For first hip joint ROM, there was no significant difference between group medians (p=0.302), this would be expected due to no interventional differences between groups at this milestone. However, all other functional milestones were achieved quicker within the RAPID group, with all differences reaching statistical significance as shown in ***Table 4-17***

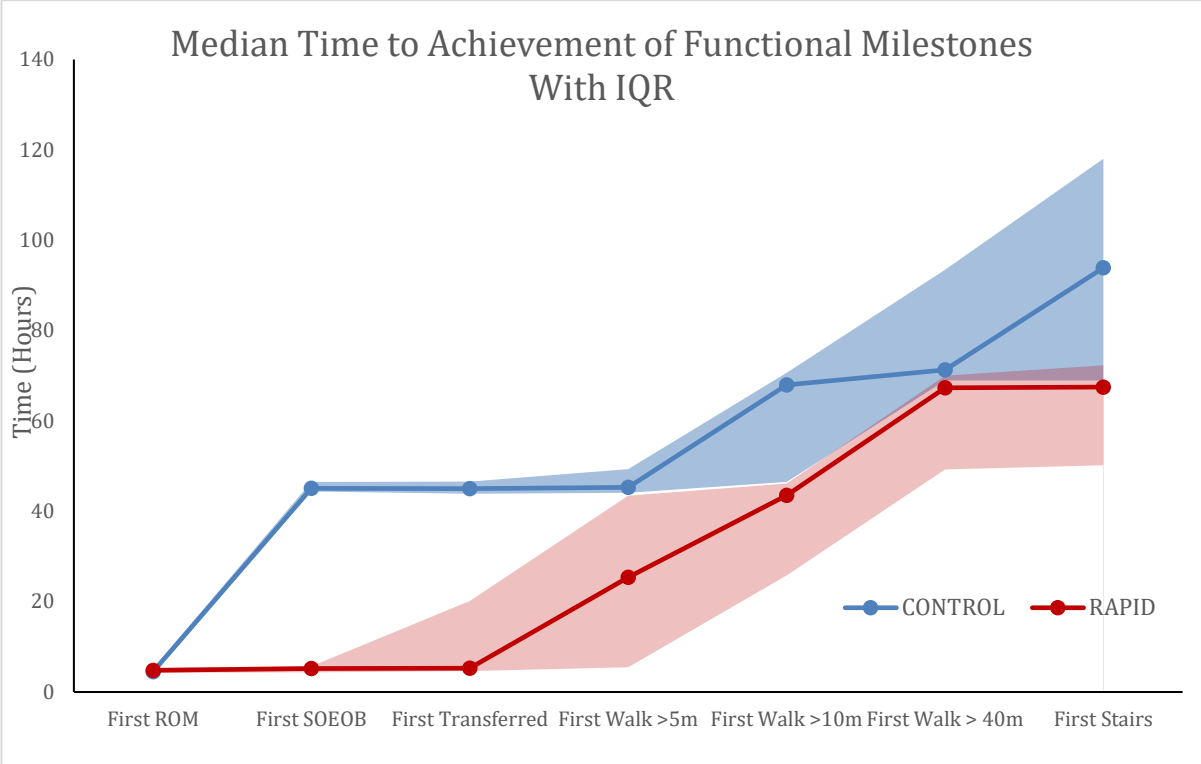


Figure 24 - Graph - Time to functional milestones between groups (Displayed with IQR limits)

ROM = Range of motion, SOEOB = sit on edge of bed, T/F = transfer to the bedside chair

Table 4-17 - Descriptive and Comparison Statistics for Functional Milestone Variables

Variable	*Descriptive Statistic*	*Control Group*	*Rapid Group*	*Difference between Mean/Median*	*Significance*
Length of stay (Days)	Mean (SD)	4.53 (3.94)	3.00 (1.41)	-1.53	0.096
	Median (IQR)	4.00 (2.00)	3.00 (1.00)	-1.00	
Time to PT Complete (Days)	Mean (SD)	4.49 (2.89)	2.88 (0.88)	-1.61	0.015
	Median (IQR)	3.97 (2.06)	2.93 (0.98)	-1.04	
Time to Functional Milestones					
First Range of Motion (Hours)	Mean (SD)	6.9 (9.8)	5.0 (0.8)	-1.9	0.302
	Median (IQR)	4.5 (1.2)	4.8 (1.4)	0.3	
First Sit on Edge of Bed (Hours)	Mean (SD)	45.2 (26.5)	5.2 (0.9)	-40.0	<0.001
	Median (IQR)	45.1 (2.8)	5.2 (1.4)	-39.9	
First Transferred to Chair (Hours)	Mean (SD)	46.9 (27.0)	12.8 (14.5)	-34.1	<0.001
	Median (IQR)	45.0 (17.6)	5.3 (20.4)	-39.7	
First Walk >5m (Hours)	Mean (SD)	49.9 (30.0)	28.1 (20.5)	-21.8	0.011
	Median (IQR)	45.3 (23.2)	25.4 (38.1)	-19.9	
First Walk >10m (Hours)	Mean (SD)	60.0 (29.9)	40.0 (12.7)	-20.0	0.009
	Median (IQR)	68.0 (25.8)	43.5 (20.8)	-24.5	
First Walk >40m (Hours)	Mean (SD)	81.4 (34.7)	60.4 (21.5)	-20.9	0.017
	Median (IQR)	71.3 (25.8)	67.3 (24.0)	-3.9	
First Independent Stairs	Mean (SD)	107.5 (69.4)	65.8 (23.9)	-41.6	0.010
	Median	93.9 (49.6)	67.5 (23.7)	-26.4	

PT Complete = Physiotherapy Complete for discharge, SD = Standard Deviation, IQR = Interquartile Range

4.15.4.9 Post-Operative Complications

Table 4-18: Results of post-operative complications

	Severity Classification	*Individual Instances*		*In Unique Patients*	
Complication	Grade	Control	RAPID	Control	RAPID
Apnoea	IVa	1	0	1	0
Blood Transfusion	II	1	0	1	0
Pulmonary Embolism	II	1	0	1	0
Orthostatic Hypotension	I	5	6	5	4
Wound Ooze	I	0	2	0	2
PONV*	I	4	3	4	2
Bruising Around Op-Site	I	0	1	0	1
Chest Pain	I	0	1	0	1
Dizziness	I	2	0	1	0
Pain limiting Mobility	I	1	0	1	0
Post-Operative Confusion	I	1	0	1	0
Slow Mobility Progress	I	1	0	1	0
Syncope	I	1	0	1	0

**PONV = Post-operative nausea and vomiting*

Post-operative complications were classified for severity using the Clavien-Dindo classification system (Dindo et al. 2004) detailed in **Table 4-19** below:

Table 4-19: Clavien-Dindo classification

Grade	*Subgrade*	*Definition:*
I		Any deviation from the post-operative course without the need for pharmacological treatment, or surgical, endoscopic and radiological interventions. Allowed Therapeutic regimens are drugs such as antiemetics, antipyretics, analgesics, diuretics, electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside
II		Requiring pharmacological treatment with drugs other than allowed for grade I complications. Blood transfusion and total parenteral nutrition are also included.
III		Requiring surgical, endoscopic or radiological intervention
	A	Intervention not under general anaesthesia
	B	Intervention under general anaesthesia
IV		Life threatening complications (Including CNS complications) requiring intensive care management
	A	Single organ dysfunction
	B	Multi-organ dysfunction
V		Death

(Reproduced from (Dindo et al. 2004) with permission from Wolters Kluwer Health Inc. under licence number 5474770173829)

Orthostatic hypotension (defined using the Freeman et al. 2011 published consensus definition of a sustained reduction in systolic blood pressure of at least 20mmHg or diastolic blood pressure of at least 10mmHg within three minutes of postural challenge) was the most common complication in both groups, seen in 9 different patients in total, with one patient in the intervention group experiencing three instances during their inpatient hospital stay. Although the consensus definition states that orthostatic hypotension may be symptomatic or asymptomatic, in this study only participants who experienced symptoms of orthostatic hypotension were investigated and the complication confirmed with non-invasive blood pressure readings.

Post-operative nausea and vomiting was the next most common complication to affect both groups, being observed in four of the control group and two of the intervention group, one of which experienced two episodes of PONV.

There were three incidences of post-operative complications classified as higher than grade I. One instance of pulmonary embolism, one instance of low haemoglobin requiring blood transfusion and one instance of apnoea which required intubation and ventilation, with an admission to intensive care. All these very serious complications were observed within the control group.

There were two incidences of post-operative wound ooze within the RAPID group, while none observed within the control group, which could be attributed to the intervention and delayed discharge with both of those individual participants.

4.15.4.10 Post-Operative Pain

Overall, higher PNRS scores were observed on the day-of-surgery for participants within the RAPID group when compared to controls. However, this trend was reversed on post-operative day 1 both at rest and on hip joint range-of-motion. Comparison testing however indicated no significant differences between groups.

When comparing the first-time participants walked post-operatively, in the RAPID group, Mean PNRS scores were observed as 1.16 points lower compared to the control group, however, this also did not reach statistical significance (p=0.582). (**Table 4-20**)

Table 4-20: Descriptive statistics for Pain numerical rating scale

Descriptive Statistics – Pain Numerical Rating Scale Data							
Day 0 Pain Numerical Rating Scores							
Circumstance	RAPID Group		Control Group		Difference Between Groups		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean	Median	Significance
PNRS at Rest	1.79 (1.97)	1.50 (3.00)	1.12 (1.73)	0.00 (2.00)	0.67	1.50	0.309
PNRS on Hip ROM	3.00 (2.99)	2.00 (4.00)	2.41 (2.27)	2.00 (5.00)	0.59	0.00	0.683
PNRS on Walking	3.57 (3.01)	3.50 (6.00)	N/A	N/A	N/A	N/A	N/A
Day 1 Pain Numerical Rating Scores							
PNRS at Rest	2.36 (2.59)	1.00 (4.00)	2.72 (1.99)	3.00 (3.00)	-0.36	-2.00	0.708
PNRS on Hip ROM	3.79 (2.49)	3.50 (4.00)	4.78 (2.58)	5.00 (3.50)	-0.99	-1.50	0.322
PNRS on Walking	3.86 (2.48)	4.00 (4.00)	4.73 (2.40)	5.00 (2.50)	-0.87	-1.00	0.892

PNRS = Pain numerical rating scale, ROM = Range of motion, SD= Standard deviation, IQR = Interquartile range

4.15.5 Patient Experience

There was no missing data, with questionnaires completed for all 34 participants. For questions 5 and 6 with an open-ended comments option not all participants opted to add comments.

4.15.5.1 Quantitative Results:

All the numerical questionnaire responses suggested no significant differences between intervention and control groups, as shown in **Table 4-21** below.

Table 4-21 – Responses to numerical survey data

	Control - Mean (SD)	*RAPID – Mean (SD)*	*Difference Between Groups*	*Significance*
Do you think the hospital staff did all they could to help control your pain?	9.87 (0.516)	9.88 (0.485)	0.01	p=0.575
Overall, how was your experience of physiotherapy following your operation?	9.93 (0.258)	9.88 (0.332)	-0.05	p=1.000
Overall, how was your experience of your overall hospital treatment?	9.87 (0.352)	9.88 (0.332)	0.01	p=0.349
Did you have confidence and trust in the physiotherapists treating you?	9.93 (0.258)	9.94 (0.243)	0.01	p=0.551
How beneficial was walking early after your operation?	9.60 (0.737)	9.41 (1.326)	-0.19	p=0.960
How well was your progression with your physiotherapist paced to suit you?	9.80 (0.561)	9.82 (0.529)	0.02	p=0.654

SD = Standard deviation

4.15.5.2 Open-Ended Survey Questions:

For question five, 9 participants opted to make no comment, meaning that 25 individual comments were made on this question. For question six, 13 participants opted to make no comment, meaning that 21 individual comments were made on this question.

Although there was too limited a quantity to develop a theoretically saturated analysis of participant experience, reading the questionnaire comments grouped respective to their randomised group, with thematic analysis, the following themes emerged:

Question 5: How Beneficial Was Walking Early After your Operation?

Question 6: How Well Was Your Progression with Your Physiotherapist Paced to Suit You?

Confidence

Confidence was the most explicitly mentioned emotion when participants were asked how beneficial early walking was for them, with several quotes indicating that early ambulation influenced participant confidence in the outcome of the operative procedure:

"It gave me confidence that op went well" (RAPID Group)

"Knowing very quickly that I had use of both legs and able to stand, move, sit and stand up again built my confidence in the procedure" (RAPID Group)

"Gave me confidence by starting early" (RAPID Group)

This was also reflected by comments within the control group:

"Walking as soon as possible after the operation gives confidence" (Control Group)

The Impact of the Physical Experience

All comments pertaining to negative participant experiences directly and explicitly discussed empirical 'symptoms' as the causative factor, both within the RAPID group and within the control group:

"I was sick the day afterwards, which may have prejudiced me against walking early" (RAPID Group)

"I was only up one day after operation before I became unwell and was bed ridden again" (Control Group)

"After day 1 my progress was delayed because of a dangerously low BP and anaemia which resulted in the need for a blood transfusion" (Control Group)

These quotations suggest a direct link between the manifestation of physical symptoms and patient experience.

Recovery Management

Through both the RAPID and Control group participant responses, the way they self-managed and were personally managed through their recovery by healthcare professionals appeared to impact on their overall experience. The role of the physiotherapist in recovery pacing and guidance appeared frequently, and particularly within the control group appeared to impact positively on the lived experience:

"I cannot fault the way the whole physio team taylored and retaylored their programme to meet my changing needs" (Control Group)

"Always encouraged but never pushed or forced beyond my capabilities" (Control Group)

This was also reflected in comments from the RAPID group cohort:

"First class supervision throughout. No pressure to progress, just engagement. It worked well" (RAPID Group)

"The physios were all very helpful and good at supporting me, especially if I didn't understand something straight away" (RAPID Group)

While providing indications of potential themes related to patient experience of day-zero ambulation, comments to the open-ended survey questions provided a limited volume of data for the formulation of thematic analysis, lacking the required richness, and lacking the ability to clarify participant thoughts and feelings. Consequently, no conclusions can be drawn from this data, other than to provide potential topics for further exploration.

4.15.5.3 Validity

Content validity of the questionnaire was reviewed using guidance from Bolarinwa 2015. Construct and criterion-related validity were not reviewed as scores were not combined into a single score or designed to be compared against a known 'gold-standard' measure.

Content Validity:

Consideration of content validity was carried out by comparing the questionnaire questions in reference to the NHS patient experience framework (NHS 2011) (Appendix 20) and through readability testing using the University of Nottingham readability calculator using the SMOG (Simplified measure of gobbledygook) advocated for testing healthcare literature for understanding within the UK (Rowlands 2013).

Within this comparison, all the questions showed direct relevance in relating to domains within the NHS patient experience framework.

Readability was assessed for each question individually (Appendix 21), and indicated a readability level equivalent to a UK broadsheet newspaper/UK GCSE level education. Although these scores were higher than ideal for healthcare literature, higher scores were attributable to polysyllabic words such as 'physiotherapy' and 'experience' which could not be omitted or adapted without losing the overall meaning of the question.

4.15.5.4 Potential Bias

Crow et al. 2002 produced a systematic review analysing bias within healthcare-based patient satisfaction survey methods. The findings within this paper were used to analyse the strengths and weaknesses of this study's questionnaire shown in **Table 4-22** below:

Table 4-22: Patient experience questionnaire strengths and weaknesses analysis

Strengths	*Weaknesses*
Easy to administer Methods facilitate all participants to respond – reducing the risk of non-response bias Questionnaires anonymised Inclusion of open-ended questions and comments sections – provide opportunity for richer data Sequencing follows guidance of moving from generic topics to specific areas of experience.	The questionnaire contains pre-selected issues – may miss issues which may be more important to the patient. Location – while completing the questionnaire on site, patients are less likely to express dissatisfaction, leaving the questionnaire open to socially desirable response bias Questionnaire is completed by the treating team / organisation – lending towards socially desirable response bias.

	Questions are short and as jargon free as possible Physiotherapy care is ending at the completion of the questionnaire – less motivation for cognitive consistency pressure bias.	

4.16 Discussion and Learning

4.16.1 Scientific Findings

4.16.1.1 Length of Stay, time to physiotherapy complete and functional milestones

This study showed a trend suggesting an increase in speed of recovery when day-zero ambulation was employed. While this study was not powered to draw conclusions from the findings, time to physiotherapy complete to leave hospital and time to functional milestones showed a statistically significant difference between groups, with length of stay coming close to statistical significance, giving a strong indication that proceeding to a fully powered study would be valuable.

4.16.1.2 Pain Numerical Rating Scale Scores

This feasibility study indicated no significant differences between groups in post-operative pain scores. However, as discussed below, this outcome is open to confounding factors.

4.16.1.3 Post-Operative Complications

This study gives an indication that day-zero ambulation is a safe intervention to research within this patient cohort with no high severity complications within the intervention group.

With respect to low severity complications, most complications were seen in equal representations in both groups; with the exception being post-operative wound ooze and bruising around the wound site. This is something to consider when examining the results of a fully powered study as theoretically day-zero ambulation could affect early wound healing and be a direct cause of wound ooze problems.

4.16.1.4 Patient Experience

Questionnaire data suggested no significant differences between patient experience with day-zero ambulation.

4.16.1.5 Representativeness of the Sample

This feasibility study showed baseline group characteristics which were comparable between groups, indicating that randomisation appears to have been successful in minimising group differences and when compared with the latest National Joint Registry statistics for age and gender of total hip replacements, the sample seen within this feasibility study is comparable to the wider population (**Table 4-23**).

Table 4-23: Representativeness of the sample compared with national data

	Feasibility Study Sample	*NJR 2017 Statistics*	*Difference*
Age	67.1	68.7	1.6
Gender	67.5% Female	60% Female	7.5%

(National Joint Registry for England, Wales 2017)

Roberts & Torgerson (1999) recommend that where there is a known moderate association between the covariate and the test variable, that chance bias may be appreciable when the group imbalance exceeds 5%. For the variables compared above, gender did exceed this at 7.5% difference between groups. However, with the increased numbers recruited within a fully powered study this difference would likely be further addressed by randomisation.

4.16.2 Feasibility of a Fully Powered Study

4.16.2.1 Sample Size Calculation

The following descriptive statistics in **Table 4-24** were used in sample size calculation based on the primary outcome measure of length of stay:

Table 4-24: Sample size calculation

Allocated Group			Statistic	Std. Error
Control	Mean		4.53	.955
	95% Confidence Interval for Mean	Lower Bound	2.50	
		Upper Bound	6.55	
	5% Trimmed Mean		3.87	
	Median		4.00	
	Variance		15.515	
	Std. Deviation		3.939	
	Minimum		2	
	Maximum		19	
	Range		17	
	Interquartile Range		2	
	Skewness		3.452	.550
	Kurtosis		13.004	1.063
RAPID	Mean		3.00	.343
	95% Confidence Interval for Mean	Lower Bound	2.27	
		Upper Bound	3.73	
	5% Trimmed Mean		2.94	

	Median	3.00	
	Variance	2.000	
	Std. Deviation	1.414	
	Minimum	1	
	Maximum	6	
	Range	5	
	Interquartile Range	1	
	Skewness	1.202	.550
	Kurtosis	.896	1.063

t tests - Means: Difference between two independent means (two groups)

Analysis: A priori: Compute required sample size

Input: Tail(s) = Two

Effect size d = 0.5170616

α err prob = 0.05

Power (1-β err prob) = 0.9

Allocation ratio N2/N1 = 1

Output: Noncentrality parameter δ = 3.2701847

Critical t = 1.9750921

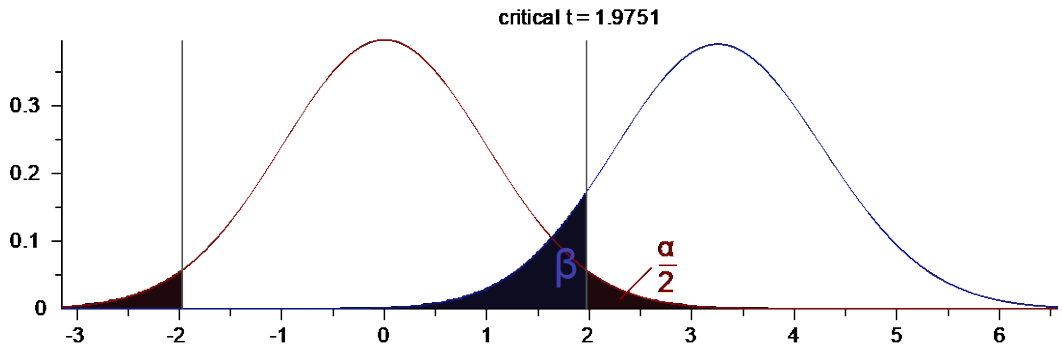
Df = 158

Sample size group 1 = 80

Sample size group 2 = 80

Total sample size = 160

Actual power = 0.9015233



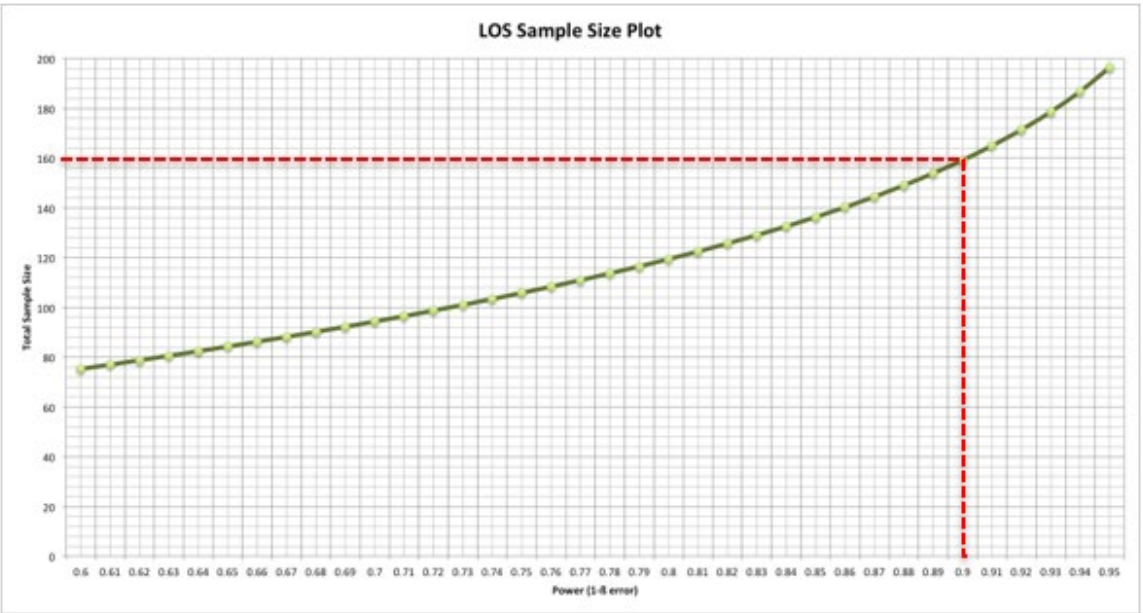


Figure 25: Sample size power graph

Sample-size calculation indicates a total of 160 participants and is based on a clinically significant difference in length of stay showing a median reduction of 1 day.

Sample size calculation was completed following advice from a statistician and using the software package G*Power 3.1 (Franz Faul 2007; Faul et al. 2009). A value of 0.05 was used for the α-error and a value of 0.10 for the β-error as within convention for a clinical trial (Banerjee et al. 2009; Machin et al. 2009). Although data were found to be non-parametric, sample size calculation was completed using a t-test difference between two independent means based on statistician advice and following the advice presented within Bausell-Barker & Yu-Fang (2002) book on sample size within experimental research. Under this advice, it is suggested that if the investigator feels especially insecure about a sample size calculation based on non-normality of data that the computation should be carried out using a power (1-β error) of 0.9.

It was also statistician advice that as the projected numbers within the power calculation were approaching n=200 then it can be assumed that central-limit-theorem would apply to data collected, making a sample size calculation in this instance based on a t-test appropriate.

Gupta et al. (2016) recommends accounting for potential dropout when determining final sample size for recruitment by increasing the sample size by the expected dropout rate. No dropouts were observed within this feasibility study, nevertheless dropouts could occur within the fully-powered study. As such, a low anticipated dropout rate of 10% or less was expected, and the sample size increased by 10% to adjust for this. This 10% increase to account for dropout, resulted in a total sample size of 176 comprised of 88 participants per group.

4.16.2.2 Recruitment

For a required sample size of 176, the following time periods for recruitment in **Table 4-25** are indicated:

Table 4-25: Recruitment rate projections

Recruitment Rate (Per Working Day):	*Anticipated Recruitment Time*
1.5	30 months
1.9	24 months
2.4	19 months

These figures suggested recruitment was feasible within a time-period conducive with the resources of the research team.

The recruitment rate of 1.5-2.4 participants per week appears favourable when put in comparison with published recruitment rates. Walters et al. 2017 found an average recruitment rate of 0.92 patients per month within RCTs.

4.16.2.3 Study Logistics

This study highlighted the following weaknesses in the logistical implementation:

<u>Reliability of participants receiving PIS:</u>

During the beginning of this study, there were a number of potential participants who did not receive the study PIS prior to screening for recruitment. This resulted in 12.5% of the potential participants screened who were then not eligible for recruitment. Altering the practice for this and posting the study documents improved this dramatically over the last 8 weeks of the feasibility study and must be recommended for a fully powered study.

<u>Reliance on the CI:</u>

The sole reliance on the study CI for recruitment was a clear limitation within this feasibility study, with recruitment stalling completely when the CI was absent. This was both due to contingency plans for CI absence not being in place, but also through the remainder of the research team not trained to be able to gain informed consent. While recruitment being carried out solely by the CI is desirable in order to protect against study protocol breaches, in this case it could seriously affect the recruitment rate and the study-running period, with periods of absence inevitable within a 24-month recruitment period.

Other Evening Workload on Therapists:

Evening treatment for trial participants was completed by a physiotherapist already working an evening shift; with the purpose of treating other patients who had undergone gone day-case surgery. Adding trial participants to this workload does have the potential to cause a conflict of interest as to which patient should be treated first or altogether.

While clashes of clinical caseload with trial participant treatment were not an observed problem, it was highlighted within the debrief minutes (Appendix 16) that this could be a potential risk.

Duplication of Data Entry:

Paper systems for data collection and entry led to the research team having to re-enter the same data onto several different forms. One example of this is in the entry of any post-operative complications that befell the participant on to the case-report form, this information was also required to be entered into the study adverse events log. These practices both increase the burden on the research staff, but also leave opportunity for missing data or incorrect data entry. Therefore, simplifying the collection and logging of data to eliminate duplication is recommended.

4.16.3 Limitations

4.16.3.1 Follow-up period

Methods used within this study only provide sensitivity for the identification of post-operative complications occurring within the inpatient period. While this was chosen for pragmatic reasons, it means that post-discharge complications would not be picked up by this study and correlations with day-zero ambulation missed. Certainly, some of the common post-operative complications expected within this patient cohort have incidence time-courses outside of the expected inpatient period. For example White et al. 1998 found that 76% of thromboembolic events were diagnosed post-discharge following THR, with 50% of these diagnosed more than 17 days post-operatively. This is reflected in guidelines for VTE pharmacological prophylaxis to continue for 35 days post-operatively (Falck-Ytter et al. 2012).

4.16.3.2 Unaccounted Confounding Factors:

Pharmacological management of post-op pain:

Although participants were treated using a standardised post-operative analgesia regime (Appendix 10), there is room for considerable variation within this regime for pharmacological analgesia dosing appropriate to patient's pain scores. Indeed, these scores are actively controlled

for by nurses, throughout the inpatient stay. While within the standardised regime, paracetamol and NSAIDs (where appropriate) are provided at the same doses, both strong and weak opioids may be delivered via different drugs, formulations, doses and at time-intervals. Fischer et al. (2008) produced a literature review examining analgesia following total knee replacement and included two different studies which showed strong opioid medications were superior to placebo control in reducing post-operative pain scores (Ahdieh et al. 2004; Cheville et al. 2001). With opioid analgesia having a proven efficacy, and the expectation that in a fully powered study, the consumption of opioid analgesia will vary between participants this must be considered a major confounding factor in examining post-operative pain scores.

Co-morbidities

While the inclusion and exclusion criteria have been left broad within this study to enable a cohort representative of the target population, pre-existing medical conditions could be a confounder for some of the outcome measures used. Huang et al. (2011) presented increasing numbers of pre-operative co-morbidities as positively correlated with length of stay. Patients with a Charlston comorbidity index of ≥2 needed an extra 1.61 days in hospital. The presence of co-morbidity has also be shown to increase the overall care episode cost to THR (Rosas et al. 2017) and Singh & Lewallen (2013) showed increased risk of moderate to severe post-operative pain related to both medical co-morbidities and anxiety and depression. As such this should be a covariate which need measuring or controlling for within a fully-powered RCT.

4.16.3.3 Incidence of post-operative nausea and vomiting

One of the most common post-operative complications seen within this feasibility study was PONV, similarly to pain scores discussed above, incidences of this aim to be controlled with the use of antiemetic medications. Through this, incidences of PONV may be artificially adjusted. Considering the findings of Raphael et al. (2011) where higher incidences of PONV were observed in patients who underwent fast track total joint arthroplasty, data collection of the consumption of antiemetic medications may help to provide a greater depth of information on this and account for this confounding factor.

4.16.3.4 Patient experience

Data collected from the participant experience questionnaire provided some useful quantitative data for comparing groups across specific questions, with the purpose of generalisability.

However, comments to the open-ended survey questions didn't provide sufficient data for the formulation of thematic analysis, lacking the required richness to be able to draw conclusions from the data, and lacking the ability to clarify participant thoughts and feelings. While the use of questionnaires in collecting participant experience data offers the strengths of enabling the researcher to collect large amounts of data and generalise findings due to the standardisation of response questions, the data gathered did not provide a sufficiently rich evaluation of patient experience to be able to properly complement and provide context to the quantitative findings. This is a key limitation of questionnaire research, with the researcher having no opportunity to follow-up on ideas or issues raised. Furthermore, participants can find questionnaires frustratingly restrictive in allowing them to express their experience. In this research, as the questionnaire had been collated by the researcher, this also opens the potential for bias, where questions could be coded towards the researchers way of thinking (Denscombe 2014). Proper examination of participant experience would warrant a different research approach.

4.16.3.5 Functional milestones outcome unvalidated

While the collection of functional milestone time stamps provides information on return to set levels of function, this is not a measurement of function validated in literature. This could leave future research findings open to challenge of their validity to measure physical function.

4.16.3.6 Single Centre Study

This feasibility study was conducted as a single centre study selected as the full-time workplace of the researcher. However, single centre studies are seen as inferior to a multi-centre design within the hierarchy of evidence (Evans 2003). And while achieving a high level of internal validity, are recognised as being limited in their external validity, susceptible to over-estimating effect size and there are examples of their findings being contradicted by later conducted multi-centre studies (Bellomo et al. 2009). Ideally, with adequate funding and a larger research team the planned fully powered study would have been conducted as a multi-centre study. This would strengthen the external validity of the findings by reducing potential influences of local biases.

4.16.4 Recommendations for Improvement

4.16.4.1 Scientific Quality Improvements

Based on the limitations of the feasibility study identified above, the following recommendations shown in **Table 4-26** were made to improve the scientific quality of any subsequent fully powered RCT.

Table 4-26: Methodological recommendations for scientific quality improvement

Recommendation	*Rationale*
Extension of the post-operative follow-up period	To identify post-operative complications which may have causality to the intervention but occur outside the inpatient period.
Collection or controlling for consumption of anti-emetic and analgesic medications	To address these as confounders to findings on the incidence of PONV and pain experience. To provide a greater depth of information on pain experience
Stratification of randomisation based on co-morbidities	To ensure balance of participants with high numbers or severity of comorbidities between groups.
Collection of a validated functional measure	To improve validity of study findings on functional recovery.
Conduct a nested qualitative study to examine patient experience	To further examine in detail the patient's lived experience of day-zero ambulation using a methodology which provides a richer exploration. Austin & Sutton 2014 summarised the value of qualitative research as complimentary to quantitative research in healthcare where numerical data is insufficient to capture how patients feel about their care.
Conduct the fully-powered study as a multi-centre study	This would strengthen the study by raising its ranking within the hierarchy of evidence for quantitative research (Evans 2003). Reduce the influence of local bias and improve external validity and generalisability to other UK hospitals.

4.16.4.2 Study Governance / Management Improvements

The insight gained from this study would suggest the following improvements to address the study management or governance issues discussed above:

4.16.4.2.1 Development of a Study Database

Development of a study database, with the following aims:

- Provide one central point for data entry and remove data duplications
- To generate electronic PIS, screening, enrolment and adverse events logs

4.16.4.2.2 Multiple Staff Able to Recruit

The training and delegation to at least two other members of staff to be able to formally consent, randomise and recruit participants to the study.

4.16.4.2.3 Recruitment Sensitive to the Normal Clinical Caseload

Evening workloads for the clinical team involved in treating trial participants are predictable in advance based on theatre timetables. When recruiting it is recommended that the recruiter check the evening workload and not recruit on this particular day if a conflict of interest may be anticipated.

5 - Study Amendments

5.1 Introduction

This chapter discusses the recommendations made following the feasibility study and how the author considered these either for rejection or translation into study amendments. This includes the practical considerations, impact on the research team and the ethical considerations of the proposed changes.

5.2 Use of a Single-Centre RCT

Adopting a multi-centre RCT design would have added some significant strengths to the design of the present study and raised it higher in the hierarchy of evidence by enhancing the external validity of the findings (Bellomo et al. 2009). It could also have accelerated subject recruitment within the fully powered study minimising the duration of data collection. However, despite these advantages the author deemed it most appropriate to maintain a single-centre design for several reasons. Firstly, the current study was conducted without funding and was made up of a volunteer research team. Assembly of this team and conduct of this RCT without funding was possible due to the professional relationships the chief investigator had developed within the clinical team. It was unlikely to be possible to assemble a similar team in other sites unfamiliar to the author. Similarly, the author conducted this PhD part-time alongside a full-time clinical position – this would have limited the author's ability to travel to other trial centres to properly support nominated investigators. These reasons are reflected in other advantages of single-centre RCTs with them being cheaper, simpler and easier to conduct, and often do not require the protracted negotiations to agree a study protocol which is often a struggle within multi-centred studies. Furthermore on a single site, the author was able to directly monitor data collection and ensure that the trial protocol was strictly followed, ensuring complete data and no breaches in the study protocol. Also, as discussed in 1.2, ERAS pathways do differ between hospital sites, while this brings real-world variation and external validity, it would have reduced the internal validity delivered.

5.3 Amendments

The following recommendations were taken forwards and adapted into amendments to the study protocol for the fully powered RCT:

- 3-Month telephone follow-up
- Collection of pharmacological antiemetic and opioid consumption
- Stratification of randomisation
- Collection of the mILOA score as a validated measure of function
- Nested qualitative study

Justifications and specifics of these are discussed in detail in 6.2.4

5.3.1 Increasing follow-up period

As discussed in section 4.16.3.1, one of the limitations of the feasibility was in its inability to identify post-operative complications after hospital discharge. However, there is some debate about what the optimum post-operative follow-up period should be before morbidity and mortality is no longer related to the surgical care provided. Commonly within published research, either a 30-day or 90-day follow-up period is used for surgery related morbidity and mortality (Liao & Lu 2016; Jorgensen et al. 2016; Berstock et al. 2014). The author was unable to identify published guidance on this topic directly relating to the orthopaedic speciality.

While carried out within oesophagectomy patients Talsma et al. 2014 found that the use of a 30-day mortality metric yielded a sensitivity of only 33% and specificity of 100%, whereas a 90-day mortality metric had a much improved sensitivity of 74% and specificity of 96%. This study also found that extending the follow-up period beyond 90 days resulted in the inclusion of complications unrelated to the surgical intervention. Overall, Talsma et al advocates the use of a composite measure of in-hospital mortality and 90-day mortality to give the optimum balance of sensitivity and specificity. This time period also fits with the work of Healy et al. 2016 where related death, readmission and thromboembolic disease were defined as occurring within the first 3 post-operative months. Consequently, although there is debate, a 90-day follow-up period appears to be the best choice for balancing sensitivity and specificity while being able to justify the assumption of causality from the target intervention. Unfortunately, this PhD project lacked the resources to make this assessment face-to-face. Consequently, the author's decision was to conduct the follow-up as a telephone call and examination of the hospital patient records to identify any incidence of complications and re-admissions within this period.

5.3.2 Collection of opioid and anti-emetic consumption

Through conduct and evaluation of the feasibility study, it was recognised that several confounding factors may have been left unaccounted for, including the degree to which patients received pharmacological treatment for the common post-operative effects of pain and PONV. It was therefore recommended that any subsequent fully powered study control for or measure this. It would be unethical to look to control for these treatments between groups as they form a core part of the standard pathway in helping patients to remain symptom controlled post-operatively, as such the author made consideration of measuring these variables.

The process of collecting and collating analgesic consumption and antiemetic consumption would increase the burden on the research team in the form of retrospective review of the inpatient drug charts and recording findings. Also, this process would need to be carried out by a clinician with some expertise in clinical pharmacology in order to ensure data accuracy. Despite this workload, the author felt it critical to account for these potential confounders in order to protect the validity of the fully powered study's findings relating to PONV incidence and post-operative pain scores. Indeed Raphael et al. 2011, presented morphine consumption alongside pain numerical rating scores, enabling them to indicate lower pain scores in the intervention group but also within the context of reduced opioid consumption lending credibility and context to the findings.

In light of the standardised analgesic pathway employed (Appendix 10) the administration of simple analgesia (paracetamol and non-steroidal anti-inflammatory medications) was designed to be standardised across both groups. As such, the only expected variation between groups was in the consumption of opioid based analgesia which is used as required. The author therefore deemed it unnecessary to record the consumption of paracetamol or NSAID analgesia and ultimately decided to amend the study to include a review of the inpatient medication charts by the CI on discharge to identify and record the consumption of opioid and antiemetic class medications across the inpatient stay.

5.3.3 Stratification of randomisation based on co-morbidities

As discussed in the previous chapter, pre-operative co-morbidities could confound the results of many of the outcomes suggested for this study. While certain comorbidities could be accounted for within the inclusion or exclusion criteria, this would limit the available cohort for recruitment and bring the current study in line with previous studies where selection bias limited how representative the sample was of a normal UK THR population.

The author considered the options of measuring the incidence and severity of co-morbidities within the recruited cohort and adding this to baseline comparison analysis. This may have been sufficient, as the author expected low numbers of prospective participants with high numbers of or severity of comorbidities. This cohort would be unlikely to be undergoing surgery due to increased surgical risk and unlikely to pass through the study inclusion and exclusion criteria. However, within the study by Huang et al. (2011) the Charlston Comorbidities index (CCI) was used to investigate the impact of comorbidities on length of stay, with a score of equal to or greater than 2 shown to correlate with increased length of stay. This metric has been validated and shown to have excellent reliability when used with a total joint replacement cohort (Bjorgul et al. 2010). This work provides a clear dichotomisation point in the CCI measure which can be used to create well-reasoned strata. Decision to perform stratified randomisation was made both to balance groups on the known prognostic factor of CCI and also to supplement the learning of the researcher in using another method of randomisation. Consequently, the author decided to emulate the work of Huang et al and opt to stratify group randomisation based on a CCI score of greater than or equal to two.

In practical terms this meant the calculation of the CCI during pre-operative screening and stratification of randomisation built into the sealed envelope method of randomisation by the study sponsor.

5.3.4 Collection of the modified IOWA level of assistance score as a functional measure

One of the feasibility study findings was that research findings on functional recovery could be challenged in their validity based on the study not employing a validated measure of function. As such the author did deem it appropriate to employ a validated functional measure. There are many different validated measures of function available with varying degrees of complexity. The following functional outcome measures were considered for use and discounted for the following reasons shown in **Table 5-1**:

Table 5-1: Discounted functional outcome measures

Functional Outcome Measure	*Positives*	*Limitations to this Study*
Timed Up and Go Test	• Excellent test-retest reliability in elderly adults and in patients post THR (Kennedy et al. 2005; Steffen TM, Hacker TA 2002) • Excellent inter-rater reliability (Wright et al. 2011)	• Intrarater reliability affected by performing multiple assessments (Van Hedel et al. 2005) • Small effect response to physiotherapy (French et al. 2010)

	• Excellent correlation with other measures (Berg balance, Gait speed and Barthel index, KOOS) (Sabirli et al. 2013; Richardson 1991) • Predictive of falls risk (Bhatt et al. 2011)	• Requires operational space and setup • Extra time required from assessing clinician • May not be appropriate to use in the early stages of post-op rehabilitation.
6 Minute walk test or 2 Minute walk test.		• 6-minute walking time may not be appropriate with all participants or at early stages in post-operative rehabilitation • Participant must be able to mobilise without assistance.
Patient specific Functional Scale	• Excellent reliability and validity shown with joint dysfunction (Chatman et al. 1997)	• Activities are specific to the patient – not so easy to compare function across participants
Functional Independence Measure		• Licence required • Several criterions not relevant within an orthopaedic population (Eating, cognition, bladder and bowel control) • 30-45 mins to complete • All validating research specific to a stroke population
WOMAC	• Specifically designed for THR • Able to stratify for pain, function and stiffness • Excellent test-retest reliability for pain and function. (Whitehouse et al. 2008) • Excellent internal consistency (Kapstad et al. 2010; Quintana et al. 2005) • Excellent construct validity (Davis et al. 2009; Kapstad et al. 2010)	• Licence required • Extra 12 mins per participant required to complete • Designed to be retested at 6 months, not again within an inpatient period.
Barthel Index	• Fair to good inter-rater reliability when used within an elderly population (Richards et al. 2000)	• Designed for and only well evidenced within stroke population. • Several sections of the measure are not relevant to an elective orthopaedic population, eg. Feeding, and bladder and bowel control.

		• Requires 20 mins of direct assessment time with the patient.

WOMAC = Western Ontario and McMasters Universities Arthritis Index

For measuring functional change within the inpatient period, the modified Iowa level of assistance scale appears to be the best choice for the following reasons:

- Therapist completed within normal working practices – minimal burden on participants and therapists
    - Reducing burden on the research team is likely to yield a more complete dataset.
- Sensitive within a short time period and appropriate to be used within an inpatient period
- Validated for use within a THR population (Shields, Lori J Enloe, et al. 1995)
- Excellent inter-rater reliability, good known groups validity and responsiveness within an inpatient stay (Kimmel et al. 2016)

In order to simplify procedures for the research team clinicians, the author decided to carry out an mILOA measure at the end of each physiotherapy session.

5.3.5 Nested Qualitative Study

The author did make the decision to conduct a nested qualitative study alongside the fully-powered RCT. As previously mentioned in 1.4, the author has decided to omit the nested study from this thesis due to the overall size and complexity of the project. There are plans to write-up and disseminate this at a later date.

5.3.6 Development of a study database

During the feasibility study, collected data was collated within a spreadsheet. This created some duplication of data entry for example with the study adverse events log.

To ensure ease of data collection, automatic validation of entered data and minimisation of duplication the author developed a dedicated study database (Shown in Figure 26). This also integrated processes for generation of the study screening log, enrolment log, adverse events log and generation of a worklist for 3-month follow-up telephone calls.

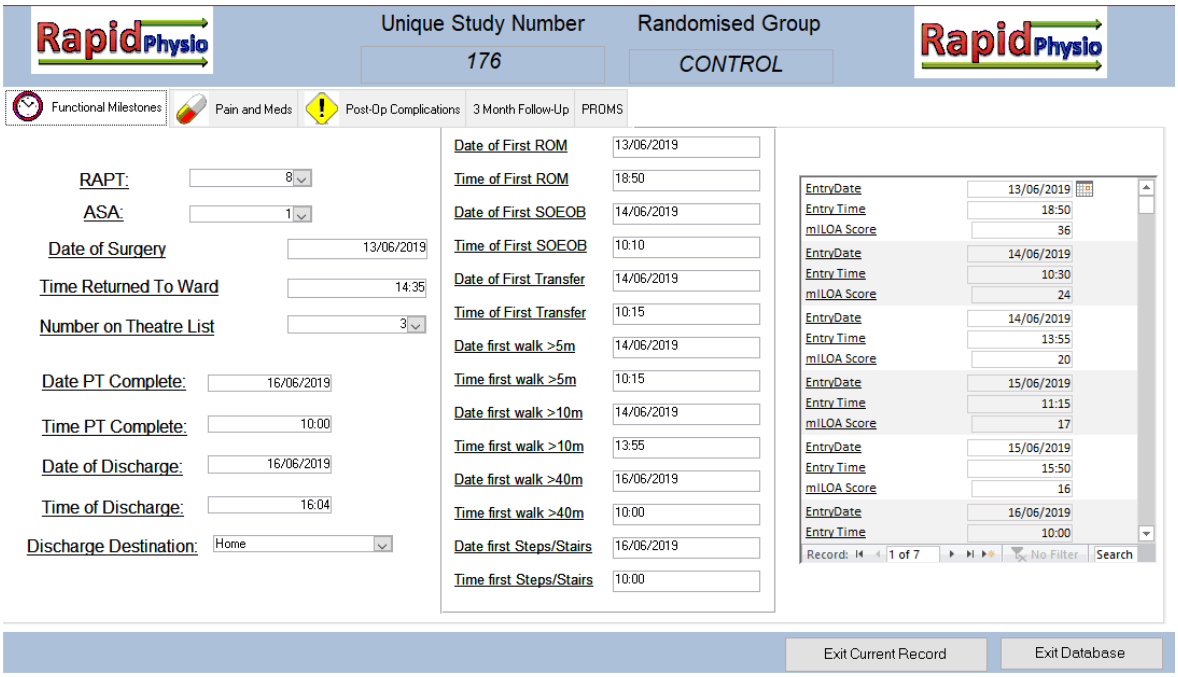


Figure 26 - Screenshot fully powered study database

5.3.7 Training more study recruiters

The author organised the training of two other members of the research team to be able to enrol participants onto the study.

5.4 Ethics

Favourable opinion was obtained from the Hampshire B research ethics committee for the amendments discussed in this chapter, leading to the fully powered study presented in the following chapter.

Of note there were some additional ethical considerations which came with these amendments:

5.4.1 Reduction in recruitment numbers through sample size calculation

Pre-feasibility study, the author had carried out a sample-size calculation based on standard care service level data, a proposed minimally clinically important difference of 1-day median reduction in length of stay and a power of 90%. This produced a sample size requirement of 212. As the feasibility data were collected through trialling the intervention of interest it provided a much more appropriate dataset on which to base a sample-size calculation. The resulting sample-size calculation detailed in 4.16.2.1 indicated a total of 176 participants should be recruited. This constituted a reduction in participants of 36. This was accordingly reported to the REC.

5.4.2 Increased burden on participants with additional follow-up

The addition of a post-discharge telephone follow-up, while providing scientific rigour did increase the burden on research participants. The PIS was adjusted accordingly, and prospective participants were informed of the intention to follow-up at 3 months post-op as part of the informed consent procedures. The research team aimed to limit the burden of the telephone call as much as possible by checking participants were happy and available to talk upon commencing the call.

5.4.3 Clinical need identified at 3 Month telephone follow-up

By carrying out a telephone follow-up, there was the potential that participants could disclose an urgent or increased clinical need to the research team after they had been discharged from hospital. Mechanisms were developed that in the instance of this, the CI would be notified, and the appropriate onward referral would be made either to the participant's orthopaedic consultant, their local physiotherapy service or to emergency services for follow-up and investigation. This was deemed satisfactory by the REC.

6 - Fully Powered RCT

6.1 Introduction

This section details the aims, methodology, results and interpretation of findings from the fully powered RCT having integrated the findings and recommendations discussed in the previous chapter into the study design. This fully powered study was registered by the study sponsor with clinicaltrials.gov under the following title and registration details:

Does Rapid Mobilisation as Part of an Enhanced Recovery Pathway Improve Length of Stay, Return to Function and Patient Experience Post Primary Total Hip Replacement? A Randomised Controlled Trial

Trial registration
ClinicalTrials.gov Identifier: NCT02428829
Research ethics committee reference: 15/SC/0018

Based on the findings presented in chapters 2 and 4, current published research and feasibility study data suggests that day-zero ambulation may have potential benefits in reducing length of hospital stay and speeding up functional recovery following total hip replacement surgery. However, as discussed in section 2.5.3, methodological limitations in the existing research base give little confidence of these effects being caused by day-zero ambulation in isolation. Using recommendations from the feasibility study, this study was conducted to address some of the weaknesses in the existing knowledge using a gold-standard RCT research design (Cope 2015), and employing a methodology to the highest quality available to the researcher within available resources.

This trial was conducted within a specialist elective orthopaedic unit at the Royal Bournemouth Hospital between October 2016 to September 2019. As this chapter concerns a randomised controlled trial it has been written using the CONSORT guidance (Schulz et al. 2010) and contains all of the relevant elements suggested within the 2010 CONSORT checklist.

6.2 Trial Objectives

6.2.1 Primary Objective

To evaluate the effectiveness of a rapid mobilisation physiotherapy protocol in reducing the length of hospital stay for patients having undergone primary total hip replacement (THR).

In particular, to test the hypothesis that a rapid mobilisation protocol will significantly reduce length of hospital stay following THR when compared to standard care.

6.2.2 Secondary Objectives

- To evaluate the impact of a rapid mobilisation physiotherapy protocol on the patient experience of post-operative physiotherapy care
    - Hypothesis: *That rapid mobilisation will improve patient experience of post-operative physiotherapy when compared to standard care.*

- To evaluate whether a rapid mobilisation physiotherapy protocol will affect the time taken for patients to be deemed physiotherapy ready for hospital discharge.
    - Hypothesis: *That rapid mobilisation will reduce the time taken for patients to be deemed physiotherapy ready to leave hospital when compared to standard care.*

- To evaluate whether a rapid mobilisation physiotherapy protocol will affect the time taken for patients to reach functional milestones post-operatively.
    - Hypothesis: *Rapid mobilisation will reduce the time taken for patients to reach functional milestones post-operatively when compared to standard care*
    - *See below for details of functional milestones*

- To evaluate whether a rapid mobilisation physiotherapy protocol will affect daily modified Iowa Level of Assistance Scale (mILOA) scores.
    - Hypothesis: *That rapid mobilisation will significantly improve daily mILOA scores post-operatively when compared to standard care.*

- To determine if implementing a rapid mobilisation physiotherapy protocol will affect the incidence of post-operative complications.

- Hypothesis: *Rapid mobilisation post-operatively will reduce the incidence of post-operative complications when compared to standard care*

- To determine whether a rapid mobilisation physiotherapy protocol will affect post-operative pain scores when attempting mobility for the first time.
    - Hypothesis: *Rapid mobilisation post operatively will reduce the levels of pain as measured using a numerical pain rating scale reported by patients on initial mobility when compared with standard care.*

- To determine whether a rapid mobilisation physiotherapy protocol will affect the amount of anti-emetic medications consumed within the inpatient stay period.
    - Hypothesis: *Rapid mobilisation will cause no significant change in the post-operative inpatient consumption of anti-emetic medications when compared to standard care.*

- To determine whether a rapid mobilisation physiotherapy protocol will affect the amount of opioid analgesia medications consumed during the acute hospital inpatient stay.
    - Hypothesis: *Rapid mobilisation will reduce the total amount of opioid analgesia consumed during the acute inpatient stay period when compared to standard care.*

- To determine whether a rapid mobilisation physiotherapy protocol will significantly reduce the financial cost-to-hospital for a primary THR
    - Hypothesis: *Rapid mobilisation will significantly reduce the overall cost to the hospital for completing a primary THR when compared to the cost of standard care cost for the procedure and post-operative recovery up until hospital discharge.*

6.2.3 Primary Endpoint

Primary analysis was length of hospital stay following surgery, measured to the nearest day, calculated from the date of the operation to the date the patient was discharged from hospital.

6.2.4 Secondary Endpoints

6.2.4.1 Patient Experience:

Assessed with a specific patient experience questionnaire, where patients were asked to rate their experience between 0 and 10. Zero representing the worst and ten the best experience. Questions 1, 3 and 4 are adopted from the CQC inpatient survey 2013 (Care Quality Commission 2013)

1. Do you think the hospital staff did everything they could to help control your pain? (Possible Responses: 0 - 10)
2. Overall, how was your experience of physiotherapy following your operation? (Possible Responses: 0 - 10)
3. Overall, how was your experience of your overall hospital treatment? (Possible Responses: 0 - 10)
4. Did you have confidence and trust in the physiotherapists treating you? (Possible Responses: 0 - 10)
5. How beneficial was walking early after your operation? (Possible Responses: 0 - 10. Section for comments)
6. How well was your progression with your physiotherapist paced to suit you? (Possible Responses: 0 - 10. Section for comments)

Although not validated, this method was devised due to a lack of validated patient experience measures specific to an orthopaedic patient group (Jones et al. 2014).

Participants were asked for any general comments during a 3-month post-operative telephone follow-up. The purpose of these questionnaires and comments was for triangulation with qualitative study data which will be written up outside of the PhD project.

6.2.4.2 Achievement of Functional Milestones and mILOA Scores:

<u>Functional Milestones:</u>

Measured in number of hours post-operatively:

1. First voluntary movement of the new prosthetic hip joint.
2. First sit on the edge of the bed.
3. First transfer from bed to chair using a walking frame or appropriate walking aid.
4. First walk of greater than or equal to 5 meters using a walking frame and appropriate physiotherapy support.

5. First walk of greater than or equal to 10 meters using a walking frame / pair of elbow crutches independently.
6. First walk of greater than or equal to 40 meters using a pair of elbow crutches independently.
7. First completion of a step or stairs independently using elbow crutches.

The treating physiotherapist recorded the date and time that participants completed the above milestones. From this, the time taken to reach the milestone was calculated from the time they returned to the ward following their operation.

6.2.4.3 mILOA

mILOA scores were recorded for each patient following physiotherapy session. The original ILOA measure has been shown to be valid and reliable for use within an elective orthopaedic population (Shields, Lori J Enloe, et al. 1995)and the mILOA shown to have excellent inter-rater reliability and known-group validity within an elective orthopaedic cohort (Kimmel et al. 2016)

The mILOA was selected over the ILOA for the following reasons:

- Easy practical application within the ward to maximise compliance with data collection as:
    - No extra equipment required
    - Minimal changes to current rehabilitation practices.
- ILOA measures walking over a maximum of 13.4m (Jesudason & Stiller 2002). The mILOA includes a walking distance measure to >40m and therefore more aligned to common discharge criteria (Enloe et al. 1996) post THR.

6.2.4.4 Incidence of Post-Operative Complications:

The number of patients who experienced a post-operative complication was recorded and the nature of the complication was selected from a list of categories:

- Post-operative orthostatic hypotension
    - Defined as a reduction in systolic blood pressure of >20mmHg **and** with symptoms of postural hypotension
- Syncope
- Deep Vein Thrombosis
    - As confirmed by radiological imaging
- Pulmonary Embolism
    - As confirmed by CTPA

- Excessive wound ooze
  - This constitutes any wound ooze that escapes the 'op-site' dressing.
- Post-operative Respiratory Tract Infection
  - As confirmed by medical diagnosis
- Blood Transfusion Required and delivered
  - Determined once the patient has received ≥ 1 unit of blood.
- MI
  - Confirmed via ECG, troponin blood test and medical diagnosis.
- CVA
  - Confirmed by radiological imaging and medical diagnosis
- Bowel Obstruction
  - Confirmed by radiological imaging and medical diagnosis
- Other

This data was collected throughout hospital admission, and then followed up at 3 months via telephone where the participants were asked to disclose any post-discharge complications. See 3-month telephone follow-up form (Appendix 23).

6.2.4.5 Pain on Day 0 and Day 1 Physiotherapy:

This was collected as a patient reported pain numerical rating score (PNRS), with the patient asked to rate their pain level at rest, when moving the joint and on ambulation.

PNRS was selected for pain measurement for the following reasons:

- A familiar pain outcome measure used routinely in the clinical setting was included in the present study
- Well-evidenced validity and reliability (Jensen & McFarland 1993; Herr et al. 2004; Bijur et al. 2003; Ferreira-Valente et al. 2011)

PNRS was collected in the above activities on both day 0 and day 1 post-op.

6.2.4.6 Consumption of anti-emetic medications:

The types and amount of anti-emetic medications consumed throughout the post-operative inpatient stay was collected for each participant. These were obtained through post-discharge review of the participant's in-patient drug chart records. These were collated into the number of individual doses required for each participant.

6.2.4.7 Consumption of opioid analgesia medications:

The types and amounts of opioid analgesia medications consumed throughout the inpatient stay were collected for each participant. This data was obtained through post-discharge review of the participant's inpatient drug charts.

Opioid medications were collated into a total opioid consumption value across their post-operative inpatient stay using the opioid conversion guidance provided in the British National Formulary 2017 (BNF 2017). Conversion guidelines were used to convert all opioid type medications delivered into equivalent doses of oral morphine for comparison. These were analysed for total consumption, but also divided per day of inpatient stay to give an opioid consumption per inpatient day preventing inflation of opioid consumption measures in participants who had extended inpatient stays.

This measure was included to provide richer information about the effect of day-zero ambulation on pain experience. While other forms of pharmacological analgesia are used post-operatively, opioid class medications form the standard 'when necessary' analgesia available to participants on request. Consequently, it is in the consumption of opioid medications that pharmacological analgesic consumptions differ between patients in this cohort.

6.2.4.8 Cost Analysis:

Data on any differences identified in length of hospital stay were used to calculate the financial impact of RAPID mobilisation. A figure of £346 of cost per bed day per patient was used (NHS Improvement 2018). This figure, provided through the department of health reference costs is designed to incorporate all ward costs of excess bed day usage including routine blood tests, medications, dressings and therapies. This includes acute inpatient rehabilitation costs (Department of Health 2015). UK health reference costs are periodically updated. The most up to date published health reference costs were used at the time of analysis.

6.3 Methods

6.3.1 Trial Design

A single-centre, non-blinded, parallel group, randomised controlled trial of patients undergoing primary THR.

6.3.2 Participants

6.3.2.1 Number of Participants and Participant Selection

Sample size calculation detailed in 4.16.2.1 indicated 176 participants required to form 88 participants in each randomised group.

Patients awaiting a primary THR were screened for eligibility on the ward prior to their operation and if suitable were approached and invited to participate, providing written informed consent if they chose to participate.

6.3.2.2 Inclusion Criteria

Table 6-1: Fully powered RCT inclusion criteria

Inclusion Criteria	*Rationale*
Any Age > 18 years	To keep the recruited sample representative of a UK elective THR population. To ensure recruitment of adults only.
Able to give informed written consent Able to understand verbal and written communication in English	To ensure proper compliance with informed consent procedures.
Returned from theatre > 4 hours Primary unilateral THR No intraoperative complications Post-operative weightbearing status: Fully weight bearing Weight bearing as tolerated	To reduce risk of harm to the participants by ensuring that spinal anaesthetics have resolved. To ensure that research findings are not confounded by including surgeries with more complex and restrictive rehabilitation protocols.
Adequate home support to facilitate early discharge	To ensure research findings are not confounded by delayed discharges due to social delays.

6.3.2.3 Exclusion Criteria

Table 6-2: Fully powered RCT exclusion criteria

Exclusion Criteria	*Rationale*
No current or historical serious co-morbidities in particular: Cerebro-Vascular Accident Myocardial Infarction Pulmonary Embolism (PE) Deep Vein Thrombosis (DVT) Diabetes Mellitus (DM) Significant intra or post-operative wound ooze Poor pre-morbid mobility/level of function (House or wheelchair bound) Clinical signs of DVT or PE Altered Weight-Bearing status Repair to abductor muscle complex Peripheral nerve block as part of anaesthetic	To reduce risk of harm to the participants by ensuring that participants are not at high risk of cardiovascular complications. To ensure that research findings are not confounded by: including surgeries with more complex and restrictive rehabilitation protocols common post-operative complications more likely due to past medical factors.
Concomitant procedure at time of THR Participation in any other research trials	To ensure research findings are not confounded by existing medical conditions likely to affect recovery or by other experimental research.

6.3.2.4 Premature Withdrawal

Participants were free to withdraw from the study at any point or a participant could have been withdrawn by the CI for safety reasons. There were no withdrawals observed within this study.

If a participant declined a session of physiotherapy, this did not constitute withdrawal. In this case, all attempts were made to follow-up the participant as per protocol.

6.3.2.5 Settings and Locations

This study took place on a UK specialist orthopaedic ward at the Royal Bournemouth Hospital, part of the University Hospitals Dorset NHS Foundation Trust.

6.3.2.6 Informed Consent Procedures

Written and informed consent was obtained by a suitably qualified member of the research team at study entry. Patients were made aware of the trial at the time of invite to a pre-operative education group session (approximately 1-2 weeks prior to admission) with a study information sheet posted (Appendix 24) with the patient invite. This provided potential participants with more than 24 hours to consider the written information. The written information contained details of the study team providing the potential participant an avenue to raise any questions regarding the study prior to their surgical admission.

Following admission and prior to surgery, a member of the research team screened the medical records of interested potential participants to confirm they met the eligibility criteria. Those who passed the initial screening stage were provided with another copy of the information sheet and given adequate time to read and ask a senior member of the research team any questions about the study. If the participant wished to speak directly to the CI, then this happened prior to formal consenting.

All gathering of formal informed consent was completed by the CI or a senior member of the research team who had undergone the relevant study protocol and GCP training using the study consent form show in Appendix 25. The research team recognised that the patient was also required to give informed consent for their surgical procedure within the same time period. In cases where the patient did not have enough time to consider participation for any reason (for example logistical reasons), then consenting did not go ahead and the patient was not included in the study. A senior member of the research team countersigned all written consent forms prior to the participant's commencement on the study, with the participant provided with a copy of any signed documents. The CI or member of the research team explained to each prospective participant that their freedom to refuse any involvement in the study or withdraw their consent at any point during the study for any reason without it resulting in any future detriment to their care.

6.3.2.7 Screening Procedures

Potential participants were screened in two phases by a member of the research team.

Participants underwent initial screening prior to their surgery and written informed consent gained if they wished to take part. The second screen happened after return to the ward following their operation to screen for any intra-operative complications that may affect the inclusion/exclusion criteria.

This method of screening was chosen as the most ethical method, enabling informed consent to be gathered prior to the potential participants undergoing anaesthesia. A participant was only classed as entered onto the study following passing the second stage of screening. Any patients who did not pass through the second stage of screening were informed by a senior member of the research team that they would not be enrolled into the study and the reason why.

6.3.2.8 Randomisation Procedure

Randomisation into concealed sequentially numbered envelopes was carried out by the study sponsor, using a stratified, computer generated, block randomisation method. Randomisation of participants took place following a participant's return from theatre and passing of the second stage of screening. Participants were randomized on a 1:1 ratio by opening a series of numbered envelopes stored in the study file provided by the Sponsor. A sequence of opaque envelopes containing a group allocation (either 'CONTROL Group' or 'RAPID Group') were opened in chronological order with the original slip kept with the patient's case report form for verification and monitoring purposes.

Randomisation was stratified based on the Charlson co-morbidities index (CCI)(Charlson et al. 1987)(Appendix 27). This was in response to the recommendations of the feasibility study. Sealed envelopes were provided by the study sponsor, representatives of which were at no time involved in the recruitment of participants to ensure allocation concealment. Randomisation was completed by the CI or a suitably trained senior member of the research team. Once randomised, the participants were entered onto the enrolment log.

6.3.3 Interventions

6.3.3.1 Schedule of Treatment

The RAPID group was seen by a physiotherapist to attempt walking from 4 hours post operatively, on the day of their surgery.

The control group received standard physiotherapy in line with current hospital protocol including first walking approximately 24 hours post operatively.

See below protocol in **Table 6-3** for full physiotherapy post-operative intervention for both RAPID and CONTROL groups.

Table 6-3 Physiotherapy treatment schedule for RAPID and CONTROL groups

	RAPID GROUP	CONTROL GROUP
Pre op	Information booklet given Commence discharge planning Attend Information class Occupational therapy home visit	
Day of surgery (within 18 hours of surgery)	Check op notes for procedure, type of anaesthetic/nerve block, post op instructions RAPT score to be completed Standard post-operative neurovascular examination Reinforce hip precautions Circulatory exercises Respiratory exercises Static gluteal and quadriceps exercises Hip ROM exercises (abduction and flexion) Patient to continue exercises hourly Oxygen therapy to maintain SaO2 if required (as documented on drugs chart)	Check op notes for procedure, type of anaesthetic/nerve block, post op instructions RAPT score to be completed Standard post-operative neurovascular examination Reinforce hip precautions Circulatory exercises Respiratory exercises Static gluteal and quadriceps exercises Hip ROM exercises (abduction and flexion) Patient to continue exercises hourly Oxygen therapy to maintain SaO2 if required (as documented on drugs chart)
Day of Surgery Rapid Mobilisation	Check patient meets inclusion/exclusion criteria for rapid mobilisation. Assess patient suitability for mobilising (See below) Assess pain using Numerical Rating Scale at rest and on movement. Mobilise with ZF as tolerated (2 persons to assist) Consider discharge plans/date/destination	
Day 1	Standard post-operative neurovascular examination Assess pain using Numerical Rating Scale at rest and on movement Check patient's recall of precautions Assess patient for suitability for ambulation Mobilise with walking frame as tolerated Progress to ambulation with elbow crutches when ready Encourage independence and progressive distance with mobilising Oxygen therapy to maintain SaO2 if required (as documented on drugs chart)	Standard post-operative neurovascular examination Assess pain using Numerical Rating Scale at rest and on movement Check patient's recall of precautions Bed exercises as per day of surgery Assess patient for suitability for mobilising Mobilise with walking frame as tolerated (2 persons to assist) Oxygen therapy to maintain SaO2 (as documented on drugs chart) Review p.m. as required. Encourage exercises Consider discharge plans/date/destination Review for physiotherapy session morning and afternoon.

	Teach active exercises in standing with both legs (abduction, flexion and extension) Review for physiotherapy session morning and afternoon. Discharge if required criteria are met and medically fit for discharge	Discharge if required criteria are met and medically fit for discharge
Day 2	Progress mobility – independence, distance, walking aids Check independent with active standing exercises Step/stair practice Advise on progression of mobility/walking aids/first 6/52 at home Outpatient physiotherapy referral if justified Review for physiotherapy sessions morning and afternoon. Discharge if required criteria are met and medically fit for discharge	Encourage independence and distance with mobilising with walking frame Progress onto elbow crutches when ready Check participant's recall of precautions Teach active exercises in standing with both legs (abduction, flexion and extension) Review for physiotherapy sessions morning and afternoon. Discharge if required criteria are met and medically fit for discharge
Day 3	Continue mobility progression and exercise as above Review for physiotherapy sessions morning and afternoon. Discharge if required criteria are met and medically fit for discharge	Progress mobility – independence, distance, walking aids Start/continue with active standing exercises both legs (abduction, flexion, extension) Step/stair practice Advise on progression of mobility/walking aids/swelling management/first 6/52 at home Outpatient physiotherapy referral if justified Continue with above until completed Review for physiotherapy sessions morning and afternoon. Discharge if required criteria are met and medically fit for discharge
Day 3+	Continue mobility progression and exercise as above Review for physiotherapy sessions morning and afternoon. Discharge if required criteria are met and medically fit for discharge	Continue mobility progression and exercise as above Review for physiotherapy sessions morning and afternoon. Discharge if required criteria are met and medically fit for discharge
Discharge Criteria	Discharge when required criteria are met: Safe and independent mobility with appropriate walking aid Safe and independent on steps/stairs Patient able to recall hip precautions Patient can complete active standing exercises Patient will be able to manage adequately at home	
Post Discharge –	Continue with advanced exercises until good ROM and strength Continue to adhere to precautions (for 3 months post op). This will be reviewed at follow up appointment Gradually increase distance walked Reduce use of walking aids as able over 6 weeks	

first 6 weeks	Review with surgeon at 6 weeks Patients must sleep on back for first 6/52. If they can't sleep on their back they can lie on the operated side with a pillow between their legs
6 weeks +	Can drive if surgeon allows at 6/52 review Continue to increase walking distance, ROM and strength Can start swimming when good mobility, wound healed. Access pool via stairs not ladder. No breast stroke allowed Can cycle once precautions have stopped, providing the patient is very careful No flying for at least 6 weeks. General rule is 3/12 short haul, 6/12 long haul (at surgeons discretion).

6.3.3.2 Schedule of Assessment

Outcome measures were assessed according to the schedule below in **Table 6-4**:

Table 6-4: Fully powered study schedule of assessment

Time Period **Outcome**	Surgery	Post-Op Mobilising	Post-Op Stay	Discharge	3 Months Post-Discharge
Length of stay				✓	
Time to Physiotherapy Complete			✓	✓	
Patient Satisfaction Questionnaire				✓	
Functional Milestones		✓	✓	✓	
Post-Op Complications		✓	✓		✓
Pain Scores		✓	✓		
Participant Comments					✓
mILOA		✓	✓	✓	

Following discharge, participants were telephoned approximately 90 days post-discharge to gather detail of any post-discharge complications and invite open comments about their experience. For participants who did not answer, several attempts were made to contact them via telephone at different times of day. If after three attempts contact was unsuccessful, hospital computer records were reviewed for any admissions or documented post-discharge complications within clinic letters and these recorded.

6.3.4 End of Study Definition

The study ended once telephone follow-up at 3 months had been completed for the last participant.

6.3.5 Participant Withdrawal

Within the above schedule of assessment guidelines, there were no withdrawals from this study.

6.3.6 Safety Reporting

6.3.6.1 General Definitions

6.3.6.1.1 Adverse Event (AE)

An AE is any untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporarily associated with study activities.

6.3.6.1.2 Serious Adverse Event (SAE)

An SAE fulfils at least one of the following criteria:

- Is fatal – results in death (NOTE: death is an outcome, not an event)
- Is life-threatening
- Requires inpatient hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is otherwise considered medically significant by the Investigator

The following adverse events may prolong the period of existing hospitalisation but are common complications following surgery of the nature of a THR. Consequently, they were treated as AEs and were reported as such:

- Orthostatic Hypotension resulting in syncope
- Excessive Wound ooze from THR wound:
  - escaping the dressing
  - Lasting > 3 days.
  - Was a cause of delaying discharge
- Hb < 85g/L post operatively
- Symptomatic of low Hb
- Fatigue
- Post-operative confusion

- Constipation
- Urinary Retention
- Dehydration
- Post-Operative nausea and vomiting
- Pain relating to the THR operation
- Slow progress with rehabilitation
- Hypoglycaemia

The CI or other senior investigators could choose to class any of the above as an SAE based on clinical judgement and circumstances if required.

6.3.7 Adverse Events or Reactions

For the purpose of this study, the following adverse events were commonly expected and therefore were not recorded as AEs in the study file:

- Nausea and vomiting
- Pain related to the operation
- Orthostatic hypotension not resulting in syncope
- Slow Progress with rehabilitation
- Constipation
- Dehydration
- Fatigue
- Wound ooze

6.3.8 Statistical Considerations

6.3.8.1 Primary Endpoint Effectiveness Analysis

A ≥ 1 day difference in median length of stay was considered clinically significant.

This was devised from a calculation that a saving 1 day of bed stay time would allow the ward at RBH to save 15 bed days per week, potentially allowing three extra total hip replacements to be completed per week. This was based on the department throughput at the time of this research of completing approximately 15 THRs per week.

6.3.8.2 Secondary Endpoint Effectiveness Analysis

<u>Time to Physiotherapy Complete:</u>

Based on clinical experience a reduction of ≥4 hours was deemed clinically significant.

On current standard care patients receive two physiotherapy sessions per day. Earlier physiotherapy completion of ≥4 hours would reduce the number of physiotherapy sessions required by ≥1.

Patient Experience:

The following effectiveness guides were used for each question of the patient experience questionnaire:

- Do you think the hospital staff did everything they could to help control your pain?
  - Effectiveness: No significant differences between groups or pain better controlled
- Overall, how was your experience of physiotherapy following your operation?
  - Effectiveness: No significant differences between groups or better perception of physiotherapy experience.
- Overall, how was your experience of your overall hospital treatment?
  - Effectiveness: No Significant differences between groups or better
- Did you have confidence and trust in the physiotherapists treating you?
  - Effectiveness: No significant differences between groups or better
- How beneficial was walking early after your operation?
  - Effectiveness = ≥ 10% difference between groups
- How well was your progression with your physiotherapist paced to suit you?
  - Effectiveness = ≥ 10% difference between groups.

The figure of ≥ 10% difference between groups was selected on advice from the hospital patient engagement team as a benchmark value used within other patient satisfaction questionnaires at RBCH.

Achievement of Functional Milestones:

A reduction of ≥ 4 hours in the time taken to reach a functional milestone was considered clinically significant.

This was reasoned as patients on the current standard protocol receive two physiotherapy sessions per day, and earlier achievement of functional milestones would allow earlier progression in the next treatment session.

mILOA Scores:

A difference of 5.8 points between groups on comparable post-operative days was considered clinically significant. 5.8 being indicated as the minimal detectable change in literature (Kimmel et al. 2016)

Incidence of Post-Operative Complications:

No significant differences between groups or any reduction in post-operative complications was considered clinically significant.

Post-Operative Numerical Pain Scores:

No significant differences between groups or any reduction in post-operative numerical pain rating was considered clinically significant.

Consumption of opioid medications:

No significant differences between groups or any reduction in post-operative inpatient collated opioid consumption was considered clinically significant.

Consumption of anti-emetic medications:

No significant differences between groups or any reduction in post-operative inpatient anti-emetic consumption was considered clinically significant.

Cost-Analysis:

A financial saving of £10,000 per annum was considered clinically significant based on feedback from the orthopaedic directorate management team at RBCH, see attached email correspondence (Appendix 28). With the reported cost to the NHS of completing a primary THR of £7620 covering surgical costs, prosthesis, post-operative hospital stay, adaptive aids and medication costs and 12 months of post discharge outpatient care (Edlin et al. 2012; NICE 2014) and would therefore allow funding for 1 extra primary THR per annum.

6.3.9 Sample Size

Sample size calculation (detailed in 4.13.3) indicated 160 participants required. A 10% increase was included to account for dropout, resulting in a total sample size of 176.

6.3.10 Statistical Methods

6.3.10.1 Testing for normality

As within the feasibility study data were tested for normality in order to establish the use of parametric or non-parametric comparison testing. Peat & Barton 2014 advocate using a summary of several indicators for normality of distribution when determining distribution shown in **Table 6-5**.

Table 6-5: Testing for Normality Methods

Relationship between the Mean and Median:	The difference between the mean and median was calculated and expressed as a percentage of the mean. A small percentage difference indicated a likely normal distribution, with a large difference indicating non-normality.
Standard deviation	The mean +/- two times the standard deviation was calculated to give an estimated range which 95% of the values should lie within if a normal distribution was present. This was then compared to the actual maximum and minimum observed values for proximity. Values which differed significantly from the minimum and maximum values indicate non-normality.
Skewness and Kurtosis	Skewness and kurtosis values were inspected, with values above +1 and below -1 indicating a tendency away from normal and a value above +3 or below -3 indicating that the distribution is not normal
Statistical testing for normality	A Shapiro-wilk test was used to test for normality of distribution
Plots	All plots were inspected and assessed for normality of distribution using the following guidance from Pete and Barton 2014: **Histograms**: Reviewed for the approximation of a bell-shaped normal distribution curve and for any gaps within the dataset. **Q-Q Plot**: Reviewed and considered how close points fell to the expected normal distribution line.

	Box Plots: The length of the whiskers to be within 1.5 times the spread of the inter-quartile range. These plots were also used to identify outliers and extreme values.

As such, variables were reviewed with this method, and the findings summarised in a meta-summary table, with domains indicating non-normal distribution highlighted in red (**Table 6-6**). Full detail of testing for normality is provided in Appendix 31.

