Biomechanical Effects of Manual Therapy in Patients with Acute Non-specific Low Back Pain – A Feasibility Study

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Abstract

Background:
The cause of non-specific low back pain (NSLBP) is unclear; however, mechanical factors are thought to contribute to pain and dysfunction. Manual therapy is a commonly sought treatment for NSLBP and has been demonstrated to be effective in reducing pain and disability, however, some patients respond to manual therapy and others do not.
This study aimed to explore the feasibility of conducting a full-scale trial investigating the biomechanical effects of manual therapy. Much of the study was carried out during the Covid-19 pandemic, as such a parallel study was conducted to explore feasibility pre-Covid-19 and within the Covid-19 era.
Secondary aims included exploring whether lumbar intervertebral motion changed following a course of manual therapy; and whether those who responded to manual therapy have different intervertebral motion to those who did not.
Methods:
A Public and Patient Involvement Process assisted in finalising the trial method and development of the trial material, particularly the Home Management Booklet.
Sixteen participants with acute NSLBP were recruited from the AECC University College Clinic to the two-armed randomised controlled trial which consisted of a group who received manual therapy and home advice and a group who only received home advice. The home advice consisted of a Home Management Booklet containing information on analgesia, hot and cold packs, and postural advice. Manual therapy consisted of spinal manipulative therapy, mobilisation, and soft tissue therapy. Baseline and follow up measurements included weight bearing and recumbent flexion and extension quantitative fluoroscopy sequences. Continuous intervertebral motion variables included range of motion, disc height, translation, initial attainment rate, motion sharing inequality and variability. Patient Reported Outcomes Measures of Bournemouth Questionnaire and Roland Morris Disability Index-24 were obtained at baseline and follow up to determine responders (at least a minimal clinically important change) and non-responders to manual therapy.
The parallel study collected retrospective data from outpatient clinic files to match new patients presented against the trial's inclusion/ exclusion criteria both pre-Covid-19 and within the Covid-19 era to calculate number of patients who would have been eligible for the trial. The feasibility of a full-scale study was assessed utilising the recruitment and retention data. Sample size for a future full-scale study was calculated.
Results:
Pre-Covid-19, 9.8% (n=100), and within Covid-19 10.8% (n=59), of low back pain patients would have been eligible for the trial. During the trial, 45 patents were eligible for the trial, of the 28 patients approached, 16 (57%) consented onto the trial. One out of the eight participants in the non-manual therapy group withdrew due to Covid-19, there were no withdrawals in the manual therapy group.
Sample size calculated for investigating all biomechanical variables in a future full-scale trial was 83115 participants; for investigating motion share inequality and variability only was 328 participants.
Conclusion:
A full-scale trial investigating all possible quantitative fluoroscopy intervertebral motion variables is not feasible. Should only motion sharing inequality and variability be utilised a full-scale trial may be feasible as a multi-researcher, multi-site trial, with the addition of additional recruitment centres.

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Dedication

My Husband, George

I cannot begin to express my unfailing gratitude and love. Thank you for your constant support and encouragement throughout my degree. You have my whole heart for my whole life.

My 'working from home' office mates, Scrumpy, Ralph and Toggle

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Content from this thesis has been published and presented at conferences as follows:

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- World Federation of Chiropractic Conference. 2021:
    - Poster Presentation of published work: Stakeholder Involvement in the Development of Trial Material for a Clinical Trial.

Abbreviations

Abbreviation	Meaning
_BL	Baseline measurement
_FU	Follow up Measurement
ADL	Activities of Daily Living
AE	Adverse Event
AECC UC	AECC University College
ALARP	As low as reasonably practicable
BAME	Black, Asian and minority ethnic
BBC	British Broadcast Corporation
BCA	British Chiropractic Association
BMI	Body Mass Index
BQ	Bournemouth Questionnaire
COS	Core Outcome Set
CT	Computerised Tomography
HRA	Health Research Authority
IAR	Initial Attainment Rate
ICC	Intra class correlation
IRAS	Integrated Research Application System
IV-ROM	Intervertebral range of motion
LBP	Low back pain
MCIC	Minimally Clinically Important Change
MDC	Minimal Detectable Change
MRI	Magnetic Resonance Imaging
MSI	Motion Sharing Inequality
MSV	Motion Sharing Variability
MT	Manual Therapy
NICE	National Institute for Health and Care Excellence
non-MT	Non-manual Therapy
NRS	Numerical Pain Rating Scale
NSAID	Non-steroidal Anti-Inflammatory Drug
NSLBP	Non-specific low back pain
ODI	Oswestry Disability Index

PPE	Personal Protection Equipment
PPI	Public and Patient Involvement
PROMs	Patient Reported Outcomes Measures
QF	Quantitative Fluoroscopy
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
Rec	Recumbent
RMDS-24	Roland Morris Disability Score 24
ROM	Range of Motion
SAE	Serious Adverse Event
SD	Standard Deviation
SEM	Standard Error of Measurement
SMT	Spinal Manipulative Therapy
UK	United Kingdom
VBU	Vertebral Body Units
WB	Weight Bearing
WHO	World Health Organisation
YLD	Years lived with disability

1. Introduction

1.1. Statement of the Problem

Low back pain (LBP) is the most common musculoskeletal complaint worldwide (Deyo et al. 1991; Hoy et al. 2010; Hoy et al. 2012; Maher et al. 2017). Globally, it is the leading cause of working days lost, which results in substantial economic cost (Deyo et al. 1991; Hartvigsen et al. 2018). In the UK alone, work-related lower back disorders accounted for 3.2 million working days lost in 2016 (Health and Safety Executive 2017). Equally, LBP results in a huge medical burden globally and nationally (Deyo et al. 1991; Hartvigsen et al. 2018). Consequently, it is one of the major global public health problems (Buchbinder et al. 2018).

Estimates from the Global Burden of Disease Study in 2017 (GBD 2017 SDG Collaborators 2018) suggested the global point prevalence of LBP to be 7.5%, which equates to an estimated 577.0 million people with LBP at any one time. Prevalence was higher in females than males (8.01% verses 6.94%) and increased with age, peaking at ages 80 – 89 years of age. LBP was the leading global cause of years lived with disability (YLD) and was estimated to be 64.9 million. Again, YLD was higher in females than males and peaked at 45 – 49 years of age. The prevalence of LBP has decreased slightly (not significantly), however YLD has increased (not significantly) since 1990 (GBD 2017 SDG Collaborators 2018; Wu et al. 2020). It is suggested that increasing population numbers may be influencing this increase in YLD (Wu et al. 2020). Equally, people are living longer, and aging may be coupled with pain which may result in restriction of social and physical functioning (Dionne et al. 2006). Factors such as increasing population obesity and sedentary lifestyle may be a contributing factor (Hoy et al. 2010; Hoy et al. 2012).

LBP is commonly described as pain in the lower back between the bottom of the rib cage (twelfth rib) and the buttock folds. It is defined as pain that lasts for at least one day, with or without pain referral into one or both legs (NICE 2019). It is estimated that 90 – 99% of LBP is diagnosed as non-specific low back pain (NSLBP) (Itz et al. 2013; Hartvigsen et al. 2018). A diagnosis of NSLBP simply means that the pain is unlikely to be due to a serious problem such as cancer, infection, fracture, nerve root pain or as part of more widespread inflammation (NICE 2019).

As the name implies, the specific cause of NSLBP is unclear (NICE 2019) or maybe more accurately, a symptom for which reliable identification of the pathology is not possible (Balagué et al. 2012). Various factors have been identified as possibly pain causing or influence the development of pain (Balagué et al. 2012). It is suggested that nociceptive factors play a major role in NSLBP, and pain can arise from the anatomical structures in the lumbopelvic area, such as

bones, intervertebral discs, joints, ligaments, muscles, neural structures and blood vessels (Balagué et al. 2012). Mechanical pain refers to pain caused by abnormal stress on anatomical structures causing injury and pain; or once injured, normal stress on painful anatomical structures causing an increase in pain (Kirkaldy-Willis and Bernard 1999; Panjabi 2003). It is suggested that mechanical factors, such as sitting, awkward postures, standing and walking, and manual handling, may not be singularly responsible for the development of LBP, but contributory (Roffey et al. 2010b, 2010a, 2010d, 2010c; Wai et al. 2010). However, obesity, as well as physical disuse and deconditioning (or an increase in sedentary lifestyle) have been associated with increased incidence of LBP (Shiri et al. 2010; Verbunt et al. 2010).

Equally, there are multiple mechanisms which may alter the way nociceptive information is processed which can result in enhanced pain sensitivity (hyperalgesia). These mechanisms can be either peripheral or central. Post-injury inflammation can enhance nociceptive sensitivity resulting in peripheral sensitisation, whereas centrally normally sub-threshold nociceptive information results in increased responsiveness of spinal nociceptive neurons (Latremoliere and Woolf 2009; Klyne et al. 2019). But whether this occurs in acute LBP patients remains to be seen and as such acute LBP is thought to be more mechanical in origin (Klyne et al. 2019).

According to the International Classification of Disease (ICD-11), chronic pain is defined as pain lasting more than three months (Treede et al. 2019). The definition of acute pain is less homogenous, with some indicating that acute is less than four weeks (Qaseem et al. 2017), or six weeks (van Tulder et al. 2006), with the addition of a subacute category lasting up to twelve weeks. Whereas others suggest that acute pain is less than twelve weeks, without a subcategory (Itz et al. 2013). The European Guidelines for acute NSLBP suggest that it is self-limiting for most people (90% of patients recover within the first six weeks) (van Tulder et al. 2006). Equally, National Institute for Health and Care Excellence (NICE) Referral Advice for general practitioners suggest spontaneous recovery of LBP can be expected within six weeks (NICE 2002). However, literature suggests this is not necessarily the case (Menezes Costa et al. 2012; Itz et al. 2013; Kongsted et al. 2016). In a systematic review of the clinical course of NSLBP, it is suggested that only 33% of patients spontaneously recover within the first three months (Itz et al. 2013). A potential difference in percentage of patients who spontaneously recover may be due to the difference in opinion on what ’recovery’ means. Some literature considers ’recovery’ as ’return to work’ (Andersson 1999). However, it is entirely possible that some patients returning to work may still be experiencing pain and dysfunction. Equally, some literature considers ’recovery’ as a minimal clinically important change (MCIC) in pain and dysfunction, and not necessarily a complete resolution of symptoms. Thus, due to the heterogeneity in the literature, potentially the

percentage of patients who 'recover' within the first three months lies between 90% (van Tulder et al. 2006) and 33% (Itz et al. 2013). Arguably more important is that 57% to 71% of patients still report some pain up to one year after onset (Itz et al. 2013). This highlights the importance of exploring potential causes and treatment options for acute NSLBP to reduce the chances of a person's acute pain becoming chronic.

The NICE Guidelines for the non-invasive treatment for low back pain and sciatica (NICE 2019) suggest that manual therapy be considered for managing low back pain, but only as part of a treatment package including exercise, with or without psychological therapy. Manual therapy is defined as *"any manual technique that moves one or more joints within normal ranges of motion and aims at improving joint motion or function"* (Stochkendahl et al. 2018). Most guidelines for the management of acute low back pain recommend manual therapy (Globe et al. 2016; Qaseem et al. 2017; Wong et al. 2017b; Bussieres et al. 2018; Oliveira et al. 2018; Stochkendahl et al. 2018). Exercise is recommended by two guidelines for the management of low back pain (Stochkendahl et al. 2018 and NICE 2019). While Stochkendahl et al. (2018) specifies the guideline is for the management of acute low back pain, NICE (2019) do not provide a time scale. It is suggested that supervised exercises or an exercise class is prefered (Stochkendahl et al. 2018), taking patients needs, preferences, and capabilities into account (NICE 2019). While it is recognised that exercise may be beneficial as a treatment in patients with acute low back pain, there is heterogeneity within the literature regarding evidence for the type and mode of delivery of an exercise program. Equally, there is heterogeneity in the literature regarding the effect of the different types and modes on delivery on lumbar biomechanics.

1.2. Purpose of the Study

This thesis will focus on the mechanical nature of acute NSLBP, specifically exploring biomechanical effects of manual therapy. Manual therapy has demonstrated effectiveness in some patients (Paige et al. 2017; Stochkendahl et al. 2018). Manual therapy encompasses a package of care which includes spinal manipulative therapy (SMT), mobilisation, soft tissue work (massage and stretching) and trigger point therapy (Harvey et al. 2003). SMT is recommended in most guidelines for the non-invasive management of NSLBP (Globe et al. 2016; Qaseem et al. 2017; Wong et al. 2017b; Bussières et al. 2018; Oliveira et al. 2018; Stochkendahl et al. 2018; NICE 2019). Evidence suggests that among patients with acute NSLBP, SMT is associated with moderate improvement in pain (Paige et al. 2017; Stochkendahl et al. 2018) and physical function (Paige et al. 2017). It is suggested that manual therapy can decrease spinal stiffness (Fitz et al. 2018) and/

or is intended to increase intervertebral motion (Bergmann and Petersen 2011). However, some patients respond to manual therapy, while others do not. The reason for this remains unclear.

The intervertebral effects of manual therapy have been investigated, however previous research has been largely in the area of immediate effects on mechanical models (Keller et al. 2002), animals (Funabashi et al. 2017b; Funabashi et al. 2018), or cadaveric specimens (Ianuzzi and Khalsa 2005b, 2005a). Measuring the intervertebral effects of manual therapy *in vivo* in humans, which is required to determine if intervertebral motion can be changed in patients, is challenging. Modalities such as Magnetic Resonance Imaging (MRI), computerised tomography (CT) and bi-planar x-ray studies have been found to be impractical, with poor reliability and issues with continuous motion image acquisition (Breen et al. 2012a). Fluoroscopy, however, is capable of capturing continuous spinal motion, and with less radiation than static x-ray (Mellor et al. 2014b). When fluoroscopy is coupled with semi-automated computer processing algorithms, continuous intervertebral motion variables throughout the movement can be obtained, this is referred to as Quantitative Fluoroscopy (QF) (Breen et al. 2012a). Previous QF research has demonstrated a difference between intervertebral motion in patients with chronic NSLBP and pain-free persons (Mellor et al. 2014; Breen and Breen 2018). However, intervertebral motion measured by QF has not previously been investigated in patients with acute NSLBP.

This study explored the feasibility of a trial investigating intervertebral motion in participants with acute NSLBP, before and after a course of manual therapy. Not all participants were expected to respond to treatment, so the study also explored differences in intervertebral motion between participants who responded to manual therapy and those who did not. Response to manual therapy was determined using Patient Reported Outcomes Measures (PROMs), and responders were defined as those with at least a MCIC.

1.2.1. Research Questions:

- In patients with acute non-specific low back pain, does lumbar intervertebral movement change following a course of manual therapy?
- In patients with acute non-specific low back pain, do those who respond to manual therapy (established by PROMs) have different intervertebral movement to those who do not?

1.3. Objectives of the Study

1.3.1. Primary Objectives

The primary objective of this study was to determine the feasibility of conducting a full-scale trial. This study aimed to answer the question "Can a full-scale study of the biomechanical effects of manual therapy be done?". A feasibility study was used to identify and understand parameters that may affect the implementation and execution of a full-scale trial (NIHR 2019a).

Parameters may include (NIHR 2019a):

- An exploration of participant recruitment (such as, whether the recruitment strategies are sufficient to recruit the number of patients required for a full-scale trial).
- Number of patients eligible for the trial, as well as conversion to consenting participants.
- Appropriateness of inclusion and exclusion criteria.
- Willingness of participants to be randomised.
- Practicality of obtaining baseline and trial measurements in the proposed setting.
- Characteristics of proposed outcomes measures or appropriateness of outcomes measures to answer the research question.
- Practicality of delivering the intervention in the proposed setting.
- Acceptability of the intervention to participants and intervention compliance.
- Standard deviation of the outcome measure, which is needed to estimate sample size for a full-scale trial.
- Time needed to collect and analyse data.

Recruitment to the clinical trial took place in the Covid era (February 2020 – April 2021), as such the data collected would not have represented the feasibility of conducting the trial outside of a pandemic. For this reason, a parallel study collecting retrospective data from clinic files was carried out to explore the feasibility of conducting a full-scale study outside of the Covid-19 pandemic.

1.3.2. Secondary Objectives

A feasibility study may generate data on the outcome of interest, but analysis of the outcome of interest is not the primary aim (NIHR 2019a). In this study, the small participant numbers meant that the study was insufficiently powered to gain meaningful outcomes. However, data from this study was analysed to aid power calculations and to estimate sample size of a full-scale trial (Eldridge et al. 2016; NIHR 2019a).

The secondary objective measures utilised in this study included:

- QF measurements: Intervertebral angular range of motion, translation, laxity (initial attainment rate), disc height, intervertebral motion share and variability.
- PROMs questionnaires: Bournemouth Questionnaire and Roland Morris Disability Index-24.

1.4. Organisation of Thesis

The thesis was written in an integrated or alternative thesis format. As such, some chapters appear in the format of publishable journal articles. Chapters which have been prepared, submitted, or published, are indicated at the beginning of the relevant chapters.

The thesis still follows a traditional thesis flow (See table 1.1); however, seven chapters have been written as publishable journal articles.

Table 1.1: Organisation of Thesis

	Traditional Thesis	**Integrated Thesis (Chapters written in journal article format)**
Chapter 1	Introduction	
Chapter 2	Background	
Chapter 3	(Literature review)	Is There Intersegmental Change in the Lumbar Spine Following Spinal Manipulative Therapy and Mobilisation?
Chapter 4	Literature Review	
Chapter 5	Methods	
Chapter 6	(Methods)	The Development of the Home Management Booklet
Chapter 7	(Methods)	Usability Testing as an Aid to Design a Person-centred Trial (published)
Chapter 8	(Methods)	Stakeholder Involvement in Trial Material Development (published)
Chapter 9	(Results)	Comparison of Low Back Pain Population in the Covid-19 era and pre-Covid-19
Chapter 10	(Results)	Biomechanical Effects of Manual Therapy in Acute Low Back Pain Patients – Primary Objectives
Chapter 11	(Results)	Biomechanical Effects of Manual Therapy in Acute Low Back Pain Patients – Secondary Objectives
Chapter 12	Discussion	

2. Background

2.1. Introduction

To enable exploration of intervertebral motion of the lumbar spine, an understanding of gross anatomy and movement of the lumbosacral spine is essential. This chapter begins by outlining normal lumbosacral anatomy and intervertebral motion. Although there is a paucity of literature relating to intervertebral motion in acute NSLBP, existing literature has been explored for each intervertebral motion parameter.

As manual therapy is a commonly sought treatment for acute NSLBP, the chapter follows on to outline how manual therapists examine intervertebral motion and manage what is thought of as aberrant intervertebral motion clinically. The theoretical models for the effects of manual therapy have also been explored in this chapter.

2.2. The Spine

The human spine gives the body structure and support to enable the body to keep upright, while allowing flexibility and movement. The human spine is inherently unstable without the active involvement of the spinal ligaments and musculature (Oxland 2016). The spine is subdivided into five regions according to their anatomical appearance. Typically, the cervical spine consists of seven vertebrae, the thoracic spine consists of twelve vertebrae, the lumbar spine consists of five vertebrae, the sacrum consists of five fused vertebrae, and the coccyx consists of three to five small, fused vertebrae (Moore et al. 2018) (See Figure 2.1).

The lumbar spine vertebrae are large and carry the weight of the upper torso and head. The lumbar vertebrae also protect the conus medullaris and cauda equina, which connect the brain to the lower half of the body (Moore et al. 2018). The lumbar spine allows more range of motion than the thoracic spine (due to the presence of ribs), but less than the cervical spine (Moore et al. 2018).

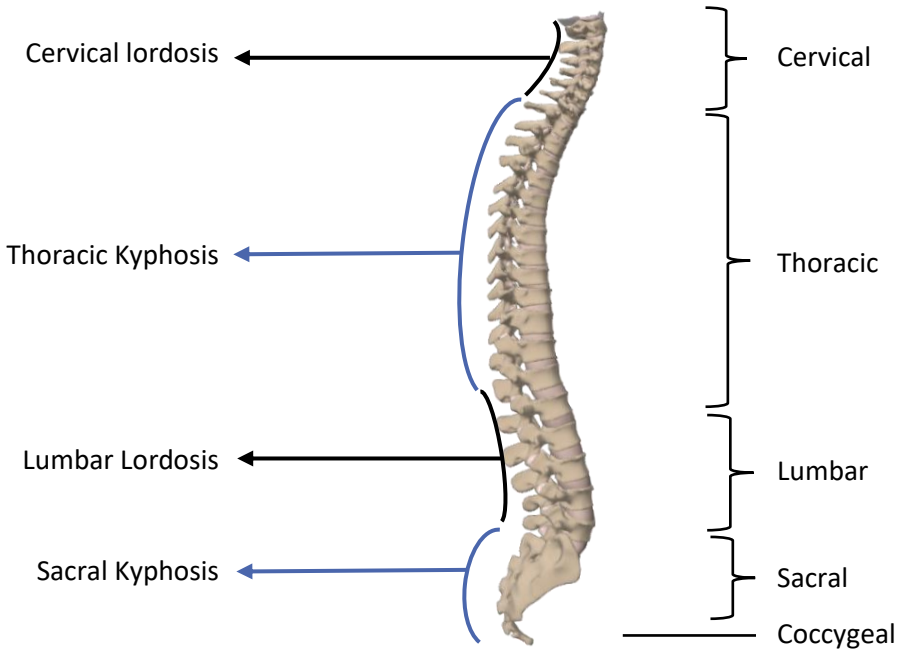

Figure 2.1: The vertebral column, including vertebral regions and curves (Figure reproduced with kind permission from ©Primal Pictures. All rights reserved (2021b))

2.3. Spinal Curves

The human spine is curved, with two primary curves of the thoracic kyphosis and sacral kyphosis which are present from birth, and two secondary curves of the cervical lordosis and lumbar lordosis which appear approximately seven months after birth (Moore et al. 2018) (See Figure 2.1). The average lumbar lordosis angle in a standing position range from 49.8° (±11.1) (Yasutsugu et al. 2019) to 63° (±15) (De Carvalho et al. 2010). It is suggested that females have a significantly larger lumbar lordosis angle than males (Arshad et al. 2019b). Whether a relationship between lumbar lordosis and LBP exists is difficult to determine due to the heterogeneity in the measurement method (Been and Kalichman 2014) as well as the heterogeneity in LBP study inclusion and exclusion criteria (Chun et al. 2017). However, Chun et al. (2017) suggest that chronic LBP is associated with a smaller lumbar lordotic angle. The extent to which spinal curves play a role in in the onset or perpetuation of acute LBP, if any, is unknown.

2.4. Functional Spinal Unit (Motion Segment)

A functional spinal unit (or motion segment) comprises of two vertebrae, the intervertebral disc, the facet joints, and the surrounding soft tissues (ligaments and muscles) (White and Panjabi 1990) (see Figure 2.2). According to White and Panjabi (1990), a functional spinal unit is *"the*

smallest physiological motion unit of the spine to exhibit biomechanical characteristics similar to those of the entire spine" (White and Panjabi 1990, p.49).

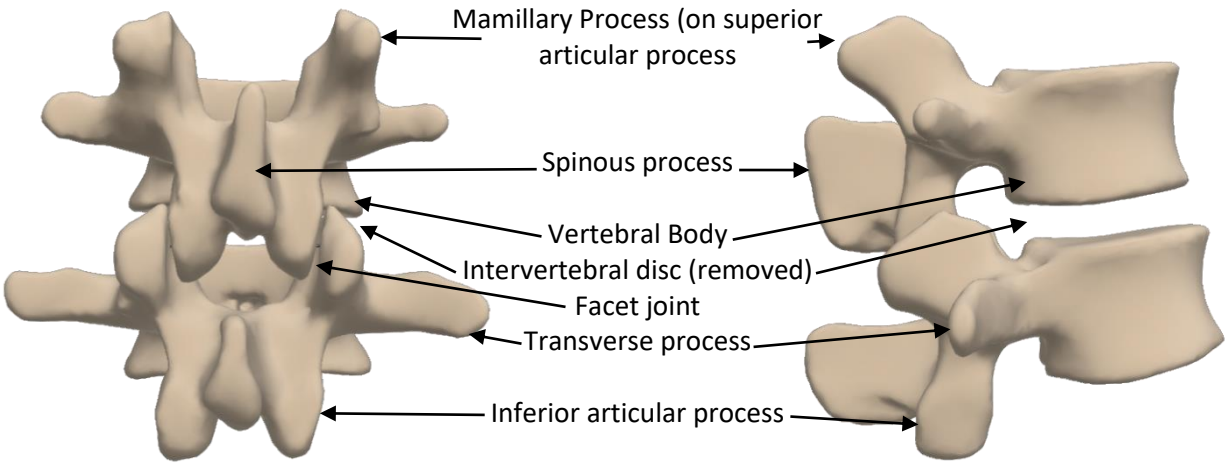

Figure 2.2: Lateral and posterior views of a Functional Spinal Unit (Figure reproduced with kind permission from ©Primal Pictures. All rights reserved (2021a))

Structures of the functional spinal unit have nociceptor receptors, which upon detecting noxious stimuli (pressure, temperature, chemical) relay signals to the brain which can be perceived as pain. The brain can perceive pain as local (at the site of the stimuli), or as referred pain (further away from the site of the stimuli) (McMahon et al. 2013). The facet joint capsule, the outer one-third of the intervertebral disc, the vertebra (periosteum and marrow), and the ligaments surrounding the functional spinal unit contain nociceptive receptors. As such, the brain can perceive pain as local, or referred in a particular pattern known as a sclerotome referral pattern of pain (McMahon et al. 2013). Equally, the muscles surrounding the functional spinal unit, as well as the muscles of the lower back and buttocks, contain nociceptive receptors. As such the brain can also perceive pain as local or referred in a particular pattern known as myotome referral pattern of pain (McMahon et al. 2013). The spinal cord does not descend as far as the mid to lower lumbar spine and as such cord compression cannot occur, however, nerve root sensitisation can occur. Depending on the cause (cauda equina compression or vertebral foramen compression), this could be perceived as local pain or referred pain in a radicular pain referral pattern (McMahon et al. 2013).

Due to the low specificity of imaging and diagnostic methods, it is not always possible to identify the painful structure (Knezevic et al. 2021). Furthermore, pain is not simply biological, but a complex dynamic interaction between biological, social and psychological factors (biopsychosocial model of pain) (Knezevic et al. 2021). For this reason, identifying the cause of pain and pain management can be complex.

2.4.1. Facet Joints

The articular processes are surrounded by a ligamentous joint capsule, which is filled with synovial fluid, together they form the facet joint (Moore et al. 2018). The orientation of the facet joints in the lumbar spine change, going from slightly more sagittally orientated at L1-L2 to slightly more coronally orientated at L5-S1, however there is much normal anatomical variance (Boden et al. 1996). Facet joints orientated in the coronal plane resist more anterior translation, and less axial rotation. Facet joints orientated in the sagittal plane resist more axial rotation, and less anterior translation (Adams et al. 1980; White and Panjabi 1990). Gliding of the articular surfaces permits flexion and extension, however, due to the orientation of the facets, pure motion of lateral flexion and axial rotation are unobtainable. During lateral flexion there is coupled motion with axial rotation and vice versa. During lateral flexion, axial rotation is such that the spinous process points in the same direction as lateral flexion (White and Panjabi 1990).