Table 6-6 Testing for Normality Meta-Table

Variable	Mean to Median Relationship		Mean ± SD – Good Approximation?		Skewness and Kurtosis		Shapiro-Wilk Test		Plots		Overall Decision
	Control	Rapid	Control	Rapid	Control	Rapid	Control	Rapid	Control	Rapid	Distribution
Length of stay (Days)	11.7%	0.0%	No	No	No	No	No	No	No	No	Non-normal
Time to Discharge	13.2%	5.9%	No	No	No	No	No	No	No	No	Non-normal
Time to PT Complete	11.6%	1.7%	No	No	No	No	No	No	No	No	Non-normal
Time to First ROM	34.8%	4.0%	No	No	No	No	No	No	No	No	Non-normal
Time to First SOEOB	0.2%	0.0%	Yes	No	No	No	No	No	No	No	Non-normal
Time to First T/F	4.1%	58.6%	No	No	No	No	No	No	No	No	Non-normal
Time to First Walk >5m	9.2%	9.6%	No	No	No	No	No	No	No	No	Non-normal
Time to First Walk >10m	13.3%	11.3%	No	No	No	No	No	No	No	No	Non-normal
Time to First Walk >40m	12.4%	11.4%	No	No	No	No	No	No	No	No	Non-normal
Time to First Stairs	12.7%	2.6%	No	No	No	No	No	No	No	Yes	Non-Normal
Day 0 Pain at Rest	100.0%	20.0%	No	No	No	No	No	No	No	No	Non-Normal
Day 0 Pain on ROM	20.0%	25.0%	No	No	Yes	Yes	No	No	No	No	Non-Normal
Day 1 Pain at Rest	28.0%	14.0%	No	No	Yes	Yes	No	No	No	No	Non-Normal
Day 1 Pain on ROM	14.0%	1.2%	Yes	Yes	Yes	Yes	No	No	No	No	Non-Normal
Day 1 Pain on Ambulation	12.7%	7.0%	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Non-Normal
Pain of First Ambulation	10.5%	12.0%	Yes	Yes	Yes	Yes	Yes	No	No	No	Non-Normal
Total Opioid Consumption	29.6%	34.8%	No	No	No	No	No	No	No	No	Non-Normal
Total Antiemetic Consumption	32.4%	12.7%	No	No	No	No	No	No	No	No	Non-Normal

ROM = Range of motion, PT = physiotherapy, SOEOB = Sit on edge of bed

6.3.10.2 Logarithmic Transformation

Logarithmic transformation was considered for suitability within this study to bring the data into normal distribution in order to permit parametric testing. However, as warned by Feng et al. (2014), skewed biomedical data is often not amenable to transformations and can cause problems. As shown in Appendix 31, logarithmic transformation of this study's data did not result in normally distributed transformed data. Furthermore, Feng cautions the use of transformed data in making inferences about the original data, as often transformed data shares little in common with the original data. As such, logarithmic transformation was not used in this study both as parametric testing assumptions would still have been violated, and also to retain clinical relevance of the examined data for hypothesis testing.

6.3.10.3 Testing for Outliers:

Outliers were identified using the box plots and Mahalanobis distances calculated:

Mahalanobis distance calculations were then used to identify any multivariate outliers across the seven complete numerical variables examined. Mahalanobis distance values were then evaluated using critical values of chi-squared to seven degrees of freedom relating to the number of variables. P-values less than 0.001 were deemed multivariate outliers. Through this method, four participants were identified as multivariate outliers. This process is detailed in Appendix 32.

Identified outliers were then assessed via medical records review for potential reasons as to why the outlier occurred and shown below in Table 6-7.

Table 6-7: Multivariate Outlier Detail Assessment

Subject Number	*Group*	*Reasons for outlying data*
006	CONTROL	Remained as an inpatient for 11 days post-op Delayed discharge due to: Multiple episodes of orthostatic intolerance delaying functional progression of rehabilitation and discharge

		New diagnosis of CKD during inpatient prompting medical delay to discharge.
030	RAPID	Remained as an inpatient for 5 days post-op Multiple episodes of syncope prevented progression of functional independence and therefore discharge.
037	CONTROL	Remained as an inpatient for 18 days post-op Two dislocations of operated hip during inpatient period which was eventually revised to dual mobility hip day 14 post-op due to recurrent instability.
096	CONTROL	Remained as an inpatient for 6 days post-op Persistent orthostatic intolerance, syncope and a mechanical fall post-op delayed mobility progression and discharge.

No outliers were due to erroneous data collection or handling; all genuine values. All outliers were related to medical or post-operative complications delaying recovery and skewing time to functional milestones and time to discharge to the right. All of these complications are recognised as associated with THR and/or the subsequent post-operative recovery.

6.3.10.4 Dealing with Outliers

Given all outliers were genuine values, with variation due to medical or post-operative complications associated with THR it was appropriate to retain these values within the dataset as they reflect variation expected within a real-world THR population.

Non-parametric statistical testing was therefore selected due to non-normal distribution of data and retaining of outliers.

6.3.10.5 Baseline Characteristics:

The following baseline characteristics were analysed for all patients:

- Age
- Gender
- Number on theatre list
- Charlson Comorbidities Index (Charlson et al. 1987)

- American society of Anaesthesiologists physical status classification score (ASA Score) (Daabiss 2011)
- Risk assessment and prediction tool score (RAPT Score) (Hansen et al. 2015)

Descriptive statistics were observed between groups and where appropriate, statistical comparison was completed to describe any differences between groups at baseline. The above baseline measures were tested using the Shapiro-Wilk test and through plot observation and deemed non-normally distributed. Therefore comparison testing employed non-parametric testing using the Wilcoxon Mann-Whitney Test.

6.3.10.6 Primary and Secondary Endpoint Data:

Statistical analysis compared the difference between the two groups for outcomes in **Table 6-8** as follows:

Table 6-8: Statistical testing methods for each outcome

Endpoint	*Data Type*	*Distribution Result*	*Statistical Testing Strategy*
Length of Stay	Interval	Non normally distributed	Mann-Whitney Test
Patient experience questionnaire	Ordinal data	Non normally distributed	Mann Whitney Test
Time to completion of functional milestones	Interval data Time to each functional milestone compared individually	Non normally distributed	Mann-Whitney Test
Post-Operative Complications	Categorical data	Non normally distributed	Described in frequencies Compared using Chi Squared test
Anti-emetic consumption	Interval data To be analysed individually for each drug	Non normally distributed	Mann-Whitney Test
Opioid consumption	Interval data	Non normally distributed	Mann-Whitney Test

All statistical tests were carried out using R: (R Core Team 2021) in the software package R-Studio (Rstudio 2020). Where appropriate, 95% confidence intervals are reported. Where statistical analysis uses non-parametric methods, interquartile ranges are reported.

6.3.10.7 Modified IOWA level of assistance statistical testing

mILOA scores were considered separately, as the nature of the data precluded the use of traditional comparison testing as the data was longitudinal repeated measures data, recorded at differing time-points and with differing numbers of measures per participant.

Consequently, the data characteristics violate assumptions of normal distribution and common variance required for the use of ANOVA based analysis methods. Consequently, simple ANOVA, repeated measures ANOVA and MANOVA would have been inherently flawed if employed.

Several statistical analysis methods were considered and trialled, including mixed effects linear regression and mixed effects logistic regression. Both methods proved unsuitable due to violating assumptions relied on by these modelling methods. Details of this process of modelling and checking are detailed in Appendix 33.

Following ruling out mixed effects modelling, survival analysis was selected for the analysis of dichotomised mILOA data.

6.3.10.7.1 Dichotomisation

Exploratory analysis highlighted poor model fits, with heavy tails on residual plots due to the dataset containing many extreme values. This was due to the nature of the collected mILOA data with all participants scoring the same high mILOA score on exiting theatre and many scoring very similar low values on final assessment before discharge.

While transformation of data was trialled, it was not possible to achieve an approximately normal distribution to allow a good fit of the data when modelling.

Ultimately as a result, data was dichotomised into a dependent or independent status based on the mILOA score. The threshold of <7 was used as functionally independent based on the threshold previously used by (Hoogeboom et al. 2015). To support this decision, only 2 participants (1%) were discharged with an mILOA score >6.

6.3.10.7.2 Survival Analysis

Following the exclusion of mixed effects logistic regression due to violation of assumptions, survival analysis was selected as the final chosen method for analysis of mILOA data. This was appropriate with the event of regaining functional independence expected to be time-dependant. In addition, survival analysis is appropriate for the analysis of non-parametric data, commonly used with positively skewed time data and able to deal with censored data from any participants who didn't reach functional independence (Collett 2015).

Kaplan-Meier plots were used to observe the relationship between groups and a log-rank test used for statistical comparison. Finally, a Cox proportional hazards method was used to compare the effect of intervention group on functional independence in the presence of other known covariates of gender, Charlson comorbidities index and ASA scores.

6.4 Results

All raw study dataset for this RCT has been uploaded through the University of Southampton at DOI: https://doi.org/10.5258/SOTON/D2377.

6.4.1 Participant Flow

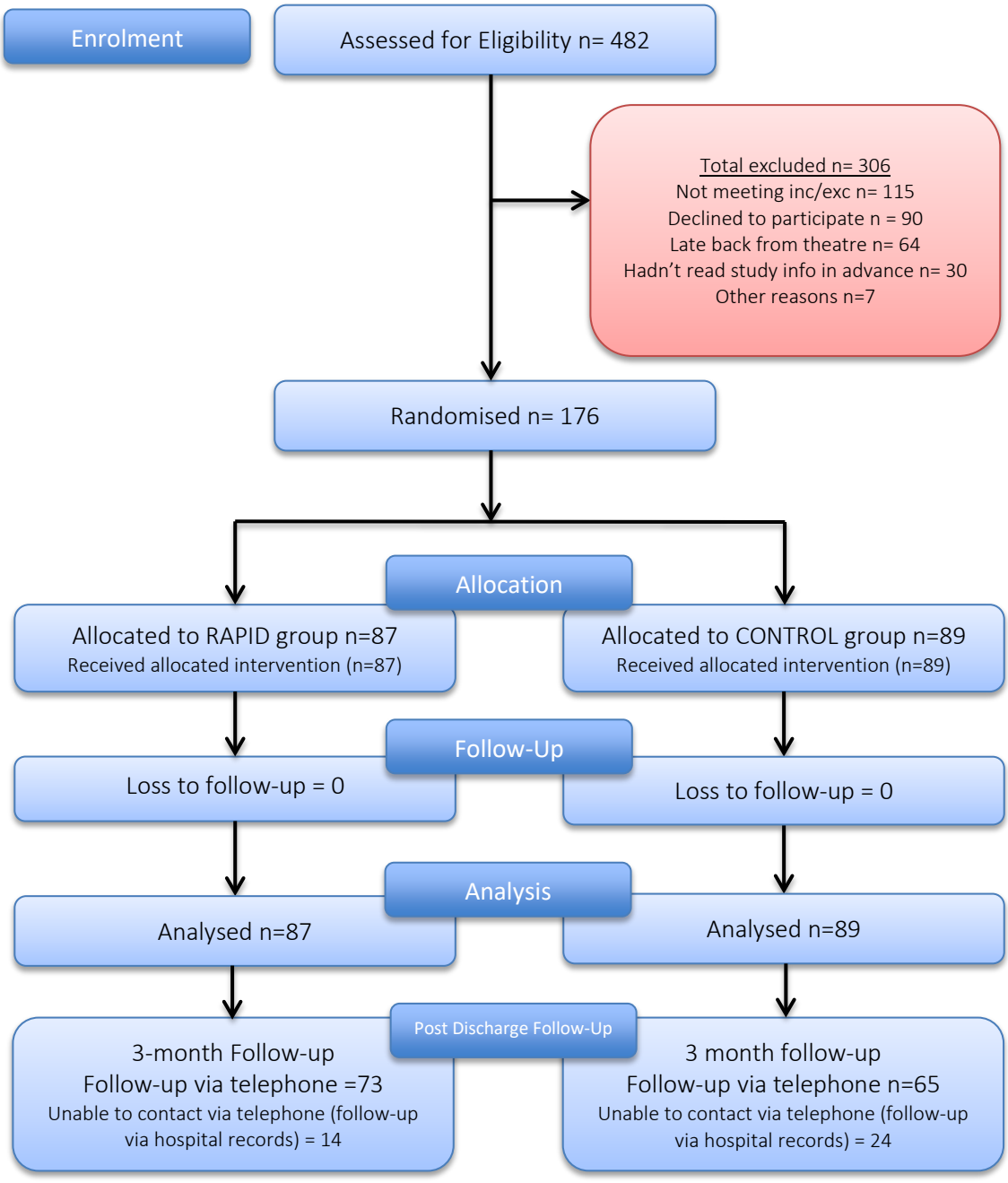


Figure 27: Fully powered RCT participant flow diagram

6.4.2 Recruitment and follow-up

Participants were recruited for just over 31 months between October 2016 to May 2019. Recruitment ended when sufficient numbers of participants were reached according to the sample size calculation carried out before study commencement.

Telephone call follow-ups were completed at median 92 days for the control group and 96 days for the Rapid group, there was no statistically significant difference in follow-up time between groups (p=0.3722). 38 participants were not reached for telephone conversation follow-up; therefore, hospital records were used to identify any post-op complications or readmissions after discharge and as planned, they were retained for analysis.

6.4.3 Baseline Data

Normality testing for baseline data is presented in full in Appendix 31. Baseline data is shown below in **Table 6-9**. There were no significant differences in baseline characteristics between groups

Table 6-9: Baseline Group Characteristics

	CONTROL Group (n=89)		*RAPID Group (n=87)*		*Median Difference*	*P value*
	Mean(SD)	Median(IQR)	Mean(SD)	Median(IQR)		
Age (Years)	66.8(10.68)	68(63-73)	68.23(7.94)	69(64-73)	2	0.5233
CCI Score	0.24 (0.62)	0(0-0)	0.1(0.34)	0(0-0)	0	0.2244
RAPT Score	9.39(1.89)	10(8-11)	9.25(1.84)	10(8-10.5)	0	0.5781
No. on Theatre List	2.47(1.3)	2(2-3)	2.59(1.22)	3(2-3)	1	0.3272
ASA Score	1.80(0.46)	2(2-2)	1.83(0.38)	2(2-2)	0	0.5863
Time to telephone follow-up (days)	103(32)	92(84-114)	105(25)	96(88-113)	4	0.3722
Gender: Male		n = 43 (48%)		n = 40 (46%)	2%	N/A

CCI = Charlson comorbidities index (Charlson et al. 1987), RAPT = Risk Assessment and Prediction Tool (Hansen et al. 2015), ASA = American society of anaesthesiologists score (Daabiss 2011)

6.4.4 Outcome: Length of Stay

Median length of stay was 3 days for both groups. However as shown in Figure 28 the CONTROL group had a much wider distribution than the RAPID group, which on comparison testing showed a statistically significant difference between groups p=0.02

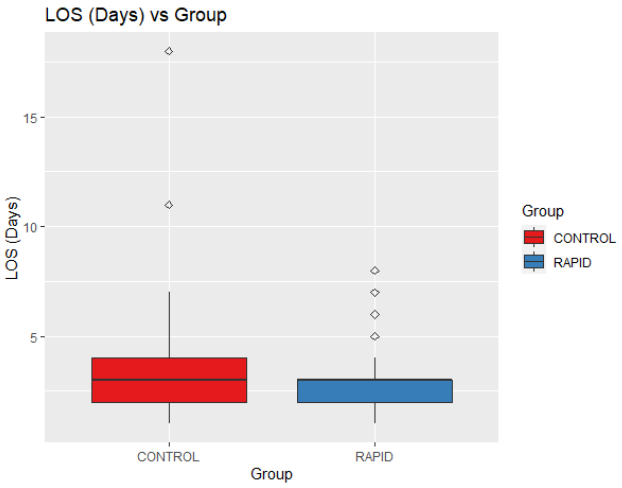


Figure 28 Boxplot - Length of stay by Group

Median values are equal, but the IQR within the RAPID group presents as less than half the IQR in the Control Group

When presented as a cumulative percentage of participants who were discharged from hospital on each post-operative day (shown in Table 6-10), this distribution is shown, with the RAPID group seeing 82.8% of participants discharged by post-operative day, while the CONTROL group discharged 65.2% of participants by the same time-point.

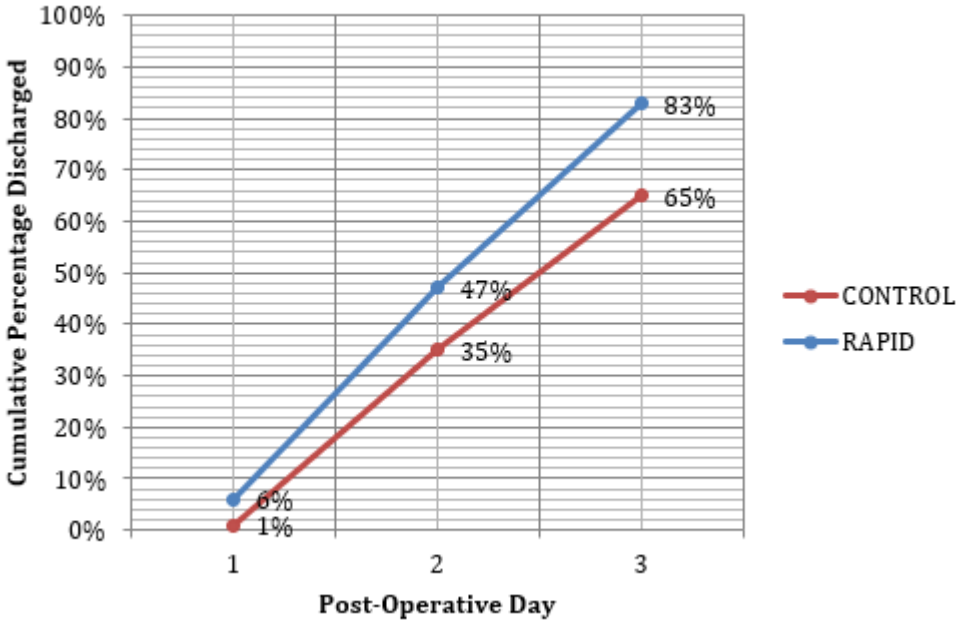


Figure 29: Cumulative percentage discharged by post-operative day

Table 6-10: Numbers discharged each post-operative day

Numbers discharged on each post-operative day									
Group	Day of Discharge	1	2	3	4	5	6	7	>7
CONTROL Group	N	1	30	27	16	6	5	2	2
	Cumulative %	1.1%	34.8%	65.2%	83.1%	89.9%	95.5%	97.8%	100.0%
RAPID Group	N	5	36	31	4	1	3	0	0
	Cumulative %	5.7%	47.1%	82.8%	87.4%	90.8%	95.4%	96.6%	100.0%

When median time to discharge was taken in hours, participants in the RAPID group left hospital 5.6 hours earlier than participants in the control group (p=0.03), shown below in **Table 6-11**.

Table 6-11: Length of hospital stay results

Variable	*Descriptive Statistic*	*Control Group*	*Rapid Group*	*Difference between Groups*	*Significance*
Length of stay (Days)	Mean (95% CI)	3.47 (3.0 to 3.9)	2.94 (2.62 to 3.3)	0.53 (-0.03 to 1.09)	**0.02151**
	Median (IQR) (95%CI)	3 (2 to 4) (3.0 to 3.5)	3 (2 to 3) (2.5 to 3.0)	0 (0.0 to 1.0)	
Time to Discharge (Hours)	Mean (95% CI)	84.7 (73.7 to 95.7)	72.2 (64.5 to 79.8)	12.5 (-0.8 to 25.9)	**0.02997**
	Median (IQR) (95% CI)	73.5 (51.6 to 96.9) (71.8 to 85.1)	67.9 (50.7 to 74.9) (60.9 to 71.9)	5.6 (0.34 to 20.3)	
Time to PT Complete (Hours)	Mean (95% CI)	72.6 (62.2 to 83.0)	53.3 (47.8 to 58.8)	19.3 (7.6 to 31.1)	**P<0.0001**
	Median (IQR) (95% CI)	66.8 (46.8 to 74.1) (58.7 to 70.3)	47.3 (43.3 to 67.9) (46.1 to 57.0)	19.5 (3.3 to 22.1)	

95% CI = 95% Confidence Interval, IQR = Interquartile range

6.4.5 Outcome: Time to physiotherapy ready to leave hospital

Participants within the Rapid group were deemed physiotherapy fit to leave hospital a median 19.6 hours earlier than participants in the control group (p<0.0001).

6.4.6 Outcome: Functional milestones

With the exception of time to first ROM which was expected to occur at similar times in both groups, all functional milestones were achieved earlier within the Rapid group than the control group (p<0.0001). These outcomes are presented below in **Table 6-12**.

Table 6-12: Functional Milestones Results

Time to Functional Milestones					
		CONTROL	**RAPID**	**DIFFERENCE**	Significance
First ROM (Hours)	Mean	5.6	5.5	0.1	0.9563
	(95% CI)	(4.9 to 6.3)	(4.9 to 6.2)	(-0.9 to 1.0)	
	Median	4.75	4.75	0.0	
	(IQR)	(4.2 to 6.0)	(4.3 to 5.6)		
	(95% CI)	(4.7 to 5.3)	(4.7 to 5.2)	(-0.3 to 0.3)	
First SOEOB (Hours)	Mean	20.7	7.0	13.7	**P<0.0001**
	(95% CI)	(20.2 to 21.2)	(5.9 to 8.1)	(12.5 to 14.9)	
	Median	20.8	5.0	15.8	
	(IQR)	(19.1 to 22.3)	(4.3 to 6.2)		
	(95% CI)	(20.2 to 21.2)	(5.0 to 5.8)	(14.5 to 15.8)	
First Transferred to Chair (Hours)	Mean	27.5	12.1	15.4	**P<0.0001**
	(95% CI)	(19.3 to 35.7)	(9.5 to 14.7)	(6.8 to 23.9)	
	Median	21.3	5.7	15.6	
	(IQR)	(19.7 to 23.8)	(4.5 to 19.0)		
	(95% CI)	(20.9 to 22.4)	(6.0 to 12.7)	(13.2 to 15.7)	
First Walk >5m (Hours)	Mean	32.0	13.9	18.1	**P<0.0001**
	(95% CI)	(23.5 to 40.5)	(11.0 to 16.8)	(9.2 to 27.0)	
	Median	22.2	5.8	16.4	
	(IQR)	(20.2 to 28.3)	(4.5 to 20.3)		
	(95% CI)	(21.8 to 31.7)	(10.7 to 14.0)	(13.8 to 16.6)	
First Walk >10m (Hours)	Mean	41.5	25.5	36	**P<0.0001**
	(95% CI)	(32.3 to 50.8)	(22.6 to 28.3)	(6.4 to 25.7)	
	Median	26.9	21.4	5.5	
	(IQR)	(23.1 to 46.0)	(19.3 to 23.6)		
	(95% CI)	(32.9 to 36.4)	(20.7 to 22.9)	(3.9 to 15.9)	
First Walk >40m (Hours)	Mean	65.3	44.3	21.0	**P<0.0001**
	(95% CI)	(54.7 to 75.8)	(38.6 to 50.0)	(9.0 to 32.9)	
	Median	49.8	44.5	4.8	
	(IQR)	(44.8 to 70.5)	(23.9 to 48.5)		
	(95% CI)	(54.6 to 61.0)	(35.4 to 46.5)	(5.6 to 23.0)	
First Independent Stairs	Mean	71.8	52.9	18.9	**P<0.0001**
	(95% CI)	(61.7 to 81.8)	(47.4 to 58.3)	(7.5 to 30.3)	
	Median	66.8	47.3	19.5	
	(IQR)	(46.8 to 74.0)	(43.3 to 67.5)		
	(95% CI)	(58.5 to 70.2)	(46.0 to 56.5)	(3.3 to 22.2)	

ROM = Range of motion, SOEOB = sit on edge of bed, 95% CI = 95% Confidence Interval, IQR = Interquartile range

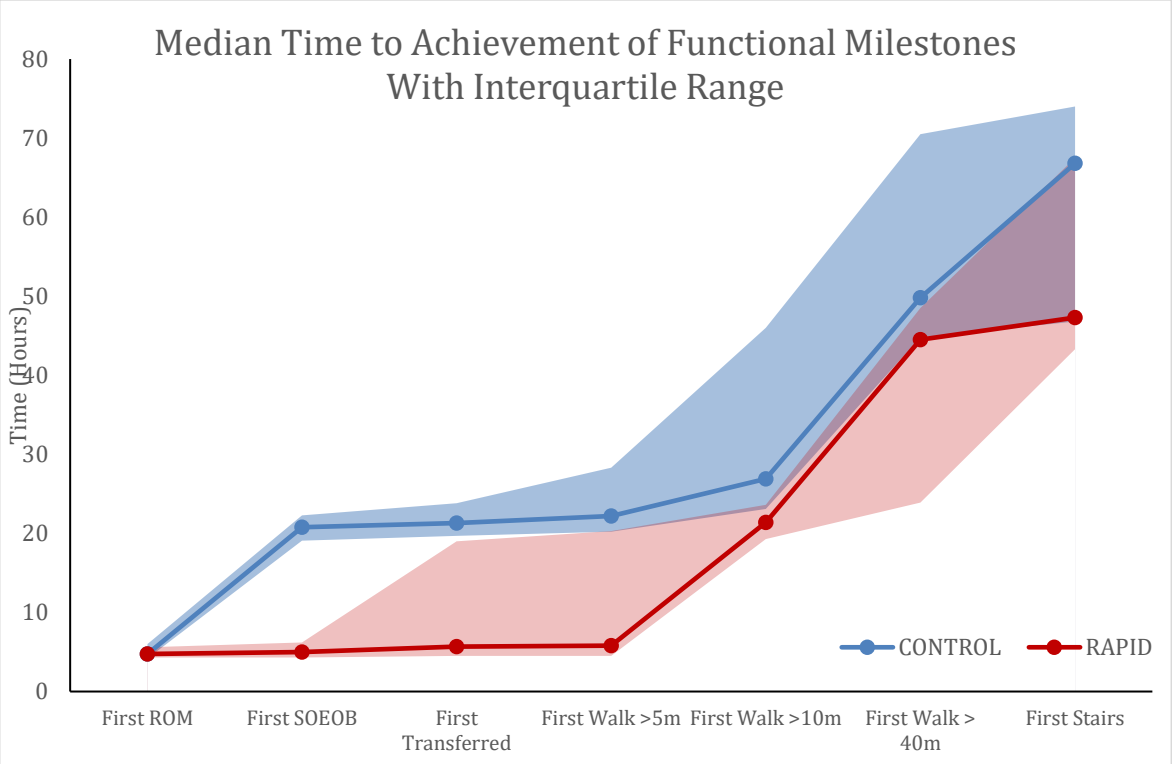


Figure 30 Graph - Median time to achieve post-operative functional milestones (Shown with interquartile range boundaries)

Represented graphically, the RAPID group had reduced time to functional milestones throughout the inpatient period, this was most pronounced in achieving initial transfers and walking and on first managing stairs, with less difference in the 10m and 40m walking distances.

6.4.7 Outcome: Modified IOWA Level of Assistance Scores

There were 1310 individual mILOA scores collected within this study.

6.4.7.1 Exploratory Analysis

Exploratory analysis plotted for the entire cohort as expected showed an inverse correlation with mILOA score decreasing as time post-operatively increased.

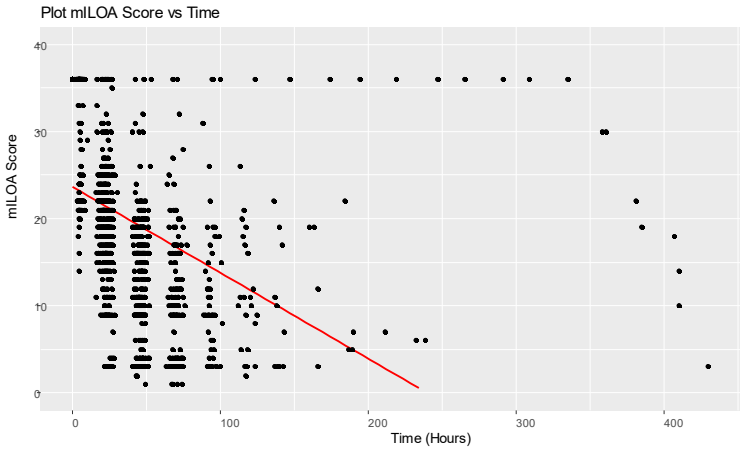


Figure 31 Whole cohort plot for mILOA scores

This relationship was broken down by group as the independent variable and potential covariates to observe for correlation

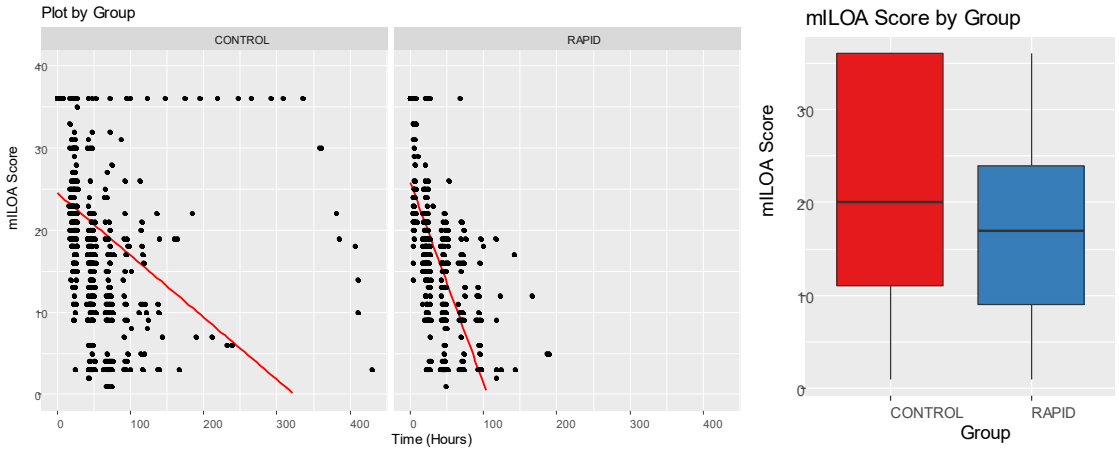


Figure 32 mILOA plot by treatment group

Differences in the gradient of change and boxplot parameters for mean and IQR was observed between groups, with a steeper gradient within the Rapid group compared to the control suggesting a difference between intervention and control groups in rate of functional recovery.

Plots compared for each of the potential covariates:

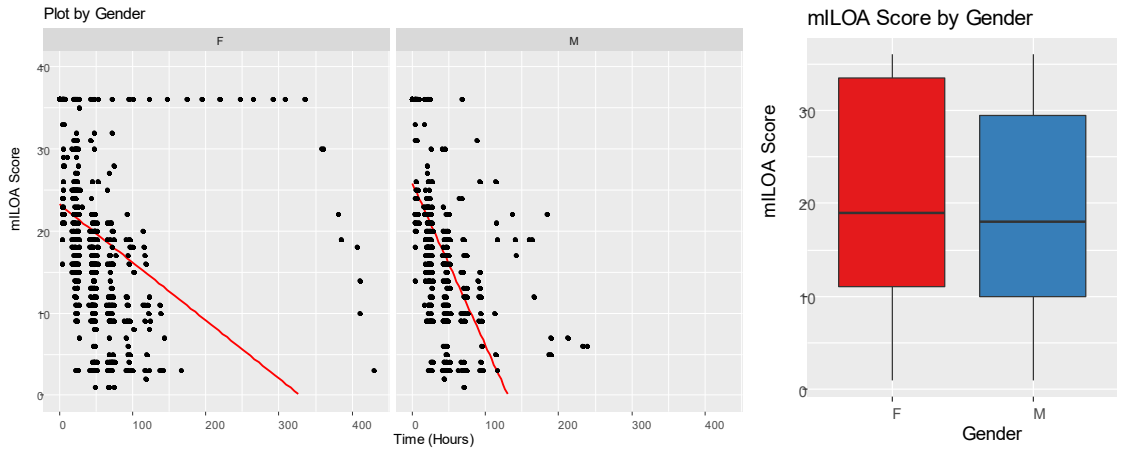


Figure 33 mILOA plot by gender

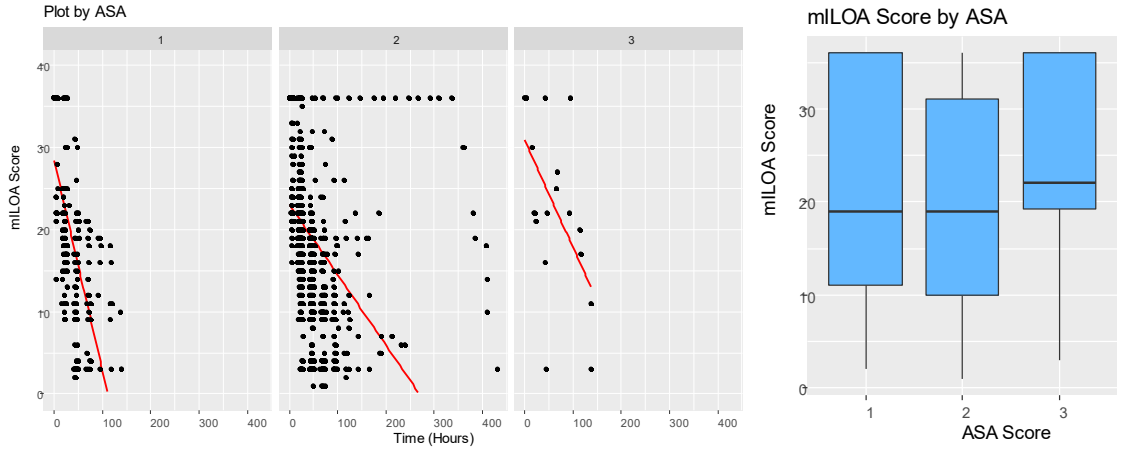


Figure 34 mILOA scores by ASA

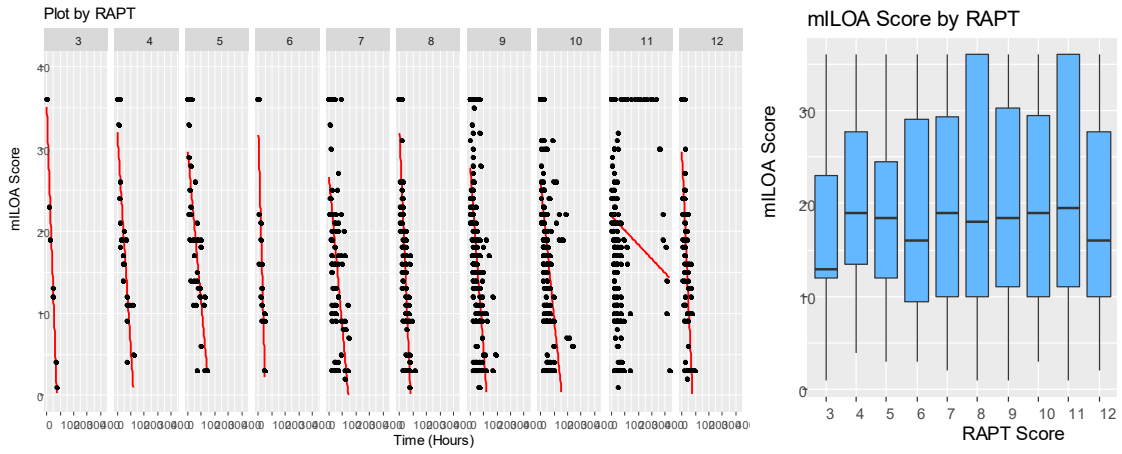


Figure 35 mILOA plot by RAPT

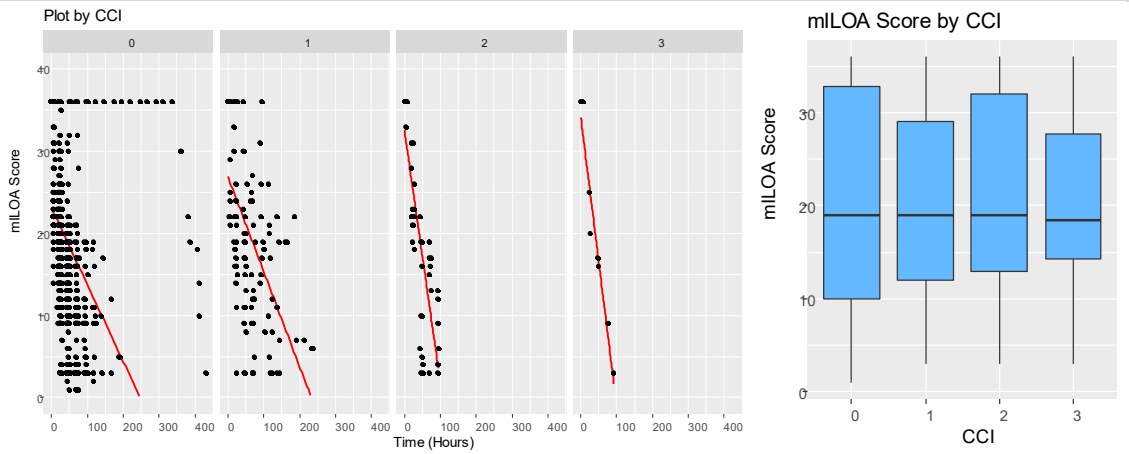


Figure 36 mILOA scores by CCI score

Like group, gender also showed a difference in gradient and in boxplot appearance. Other covariates did not appear to show correlation between RAPT, ASA and CCI scores on mILOA score change over time.

6.4.7.2 Exploratory analysis by functional independence

Exploratory analysis of dichotomised mILOA data (Shown in **Table 6-13**) showed a difference between groups when plotting functional independence over time, with participants in the control group appearing to remain dependent for longer than those in the Rapid group.

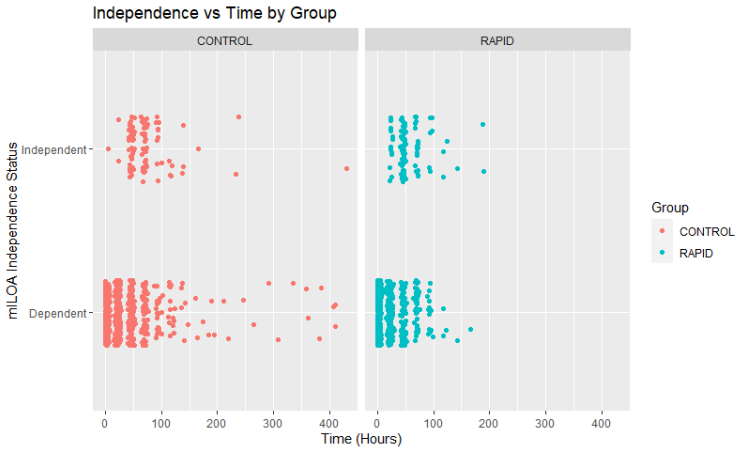


Figure 37: Exploratory Analysis mILOA data based on treatment group

Similar plots for other suspected covariates showed a similar pattern for gender, with females appearing to remain dependent for longer than males. Other categorical variables of ASA and RAPT did not appear to show clear patterns of a correlation with independence status. CCI appears to show the opposite of the expected correlation, with lower scores associated with extended dependence where we would expect participants with higher numbers or severity of

comorbidities to remain dependant for longer. This relationship however was due to very few participants scoring >1 on this measure, skewing the results.

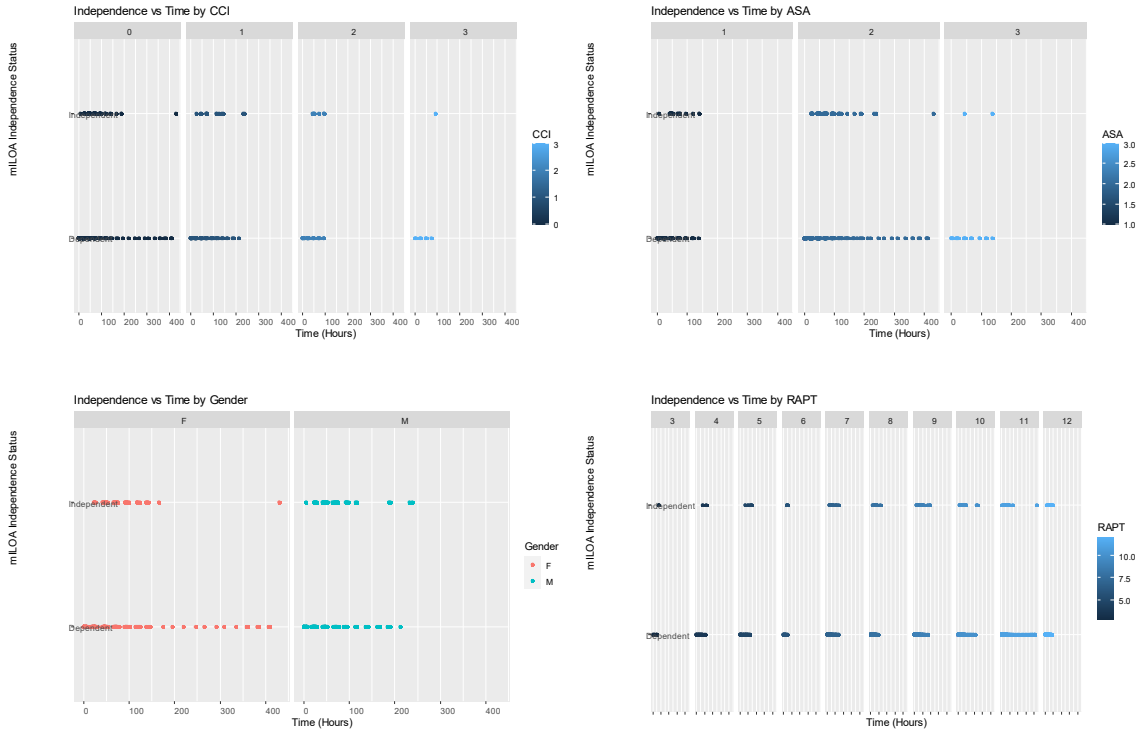


Figure 38: Exploratory Analysis mILOA data based on other categorical covariates

Plotted for age, there appears to be no obvious relationship between advancing age and prolonged dependence, with some of the longest periods of dependence observed in participants at the younger end of the cohort.

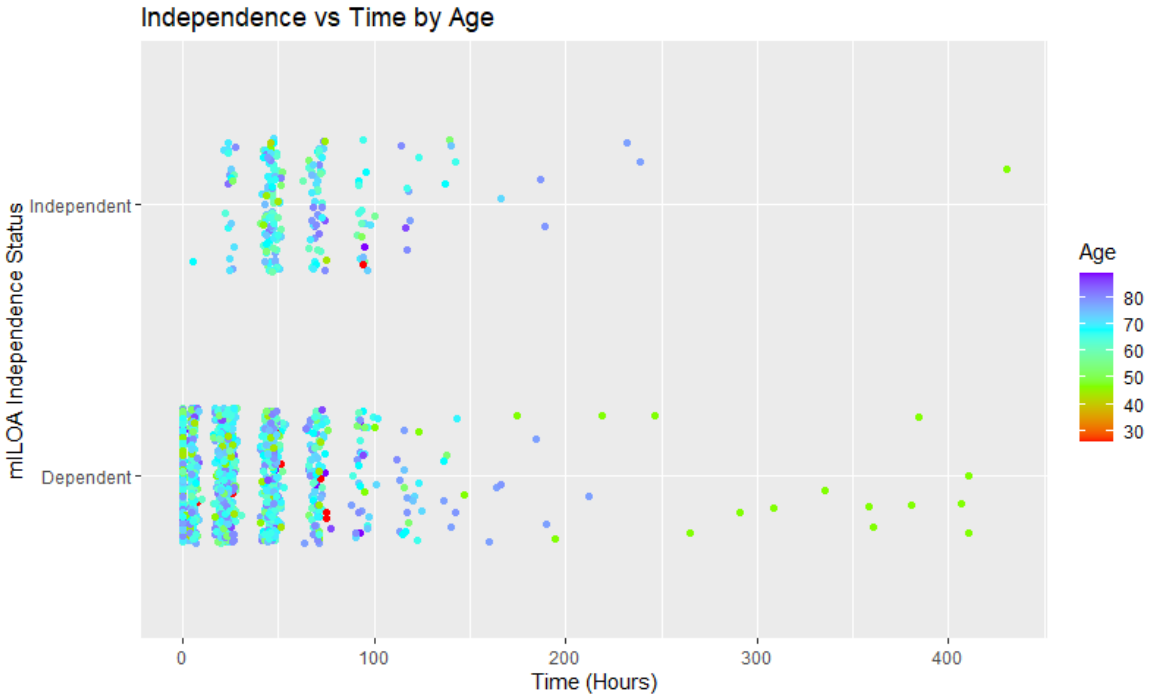


Figure 39: Exploratory Analysis mILOA data based on age

Table 6-13: Dependence status broken down by potential covariates

	Dependent (N=1106)	***Independent (N=204)***	***Overall (N=1310)***
Group			
CONTROL	620 (56.1%)	101 (49.5%)	721 (55.0%)
RAPID	486 (43.9%)	103 (50.5%)	589 (45.0%)
Gender			
F	629 (56.9%)	103 (50.5%)	732 (55.9%)
M	477 (43.1%)	101 (49.5%)	578 (44.1%)
Age			
Mean (SD)	67.4 (10.1)	67.8 (9.34)	67.5 (9.95)
Median [Min, Max]	68.5 [26.0, 89.0]	69.0 [26.0, 89.0]	69.0 [26.0, 89.0]
RAPT			
Mean (SD)	9.23 (1.92)	9.33 (1.85)	9.24 (1.91)
Median [Min, Max]	9.00 [3.00, 12.0]	9.50 [3.00, 12.0]	9.00 [3.00, 12.0]
CCI			
Mean (SD)	0.205 (0.533)	0.176 (0.514)	0.201 (0.530)
Median [Min, Max]	0 [0, 3.00]	0 [0, 3.00]	0 [0, 3.00]
ASA			
Mean (SD)	1.83 (0.417)	1.82 (0.411)	1.83 (0.416)
Median [Min, Max]	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]

RAPT = Risk assessment and prediction tool score, CCI = Charlson comorbidities index score, ASA = American society of anaesthesiologists score

6.4.7.3 Survival Analysis

Numerical summary of survival analysis data is presented in **Table 6-14**. Median time to functional independence was observed at 118.5 (CI 94.92 to 238.55) hours in the control group and 72.25 (CI 69.83 to 94.58) in the RAPID group. Kaplan-Meier plots for survival function and cumulative hazard are presented in Figure 40 and Figure 41 respectively. Log rank test indicated a statistically significant difference between groups for time to gain functional independence (p <0.001)

Table 6-14: Numerical summary of time to functional independence data

Group	*Records*	*events*	**rmean*	**se(rmean)*	*Median*	*0.95LCL*	*0.95UCL*
Control	721	101	217.96381	16.649620	118.50	94.92	238.55
Rapid	589	103	89.69766	5.726464	72.25	69.83	94.58

**Rmean = mean time to functional independence, *se(rmean) = standard error of mean*

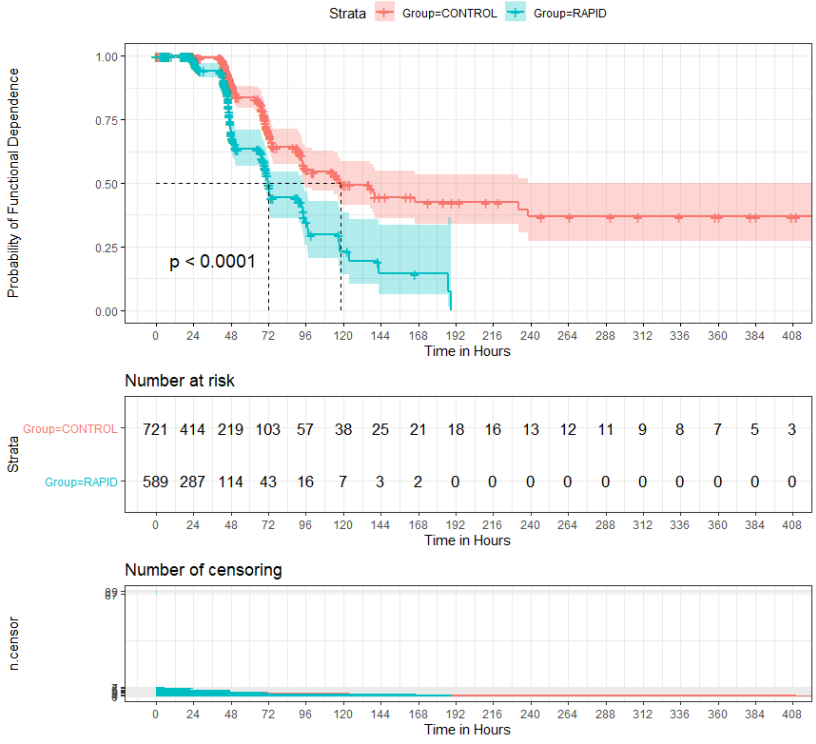


Figure 40 Kaplan-Meier plot of survival function – shown with 95% confidence intervals

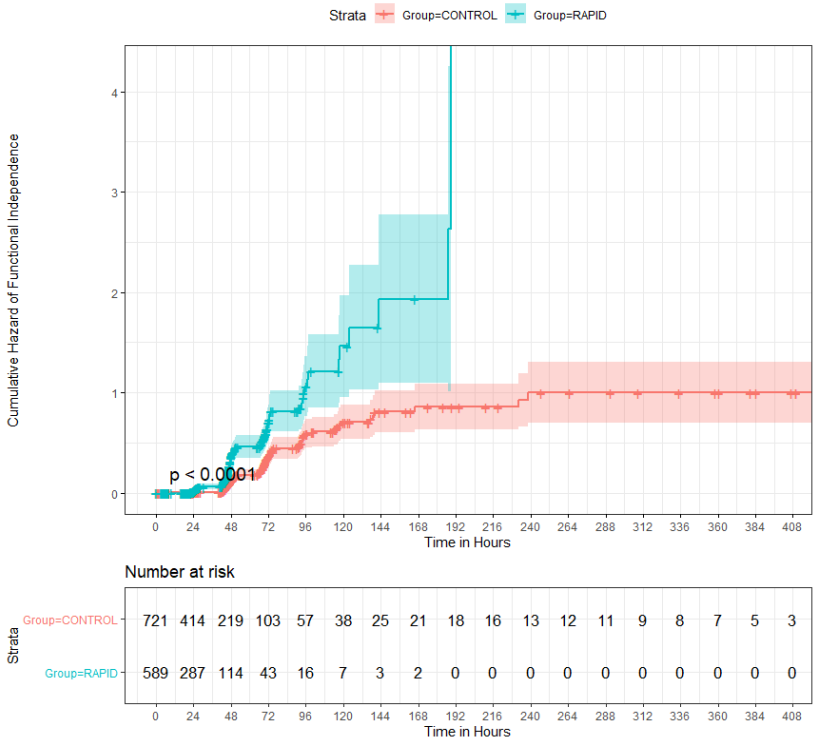


Figure 41 Kaplan-Meier plot by cumulative hazard – Shown with 95% confidence intervals

Multivariate Cox proportional hazard

When presented in a multivariate analysis with other covariates, participants within the RAPID group had just over double the odds (Hazard ratio 2.06 (CI 1.55 to 2.74)) of being functionally independent at a given time-point when compared to the control group (p<0.001) (See **Table 6-15**). In addition, male participants had a 1.75 (CI 1.32 to 3.90) times the odds of being functionally independent (p<0.001)

Table 6-15 Cox proportional hazards results

	Coefficient	*Hazard Ratio*	*SE(coefficient)*	*95% CI LCL*	*95% CI UCL*	*Wald statistic*	*P*
Group: RAPID	0.7238	2.0622	0.1448	1.5527	2.739	4.999	<0.001*
Gender: Male	0.5613	1.7529	0.1441	1.3216	2.325	3.895	<0.001*
ASA > 2	-0.577	0.5655	0.7175	0.1386	2.308	-0.794	0.427
CCI > 1	-0.2656	0.7667	0.3288	0.4025	1.460	-.0808	0.419
					Likelihood ratio test= 48.71	on 4 df,	p<0.001*
					Wald test = 48.87	on 4 df,	p<0.001*

	Score (logrank) test = 51.60 on 4 df, p<0.001*

SE = standard error of coefficient, ASA = American society of anaesthesiologists score, CCI = Charlson comorb idities index score

This is presented graphically within Figure 42, showing treatment group as the most significant var iable in reaching functional independence.

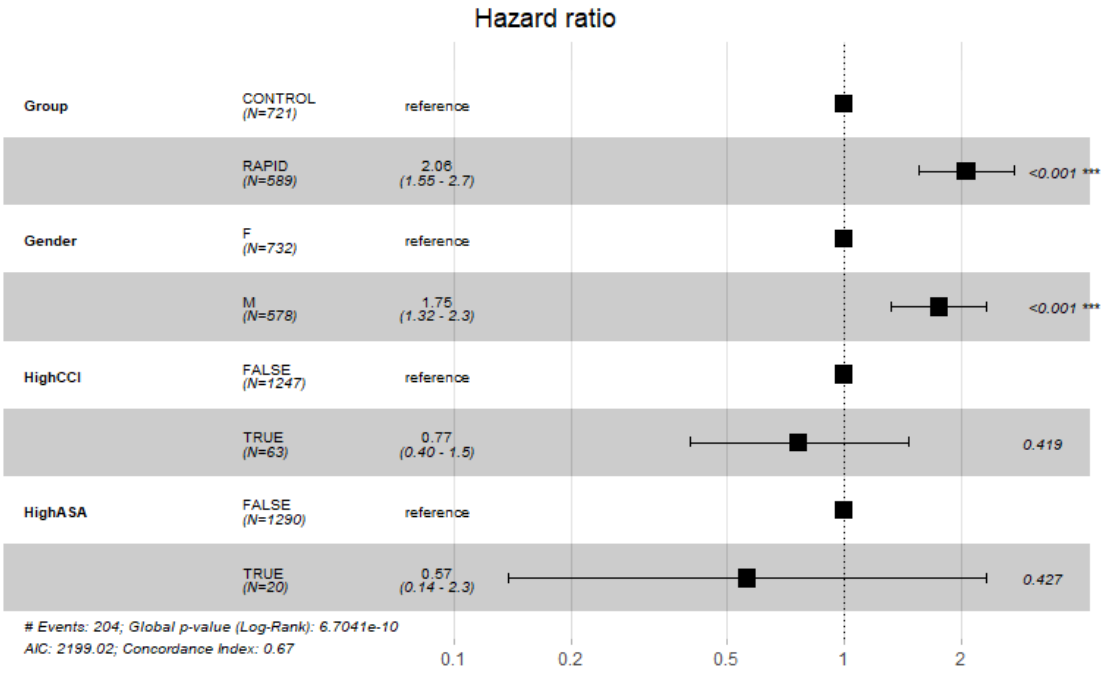


Figure 42 Forest plot. Multivariate Cox proportional hazards

Model assumption checking:

Schoenfeld residuals used to test for proportional hazards assumption of Cox method. Graphical e xamination of schoenfeld residual plots (Figure 43) showed relatively horizontal lines, with no patt erns of departure from the expected zero line with time. However, the gender covariate was stati stically significant on testing (See **Table 6-16**).

Table 6-16 Schoenfeld residuals for Cox proportional hazards model

	Chi- Squared Statistic	*Degrees of Freedom*	*p-value*
Group	0.837	1	0.360
Gender	6.096	1	0.014
ASA > 2	0.143	1	0.706
CCI > 1	4.524	1	0.033
GLOBAL	11.933	4	0.018

ASA = American society of anaesthesiologists score, CCI = Charlson comorbidities index score

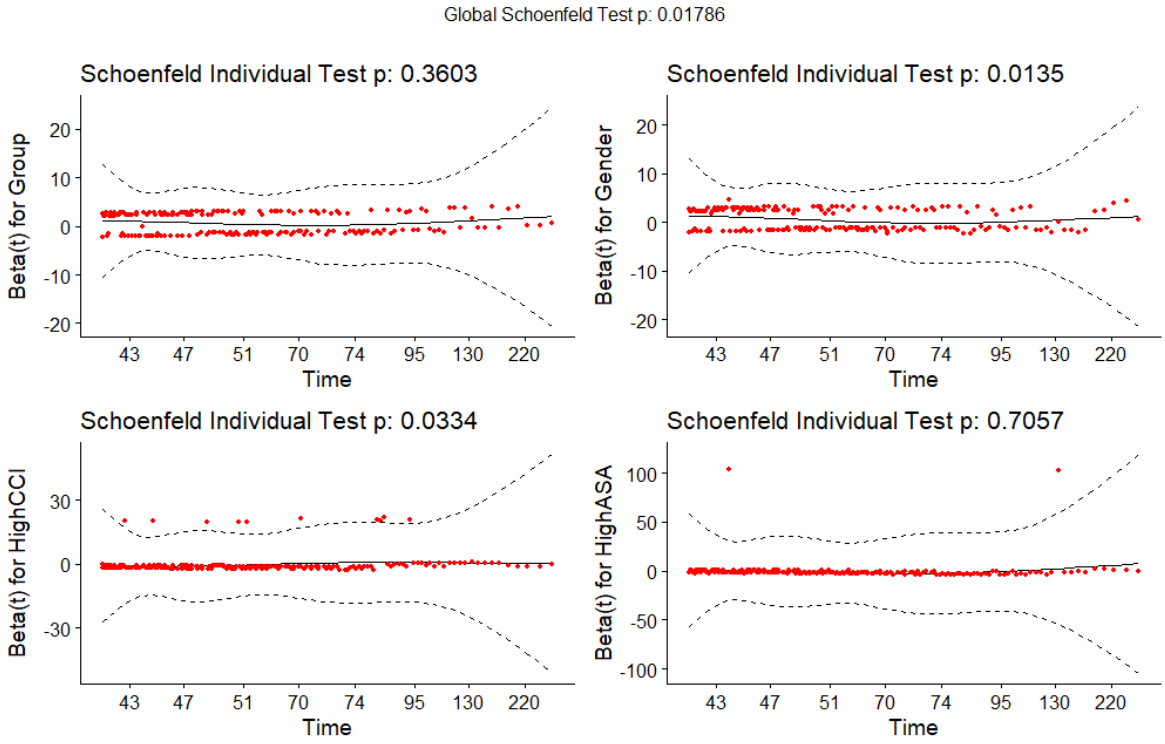


Figure 43 Schoenfeld residual plots

The statistical significance of gender Schoenfeld residuals was deemed due to the nature of the data as males reached functional independence sooner than females. This is shown in Figure 44; non-convergence of the survival curves indicates the proportional hazards assumptions holds within this dataset.

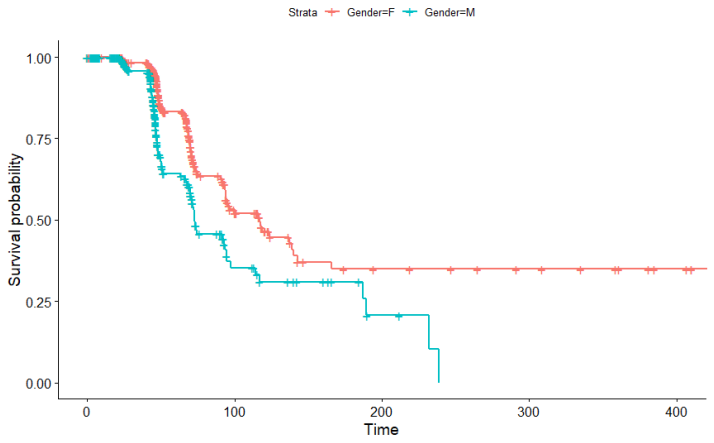


Figure 44 Survival analysis based on Gender

6.4.8 Incidence of post-operative complications and readmissions

Incidences of post-operative complications broken down by group are shown below in Table 6-17. Complications are classified according to the clavien-dindo classification of severity.

Table 6-17: Post-op complications by clavien-dindo classification of severity. (*Inclusive of all complications recorded including post hospital discharge)***.**

Clavien-Dindo Classification	***Complication***	***CONTROL GROUP***	***RAPID GROUP***
1	Atrial Fibrilation	1	2
	Bradycardia	1	0
	Chronic Kidney Disease	1	0
	Confusion	1	1
	Constipation	1	0
	Dizziness	14	9
	Fall	1	2
	Fatigue	3	0
	Haematoma	1	0
	Headache	1	0
	Hyponatraemia	2	0
	Hypotension	4	1
	Hypoxia	1	0
	Leg length discrepancy	3	0
	Low back pain	2	0
	Orthostatic Hypotension	39	9
	Other	12	5
	Persistent Oedema	3	2
	Persistent Pain	8	4
	Post Operative Nausea and Vomiting	36	23
	Post-op Anaemia	2	0
	Pyrexia	1	0
	Systemic Inflammatory Response Syndrome	1	0
	Syncope	4	6
	Tachycardia	0	1
	Transient Ischaemic Attack	0	1
	Trendelenberg Gait	2	1
	Uncontrolled Pain	5	3
	Urinary Retention	2	2
	Wound Ooze	19	26
2	Blood Transfusion	3	0
	Cellulitis	1	0
	Deep Vein Thrombosis	0	1
	Infective Exacerbation of COPD	0	1
	Pulmonary Embolism	1	1
	Urinary Tract Infection	1	1
	Wound Infection	7	6
3	THR Dislocation	2	2
	(Closed Reduction of dislocated THR)	1	2
	Fracture	0	1

	Perforated Bowel	1	0
	Revision THR	1	1
4	Death	1	0

COPD = Chronic obstructive pulmonary disease

Comparison testing between groups for post-operative complications showed no significant difference in the incidence rate when considered for all classifications of post-operative complications (p=0.1495). There were 19 complications deemed serious (classified as > 1 on the clavien-dindo classification) within the control group, and 14 within the RAPID group. Once again there were no statistically significant differences between groups (p=0.6564). Broken down into the most common complications expected within a THR cohort (Dizziness, PONV, Wound Ooze and Orthostatic Hypotension), all of these except for wound ooze saw a reduced rate within the rapid group when compared with the control group. On comparison testing this did reach statistical significance (p=0.002). However, there were seven more instances of post-operative wound ooze (36%) in the RAPID group when compared to the control group.

There were 17 incidences of complications classified as "other". The natures of these are shown in Appendix 35. There were four incidences of dislocation of THR observed, this constituted only two individuals; one from each group, both of which suffered two dislocations each. The participant within the control group was treated with one closed reduction and then revision THR following the second dislocation. The participant within the RAPID group was treated with two closed reductions of the THR. The single fracture recorded within the RAPID group was due to a mechanical fall and was treated with the only revision THR observed within the RAPID group.

Complications post discharge:

Incidence of complications occurring post discharge are shown in Table 6-18. Comparison testing between groups for post-op complications showed no statistically significant differences between groups (p=0.3233).

Table 6-18 Post-operative complications occurring post hospital discharge

Clavien-Dindo Classification	***Complication***	***CONTROL GROUP***	***RAPID GROUP***
1	Atrial Fibrillation	0	1
	Fall	0	2
	Hyponatraemia	2	0
	Leg length discrepancy	3	0
	Low back pain	2	0
	Other	7	3
	Persistent Oedema	3	2
	Persistent Pain	8	4
	Post Operative Nausea and Vomiting	1	0

	Syncope	1	0
	Trendelenberg Gait	2	1
	Wound Ooze	3	2
2	Cellulitis	1	0
	Deep Vein Thrombosis	0	1
	Pulmonary Embolism	0	1
	Urinary Tract Infection	0	1
	Wound Infection	7	6
3	THR Dislocation	0	2
	Fracture	0	1
	Perforated Bowel	1	0
	Revision THR	0	1
4	Death	1	0

Readmissions:

There was a total of eight readmissions across the 176 study participants. Four of these occurred within the RAPID group and four within the CONTROL group. This gave comparable readmission rates between groups of 4.6% within the RAPID group and 4.5% within the CONTROL group. Within the RAPID group, reasons for readmission were peri-prosthetic fracture following a mechanical fall, pulmonary embolism, urinary tract infection with associated AF and dislocation of the THR. Within the CONTROL group, reasons for readmission were wound infection, myocardial infarction, impaired swallowing and intra-abdominal perforation.

6.4.9 Post-operative Pain

Pain scores were similar between groups when compared, with no statistical difference in day 0 or day 1 scores (see Table 6-19). However, pain on first post-operative ambulation was a median of one point lower within the rapid group than the control group, reaching statistical significance (p=0.0059).

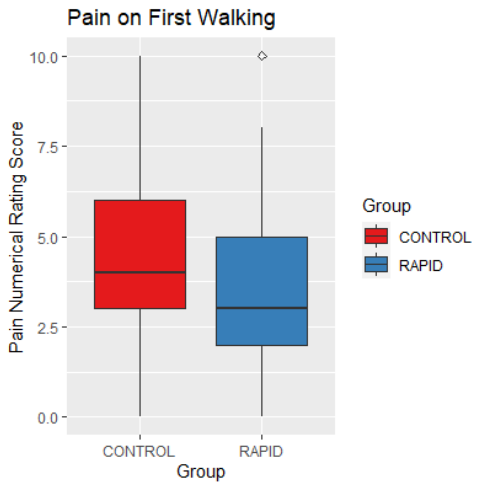


Figure 45 Box-plot pain scores on first ambulation

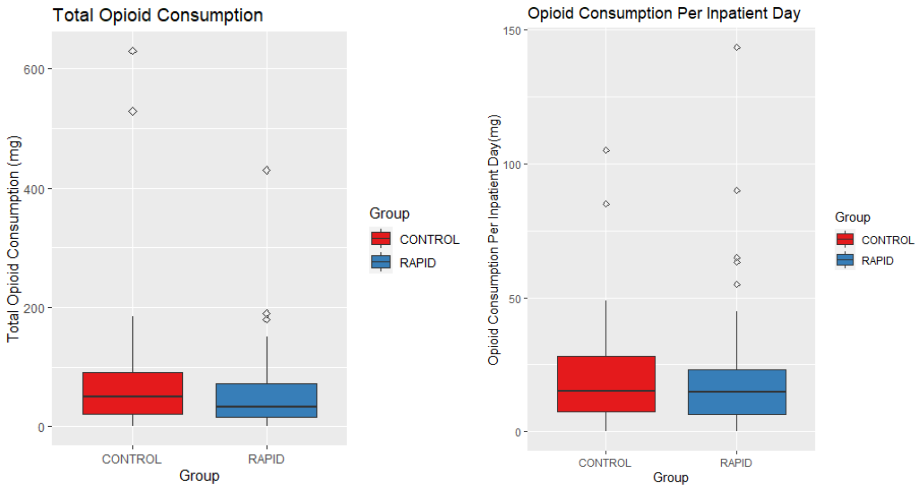
Table 6-19: Post-operative pain scores

Post-Operative Pain Scores					
		Control	**Rapid**	**Difference**	**p-value**
Day 0 Pain at Rest	Mean (95% CI)	1.36 (0.9 to 1.8)	1.25 (0.9 to 1.6)	-0.11 (-0.4 to 0.7)	
	Median (IQR) (95% CI)	0 (0 to 2) (2.5 to 3.5)	1 (0 to 2) (2.0 to 2.5)	1 (0.0 to 0.0)	p=0.7363
Day 0 Pain on ROM	Mean (95% CI)	2.51 (2.0 to 3.0)	2.68 (2.1 to 3.2)	0.17 (-0.9 to 0.6)	
	Median (IQR) (95% CI)	2 (0 to 4) (3.0 to 4.0)	2 (0 to 4) (3.0 to 4.0)	0 (-0.9 to 1.3)	p=0.6825
Day 1 Pain at Rest	Mean (95% CI)	2.76 (2.2 to 3.3)	2.33 (1.9 to 2.8)	-0.43 (-0.3 to 1.2)	
	Median (IQR) (95% CI)	2 (0 to 5) (3.0 to 4.0)	2 (0 to 4) (2.5 to 3.5)	0 (0.0 to 0.9)	p=0.4348
Day 1 Pain on ROM	Mean (95% CI)	4.38 (3.9 to 4.9)	3.95 (3.4 to 4.5)	-0.43 (-0.3 to 1.2)	
	Median (IQR) (95% CI)	5 (2 to 6) (4.0 to 5.0)	4 (2 to 5) (4.0 to 5.0)	-1 (0.0 to 1.0)	p=0.2609
Day 1 Pain on Walking	Mean (95% CI)	4.58 (4.0 to 5.1)	4.30 (3.8 to 4.8)	-0.28 (-0.5 to 1.0)	
	Median (IQR) (95% CI)	4 (3 to 6) (4.0 to 5.5)	4 (1.5 to 4.0) (4.0 to 5.0)	0 (-1.0 to 1.0)	p=0.5008
First Walk	Mean (95% CI)	4.47 (3.9 to 5.0)	3.41 (2.9 to 3.9)	-1.06 (0.3 to 1.8)	
	Median (IQR) (95% CI)	4 (3 to 6) (4.0 to 5.5)	3 (3 to 5) (3.0 to 4.0)	-1 (0.0 to 2.0)	p=0.0059

SD = Standard deviation, IQR = interquartile range, ROM = range of motion

6.4.10 Post-op opioid analgesic consumption

Median total consumption of opioid analgesia was lower within the Rapid group across admission at 34mg than in the control group at 50mg, however this did not reach statistical significance (p=0.125). When analysed in opioid consumption per inpatient day, there was no difference between groups (p=0.2918). Full statistics are shown in Table 6-20.



6.4.11 Post-op antiemetic consumption

There was no difference between groups in the number of antiemetic doses administered across admission with a median of 2 doses in both the Control group and the RAPID group (p=0.3627).

Table 6-20: Pharmacological Outcome Measures

Opioid and Antiemetic Consumption Measures					
		Control Group	Rapid Group	Difference	Significance
Total Opioid Consumption (mg as morphine equivalent**)**	Mean (95% CI)	71.04 (52 to 90)	54.91 (42 to 68)	-16.13 (-6.9 to 39.2)	p=0.1250
	Median (IQR) (95% CI)	50 (21 to 91) (53 to 77)	34 (16 to 72) (43 to 69)	-16 (-2 to 23)	
Opioid Consumption Per Inpatient Day (mg as morphine equivalent**)**	Mean (95% CI)	19.30 (16 to 23)	18.66 (14 to 23)	-0.64 (-5.0 to 6.3)	p=0.2918
	Median (IQR) (95% CI)	15.00 (8 to 28) (16 to 22)	14.95 (7 to 23) (15 to 21)	-0.05 (-1.7 to 6.0)	
Total antiemetic consumption (number of doses**)**	Mean (95% CI)	2.96 (2 to 4)	2.29 (2 to 3)	-0.67 (-0.4 to 1.8)	p=0.3627
	Median (IQR) (95% CI)	2 (0 to 4) (3.0 to 4.5)	2 (0 to 3) (2.0 to 3.0)	0 (-0.0 to 1.0)	

95% CI = 95% Confidence intervals, IQR = Interquartile range

6.4.12 Financial Impact of DZM

Although median length of stay was 3 days for both groups, there was reduced variation within the RAPID group meaning there were differing numbers of total bed days. The total number of bed days used in the control group was 309 compared to 256 in the RAPID group. Using the reference cost of £346 per bed day, the total cost of bed days in the Control group was £106,914 compared to £88,576 within the RAPID group. Overall, this saw a saving on bed days of £18,338 in the RAPID group equating to a 17% reduction (Shown in **Table 6-21**).

Table 6-21 Bed day costs by treatment group

Group	*Total bed days*	*Total Cost (Based on £346 per bed day)*
CONTROL	309	£106,914.00
RAPID	256	£88,338.00
Difference	53	£18,338.00

6.4.13 Participant Experience

174 participant experience questionnaires were completed and collected prior to participant discharge from hospital. Results are presented in Table 6-22. There were minimal differences in questionnaire responses between groups. Although questions 2, 4 and 6 did show a statistically significant difference in favour of the RAPID group, none of these reached the predefined clinically significant threshold.

Table 6-22 Participant Experience Questionnaire Results

Participant Experience Questionnaire Results					
		Control Group	Rapid Group	Difference	Significance
Question 1 *"Do you think the hospital staff did everything they could to help control your pain?"*	Mean (SD)	9.80(0.53)	9.91(0.29)	0.11	p=0.172
	Median (IQR)	10(10-10)	10(10-10)	0	
Question 2 *"Overall, how was your experience of physiotherapy following your operation?"*	Mean (SD)	9.82(0.39)	9.92(0.47)	0.10	**p=0.006**
	Median (IQR)	10(10-10)	10(10-10)	0	
Question 3 *"Overall, how was your experience of your overall hospital treatment?"*	Mean (SD)	9.66(0.71)	9.81(0.47)	0.15	p=0.122
	Median (IQR)	10(10-10)	10(10-10)	0	
Question 4 *"Did you have confidence and trust in the physiotherapists treating you?"*	Mean (SD)	9.88(0.37)	9.97(0.18)	0.09	**p=0.048**
	Median (IQR)	10(10-10)	10(10-10)	0	

Question 5 *"How beneficial was walking early after your operation?"*	Mean (SD)	9.52(1.02)	9.55(1.14)	0.03	p=0.225
	Median (IQR)	10(9-10)	10(10-10)	0	
Question 6 *"How well was your progression with your physiotherapist paced to suit you?"*	Mean (SD)	9.84(0.40)	9.93(0.40)	0.09	**p=0.013**
	Median (IQR)	10(10-10)	10(10-10)	0	

SD = standard deviation, IQR = interquartile range

6.4.14 Harms

Other than the post-operative complications recorded as part of secondary end-point analysis above, there were no other harms to participants or other unintended effects.

6.5 Discussion

This study aimed to examine the multi-factorial quality of day-zero ambulation following primary uncomplicated THR. Throughout the previous section we have seen the following key findings:

- The same median length of hospital stay in both groups, but with less variation in the interventional group reaching statistical significance with an associated financial saving.
- Participants in the intervention group achieving physiotherapy discharge criteria a median 19.5 hours earlier
- Faster achievement of functional milestones and return to functional independence.
- No significant differences in incidence of post-operative complications, participant experience, post-operative pain score and consumption of opioid analgesia or anti-emetic medications.

The discussion within this chapter will handle the interpretation of the present study's results and consideration against existing literature, structured by the main planned outcomes for this study including length of hospital stay, functional recovery, incidence of post-operative complications, post-operative pain and patient experience. The implications of these findings are discussed in detail within Chapter 7.

6.5.1 Recruitment

Although not within the original planned outcomes of this trial, comment must be made as to the numbers of participants who were not recruited. Staffing within this study included a physiotherapist on duty until 9pm, requiring that any participants needed to return to the ward by 16:30 in order for them to have recovered on the ward for 4 hours post-op and allow the physiotherapist a practical amount of time to assess and provide intervention. 13% of participants who provided informed consent to take part in this study were unable to be recruited as they returned to the ward too late to receive physiotherapy on the same day as surgery. This raises practical questions for service providers on how late into the evening physiotherapy staffing would be required in order to employ day-zero ambulation successfully.

Additionally, 19% of participants who were approached declined participation. While reasons for declining were not collected, this may indicate a reduced acceptance of or confidence in this intervention from a patient perspective and may warrant further research.

6.5.2 Length of hospital stay

While median length of stay was the same in both groups, there was a significantly reduced variation in length of stay observed within the intervention group. The time taken for participants to be physiotherapy ready to leave hospital was also significantly reduced in the intervention group. The difference between these metrics was due to participants having outstanding medical discharge criteria to fulfil before they could be discharged, for example; passing urine after decatheterisation, opening bowels and ensuring pain was well controlled.

While there have been quite a few published studies which reported larger relative reductions in length of stay, the effect sizes vary dramatically between studies with the highest reduction of 6.45 days (den Hertog et al. 2012) and the lowest at 0.21 days (Juliano et al. 2011). Improved performance of contemporary control groups in length of stay data is most likely responsible for reduced effect sizes observed in more modern research, giving less potential for improved length of stay figures than was seen in earlier research. An example of this can be shown when comparing Larsen, Hansen, et al. (2008) with the current study. Larsen et al reported a control group length of stay of eight days and an intervention group of length of stay of 5 days, whereas in this study the control group far outperformed the Larsen et al intervention group with a median length of stay of 3 days. This creates a ceiling effect in more recent studies as to the effectiveness of day-zero ambulation, meaning that we cannot and should not expect the effect sizes reported in some of the early findings in this field. This is the principle cause for statistical heterogeneity in length of stay data when attempting meta-analysis across the range of publications in this field. Furthermore, as discussed in 2.5.3 most previously published studies had methodological limitations and concomitant interventions, making it difficult to be confident the effect size was attributable to day-zero ambulation.

The length of stay findings observed and reported within this study support the findings of the other more recent publications on this topic (Okamoto et al. 2016; Juliano et al. 2011; Karim et al. 2016). Most closely supporting the other recent RCT findings of Okamoto et al. 2016, seeing a significant reduction in time to physiotherapy complete, but with this not translating directly into a reduced median length of stay. While Juliano et al. 2011 showed much more modest effect sizes than other published literature, on critical appraisal it has one of the more robust methodologies, was specific to THR and had a good representative population sample. This provides confidence that the true effect size attributable to day-zero ambulation as an isolated intervention is more modest than observed in several previous studies. This suggests that contemporaneity is important in this field, as standard length of stay observed in some earlier studies were far beyond what might be expected for modern day elective arthroplasty in the UK. Combining

results from only contemporary studies may reduce statistical heterogeneity and make meta-analysis more viable.

Many of the previous drivers for day-zero ambulation have been around reducing length of stay and the financial savings purported to come with this. This study indicates that while day-zero ambulation may not reduce median length of stay significantly, the more substantive effects of this intervention look to be in reducing the variation seen in length of stay, speeding functional recovery and return to independence within the inpatient period.

6.5.3 Functional recovery

Some of the clearest differences between groups within this study were seen in measures of post-operative function, with patients achieving functional milestones significantly earlier in their recovery and gaining functional independence quicker when day-zero ambulation was utilised. Although other studies measured function in different ways, the findings of this study support the publications of Banerjee (2014); Karim et al. (2016) and den Hertog et al. (2012) in observing quicker functional recovery. Previously, only Juliano et al. (2011) had published findings of no significant differences in function within the inpatient recovery period.

6.5.4 Post-Op Complications

This study found no significant differences in incidences of post-operative complications between groups, supporting several other published works (Berger et al. 2009; Wellman et al. 2011; Gulotta et al. 2011; Banerjee 2014; Khan et al. 2014; Klein et al. 2017; Pollock et al. 2016).

A strength of the current study was in breaking down complications according to severity, adding weight to the argument that day zero ambulation is safe; with no increase in incidence of serious complications. Several other studies support this with findings of:

- Reduced or no difference in incidence of DVT/PE (Berger et al. 2009; Husted, Otte, Billy B Kristensen, et al. 2010; Jorgensen et al. 2016; Klein et al. 2017)
- No increase in dislocation rates (Andersen et al. 2009)(Husted, Otte, Billy B. Kristensen, et al. 2010; Klein et al. 2017; Andersen et al. 2009)
- No increase in risk of falls (Jorgensen & Kehlet 2013)
- No significant differences or improvements in mortality rate (Jorgensen & Kehlet 2013; Khan et al. 2014; Malviya et al. 2011; Savaridas et al. 2013; Pitter et al. 2016)
- No significant differences or reductions in readmission rates (Jorgensen & Kehlet 2013; Robbins et al. 2014; Husted, Otte, Billy B. Kristensen, et al. 2010; Dorr et al. 2010; Khan et al. 2014; Raphael et al. 2011; Stambough et al. 2015; Klein et al. 2017)
- Reduction in post-operative blood transfusion rate (Khan et al. 2014)

- Reduced rates of 30-day myocardial infarction (Khan et al. 2014)
- No significant difference in the incidence of infection (Klein et al. 2017)

Furthermore, within the present study, there was a reduced incidence of complications commonly associated with this patient population. Reduced incidence of post-operative dizziness was also observed by Gulotta et al. (2011). This study also showed reduced incidences of PONV and orthostatic intolerance, contradicting the findings of Raphael et al. 2011 and Jans et al. 2015 respectively who both observed higher incidences of these complications.

The sole domain where day-zero ambulation did not perform as well as the control group was in incidence of post-operative wound ooze, observing a 36% higher incidence in the intervention group. This finding was limited to the inpatient period of recovery and was not observed post-discharge.

Several studies have investigated risk factors for prolonged wound drainage following joint arthroplasty, and while factors such as morbid obesity, smoking, alcohol consumption and comorbidities such as diabetes have been shown to be significant contributors, early mechanical stresses through the wound has not been published as a known contributor (Patel et al. 2007; Shahi et al. 2019a). However, prolonged wound drainage has been linked with an increased risk of surgical site infection (Saleh et al. 2002; Patel et al. 2007), and surgical site infection is well documented as a risk factor for peri-prosthetic joint infection (Zhu et al. 2015a; Berbari et al. 1998; Shahi et al. 2019b).

This becomes important when coupled with the findings of Amlie et al. 2016, who observed an increase in the incidence of revision arthroplasty due to deep infection in patients who had undergone hip arthroplasty via a fast track pathway inclusive of day of surgery ambulation.

While the current study didn't observe higher numbers of revision surgeries or surgical site infections in either group, it does raise questions that perhaps day-zero ambulation prolongs wound drainage due to earlier mechanical forces through the wound site, thereby providing an increased risk of surgical site infection and raising the risk of deep infection.

In contrast, while their study used no comparison group, Klapwijk et al. (2017), saw an 11.7% incidence of wound ooze across both the inpatient and outpatient phases in patients who underwent day-zero ambulation (11 incidences out of 94 patients). This figure is still significantly less than the present study observed within its control group (21%). Finally, although not proven in research, prolonged wound drainage could theoretically contribute to an increased risk of hypertrophic scarring.

Further research is recommended in this area, and in the meantime, consider carefully the suitability of day-zero ambulation in individuals who are at high risk of infection or prolonged wound ooze due to clotting concerns.

6.5.5 Pain Experience

Within this study, day-zero ambulation did not adversely affect the post-operative pain numerical ratings, with this finding supported by the intra-study findings on opioid analgesia consumption and participant experiences of pain discussed in 6.5.7 and 6.5.10 respectively.

While other published studies have reported reductions in post-operative pain numerical ratings for patients treated with day zero ambulation (Bottros et al. 2010; Raphael et al. 2011; Smith et al. 2012), all of these studies made concomitant changes to the analgesia regimen used with intervention group participants, likely significantly affecting their results. Further larger scale observational studies and multi-centre studies would be helpful in determining the true effect of day-zero ambulation on pain scores.

6.5.6 Pain on first ambulation

The present study did observe reduced pain in the Rapid group when participants ambulated for the first time following their THR. This improved level of analgesia is likely to be related to latent activity of the spinal anaesthetic, and local infiltration analgesia still being active when attempting ambulation on day zero. In TKR patients, Krenzel et al. (2009) showed that a single bolus local infiltration analgesia was able to affect pain for the first 12 hours, but showed no pain improvement beyond this and in Andersen et al. (2007) for the first 8 hours. Employing day zero ambulation may be making the most of LIA within the initial post-operative period.

6.5.7 Opioid Consumption

Previous published research has seen mixed results, with Raphael et al. (2011) reporting significantly less opioid consumption in their fast-track group than with standard care. However, den Hertog et al. (2012) reported results in contradiction to this with consumption of analgesics being higher over the first two post-operative days than standard care. The current study agrees with neither and occupies a more middle ground that day-zero ambulation does not appear to have any significant differences on opioid consumption. However, within this study, opioid consumption was only measured within the inpatient phase of recovery, meaning that participants who remained in hospital longer had longer opportunity to consume a larger total opioid amount, or to have a reduced mean consumption per day with a prolonged length of stay where pain would be expected to reduce as post-operative time increases.

6.5.8 Antiemetic consumption

This study saw no significant differences in anti-emetic consumption during the inpatient phase of recovery between groups. This appears to be at odds with the incidence of PONV, which was observed as higher within the Control group with 36 incidences compared with 23 incidences in the Rapid group, and the consumption of the opioid analgesia being the same between groups.

This may be due to nursing practices specific to the unit where this study was conducted, and may be observed differently in other units which may offer a more prophylactic, aggressive and/or multi-modal approach to antiemetic medications. Nonetheless, observing equal anti-emetic use between the groups in the present study adds confidence to findings on incidence of PONV, with a major potential confounder accounted for. Also, as with opioid consumption, this study only examined the use of anti-emetic medications up to hospital discharge, meaning that any outpatient phase consumption would not have been captured. Raphael et al. (2011) observed the opposite finding, with increased rates of PONV in their fast-track group; which included day-zero ambulation, although within this study they suggest this finding may be due to different event recording between groups. As such, with two studies providing contrasting results, further research is required on this topic.

6.5.9 Financial impact

This study saw a 17% saving in cost on bed days between groups. Extrapolated to the same hospital across 2019 could have seen this saving on 713 THRs, equating to a potential annual saving of more than £145,000 on bed days. While this in itself indicates a benefit, the impact of more bed day availability could have further impacts on improving operative throughput and waiting lists.

While the current study was single-centred and therefore specific to the unit examined, two other studies have observed financial savings with savings of $4000 USD and $10,471 USD per patient respectively (Larsen 2009; Andreasen et al. 2017). While the present study's findings are more modest in comparison, both of these previous studies examined cost-savings across the entirety of the patient pathway, whereas the present study was based purely on bed day savings. Despite this, all published studies contribute to a trend of cost saving from the implementation of day-zero ambulation.

6.5.10 Participant Experience

While already recognised during the feasibility study as a method with some significant limitations in examining participant experience of day-zero ambulation. For generalisability, quantitative responses to the questionnaire used in the present study indicate that day-zero ambulation does

not result in a poorer patient experience, with no differences seen between groups. This does support the findings of Husted et al. (2009) who also reported no significant differences in their questionnaire gathered data. However, within the Husted study, the participant experience questionnaire was not validated or published making it difficult to appraise the reliability and validity of its findings. Beyond this, quantitative findings alone lack the richness to draw further conclusions as to how or why. Responses to open-ended survey questions will be examined in triangulation with quantitative results and semi-structured interview findings not included within this thesis as part of the nested qualitative study.

6.6 Limitations

This study has several limitations

6.6.1 Single Centre Study

This study was conducted as a single centre study in a specialist elective orthopaedic unit. As such, the findings of this study can be considered specific to the research site. While this site is mostly representative of elective orthopaedic services within the UK, findings would be strengthened by future research being conducted multi-centre.

6.6.2 Blinding

Within this type of study, it was not possible to blind participants to the treatment they received as they were active participants in this. Similarly, blinding of the treating clinicians was not possible.

However, while possible, assessor blinding was not used in this study. This was for pragmatic reasons with the study being conducted without funding and with a small research team as part of a PhD programme.

6.6.3 Opioid and antiemetic consumption

Collection of opioid and antiemetic consumption within the present study was limited to the inpatient phase of recovery. As such, this study would not be sensitive to between group variation of these medications consumed following discharge from hospital.

6.6.4 Participant Experience

The main limitation was that experience questionnaires were given to participants and collected by members of the physiotherapy team responsible for the care of the participant. Although anonymous and with the same conditions across groups, questionnaire responses may still have been subject to response bias.

6.6.5 Economic analysis

While this study reported a financial saving relating to bed-day savings, the calculation of this was significantly simplified in comparison to a properly designed and implemented economic evaluation study. Due to this study being unfunded and conducted with limited resources it was never designed to perform a full economic evaluation. While the excess bed days reference cost used within this study claimed to incorporate all ward costs, this figure is a crude national figure and may not be representative of all UK units. The two most recent economic reports of orthopaedic services in the UK have shown variability in cost between sites for the delivery of THR (Briggs 2015; GIRFT 2020). Furthermore, there may have been other costs or saving incurred in other healthcare costs or non-healthcare costs which were not accounted for within this study.

6.7 Conclusion

Day-zero ambulation following primary elective THR is safe and does not adversely influence patient experience and post-operative pain. The present study provides evidence that it speeds functional recovery within the inpatient phase of rehabilitation. While changes in length of stay were modest, day-zero ambulation appears to reduce variation in length of hospital stay, which in the case of this study led to a reduction in total bed days required in the intervention group and a subsequent cost-saving.

7 - Discussion

7.1 Introduction

7.1.1 Reminder of research aims and hypotheses

As a reminder, this study aimed to answer the following overarching research question 'what is the effect of a Rapid ambulation physiotherapy protocol when compared to standard care on:

- Length of hospital stay
- Patient experience
- Time taken for participants to be physiotherapy ready for discharge
- Functional recovery
- Incidence of post-operative complications
- Post-operative pain
- Post-operative antiemetic and opioid consumption
- The financial cost-to-hospital of a primary THR

While the discussion in Chapter 6 summarises this study's empirical findings in context of the wider literature, this chapter aims to discuss the implications and real-world application of these findings.

7.1.2 Summary of key findings

Systematic Review

- Limitations in the published literature give low confidence in how much day-zero ambulation affects length of stay
- There is a lack of high-quality evidence examining how day-zero ambulation may affect post-operative pain, functional recovery and participant experience

Fully Powered RCT

- Statistically significant difference in median length of stay seen through reduced variation in length of stay when day-zero ambulation was employed.

Day-zero ambulation resulted in:

- Significantly reduced time taken to be physiotherapy ready to leave hospital.
- Significantly faster achievement of functional milestones in recovery
- Significantly reduced time to reach functional independence post-operatively
  - With day-zero ambulation being the most significant predictive factor of early functional independence compared with other co-variates.
- No significant differences in the incidence of post-operative complications
- Reduced incidence of post-operative dizziness, PONV and orthostatic hypotension.
- Increased incidence of post-operative wound ooze.
- No significant differences in post-operative pain on day 0 or day 1.
- Significantly reduced pain on initial ambulation
- No significant differences in the consumption of opioid analgesia or anti-emetic medications.
- Financial saving of 17% on reduced bed days across the study cohort
- No clinically important differences in participant experience based on questionnaire data.

7.2 Implications

7.2.1 Length of stay and Service Efficiency

As discussed in 6.5.2, this research observed an identical median length of stay of 3 days across both groups. While the findings did not show a difference of 1 day between group medians as was required for clinical significance, it did observe a difference of 1 day in the interquartile range between groups. This indicates reduced spread in length of stay data from the median. In turn meaning that day-zero ambulation reduced the variation in length of stay compared to standard care.

One factor affecting the rate of flow through elective orthopaedic pathways is having ward beds available for post-operative patients to occupy during their recovery. Admissions are planned by predicting when a bed will become available based on an expected length of stay. Although anecdotal evidence, observations in clinical practice of how variation and unpredictability in length of stay can lead to an unavailability of hospitals beds due to unexpectedly delayed discharges. This leads to cancellations of planned surgeries to the detriment of the patient and waste of surgeon and theatre time. Sahraoui & Elarref (2014) reported a nearly 18% late cancellation rate in elective orthopaedic surgery, of which 26% was related to overbooking and bed availability problems. Reduced variation in length of stay indicates a better ability to predict length of stay and consequently the rate of flow through the elective pathway.

If translated into mainstream practice, this would be likely to lead not only to financial efficiencies, but also result in bed-day savings. This may therefore improve confidence in operative planning, reduce rates of cancelling elective surgeries, and increase operative throughput. As discussed in section 1.1, various population demographic factors are leading to increasing demand for arthroplasty surgeries. With orthopaedic NHS waiting lists having increased by 59% since April 2018 (Figure 46 **– Trend of increasing numbers of people in England awaiting elective orthopaedic procedures**), optimising the flow through elective pathways is critical to keep up with demand. Consequently, post-operative day-zero ambulation is a low-cost service change, with potentially high value returns for service managers and commissioners.

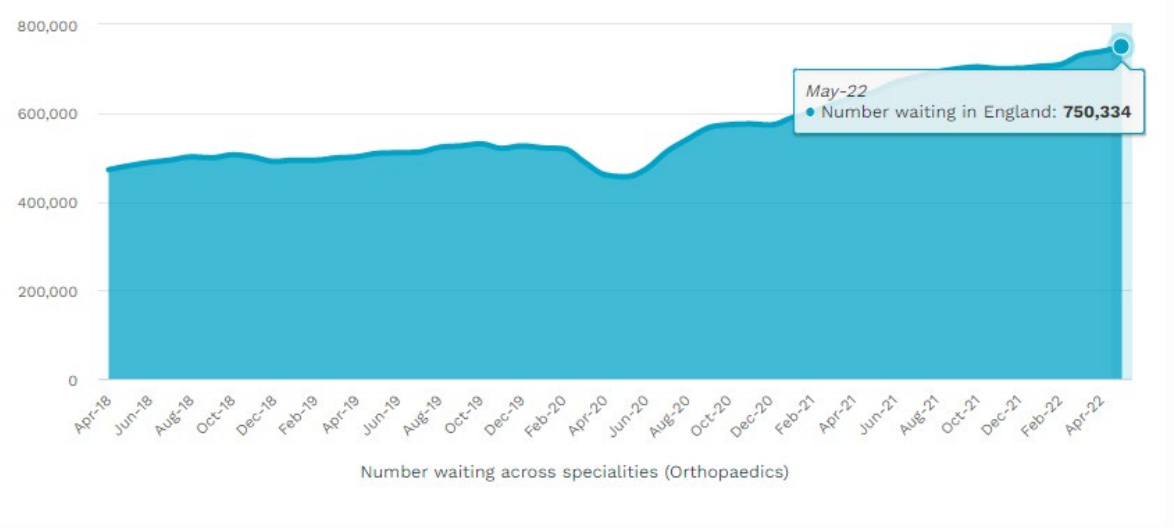


Figure 46 – Trend of increasing numbers of people in England awaiting elective orthopaedic procedures (Lane Clark & Peacock 2022)

If we compare waiting list numbers in Figure 46, with the number of completed hip procedures reported by the National Joint Registry (njrcentre.org.uk 2022) graphically shown in Figure 47, we see a plateau in numbers of surgeries carried out between 2014 and 2019, despite a steady and continuing increase in waiting list numbers. This suggests that the national capacity for the delivery of elective hip procedures had been reached some years ago, and in the absence of increased funding and resource, orthopaedic departments will need low-cost efficiency savings in order to have any hope of keeping up with national demand.

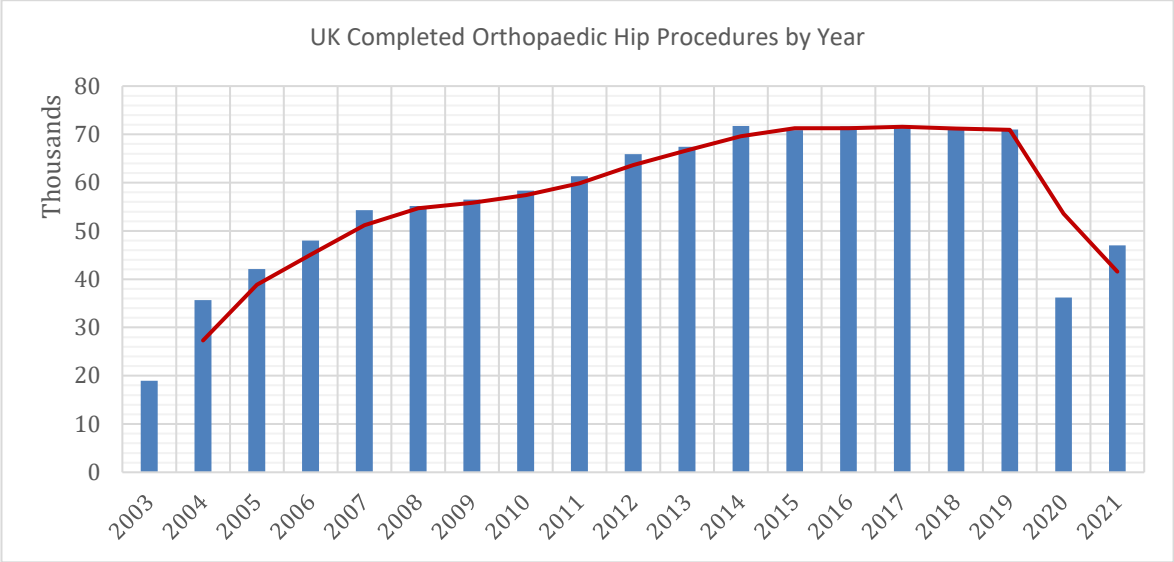


Figure 47 Numbers of hip arthroplasty procedures carried out each year - Collated from National Joint Registry Stats Online Data up to 25/07/2022 (Please note impact of the COVID-19 pandemic from 2020 onwards)

The COVID-19 pandemic has only served to worsen this picture, with the numbers of hip procedures completed in 2020 being the lowest seen in 16 years. However, even before impact of COVID-19, several providers across the world have embarked on trialling 'outpatient' hip arthroplasty where patients receive their surgery and are discharged home within a single day. This approach has so far been selective in which patients it is appropriate for, opting for the youngest and fittest patients for safety and effectiveness reasons due to no overnight stay. This is reflected in the published literature with most studies examining outpatient THR having used selective recruitment based on age, minimal comorbidities and good social support (Berger et al. 2009; Hartog et al. 2015; Dorr et al. 2010; Klein et al. 2017). All of these studies reported the average ages of their cohorts in the 50s, far below the median age category for THR in the UK of between 75-79 (NHS England 2020), meaning that researched populations are not at this time representative of the wider population served. As an intervention, day-zero ambulation can be a component in both outpatient THR and inpatient THR pathways, meaning the current study is likely to have relevance, even if there is an increase in research and the adoption of increased outpatient arthroplasty. Also, there are always likely to be patient cohorts who are not suitable for outpatient THR due to risk and compassion.

Ultimately, day-zero ambulation is an intervention designed to help patients achieve their physiotherapeutic discharge goals. Not all participants achieved early discharge, with other medical and nursing discharge criteria holding them in hospital, such as deranged post-operative blood results, medical complications or delays in the availability of family in providing social support to name a few examples. This was observed through the difference in time taken to be

deemed physiotherapy ready to leave hospital versus the actual length of stay. Further optimisation of these delay factors could further reduce length of stay and length of stay variability.

Another observation from this study was that despite all participants receiving two physiotherapy sessions per day during their inpatient period, the bed day savings observed within the RAPID group resulted in less inpatient days over which physiotherapy needed to be provided (Shown in **Table 7-1**). This meant that the total number of physiotherapy sessions delivered to the RAPID group was 18% lower than observed in the CONTROL group. This suggests that day-zero ambulation may ultimately reduce the burden on inpatient orthopaedic physiotherapy services.

Table 7-1 Number of physiotherapy sessions delivered per group

	CONTROL Group	RAPID Group	Difference	% Difference
Number of Physiotherapy Sessions	721	589	132	18.3%

Although this can be considered a low-cost intervention, any adoption of day-zero ambulation as an established service change would require increased staffing of post-operative physiotherapy teams. For example, in order to treat patients operated on later in the day, physiotherapy would have to run later into the evening, perhaps until 9 or-10pm. This may require some investment or could have some knock-on effects on service delivery at other times during the day and could prove challenging across a 7-day service. However, as seen above, this may be offset by reducing the overall number of physiotherapy contacts needed as an inpatient.

7.2.2 Function

The present study provides a good indication that during the inpatient phase of recovery, day-zero ambulation results in a speedier achievement of physical function and functional independence. As discussed in 6.5.3, other published works were mostly in agreement with this finding (Banerjee 2014; Karim et al. 2016; den Hertog et al. 2012), with only Juliano et al. (2011) in disagreement, showing no significant differences between groups. Unfortunately, of the three studies with supportive results, two examined day-zero ambulation in TKR only (Banerjee 2014; den Hertog et al. 2012). However, Karim et al. (2016) although looking at walking distance as the sole functional outcome, reported results which showed a similar pattern to that observed in this study, showing a very similar trend to that seen within Figure 30 in the results of the current study, whereby there appears to be a greater functional difference between groups at the

beginning of the inpatient phase of recovery. However, this functional gap narrowed as post-operative time increases.

Although neither this study, or Karim et al. (2016) examined post-operative function over a longer follow-up period, this suggests that the functional benefits of day-zero ambulation are reaped mainly within the inpatient period and not lasting in effect. While the functional effects may be short lived, earlier functional independence is likely to reduce the burden of care on nursing teams and release nurses to focus on high acuity patients, secondarily contributing to operational efficiency and service quality. Furthermore, it would be logical that earlier post-operative independence and faster return to function is preferential for and mentally beneficial to the patient, fostering an improved experience. However, the author was unable to find any published works pertaining to the mental health benefits of early functional independence, or any studies examining the lived experience of transient post-operative dependence in an orthopaedic cohort.

The present study and all previously identified studies on this topic focus on functional mobility and not on other domains of function which may be as important or potentially more important to patients, such as gaining independence in personal care activities, activities of daily living and post-discharge return to hobbies and activities. Further research would be required to confirm suspicions that there are no lasting differences in function between groups and to examine function through more comprehensive measures of function including personal care and return to hobbies and activities. These lines of enquiry would suit such approaches as multi-disciplinary or user led research to focus on issues important to patients and carers.

7.2.3 Post-op Complications

The primary outcome of this study was to examine intervention effectiveness on length of stay, consequently, this study was powered to this effect. As is common in RCTs which report adverse events findings (Phillips et al. 2019), the current study was never powered to detect significant or clinically important differences in adverse events. Nearly all of the serious post-operative complications expected following THR have an expected incidence of less than 2% (Heo et al. 2020) making the numbers required to power a study to compare this between groups prohibitively high to recruit within the scope of this PhD project.

When examining the wider published literature on this topic, there are a wealth of papers examining readmission rates, complication rates and mortality. While most of the literature paints a positive picture of complication rates, there are a lack of comparative studies on this topic. Almost all authors have published complication rates through observational study designs, lacking

a control or comparison group upon which to judge the influence of day-zero ambulation. Within these studies all report acceptable or favourable readmission rates (Berger et al. 2009; Husted et al. 2008; Husted, Otte, Billy B. Kristensen, et al. 2010; Robbins et al. 2014; Dorr et al. 2010; Gulotta et al. 2011; Khan et al. 2014; Stambough et al. 2015). No significant differences or improvements in complication rates (Husted, Otte, Billy B Kristensen, et al. 2010; Jorgensen et al. 2013; Banerjee 2014; Gulotta et al. 2011; Khan et al. 2014; Krenk et al. 2014; Jorgensen & Kehlet 2013; Klein et al. 2017) and no significant differences or improvements in post-operative mortality (Husted, Otte, et al. 2011; Husted, Otte, Billy B. Kristensen, et al. 2010; Jorgensen & Kehlet 2013; Khan et al. 2014; Malviya et al. 2011; Savaridas et al. 2013). Within most categories of post-operative complications, this study supports these findings, with no significant differences in complication rates. The one exception to this was an increased incidence of post-operative ooze. As such, this is discussed in detail in the next section.

To the author's knowledge, there are only three published studies which indicate increased incidence of adverse events associated with day-zero ambulation. Raphael et al. (2011) found a much higher incidence of PONV within their intervention group. The results of the current study contradict this, with reduced PONV rates observed within the RAPID group. Of note, Raphael's study did also operate different analgesic pathways between groups, and this may be the more likely culprit of the increased PONV rates observed.

While not containing a comparison group, Pitter et al. (2016) examined pathways inclusive of day-zero ambulation in participants over 85 years of age and reported higher than expected readmission rates of 14.2% after 30 days, and 17.9% after 90 days. While the present study did not restrict participation in the research based on age, the median age of the sample cohort (69) was well below the age of 85 years. As such this study cannot challenge the findings of Pitter et al. (2016), meaning that the question of safety in the very elderly category of patients remains.

The present research mirrors much of the current literature base in examining complications up to a period of 90 days post-operatively. This is selected most often as the tipping point whereby causality is most likely to be related to surgery and post-surgical interventions. As such, there is little published information about complications or readmissions after this time period. One of the main areas of increased complication rate observed within this study was in wound healing and prolonged post-operative ooze. As such, this is discussed in detail in the next section.

7.2.3.1 Wound Healing

Within this study we observed an increased rate of post-operative wound ooze associated with day-zero ambulation. In normal physiological conditions, injuries limited to the epidermis layer of the skin heal very efficiently and with little to no scarring. This means that the epithelial barrier protecting the body against infection can be restored quickly with minor lesions limited to the epidermis. However, injuries to the deeper dermal layer as seen within the deep incision made for hip arthroplasty require longer healing times leading to scar formation. This loses the original tissue structure and function and prolongs the time period for the restoration of the functional barrier of the skin. Ireton et al. (2013) found that within the first 4 post-operative days, the surgical wound has minimal inherent strength, with the dermal edges only held together with a haemostatic plug and sutures. Disruption of the normal tissue healing response can result in delayed wound healing, excessive scarring, or in extreme cases chronic wounds (Eming et al. 2014). In light of this Barnes et al. (2017) advocates the minimisation of mechanical forces in the wound environment to improve wound healing and reduce scar formation

As such mechanical disruption of the wound could be the mechanism by which an increased incidence of prolonged wound ooze was observed in participants who started ambulation on day zero. Physiologically, ambulation is likely to mobilise the wound edges, and could feasibly disrupt the fibrin scaffolds which begin forming within the first 48 hours of wound healing (Phillips 2000).

It is unclear from this research whether earlier ambulation provides a significantly greater mechanical disruption to the wound than would be seen in standard care, but the median 16.4 hours longer the control group had for fibrinogenesis to occur prior to ambulation could explain the lower incidence of excessive or prolonged wound drainage observed. When this is coupled with other research, the picture of risk increases, with prolonged wound drainage shown to be predictive of superficial surgical site infection (Saleh et al. 2002), with Patel et al. (2007) showing each day of prolonged wound drainage increased the risk of wound infection by 42%.

Concerningly, persistent wound drainage, wound dehiscence, and superficial surgical site infection have all been shown to be risk factors in the development of peri-prosthetic joint infection (Zhu et al. 2015b; Shahi et al. 2019a; Kapadia et al. 2016). Peri-prosthetic joint infection is considered one of the most challenging complications following THR, responsible for 19% of early revision surgeries (within 2 years or the original surgery) and 9.9% of revisions across the lifespan of the arthroplasty (Kelmer et al. 2021). Indeed, Amlie et al. (2016) showed a three times increased risk of revision surgery due to deep infection within 3 months post-surgery in a cohort of patients who underwent day-zero ambulation compared to standard care. In addition, while less serious in implications than infective complications, day-zero ambulation could theoretically

contribute to the development of more hypertrophic or keloid scars and a less aesthetically pleasing scar for the patient.

While the benefits of day-zero ambulation seem to outweigh these risks, it may be prudent to consider the appropriateness of day-zero ambulation in patients who hold known risk factors for delayed wound healing such as, morbid obesity, vascular compromise, diabetes mellitus, rheumatoid arthritis, ongoing corticosteroid therapy, nutritional compromise, immunological compromise or a history of wound healing problems or leg ulcers (Patel et al. 2007; Shahi et al. 2019a).

Within the current study, co-morbidity of vascular, nutritional or immunological compromise and active corticosteroid treatment were not observed as part of the study cohort, and screened prospective participants were excluded for safety. As such, adopting day-zero ambulation wholesale could expose people who have increased risk of wound drainage problems than was representative in this study's cohort. In Amlie et al's (2016) study, the research team were clear that because their fast-track pathway included a combination of changes from standard care including day-zero ambulation, altered anaesthetic medications, the use of COX-2 inhibitors, the use of uncemented prosthetic components and high volume local anaesthetics meaning they were unable to attribute an increase in revision surgery rate to any one particular intervention. Consequently, advice from their study was to use caution when employing fast-track pathways in patients already at high risk for infection. Considering this PhD project's findings, day-zero ambulation could well have been a contributing factor to the Amlie et al study's findings. Accordingly, this researcher would advise caution in the use of day-zero ambulation at this time with patient's already at high risk of delayed wound healing. Further research in this area could investigate safety in these higher risk cohorts and identify the effects of day-zero ambulation on pathological scar formation.

7.2.4 Post-op pain

The present study found no significant difference in post-operative pain whether participants started ambulation on day 0 or day 1. In practical terms, this means this study supports the use of day-zero ambulation given the positive effects observed within other outcomes, without any adverse effects on pain.

Theoretical mechanical wound disruption associated with day-zero ambulation could trigger increased pain through increasing the release of inflammatory cytokines and prolonging capillary drainage and haematoma formation. While the author was unable to find any publications

evidencing this physiologically, Klein et al. (2017) observed an increased rate of haematoma formation in their patients who underwent day-zero ambulation in combination with aggressive anticoagulation. This potential upregulation of inflammatory cascades and haematoma formation are both potential mechanisms for triggering nociceptive pain pathways. As such, day-zero ambulation could be expected to trigger a latent increased pain response in the patient on subsequent post-operative days.

However, this was not observed in the present study, with no significant differences in day 1 pain scores between groups. Additionally, pain during first ambulation was significantly lower within the intervention group. This is likely to be due day-zero ambulation capitalising on the residual effects of peri-operative pain management and spinal anaesthetics; keeping the patient more comfortable during their first ambulation. While the pain numerical rating scale used within this study is well validated and simple to administer, the author recognises the limitations in using the numerical rating scale in evaluating pain of being one dimensional and not accounting for the complexities of the pain experience.

As was seen within Chapter 2's systematic review, there were no pre-published studies which examine pain that reached a high enough methodological standard to be included in the present systematic review. Indeed, the present study is the first RCT to report the effects of day-zero ambulation on post-operative acute pain following THR. Furthermore, this study examined and reported on the significant confounder in this domain of opioid analgesic consumption, which is most often employed as a mixture of regular administration and patient requested administration. This means that consumption rates have the potential to differ widely between individuals and directly affect post-operative pain.

Within the wider literature, there are two studies which align with the current study's findings. Temporiti et al. (2020) showed no significant differences in post-operative pain between groups, and Andersen et al. (2009), reported 'acceptable' median pain scores in their observed population, but did not include a comparison group. There are several studies which have reported reduced pain outcomes, but are restricted in their applicability to this research as they contain significant concomitant analgesia pathway differences between groups (e.g. Bottros et al. 2010; Isaac et al. 2005; Raphael et al. 2011) or only examined participants undergoing TKR (e.g. Holm et al. 2010; Isaac et al. 2005). Of interest, while examining TKR only, den Hertog et al. (2012) reported increased analgesic consumption within the intervention group over the first two post-operative days in comparison with their control group. The present study did not break down analgesic consumption to specific days of administration and therefore cannot support or contradict the findings of den Hertog et al. It is feasible the same effect could have occurred

within the present study. This may warrant further investigation, with analgesic consumption also examined over a longer post-operative duration.

While examining post-op pain over this time period should cover the period of peak pain which has been reported to take place on POD 1 (Wylde et al. 2011), this study will not have been sensitive to differences in post-operative pain later on in the inpatient stay or following discharge.

7.2.5 Patient Experience

As highlighted in Chapter 2 there is very little published research focussing on patient experience of day-zero ambulation following THR. This study's questionnaire based findings suggest no clinically important difference in patient experience between groups, and doesn't contradict the only other study which has published survey data on this (Husted et al. 2009).

Practically the present study indicates that day-zero ambulation could be implemented, without concern of adversely affecting patient experience. However, more research is needed to properly present a richer picture of how day-zero ambulation affects the experience of post-operative recovery.

7.3 Strengths of this Research

Overall, this PhD project had some significant strengths in addressing the research question, allowing it to make a unique contribution to the body of evidence in this domain. This section discusses the key strengths of this study in detail.

7.3.1 Isolation of Day-Zero Ambulation as an Intervention

To the author's knowledge the present study is the only study to have isolated day-zero ambulation as an intervention with participants solely undergoing THR. Several other studies have isolated day-zero ambulation as an intervention (Chen et al. 2012; den Hertog et al. 2012; Karim et al. 2016) but amalgamated results with participants undergoing TKR. Okamoto et al. (2016) did isolate day-zero ambulation as the sole intervention with participants undergoing hip surgery, however, their study cohort was inclusive of participants undergoing hip resurfacing.

7.3.2 Reporting Non-Parametric Descriptive Statistics

None of the studies reviewed as part of the systematic review reported their results in terms of the median. In fact, within the wider literature, only 3 published studies were identified which did report length of stay data in terms of the median (Husted, Lunn, et al. 2011; Jorgensen et al. 2013; Banerjee 2014). Unfortunately, these studies, while reporting non-parametric statistics, were not

designed to examine the effectiveness of day-zero ambulation. Husted, Lunn, et al. (2011) looked retrospectively at reasons for delayed discharge and had no comparison groups based on intervention. Jorgensen et al. (2013) were examining the use of thromboprophylaxis in a day-zero ambulation cohort and Banerjee (2014) only examined participants undergoing TKR.

By reporting non-parametric descriptive statistics, this study adds to this field of research by providing a more robust and reliable measure of central tendency. In addition, the subsequently used non-parametric comparative testing has been shown to have large power advantages compared to parametric testing in non-normally distributed data (Bridge & Sawilowsky 1999). Furthermore, reporting interquartile range allowed us to observe the difference in spread of length of stay data between the two different groups, showing that the spread of the data in the intervention group was reduced.

7.3.3 Robust and rigorous literature review and background

It is the author's opinion that this project's literature review served as a rigorous basis from which to design the empirical research presented as part of this PhD. The author went to great lengths to ensure rigor and quality by selecting a systematic review methodology, choosing clear eligibility criteria focussed on high methodological quality, and using multiple layers of Cochrane recommended tools (The Cochrane Collaboration 2008) to assess and appraise quality of methodology, publication and risk of bias.

This provided important focus on the methodological limitations seen in preceding research and allowed the author to design an empirical study to address these limitations and make a unique and valuable contribution to this research field.

7.3.4 Properly conducted feasibility study with highly relevant sample size calculation

As discussed within section 4.1, conducting a feasibility study can be burdensome, but provides some definite advantages in helping to develop and improve the research methodology before conducting the main RCT. This was certainly the case in this project, where the feasibility study led to some significant learning and some major study amendments for the fully powered RCT. Below is discussed some of the specific impacts the feasibility study had on strengthening this project:

Strength of key variable relationships and sample size calculation:

The conduct of a feasibility study gave indication that there was likely to be a causal relationship between the intervention and key outcome measures with length of stay within the feasibility study intervention group observed as a median of 1 day shorter. This gave confidence to the researcher that this line of enquiry was worth further pursuit. Furthermore this data also allowed sample sized calculation using highly relevant data which resulted in a reduction of the target

recruitment numbers as discussed in section 5.4.1. This not only saved study resource, but limited experimental exposure to the correct number of participants, limiting risk and improving the ethical standpoint of the study.

Participant recruitment:

Assessment of procedures for recruitment which took place within the feasibility study allowed some small but significant adjustments to how study information was provided to potential participants and how informed consent was obtained. This affected the recruitment rate significantly. Had a feasibility study not been conducted and these issues addressed, recruitment of the full study cohort may have taken significantly longer and been prohibitive to this piece of research being completed within the allotted PhD tenure.

Identification of unaccounted for confounders:

The feasibility study served to identify and give recommendations for three significant confounders which could have impacted on the scientific validity of the main study's findings. By adopting these recommendations to carry out stratified randomisation and report data for pharmacological analgesia and anti-emetic consumption, the study's findings reach a higher level of validity.

Experience as a novice researcher and clinical research team:

This project was the first embarking of the author as a researcher, and for most of the small clinical research team their first involvement in research. As such, there was a good degree of naivety when entering this process. Conducting a feasibility study allowed both the lead researcher and research team to become familiar with research governance processes, conduct of the required training and correct completion of the study documentation. This experience meant the research team commenced the fully powered study with an existing understanding of the processes and conduct expected of them. While not evidenced, the researcher believes this was extremely helpful in preventing protocol breaches and ensuring the completeness of the data collected.

Trial of data analysis methods and data management:

Once again, as a novice, this was the researchers first experience of collecting, managing, collating and analysing trial data. This experience helped in identifying useful ways of managing and analysing the data. An example of this was in the researcher seeing value in building a trial database to ensure better data collation and storage for the main study, where the volume and complexity of data was expected to be much greater. Similarly, another example was in the

employment of the Clavien-Dindo classification (Dindo et al. 2004) of post-operative complications in order to make more sense of the trial data.

7.3.5 Using an RCT design

The author selected an RCT design with the aim of producing the highest quality of research available within the resources and time available. This design helps to fill a gap in the research with a study which is high on internal validity and low in risk of bias.

7.3.6 End point analysis designed to cover all domains of quality in healthcare – efficiency, effectiveness and patient experience.

This study aimed for end point analyses to examine all of the domains of quality in healthcare (Darzi 2008b). The author feels this is a big strength in improving the relevance of the findings from the current study to clinicians considering day-zero ambulation as a physiotherapeutic intervention.

7.4 Limitations – (What Can't the Results Tell Us?)

7.4.1 Single Centre Trial Design

As discussed in 6.6, a single centre design is one of the weaknesses of this research, reducing the external applicability of this study's findings. A study combining 29 meta-analyses comparing single and multi-centre trials showed that single-centre trials generally show larger intervention effects than multi-centre trials (Bafeta et al. 2012). In addition, Bellomo et al. (2009) advocates that changes to practice guidelines should not be based on evidence from single-centre trials and that careful consideration of the trial methodology and relevance of the clinical context is critical to relating the trial findings to a clinician's clinical setting. This paper also discusses the risk of the findings of single-centre trials being contradicted when examined at a multi-centre level. Furthermore, that single centre trials are typically delivered by a single protagonist who has a-typical expertise and commitment not reflected in standard practice (Bellomo et al. 2009). As a result, the practical delivery of an intervention in practice can be much tougher than indicated from a single-centre trial.

Unfortunately, conducting this trial as a multi-centre study was not feasible within the scope of this PhD project, lacking the required funding and workforce. However, the author feels that the chosen setting is well representative of UK orthopaedic practice and has provided detailed treatment protocols to allow any future readers of this work to compare practice within this study, to practice in their setting.

7.4.2 No Assessor Blinding

While participant blinding was not possible with this intervention, assessor blinding would have been an advantage. Again, this PhD study was unfunded and was consequently conducted by a small research team made up of volunteers. Consequently, it was not feasible to conduct this research with some of the team working as blinded assessors, as all research team staff were required to provide clinical care to participants across their admission.

Research has shown that not blinding assessors can affect study outcomes, Hróbjartsson et al. (2012) showed a 36% exaggeration in odds ratios for binary outcomes. While this casts doubt on this project's finding, there are limitations to assessor blinding itself with implementation of blinding being inconsistent and unsuccessful in more than 50% of trials examined (Monaghan et al. 2021). In the present study, where double blinding would not have been possible due to the active participation required of the intervention, the risk of unblinding incidents through participants revealing to assessors would have been high.

7.4.3 Complex Intervention Research

This thesis was designed to focus on examining the effectiveness of day-zero ambulation as an isolated intervention. This focus was selected in order to answer the binary question of effectiveness, and also address some of the limitations in existing research of examining day-zero ambulation as part of a pathway of concomitant interventions. As has been discussed in 7.3.1, this can be considered a strength of this research. However, if considered through the lens of the MRC framework for evaluating complex interventions (Skivington et al. 2021), this paper highlights how this may also be a limitation of this research.

The MRC framework defines complex interventions as interventions which can be complex in delivery or are complex due to the context within which they are delivered. As discussed in previous chapters, day-zero ambulation in practice does not sit alone as a sole intervention, but rather as a part of a complex pathway. Within a complex pathway such as this, it is arguable how possible or reflective of real-world practice it is to isolate day zero ambulation, as the intervention will be influenced by and could directly influence the context it is delivered within.

The MRC framework advocates the evaluation of complex interventions in the context and flexibility with which it is likely to be employed in practice. This allows judgement of the intervention alongside contextual system factors which may influence the effectiveness of the intervention and also observe effects that the intervention may have on the wider system.

The present research wasn't designed with this in mind and did not have the flexibility in intervention delivery to be predictive of implementation across a range of different hospitals or providers. As such, this research is limited when answering how effective day-zero ambulation is as a complex intervention and the practical advice on how it fits within an elective orthopaedic pathway.

7.4.4 Collection of socio-economic or broader demographic information

While this research did collect some demographic information about the sampled cohort, this was limited to age, gender, CCI scores and ASA scores. There could be an argument that other socio-economic or demographic factors which could have been covariates have been overlooked. Indeed Alvarez et al. (2022) literature review of studies conducted in the United States showed that socioeconomic status could influence patients receiving arthroplasty surgery, with those from lower incomes 5-10% less likely to undergo THR surgery, lower household income was also linked with increased risk of post-operative THR dislocation and 30 day readmissions, but at a lower risk of infection, prolonged hospital stay and blood transfusion. Furthermore Allen (2010) reported increased pain and functional limitations in African-Americans than Caucasians with knee osteoarthritis and Mehta et al. (2018) systematic review reported all included studies found increased pain and reduced function following THR in black ethnic patients. While these results are specific to the United States and a private healthcare system, similar factors could be occurring in UK practice. Collection of more detailed socioeconomic and demographic information such as ethnicity and household income would have enabled the screening of these factors as potential covariates and for baseline comparison between groups. Future research could look to collect this level of demographic information.

7.4.5 Using a questionnaire methodology to measure participant experience

As previously stated, this thesis was unable to include results from the nested qualitative study included within this piece of research. Although the write up and publication of these findings is planned and will eventually supplement the questionnaire data, at this point in time, the author must reflect on the limitations of reporting questionnaire data in isolation.

The content of the employed questionnaire was mainly based on the CQC inpatient survey, providing some reassurance as to the content and construct validity, as well as making the findings highly relevant to frontline clinicians and service leaders. We were also able to obtain an excellent response rate of 99%, where more than 80% is considered the standard for publication

(Fincham 2008). While questionnaires allow sampling of many participants to gather information on their experience, they have several limitations when attempting to answer the research questions. They lack richness in examining patient experience as unlike interviews, the researcher is unable to follow-up or clarify statements, observations or issues highlighted within the questionnaire responses. As such, this makes it difficult to provide a context against which to present quantitative findings and may not help in highlighting new lines of enquiry or in generating ideas for improvement.

7.5 Researcher's Journey and Reflection

This section is reflective and therefore is written within the first person

At concept, this was a topic I had an interest in and was derived from a question within my clinical practice which I could not find a satisfactory answer to within the existing literature. This research project was originally commenced outside of the guidance of this PhD programme and was adopted onto the Doctoral Programme at the University of Southampton towards the end of the feasibility study data collection.

Although I had no experience in designing or conducting research, I felt that I could gain the knowledge and skills in order to answer this question, both for myself, and for any other clinicians out there in the same situation as me. On reflection, there was a degree of naivety involved in selecting and embarking on an RCT design, particularly as I aimed to deliver this without any dedicated funding. At this stage in my journey, I knew I would be working hard, but didn't appreciate fully that I would struggle to deliver this research by working alone.

Conducting the feasibility study brought realisation that it was unrealistic for me to be able to conduct all the different elements required in the promotion, recruitment, conduct, data management and safety reporting required of this RCT on my own. Fortunately, throughout this journey, I was fortunate to have fostered excellent relationships with the team of clinicians which I eventually assembled as my research team. Their willingness and hard work above and beyond their normal clinical roles made it possible to deliver this research.

As the researcher, I am very proud to have been able to see this piece of research through. I believe that conducting a fully powered RCT as part of my research project, although challenging has been an excellent way to learn and suits my style of experiential learning.

7.5.1 Would I do anything differently?

While this project has been fascinating to investigate, it has proved to be quite an extreme way to embark as a novice researcher.

Throughout the project, my decisions on research design and conduct have been driven by a desire to create the highest quality of research which I could manage. As such, my first proper involvement in research was as Chief Investigator in my own RCT with many of my decisions uncompromising in selecting the more challenging route to ensure rigor in my research. An example of this was in adding a 3-month follow-up telephone call to all participants, which created a significant amount of work in contacting participants and reviewing medical records. While admirable, this did lead to a project which escalated in scale beyond that which was required for this PhD programme.

Another prime example of this is being unable to include the nested qualitative study as part of this thesis. This learning has given me some appreciation of the large teams and funding usually required to conduct an RCT and I now appreciate why many of the previously published authors on this topic have opted for study designs lower in the hierarchy of evidence.

Despite this, I feel the learning and rewards of conducting a fully powered RCT outweighed the trials of carrying out this type of research, and as such I would select this design again. However, if I were to offer some advice to myself embarking on this journey for the first time again, it would be to join the PhD programme full-time. Conducting a research project of this size and complexity part-time alongside a demanding clinical role has been an enormous challenge and has been the principle factor in the duration of this PhD project spanning 7 years.

7.6 Nested Qualitative Study

As explained earlier within this thesis document, in order to further explore the domain of patient experience I conducted a nested qualitative study. Although this study is not reported on within this thesis, this nested study aims to provide context to the findings of the fully powered RCT, and potentially pose questions for further investigation into day-zero ambulation which have not been previously recognised.

The aim is for this nested study to be published as a research paper in its own right at a later date, alongside the quantitative study.

An abstract summary of this work is shown in Appendix 37.

7.7 Conclusions

To the authors knowledge this is the only RCT to examine the effect of day-zero ambulation following elective THR in a UK population. It also appears to be the only RCT examining outcomes across the domains of healthcare quality defined by Darzi (2008), which includes patient experience, safety and multifactorial effectiveness of care alongside outcomes to measure service efficiency.

The findings of this project compliment existing knowledge in this field with a high-quality methodology and study design (discussed in 7.3), something which has been lacking in the wider research as identified in Chapter 2. Furthermore, the project findings on post-operative wound ooze raise awareness of this potential pitfall with this intervention, something which has not been examined or reported in other studies.

7.7.1 Recommendations

7.7.1.1 Practical Applications

In conclusion, this PhD thesis has made a unique contribution to the evidence base on day-zero ambulation by using a high-quality methodology, and isolating day-zero ambulation as an intervention. This study can advocate for the use of day-zero ambulation in most patients within primary elective THR cohorts. Day-zero ambulation is low-cost, appears safe, and has benefits in faster functional recovery, earlier return to independence, reduced variability in length of hospital stay and potential cost-savings through cumulative bed day savings without compromising post-operative pain experience or overall patient experience.

However, day-zero ambulation may increase the risk of post-operative wound ooze, which could lead to furthermore serious complications and therefore should be used with caution or avoided in patients who hold risk factors making them already at higher risk of post-operative delayed wound healing.

7.7.2 Further development of this research

To follow-on and further develop this research study, this author would recommend seeking funding to be able to proceed to a multi-centre or cluster RCT design, overcoming some of the limitations presented within this study. This research could also look further into the operational effect of reduced variation in length of stay, and whether day-zero ambulation has real world effects on service level metrics such as surgical throughput and incidence of cancelled surgeries due to bed blocking. As part of this, strong consideration should be given to the design of this

research within the MRC framework for the evaluation of complex interventions. A multi-centre or cluster design could provide the flexibility in intervention delivery to allow the evaluation of contextual factors on practical success, and the influence of day-zero ambulation on the wider pathway. This would be further strengthened by including a full economic analysis with consideration given to the collection of cost data beyond length of stay. This could include costs for medications, subsequent general practitioner visits and/or readmission costs.

Following the production of a multi-centre RCT, I believe that this field of research could be strengthened through meta-analysis using only the most contemporary studies. This is likely to produce a meta-analysis result which is less subject to significant heterogeneity and therefore viable in producing a representative effect-size, but also of relevance within existing modern enhanced recovery pathways.

Another core outcome which should be targeted for future research is in how day-zero ambulation affects the longer term functional outcomes of patients across more traditional long term follow-ups periods such as patient reported outcome measures at one year post-operatively. The author will proceed to write-up and publish the nested qualitative study to directly add context and supplement the findings presented in this thesis.

7.7.3 Broader Future Research

This project would advocate for the following further research around the topic of day-zero ambulation:

Further investigation into the incidence of wound ooze and safety of day-zero ambulation in patient groups at higher risk of delayed wound healing or prolonged wound ooze issues. This should focus on a longer post-operative follow-up period and specifically look for differences in the incidence of peri-prosthetic infection whether conservatively monitored and managed, or treated with revision surgery. Although of less importance, this research could also look to examine the effect of day-zero ambulation on incidence of pathological scar formation and patient satisfaction with scar aesthetics.

Further investigation into the effect of day-zero ambulation on post-operative pain, looking to measure pain over a longer post-operative period and look for time related patterns in analgesic consumption.

Further research into the effects of day-zero ambulation on return to independence in function beyond mobility. In particular examining the effect of day-zero ambulation on time taken for independent return to personal care, activities of daily living and return to hobbies and activities.

Appendix 1 Literature Search Strategy

Search Number	Databases Searched	Search Terms and Limits	Number of Results	Comments on Results
S1	MEDLINE, CINAHL,	THR **OR** “total hip replacement” **OR** THA **OR** “total hip arthroplasty” **OR** ‘joint replacement’	76047	N/A
S2	MEDLINE, CINAHL, AHMED	Rapid **OR** Accelerated **OR** “fast-track” **OR** “fast track” **OR** "day zero" **OR** "day 0"	745184	N/A
S3	MEDLINE, CINAHL, AHMED	Ambulat* **OR** walking **OR** mobilisation **OR** mobilization	364330	N/A
S4	MEDLINE, CINAHL, AHMED	S1 AND S2 AND S3 **Since 2005**	309	63 identified via title for further investigation
S5	EMBASE	THR **OR** “total hip replacement” **OR** THA **OR** “total hip arthroplasty” **OR** "joint replacement"	59893	N/A
S6	EMBASE	Rapid **OR** Accelerated **OR** “fast-track” **OR** “fast track” **OR** "day zero" **OR** "day 0"	835264	N/A
S7	EMBASE	Ambulat* **OR** walking **OR** mobilisation **OR** mobilization	334050	N/A
S8	EMBASE	S5 **AND** S6 **AND** S7 - **Since 2005**	180	14 further papers identified via title for further investigation

Appendix 2 Literature Search Meta Summary Table

No	Authors	Title	Study Type and (Hierarchy Rank)	Study Purpose	Sample Size	Outcome Measures	Relevant Findings	Specific Methodological Strengths	Relevant Methodological Weaknesses
1	(Andersen et al. 2009)	Sub-acute pain and function after fast-track hip and knee arthroplasty	Prospective, consecutive observational study (6)	To describe the prevalence and intensity of sub-acute pain, opiate consumption, side-effects and function at 1-10 and 30 days post fast-track THR or TKR	N = 100 50 THR 50 TKR	Self-assessment: Pain VAS PONV Type and total use of opioids Did patient leave home each day	Acceptable levels of post-op sub-acute pain in patient's discharged early following fast-track rehab protocol When a multi-modal analgesia regimen used	Standard operative procedures Separate results presented for THR and TKR THR – representative demographics	Observational study – no comparison with standard care Is leaving the house each day representative of function? Conclusions based on THR and TKR combined
2	(Berger et al. 2009)	Newer anaesthesia and rehabilitation protocols enable outpatient hip replacement in selected patients	Observational study (6)	To assess the feasibility and safety of outpatient THR	N = 150	Rate of hospital discharge on the day of surgery Average time to discontinue the use of walking aids Readmission rate	Recommended outpatient THR as safe No major complications – 2 x visits to A&E within the first 2 weeks post D/C Average time to wean from walking aids 4.1 days No incidences of DVT/PE All patients discharged home on the same day as surgery	PT commenced 5-6 hours post-op 3 month follow-up Specific to THR	Significant other pathway changes: Analgesia, surgical approach/technique, anti-emetic regime changes Dedicated nurse to manage D/C delay factors Aggressive treatment of hypotension including blood transfusion Pre-operative gait training Selection bias – patients opting in/out of intervention at will. Large proportion of young patient s

									74% male No control group – no comparison No randomisation in selection
3	(Berger 2007)	A comprehensive approach to outpatient total hip arthroplasty	Description of post-operative protocol for outpatient THR used locally.	To describe the protocol used for outpatient THR used locally	N/A	None	None	N/A	Not an experimental paper Doesn't provide empirical data about effectiveness
4	(Husted 2012)	Fast-track hip and knee arthroplasty: Clinical and organisational aspects	Doctoral thesis paper – summarises the findings of other research papers completed as part of authors doctorate	Summarise the findings of doctoral project on fast-track hip and knee arthroplasty	N/A	N/A	Summary of findings discussed in other papers reviewed.	N/A	N/A
5	(Husted et al. 2009)	What determines length of stay after total hip and knee arthroplasty? A nationwide study in Denmark	Retrospective audit (6)	To identify logistical and clinical areas of importance for length of stay (LOS) by identifying departments with short and long LOS and to evaluate their set-up To evaluate patient satisfaction in relation to LOS.	8 Departments 563 patients for satisfaction follow-up.	Identification of any clinical or organisational differences between departments Patient satisfaction between departments	Mean LOS for TKR and THR was 7.4 Shorter LOS seen in specialised units The two departments with the shortest LOS routinely commenced mobility on the day of surgery No significant differences in patient satisfaction between departments – regardless of LOS		Audit methodology Doesn't specifically compare rapid mobilisation with anything – was just present in two departments No clear explanation of how patient satisfaction was measured
6	(Husted et al. 2008)	Predictors of length of stay and patient satisfaction after hip and knee replacement surgery: Fast-track experience in 712 patients	Prospective Descriptive study (6)	To identify patient characteristics associated with LOS and patient satisfaction after total hip and knee replacement surgery	N = 712	LOS Readmissions Patient satisfaction	Some characteristics were predictive of reduced LOS Age Gender: Male Not living alone Pre-op use of walking aids Weekday of surgery. ASA score Need for blood T/F 8% of patients stayed more than 5 days	Unaltered post-op pain management programme Patients treated under fast-track mobilisation	THR and TKR Intervention group only. Therefore only descriptive data – not able to compare with standard care No clear explanation of how patient satisfaction was measured – apart from mentioning questionnaires

							Correlation between LOS and some aspects of satisfaction: Information given Operating room stay Nursing Pain treatment Doctors rounds LOS Entire stay overall 5% of THR readmitted within 3 months 2% needed additional surgery 22% of THR needed blood transfusion		
7	(Husted, Lunn, et al. 2011)	Why still in hospital after fast-track hip and knee arthroplasty?	Case Control Study (5)	To determine the specific reasons why patients remain hospitalised during the first 1-3 days post THR and TKR	N = 207	LOS Reasons for not being discharged – assessed twice daily	Median LOS = 2 days for THR and TKR Mean LOS = 2.2 days Pain, dizziness and muscle weakness main reasons for delaying discharge PONV on days 0 and 1 <13%	Standard operative procedures Patients treated under fast-track mobilisation	No control group / no comparison Examined both THR and TKR
8	(Husted, Otte, et al. 2011)	Fast-track revision knee arthroplasty	Descriptive study (6)	To assess whether patients undergoing revision TKR might benefit from fast-track surgery	N = 29	LOS Morbidity Mortality Patient satisfaction	Median LOS 2 days No deaths within 3 months 2 readmissions within 3 months Patient satisfaction was high – median = 10		Selected sample No control group or comparison group Not clear as to how patient satisfaction was measured
9	(Husted, Otte, Billy B. Kristensen, et al. 2010)	Readmissions after fast-track hip and knee arthroplasty	Quality control study (6)	To determine if using fast-track surgery for THR or TKR increases post discharge readmission rates	N = 1731	90 day readmission rates 90 day death rates	LOS decreased from the start of the study (6.3) to 3.9 days for THR and 4.6 to 3.1 days for TKR Death rate = 0.8% within 90 days Risk of death due to VTE = 0.17% Overall surgery related mortality rate of 0.35% 225 pts readmitted 103 readmitted after THR = 10.9%	Large participant numbers 90 day follow-up period	No control group Progressive pathway changes over the course of data collection 2004-2008. Changes in analgesia No comparison between groups Relies on the findings from other studies to make the conclusions that fast-track surgery reduced

							Higher risk of readmission after TKR than THR 749 days of hospitalisation required due to readmission after THR Incidence of PE after THR = 0.21% 2 confirmed DVTs in the THR group 51 dislocations within 33 pts within 90 days Significantly reduced rate of dislocation with reduced LOS. No increase in readmission rates Dislocation rate does not increase by using fast-track surgery.		
10	(Husted, Otte, Billy B Kristensen, et al. 2010)	Low risk of thromboembolic complications after fast-track hip and knee arthroplasty	Descriptive Study (6)	To determine the risk of post-operative VTE and VTE related death post fast-track THR or TKR	N = 1977	30 and 90 day readmission rates Focussing on DVT, PE or sudden death	Pts stopped LMWH on hospital D/C 3 deaths related to clotting episodes – overall VTE related mortality of 0.15% In the last 2 years with shortest LOS. Risk of PE was 0% after THR In the last 2 years with shortest LOS risk of DVT was 0.51% after THR Very low rates of clinically symptomatic VTE and deaths	Large participant numbers 90 day follow up period	No control group Changes in analgesia treatment part way through data collection No comparison between groups Relies on the findings from other studies to make the conclusions that fast-track surgery reduced
11	(Jans et al. 2015)	Decreased heart rate variability responses during early post-operative mobilisation	Descriptive Study (6)	To identify and characterize possible abnormal autonomic postural responses that could contribute to	n = 23	Arterial pressure responses to postural change	39% incidence of orthostatic intolerance at 6hrs post-op 22% OI at 24 hours Drop of 18mmHg sitting to standing 6hrs post op Highlights orthostatic hypotension as a potential problem with RAPID patients		Small participant numbers No comparison between groups

				the pathophysiology of postoperative impaired arterial pressure regulation					
12	(Jans et al. 2012)	Orthostatic intolerance during early mobilization after fast-track hip arthroplasty	Descriptive Study (6)	To determine the incidence rate of orthostatic intolerance after primary unilateral THR	n = 26	Incidence of post-op orthostatic intolerance	11 (42%) and five (19%) patients had OI 6 and 24h after surgery, respectively At 6hrs, 9 showed objective systolic BP drop. No association between OI and bleeding, postoperative Hb concentration, or opioid use.		Small participant numbers No comparison group
13	(Jørgensen & Kehlet 2013)	Fall-related admissions after fast-track total hip and knee arthroplasty – cause of concern or consequence of success?	Observational Study (6)	To examine the risk and incidences of falls post fast-track orthopaedic surgery	n = 5145	Falls related hospital admissions within 90 day follow-up Length of time to fall Falls related injuries Circumstances of fall	1.6% readmission rate due to fall 73.5% classified as surgery related falls Falls were most frequent during the first week post-discharge. Risk factors for falls: Age, living alone, pharmacological treatment for psychiatric disease.	Large participant numbers	No comparison group Inclusive of both THR and TKR

							Shorter length of stay did not increase the risk of surgery related falls.		
14	(Jorgensen & Kehlet 2013)	Role of patient characteristics for fast-track hip and knee arthroplasty	Quality control study - Observational (6)	Report data on characteristics of patients undergoing fast track primary THR or TKR Is fast-track joint replacement surgery for everyone	n = 3112	Mortality Median LOS Hospital readmission rate	Mortality 0.22% at 30 days, 0.42% at 90 days Hospital readmission rate = 6.6% within 30 days, 9.3% within 90 days. 0.38% of confirmed DVT/PE 1.8% incidence of suspected infection 91% of patients had a LOS ≤ 4 days with no significant increases in mortality or readmissions most older patients can be successfully included in a standardized fast-track THA/TKA programme	Large participant numbers	Inclusive of both THR and TKR No comparison with a control group Results compared with results in other studies instead
15	(Jorgensen et al. 2013)	Thromboprophylaxis only during	Prospective cohort study (4)	Investigate the incidence of any symptomatic thromboembolic events with	n = 4924	Occurrence of symptomatic	median LOS = 2days 8.1% readmission rate	Large participant numbers	Inclusive of both THR and TKR

		hospitalisation in fast-track hip and knee arthroplasty, a prospective cohort study		only in-hospital prophylaxis if LOS≤5 days after fast-track THA and TKA.		thrombo-embolic events	1.12% incidence of TEEs Only 0.14% of these were in hospital 0.41% VTE = 0.11% PE and 0.3% DVT 0.09% surgery related deaths The numbers of symptomatic VTE were lower or comparable to the RCTs with prophylaxis of 10– 35 days	Unselected patients	Very small comparison group No random selection
16	(Larsen 2009)	Cost-effectiveness of accelerated perioperative care and rehabilitation after total hip and knee arthroplasty	Piggyback study of an RCT Cost-utility study (2)	Compare the cost-effectiveness of a peri-operative accelerated care and rehabilitation protocol. Over the first post-operative year	N =87	Average reduction in cost QALY gain	Average cost reduction of approx. $4000 US Significant cost reduction Additional QALY gain of 0.08	Based on RCT data in Larsen 2008 Realistic Inc./Exc criteria	As with Larsen 2008 Pre-intervention HRQoL difference between groups

							Intervention significantly less costly and significantly more effective		
17	(Larsen, Sørensen, et al. 2008)	Accelerated perioperative care and rehabilitation intervention for hip and knee replacement is effective: A randomized clinical trial involving 87 patients with 3 months of follow-up	RCT (2)	To trial the efficacy of a 'true' accelerated surgical pathway post total joint replacement on LOS and quality of life.	n = 87	LOS EQ5D Scores at 3 months	Mean LOS reduced from 8 days to 5 days Greater gain of QoL in intervention group as measured through EQ5D - increase of an extra 0.88 on EQ5D in intervention group Median LOS reduced by 3 days	RCT design Direct comparison between groups Realistic Inc/Exc criteria	Inclusive of THR, TKR and UKR Several other significant changes: Analgesic pathway changed Introduction of different education programme pre-op nutrition screening different anti-emetic prophylaxis Used mean to report the LOS change - however known to be skewed data
18	(O'Brien et al. 2005)	Day two post-operative 'fast-track' discharge following primary total hip replacement	Cohort Study	N/A	N/A	N/A	N/A	N/A	Excluded: Participants did not undergo mobilisation on day zero

19	(Petersen et al. 2008)	Self-reported functional outcome after primary total hip replacement treated with two different perioperative regimes: a follow-up study involving 61 patients	RCT	To assess the usefulness of optimization of perioperative care during admission on self- Reported functional outcome after THR. Comparison with an age matched healthy cohort	n = 79	N/A	N/A	Specific to THR Randomisation	Mobility did not start until post-op Day 1 - Omitted from Lit Review
20	(Robbins et al. 2014)	A multidisciplinary total hip arthroplasty protocol with accelerated postoperative rehabilitation: does the patient benefit?	Cohort Study – Retrospective review (4)	To analyse the benefits of accelerated rehabilitation in patients post THA	N = 590	LOS Discharge destination Hospital readmission rate	Significant reduction in LOS LOS Control = 3.38 days Intervention = 2.06 days Significant reduction in the proportion of patients discharged to inpatient rehabilitation facilities Reduction in the rate of hospital readmissions	Specific to THR	Concomitant changes in: Analgesia pathway Patient education Convenience selective sampling Differing surgical techniques between surgeons
21	(Schneider et al. 2009)	Predictive factors influencing fast track rehabilitation following primary total hip and knee arthroplasty	Cohort study	N/A	N/A	N/A	N/A	N/A	Mobility did not start until Post-op Day 1. Omitted from Lit Review

22	(Sharma et al. 2009)	Factors influencing early rehabilitation after THA: a systematic review	Systematic Review	Examine the following factors: Minimally invasive THR Multi-modal analgesia Hip precautions Pre-habilitation	Included 16 articles	N/A	N/A	N/A	Omitted: Did not examine Day 0 mobilisation
23	(Specht et al. 2015)	Nursing in fast-track total hip and knee arthroplasty: A retrospective study	Descriptive study – Retrospective analysis (6)	Describe increased activity in THR and TKR in an orthopaedic unit, the setup of a fast track programme and its impact on nursing care	Not clear	Nursing hours per patient day (NHPPD)	Increased surgical activity was enabled with the use of an accelerated pathway Increase in the complexity and specialist nature of tasks carried out by nursing staff Increasing number of patients to care for per nurse.		Examines the same cohorts as reviewed in research by Husted et al. Multiple changes to pathway. Doesn't consider the impact on the patient, more from the logistical perspective and pressures on the nursing team. No direct comparison of the effectiveness of day zero mobilisation.
24	(Bottros et al. 2010)	A rapid recovery programme after total hip arthroplasty	Cohort Study (4)	To investigate the effectiveness of a rapid recovery programme post	N = 103	LOS Cumulative distance walked	Significant reduction in LOS Control = 4.47	Specific to THR	No randomisation Concomitant changes in analgesic pathway

				THA, including posterior approach surgery, specific pain management and early ambulation		Pain VAS Harris hip score	Rapid = 3.5 Higher percentage of patients in the rapid group were able to be discharged directly home. No significant differences in Harris hip score Lower pain scores in rapid group POD 1-3 (Mean difference of 3.39 POD 2)		Mean LOS reduction reported – is the dataset skewed however? Not equal numbers between groups control =73, rapid = 30
25	(Dawson-Bowling et al. 2014)	A multidisciplinary enhanced recovery programme allows discharge within two days of total hip replacement; three- to five-year results of 100 patients.	Descriptive Study (6)	To review the efficacy of a 'short stay protocol' following total hip replacement	N = 100	LOS Clinical outcome scores SF-36 Oxford hip score MDP VAS	LOS reported as 1.99 days (mean) No comparison of functional scores such as OHS, MDP and SF-26 due to methodology.	Specific to THR Carried out in the UK	Concomitant changes: Altered surgical technique Half day pre-admission joint school Data reported as non-parametric – chose to present mean rather than median. No comparison data / group

26	(Stewart 2012)	Joint Replacement and Rapid Mobilization A Clinical Perspective on Rapid Arthroplasty Mobilization Protocol	Protocol Description						Exclude: Protocol description No data on the effectiveness of day zero mobilisation
27	(Tayrose et al. 2013)	Rapid mobilization decreases length-of-stay in joint replacement patients	Cohort study (4)	Assess the impact of rapid rehabilitation beginning in the recovery room on length-of-stay after primary hip and knee arthroplasty	n = 900	LOS	LOS reduced from 4.4 in control group to 3.9 in intervention group 74% of patients in the intervention group achieved mobility day 0 Decreased need for other services or care.	no changes to other elements of the enhanced recovery pathway	Potential for selection bias No randomisation Some significant baseline differences between groups: Presence of co-morbidities Operation table time Blood loss Co-analysis of THR and TKR No pre-selection of patient's - but theatre list adjusted to suit trial Other studies were running at the same

									time with aims to reduce LOS
28	(Wellman et al. 2011)	Implementation of an accelerated mobilization protocol following primary total hip arthroplasty: impact on length of stay and disposition	Cohort study (4)	Hypothesis: Combining tissue preserving techniques and un-cemented implants with immediate mobilisation on the day of surgery would decrease the length of stay without adverse effects on complications or readmissions	n = 218	LOS Discharge destination	LOS Control = 3.54 Intervention group = 1.65 99% of patients able to return directly home. No difference in post-op complications rate		Intervention group used a different surgical technique No randomisation to groups Used pre-emptive autologous blood transfusion Difference of anaesthetic regimes between groups Significantly young mean age in intervention group No statistical comparison between groups
29	(Antrobus & Bryson 2011)	Editorial Discussion							Excluded: Discussion paper – no empirical evidence of the effectiveness of day zero mobilisation

30	(Bandholm & Kehlet 2012)	Physiotherapy exercise after fast-track total hip and knee arthroplasty: Time for reconsideration?							Omitted: Discussed very early physiotherapy exercise post THR or TKR but did not specifically look at early mobilisation or provide any empirical analysis of its effectiveness
31	(Banerjee 2014)	The efficacy of multimodal high-volume wound infiltration in primary total knee replacement in facilitating immediate post-operative pain relief and attainment of early rehabilitation milestones	Cohort Study (4)	The efficacy of multimodal high-volume wound infiltration in primary total knee replacement in facilitating immediate post-operative pain relief and attainment of early rehabilitation milestones	n = 64	LOS Time to transfer Time to walk 3m with frame Complication rate	No significant difference in time to be able to transfer from the bed to chair Significant reduction of time until able to walk 3m with a frame. 29.3 hours in intervention group 48.8 hours in control group Reduction of 1 day in median length of stay in intervention group		Retrospective design no randomisation No comparison with standard care practices Wasn't the purpose of this study to examine the efficacy of day zero mobilisation Looked at TKR only Both groups had potential to have been walking for the first time on Day 0

							No significant post-operative complications within 48 hours.		
32	(Bennett et al. 2007)	Comparison of Immediate Postoperative Walking Ability in Patients Receiving Minimally Invasive and Standard-Incision Hip Arthroplasty	RCT	Compared walking ability in patients who had undergone minimally invasive THR vs standard incision THR	n = 100	Gait analysis - temporospacial parameters		used participant blinding	Omitted: Day zero mobilisation was not used or examined Mobility examined on first ambulatory day or day 2.
33	(Chen et al. 2012)	Effect of Immediate Postoperative Physical Therapy on Length of Stay for Total Joint Arthroplasty Patients	Cohort Study (4)	Measure the effect of rehabilitation in the early postoperative period on hospital LOS. Hypothesis: That early rehabilitation alone on the day of surgery could shorten the hospital LOS, regardless of other interventions	n = 128	LOS	LOS 2.81 in intervention group in control group Increased walking distance on POD in intervention group	Isolated day zero mobilisation as a treatment	included both THR and TKR patients No randomisation - inclusion for intervention was based on timing and physiotherapy availability - Convenience sampling Only 25 participants were in intervention group. Control group still got out of bed day zero

									with nurses - they just did not walk or see a PT
34	(den Hertog et al. 2012)	Pathway-controlled fast-track rehabilitation after total knee arthroplasty: a randomized prospective clinical study evaluating the recovery pattern, drug consumption, and length of stay	RCT (2)	Examine the effect of early rehabilitation on functional scores, pain and length of stay post TKR.	n = 147	AKSS WOMAC Consumption of concomitant analgesic drugs LOS	Significant increase in AKSS scores in intervention group when compared with standard care in early stages only Significant increase in WOMAC scores in intervention group when compared with standard care in early stages only Analgesia consumption higher in first 2 days with intervention group, but over the 3 month follow-up was significantly lower than standard care group LOS significantly reduced: Intervention Group = 6.75 days	RCT design Looked specifically at day zero mobilisation	Looked at TKR only Control group did not mobilise until POD 2 LOS figures are still very high compared to what is seen in the UK.