2.4.2. Intervertebral Disc

The intervertebral disc is found between two adjacent vertebral bodies and consists of a peripheral annulus fibrosus and a central nucleus pulposus. The annulus fibrosus consists of concentric fibrous collagen rings which surround the semi-fluid like substance of the nucleus pulposus (Moore et al. 2018). The two elements are strong enough to allow transfer loading through the spine without collapse and are deformable enough to allow intervertebral motion (Bogduk 2012). Disc height increases from L1-L2 to L4-L5, and discs are wedge shaped, wider anteriorly and narrower posteriorly (Moore et al. 2018).

In a healthy disc, during lumbar spine flexion the anterior disc is compressed and bulges anteriorly, pushing the nucleus pulposus posteriorly. During this motion the posterior disc is subject to tension, pulling the fibres of the anulus fibrosis taught resisting the nucleus pulposus from excessive posterior movement (White and Panjabi 1990; Bogduk 2012). During extension, the opposite occurs.

2.5. Lumbosacral Junction

The lumbosacral junction is between L5 and the sacrum and has the same characteristics as the lumbar intervertebral joints (Moore et al. 2018). The intervertebral disc is the largest, and most wedge shaped, of the lumbar spine (Moore et al. 2018). The relationship between the lumbar spine and the sacrum is unique as it is the junction between the lumbar lordosis and the sacral kyphosis. It is thought that a change in sacral angle (angle between sacral base and horizontal plane) may correlate with chronic NSLBP (Caglayan et al. 2014), however, in one study acute NSLBP patients had similar sacral angles to pain free participants (Naqvi et al. 2020).

2.6. Transitional Vertebrae

The term *"lumbosacral transitional vertebra"* refers to either the lowest lumbar vertebra resembling S1 (a sacralised lumbar vertebra), or a failure of S1 to fuse (partially or completely) to the other sacral elements (a lumbarised sacrum). It is suggested that in the global general population prevalence is between 4% - 30% (Konin and Walz 2010). It is thought to be a genetic developmental variation; however traumatic or pathological fusion patterns cannot be ruled out (Barnes 1994). The presence of transitional vertebrae can be more prevalent within geographic areas. Archaeological explorations in the South of England, such as the remains examined from the sunken ship the Mary Rose, had a higher prevalence of 38.3% (Drew and Kjellström 2021).

According to the Castellvi Classification (Castellvi et al. 1984), there are four types of lumbosacral transitional vertebrae:

- Type I: Enlarged and dysplastic transverse process of at least 19mm:
    - Type Ia: Unilateral
    - Type Ib: Bilateral
- Type II: Pseudo-articulation of enlarged transverse process with sacrum with incomplete lumbarisation/ sacralisation:
    - Type IIa: Unilateral
    - Type IIb: Bilateral
- Type III: Enlarged transverse process fused with sacrum with complete lumbarisation/ sacralisation:
    - Type IIIa: Unilateral
    - Type IIIb: Bilateral
- Type IV: Type IIa on one side and type IIIa on the contralateral side.

Whether a relationship between lumbosacral transitional vertebrae and LBP exists is difficult to ascertain. However, it is suggested that a lumbosacral transitional vertebra is correlated with LBP, but whether it causes LBP is controversial (Gopalan and Yerramshetty 2018). Potentially, type III and type IV sacralisation may alter the biomechanics of the spine by putting more pressure on the L4-L5 motion segment causing LBP which is what occurs in Bertolotti's Syndrome (Quinlan et al. 2006). There is little literature relating to lumbarisation and the relationship with LBP.

2.7. Biomechanics of the Lumbosacral Spine

2.7.1. Intervertebral Motion

Flexibility is the ability of a structure to deform under the application of a load. Stiffness is the opposite and refers to the resistance offered to the application of a load (White and Panjabi 1990). These definitions are simplistic and potentially do not represent the complexity of intervertebral motion. The definitions imply that there is a linear relationship between load and deformation, however, this is not true in the spine. White and Panjabi (1990) suggest that there are two distinct phases of joint movement (See Figure 2.3). The first phase, providing little resistance and deforming easily, is known as the neutral zone and occurs closest to the start of the range of motion. The second, providing more resistance at an increasing rate, is known as the elastic zone and occurs for the remainder of the physiologic range of motion. The total range of motion is then the sum of the neutral zone and the elastic zone and a reduction in range of motion (ROM) can indicate overall spinal stiffness (Widmer et al. 2019).

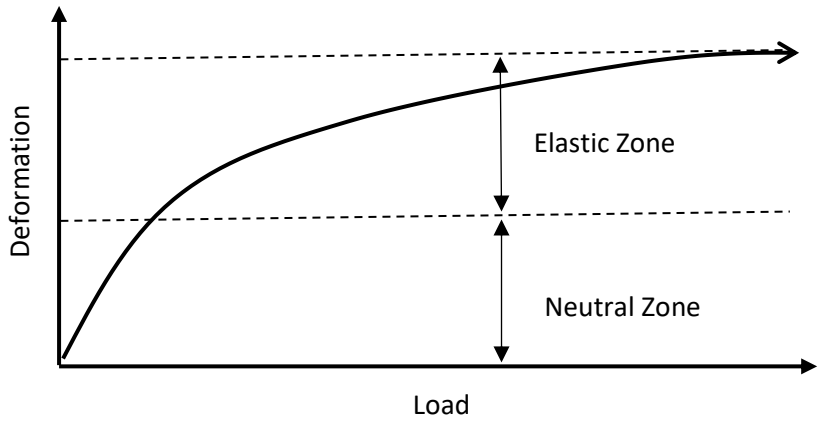

Figure 2.3: The load-deformation curve of a joint. The load-deformation curve is divided into two parts: the neutral zone, and elastic zone. Modified from White and Panjabi (1990).

The theoretical concept of the neutral zone is commonly accepted, however, there is little consensus on the method for mathematically calculating the neutral zone and a "gold standard" has yet to be established (Di Pauli von Treuheim et al. 2020). Nevertheless, the neutral zone gives an indication of joint laxity. Using the neutral zone theory, Panjabi (1992) defines instability as *"a significant decrease in the capacity of the stabilizing system of the spine to maintain the intervertebral neutral zones within the physiological limits"* (Panjabi 1992, p.394). Joint laxity is an indication of joint instability and is characterised by an increase in the neutral zone. Conversely, the neutral zone also gives an indication of joint stiffness which demonstrates an increase in the stabilising system of the spine and is characterised by a decrease in the neutral zone.

2.7.2. Range of Motion (ROM)

Total lumbar spine range of motion (ROM) is calculated from the sum of the intervertebral motion from L1-S1. The intersegmental contributions vary and depend on the movement performed. During flexion, two patterns of intervertebral contributions can be seen from the literature. The first pattern is of decreasing contribution from L1-L2 to L5-S1 which can be seen in studies which limit ROM to between 35°-45° of flexion, demonstrating a cascade of movement from the top of the lumbar spine to the bottom. The second pattern is of increasing contribution from L1-L2 to L4-L5, with a decrease in contribution to L5-S1 which can be seen in studies with moderate to full ROM of flexion (Widmer et al. 2019).

Very few studies have included the measurement of extension, however, it is suggested that the pattern of intervertebral contribution for extension demonstrates high contribution of L1-L2 and L5-S1, with a decrease in the intermediate levels (Widmer et al. 2019).

The magnitude of total lumbar ROM (L1-S1) varies between publications, with Kapandji (1974) estimating 60° of lumbar flexion and 35° lumbar extension; White and Panjabi (1990) estimating 78° for combined flexion and extension; and Magee and Manske (2020) estimating 40°-60° for flexion and 20°-35° for extension. The ROM measurement range can be dependent on the measuring tool being used. For example, total lumbar spine flexion ROM (L1-S1) in pain free participants measured using x-ray was 51° on average (Pearcy et al. 1985), however, in a different study, when measured with a goniometer the average was 56.4° (Van Herp et al. 2000). The ROM measurement is also dependant on whether the participant motion was to their full ROM or limited based on the study protocol. For example, when pain free participants were limited to 40° of flexion, the total lumbar spine flexion ROM (L1-S1) measured using video fluoroscopy was 38.6° (Wong et al. 2006). Furthermore, it is suggested that ROM increases throughout the day and as such the measurement may be dependent on the time of day it was obtained (Ensink et al. 1996).

It is also suggested that total lumbar ROM significantly decreases with age and is affected by the sex of the participant, with flexion ROM being significantly greater in males, whereas extension ROM was greater in females (Arshad et al. 2019b). As demonstrated, there is much variation in the literature on total lumbar ROM.

There is evidence to suggest that participants with LBP demonstrate reduced lumbar regional ROM (Laird et al. 2014; Vaisy et al. 2015). Vaisy et al. (2015) suggests that participants with chronic LBP display up to 10%-15% decrease in flexion ROM (L1-S1), the reduction in ROM was negatively correlated with self-reported pain. In contradiction to this, in a study comparing chronic NSLBP patients with pain free controls, intervertebral ROM was found to be highly variable with no significant differences between the two groups (Mellor et al. 2014a). There is little literature on the relationship between ROM and acute NSLBP.

2.7.3. Translation

Translation is anterior or posterior movement of the vertebra above versus the vertebra below. Translational contribution is the percentage translational motion of a vertebra, in relation to the sum of all lumbar spine translations (Widmer et al. 2019). During lumbar spine flexion, the contribution pattern is very similar to that of ROM contributions, whereby translation increases from L1-L2 to L4-L5 and decreased to L5-S1. The extent to which the slightly more coronal orientation of the facets of L5-S1 limit translation is unknown. As intervertebral angular ROM and translation positively correlate, potentially the L4-L5 intervertebral joint is under the most stress which may be a reason for the higher prevalence of joint degeneration at this level (Widmer et al. 2019).

The term *"stability"* in the literature has been used to represent various mechanical theories. *"Mechanical stability is defined as the ability of a structure to return to its original state after being subjected to a perturbation"* (Oxland 2016, p.820). A mechanically unstable spine may experience buckling under compressive loads, which may result in clinical symptoms. It is thought that the spine is inherently unstable without the active involvement of the spinal musculature (Oxland 2016).

NSLBP has been linked to instability and an alteration in muscle control of the trunk (van Dieën et al. 2019). Translation is typically measured when instability is suspected or a loss of muscular or ligamentous restraint (Leone et al. 2007). In a patient, if intervertebral translation exceeds 4mm, and the patient experiences significant symptoms, fusion surgery may be offered (Leone et al. 2007). However, Posner et al. (1982) suggested the cut off for intersegmental instability should be 8% of the vertebral body unit (VBU), which when using the standard VBU of 35mm is only 2.8mm.

Population variability and a lack of standardised measurement protocols can make a definitive cut off difficult to obtain (Leone et al. 2007).

2.7.4. Degeneration and the Three Joint Complex

The three joint complex consists of the intervertebral disc and the two facet joints of a functional spinal unit. Changes affecting the intervertebral disc affect the facet joints and vice versa (Kirkaldy-Willis and Bernard 1999). It is not possible to ascertain which occurs first, changes to the disc or to the facets. For ease of explanation, the degenerative process in the disc will be discussed, followed by the degenerative process of the facet joints. However, it is likely they occur simultaneously (Kirkaldy-Willis and Bernard 1999).

Changes can occur in the disc due to high or prolonged loading, or tissue damage. Tissue damage may be caused by connective tissue disorders, impaired metabolite transport within the disc, inadequate disc nutrition, or tissue fatigue which can result in a permanent loss of disc height (Bogduk 2012).

Dynamic (un-sustained) loading of the intervertebral disc can be anabolic and promote disc repair, equally disc height recovery is faster than sustained loading (Chan et al. 2011). Conversely, sustained loading of the intervertebral disc causes loss of disc height gradually, this is termed creep. Most creep is due to water expulsion. Water moves from an area of high pressure to an area of low pressure. When the loading is decreased or removed, the disc recovers by sucking the water back into it due to negative pressure (Bogduk 2012). Recovery from creep in the disc takes longer than creep itself, however recovery is possible (Bogduk 2012).

Following prolonged sustained creep, damage can occur to the fibres of the annulus fibrosus leading to more permanent disc height loss (Bogduk 2012). This disc damage is known as disc degeneration. Degeneration can occur at any age, but it is most common in older people (Bogduk 2012). Intervertebral degeneration is potentially considered a normal age-related change, and not necessarily a disease process (Benoist 2003).

Kirkaldy-Willis and Bernard (1999) suggest there are three phases of degeneration, stage I is the dysfunction phase, stage II is the unstable phase, and phase III is the stabilisation phase. First, a number of small circumferential tears in the annulus fibrosus occur. These tears become larger and form radial tears which pass from the annulus fibrosus to the nucleus pulposus. These radial tears increase in size and number until there is complete disc disruption internally. This leads to greater disc height loss. Due to the loss of integrity of the annulus fibrosus, the disc bulges, and following further damage the disc can be seen as a thin slit of fibrous tissue between the vertebral

bodies (disc reabsorption). Finally, bony osteophytes appear around the disc circumference as a stabilisation mechanism (Kirkaldy-Willis and Bernard 1999).

Disc height loss brings the two adjacent vertebral bodies closer together and increases the load on the facet joints. For this reason, the three phases of degeneration also affect the facet joints. The earliest change in the facets is synovitis, which is inflammation of the synovial lining of the joint capsule. Later degeneration of the articular cartilage occurs, and this increases and becomes more visible on imaging. The degeneration of the articular cartilage reduces the joint space, resulting in the surrounding joint capsule becoming lax and allowing increased movement within the joint. Continuing degeneration results in the formation of osteophytes which produces enlargement of the articular processes to stabilise the joint (Kirkaldy-Willis and Bernard 1999).

A summary table of Kirkaldy-Willis and Bernard's Phases of Degeneration can be seen in Table 2.1.

Table 2.1: Phases of Degeneration modified from Kirkaldy-Willis and Bernard (1999).

Phase of Degeneration	**Disc**	**Facet**
Dysfunction	Circumferential and radial tears	Synovitis
Unstable Phase	Internal disc disruption; disc reabsorption	Degeneration; capsular laxity
Stabilisation	Osteophytosis	Enlargement of articular processes

Practically, grading degeneration can be difficult and there are different grading systems for different imaging modalities. However, literature suggests that during the movements of flexion and extension the overall ROM does follow the theory of Kirkaldy-Willis and Bernard (1999) with an initial increase in ROM during the instability phase followed by a decrease in ROM in the stabilisation phase (White and Panjabi 1990; Mimura et al. 1994; Fujiwara et al. 2000). Tanaka et al. (2001), suggests this is true for the lower lumbar levels, but potentially not for the higher lumbar levels whereby there is a progressive pattern of decreasing ROM, particularly in advanced disc degeneration.

Studies agree that there is an increase in the neutral zone, indicating an increase in joint laxity until bony stabilisation of the joints occur (White and Panjabi 1990; Mimura et al. 1994; Fujiwara et al. 2000; Tanaka et al. 2001; Kettler et al. 2011). Translational changes indicate that they remain within normal limits, with an increase in the instability phase of degeneration (Widmer et al. 2019).

Intervertebral degeneration does not necessarily mean that the person will suffer from LBP. While a relationship between disc space narrowing and LBP has been suggested (Goode et al. 2013; Raastad et al. 2015; Widmer et al. 2019), there is no substantiated relationship between facet articular surface widening or osteophyte presence, and LBP (Goode et al. 2013; Widmer et al. 2019).

2.7.5. Aberrant Motion

The lumbar spine is a dynamic chain that requires the simultaneous movement of the intervertebral joints to achieve motion. Which means that altered or aberrant motion in one spinal joint can result in changes to the motion within adjacent joints (du Rose et al. 2018). Altered or aberrant motion may mean that joint is moving too much (hypermobility) or too little (hypomobility), either statically or dynamically, which can have a knock-on effect on other intervertebral joints in the lumbar spine.

Motion Sharing Inequality (MSI) is the average difference between the functional spinal unit that performs the lowest rotational motion as a proportion of all the measured spinal motion (L2-S1), and that which performs the highest proportional motion during the movement of flexion and extension (Breen and Breen 2018). A heightened MSI may be a result of stiffness at one or more levels, or hypermobility at one or more levels. Thus, the measurement of MSI can provide an indication of spinal aberrant motion. There is a small, but conflicting pool of literature with some suggesting that chronic low back pain patients demonstrate a greater MSI than matched controls (Breen and Breen 2018). Equally, patients with treatment resistant LBP (including surgical or interventional procedures) demonstrated a greater MSI than matched controls (Breen et al. 2018). However, in a later study by Breen and Breen (2020), no significant differences were found between patients with chronic NSLBP and controls. There is a paucity of literature relating to patient with acute NSLBP.

2.8. Patient Examination

The evaluation and management of musculoskeletal disorders, like acute NSLBP, is a primary focus of musculoskeletal health professionals, such as chiropractors, osteopaths, and

physiotherapists. Patient evaluation or examination is designed to progressively narrow down the location of pain, and potentially the structures eliciting pain, and therefore inform diagnosis and management. Currently, there is little agreement on how to identify the pain causing structures, particularly in the case of NSLBP. However, the clinical presentation can direct the diagnostic process. A commonly used pneumonic for locating a treatment site is P.A.R.T.S (Triano et al. 2013) (See Table 2.2). Other patient examinations do exist; however, it is mostly only the order of the examination which is altered. For example, completing all the assessments while the patient is standing, then sitting, then lying down (Magee and Manske, 2020). Table 2.2 indicates the recommendations for the use of each of the components of P.A.R.T.S based upon the level of the supporting evidence (Triano et al. 2013). Looking at the table, a recommendation of 'favourable' indicates for general use by clinicians to determine site of care; 'favourable with limitations' indicates favourable for determining site of care although limits exist such as number and quality of studies, limited generalisability, etc.; 'unclear' indicates that based on the evidence available, it is unclear whether or not the procedure should be recommended for use; 'unfavourable with exceptions' indicates that the procedure is not recommended for general use but may be used in limited circumstances; 'unfavourable' indicates the procedure is not recommended for use (limited number of studies, significant flaws in methods, not generalisable, high quality evidence against validity and/ or reliability).

Table 2.2: A summary of P.A.R.T.S, together with the quality assessment and recommendation of use. Table modified from Triano et al. (2013).

Evaluation Method		Summary	Evidence	Recommendation
Pain History:		Gives context to the complaint and increases the reliability of the interpretation of physical examination findings	Moderate	Favourable
Pain provocation:	Tenderness	Localises region/ tissue of involvement	High	Favourable
	Orthopaedic test	Pain with movement localises region/ tissue of involvement	High	Favourable
Asymmetry:	Posture	Antalgia, kyphosis, lordosis, scoliosis	High	Favourable
		Localising to site of care	High	Unfavourable
	Stiffness (manual palpation)	Passive physiologic/ accessory motion, joint spring, over-pressure testing	High	Unclear
	Stiffness (instrumented)		Low	Favourable with limitations
	Palpation (static)	Identifying major anatomical landmarks	High	Favourable with limitations
	Palpation (motion)	Enhanced if pain provocation present	High	Favourable with limitations
	Manual Muscle Testing	Strength grading to localise nerve root involvement	Moderate	Favourable
		Location of non-pathologic altered function	Moderate	Unfavourable
Range of Motion:		Localisation to region	High	Favourable
Tissue temperature, texture, tone:		Paraspinal skin temperature in locating site of care	High	Unfavourable
		Skin rolling	Moderate	Favourable
Specialised testing:	Sensation Testing	Location of sensory deficit	High	Favourable
	Radiographic Imaging	Location of site of pain	High	Unfavourable

Much of the patient examination is used for location of painful site. However, some of the evaluation is aimed at intervertebral motion evaluation. These are referred to in Table 2.2 as stiffness (manual palpation) and palpation (motion).

To explore the evaluation of intervertebral motion, an understanding of joint motion is needed. Figure 2.4 represents the theoretical movement of a joint and was first proposed by Sandoz (Sandoz 1976). While revised Sandoz models have been proposed (Vernon and Mrozek 2005), the theoretical model of Sandoz is still used to represent joint motion today. Movement in the neutral area is also known as joint play or accessory motion of the joint. Movement from neutral to the physiologic barrier represents active ROM and movement from neutral to the elastic barrier represents passive ROM. End play is represented by 'EP' and the paraphysiological space is represented by 'PH' on Figure 2.4. The anatomical limit represents the barrier, which when crossed, will result in joint injury.

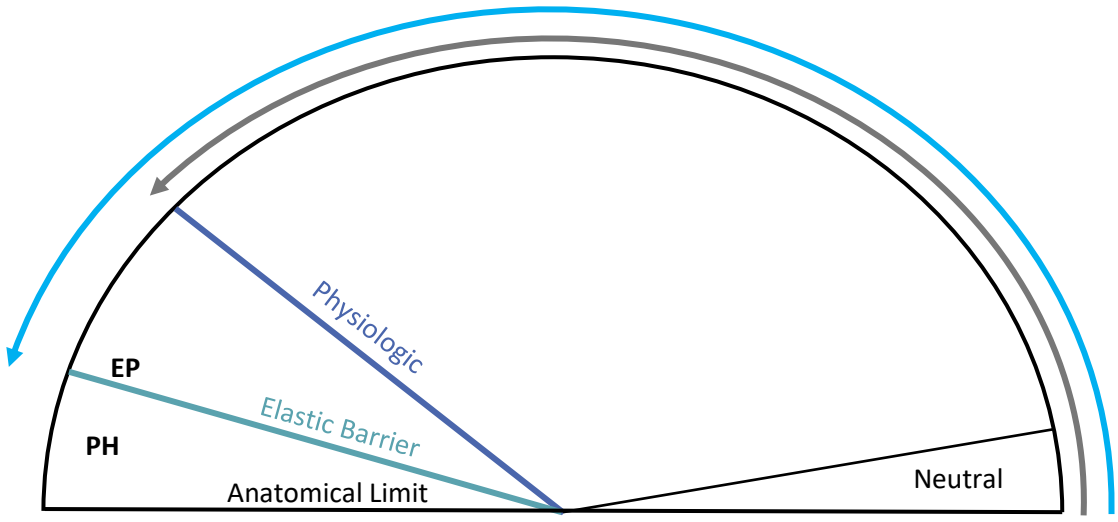

Figure 2.4: Modified Sandoz Diagram representing joint movement (Sandoz 1976). 'EP' represents end play and 'PH' represents the paraphysiological space. The grey arrow represents active ROM; the blue arrow represents passive ROM.

2.8.1. Accessory Joint Motion

The assessment of stiffness (manual palpation) is also known as accessory joint motion or joint play and can be used to evaluate motion of the intervertebral joints in the neutral area (See figure 2.4). The patient is positioned prone, and pressure is applied to the skin over the bony structures

of the spine (spinous process, transverse process) to assess for hypermobility or hypomobility (Bergmann and Peterson 2011). According to Abbott et al. (2005) accessory joint motion is specific for the identification of joint hypermobility (specificity 89%) but showed poor sensitivity (29%). In other words, using accessory joint motion, clinicians were able to identify those without the disorder (specificity), but struggle to identify those with the disorder (sensitivity). When using accessory joint motion for the identification of hypomobility, clinicians were able to detect large differences in spinal stiffness, but less able to detect smaller differences (Kawchuk et al. 2019). It is suggested that there is a physiological limit to clinician palpation sensitivity which may limit the ability to identify small changes in spinal stiffness (Kawchuk et al. 2019). When using accessory joint motion for the identification of hypomobility, inter-therapist reliability was high with a Kappa coefficient of 0.94 (Downey et al. 1999), and intra-therapist reliability was weak with a Kappa Coefficient of 0.56 (Horneij et al. 2002). Reliability of accessory motion may be affected by factors such as loading frequency (Lee and Svensson 1993), force used (Simmonds et al. 1995), intra-abdominal pressure (Hodges et al. 2005) and trunk muscle activity (Shirley et al. 1999). Equally, clinicians are less reliable at identifying the vertebral level number being marked (Downey et al. 1999; Mieritz and Kawchuk 2016). The reliability of the evaluation increases in symptomatic patients who provide pain feedback during the evaluation (Maher and Adams 1994).

2.8.2. Motion Palpation

The assessment of palpation (motion) is also known as motion palpation and is used to evaluate end play (See Figure 2.4, page 38). End play is evaluated by applying additional overpressure to the specified joint at the end of passive range of motion to assess for hypomobility or hypermobility (Bergmann and Peterson 2011). When identifying hypomobile joint motion, there is little agreement in the literature on inter-therapist reliability, with a Kappa coefficient range from 0.14 (Haas et al. 1995) up to 0.70 (Lundberg and Gerdle 1999; Landel et al. 2008). There is moderate agreement in the literature that intra-therapist reliability is also poor when identifying hypermobile segments with a Kappa coefficient range from 0.21 (Qvistgaard et al. 2007) up to 0.29 (Landel et al. 2008). It has even been suggested that the identification of altered motion is due to chance alone (Love and Brodeur 1987), however, it should be noted that this study utilised students as therapists who potentially lack the psychomotor skills or experience. Whether repeated motion palpation on the same participant reduced the hypomobility and made the joints more mobile is a possible explanation for the poor reliability, however to what extent repeated measures would have reduced hypomobility is unknown.

It is evident that there is a lack of evidence supporting the reliability of both accessory joint motion evaluation and motion palpation, which is mirrored in Table 2.2. (Page 37). As such, there is a lack of a reliable bed side method of assessing intervertebral motion. For this reason, research has moved toward spinal imaging for a more reliable exploration into intervertebral motion.

2.9. Manual Therapy

The term 'manual therapist' encompasses chiropractors, osteopaths and physiotherapists. While there are differences between the professions in terms of philosophy, there is commonality in the treatment packages provided by each profession (Harvey et al. 2003). To standardise treatment provided in the UK Back pain Exercise and Manipulation (UK BEAM) trial, a treatment package of manual therapy was agreed by professions to include spinal manipulative therapy; spinal mobilisation; trigger point therapy (a way of reducing tension in muscles); and soft tissue techniques (massage and stretching) (Harvey et al. 2003).

The optimal treatment guideline for manual therapy in the treatment of acute NSLBP is difficult to ascertain. Much of the difficulty is resulting from the heterogeneity of the literature. Methodologies differ in terms of multi-modal or uni-modal treatment protocols; what treatment protocols are being compared; the outcomes being measured and whether patient improvement is assessed as any reduction in pain and/ or disability, a MCIC, or complete resolution of pain and/ or disability. As an addition to the complexity in investigating an optimal treatment guideline, there is evidence to suggest that some patients respond better to manual therapy than others. This will be explored further in the literature review (See Section 4.5.2.).