							Standard care group = 13.20		
35	(Dorr et al. 2010)	Outpatient total hip arthroplasty	Descriptive study (6)	Research Questions: How many patients would elect to go home the same day Was same day discharge safe Was there any benefit for those that went home? Hypothesis: that same day discharge would be safe (no medical complications and no readmissions) and beneficial for those patients who chose it.	n = 52	% enrolled Readmission rate	36% enrolled out of 192 77% of enrolled patients achieved same-day discharge At 6 week FU (96%) of 52 patients were satisfied with the decision to have same day surgery and would choose same day surgery again (87%) believed that same day surgery gave them more confidence and accelerated their recovery		Selection bias - patients under 65 yo only No randomisation - volunteer sampling used No control group comparison Used minimally invasive surgical technique Non-validated satisfaction questions

							No objective physical benefit from same-day discharge No readmissions		
36	(Gulotta et al. 2011)	Fast Track THR: One Hospital's Experience with a 2-Day Length of Stay Protocol for Total Hip Replacement	Cohort Study (4)	To compare a fast-track pathway including day of surgery mobility with standard care for: Length of stay Safety and feasibility. Determine what barriers exist to 2-day discharge.	n = 283	LOS readmission rate complication rate	No differences in incidence of complications, readmissions or re-operations at 1 year follow-up Average LOS reduced in intervention group. days in fast-track group 4.1 days in control group 58% of patients in the intervention group discharged within two post-op days lower rate of postoperative dizziness in the fast track	matching controls for demographics	No randomisation to groups used

							group (18.8%) compared to the control group (41.8%)		
37	(Juliano et al. 2011)	Initiating Physical Therapy on the Day of Surgery Decreases Length of Stay Without Compromising Functional Outcomes Following Total Hip Arthroplasty	Retrospective Observational Study (6)	Examine whether the implementation of a new multidisciplinary clinical pathway, which began PT on the day of surgery (DOS) rather than POD1 would reduce LOS for patients undergoing THA while in the acute care setting. To assess the functional milestones achieved by these patients during the hospital stay and whether or not the shortened length of stay resulted in patients being discharged with fewer of the milestones being reached	N = 408	LOS Attainment of functional milestones	Reduction in LOS of 0.21 days seen in the intervention group – this reached statistical significance Control =3.48 Intervention = 3.27 Shortened LOS did not reduce the achievement of functional outcomes 67% of intervention group discharged in 3 days or less This was 57% in the control group	Specific to THR High participant numbers	No co-morbidities Did not account for other non-medical factors which may have affected LOS No randomisation

38	(Holm et al. 2011)	Thigh and Knee Circumference, Knee-Extension Strength, and Functional Performance After Fast-Track Total Hip Arthroplasty	Descriptive study (6)	(1) quantify knee-extension strength and functional performance deficits at discharge after fast-track THA (2) investigate whether changes in thigh and knee circumferences (oedema or swelling) or hip pain were related to changes in knee-extension strength and functional performance after fast-track	N = 24	knee-extension strength, functional performances: TUAG 30 second chair stand test 10m walk test thigh and knee joint circumferences, hip pain.	Mean 6% increase in thigh circumference Mean 3% increase in knee circumference Mean reduction in knee-extension power of 32% on hospital discharge Mean 114% reduced performance in TUAG Mean 30% reduction in performance 30 Sec Stand test Mean 50% reduction in performance in 10m walk test Above changes in circumference did not correlate with reduced strength Increased knee circumference did correlate with poorer functional performances.	Assessor blinding to pre-op data – attempt to avoid recall bias Specific to THR	Convenience sampling Large majority of female patients Doesn't examine the difference between fast track and standard care All participants mobilised Day 0 Low participant numbers

39	(Holm et al. 2010)	The role of pain for early rehabilitation in fast track total knee arthroplasty	Descriptive study (6)	To investigate the relationship between early functional mobility and pain intensity on the first two post- operative days after surgery and on the planned DOD	N = 100	Cumulated Ambulation Score Pain intensity VAS Knee AROM TUAG test	90% of participants managed to walk independently with median pain intensity of ≤ 5. Median LOS = 3		Only examined post TKR not THR Design doesn't allow for comparison between groups
40	(Husted et al. 2015)	Low manipulation prevalence following fast-track total knee arthroplasty							Excluded: Only outcome measure was rate of manipulation under anaesthetic – no outcomes relevant to THR.
41	(Husted, Solgaard, et al. 2010)	Care principles at four fast-track arthroplasty departments in Denmark	Descriptive study						Excluded: Analyses just the logistical and clinical pathways used in 4 different fast track Danish centres for joint replacement. No new experimental data or findings relating to day zero mobilisation

42	(Isaac et al. 2005)	Accelerated rehabilitation after total knee replacement	Cohort study (4)	To assess if significant reductions in length of stay could be achieved with optimisation of the patient pathway post TKR	N =120	LOS Pain VAS scores Readmission rates	Mean LOS control = 6.6 days Mean LOS intervention group = 3.6 days. Statistically significant No blood transfusions required in accelerated group Observed lower pain scores but not enough data to reach statistical comparison Readmission rate 5.9% with intervention group (not compare with control		No randomisation to groups Control group under different consultant care Differences in other pathway elements: Surgical technique Anaesthetic Analgesia protocol Pre-assessment procedures. LOS the only outcome measure compare with a control group Only looked at TKR
43	(Ishiguro et al. 2013)	Day zero ambulation under modified femoral nerve block after minimally invasive surgery for total knee arthroplasty: preliminary report	Descriptive study		N = 25		No clinically relevant findings relating to day zero mobilisation		Excluded: Only examined patients undergoing TKR Minimally invasive surgical technique also Main study aim was to examine the use of a

									modified femoral nerve block
44	(Kehlet 2013)	Fast-track hip and knee arthroplasty Fast-track	Comment editorial	Summary statement	N/A	N/A	No empirical findings about the efficacy, safety or experience of early post-operative mobilisation	N/A	Excluded: Summary statement – no empirical evidence
45	(Kehlet & Søballe 2010)	Fast-track hip and knee replacement — what are the issues?	Guest editorial	Summary statement	N/A	N/A	No empirical findings about the efficacy, safety or experience of early post-operative mobilisation	N/A	Excluded: Summary statement – no empirical evidence
46	(Khan et al. 2014)	Reduced short-term complications and mortality following Enhanced Recovery primary hip and knee arthroplasty: results from 6,000 consecutive procedures	Cohort study (4)	To report on the 90 day safety	N = 6000	LOS Readmission rates Rates of post-operative complications Mortality rates	Median LOS reduced by 3 days in the intervention group (Stat Sig) No difference in readmission rates between groups Reduced requirement for blood transfusion or return to theatre in the intervention group (Stat Sig)	No loss to follow-up Large participant numbers	Inclusive of both THR and TKR Different anaesthetic and analgesic regimes between groups Differences in patient education between groups No randomisation – consecutive patient selection Differences between groups in gender and co-morbidities

							Intervention group had statistically significant reduction in 30 day MI rates and death No significant differences in incidence of stroke, gastro-intestinal bleeding, pneumonia, deep-vein-thrombosis or pulmonary embolism Improved 30 day and 90 day mortality rates in intervention group.		
47	(Krenk et al. 2012)	Delirium in the fast-track surgery setting	Descriptive Study (6)	To investigate the incidence rate of post-operative delirium or cognitive decline following fast track THR or TKR	No participant numbers reported	Incidence of post-op delirium Incidence of post-op cognitive decline	The fast-track concept with early mobilisation, multimodal opioid-sparing analgesia and short LOS seems to be beneficial in preserving cognitive abilities in the elderly		Summary of two studies No first hand comparison with standard care – comparison with previous literature. No reported participant numbers
48	(Larsen, Hansen, et al. 2008)	Hip arthroplasty patients benefit from accelerated perioperative care and rehabilitation A quasi-	Effectiveness trial (6)	To investigate whether HRQOL was improved post-operatively in primary THA patients in patients who underwent accelerated	N = 98	EQ5D at 3 months	Clinically relevant difference in health related quality of life in favour of the accelerated group.		Pre-op assessment differences between groups. Differences in nutrition

		experimental study of 98 patients		perioperative care and rehabilitation intervention compared to those who underwent standard care					
59	(Lenssen et al. 2006)	Efficiency of immediate postoperative inpatient physical therapy following total knee arthroplasty: an RCT					•	•	• Excluded: Did not include day zero mobilisation as an intervention
50	(Malviya et al. 2011)	Enhanced recovery program for hip and knee replacement reduces death rate	Cohort Study (4)	To examine the influence of an enhanced recovery pathway including day zero mobilisation affects early morbidity and mortality rates after primary joint replacement	n = 4500	30 day and 90 day mortality rates LOS Complication rates	• Significant reduction in 30 and 90 day mortality rates in enhanced recovery group • 30 day: • Control: 0.5% • ER: 0.1% • 90 Day: • Control: 0.8% • ER:0.2%	• Large participant numbers	• Differences in patient education, analgesia, anaesthetics, tranexamic acid as well as mobility change. • No randomisation - consecutive sampling.

							• Significant reduction in LOS		
51	(Raphael et al. 2011)	Easily adoptable total joint arthroplasty program allows discharge home in two days	Historical cohort study (4)	Determine whether a fast-track model of care could reduce length of hospital stay following total hip and knee arthroplasty while maintaining a high level of patient safety and satisfaction	n = 200	LOS Patient reported pain scores	• Patients in the fast-track group were discharged 69 hours earlier than control group. • All but one patient discharged by POD 3 in fast track group - only 8 managed this in standard care group • Lower pain scores in fast track group • Lower opioid consumption fast-track group	•	• Concomitant pathway changes in intervention group. Differences in Pre-op education and expectation management • Post-op analgesia regime. • Included both THR and TKR • No detailed measure of satisfaction - based on telephone feedback - not discussed with supporting evidence. • Linear design

							• Significantly more events of nausea and PONV in fast-track group. • No significant differences in 30 day readmission rates		
52	(Savaridas et al. 2013)	Reduced medium-term mortality following primary total hip and knee arthroplasty with an enhanced recovery program	Cohort Study (4)	To report on longer term mortality following the use of an enhanced recovery programme after major joint replacement	n = 4500	2 year survival rates	• 2 year survival rates significantly better in intervention group 2.7% vs 3.8% • Survival benefit appears to remain up to 3.7 years post-op	• Large participant numbers	• Differences in patient education, analgesia, anaesthetics, tranexamic acid as well as mobility change. • No randomisation - consecutive sampling.
53	(Smith et al. 2012)	Rehabilitation implications during the development of the Norwich Enhanced Recovery Programme (NERP) for patients following total knee	Secondary analysis of service change (6)	Report the early findings of the initial 95 patients who followed the developing Norwich Enhanced Recovery Programme (NERP) in terms of function and pain at discharge, length of stay, need for outreach physiotherapy services and	N = 95	ILOA scores	• Less than 46% of patients were able to commence day 0 mobilisation due to reduced sensory-motor output, dizziness, nausea and pain.	•	• Included THR and TKR • No control group / comparison with standard care.

		and total hip arthroplasty		complications during the initial six post-operative weeks.			• Significantly reduced pain scores for patients who achieved mobility on day 0. • Earlier functional improvement for those patients who achieved mobility day 0.		
54	(Stambough et al. 2015)	Rapid Recovery Protocols for Primary Total Hip Arthroplasty Can Safely Reduce Length of Stay Without Increasing Readmissions	Descriptive Study (6)	Investigate the impact of incremental perioperative practice changes and the adoption of specific rapid recovery protocols on hospital LOS and readmission rates in primary THAs	N = 1751	LOS 30 day readmission status	• LOS significantly decreased as each stage of the pathway was implemented (no change in median when early mobilisation introduced compared to previous stage) • No change in readmission rates (did not reach statistical significance)	•	• Consecutive recruitment • Linear design • Examined other significant pathway changes also
							•	•	•

55	(Sahu et al. 2018)	Influence of Early Physiotherapy Intervention on Pain, Joint Range of Motion and Quality of Life in Unilateral Hip Joint Replacement Surgery					•	•	• Excluded – Did not use day zero mobilisation
56	(Okamoto et al. 2016)	Day-of-Surgery Mobilization Reduces the Length of Stay After Elective Hip Arthroplasty	RCT (2)	Determine the effect of day 0 mobilisation on time to readiness for discharge and LOS.	N=126	LOS Time to readiness to discharge	• Significant reduction in time to PT complete No significant differences in LOS Significant reduction in the proportion of patients staying >72 hours	• Specific to hip Only changed PT intervention RCT 3-month readmission follow-up • ****Good Study****	• Strict inc/exc criteria • Inclusive of hip resurfacing used unpaired t-test - but I would expect the data to be non-parametric No power calculation
57	(Larsen et al. 2017)	Feasibility of day-case total hip arthroplasty: a single-centre observational study	Feasibility Study	Examine the feasibility of outpatient THR.	N=20	LOS (hours) Adverse events with 6 week FU.	• 85% of those included were able to leave hospital on DOS • Reduced in hospital time with Day case surgery.	• Compliance with STROBE statement. • Specific to THR	• Excluded: Not powered as a full study. • Non-blinded • Non-randomised • Only included the first patient on theatre list for the day. • Not a true same-day discharge –

									• patients left unit to a hotel where they remained overseen by a nurse. • Both groups underwent day 0 mobilisation.
58	(Klapwijk et al. 2017)	The first 6 weeks of recovery after primary total hip arthroplasty with fast track: A diary study of 94 patients	Observational Study (6)	To examine patient experience over the first 6 weeks following fast-track THR.	N=101	Diary of specific questionnaires: HOOS OHS EQ-5D 12 Item health survey (SF-12) ICOAP	Pain gradually decreased over the first 6 weeks. Analgesia consumption decreased gradually over the first 6 weeks. 11 incidences of inpatient wound ooze. 7 incidences of persistent wound ooze as an outpatient. Improvement in functional	Specific to THR	No power calculation Baseline significant differences between inpatient and outpatient groups – in Age and ASA No randomisation to treatment – as patients naturally performed. Results do not compare groups. Just descriptives of both groups combined. No specific examination of 'patient experience' all carried out through PROMS and set questionnaires.
59	(Gromov et al. 2017)	Feasibility of outpatient total hip and knee arthroplasty in unselected patients	Observational Study (6)	To identify the proportion of patients suitable for outpatient THA and TKA in an unselected patient population.	N=557	Fulfilment of set criteria for outpatient surgery.	54% fulfilled the set criteria to be eligible for outpatient surgery. 28% of THR patients were able to be discharged on the DOS.	Unselected population. Broad inclusion and exclusion criteria.	Combined both THR and TKR. Sponsorship by surgical implant company. Results appear to have been influenced by some patients

				Investigate the proportion of patients who can be discharged on the DOS Identify reasons for preventing D/C on the DOS.		Proportion discharged on Day0 Reasons for non-discharge on day 0	Lack of safe mobility was the principle reason for missing discharge on DOS. Female Sex and being >1 on operating list significantly increased the risk of missing DOS discharge. Chances of discharge on DOS ranged between 9% and 68%. Actual DOS discharge rates were 13-15% of the entire population. Summarises that although a good proportion of patients may be eligible, considerably less managed same-day-discharge.		lacking motivation for same-day-discharge.
60	(Andreasen et al. 2017)	Time-driven Activity-based Cost of Fast-Track Total Hip and Knee Arthroplasty	Observational Study (6)	Investigate the effect of fast-track THR and TKR on the costs of providing the operations.	THR = 229 TKR = 196	Time driven activity based costing	Median LOS = 2 days Providing fast-track surgery cost approx. $2500 dollars excluding the implant cost. This is lower than costs reported in previous studies.	Calculation method appears good – TDABC method.	Combined both TKR and THR. Two different sites with two different post-op protocols (although results were stratified to this)
61	(Pitter et al. 2016)	Postoperative morbidity and discharge destinations after fast-track hip and	Observational Study (6)	Investigate the rates of complications following fast-	N=522	Causes of LOS>4 days.	Mean LOS=4.3 days 23.7% had >4 day LOS – main reason anaemia.	This study looked specifically at patients over 85 years – high-risk group.	Comes from the LCDB database – many other studies reporting on this also

		knee arthroplasty in patients older than 85 years		track surgery with cohorts >85 years of age.		Causes of 90-day readmissions. Proportion of patients with non-home discharge destination 90-day mortality rates.	6.9% had non-home discharge 14.2% readmission after 30 days 17.9% after 90 days (24.3% due to falling) 2% 90 day mortality rate	Excellent data completeness Non-selective sampling.	– therefore looking at the same cohort. Combines both THR and TKR. Non-comparative study
62	(Chua et al. 2017)	Early mobilisation after total hip or knee arthroplasty: A multicentre prospective observational study	Observational – prospective single group cohort study	Investigate the proportion of patients who did achieve day 0 mobilisation across multiple centres. What factors influenced this	N=1807 THR = 818 TKR = 989	Which POD patient achieved mobilisation	18% of THR patients had a complication Only 9.4% of THR patients achieved day 0 mob. Which hospital site was linked with time-to-mobilisation, as was male gender, anterior approach, no spinal block, no indwelling catheter and no complications	Results also presented as joint specific. Large cohorts	Excluded: Didn't examine the efficacy of day 0 mobilisation. Combination of THR and TKR. Not investigating the efficacy of day 0 mobilisation, but more looking at feasibility. Non-validated modified version of Clavien-Dindo classification method.
63	(Goyal et al. 2017)	Otto Aufranc Award: A Multicenter, Randomized Study of Outpatient versus Inpatient Total Hip Arthroplasty	Prospective RCT	Comparing outcomes between outpatient THR and inpatient THR	N=220	PNRS Harris hip score	Increased PNRS in outpatient group day 1 post op, no difference by 4 weeks. No difference in Harris hip scores at 4 weeks.	RCT design Mostly appropriate inc/exc Intention to treat analysis used.	Only patients younger than 75 years old Appears that both groups underwent day zero mobilisation.

							No difference in re-operation rates between groups	No loss to follow-up	Conducted in two differing centres. One high throughput centre and one a community hospital. Patients were allowed to 'move between groups depending on their preference'. Underpowered to assess for complications. Excluded: No comparison based on day 0 mobilisation.
64	(Karim et al. 2016)	Does Accelerated Physical Therapy After Elective Primary Hip and Knee Arthroplasty Facilitate Early Discharge?	Retrospective service change evaluation - cohort study (4)	To evaluate the introduction of a service change towards day 0 mobilisation.	N=116 for THR	LOS Distance walked on first PT session.	No significant differences in mean LOS. Higher proportion of pts achieving discharge on day 1	Comparative study Exceeded power calculation requirements. Isolated use of day zero mobilisation as the intervention.	Inclusive of both THR and TKR. No randomisation – appears to be selective group allocation. Also changed to minimally invasive surgical technique
65	(Jørgensen et al. 2016)	Preoperative prediction of potentially preventable morbidity after fast-track hip and knee arthroplasty: A	Retrospective review of previous prospective study data.	To attempt to develop a numerical score to identify patients at high risk of medical or surgical complications	N=8737	Incidence of complications	Statistically possible to predict – but not clinically relevant – due to problems with developing strategies to prevent complications		Excluded: Not examining the efficacy of day 0 mobilisation.

		detailed descriptive cohort study							Inclusive of both THR and TKR. No comparison / investigation into the efficacy of day 0 mobilisation.
66	(Vesterby et al. 2017)	Telemedicine support shortens length of stay after fast-track hip replacement: A randomized controlled trial							Excluded: Telemedicine system was the intervention. DOS mob was used in both groups – no comparison based on this.
67	(Klein et al. 2017)	Same Day Total Hip Arthroplasty Performed at an Ambulatory Surgical Centre: 90-Day Complication Rate on 549 Patients	Prospective cohort study – single group (6)	To investigate the incidence of complications following outpatient THR	N=549	Incidence of complications	1% dislocation rate 6% haematoma requiring irrigation 0.9% infection 0.5% VTE 0.5% readmission Paper concluded that outpatient THR was safe in a selected population.	Large participant numbers	Minimally invasive surgical technique used. Non-randomised – selected sampling. Wide variation in follow-up times range = 3-2689 days Poor clarity on outcome measures selected. No comparison group.

68	(Jans et al. 2016)	Postoperative anaemia and early functional outcomes after fast-track hip arthroplasty: A prospective cohort study	Prospective cohort study – single group	To assess the relationship between post-op anaemia and functional mobility performance following fast-track THR	N=122	TUG 6MWT Up to 2 weeks post-op	Weak correlation between severity of post-op anaemia and reduction in functional outcomes performance. Correlations were not clinically significant.	Blinding of assessors STROBE compliance with write-up Specific to THR Clear sample size considerations and methodology	Excluded: Not examining the efficacy of day 0 mobilisation. Convenience sampling – potential for selection bias No comparison group as to the effectiveness of day zero mobilisation.
69	(Jørgensen & Kehlet 2016)	Early thromboembolic events ≤ 1 week after fast-track total hip and knee arthroplasty	Observational descriptive study (6)	To investigate the incidence rate of TEE post fast-track joint replacement	N=13,775	Incidence of in hospital TEE or TEE within the first week post-op. Also 30-day review of incidence of TEE, TIA or ACS.	Study did not compare with a control group. Comparison with national data in Denmark on incidences. Reported reduced incidence in this study compared to national statistics for both TEE and MI	Large cohort numbers.	Inclusive of both THR and TKR. No direct comparison group – use of national statistics instead.
70	(Hartog et al. 2015)	Total hip arthroplasty in an outpatient setting in 27 selected patients	Feasibility study (6)	Report of descriptive data in a patient cohort	N=27	PROMS EQ5D at 6 weeks and 3 months	Unable to compare the effectiveness of day 0 mobilisation as there was no control group. Results were reported as favourable with improvements in PROMS, however, this could have been the case even without 'day-case THR'	Not too strict inclusion criteria	Low participant numbers No randomisation No comparison group – unable to ascertain the effectiveness of the intervention.

							More provides indication on feasibility		
71	(Amlie et al. 2016)	A trend for increased risk of revision surgery due to deep infection following fast-track hip arthroplasty	Interrupted time series study (4)	To investigate any link between fast-track THR inclusive of day 0 mobilisation and revision surgery due to deep infection.	N=4406	Rates of revision surgery within 3 months related to deep infection.	Significant increase in the incidence of revision surgery due to deep infection within the first 3 months post-op. 0.5% in control group 1.67% in intervention group >3x increase in risk.	Specific to THR Large number of participants.	Several confounders – change of component type and fixation from cemented to uncemented at the beginning of the fast-track period. Stepwise discontinuation of fast track elements. Is 3 months a bit of a short follow-up for something like revision surgery – only accounts for early onset peri-prosthetic infections. Delayed onset of 3-12months with less virulent organisms likely to be missed. Did not evaluate minor infections.
72	(Stambough et al. 2016)	Contemporary Strategies for Rapid Recovery Total Hip Arthroplasty	Symposium write-up						Excluded: Summary statement - No empirical findings.

73	(Pollock et al. 2016)	Outpatient Total Hip Arthroplasty, Total Knee Arthroplasty, and Unicompartmental Knee Arthroplasty	Systematic Review (1)	Review literature for the safety and feasibility of outpatient arthroplasty (THR, TKR, UKR)	17 studies included	N/A	Similar outcomes from outpatient arthroplasty in terms of complication rates and clinical outcomes but with reduced LOS and cost savings. However – lack of high-level evidence.	Clear search and appraisal methodology Well conducted review PRISMA statement for write-up 2 x independent reviewers	Not specific to THR No RCTs included Only 4 included studies had a control group Majority of studies had a selected population – inherent selection bias
74	(Yager & Stichler 2015)	The Effect of Early Ambulation on Patient Outcomes for Total Joint Replacement							Excluded - Classed joint ROM within the ambulation on day of surgery category. No clear treatment protocol. Main intervention was education of therapy staff to increase the above stats, not walking day of surgery.
75	(Krenk et al. 2014)	Cognitive dysfunction after fast-track hip and knee replacement	Observational Study – Prospective (6)	To investigate the incidence of post-operative cognitive dysfunction in patients who underwent fast-track TJR which included day 0 mobilisation	N=220	Neuropsychological tests: Visual-verbal learning test Concept shifting test Stroop colour word test	Lower incidence of post-op cognitive dysfunction than seen in previous studies. Incidence of 9.1% at 1-2 weeks post-op.	Large proportion of cohort underwent THR. Good standardised surgical protocol. Clear anaesthetic protocol.	Not specific to THR – included TKR also Only consultant carried out operations Multimodal fast track intervention – not able to isolate the effects of day 0 mobilisation.

						Letter digit coding task		Variations in analgesic regime used. Multi-centre	
76	(Galbraith et al. 2017)	Enhanced recovery protocols in total joint arthroplasty: a review of the literature and their implementation	Literature Review	Reviews the different elements of ERAS and the evidence behind each of them.	? number of studies included – Not stated	N/A	Day-zero mobilisation section based on LOS only	Specific section considering day zero mobilisation Study type	Excluded: Only inclusive of two papers which are included within this review already. No clear literature search methodology. No clear appraisal of the quality of included literature. Day zero mobilisation section only included 2 papers.
77	(Den Hartog et al. 2017)	Which patient-specific and surgical characteristics influence postoperative pain after THA in a fast-track setting?							Excluded – Not clear if Day 0 mobilisation was used. Selected intervention was analgesia regime not day 0 mobilisation.
78	(Mears et al 2017)	Fast track hip and knee arthroplasty is possible and safe for the over 80 patient							Excluded: Abstract Only – Does not appear to investigate day zero mobilisation. Two groups

									based on above or below 80 years of age.
79	(Temporiti et al. 2020)	Does walking the day of total hip arthroplasty speed up functional independence? A non-randomized controlled study	Non-randomised controlled study (4)	To investigate the effect of day zero mobilisation on functional independence post THR	N=71	FIM HHS PNRS EQ5D	Showed statistically significant difference in FIM scores favouring day zero mobilisation at both 3 and 7 days post-op.	Specific to THR Good well validated outcome measures Representative inc/exc criteria	Non-randomised – convenience sample No power calculation- could be underpowered Only 7 day follow-up period Lower baseline age in intervention group No published MCID for FIM in THR – unclear as to the clinical relevance of findings. No baseline measure of co-morbidities *participants who failed to walk day zero in the intervention group were automatically excluded*
80	(Mariorenzi et al. 2020)	Outpatient Total Joint Arthroplasty: A Review of the Current Stance and Future Direction.	Literature Summary	Summarise the current standpoint on outpatient joint arthroplasty	N/A				Excluded: No empirical findings Summarises both THR and TKR together. No literature search or appraisal detail.

81	(Nassar et al. 2020)	Rapid recovery following hip and knee arthroplasty using local infiltration analgesia: length of stay, rehabilitation protocol and cost savings	Cohort study						Excluded: Investigating the efficacy of LIA and not day zero mobilisation
82	(Hoeffel et al. 2019)	Outcomes of the First 1,000 Total Hip and Total Knee Arthroplasties at a Same-day Surgery Centre Using a Rapid-recovery Protocol	Observational study						Excluded: No comparison group to determine the efficacy of day 0 mobilisation.
83	(Fraser et al. 2018)	Identifying Reasons for Failed Same-Day Discharge Following Primary Total Hip Arthroplasty	Pilot observational study	Identify reasons for failed discharge on the day of surgery.	N = 106	Reasons for failed discharge	28% failed same day discharge Principal reasons were: Pt preference Dizziness / low BP Failed to reach PT goals Risk factors: RA Number of allergies	Prospective design Specific to THR	Excluded: Pilot study – no power calculation. Selected cohort for intervention Age limited to under 75 No specific investigation of day 0 mobilisation.

Additional Papers Considered Between Literature Review and Completion of Thesis:

84	(Bristol 2021)	Early ambulation in hip replacement patients regarding length of hospital stay	Retrospective notes review	To see if standing or walking before 8 hours post-operative decreased overall length of hospital stay	N = 92	Length of stay	Mean LOS for ambulation within 8 hours = 2.83 days Mean LOS for control group was 5.14 days	Specific to THR	No sample size calculation No analysis of data for normality of distribution Retrospective design No randomisation Single centre
85	(Elmoghazy et al. 2022)	Conventional versus fast track rehabilitation after total hip replacement: A randomized controlled trial	RCT (2)	To investigate the effect of day-zero ambulation on LOS and functional outcomes following THR	N=60	Length of Stay Harris Hip Score WOMAC	LOS 4.5 days in the intervention group versus 7.8 in control group. (p<0.001) Improved Harris hip scores at 6 (p=0.013) and 12 weeks post-op in intervention group. (p=0.002) Improved WOMAC score at 6 weeks post-op (p=0.08)	Specific to THR Randomisation Intervention limited to day-zero ambulation	LOS less than 3 days was actively prevented due to German DRG system dictating financial reductions for shorter LOS No statistical comparison testing for baseline measures Appears to be significant differences in baseline measures favouring intervention group for age (Control =72, Intervention = 65), gender (Control 1:2, Intervention 2:2) and pre-op

									Harris hip scores (Control = 41, Intervention = 49.6) Difference in Harris hip score between groups not dissimilar to the difference observed at baseline.

Appendix 3 Qualitative Search Strategy

Search Number	Databases Searched	Search Terms and Limits	Number of Results	Comments on Results
S1	MEDLINE, CINAHL, AHMED	THR **OR** “total hip replacement” **OR** THA **OR** “total hip arthroplasty” **OR** ‘joint replacement’	76,446	N/A
S2	MEDLINE, CINAHL, AHMED	Rapid **OR** Accelerated **OR** “fast-track” **OR** “fast track” **OR** "day zero" **OR** "day 0"	742,862	N/A
S3	MEDLINE, CINAHL, AHMED	Ambulat* **OR** walking **OR** mobilisation **OR** mobilization	369,335	N/A
S4	MEDLINE, CINAHL, AHMED	“patient experience” **OR** “patient satisfaction” **OR** “lived experience” **OR** phenomenology* **OR** qualitative	472,144	N/A
S5	MEDLINE, CINAHL, AHMED	S1 **AND** S2 **AND** S3 **AND** S4 Limits: **Since 2005, English Language, Full Text**	22	8 Identified via title and abstract for further investigation
S6	EMBASE	THR **OR** “total hip replacement” **OR** THA **OR** “total hip arthroplasty” **OR** “joint replacement”	60638	N/A
S7	EMBASE	Rapid **OR** Accelerated **OR** “fast-track” **OR** “fast track” **OR** "day zero" **OR** "day 0"	848141	N/A
S8	EMBASE	Ambulat* **OR** walking **OR** mobilisation **OR** mobilization	339794	N/A
S9	EMBASE	“patient experience” **OR** “patient satisfaction” **OR** “lived experience” **OR** phenomenology* **OR** qualitative	394177	N/A
S10	EMBASE	S5 **AND** S6 **AND** S7 **AND** S8 Limits: **Since 2005, English Language, Full Text**	19	1 identified via title and abstract for further investigation

Appendix 4 Risk of Bias Assessments

The Risk Of Bias In Non-randomized Studies – of Interventions (ROBINS-I) assessment tool

(version for cohort-type studies)

Version 19 September 2016

ROBINS-I tool (Stage I): At protocol stage

Specify the review question

Participants	People who have undergone unilateral primary and uncomplicated THR
Experimental intervention	Day zero-ambulation
Comparator	Standard post-operative care (ambulation day 1 or greater)
Outcomes	Length of stay, post-operative complications, post-operative pain.

List the confounding domains relevant to all or most studies

Age, pre-morbid mobility and function, pre-existing co-morbidities

List co-interventions that could be different between intervention groups and that could impact on outcomes

Analgesia pathway, surgical techniques, surgical approach, post-operative weight-bearing, post-operative discharge criteria.

ROBINS I Tool Assessment for Risk of Bias

Study / Article:

Robbins, C. E., Casey, D., Bono, J. V, Murphy, S. B., Talmo, C. T., & Ward, D. M. (2014). A multidisciplinary total hip arthroplasty protocol with accelerated postoperative rehabilitation: does the patient benefit? *American Journal of Orthopedics (Belle Mead, N.J.)*, *43*(4), 178–181. Retrieved from www.amjorthopedics.com

Reference Number:

20

Study Classification:

Cohort Study

Reviewer: Christopher Efford and Catherine Holdsworth

ROBINS-I tool (Stage II): (Robbins et al. 2014)

Specify a target randomized trial specific to the study

Design	Individually randomized / ~~Cluster randomized / Matched (e.g. cross-over)~~
Participants	People who have undergone open primary THR via postero-lateral approach without complications.
Experimental intervention	Day-Zero ambulation in isolation
Comparator	Standard care including ambulation day 1 or greater

Is your aim for this study…?

☑ to assess the effect of *assignment to* intervention

☐ to assess the effect of *starting and adhering to* intervention

Specify the outcome

Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table). Specify whether this is a proposed benefit or harm of intervention.

Length of stay

Specify the numerical result being assessed

In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

2.06 days experimental (No numerical CI presented), 3.38 days Control (No numerical CI Presented)

Preliminary consideration of confounders

Complete a row for each important confounding domain (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as potentially important.

"Important" confounding domains are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. "Validity" refers to whether the confounding variable or variables fully measure the domain, while "reliability" refers to the precision of the measurement (more measurement error means less reliability).

(i) Confounding domains listed in the review protocol				
Confounding domain	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator?
Age	Yes	No	Yes	Experimental – reduced mean age in experimental group
Pre-Morbid Function	No	No	N/A	N/A
Co-morbidities	No	No	N/A	N/A
Anaesthetic type	No	No	N/A	No

Blood Loss	No	No	N/A	N/A
Time of day of surgery	No	No	N/A	N/A
Duration of surgery	No	No	N/A	N/A
Surgical Technique	Yes	No	Yes	Neither
Arthroplasty type	Yes	No	Yes	N/A – exclusive to THR
Gender	Yes	No	Yes	Neither – appears balanced between groups.

(ii) Additional confounding domains relevant to the setting of this particular study, or which the study authors identified as important				
Confounding domain	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator?
			Yes / No / No information	Favour experimental / Favour comparator / No information

* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of intervention; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that “no statistically significant association” is not the same as “not predictive”.

Preliminary consideration of co-interventions

Complete a row for each important co-intervention (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as important.

"Important" co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention.

(i) Co-interventions listed in the review protocol		
Co-intervention	Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)?	Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator
Analgesic Pathway	Yes	Presented for each surgeon – but not by group
Catheterisation	No	N/A
LIA	Yes	Presented for each surgeon – but not by group
Staff Availability	No	N/A

(ii) Additional co-interventions relevant to the setting of this particular study, or which the study authors identified as important		
Co-intervention	Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)?	Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator

Pre-operative education	No	Favour experimental
More physiotherapy sessions	No	Favour experimental
		Favour experimental / Favour comparator / No information
		Favour experimental / Favour comparator / No information

Risk of bias assessment

Responses underlined in green are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Signalling questions	Description	Response options
Bias due to confounding		
1.1 Is there potential for confounding of the effect of intervention in this study? **If N/PN to 1.1:** the study can be considered to be at low risk of bias due to confounding and no further signalling questions need be considered	Many theorised confounding domains not measured or accounted for	Y
If Y/PY to 1.1: determine whether there is a need to assess time-varying confounding:		

1.2. Was the analysis based on splitting participants' follow up time according to intervention received? **If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6) **If Y/PY**, go to question 1.3.	No	N
1.3. Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome? **If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6) **If Y/PY**, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8)	N/A	NA / Y / PY / PN / N / NI

Questions relating to baseline confounding only

1.4. Did the authors use an appropriate analysis method that controlled for all the important confounding domains?	Only descriptions for age and gender. Values presented for intervention group and then whole study cohort, no control group values.	N
1.5. **If Y/PY to 1.4**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?	N/A	NA
1.6. Did the authors control for any post-intervention variables that could have been affected by the intervention?	No	N
Questions relating to baseline and time-varying confounding		
1.7. Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding?	No.	NA
1.8. **If Y/PY to 1.7**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?	N/A	NA

Risk of bias judgement	Critical	**Critical**
Optional: What is the predicted direction of bias due to confounding?		Favours experimental

Bias in selection of participants into the study		
2.1. Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention? **If N/PN to 2.1:** go to 2.4	*Note – participants selected for intervention group – allocation open to bias	N

2.2. **If Y/PY to 2.1**: Were the post-intervention variables that influenced selection likely to be associated with intervention? 2.3 **If Y/PY to 2.2**: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome?	N/A N/A	NA NA
2.4. Do start of follow-up and start of intervention coincide for most participants?	Yes	Y
2.5. **If Y/PY to 2.2 and 2.3, or N/PN to 2.4**: Were adjustment techniques used that are likely to correct for the presence of selection biases?	N/A	NA
Risk of bias judgement	Low	Low / Moderate / Serious / Critical / NI
Optional: What is the predicted direction of bias due to selection of participants into the study?	N/A	Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Bias in classification of interventions		
3.1 Were intervention groups clearly defined?	Yes	Y
3.2 Was the information used to define intervention groups recorded at the start of the intervention?	Yes	Y
3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome?	Yes – Participants were selected for intervention – surgeon selection	Y
Risk of bias judgement	Serious	**Serious**
Optional: What is the predicted direction of bias due to classification of interventions?	Favours experimental	Favours experimental

Bias due to deviations from intended interventions	
If your aim for this study is to assess the effect of assignment to intervention, answer questions 4.1 and 4.2	

4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice?	All deviations within normal practice	N
4.2. **If Y/PY to 4.1**: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome?	N/A	NA
If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6		
4.3. Were important co-interventions balanced across intervention groups?	N/A	
4.4. Was the intervention implemented successfully for most participants?	N/A	
4.5. Did study participants adhere to the assigned intervention regimen?	N/A	
4.6. **If N/PN to 4.3, 4.4 or 4.5**: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention?	N/A	NA
Risk of bias judgement	Low	**Low**

Optional: What is the predicted direction of bias due to deviations from the intended interventions?	Favours neither	Unpredictable

Bias due to missing data		
5.1 Were outcome data available for all, or nearly all, participants?		Y
5.2 Were participants excluded due to missing data on intervention status?		N
5.3 Were participants excluded due to missing data on other variables needed for the analysis?		N
5.4 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Are the proportion of participants and reasons for missing data similar across interventions?	N/A	NA

5.5 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Is there evidence that results were robust to the presence of missing data?	N/A	NA
Risk of bias judgement	Low	**Low**
Optional: What is the predicted direction of bias due to missing data?	N/A	N/A

Bias in measurement of outcomes		
6.1 Could the outcome measure have been influenced by knowledge of the intervention received?	LOS – measurable when pt leaves hospital	N
6.2 Were outcome assessors aware of the intervention received by study participants?	Group allocation and assessment doesn't appear to be concealed	Y
6.3 Were the methods of outcome assessment comparable across intervention groups?	Yes	Y
6.4 Were any systematic errors in measurement of the outcome related to intervention received?	No	N

Risk of bias judgement	Moderate	**Moderate**
Optional: What is the predicted direction of bias due to measurement of outcomes?	Unpredictable	Unpredictable

Bias in selection of the reported result		
Is the reported effect estimate likely to be selected, on the basis of the results, from...		
7.1. ... multiple outcome *measurements* within the outcome domain?	No	N
7.2 ... multiple *analyses* of the intervention-outcome relationship?	No	N
7.3 ... different *subgroups*?	No	N
Risk of bias judgement	Low	**Low**

Optional: What is the predicted direction of bias due to selection of the reported result?	N/A	N/A

Overall bias		
Risk of bias judgement	Critical	Critical
Optional: What is the overall predicted direction of bias for this outcome?	Favours experimental	Favours experimental

ROBINS I Tool Assessment for Risk of Bias

Study / Article:

Husted, H., Hansen, H.C., Holm, G., Bach-Dal, C., Rud, K., Andersen, K.L. & Kehlet, H., (2009) What determines length of stay after total hip and knee arthroplasty? A nationwide study in Denmark. *Archives of Orthopaedic and Trauma Surgery*, 130(2), pp.263–268. Available at: http://dx.doi.org/10.1007/s00402-009-0940-7.

Reference Number:

71

Study Classification:

Cohort Study

Reviewer:

Christopher Efford and Catherine Holdsworth

ROBINS-I tool (Stage II): (Husted et al. 2009)

Specify a target randomized trial specific to the study

Design	Individually randomized / ~~Cluster randomized / Matched (e.g. cross-over)~~
Participants	People who have undergone open primary THR via postero-lateral approach without complications.
Experimental intervention	Day-Zero ambulation in isolation
Comparator	Standard care including ambulation day 1 or greater

Is your aim for this study…?

☑ to assess the effect of *assignment to* intervention

☐ to assess the effect of *starting and adhering to* intervention

Specify the outcome

Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table). Specify whether this is a proposed benefit or harm of intervention.

Incidence of revision surgery within 3 months of primary operation due to deep infection.

Specify the numerical result being assessed

In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

1.67% rate of infection related revision surgery during fast track period (n = 4 of 239). 'adjusted risk of revision surgery due to deep infection during the first 3 postoperative months that was more than three times higher (OR = 3.3, 95% CI 1.125–9.772, p = 0.03)than patients who had standard THA'

Preliminary consideration of confounders

Complete a row for each important confounding domain (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as potentially important.

"Important" confounding domains are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. "Validity" refers to whether the confounding variable or variables fully measure the domain, while "reliability" refers to the precision of the measurement (more measurement error means less reliability).

(i) Confounding domains listed in the review protocol				
Confounding domain	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator?
Age	Yes	No	YES	Not enough information
Pre-Morbid Function	No	Yes	N/A	N/A
Co-morbidities Measured using ASA	Yes	No	Yes	N/A
Anaesthetic type	No	No	No	No information

Blood Loss	No	No	No	No information
Time of surgery	No	No	No	No information
Duration of surgery	Yes	No	No	Not enough information
Surgical Technique	No	Yes –standard technique and approach used	N/A	N/A
Arthroplasty type	No	Yes – All THRs	N/A	N/A
Gender	Yes	No	Yes	None – appears balanced

(ii) Additional confounding domains relevant to the setting of this particular study, or which the study authors identified as important				
Confounding domain	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator?
BMI	Yes	No	No – not measured in all participants	Not enough information

Surgery Duration	Yes	No	No	Not enough information
LOS	Yes	No	Yes	Not enough information

* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of intervention; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that “no statistically significant association” is not the same as “not predictive”.

Preliminary consideration of co-interventions

Complete a row for each important co-intervention (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as important.

"Important" co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention.

(i) Co-interventions listed in the review protocol		
Co-intervention	Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)?	Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator
Analgesic Pathway	No	Favour experimental ~~/ Favour comparator / No information~~
Catheterisation	No information	~~Favour experimental / Favour comparator~~ / No information
LIA	No	Favour experimental ~~/ Favour comparator / No information~~
Staff Availability	No	~~Favour experimental / Favour comparator /~~ No information

(ii) Additional co-interventions relevant to the setting of this particular study, or which the study authors identified as important		
Co-intervention	Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)?	Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator
Cessation of negative vacuum suction drain	No	~~Favour experimental / Favour comparator /~~ No information
Antibiotic regimen	Yes –Standard across both groups	~~Favour experimental / Favour comparator /~~ No information
		Favour experimental / Favour comparator / No information
		Favour experimental / Favour comparator / No information

Risk of bias assessment

Responses underlined in green are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Signalling questions	Description	Response options
Bias due to confounding		
1.1 Is there potential for confounding of the effect of intervention in this study? **If N/PN to 1.1:** the study can be considered to be at low risk of bias due to confounding and no further signalling questions need be considered	Yes	Y / ~~PY~~ / ~~PN / N~~
If Y/PY to 1.1: determine whether there is a need to assess time-varying confounding:		

1.2. Was the analysis based on splitting participants' follow up time according to intervention received? **If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6) **If Y/PY**, go to question 1.3.	No – Retrospective review	~~NA / Y / PY / PN~~ / N ~~/ NI~~
1.3. Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome? **If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6) **If Y/PY**, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8)	N/A	NA / Y / PY / PN / N / NI

Questions relating to baseline confounding only

1.4. Did the authors use an appropriate analysis method that controlled for all the important confounding domains?	Yes | Results were stratified according to all measured confounding domains	~~NA /~~ Y ~~/ PY~~ ~~/ PN / N~~ ~~/ NI~~
1.5. **If Y/PY to 1.4**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?	Probably Yes | Age, Gender, BMI ASA, surgery duration, LOS, surgery type and prosthesis type. BMI, ASA and Surgery duration not collected for all	~~NA /~~ Y ~~/~~ PY ~~/ PN / N~~ ~~/ NI~~
1.6. Did the authors control for any post-intervention variables that could have been affected by the intervention?	No	~~NA /~~ ~~Y / PY~~ ~~/ PN~~ / N ~~/ NI~~
Questions relating to baseline and time-varying confounding		
1.7. Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding?	Yes	~~NA /~~ Y ~~/ PY~~ ~~/ PN / N~~ ~~/ NI~~

1.8. **If Y/PY to 1.7**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?	Yes	~~NA /~~ Y ~~/ PY / PN / N / NI~~
Risk of bias judgement	Moderate	~~Low /~~ Moderate ~~/ Serious / Critical / NI~~
Optional: What is the predicted direction of bias due to confounding?	No evidence for favour towards either group.	~~Favours experimental / Favours comparator /~~ Unpredictable

Bias in selection of participants into the study		
2.1. Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention? **If N/PN to 2.1:** go to 2.4	No | All patients operated on within selected dates were reviewed.	~~Y / PY /~~ PN ~~/~~ N ~~/ NI~~

2.2. **If Y/PY to 2.1**: Were the post-intervention variables that influenced selection likely to be associated with intervention?	N/A	NA ~~/ Y / PY~~ / PN / N ~~/ NI~~
2.3 **If Y/PY to 2.2**: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome?	N/A	NA ~~/ Y / PY~~ / PN / N ~~/ NI~~
2.4. Do start of follow-up and start of intervention coincide for most participants?	Yes	Y / PY ~~/ PN / N / NI~~
2.5. **If Y/PY to 2.2 and 2.3, or N/PN to 2.4**: Were adjustment techniques used that are likely to correct for the presence of selection biases?	N/A	NA ~~/ Y / PY~~ / ~~PN / N / NI~~
Risk of bias judgement	Low	Low ~~/ Moderate / Serious / Critical / NI~~

Optional: What is the predicted direction of bias due to selection of participants into the study?	No evidence for favour towards either group.	~~Favours experimental / Favours comparator / Towards null /Away from null /~~ Unpredictable

Bias in classification of interventions		
3.1 Were intervention groups clearly defined?	Yes	Y ~~/ PY / PN / N / NI~~
3.2 Was the information used to define intervention groups recorded at the start of the intervention?	Probably yes | Determined by dates which participants underwent surgery	~~Y~~ / PY ~~/ PN / N / NI~~
3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome?	Review of medical records – unlikely to have been subject to misclassification	~~Y / PY~~ / PN ~~/~~ / N ~~/ NI~~
Risk of bias judgement	Low	Low ~~/ Moderate / Serious / Critical / NI~~
Optional: What is the predicted direction of bias due to classification of interventions?	No evidence for favour towards either group.	~~Favours experimental / Favours comparator / Towards null /Away from null /~~ Unpredictable

Bias due to deviations from intended interventions		
If your aim for this study is to assess the effect of assignment to intervention, answer questions 4.1 and 4.2		
4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice?	Probably Yes |	~~Y /~~ PY ~~/~~ PN / N ~~/ NI~~
4.2. **If Y/PY to 4.1**: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome?	Cemented v uncemented change and analgesic pathway changes during the course of the study	~~NA /~~ Y ~~/ PY~~ ~~/~~ PN / N ~~/ NI~~
If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6		
4.3. Were important co-interventions balanced across intervention groups?	N/A	Y / PY / PN / N / NI
4.4. Was the intervention implemented successfully for most participants?	N/A	Y / PY / PN / N / NI
4.5. Did study participants adhere to the assigned intervention regimen?	N/A	Y / PY / PN / N / NI

4.6. **If N/PN to 4.3, 4.4 or 4.5**: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention?	N/A	NA / Y / PY / PN / N / NI
Risk of bias judgement	Difference between the groups in numbers of cemented and uncemented prosthesis was balanced	~~Low /~~ Moderate ~~/ Serious / Critical / NI~~
Optional: What is the predicted direction of bias due to deviations from the intended interventions?	No evidence for favour towards either group.	~~Favours experimental / Favours comparator / Towards null /Away from null /~~ Unpredictable

Bias due to missing data		
5.1 Were outcome data available for all, or nearly all, participants?	No | Some confounding data not collected for all participants. BMI, ASA and surgery duration	Y / PY ~~/ PN /~~ N ~~/ NI~~
5.2 Were participants excluded due to missing data on intervention status?	No	~~Y / PY /~~ PN / N ~~/ NI~~
5.3 Were participants excluded due to missing data on other variables needed for the analysis?	No	~~Y / PY /~~ PN / N ~~/ NI~~

5.4 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Are the proportion of participants and reasons for missing data similar across interventions?	No	~~NA /~~ ~~Y / PY~~ ~~/ PN~~ / N ~~/ NI~~
5.5 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Is there evidence that results were robust to the presence of missing data?	Significant numbers – standard care group was very large	~~NA /~~ ~~Y / PY~~ ~~/ PN / N~~ ~~/ NI~~
Risk of bias judgement	Serious	~~Low / Moderate /~~ Serious / ~~Critical / NI~~
Optional: What is the predicted direction of bias due to missing data?	No evidence for favour towards either group.	Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Bias in measurement of outcomes		
6.1 Could the outcome measure have been influenced by knowledge of the intervention received?	No | Retrospective data review – not aware study would take place at the time of the intervention.	~~Y / PY~~ ~~/ PN /~~ ~~N~~ / ~~NI~~

6.2 Were outcome assessors aware of the intervention received by study participants?	Yes	Y ~~/ PY~~ / PN / N ~~/ NI~~
6.3 Were the methods of outcome assessment comparable across intervention groups?	Probably Yes	~~Y~~ / PY ~~/ PN / N~~ / NI
6.4 Were any systematic errors in measurement of the outcome related to intervention received?	Probably No	~~Y / PY~~ / PN ~~/ N~~ / NI
Risk of bias judgement	Low	Low ~~/ Moderate / Serious / Critical / NI~~
Optional: What is the predicted direction of bias due to measurement of outcomes?	No evidence for favour towards either group.	Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Bias in selection of the reported result		
Is the reported effect estimate likely to be selected, on the basis of the results, from...		

7.1. ... multiple outcome *measurements* within the outcome domain?	No	~~Y / PY~~ / PN / N ~~/ NI~~
7.2 ... multiple *analyses* of the intervention-outcome relationship?	No	~~Y / PY~~ / PN / N ~~/ NI~~
7.3 ... different *subgroups*?	No | All sub-groups were presented	~~Y / PY~~ / PN / N ~~/ NI~~
Risk of bias judgement	Low	Low ~~/ Moderate / Serious / Critical / NI~~
Optional: What is the predicted direction of bias due to selection of the reported result?	No evidence for favour towards either group.	~~Favours experimental / Favours comparator / Towards null /Away from null /~~ Unpredictable

Overall bias		
Risk of bias judgement	Serious	~~Low / Moderate~~ / Serious ~~/ Critical / NI~~

Optional: What is the overall predicted direction of bias for this outcome?		Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

ROBINS I Tool Assessment for Risk of Bias

Study / Article:

Juliano, K., Edwards, D., Spinello, D., Capizzano, Y., Epelman, E., Kalowitz, J., Lempel, A. & Ghomrawi, H., (2011) Initiating physical therapy on the day of surgery decreases length of stay without compromising functional outcomes following total hip arthroplasty. *Archives of Orthopaedic and Trauma Surgery*, 7(1), pp.16–20.

Reference Number:

37

Study Classification:

Correlation Study

Reviewer:

Christopher Efford and Catherine Holdsworth

ROBINS-I tool (Stage II): (Juliano et al. 2011)

Specify a target randomized trial specific to the study

Design	Individually randomized / ~~Cluster randomized / Matched (e.g. cross-over)~~
Participants	People who have undergone open primary THR via postero-lateral approach without complications.
Experimental intervention	Day-Zero ambulation in isolation
Comparator	Standard care including ambulation day 1 or greater

Is your aim for this study…?

☑ to assess the effect of *assignment to* intervention

☐ to assess the effect of *starting and adhering to* intervention

Specify the outcome

Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table). Specify whether this is a proposed benefit or harm of intervention.

Length of hospital stay

Specify the numerical result being assessed

In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

LOS – reduction of 0.21 days in LOS in intervention when compared to control (p=0.014)

Preliminary consideration of confounders

Complete a row for each important confounding domain (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as potentially important.

"Important" confounding domains are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. "Validity" refers to whether the confounding variable or variables fully measure the domain, while "reliability" refers to the precision of the measurement (more measurement error means less reliability).

(i) Confounding domains listed in the review protocol				
Confounding domain	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator?
Age	Yes	No	Yes	Unclear – means between groups comparable, not shown in comparison testing however.
Pre-Morbid Function	Yes in terms of pre-morbid walking aid and distance	No	Yes	Experimental – better premorbid – didn't quite reach statistical sig.
Co-morbidities Measured using ASA	No	No	N/A	N/A

Anaesthetic type	No	No	N/A	Not collected or discussed
Blood Loss	No	No	No	Not collected or discussed
Time of surgery	Yes – in day of the week	No	Partially	Time of surgery will have had an effect on selection.
Duration of surgery	No	No	No	Not collected or discussed
Surgical Technique	No	No	No	Not collected or discussed
Arthroplasty type	Yes	Yes	N/A	All THR pts
Gender	Yes	No	Yes	No - significant differences between groups

(ii) Additional confounding domains relevant to the setting of this particular study, or which the study authors identified as important				
Confounding domain	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator?

Operation side	Yes	No	Yes	No - significant differences between groups
Day of the week operated on	Yes	No	Yes	No - significant differences between groups
Ethnic Race	Yes	No	Yes	No - significant differences between groups

* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of intervention; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that “no statistically significant association” is not the same as “not predictive”.

Preliminary consideration of co-interventions

Complete a row for each important co-intervention (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as important.

"Important" co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention.

(i) Co-interventions listed in the review protocol		
Co-intervention	Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)?	Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator
Analgesic Pathway	No – not discussed	Unclear
Catheterisation	No – not discussed	Unclear
LIA	No – not discussed	Unclear
Staff Availability	No – not discussed	Unclear

(ii) Additional co-interventions relevant to the setting of this particular study, or which the study authors identified as important

Co-intervention	Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)?	Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator
		Favour experimental / Favour comparator / No information
		Favour experimental / Favour comparator / No information
		Favour experimental / Favour comparator / No information
		Favour experimental / Favour comparator / No information

Risk of bias assessment

Responses underlined in green are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Signalling questions	Description	Response options
Bias due to confounding		
1.1 Is there potential for confounding of the effect of intervention in this study? **If N/PN to 1.1:** the study can be considered to be at low risk of bias due to confounding and no further signalling questions need be considered	Yes	Y Agreed Response: Yes
If Y/PY to 1.1: determine whether there is a need to assess time-varying confounding:		

1.2. Was the analysis based on splitting participants' follow up time according to intervention received? **If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6) **If Y/PY**, go to question 1.3.	No	NA / Y / PY / PN / N / NI Agreed Response: No
1.3. Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome? **If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6) **If Y/PY**, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8)	N/A	NA / Y / PY / PN / N / NI

Questions relating to baseline confounding only

1.4. Did the authors use an appropriate analysis method that controlled for all the important confounding domains?	No - No stratification or adjustment for confounding factors.	N Agreed Response: No
1.5. **If Y/PY to 1.4**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?	N/A	NA
1.6. Did the authors control for any post-intervention variables that could have been affected by the intervention?	Yes – Patients who were discharged to rehab or were readmitted were excluded.	Y Agreed Response: Yes
Questions relating to baseline and time-varying confounding		

1.7. Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding?	N/A	NA / Y / PY / PN / N / NI
1.8. **If Y/PY to 1.7**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?	N/A	NA / Y / PY / PN / N / NI
Risk of bias judgement	Serious	**Serious** Agreed Response: Serious
Optional: What is the predicted direction of bias due to confounding?	Baseline measures do appear to favour experimental group although not statistically significant. Several confounding domains not measured / considered (comorbidities, pain/analgesia)	Favours experimental

Bias in selection of participants into the study

2.1. Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention? **If N/PN to 2.1:** go to 2.4	Yes - Participants excluded based on outcome – discharge to rehabilitation or readmitted. Therefore selection excluded the 'worst' performers.	Y Agreed Response: Yes
2.2. **If Y/PY to 2.1**: Were the post-intervention variables that influenced selection likely to be associated with intervention?	Yes – Slow rehab and inability to return directly home. Intervention could have been a potential cause of these outcomes.	Y Agreed Response: Yes
2.3 **If Y/PY to 2.2**: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome?		Y Agreed Response: Yes
2.4. Do start of follow-up and start of intervention coincide for most participants?	Yes	Y Agreed Response: Yes

2.5. **If Y/PY to 2.2 and 2.3, or N/PN to 2.4**: Were adjustment techniques used that are likely to correct for the presence of selection biases?	No specific analysis methods	N Agreed Response: No
Risk of bias judgement	Serious	**Serious** Agreed Response: Serious
Optional: What is the predicted direction of bias due to selection of participants into the study?	Exclusion of patients who functionally would have been the poorest performers.	Away from null

Bias in classification of interventions		
3.1 Were intervention groups clearly defined?	Yes	Y Agreed Response: Yes

3.2 Was the information used to define intervention groups recorded at the start of the intervention?	Yes	Y Agreed Response: Yes
3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome?	No clear evidence on how participants were selected for intervention or control.	N Agreed Response: No
Risk of bias judgement	Moderate	**Low** Agreed Response: Low
Optional: What is the predicted direction of bias due to classification of interventions?		Unpredictable

Bias due to deviations from intended interventions

If your aim for this study is to assess the effect of assignment to intervention, answer questions 4.1 and 4.2		
4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice?	No – No evidence to suggest significant pathway deviations.	N Agreed Response: No
4.2. **If Y/PY to 4.1**: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome?	N/A	NA
If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6		
4.3. Were important co-interventions balanced across intervention groups?	N/A	Y / PY / PN / N / NI
4.4. Was the intervention implemented successfully for most participants?	N/A	Y / PY / PN / N / NI
4.5. Did study participants adhere to the assigned intervention regimen?	N/A	Y / PY / PN / N / NI

4.6. **If N/PN to 4.3, 4.4 or 4.5**: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention?	N/A	NA / Y / PY / PN / N / NI
Risk of bias judgement	Low	**Low** Agreed Response: Low
Optional: What is the predicted direction of bias due to deviations from the intended interventions?		Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Bias due to missing data		
5.1 Were outcome data available for all, or nearly all, participants?	Yes – No documented loss to follow-up or missing data. Note: Rehospitalisation participants excluded.	PY Agreed Response: PY

5.2 Were participants excluded due to missing data on intervention status?	No concerns	N Agreed Response: No
5.3 Were participants excluded due to missing data on other variables needed for the analysis?	No concerns	N Agreed Response: No
5.4 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Are the proportion of participants and reasons for missing data similar across interventions?	N/A	NA
5.5 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Is there evidence that results were robust to the presence of missing data?	N/A	NA

Risk of bias judgement	Low	**Low** Agreed Response: Low
Optional: What is the predicted direction of bias due to missing data?		Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Bias in measurement of outcomes		
6.1 Could the outcome measure have been influenced by knowledge of the intervention received?	LOS clearly defined as a time-point	N Agreed Response: No

6.2 Were outcome assessors aware of the intervention received by study participants?	Very likely – retrospective review so assessors would likely have been the treating clinicians	PY Agreed Response: PY
6.3 Were the methods of outcome assessment comparable across intervention groups?	No concerns. Of note – no clarity on specific discharge criteria - ? differences highlighted in Table 3 – milestone achievement.	PY Agreed Response: PY
6.4 Were any systematic errors in measurement of the outcome related to intervention received?	No concerns	N Agreed Response: PN

Risk of bias judgement	Moderate	**Moderate** Agreed Response: Moderate
Optional: What is the predicted direction of bias due to measurement of outcomes?		Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Bias in selection of the reported result		
Is the reported effect estimate likely to be selected, on the basis of the results, from... 7.1. ... multiple outcome *measurements* within the outcome domain?	No concerns	N Agreed Response: No

7.2 ... multiple *analyses* of the intervention-outcome relationship?	No concerns	N Agreed Response: No
7.3 ... different *subgroups*?	No sub-grouping	N Agreed Response: No
Risk of bias judgement	Low	**Low** Agreed Response: Low
Optional: What is the predicted direction of bias due to selection of the reported result?	N/A	Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall bias

Risk of bias judgement	Serious	**Serious** Agreed Response: Serious
Optional: What is the overall predicted direction of bias for this outcome?	Favours experimental	Favours experimental

ROBINS I Tool Assessment for Risk of Bias

Study / Article:

Karim, A., Pulido, L. & Incavo, S., (2016) Does Accelerated Physical Therapy After Elective Primary Hip and Knee Arthroplasty Facilitate Early Discharge? *American journal of orthopedics (Belle Mead, N.J.)*, 45(6), pp.E337–E342. Available at: https://www.amjorthopedics.com/sites/default/files/ajo04509337e.PDF [Accessed February 21, 2018].

Reference Number:

64

Study Classification:

Cohort Study

Reviewer:

Christopher Efford and Catherine Holdsworth

ROBINS-I tool (Stage II): (Karim et al. 2016)

Specify a target randomized trial specific to the study

Design	Individually randomized / ~~Cluster randomized / Matched (e.g. cross-over)~~
Participants	People who have undergone open primary THR
Experimental intervention	Day-Zero ambulation in isolation
Comparator	Standard care including ambulation day 1 or greater

Is your aim for this study…?

☑ to assess the effect of *assignment to* intervention

☐ to assess the effect of *starting and adhering to* intervention

Specify the outcome

Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table). Specify whether this is a proposed benefit or harm of intervention.

Length of hospital stay

Specify the numerical result being assessed

In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

THR and TKR – Intervention group LOS 2.27 days (95% CI 2.15 to 2.39) Control group LOS 2.45 days (95% CI 2.23 – 2.67) Specific to THR – Intervention group LOS 2.26 days (95% CI 2.0 to 2.5) Control group LOS 2.5 days (95% CI 2.2 – 2.8)

Preliminary consideration of confounders

Complete a row for each important confounding domain (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as potentially important.

"Important" confounding domains are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. "Validity" refers to whether the confounding variable or variables fully measure the domain, while "reliability" refers to the precision of the measurement (more measurement error means less reliability).

(i) Confounding domains listed in the review protocol				
Confounding domain	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator?
Age	Yes	No	Yes	Unclear – no statistical comparison testing
Pre-Morbid Function	No	No	N/A	N/A
Co-morbidities Measured using ASA	Yes	No	N/A	Unclear – no statistical comparison testing. ? increased ASA in Control group

Anaesthetic type	Yes	No	Yes	Unclear – no statistical comparison testing.
Blood Loss	Yes	No	Yes	Favours experimental – significantly higher blood loss in control group.
Time of day of surgery	No	No	N/A	Significant factor in group allocation.
Duration of surgery	Yes	No	Yes	Unclear – no statistical comparison testing. Appears comparable
Surgical Technique	Yes	No	Yes	Unclear – no statistical comparison testing. Some minimally invasive surgery. Unable to compare between groups.
Arthroplasty type	Yes	Yes	N/A	N/A
Gender	Yes	No	Yes	Similar proportions across groups.

(ii) Additional confounding domains relevant to the setting of this particular study, or which the study authors identified as important

Confounding domain	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator?

* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of intervention; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that “no statistically significant association” is not the same as “not predictive”.

Preliminary consideration of co-interventions

Complete a row for each important co-intervention (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as important.

"Important" co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention.

(i) Co-interventions listed in the review protocol		
Co-intervention	Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)?	Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator
Analgesic Pathway	No – not discussed	Unclear
Catheterisation	No – not discussed	Unclear
LIA	No	Neither – the same used for both groups
Staff Availability	No	Described as a factor in group allocation

(ii) Additional co-interventions relevant to the setting of this particular study, or which the study authors identified as important		
Co-intervention	Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)?	Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator

Minimally invasive surgical techniques	No	No information – unclear of the balance of this across groups.
		Favour experimental / Favour comparator / No information
		Favour experimental / Favour comparator / No information
		Favour experimental / Favour comparator / No information

Risk of bias assessment

Responses underlined in green are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Signalling questions	Description	Response options
Bias due to confounding		
1.1 Is there potential for confounding of the effect of intervention in this study? **If N/PN to 1.1:** the study can be considered to be at low risk of bias due to confounding and no further signalling questions need be considered	Yes Differing blood loss between groups Unclear balance across groups for minimally invasive surgical technique.	Y Agreed Response: Yes
If Y/PY to 1.1: determine whether there is a need to assess time-varying confounding:		

1.2. Was the analysis based on splitting participants' follow up time according to intervention received? **If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6) **If Y/PY**, go to question 1.3.	No	N Agreed Response: No
1.3. Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome? **If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6) **If Y/PY**, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8)	N/A	NA

Questions relating to baseline confounding only

1.4. Did the authors use an appropriate analysis method that controlled for all the important confounding domains?	Probably No – results were stratified for type of arthroplasty but not for other confounders.	PN Agreed Response: Probably No
1.5. **If Y/PY to 1.4**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?	N/A	NA
1.6. Did the authors control for any post-intervention variables that could have been affected by the intervention?	No	N Agreed Response: No
Questions relating to baseline and time-varying confounding		

1.7. Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding?	N/A	NA
1.8. **If Y/PY to 1.7**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?	N/A	NA
Risk of bias judgement	Serious	**Serious** Agreed Response: **Serious**
Optional: What is the predicted direction of bias due to confounding?	Good coverage of confounders – blood loss shown to be significantly different between groups.	Favours experimental

Bias in selection of participants into the study

2.1. Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention? **If N/PN to 2.1:** go to 2.4	Yes – Group allocation based on ability to ambulate on day 0. Those that failed intervention for whatever reason, including choice became the control group. A few exclusions due to outcomes or complications.	Y Agreed Response: Yes
2.2. **If Y/PY to 2.1**: Were the post-intervention variables that influenced selection likely to be associated with intervention?	Yes	Y Agreed Response: Yes
2.3 **If Y/PY to 2.2**: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome?	Yes	Y Agreed Response: Yes
2.4. Do start of follow-up and start of intervention coincide for most participants?	Yes	Y

2.5. **If Y/PY to 2.2 and 2.3, or N/PN to 2.4**: Were adjustment techniques used that are likely to correct for the presence of selection biases?	No specific analysis methods	N
Risk of bias judgement	Serious	**Serious** Agreed Response: **Serious**
Optional: What is the predicted direction of bias due to selection of participants into the study?	Group allocation method could favour experimental group. It would be expected that participants who failed the mobility intervention could take longer to recover.	Towards experimental

Bias in classification of interventions		
3.1 Were intervention groups clearly defined?	Yes	Y Agreed Response: Yes

3.2 Was the information used to define intervention groups recorded at the start of the intervention?	Yes	Y Agreed Response: Yes
3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome?	Likely to expect participants who failed day 0 ambulation to do poorly.	N Agreed Response: No
Risk of bias judgement	Serious	**Low** Agreed Response: Low
Optional: What is the predicted direction of bias due to classification of interventions?	Favours experimental	Favours experimental

Bias due to deviations from intended interventions

If your aim for this study is to assess the effect of assignment to intervention, answer questions 4.1 and 4.2		
4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice?	No – Only small deviations which can be considered part of normal practice.	N Agreed Response: No
4.2. **If Y/PY to 4.1**: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome?	N/A	NA
If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6		
4.3. Were important co-interventions balanced across intervention groups?	N/A	Y / PY / PN / N / NI
4.4. Was the intervention implemented successfully for most participants?	N/A	Y / PY / PN / N / NI

4.5. Did study participants adhere to the assigned intervention regimen?	N/A	Y / PY / PN / N / NI
4.6. **If N/PN to 4.3, 4.4 or 4.5**: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention?	N/A	NA / Y / PY / PN / N / NI
Risk of bias judgement	Low	**Low** Agreed Response: Low
Optional: What is the predicted direction of bias due to deviations from the intended interventions?		Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Bias due to missing data

5.1 Were outcome data available for all, or nearly all, participants?	Yes – No evidence of missing data	Y Agreed Response: Yes
5.2 Were participants excluded due to missing data on intervention status?	No concerns	N Agreed Response: No
5.3 Were participants excluded due to missing data on other variables needed for the analysis?	No concerns	N Agreed Response: No
5.4 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Are the proportion of participants and reasons for missing data similar across interventions?	N/A	NA

5.5 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Is there evidence that results were robust to the presence of missing data?	N/A	NA
Risk of bias judgement	Low	**Low** Agreed Response: Low
Optional: What is the predicted direction of bias due to missing data?	Unpredictable	Unpredictable

Bias in measurement of outcomes		
6.1 Could the outcome measure have been influenced by knowledge of the intervention received?	LOS clearly defined as a time-point	N Agreed Response: No

6.2 Were outcome assessors aware of the intervention received by study participants?	Very likely. No mention of blinding. Retrospective study – therefore would not expect biases from non-blinding.	PY Agreed Response: PY
6.3 Were the methods of outcome assessment comparable across intervention groups?	No concerns	Y Agreed Response: Yes
6.4 Were any systematic errors in measurement of the outcome related to intervention received?	No concerns	N Agreed Response: No
Risk of bias judgement	Moderate	**Low** Agreed Response: Low

Optional: What is the predicted direction of bias due to measurement of outcomes?		Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Bias in selection of the reported result		
Is the reported effect estimate likely to be selected, on the basis of the results, from... 7.1. ... multiple outcome *measurements* within the outcome domain?	Did report on measures not included in the planned methodology	PN Agreed Response: PN
7.2 ... multiple *analyses* of the intervention-outcome relationship?	No concerns	N Agreed Response: No

7.3 ... different *subgroups*?	Sub groups for type of arthroplasty, but all results presented.	N Agreed Response: No
Risk of bias judgement	Low	**Low** **Agreed Response:** **Low**
Optional: What is the predicted direction of bias due to selection of the reported result?	N/A	Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall bias

Risk of bias judgement	Serious	**Serious** **Agreed Response:** **Serious**
Optional: What is the overall predicted direction of bias for this outcome?	Favours experimental	Favours experimental

ROBINS I Tool Assessment for Risk of Bias

Study / Article:

Khan, S.K., Malviya, A., Muller, S.D., Carluke, I., Partington, P.F., Emmerson, K.P. & Reed, M.R., (2014) Reduced short-term complications and mortality following Enhanced Recovery primary hip and knee arthroplasty: results from 6,000 consecutive procedures. *Acta orthopaedica*, 85(1), pp.26–31. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3940988&tool=pmcentrez&rendertype=abstract.

Reference Number:

46

Study Classification:

Cohort Study

Reviewer:

Christopher Efford and Catherine Holdsworth

ROBINS-I tool (Stage II): (Khan et al. 2014)

Specify a target randomized trial specific to the study

Design	Individually randomized / ~~Cluster randomized / Matched (e.g. cross-over)~~
Participants	People who have undergone open primary THR
Experimental intervention	Day-Zero ambulation in isolation
Comparator	Standard care including ambulation day 1 or greater

Is your aim for this study…?

☑ to assess the effect of *assignment to* intervention

☐ to assess the effect of *starting and adhering to* intervention

Specify the outcome

Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table). Specify whether this is a proposed benefit or harm of intervention.

Post-operative complications

Specify the numerical result being assessed

In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

Preliminary consideration of confounders

Complete a row for each important confounding domain (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as potentially important.

"Important" confounding domains are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. "Validity" refers to whether the confounding variable or variables fully measure the domain, while "reliability" refers to the precision of the measurement (more measurement error means less reliability).

(i) Confounding domains listed in the review protocol				
Confounding domain	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator?
Age	Yes	No	Yes	Slightly younger cohort in the experimental group p=0.05
Pre-Morbid Function	No	No	N/A	N/A
Co-morbidities	Yes	No	N/A	Favour comparator –more prevalent comorbidities in experimental group.
Anaesthetic type	Yes	No	Yes	Neither – Standardised

Blood Loss	No	No	N/A	N/A
Time of day of surgery	No	No	N/A	N/A
Duration of surgery	No	No	N/A	N/A
Surgical Technique	Yes	No	Yes	Neither – Standardised
Arthroplasty type	Yes	No	Yes	Unclear although higher proportion TKR in experimental group
Gender	Yes	No	Yes	Higher % males in comparator group. Could favour control.

(ii) Additional confounding domains relevant to the setting of this particular study, or which the study authors identified as important				
Confounding domain	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator?

* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of intervention; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that “no statistically significant association” is not the same as “not predictive”.

Preliminary consideration of co-interventions

Complete a row for each important co-intervention (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as important.

"Important" co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention.

(i) Co-interventions listed in the review protocol		
Co-intervention	Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)?	Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator
Analgesic Pathway	Yes	Neither – Standardised
Catheterisation	No – not discussed	Unclear
LIA	Yes	Neither – Standardised
Staff Availability	No	Unclear – not discussed

(ii) Additional co-interventions relevant to the setting of this particular study, or which the study authors identified as important

Co-intervention	Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)?	Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator
Pre-operative education	No	Neither –Standardised
		Favour experimental / Favour comparator / No information
		Favour experimental / Favour comparator / No information
		Favour experimental / Favour comparator / No information

Risk of bias assessment

Responses underlined in green are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Signalling questions	Description	Response options
Bias due to confounding		
1.1 Is there potential for confounding of the effect of intervention in this study? **If N/PN to 1.1:** the study can be considered to be at low risk of bias due to confounding and no further signalling questions need be considered	Yes Several baseline differences between groups. Age, gender, arthroplasty type, comorbidities.	Y
If Y/PY to 1.1: determine whether there is a need to assess time-varying confounding:		

1.2. Was the analysis based on splitting participants' follow up time according to intervention received? **If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6) **If Y/PY**, go to question 1.3.	No	N
1.3. Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome? **If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6) **If Y/PY**, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8)	N/A	NA

Questions relating to baseline confounding only

1.4. Did the authors use an appropriate analysis method that controlled for all the important confounding domains?	Yes – Confounders described	Y
1.5. **If Y/PY to 1.4**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?	Yes – All appear to be measured validly	Y
1.6. Did the authors control for any post-intervention variables that could have been affected by the intervention?	No	N
Questions relating to baseline and time-varying confounding		
1.7. Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding?	N/A	NA

1.8. **If Y/PY to 1.7**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?	N/A	NA
Risk of bias judgement	Moderate	**Moderate**
Optional: What is the predicted direction of bias due to confounding?	Favours control group.	Favours control

Bias in selection of participants into the study		
2.1. Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention? **If N/PN to 2.1:** go to 2.4	No – all patients included.	N

2.2. **If Y/PY to 2.1**: Were the post-intervention variables that influenced selection likely to be associated with intervention?	N/A	NA
2.3 **If Y/PY to 2.2**: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome?	N/A	NA
2.4. Do start of follow-up and start of intervention coincide for most participants?	Yes	Y
2.5. **If Y/PY to 2.2 and 2.3, or N/PN to 2.4**: Were adjustment techniques used that are likely to correct for the presence of selection biases?	NA	NA
Risk of bias judgement	Low	**Low**
Optional: What is the predicted direction of bias due to selection of participants into the study?	N/A	

Bias in classification of interventions		
3.1 Were intervention groups clearly defined?	Yes – Table 1	Y
3.2 Was the information used to define intervention groups recorded at the start of the intervention?	Yes	Y
3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome?	No.	N
Risk of bias judgement	Low	**Low**
Optional: What is the predicted direction of bias due to classification of interventions?		

Bias due to deviations from intended interventions	
If your aim for this study is to assess the effect of assignment to intervention, answer questions 4.1 and 4.2	

4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice?	No – Some deviations over the course of study pathway on anticoagulation and prophylactic antibiotics.	N
4.2. **If Y/PY to 4.1**: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome?	N/A	NA
If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6		
4.3. Were important co-interventions balanced across intervention groups?	N/A	Y / PY / PN / N / NI
4.4. Was the intervention implemented successfully for most participants?	N/A	Y / PY / PN / N / NI
4.5. Did study participants adhere to the assigned intervention regimen?	N/A	Y / PY / PN / N / NI
4.6. **If N/PN to 4.3, 4.4 or 4.5**: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention?	N/A	NA / Y / PY / PN / N / NI

Risk of bias judgement	Low	**Low**
Optional: What is the predicted direction of bias due to deviations from the intended interventions?		Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Bias due to missing data		
5.1 Were outcome data available for all, or nearly all, participants?	Yes – No evidence of missing data	Y
5.2 Were participants excluded due to missing data on intervention status?	No concerns	N
5.3 Were participants excluded due to missing data on other variables needed for the analysis?	No concerns	N
5.4 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Are the proportion of participants and reasons for missing data similar across interventions?	N/A	NA

5.5 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Is there evidence that results were robust to the presence of missing data?	N/A	NA
Risk of bias judgement	Low	**Low**
Optional: What is the predicted direction of bias due to missing data?	Unpredictable	Unpredictable

Bias in measurement of outcomes		
6.1 Could the outcome measure have been influenced by knowledge of the intervention received?	LOS clearly defined as a time-point	N
6.2 Were outcome assessors aware of the intervention received by study participants?	Yes	Y
6.3 Were the methods of outcome assessment comparable across intervention groups?	No concerns	Y

6.4 Were any systematic errors in measurement of the outcome related to intervention received?	No concerns	N
Risk of bias judgement	Low	**Low**
Optional: What is the predicted direction of bias due to measurement of outcomes?		Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Bias in selection of the reported result		
Is the reported effect estimate likely to be selected, on the basis of the results, from...		
7.1. ... multiple outcome *measurements* within the outcome domain?	No concerns	N
7.2 ... multiple *analyses* of the intervention-outcome relationship?	No concerns	N
7.3 ... different *subgroups*?	No subgroups	N

Risk of bias judgement	Low	**Low**
Optional: What is the predicted direction of bias due to selection of the reported result?	N/A	Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall bias		
Risk of bias judgement	Moderate	**Moderate**
Optional: What is the overall predicted direction of bias for this outcome?	Favours control	Favours control

ROBINS I Tool Assessment for Risk of Bias

Study / Article:

Sibia, U.S., MacDonald, J.H. & King, P.J., (2016) Predictors of Hospital Length of Stay in an Enhanced Recovery After Surgery Program for Primary Total Hip Arthroplasty. Journal of Arthroplasty, 31(10), pp.2119–2123. Available at: http://dx.doi.org/10.1016/j.arth.2016.02.060. [Accessed September 16, 2020].