2.9.1. Spinal Manipulative Therapy (SMT) and Mobilisation

SMT is used to increase intervertebral ROM or decrease joint hypomobility and utilises either a long lever or short lever technique. A long lever technique uses contacts at leverage points distant to the affected joint, whereby a short lever technique uses direct contact onto the affected joint. SMT is characterised by a low amplitude dynamic thrust of controlled velocity and direction (Bergmann and Peterson 2011). Referring to the Sandoz Diagram (see Figure 2.4, page 38), SMT is moving through the elastic barrier into the paraphysiological space and is commonly associated with a cavitation (Bergmann and Peterson 2011).

Mobilisation is a passive, rhythmic, graded motion applied in the physiological ROM (Bergmann and Peterson 2011). Mobilisation may be carried out regionally using long levers to increase regional ROM, or locally using short levers to increase intervertebral ROM. Included under the umbrella of mobilisation is manual traction-distraction. There are four grades of mobilisation

ranging from grade I (close to neutral), up to grade IV (close to the elastic barrier) (Maitland 2007) (See Figure 2.4, page 38). It is not usually associated with a cavitation (Bergmann and Peterson 2011).

The aim of both SMT and mobilisation are to decrease joint hypomobility and increase ROM, both intervertebral and regional. However, there are contraindications to SMT and mobilisation. The term *"relative contraindication"* indicates that clinical judgement should be used as to whether to treat the patient, or treatment should be modified (WHO 2005). The term *"absolute contraindication"* indicates that treatment may place the patient at risk of injury and as such should not be treated using SMT or mobilisation (WHO 2005). Conditions on the list of *"absolute contraindications"* are of a serious nature and are not considered within the realm of NSLBP, and include trauma (fracture or dislocation), tumour, infection, inflammation, or spinal cord compression.

Evidence suggests that among patients with acute NSLBP, SMT is associated with moderate improvement in pain (Paige et al. 2017; Stochkendahl et al. 2018) and function (Paige et al. 2017). A Cochrane review on SMT for the treatment of acute LBP concluded that SMT is no more effective than inert interventions, sham SMT, or when added to another intervention (such as exercise) (Rubinstein et al. 2012). However, both Rubinstein et al. (2012) and Paige et al. (2017) indicate that heterogeneity of literature can make comparisons between interventions difficult. Equally, much of the literature is deemed low quality due to the inability to blind either the patient, clinician, or both. The quality assessment of a trial, or risk of bias assessment, is designed to reassure the reader that the result of the trial is not bias and can be trusted (Elkins et al. 2010). Blinding of the patient, clinician, or both reduces the risk of bias. However, in manual therapy trials it is very difficult to ensure blinding. Equally, it is difficult to perform a convincing sham SMT, without inadvertently providing some form of treatment. For this reason, risk of bias assessment tools designed for use in manual therapy trials should be considered. One such tool is the PEDro tool, however blinding is still included in the checklist (Elkins et al. 2010).

It is recommended that the decision to use SMT as a treatment should be based upon cost, preference of the clinician and patient, and relative safety of manual therapy compared to other treatment options (Rubinstein et al. 2012). SMT of the lumbar spine and pelvis (sacroiliac joints) is considered minimal risk for serious adverse events (SAE). It has been calculated that less than 1 in 3.7 million patients will experience a SAE, such as a worsening disc lesion or cauda equina syndrome (Oliphant 2004). However, mild transient discomfort post-treatment (lasting up to 2

days) is considered common and can occur in 50% - 67% of patients (Oliphant 2004; Paige et al. 2017).

Few studies have investigated dose response of SMT for the treatment of acute NSLBP using SMT. Globe et al. (2016) acknowledge that frequency and duration of manual therapy treatment may be influenced by individual patient factors. However, they recommend a typical trial of care for acute NSLBP of 2 – 3 times a week for 2 – 4 weeks. Fritz et al. (2018) and Haas et al. (2014) suggest that a dose response for SMT treatment is difficult to ascertain due to the complexity of the individual case of a patient with acute NSLBP. Potentially, much of the debate in the literature may be due to a lack of understanding of the underlying mechanism of treatment. Much is still unknown about what effect SMT has on the patient.

2.9.2. Soft tissue techniques and Trigger Point Therapy

Massage uses slow firm strokes which is intended to ease muscle tension and increase blood flow (Cafarelli and Flint 1992; Mori et al. 2004). Specific points targeted during massage are known as *"myofascial trigger points"* (Donnelly 2018). A trigger point is defined as a hypersensitive spot in a palpable taut band of skeletal muscle that when stimulated or compressed may result in referred pain or a local muscle twitch response (Donnelly 2018). Compression of these trigger points is effective for treating musculoskeletal pain (Hains and Hains 2000; Hains 2002) and is thought to be more effective than superficial massage alone (Borg-Stein 2006). It is suggested that compression of trigger points in the low back and gluteal region significantly decreased pain and increased lumbar regional ROM in acute NSLBP patients (Takamoto et al. 2015).

Although light massage should not result in bruising, it is not uncommon for bruising to occur during trigger point therapy, particularly when manual compression is used (Donnelly 2018).

2.9.3. Theoretical Mechanisms of Manual Therapy

The clinical effects of manual therapy are thought to be in response to mechanical, neurophysiological, or psychosocial mechanisms (Bialosky et al. 2009), potentially working simultaneously. Bialosky et al. (2009) has developed a detailed theoretical model to explore the clinical effects associated with manual therapy (see Figure 2.5).

The theoretical model suggests that a mechanical stimulus, such as SMT or mobilisation, initiates a number of potential mechanical and neurophysiologic effects which produce the clinical outcomes associated with manual therapy in the treatment of musculoskeletal pain. The theoretical model attempts to account for the complex interactions of the central and peripheral nervous system which modulates the pain experience. As direct observations of the central and

peripheral nervous system are potentially not possible due to the lack of reliable imaging and the ethical implications of invasive research methods in humans, the mechanical and neurophysiologic responses are utilised to explore the mechanisms at play (Bialosky et al. 2009).

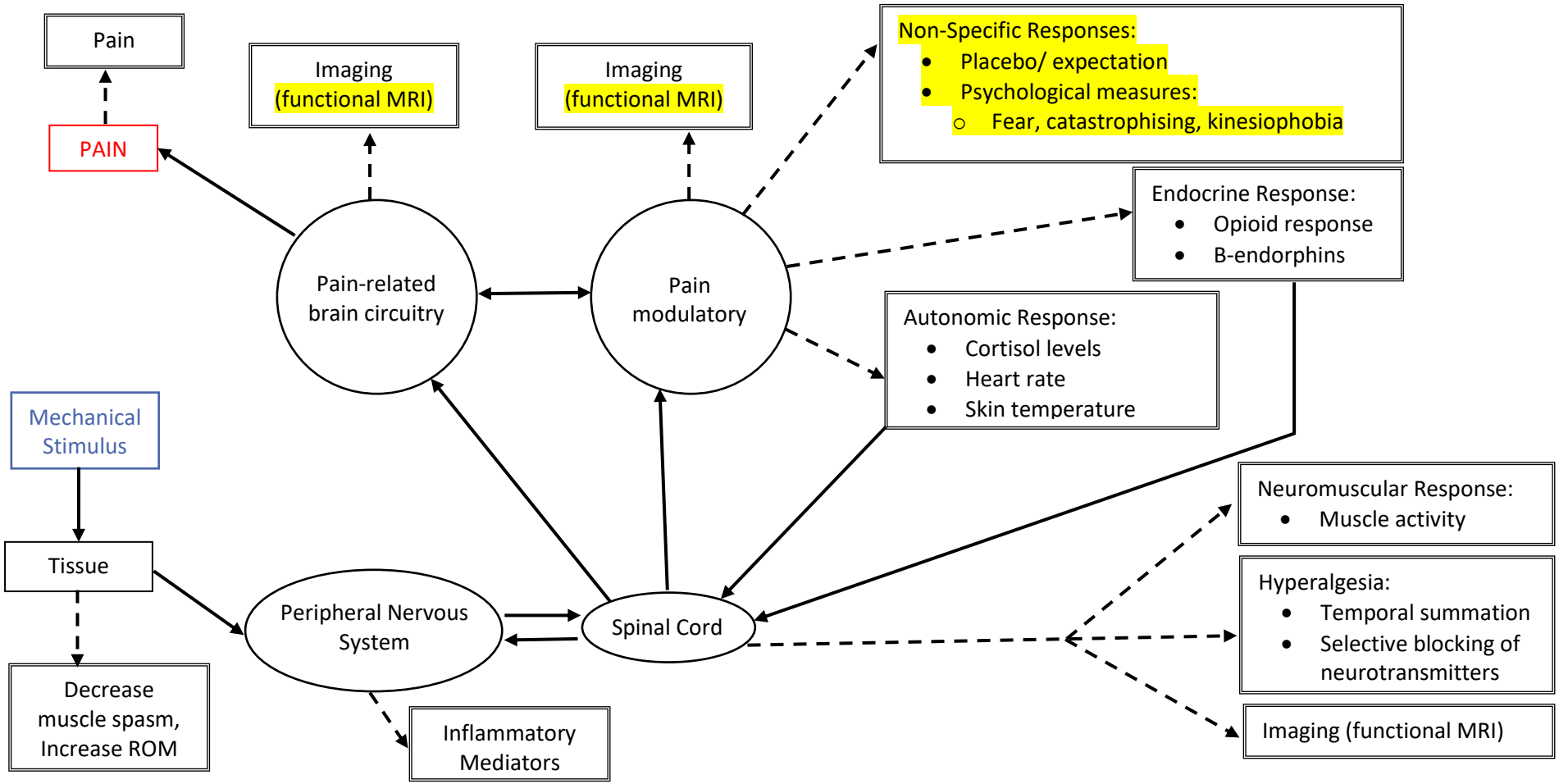

Figure 2.5: Comprehensive model of proposed mechanisms of manual therapy (Modified from Bialosky et al. (2009, p.533). Solid arrows denote a direct mediating effect. Broken arrows denote an associative relationship which may include an association between a construct and its measure. Double-weighted boxes indicate the measurement of a construct.

The following sections discuss the mechanical and neurophysiological responses to manual therapy as outlined by Bialosky et al. (2009).

2.9.3.1. Mechanical Stimulus Effect on Tissue

2.9.3.1.1. Facet Joint Gapping

During manual therapy, the facet joints are gapped (Cramer et al. 2012). Theoretically, this could lead to a breakdown in facet capsule adhesions, although adhesions have not been found to be the primary restrictor of joint movement (Zusman 1986). It has also been proposed that the stretching of the facet joint capsule facilitates inhibition of reflex muscle contraction and reduced muscle tension in the muscles surrounding the facet joint (Zusman 1986; Maigne and Vautravers 2003).

2.9.3.1.2. Diffusion of Water in the Intervertebral Disc

Beattie et al. (2009) suggests that mobilisation of L5-S1 significantly increased diffusion of water within degenerative intervertebral discs, however, this phenomenon was not observed in degenerative intervertebral discs of L1-L2 to L4-L5. As such, mobilisation may have an influence on water diffusion, but this would require further research in the area to establish this relationship.

2.9.3.1.3. Increasing Spinal Motion

Pain in the musculature surrounding the functional spinal unit may activate paraspinal muscles resulting in a decrease in spinal motion (Solomonow et al. 1998). Only one study demonstrated immediate decrease in measured lumbar spine stiffness, with decreased pain and increased overall lumbar ROM after one session of mobilisation in patients with LBP. Patients could also tolerate a greater mechanically applied load to the spine immediately following treatment (Shum et al. 2013).

2.9.3.2. Neurophysiological Mechanisms

2.9.3.2.1. Inflammatory Mediators

Musculoskeletal injuries induce an inflammatory response in tissues which initiates the healing process. Inflammation is associated with an increase in cytokines which can directly or indirectly act on nociceptive neurons and produce pain. This increase has also been seen in patients with discogenic LBP (Burke et al. 2002). It is suggested that there is a reduction in blood and serum cytokines in individuals receiving manual therapy, which was not observed in those not receiving manual therapy (Teodorczyk-Injeyan et al. 2006). It should be noted that inflammation of a joint is a relative contraindication for SMT, depending on the cause.

2.9.3.2.2. Sympathetic Nervous System

A recent systematic review investigating the effect of spinal mobilisation on the sympathetic nervous system concluded that there is a demonstrated relationship between manual therapy and

sympathetic excitation (Kingston et al. 2014). There is strong evidence to suggest a positive change in skin conductance, respiratory rate, blood pressure, and heart rate among the healthy population (Kingston et al. 2014). However, only one study investigated changes in sympathetic excitation in a symptomatic population, suggesting that further research is needed to establish a relationship between sympathetic excitation and manual therapy in NSLBP patients. Currently, there is a paucity of literature exploring the link between reduced sympathetic excitation and hypomobility. Potentially if a link was established, then further research could be conducted to determine if manual therapy on the hypomobile segments effected the sympathetic excitation. There is limited clinical application of manual therapy increasing sympathetic excitation if this increase exists in both asymptomatic and symptomatic patients.

2.9.3.2.3. Pain Inhibition

It has been suggested that manual therapy acts as a counter irritant to modulate pain (Boal and Gillette 2004) and effectively *"bombards the central nervous system with sensory input from the muscle proprioceptors"* (Pickar and Wheeler 2001, p.9). Malisza et al. (2003) demonstrated that manual therapy decreases activation of the dorsal horn of the spinal cord in rats. However, to explore this phenomenon in humans would be almost impossible due to the ethical implications of the invasive procedure, and as such the neurophysiological responses are utilised to create the theoretical mechanism. The neurophysiological responses to manual therapy which support this mechanism include hypoalgesia (Mohammadian et al. 2004; George et al. 2006), decreased afferent discharge (Colloca et al. 2000; Colloca et al. 2003a), decreased motor neuron activity (Bulbulian et al. 2002; Dishman and Burke 2003), and changes in muscle activity (Herzog et al. 1999; Symons et al. 2000).

2.9.3.2.4. Supraspinal Mechanisms

Malisza et al. (2003) applied joint based manual therapy to the lower extremity of rats following a capsaicin injection (chemical irritant derived from chilli peppers). Functional MRI of the supraspinal region quantified the response of the hind paw to light touch and a trend was noted towards the decrease in activation of the supraspinal regions associated with central pain processing such as the anterior cingular cortex, amygdala, periaqueductal grey, and rostral ventromedial medulla (Malisza et al. 2003). There is little literature relating to supraspinal mechanisms in humans.

2.9.3.2.5. Psychosocial Mechanisms

Patient expectation of effectiveness of manual therapy is associated with outcome of treatment. In other words, if patients think that manual therapy will decrease their pain, they have a more positive outcome from the treatment (Kalauokalani et al. 2001). Fear avoidance can function as both a

treatment effect modifier (baseline variable that influences the relationship between the intervention and the outcome) and treatment effect mediator (factors that have an intermediary role in the link between treatment and outcome) (Hill and Fritz 2011). Whereas self-efficacy, personal control, and pain catastrophising can act as a treatment mediator (Hill and Fritz 2011).

Interestingly, it is thought that manual therapy improves psychological outcome of patients when compared to verbal interventions alone (Williams et al. 2007).

2.10. Patient Education

Healthcare providers are expected to deliver information and patient education to improve patients' understanding of their condition as part of the management plan for NSLBP. This information can be delivered in face-to-face appointments or via booklets and leaflets. The information to be delivered includes patient education on their back pain and reassurance that their back pian is not from a serious cause; staying active and avoiding bed rest; pharmacological recommendations; and when to use superficial heat or cold. This is explored further in Chapter 6.

3. Is There Intervertebral Motion Change in the Lumbar Spine Following Spinal Manipulative Therapy and Mobilisation?

3.1. Introduction:

This chapter is in the format of a publishable paper and forms part of the literature review. Following on from the Background Chapter (See Chapter 2), theoretically manual therapy initiates mechanical and neurophysiologic effects. The scope of this feasibility study was to explore the intersegmental mechanical effects of manual therapy and as such, a systematic review was carried out to identify previous studies exploring intervertebral motion change in the lumbar spine following SMT and mobilisation.

3.2. Background:

To answer the question **"Is There Intervertebral Motion Change in the Lumbar Spine Following Spinal Manipulative Therapy (SMT) and Mobilisation?"** is a challenge. The reason for this is the number of SMT and mobilisation variables, and the effect each variable may have on intervertebral motion.

SMT can be delivered manually by a clinician (Bergmann and Peterson 2011), or mechanically by commonly used high velocity, low amplitude instruments such as Activator (Activator Methods International Ltd., USA), Chiropractic Adjusting Tool (JTECH Medical Industries Inc., USA), Impulse Adjusting Instrument (Neuromechanical Innovations, USA) or other custom-made SMT tools (Keller et al. 2006). The patient can be positioned differently, such as prone or side-lying, prepositioning the joint to assist with the SMT (Triano and Schultz 1997; Bergmann and Petersen 2011; Evans 2010). SMT can be delivered to different contact sites on the vertebra (such as the spinous process, facet joint or transverse process); at different angles (such as posterior to anterior, posterior to anterior with an inferior to superior angle, or posterior to anterior with a medial to lateral angle); or delivered to adjacent vertebra to affect the vertebra of interest (Evans 2010; Bergmann and Peterson 2011). The impulse thrust can be delivered using different force, speed, and acceleration (Gelley et al. 2015). The same variables can be applied to mobilisation; additionally, mobilisation can be a holding technique; a repeated passive regional movement moving the area of interest through physiological range of motions (ROM); or more specific oscillatory motions in a particular direction in relation to an individual vertebra (Bergmann and Petersen 2011). This introduces an additional variable of frequency. Due to the variations in technique, it is essential that studies accurately describe the SMT or mobilisation protocol employed to allow meaningful comparison across studies.

Equally, intersegmental change may be influenced by whether the outcome measure is recorded immediately (real time effects) after the delivery of the intervention or after a defined period of follow-up (short to long term effects). Most studies refer to outcomes from real time (immediate), and do not explore the lasting effect of SMT and mobilisation on vertebral or intervertebral motion. However, it has been suggested that SMT and mobilisation are associated with short term biomechanical effects (Gál et al. 1997; Colloca et al. 2006), but not lasting change in motion (Tullberg et al. 1998).

3.2.1. SMT delivery method

Previous literature related to SMT delivery methods included porcine studies (Funabashi et al. 2016; Funabashi et al. 2017b), ovine studies (Colloca et al. 2006; Keller et al. 2006) and frozen human lumbar spine specimens (Ianuzzi and Khalsa 2005b).

Force is supplied by an object, such as a hand in the case of manual SMT or a tool in the case of mechanical SMT, and applied to a movable object, such as a vertebra (Bird and Ross 2015). The force created by SMT can vary considerably between manual and mechanical delivery. To obtain an idea of how fast a force is applied, 'time to peak' is measured. This is expressed in seconds (s) or milliseconds (ms), and is neither speed nor acceleration, but merely an indication of the time taken for force to reach maximum. Load is an applied force on an immovable object which can result in deformation of the object (Bird and Ross 2015). Loads experienced by spinal structures such as facet joint capsules, ligaments, discs and surrounding soft tissues can create injuries if the magnitude of the load is beyond anatomical failure. For this reason, loads on spinal structures have been explored for both manual and mechanical SMT (Funabashi et al. 2016; Funabashi et al. 2017a).

When different SMT delivery methods were compared, such as manual therapy (clinician), Activator, and an actuator motor, unique vertebral loading characteristics were observed (Funabashi et al. 2017b). Manual therapy (524N, 220ms time to peak) and actuator motor (300N, 112.5ms time to peak) generated the greatest force, with Activator generating less force (120N) but a much quicker time to peak (99ms) (Funabashi et al. 2017b). When different SMT methods were compared, such as Activator, Chiropractic Adjusting Tool, and Impulse Adjusting Instrument, again unique vertebral loading characteristics were observed (Keller et al. 2006). For comparison, the medium settings were utilised as the Activator force was similar (121N) for this setting as found in Funabashi et al. (2017b). The Chiropractic Adjusting Tool delivered 237N and the Impulse Adjusting Instrument delivered 245N. The greatest force, delivered by the Impulse Adjusting Instrument, also produced the greatest posterior-anterior displacement, however, the Activator on the high setting delivered the lowest

force of 114N but produced one of the highest posterior-anterior displacements (Keller et al. 2006). Thus, indicating that displacement was not solely due to magnitude of force alone.

Speed is measured as rate of change of distance (Bird and Ross 2015); however, the vertebra moves a very small distance and as such when referring to SMT, speed is defined as rate of change of displacement (mm/s). Acceleration is rate of change of speed (Bird and Ross 2015), or when referring to SMT, acceleration is rate of change of rate of change of displacement (mm/s^2) (See Figure 3.1). SMT should accelerate through the thrust until desired displacement has been achieved (Gelley et al. 2015). Acceleration varies greatly depending on whether the SMT is delivered manually or mechanically.

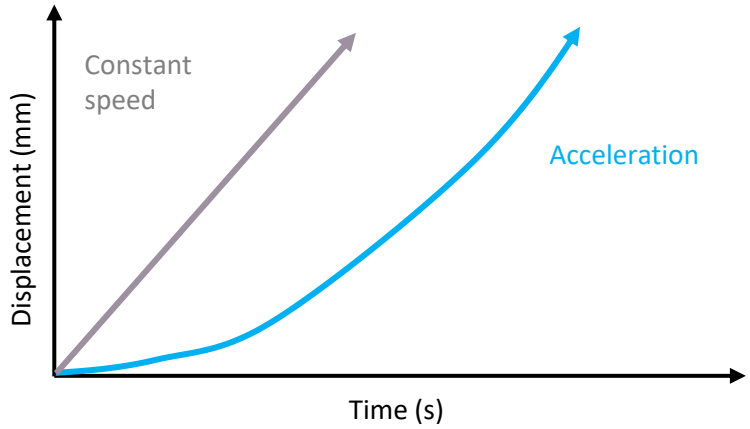

Figure 3.1: Displacement-time graph indicating constant speed (grey line) and acceleration (blue line).

The speed at which SMT is delivered can influence vertebral movement, the faster the force delivered to the vertebra of interest, the greater the movement measured (Colloca et al. 2006). However, in a study by Keller et al. (2006), the Impulse Adjusting Tool (on a medium setting), which delivers the greatest acceleration did not deliver the largest intervertebral displacement. The Activator (on a medium setting) which delivers less acceleration than the Impulse Adjusting Tool delivered the greatest intervertebral displacement (Keller et al. 2006). In other words, the speed (rate of change of displacement) of the adjustment effects the amount of intervertebral displacement, but not the acceleration (measured in mm/s^2).

Regarding load on spinal structures, the magnitude of force (100N, 300N and 500N) did not create significant differences in the loads experienced by the spinal tissues and spinal structures (Funabashi et al. 2017a). Thus, indicating that spinal tissues were able to dissipate the force. However, speed of

force did, with higher speed resulting in a unique pattern of facet joint capsule strain (Ianuzzi and Khalsa 2005b). A limitation of this study was that SMT was applied to the anterior body of a dissected human spine in an anterior-posterior direction, which was an SMT direction that would not normally occur in clinical practice and is therefore of questionable clinical value (Ianuzzi and Khalsa 2005b).

Literature suggests that SMT does not produce significantly greater tissue strain or spinal tissue loading than passive motion or mobilisation, suggesting that SMT was biomechanically safe (Ianuzzi and Khalsa 2005a; Funabashi et al. 2016). More importantly, SMT does not generate spinal tissue loading which will take the tissues beyond their structural limit causing damage (Funabashi et al. 2016).

3.2.2. Contact site

Previous literature related to contact site include porcine studies (Funabashi et al. 2017a; Funabashi et al. 2018), ovine studies (Colloca et al. 2006; Keller et al. 2006); spinal models (Keller et al. 2002); anaethatised symptomatic human studies (Colloca et al. 2003a; Keller et al. 2003) and frozen lumbar spine specimens (Ianuzzi and Khalsa 2005b, 2005a).

The contact site of SMT on the vertebra of interest can affect intervertebral motion (Funabashi et al. 2017a). For example, SMT applied to a vertebral transverse process created greater vertebral rotation than SMT applied to facet joints (Funabashi et al. 2017a). Thrusts delivered to facet joints demonstrated greater coupled motion (axial displacement, medial to lateral displacement, and posterior to anterior displacement) than thrusts delivered to the spinous process (axial displacement, and posterior to anterior displacement) (Keller et al. 2003).

The contact site of SMT can alter the load experienced by the spinal tissues (Funabashi et al. 2017a; Funabashi et al. 2018). In an intact porcine cadaver, greater superior-inferior load was observed when SMT was applied to the facet joints than when applied to the transverse processes (Funabashi et al. 2017a). SMT between bony prominences or on soft tissue create the least spinal tissue loading, indicating that soft tissues dissipate the forces (Funabashi et al. 2018). This demonstrates that application site on the vertebra of interest may alter SMT load distribution within spinal tissues (Funabashi et al. 2017a). This supports the theory that SMT should be specific in terms of contact site on the vertebra undergoing SMT.

However, SMT does not just influence the vertebra being acted upon. SMT applied to the vertebra of interest produced the greatest displacement (Keller et al. 2003), however, SMT can produce

posterior-anterior displacement in adjacent vertebrae as well (Keller et al. 2003; Colloca et al. 2006). This can occur up to two to four vertebral levels away from the thrust site (Colloca et al. 2003a).

SMT applied to L3 vertebra, the L3 posterior-anterior vertebral displacement was up to 2.4mm during SMT (100N mechanically delivered to a model of the spine) (Keller et al. 2002). When SMT of 380.2N was mechanically delivered (Impulse adjusting tool) to the T12 spinous process of sheep, the posterior-anterior displacement of L1 on L2 was 1.76mm (±1.55mm) (Keller et al. 2006). Potentially to make comparison easier, in the same study when SMT of 121N was applied using Activator to the T12 spinous process, posterior-anterior displacement exceeded 0.6mm (Keller et al. 2006). Keller et al. (2003) found when SMT was delivered to L5 and S1 by Activator (150N) the average vertebral displacement of L3 and L1 was 0.48mm (range 0.15 – 0.81). While there is a great deal of difference in the force applied, as well as the specimen, there is evidence to support the theory that there is a decreasing effect on posterior-anterior displacement the further away from the vertebra undergoing SMT.

This effect decreased significantly if the thrust site was caudal to the vertebra of interest, compared with cranial to the vertebra of interest (Keller et al. 2003). However, patterns of observed facet joint capsule strain (which is an indication of load) during SMT delivered to the level distally or caudally to the vertebra of interest, suggests that SMT force effects adjacent vertebra load on the facet joint capsules as much as the vertebra of interest. A limitation of this study was that SMT was applied to the anterior body of a dissected human spine in an anterior-posterior direction, which is an SMT direction that would not normally occur in clinical practice (Ianuzzi and Khalsa 2005b, 2005a). This potentially suggests that site specificity of SMT (SMT to the level of interest) may not be as essential as previously thought.

3.2.3. Direction of SMT delivery

Previous literature relating to direction of SMT delivery include a model of the human lumbar spine only (Keller et al. 2002). There were no significant differences in posterior-anterior displacement between a posterior-anterior thrust and posterior-anterior thrust with up to 20° caudal inclination (Keller et al. 2002). However, there was increasing flexion-extension rotation from approximately 5° of caudal inclination (Keller et al. 2002). This is the only study which investigated this parameter and as such, the effect of rotation of the vertebra during SMT is unknown.

3.2.4. Comparison of SMT and Mobilisation

Frequency is the rate at which something occurs over a period of time (Bird and Ross 2015). Frequency indicates there is repeated motion and is a measurement used mostly for mobilisation. In mobilisation, frequency indicates the number of repeated motions within a time frame and is

measured in Hertz (Hz). In most of the studies where frequency is reported, the mobilisation is delivered mechanically and not manually on dissected specimens or spinal models. For this reason, the frequencies demonstrated are relatively high (up to 19Hz) and most likely unobtainable manually (Keller and Colloca 2007). In some literature, frequency of oscillations has been reported, however, the meaning of this can be different. Frequency of oscillations can refer to repeat motions of a mobilisation (Bergmann and Peterson 2011), or it can refer to the oscillations which occur in the functional spinal unit and surrounding soft tissue in response to SMT. It is thought than an initial oscillatory response to SMT is governed by the ligaments and disc. This may be followed by a secondary phase which is thought to be caused by reflex muscular contraction (Solinger 1996).

Literature relating to porcine (Funabashi et al. 2016; Funabashi et al. 2017b) and spinal models (Keller and Colloca 2002; Keller et al. 2002) have compared the biomechanical effects of mobilisation and SMT.

SMT created significantly greater posterior-anterior force (the direction of the thrust) compared to repeated regional passive movements in the physiological direction during mobilisation. However, SMT did not generate different loads in the surrounding soft tissue of an intact porcine specimen. Again, indicating the force from an SMT dissipates throughout the tissues). However, SMT generated greater posterior load on the intervertebral disc (Funabashi et al. 2017b).

Keller and Colloca (2002) compared SMT (manual), SMT (mechanical), quasi-holding and oscillatory localised mobilisation using a model of the lumbar spine. They concluded that differences in intersegmental motion were similar for the different therapy types (Keller and Colloca 2002; Keller et al. 2002). However, when forces were applied to the L3 vertebrae, the L3 displacement was up to 2.4mm (SMT) and 8.23mm (oscillatory mobilisation at 2Hz) (Keller et al. 2002). Potentially, up to 1.48° of flexion-extension rotation was observed in oscillatory mobilisation (Keller et al. 2002). Interpreting these finding, while L3 moved significantly, the movement of L3 on L4 (intersegmental motion) was similar between the methods of delivery. It is possible that due to the 'stripped down' nature of the spinal models, the damping effect of the soft tissues, as well as the stabilising structures of the ligaments and motor system, were not adequately represented.

The rate of oscillations, in this instance oscillations were the continued motion of the vertebra immediately following the impulse and can continue for up to 160 milliseconds, may differ between SMT and mobilisation. There is evidence to suggest that the rate of oscillations may affect the magnitude of intersegmental motion (Keller and Colloca 2002; Keller et al. 2006). Oscillations would need to reach 38 – 50Hz in order for intersegmental motion to increase 2.74-fold which can occur

during mobilisation (Keller and Colloca 2002). Again, a limitation of this study is the use of a spinal model.

3.2.5. Stiffness

Stiffness is defined as force (N) divided by displacement (mm). However, the force-displacement relationship is not linear and as such studies differ in how stiffness is calculated (See Figure 3.2). Stiffness may be calculated at the beginning of the curve (referred to as the toe region) where little force is required for a relatively large displacement (Kumar 2011, 2012); the middle of the curve (referred to as the linear region) (Caling and Lee 2001; Shirley et al. 2002; Wong et al. 2015); or the maximum force and displacement.

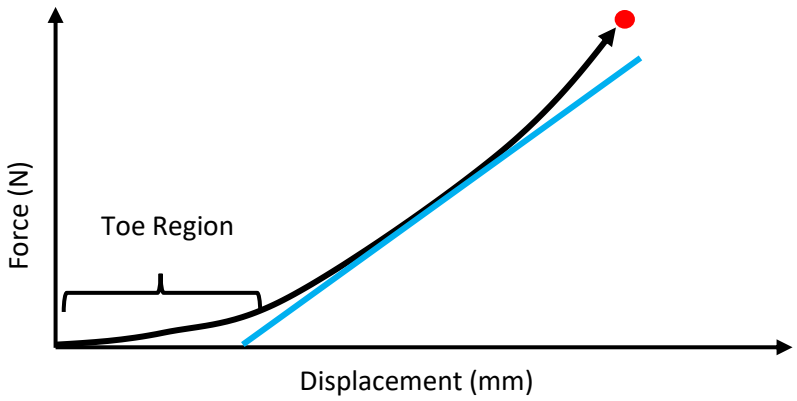

Figure 3.2: Force-displacement curve. The blue line indicates the linear region, the red dot indicates maximum force and displacement.

3.2.6. Aims

The *in vivo* lumbar spine consists of multiple functional spinal units and surrounding soft tissue working in unison to create movement. When using models (Keller and Colloca 2002; Keller et al. 2002) or dissected mammal spines (Ianuzzi and Khalsa 2005a, 2005b), the lumbar spine is 'stripped down' and simplified, effectively losing the ligamentous, muscular and motor (neurological) aspect of joint stabilisation. As such, while the use of models can assist with building theoretical frameworks, until assessed *in vivo*, they remain theoretical or predictive. While porcine specimens are thought to be closely related to human lumbar spines in terms of geometry in the coronal plane and in terms of disc structure, it should be recognised that porcine, as well as feline and ovine specimens are optimised for quadruped motion and not for biped motion as in humans. For this

reason, the aim of the systematic review was to explore the available literature relating to live symptomatic and asymptomatic humans.

3.3. Method:

Relevant peer reviewed literature was systematically searched. The literature search took place in July 2020 and repeated in June 2022. It included the electronic databases of Pubmed, Web of Science, Medline, Cochrane and CINAHL. The search terms and subject headings used can be seen in Table 3.1. Due to the number of journal articles relating to “vertebrate” and “cervix”, the search was modified to exclude these terms. As the focus of the thesis was LBP, only journal articles relating to lumbar spine (including L5-S1 and T12-L1) were included. The search was limited to human studies in English journal articles only, no time limit was applied to ensure all relevant information was obtained.

Table 3.1: Search terms and narrowing terms used for the search strategy to answer the question, is there intersegmental change following spinal manipulative therapy and mobilisation?

Theme:	**Search Terms and Subject Headings:**
Manual Therapy	"Spinal Manipulat*" "Lumbar Manipulat*" "Manual Therapy" (manipulat* or mobiliz* or mobilis*) adj5 (spine* or spinal) Subject Headings: Manipulation, Spinal/ Chiropractic/ Vertebrae/ Intervertebral Disc/
Segmental movement	Segmental Intersegmental Inter-segmental Vertebra* Intervertebra* Inter-vertebra* (change* or alter* or increase or decrease) adj5 (segment* or intersegment*) (change* or alter* or increase or decrease) adj5 (vertebra* or intervertebral*)
Biomechanics	Biomechanic* phenomena* Kinematic* Kinetic* Stiff* "Spinal Stiffness" mechanobiological phenomena* Subject Headings: Biomechanical Phenomena/

Following the removal of duplicates, titles and abstracts were screened to identify relevant, possibly relevant, and irrelevant studies. Relevant and possibly relevant studies were then read in full text to determine eligibility. Studies were deemed eligible if they contained information on lumbar intervertebral joint motion from either SMT or mobilisation. A manual review of the articles' reference lists was used as an additional data source. The included peer reviewed journal articles were assessed using the Physiotherapy Database Scale (PEDro 2020) (Appendix A). The scale considers randomisation, concealment of allocation, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases.

Data relating to SMT and mobilisation variables, and the effect on intervertebral movement, were extracted. Data were tabulated to compare the literature, where outcomes were outside of the scope of this review (for example, effect of lumbar SMT on the thoracic spine ROM), they were not included in the data extraction.

3.4. Results

The literature search identified 458 peer-reviewed journal articles. Following the removal of duplicates, phase one of screening (title and abstracts) reduced the number of peer-reviewed articles to 20. Phase two of screening (review of full text articles) reduced the number of peer-reviewed articles to 11. Articles excluded during phase two screening included commentary (n=1); letter to the editor (n=1); a systematic or narrative review, where no intervertebral motion data were included (n=3); full text articles which were unavailable (pre-1990) (n=2); outcomes which were measures of regional motion and not intervertebral motion (n=2). Two additional articles were included following reference list reviews (See Figure 3.3).

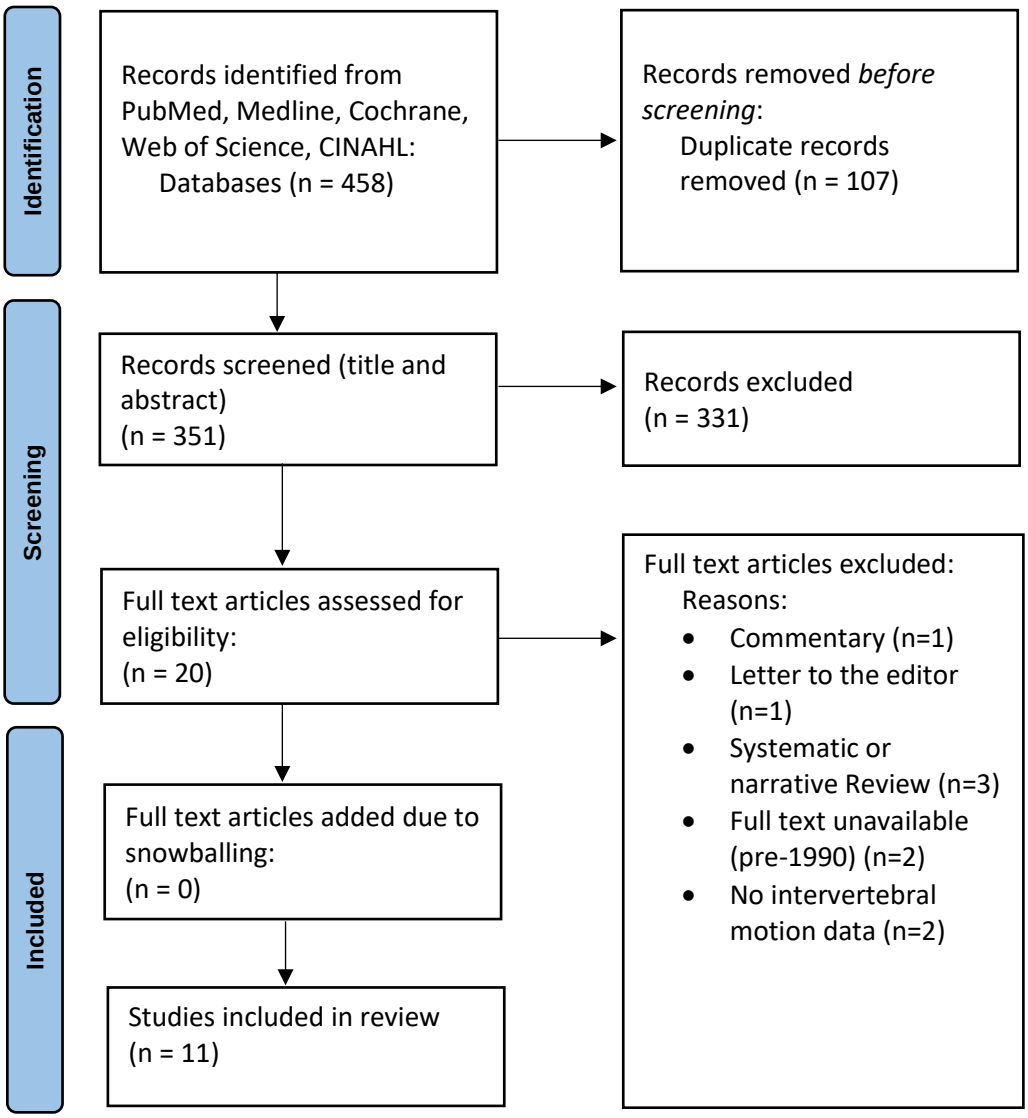

Figure 3.3: PRISMA Flow Diagram. Presentation of the procedure for the literature search for the narrative review entitled: Is There Intersegmental Change Following Spinal Manipulative Therapy and Mobilisation?

A summary of the data extraction can be seen in Table 3.2. The ratio of male to female, and mean age were tabulated, together with the type of intervention; the force or frequency utilised; the objective measurements obtained; and a brief summary of the outcome. Eight journal articles explored stiffness; two explored intervertebral angle during mobilisation; and one explored joint gapping during patient positioning.

A summary of critical appraisal using the PEDro Scale (PEDro 2020) of the 11 peer reviewed articles can be seen in Table 3.3. As evidenced from Table 3.3 the level of evidence is very low for majority of the articles.

Table 3.2: Summary table of data extraction for 11 peer reviewed journal articles relating to intervertebral motion following SMT or mobilisation to the lumbar spine. Where information was not available, this has been indicated in grey.

Authors	**Sample Size (*n*)**	**Age range and sex**	**Intervention**	**Force (N), frequency Hz)**	**Objective Measurement**	**Outcome**
Allison et al. 2001	Live asymptomatic humans (n=24)	13 men, 11 women; mean age 27 (± 3), range 20 - 35	Mobilisation (clinician delivered - oscillatory)	Mean force of 146N (SD 8N) at a frequency of 1.5 Hz	Stiffness (measured in N/mm)	Two minutes' PA mobilization resulted in no significant change in the PA stiffness of the lumbar spine at the level to which the mobilization was applied (L3), or at the L1 and L5 segments (distant from mobilisation site).
Allison et al. 1998	Live asymptomatic humans (n=24)	13 men, 11 women; mean age 27 (± 3), range 20 - 35	Static force (clinician delivered)	30 N preload, followed by 100N load	Stiffness (measured in N/mm)	Stiffness of L5 was significantly lower when the load was applied in the vertical direction compared with the application of the load in the perpendicular direction (p=0.0001). Altering the angle of inclination PA load had no significant effect on PA stiffness at L1 or L3.
Caling and Lee 2001	Live asymptomatic humans (n=24)	14 male, 10 female; 24.1 (±6.0)	Mobilisation	30 N preload, followed by 100N load	Stiffness (measured in N/mm) (linear region)	Changes in force direction changes stiffness. At L3, mean stiffness was greater with posterior-anterior direction, it was 11% less when applied 10° more caudad, and 14% less than applied more cephalad. No significant difference was found at L5

Colloca et al. 2003b	Live humans, Symptomatic LBP (including LPB with leg pain) (n=18)	10 male, 8 female; 44.3 (±15.4), range 15 - 69.	SMT (activator)	150N	Radiograph (L4 and L5): Post. Disc height, post vert. height, ant disc height, ant vert. height. Mechanical impedance (Zmin1, Ns/m) and Effective stiffness (Kmin1, kN/m) at the PA natural frequency (fmin1) taken at L4 and L5 only.	There is correlation (p=0.002) between increased effective stiffness and decreased posterior lumbosacral disk height at L5/S1.
Cramer et al. 2012	Live Asymptomatic humans (n=40)	20 male, 20 female, range 18 - 30	SMT (clinician delivered)	Unknown	During the SMT - accelerometers assessed for presence of cavitation; MRI	SMT group upside joints (lt) gapped more than side posture position group only (p=0.03). A decrease in joint gapping was found on the downside (rt) with SMT group showing less of a gap decrease than side posture only (p=0.01). SMT group, men gapped more than women (p<0.002).

					measured gapping of z-joints.	No difference in sex in side posture group only. Overall, joints that cavitated gapped more than those that didn't (p=0.004). Upside joints (lt) found no relationship between cavitation and gapping (p=0.43). Joints that cavitated from SMT (n=28) had the same gapping difference as those that cavitated in the side posture only group (n=3).
Kulig et al. 2004	Asymptomatic live humans (n=20)	18 male, 2 female; mean age 31.1 (±7.0), range 22 - 43	Mobilisation	Unknown - clinician delivered mobilisation.	intervertebral angle (extension)	PA force applied at 1 spinous process caused motion at the target vertebra and this motion was propagated caudally and cranially. Motion at the target segment was always into extension.
Kulig et al. 2007	Asymptomatic live humans (n=20) and symptomatic (LBP) live humans (n=45)	Asymptomatic: 18 male, 2 female; mean age 31.1 (±7.0), range 22 - 43. Symptomatic: 18 male, 27 female; age 32.1 (±8.5)	Mobilisation	Unknown - clinician delivered mobilisation.	intervertebral angle (extension)	The symptomatic group had a larger percentage of subjects with evidence of single level segmental hypermobility than the asymptomatic group during the PA (40.0% vs. 5%) and PU (26.7% vs. 15%) procedures. Single lumbar motion-segment analysis revealed hyper-mobility in symptomatic subjects at L5 – S1 (Chi-square = 10.0, $p \leq 0.01$) and L4 – L5 (Chi-square = 4.18, $p \leq 0.05$) during the PA test.

Kumar 2011	Asymptomatic live humans (n=16)	8 male, 8 female; mean age 25.6, range 22 - 31		22.5N, 45N, 90N and 135N	Stiffness (N/mm) (toe region)	Stiffness at L2 ranged from a mean of 4.23 up to 8.49, as the force increased from 22.5N up to 135N, so did the stiffness. However, this was not a linear relationship.
Kumar 2012	Asymptomatic live humans (n=16)	8 male, 8 female; 28, range 21 - 50		22.5N, 45N, 90N and 135N	Stiffness (N/mm) (toe region)	Stiffness at L3 ranged from 5.08N/mm up to 8.79N/mm, as the force increased from 22.5N up to 135N. As the magnitude of the force increased, so did the stiffness. However, this was not a linear relationship.
Shirley et al. 2002	Asymptomatic live humans (n=18)	6 male, 12 female	Mobilisation	Unknown	Stiffness (linear region)	During mobilisation (five oscillations at 0.5Hz), the first measurements of displacement and stiffness were significantly less than the subsequent measures which were comparable to each other.
Wong et al. 2015	Asymptomatic live humans (n=57) and symptomatic (LBP) live humans (n=33)	Symptomatic mean age 32.2, asymptomatic mean age 29.7 (± 11.3)		Up to 60N	Stiffness (linear region)	Responders to SMT (defined as those reaching a MCIC in the ODI) displayed a significant decrease in spinal stiffness as compared to those who did not respond to SMT.

Table 3.3: Results of critical appraisal of the 11 included peer reviewed journal articles. The PEDro Scale (2020) to obtain a score out of 10 (excluding question 1), 0 indicates and answer of no to the question; 1 indicates an answer of yes to the question; the total score indicates the level of evidence.

Authors	**Eligibility criteria**	**Random allocation**	**Allocation concealed**	**Similar at baseline**	**Blinding of subjects**	**Blinding of therapist**	**Blinding of assessor**	**Outcome obtained from 85%**	**Received intervention**	**Between group comparison**	**Within group comparison**	**Total**
Allison et al. 2001	1	0	0	0	0	0	0	1	1	0	1	3
Allison et al. 1998	1	0	0	0	0	0	0	1	1	0	1	3
Caling and Lee 2001	1	0	0	0	0	0	0	1	1	0	1	3
Colloca et al. 2003b	1	0	0	0	0	0	0	1	1	0	1	3
Cramer et al. 2012	1	1	0	0	0	0	0	1	1	1	1	5

Kulig et al. 2004	1	0	0	0	0	0	0	1	1	0	1	3
Kulig et al. 2007	1	0	0	0	0	0	0	1	1	0	1	3
Kumar 2011	1	0	0	0	0	0	0	1	1	0	1	3
Kumar 2012	1	0	0	0	0	0	0	1	1	0	1	3
Shirley et al. 2002	1	0	0	0	0	0	0	1	1	0	1	3
Wong et al. 2015	1	0	0	0	0	0	0	1	1	0	1	3

3.5. Discussion

The PEDro Scale (PEDro 2020) was utilised to assess the quality of the included journal articles. As evidenced from Table 3.3 the level of evidence is very low for majority of the articles. There are two main reasons for this; the first being the lack of a control group or second group; the second being the lack of blinding of the participant, the practitioner, or the assessor of the outcome measures. These short falls increase the risk of bias in a study and decrease the trustworthiness in the study results. Acknowledgement has been made of the low level of evidence; however, all journal articles were included in the data extraction and discussion to gain an overarching view of the topic area (Popay et al. 2006; Siddaway et al. 2019).

3.5.1. Patient Positioning

During side-lying patient positioning, as well as the SMT delivery, the space between the articular surfaces of the facet joint increased or gapped (Cramer et al. 2012). When facet joint gapping due to side-lying patient position was compared to gapping during SMT, the upside joint (closest to the ceiling) gapped significantly more during SMT ($p=0.03$), than side-lying alone (Cramer et al. 2012). During SMT, facet joints gap significantly more in men, than women ($p<0.002$) (Cramer et al. 2012). It was suggested that facet joint gapping has a mechanical stimulus effect on spinal tissues (Zusman 1986) (See Section 2.9.3.1.1).

3.5.2. Mobilisation

Mobilisation of the lumbar spine was applied to each spinous process and changes to intervertebral angles were measured using MRI *in vivo* (Kulig et al. 2004). When posterior-anterior force was applied to L5, there was an increase in extension intervertebral angle at L5-S1 by 3.6° (±1.1). However, the lumbar segments cranially to L5 also showed an increase in extension intervertebral angle decreasing gradually from L4-L5 to L1-L2 (Kulig et al. 2004). Interestingly, in this study three out of twenty participants demonstrated paradoxical motion when posterior-anterior force was applied to L3, L4-L5 and L5-S1 moved into flexion. When force is applied to L1, L1-L2; L2-L3 and L3-L4 move into extension, however, some participants did not move at L3-L4 (n=6), L4-L5 (n=4) and L5-S1 (n=2). When force is applied to L2, L2-L3 moved into extension, however, L4-L5 and L5-S1 most participants moved into flexion, the remaining participants demonstrated no movement at L4-L5 (n=7) and L5-S1 (n=4) (Kulig et al. 2004). Interpreting these findings, when the contact point was caudal, there was more motion in the vertebra above than if the contact point was cranial. This appears to be converse to what occurs in SMT, vertebral posterior-anterior displacements decreased significantly if contact point was caudal to the vertebra of interest, compared with cranial to the vertebra of interest (Keller et al. 2003).

3.5.3. Stiffness

Kumar (2012) defined stiffness as the toe region of the force-displacement curve. Stiffness at L3 ranged from 5.08N/mm up to 8.79N/mm, as the force increased from 22.5N up to 135N (Kumar 2012). Wong et al. (2015) defined stiffness at the linear region of the force-displacement curve and compared stiffness between symptomatic and asymptomatic participants. They reported stiffness at L3 to be 5.76N/mm in the symptomatic group and 5.44N/mm in the asymptomatic group. If the data from the two studies are tabulated (See Table 3.4), what was evident is that there is a relationship between magnitude of force and stiffness. As force increases, as does stiffness, however this relationship was not linear.

Table 3.4: Tabulated data comparing force to stiffness derived from Kumar (2012) and Wong et al. (2015).

Force (N)	**Stiffness (N/mm)**
22.5 (Kumar 2012)	5.08 (±0.43)
45 (Kumar 2012)	5.30 (±0.28)
60 (Wong et al. 2015)	Symptomatic (responders to SMT): 5.76 (±1.20) Symptomatic (non-responders to SMT: 5.44 (±1.36) Asymptomatic: 5.56 (±1.19)
90 (Kumar 2012)	6.53 (±0.28)
135 (Kumar 2012)	8.79 (±0.45)

A feline study by Edgecombe et al. (2015) suggest that the application site of SMT can influence stiffness. Significant post-SMT changes (relative to control) were observed when the SMT was applied to the lumbar spinous process and lamina (Edgecombe et al. 2015). However, no significant changes in stiffness were observed when SMT was applied to the mammillary process or the spinous process of vertebra below. When stiffness was measured in adjacent vertebra in a human study, there were no significant differences in L1 and L5 when mobilisation was applied to L3 spinous process (Allison et al. 2001).

The direction at which the force is applied can affect the stiffness measure (Caling and Lee 2001). At L3, mean stiffness was greatest when the force was delivered in a posterior-anterior direction, stiffness was 11% less when applied in a caudad direction, and 14% less than applied in a cephalad direction. Interestingly, no significant differences in force direction and stiffness were

found at L5 (Caling and Lee 2001). However, the direction in which stiffness is measured does alter the measurement of stiffness. During a holding mobilisation (force in a posterior-anterior direction held for as long as participant can hold their breath), stiffness was significantly lower when measured posterior-anterior, than medial-lateral (Allison et al. 1998).

The number of mobilisations may influence the measurement of stiffness. During mobilisation (five oscillations at 0.5Hz), Shirley et al. (2002) found stiffness to be the least during the first oscillation, the subsequent oscillations were stiffer and more comparable to each other.

In a study utilising anaesthetised sheep, stiffness was calculated as peak force divided by peak displacement (N/mm) (Keller and Colloca 2007). Stiffness was measured in constant frequencies of 2Hz (5.41N/mm), 6Hz (6.45N/mm) and 11.7Hz (11.8N/mm), as well as a sweeping frequency of 0.5 – 19.7Hz (minimum of 5.77 to maximum of 14.1N/mm). The study concluded that stiffness increased with increasing frequency, there was little difference between constant frequency or sweeping frequency (Keller and Colloca 2007).

It is thought that repeated measures testing may influence the measurement of spinal motion. The reason for this is that repeated motion is one of the ways mobilisation is carried out and as such is utilised as a treatment. The extent to which repeated measures influences spinal motion as an outcome measure is unknown.

3.5.4. Studies that included acute NSLBP participants

During posterior-anterior mobilisation, there were no significant differences in intervertebral angles between patients experiencing NSLBP and their pain-free counterparts (Kulig et al. 2007). The largest amount of intervertebral angle change during mobilisation was at L1-L2 in asymptomatic participants (3.9° ± 1.7) and at L2-L3 in symptomatic participants (4.3° ±1.5). The least amount of motion was measured at L4-L5 for both groups (Kulig et al. 2007). In this study, participants demonstrating intervertebral angle motion of more than the asymptomatic group's mean ±2 standard deviations were considered hypermobile, those demonstrating less were considered hypomobile. Only 4.4% of the symptomatic group and 10% of the asymptomatic group demonstrated hypomobility at one motion segment (Kulig et al. 2007). Thus, symptomatic participants demonstrated greater intersegmental mobility than their pain-free counterparts. However, Wong et al. (2015) explored stiffness in NSLBP participants following SMT. Participants who responded to SMT (determined by obtaining MCIC in ODI) demonstrated a significant decrease in stiffness in contrast to their non-responsive counterparts.

3.6. General

Gaining an understanding of intervertebral motion in humans is very difficult. This is largely due to the large number of variables which can be introduced during SMT and mobilisation. Variables such as SMT delivery method, contact site, direction of SMT delivery have not been explored in a live human population. Thus, exploring the relationship between displacement and speed, acceleration and force is theoretical. Equally, the difference in biomechanics between SMT and mobilisation has not been explored in a human population and as such remains theoretical as well.