Reference Number:

129

Study Classification:

Case Control Study

Reviewer:

Christopher Efford and Catherine Holdsworth

ROBINS-I tool (Stage II): (Sibia et al. 2016)

Specify a target randomized trial specific to the study

Design	Individually randomized / ~~Cluster randomized / Matched (e.g. cross-over)~~
Participants	People who have undergone open primary THR via postero-lateral approach without complications.
Experimental intervention	Day-Zero ambulation in isolation
Comparator	Standard care including ambulation day 1 or greater

Is your aim for this study…?

☑ to assess the effect of *assignment to* intervention

☐ to assess the effect of *starting and adhering to* intervention

Specify the outcome

Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table). Specify whether this is a proposed benefit or harm of intervention.

Length of stay

Specify the numerical result being assessed

In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

Odds Ratio – 3.93 times more likely to stay > 1 day post-operatively if not ambulating day zero (CI 2.30 to 6.72) (p<0.001)

Preliminary consideration of confounders

Complete a row for each important confounding domain (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as potentially important.

"Important" confounding domains are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention. "Validity" refers to whether the confounding variable or variables fully measure the domain, while "reliability" refers to the precision of the measurement (more measurement error means less reliability).

(i) Confounding domains listed in the review protocol				
Confounding domain	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator?
Age	Yes	No	Yes	Experimental – reduced mean age in experimental group
Pre-Morbid Function	No	No	N/A	N/A
Co-morbidities	Yes	No	Yes	Unable to tell
Anaesthetic type	Yes	No	Yes	No
Blood Loss	Yes	No	Unable to tell – likely yes	N/A

Time of day of surgery	Yes	No	Unable to tell – likely yes	Experimental – accounted for in analysis
Duration of surgery	Yes	No	Unable to tell – likely yes	N/A
Surgical Technique	Yes	No	Yes	Neither
Arthroplasty type	Yes	No	Yes	N/A – exclusive to THR
Gender	Yes	No	Yes	Gender part of the examined variables

(ii) Additional confounding domains relevant to the setting of this particular study, or which the study authors identified as important				
Confounding domain	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding domain measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is failure to adjust for this variable (alone) expected to favour the experimental intervention or the comparator?
			Yes / No / No information	Favour experimental / Favour comparator / No information

* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of intervention; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that “no statistically significant association” is not the same as “not predictive”.

Preliminary consideration of co-interventions

Complete a row for each important co-intervention (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as important.

"Important" co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention.

(i) Co-interventions listed in the review protocol		
Co-intervention	Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)?	Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator
Analgesic Pathway	No	Unable to tell – not described
Catheterisation	No	N/A
LIA	No	Unable to tell – not described
Staff Availability	No	N/A

(ii) Additional co-interventions relevant to the setting of this particular study, or which the study authors identified as important		
Co-intervention	Is there evidence that controlling for this co-intervention was unnecessary (e.g. because it was not administered)?	Is presence of this co-intervention likely to favour outcomes in the experimental intervention or the comparator
Pre-operative education	No	Appears the same across groups

		Favour experimental / Favour comparator / No information
		Favour experimental / Favour comparator / No information

Risk of bias assessment

Responses underlined in green are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Signalling questions	Description	Response options
Bias due to confounding		
1.1 Is there potential for confounding of the effect of intervention in this study? **If N/PN to 1.1:** the study can be considered to be at low risk of bias due to confounding and no further signalling questions need be considered	Many theorised confounding domains – mostly measured or accounted for – however there is potential.	Y Agreed Response: Yes
If Y/PY to 1.1: determine whether there is a need to assess time-varying confounding:		
1.2. Was the analysis based on splitting participants' follow up time according to intervention received? **If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6) **If Y/PY**, go to question 1.3.	No	N Agreed Response: No

1.3. Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome? **If N/PN**, answer questions relating to baseline confounding (1.4 to 1.6) **If Y/PY**, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8)	N/A	NA / Y / PY / PN / N / NI

Questions relating to baseline confounding only		
1.4. Did the authors use an appropriate analysis method that controlled for all the important confounding domains?	Logistic regression looked at most potential confounders as potential predictors. However, base descriptive data for each domain was not presented.	PY **Agreed Response:** **PY**
1.5. **If Y/PY to 1.4**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?	Unable to tell how some were measured such as surgical times, blood loss	Y Agreed Response: Yes

1.6. Did the authors control for any post-intervention variables that could have been affected by the intervention?	No	N **Agreed Response:** **No**
Questions relating to baseline and time-varying confounding		
1.7. Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding?	N/A	NA
1.8. **If Y/PY to 1.7**: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?	N/A	NA
Risk of bias judgement	Moderate	**Low** **Agreed Response:** **Low**
Optional: What is the predicted direction of bias due to confounding?		Unable to tell

Bias in selection of participants into the study		
2.1. Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention? **If N/PN to 2.1:** go to 2.4	No – all people who underwent THR within the study were included	N Agreed Response: No
2.2. **If Y/PY to 2.1**: Were the post-intervention variables that influenced selection likely to be associated with intervention?	N/A	NA
2.3 **If Y/PY to 2.2**: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome?	N/A	NA
2.4. Do start of follow-up and start of intervention coincide for most participants?	Yes	Y Agreed Response: Yes

2.5. **If Y/PY to 2.2 and 2.3, or N/PN to 2.4**: Were adjustment techniques used that are likely to correct for the presence of selection biases?	N/A	NA
Risk of bias judgement	Low	Low Agreed Response: Low
Optional: What is the predicted direction of bias due to selection of participants into the study?	N/A	Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Bias in classification of interventions		
3.1 Were intervention groups clearly defined?	Yes	Y **Agreed Response:** **Yes**

3.2 Was the information used to define intervention groups recorded at the start of the intervention?	Yes	PY **Agreed Response:** **PY**
3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome?	Yes – All data collected retrospectively. Threshold for groups classification open to adjustment after outcome.	Y **Agreed Response:** **Yes**
Risk of bias judgement	Moderate	**Moderate** **Agreed Response:** **Moderate**
Optional: What is the predicted direction of bias due to classification of interventions?	NA	NA

Bias due to deviations from intended interventions	
If your aim for this study is to assess the effect of assignment to intervention, answer questions 4.1 and 4.2	

4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice?	No	N Agreed Respone: No
4.2. **If Y/PY to 4.1**: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome?	N/A	NA
If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6		
4.3. Were important co-interventions balanced across intervention groups?	N/A	
4.4. Was the intervention implemented successfully for most participants?	N/A	
4.5. Did study participants adhere to the assigned intervention regimen?	N/A	
4.6. **If N/PN to 4.3, 4.4 or 4.5**: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention?	N/A	NA

Risk of bias judgement	Low	**Low** Agreed Respone: Low
Optional: What is the predicted direction of bias due to deviations from the intended interventions?	Favours neither	Unpredictable

Bias due to missing data		
5.1 Were outcome data available for all, or nearly all, participants?	No evidence of or discussion of missing data	Y Agreed Respone: Yes
5.2 Were participants excluded due to missing data on intervention status?	N/A	N Agreed Respone: No

5.3 Were participants excluded due to missing data on other variables needed for the analysis?		N Agreed Respone: No
5.4 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Are the proportion of participants and reasons for missing data similar across interventions?	N/A	NA
5.5 **If PN/N to 5.1, or Y/PY to 5.2 or 5.3**: Is there evidence that results were robust to the presence of missing data?	N/A	NA
Risk of bias judgement	Low	**Low** Agreed Respone: Low
Optional: What is the predicted direction of bias due to missing data?	N/A	N/A

Bias in measurement of outcomes

6.1 Could the outcome measure have been influenced by knowledge of the intervention received?	LOS – measurable when pt leaves hospital	N Agreed Respone: No
6.2 Were outcome assessors aware of the intervention received by study participants?	Group allocation based on outcome – blinding not possible N/A – All participants received the same intervention.	Y Agreed Respone: N/A
6.3 Were the methods of outcome assessment comparable across intervention groups?	Yes	Y
6.4 Were any systematic errors in measurement of the outcome related to intervention received?	No	N
Risk of bias judgement	Moderate	**Moderate** Agreed Respone: Low

Optional: What is the predicted direction of bias due to measurement of outcomes?	Unpredictable	Unpredictable

Bias in selection of the reported result		
Is the reported effect estimate likely to be selected, on the basis of the results, from... 7.1. ... multiple outcome *measurements* within the outcome domain?	No	N Agreed Respone: No
7.2 ... multiple *analyses* of the intervention-outcome relationship?	No	N Agreed Respone: No
7.3 ... different *subgroups*?	No	N Agreed Respone: No

Risk of bias judgement	Low	**Low** Agreed Respone: Low
Optional: What is the predicted direction of bias due to selection of the reported result?	N/A	N/A

Overall bias		
Risk of bias judgement	Moderate	Moderate Agreed Respone: Moderate
Optional: What is the overall predicted direction of bias for this outcome?	N/A	N/A

The file below contains details of the Risk of Bias 2.0 assessment carried out for studies which used an RCT design (Larsen 2009; Okamoto et al. 2016)

RAPID RoB 2 CE.xlsm

Appendix 5 Literature Review Checklists

STROBE Checklists:

STROBE Checklist	Husted et al 2009	Robins et al 2014	Juliano et al 2011	Karim et at 2016	Sibia et al 2016
Title and Abstract	✓	✓	✓	×	✓
Introduction					
Background / Rationale	✓	✓	✓	✓	✓
Objectives	✓	✓	✓	✓	✓
Methods					
Study design	✓	✓	✓	✓	✓
Setting	✓	✓	✓	✓	✓
Participants	✓	✓	✓	✓	✓
Variables	×	✓	✓	✓	✓
Data Sources / Management	✓	✓	✓	✓	✓
Bias	×	✓	✓	✓	✓
Study size	×	×	✓	✓	×
Quantitative variables	✓	✓	✓	✓	✓
Statistical methods	✓	✓	✓	✓	✓
Results					
Participants	×	✓	✓	✓	✓
Descriptive Data	×	✓	✓	✓*	✓
Outcome Data	×	✓	✓	✓	✓
Main Results	×	✓	×	✓	✓
Other analyses	×	N/A	×	N/A	✓
Discussion					
Key results	✓	✓	✓	✓	✓
Limitations	×	✓	✓	✓	×
Interpretation	×	✓	✓	✓	✓
Generalisability	×	✓	✓	×	✓
Other Information					
Funding	×	×	×	×	✓

*This study was not explicit about duration of time to follow-up

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item (Larson et al 2008.)	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	✓ 149.
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	✓ 149.
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	✓ 149.
	2b	Specific objectives or hypotheses	X.
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	✓ 149 150.
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A.
Participants	4a	Eligibility criteria for participants	✓ 150
	4b	Settings and locations where the data were collected	✓ 150.
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	✓ 151.
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	✓ 152.
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A.
Sample size	7a	How sample size was determined	✓ 150.
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A.
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	✓ 150
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	✓ 150.
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	✓ 150.
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	✓ 150
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	x

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Okamoto et al 2016.

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	X
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2227
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	✓ 2228
	2b	Specific objectives or hypotheses	✓ 2228
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	X
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	✓ 2228
Participants	4a	Eligibility criteria for participants	✓ 2228
	4b	Settings and locations where the data were collected	✓ 2228
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	✓ 2228
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	✓ 2228
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	X
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	X
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	X
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	X
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	X
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	✓ 2228

PRISMA Checklist:

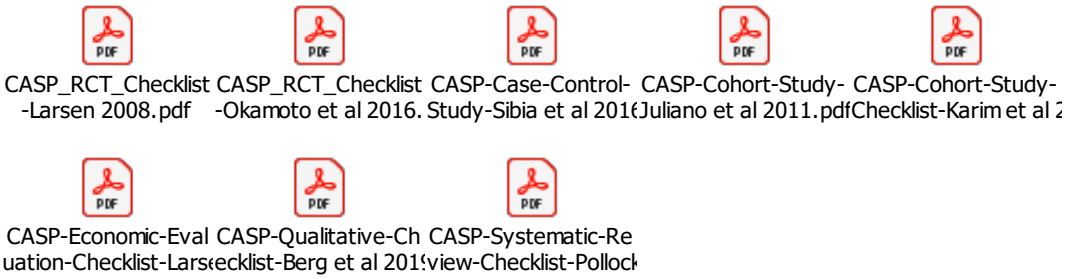
Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	✓ Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	✓ Page 1 + 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	✓ Page 2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	✓ Page 2
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	✓ Page 2
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	✓ Page 2
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	✓ Appendix
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	✓ Page 2+3
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	✓ Page 2/3
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	✓ Page 3
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	✓ Page 3
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	✓ Page 3
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	✓ Page 3
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	×

Section and Topic	Item #	Checklist item	Location where item is reported
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	×
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	×
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	×
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	×
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	×
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	✓ Page 3 /10
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	✓ Page 3
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	✓ Page 3
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	×
Study characteristics	17	Cite each included study and present its characteristics.	✓ Pages 4-9
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	✓ Appendix
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	✓ Pages 4-9
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	✓ Page 10
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	✓ Page 10
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	✓ Pages 6-7
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	×
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	×
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	✓ Pages 10-12

Section and Topic	Item #	Checklist item	Location where item is reported
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	✓ Pages 12-14
	23b	Discuss any limitations of the evidence included in the review.	✓ Page 14
	23c	Discuss any limitations of the review processes used.	✓ Page 14
	23d	Discuss implications of the results for practice, policy, and future research.	✓ Page 14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	×
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	×
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	×
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	×
Competing interests	26	Declare any competing interests of review authors.	×
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	×

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
For more information, visit: http://www.prisma-statement.org/

Appendix 6 CASP Checklists



Appendix 7 Protocol for the Reporting of Adverse Events

This appendix contains an extract from the trial protocol used in both the feasibility study and Fully Powered RCT to provide procedure for the investigation and reporting of adverse and serious adverse events.

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5. Safety Reporting

5.1 General Definitions

5.1.1 Adverse Event (AE)

An AE is any untoward medical occurrence in a subject to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporarily associated with study activities.

5.1.2 Serious Adverse Event (SAE)

An SAE fulfils at least one of the following criteria:

- Is fatal – results in death (NOTE: death is an outcome, not an event)
- Is life-threatening
- Requires inpatient hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is otherwise considered medically significant by the Investigator

The following adverse events may impact on prolonging the period of existing hospitalisation but are common complications following surgery of the nature of a THR. Consequently they will be treated as AEs and reported as such:

- Orthostatic Hypotension resulting in syncope
- Excessive Wound ooze from THR wound:
  - escaping the dressing
  - lasting > 3 days.
  - Was a cause of delaying discharge
- Hb < 85g/L post operatively
- Symptomatic of low Hb
- Fatigue
- Post-operative confusion
- Constipation
- Urinary Retention
- Dehydration
- Post-Operative nausea and vomiting
- Pain relating to the THR operation
- Slow progress with rehabilitation
- Hypoglycaemia

The CI or other senior investigators can choose to class any of the above as an SAE based on clinical judgement and circumstances if required.

5.1 Investigators Assessment

Medical judgement should be exercised in deciding whether an AE is serious in other situations. Important AEs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

5.2.1 Seriousness

The seriousness of the event would be assessed by a medic based in the clinical setting which in which the patient is based. This would then be reported to the chief investigator.

Decision on whether the event is serious would be made according to the definitions given in section 5.1.

5.2.2 Causality

The Chief Investigator must assess the causality of all serious adverse events in relation to the trial treatment according to the definition given.

Expectedness

The investigator must assess the expectedness of all SAEs according to the definition given. If the SAE is unexpected and related, then it needs immediate reporting.

5.2.4 Severity

The Investigator must assess the severity of the event according to the following terms and assessments. The intensity of an event should not be confused with the term "serious" which is a regulatory definition based on patient/event outcome criteria.

Mild: Some discomfort noted but without disruption of daily life

Moderate: Discomfort enough to affect/reduce normal activity

Severe: Complete inability to perform daily activities and lead a normal life

5.3 Notification and reporting Adverse Events or Reactions

If the AE is not defined as serious, the AE is recorded in the study file and the participant is followed up by the research team. The AE is documented in the participants' medical notes.

For the purpose of this study, the following adverse events would be commonly expected and therefore do not need to be recorded in the study file:

- Nausea and vomiting
- Pain related to the operation
- Orthostatic hypotension not resulting in syncope
- Slow Progress with rehabilitation
- Constipation
- Dehydration
- Fatigue
- Wound ooze

5.4 Notification and Reporting of Serious Adverse Events

5.4.1 Serious Adverse Event (SAEs) that are considered to be 'related' and 'unexpected' are to be reported to the hospital research department within 24 hours of learning of the event and to the Main REC within 15 days in line with the required timeframe.

5.5 Urgent Safety Measures

The CI may take urgent safety measures to ensure the safety and protection of the clinical trial subjects from any immediate hazard to their health and safety, in accordance with Regulation 30. The measures should be taken immediately. In this instance, the approval of the Licensing Authority Approval prior to implementing these safety measures is not required. However, it is the responsibility of the CI to inform the Main Research Ethics Committee (via telephone) of this event **immediately**.

The CI has an obligation to inform both the Main Ethics Committee **in writing within 3 days**, in the form of a substantial amendment.

Appendix 8 PPIE Focus Group Planned Questions

excellent care for every patient, every day, everywhere

The Royal Bournemouth and Christchurch Hospitals NHS
NHS Foundation Trust

RapidPhysio

RAPID Patient Focus Group Questions Version 1 Dated 28/07/2014

Thank you for attending this focus group, through open discussion of your opinions and questions around this research study we aim to gather information for patients which we can then use to change the study to include patient views as much as possible.

As part of this focus group we would like you to consider the following questions:

1. What do you think of the idea for the study?
2. How do you feel about the information sheet we would provide our patients with?
    a. Is it clear and understandable? If not what parts could do with changing?
    b. Is there anything you think is missing?
3. Do you feel that there are any ethical problems with the study?
4. As a patient would you have any concerns which have not been dealt with in the patient information sheet?
5. Of all the things discussed today what do you feel is the most important?

Thank you for providing some valuable feedback on the design process for this study. As you have had a key part in the development of this study we would be happy to provide you with a summary of the results at the end of the study. If you would like to receive this then please leave your name and address or email address at the end of the focus group.

Appendix 9 PPIE Focus Group Minutes

excellent care for every patient, every day, everywhere

The Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust

Orthopaedic Focus Group

1st October 2014 @ 10.00am – 12.00pm

Royal Bournemouth Hospital

Sue Mellor welcomed the patient in attendance and introductions were made. Whilst multiple patients were invited, there was only one attendee.

The purpose of the focus group meeting was explained by Chris Efford, Senior Orthopaedic Physiotherapist, leading a study to investigate changing the physiotherapy treatment of patients who had undergone a hip replacement. This entails encouraging patients to get up and move the same day as their operation. There was some evidence available which advocated this as best practice but research was potentially was flawed and unproven. Therefore the Trust is investing in research for the department lead by CE.

This means introducing a major change for patients from a physical and psychological perspective.

Physio dept. initial thoughts about gains were:

- reduction in length of time spent in hospital
- increase in mobility quicker
- reduce risk of blood clots
- reduce risk of thrombosis
- reduce risk of heart attack

Patient in attendance had a hip replacement within 7 days. He had been let out of hospital earlier than planned. Operation was on a Tuesday and he was mobilised from bed on Wednesday. He stressed that to engage patients to become involved in the study, a lot will depend on individual patient and they should expect a reasonable rest period post operatively:

Patient perspective:

- initially rejected the concept completely, thought was unrealistic time frame and would not have been personally ready.

- noted that elderly / unfit patients would still be experiencing the side effects of anaesthesia
- expected rest period was a minimum of 4 to 6 hours if concept to proceed
- if operation in afternoon then unrealistic to get patient up on the same day
- Patient dependent – e.g. spinal injection (unable to feel lower back 6 hours after op) Stated need comprehensive pain management
- Patient had felt faint when first getting up and felt he had lost ability to walk because of injection (spinal) and thus would have felt unsafe and at risk of falling.
- The day after, he had felt comfortable both from a pain and confidence viewpoint. Noted this was focused on saving Trust money by releasing beds and may not be in the patients best interests.

Chris read through draft information prepared to inform patients of the study.

Following points were noted:

- study title was not important from patient perspective
- information highlighting / stating that participation is entirely **voluntary**
- further information stating 'research indicates ……'(benefits to patient)

The criteria for participation was clarified, information was gathered both before and after surgery. It was hoped to trial 50% of patients using new protocol and remainder to receive treatment as at present. In was noted by CE that not all patients would be participants and they would be reviewed on the day of surgery and only included if assessed as appropriate based on clinical assessment. It was also noted that patients could remove themselves from the trial at any time, including on the day of surgery.

Patient queried the evidence; both what it would be beneficial to the patient and when it would be available to those participating?

Consideration needs to be given from patient viewpoint e.g.

- has it helped me start doing things and return to normal life quicker?
- not just to get us out of the hospital quicker
- phone call from physio dept approx. 10 days after surgery to enquire if any difficulties would be well received?
- consideration also to be given to information from patient given at consultant post op check up

Feedback regarding study could be given to those taking part after a period of time when enough data had been gathered.

Patient felt he would sign up to participate but needed to know what the benefits to him personally would be and it was very much dependent on lifestyle e.g. some will welcome a rest in hospital when others will want to get up and walking as quickly as possible.

Discussion took place regarding further advantages from Physio perspective including, analgesia still being present in joint which in turn may make patients more comfortable when moving on same day.

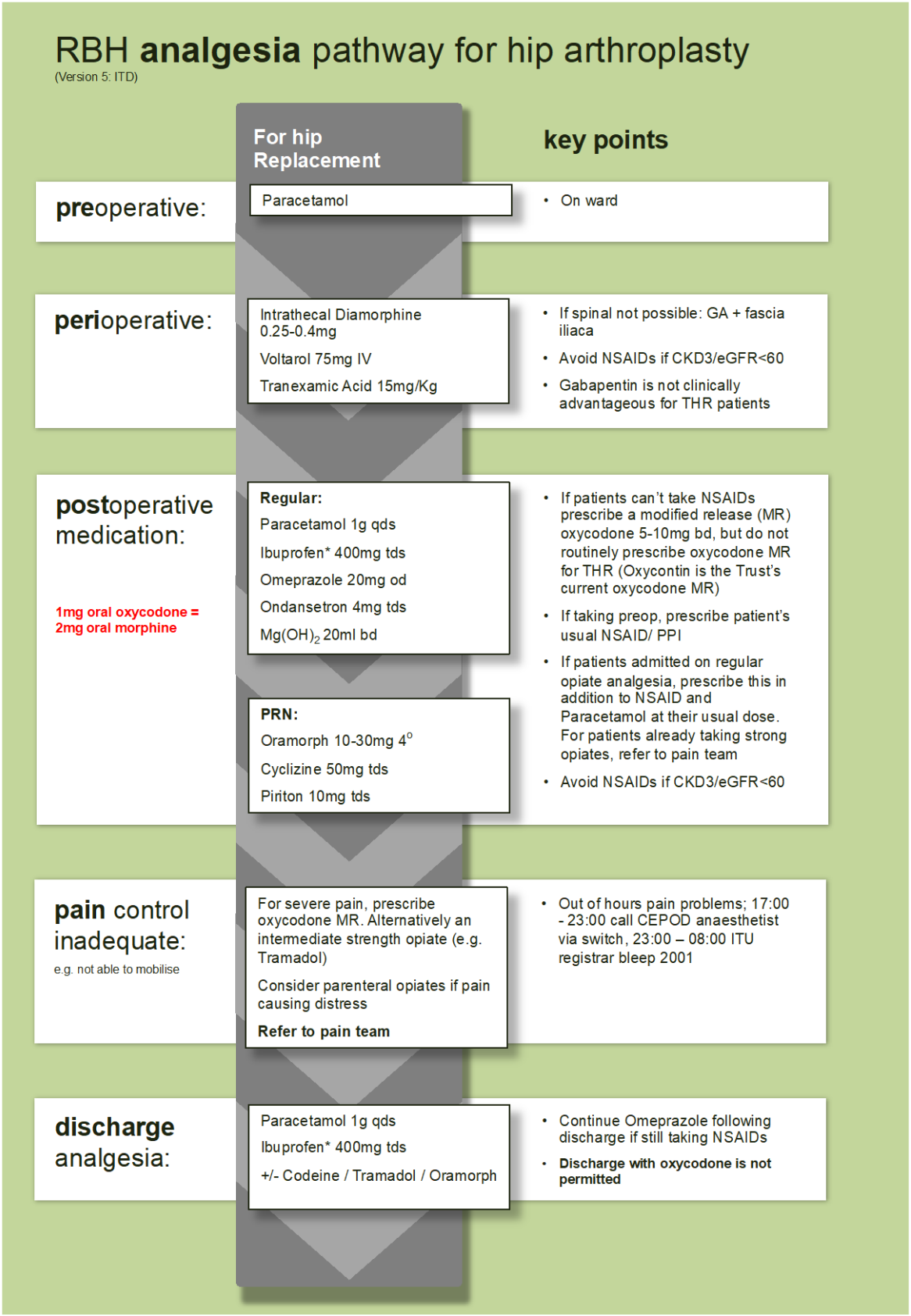
A group education meeting is currently provided for patients one or two weeks prior to their procedures and information about the study would be offered at this point.

Patient felt it important that information be presented in plain English.

Literature should also emphasise that it is a 'study' and not guarantee anything and be very clear about any 'benefits'.

We hope this a full and representation of the event is useful for you. If you would wish to discuss in any detail please make an appointment and we are happy to discuss.

Appendix 10 Standardised Anaesthetic and Analgesic Pathway



Appendix 11 Post-operative Physiotherapy Protocols

Total Hip Replacement (Day 0 Mobilisation Patients)	
Pre op	• Information booklet given out at PAC or pre-op group or ward • RAPT to be completed at pre-op group or OT home visit • Commence discharge planning • Attend Information class • OT home visit
Day of surgery (within 18 hours of surgery)	• RAPT score to be completed if not yet done • Standard post-operative checks • Reinforce precautions • Circulatory exercises • Respiratory exercises • Static gluteal and quadriceps exercises • Hip ROM exercises with sliding board (abduction and flexion) • Patient to continue exercises hourly • Oxygen therapy to maintain SaO2 if required (as documented on drugs chart)
Day of Surgery Rapid Mobilisation	• Check patient meets inclusion/exclusion criteria for rapid mobilisation. • Assess patient suitability for mobilising (See below) • Assess pain using Numerical Rating Scale at rest and on movement. • Mobilise with ZF as tolerated (2 persons to assist) • Consider discharge plans/date/destination
Day 1	• Standard post-operative checks • Assess pain using Numerical Rating Scale at rest and on movement • Check patient's recall of precautions • Assess patient for suitability for mobilising • Mobilise with ZF as tolerated • Progress onto elbow crutches when ready • Encourage independence and distance with mobilising • Oxygen therapy to maintain SaO2 if required (as documented on drugs chart) • Review p.m. to continue as required. • Teach active exercises in standing with both legs (abduction, flexion and extension)

Day 2	• Progress mobility – independence, distance, walking aids • Check independent with active standing exercises • Step/stair practice • Advise on progression of mobility/walking aids/first 6/52 at home • Outpatient physio/community physio if justified • Discharge when required criteria are met: • Safe and independent mobility with appropriate walking aid • Safe and independent on steps/stairs • Patient able to recall precautions • Patient can complete active standing exercises • Patient will be able to manage adequately at home
Day 3	• Continue with above until completed • Ensure discharge criteria are met as above.
Post Discharge – first 6 weeks	• Continue with advanced exercises until good ROM and strength • Continue to adhere to precautions (for 3 months post op). This will be reviewed at follow up appointment • Gradually increase distance walked • Reduce use of walking aids as able over 6 weeks • Review with surgeon at 6 weeks • Patients must sleep on back for first 6/52. If they can't sleep on their back they can lie on the operated side with a pillow between their legs
6 weeks +	• Can drive if surgeon allows at 6/52 review • Continue to increase walking distance, ROM and strength • Can start swimming when good mobility, wound healed. Access pool via stairs not ladder. No breast stroke allowed • Can cycle once precautions have stopped, providing the patient is very careful • No flying for at least 6 weeks. General rule is 3/12 short haul, 6/12 long haul (at surgeons discretion).

Any other Surgeon/post op instructions should supersede these guidelines

Assessment criteria for Suitability for Mobilising:

Stable blood pressure and other nursing observations

Adequate knee extension power assessed by a qualified physiotherapist

Total Hip Replacement – Control Group	
Pre op	• Information booklet provided at pre admissions clinic • Attend pre-operative information group • OT home visit
Day of surgery (if appropriate but usually day 1)	• Check op notes for procedure, type of anaesthetic/nerve block, post op instructions • Issue with THR booklet if patient does not already have one • RAPT to be completed – refer to BCHA if appropriate • Standard post-operative checks • Reinforce precautions • Circulatory exercises • Respiratory exercises • Static gluteal and quadriceps exercises • Patient to continue above exercises hourly • Hip ROM exercises with sliding board (abduction and flexion) **only** with Physiotherapist and **only** if full sensation at hip
Day 1	• Complete RAPT if not yet done – refer to BCHA if appropriate • Standard post-operative checks • Assess pain using Numerical Rating Scale at rest and on movement • Reinforce precautions • Bed exercises as per day of surgery • Assess patient for suitability for mobilising (including Hb) See Below • Mobilise with ZF as tolerated (2 persons to assist) • Oxygen therapy to maintain SaO2 (as documented on drugs chart) • Review p.m. as required. Encourage exercises • Consider discharge plans/date/destination • Document RAPT, day 1 pain scores and date/time of joint mobilisation and walk on database
Day 2	• Encourage independence and distance with mobilising with zf • Progress onto elbow crutches when ready • Check patient's recall of precautions • Commence advanced exercise if patient mobilising well- standing exercises both legs (abduction, flexion, extension) • Review p.m. to continue as required

Day 3 (discharge)	• Progress mobility – independence, distance, walking aids
	• Start/continue with active standing exercises both legs (abduction, flexion, extension)
	• Step/stair practice
	• Advise on progression of mobility/walking aids/swelling management/first 6/52 at home
	• Outpatient physio/community physio if justified
	• Continue with above until completed
	• Ensure discharge criteria are met:
	  ○ Safe and independent mobility with appropriate walking aid
	  ○ Safe and independent on steps/stairs
	  ○ Patient able to recall precautions
	  ○ Patient can complete active standing exercises
	  ○ Patient will be able to manage adequately at home

Post discharge – first 6 weeks	• Continue with advanced exercises until good ROM and strength • Continue to adhere to precautions (for 3 months post op). This will be reviewed at follow up appointment • Gradually increase distance walked • Reduce use of walking aids as able over 6 weeks • Review with surgeon at 6 weeks • Patients must sleep on back for first 6/52. From 6 weeks they can lie on the operated side with a pillow between their legs
6/52 +	• Can drive if surgeon allows at 6/52 review • Continue to increase walking distance, ROM and strength • Can start swimming when good mobility, wound healed. Access pool via stairs not ladder. No breast stroke allowed • Can cycle once precautions have stopped, providing the patient is very careful • No flying for at least 6 weeks. General rule is 3/12 post op. Consultant clearance is required for earlier short haul flying • Can lie on operated hip with a pillow between knees

Any other Surgeon/post op instructions should supersede these guidelines

Assessment criteria for Suitability for Mobilising:

Stable blood pressure and other nursing observations

Adequate knee extension power assessed by a qualified physiotherapist

Appendix 12 Standard THR exercises

The Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust

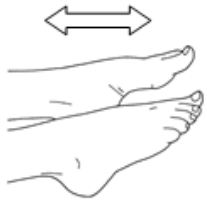
Exercises following your Total Hip Replacement

Early Exercises

You should start these exercises 1 –3 as soon as you are able to after your operation. These are designed to reduce the risks associated with being on bed rest. You should not complete exercises 4 and 5 until you have seen your physiotherapist, they will show you how to complete these correctly.

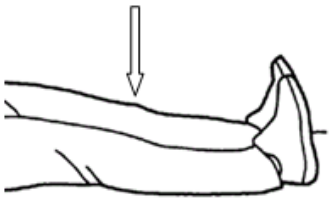
Exercise 1

When lying or sitting, bend and straighten your ankles briskly. Repeat this **10 times every hour.**



Exercise 2

Sitting in bed with your legs out straight. Pull your toes towards you and push your knees down firmly into the bed. Repeat this **10 times every hour.** Also squeeze your buttocks together **10 times every hour.**



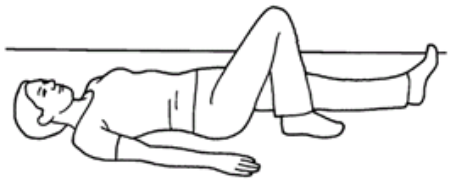
Exercise 3

Sitting in bed, lift one arm up above your head then return it to your side. Repeat with the other arm. Repeat this **10 times every hour** with both arms. Take care if you have a drip in your arm.

Additionally regularly take **3 deep breaths** in through your nose then out through your mouth.

Exercise 4

Lie on your back with your leg out straight on the bed. Bend and straighten your hip and knee by sliding your foot up and down the bed. Repeat this **10 times every hour.**



Exercise 5

Lie on your back with your leg out straight on the bed. Slowly slide your leg out to the side then back to the middle. Repeat this **10 times every hour.**

Advanced Exercises

Your physiotherapist will go through these exercises with you when appropriate. You should do these **every hour whilst in hospital** and then continue these **3– 4 times a day once home.**

Exercise 1

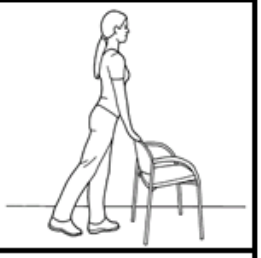
Stand up straight holding onto a support. Slowly lift your leg out to the side then return it to the starting position. Aim to repeat this **10 times with each leg.**

Exercise 2

Stand up straight holding onto a support. Slowly lift your knee up in front of you then return it to the starting position. Aim to repeat this **10 times with each leg.**

Exercise 3

Stand up straight holding onto a support. Slowly move your leg out behind you, keeping your knee straight, then return it to the starting position. Aim to repeat this **10 times with each leg.**



Exercise 4

Stand up straight holding onto a support with your feet hip width apart. Slowly bend your knees and lower your body a few inches whilst keeping your back straight. Hold this position for 5 seconds then slowly straighten your knees and return to the starting position. Aim to repeat this **10 times.**

Hip Precautions

(You should follow these for 3 months unless told otherwise by your surgeon or physiotherapist)

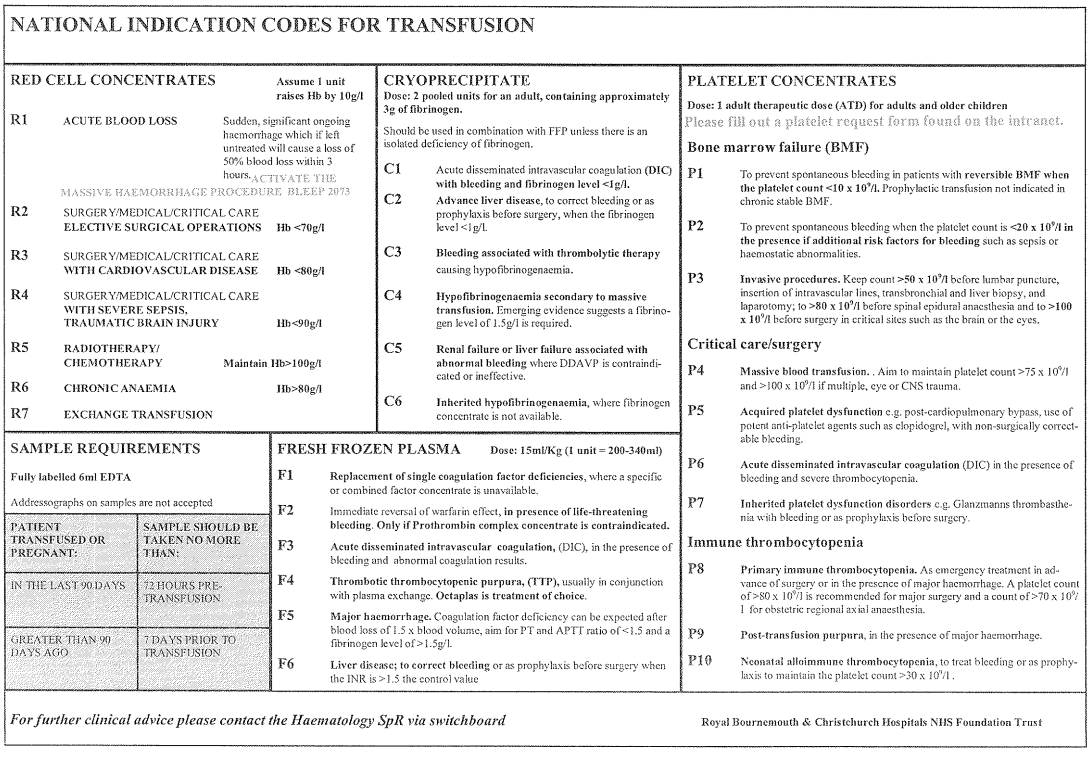
DO NOT cross you legs or ankles

DO NOT bring your knee higher than your hip

DO NOT reach down past your knees

DO NOT twist your body

Appendix 13 Local Blood Transfusion Request Form



NATIONAL INDICATION CODES FOR TRANSFUSION

RED CELL CONCENTRATES — Assume 1 unit raises Hb by 10g/l

R1	ACUTE BLOOD LOSS	Sudden, significant ongoing haemorrhage which if left untreated will cause a loss of 50% blood loss within 3 hours. ACTIVATE THE MASSIVE HAEMORRHAGE PROCEDURE BLEEP 2073	
R2	SURGERY/MEDICAL/CRITICAL CARE ELECTIVE SURGICAL OPERATIONS		Hb <70g/l
R3	SURGERY/MEDICAL/CRITICAL CARE WITH CARDIOVASCULAR DISEASE		Hb <80g/l
R4	SURGERY/MEDICAL/CRITICAL CARE WITH SEVERE SEPSIS, TRAUMATIC BRAIN INJURY		Hb<90g/l
R5	RADIOTHERAPY/ CHEMOTHERAPY	Maintain	Hb>100g/l
R6	CHRONIC ANAEMIA		Hb>80g/l
R7	EXCHANGE TRANSFUSION		

CRYOPRECIPITATE

Dose: 2 pooled units for an adult, containing approximately 3g of fibrinogen.

Should be used in combination with FFP unless there is an isolated deficiency of fibrinogen.

- C1 Acute disseminated intravascular coagulation **(DIC) with bleeding and fibrinogen level <1g/l.**
- C2 **Advance liver disease**, to correct bleeding or as prophylaxis before surgery, when the fibrinogen level <1g/l.
- C3 **Bleeding associated with thrombolytic therapy** causing hypofibrinogenaemia.
- C4 **Hypofibrinogenaemia secondary to massive transfusion.** Emerging evidence suggests a fibrinogen level of 1.5g/l is required.
- C5 **Renal failure or liver failure associated with abnormal bleeding** where DDAVP is contraindicated or ineffective.
- C6 **Inherited hypofibrinogenaemia**, where fibrinogen concentrate is not available.

PLATELET CONCENTRATES

Dose: 1 adult therapeutic dose (ATD) for adults and older children

Please fill out a platelet request form found on the intranet.

Bone marrow failure (BMF)

- P1 To prevent spontaneous bleeding in patients with **reversible BMF when the platelet count <10 x 10^9/l.** Prophylactic transfusion not indicated in chronic stable BMF.
- P2 To prevent spontaneous bleeding when the platelet count is **<20 x 10^9/l in the presence if additional risk factors for bleeding** such as sepsis or haemostatic abnormalities.
- P3 **Invasive procedures.** Keep count **>50 x 10^9/l** before lumbar puncture, insertion of intravascular lines, transbronchial and liver biopsy, and laparotomy; to **>80 x 10^9/l** before spinal epidural anaesthesia and to **>100 x 10^9/l** before surgery in critical sites such as the brain or the eyes.

Critical care/surgery

- P4 **Massive blood transfusion.** . Aim to maintain platelet count >75 x 10^9/l and >100 x 10^9/l if multiple, eye or CNS trauma.
- P5 **Acquired platelet dysfunction** e.g. post-cardiopulmonary bypass, use of potent anti-platelet agents such as clopidogrel, with non-surgically correctable bleeding.
- P6 **Acute disseminated intravascular coagulation** (DIC) in the presence of bleeding and severe thrombocytopenia.
- P7 **Inherited platelet dysfunction disorders** e.g. Glanzmanns thrombasthenia with bleeding or as prophylaxis before surgery.

Immune thrombocytopenia

- P8 **Primary immune thrombocytopenia.** As emergency treatment in advance of surgery or in the presence of major haemorrhage. A platelet count of >80 x 10^9/l is recommended for major surgery and a count of >70 x 10^9/l for obstetric regional axial anaesthesia.
- P9 **Post-transfusion purpura**, in the presence of major haemorrhage.
- P10 **Neonatal alloimmune thrombocytopenia**, to treat bleeding or as prophylaxis to maintain the platelet count >30 x 10^9/l .

SAMPLE REQUIREMENTS

Fully labelled 6ml EDTA

Addressographs on samples are not accepted

PATIENT TRANSFUSED OR PREGNANT:	SAMPLE SHOULD BE TAKEN NO MORE THAN:
IN THE LAST 90 DAYS	72 HOURS PRE-TRANSFUSION
GREATER THAN 90 DAYS AGO	7 DAYS PRIOR TO TRANSFUSION

FRESH FROZEN PLASMA **Dose: 15ml/Kg (1 unit = 200-340ml)**

- F1 **Replacement of single coagulation factor deficiencies**, where a specific or combined factor concentrate is unavailable.
- F2 Immediate reversal of warfarin effect, **in presence of life-threatening bleeding. Only if Prothrombin complex concentrate is contraindicated.**
- F3 **Acute disseminated intravascular coagulation,** (DIC), in the presence of bleeding and abnormal coagulation results.
- F4 **Thrombotic thrombocytopenic purpura, (TTP),** usually in conjunction with plasma exchange. **Octaplas is treatment of choice.**
- F5 **Major haemorrhage.** Coagulation factor deficiency can be expected after blood loss of 1.5 x blood volume, aim for PT and APTT ratio of <1.5 and a fibrinogen level of >1.5g/l.
- F6 **Liver disease; to correct bleeding** or as prophylaxis before surgery when the INR is >1.5 the control value

For further clinical advice please contact the Haematology SpR via switchboard

Royal Bournemouth & Christchurch Hospitals NHS Foundation Trust

The Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust

BLOOD TRANSFUSION

The Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust

Appendix 14 Local Venous Thromboembolism Policy

DALTEPARIN (LMWH) TREATMENT DOSES

Prescribe on Parenteral Anticoagulation Prescription (Dalteparin) Use actual body weight when dosing – DO NOT USE ESTIMATES.

Dalteparin should be given subcutaneously (SC), preferably with the patient lying down. Inject into the SC tissue of the anterolateral or posterolateral abdomen, or lateral part of the thigh, alternating from the left to right side. Vertically introduce the whole length of the needle into the thickness of the skin held between the thumb and forefinger. Hold the skin throughout the duration of the injection. Do not rub the injection site (helps to avoid bruising).

Overdose

Protamine sulphate only partially reverses the effect of dalteparin so additional measures may be required if bleeding is uncontrollable and life-threatening.

Consult Haematologist for advice

Complications

Bleeding

Osteoporosis is a complication of long-term heparin use only

Hyperkalaemia; The risk appears to increase with duration of therapy, but is usually reversible. Serum potassium should be measured in those at risk

Heparin-induced thrombocytopenia (HIT) with thromboembolism (HITT)

Monitor platelets days 1 & 5 then every 3rd to 5th day. Consult Haematology if ≥ 50% reduction is observed

Renal function

Renal function must be checked before prescribing, there have been reports of retroperitoneal bleeds in patients where an excessive dose of dalteparin was administered in renal impairment.

1. STANDARD TREATMENT DOSE: ONCE daily – 18.00 (Table printed on prescription chart)

Dalteparin Standard Treatment Dose - 200 units/kg daily s/c (CrCl ≥30mL/min)		Dosing in renal impairment	
Body weight kg	Minimal bleeding risk (OD dosing) units	CrCl < 30 to 20mL/min	Prescribe BD dose as table below Long term >10 days, with Anti-Xa monitoring
< 46	7500		
46 to 56	10000		
57 to 68	12500	CrCl < 20mL/min	Prescribe IV unfractionated heparin on separate prescription
69 to 82	15000		
> 82	18000		

PATIENTS WITH INCREASED BLEEDING RISK: (Table printed on prescription chart)
In patients who are at increased risk of bleeding e.g. following haemorrhagic stroke, severe liver or renal failure, thrombocytopenia or defective platelet function, consider a dose of 100 units/kg TWICE daily – 08.00 &18.00

Dalteparin Treatment Dose 100 units/kg BD s/c (CrCl ≥30mL/min)			Dosing in renal impairment	
Body weight kg	AM 08.00 (units)	PM 18.00 (units)	CrCl <30 to 20mL/min	Dose as table Long term > 10 days, with Anti-Xa monitoring
< 46	5000	2500		
46 to 56	5000	5000		
57 to 68	7500	5000	CrCl < 20mL/min	Prescribe IV unfractionated heparin on separate prescription
69 to 82	7500	7500		
> 82	10000	7500		

SURGICAL BRIDGING WARFARINISED PATIENTS & PREGNANCY
HIGH RISK (needs therapeutic dose of dalteparin) – mechanical heart valves and AF:
In pregnancy and in patients with mechanical heart valves or AF who require surgical bridging (potentially HIGH risk for VTE) prescribe a dose of 100 units/kg TWICE daily – NOTE weight banding alters in this group of patients

Dalteparin in Pregnancy & for Surgical Bridging in Patients with Mechanical Heart Valves or AF 100 units/kg BD s/c (CrCl ≥30mL/min)			Dosing in renal impairment	
Body weight kg	AM (08.00) (units)	PM (18.00) (units)	CrCl < 30 to 20mL/min	Short term: dose as table Long term > 10 days, dose as table with Anti-Xa monitoring
< 50	5000	5000		
50 to 69	7500	5000		
70 to 79	7500	7500	CrCl < 20mL/min	Prescribe IV unfractionated heparin on separate prescription
80 to 89	10000	7500		
> 89	10000	10000		

HIGH RISK – other patients
Other patients requiring surgical bridging who have been assessed as HIGH risk should be also be prescribed dalteparin as in table 3 above.

MODERATE RISK (needs high prophylactic dose of dalteparin)
Patients assessed as moderate risk should be prescribed a dose of 100 units/kg ONCE daily -18.00

Dalteparin Treatment Dose - 100 units/kg daily s/c (CrCl ≥30mL/min)		**Dosing in renal impairment**	
Body weight kg	**Minimal bleeding risk (OD dosing) units**	CrCl < 30 to 20mL/min	Short term: dose as table

< 46	**5000**		Long term > 10 days, Anti-Xa monitoring and discuss levels with
46 to 56	**5000**		
57 to 68	**7500**	CrCl < 20mL/min	Prescribe IV unfractionated heparin on separate prescription
69 to 82	**7500**		
> 82	**10000**		

LOW RISK (needs prophylactic dose of dalteparin)
Prescribe 5000 units ONCE daily on the in-patient medication chart
If having over 10 days treatment and CrCL< 20mL/min prescribe unfractionated heparin 5000iu s/c BD

EXTENDED TREATMENT OF VENOUS THROMBOEMBOLISM IN ONCOLOGY PATIENTS

Month 1 = Prescribe standard treatment dose as stated above
Months 2 to 6 = 150 units/kg SC daily, using the table below for dosing

Weight (kg)	Daily Dose (units)
< 56	**7500**
57 to 68	**10000**
69 to 82	**12500**
83 to 98	**15000**
> 98	**18000**

POINTS TO REMEMBER:

- LMWH mainly inhibit prothrombinase

- Relevance of continuing treatment beyond 6 months should be evaluated according to individual risk/benefit ratio
- Dose modifications in chemotherapy-induced thrombocytopenia: Platelets 50 to 100 x 10^9/L - decrease daily dalteparin dose by 2500units until platelets ≥ 100 x 10^9/L
- Platelets < 50 x 10^9/L - discontinue dalteparin until platelets
  - 50 x 10^9/L

- (Factor Xa) and weakly inhibit thrombin (Factor IIa)
- Dalteparin only moderately affects the APTT ratio, this should only be measured in suspected overdose and not be monitored routinely.
- Anti-Factor Xa level can be used to monitor the anticoagulant effect but has limited predictive value for bleeding complications or antithrombotic efficacy.

Contra-indications

- Known bleeding disorders, e.g. haemophilia
- Pre-existing thrombocytopenia with platelet count < 75 x 10^9/L History of heparin-induced thrombocytopenia (HIT)
- Hypersensitivity to heparins Peptic ulcer
- Recent cerebral haemorrhage Major / life threatening bleeding
- Severe hypertension – Systolic BP > 230 mmHg + Diastolic BP > 120mm Hg Severe liver disease with oesophageal varices
- Major trauma
- Recent eye, brain, spinal cord surgery Acute bacterial endocarditis

Cautions

- Concomitant use of drugs that increase bleeding Liver disease
- Renal impairment Recent surgery
- Pre-existing diseases or concomitant use of drugs that cause hyperkalaemia Osteoporosis

Monitoring

- Routine monitoring of anticoagulant effect is not required except in special circumstances below Patients having treatment doses for more than 10 days with a creatinine clearance < 30 to 20mL/min Obesity (BMI > 30kg/m^2)
- Pregnancy
- Those at increased risk of bleeding

Samples for anti-Factor Xa activity are taken 3 to 4 hours after injection to check peak levels, for BD dosing the sample should be taken after the morning dose . Contact haematology medics if 3 to 4 hour post-Dalteparin anti-Xa levels are < 1 or > 2units/mL for OD dosing, < 0.5 or > 1units/mL for BD dosing and for all pregnant patients. If levels are within this range re-check levels within 5 to 7 days.

DALTEPARIN (LMWH) PROPHYLATIC DOSES

Prescribe on in-patient medication chart

PROPHYLAXIS FOR VENOUS THROMBOEMBOLISM

All adult patients (aged ≥ 18 yr) admitted to hospital must be risk assessed for venous thromboembolism. Use of low molecular weight heparin reduces incidence of venous thromboembolism by at least 50%, with no increased risk of bleeding

Continue prophylaxis until patient is no longer at increased risk of VTE. Consider patient's level of mobility prior to admission. Usual maximum is 14 days for medical patients and in surgical patients generally 5 to 7 days.
Use is extended in major cancer surgery and some orthopaedic procedures

General measures: Do not allow patient to become dehydrated. Encourage patient to mobilise

Precautions - LMWH

If patient normally receives anticoagulant and INR sub-therapeutic contact anticoagulation management team. Out-of-hours, contact on-call Haematologist via SWITCHBOARD
Monitor for any bleeding
If renal function deteriorates CrCl < 20mL/min use unfractionated heparin
Insertion of a spinal/epidural catheter, lumbar puncture or a deep peripheral nerve block – do not undertake within 12 hr following administration of prophylactic LMWH
LMWH can be administered 6 hr after withdrawal of a spinal/epidural catheter

Medical and surgical Patients (CrCl ≥ 20mL/min):

<50 kg	**2500 units once daily**
50kg – 99kg	**5000 units once daily**
100kg – 150kg	**5000 units twice daily**
➢ **150kg**	**7500 units twice daily**

In patients with severe renal failure (CrCl < 20ml/min):

Short term (up to 10 days) - above doses for 10 days then unfractionated heparin 5000 units BD (irrespective of weight) Long term (more than 10 days) - unfractionated heparin 5000 units S/C BD

Monitoring for HIT (Heparin Induced Thrombocytopenia

Monitoring is only required if the patient has received unfractionated heparin in the preceding 100 days before starting LMWH (see below). Risk of HIT with LMWH on its own is very low hence monitoring no longer recommended.

If the patient has had unfractionated heparin in the preceding 100 days then:
if dalteparin prophylaxis is required for > 5 days, check baseline FBC and check again between days 5 to 7 and between days 10 to 14 for outpatients and discharges and day 6 and day 14 for inpatients to exclude heparin-induced thrombocytopenia
if platelet count is < 150 x 10^9/L or lower than baseline platelet count by > 50%, stop dalteparin, investigate for HIT and switch to alternative prophylaxis (discuss with Haematologist)

PLEASE REFER TO FULL GUIDELINES ON INTRANET

Appendix 15 Participant Experience Questionnaire

Patient Satisfaction Questionnaire

Please answer the following Questions in relation to your physiotherapy treatment during your tim in hospital: Rate your experience from 0 - 10.

0 being the worst and 10 being the best

1.	Do you think the hospital staff did everything they could to help control your pain?*										
	0	1	2	3	4	5	6	7	8	9	10
2.	Overall, how was your experience of physiotherapy following your operation?										
	0	1	2	3	4	5	6	7	8	9	10
3.	Overall, how was your experience of your overall hospital treatment?*										
	0	1	2	3	4	5	6	7	8	9	10
4.	Did you have confidence and trust in the physiotherapists treating you?*										
	0	1	2	3	4	5	6	7	8	9	10
5.	How beneficial was walking early after your operation?										
	0	1	2	3	4	5	6	7	8	9	10
	Any Comments:										
6.	How well was your progression with your physiotherapist paced to suit you?										
	0	1	2	3	4	5	6	7	8	9	10
	Any Comments:										
	Below to be Completed by Physiotherapist										
	Which Group was this patient part of? (*Please Circle)*										

Appendix 16 Feasibility Study Debrief Minutes

Meeting Minutes

Call to order

A meeting of The RAPID study research team was held at Royal Bournemouth Hospital on 15/12/2015.

Attendees:

Attendees included.

Mr Christopher Efford – Chief Investigator
Mr Ross Darch – Therapy Team Leader
Mr Aaron Bailie – Senior Physiotherapist
Mrs Jennifer White – Senior Physiotherapist

Members not in attendance

Members not in attendance included.

Nil

Minutes:

The purpose of this meeting was to debrief following the completion of the feasibility phase of the RAPID research study in order to gain opinion and ideas on the strengths and weaknesses of the research design and implementation strategy.

CE introduced the meeting and requested open and honest feedback from the members of the team who had been involved with the RAPID study so far. Agenda topics for the meeting were introduced to be worked through methodologically.

Informed Consent Procedures:

Each attendee was asked for their feedback on this element of the study so far.

AB expressed that he felt participants were presented with the appropriate level of information and appeared well informed about the study both before and after consent procedures/enrolment. CE agreed that the level of information is fulfilling the requirements for proper ethical informed consent standards, and if anything potentially over-states the risks in the participant information sheet, as none of them are substantiated in evidence.

However, CE pointed out that this was dependent on potential participants attending the pre-operative education session. Those that had failed to attend the education session approximately one week prior to admission had not received the participant information pack. This led to a number of potential participants in the first 11 weeks of the feasibility study not being eligible for recruitment, as they had not had a sufficient amount of time to ethically consider their participation. After changing the procedure for sending out participant information sheets this problem was not encountered again for the rest of the study.

AB felt that one of the main limitations of the informed consent and recruitment process is that there is only the CI is trained to obtain written informed consent. This has meant that on days when the CI is not available for reasons such as annual leave or time-in-lieu recruitment is essentially suspended.

RD explained that it would be possible to book more members of the team for the trusts informed consent training.

Randomisation and Enrolment:

All attendees agreed that the delegation log has been clear as to which members of the team carry out these duties, and the process itself is straightforward and clear with no problems identified.

Implementation of Day 0 Mobilisation:

CE, AB and RD have all had experience of attempting day 0 mobilisation with an enrolled participant. All agreed that the safety checks for appropriate neurovascular recovery from the spinal anaesthetic were sufficient and provided a safe basis for mobilisation at this stage.

Overall, it was felt that the majority participants had coped well with day 0 mobilisation, with very few incidences of syncope, and with the physiotherapists reacting appropriately to warning signs of orthostatic hypotension that could lead to syncope. RD and AB expressed that post-operative nausea and vomiting appeared fairly common within the cohort.

There were no issues with any participant having an active spinal anaesthetic preventing day 0 mobilisation. The main limitations to early mobilisation were nausea and vomiting, and dizziness.

Overall, the team felt that beginning day 0 mobilisation with participants in the evening was safe and within resource capacity, with arrangement made for health-care assistant staff assisting for safety when there is only one physiotherapist left on the ward into the evening.

RD suggested that when recruiting, it would need to be taken into account the level of caseload expected for day-surgery post-operative physiotherapy to ensure that resources weren't stretched, but so far this had not been a problem. CE felt that this was also the case for documenting the PIS log and being able to identify which participants would be arriving in hospital on what day and eligible for recruitment, as this was complicated at times by cancelled surgeries or rearrangement of the site of surgery or order of the theatre list.

All attendees agreed that there were no concerns with physical equipment limiting the study. However, AB suggested that although a spreadsheet system for collating collected data had been fine, when looking to collect larger numbers, a more robust and user friendly way of collating data would be preferable such as a database.

Serious Adverse Events:

CE fed back that there had been two serious adverse events during the course of the feasibility study. Both of these were within the control group and felt to be unrelated to the research study. Both were reported and dealt with appropriately and to the satisfaction of the study sponsor.

Data Collection:

CE fed back that most of the data collected was complete, with only patient experience questionnaire missing. This was due to a member of staff working at the weekend and forgetting to ask the participant to complete the questionnaire. On discussion the team felt that a contributing factor to this being that the questionnaires are kept within the study folder rather than close at hand within the patient notes where the treating therapist would notice it.

AB suggested that when a participant is enrolled, a blank patient experience questionnaire is placed with the rest of their study documentation to remind the treating therapist to ensure it is completed.

All attendees reported that the study paperwork was clear, and not too burdensome to compete alongside the regular patient notes written.

Research Team Communication:

RD, AB and JW all felt that communication within the senior physiotherapists conducting the study was sufficient and working well. However junior staff newly rotating into the team, although not having direct contact with the trial participants until undergoing protocol training, had come up against potential participants asking questions about the study which they did not feel equipped to answer.

RD suggested ensuring that junior staff had an introduction to the study and how/who to pass queries onto early on in their rotation instead of waiting for full protocol training.

RD felt as the team leader that the team engagement with the study had been good and that the team was proud to be hosting some original research.

RD also raised that there had been a period of limited staffing due to injury and sickness time for 2 members of staff simultaneously. However, the team felt that the conduct of the study had not felt a knock-on effect from this and research participants were still dealt with appropriately.

Any Other Comments:

AB expressed that he would be keen to become involved in assisting to run the study more.

Christopher Efford **15/12/2015**

Signed Date

Appendix 17 Researcher Development Framework Meta-Table

Researcher Development Framework Meta-Table – Christopher Efford Self-Evaluation Post-Feasibility Study

Domains and Sub-Domains	Phase 1	Phase 2	Phase 3	Phase 4	Phase 5	Comments
Domain A – Knowledge and Intellectual Abilities						
A1 – Knowledge Base						
Participant Knowledge	Achieved	□	□	□	□	Completed comprehensive literature review in my topic area
Research Methods – Theoretical Knowledge	Achieved	□	□	□	□	
Research Methods – Practical Application	Achieved	□	□	□	□	Haven't yet used a range of research techniques and not yet with confidence
Information Seeking	□	□	□	□	□	Need more development in recognising the importance of

						bibliometrics and citations and more practice in recognising the strengths and weaknesses of literature searches
Information literacy and management	Achieved					Limited understanding of metadata
Languages	Achieved					Progressing within this dimension but technical language is not deep yet, particularly across a variety of research methods
Academic literacy and numeracy	Achieved					Developing knowledge of statistical procedures, however I don't present complex ideas with clarity very easily and am still developing my academic writing skills
A2 - Cognitive Abilities						
Analysing	Achieved					I am still developing my analytical skills, and need to develop understanding of a range of methods.

Synthesising	Achieved	□	□	□	□	At times, guidance is required for the synthesis of information and ideas, I am happy to throw ideas around but they may be fairly one-dimensional
Critical Thinking	□	□	□	□	□	I am beginning to recognise different paradigms, but poor knowledge of qualitative work. I can theorise assumptions, although this takes time and reflection
Evaluating	Achieved	□	□	□	□	I am able to basically evaluate my own work, but haven't applied this to other less experienced researchers
Problem Solving	Achieved	□	□	□	□	I have no significant experience yet of analysing and interpreting research results.
A3 – Creativity						

Inquiring Mind	Achieved	Achieved	□	□	□	I am very motivated to learn and develop, actively seeking new learning opportunities
Intellectual Insight	Achieved	□	□	□	□	I work well independently and with initiative. I need to develop my own conceptual approach / intellectual position.
Innovation	□	□	□	□	□	I have not yet been involved in any interdisciplinary research. All my research work / ideas have come from a clinical context.
Argument Construction	□	□	□	□	□	I have not yet had the need or opportunity to academically defend my research ideas.
Intellectual Risk	□	□	□	□	□	I have not yet put myself in a situation in front of an audience with my ideas, I feel nervous about this currently.

Domain B – Personal Effectiveness

B1 – Personal Qualities						
Enthusiasm	Achieved	Achieved	Achieved	Achieved	□	I have a huge amount of enthusiasm for my research and work to inspire others within this research area
Perseverance	Achieved	Achieved	Achieved	Achieved	Achieved	Within a personal context I have been very persistent in often isolated situations in order to make my research succeed
Integrity	Achieved	Achieved	□	□	□	I am not yet advising other on how to conduct their research and have had little guidance in research practice except for GCP training
Self-Confidence	Achieved	Achieved	□	□	□	I am not yet confident in seeking challenges for my ideas, but I am happy to seek challenges for my skills – for example joining a journal editorial board.

Self-Reflection	Achieved	Achieved	Achieved	Achieved	Achieved	I often lead by example, and am consistently seeking ways to improve my performance.
Responsibility	Achieved	Achieved	Achieved	□	□	I have taken sole responsibility for beginning my research project and in building and leading the research team – prior to my enrolment on the Doctorate and advice from my supervisors
B2 – Self-Management						
Preparation and Prioritisation	Achieved	Achieved	□	□	□	I am not yet familiar enough with the wider research base to anticipate research trends
Commitment to Research	□	□	□	□	□	I have not achieved phase 1, as I have not yet completed my first project.
Time Management	Achieved	□	□	□	□	I work hard to manage my own time and research project, with plans of how I will manage this. However, lack

						of experience has left some of my time targets unrealistic.
Responsiveness to Change	Achieved	□	□	□	□	From a research aspect I haven't had to manage a great deal of change yet
Work-Life Balance	□	□	□	□	□	Balancing being a father, work, study, research and social has been challenging. I tend to focus in one direction at a time to the detriment of the others rather than balancing well
B3 – Professional and Career Development						
Career Management	Achieved	□	□	□	□	I am a strong communicator and at developing a network of people. However without a clear career target in mind.
Continuing Professional Development	Achieved	Achieved	□	□	□	I am not sure what my potential within the job market is, however I am good at seeking skill development, learning and new opportunities.

Responsiveness to opportunities	□	□	□	□	□	In my clinical professional life, I seek, and sometimes self-generate opportunities. I have not yet extended this within a research or academic context.
Networking	□	□	□	□	□	Not yet achieved phase 1 – It is one of my main weaknesses in engaging with societies and networks outside of face-to-face contact.
Reputation and Esteem	□	□	□	□	□	I have not dedicated any time to establishing my own reputation or becoming known within the research community – Currently I worry about feeling like an impostor as a very novice researcher.

Domain C – Research Governance and Organisation

C1 – Professional Conduct

Health and Safety	Achieved	Achieved	□	□	□	Within a clinical context I am the health and safety lead, but not within an academic/research setting
Ethics, Principles and Sustainability	Achieved	□	□	□	□	I am aware of research ethics and practicalities, but mostly within my own research, and I do not feel well read on this topic.
Legal Requirements	Achieved	□	□	□	□	I have a basic understanding of data protection and other relevant legislation and how it affects my conduct and study management – however I do not feel confident I know the ins and outs of the legislation
IPR and Copyright	□	□	□	□	□	I admit I have a poor understanding of data ownership rules
Respect and Confidentiality	Achieved	□	□	□	□	I always work to respect the rights of my research participants – but have

						not been in a situation to advise other researchers on this.
Attribution and Co-Authorship	□	□	□	□	□	I admit I have a poor understanding of co-authorship rules / etiquette
Appropriate Practice	Achieved	□	□	□	□	I understand rules of plagiarism and integrity within my writing. However, my knowledge is not sufficient to advise others with any confidence.
C2 – Research Management						
Research Strategy	Achieved	Achieved	Achieved	□	□	My research project has been developed with a very clear multifactorial strategy taking into account the interests of all stakeholders.
Project Planning and Delivery	Achieved	□	□	□	□	I am still within the management of my first major project and am developing my project management skills

Risk Management	Achieved	□	□	□	□	I am able to assess basic risks within clinical settings and in my own research. I have little experience in conducting thorough risk analyses.
C3 – Finance, Funding and Resources						
Income and Funding Generation	□	□	□	□	□	Within my experience so far I have only worked with unfunded research
Financial Management	□	□	□	□	□	Unfortunately I have had no professional experience of financial management
Infrastructure and Resources	Achieved	□	□	□	□	I have a clinical grounding of resource management, however, some naivety to resource use. When it is unfunded, I am able to tap into what I need.
Domain D: Engagement, Influence and Impact						
D1 – Working with Others						

Collegiality	Achieved	Achieved	Achieved	□	□	Professionally I am accustomed to working closely with and supporting colleagues, including delivering supervision, coaching and clinical skill development.
Team Working	Achieved	Achieved	Achieved	□	□	I have considerable experience working within a clinical team and just need to work to transfer these skills to a research setting.
People Management	Achieved	□	□	□	□	Still working to establish my individual management style and improve my delegation skills
Supervision	□	□	□	□	□	Not yet achieved phase 1: Not yet involved in the supervision/support of undergraduate students except from a placement educator perspective. No experience of academic supervision
Mentoring	□	□	□	□	□	Not yet achieved phase 1: Only teaching currently within a clinical

						context and not within an academic setting.
Influence and Leadership	Achieved	□	□	□	□	This is one of my strengths within my research as it has been led and designed with minimal support and based around producing real world outputs. I have not yet begun to extend my influence/leadership beyond my own research.
Collaboration	□	□	□	□	□	I am aware of the value of working in collaboration, but so far have not produced any work in collaboration. I am guilty of flying solo at times.
Equality and Diversity	Achieved	Achieved	□	□	□	I work hard to maintain equality and diversity within my research and clinical practice. But can develop by impressing this behaviour in others

D2 – Communication and Dissemination

Communication Methods	□	□	□	□	□	I can develop my approach to constructing written and verbal arguments
Communication Media	□	□	□	□	□	I am an effective presented and communicate well face-to-face. However, my web presence as a researcher is currently poor.
Publication	□	□	□	□	□	I have not yet published any original research.
D3 – Engagement and Impact						
Teaching	□	□	□	□	□	I currently have very limited experience of teaching outside of clinical educator context. This is something I plan to develop over the next few years
Public Engagement	□	□	□	□	□	I understand the value of public engagement within decision making and research, however, I have not yet

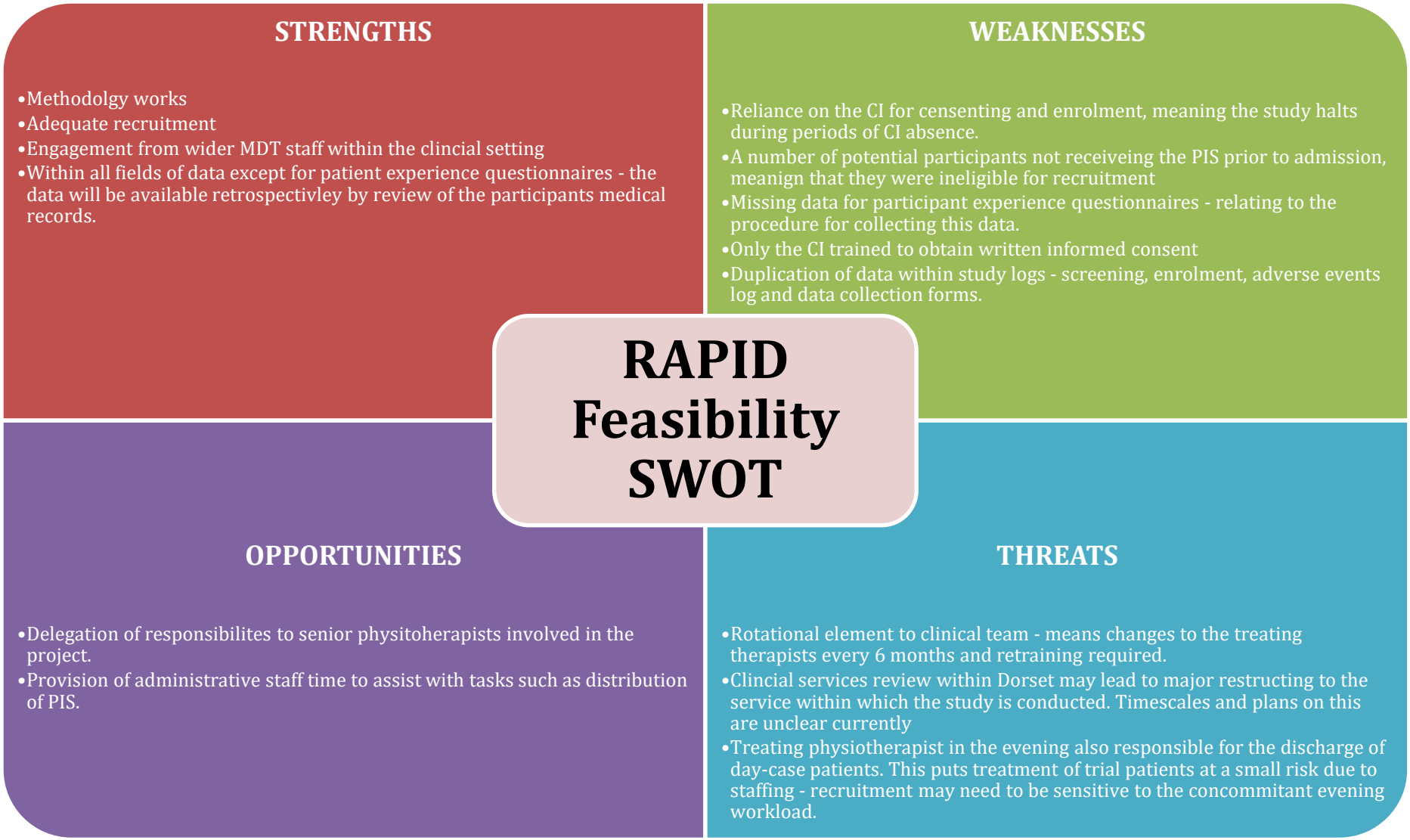
						been in a position to present any aspects of y research at public events
Enterprise	□	□	□	□	□	I have so far given very little thought to the commercial side of my research. With much of my focus being around efficacy and quality for patients.
Policy	Achieved	□	□	□	□	My experience with setting up research and with previous trade union representation have given me a good overview of policy and their situational context.
Society and Culture	Achieved	□	□	□	□	Through previous leadership training, I understand the concepts of organisational culture and social responsibility.
Global Citizenship	Achieved	□	□	□	□	I have an understanding of where my research project sits within the national and international

						developments within this field. I have not yet begun to speak to the international research community.

Appendix 18 SWOT Analysis – Chief Investigator Management Skills


STRENGTHS
•Enthusiasm and perseverence in making the research succeed, having had to be adaptable at times to keep the project on track or develop ot further.
•Confidence in my own skills at being able to run the study effectively
•Self-reflection and learning from this - learning from mistakes and areas of the project setup which havent gone totally smoothly
•Responsibility to the project with independence.
•Professional development in seeking and developing new skill and putting them into practice.
•Clear research strategy with clear end goals for real world outcomes grounded in clinical practice.
•Support network to seek help with research
•Working with others and teamworking
•Verbal communication
WEAKNESSES
•Understanding of research funding due to this being an unfunded project
•Little experience of research governance or project management in the past.
•No previously published work or work at a publishable level.
•Work-Life balance
•Some naievity around the project infrastructure and resources - I have just taken what I can get.
•Little experience of academic teaching or working within different research paradigms
Research Management SWOT Analysis
(Based on Vitae RDF)
OPPORTUNITIES
•Reflective learning from this feasibility study
•Engagement with academic supervisors
•Practice at running a study
•DClinP modules
•The research team around me - developing my trust in them to allow me to delegate.
•Higher level managerial support and the influence this brings
•Annual leave and planning some down-time
THREATS
•Work life balance
•Burden of recruitment
•Financial - tuition fees

Appendix 19 SWOT Analysis – Management RAPID Study


STRENGTHS
•Methodolgy works
•Adequate recruitment
•Engagement from wider MDT staff within the clincial setting
•Within all fields of data except for patient experience questionnaires - the data will be available retrospectivley by review of the participants medical records.
WEAKNESSES
•Reliance on the CI for censenting and enrolment, meaning the study halts during periods of CI absence.
•A number of potential participants not receiveing the PIS prior to admission, meanign that they were ineligible for recruitment
•Missing data for participant experience questionnaires - relating to the procedure for collecting this data.
•Only the CI trained to obtain written informed consent
•Duplication of data within study logs - screening, enrolment, adverse events log and data collection forms.
RAPID Feasibility SWOT
OPPORTUNITIES
•Delegation of responsibilites to senior physitoherapists involved in the project.
•Provision of administrative staff time to assist with tasks such as distribution of PIS.
THREATS
•Rotational element to clinical team - means changes to the treating therapists every 6 months and retraining required.
•Clincial services review within Dorset may lead to major restructing to the service within which the study is conducted. Timescales and plans on this are unclear currently
•Treating physiotherapist in the evening also responsible for the discharge of day-case patients. This puts treatment of trial patients at a small risk due to staffing - recruitment may need to be sensitive to the concommitant evening workload.

Appendix 20 NHS Patient Experience Framework

NHS

NHS Patient Experience Framework

In October 2011 the **NHS National Quality Board (NQB)** agreed on a working definition of patient experience to guide the measurement of patient experience across the NHS. This framework outlines those elements which are critical to the patients' experience of NHS Services.

- **Respect for patient-centred values, preferences, and expressed needs,** including: cultural issues; the dignity, privacy and independence of patients and service users; an awareness of quality-of-life issues; and shared decision making;
- **Coordination and integration of care** across the health and social care system;
- **Information, communication, and education** on clinical status, progress, prognosis, and processes of care in order to facilitate autonomy, self-care and health promotion;
- **Physical comfort** including pain management, help with activities of daily living, and clean and comfortable surroundings;
- **Emotional support** and alleviation of fear and anxiety about such issues as clinical status, prognosis, and the impact of illness on patients, their families and their finances;
- **Welcoming the involvement of family and friends,** on whom patients and service users rely, in decision-making and demonstrating awareness and accommodation of their needs as care-givers;
- **Transition and continuity** as regards information that will help patients care for themselves away from a clinical setting, and coordination, planning, and support to ease transitions;
- **Access to care** with attention for example, to time spent waiting for admission or time between admission and placement in a room in an in-patient setting, and waiting time for an appointment or visit in the out-patient, primary care or social care setting.

This framework is based on a modified version of the Picker Institute Principles of Patient-Centred Care, an evidence based definition of a good patient experience. When using this framework the NHS is required under the Equality Act 2010 to take account of its Public Sector Equality Duty including eliminating discrimination, harassment and victimisation, promoting equality and fostering good relations between people.