Much of the difficulty in carrying out human studies lies in the measurement method. Many of the studies exploring real time displacement have used invasive procedures to apply rods to the vertebrae, which is ethically not possible in a live human population. Until a more ethical, but accurate method can be devised, this will remain a difficult area to explore.

There are a number of human studies exploring mobilisation and lumbar stiffness. Studies use different ways of measuring stiffness, making comparisons between studies difficult. Potentially, an agreement between spinal stiffness researchers would be advantageous going forward.

There is evidence to suggest that the measurement of stiffness requires a number of patient-related, as well as environmental factors to be controlled (Wong and Kawchuk 2017). Patient-related factors which can affect the measurement of spinal stiffness include trunk extensor contraction; abdominal muscle contraction; intra-abdominal pressure; where in the respiratory cycle the measurement is taken; the participants' gender; and the participants fat percentage (Wong and Kawchuk 2017). The environmental factors which can affect the measurement of spinal stiffness include load force, frequency, speed, and angle; testing position; constraint of the pelvis or rib cage; and padding of the test surface (Wong and Kawchuk 2017). There is very little mention of these factors in the articles included in this narrative review. For this reason, the accuracy of the measure of stiffness needs to be explored further. However, test-retest reliability was good, ranging from an ICC of 0.77 – 0.79 (Lee and Evans 1992; Wong et al. 2013).

There is very literature relating to short term or long-term biomechanical effects of SMT or mobilisation. With the development of imaging, such as quantitative fluoroscopy, this is an area future research should look to expand into.

3.7. Conclusion

Spinal stiffness is affected by magnitude of force, direction, contact site on vertebra of interest, number of mobilisation oscillations and whether the oscillations are static or sweeping. NSLBP

patients who responded to treatment demonstrated reduced stiffness post treatment than those who did not respond to treatment.

Future research should look towards exploring short-term and long-term effects of SMT and mobilisation, particularly with the development of new imaging modalities.

4. Literature Review

4.1. Introduction

Much of the previous chapter relates to what is occurring in the lumbar spine at the time of SMT and mobilisation (immediate effects), and how various parameters of SMT and mobilisation effect intersegmental motion. This chapter explores methods of measuring intervertebral motion *in vivo*, including which intervertebral measurements can be obtained. The chapter outlines how intervertebral motion can be measured to explore short term and long terms effects of manual therapy. The literature search took place from September 2018 until March 2021 and included the electronic databases of PubMed, Web of Science, Medline, Cochrane and CINAHL. Search terms included (Imaging OR CT OR MRI OR "planar x-ray" OR x-ray OR EOS OR Quantitative Fluoroscopy OR Motion Capture) AND (biomechanics OR kinematics) AND (lumbar OR "low back pain" OR NSLBP).

This chapter also explores how to determine if manual therapy is clinically effective, what measuring tools can be utilised, and if all patients respond to treatment. The literature search took place from September 2018 until March 2021 and included the electronic databases of PubMed, Web of Science, Medline, Cochrane and CINAHL. Search terms included (PROM OR "Core outcome set" OR "pain scale" OR "disability questionnaire" OR "health related quality of life" OR "physical functioning" OR questionnaire) AND (lumbar OR "low back pain" OR NSLBP).

4.2. How Can Intervertebral Motion be Measured *in vivo*?

An invasive approach includes roentgen stereophotogrammetry which involves metal markers surgically implanted into the vertebrae. The motion is then measured via bi-planar radiographs of the lumbar spine in six positions (Johnsson et al. 1990; Axelsson et al. 1992; Leivseth et al. 1998; Axelsson and Karlsson 2004). Not only is this invasive, but the radiation dose approaches 2.6mSv. To put this into context, the average annual background radiation dose in the UK (excluding Cornwall) is 2.7mSv (Public Health England 2011). Another invasive approach is percutaneous intra-pedicle screws which involves surgically implanting screws and rods into a functional spinal unit of the lumbar spine to assess the relationship between pain and vertebral motion in LBP patients (Dickey et al. 2002). This is highly invasive and requires a surgical procedure to insert and remove the intra-pedicle screws.

However, intervertebral motion can be viewed and measured non-invasively using imaging modalities. The intervertebral motion variables of angular intervertebral range of motion (IV-ROM), disc height and translation can be viewed using static imaging by comparing neutral views

to flexion and extension views. However, to really explore aberrant motion patterns, continuous motion imaging is required. Many of the imaging modalities use ionising radiation, and as such there is the additional need to keep the radiation dose as low as reasonably practicable (ALARP) (HSE 2021). Ethically, the risk and reward of the use of ionising radiation needs to be considered (HSE 2021). Particularly in a research setting where, under what is considered normal management of the condition, imaging would not normally be carried out.

Radiation dose is measured in three ways. Absorbed dose (measured in milli-gray (mGy)) is the concentration of energy deposited in tissue as a result of an exposure to ionising radiation. Equivalent dose (measured in millisievert (mSv)) takes the damaging properties of different types of radiation into account. Lastly, effective dose is a calculated value (measured in mSv) which takes into account the absorbed dose, relative harm level of radiation and sensitivities of each organ to radiation. The effective radiation dose will be used to compare imaging modalities.

Table 4.1 is a summary of the imaging modalities, their effective radiation dose (mSv), the intervertebral motion variables which can be obtained and whether the imaging modality can obtain continuous motion images. The table has been compiled utilising the imaging modality literature.

Table 4.1: Summary of imaging modalities, imaging views, radiation dose (mSv), intervertebral motion variables which the modality can be used to measure, and whether the imaging modality can view continuous motion.

Imaging Modality	**Views**	**Radiation Dose (mSv)**	**Intervertebral Motion Variables**	**Continuous Motion (Yes/ No)**
Planar X-Ray	Lumbar neutral, full flexion, full extension	1.3	IV-ROM, translation, disc height	No
Biplanar x-ray	Lumbar neutral (three views)	1.3	None	No
EOS	Full spine neutral (PA view)	0.07 – 0.23	None	No
	Full spine neutral (Lateral view)	0.13 – 0.37	None	No
Cineradiography	No longer used due to the multiple x-ray exposures required, and the high effective radiation dose to the patient.			
CT	Abdomen and pelvis view	10	Translation, disc height	No
MRI	Abdomen and pelvis view	None	Translation, disc height	No
Fluoroscopy	Standing flexion and extension; recumbent flexion and extension	0.67-0.69	IV-ROM, translation, initial attainment rate, disc height, motion sharing inequality and motion sharing variability	Yes
Motion Capture	Flexion, extension	None	None	Yes

4.2.1. X-Ray

4.2.1.1. Planar X-Ray

Standing lumbar x-rays can be utilised to measure intervertebral motion, such as IV-ROM (Leone et al. 2007), translation (Frobin et al. 1997; Pitkänen et al. 2002) and disc height (Frobin et al. 1997). Measurements are effectively static measurements of end ROM in the sagittal plane (flexion and extension), compared to neutral. As such, continuous motion data is not available, and it is not possible to explore aberrant motion patterns. According to Public Health England (2008), a lumbar spine series of three views delivers a total effective dose of 1.3 mSv.

4.2.1.2. Biplanar X-Ray

Standing biplanar lumbar x-ray can be utilised to reconstruct a three-dimensional (3D) image of the lumbar spine. When reconstructing the lumbar spine at least two views are required, one posterior-anterior view and one lateral view (Dansereau and Stokes 1988; Moura et al. 2011). However, it is not uncommon for a third view to be used of a 20° angled down posterior-anterior view (Cheriet et al. 2007). Radio-opaque markers or pellets of known 3D coordinates are used to define a reference for the 3D construction (Cheriet et al. 2007; Moura et al. 2011). For exploration of the lumbar spine in neutral it would require up to three views and up to 1.3mSv of effective radiation dose. In order to explore intervertebral motion, flexion, neutral and extension would be required resulting in up to a total of nine radiographs and a total effective dose of up to 3.9 mSv. For this reason, biplanar x-ray is seldom used to explore intervertebral motion, but is used more for measurement of Cobb's angle for scoliosis, kyphosis and lordosis in neutral (Moura et al. 2011).

4.2.1.3. EOS®

EOS® is a biplanar x-ray imaging system manufactured by EOS Imaging (ATEC Spine, California, USA) which produces high quality images with less radiation (McKenna et al. 2012; Melhem et al. 2016). EOS® image acquisition can be performed standing, seated, or squatting and full body length images can be obtained. EOS® is able to take posterior-anterior and lateral views simultaneously, and a well-trained operator is able to create a 3D image in up to ten minutes (McKenna et al. 2012). It is estimated that the effective radiation for EOS® is between 5.2 to 13.1 times less than x-ray for a posterior-anterior spine view, and between 6.2 to 15.1 times less for a lateral spine view (McKenna et al. 2012; Melhem et al. 2016; Law et al. 2017; Hamzian et al. 2021). Although this relatively new technology is evolving, currently full flexion or extension views are not possible and as such it is not possible to explore intervertebral motion. The system is

mostly used for kyphosis and lordosis measurements (Abrisham et al. 2020; Garg et al. 2020), as well as scoliosis assessments and monitoring (Pasha et al. 2016; Law et al. 2017; Garg et al. 2020).

4.2.2. Magnetic Resonance Imaging (MRI)

MRI is a non-invasive diagnostic tool which provides the most accurate delineation of soft-tissue and osseous structures enabling detection of abnormalities with great sensitivity (Michelini et al. 2018). Dynamic or kinetic MRI often uses an open scanner which allows upright scanning (seated or recumbent), at the cost of lower resolution (Michelini et al. 2018). MRI is used to measure lumbosacral angle, lordosis angle, disc height and interspinous distance between two adjacent vertebrae (Michelini et al. 2018) and can potentially use these measurements together with classification of lumbar degeneration to gain a greater understanding of the effect of disc and facet degeneration (Lee et al. 2015). The limitation of the use of MRI in motion studies is the need for the participant to remain still while the images are acquired (Morishita et al. 2008). For this reason, participants are moved into various degrees of flexion and extension to hold this position while the image is acquired, and as such continuous motion cannot be measured. The use of dynamic MRI has been coupled with planar x-rays to provide a greater sensitivity to assess lumbar instability and its possible cause (Lee et al. 2021). An advantage of using MRI is that it does not require ionising radiation to obtain the images, however, it is expensive.

4.2.3. Computerised Tomography (CT)

Arguably, CT provides the best osseus detail and has the ability to create 3D bone images (Kim et al. 2003). The effective radiation dose is 10mSv for an abdominal and pelvic CT (Public Health England 2008), and similar to MRI, the limitation of CT in motion studies is the need for the participant to remain still while the images are acquired. As the radiation dose is very high, to take multiple CT scans to view neutral, flexion and extension is not ethical and as a result is very seldom used to explore intervertebral motion.

4.2.4. Cineradiography

Cineradiography involves taking a rapid succession of x-rays to create what is effectively a moving picture. The oldest surviving cineradiography sequence were created by Brailsford in 1934 who recorded motion of four acrobats with x-rays at 16 frames per second (Brailsford 1934). The radiation dose would have been very high and for this reason not for general use. It was, however, the precursor to the development of video fluoroscopy.

4.2.5. Quantitative Fluoroscopy (QF)

QF combines fluoroscopy (moving x-rays), together with an automated computer processing algorithm to calculate intervertebral motion variables such as IV-ROM, disc height, translation, initial attainment rate (laxity), motion sharing inequality and motion sharing variability (Breen et al. 2012b). The advantage of QF is that it is able to view continuous motion of the lumbar spine with relatively low effective radiation dose. For this reason, multiple views can be taken (standing flexion and extension; recumbent flexion and extension) to explore spinal motion with an effective radiation dose of 0.67 – 0.69mSv (this study). A limitation of QF is the reduced resolution. Arguably a diagnostic grade x-ray resolution is not necessary for biomechanical measurements, however, fluoroscopy images are not appropriate for bony pathology diagnosis.

4.2.6. Motion Capture

Motion capture is the process of digitally recording the way people move. Motion tracking devices, such as accelerometers and electromagnetic sensors, are capable of measuring dynamic motion. They have a high temporal resolution, but compared to MRI, biplanar X-ray and fluoroscopy, relatively low spatial resolution. For this reason, motion capture is not used to explore intervertebral motion, but rather larger areas such as upper lumbar spine or lower lumbar spine (Mazzone et al. 2016; Zwambag et al. 2019; Pourahmadi et al. 2020).

4.3. Which Imaging Views are the Most Useful?

4.3.1. Sagittal, coronal, or transverse plane views?

There are three planes of motion to choose from when assessing intervertebral motion, sagittal (flexion and extension), coronal (lateral flexion) and transverse (axial rotation). It is not feasible to assess axial rotation with any uniplanar imaging as the images would need to be taken from superior to inferior, which is both impractical and individual bones would be impossible to discern. It is possible to explore intervertebral motion of lateral flexion, however, due to the orientation of the facets pure motion is unobtainable. Lateral flexion of the vertebra is combined with a significant amount of axial rotation to create the torso movement of lateral flexion (Pearcy et al. 1985). Thus, making uniplanar images difficult to analyse accurately. Flexion and extension in the lumbar spine are more pure movements with very little (if any) axial rotation or lateral flexion, equally there is relatively more intervertebral ROM during these movements. Together, these make the sagittal plane preferable when exploring intervertebral motion using a radiographic method.

4.3.2. Weight bearing versus Recumbent Intervertebral Motion

In general, planar x-rays and EOS® are carried out standing; CT is carried out recumbent; and bi-planar x-ray, MRI and QF can be either standing or recumbent.

Intervertebral motion measurement will be affected by whether it is carried out weight bearing (standing) or recumbent. It is assumed that there will be no muscular or motor influence with recumbent passive motion (Mellor et al. 2009; Breen et al. 2012b), thus, providing a greater understanding of the passive holding elements such as discs, vertebral bodies, facet joints and ligaments. Conversely, weight bearing includes the simultaneous function of the passive holding elements, the active spinal musculature, and the neural/ motor control system.

Theoretically, by comparing weight bearing (standing) to recumbent, which can be done using QF it may be possible to understand the biomechanics of the passive holding elements versus the muscular and motor control elements.

4.4. Which Intervertebral Motion Variables Can Be Measured?

4.4.1. Stiffness

Accessory joint motion has been discussed in section 2.8.1. This section will focus on mechanically assisted spinal stiffness-testing devices. There are a number of models used within the literature (Keller et al. 2002; Colloca et al. 2003b; Stanton and Kawchuk 2009; Kumar and Stoll 2011; Kumar 2012; Wong et al. 2013). In general, the device consists of a load cell that measures indentation forces (measured in Newtons (N)), together with displacement sensors which detect the displacement (measured in millimetres (mm)) during indentation. The operator manually controls indentation force, speed, and direction (Wong and Kawchuk 2017). Stiffness is calculated using the force-displacement curve (See Figure 3.2, page 50). When calculating stiffness using the linear region, there are different thoughts on the magnitude of force used to calculate stiffness, with some indicating 30N to 90N of force (Latimer et al. 1996) and others indicating 5N to 60N ((Fritz et al. 2011). The start of the force-displacement curve where relatively little force is required to produce a large displacement is known as the toe region, with some indicating that the magnitude of force used to calculate stiffness is 0N to 30N (Latimer et al. 1996).

There is little consistency in the literature on how stiffness is measured with some literature suggesting stiffness is the measure of the toe region (Kumar 2012); some literature suggesting stiffness is the measure of the linear region (Kumar and Stoll 2011; Kumar 2012; Björnsdóttir et al. 2016); and some literature suggesting stiffness as the final loading force and the overall displacement (Wong et al. 2015) (See Figure 3.2, page 50). It is thought that spinal stiffness is a

measure of intervertebral motion, however, to obtain a stiffness measurement of intervertebral motion both patient-related, as well as environmental factors need to be controlled. Patient-related factors which can affect the measurement of spinal stiffness include trunk extensor contraction; abdominal muscle contraction; intra-abdominal pressure; where in the respiratory cycle the measurement is taken; the participants' gender; and the participants fat percentage (Wong and Kawchuk 2017). The environmental factors which can affect the measurement of spinal stiffness include load force, frequency, speed, and angle; testing position; constraint of the pelvis or rib cage; and padding of the test surface (Wong and Kawchuk 2017). This many controllable and uncontrollable factors brings into question the validity of the measurement. However, test-retest reliability was good, ranging from an ICC of 0.77 – 0.79 (Lee and Evans 1992; Wong et al. 2013).

4.4.2. Intervertebral Motion Variables

There are a number of intervertebral motion variables which can be measured using quantitative fluoroscopy (QF). Arguably, the six most useful intervertebral variables include angular intervertebral range of motion (IV-ROM); initial attainment rate or laxity; translation; disc height; motion sharing inequality (MSI) and motion sharing variability (MSV).

Debatably, an addition to the list should include Centre of Rotation (COR). Centre of rotation is defined as the point around which a motion segment appears to move (Funabashi et al. 2020). It has been thought to indicate aberrant intersegmental motion which may be related to spinal instability (Widmer et al. 2019). However, the measurement of COR is associated with inaccuracies, such as large error magnification (Panjabi 1979), projection errors, and errors due to coupled motion (Wachowski et al. 2010). There is large variability in the literature, with COR spreading beyond the boundaries of the vertebral bodies (Pearcy and Bogduk 1988; Yoshioka et al. 1990; Aiyangar et al. 2017). For these reasons, potentially COR is neither a valid nor reliable measurement.

4.4.2.1. Angular Intervertebral Range of Motion (IV-ROM)

Angular intervertebral range of motion (IV-ROM) is the maximum intervertebral angular displacement during flexion and extension (Breen et al. 2019b). Figure 4.1 is an example of a motion graph produced for weight bearing flexion and return. It demonstrates the change in intervertebral angular range of motion during the sequence. As noted from the graph, the maximum intervertebral angular displacement does not necessarily coincide with the maximum torso flexion, indicating the advantage of this measurement over that from static radiographs.

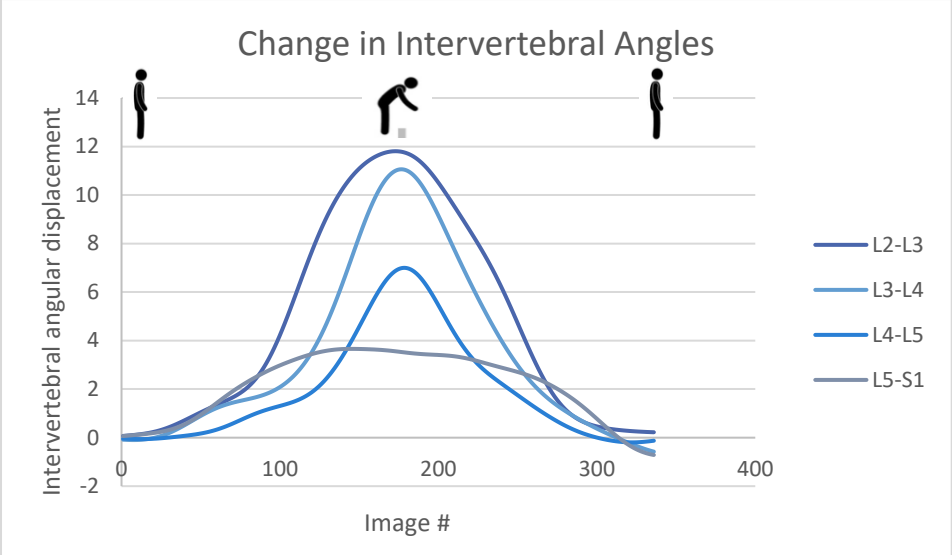

Figure 4.1: Motion graph of weight bearing flexion and return, demonstrating change in intervertebral angular displacement (measured in degrees) during flexion weight bearing and return to neutral.

Figure 4.2 is an example of a motion graph demonstrating paradoxical motion at L5-S1. As evident from the graph, L5-S1 segment moves in the opposite direction to the torso movement and is indicated by the negative measurement of intervertebral angular range of motion.

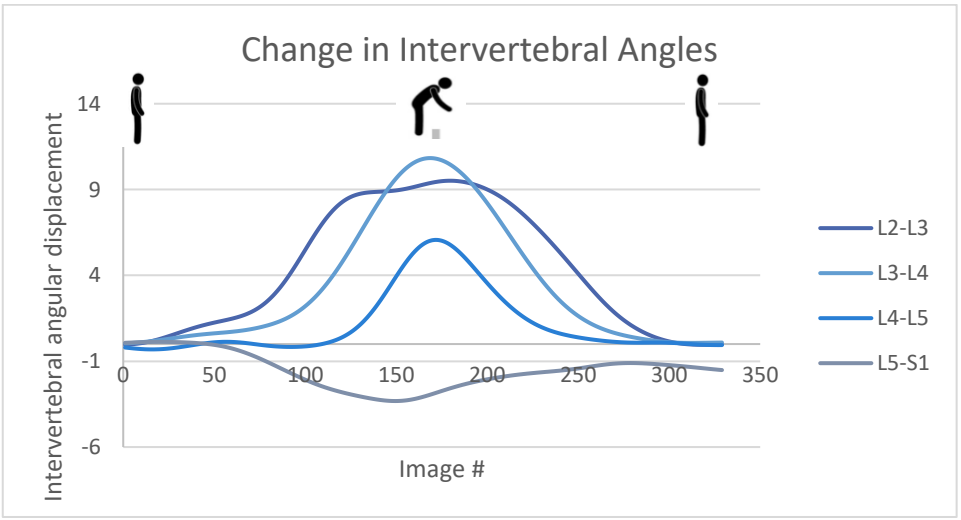

Figure 4.2: A motion graph of weight bearing flexion and return, demonstrating paradoxical motion of L5-S1, which is indicated by the negative measurement of intervertebral angular range of motion.

Du Rose and Breen (2016b) explored the reliability of measuring IV-ROM in the lumbar spine and found the intra class correlation (ICC) for intra-observer and inter-observer reliability to be 0.96 and 0.94 respectively, thus demonstrating excellent reliability. The recumbent flexion minimal detectable change (MDC) was 4.66°, and weight bearing flexion was 9.10° (Breen et al. 2019b). According to White and Panjabi (1990), each motion segment potentially has a maximum of 14° IV-ROM, therefore the MDC or error in the measurement is high. As intra- and inter-observer reliability is high, the error in the measurements appear to be related to something inherent in the measurement technique itself, rather than observer error. However, exploring changes in angular IV-ROM following an intervention, it would be almost impossible for changes to be larger than the MDC, and if they were they would most likely be beyond the anatomical limit for the joint. This brings into question the usefulness of the measurement in intervention studies.

4.4.2.2. Motion Sharing Inequality (MSI) and Motion Sharing Variability (MSV)

Motion Sharing Inequality (MSI) is derived from intervertebral angular motion. Figure 4.3 represents change in intervertebral angular ROM from neutral to flexion and return to neutral during weight bearing. The x-axis represents image number. There are approximately 340 images acquired during the motion. Image number is converted to motion cycle percentage (See Figure 4.4)

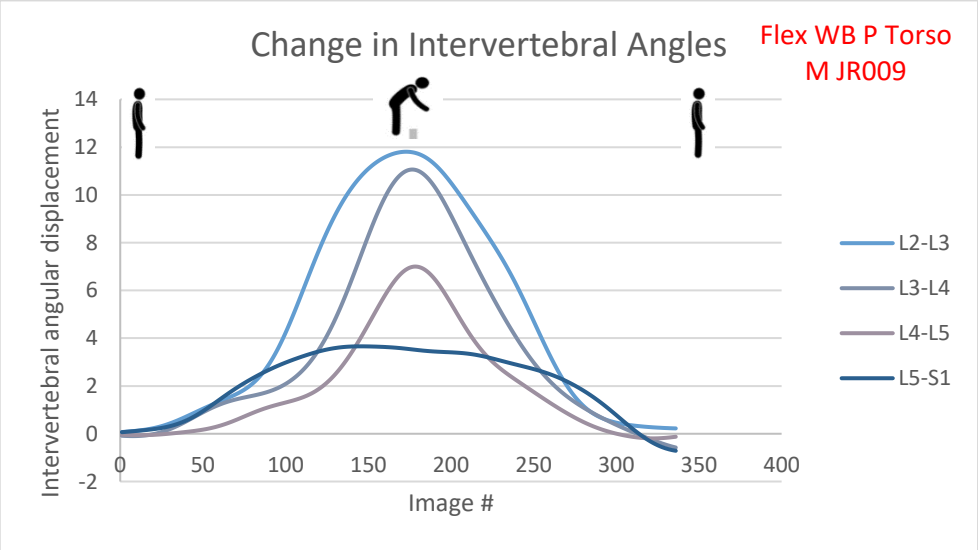

Figure 4.3: Change in intervertebral angular ROM from neutral to flexion and return to neutral during weight bearing. The x-axis represents image number (Modified from To et al. 2020).

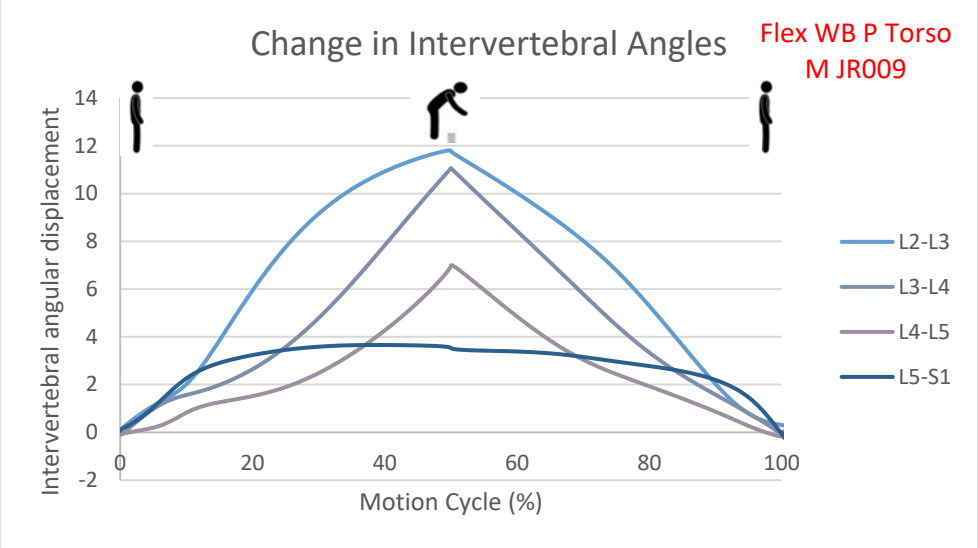

Figure 4.4: Change in intervertebral angular ROM from neutral to flexion and return to neutral during weight bearing. The x-axis represents motion cycle percentage (Modified from To et al. 2020).

Intervertebral angular displacement is proportionally scaled as a ratio of the overall lumbar spine angular ROM from L2-S1 (See Figure 4.5). Changes in the IV-ROM from the neutral position are small at the start and the end of the motion sequence. These data points are close to the error measurement of QF (0.52° per intervertebral joint) and as such they are removed. The middle 80% of the motion is used to calculate MSI.

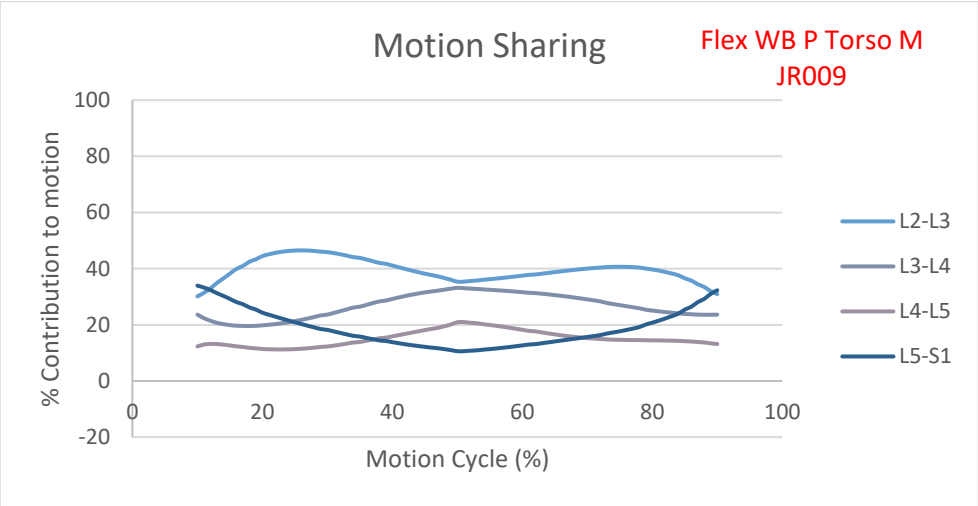

Figure 4.5: Proportionally scaled intervertebral anglar displacement during the motion cycle of flexion weight bearing (Modified from To et al. 2020).

MSI is calculated as the average proportional contribution to the ROM across all points in the fluoroscopy sequence While MSV is the standard deviation of the range of proportional intervertebral motion (To et al. 2020) (See Figure 4.6). In Figure 4.6, the average proportional contribution is 26.6%. MSI is calculated as 0.266, and MSV is calculated as 0.041.

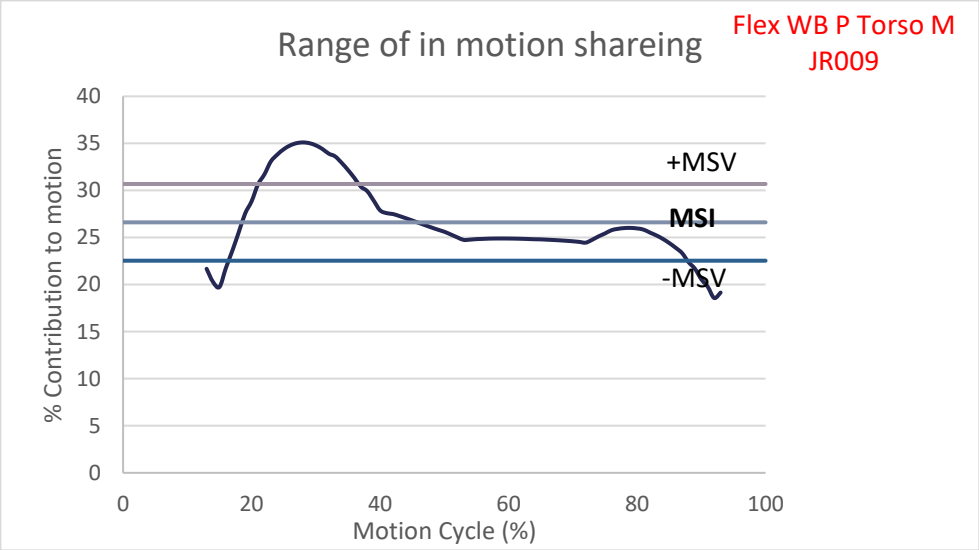

Figure 4.6: MSI is the average of the range of proportional intervertebral motion, while MSV is the standard deviation of the range of proportional intervertebral motion (Modified from To et al. 2020).

A high MSI indicates a large difference in contribution to the ROM (L2-S1) by the intervertebral segments, a low MSI indicates that the contribution of the intervertebral segments is similar across the ROM (L2-S1). Motion Sharing Variability (MSV) is calculated as the square root of the variance (or standard deviation) of these differences throughout the motion (To et al. 2020) (See Figure 4.4).

Breen et al. (2019b) reports flexion weight bearing to have moderate reliability (ICC of MSI 0.76; ICC of MSV 0.65); extension weight bearing to have moderate to poor reliability (ICC of MSI 0.57; ICC of MSV 0.41); flexion recumbent moderate to have poor reliability (ICC of MSI 0.61; ICC of MSV 0.41); and extension weight bearing to have poor reliability (ICC of MSI 0.43; ICC of MSV 0.14). The pool of existing data on MSI and MSV is small and as such what is considered average or 'normal' MSI and MSV has yet to be determined.

4.4.2.3. Initial Attainment Rate (IAR)

Laxity is defined as a kinematic measure which reflects intervertebral restraint in response to external forces (Mellor et al. 2009). It is a part of the range of physiologic movement, measured from the neutral position of the joint, within which motion is met with minimal internal resistance. Panjabi (1992) also term this the neutral zone (See Figure 2.3, page 30). The measurement of laxity *in vivo* is problematic without invasive procedures, for this reason exploration has been mostly cadaveric studies (Panjabi 1992; Crawford et al. 1998). As such, Teyhen et al. (2007) and Breen *et al.* (2015) investigated whether initial intervertebral attainment rate could be used as an indicator of laxity. Breen et al. (2015) investigated initial intervertebral attainment rate and neutral zone in porcine models and found the correlation to be strong (right lateral flexion ($r_s = 0.55$, $p = 0.0012$); left lateral flexion ($r_s = 0.75$, $p = 0.0002$)). However, this study used dissected porcine models going into lateral bending and as such findings may differ *in vivo* going into forward flexion and extension. Equally, the removal of the porcine model musculature and surrounding trunk may influence the neutral zone and as a result be different from the neutral zone *in vivo* (Kanayama et al. 1996). Teyhen et al. (2007) explored initial attainment rate in individuals with LBP (chronic pain with aberrant movement patterns), and those without. In this study it was noted that participants with LBP were more hypomobile, with decreased initial attainment rate during flexion weight bearing, than their pain-free counterparts. It was agreed by an international forum that initial attainment was to be calculated as the gradient of the intervertebral motion angle of the first 10° of platform (or moving table) motion (Breen et al. 2012b). The 10° cut off is an arbitrary number (Breen et al. 2012b), but as agreed at the international forum, this cut off will be used for all future research into IAR, thus making meaningful comparisons possible between studies.

4.4.2.4. Translation

Sagittal translation is anterior or posterior movement of the vertebra above versus the vertebra below. Translation is calculated by a line drawn from the centre of each vertebra to the coinciding bisectrix line. These lines cross the bisectrix line at 90-degree angles to the bisector's gradient (Frobin et al. 1997) (See Figure 4.7). Translation is the distance between where the two lines cross (Black arrow on bisectrix line) and is measured in vertebral body units (VBU). Frobin (1997) assumes the vertebral body depth to be 35mm, therefore, by multiplying the VBU by 35, measurements can be made into millimetres. This method removes the effect of rotation on translation (Frobin et al. 1997). Translation is typically measured when instability is suspected or a loss of restraint (Leone et al. 2007). Breen et al. (2019a) explored intra subject repeatability of QF in the measurement of lumbar intervertebral flexion translation. The study explored ICC and MDC

during passive recumbent flexion and active weight bearing flexion in 55 asymptomatic participants. ICC demonstrated moderate reliability (between 0.5 and 0.75 (Koo and Li 2016)). During passive recumbent flexion the MDC was 1.33mm and during active weight bearing flexion the MDC was 1.97mm. It should be noted that these measurements were carried out while the pelvis was restricted to movement and the participants were guided through the movement as part of the QF protocol. When the pelvis is not restricted and the participant was free to move uncontrolled, the measurement errors at L5 – S1 approached 4mm, which is the cut off measurement for potential surgical intervention (Leone et al. 2007). As such, using the controlled QF protocol reduces the measurement error, however, to what extent the participants pelvic restraint effects the measurement of translation is unquantifiable.

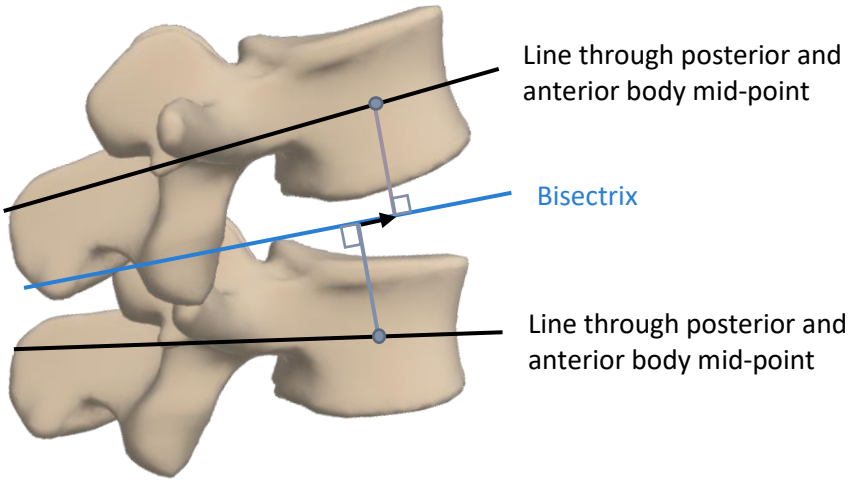

Figure 4.7: Measurement of translation using the method described by Frobin et al. 1997 (Figure modified from Frobin et al. 1997 using figure reproduced with kind permission from ©Primal Pictures. All rights reserved Primal Pictures (2021a)).

4.4.2.5. Disc Height

Anterior disc height is the sum of the perpendicular distances of the anterior–inferior corner of the vertebra above and the anterior–superior corner of the vertebra below, from the bisectrix between the two vertebral body mid-planes (Frobin et al. 1997) (See Figure 4.8). Disc height is also calculated in VBU for flexion and extension and can be converted to millimetres by multiplying by 35. For extension, the ICC for intra-observer and inter-observer reliability is 0.65-0.97 and 0.49-0.97 respectively (moderate to excellent). For flexion, ICC for intra-observer and inter-observer reliability is 0.24-0.88 (poor to good) and 0.64-0.99 respectively (moderate to

excellent) (Breen 2011). The average lumbar disc height in men is approximately 5.6 mm (±1.1) and in females is 4.8 mm (±0.8) at T12-L1, increasing at each level to an average disc height in men of 8.8 mm (±1.6) and in females of 8.6 mm (±1.8) at L5-S1 (Bach et al. 2018). The MDC for minimum anterior disc height during flexion recumbent is 4.02 mm and flexion weight bearing is 4.39 mm. The MDC for maximum anterior disc height during extension recumbent is 5.27 mm and extension weight bearing is 5.64 mm (Breen et al. 2019b). The MDC was calculated by pooling the intervertebral levels, which may account for the large MDC. MDC is calculated from the standard deviation, and by pooling the data the smaller disc heights of L2-L3 will be pooled with the larger disc heights of L5-S1 thus creating a larger standard deviation which will result in a larger MDC. As such, while the measurement demonstrated moderate to excellent reliability, the use of the measurement in interventional studies looking for potential differences may not be useful. It would be almost anatomically impossible for a change in intervertebral disc height to be more than the MDC.

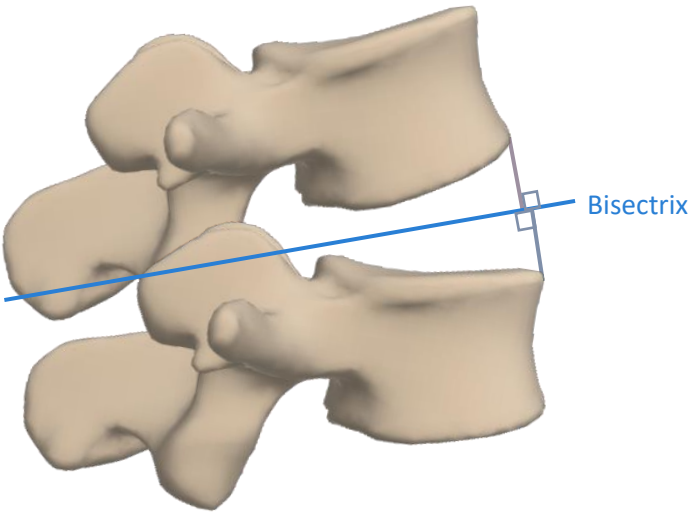

Figure 4.8: Measurement of anterior disc height in the neutral position using the method described in Frobin et al. 1997 (Figure modified from Frobin et al. 1997 using figure reproduced with kind permission from ©Primal Pictures. All rights reserved Primal Pictures (2021a)).

4.5. How to Determine if Manual Therapy is Clinically Effective?

To determine if manual therapy is clinically effective, there needs to be a way of measuring clinical outcomes. While there are objective measures which can be used such as intervertebral motion variables, the subjective measures of patient reported outcomes measures (PROMs) informs the clinician of how the patient feels they are progressing in response to treatment.

Patients who do demonstrate positive response to treatment are termed ‘responders’, and those who do not are termed ‘non-responders’.

4.5.1. Patient Reported Outcomes Measures (PROMs)

Patient-reported outcome measures (PROMs) are health questionnaires that are completed by patients before and after treatment to indicate whether their health, condition or symptoms have changed (Black and Jenkinson 2009). There are a number of PROMs used to assess patients with LBP, however the heterogeneity in the choice of questionnaires used in clinical trials can make comparisons between outcomes difficult. This can be improved by agreeing on a standardised core outcome set (COS) to be measured. Work within this area is dominated by two authors, Deyo et al. (1998) and Chiarotto et al. (2015) (endorsed by International Association for the Study of Pain). In 1998, Deyo et al. and a panel of international back pain researchers developed a core set of five domains which should be included for LBP. These domains included pain symptoms (such as pain intensity or how bothersome pain has been); function (how much pain interfered with activities); well-being; disability (reducing social activities or being unable to perform activities of daily living (ADL)); and satisfaction with care (such as Patient Global Impression of Change). The domains were updated in 2015 by Chiarotto et al. (2015) who reduced the number to four using a Delphi method. The proposed domains were physical function (which includes function and disability); pain intensity; health related quality of life (a more specific measure of well-being) and number of deaths. Satisfaction of care was not deemed a core domain as it was too broad and could include everything from patient treatment; waiting time; amiability of providers and receptionists; and other contextual effects. As such, a global measurement of satisfaction of care provides an incomplete understanding of what aspects of care the patient finds satisfying (Leininger et al. 2014). Equally, the social effect of disability was removed. What individuals deem as a social activity could have different connotations for different people and therefore could be seen as an ambiguous question. It was also suggested that this could be replaced in part by physical functioning and work productivity. Chiarotto et al. (2015) did, however, include number of deaths as a core outcome to be stated in all LBP research. Neither Deyo et al. (1998), nor Chiarotto et al. (2015) were exploring core outcomes in a manual therapy context. They were discussing LBP outcomes (which may have included not only NSLBP, but LBP of a serious origin) from a broad surgical, medical, and manual therapy point of view. This may have led to Chiarotto et al. (2015) including number of deaths as a core outcome. There are no reports of death directly attributable to manual therapy of the low back. This may not demonstrate a lack of evidence, moreover it may demonstrate that death attributed to manual therapy of the lumbar spine is rare.

The selection of a PROM should be based upon its measurement properties (such as reliability, validity and responsiveness) and feasibility of use in the target population (Prinsen et al. 2016). Validity is defined as how well the questionnaire measures what it is supposed to. In order for a questionnaire to be valid, the participant needs to understand what the questionnaire is asking (comprehension), and the questionnaire needs to have an adequate scope to cover all areas being investigated (comprehensive). Reliability is whether the same questionnaire will give the same repeated results under the same conditions.

4.5.1.1. Pain Intensity Questionnaires

The three most used pain intensity questionnaires include Numerical Pain Rating Scale (NRS), Visual Analogue Scale (VAS), and Brief Pain Inventory (BPI). Assessing all three questionnaires, Robinson-Papp et al. (2015) indicated it may not be possible to measure pain in a meaningful way. For example, one person's *"worst pain imaginable"* may not be the same as another person's *"worst pain imaginable"* and therefore reduces the validity of pain intensity questionnaires. Equally, all three questionnaires ask the participant to rate their pain over the last 24 hours and give one number as an average over the last 24 hours, this averaging of pain can lead to inconsistent reporting and therefore effect the validity and reliability of the questionnaires. As such, none of the pain intensity questionnaires are especially valid or reliable. The NRS appears to be the most used pain intensity questionnaire in the literature (Clohesy et al. 2018), however, frequency of use does not necessarily mean it is the most appropriate of the three questionnaires assessed. It is suggested that the NRS is easier for patients to understand, predominantly elderly patients, and can be easily administered as a paper version, over the telephone or with a digital device (Chiarotto et al. 2018a). It is possible that this convenience is the reason why it is used the most, that is not to say it does not have limitations. The NRS 2-point minimal clinically important change (MCIC) value commonly proposed for this instrument is smaller than the NRS MDC (Chiarotto et al. 2018b). As such, the NRS may not be able to distinguish between the smallest detectable changes and the real changes (Chiarotto et al. 2018b). For this reason, incremental changes in chronic patients may not be demonstrated in this questionnaire. The NRS does, however, demonstrate the greatest responsiveness of all three questionnaires when looking at acute LBP patients (Chiarotto et al. 2018b). As such, while recognising the limits of this single question pain questionnaire, the NRS is potentially the best questionnaire for studies with patients suffering from acute NSLBP.

4.5.1.2. Physical Function Questionnaires

LBP is debilitating and may result in changes in physical functioning for patients. The most used physical function questionnaires include Roland Morris Disability Scale (RMDS-24) and Oswestry

Disability Index (ODI 2.1a). According to Chiarotto et al. (2018c), RMDS-24 has sufficient comprehensibility, but insufficient comprehensiveness. It was noted that the RMDS-24 lacked questions related to leisure and exercise activities when compared to the ODI 2.1a and is therefore deemed less valid than the ODI 2.1a. However, Hush et al. (2010) suggested that the RMDS-24 may be more appropriate in acute LBP as leisure and exercise are arguably more relevant to a chronic pain patient. Thus, the RMDS-24 is more valid than the ODI 2.1a for acute LBP patients, which may affect questionnaire responsiveness. The RMDS-24 is thought to be more responsive in acute LBP patients, however, evidence is conflicting for both questionnaires when assessed for responsiveness in chronic LBP patients (Chiarotto et al. 2018c). The ODI 2.1a is thought to be more reliable than the RMDS-24. This may be due to ODI 2.1a having more literature relating to reliability and is therefore deemed more reliable than the RMDS-24 (Chiarotto et al. 2018c). The ODI 2.1a has been used more frequently in the literature than the RMDS-24 (Clohesy et al. 2018) and as such it may be a case of absence of evidence, rather than evidence of absence. The RMDS-24 has a slightly higher measurement of MDC; however, it is suggested that neither questionnaire is able to discriminate between MDC and MCIC (Chiarotto et al. 2018c). While recognising the limits of physical function questionnaires, the RMDS-24 is potentially the best questionnaire for studies with patients suffering from acute NSLBP.

Randomised controlled trials (RCTs) commonly analyse differences between the group means. If the difference is more than the MCIC, the treatment is assumed to be effective. Regarding the RMDS-24 in LBP patients, between group change difference of 2 points is considered clinically important. However, it is possible that individual patients demonstrate a MCIC (Ostelo et al. 2008). A within patient change of 4 or 5 points is recognised as the threshold for a clinically important improvement (Roland and Fairbank 2000; Stratford and Riddle 2016). In some cases, it may be more reasonable to analyse individual responses, rather than group responses. According to a consensus statement developed by Ostelo et al. (2008), 30% within patient change may be considered a clinically meaningful improvement.

Stratford and Riddle (2016) introduce the concept of threshold target value for success, in other words when is a person considered functioning or dysfunctioning? This literature suggests a change of between 2 – 4 points depending on the occupation or activeness of the patient (Kamper et al. 2010; Stratford and Riddle 2016). Thus, it is suggested that investigators apply a minimum RMDS-24 value of 4 – 5 points to be eligible for the study, this allows for a patient to have a MCIC. However, if one considers both the threshold target value for success and the MCIC, a minimum eligibility score of 8 or 9 points might be more appropriate (i.e., 4-point target value plus a change of 4 or 5 points) (Stratford and Riddle 2016). By limiting the study to participants

who have a RMDS-24 of over 9 points out of 24, the study is potentially only investigating a subset of a population of patients who have are struggling with physical functioning which may in turn be a study limitation. As such, serious consideration of what the study hopes to achieve should be evaluated before limiting participants to patients with a RMDS-24 of 9 or above.

4.5.1.3. Health Related Quality of Life

The most used health related quality of life questionnaires includes EuroQuol-5D-5L (EQ-5D-5L), Patient-Reported Outcome Measurement Information System Global Health (PROMIS-GH-10), Short Form 12 (SF-12), Musculoskeletal Health Questionnaire (MSK-HQ), and Bournemouth Questionnaire (BQ). Health related quality of life is defined as *"physical, psychological, and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations, perceptions"* (Chiarotto et al. 2018d). It should be noted that there is no consensus on the definition of health-related quality of life and other definitions do exist. The definition by Chiarotto et al. (2018d) has been used as it encompasses the three major subdomains of physical, mental, and social which are included in the questionnaires being considered. It should be noted that most health-related quality of life questionnaires have very low content validity and very little or limited public or patient involvement (PPI) in the development of the questionnaire. This is not unusual as it is only recently that PPI studies are becoming more popular, however, this is something which needs to be addressed using a target population to understand what health related quality of life means to a patient with LBP. PROMIS-GH-10 was developed to assess global health in patients with chronic conditions and not specifically LBP. As such, there is a paucity of literature relating to validity, reliability, measurement error and responsiveness in acute LBP patients. There is a paucity of literature regarding the use of SF-12 in LBP patients, however, the SF-12 was developed using regression models from the SF-36. The SF-36 has been used to evaluate health related quality of life in LBP patients, both acute and chronic (Chiarotto et al. 2018d). There is low quality evidence of sufficient test-retest reliability and validity. Equally there is low to medium quality evidence for responsiveness (Chiarotto et al. 2018d). There is a paucity of literature related to EQ-5D-3L and EQ-5D-5L and their use in LBP patients. The MSK-HQ was developed as a general musculoskeletal questionnaire (Hill et al. 2016). This questionnaire was developed with patient involvement and patients reported the questionnaire to be *"easy to understand"* and *"highly relevant"* (Hill et al. 2016). The questionnaire was relatively new and there is little literature pertaining to its use in LBP patients. There was a concern with how to interpret scores as to whether it is more reliable to interpret subdomain scores individually or the total questionnaire score when examining change. Equally there was a concern regarding the recommended two week follow up schedule. As the questionnaire has mainly been examined in

chronic LBP patients, two weeks was considered a short time frame to have sufficient change in the patient's condition to be a measurable change in the questionnaire score (Gibbons and Fitzpatrick 2018). The BQ has been investigated for its use in acute and chronic LBP patients. The BQ is a seven-question questionnaire which consists of the Numerical Pain Scale (for pain intensity); four health related quality of life questions (particularly focusing on depression and anxiety); and two physical functioning questions (Bolton and Breen 1999). The post-treatment BQ includes an eighth question of the global impression of change (Bolton and Breen 1999). There is a paucity of literature relating to the questionnaire, however, the available literature is positive for its use in LBP patients (Hurst and Bolton 2004). The questionnaire demonstrates high sensitivity and specificity in distinguishing clinically significant improvement from non-improvement in LBP patients (Hurst and Bolton 2004). Controversially the questionnaire was deemed to be not a useful instrument to identify baseline status, monitor or predict progress in chiropractic patients having persistent/ chronic LBP (Larsen and Leboeuf-Yde 2005). However, it was argued that the questionnaire was not designed for this use (Jahn et al. 2006), nor is this study exploring chronic LBP. In acute NSLBP patients, a change of at least 26 points (out of a maximum of 70 points) in the BQ is considered a MCIC (Newell and Bolton 2010).

4.5.1.4. Predictors of outcome questionnaire

Although not one of the COS, predictors of performance tools can be useful, one of which is the STarT Back Tool or questionnaire. The STarT Back tool was initially developed by Hill et al. (2008) as a screening tool to identify prognostic indicators in patients with low back pain, such as referred leg pain, comorbid pain, disability (2 items), bothersomeness, catastrophizing, fear, anxiety, and depression. The tool is designed to be quick and easily analysed by the practitioner. It allows the practitioner to identify patients with high, medium and low risk of poor prognosis and provide stratified treatment accordingly. A randomised controlled trial (RCT) carried out with physiotherapists in the UK found that outcomes of patients can be improved by using a stratified approach to primary care management of low back pain (Hill et al. 2011), this result was not replicated in the USA where stratified care was not significantly different to non-stratified care (Cherkin et al. 2018). Interestingly, although the STarT Back tool was designed to allow stratification of care to reduce the burden on primary health care practitioners, the tool has rarely been used for this purpose. Moreover, it has been studied as a predictor of patient outcome in primary care and physiotherapy. There are few studies related to its use in Chiropractic, Khan (2017) noted that the tool has some predictive ability but more in patients with more than two weeks of pain or if the screen is done two days post initial visit. There are no stratified treatment studies within a chiropractic setting. Stratified care would not be appropriate to answer the

research questions of this study. Equally, the tool as a predictor has inconsistent finding within the literature. Within the trial leg pain patients as well as patients with comorbidities will not be recruited as part of the inclusion/ exclusion criteria; disability will be assessed via the RMDQ and fear; anxiety and depression will be assessed using the BQ. As such, the use of the STarT Back tool was not considered appropriate for this study.

4.5.2. Responders versus Non-Responders

The meaning of the term 'responder' differs in the literature, with some literature defining a responder as someone who has had any positive change in their condition (Andersson 1999; van Tulder et al. 2006); some literature defining a responder as someone who has reached the MCIC (Itz et al. 2013; Kongsted et al. 2016); and some literature defining a responder as someone who has had complete resolution of symptoms (Itz et al. 2013).