DH Department of Health

Gateway reference number 17273

Appendix 21 Questionnaire Readability Assessment

Question 1: Do you think the hospital staff did everything they could to help control your pain?*

Number of characters (without spaces) :	69.00
Number of words :	15.00
Number of sentences :	1.00
Average number of characters per word :	4.60
Average number of syllables per word :	1.60
Average number of words per sentence:	15.00

Indication of the number of years of formal education that a person requires in order to easily understand the text on the first reading

Gunning Fog index :	11.33

Approximate representation of the U.S. grade level needed to comprehend the text :

Coleman Liau index :	9.29
Flesch Kincaid Grade level :	9.14
ARI (Automated Readability Index) :	7.74
SMOG :	10.75

Flesch Reading Ease :	56.25

Question 2: Overall, how was your experience of physiotherapy following your operation?

Number of characters (without spaces) :	64.00
Number of words :	10.00
Number of sentences :	1.00
Average number of characters per word :	6.40
Average number of syllables per word :	2.50
Average number of words per sentence:	10.00

Indication of the number of years of formal education that a person requires in order to easily understand the text on the first reading

Gunning Fog index :	20.00

Approximate representation of the U.S. grade level needed to comprehend the text :

Coleman Liau index :	18.90
Flesch Kincaid Grade level :	17.81
ARI (Automated Readability Index) :	13.71
SMOG :	15.25

Flesch Reading Ease :	-14.81

Question 3: Overall, how was your experience of your overall hospital treatment?

57.00

Number of characters (without spaces) :	
Number of words :	10.00
Number of sentences :	1.00
Average number of characters per word :	5.70
Average number of syllables per word :	2.10
Average number of words per sentence:	10.00

Indication of the number of years of formal education that a person requires in order to easily understand the text on the first reading	
Gunning Fog index :	20.00

Approximate representation of the U.S. grade level needed to comprehend the text :	
Coleman Liau index :	14.77
Flesch Kincaid Grade level :	13.09
ARI (Automated Readability Index) :	10.42
SMOG :	13.95

Flesch Reading Ease : 19.03

Question 4: Did you have confidence and trust in the physiotherapists treating you?

Number of characters (without spaces) :	60.00
Number of words :	11.00

Number of sentences :	1.00
Average number of characters per word :	5.45
Average number of syllables per word :	1.82
Average number of words per sentence:	11.00

Indication of the number of years of formal education that a person requires in order to easily understand the text on the first reading	
Gunning Fog index :	11.67

Approximate representation of the U.S. grade level needed to comprehend the text :	
Coleman Liau index :	13.60
Flesch Kincaid Grade level :	10.15
ARI (Automated Readability Index) :	9.76
SMOG :	10.75

Flesch Reading Ease : 41.85

Question 5: How beneficial was walking early after your operation?

Number of characters (without spaces) :	46.00
Number of words :	8.00
Number of sentences :	1.00
Average number of characters per word :	5.75

Average number of syllables per word :	2.25
Average number of words per sentence:	8.00

Indication of the number of years of formal education that a person requires in order to easily understand the text on the first reading	
Gunning Fog index :	13.20

Approximate representation of the U.S. grade level needed to comprehend the text :	
Coleman Liau index :	14.32
Flesch Kincaid Grade level :	14.08
ARI (Automated Readability Index) :	9.65
SMOG :	10.75

Flesch Reading Ease :	8.37

Question 6: How well was your progression with your physiotherapist paced to suit you?

Number of characters (without spaces) :	62.00
Number of words :	12.00
Number of sentences :	1.00
Average number of characters per word :	5.17
Average number of syllables per word :	1.83
Average number of words per sentence:	12.00

Indication of the number of years of formal education that a person requires in order to easily understand the text on the first reading

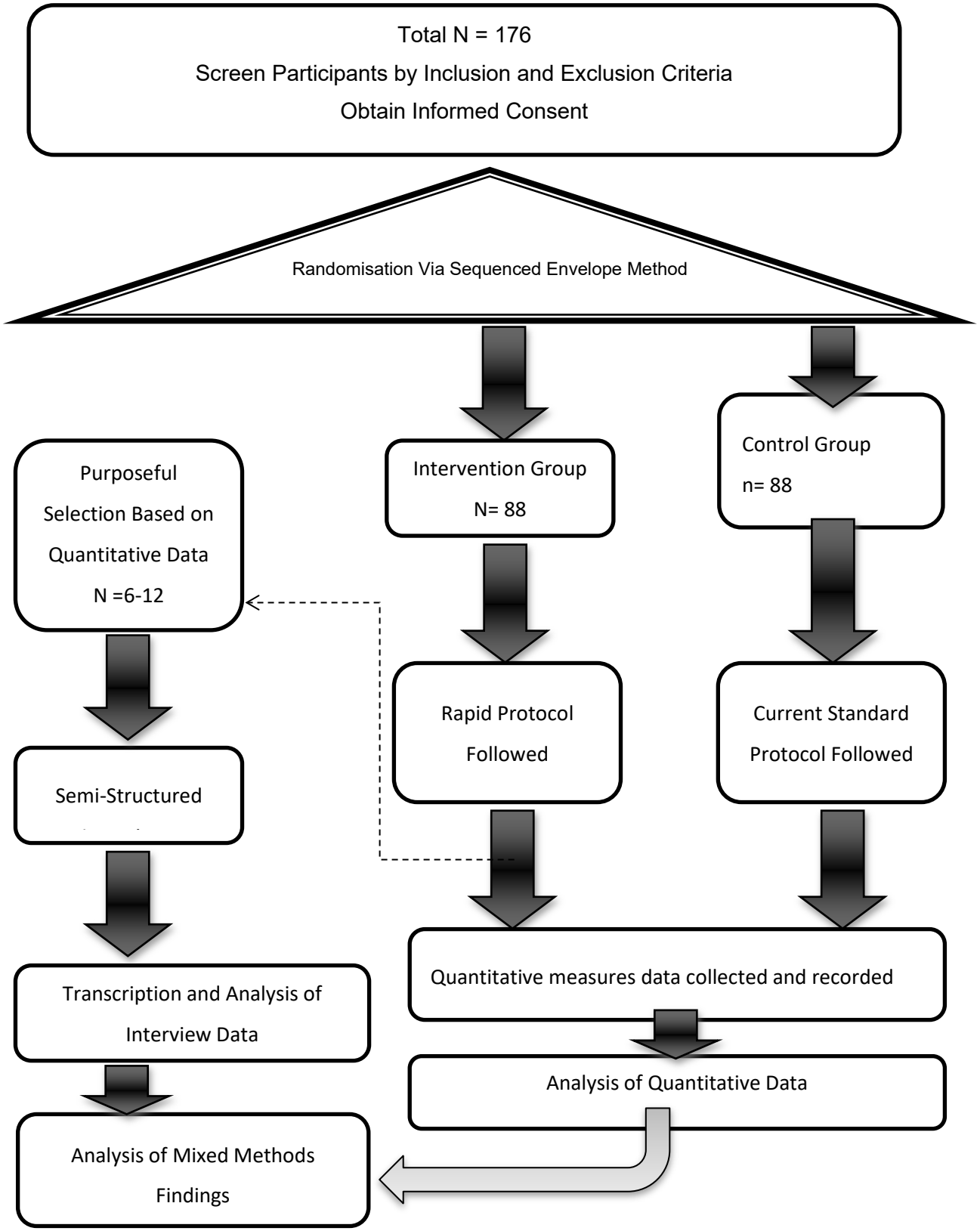
Gunning Fog index :	11.47

Approximate representation of the U.S. grade level needed to comprehend the text :

Coleman Liau index :	12.13
Flesch Kincaid Grade level :	10.72
ARI (Automated Readability Index) :	8.90
SMOG :	10.75

Flesch Reading Ease :	39.56

Appendix 22 Study Scheme Diagram



Appendix 23 3-Month Telephone Follow-up Form

RAPID Study 3-Month Telephone Follow-Up

Date of Op:		**Date of Discharge:**	
Date of Telephone f/u		**Unique Study Number:**	

Post-Op Complications - Since Discharge

	Complication	Tick	Comments:
	Deep Vein Thrombosis		
	Pulmonary Embolism		
	Wound Ooze Issues		
	Wound Infection		
	Blood Transfusion		
	CVA		
	Orthostatic Hypotension		
	Syncope		
	Respiratory Tract Infection		
	MI		
	Bowel Obstruction		

Other Complications

	Complication:	
	Comments:	

Any Participant Volunteered Comments on their experience?

Print Name	Job Title	Signed

Appendix 24 Participant Information Sheet

RAPID Participant Information Sheet Version 4 Dated 30/08/2016

1. Study Title:

Does Rapid Mobilisation as Part of an Enhanced Recovery Pathway Improve Length of Stay, Return to Function and Patient Satisfaction Post Primary Total Hip Replacement? A Randomised Controlled Trial

2. Invitation Paragraph:

During your admission for your hip replacement you may be invited to take part in a research study. Before you make any decision it is important that you understand why the research study is being done and what it would involve for you.

Please take your time to read through the following information carefully. You may talk to others about the study if you wish. Please ask us if there is anything that you are not clear about or would like extra information on. One of our team will happily go through the information sheet with you.

This information sheet will aim to inform you of the purpose of the study, and give you more details about how the study is run.

3. What is the Purpose of this Study?

Following total hip replacement surgeries, recent evidence suggests that walking early after your operation can improve your recovery times and function. Currently most patients having had a total hip replacement walk for the first time on the day after their operation.

This study aims to investigate whether starting walking on the same day of the operation improves a patient's recovery and reduces the length of time they need to stay in hospital for.

4. What will happen to me if I do take part?

This is a randomised trial, because we don't know which way of treating patients is best. To find out, we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same to start with, each patient is put into a group by chance (randomly).

If you decide to take part in the study, you will either start walking on the day of your operation, (we will call this group the RAPID group), or follow the current standard care protocol, (we call this group the control group). Half of the patients in the study will be in the RAPID group and half in the control

group. You have a 50% chance of receiving the treatment we are testing (walking on the day of your operation). A member of the research team will come and see you following your operation and will let you know which group you have been randomly allocated to.

You will also be issued with a unique study number. Only the clinical team involved in the research at the hospital will be able to identify you by this code. The team will hold this information securely at the hospital at all times in accordance with the data protection act and local hospital policies.

On the day of your surgery, those patients who have been allocated into the RAPID group will be seen by our physiotherapy team with the aim to start walking. Those patients in the control group will be seen by our physiotherapy team to be taught and go through some bed exercises. Although rare, if you had any serious complications as part of your operation you would be automatically withdrawn from the study at this stage.

The rest of your physiotherapy care in hospital will be progressed by a physiotherapist at a rate which your physiotherapist feels is appropriate to you, which is exactly the same as it would be if you were not to participate in the study. This is the same for both groups.

Your physiotherapist and the research team will be observing your recovery while you are in hospital and also recording the medications you are given over the course of your stay in hospital.

After leaving hospital, you will be contacted via telephone by one of the research team to check if you had any complications in your recovery after hospital discharge.

5. Why may I be invited to take part?

You may be invited to take part as you will be having a total hip replacement operation on the Derwent suite. Your suitability for the study, should you wish to take part will be reviewed by a member of the research team on the day of your operation.

6. Do I have to take part?

It is up to you whether you decide to join the study or not. We will describe the study and go through the information sheet with you. If you do decide to take part, we will then ask you to sign a consent form.

If you do decide to take part, you are still free to withdraw from the study completely at any time and you are not required to give a reason. A decision to withdraw or not to take part will not affect any of the care you receive. Any information we have collected from you up to this point as part of the study would be kept and used in the study results.

A decision not to take part or to withdraw from this study will in no way affect the routine standard of care that you receive.

7. What are the Potential Risks?

We do not envisage any significant risks from you taking part. Some potential risks may be:

- Slower wound healing
- Risk of falling when attempting to walk

These risks will be minimised by the careful monitoring of your wound by our hospital nursing team and your suitability for walking will be closely assessed by your physiotherapist. When walking for the first time after your operation you will be accompanied by two of the physiotherapy staff.

There may be some symptoms associated with walking very early after the operation, these are listed below:

- Nausea and vomiting
- Low blood pressure when getting up for the first time. This can lead to fainting in some patients.

If you should suffer with any symptoms you should let the hospital research team know immediately.

8. What are the Possible Benefits?

We cannot promise that the study will help you but the information we get from this study will hopefully help us to treat patients who have had a total hip replacement better in the future. If you begin walking on the day of your operation, and the study shows that it speeds up recovery following a hip replacement then you may have benefited directly from taking part.

The study only requires the time commitment from you for a telephone call after you leave hospital, as all other treatments and measurements will take place within your normal expected hospital stay. You will not be required to participate in anything after your follow-up telephone call and your details will always remain confidential.

9. What happens when the study stops?

We are happy to send you a copy of the final results of the study. If you would like to receive this then you can provide us with an email or postal address and we will send them on to you.

The results of the study will be published in medical journals. No individual patients will be identified in these reports.

10. What if there is a problem?

Any complaints about the way you have been dealt with during the study, or any possible harm you might suffer will be assessed by the chief investigator running the study.

If you have a concern about any aspect of this study, you should ask to speak to a member of the research team who will do their best to answer your questions (telephone 01202 726221). If you remain unhappy and wish to complain formally, you can do this via the Legal Services and Complaints department (01202 704452). Alternatively, you can contact the Patient Advice and Liaison Service (PALS): Jennie Moffat Tel: 01202 704886

In the event that something does go wrong and you are harmed during the research the normal National Health Service complaints mechanisms will be available to you.

If any complications happen during your time taking part in the study, please inform the physiotherapist treating you as soon as you can.

11. Will my taking part in the study be confidential?

Yes. All personal information will be kept confidential.

With your permission your GP will be informed of your decision to participate. Parts of your medical records will be accessed by members of the research team. We will follow ethical and legal practice and all information about you will be handled in confidence. Our procedures for handling, sharing, processing, storage and the destruction of medical data are compliant with the Data Protection Act 1998. Data on you will be stored according to the principles of the Data Protection Act. If any information is made available to outside bodies your name and details will be kept confidential and any publications from the study will not identify you in any way.

Data about you will be stored on a secure computer. The research team and your physiotherapists only would have authorization to access this information.

12. Will any extra tests such as blood tests or X-rays be done as part of the study?

No, the study does not involve any extra tests.

13. Who is organising and funding this research?

This study will be organised and run by the orthopaedic physiotherapy team at the Royal Bournemouth Hospital.

The research team are not being paid for including you in the study.

14. What will happen to the results of the research study?

The results of this study will be presented at conferences and published in a scientific journal. This is to help other therapists decide if walking on the day of total hip replacement surgery can be beneficial. You will not be identified in any publication of the results.

15. Who has reviewed the study?

The Royal Bournemouth and Christchurch NHS Foundation Trust Research Department and the Hampshire B Research Ethics Committee have approved this study for conduct in the Royal Bournemouth Hospital.

16. What do I do next?

If you would like to participate in this study, please inform one of the researchers who will arrange for you to sign the enclosed informed consent form.

If you would like further information please do not hesitate to contact the Chief Investigator named below.

Thank you for taking the time to read this information sheet.

17. Contacts

Christopher Efford, Senior Orthopaedic Physiotherapist Tel: 01202 726221

Appendix 25 Participant Consent Form

Patient Identification Number for this trial:

CONSENT FORM

Title of Project: RAPID Study. Does Rapid Mobilisation as Part of an Enhanced Recovery Pathway Improve Length of Stay, Return to Function and Patient Satisfaction Post Primary Total Hip Replacement? A Randomised Controlled Trial

Name of Researcher: **Christopher Efford – Senior Orthopaedic Physiotherapist**

Please initial all boxes

1. I confirm that I have read and understand the information sheet dated 30/08/2016 (version 4) for the above study. ☐

2. I have spoken with the above researcher and understand what my involvement in the study will entail. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

3. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

4. I understand that relevant sections of my medical notes and data collected during, may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

5. I understand that any data or information used in any publications which arise from this study will be anonymous. I understand that all data will be stored securely and is covered by the data protection act. ☐

6. I understand that I may be approached to take part in another study associated to this one, but that there is no obligation for me to take part in this second study. ☐

6. I agree to my GP being informed of my participation in the study. ☐

7. I agree to take part in the above study. ☐

Name of Participant	Date	Signature

Name of Person Taking Consent	Date	Signature

Appendix 26 Participant Experience Questionnaire

Patient Satisfaction Questionnaire

Please answer the following Questions in relation to your physiotherapy treatment during your time in hospital: Rate your experience from 0 - 10.

0 being the worst and 10 being the best

1.	Do you think the hospital staff did everything they could to help control your pain?*										
	0	1	2	3	4	5	6	7	8	9	10
2.	Overall, how was your experience of physiotherapy following your operation?										
	0	1	2	3	4	5	6	7	8	9	10
3.	Overall, how was your experience of your overall hospital treatment?*										
	0	1	2	3	4	5	6	7	8	9	10
4.	Did you have confidence and trust in the physiotherapists treating you?*										
	0	1	2	3	4	5	6	7	8	9	10
5.	How beneficial was walking early after your operation?										
	0	1	2	3	4	5	6	7	8	9	10
	Any Comments:										
6.	How well was your progression with your physiotherapist paced to suit you?										
	0	1	2	3	4	5	6	7	8	9	10
	Any Comments:										

Below to be Completed by Physiotherapist

Which Group was this patient part of? (*Please Circle)*		
RAPID Group		Control Group

Appendix 27 Charlston Co-Morbidities Index

One Point

- Myocardial infarction (history, not ECG changes only)
- Congestive heart failure
- Peripheral disease (includes aortic aneurysm >= 6 cm
- Cerebrovascular disease: CVA with mild or no residual or TIA
- Dementia
- Chronic pulmonary disease
- Connective tissue disease
- Peptic ulcer disease
- Mild liver disease (without portal hypertension, includes chronic hepatitis)
- Diabetes without end-organ damage (excludes diet-controlled alone)

Two Points

- Hemiplegia
- Moderate or severe renal disease
- Diabetes with end-organ damage (retinopathy, neuropathy,nephropathy, or brittle diabetes)
- Tumor without metastasis (exclude if > 5 y from diagnosis)
- Leukemia (acute or chronic)
- Lymphoma

Three Points

- Moderate or severe liver disease

Six Points

- Metastatic solid tumor
- AIDS (not just HIV positive)

Appendix 28 Email Correspondence – Financial Significance

RE: What is a significant financial saving in elective orthopaedics?

Cowan, Neil
Sent: 26 November 2015 09:29
To: Efford, Christopher

Chris,
Most interesting indeed.
Over £10k gets my attention. You will need to factor into the cost savings the cost of physio time and any consumables so it is only the net benefit.
Suggest that you raise this in Sept 16 as a potential saving and we can then plan it in from April 2017 (to meet budget setting timescales) as will need budget for physio time and any extras plus accept additional income target to offset.
Sakis also mentioned to me there is analgesia which has a 72 hour lifespan coming onto the market (same drug just longer lasting) to also reduce LoS, maybe these could run in tandem?
Hope this is helpful?
Neil

Neil Cowan
Interim Directorate Manager
Orthopaedic Directorate
Care Group A

☏ 01202 70(4481)
Email: neil.cowan@rbch.nhs.uk

Providing excellent care for our patients
reflecting the care we expect for our families

From: Efford, Christopher
Sent: 24 November 2015 16:10
To: Cowan, Neil
Subject: RE: What is a significant financial saving in elective orthopaedics?

Hi Neil

Thank you for your quick reply,

As a quick summary, RAPID is a clinical trial which we have been running here at RBH since April 2015. It is a trial looking at commencing walking with a physiotherapist approximately 4-6 hours post-operatively. It has full ethical approval through Hampshire B REC and is registered with clincialtrials.gov.

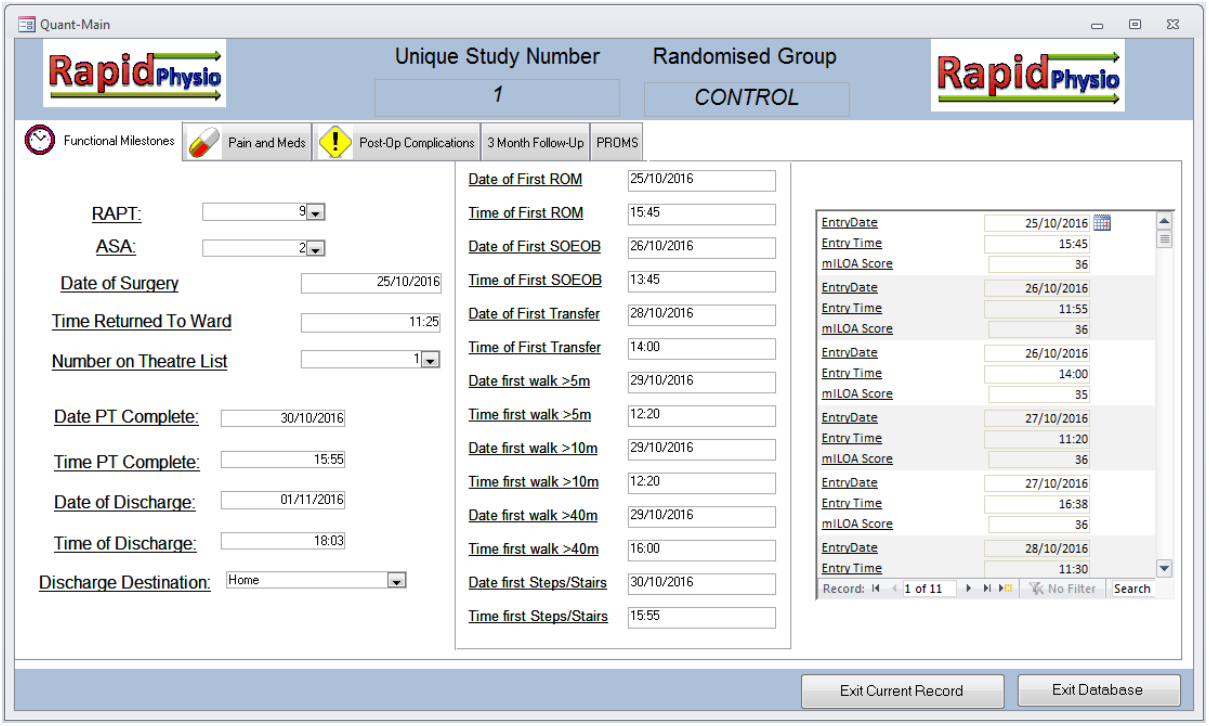
Outcome measures we are currently looking at are:

Length of stay
Time to reach functional milestones in recovery (eg, time to first walk > 40m)
Time to being physiotherapy complete to leave hospital
Incidence rates of post-operative complications
Post-operative pain scores
Patient experience

Also, I am currently in the process of drafting a request with ethics for amendments which would allow me to include the following outcomes/analyses:

Patient experience in more detail

Appendix 29 Screenshot of MS Access Database



Appendix 30 Case Report Form

RAPID Study Data Collection Form (Example Form)			
Formal Consenting Completed (Tick):	☐	Signed by Enroller	
Date of Op:		**Number on Theatre List:**	
Time RTW:		**Unique Study Number:**	
Randomised Group (Tick)			
RAPID	☐	CONTROL	☐

Functional Milestones

	Milestone	Date:	Time:
	Joint First Mobilised		
	First SOEOB		
	First Transferred Bed-Chair		
	First Walked > 5m		
	First Walked > 10m		
	First Walked > 40m		
	First Independent on Steps or Stairs		

Pain Scores Day 0

Pain at Rest	/10	Pain on Movement	/10	Pain on Mobilisation	/10

Pain Scores Day 1

Pain at Rest	/10	Pain on Movement	/10	Pain on Mobilisation	/10

Discharge Information

		Date:	Time:
	Physiotherapy Complete		
	Actual Date of Discharge		
	Discharge Destination		
	Pt Experience Questionnaire Completed.	☐	

Post-Op Complications (If more than 2 Complications PTO)

	Complete as required for each post-operative complication.			
1	Date:		Time:	
	Complication:			
	Notes/Detail:			
2	Date:		Time:	
	Complication:			
	Notes/Detail:			

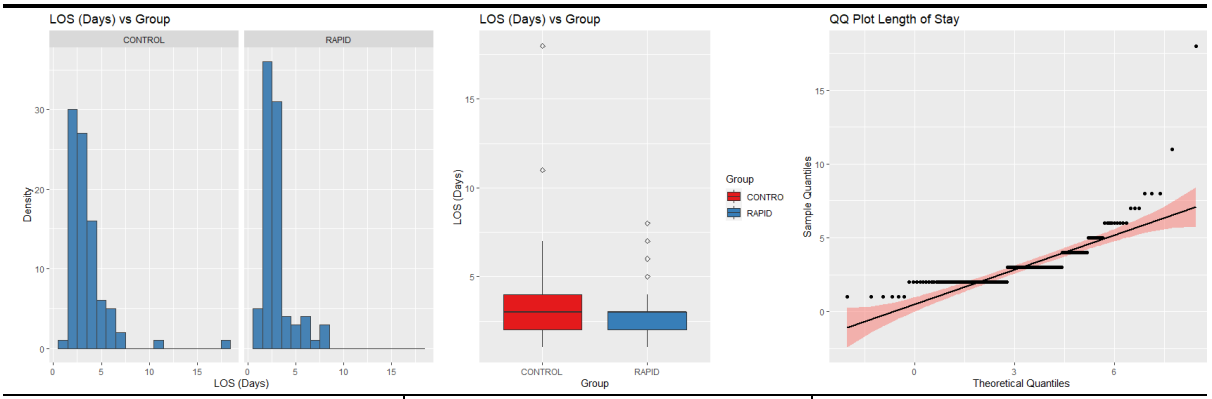
Print Name	Job Title	Signed

Appendix 31 Checking for Normality of Data

Skewness and Kurtosis

Variable	Group	Skewness	Interpretation	Kurtosis	Interpretation
Time to First ROM	**Control**	3.25	Non-Normal	11.61	Non-Normal
	Rapid	3.96	Non-Normal	16.27	Non-Normal
ime to First SOEOB	**Control**	0.13	Normal	-0.32	Normal
	Rapid	2.18	Severe Skew	3.37	Non-Normal
Time to First T/F	**Control**	8.47	Non-Normal	73.85	Non-Normal
	Rapid	2.21	Severe Skew	6.03	Non-Normal
Time to First Walk >5m	**Control**	7.6	Non-Normal	63.17	Non-Normal
	Rapid	1.66	Moderate Skew	2.66	Moderate Skew
Time to First Walk >10m	**Control**	6.48	Non-Normal	49.92	Non-Normal
	Rapid	2.04	Severe Skew	4.09	Non-Normal
Time to First Walk >40m	**Control**	4.65	Non-Normal	28	Non-Normal
	Rapid	2.39	Severe Skew	8.97	Non-Normal
Time to First Stairs	**Control**	4.96	Non-Normal	32.91	Non-Normal
	Rapid	2.2	Severe Skew	8.02	Non-Normal
Time to PT Complete	**Control**	4.72	Non-Normal	29.17	Non-Normal
	Rapid	2.14	Severe Skew	7.59	Non-Normal
Time to Discharge	**Control**	3.86	Non-Normal	21.14	Non-Normal
	Rapid	1.82	Moderate Skew	3.21	Non-Normal
LOS (Days)	**Control**	3.85	Non-Normal	20.9	Non-Normal
	Rapid	1.82	Moderate Skew	3.21	Non-Normal
Day 0 Pain at Rest	**Control**	1.46	Moderate Skew	1.45	Moderate Skew
	Rapid	1.86	Moderate Skew	4.62	Non-Normal
Day 0 Pain on ROM	**Control**	0.75	Normal	-0.2	Normal
	Rapid	0.89	Normal	0.11	Normal
Day 1 Pain at Rest	**Control**	0.85	Normal	-0.18	Normal
	Rapid	0.8	Normal	-0.1	Normal
Day 1 Pain on ROM	**Control**	0.28	Normal	-0.62	Normal
	Rapid	0.21	Normal	-0.79	Normal
Day 1 Pain on Ambulation	**Control**	0.19	Normal	-0.57	Normal
	Rapid	0.21	Normal	-0.54	Normal
Pain on First Ambulation	**Control**	0.2	Normal	-0.7	Normal
	Rapid	0.52	Normal	-0.3	Normal
Total Opioid Consumption	**Control**	4.07	Non-Normal	20.7	Non-Normal
	Rapid	2.89	Moderate Skew	13.5	Non-Normal
Total Antiemetic Consumption	**Control**	3.64	Non-Normal	18.2	Non-Normal
	Rapid	2.66	Moderate Skew	8.84	Non-Normal

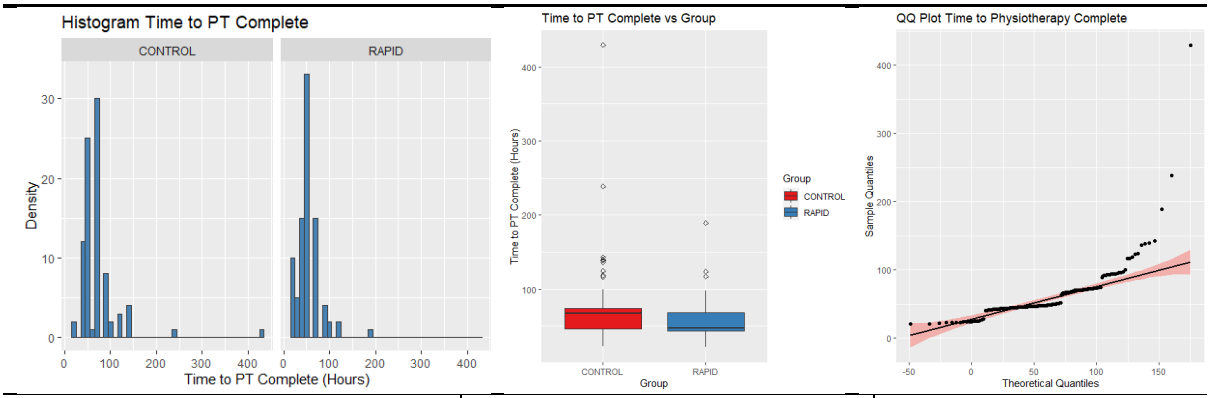
LOS (Days)



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND

Shapiro-Wilk Normality Test	W	p-value
Control Group	0.62742	<0.001
Rapid Group	0.75696	<0.001

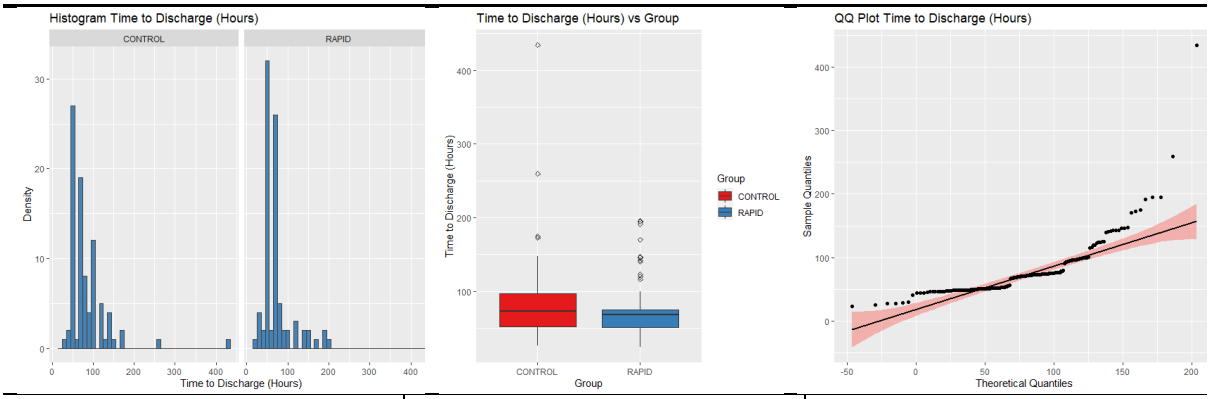
Time to PT Complete



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND

Shapiro-Wilk Normality Test	W	p-value
Control Group	0.55512	<0.001
Rapid Group	0.79562	<0.001

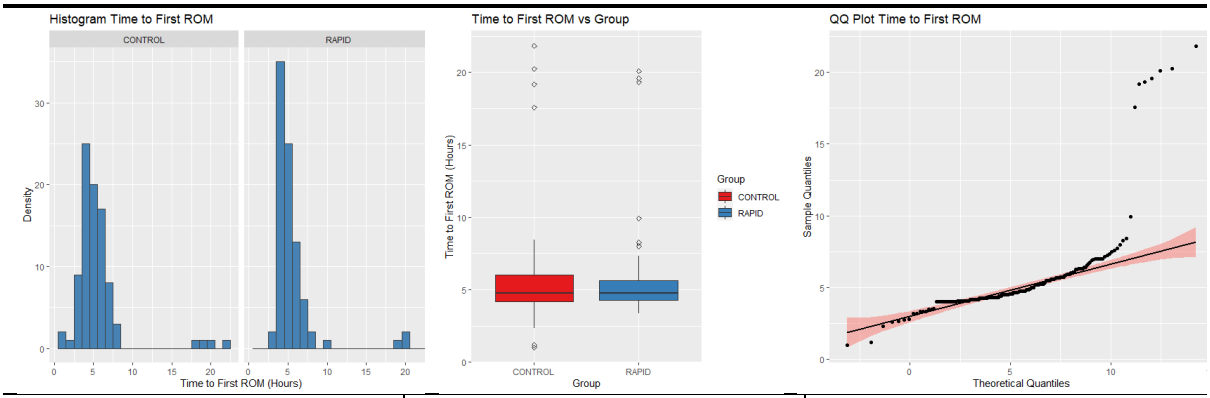
Time to Discharge (Hours)



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND

Shapiro-Wilk Normality Test	W	p-value
Control Group	0.64490	<0.001
Rapid Group	0.78006	<0.001

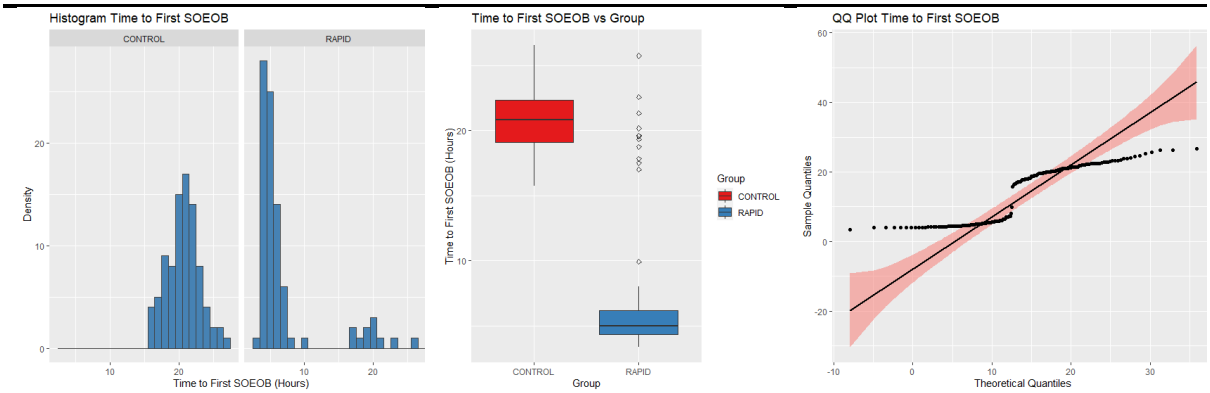
Time to First ROM



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND

Shapiro-Wilk Normality Test	W	p-value
Control Group	0.60795	<0.001
Rapid Group	0.49016	<0.001

Time to First Sit on Edge of Bed

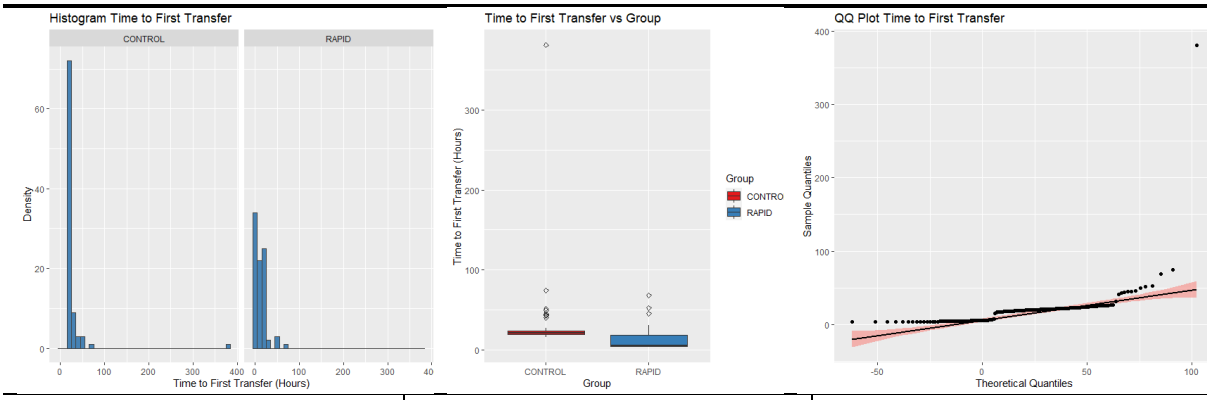


Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND

Shapiro-Wilk Normality Test	W	p-value
Control Group	0.98755	<0.001

Rapid Group	0.58122	<0.001

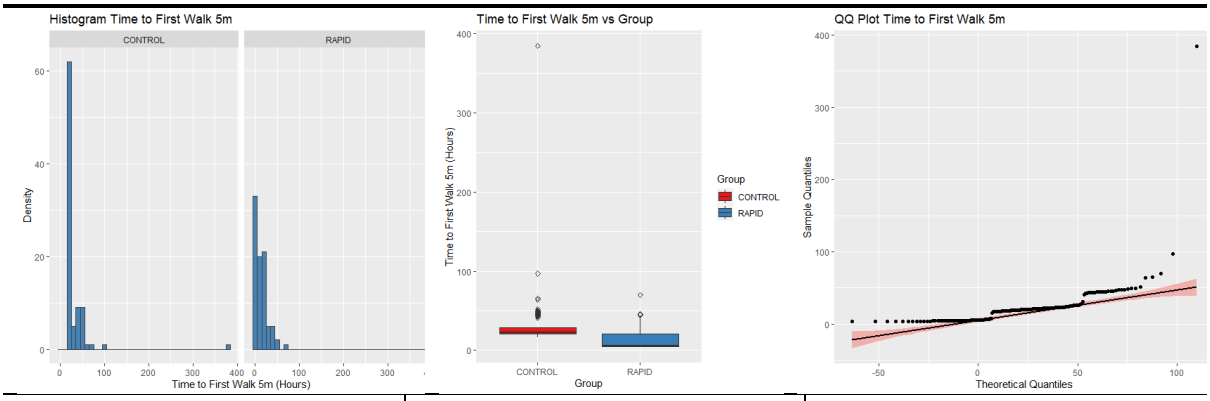
Time to First Transfer



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND

Shapiro-Wilk Normality Test	W	p-value
Control Group	0.18899	<0.001
Rapid Group	0.68708	<0.001

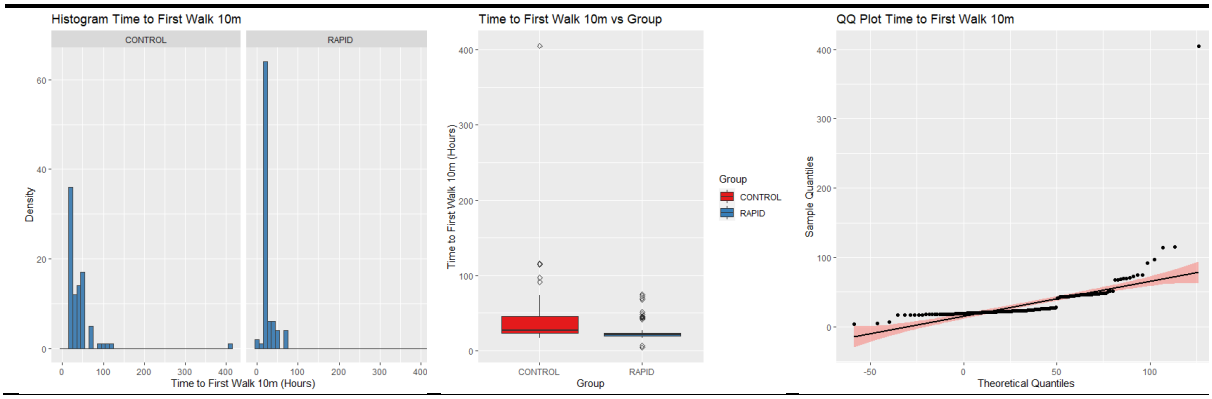
Time to first walk 5m



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND

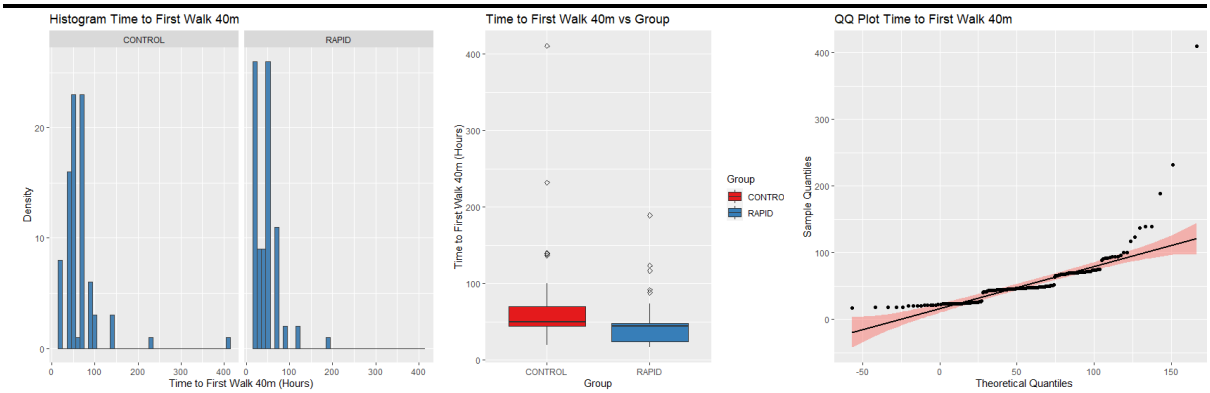
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.28859	<0.001
Rapid Group	0.73741	<0.001

Time to first walk 10m



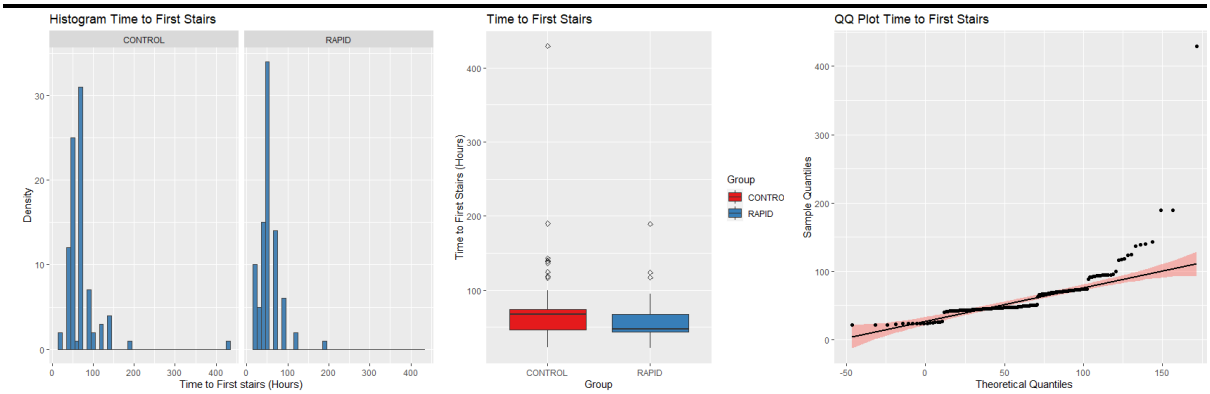
Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.40598	<0.001
Rapid Group	0.69345	<0.001

Time to first walk 40m



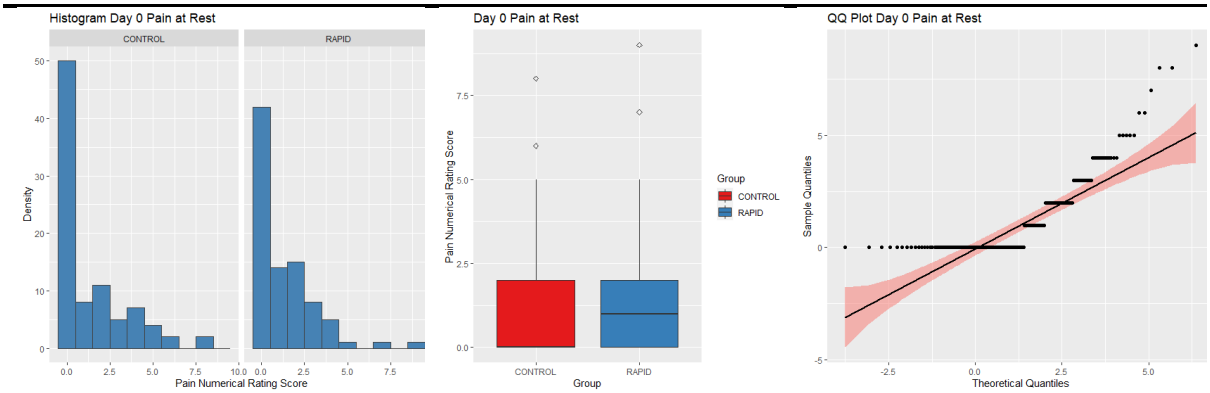
Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.55662	<0.001
Rapid Group	0.76395	<0.001

Time to first managing stairs



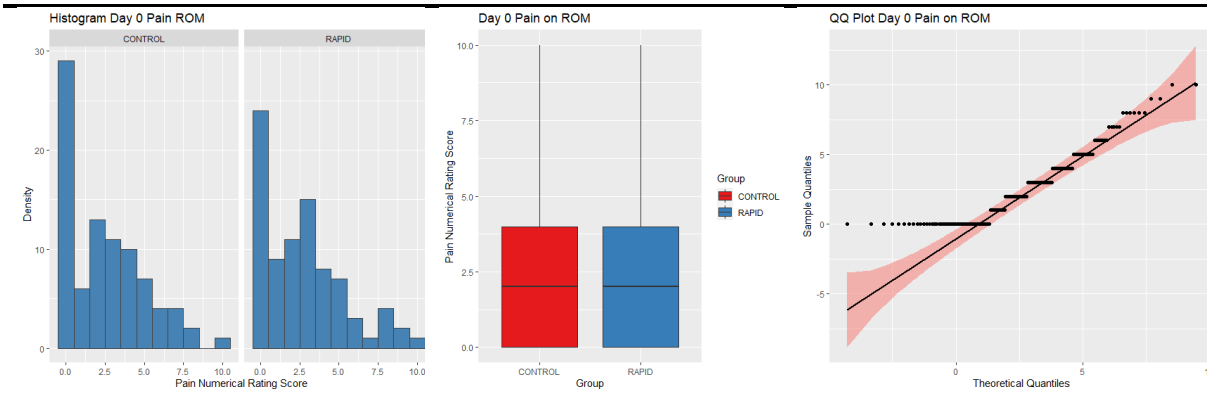
Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.55239	<0.001
Rapid Group	0.78745	<0.001

Day 0 Pain at Rest



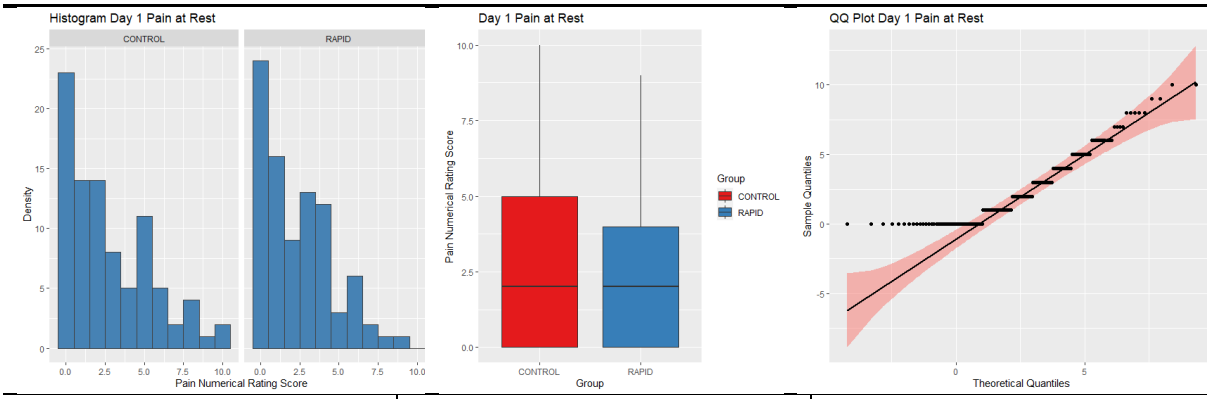
Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.72974	<0.001
Rapid Group	0.74935	<0.001

Day 0 Pain on ROM



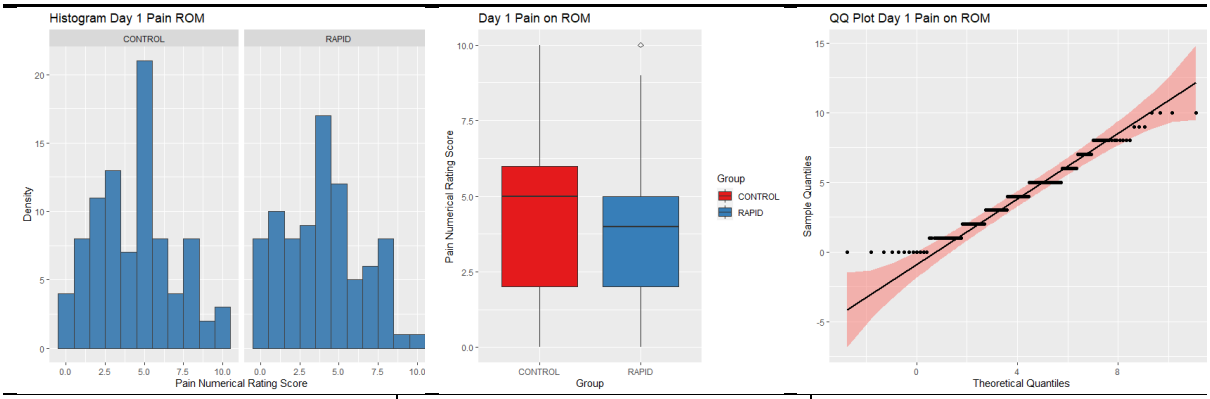
Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.88448	<0.001
Rapid Group	0.88347	<0.001

Day 1 Pain at rest



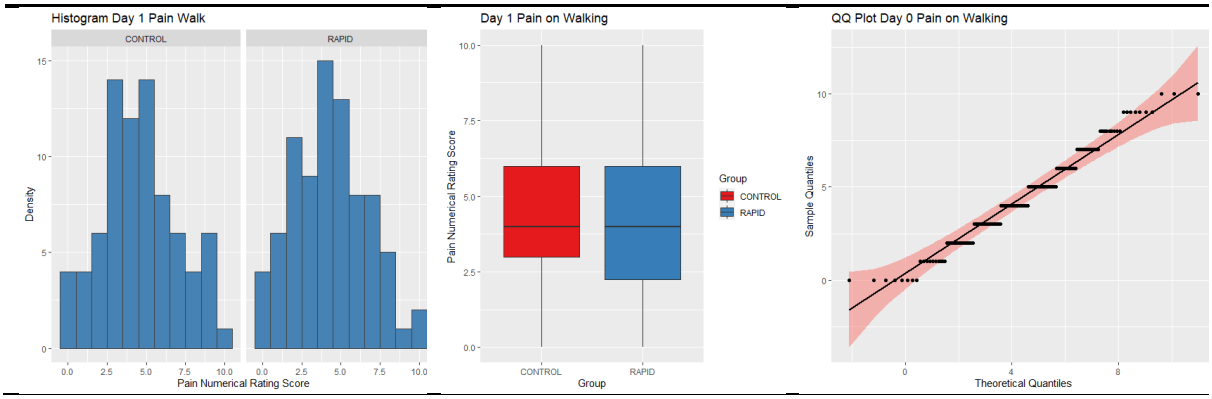
Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.88125	<0.001
Rapid Group	0.88907	<0.001

Day 1 Pain on ROM



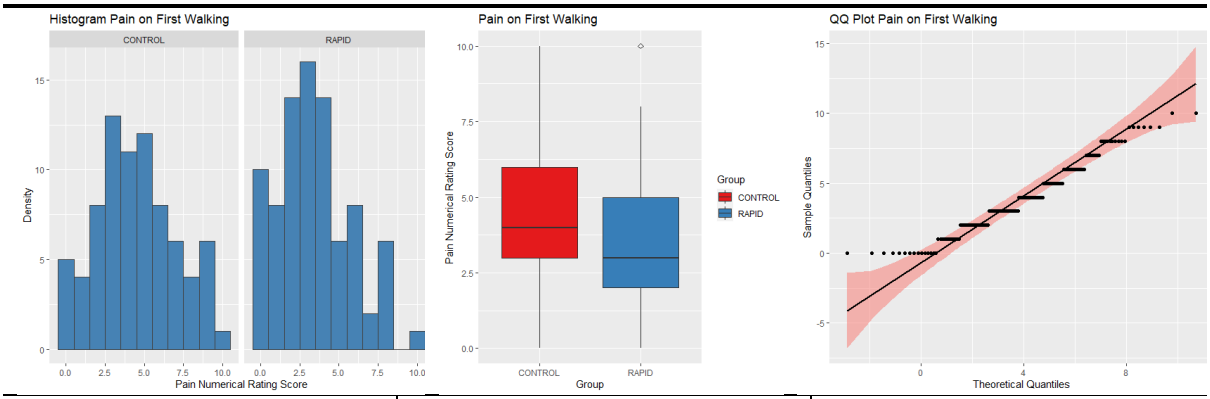
Histogram Appearance: ND	Boxplot Appearance: ND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.96124	0.009
Rapid Group	0.95651	0.005

Day 1 pain on walking



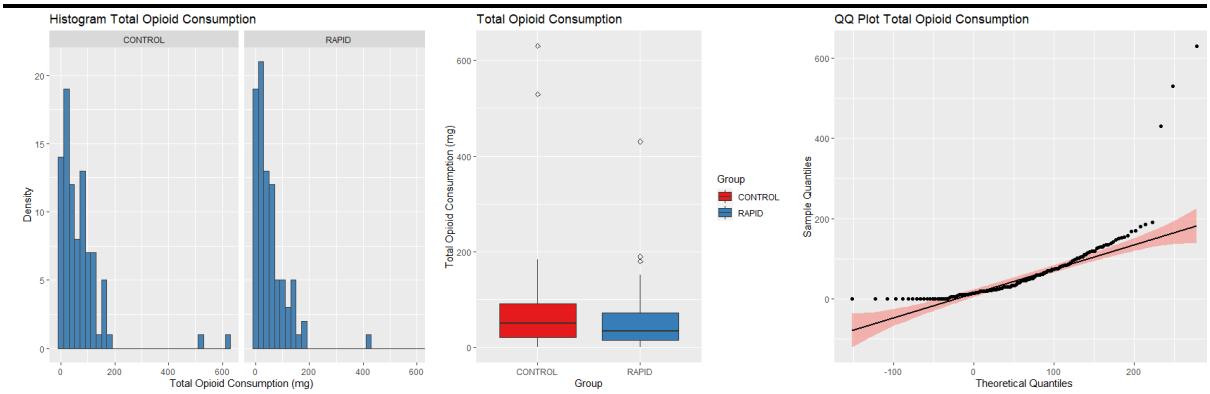
Histogram Appearance: ND	Boxplot Appearance: ND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.96752	0.042
Rapid Group	0.97186	0.068

Pain on first walking



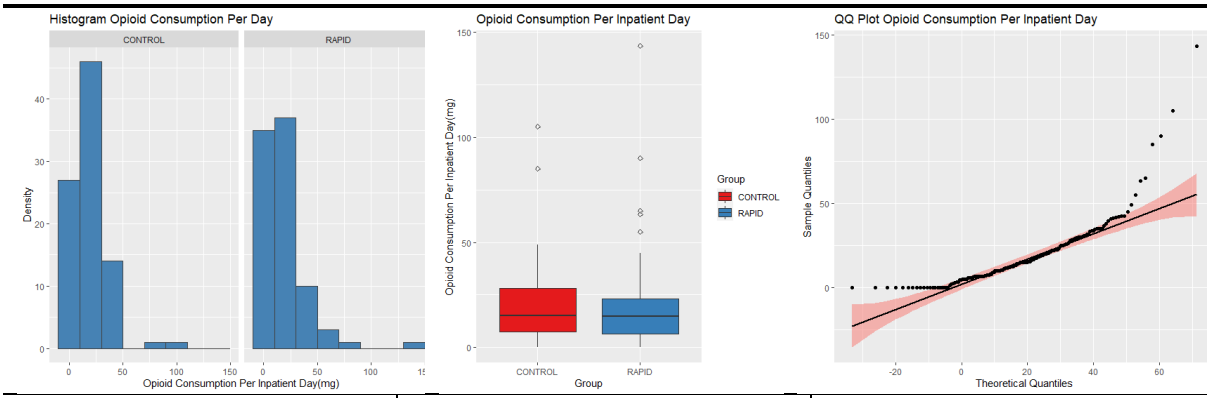
Histogram Appearance: ND	Boxplot Appearance: ND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.96601	0.035
Rapid Group	0.94600	0.001

Total Opioid Consumption



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.59489	<0.001
Rapid Group	0.74220	<0.001

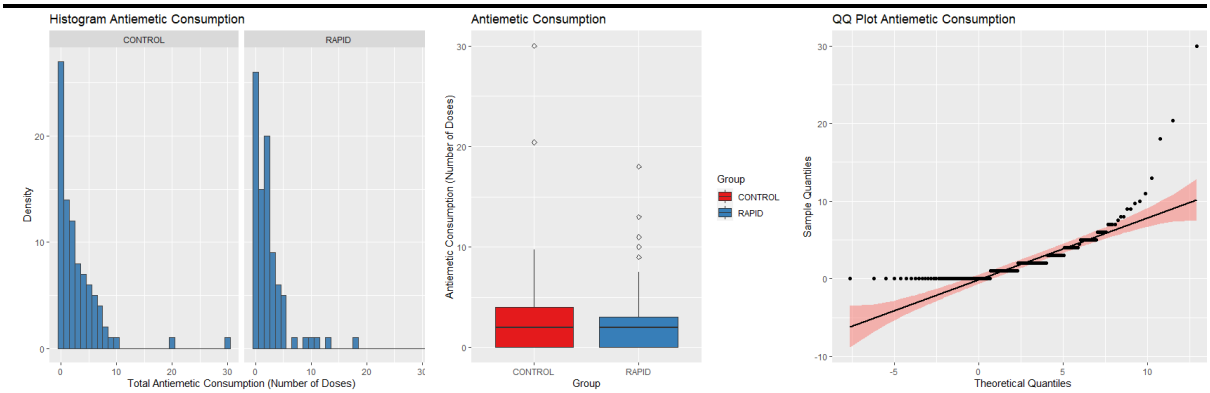
Opioid Consumption Per Inpatient Day



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND

Shapiro-Wilk Normality Test	W	p-value
Control Group	0.81770	<0.001
Rapid Group	0.71693	<0.001

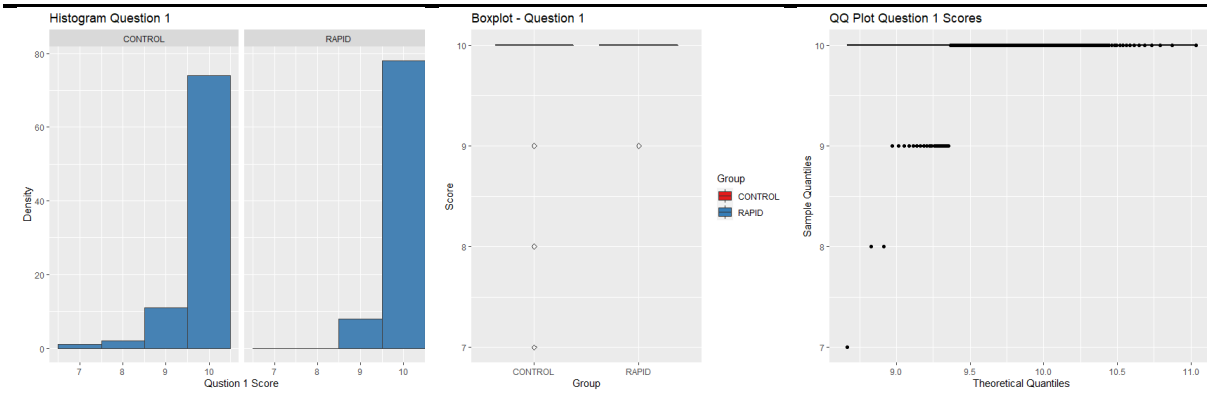
Anti-emetic Consumption



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND

Shapiro-Wilk Normality Test	W	p-value
Control Group	0.63364	<0.001
Rapid Group	0.69806	<0.001

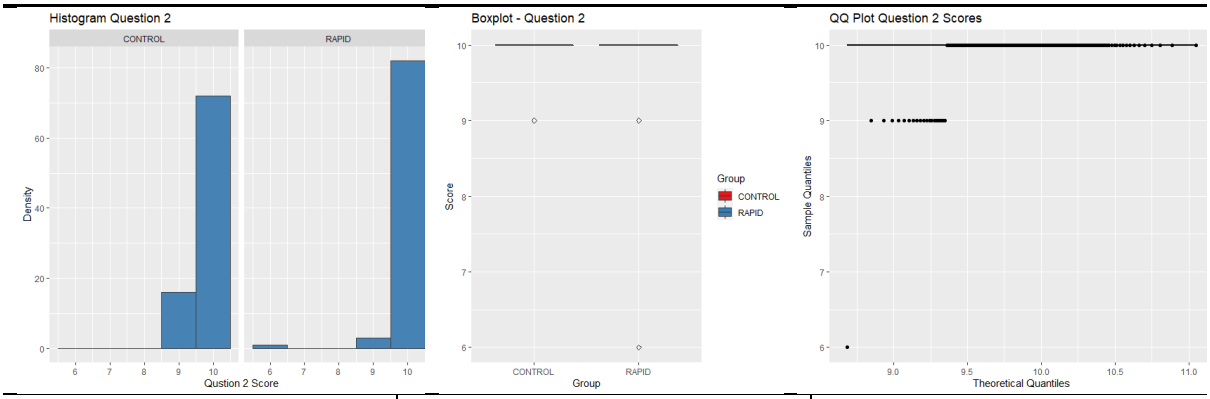
Participant Experience Questionnaire – Q1



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND

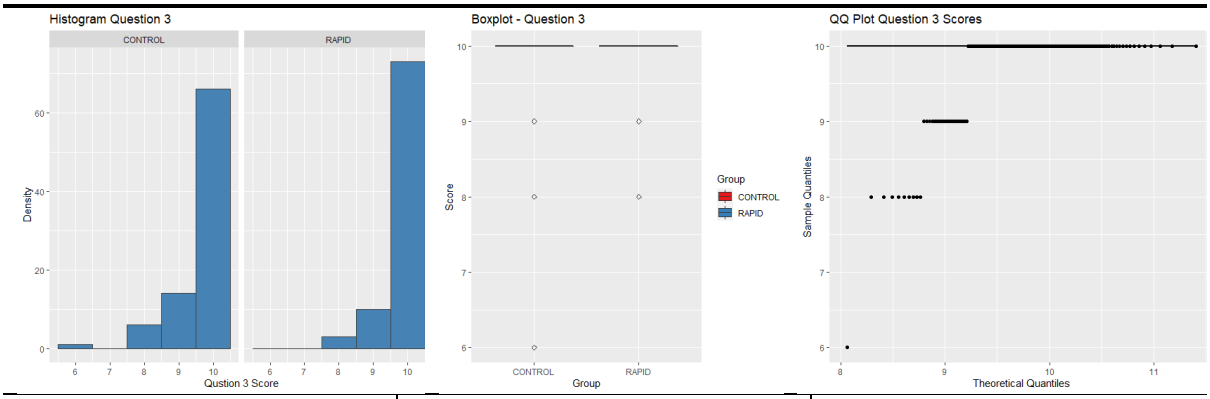
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.44075	<0.001
Rapid Group	0.32871	<0.001

Participant Experience Questionnaire – Q2



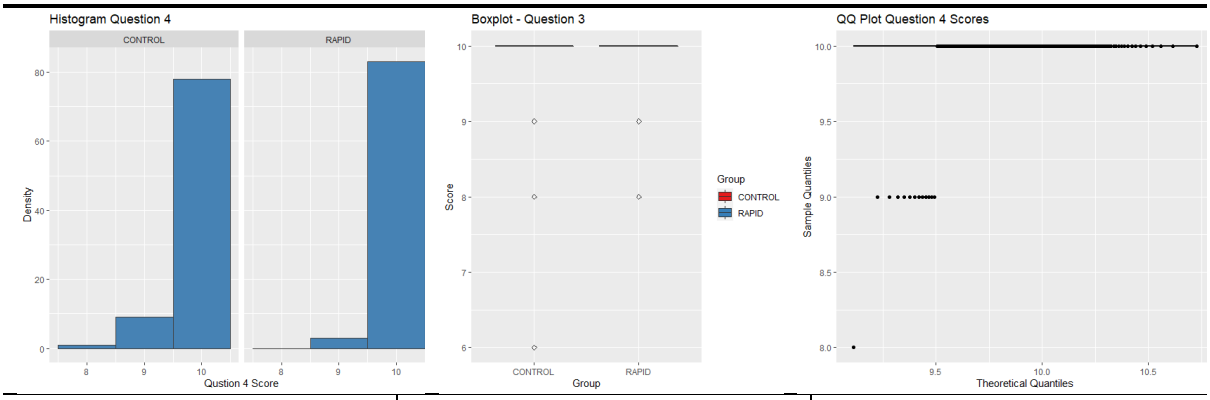
Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.46861	<0.001
Rapid Group	0.17031	<0.001

Participant Experience Questionnaire – Q3



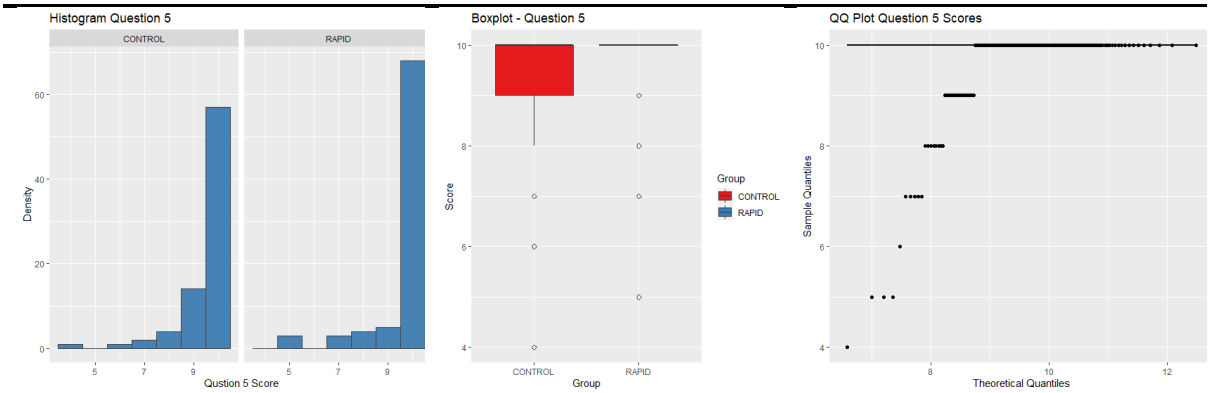
Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.54483	<0.001
Rapid Group	0.43984	<0.001

Participant Experience Questionnaire – Q4



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.37649	<0.001
Rapid Group	0.17866	<0.001

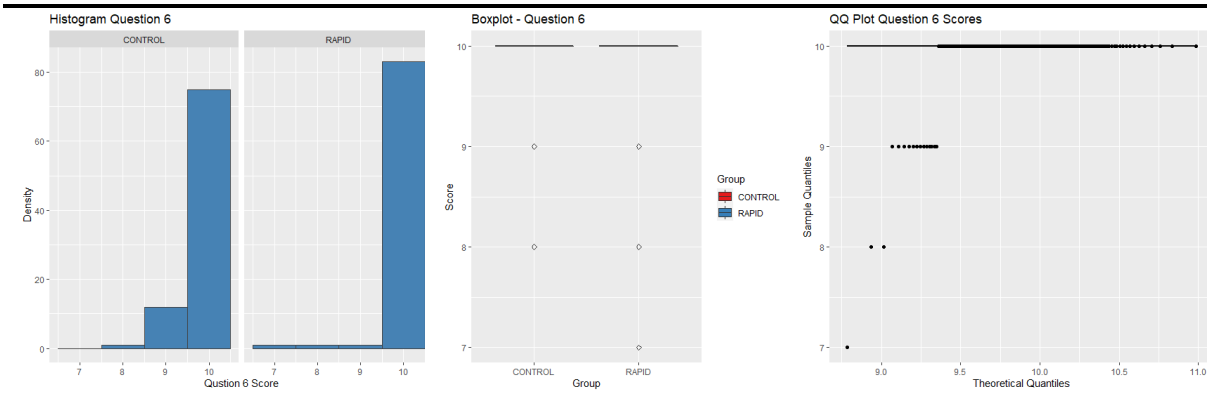
Participant Experience Questionnaire – Q5



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND

Shapiro-Wilk Normality Test	W	p-value
Control Group	0.53550	<0.001
Rapid Group	0.45159	<0.001

Participant Experience Questionnaire – Q6



Histogram Appearance: NND	Boxplot Appearance: NND	Q-Q Plot Appearance: NND

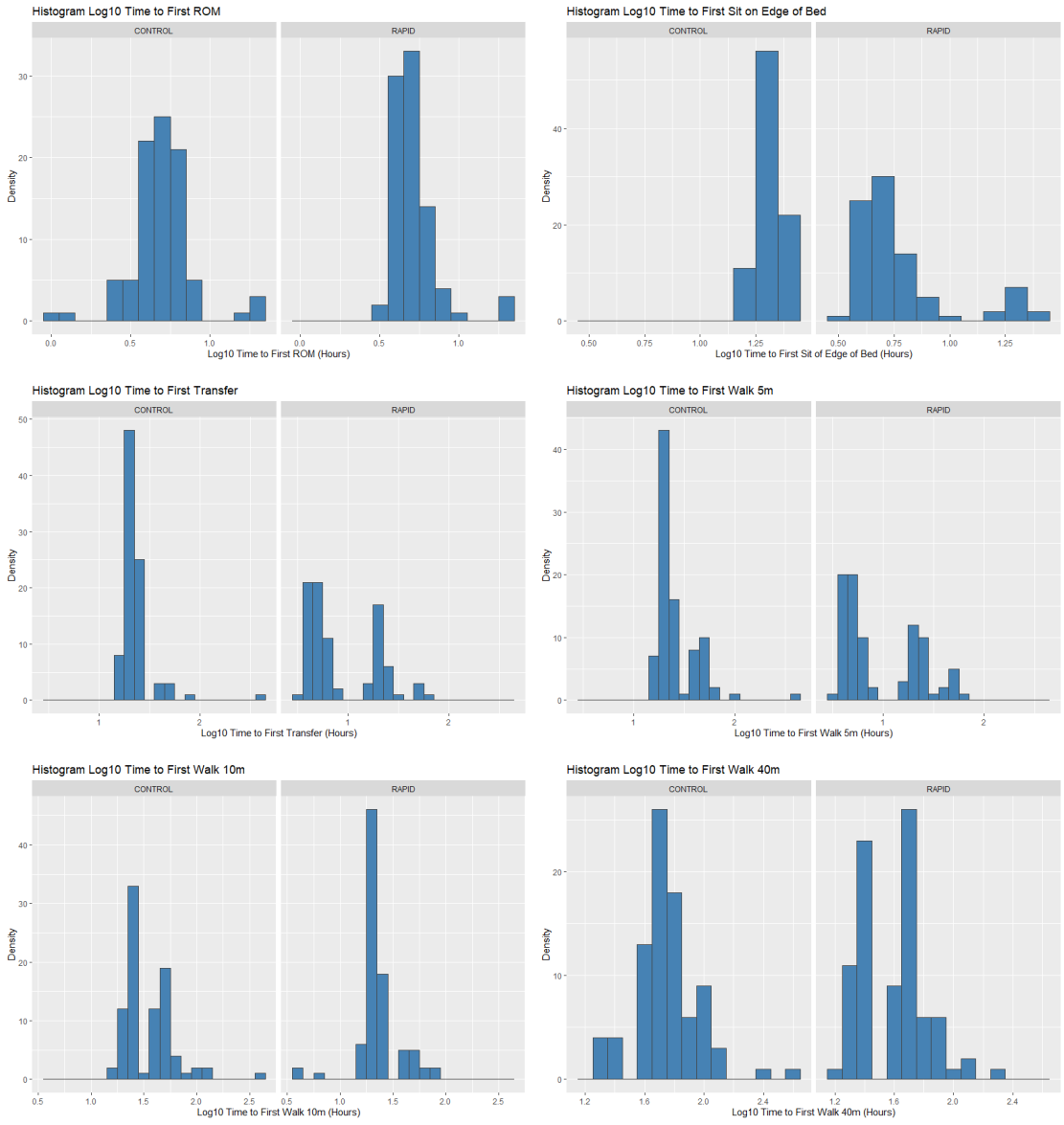
Shapiro-Wilk Normality Test	W	p-value
Control Group	0.43622	<0.001
Rapid Group	0.17106	<0.001

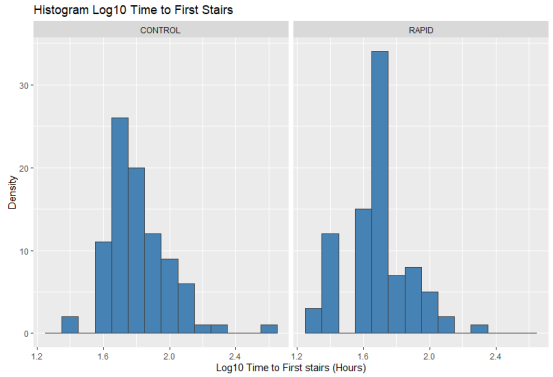
Base 10Logarithmic Transformation and Shapiro-wilk Testing

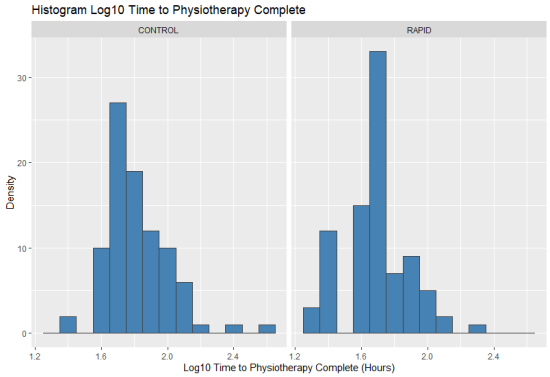
Log^{10} Variable	**Group**	**Shapiro-Wilk W Statistic**	**p-value**	**Distribution Interpretation**
Time to First ROM	**Control**	0.8735	<0.001	Non-Normal
	Rapid	0.7347	<0.001	Non-Normal
Time to First SOEOB	**Control**	0.9870	0.5243	Normal
	Rapid	0.7263	<0.001	Non-Normal
Time to First T/F	**Control**	0.5595	<0.001	Non-Normal
	Rapid	0.8231	<0.001	Non-Normal
Time to First Walk >5m	**Control**	0.7287	<0.001	Non-Normal
	Rapid	0.8335	<0.001	Non-Normal
Time to First Walk >10m	**Control**	0.8611	<0.001	Non-Normal
	Rapid	0.7928	<0.001	Non-Normal
Time to First Walk >40m	**Control**	0.9113	<0.001	Non-Normal

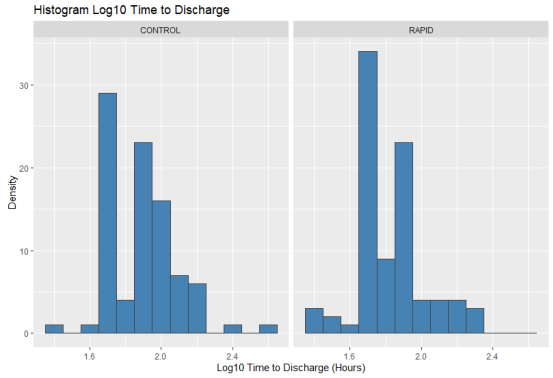
	Rapid	0.9246	<0.001	Non-Normal
Time to First Stairs	**Control**	0.8996	<0.001	Non-Normal
	Rapid	0.9187	<0.001	Non-Normal
Time to PT Complete	**Control**	0.8963	<0.001	Non-Normal
	Rapid	0.9240	<0.001	Non-Normal
Time to Discharge	**Control**	0.9273	<0.001	Non-Normal
	Rapid	0.9268	<0.001	Non-Normal
LOS (Days)	**Control**	0.8859	<0.001	Non-Normal
	Rapid	0.8748	<0.001	Non-Normal

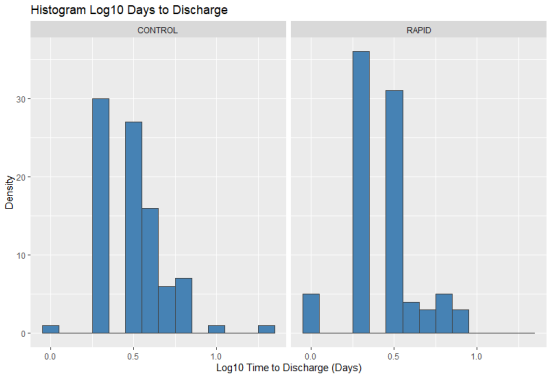
Log10 Histograms:




Histogram Log10 Time to First Stairs
CONTROL
RAPID
Density
Log10 Time to First stairs (Hours)


Histogram Log10 Time to Physiotherapy Complete
CONTROL
RAPID
Density
Log10 Time to Physiotherapy Complete (Hours)


Histogram Log10 Time to Discharge
CONTROL
RAPID
Density
Log10 Time to Discharge (Hours)


Histogram Log10 Days to Discharge
CONTROL
RAPID
Density
Log10 Time to Discharge (Days)

Appendix 32 Identification of Outliers

Mahalanobis Distance

Mahalanobis distances were calculated for all numerical variables with complete data to identify multivariate outliers. Identified outliers are shown in the table below highlighted in yellow

Study No	Mahalanobis Distance	P Value
1	9.795219	0.20048
2	1.818942	0.96918
3	1.931605	0.96353
4	1.90886	0.96471
5	2.871226	0.89665
6	33.847015	**0.00002**
7	3.265592	0.85939
8	1.918572	0.96421
9	7.304268	0.3979
10	1.700456	0.97455
11	7.550469	0.37389
12	3.65818	0.8182
13	5.544288	0.59385
14	8.714287	0.27383
15	1.858271	0.96727
16	6.052766	0.5336
17	4.74301	0.69129
18	7.193633	0.409
19	1.891416	0.9656
20	1.798291	0.97016
21	3.31638	0.85427
22	23.296161	0.00151
23	4.519548	0.71836
24	21.051404	0.00369
25	3.770616	0.80579
26	3.295017	0.85644
27	6.952479	0.43384
28	2.664377	0.91422
29	3.657451	0.81828
30	30.254303	**0.00009**
31	13.365832	0.06368
32	4.482733	0.7228
33	10.831959	0.14612
34	2.629024	0.91707
35	2.842138	0.89921
36	1.877576	0.9663
37	157.65525	**0**
38	3.652309	0.81884
39	3.471515	0.83823
40	3.157257	0.87008
41	4.645488	0.70313
42	4.438294	0.72813
43	1.485217	0.98282
44	7.497196	0.37901
45	6.002499	0.53946
46	3.664999	0.81745
47	2.987168	0.88619
48	5.03758	0.65538
49	3.536401	0.83136
50	3.387307	0.84701
51	1.466197	0.98346
52	5.438218	0.60665
53	7.351365	0.39323
54	8.052445	0.32799
55	9.790887	0.20074
56	9.244036	0.23561
57	15.187583	0.03367
58	2.45514	0.93044
59	9.58114	0.21358
60	1.997481	0.95998
61	2.313779	0.94046
62	1.913009	0.9645
63	1.930879	0.96357
64	2.924696	0.89188
65	1.524182	0.98146
66	4.804802	0.68377
67	8.559757	0.28583
68	3.487072	0.83659
69	1.831275	0.96859
70	1.459118	0.98369
71	5.854941	0.55679
72	15.372287	0.03151
73	2.369942	0.93657
74	5.012402	0.65845
75	20.997829	0.00377
76	22.655405	0.00196
77	3.967165	0.78355
78	2.209656	0.94733
79	13.072945	0.07035
80	3.837794	0.79826
81	5.726192	0.57206
82	1.090846	0.99323
83	1.312758	0.98809
84	4.858092	0.67728
85	6.494156	0.48337
86	4.599318	0.70873
87	3.511737	0.83398
88	10.615367	0.1563
89	3.468309	0.83857
90	20.876775	0.00396
91	1.706056	0.97431
92	2.568827	0.92183
93	7.122932	0.41619
94	1.781022	0.97096
95	14.577355	0.04182
96	51.516089	**0**
97	4.681842	0.69872
98	1.426064	0.98476
99	2.656414	0.91487
100	3.417069	0.84393
101	2.959694	0.88871
102	1.823687	0.96895
103	3.056078	0.87977
104	2.480059	0.92859
105	4.305604	0.74398
106	3.299178	0.85602
107	8.07245	0.32625
108	23.535232	0.00137
109	8.463485	0.2935
110	11.802499	0.10724
111	18.068953	0.01166
112	16.843009	0.01844
113	7.332263	0.39512
114	1.755727	0.97212
115	3.324098	0.85349
116	2.207158	0.94749
117	1.981716	0.96085

This method identified four participants as multivariate outliers. Each of these underwent an individual review of the medical records to investigate reasons for this.

Appendix 33 Statistical Analysis R Code

This appendix contains the raw R-Code used for statistical analysis of all variables explored within the main study except for mILOA data which is shown in Appendix 32. This is provided for transparency and reproducibility.

All raw study dataset for this RCT has been uploaded through the University of Southampton at DOI: https://doi.org/10.5258/SOTON/D2377.

```
######################
#                    #
#  Quant Main Code   #
#                    #
######################

#Dataset Info

# Treatment groups:
#--------------------
#      RAPID   (Participants commenced walking on the day of surgery)
#      CONTROL (Participants received standard care)

# CCI: Charlston-Comorbidities Index
#--------------------
# Validated score based on the number and severity of medical co-morbidities
# 0 : no co-morbidities
# Score increases the number and severity of medical co-morbidities increases

# RAPT: score based on the patient's pre-morbid function and social support
#--------------------
# It is designed to be predictive of how long people may stay in hospital for
# 12 predicted as needing the shortest time to recover
# 1 predicted as taking the longest

# ASA       American society of Anaesthesiologists Score
#--------------------
# Measure estimate of how risky a patient is to anaesthetise.
# 1 : minimal risk
# score increases the risk increases.

# No_Th_List
#--------------------
# The order in the day patients were operated on
```

```
# Typically: 6 surgeries completed per day

#LOS
#--------------------
#Length of stay in hospital in days

#~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~#

# Installed R packages

library(psych)
library(tidyverse)
library(stats)
library(car)
library(qqplotr)
library(plyr)

#Review data structure
str(Q_Main)

#Set as Factor
Q_Main$Study_No<-as.factor(Q_Main$Study_No)
Q_Main$Group <- as.factor(Q_Main$Group)
Q_Main$Gender <- as.factor(Q_Main$Gender)

#Identification of Outliers

Q_Main$Mahal <- mahalanobis(Q_Main[,c(2,6,7,8,9,10,24)],
colMeans(Q_Main[,c(2,6,7,8,9,10,24)]), cov(Q_Main[,c(2,6,7,8,9,10,24)]))
Q_Main$MDp <- pchisq(Q_Main$Mahal, df=7, lower.tail=FALSE)
Q_Main$MDp <- round(Q_Main$MDp, 5)

#Baseline measures analysis
#---------------
##AGE##

#Age Descriptives
describeBy(Q_Main$Age,group = Q_Main$Group)
#Age boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=Age,fill=Group))+
  geom_boxplot(outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Age vs Group")+
  xlab('Group')+
  ylab('Age')
```

```
#Histogram
ggplot(data=Q_Main,aes(x=Age))+
  geom_histogram(binwidth = 3, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Age")+
  facet_grid(. ~ Group)+
  xlab('Age')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = Age)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Age")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$Age[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$Age[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$Age~Q_Main$Group)
#---------------
##CCI##

#CCI Descriptives
describeBy(Q_Main$CCI,group = Q_Main$Group)
#CCI boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=CCI,fill=Group))+
  geom_boxplot(outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("CCI vs Group")+
  xlab('Group')+
  ylab('CCI')
#Histogram
ggplot(data=Q_Main,aes(x=CCI))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram CCI")+
  facet_grid(. ~ Group)+
  xlab('CCI Score')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = CCI)) +
```

```
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot CCI")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$CCI[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$CCI[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$CCI~Q_Main$Group)
#---------------
##RAPT##

#RAPT
describeBy(Q_Main$RAPT,group = Q_Main$Group)
#RAPT boxplot
par(mfrow=c(1,3))
ggplot(data=Q_Main,aes(x=factor(Group),y=RAPT,fill=Group))+
  geom_boxplot(outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("RAPT vs Group")+
  xlab('Group')+
  ylab('RAPT')
#Histogram
ggplot(data=Q_Main,aes(x=RAPT))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram RAPT")+
  facet_grid(. ~ Group)+
  xlab('RAPT score')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = RAPT)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot RAPT")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$RAPT[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$RAPT[Q_Main$Group=="RAPID"])
```

```
#Mann-Whitney Test
wilcox.test(Q_Main$RAPT~Q_Main$Group)
#---------------
##Number on Theatre List##

#Number on Theatre List
describeBy(Q_Main$Number.on.Theatre.List ,group = Q_Main$Group)
#Number on Theatre List Boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=Number.on.Theatre.List,fill=Group))+
  geom_boxplot(outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Number on Theatre List vs Group")+
  xlab('Group')+
  ylab('Number on Theatre List')
#Histogram
ggplot(data=Q_Main,aes(x=Number.on.Theatre.List))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Number on Theatre List Histogram")+
  facet_grid(. ~ Group)+
  xlab('Density')+
  ylab('Number on Theatre List')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = Number.on.Theatre.List)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Number on Theatre List")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$Number.on.Theatre.List[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$Number.on.Theatre.List[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$Number.on.Theatre.List~Q_Main$Group)
#---------------
##ASA##

#ASA
describeBy(Q_Main$ASA,group = Q_Main$Group)
#ASA boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=ASA,fill=Group))+
  geom_boxplot(outlier.colour=NA)+
```

```
  scale_fill_brewer(palette='Set1')+
  ggtitle("ASA vs Group")+
  xlab('Group')+
  ylab('ASA')
#Histogram
ggplot(data=Q_Main,aes(x=ASA))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("ASA Histogram")+
  facet_grid(. ~ Group)+
  xlab('ASA Score')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = ASA)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot ASA Score")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$ASA[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$ASA[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$ASA~Q_Main$Group)
#---------------

#  OUTCOMES  #

#---------------

#****** LOS ******#
describeBy(Q_Main$Days_Discharge,group = Q_Main$Group)
IQR(Q_Main$Days_Discharge[Q_Main$Group=="CONTROL"])
IQR(Q_Main$Days_Discharge[Q_Main$Group=="RAPID"])
#LOS boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=Days_Discharge,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("LOS (Days) vs Group")+
  xlab('Group')+
  ylab('LOS (Days)')
#Histogram
ggplot(data=Q_Main,aes(x=Days_Discharge))+
```

```
   geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
   scale_fill_brewer(palette='Set1')+
   ggtitle("LOS (Days) vs Group")+
   facet_grid(. ~ Group)+
      xlab('LOS (Days)')+
      ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = Days_Discharge)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Length of Stay")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$Days_Discharge[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$Days_Discharge[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$Days_Discharge~Q_Main$Group)

#******#

#---------------
# Time to PT Complete #
describeBy(Q_Main$TT_PT_Complete,group = Q_Main$Group)
IQR(Q_Main$TT_PT_Complete[Q_Main$Group=="CONTROL"])
IQR(Q_Main$TT_PT_Complete[Q_Main$Group=="RAPID"])
#TT PT complete boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=TT_PT_Complete,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Time to PT Complete vs Group")+
  xlab('Group')+
  ylab('Time to PT Complete (Hours)')
#Histogram
ggplot(data=Q_Main,aes(x=TT_PT_Complete))+
  geom_histogram(binwidth = 10, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Time to PT Complete")+
  facet_grid(. ~ Group)+
  xlab('Time to PT Complete (Hours)')+
  ylab('Density')
#QQPlot
```

```
ggplot(data = Q_Main, mapping = aes(sample = TT_PT_Complete)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Time to Physiotherapy Complete")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$TT_PT_Complete[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$TT_PT_Complete[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$TT_PT_Complete~Q_Main$Group)

#---------------
# Time to Discharge - Hours #
describeBy(Q_Main$TT_Discharge,group = Q_Main$Group)
IQR(Q_Main$TT_Discharge[Q_Main$Group=="CONTROL"])
IQR(Q_Main$TT_Discharge[Q_Main$Group=="RAPID"])
#TT Discharge boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=TT_Discharge,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Time to Discharge (Hours) vs Group")+
  xlab('Group')+
  ylab('Time to Discharge (Hours)')
#Histogram
ggplot(data=Q_Main,aes(x=TT_Discharge))+
  geom_histogram(binwidth = 10, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Time to Discharge (Hours)")+
  facet_grid(. ~ Group)+
  xlab('Time to Discharge (Hours)')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = TT_Discharge)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Time to Discharge (Hours)")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$TT_Discharge[Q_Main$Group=="CONTROL"])
```

```
shapiro.test(Q_Main$TT_Discharge[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$TT_Discharge~Q_Main$Group)

#~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~#
#                FUNCTIONAL MILESTONES                    #
#~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~#

#---------------
# Time to First ROM#
describeBy(Q_Main$TTFirst_ROM,group = Q_Main$Group)
IQR(Q_Main$TTFirst_ROM[Q_Main$Group=="CONTROL"])
IQR(Q_Main$TTFirst_ROM[Q_Main$Group=="RAPID"])
#Time to First ROM boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=TTFirst_ROM,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Time to First ROM vs Group")+
  xlab('Group')+
  ylab('Time to First ROM (Hours)')
#Histogram
ggplot(data=Q_Main,aes(x=TTFirst_ROM))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Time to First ROM")+
  facet_grid(. ~ Group)+
  xlab('Time to First ROM (Hours)')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = TTFirst_ROM)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Time to First ROM")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$TTFirst_ROM[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$TTFirst_ROM[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$TTFirst_ROM~Q_Main$Group)

#---------------
```

```
# Time to First SOEOB#
describeBy(Q_Main$TTFirst_SOEOB,group = Q_Main$Group)
IQR(Q_Main$TTFirst_SOEOB[Q_Main$Group=="CONTROL"])
IQR(Q_Main$TTFirst_SOEOB[Q_Main$Group=="RAPID"])
#Time to First ROM boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=TTFirst_SOEOB,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Time to First SOEOB vs Group")+
  xlab('Group')+
  ylab('Time to First SOEOB (Hours)')
#Histogram
ggplot(data=Q_Main,aes(x=TTFirst_SOEOB))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Time to First SOEOB")+
  facet_grid(. ~ Group)+
  xlab('Time to First SOEOB (Hours)')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = TTFirst_SOEOB)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Time to First SOEOB")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$TTFirst_SOEOB[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$TTFirst_SOEOB[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$TTFirst_SOEOB~Q_Main$Group)

#---------------
# Time to First Transfer#
describeBy(Q_Main$TTFirst_TF,group = Q_Main$Group)
IQR(Q_Main$TTFirst_TF[Q_Main$Group=="CONTROL"])
IQR(Q_Main$TTFirst_TF[Q_Main$Group=="RAPID"])
#Time to First ROM boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=TTFirst_TF,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Time to First Transfer vs Group")+
  xlab('Group')+
```

```
  ylab('Time to First Transfer (Hours)')
#Histogram
ggplot(data=Q_Main,aes(x=TTFirst_TF))+
  geom_histogram(binwidth = 10, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Time to First Transfer")+
  facet_grid(. ~ Group)+
  xlab('Time to First Transfer (Hours)')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = TTFirst_TF)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Time to First Transfer")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$TTFirst_TF[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$TTFirst_TF[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$TTFirst_TF~Q_Main$Group)

#---------------
# Time to First Walk 5m#
describeBy(Q_Main$TTFirstWalk5m,group = Q_Main$Group)
IQR(Q_Main$TTFirstWalk5m[Q_Main$Group=="CONTROL"])
IQR(Q_Main$TTFirstWalk5m[Q_Main$Group=="RAPID"])
#Time to First ROM boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=TTFirstWalk5m,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Time to First Walk 5m vs Group")+
  xlab('Group')+
  ylab('Time to First Walk 5m (Hours)')
#Histogram
ggplot(data=Q_Main,aes(x=TTFirstWalk5m))+
  geom_histogram(binwidth = 10, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Time to First Walk 5m")+
  facet_grid(. ~ Group)+
  xlab('Time to First Walk 5m (Hours)')+
  ylab('Density')
```

```
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = TTFirstWalk5m)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Time to First Walk 5m")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$TTFirstWalk5m[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$TTFirstWalk5m[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$TTFirstWalk5m~Q_Main$Group)

#---------------
# Time to First Walk 10m#
describeBy(Q_Main$TTFirstWalk10m,group = Q_Main$Group)
IQR(Q_Main$TTFirstWalk10m[Q_Main$Group=="CONTROL"])
IQR(Q_Main$TTFirstWalk10m[Q_Main$Group=="RAPID"])
#Time to First ROM boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=TTFirstWalk10m,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Time to First Walk 10m vs Group")+
  xlab('Group')+
  ylab('Time to First Walk 10m (Hours)')
#Histogram
ggplot(data=Q_Main,aes(x=TTFirstWalk10m))+
  geom_histogram(binwidth = 10, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Time to First Walk 10m")+
  facet_grid(. ~ Group)+
  xlab('Time to First Walk 10m (Hours)')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = TTFirstWalk10m)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Time to First Walk 10m")+
  theme(legend.position = "none")
#Test for normality
```

```
shapiro.test(Q_Main$TTFirstWalk10m[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$TTFirstWalk10m[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$TTFirstWalk10m~Q_Main$Group)

#---------------
# Time to First Walk 40m#
describeBy(Q_Main$TTFirstWalk40m,group = Q_Main$Group)
IQR(Q_Main$TTFirstWalk40m[Q_Main$Group=="CONTROL"], na.rm = TRUE)
IQR(Q_Main$TTFirstWalk40m[Q_Main$Group=="RAPID"],na.rm = TRUE)
#Time to First ROM boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=TTFirstWalk40m,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Time to First Walk 40m vs Group")+
  xlab('Group')+
  ylab('Time to First Walk 40m (Hours)')
#Histogram
ggplot(data=Q_Main,aes(x=TTFirstWalk40m))+
  geom_histogram(binwidth = 10, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Time to First Walk 40m")+
  facet_grid(. ~ Group)+
  xlab('Time to First Walk 40m (Hours)')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = TTFirstWalk40m)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Time to First Walk 40m")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$TTFirstWalk40m[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$TTFirstWalk40m[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$TTFirstWalk40m~Q_Main$Group)

#---------------
# Time to First Manage Stairs#
describeBy(Q_Main$TTFirst_Stairs,group = Q_Main$Group)
#Time to First ROM boxplot
```

```
ggplot(data=Q_Main,aes(x=factor(Group),y=TTFirst_Stairs,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Time to First Stairs")+
  xlab('Group')+
  ylab('Time to First Stairs (Hours)')
#Histogram
ggplot(data=Q_Main,aes(x=TTFirst_Stairs))+
  geom_histogram(binwidth = 10, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Time to First Stairs")+
  facet_grid(. ~ Group)+
  xlab('Time to First stairs (Hours)')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = TTFirst_Stairs)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Time to First Stairs")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$TTFirst_Stairs[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$TTFirst_Stairs[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$TTFirst_Stairs~Q_Main$Group)

#~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~#
#                       PAIN SCORES                       #
#~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~#

#---------------
# Day 0 Pain --- REST#
describeBy(Q_Main$Day0_Pain_Rest,group = Q_Main$Group)
IQR(Q_Main$Day0_Pain_Rest[Q_Main$Group=="CONTROL"])
IQR(Q_Main$Day0_Pain_Rest[Q_Main$Group=="RAPID"])
#Boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=Day0_Pain_Rest,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Day 0 Pain at Rest")+
  xlab('Group')+
  ylab('Pain Numerical Rating Score')
```

```
#Histogram
ggplot(data=Q_Main,aes(x=Day0_Pain_Rest))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Day 0 Pain at Rest")+
  facet_grid(. ~ Group)+
  xlab('Pain Numerical Rating Score')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = Day0_Pain_Rest)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Day 0 Pain at Rest")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$Day0_Pain_Rest[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$Day0_Pain_Rest[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$Day0_Pain_Rest~Q_Main$Group)

#---------------
# Day 0 Pain ROM#
describeBy(Q_Main$Day0_Pain_ROM,group = Q_Main$Group)
IQR(Q_Main$Day0_Pain_ROM[Q_Main$Group=="CONTROL"])
IQR(Q_Main$Day0_Pain_ROM[Q_Main$Group=="RAPID"])
#Boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=Day0_Pain_ROM,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Day 0 Pain on ROM")+
  xlab('Group')+
  ylab('Pain Numerical Rating Score')
#Histogram
ggplot(data=Q_Main,aes(x=Day0_Pain_ROM))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Day 0 Pain ROM")+
  facet_grid(. ~ Group)+
  xlab('Pain Numerical Rating Score')+
  ylab('Density')
#QQPlot
```

```
ggplot(data = Q_Main, mapping = aes(sample = Day0_Pain_ROM)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Day 0 Pain on ROM")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$Day0_Pain_ROM[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$Day0_Pain_ROM[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$Day0_Pain_ROM~Q_Main$Group)

#---------------
# Day 1 Pain REST#
describeBy(Q_Main$Day1_Pain_Rest,group = Q_Main$Group)
IQR(Q_Main$Day1_Pain_Rest[Q_Main$Group=="CONTROL"])
IQR(Q_Main$Day1_Pain_Rest[Q_Main$Group=="RAPID"])
#Boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=Day1_Pain_Rest,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Day 1 Pain at Rest")+
  xlab('Group')+
  ylab('Pain Numerical Rating Score')
#Histogram
ggplot(data=Q_Main,aes(x=Day1_Pain_Rest))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Day 1 Pain at Rest")+
  facet_grid(. ~ Group)+
  xlab('Pain Numerical Rating Score')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = Day1_Pain_Rest)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Day 1 Pain at Rest")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$Day1_Pain_Rest[Q_Main$Group=="CONTROL"])
```

```
shapiro.test(Q_Main$Day1_Pain_Rest[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$Day1_Pain_Rest~Q_Main$Group)

#---------------
# Day 1 Pain ROM#
describeBy(Q_Main$Day1_Pain_ROM,group = Q_Main$Group)
IQR(Q_Main$Day1_Pain_ROM[Q_Main$Group=="CONTROL"])
IQR(Q_Main$Day1_Pain_ROM[Q_Main$Group=="RAPID"], na.rm = TRUE)
#Boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=Day1_Pain_ROM,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Day 1 Pain on ROM")+
  xlab('Group')+
  ylab('Pain Numerical Rating Score')
#Histogram
ggplot(data=Q_Main,aes(x=Day1_Pain_ROM))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Day 1 Pain ROM")+
  facet_grid(. ~ Group)+
  xlab('Pain Numerical Rating Score')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = Day1_Pain_ROM)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Day 1 Pain on ROM")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$Day1_Pain_ROM[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$Day1_Pain_ROM[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$Day1_Pain_ROM~Q_Main$Group)

#---------------
# Day 1 Pain Walk#
describeBy(Q_Main$Day1_Pain_Walk,group = Q_Main$Group)
IQR(Q_Main$Day1_Pain_Walk[Q_Main$Group=="CONTROL"], na.rm = TRUE)
IQR(Q_Main$Day1_Pain_Walk[Q_Main$Group=="RAPID"], na.rm = TRUE)
```

```
#Boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=Day1_Pain_Walk,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Day 1 Pain on Walking")+
  xlab('Group')+
  ylab('Pain Numerical Rating Score')
#Histogram
ggplot(data=Q_Main,aes(x=Day1_Pain_Walk))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Day 1 Pain Walk")+
  facet_grid(. ~ Group)+
  xlab('Pain Numerical Rating Score')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = Day1_Pain_Walk)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Day 0 Pain on Walking")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$Day1_Pain_Walk[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$Day1_Pain_Walk[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$Day1_Pain_Walk~Q_Main$Group)

#Pain on First Walk#
#---------------
describeBy(Q_Main$FirstWalkPain,group = Q_Main$Group)
IQR(Q_Main$FirstWalkPain[Q_Main$Group=="CONTROL"], na.rm = TRUE)
IQR(Q_Main$FirstWalkPain[Q_Main$Group=="RAPID"], na.rm = TRUE)
#Boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=FirstWalkPain,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Pain on First Walking")+
  xlab('Group')+
  ylab('Pain Numerical Rating Score')
#Histogram
ggplot(data=Q_Main,aes(x=FirstWalkPain))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
```

```
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Pain on First Walking")+
  facet_grid(. ~ Group)+
  xlab('Pain Numerical Rating Score')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = FirstWalkPain)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Pain on First Walking")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$FirstWalkPain[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$FirstWalkPain[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$FirstWalkPain~Q_Main$Group)

#~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~#
#               PHARMACOLOGICAL MEASURES                  #
#~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~#

# Total Opioid Consumption#
describeBy(Q_Main$TOTAL_OPIOID,group = Q_Main$Group)
IQR(Q_Main$TOTAL_OPIOID[Q_Main$Group=="CONTROL"], na.rm = TRUE)
IQR(Q_Main$TOTAL_OPIOID[Q_Main$Group=="RAPID"], na.rm = TRUE)
#Boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=TOTAL_OPIOID,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Total Opioid Consumption")+
  xlab('Group')+
  ylab('Total Opioid Consumption (mg)')
#Histogram
ggplot(data=Q_Main,aes(x=TOTAL_OPIOID))+
  geom_histogram(binwidth = 20, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Total Opioid Consumption")+
  facet_grid(. ~ Group)+
  xlab('Total Opioid Consumption (mg)')+
  ylab('Density')
#QQPlot
```

```
ggplot(data = Q_Main, mapping = aes(sample = TOTAL_OPIOID)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Total Opioid Consumption")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$TOTAL_OPIOID[Q_Main$Group=="CONTROL"])
shapiro.test(Q_Main$TOTAL_OPIOID[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$TOTAL_OPIOID~Q_Main$Group)

#-----------------
# Anti-emetic Consumption#
describeBy(Q_Main$Antiemetic...Total.Doses,group = Q_Main$Group)
IQR(Q_Main$Antiemetic...Total.Doses[Q_Main$Group=="CONTROL"])
IQR(Q_Main$Antiemetic...Total.Doses[Q_Main$Group=="RAPID"])
#Boxplot
ggplot(data=Q_Main,aes(x=factor(Group),y=Antiemetic...Total.Doses,fill=Group))+
  geom_boxplot(outlier.shape=5)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Antiemetic Consumption")+
  xlab('Group')+
  ylab('Antiemetic Consumption (Number of Doses)')
#Histogram
ggplot(data=Q_Main,aes(x=Antiemetic...Total.Doses))+
  geom_histogram(binwidth = 1, color = "grey26", fill = "steelblue")+
  scale_fill_brewer(palette='Set1')+
  ggtitle("Histogram Antiemetic Consumption")+
  facet_grid(. ~ Group)+
  xlab('Total Antiemetic Consumption (Number of Doses)')+
  ylab('Density')
#QQPlot
ggplot(data = Q_Main, mapping = aes(sample = Antiemetic...Total.Doses)) +
  geom_qq_band(bandType = "pointwise", mapping = aes(fill = "Confidence Band"),
alpha = 0.5) +
  stat_qq_line() +
  stat_qq_point() +
  labs(x = "Theoretical Quantiles", y = "Sample Quantiles")+
  ggtitle("QQ Plot Antiemetic Consumption")+
  theme(legend.position = "none")
#Test for normality
shapiro.test(Q_Main$Antiemetic...Total.Doses[Q_Main$Group=="CONTROL"])
```

```
shapiro.test(Q_Main$Antiemetic...Total.Doses[Q_Main$Group=="RAPID"])
#Mann-Whitney Test
wilcox.test(Q_Main$Antiemetic...Total.Doses~Q_Main$Group)

#~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~#
#                POST-OP COMPLICATIONS                    #
#~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~#

#Set as Factor
Post.opComp$StudyID<-as.factor(Post.opComp$StudyID)
Post.opComp$GROUP <- as.factor(Post.opComp$GROUP)
Post.opComp$PostDCComp <- as.factor(Post.opComp$PostDCComp)
Post.opComp$CDC <- as.numeric(Post.opComp$CDC)
Post.opComp$Post.Op.Complication <- as.factor(Post.opComp$Post.Op.Complication)

str(Post.opComp)

#Table of post-op complications
table(Post.opComp$Post.Op.Complication, Post.opComp$GROUP)

#Filter Data by CD Classification
CDC1 <- Post.opComp[Post.opComp$CDC=="1",]
CDC2 <- Post.opComp[Post.opComp$CDC=="2",]
CDC3 <- Post.opComp[Post.opComp$CDC=="3",]
CDC4 <- Post.opComp[Post.opComp$CDC=="4",]
CDC5 <- Post.opComp[Post.opComp$CDC=="5",]
CDC6 <- Post.opComp[Post.opComp$CDC=="6",]
HighCDC <- Post.opComp[Post.opComp$CDC>1,]
PostDC <- Post.opComp[Post.opComp$PostDCComp == TRUE,]
#Other complications for appendix
OtherComp <- Post.opComp[Post.opComp$Post.Op.Complication == "Other",]

#Tables by CD Classification
CD1T <- table(CDC1$Post.Op.Complication, CDC1$GROUP)
CD2T <- table(CDC2$Post.Op.Complication, CDC2$GROUP)
CD3T <- table(CDC3$Post.Op.Complication, CDC3$GROUP)
CD4T <- table(CDC4$Post.Op.Complication, CDC4$GROUP)
CD5T <- table(CDC5$Post.Op.Complication, CDC5$GROUP)
CD6T <- table(CDC6$Post.Op.Complication, CDC6$GROUP)


#Write Tables
write.csv(CD1T, "CDC1Table.csv")
write.csv(CD2T, "CDC2Table.csv")
```

```
write.csv(CD3T, "CDC3Table.csv")
write.csv(CD4T, "CDC4Table.csv")
write.csv(CD5T, "CDC5Table.csv")
write.csv(CD6T, "CDC6Table.csv")

#Table for post-DC Complications
table(PostDC$Post.Op.Complication, PostDC$GROUP)

#Chi-Sq test for incidence of post-op complications by group
chisq.test(Post.opComp$Post.Op.Complication, Post.opComp$GROUP, correct =
FALSE)

#Chi-Sq test for Complications with High CDC
chisq.test(HighCDC$Post.Op.Complication, HighCDC$GROUP, correct = FALSE)

#Chi-Sq test for common complications
chisq.test(CommonComp$Post.Op.Complication, CommonComp$GROUP, correct =
FALSE)

#Chi-Sq test for Complications post-DC
chisq.test(PostDC$Post.Op.Complication, PostDC$GROUP, correct = FALSE)
```

Appendix 34 mILOA Data – Determining Statistical Modelling Methodology

This appendix details the preliminary analysis of mILOA data and the process by which mixed effects logistic regression and mixed effects logistic regression were discounted and survival analysis identified as the selected statistical methodology.

Complexity of mILOA data

While originally planned to be analysed with traditional comparison testing such as T-test or Mann-Whitney testing. Once collected and reviewed the nature of the data was longitudinal repeated measures data, recorded at differing time-points and with differing numbers of measures per participant. Consequently, traditional statistical comparison was unsuitable for analysis.

In addition, the data characteristics violate many of the assumptions required for the use of ANOVA based analysis methods. Consequently, simple ANOVA, repeated measures ANOVA and MANOVA would have been inherently flawed if employed.

Garcia & Marder 2017 advocates the use of mixed effects regression as a method robust to handle irregularly timed, unbalanced and missing data. This includes employing 'random effects' which can describe cluster specific trends over time such as trends within individual participants.

Consequently, mixed effects regression was explored to be able to deal with these data complexities. Within this approach it was thought mILOA scores could be tested alongside other potential covariates for effectiveness and effect size.

Selection of Fixed and Random effects

Group allocation as the dependent variable was selected as the first fixed effect.

Previous publications informed the covariates considered for inclusion as fixed effects. Hoogeboom et al. 2015 found that increased age, female gender and BMI were predictive of delayed functional recovery, Holm et al. 2014 supported increasing age as a predictive factor. Elings et al. 2015 found increased ASA scores and co-morbidity status were important factors in predicting delayed discharge. Conversely Hewlett-Smith et al. 2020 found no strong evidence that any of these factors were strong predictors for inpatient recovery after THR.

With some debate within the literature on which factors could be covariates for functional recovery, the following were considered for inclusion as fixed effects:

- Age
- Gender
- ASA Score
- CCI Score
- RAPT Score

Individual participant number was selected as the sole random effect allowing intercepts to vary between participants, therefore accounting for repeated measures taken from each subject.

Mixed effects modelling

Modelling appeared to show a clear difference between groups ($p<0.001$) when modelled without covariates as fixed effects. However, examination of residuals showed heavy tails within the QQ-plot suggesting many extreme values.

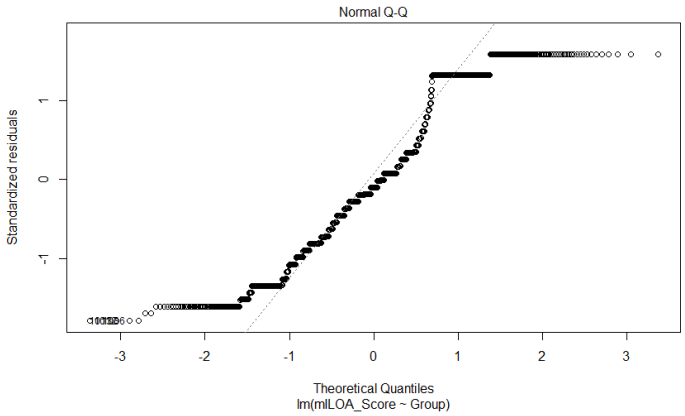


Figure 48: Initial modelling QQ plot

This was confirmed by observing a frequency table for mILOA scores, with a high frequency of scores of 36 and 3. This was due to 36 being the starting baseline for each participant after leaving theatre, and 3 being the most commonly achieved functional score allowing participants to meet criteria for hospital discharge.

Table 0-1 Frequency table of mILOA scores

	mILOA Score																																	
	1	2	**3**	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	**36**
n	5	3	**149**	27	10	9	6	4	68	46	40	25	30	21	40	65	48	43	81	32	41	75	14	25	27	15	5	5	3	14	7	3	4	0	1	**319**

These data characteristics were causing problems with model validity using mixed effects modelling. Consequently the decision was made to dichotomise mILOA scores to allow analysis using mixed effects logistic regression.

Dichotomisation

Data was dichotomised into a functionally dependent or independent status based on the mILOA score. The threshold of <7 was used as functionally independent based on this value being used by (Hoogeboom et al. 2015). To support this decision, only 2 participants (1%) were discharged with an mILOA score >6.

Table 0-2 Frequency mILOA scores on discharge

mILOA Score on Discharge	***N***
1	4
2	2
3	142
4	17
5	5
6	4
7	1
9	1

This was a radical decision in the handling of the mILOA data, but was taken as retaining the full richness of mILOA data was preventing any reliable statistical analysis of this data.

Mixed effects logistic regression

Mixed effects logistic regression was trialled; examining the dependent variable of interventional group and potential covariates against the odds of being functionally independent. Results below are presented as odds ratios for each covariate.

Logistic regression modelling appeared to show that increased time post-surgery was the strongest predictor of independence, with participants in the RAPID group 2.78 times (CI 1.39 to 5.57, p = 0.004) more likely to be independent at any point in time than participants in the CONTROL group. Gender was also a strong predictor with males 2.74 times (CI 1.30 to 5.76, p = 0.008) times more likely to be independent at any given time-point. Other covariates of Age and RAPT, CCI and ASA scores did not reach statistical significance as predictors.

Table 0-3: Predictors for functional independence

	Functionally Independent (mILOA Score <7)		
Predictors of Independence	*Odds Ratio (OR)*	*95% Confidence Interval*	*p-value*
Intercept	0.05	0.01 – 0.20	**<0.001**
Group (Reference: RAPID)	2.78	1.39 – 5.57	**0.004**
Time Post-Op (in hours)	4.41	2.47 – 7.89	**<0.001**
CCI	0.64	0.39 – 1.07	0.092
RAPT	1.04	0.90 – 1.21	0.567
Gender (Reference: Males)	2.74	1.30 – 5.76	**0.008**
Age (Mean-Centered)	1.34	0.94 – 1.92	0.102
Interaction: Group (RAPID)*Gender (Males)	0.47	0.18 – 1.23	0.122
Interaction: Group (RAPID)*Age	0.66	0.39 – 1.12	0.125
Random Effects			
σ^2	3.29		
$\tau_{00\ Study\_Number}$	1.08		
ICC	0.25		
$N_{\ Study\_Number}$	176		
Observations	1310		
Marginal R^2 / Conditional R^2	0.329 / 0.495		

Model checking was carried out using the 'DHARMa' package(Hartig 2018) within R. Residual plots for the overall model shown in Figure 51 showed problems.

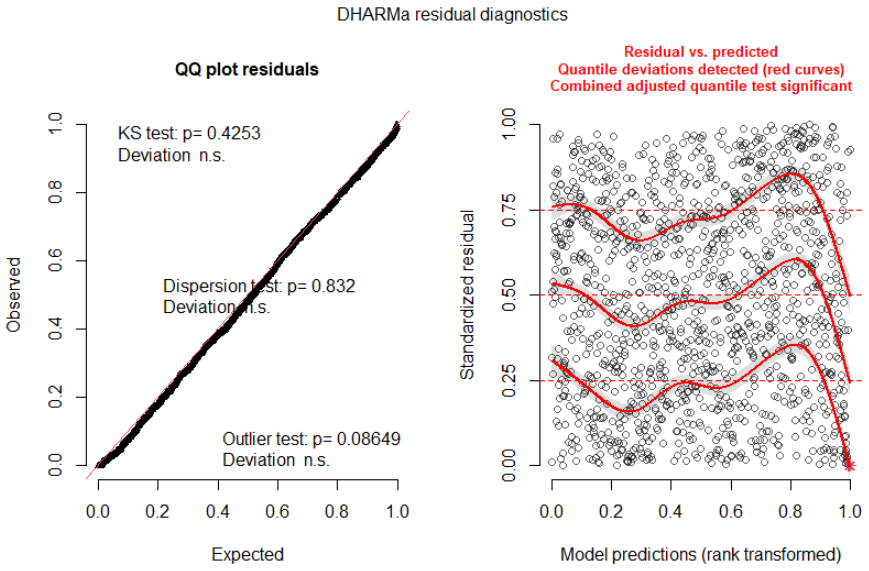


Figure 49 Mixed effects logistic regression residual plots

Residuals were then broken down into each covariate to identify any specific problem covariates as shown in Figure 50. This identified the variable of time as the problematic covariate within the model.

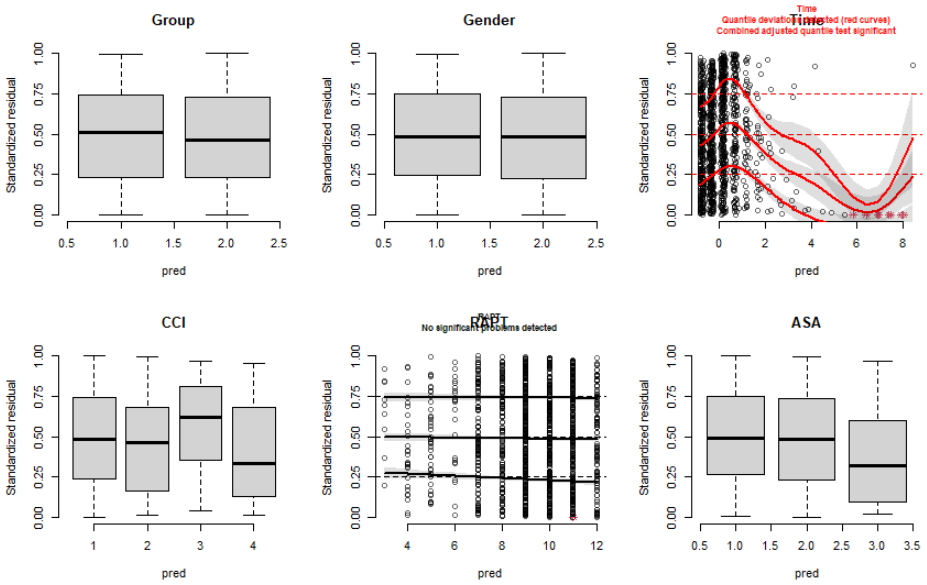


Figure 50 Mixed effects logistic regression broken down by covariate

With time to becoming functionally independent a variable of significant interest, omission of this covariate from modelling was not an option

Survival analysis

After ascertaining that mixed effects logistic regression would also not be suitable for the analysis of mILOA data, it was finally decided to opt for survival analysis. Details and reasoning for this are explained in the main text in section 6.3.10.6.2.

Appendix 35 mILOA Statistical Analysis R Code

This appendix contains the raw R-Code used for statistical analysis of mILOA data including descriptive analysis, attempts at simple logistic regression, mixed effects logistic regression and the survival analysis which eventually formed the study findings. This is provided for transparency and reproducibility.

```
# Dataset Info

# Treatment groups:
#--------------------
#      RAPID   (Participants commenced walking on the day of surgery)
#      CONTROL (Participants received standard care)

# mILOA_Score Validated measure of independence – modified Iowa level of assistance score.
#--------------------
# 36 : fully dependent (starting score at the time of operation)
#  0 : fully independent.

# Measures were taken ~twice per day [inpatient period]
# – number of measures per patient varied depending on length of stay.

# CCI: Charlston-Comorbidities Index
#--------------------
# Validated score based on the number and severity of medical co-morbidities
# 0 : no co-morbidities
# Score increases the number and severity of medical co-morbidities increases

# RAPT: score based on the patient's pre-morbid function and social support
#--------------------
# It is designed to be predictive of how long people may stay in hospital for
# 12 predicted as needing the shortest time to recover
# 1 predicted as taking the longest

# ASA       American society of Anaesthesiologists Score
#--------------------
# Measure estimate of how risky a patient is to anaesthetise.
# 1 : minimal risk
# score increases the risk increases.

# No_Th_List
#--------------------
# The order in the day patients were operated on
# Typically: 6 surgeries completed per day
```

```
# Installed R packages
library(dplyr)
library(tidyverse)
library(qqplotr)
library(MASS)
library(openxlsx)
library(lattice)
library(lme4)
library(DHARMa)
library(sjPlot)
library(table1)
library(survival)
library(survminer)
library(greg)

#Observe mILOA structure
str(mILOA)

#Set mILOA_Indep as Factor
mILOA[mILOA$mILOA_Indep == 0,]$mILOA_Indep <- "Dependent"
mILOA[mILOA$mILOA_Indep == 1,]$mILOA_Indep <- "Independent"
mILOA$mILOA_Indep <- as.factor(mILOA$mILOA_Indep)
mILOA$Study_Number<-as.factor(mILOA$Study_Number)
mILOA$Group <- as.factor(mILOA$Group)

#Descriptives information and plots

#XY plot of mILOA change by subject number and other factors
#Whole cohort plot with line
qplot(TT_mILOA_Hours, mILOA_Score, data = mILOA)+
  geom_smooth(method = "lm", se=FALSE, color="red", formula = y ~ x) +
  geom_point() +ylim(0,40)+
  ggtitle("Plot mILOA Score vs Time")+
  xlab('Time (Hours)')+
  ylab('mILOA Score')
#Trellis plot by subject number
xyplot(mILOA_Score~TT_mILOA_Hours|Study_Number, data = mILOA, layout =
c(6,6,5), type =c("p","r"), pch = 20)
#Plot by gender with line
ggplot(data=mILOA,aes(x=TT_mILOA_Hours,y=mILOA_Score,group=Study_Numbe
r,colour=Group))+
  geom_line(size=0.7)+
  geom_point(size=1,shape=20)+
  scale_fill_brewer(palette='Set1')+
```

```
  facet_grid(. ~ Gender)+
  ggtitle("Plot by Gender")+
  xlab('Time (Hours)')+
  ylab('mILOA Score')
qplot(TT_mILOA_Hours, mILOA_Score, data = mILOA, facets = .~mILOA$Gender)+
  geom_smooth(method = "lm", se=FALSE, color="red", formula = y ~ x) +
  geom_point() +ylim(0,40)+
  ggtitle("Plot by Gender")+
  xlab('Time (Hours)')+
  ylab('mILOA Score')
#Plot by ASA with line
qplot(TT_mILOA_Hours, mILOA_Score, data = mILOA, facets = .~mILOA$ASA)+
  geom_smooth(method = "lm", se=FALSE, color="red", formula = y ~ x) +
  geom_point() +ylim(0,40)+
  ggtitle("Plot by ASA")+
  xlab('Time (Hours)')+
  ylab('mILOA Score')
#Plot by RAPT with line
qplot(TT_mILOA_Hours, mILOA_Score, data = mILOA, facets = .~mILOA$RAPT)+
  geom_smooth(method = "lm", se=FALSE, color="red", formula = y ~ x) +
  geom_point() +ylim(0,40)+
  ggtitle("Plot by RAPT")+
  xlab('Time (Hours)')+
  ylab('mILOA Score')
xyplot(mILOA_Score~TT_mILOA_Hours|RAPT, data = mILOA, col="steelblue4",
xlab = "Time in Hours", ylab = "mILOA Score", main = "mILOA by RAPT", type
=c("p","r"), pch = 20)
#Plot by CCI with line
qplot(TT_mILOA_Hours, mILOA_Score, data = mILOA, facets = .~mILOA$CCI)+
  geom_smooth(method = "lm", se=FALSE, color="red", formula = y ~ x) +
  geom_point() +ylim(0,40)+
  ggtitle("Plot by CCI")+
  xlab('Time (Hours)')+
  ylab('mILOA Score')
#Plot by treatment group with line
ggplot(data=mILOA,aes(x=TT_mILOA_Hours,y=mILOA_Score,group=Study_Numbe
r,colour=Group))+
  geom_point(size=1.5,shape=19)+
  scale_fill_brewer(palette='Set1')+
  facet_grid(. ~ Group)+
  ggtitle("Plot by Group")+
  xlab('Time (Hours)')+
  ylab('mILOA Score')
qplot(TT_mILOA_Hours, mILOA_Score, data = mILOA, facets = .~mILOA$Group)+
  geom_smooth(method = "lm", se=FALSE, color="red", formula = y ~ x) +
```

```
  geom_point() +ylim(0,40)+
  ggtitle("Plot by Group")+
  xlab('Time (Hours)')+
  ylab('mILOA Score')

#Boxplots by:
#Group
ggplot(data=mILOA,aes(x=Group,y=mILOA_Score,fill=Group))+
  geom_boxplot(outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("mILOA Score by Group")+
  theme(legend.position='none')+
  xlab('Group')+
  ylab('mILOA Score')
#CCI
ggplot(data=mILOA,aes(x=factor(CCI),y=mILOA_Score))+
  geom_boxplot(fill='steelblue1',outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("mILOA Score by CCI")+
  xlab('CCI')+
  ylab('mILOA Score')
#CCI by Group
ggplot(data=mILOA,aes(x=factor(CCI),y=mILOA_Score,fill=Group))+
  geom_boxplot(outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("mILOA Score by CCI Score")+
  xlab('CCI Score')+
  ylab('mILOA Score')

#ASA
ggplot(data=mILOA,aes(x=factor(ASA),y=mILOA_Score))+
  geom_boxplot(fill='steelblue1',outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("mILOA Score by ASA")+
  xlab('ASA Score')+
  ylab('mILOA Score')
#ASA by Group
ggplot(data=mILOA,aes(x=factor(ASA),y=mILOA_Score,fill=Group))+
  geom_boxplot(outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("mILOA Score by ASA Score")+
  xlab('ASA Score')+
  ylab('mILOA Score')

#Gender
ggplot(data=mILOA,aes(x=Gender,y=mILOA_Score,fill=Gender))+
  geom_boxplot(outlier.colour=NA)+
```

```
  scale_fill_brewer(palette='Set1')+
  ggtitle("mILOA Score by Gender")+
  theme(legend.position='none')+
  xlab('Gender')+
  ylab('mILOA Score')
#Gender by Group
ggplot(data=mILOA,aes(x=factor(Gender),y=mILOA_Score,fill=Group))+
  geom_boxplot(outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("mILOA Score by Gender")+
  xlab('Gender')+
  ylab('mILOA Score')
#RAPT
ggplot(data=mILOA,aes(x=factor(RAPT),y=mILOA_Score))+
  geom_boxplot(fill='steelblue1',outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("mILOA Score by RAPT")+
  xlab('RAPT Score')+
  ylab('mILOA Score')
#RAPT by Group
ggplot(data=mILOA,aes(x=factor(RAPT),y=mILOA_Score,fill=Group))+
  geom_boxplot(outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("mILOA Score by RAPT")+
  xlab('RAPT')+
  ylab('mILOA Score')
#Number on Theatre List
ggplot(data=mILOA,aes(x=factor(No_Th_List),y=mILOA_Score))+
  geom_boxplot(fill='steelblue1',outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("mILOA Score by Number on Theatre List")+
  xlab('Number on Theatre List')+
  ylab('mILOA Score')
#Number on Theatre List by Groups
ggplot(data=mILOA,aes(x=factor(No_Th_List),y=mILOA_Score, fill=Group))+
  geom_boxplot(outlier.colour=NA)+
  scale_fill_brewer(palette='Set1')+
  ggtitle("mILOA Score by Number on Theatre List")+
  xlab('Number on Theatre List')+
  ylab('mILOA Score')


#Data exploration for dichotomised data:
#Catergorical Variables
ggplot(data = mILOA, aes(x = Group, fill=mILOA_Indep)) +
```

```
  geom_bar(position = "fill") +
  labs(y = "Proportion",
       fill = "Independence",
       title = "Independence vs. Group")
ggplot(data = mILOA, aes(x = Gender, fill = mILOA_Indep)) +
  geom_bar(position = "fill") +
  labs(y = "Proportion",
       fill = "Independence",
       title = "Independence vs. Gender")
ggplot(data = mILOA, aes(x = ASA, fill = mILOA_Indep)) +
  geom_bar(position = "fill") +
  labs(y = "Proportion",
       fill = "Independence",
       title = "Independence vs. ASA")
ggplot(data = mILOA, aes(x = CCI, fill = mILOA_Indep)) +
  geom_bar(position = "fill") +
  labs(y = "Proportion",
       fill = "Independence",
       title = "Independence vs. CCI")
ggplot(data = mILOA, aes(x = RAPT, fill = mILOA_Indep)) +
  geom_bar(position = "fill") +
  labs(y = "Proportion",
       fill = "Independence",
       title = "Independence vs. RAPT")

# Plot Independence status over time by Group
ggplot(data=mILOA,aes(x=TT_mILOA_Hours,y=mILOA_Indep,group=Study_Numb
er,colour=Group))+
       geom_jitter(height = 0.2,shape=19)+
       scale_fill_brewer(palette='Set1')+
       facet_grid(. ~ Group)+
       ggtitle("Independence vs Time by Group")+
       xlab('Time (Hours)')+
       ylab('mILOA Independence Status')
#CCI
ggplot(data=mILOA,aes(x=TT_mILOA_Hours,y=mILOA_Indep,group=Study_Numb
er,colour=CCI))+
  geom_point(size=1.5,shape=19)+
  scale_fill_brewer(palette='Set1')+
  facet_grid(. ~ CCI)+
  ggtitle("Independence vs Time by CCI")+
  xlab('Time (Hours)')+
  ylab('mILOA Independence Status')
#ASA
ggplot(data=mILOA,aes(x=TT_mILOA_Hours,y=mILOA_Indep,group=Study_Numb
er,colour=ASA))+
  geom_point(size=1.5,shape=19)+
```

```
  scale_fill_brewer(palette='Set1')+
  facet_grid(. ~ ASA)+
  ggtitle("Independence vs Time by ASA")+
  xlab('Time (Hours)')+
  ylab('mILOA Independence Status')
#RAPT
ggplot(data=mILOA,aes(x=TT_mILOA_Hours,y=mILOA_Indep,group=Study_Numb
er,colour=RAPT))+
  geom_point(size=1.5,shape=19)+
  scale_fill_brewer(palette='Set1')+
  theme(axis.text.x=element_blank())+
  facet_grid(. ~ RAPT)+
  ggtitle("Independence vs Time by RAPT")+
  xlab('Time (Hours)')+
  ylab('mILOA Independence Status')
#Gender
ggplot(data=mILOA,aes(x=TT_mILOA_Hours,y=mILOA_Indep,group=Study_Numb
er,colour=Gender))+
  geom_jitter(height=0.2,shape=19)+
  scale_fill_brewer(palette='Set1')+
  facet_grid(. ~ Gender)+
  ggtitle("Independence vs Time by Gender")+
  xlab('Time (Hours)')+
  ylab('mILOA Independence Status')
#Age
ggplot(data=mILOA,aes(x=TT_mILOA_Hours,y=mILOA_Indep,group=Study_Numb
er,colour=Age))+
      geom_jitter(height=0.25,shape=19)+
      scale_fill_brewer(palette='Set1')+
      scale_colour_gradientn(colours=rainbow(4))+
      ggtitle("Independence vs Time by Age")+
      xlab('Time (Hours)')+
      ylab('mILOA Independence Status')

#Continuous Variables
ggplot(data = mILOA, aes(x = Group, y = Age, fill = mILOA_Indep)) +
  geom_boxplot(alpha=0.7) +
  scale_fill_brewer(palette="Dark2")

#Table categorical
table1(~Group+Gender+Age+RAPT+CCI+ASA|mILOA_Indep, data=mILOA)

# Plot the study number mean of mILOA_Score  Vs. the study number ID (subject)
# visualising the study number variation
# ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
```

```
mean.group <- aggregate(mILOA_Score ~ Study_Number, data = mILOA, mean)

# Add a line at the grand mean of mILOA_Score (mean across study number IDs)
par(mfrow=c(1,1))
qplot(mean.group[,1], mean.group[,2], ylab='Group Mean of mILOA Score',
xlab='Subject')+
  geom_hline(yintercept = mean(mILOA$mILOA_Score,na.rm = TRUE))

#Clear difference between intervention/control groups
model01<-lm(mILOA_Score ~ Group, data = mILOA)
summary(model01)
par(mfrow=c(2,2))
plot(model01)

#heavy tails on QQplot

# table to show extreme values - justification for dichotomisation of response
# Many extreme scores:  157 1-3s and 318 36s
table(mILOA$mILOA_Score)

#-----
#Decision to use logistic regression modeling with dichotomized mILOA score:
# Threshold score based on Hoogeboom et al 2015. Score of < 7 considered to be
functionally independent.
# Scores at discharge in this study reviewed for frequency
discharge.score <- aggregate(mILOA_Score ~ Study_Number, data = mILOA, min)
discharge.score$mILOA_Score<-as.factor(discharge.score$mILOA_Score)
count(discharge.score, mILOA_Score)
#Only 2 participants were discharged with a score >6 (1%) - Justification to accept
6 and below as the dichotomisation threshold.


#Scale time to mILOA
mILOA$TT_mILOA_Hours <- scale(mILOA$TT_mILOA_Hours, center = TRUE, scale
= TRUE)

#Scale Age
mILOA$Age <- scale(mILOA$Age, center = TRUE, scale = TRUE)

#Simple Logistic regression
logistic1 <- glm(mILOA_Indep ~ Group, data = mILOA, family="binomial")
summary(logistic1)
# Doesn't account for repeated measures or time - not considered as a valid
model yet.

#Mixed effects logistic regression required to add the appropriate factors
```

```
#Add random intercept for Study_Number - I think this allows grouping for
subject number
logistic2 <- glmer(mILOA_Indep ~ Group +(1|Study_Number), data = mILOA,
family="binomial")
summary(logistic2)
#Doesn't account for the relationship of mILOA change over time - not considered
a valid model yet.

#Time to mILOA score known to be a significant predictor of outcome therefore
added as first fixed variable
logistic3 <- glmer(mILOA_Indep ~ (Group + TT_mILOA_Hours)
+(1|Study_Number), data = mILOA, family="binomial")
summary(logistic3)
# Now incorporates time and random intercept by subject number.
# Shows group to be significant
#AIC = 1054.6

#~~~~~ Now to improve the model ~~~~~#

#Trial age as fixed effect
logistic4 <- glmer(mILOA_Indep ~ (Group + TT_mILOA_Hours+Age)
+(1|Study_Number), data = mILOA, family="binomial")
summary (logistic4)
#AIC ISQ and p value for Age 0.42 - Age not particularly helpful within this model.

#Compare models with ANOVA
anova (logistic3, logistic4)
# p=0.4229 AIC in favour of logistic3

#Remove Age
#Include Gender as fixed effect
logistic5 <- glmer(mILOA_Indep ~ (Group + TT_mILOA_Hours+Gender)
+(1|Study_Number), data = mILOA, family="binomial")
summary(logistic5)
# Marginally better AIC (1049.0) with the same degrees of freedom, Gender looks
to be significant

#Compare logistic3 with logistic5 using ANOVA
anova (logistic3, logistic5)
# p = 0.005755, AIC in favour of logistic5

#Residual diagnostics for logistic5 || for comparison with final model later
simulationOutputLog5 <- simulateResiduals(fittedModel = logistic5, plot = T)
testResiduals(simulationOutputLog5)
```

```
#Trial CCI as fixed effect
logistic6 <- glmer(mILOA_Indep ~ (Group + TT_mILOA_Hours+Gender+CCI)
+(1|Study_Number), data = mILOA, family="binomial")
summary(logistic6)
#AIC ISQ, CCI appears non-significant
anova (logistic5, logistic6)
## AIC ISQ, p=0.1627

#remove CCI
#Include RAPT
logistic7 <- glmer(mILOA_Indep ~ (Group + TT_mILOA_Hours+Gender+RAPT)
+(1|Study_Number), data = mILOA, family="binomial")
summary(logistic7)
anova (logistic5, logistic7)
#p = 0.61, Poorer AIC and RAPT appears non-significant

#Remove RAPT
#Trial factors by group
logistic8 <- glmer(mILOA_Indep ~ (Group + TT_mILOA_Hours+Gender*Group)
+(1|Study_Number), data = mILOA, family="binomial")
summary(logistic8)
#Compare models with ANOVA
anova(logistic5, logistic8)
#AIC = 1047.9 favoring logistic 8, p = 0.08043

# Add all potential co-variants
logistic9 <- glmer(mILOA_Indep ~ (Group +
TT_mILOA_Hours+CCI+RAPT+Gender*Group + Age*Group) +(1|Study_Number),
data = mILOA, family="binomial")
summary(logistic9)


#Table of Coefficients#
tab_model(logistic8)
tab_model(logistic9)
tab_model(logistic9,
        string.pred = "Predictors of Independence",
        pred.labels = c("Intercept",
                        "Group (Reference: RAPID)",
                        "TT (in hours)",
                        "CCI",
                        "RAPT",
                        "Gender (Reference: Males)",
                        "Age (Mean-Centered)",
                        "Interaction: Group (RAPID)*Gender (Males)",
                        "Interaction: Group (RAPID)*Age"),
        string.est = "Odds Ratio (OR)",
```

```
        string.ci = "95% Confidence Interval",
        string.p = "p-value")

#--- Logistic Regression Diagnostics for logistic 8 ---#

#Using DHARMa package
#Simulate residuals
simulationOutput <- simulateResiduals(fittedModel = logistic9, plot = T)
plot(simulationOutput)
#Unsure on interpretation of this. QQ plot looks good to me, but I don't
understand the implications of 'Quantile deviations detected'
#Check residuals by predictors
par(mfrow = c(2,3))
plotResiduals(simulationOutput, mILOA$Group)
plotResiduals(simulationOutput, mILOA$Gender)
plotResiduals(simulationOutput, mILOA$TT_mILOA_Hours)
plotResiduals(simulationOutput, mILOA$CCI)
plotResiduals(simulationOutput, mILOA$RAPT)
plotResiduals(simulationOutput, mILOA$ASA)
#Other checking tools:
testResiduals(simulationOutput)
#Uniformity test Kolmogorov-Smirnov test - p=0.05339. Interpretation, there is
NOT uniformity in the distribution of residuals v expected
#Dispersion test - appears to be no significant dispersion both in test statistics,
QQ-plot and histogram p = 0.744
#Outliers test - appears to be significant

?#Checking assumptions

?#Checking linearity not applicable due to no continuous predictor variables used
in the final model.

?#Checking for influentials



#Multicollinearity
car::vif(logistic9)
# VIF(Variance inflation factors) values <5. No problematic collinearity

#
mILOA$TT_mILOA_Hours3<- cut(mILOA$TT_mILOA_Hours, breaks=c(-Inf, 8, 24,
48, 120,  Inf), levels=c(1,2,3,4,5) , labels=c("Less than 8 hours", "Under one day",
"Between two days", "Under 5 days", "More than 5 days"))
```

```
#--------------------------------
#Logistic regression not possible due to above.
#
#Model negative binomial without time - won't work because some participants
didn't achieve independence.

###################################
#                                 #
#     SURVIVAL ANALYSIS       #
#                                 #
###################################

#Move on to survival analysis

#Dataset reloaded to remove scaling

#Build the survival model
mILOASA <- Surv(time = mILOA$TT_mILOA_Hours, event =
mILOA$mILOA_Indep)
KM.Model <- survfit(formula = mILOASA ~ Group, data = mILOA)

#Plot Kaplan-Mayer plot
ggsurvplot(KM.Model, data = mILOA, pval = TRUE, conf.int = TRUE,
         xlab = "Time in Hours",
         ylab = "Probability of Functional Dependence",
         ncensor.plot = TRUE,
         break.time.by = 24,
         risk.table = TRUE, surv.median.line = "hv",
         ggtheme = theme_bw())
#By cumulative event
ggsurvplot(KM.Model, data = mILOA, pval = TRUE, conf.int = TRUE,
         risk.table = TRUE, surv.median.line = "hv",
         xlab = "Time in Hours",
         ylab = "Proportion Functionally Independent",
         break.time.by = 24,
         ggtheme = theme_bw(),
         fun = "event")
#by cumulative hazard
ggsurvplot(KM.Model, data = mILOA, pval = TRUE, conf.int = TRUE,
         risk.table = TRUE, surv.median.line = "hv",
         xlab = "Time in Hours",
         ylab = "Cumulative Hazard of Functional Independence",
         break.time.by = 24,
         ggtheme = theme_bw(),
         fun = "cumhaz")
#Summary Kaplan-Mayer
summary(KM.Model)
```

```
summary(KM.Model)$table

#Log-Rank Test
survdiff(mILOASA ~ Group, data = mILOA)

#-----------------------------------------------------------------

#Look at univariate Cox analyses - Cox proportional hazards model
#Make other covariates binomial in order to add to forest plot
#CCI>1 (Based on stratification of randomisation used in study)
mILOA$HighCCI <- ifelse(mILOA$CCI >=2, TRUE, FALSE)
mILOA$HighCCI <- as.factor(mILOA$HighCCI)
#ASA>2
mILOA$HighASA <- ifelse(mILOA$ASA >2, TRUE, FALSE)
mILOA$HighASA <- as.factor(mILOA$HighASA)

#Group
fit.coxphGrp <- coxph(mILOASA ~ Group,
                      data = mILOA)
summary(fit.coxphGrp)
#Gender
fit.coxphGender <- coxph(mILOASA ~ Gender,
                         data = mILOA)
summary(fit.coxphGender)
#CCI
fit.coxphCCI <- coxph(mILOASA ~ HighCCI,
                      data = mILOA)
summary(fit.coxphCCI)
#ASA
fit.coxphASA <- coxph(mILOASA ~ HighASA,
                      data = mILOA)
summary(fit.coxphASA)

ggforest(fit.coxph, data = mILOA)

#Make other covariates binomial in order to add to forest plot
#CCI>1
mILOA$HighCCI <- ifelse(mILOA$CCI >=2, TRUE, FALSE)
mILOA$HighCCI <- as.factor(mILOA$HighCCI)
#ASA>2
mILOA$HighASA <- ifelse(mILOA$ASA >2, TRUE, FALSE)
mILOA$HighASA <- as.factor(mILOA$HighASA)

#Replot forest plot with extra covariates
fit.coxph <- coxph(mILOASA ~ Group + Gender + HighCCI + HighASA,
```

```
                data = mILOA)
ggforest(fit.coxph, data = mILOA)

summary(fit.coxph)

confint(fit.coxph)

#Generate Schoenfeld residuals

cz  <-  cox.zph(fit.coxph)

print(cz)

# Plots of the Schoenfeld residuals

ggcoxzph(cz)

#Looking for influential observations
ggcoxdiagnostics(fit.coxph, type = "deviance",
                linear.predictions = FALSE, ggtheme = theme_bw())

# Due to gender
KM.gender <- survfit(formula = mILOASA ~ Gender, data = mILOA)
ggsurvplot(KM.gender, data = mILOA)

# Deviation from a zero-slope line is evidence that the proportional
# hazards assumption is violated

#Attempt to improve residuals by adding time interaction to problem covariate
fit.coxph <- coxph(mILOASA ~ Group + Gender*TT_mILOA_Hours + HighCCI +
HighASA,
                data = mILOA)
ggforest(fit.coxph, data = mILOA)

summary(fit.coxph)

confint(fit.coxph)

#Generate Schoenfeld residuals

cz  <-  cox.zph(fit.coxph)

print(cz)

# Plots of the Schoenfeld residuals

ggcoxzph(cz)
```

```
#-------------------------------------------------------------
```

Appendix 36 Post-op complications classified as 'other'

Recovery Phase	Days Post-op	CDC	Group	Detail
Inpatient	2	1	CONTROL	Abdominal pain. Likely adverse reaction in oxycontin
Inpatient	5	1	CONTROL	Loose stools due to aperients - restricted physiotherapy session
Post Discharge	14	1	CONTROL	Withdrawal symptoms when weaning from opioids
Post Discharge	85	1	CONTROL	Diverticulitis - treated by GP
Post Discharge	49	1	CONTROL	Leg Ulcer - anteromedial shin. Participant hit leg on a table and developed a leg ulcer. Managed by GP and no admission required. Thought unrelated to THR or THR recovery. Osteomyelitis ruled out with XR
Post Discharge	102	1	CONTROL	Left sided chest pain. Readmitted to PGH. Elevated Trop-T and chest pain. Believed to by musculoskeletal in nature.
Post Discharge	11	1	RAPID	Allergic reaction of unknown cause. GP treated with cetirizine
Inpatient	3	1	CONTROL	Low in mood - patient reported very low in mood and fatigued.
Post Discharge	7	1	RAPID	Staples uncomfortable
Post Discharge	11	1	CONTROL	Odynophagia - presented at A&E and admitted
Post Discharge	7	1	CONTROL	Blood blister on thigh - had district nurse to dress for 1 week.
Post Discharge	14	1	RAPID	Blister above wound.
Inpatient	1	1	CONTROL	Coffee ground vomit overnight but didn't limit mobility. No further investigation needed.
Inpatient	2	1	RAPID	Chest Pain - Diagnosed as ADR to oramorph - fully resolved
Inpatient	2	1	RAPID	Feeling generally unwell - did not want to mobilise too far in case it got worse.
Post Discharge	95	1	CONTROL	Quadriceps weakness causing functional limitation
Inpatient	2	1	CONTROL	Clunking in hip - reports clunking sensation with pain in standing.

Appendix 37 Abstract Nested Qualitative Study so Far

Title

What is it like to be a Patient Treated using a RAPID Mobilisation Protocol Post Total-Hip Replacement? A Nested Qualitative Study

Objectives

- To explore the patient lived experience of a RAPID mobilisation protocol on their consequent post-operative recovery.
- To provide a rich description of the lived experience of day-zero ambulation following THR which can provide context to RCT quantitative findings.

This objective is set with the overall outcome of informing the effectiveness of a RAPID mobilisation protocol in how it affects patient experience.

Study Design

A nested qualitative study using a thematic analysis method, employing semi-structured interviews with a stratified purposeful sample of participants selected from the RCT cohort.

Progress Report

This nested study has completed data collection and transcription from 6 semi-structured interviews and is moving into the analysis phase of the study. These findings will then be triangulated against participant experience questionnaires completed within the fully powered RCT and with comments raised at the 3-month post-operative telephone follow-up.

Glossary of Terms

This glossary of terms focusses on terms specific to the orthopaedic speciality medicine which is the speciality this research is focussed within.

Anitbiotic prophylaxis	Administration of anti-biotics without the presence of diagnosed infection for the prevention of infection complications post-surgery.
Arthroplasty	Orthopaedic surgical procedure to replace joint surfaces with artificial components to treat arthritis
Closed reduction	Surgical procedure to correct a fracture, dislocation or hernia without; using an incision.
Colorectal	Medical speciality relating to the colon and rectum or entire large bowel
Elective surgery	Surgery that is scheduled in advance because it does not involve a medical emergency
Functional dependence	Where a person requires the assistance of one or more other people in order to carry out a functional task.
Functional recovery	The process of regaining ability to complete functional tasks independently or with reducing assistance
Intra-operative complications	Surgical or medical complications which occur while the operation is taking place.
Leg length discrepancy	A difference in leg lengths which becomes clinically significant at more than 3 cm difference.
Local infiltration analgesia	Pain relieving medications which are delivered directly to the joint during or after surgery. This can be via injection or catheter.
Mobilisation	Walking
Orthopaedic	Surgical speciality relating to the assessment and treatment of disorders of the musculoskeletal system.
Orthostatic intolerance	The development of symptoms when standing, which are relieved when reclining
Peri-prosthetic fracture	A complete or partial break in the continuity of the bone around a prosthetic implant
Peri-prosthetic infection	An infection sited around a prosthetic implant
Posterolateral approach	An approach to doing a total hip replacement surgery where the incision lies at the back and lateral side of the gluteal region.
Post-operative complications	Surgical or medical complications which occur after the operation has finished
Primary (THR)	A hip replacement delivered in a joint which has not previously undergone hip replacement surgery
Range of motion	The angular distance that a joint can move
Repair to abductor complex	Surgical repair to the abductor muscles of the hip which lie in the gluteal region

Revision THR	A hip replacement delivered in a joint which already has a hip replacement in situ.
Surgical site infection	An infection that occurs at the site of the surgical incision
THR dislocation	Dislocation of the artificial hip joint – the displacement of the prosthetic humeral head from the prosthetic acetabulum.
Thromboprophylaxis	Any preventative measures or medications to reduce the risk of the formation of blood clots
Total hip arthroplasty	Surgery to relived pain in the hip by surgically removing and replacing articular joint surfaces with artificial components
Total hip replacement	Surgery to relived pain in the hip by surgically removing and replacing articular joint surfaces with artificial components
Trendelenberg's gait	A gait pattern which is compensatory during stance phase to the weak gluteal side
Unilateral (THR)	Carried out on a single side of the body (left or right)
Weight Bearing Status	The guidance on the ability of the body to support weight after surgery
Wound drainage	The discharge of fluid from a wound, sore or cavity

List of References

Ahdieh, H., Ma, T., Babul, N. & Lee, D., (2004) Efficacy of oxymorphone extended release in postsurgical pain: A randomized clinical trial in knee arthroplasty. *Journal of Clinical Pharmacology*, 44(7), pp.767–776.

Allen, K.D., (2010) Racial and ethnic disparities in osteoarthritis phenotypes. *Current Opinion in Rheumatology*, 22(5), pp.528–532.

Allman, K. & Wilson, I., (2012) *Oxford Handbook of Anaesthesia* 4th ed., Oxford: Oxford University Press.

Alvarez, P.M., McKeon, J.F., Spitzer, A.I., Krueger, C.A., Pigott, M., Li, M. & Vajapey, S.P., (2022) Socioeconomic factors affecting outcomes in total knee and hip arthroplasty: a systematic review on healthcare disparities. *Arthroplasty*, 4(1). Available at: https://doi.org/10.1186/s42836-022-00137-4.

Amlie, E., Lerdal, A., Gay, C.L., Høvik, Ø., Nordsletten, L. & Dimmen, S., (2016) A trend for increased risk of revision surgery due to deep infection following fast-track hip arthroplasty. *Advances in Orthopedics*, 2016.

Andersen, L.J., Poulsen, T., Krogh, B. & Nielsen, T., (2007) Postoperative analgesia in total hip arthroplasty: A randomized double-blinded, placebo-controlled study on peroperative and postoperative ropivacaine, ketorolac, and adrenaline wound infiltration. *Acta Orthopaedica*, 78(2), pp.187–192. Available at: http://www.tandfonline.com/doi/full/10.1080/17453670710013663 [Accessed February 25, 2021].

Andersen, L.Ø., Gaarn-Larsen, L., Kristensen, B.B., Husted, H., Otte, K.S. & Kehlet, H., (2009) Subacute pain and function after fast-track hip and knee arthroplasty. *Anaesthesia*, 64, pp.508–513.

Andreasen, S.E., Holm, H.B., Jørgensen, M., Gromov, K., Kjærsgaard-Andersen, P. & Husted, H., (2017) Time-driven Activity-based Cost of Fast-Track Total Hip and Knee Arthroplasty. *Journal of Arthroplasty*, 32(6), pp.1747–1755. Available at: https://www.clinicalkey.com/service/content/pdf/watermarked/1-s2.0-S0883540316309251.pdf?locale=en_US [Accessed February 21, 2018].

Bibliography

Antrobus, J.D. & Bryson, G.L., (2011) Enhanced recovery for arthroplasty: good for the patient or good for the hospital? *Canadian journal of anaesthesia = Journal canadien d'anesthésie*, 58(10), pp.891–4, 894–6. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21833818.

Arthritis Research UK, (2013) Osteoarthritis in general practice. *The Medical Press*, 222, pp.253–258. Available at: http://www.arthritisresearchuk.org/arthritis-information/data-and-statistics/osteoarthritis.aspx. [Accessed June 24, 2014].

Austin, Z. & Sutton, J., (2014) Qualitative research: getting started. *The Canadian journal of hospital pharmacy*, 67(6), pp.436–40. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25548401%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4275140.

Bafeta, A., Dechartres, A., Trinquart, L., Yavchitz, A., Boutron, I. & Ravaud, P., (2012) Impact of single centre status on estimates of intervention effects in trials with continuous outcomes: Meta-epidemiological study. *BMJ (Online)*, 344(7846). Available at: https://www.bmj.com/content/344/bmj.e813 [Accessed July 11, 2022].

Bandholm, T. & Kehlet, H., (2012) Physiotherapy exercise after fast-track total hip and knee arthroplasty: Time for reconsideration? *Archives of Physical Medicine and Rehabilitation*, 93(7), pp.1292–1294. Available at: http://dx.doi.org/10.1016/j.apmr.2012.02.014.

Banerjee, A., Chitnis, U.., Jadhav, S.L., Bhawalkar, J.S. & Chaudhury, S., (2009) Hypothesis testing, type I and type II errors. *Industrial Psychiatry Journal*, 18(2), pp.127–131. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2996198/.