Manual therapy is associated with moderate improvement in pain (Paige et al. 2017; Stochkendahl et al. 2018) and physical function (Paige et al. 2017). However, some patients respond to treatment, and others do not. While some suggest that psychological factors may play a role in patients' response (Waddell et al. 1993; Mondloch et al. 2001; Hill and Fritz 2011); others have developed clinical prediction rules to explore likely responders to manual therapy (Flynn et al. 2002; Childs et al. 2004). Clinical Prediction Rules are based on observations of patients with LBP who report clinical improvements (measured by modified ODI 2.1a). Childs et al. (2004) noted patients were most likely to benefit from manual therapy if they met four or more of the criteria: symptom duration less than sixteen days; no symptoms distal to knee; score less than nineteen on a fear-avoidance measure; at least one hypomobile lumbar intervertebral segment; and at least one hip with more than 35° of internal rotation. The presence of at least four of the criteria can increase the probability of a positive response to manual therapy by up to 45%-95% (Flynn et al. 2002). However, systematic reviews of clinical prediction rules for LBP concluded that none of the rules had been sufficiently validated for implementation into clinical practice (May and Rosedale 2009; Haskins et al. 2012). These studies suggest that there is a biomechanical or neurophysiological mechanism exerting a clinical effect. However, literature is limited in this area (Colloca et al. 2003a; Cramer et al. 2006; Lalanne et al. 2009; Wong et al. 2015). There is limited literature which utilises a control group (symptomatic, no treatment) to establish whether the effect is as a result of the intervention or other factors. Equally, there is limited literature which utilises an asymptomatic group to establish absolute magnitude of effect, if any.

There is no literature relating to measured lumbar spine intervertebral changes following manual therapy in responders versus non-responders. Wong et al. (2015) found responders to manual

therapy for LBP demonstrated an immediate decrease in spinal stiffness (calculated using the slope of the linear region) in comparison to non-responders who showed no change to spinal stiffness. Responders were defined as those who reached at least a MCIC in a modified ODI.

4.6. Summary of Literature Review

Manual Therapy is a commonly sought treatment for acute NSLBP. Patients undergoing SMT treatment report a decrease in pain and dysfunction. Among other clinical effects, manual therapy reportedly decreases spinal stiffness and/ or increases ROM. However, some patients respond to treatment and others do not. Response to treatment is measured using PROMs. NPS (pain intensity) and RMDS-24 (physical function) are valid questionnaires in the acute LBP population. The SF-12 or BQ could be utilised to measure health related quality of life in acute LBP patients.

The reason for difference in treatment response is elusive and may be related to mechanical factors. Manual therapy can create immediate biomechanical effects, but short-term and long-term biomechanical effects are still being investigated.

Manual palpation is not particularly reliable, and as such there has been a move to imaging. Static imaging can only provide biomechanical information on the difference between neutral and end range of motion only. Fluoroscopy image sequences can provide biomechanical information during continuous intervertebral motion and uses relatively low ionising radiation.

The most useful imaging sequences are flexion and extension. Partly due to these movements being pure movements without rotation or lateral flexion, thus there is less overlap of spinal structures. Equally, partly due to these movements having relatively large intervertebral ROM. Weight bearing, and recumbent sequences are useful to compare passive resistance of structures to active muscle recruitment and motor control.

When coupled with a semi-automated computer algorithm process, QF provides measurements of intervertebral motion. These measurements include IV-ROM, MSI, MSV, IAT, translation and disc height.

5. Methods

5.1. Introduction

This chapter outlines the methods utilised for the feasibility study. The study methods included a Home Management Booklet for all participants, the development of the booklet can be seen in Chapter 6. During the final design phase of the study, a Patient and Public Involvement Process was carried out to assist with making the trial person-centred (See Chapter 7). Once the method had been solidified, all trial material for the participants were sent to volunteer stakeholders to assist with readability and understanding (See Chapter 8).

The trial took place during the height of the Covid-19 pandemic, this resulted in alterations to the trial method after the trial had begun. Both the original trial method, as well as the alterations, have been included in this chapter.

5.2. Study Design

To meet the aims and objectives of the study (See Section 1.2 and 1.3), a feasibility study was designed to inform the development of a full-scale randomised controlled trial (RCT) exploring changes in intervertebral motion following a course of manual therapy.

The study was a two-arm randomised controlled trial (RCT) which collected primary empirical data. The control was an active treatment concurrent control, meaning that both groups received treatment and a comparison between treatment outcomes could be made (Nair 2019; Higgins et al. 2022). It had a parallel group design, meaning participants are randomised into one group and remained in their assigned group for the duration of the trial, until they completed the trial (Nair 2019; Higgins et al. 2022).

5.3. Stakeholder Involvement

To aid the design of a person-centred study, a Public and Patient Involvement process was carried out. This consultation process is presented in Chapter 7.

Once the trial design had been established, a stakeholder involvement process was carried out to explore the readability and understanding of the trial material. This process is presented in Chapter 8.

5.4. Trial Setting

The trial was a single centre trial, meaning that recruitment; measurements; interventions; and if required, continuation of care took place at the AECC University College (AECC UC) Clinic.

5.5. Trial Duration

The trial opened to recruitment on 10 February 2020. The trial was due to close when either all participants had been recruited or on 23 December 2020. Recruitment and retention were being explored as part of this feasibility study.

Due to the impact of Covid-19, the trial closed for the UK National Lockdown One on 20 March 2020 (See Figure 5.1). On the same date the AECC UC Clinic closed to patients. At this time, the trial was halted indefinitely for recruitment and the Sponsor informed. There was no loss to follow up, recruited participants completed the trial, and there were no active participants on the trial at the time. In preparation for the reopening of the trial an AECC UC Clinic risk assessment was completed for both staff and patients. A Bournemouth University (BU) risk assessment was completed for the research team and approval was sought and received from the Sponsor to continue the trial. The AECC UC Clinic reopened to new patients on 4 August 2020, at which time the trial reopened for recruitment.

Shortly after recruitment recommenced, an equipment fault meant no fluoroscopy investigations could take place. As a result, the trial was temporarily halted for recruitment from 18 August 2020 until 16 September 2020 (See Figure 5.1). There was one participant who was on the trial. It was agreed that the participant would continue the trial, and the lack of fluoroscopic data would be recorded as missing data.

Due to rising National Covid-19 cases, the country entered National Lockdown Two. The lockdown was announced on 1 November 2020 and came into effect on 5 November 2020. As the AECC UC Clinic was able to remain open under government guidelines, a BU assessment of trial risk was carried out and the trial was approved for continuation on 5 November 2020. No recruitment time was lost and no loss to follow up was recorded.

Before Covid-19, the AECC UC Clinic opening hours were Monday to Friday 11:00 – 19:00 and Saturday 09:00 – 12:00. There were approximately 130 – 150 chiropractic interns who could work up to four full days in the Clinic a week. In the Covid-19 era, this was reduced to opening hours of 10:30 – 17:00, Monday to Friday. Chiropractic interns were divided into bubbles, each bubble working one morning and one afternoon shift a week. As such, the clinic experienced a reduction in opening hours as well as resources. To mitigate the ongoing impact of Covid-19 on the number of new patients presenting to the AECC UC Clinic, as well as recruitment time lost, the trial was extended until the end of March 2021.

Furthermore, the trial closed for recruitment during the 2020 festive period (10 December 2020 until 4 January 2021). There was no loss to follow up recorded and all active participants completed the trial before this planned closure. Due to the rise in Covid-19 cases National Lockdown Three was announced on 4 January 2021, with immediate effect. Although the AECC UC Clinic was able to open on 4 January 2021, the trial was temporarily halted pending BU approval of research trial risk assessment. The trial reopened on 19 January 2021 (See Figure 5.1).

The trial closed to recruitment on 19 March 2021 and closed to follow up on 2 April 2021.

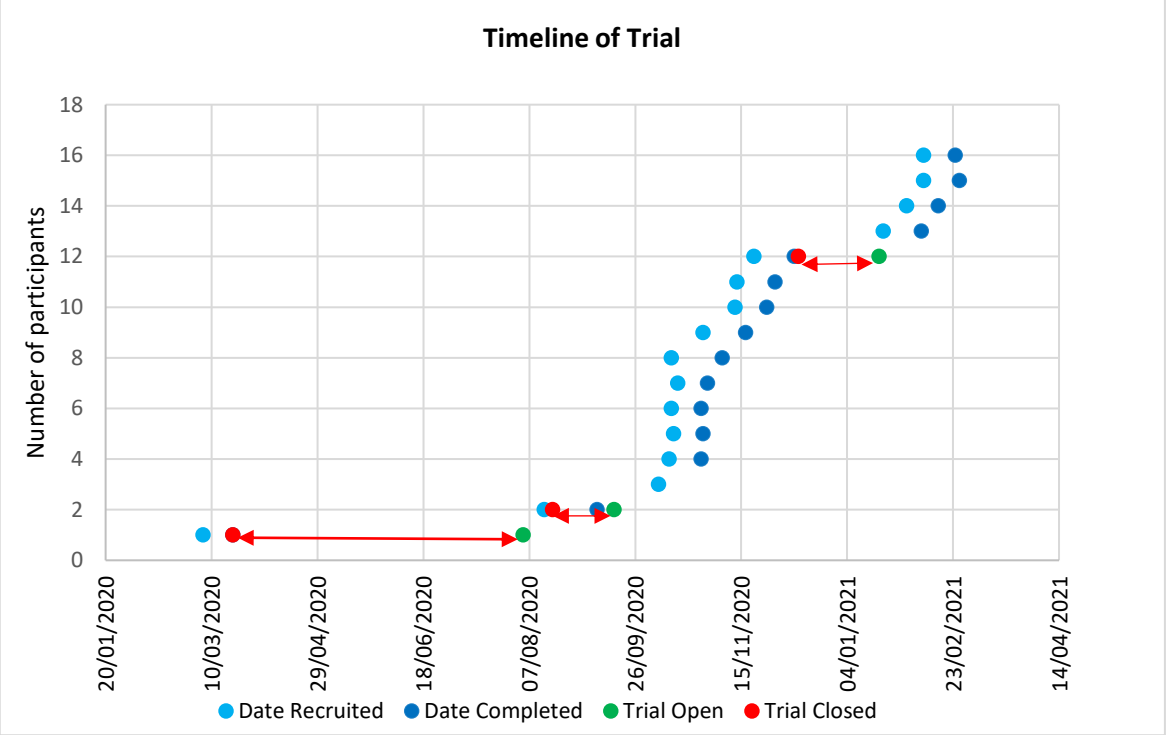

Figure 5.1: Timeline of trial. The figure plots when participants were recruited, and if they completed. The red lines in the figure indicate the time periods when the trial was closed, and when it re-opened. The first closure period indicated National Lockdown One; the second closure period indicated the breakdown of the fluoroscope; the third closure period indicates Christmas closure coupled with National Lockdown Three.

5.6. Sample Size

There is much debate in the literature regarding optimal sample size for a feasibility study (Lancaster et al. 2004; Julious 2005; Sim and Lewis 2012; Billingham et al. 2013; Whitehead et al. 2016; Bell et al. 2018). Suggested participant numbers per arm of a RCT range from 12 (Julious

2005) to 36 (Billingham et al. 2013). It may be possible to calculate the optimal sample size, however, this may not be known in the development stage of a trial and depends largely on previous work done in the subject area (Whitehead et al. 2016).

If optimal sample size cannot be calculated, the literature suggests using 'rule of thumb' sample size numbers of 12 participants per RCT arm, with an additional 20% to allow for loss to follow up (Browne 1995; Julious 2005). Some literature focuses on ensuring that there are sufficient participants in the trial to enable analysis of an outcome. Equally, the literature urges researchers not to under-recruit participant numbers to avoid underpowered studies. If the feasibility study data is used to perform a power calculation for a full-scale trial, the full-scale trial number of participants may be incorrect, thus effecting the validity and reliability of the outcome of interest (Halpern et al. 2002; Thabane et al. 2010; Sim and Lewis 2012). As such, authors have suggested a higher number of participants be recruited to the study (Sim and Lewis 2012; Billingham et al. 2013; Whitehead et al. 2016). Conversely, the literature urges researchers not to over-recruit for a feasibility study as it may raise ethical questions relating to the exposure of more participants to inconvenience and possible risk of harm associated with the study (Sim and Lewis 2012). Taking this into account, authors have generally suggested a smaller number of participants (Browne 1995; Julious 2005).

Going back to the primary aim of a feasibility study, it is not to evaluate the outcome of interest, but to evaluate whether a full-scale trial can be done (Eldridge et al. 2016). As such, Thabane et al. (2010) does not suggest a particular sample size for a feasibility trial. Rather they suggest that sufficient number of participants are recruited in order to assess whether recruitment, resources and management of a full-scale trial is feasible. With this in mind, Bell et al. (2018) suggests a sample size of between 12 – 35 participants per arm of a RCT. However, they strongly advise that the sample size be dictated by number of participants who qualify for the study, recruitment rates and retention rates. Consequently, sample size for a feasibility study should have a set target but reaching the target should not be the main focus of the feasibility trial.

Due to the lack of previous trials within this study population which have explored intervertebral motion using QF, a formal sample size calculation could not be carried out. As such, a target of 15 participants per group was chosen for this study. This is in keeping with the current literature for feasibility study sample sizes of 12 participants per group, with an additional 20% to allow for loss to follow up (Browne 1995; Julious 2005). It was felt that this sample size was large enough to inform about the practicalities of carrying out a full-scale trial.

However, due to the impact of Covid-19, as well as the trial interruptions (outlined in Section 5.5), it was not possible to recruit 15 participants per group. At the close of the trial for the festive period in 2020, the trial had recruited 12 participants, the research team took the decision to extend the trial until the end of March 2021. In January 2021, the increasing national Covid-19 cases led to National Lockdown Three, at which time the research team had concerns about the research team and participant safety. The decision was made to continue recruitment until even numbers were obtained for each arm of the RCT. As such, the research team took the decision to close the trial with 8 participants per group. This was achieved in the extended trial period as such the trial closed on 2 April 2021.

5.7. Participant Eligibility Criteria

As the definitions of acute LBP vary, it was important to clearly define the population under investigation. As such participant inclusion and exclusion criteria are outlined in Table 5.1.

Table 5.1: Inclusion and Exclusion criteria for the trial.

Inclusion Criteria	**Exclusion Criteria**
Patients with acute NSLBP, without leg pain, of at least 2 weeks duration, but no more than 4 weeks duration	Patients who cannot understand written English and unable to provide full informed consent.
Patients between the ages of 18 and 65	Patients who are currently involved in another research study
	Patients with a BMI over 30 (less likely to obtain the required information from the images)
	Pregnancy or potentially pregnant
	Previous ionising radiation exposure within the last 6 months greater than 8mSv.
	Previous lumbar spine surgery, as well as recent abdominal or pelvic surgery (within the last 12 months).
	Scoliosis or positive Adams forward Bending Test for Scoliosis.
	Diagnosed Osteoporosis (Bone Density Scan)
	Patients with a numeric pain scale of 8 or more, or 2 or less, taken at the New Patient Examination Appointment.
	Manual therapy already received for this episode of NSLBP
	Litigation or compensation pending
	Diagnosis of depression (by a medical doctor) within the last 12 months.

5.7.1. Inclusion Criteria

The inclusion criteria identified a specific patient population with acute NSLBP. Research suggests that a significant number of patients with acute NSLBP will improve significantly, without treatment, within two weeks. Patients who still experience NSLBP after two weeks are less likely to improve without treatment (Itz et al. 2013). As such, this trial sought participants who had experienced LBP for two weeks or more to decrease the chance that a favourable outcome after manual therapy was due to the natural progression of the condition.

The inclusion criteria reflect the age range of interest. The lower age limit of 18 reflects the age a person is considered an adult (UNICEF UK 1990). The age of consent is 16 years of age in England, and as such the participants of 18 and above were able to independently consent to the research trial (General Chiropractic Council 2016; HRA 2020a).

The upper age limit reflects the typical age limit for clinical trials (Shenoy and Harugeri 2015). This age limit is also used for many studies investigating LBP. However, the decision of an upper age limit for LBP trials is not simple. The elderly population is poorly represented in LBP trials and as such, there is a need for the inclusion of elderly participants to broaden the understanding of LBP in this population. However, the inclusion of elderly participants may add an additional confounding variable which may influence the results of a trial.

The World Health Organisation (WHO) define elderly as 60 years of age and above in some cases (WHO 2018), and 65 years of age and above in others (WHO 2001). Elderly patients (65 or over) with LBP experience lower recovery rates (Deyo et al. 2015), more severe symptoms (Donelson et al. 2012) and a higher risk of chronicity (Macfarlane et al. 2012). When investigating asymptomatic participants, participants over the age of 51 demonstrated a statistically significant decrease in physiologic ROM and an increase in stiffness of the spine when compared to younger counterparts (Wong et al. 2004). However, this feasibility study was exploring change in intervertebral motion before treatment versus after treatment, whether age will influence the results is unknown. There is evidence to suggest that older patients (60 years of age and above) have a similar treatment response to manual therapy, exercise and pain medication when compared to younger adults (18 – 59 years of age) (Ferreira et al. 2014). For the purposes of this feasibility study, it was decided that the upper age limit would be 65 years of age in keeping with the typical age limit for clinical trials.

5.7.2. Exclusion Criteria

Some of the exclusion criteria excluded patients for reasons which may make attaining the required information from the images difficult or be potentially harmful. Equally, where manual therapy may be contraindicated (relative or absolute).

5.7.2.1. Participants with a Body Mass Index (BMI) of 30 or more were excluded. BMI is calculated by dividing an adult's weight in kilograms by their height in metres squared (NHS 2019). Patients with a BMI of more than 30 are in the obese range and can lower the contrast resolution of the fluoroscopic images due to the greater amount of soft tissue in the x-ray beam path. This has a direct consequence of reducing the tracking program's ability to define the borders of the vertebral body. Equally, the

higher the BMI, the higher the dose of effective radiation required to gain images of sufficient resolution (Mellor et al. 2014b).

5.7.2.2. Participants who were pregnant or potentially pregnant were excluded. The effects of ionising radiation exposure in pregnancy to the foetus include cell death (leading to foetus death); foetal malformation; developmental abnormalities or growth retardation; and cancer (Lowe 2019). There is a paucity of evidence indicating the minimum level of radiation which may cause these effects, and what evidence is available is inconsistent. The estimated effective radiation dose for a lumbar spine x-ray series for an average adult is 1.3 mSv (Public Health England 2008). The estimated effective radiation dose for a lumbar spine x-ray series for a foetus is 1.1 – 10 mSv which is considered low-moderate risk for the foetus (Lowe 2019). Due to the exploratory nature of this study, any risk to the foetus was unnecessary and as such participants who were pregnant or potentially pregnant were excluded.

5.7.2.3. Medical radiation exposure with an effective dose of greater than 8mSv may include a CT scan of chest, abdomen or pelvis or interventional procedures under radiological control such as angiography (Public Health England 2008). Previous ionising radiation exposure within the previous six months of greater than 8mSv means that the patient has already had a large effective radiation dose, the cumulative radiation dose of the trial to the participant may be potentially harmful. As such, participants who had previous effective radiation dose of greater than 8 mSv were excluded from the trial.

5.7.2.4. Patients who have had previous lumbar spine surgery, or recent abdominal or pelvic surgery (within the last 12 months) were excluded from the study. According to the WHO, post-surgical joint manipulation may be an absolute or relative contraindication to spinal manipulation depending on the outcome of the clinical examination (WHO 2005). Lumbar spine fusion or stabilisation surgery may affect the biomechanics of the lumbar spine and introduce a confounding variable to the objective data of interest.

5.7.2.5. Patients who have a scoliosis (diagnosed or observed) were excluded from the study. A scoliosis is defined as a lateral deviation of the spine from the normal vertical line, consisting of lateral flexion of the spine with a vertebral rotational component (Weinstein and Flynn 2013). The presence of a scoliosis may make the borders of the vertebrae unclear or overlap on the fluoroscopic images, which can make the border tracking process difficult, and obtaining the required information less likely. Equally,

the scoliosis may affect the movement of the spine introducing a confounding variable to the objective data of interest.

5.7.2.6. Patients who have been diagnosed with Osteoporosis using a Bone Density Scan were excluded from the study. Reduced bone density can leave the images with a washed-out appearance (reduced contrast) and can make obtaining the measurements from the fluoroscopic images difficult. Equally, Osteoporosis can result in bone demineralisation which represents an absolute-to-relative contraindication to spinal manipulation due to increased risk of pathological fractures (WHO 2005).

5.7.2.7. Patients with a numeric pain scale of 8 or more, or 2 or less, taken at the New Patient Examination Appointment were excluded. The upper limit reflects the ability of the participant to have sufficient ROM to participate in the fluoroscopy investigation. The lower limit reflects the limitation of the NPS. The MCIC for NPS is 2-points, as such to allow participants to demonstrate a change the lower limit for participants was set at 2 (Chiarotto et al. 2018b).

5.7.2.8. Poor psychological health is associated with negative prognosis. This could mean that participants may report distorted information relating to pain intensity or physical function, independent of changes in intervertebral motion. As such, patients with a history of diagnosed depression (by a medical doctor) within the previous 12 months (this is the time frame employed by the World Health Organisation World Mental Health Survey Initiative as constituting “major depression”) (Demyttenaere et al. 2007) were excluded. For similar reasons, patients with pending litigation or compensation claims were excluded (Jacobs 2013).

5.7.2.9. Participants who may not understand sufficient English to fully understand the Participant Information Sheet or provide full informed consent were excluded from the trial (HRA 2020a). As the trial is a feasibility study, translating the Participant Information Sheet and Consent forms were not considered.

5.8. The Trial Procedure

Table 5.2 outlines the trial schedule for participants from booking a New Patient Examination Appointment at the AECC UC to completion of the trial.

Table 5.2: Trial schedule for participants taking part in the trial, from potential patient identification to trial completion.

<table>
<tr><td>Recruitment:</td><td>Day -4 to day 0</td><td colspan="2">Patient identified.
Patient eligibility established.</td></tr>
<tr><td>Baseline Measurements:</td><td>Day 0</td><td colspan="2">Participant consented into trial.
Bournemouth Questionnaire; Roland-Morris Disability Questionnaire – 24; Pre-fluoroscopy questionnaire; Pregnancy statement and pregnancy test (for women of childbearing age (18 – 49); fluoroscopy.</td></tr>
<tr><td colspan="2" rowspan="2">Intervention:
Day 0 to day 14</td><td colspan="2">Both groups received a home management booklet.</td></tr>
<tr><td>Group 1: Five manual therapy appointments within two weeks. The first appointment is on the same day as the baseline measurement (day 0), the fifth appointment is on the same day as the final measurement (day 14).</td><td>Group 2: One appointment (no treatment given) on day 7.</td></tr>
<tr><td>Follow up Measurements:</td><td>Day 14</td><td colspan="2">Bournemouth Questionnaire; Roland-Morris Disability Questionnaire – 24; Pre-fluoroscopy questionnaire (pregnancy statement); fluoroscopy.</td></tr>
</table>

5.9. Identification and Recruitment of Participants

Initial identification of potential participants was through the New Patient Examination Appointment booking system at the AECC UC Clinic. It was normal practice for the reception staff to enquire what the presenting complaint was or area of the body it involved. Patients who indicated that they were suffering from LBP were flagged on the clinic booking system (ClinicOffice V5, Pioneer Software, UK).

Potential participants were identified by a chiropractic intern, who carried out the New Patient Examination. A chiropractic intern was a final year chiropractic student (fifth year) who was permitted to examine and treat patients under the supervision of qualified chiropractic clinicians.

It was normal practice for the chiropractic interns to present the case to a Clinic Tutor to ensure all aspects of the history and physical examination had been completed and to potentially triage patients who require referral or immediate treatment. It is at this stage the doctoral researcher identified patients who were diagnosed with NSLBP and within the inclusion criteria (see Table 5.1), these patients were approached by the doctoral researcher.

Patients were approached in the privacy of the treatment room with the intern present. The patient was welcome to request the presence of a family member or nominated person. A summary of the study was discussed with the patient and any of their questions answered. If a patient was not interested in the trial, no further contact was made by the doctoral researcher and their care continued with the chiropractic intern. If a patient was interested, the doctoral researcher clarified with the patient the trial exclusion criteria (see Table 5.1) and an eligibility checklist completed (Appendix B). Patients eligible for the study were given a Participant Information Sheet (Appendix C) to read and time to think about their participation. Patients were given three options; they could verbally consent to the trial at the New Patient Examination Appointment and make an appointment for baseline data capture; they could contact the researcher by telephone to verbally consent to join the trial and make an appointment for baseline data capture; or they could verbally consent to a follow up telephone call from the researcher after 24 hours. Patients who required longer to decide whether to join the study were not rushed into a decision, however they were informed that they may no longer be eligible for the trial if they no longer fulfilled the eligibility criteria.

Patients who decided not to be part of the study were asked if they would like to provide a reason. Following this, they had no further contact from the research team.

5.9.1. Consent

Participants were asked to sign an informed Consent Form (Appendix D) before they were enrolled onto the study. The signing of the consent form was witnessed by the doctoral researcher. Participants were reminded that they could withdraw their consent at any time, and without giving a reason. Their withdrawal from the study would not affect their treatment at the AECC UC Clinic. The consent process also enabled the participants to consent to voluntary additions, such as agreeing to be contacted by the research team with the final trial results, as well as requesting their fluoroscopy images for their personal records.

5.9.2. Randomisation

The study utilised block randomisation which ensured the number of participants in each group remained similar at all times, and ultimately resulted in equal group sample sizes. Block

randomisation is a useful tool when designing a feasibility study, as the study could potentially be halted if needed at the end of a block, while group sample sizes remain even (Sealed Envelope 2021). However, block randomisation increases the risk that the allocation process may be predictable (Efird 2011). If one treatment occurs frequently within the beginning of the block, it is reasonable to assume that the second treatment group will occur frequently in the remaining block (Efird 2011).

Participants were block randomised using the online randomisation website Sealed Envelope™ (Sealed Envelope Ltd, UK). Due to the exploratory nature of this feasibility study no stratification factors were applied, such as age or sex. A block size of five blocks of six participants was used. An equal randomisation of 1:1 was chosen to provide the greatest power for testing effectiveness (Sealed Envelope 2021).

5.10. Data Collection

It was the intension for the data collection to be carried out by the doctoral researcher. Due to the impact of Covid-19, a contingency strategy was developed in the case of the doctoral researcher falling ill. For this reason, additional team members, such as fluoroscopy operators, were placed on standby. Equally, due to Covid-19 the appointment times for the QF were lengthened to allow for additional cleaning of equipment and Covid-19 screening to take place.

5.10.1. Quantitative Fluoroscopy

Prior to the fluoroscopy investigation, participants signed a consent form specifically relating to risks of ionising radiation (Appendix E). The consent form included a pregnancy statement for female participants. Female participants of childbearing age (15 – 49 (WHO 2006)) undertook a urine dipstick pregnancy test.

Participants were then taken to the radiology room, introduced to the equipment (Siemens Arcadis Avantic VC10A digital fluoroscope (CE0123)), and briefed on the process of the fluoroscopy acquisition.

A standardised patient motion protocol was used to acquire the four fluoroscopy sequences. The motion protocol being used in this study has been developed and refined through previous studies (Breen et al. 2012a).