Banerjee, P., (2014) The efficacy of multimodal high-volume wound infiltration in primary total knee replacement in facilitating immediate post-operative pain relief and attainment of early rehabilitation milestones. *European journal of orthopaedic surgery & traumatology : orthopédie traumatologie*, 24(4), pp.571–7. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23689908.

Barnes, L.A., Marshall, C.D., Leavitt, T., Hu, M.S., Moore, A.L., Gonzalez, J.G., Longaker, M.T. & Gurtner, G.C., (2017) Mechanical Forces in Cutaneous Wound Healing: Emerging Therapies to Minimize Scar Formation. *Advances in Wound Care*, p.wound.2016.0709. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5792236/pdf/wound.2016.0709.pdf [Accessed May 1, 2018].

Bausell-Barker, R. & Yu-Fang, L., (2002) *Power Analysis for Experimental Research* 1st ed., Cambridge: Cambridge University Press.

Bellomo, R., Warrillow, S.J. & Reade, M.C., (2009) Why we should be wary of single-center trials. *Critical Care Medicine*, 37(12), pp.3114–3119. Available at: https://journals.lww.com/ccmjournal/Fulltext/2009/12000/Why_we_should_be_wary_of_single_center_trials.17.aspx [Accessed July 11, 2022].

Bennett, D., Ogonda, L., Elliott, D., Humphreys, L., Lawlor, M. & Beverland, D., (2007) Comparison of Immediate Postoperative Walking Ability in Patients Receiving Minimally Invasive and Standard-Incision Hip Arthroplasty. A Prospective Blinded Study. *Journal of Arthroplasty*, 22(4), pp.490–495.

Berbari, E.F., Hanssen, A.D., Duffy, M.C., Steckelberg, J.M., Ilstrup, D.M., Harmsen, W.S. & Osmon, D.R., (1998) Risk factors for prosthetic joint infection: Case-control study. *Clinical Infectious Diseases*, 27(5), pp.1247–1254.

Berg, U., Berg, M., Rolfson, O. & Erichsen-Andersson, A., (2019) Fast-track program of elective joint replacement in hip and knee - Patients' experiences of the clinical pathway and care process. *Journal of Orthopaedic Surgery and Research*, 14(1). Available at: https://doi.org/10.1186/s13018-019-1232-8 [Accessed May 15, 2020].

Berger, R. a, (2007) A comprehensive approach to outpatient total hip arthroplasty. *American journal of orthopedics (Belle Mead, N.J.)*, 36(9 Suppl), pp.4–5. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17948159.

Berger, R.A., Sanders, S.A., Thill, E.S., Sporer, S.M. & Della Valle, C., (2009) Newer anesthesia and rehabilitation protocols enable outpatient hip replacement in selected patients. *Clinical Orthopaedics and Related Research*, 467(6), pp.1424–1430.

Berkman, N.D., Lohr, K.N., Ansari, M., McDonagh, M., Balk, E., Whitlock, E., Reston, J., Bass, E., Butler, M., Gartlehner, G., Hartling, L., Kane, R., McPheeters, M., Morgan, L., Morton, S.C., Viswanathan, M., Sista, P. & Chang, S., (2008) *Grading the Strength of a Body of Evidence When Assessing Health Care Interventions for the Effective Health Care Program of the Agency for Healthcare Research and Quality: An Update*, Agency for Healthcare Research and Quality. Available at: www.effectivehealthcare.ahrq.gov/reports/final.cfm. [Accessed April 5, 2022].

Berstock, J.R., Beswick, A.D., Lenguerrand, E., Whitehouse, M.R. & Blom, A.W., (2014) Mortality after total hip replacement surgery. *Bone & Joint Research*, 3(6), pp.175–182. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4054013/pdf/bonejointres-03-175.pdf

[Accessed April 27, 2018].

Bhatt, T., Espy, D., Yang, F. & Pai, Y.C., (2011) Dynamic gait stability, clinical correlates, and prognosis of falls among community-dwelling older adults. *Archives of Physical Medicine and Rehabilitation*, 92(5), pp.799–805. Available at: https://www.archives-pmr.org/article/S0003-9993(11)00002-5/pdf [Accessed May 22, 2018].

Bijur, P.E., Latimer, C.T. & Gallagher, E.J., (2003) Validation of a verbally administered numerical rating scale of acute pain for use in the emergency department. *Academic Emergency Medicine*, 10(4), pp.390–392.

Bjorgul, K., Novicoff, W.M. & Saleh, K.J., (2010) Evaluating comorbidities in total hip and knee arthroplasty: available instruments. *Journal of orthopaedics and traumatology : official journal of the Italian Society of Orthopaedics and Traumatology*, 11(4), pp.203–209.

BNF, (2017) British National Formulary. *BMJ Group and Pharmaceutical Press*, 72. Available at: www.medicinescomplete.com.

Bolarinwa, O., (2015) Principles and methods of validity and reliability testing of questionnaires used in social and health science researches. *Nigerian Postgraduate Medical Journal*, 22(4), p.195. Available at: http://www.npmj.org/temp/NigerPostgradMedJ224195-3088144_083441.pdf [Accessed January 9, 2018].

Bottros, J., Klika, A.K., Milidonis, M.K., Toetz, A., Fehribach, A. & Barsoum, W.K., (2010) A rapid recovery program after total hip arthroplasty. *Current Orthopaedic Practice*, 21(4), pp.381–384.

Bridge, P.D. & Sawilowsky, S.S., (1999) Increasing physicians' awareness of the impact of statistics on research outcomes: Comparative power of the t-test and Wilcoxon Rank-Sum test in small samples applied research. *Journal of Clinical Epidemiology*, 52(3), pp.229–235.

Briggs, T., (2015) A national review of adult elective orthopaedic services in England: GETTING IT RIGHT FIRST TIME. *British Orthopaedic Association*, (March), p.68. Available at: https://www.boa.ac.uk/wp-content/uploads/2015/03/GIRFT-National-Report-Mar15..pdf.

Bristol, J., (2021) Early Ambulation in Hip Replacement Patients Regarding Length of Hospital Stay. *Journal of Orthopedics and Orthopedic Surgery*, 2(2), pp.30–34.

British Orthopaedic Association, (2022) T&O waiting list the largest for over a decade. *boa.ac.uk*. Available at: https://www.boa.ac.uk/resources/t-o-waiting-list-the-largest-for-over-a-decade.html [Accessed August 23, 2022].

BRM, (2021) Axiology - Research-Methodology. *Business Research Methodology*. Available at: https://research-methodology.net/research-philosophy/axiology-2/#_ftn3 [Accessed September 18, 2022].

Callaghan, J., Rosenburg, A. & Rubash, H., (2007) *The Adult Hip - Volume 2* 2nd Editio., Philadelphia: Lippincott Williams and Wilkins.

Care Quality Commission, (2013) Survey of adult inpatients 2013. *Care Quality Commission*. Available at: http://www.cqc.org.uk/.

CASP, (2014) CASP Checklists. *Critical Appraisal Skills Programme (CASP)*. Available at: http://www.casp-uk.net/#!casp-tools-checklists/c18f8.

Charlson, M., Pompei, P., Ales, K. & MacKenzie, C., (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *Journal of Chronic Diseases*, 40(5), pp.373–83.

Chatman, A.B., Hyams, S.P., Neel, J.M., Binkley, J.M., Stratford, P.W., Schomberg, A. & Stabler, M., (1997) The patient-specific functional scale: Measurement properties in patients with knee dysfunction. *Physical Therapy*, 77(8), pp.820–829. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9256870 [Accessed May 22, 2018].

Chen, A.F., Stewart, M.K., Heyl, A.E. & Klatt, B.A., (2012) Effect of Immediate Postoperative Physical Therapy on Length of Stay for Total Joint Arthroplasty Patients. *The Journal of Arthroplasty*, 27(6), pp.851–856. Available at: http://dx.doi.org/10.1016/j.arth.2012.01.011.

Cheville, A., Chen, A., Oster, G., McGarry, L. & Narcessian, E., (2001) A randomized trial of controlled-release oxycodone during inpatient rehabilitation following unilateral total knee arthroplasty. *The Journal of Bone and Joint Surgery*, 83-A(4), pp.572–576.

Chua, M.J., Hart, A.J., Mittal, R., Harris, I.A., Xuan, W. & Naylor, J.M., (2017) Early mobilisation after total hip or knee arthroplasty: A multicentre prospective observational study. *PLoS ONE*, 12(6). Available at: http://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0179820&type=printable [Accessed February 21, 2018].

Collett, D., (2015) *Modelling survival data in medical research, third edition*,

Cook, C. & Sheets, C., (2011) Clinical equipoise and personal equipoise: Two necessary ingredients

for reducing bias in manual therapy trials. *Journal of Manual and Manipulative Therapy*, 19(1), pp.55–57.

Cope, D.G., (2015) Conducting pilot and feasibility studies. *Oncology Nursing Forum*, 42(2), pp.196–197.

CRAC, (2011) The Vitae Researcher Development Framework — Vitae Website. *Vitae 2015 Careers Research and Advisory Centre (CRAC) Limited*. Available at: https://www.vitae.ac.uk/researchers-professional-development/about-the-vitae-researcher-development-framework/developing-the-vitae-researcher-development-framework.

Cracknell, R., (2010) The ageing population. *Key Issues for the New Parliament in 2010*, p.1. Available at: http://www.parliament.uk/documents/commons/lib/research/key_issues/Key-Issues-The-ageing-population2007.pdf [Accessed May 6, 2014].

Creswell, J.W., (2013) *Qualitative inquiry and research design: choosing among five approaches* 3rd ed., London: SAGE Publications.

Crow, R., Gage, H., Hampson, S., Hart, J., Kimber, A., Storey, L. & Thomas, H., (2002) The measurement of satisfaction with healthcare: implications for practice from a systematic review of the literature HTA Health Technology Assessment NHS R&D HTA Programme Executive summary. *Health Technology Assessment*, 6(32). Available at: http://uhra.herts.ac.uk/bitstream/handle/2299/1073/102382.pdf;sequence=1 [Accessed February 21, 2018].

Cunningham, B.P., Harmsen, S., Kweon, C., Patterson, J., Waldrop, R., McLaren, A. & McLemore, R., (2013) Have levels of evidence improved the quality of orthopaedic research? *Clinical Orthopaedics and Related Research*, 471(11), pp.3679–3686.

Daabiss, M., (2011) American society of anaesthesiologists physical status classification. *Indian Journal of Anaesthesia*, 55(2), pp.111–115.

Darzi, a, (2008a) High quality care for all: NHS Next Stage Review final report. *London Department of Health*, p.92. Available at: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_085828.pdf.

Darzi, a, (2008b) *High Quality Care For All*, Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/228836/7

432.pdf.

Davis, A.M., Perruccio, A. V., Canizares, M., Hawker, G.A., Roos, E.M., Maillefert, J.F. & Lohmander, L.S., (2009) Comparative, validity and responsiveness of the HOOS-PS and KOOS-PS to the WOMAC physical function subscale in total joint replacement for Osteoarthritis. *Osteoarthritis and Cartilage*, 17(7), pp.829–833. Available at: https://www.oarsijournal.com/article/S1063-4584(09)00017-X/pdf [Accessed May 22, 2018].

Dawson-Bowling, S.J., Jha, S., Chettiar, K.K., East, D.J., Gould, G.C. & Apthorp, H.D., (2014) A multidisciplinary enhanced recovery programme allows discharge within two days of total hip replacement; three- to five-year results of 100 patients. *Hip international : the journal of clinical and experimental research on hip pathology and therapy*, 24(2), pp.167–74. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24500823.

Dawson, J., Fitzpatrick, R., Carr, a & Murray, D., (1996) Questionnaire on the perceptions of patients about total hip replacement. *The Journal of bone and joint surgery. British volume*, 78(2), pp.185–190. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8666621.

Denscombe, M., (2014) *The good research guide : for small-scale research projects*, Maidenhead, Berkshire : Open University Press,.

Department of Health, (2015) Reference costs guidance 2014-15. *www.gov.uk*, (February), p.26. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/402356/Reference_costs.pdf.

Dindo, D., Demartines, N. & Clavien, P.-A., (2004) Classification of Surgical Complications. *Annals of surgery*, 240(2), pp.205–213. Available at: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00000658-200408000-00003.

Doleman, B., Mathiesen, O., Jakobsen, J.C., Sutton, A.J., Freeman, S., Lund, J.N. & Williams, J.P., (2021) Methodologies for systematic reviews with meta-analysis of randomised clinical trials in pain, anaesthesia, and perioperative medicine. *British Journal of Anaesthesia*, 126(4), pp.903–911. Available at: http://www.bjanaesthesia.org/article/S0007091221000131/fulltext [Accessed June 13, 2022].

Doleman, B., Lund, J. & Williams, J., (2017) Detection and prevention of publication bias in meta-analyses of postoperative analgesics: a meta-epidemiological study. *In Anaesthesia*, 72, pp.20–20.

Dorr, L.D., Thomas, D.J., Zhu, J., Dastane, M., Chao, L. & Long, W.T., (2010) Outpatient total hip arthroplasty. *The Journal of arthroplasty*, 25(4), pp.501–6. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19640672.

Edlin, R., Tubeuf, S., Achten, J., Parsons, N. & Costa, M., (2012) Cost-effectiveness of total hip arthroplasty versus resurfacing arthroplasty: economic evaluation alongside a clinical trial. *BMJ open*, 2(5), pp.1–9. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3488749&tool=pmcentrez&rendertype=abstract.

Efford, C.M., Holdsworth, C., Donovan-Hall, M. & Samuel, D., (2023) (Submitted - Not Yet Published) What is the multifactorial efficacy of day-zero ambulation post-total hip replacement surgery: A systematic review. *JBJS Reviews*, TBC(TBC), p.TBC.

Efford, C.M. & Samuel, D., (2022) Does rapid mobilisation as part of an enhanced recovery pathway improve length of stay, return to function and patient experience post primary total hip replacement? A randomised controlled trial feasibility study. *Disability and Rehabilitation*.

Eldridge, S.M., Lancaster, G.A., Campbell, M.J., Thabane, L., Hopewell, S., Coleman, C.L. & Bond, C.M., (2016) Defining feasibility and pilot studies in preparation for randomised controlled trials: Development of a conceptual framework. *PLoS ONE*, 11(3), pp.1–22.

Elings, J., Hoogeboom, T.J., van der Sluis, G. & van Meeteren, N.L.U., (2015) What preoperative patient-related factors predict inpatient recovery of physical functioning and length of stay after total hip arthroplasty? A systematic review. *Clinical rehabilitation*, 29(5), pp.477–92. Available at: http://www.scopus.com/inward/record.url?eid=2-s2.0-84930391175&partnerID=tZOtx3y1.

Elmoghazy, A.D., Lindner, N., Tingart, M. & Salem, K.H., (2022) Conventional versus fast track rehabilitation after total hip replacement: A randomized controlled trial. *Journal of Orthopaedics, Trauma and Rehabilitation*, 29(1), pp.1–6.

Eming, S., Martin, P. & Tomic-Canic, M., (2014) Wound repair and regeneration: Mechanisms, signaling, and translation. *Sci Transl Med*, 6(265), pp.1–36.

Enloe, L.J., Shields, R.K., Smith, K., Leo, K. & Miller, B., (1996) Total hip and knee replacement treatment programs: a report using consensus. *J Orthop Sports Phys Ther*, 23(1), pp.3–11. Available at: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=8749744.

ERAS Society, (2021) Orthopaedics. *ERAS Society Webpage*. Available at: https://erassociety.org/specialty/orthopaedics/ [Accessed December 22, 2021].

Euroqol Group, (1990) EuroQol - a new facility for the measurement of health-related quality of life. *Health Policy*, 16(3), pp.199–208. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10109801%5Cnhttp://linkinghub.elsevier.com/retrieve/pii/0168851090904219.

Evans, D., (2003) Hierarchy of evidence: A framework for ranking evidence evaluating healthcare interventions. *Journal of Clinical Nursing*, 12(1), pp.77–84. Available at: http://doi.wiley.com/10.1046/j.1365-2702.2003.00662.x [Accessed July 2, 2020].

Falck-Ytter, Y., Francis, C.W., Johanson, N.A., Curley, C., Dahl, O.E., Sam Schulman, Ortel, T.L., Pauker, S.G. & Clifford W. Colwell, J., (2012) Prevention of VTE in Orthopedic Surgery Patients. *CHEST Journal*, 141(2_suppl), p.e278S. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278063/pdf/112404.pdf [Accessed April 27, 2018].

Faul, F., Erdfelder, E., Buchner, A. & Lang, A.-G., (2009) Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behavior Research Methods*, 41(4), pp.1149–60. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19897823.

Feng, C., Wang, H., Lu, N., Chen, T., He, H., Lu, Y. & Tu, X.M., (2014) Log-transformation and its implications for data analysis. *Shanghai Archives of Psychiatry*, 26(2), pp.105–109.

Ferreira-Valente, M., Pais-Riberio, J. & Jensen, M., (2011) Validity of four pain intensity-rating scales. *Pain*, 152, pp.2399–2404.

Fincham, J.E., (2008) Response rates and responsiveness for surveys, standards, and the Journal. *American journal of pharmaceutical education*, 72(2), p.43. Available at: http://jcmc.indiana.edu/vol6/issue1/yun.html [Accessed August 1, 2022].

Fischer, H.B.J., Simanski, C.J.P., Sharp, C., Bonnet, F., Camu, F., Neugebauer, E.A.M., Rawal, N.,

Joshi, G.P., Schug, S.A. & Kehlet, H., (2008) A procedure-specific systematic review and consensus recommendations for postoperative analgesia following total knee arthroplasty. *Anaesthesia*, 63(10), pp.1105–1123. Available at: http://doi.wiley.com/10.1111/j.1365-2044.2008.05565.x.

Franz Faul, E.E. and A. and A.B., (2007) G * Power 3 : A flexible statistical power analysis program for the social , behavioral , and biomedical sciences. *Behaviour Research Methods*, 39(2), pp.175–191.

Fraser, J.F., Danoff, J.R., Manrique, J., Reynolds, M.J. & Hozack, W.J., (2018) Identifying Reasons for Failed Same-Day Discharge Following Primary Total Hip Arthroplasty. *Journal of Arthroplasty*, 33(12), pp.3624–3628. Available at: https://reader.elsevier.com/reader/sd/pii/S0883540318306752?token=C382F9C2ABF0EE2E7F8142CB5ADB91CE2AB765BB681B098D8A93E598819C36EBFC039E7733EAC5BCE99F9ACE608DFE62 [Accessed May 15, 2020].

Freeman, R., Wieling, W., Axelrod, F.B., Benditt, D.G., Benarroch, E., Biaggioni, I., Cheshire, W.P., Chelimsky, T., Cortelli, P., Gibbons, C.H., Goldstein, D.S., Hainsworth, R., Hilz, M.J., Jacob, G., Kaufmann, H., Jordan, J., Lipsitz, L.A., Levine, B.D., Low, P.A., Mathias, C., Raj, S.R., Robertson, D., Sandroni, P., Schatz, I., Schondorff, R., Stewart, J.M. & Van Dijk, J.G., (2011) Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome. *Clinical Autonomic Research*, 21(2), pp.69–72. Available at: http://dx.doi.org/10.1016/j.autneu.2011.02.004.

French, B., Thomas, L., Leathley, M., Sutton, C., McAdam, J., Forster, A., Langhorne, P., Price, C., Walker, A. & Watkins, C., (2010) Does repetitive task training improve functional activity after stroke? A Cochrane systematic review and meta-analysis. *Journal of Rehabilitation Medicine*, 42(1), pp.9–15.

Galbraith, A.S., McGloughlin, E. & Cashman, J., (2017) Enhanced recovery protocols in total joint arthroplasty: a review of the literature and their implementation. *Irish Journal of Medical Science*, pp.1–13.

Garcia, T.P. & Marder, K., (2017) Statistical Approaches to Longitudinal Data Analysis in Neurodegenerative Diseases: Huntington's Disease as a Model. *Current Neurology and Neuroscience Reports*, 17(2).

Gaughan, J., Mason, A., Street, A. & Ward, P., (2012) English Hospitals Can Improve Their Use of Resources: An Analysis of Costs and Length of Stay for Ten Treatments. *Centre for Health*

Economics - University of York, 78, pp.44–48. Available at: http://www.york.ac.uk/media/che/documents/papers/researchpapers/CHERP78_English_hospitals_improve_use_of_resources_analysis_costs_length_of_stay.pdf.

GIRFT, (2020) Getting It Right in Orthopaedics: REflecting on Success and Reinforcing Improvement - A follow-up report on the GIRFT national specialty report on orthopaedics. , (February), pp.1–78. Available at: https://gettingitrightfirsttime.co.uk/wp-content/uploads/2020/02/GIRFT-orthopaedics-follow-up-report-February-2020.pdf [Accessed December 15, 2021].

Glasziou, P., Irwig, L., Bain, C. & Colditz, G., (2001) *Systematic Reviews in Health Care*, Cambridge University Press. Available at: https://www-cambridge-org.soton.idm.oclc.org/core/product/A666C9C39EF7EFE628C513E630D2281E.

Goyal, N., Chen, A.F., Padgett, S.E., Tan, T.L., Kheir, M.M., Hopper, R.H., Hamilton, W.G. & Hozack, W.J., (2017) Otto Aufranc Award: A Multicenter, Randomized Study of Outpatient versus Inpatient Total Hip Arthroplasty. *Clinical Orthopaedics and Related Research*, 475(2), pp.364–372. Available at: https://link.springer.com/content/pdf/10.1007%2Fs11999-016-4915-z.pdf [Accessed February 21, 2018].

Gray, J. & Muir, A., (2001) *Evidence-Based Healthcare* 2nd ed., London: Churchill Livingston.

Gromov, K., Kjærsgaard-Andersen, P., Revald, P., Kehlet, H. & Husted, H., (2017) Feasibility of outpatient total hip and knee arthroplasty in unselected patients: A prospective 2-center study. *Acta Orthopaedica*, 88(5), pp.516–521.

Gulotta, L. V., Padgett, D.E., Sculco, T.P., Urban, M., Lyman, S.L. & Nestor, B.J., (2011) Fast Track THR: One Hospital's Experience with a 2-Day Length of Stay Protocol for Total Hip Replacement. *HSS Journal*, 7(3), pp.223–228.

Gupta, K.K., Attri, J.P., Singh, A., Kaur, H. & Kaur, G., (2016) Basic concepts for sample size calculation: Critical step for any clinical trials! *Saudi Journal of Anaesthesia*, 10(3), pp.328–331. Available at: /pmc/articles/PMC4916819/ [Accessed April 8, 2021].

Gustafsson, B.Å., Ekman, S.-L., Ponzer, S. & Heikkilä, K., (2010) The hip and knee replacement operation: an extensive life event. *Scandinavian Journal of Caring Sciences*, 24(4), pp.663–70. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20409055.

Hansen, V.J., Gromov, K., Lebrun, L.M., Rubash, H.E., Malchau, H. & Freiberg, A.A., (2015) Does

the Risk Assessment and Prediction Tool Predict Discharge Disposition After Joint Replacement? *Clinical Orthopaedics and Related Research*, 473(2), pp.597–601.

Harms, S., Larson, R., Sahmoun, a. E. & Beal, J.R., (2007) Obesity increases the likelihood of total joint replacement surgery among younger adults. *International Orthopaedics*, 31, pp.23–26.

Hartig, F., (2018) DHARMa: Residual Diagnostics for Hierarchical (Multi-Level / Mixed) Regression Models. R package version 0.2.0. *https://CRAN.R-project.org/package=DHARMa*.

Hartog, Y.M. den, Mathijssen, N.M.C., Vehmeijer, S.B.W., Den Hartog, Y.M., Mathijssen, N.M.C. & Vehmeijer, S.B.W., (2015) Total hip arthroplasty in an outpatient setting in 27 selected patients. *Acta Orthopaedica*, 86(6), pp.667–670. Available at: http://www.tandfonline.com/doi/full/10.3109/17453674.2015.1066211.

Den Hartog, Y.M., Hannink, G., Van Dasselaar, N.T., Mathijssen, N.M. & Vehmeijer, S.B., (2017) Which patient-specific and surgical characteristics influence postoperative pain after THA in a fast-track setting? *BMC Musculoskeletal Disorders*, 18(1). Available at: https://bmcmusculoskeletdisord.biomedcentral.com/track/pdf/10.1186/s12891-017-1725-8?site=bmcmusculoskeletdisord.biomedcentral.com [Accessed February 21, 2018].

Havelka, M., Lučanin, J.D. & Lučanin, D., (2009) Biopsychosocial model - The integrated approach to health and disease. *Collegium Antropologicum*, 33(1), pp.303–310.

Healy, W.L., Iorio, R., Clair, A.J., Pellegrini, V.D., Della Valle, C.J. & Berend, K.R., (2016) Complications of Total Hip Arthroplasty: Standardized List, Definitions, and Stratification Developed by The Hip Society. *Clinical Orthopaedics and Related Research*, 474(2), pp.357–364. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4709292/pdf/11999_2015_Article_4341.pdf [Accessed April 27, 2018].

Van Hedel, H.J., Wirz, M. & Dietz, V., (2005) Assessing walking ability in subjects with spinal cord injury: Validity and reliability of 3 walking tests. *Archives of Physical Medicine and Rehabilitation*, 86(2), pp.190–196. Available at: https://www.archives-pmr.org/article/S0003-9993(04)00305-3/pdf [Accessed May 22, 2018].

Heo, S.M., Harris, I., Naylor, J. & Lewin, A.M., (2020) Complications to 6 months following total hip or knee arthroplasty: Observations from an Australian clinical outcomes registry. *BMC Musculoskeletal Disorders*, 21(1), pp.1–11. Available at: https://bmcmusculoskeletdisord.biomedcentral.com/articles/10.1186/s12891-020-03612-8 [Accessed July 25, 2022].

Herr, K. a., Spratt, K., Mobily, P.R. & Richardson, G., (2004) Pain Intensity Assessment in Older Adults. *The Clinical Journal of Pain*, 20(4), pp.207–219.

den Hertog, A., Gliesche, K., Timm, J., Mühlbauer, B. & Zebrowski, S., (2012) Pathway-controlled fast-track rehabilitation after total knee arthroplasty: a randomized prospective clinical study evaluating the recovery pattern, drug consumption, and length of stay. *Archives of orthopaedic and trauma surgery*, 132(8), pp.1153–63. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3400756&tool=pmcentrez&rendertype=abstract.

Hewlett-Smith, N., Pope, R., Furness, J., Simas, V. & Hing, W., (2020) Prognostic factors for inpatient functional recovery following total hip and knee arthroplasty: a systematic review. *Acta Orthopaedica*, 91(3), pp.313–318. Available at: https://www.tandfonline.com/doi/full/10.1080/17453674.2020.1744852 [Accessed June 24, 2020].

Higgins, J.P.T., Thompson, S.G., Deeks, J.J. & Altman, D.G., (2003) Measuring inconsistency in meta-analyses. *BMJ : British Medical Journal*, 327(7414), pp.557–560.

Higgins, J.P.T., Altman, D.G., Gøtzsche, P.C., Jüni, P., Moher, D., Oxman, A.D., Savović, J., Schulz, K.F., Weeks, L. & Sterne, J.A.C., (2011) The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ (Online)*, 343(7829). Available at: http://www.bmj.com/content/343/bmj.d5928/suppl/DC1.

Hoeffel, D.P., Daly, P.J., Kelly, B.J. & Giveans, M.R., (2019) Outcomes of the First 1,000 Total Hip and Total Knee Arthroplasties at a Same-day Surgery Center Using a Rapid-recovery Protocol. *JAAOS: Global Research and Reviews*, 3(3), p.e022.

Holm, B., Bandholm, T., Lunn, T.H., Husted, H., Aalund, P.K., Hansen, T.B. & Kehlet, H., (2014) Role of preoperative pain, muscle function, and activity level in discharge readiness after fast-track hip and knee arthroplasty. *Acta Orthopaedica*, 85(5), pp.488–492.

Holm, B., Kristensen, M.T., Myhrmann, L., Husted, H., Andersen, L.Ø., Kristensen, B. & Kehlet, H., (2010) The role of pain for early rehabilitation in fast track total knee arthroplasty. *Disability and rehabilitation*, 32(4), pp.300–306.

Holm, B., Kristensen, M.T., Husted, H., Kehlet, H. & Bandholm, T., (2011) Thigh and knee circumference, knee-extension strength, and functional performance after fast-track total

hip arthroplasty. *PM & R : the journal of injury, function, and rehabilitation*, 3(2), pp.117–24; quiz 124. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21333950.

Hoogeboom, T.J., Van Meeteren, N.L.U., Schank, K., Kim, R.H., Miner, T. & Stevens-Lapsley, J.E., (2015) Risk factors for delayed inpatient functional recovery after total knee arthroplasty. *BioMed Research International*, 2015. Available at: http://dx.doi.org/10.1155/2015/167643 [Accessed June 24, 2020].

Hopewell, S., Loudon, K., Clarke, M.J., Oxman, A.D. & Dickersin, K., (2009) Publication bias in clinical trials due to statistical significance or direction of trial results. *Cochrane Database of Systematic Reviews*, 2009(1). Available at: /pmc/articles/PMC8276556/ [Accessed June 13, 2022].

Hróbjartsson, A., Thomsen, A.S.S., Emanuelsson, F., Tendal, B., Hilden, J., Boutron, I., Ravaud, P. & Brorson, S., (2012) Observer bias in randomised clinical trials with binary outcomes: Systematic review of trials with both blinded and non-blinded outcome assessors. *BMJ (Online)*, 344(7848). Available at: https://www.bmj.com/content/344/bmj.e1119 [Accessed July 11, 2022].

Huang, C.S., Cheu, Y.D., Ying, J. & Wei, M.H., (2011) Association between provider volume and comorbidity on hospital utilization and outcomes of total hip arthroplasty among national health insurance enrollees. *Journal of the Formosan Medical Association*, 110(6), pp.401–409. Available at: http://dx.doi.org/10.1016/S0929-6646(11)60059-4.

Husted, H., Solgaard, S., Hansen, T.B., Søballe, K. & Kehlet, H., (2010) Care principles at four fast-track arthroplasty departments in Denmark. *Danish medical bulletin*, 57(7), p.A4166.

Husted, H., (2012) Fast-track hip and knee arthroplasty: clinical and organizational aspects. *Acta orthopaedica. Supplementum*, 83(346), pp.1–39. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23205862.

Husted, H., Otte, K.S., Kristensen, B.B. & Kehlet, H., (2011) Fast-track revision knee arthroplasty. A feasibility study. *Acta orthopaedica*, 82(4), pp.438–40. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3237034&tool=pmcentrez&rendertype=abstract.

Husted, H., Jørgensen, C.C., Gromov, K. & Troelsen, A., (2015) Low manipulation prevalence following fast-track total knee arthroplasty. *Acta orthopaedica*, 86(1), pp.86–91. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4366662&tool=pmcentrez&rendertype=abstract.

Husted, H., Otte, K.S., Kristensen, Billy B, Ørsnes, T., Wong, C. & Kehlet, H., (2010) Low risk of thromboembolic complications after fast-track hip and knee arthroplasty. *Acta orthopaedica*, 81(5), pp.599–605.

Husted, H., Otte, K.S., Kristensen, Billy B., Orsnes, T. & Kehlet, H., (2010) Readmissions after fast-track hip and knee arthroplasty. *Archives of orthopaedic and trauma surgery*, 130(9), pp.1185–91. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20535614.

Husted, H., Hansen, H.C., Holm, G., Bach-Dal, C., Rud, K., Andersen, K.L. & Kehlet, H., (2009) What determines length of stay after total hip and knee arthroplasty? A nationwide study in Denmark. *Archives of Orthopaedic and Trauma Surgery*, 130(2), pp.263–268. Available at: http://dx.doi.org/10.1007/s00402-009-0940-7.

Husted, H., Lunn, T.H., Troelsen, A., Gaarn-Larsen, L., Kristensen, B.B. & Kehlet, H., (2011) Why still in hospital after fast-track hip and knee arthroplasty? *Acta Orthopaedica*, 82(6), pp.679–684.

Husted, H., Holm, G. & Jacobsen, S., (2008) Predictors of length of stay and patient satisfaction after hip and knee replacement surgery: fast-track experience in 712 patients. *Acta orthopaedica*, 79(2), pp.168–173.

Ibrahim, M.S., Twaij, H., Giebaly, D.E., Nizam, I. & Haddad, F.S., (2013) Enhanced recovery in total hip replacement A CLINICAL REVIEW. , 95(12). Available at: https://online.boneandjoint.org.uk/doi/pdf/10.1302/0301-620X.95B12.31303 [Accessed July 8, 2018].

Insall, J.N., Dorr, L.D., Scott, R.D. & Scott, W.N., (1989) Rationale of the Knee Society clinical rating system. *Clinical orthopaedics and related research*, (248), pp.13–14.

Ireton, J.E., Unger, J.G. & Rohrich, R.J., (2013) The role of wound healing and its everyday application in plastic surgery: A practical perspective and systematic review. *Plastic and Reconstructive Surgery*, 1(1). Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4174176/pdf/gox-1-e10.pdf [Accessed May 1, 2018].

Isaac, D., Falode, T., Liu, P., I'Anson, H., Dillow, K. & Gill, P., (2005) Accelerated rehabilitation after total knee replacement. *The Knee*, 12(5), pp.346–50. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16019214.

Ishiguro, S., Asano, N., Yoshida, K., Nishimura, A., Wakabayashi, H., Yokochi, A., Hasegawa, M.,

Sudo, A. & Maruyama, K., (2013) Day zero ambulation under modified femoral nerve block after minimally invasive surgery for total knee arthroplasty: Preliminary report. *Journal of Anesthesia*, 27, pp.132–134.

Jans, Ø., Brinth, L., Kehlet, H. & Mehlsen, J., (2015) Decreased heart rate variability responses during early postoperative mobilization – an observational study. *BMC Anesthesiology*, 15(1), p.120. Available at: http://www.biomedcentral.com/1471-2253/15/120.

Jans, Ø., Bundgaard-Nielsen, M., Solgaard, S., Johansson, P.I. & Kehlet, H., (2012) Orthostatic intolerance during early mobilization after fast-track hip arthroplasty. *British journal of anaesthesia*, 108(3), pp.436–43. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22174345.

Jans, Ø., Bandholm, T., Kurbegovic, S., Solgaard, S., Kjærsgaard-Andersen, P., Johansson, P.I. & Kehlet, H., (2016) Postoperative anemia and early functional outcomes after fast-track hip arthroplasty: A prospective cohort study. *Transfusion*, 56(4), pp.917–925. Available at: http://onlinelibrary.wiley.com/store/10.1111/trf.13508/asset/trf13508.pdf?v=1&t=jdx83jfb&s=1a6bd11f66b0ea03f881681cc19f493a4ac14947 [Accessed February 21, 2018].

Jensen, K.A., (2004) Evidence-Based Nursing Practice: 7 STEPS TO THE PERFECT PICO SEARCH. *EBSCO Health. CINAHL Complete*, 35(3), p.309. Available at: https://www.ebsco.com/sites/g/files/nabnos191/files/acquiadam-assets/7-Steps-to-the-Perfect-PICO-Search-White-Paper.pdf?_ga=2.150948341.2100990560.1548744619-666596562.1548744619 [Accessed April 7, 2021].

Jensen, M.P. & McFarland, C., (1993) Increasing the reliability and validity of pain intensity measurement in chronic pain patients. *pain*, 55(2), pp.195–203.

Jesudason, C. & Stiller, K., (2002) Are bed exercises necessary following hip arthroplasty? *The Australian journal of physiotherapy*, 48(2), pp.73–81. Available at: http://dx.doi.org/10.1016/S0004-9514(14)60201-4.

Johnson, R.B. & Onwuegbuzie, A., (2004) Mixed Methods Research: A Research Paradigm Whose Time Has Come. *Educational Researcher*, 33(14), pp.14–26.

Jones, E.L., Wainwright, T.W., Foster, J.D., Smith, J.R.A., Middleton, R.G. & Francis, N.K., (2014) A systematic review of patient reported outcomes and patient experience in enhanced recovery after orthopaedic surgery. *Annals of the Royal College of Surgeons of England*, 96(2), pp.89–94. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24780662.

Jorgensen, C.C., Jacobsen, M.K., Soeballe, K., Hansen, T.B., Husted, H., Kjaersgaard-Andersen, P., Hansen, L.T., Laursen, M.B. & Kehlet, H., (2013) Thromboprophylaxis only during hospitalisation in fast-track hip and knee arthroplasty, a prospective cohort study. *BMJ Open*, 3(12), pp.e003965–e003965. Available at: http://bmjopen.bmj.com/cgi/doi/10.1136/bmjopen-2013-003965.

Jorgensen, C.C. & Kehlet, H., (2013) Role of patient characteristics for fast-track hip and knee arthroplasty. *British Journal of Anaesthesia*, 110(6), pp.972–980. Available at: http://bja.oxfordjournals.org/lookup/doi/10.1093/bja/aes505.

Jørgensen, C.C. & Kehlet, H., (2016) Early thromboembolic events ≤ 1 week after fast-track total hip and knee arthroplasty. *Thrombosis Research*, 138, pp.37–42. Available at: https://www.clinicalkey.com/service/content/pdf/watermarked/1-s2.0-S0049384815302401.pdf?locale=en_US [Accessed February 21, 2018].

Jørgensen, C.C. & Kehlet, H., (2013) Fall-related admissions after fast-track total hip and knee arthroplasty - cause of concern or consequence of success? *Clinical interventions in aging*, 8, pp.1569–77. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3848378&tool=pmcentrez&rendertype=abstract.

Jorgensen, C.C., Petersen, M.A. & Kehlet, H., (2016) Preoperative prediction of potentially preventable morbidity after fast-track hip and knee arthroplasty: A detailed descriptive cohort study. *BMJ Open*, 6(1). Available at: http://bmjopen.bmj.com/content/bmjopen/6/1/e009813.full.pdf [Accessed February 21, 2018].

Jørgensen, C.C., Petersen, M.A. & Kehlet, H., (2016) Preoperative prediction of potentially preventable morbidity after fast-track hip and knee arthroplasty: a detailed descriptive cohort study. *BMJ open*, 6(1).

Juliano, K., Edwards, D., Spinello, D., Capizzano, Y., Epelman, E., Kalowitz, J., Lempel, A. & Ghomrawi, H., (2011) Initiating physical therapy on the day of surgery decreases length of stay without compromising functional outcomes following total hip arthroplasty. *Archives of Orthopaedic and Trauma Surgery*, 7(1), pp.16–20. Available at: http://dx.doi.org/10.1016/j.arth.2012.04.025%5Cnhttp://dx.doi.org/10.1016/j.joon.2008.07.017%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/19339559%5Cnhttp://www.ncbi.nlm.nih.go

v/pubmed/21822756%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3026104&tool=pm.

Kapadia, B.H., Berg, R.A., Daley, J.A., Fritz, J., Bhave, A. & Mont, M.A., (2016) Periprosthetic joint infection. *The Lancet*, 387(10016), pp.386–394.

Kapstad, H., Rokne, B. & Stavem, K., (2010) Psychometric properties of the Brief Pain Inventory among patients with osteoarthritis undergoing total hip replacement surgery. *Health and Quality of Life Outcomes*, 8. Available at: https://hqlo.biomedcentral.com/track/pdf/10.1186/1477-7525-8-148 [Accessed May 22, 2018].

Karim, A., Pulido, L. & Incavo, S., (2016) Does Accelerated Physical Therapy After Elective Primary Hip and Knee Arthroplasty Facilitate Early Discharge? *American journal of orthopedics (Belle Mead, N.J.)*, 45(6), pp.E337–E342. Available at: https://www.amjorthopedics.com/sites/default/files/ajo04509337e.PDF [Accessed February 21, 2018].

Kawulich, B. & Holland, L., (2012) *Doing Social Research: A global contextChapter: Qualitative data analysis*, McGraw-Hill Higher Education.

Kehlet, H., (2013) Fast-track hip and knee arthroplasty. *Lancet*, 381(9878), pp.1600–2. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23663938.

Kehlet, H. & Søballe, K., (2010) Fast-track hip and knee replacement--what are the issues? *Acta orthopaedica*, 81(3), pp.271–272.

Kelmer, G., Stone, A.H., Turcotte, J. & King, P.J., (2021) Reasons for Revision: Primary Total Hip Arthroplasty Mechanisms of Failure. *The Journal of the American Academy of Orthopaedic Surgeons*, 29(2), pp.78–87.

Kennedy, D.M., Stratford, P.W., Wessel, J., Gollish, J.D. & Penney, D., (2005) Assessing stability and change of four performance measures: A longitudinal study evaluating outcome following total hip and knee arthroplasty. *BMC Musculoskeletal Disorders*, 6(6). Available at: http://www.biomedcentral.com/1471-2474/6/3 [Accessed May 22, 2018].

Khan, S.K., Malviya, A., Muller, S.D., Carluke, I., Partington, P.F., Emmerson, K.P. & Reed, M.R., (2014) Reduced short-term complications and mortality following Enhanced Recovery primary hip and knee arthroplasty: results from 6,000 consecutive procedures. *Acta orthopaedica*, 85(1), pp.26–31. Available at:

http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3940988&tool=pmcentrez&rendertype=abstract.

Kimmel, L.A., Elliott, J.E., Sayer, J.M. & Holland, A.E., (2016) Assessing the Reliability and Validity of a Physical Therapy Functional Measurement Tool-the Modified Iowa Level of Assistance Scale-in Acute Hospital Inpatients. *Physical therapy*, 96, pp.176–182. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26045603.

Klapwijk, L.C.M., Mathijssen, N.M.C., Van Egmond, J.C., Verbeek, B.M. & Vehmeijer, S.B.W., (2017) The first 6 weeks of recovery after primary total hip arthroplasty with fast track: A diary study of 94 patients. *Acta Orthopaedica*, 88(2), pp.140–144.

Klein, G.R., Posner, J.M., Levine, H.B. & Hartzband, M.A., (2017) Same Day Total Hip Arthroplasty Performed at an Ambulatory Surgical Center: 90-Day Complication Rate on 549 Patients. *Journal of Arthroplasty*, 32(4), pp.1103–1106. Available at: http://dx.doi.org/10.1016/j.arth.2016.10.013. [Accessed February 21, 2018].

Krenk, L., Kehlet, H., Hansen, T.B., Solgaard, S., Soballe, K. & Rasmussen, L.S., (2014) Cognitive dysfunction after fast-track hip and knee replacement. *Anesthesia and Analgesia*, 118(5), pp.1034–1040.

Krenk, L., Rasmussen, L.S. & Kehlet, H., (2012) Delirium in the fast-track surgery setting. *Best Practice and Research: Clinical Anaesthesiology*, 26(3), pp.345–353. Available at: http://dx.doi.org/10.1016/j.bpa.2012.07.004.

Krenzel, B.A., Cook, C., Martin, G.N., Vail, T.P., Attarian, D.E. & Bolognesi, M.P., (2009) Posterior Capsular Injections of Ropivacaine During Total Knee Arthroplasty: A Randomized, Double-Blind, Placebo-Controlled Study. *Journal of Arthroplasty*, 24(6 SUPPL.), pp.138–143. Available at: https://pubmed.ncbi.nlm.nih.gov/19520544/ [Accessed February 25, 2021].

Kulinskaya, E., Kornbrot, D. & Gao, H., (2005) Length of stay as a performance indicator: Robust statistical methodology. *IMA Journal of Management Mathematics*, 16(4), pp.369–381.

Lane Clark & Peacock, (2022) NHS Waiting List Tracker. Available at: https://nhswaitlist.lcp.uk.com/ [Accessed July 25, 2022].

Larsen, J.R., Skovgaard, B., Prynø, T., Bendikas, L., Mikkelsen, L.R., Laursen, M., Høybye, M.T., Mikkelsen, S. & Jørgensen, L., (2017) Feasibility of day-case total hip arthroplasty: A single-centre observational study. *HIP International*, 27(1), pp.60–65. Available at:

http://journals.sagepub.com/doi/pdf/10.5301/hipint.5000421 [Accessed February 21, 2018].

Larsen, K., Sørensen, O.G., Hansen, T.B., Thomsen, P.B. & Søballe, K., (2008) Accelerated perioperative care and rehabilitation intervention for hip and knee replacement is effective: a randomized clinical trial involving 87 patients with 3 months of follow-up. *Acta orthopaedica*, 79(2), pp.149–59. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18478482.

Larsen, K., (2009) Cost-Effectiveness of Accelerated Perioperative Care and Rehabilitation After Total Hip and Knee Arthroplasty. *The Journal of Bone and Joint Surgery (American)*, 91(4), p.761. Available at: http://www.of-aarhus.dk/files/Filer/Kristian Larsens phd.pdf.

Larsen, K., Hansen, T.B. & Søballe, K., (2008) Hip arthroplasty patients benefit from accelerated perioperative care and rehabilitation: a quasi-experimental study of 98 patients. *Acta orthopaedica*, 79(5), pp.624–630.

Lees, L., (2011) Factors to consider in designing a patient satisfaction survey. *Nursing Management*.

Lenssen, A.F., Crijns, Y.H.F., Waltjé, E.M.H., van Steyn, M.J.A., Geesink, R.J.T., van den Brandt, P.A. & de Bie, R.A., (2006) Efficiency of immediate postoperative inpatient physical therapy following total knee arthroplasty: an RCT. *BMC musculoskeletal disorders*, 7, p.71.

Liao, K.-M. & Lu, H.-Y., (2016) A National Analysis of Complications Following Total Hip Replacement in Patients With Chronic Obstructive Pulmonary Disease. *Medicine*, 95(12), p.e3182. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4998405/pdf/medi-95-e3182.pdf [Accessed April 27, 2018].

Luksameearunothai, K., Chaudhry, Y., Thamyongkit, S., Jia, X. & Hasenboehler, E.A., (2020) Assessing the level of evidence in the orthopaedic literature, 2013-2018: A review of 3449 articles in leading orthopaedic journals. *Patient Safety in Surgery*, 14(1). Available at: https://doi.org/10.1186/s13037-020-00246-6 [Accessed September 2, 2022].

Machin, D., Campbell, M. & Tan, S.-B., (2009) *Sample Size Tables for Clinical Studies* 3rd ed., Chichester, West Sussex: Wiley-Blackwell.

Maltby, J., Williams, G.A., McGarry, J. & Day, L., (2014) *Research methods for nursing and healthcare* 1st ed., Taylor & Francis.

Malviya, A., Martin, K., Harper, I., Muller, S.D., Emmerson, K.P., Partington, P.F. & Reed, M.R.,

(2011) Enhanced recovery program for hip and knee replacement reduces death rate. *Acta Orthopaedica*, 82(5), pp.577–581.

Mariorenzi, M., Levins, J., Marcaccio, S., Orfanos, A. & Cohen, E., (2020) Outpatient Total Joint Arthroplasty: A Review of the Current Stance and Future Direction. *Rhode Island medical journal (2013)*, 103(3), pp.63–67.

McCulloch, R., Cottingham, P., Chrismas, B. & Pearce, O., (2017) Is It Time We Changed How We Measure Length of Stay for Hip and Knee Arthroplasty? *JAAOS: Global Research and Reviews*, 1(6), p.e032.

McGuinness, L.A. & Higgins, J.P.T., (2021) Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. In *Research Synthesis Methods*. John Wiley and Sons Ltd, pp. 55–61.

Mehta, B.Y., Bass, A.R., Goto, R., Russell, L.A., Parks, M.L., Figgie, M.P. & Goodman, S.M., (2018) Disparities in outcomes for blacks versus whites undergoing total hip arthroplasty: A systematic literature review. *Journal of Rheumatology*, 45(5), pp.717–722. Available at: www.jrheum.org [Accessed January 26, 2023].

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., Altman, D., Antes, G., Atkins, D., Barbour, V., Barrowman, N., Berlin, J.A., Clark, J., Clarke, M., Cook, D., D'Amico, R., Deeks, J.J., Devereaux, P.J., Dickersin, K., Egger, M., Ernst, E., Gøtzsche, P.C., Grimshaw, J., Guyatt, G., Higgins, J., Ioannidis, J.P.A., Kleijnen, J., Lang, T., Magrini, N., McNamee, D., Moja, L., Mulrow, C., Napoli, M., Oxman, A., Pham, B., Rennie, D., Sampson, M., Schulz, K.F., Shekelle, P.G., Tovey, D. & Tugwell, P., (2009) Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine*, 6(7). Available at: http://www.prisma-statement. [Accessed September 14, 2020].

Monaghan, T.F., Agudelo, C.W., Rahman, S.N., Wein, A.J., Lazar, J.M., Everaert, K. & Dmochowski, R.R., (2021) Blinding in clinical trials: Seeing the big picture. *Medicina (Lithuania)*, 57(7), pp.1–13.

Nassar, I., Fahey, J. & Mitchell, D., (2020) Rapid recovery following hip and knee arthroplasty using local infiltration analgesia: length of stay, rehabilitation protocol and cost savings. *ANZ Journal of Surgery*, 90(3), pp.355–359. Available at: https://onlinelibrary.wiley.com/doi/abs/10.1111/ans.15663 [Accessed May 15, 2020].

National Institute for Health and Care Excellence, (2015) Venous thromboembolic diseases : diagnosis , management and thrombophilia testing. *NICE Guideline*, (November), pp.12–15.

National Institute for Health Research. Centre for Engagement and Dissemination, (2021) *Briefing notes for researchers - public involvement in NHS, health and social care research*, Available at: https://www.nihr.ac.uk/documents/briefing-notes-for-researchers-public-involvement-in-nhs-health-and-social-care-research/27371 [Accessed May 9, 2022].

National Institute for Health Research, (2016) NIHR Glossary. *NETSCC*. Available at: http://www.nets.nihr.ac.uk/glossary?result_1655_result_page=P [Accessed October 27, 2016].

National Joint Registry, (2014) National Joint Registry. *National Joint Registry Reports*. Available at: http://www.njrreports.org.uk/hips-all-procedures-activity/H03v2NJR [Accessed May 6, 2014].

National Joint Registry for England, Wales, N.I. and the I. of M., (2017) Hip replacement edition - PUBLIC AND PATIENT GUIDE. *National Joint Registry*. Available at: http://www.njrcentre.org.uk/njrcentre/Portals/0/Documents/England/PPG/09736 NJR PPG - HIPS 2018 WEB SPREADS.pdf?ver=2018-02-08-112731-437 [Accessed May 1, 2018].

NHS, (2011) NHS Patient Experience Framework. *Department of Health*, (17273), p.17273. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/215159/dh_132788.pdf.

NHS England, (2020) Patient Profile - NHS Digital. *NHS Digital*. Available at: https://digital.nhs.uk/data-and-information/publications/statistical/patient-reported-outcome-measures-proms/finalised-hip--knee-replacements-april-2018---march-2019/patient-profile [Accessed July 25, 2022].

NHS Improvement, (2018) Reference costs 2017/18:highlights, analysis and introduction to the data. , (November). Available at: https://improvement.nhs.uk/documents/1972/1_-_Reference_costs_201718.pdf.

NICE, (2015) Blood transfusion. *NICE Guideline*, (November).

NICE, (2012) Methods for the development of NICE public health guidance. Algorithm for classifying quantitative (experimental and observational) study designs. , p.Appendix E. Available at: https://www.nice.org.uk/article/PMG4/chapter/Appendix-E-Algorithm-for-

classifying-quantitative-experimental-and-observational-study-designs [Accessed September 15, 2020].

NICE, (2014) Total hip replacement and resurfacing arthroplasty for end-stage arthritis of the hip. *NICE Technology Appraisal Guidance [TA304]*. Available at: https://www.nice.org.uk/guidance/ta304/resources [Accessed November 15, 2015].

Nilsdotter, A.K., Lohmander, L.S., Klässbo, M. & Roos, E.M., (2003) Hip disability and osteoarthritis outcome score (HOOS) - Validity and responsiveness in total hip replacement. *BMC Musculoskeletal Disorders*, 4, pp.1–8. Available at: https://bmcmusculoskeletdisord.biomedcentral.com/track/pdf/10.1186/1471-2474-4-10 [Accessed April 18, 2018].

njrcentre.org.uk, (2022) NJR Stats Online. *National Joint Registry*. Available at: https://surgeonprofile.njrcentre.org.uk/Home/StatsIndex [Accessed July 25, 2022].

O'Brien, S., Ogonda, L., Dennison, J., Doran, E., Lawlor, M., Humphreys, P., Kelly, M., Matthews, L. & Beverland, D., (2005) Day two post operative "fast-track" discharge following primary total hip replacement. *Journal of Orthopaedic Nursing*, 9(3), pp.140–145. Available at: http://login.ezproxy.library.ualberta.ca/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=rzh&AN=2009048768&site=ehost-live&scope=site.

Offredy, M. & Vickers, P., (2010) *Developing a Healthcare Research Proposal : An Interactive Student Guide*, Chichester, West Sussex: Wiley-Blackwell.

Okamoto, T., Ridley, R.J., Edmondston, S.J., Visser, M., Headford, J. & Yates, P.J., (2016) Day-of-Surgery Mobilization Reduces the Length of Stay After Elective Hip Arthroplasty. *Journal of Arthroplasty*, 31(10), pp.2227–2230. Available at: https://www.clinicalkey.com/service/content/pdf/watermarked/1-s2.0-S0883540316300481.pdf?locale=en_US [Accessed February 21, 2018].

Patel, V.P., Walsh, M., Sehgal, B., Preston, C., DeWal, H. & Di Cesare, P.E., (2007) Factors associated with prolonged wound drainage after primary total hip and knee arthroplasty. *Journal of Bone and Joint Surgery - Series A*.

Peat, J. & Barton, B., (2014) *Medical Statistics - A Giude to SPSS, Data Analysis and Critical Appraisal* 2nd ed., Chichester, West Sussex: John Wiley & Sons.

Petersen, M.K., Andersen, N.T. & Søballe, K., (2008) Self-reported functional outcome after

primary total hip replacement treated with two different perioperative regimes: a follow-up study involving 61 patients. *Acta orthopaedica*, 79(2), pp.160–167.

Petticrew, M. & Roberts, H., (2003) Evidence, hierarchies, and typologies: horses for courses. *Journal of epidemiology and community health*, 57(7), pp.527–529.

Phillips, R., Hazell, L., Sauzet, O. & Cornelius, V., (2019) Analysis and reporting of adverse events in randomised controlled trials: a review. *BMJ open*, 9(2), p.e024537. Available at: /pmc/articles/PMC6398660/ [Accessed July 26, 2022].

Phillips, S.J., (2000) Physiology of wound healing and surgical wound care. *ASAIO Journal*, 46(6), pp.2–5.

Pitter, F.T., Jørgensen, C.C., Lindberg-Larsen, M. & Kehlet, H., (2016) Postoperative morbidity and discharge destinations after fast-track hip and knee arthroplasty in patients older than 85 years. *Anesthesia and Analgesia*, 122(6), pp.1807–1815.

Pollock, M., Somerville, L., Firth, A. & Lanting, B., (2016) Outpatient Total Hip Arthroplasty, Total Knee Arthroplasty, and Unicompartmental Knee Arthroplasty. *JBJS Reviews*, 4(12), p.1. Available at: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=01874474-201612000-00004.

Popay, J., Roberts, H. & Sowden, A., (2006) Guidance on the Conduct of Narrative Synthesis in Systematic Reviews A Product from the ESRC Methods Programme. *ESRC Methods Programme*.

Purves, D., Augustine, G.J., Fitzpatrick, D., Hall, W.C., LaMantia, A.-S. & White, L.E., (2001) Physiological Changes Associated with Emotion - Neuroscience - NCBI Bookshelf. In *Neuroscience*. Sinauer Associates Inc. Available at: https://www.ncbi.nlm.nih.gov/books/NBK10829/ [Accessed May 9, 2022].

QSR International Pty Ltd, (2015) Nvivo 11 for Windows. *NVivo qualitative data analysis Software*.

Quintana, J.M., Escobar, A., Bilbao, A., Arostegui, I., Lafuente, I. & Vidaurreta, I., (2005) Responsiveness and clinically important differences for the WOMAC and SF-36 after hip joint replacement. *Osteoarthritis and Cartilage*, 13(12), pp.1076–1083. Available at: https://www.oarsijournal.com/article/S1063-4584(05)00178-0/pdf [Accessed May 22, 2018].

R Core Team, (2021) R: A Language for Statistical Computing. Available at: https://www.r-

project.org/.

Raphael, M., Jaeger, M. & van Vlymen, J., (2011) Easily adoptable total joint arthroplasty program allows discharge home in two days. *Canadian journal of anaesthesia = Journal canadien d'anesthésie*, 58(10), pp.902–10. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21822756.

Reay, P.A., Horner, B. & Duggan, R., (2015) The patient's experience of early discharge following total hip replacement. *International Journal of Orthopaedic and Trauma Nursing*, 19, pp.131–139.

Richards, S.H., Peters, T.J., Coast, J., Gunnell, D.J., Darlow, M.A. & Pounsford, J., (2000) Inter-rater reliability of the Barthel ADL Index: How does a researcher compare to a nurse? *Clinical Rehabilitation*, 14(1), pp.72–78.

Richardson, S., (1991) The Timed "Up & Go": A Test of Basic Functional Mobility for Frail Elderly Persons. *Journal of the American Geriatrics Society*, 39(2), pp.142–148. Available at: http://doi.wiley.com/10.1111/j.1532-5415.1991.tb01616.x [Accessed May 22, 2018].

Robbins, C.E., Casey, D., Bono, J. V, Murphy, S.B., Talmo, C.T. & Ward, D.M., (2014) A multidisciplinary total hip arthroplasty protocol with accelerated postoperative rehabilitation: does the patient benefit? *American journal of orthopedics (Belle Mead, N.J.)*, 43(4), pp.178–181. Available at: www.amjorthopedics.com.

Roberts, C. & Torgerson, D.J., (1999) Understanding controlled trials. Baseline imbalance in randomised controlled trials. *British Medical Journal*, 318(7203), p.185. Available at: /pmc/articles/PMC1116277/ [Accessed September 6, 2022].

Roos, E.M., Roos, H.P., Lohmander, L.S., Ekdahl, C. & Beynnon, B.D., (1998) Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *The Journal of orthopaedic and sports physical therapy*, 28(2), pp.88–96.

Rosas, S., Sabeh, K.G., Buller, L.T., Law, T. yee, Roche, M.W. & Hernandez, V.H., (2017) Medical Comorbidities Impact the Episode-of-Care Reimbursements of Total Hip Arthroplasty. *Journal of Arthroplasty*, 32(7), pp.2082–2087. Available at: https://www.clinicalkey.com/service/content/pdf/watermarked/1-s2.0-S0883540317301572.pdf?locale=en_US [Accessed April 27, 2018].

Rowlands, G., (2013) The Information Standard Workshop Understanding Health Literacy – best

practice in developing and testing health and care information Resources and useful information. *The Information Standard*, (October), pp.1–6. Available at: https://www.england.nhs.uk/wp-content/uploads/2017/02/tis-standard-health-literacy-wrkshp-handout-101013.pdf [Accessed January 9, 2018].

Rstudio, T., (2020) RStudio: Integrated Development for R. *Rstudio Team, PBC, Boston, MA URL http://www.rstudio.com/*.

Sabirli, F., Paker, N. & Bugdayci, D., (2013) The relationship between Knee Injury and Osteoarthritis Outcome Score (KOOS) and Timed Up and Go test in patients with symptomatic knee osteoarthritis. *Rheumatology International*, 33(10), pp.2691–2694. Available at: https://link.springer.com/content/pdf/10.1007%2Fs00296-012-2512-3.pdf [Accessed May 22, 2018].

Sahraoui, A. & Elarref, M., (2014) Bed crisis and elective surgery late cancellations: An approach using the theory of constraints. *Qatar Medical Journal*, 2014(1), p.1. Available at: /pmc/articles/PMC4197367/ [Accessed September 3, 2022].

Sahu, A., Kumar, K.S., Krishna, S.R. & Madhavi, K., (2018) Influence of Early Physiotherapy Intervention on Pain , Joint Range of Motion and Quality of Life in Unilateral Hip Joint Replacement Surgery. *Indian Journal of Physiotherapy and Occupational Therapy*, 12(1), pp.30–34.

Saleh, K., Olson, M., Resig, S., Bershadsky, B., Kuskowski, M., Gioe, T., Robinson, H., Schmidt, R. & McElfresh, E., (2002) Predictors of wound infection in hip and knee joint replacement: Results from a 20 year surveillance program. *Journal of Orthopaedic Research*, 20(3), pp.506–515.

Savaridas, T., Serrano-Pedraza, I., Khan, S.K., Martin, K., Malviya, A. & Reed, M.R., (2013) Reduced medium-term mortality following primary total hip and knee arthroplasty with an enhanced recovery program. A study of 4,500 consecutive procedures. *Acta orthopaedica*, 84(1), pp.40–3. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3584601&tool=pmcentrez&rendertype=abstract.

Schneider, M., Kawahara, I., Ballantyne, G., McAuley, C., MacGregor, K., Garvie, R., McKenzie, A., MacDonald, D. & Breusch, S.J., (2009) Predictive factors influencing fast track rehabilitation following primary total hip and knee arthroplasty. *Archives of Orthopaedic and Trauma Surgery*, 129(12), pp.1585–1591.

Schulz, K.F., Altman, D.C. & Moher, D., (2010) CONSORT 2010 Statement: Updated guidelines for reporting parallel group randomised trials. *Italian Journal of Public Health*.

Shahi, A., Boe, R., Bullock, M., Hoedt, C., Fayyad, A., Miller, L. & Oliashirazi, A., (2019a) The risk factors and an evidence-based protocol for the management of persistent wound drainage after total hip and knee arthroplasty. *Arthroplasty Today*, 5(3), pp.329–333. Available at: https://doi.org/10.1016/j.artd.2019.05.003.

Shahi, A., Boe, R., Bullock, M., Hoedt, C., Fayyad, A., Miller, L. & Oliashirazi, A., (2019b) The risk factors and an evidence-based protocol for the management of persistent wound drainage after total hip and knee arthroplasty. *Arthroplasty Today*, 5(3), pp.329–333.

Sharma, V., Morgan, P.M. & Cheng, E.Y., (2009) Factors influencing early rehabilitation after tha: A systematic review. *Clinical Orthopaedics and Related Research*, 467(6), pp.1400–1411.

Shields, R.K., Enloe, L J, Evans, R.E., Smith, K.B. & Steckel, S.D., (1995) Reliability, validity, and responsiveness of functional tests in patients with total joint replacement. *Physical therapy*, 75(3), pp.169–176; discussion 176-179.

Shields, R.K., Enloe, Lori J, Evans, R.E., Smith, K.B. & Steckel, S.D., (1995) Reliability, validity, and responsiveness of functional tests in patients with total joint replacement. *Physical therapy*, 75(3), pp.169–176; discussion 176-179. Available at: http://ptjournal.apta.org/content/75/3/169.

Sibia, U.S., MacDonald, J.H. & King, P.J., (2016) Predictors of Hospital Length of Stay in an Enhanced Recovery After Surgery Program for Primary Total Hip Arthroplasty. *Journal of Arthroplasty*, 31(10), pp.2119–2123. Available at: http://dx.doi.org/10.1016/j.arth.2016.02.060. [Accessed September 16, 2020].

Singh, J.A. & Lewallen, D.G., (2013) Medical and psychological comorbidity predicts poor pain outcomes after total knee arthroplasty. *Rheumatology (United Kingdom)*, 52(5), pp.916–923. Available at: https://watermark.silverchair.com/kes402.pdf?token=AQECAHi208BE49Ooan9kkhW_Ercy7Dm3ZL_9Cf3qfKAc485ysgAAAbkwggG1BgkqhkiG9w0BBwagggGmMIIBogIBADCCAZsGCSqGSIb3DQEHATAeBglghkgBZQMEAS4wEQQMfSlgI6K61wp0qFFmAgEQgIIBbCL9hRJZP4xcy_B1FgWG9tp2YMYx8c3JKtZ6CrwTgX337PA5 [Accessed April 27, 2018].

Sjøveian, A.K.H. & Leegaard, M., (2017) Hip and knee arthroplasty - patient's experiences of pain

and rehabilitation after discharge from hospital. *International Journal of Orthopaedic and Trauma Nursing*, 27, pp.28–35. Available at: https://doi.org/10.1016/j.ijotn.2017.07.001.

Skivington, K., Matthews, L., Simpson, S.A., Craig, P., Baird, J., Blazeby, J.M., Boyd, K.A., Craig, N., French, D.P., McIntosh, E., Petticrew, M., Rycroft-Malone, J., White, M. & Moore, L., (2021) A new framework for developing and evaluating complex interventions: Update of Medical Research Council guidance. *The BMJ*, 374. Available at: http://dx.doi.org/10.1136/bmj.n2061 [Accessed September 19, 2022].

Smith, T.O., McCabe, C., Lister, S., Christie, S.P. & Cross, J., (2012) Rehabilitation implications during the development of the Norwich Enhanced Recovery Programme (NERP) for patients following total knee and total hip arthroplasty. *Orthopaedics and Traumatology: Surgery and Research*, 98(5), pp.499–505. Available at: http://dx.doi.org/10.1016/j.otsr.2012.03.005.

Specht, K., Kjaersgaard-Andersen, P., Kehlet, H. & Pedersen, B.D., (2015) Nursing in fast-track total hip and knee arthroplasty: A retrospective study. *International Journal of Orthopaedic and Trauma Nursing*, 19(3), pp.121–130. Available at: http://linkinghub.elsevier.com/retrieve/pii/S1878124114000823.

Stambough, J.B., Beaule, P.E., Nunley, R.M. & Clohisy, J., (2016) Contemporary Strategies for Rapid Recovery Total Hip Arthroplasty. *Instructional course lectures*, 65(March), pp.211–224.

Stambough, J.B., Nunley, R.M., Curry, M.C., Steger-May, K. & Clohisy, J.C., (2015) Rapid recovery protocols for primary total hip arthroplasty can safely reduce length of stay without increasing readmissions. *J Arthroplasty*, 30(4), pp.521–526. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25683296.

Statista, (2022) Total Healthcare expenditure as a share of GDP in the United Kingdom from 1980-2021. *Statista Website*. Available at: https://www.statista.com/statistics/317708/healthcare-expenditure-as-a-share-of-gdp-in-the-united-kingdom/ [Accessed August 23, 2022].

Steffen TM, Hacker TA, M.L., (2002) Age-and gender-related test performance in community-dwelling elderly people: Six-minute walk test, Berg balance scale, timed up & go test, and gait speeds. *Physical Therapy*, 82(2), pp.128–137. Available at: https://academic.oup.com/ptj/article-abstract/82/2/128/2836941 [Accessed May 22, 2018].

Sterne, J.A., Hernán, M.A., Reeves, B.C., Savović, J., Berkman, N.D., Viswanathan, M., Henry, D., Altman, D.G., Ansari, M.T., Boutron, I., Carpenter, J.R., Chan, A.W., Churchill, R., Deeks, J.J., Hróbjartsson, A., Kirkham, J., Jüni, P., Loke, Y.K., Pigott, T.D., Ramsay, C.R., Regidor, D.,

Rothstein, H.R., Sandhu, L., Santaguida, P.L., Schünemann, H.J., Shea, B., Shrier, I., Tugwell, P., Turner, L., Valentine, J.C., Waddington, H., Waters, E., Wells, G.A., Whiting, P.F. & Higgins, J.P., (2016) ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. *BMJ (Online)*, 355. Available at: /pmc/articles/PMC5062054/?report=abstract [Accessed September 15, 2020].

Sterne, J.A.C., Savović, J., Page, M.J., Elbers, R.G., Blencowe, N.S., Boutron, I., Cates, C.J., Cheng, H.Y., Corbett, M.S., Eldridge, S.M., Emberson, J.R., Hernán, M.A., Hopewell, S., Hróbjartsson, A., Junqueira, D.R., Jüni, P., Kirkham, J.J., Lasserson, T., Li, T., McAleenan, A., Reeves, B.C., Shepperd, S., Shrier, I., Stewart, L.A., Tilling, K., White, I.R., Whiting, P.F. & Higgins, J.P.T., (2019) RoB 2: A revised tool for assessing risk of bias in randomised trials. *The BMJ*, 366. Available at: http://dx.doi.org/10.1136/bmj.l4898http://www.bmj.com/.

Stewart, S.P., (2012) Joint Replacement and Rapid Mobilization. *Orthopaedic Nursing*, 31(4), pp.224–229.

Talsma, A.K., Lingsma, H.F., Steyerberg, E.W., Wijnhoven, B.P.L. & Van Lanschot, J.J.B., (2014) The 30-day versus in-hospital and 90-day mortality after esophagectomy as indicators for quality of care. *Annals of Surgery*, 260(2), pp.267–273.

Taurchini, M., Del Naja, C. & Tancredi, A., (2018) Enhanced Recovery After Surgery: a patient centered process. *Journal of Visualized Surgery*, 4, pp.40–40.

Tayrose, G., Newman, D., Slover, J., Jaffe, F., Hunter, T. & Bosco, J., (2013) Rapid mobilization decreases length-of-stay in joint replacement patients. *Bulletin of the NYU Hospital for Joint Diseases*, 71(3), pp.222–226.

Temporiti, F., Draghici, I., Fusi, S., Traverso, F., Ruggeri, R., Grappiolo, G. & Gatti, R., (2020) Does walking the day of total hip arthroplasty speed up functional independence? A non-randomized controlled study. *Archives of Physiotherapy*, 10(1). Available at: https://doi.org/10.1186/s40945-020-00079-7 [Accessed May 15, 2020].

Thabane, L., Ma, J., Chu, R., Cheng, J., Ismaila, A., Rios, L.P., Robson, R., Thabane, M., Giangregorio, L. & Goldsmith, C.H., (2010) A tutorial on pilot studies: the what, why and how. *BMC Med Res Methodol*, 10(August 2016), p.1. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20053272.

The Cochrane Collaboration, (2008) *Cochrane Handbook for Systematic Reviews of Interventions*

1st ed. J. P. T. Higgins & S. Green, eds., Chichester, West Sussex: The Cochrane Collaboration and John Wiley & Sons Ltd.

Tickle-Degnen, L., (2013) Nuts and bolts of conducting feasibility studies. In *American Journal of Occupational Therapy*.

Tombs, M. & Pugsley, L., (2020) Medical Education @ Cardiff 2020 Understand Research Philosophies and Paradigms in Medical Education Why Focus on Philosophy and Paradigms? *Medical Education Cardiff*. Available at: www.cardiff.ac.uk/medicaleducation [Accessed September 23, 2021].

Turner, J.H., (2001) Positivism: Sociological. In *International Encyclopedia of the Social & Behavioral Sciences*. Pergamon, pp. 11827–11831.

UK Public Involvement Standards Deveopment Partnership, (2019) UK Standards for Public Involvement. *Nihr*, p.12. Available at: https://sites.google.com/nihr.ac.uk/pi-standards/standards [Accessed January 25, 2022].

Versus Arthritis, (2019) The state of musculoskeletal health 2019. *Versus Arthritis*, 91(5), pp.31–32.

Versus Arthritis, (2021) The State of Musculoskeletal Health 2021. *Versus Arthritis*. Available at: www.versusarthritis.org [Accessed August 23, 2022].

Vesterby, M.S., Pedersen, P.U., Laursen, M., Mikkelsen, S., Larsen, J., Søballe, K. & Jørgensen, L.B., (2017) Telemedicine support shortens length of stay after fast-track hip replacement: A randomized controlled trial. *Acta Orthopaedica*, 88(1), pp.41–47.

Voleti, P.B., Donegan, D.J., Baldwin, K.D. & Lee, G.C., (2012) Level of evidence of presentations at american academy of orthopaedic surgeons annual meetings. *Journal of Bone and Joint Surgery*, 94(8), pp.1–5.

Von-Elm, E., Altman, D.G., Egger, M., Pocock, S.J., Gøtzsche, P.C. & Vandenbroucke, J.P., (2008) Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Journal of Clinical Epidemiology*, 61(4), pp.344–349.

Wadhwa, M. & Cook, T.D., (2019) The Set of Assumptions Randomized Control Trials Make and Their Implications for the Role of Such Experiments in Evidence-Based Child and Adolescent Development Research. *New Directions for Child and Adolescent Development*, 2019(167), pp.17–37.

Wainwright, T., McDonald, D. & Burgess, L., (2017) The role of physiotherapy in Enhanced Recovery after Surgery in the intensive care unit. *ICU Management & Practice*, 17(3), pp.1–6. Available at: http://eprints.bournemouth.ac.uk/29715/3/ICU Management %281%29.pdf [Accessed January 23, 2023].

Walters, S.J., Dos Anjos Henriques-Cadby, I.B., Bortolami, O., Flight, L., Hind, D., Jacques, R.M., Knox, C., Nadin, B., Rothwell, J., Surtees, M. & Julious, S.A., (2017) Recruitment and retention of participants in randomised controlled trials: A review of trials funded and published by the United Kingdom Health Technology Assessment Programme. *BMJ Open*, 7(3), pp.1–10.

Wang, Y.C., McPherson, K., Marsh, T., Gortmaker, S.L. & Brown, M., (2011) Health and economic burden of the projected obesity trends in the USA and the UK. *The Lancet*, 378(9793), pp.815–825. Available at: http://dx.doi.org/10.1016/S0140-6736(11)60814-3.

Wellman, S.S., Murphy, A.C., Gulcynski, D. & Murphy, S.B., (2011) Implementation of an accelerated mobilization protocol following primary total hip arthroplasty: impact on length of stay and disposition. *Current reviews in musculoskeletal medicine*, 4(3), pp.84–90. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3261249&tool=pmcentrez&rendertype=abstract.

White, R.H., Romano, P.S., Zhou, H., Rodrigo, J. & Bargar, W., (1998) Incidence and time course of thromboembolic outcomes following total hip or knee arthroplasty. *Archives of internal medicine*, 158(14), pp.1525–31. Available at: https://pdfs.semanticscholar.org/53f4/fe05cb2828a734753897561c071ead94f5eb.pdf [Accessed April 27, 2018].

Whitehouse, S., Crawford, R. & Learmonth, I., (2008) Validation for the Reduced Western Ontario and McMaster Universities Osteoarthritis Index Function Scale. *Journal of Orthopaedic Surgery*, 16(1), pp.50–53. Available at: http://journals.sagepub.com/doi/pdf/10.1177/230949900801600113 [Accessed May 22, 2018].

Wright, A.A., Cook, C.E., Baxter, G.D., Dockerty, J.D. & Abbott, J.H., (2011) A Comparison of 3 Methodological Approaches to Defining Major Clinically Important Improvement of 4 Performance Measures in Patients With Hip Osteoarthritis. *Journal of Orthopaedic & Sports Physical Therapy*, 41(5), pp.319–327. Available at:

http://www.jospt.org/doi/10.2519/jospt.2011.3515.

Wylde, V., Rooker, J., Halliday, L. & Blom, A., (2011) Acute postoperative pain at rest after hip and knee arthroplasty: Severity, sensory qualities and impact on sleep. *Orthopaedics and Traumatology: Surgery and Research*, 97(2), pp.139–144.

Yager, M. & Stichler, J., (2015) The Effect of Early Ambulation on Patient Outcomes for Total Joint Replacement. *Orthopaedic Nursing*, 34(4), pp.201–202. Available at: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00006416-201507000-00008.

Zhu, Y., Zhang, F., Chen, W., Liu, S., Zhang, Q. & Zhang, Y., (2015a) Risk factors for periprosthetic joint infection after total joint arthroplasty: A systematic review and meta-analysis. *Journal of Hospital Infection*.

Zhu, Y., Zhang, F., Chen, W., Liu, S., Zhang, Q. & Zhang, Y., (2015b) Risk factors for periprosthetic joint infection after total joint arthroplasty: A systematic review and meta-analysis. *Journal of Hospital Infection*, 89(2), pp.82–89. Available at: http://dx.doi.org/10.1016/j.jhin.2014.10.008.

Zimmer.Inc, (2006) CPT ® 12/14 Hip System. *Zimmer.Inc Product Brochure*. Available at: http://www.zimmer.co.uk/medical-professionals/products/hip/cpt-hipsystem.html.