5.10.1.1. Recumbent Sequences

Fluoroscopy sequences were obtained for passive recumbent (non-weight bearing) flexion and extension (See Figure 5.2). The computer-controlled swing table was manufactured by Atlas Clinical Limited (declared conformity under MDD93/42/EEC). Participants were asked to lie on

their right side, in a foetal sleeping position, with their head on a pillow for comfort. The researcher positioned the participant with their L3-L4 disc space over the fulcrum of the table and made slight adjustments to the participants positioning to reduce axial rotation of the spine and pelvis. Lead pieces were placed over the participants gonads, breast, and thyroid. A radiographic marker was placed on the underside of the table at the fulcrum. The fluoroscope was then positioned around the participant and brief positioning exposures were taken (0.1 seconds) to ensure the participant and the radiographic marker were in the correct position for optimal image sequence quality. The radiographic marker was then removed from the table for the image sequence acquisition. The participants were informed that the upper half of the table was going to move and to remain relaxed during the movement.

The rate of motion of the swing table was set at six degrees per second with a gradual acceleration ($6°s^{-2}$) to begin the motion and deceleration ($-6°s^{-2}$) to end the motion to avoid sudden movements. The images were acquired at a rate of fifteen frames per second (fps) to reduce image blur during motion. Vertebral images from L1 – L5, as well as the sacrum, were recorded. Where the participant was particularly tall L1 was sacrificed to ensure sufficient sacrum was included to allow tracking of the vertebral movement.

- Flexion sequence: Participants were taken through the motion in ten-degree increments to help them acclimatise and 'warm up' to the movement, and to give the researchers an understanding of how well the movements were tolerated. When the participant was ready, the image sequence recording was started at the same time the swing table began the movement. Participants were taken through neutral to forty degrees of flexion and back to neutral.
- Extension sequence: The same procedure was used to obtain the extension sequence. Participants were taken through neutral to forty degrees of extension and back to neutral.

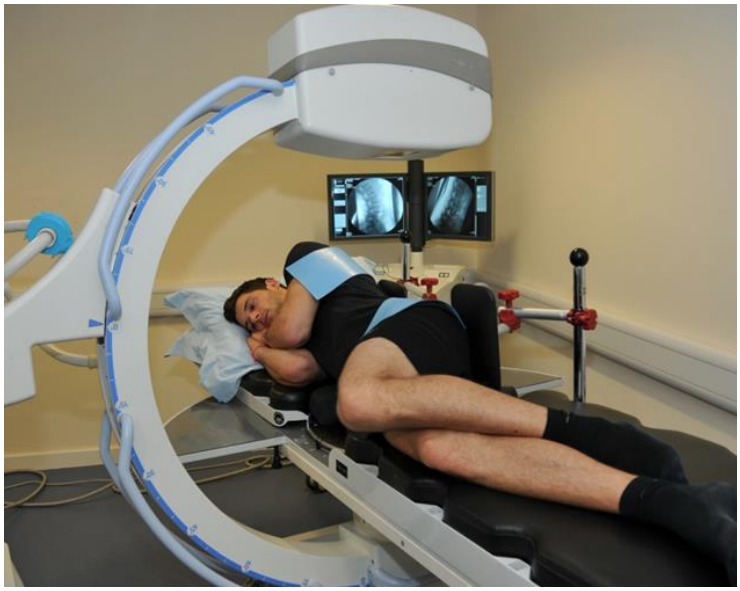

Figure 5.2: Obtaining fluoroscopy sequences of flexion and extension while participant is recumbent.

5.10.1.2. Weight bearing sequences

Fluoroscopy sequences were obtained for weight bearing flexion and extension (See Figure 5.3). The computer-controlled motion platform was manufactured by Atlas Clinical Limited (declared conformity under MDD93/42/EEC). Participants were asked to place their right side to the motion platform, with their arms in the arm support in front of them. The researcher adjusted the height of the motion platform until the centre of the motion platform rotation was aligned with the L3-L4 intervertebral disc space. Minor adjustments were made to the participants positioning to reduce axial spinal rotation. A radiographic marker was placed on the back of the motion platform. The fluoroscope was then positioned around the participant and brief positioning exposures were taken (0.1 seconds) to ensure the participant and the radiographic marker were in the correct position for optimal image sequence quality. The radiographic marker was then removed from the motion platform for the image sequence acquisition. A positioning plate was placed on the participants sacrum at S2, and a strap was placed around the participants hips at the greater trochanter level. The purpose of the plate and strap were to reduce posterior pelvic movement during flexion and extension sequences. The participants were informed that the motion platform would rotate the arm support forward and backward and to use the arm support to guide the movement without leaning their weight on it.

The rate of movement of the motion platform was six degrees per second. A gradual acceleration of $6°s^{-2}$ was used for the first six degrees of rotation and a gradual decrease of $-6°s^{-2}$ was used for

the final six degrees of movement to reduce sudden movements. The images were acquired at a rate of fifteen frames per second (fps) to reduce image blur during motion. Vertebral images from L1 – L5, as well as the sacrum, were recorded. Where the participant was particularly tall L1 was sacrificed to ensure sufficient sacrum was included to allow tracking of the vertebral movement.

- Flexion sequence: Participants were taken through the motion in twenty-degree increments to help them acclimatise and 'warm up' to the movement, and to give the researchers an understanding of how well the movements were tolerated. When the participant was ready, the image sequence recording was started at the same time the motion platform began the movement. Participants were taken through neutral to sixty degrees of flexion and back to neutral.
- Extension sequence: The same procedure was used to obtain the extension sequence; however, participants were taken through the movement in ten-degree increments. Participants were taken through neutral to twenty degrees of extension and back to neutral.

Figure 5.3: Obtaining fluoroscopy sequences of flexion and extension while participant is weight bearing.

Motion platform positions were sampled at 15 Hz and recorded. The data were used in the image analysis.

5.10.1.3. Image analysis

The fluoroscopy sequences were transferred from the fluoroscope computer to a workstation computer for enhancement and analysis. Each fluoroscopy sequence can contain up to 350 individual frames, which were extracted and transformed in JPEG files within the MATLAB Environment (R2011b).

Three frames from each sequence were enhanced to highlight the edges of each object for easier identification of the lumber vertebral and sacral bones. The raw image, together with five enhanced images were presented for each frame. The image with the clearest vertebral body and sacral borders, while producing the least amount of image noise, was chosen. This facilitated the tracking algorithms to identify vertebral body and sacrum positions in subsequent images.

Following enhancement, the researcher marked one frame (usually the first frame) from each sequence manually (See Figure 5.4). First a reference template was marked by clicking on each corner of the vertebral body (represented in yellow on the figure). Once complete a second template or tracking template was marked by clicking on the image and outlining the vertebral body and bony attachments which are not overlapped by the adjacent bone (represented by green on the figure). The manual marking of the frame was completed five times.

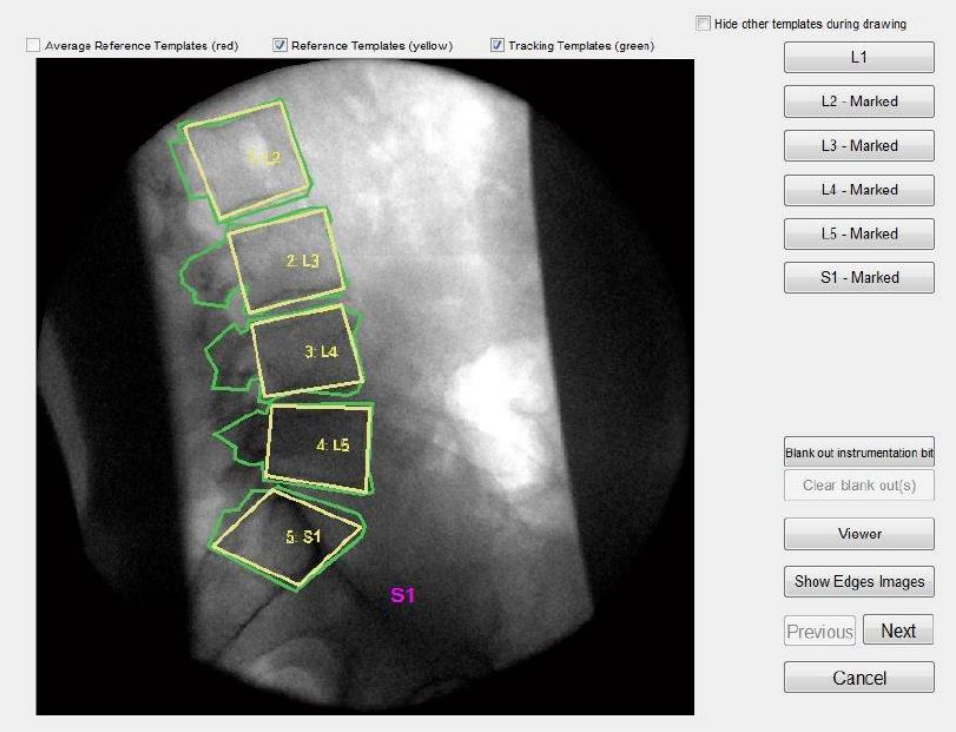

Figure 5.4: An example of the computer-based process. Automated computer processing algorithms calculate intervertebral movement variables throughout the motion.

The tracking algorithm tracks the greyscale pixel information within each marked template, as well as its location in the image. This information is used for the subsequent images in the sequence. The tracking template with the content which most correlates with the previous image is taken to be the vertebral position in this image. This process is repeated for all the images in the sequence (Muggleton and Allen 1997).

It is possible that tracking may contain errors, and the algorithm may track bowel gas or noise in the image. A manual editing process can be used to detect where in the sequence the tracking error occurred, these errors can be removed and the sequences retracked at the discretion of the researcher.

Once all tracking has been finalised, the motion platform position data is combined with the data obtained through image analysis, to allow for comparison of each segment's motion and the global trunk motion.

5.10.2. Objective Measurements

Intervertebral motion variables obtained from QF include:

- Angular range of intervertebral motion (IV-ROM) (See Section 4.4.2.1)
- Initial Attainment Rate (Laxity) (See Section 4.4.2.2)
- Sagittal translation (See Section 4.4.2.3)
- Anterior disc height (See Section 4.4.2.4)
- Motion sharing inequality (MSI) and motion sharing variability (MSV) (See Section 4.4.2.5)

Data analysis strategy can be seen in Section 11.3.1.

5.10.3. Subjective Measurements

Validated, standardised PROMs of the BQ (See Section 4.5.1.1 and 4.5.1.3) and the RMDS-24 (See Section 4.5.1.2) were used. Data analysis strategy can be seen in Section 11.3.1.

5.10.3.1. Bournemouth Questionnaire

The advantage of using the BQ is it is already in use in the AECC UC Clinic (thus not an additional research burden to the participant), and it includes the NRS.

The score for each question was recorded, as well as the total score (Appendix F for pre-treatment (baseline) and post-treatment (follow up) questionnaires).

5.10.3.2. Roland Morris Disability Scale – 24

The score for each question was recorded, as well as the total score (Appendix F).

5.10.3.3. Analgesia Diary

The use of analgesia (including name of analgesia, frequency, and dose) was recorded by the participant for the duration of the trial. It is possible that participant reported data may be less accurate, due to the reliance on memory (Drieling et al. 2016). Prescription analgesia (such as opioids) may influence PROMs in patients with acute LBP, particularly pain intensity questionnaires such as NRS (Tucker et al. 2020). Participants taking prescribed analgesia before the start of the study, were not excluded from the study, as the effect on the PROMs should theoretically be constant in the baseline and follow up measurements. However, if a participant began to take prescription analgesia during the trial, this would only affect the follow up measurement and as such, influence the trial outcomes. Participants who began to take prescription analgesia during this trial were not withdrawn as this study is exploring feasibility, rather this information was used to inform the full-scale trial.

5.11. Trial Treatment Plan

It was the intention of the doctoral researcher, a qualified chiropractor, to carry out all participant treatment appointments. However, due to Covid-19, a contingency plan was put into place in case any of the research team fell ill. As part of this plan, the original participant's student chiropractic intern was in standby to take over any appointments that needed to be covered. Due to Covid-19 the appointment times were increased to allow for additional cleaning, as well as the completion of pre-treatment Covid-19 screening.

5.11.1. Both Groups

All participants received an evidence-informed home management booklet to help manage their back pain at home. The development of the Home Management Booklet is presented in Chapter 6.

During the trial, should a participant have experienced increased pain or dysfunction, they were addressed on a case-by-case basis and appropriate advice, treatment or referral sought as required.

5.11.2. Group One: Manual therapy group

Group 1 received manual therapy. Participants received five 30-minute treatment visits in the space of two weeks, with at least one day between appointments, this is in keeping with the Clinical Practice Guideline for chiropractic care for acute NSLBP (Globe et al. 2016). It is normal practice during each appointment for a manual therapist to review the clinical picture by taking a brief history of the current complaint since the last treatment visit and carrying out a brief physical examination, and as such, this practice was maintained throughout the trial. At the final treatment visit, participant's clinical progress and need for post-trial care was discussed.

5.11.3. Group Two: Non-manual therapy group

Participants received one visit at the end of the first week to discuss their LBP and ensure the participants pain was not worsening. No physical treatment was given at this time. At the final follow up data collection appointment, participants clinical progress and need for post-trial care was discussed.

5.11.4. Post-trial Care

Once a participant completed the trial, if they wished to continue treatment, they were signposted back to the original student intern they had booked an appointment with. The intern was given access to all clinical notes taken during the trial, and treatment options were no longer restricted to the trial protocol.

For the duration of the trial, all appointments were free of charge. Any post-trial appointments were subject to the standard AECC UC Clinic fees. The AECC UC Clinic is a teaching clinic, as such fees are low. However, in line with clinic policy, no patient who has commenced treatment would be denied necessary treatment because of financial difficulties.

5.12. Ethical Approval

Following a review of the study protocol, Bournemouth University confirmed Sponsorship of the study (Appendix G). The trial was registered on ClinicalTrials.gov (NCT04155970) and gained favourable ethical opinion from the East of England – Cambridge Central Research Ethics Committee (20/EE/001) (Appendix H). Bournemouth University and the AECC UC local internal ethics also provided favourable ethical opinions for the study.

Due to the impact of Covid-19, any major and minor amendments made during the trial were approved by the Sponsor, Bournemouth University. The Research Ethics Committee were notified of changes as instructed by IRAS Guidance on Notification of Amendments (IRAS 2021a), as well as the special advice for amendments during Covid-19 (HRA 2020d).

5.13. Ethical Considerations

5.13.1. Ionising Radiation Dose to Participants

In a normative population study using the same fluoroscopy protocol (weight bearing flexion and extension, and recumbent non-weight baring flexion and extension) the mean dose was 0.77mSv (upper 3rd quartile of 0.86mSv). As there were baseline and follow up fluoroscopic sequences in this trial, the total mean dose was estimated to be 1.54mSv. The typical effective dose for a single lumbar x-ray examination is 1.3mSv (Public Health England 2008). The study adhered to the ALARP principles (HSE 2021) and strived to minimise dose by using collimation; gonadal, breast and thyroid protection; pulsed fluoroscopy and minimised exposure times (Health and Safety Executive 2021).

Fluoroscopy was carried out by a trained operator in accordance with Schedule 3 of IR(ME)R 2017, who has undergone training in these specific procedures (IR(ME)R 2017).

Participants were made aware of the dose, as well as the risks, as part of the informed consent process. It is often difficult for patients to perceive risk, as such participants were given a table of familiar risks to allow comparison (See Table 5.3). The estimated radiation dose from the trial was roughly the same amount of naturally occurring background radiation a person would receive in the United Kingdom over an 8-month period (Public Health England 2008). The normal risk of developing cancer is 1 in 2 people at some point during their life. It was very difficult to determine

the risk of inducing cancer from such low effective radiation doses; however, it was estimated that there was an additional 1 in 13 000 chance of developing cancer from this examination. There was no direct benefit to the participant from the radiation dose; however, the risk was seen as low-medium risk.

Table 5.3: Risk of ionising radiation in relation to familiar events.

Some familiar risks	**Chance they will happen**
Getting four balls in the UK national lottery (Lottery.co.uk 2021)	1 in 2 180
Dying from Sunstroke (Statistica 2017)	1 in 8 912
Dying from Canoeing (National Center for Health Statistics 2018)	1 in 10 000
Dying from Mountain Hiking (National Center for Health Statistics 2018)	1 in 15 700
Dying at a Dance Party (National Center for Health Statistics 2018)	1 in 100 000
Getting five balls in the UK national lottery (Lottery.co.uk 2021)	1 in 144 415

5.13.2. Risk of Manual Therapy

Participants may experience an adverse event (AE) of a mild transient discomfort following manual therapy (lasting up to 2 days). This may include mild bruising from trigger point therapy or tenderness related to SMT or mobilisation. This is considered common and can occur in 50% - 67% of patients (Paige et al. 2017).

SMT of the lumbar spine and pelvis (Sacroiliac joints) is considered low risk. However, the types of serious adverse events (SAE) which can occur, can be significant, meaning that some risk is present (Nielsen et al. 2017). Examples of SAE include worsening disc lesion or cauda equina syndrome (CES) (Oliphant 2004).

Should a SAE and AE have occurred, they would have been addressed on a case-by-case basis and appropriate advice, treatment or referral sought as required.

5.13.3. Incidental Radiographic Findings

It was possible an incidental radiographic finding may have been detected on fluoroscopic sequences. If there was a suspicion of an incidental finding, sequences were reviewed by an

appropriate health professional. Any important incidental findings were discussed with the patient and their permission to inform their general practitioner was sought. Detection of an incidental finding has the benefit of allowing the participant to start early treatment of their condition, but in a small number of cases these findings may have an implication for future employment or health/ life insurance. To date, a number of studies involving fluoroscopy have been carried out, no important incidental findings have been detected.

5.13.4. Participant Distress

Although considered low risk, it was possible a participant may have become distressed or upset during discussions regarding their NSLBP, particularly pertaining to pain intensity or lack of physical functioning. While every effort was made to minimise this risk, the AECC UC Clinic has a mental health first aider on duty during opening hours. Equally, the doctoral researcher was a qualified mental health first aider.

5.13.5. Evidence-informed Home Management Booklet

The evidence-based home management booklet informed participants of when to seek help from a medical professional in the case of worsening symptoms or developing new symptoms. The booklet also provided advice on rescue analgesia (hot/ cold pack and over the counter analgesia). Participants were encouraged to consult the information leaflet provided with 'over the counter' analgesia and speak to their pharmacist if they had questions or concerns.

5.13.6. Limitation of Treatment Options

The treatment options available to the participants were deliberately restricted to study changes in lumbar spine intervertebral motion following a specific treatment. The participants were made aware of this in the Patient Information Sheet, and this was reinforced during the consent process.

5.13.7. Covid-19

The ethical consideration of Covid-19 was not considered when the original ethical favourable opinion was given by the Research Ethics Committee, this is largely due to the timeline of the ethical approval process for the study being late 2019 until early February 2020. A timeline of Covid-19 in the United Kingdom, together with the effects on the trial can be seen in Table 5.4.

Table 5.4: Timeline of Covid-19 in the UK, together with the effects on the trial. National lockdowns have been highlighted in green; AECC UC Clinic has been highlighted in orange; effect on the trial has been highlighted in blue.

January 2020	• 31st Jan: First Covid-19 cases in the UK (Ball and Wace 2020)
March 2020	• 5th Mar: First death from Covid-19 in the UK (BBC News 2020b)
	• 11th Mar: WHO declares Covid-19 a pandemic (Cucinotta and Vanelli 2020)
	• 12th Mar: UK reported Covid-19 cases = 590 (GOV.UK 2020a)
	• 20th Mar: National Lockdown One (Institute for Government 2021)
	• 20th Mar: UK schools closed
	• 20th Mar: AECC UC Clinic Closed
	• 20th Mar: BCA – chiropractors move to close or telehealth only (British Chiropractic Association 2020a)
	• 20th Mar: All non-essential research halted (GOV.UK 2020b)
	• 20th Mar: Trial halted
May 2020	• 10th May: National Lockdown One eased: Government message changed from "stay home, save lives, protect the NHS" to "stay alert, control the virus" (GOV.UK 2020c)
	• 10th May: BCA - telehealth considered, with a return to risk assessed face-to-face consultations (British Chiropractic Association 2021)
June 2020	• 26th Jun: BU – guidance on return to research
August 2020	• 3rd Aug: AECC UC Clinic open to new patients
	• 3rd Aug: Trial reopened
September 2020	• Chiropractic added to list of essential workers (British Chiropractic Association 2021)
November 2020	• 5th Nov: National Lockdown Two (Institute for Government 2021)
	• (AECC UC Clinic remained open; trial remained open as approval obtained)
December 2020	• 2nd Dec: National Lockdown Two eased (Institute for Government 2021)
	• 8th Dec: first Pfizer-BioNTech vaccine was administered in UK (BBC News 2020c)
January 2021	• 5th Jan: Biweekly lateral flow tests for all AECC UC Clinic workers.
	• 6th Jan: National Lockdown Three (Institute for Government 2021)
	• (AECC UC Clinic remained open; trial closed while approval sought)
	• 19th Jan: Trial reopened (approval obtained)
March 2021	• 20th Mar: Trial closed to recruitment

On 20 March 2020 National Lockdown One began, the AECC UC Clinic closed to patients and the trial was halted indefinitely. The ethical considerations for continuing the trial were discussed by the research team, together with the trial Sponsor representative from BU. During this uncertain time, there were continuous reviews of the government guidelines, General Chiropractic Council guidelines, and BU research guidelines. As the UK began to come out of National Lockdown One, the research team prepared to reopen the trial. The AECC UC Clinic put in place one-way systems to aid social distancing; additional cleaning protocols for common areas and treatment rooms; compulsory wearing of facemasks within the building; and screening questions and temperature checks at the entrance to the building. Practitioners within the Clinic wore scrubs which remained on the property and were centrally washed at 60°, along with additional Personal Protective Equipment (See Figure 5.5). Once the relevant risk assessments were completed and approved by the Sponsor an approval letter was supplied to the research team to enable continuation of the trial (Appendix I). The trial reopened on 3 August 2020.

Figure 5.5: Personal Protection Equipment: Scrubs; mask; gloves; visor; plastic apron.

The trial continued, taking note of the Covid-19 case numbers in the area as well as nationally. However, in November 2020 the case numbers increased, and England entered National Lockdown Two. The risk assessments were re-evaluated to see if anything required altering. At the time of Lockdown Two, the trial had participants on follow up. Part of the reason to continue the trial was to enable these participants to complete the trial. The trial was able to continue (Appendix I), however, the research team continued to monitor Covid-19 cases.

In January 2021, when National Lockdown Three was announced, the risk assessments were again reviewed. However, based on National and local Covid-19 levels of infection the research team took the decision to make modifications to the participant numbers (See Section 5.6). However, the research team were very conscious of the Covid-19 numbers and at any time if participants or the team felt the risk to themselves was too high, the trial would be closed.

The trial remained open as the participants were in pain and would have been attending the AECC UC Clinic for treatment anyway (Appendix I). They were not attending the clinic purely for research purposes and as such the trial was not creating a higher risk to participants. Where possible the non-manual therapy group were offered online appointment (Zoom) instead of attending the clinic.

5.14. Comparison of Participants Pre-Covid 19 Versus in the Covid-19 Era

Due to the exploratory nature of this feasibility study, recruitment rate was considered an important outcome of the trial. To explore the impact of Covid-19 on the number of potential trial participants, a parallel retrospective data capture was carried out to compare the potential number of participants pre-Covid-19 to during Covid-19. The methods for this can be seen in Chapter 9.

5.15. Limitations of Methods

5.15.1. Blinding

It was not possible to blind either the participants, or the doctoral researcher who carried out the intervention. However, to blind the doctoral researcher from the data obtained from the PROMs, a research assistant collected the questionnaires from the participants. Each participant was assigned a randomly generated, unique study number. Names were removed from the questionnaires and replaced with their unique study number. Similarly, fluoroscopy sequences were also saved using the study number. The researcher data captured the pseudo anonymised questionnaires and analysed the data. The research assistant was the only person who has access to the master list linking participant numbers to participant names.

6. The Development of a Home Management Booklet for Patients with Acute Non-specific Low Back Pain for a Clinical Trial.

6.1. Introduction

This chapter is in the format of a publishable paper and forms part of the methods for the study. This chapter outlined the development and production of the Home Management Booklet which was provided to all participants in the study.

6.2. Background

NSLBP is the leading cause of years lost through disability in high- and middle-income countries such as the United Kingdom (UK) (Vos 2017). In the UK alone, work-related lower back disorders accounted for 3.2 million working days lost in 2016, which results in substantial loss of revenue (Health and Safety Executive 2017). There are a variety of treatment options available for LBP, such as analgesia and manual therapy which can be effective (Oliveira et al. 2018; Stochkendahl et al. 2018). The effects of these treatment options may be augmented by the addition of patient information and encouraging active patient involvement in their care (Rantonen et al. 2014).

Healthcare providers are expected to deliver information and patient education to improve patients' understanding of their condition as part of the management plan for NSLBP. One of the ways they deliver this information is via booklets or information leaflets (Sustersic et al. 2017). Booklets have been used in healthcare for decades (O'Hanrahan et al. 1980; Laher et al. 1981), and specifically for LBP since the 1980s (Roland and Dixon 1989). Information booklets on LBP can help patients cope with their condition, as well as provide reassurance relating to the seriousness of their condition and prognosis (Burton et al. 1996; Burton et al. 1999; Roberts et al. 2002).

Rantonen et al. (2014) explored the use of a booklet for LBP alone, versus a booklet used in combination with a face-to-face educational appointment and found the booklet alone was no more effective than the combination. The booklet alone, however, was more cost effective (healthcare costs) when compared to the natural progression of the condition (Rantonen et al. 2016). When a LBP booklet alone was compared to manual therapy, patients who received the booklet experienced only slightly worse outcomes in their LBP symptoms and physical function but experienced less satisfaction of care (Cherkin et al. 1998). When a booklet was used in combination with usual care or general practice (GP) care, compared to usual or GP care alone, patients in the combined group had a change in the way they thought about their condition (cognitive changes), but not about the way they felt about their condition (affective changes) (Cherkin et al. 1996). There were no significant differences in symptoms or physical function

(Cherkin et al. 1996; Coudeyre et al. 2007), however, patients in the combined group reported better satisfaction with their care (Coudeyre et al. 2007). As such, booklets might be useful alongside usual care or manual therapy. However, they should be seen as part of effective doctor-patient communication during a consultation, not as a substitute (Sustersic et al. 2017).

It is suggested that booklet content should be evidence-based and consistent with existing guidelines (Sustersic et al. 2017). Equally, the information delivered by the booklet should be consistent with the information delivered by the healthcare provider (Sustersic et al. 2017). Furthermore, booklets should be written in a way which is easy to read for all socioeconomic levels (Dixon and Park 1990), using language which is appropriate for the average level of adult literacy (The National Literacy Trust 2017).

Possibly, the LBP booklet used the most in the literature is the *Back Book* (Roland 1996). However, this book is no longer in print and is very difficult to find in large quantities. For this reason, it was decided to develop a new one for the study entitled: Biomechanical Effects of Manual Therapy – A Feasibility Study. The purpose of the booklet was to provide information and home management recommendations to the participants of the trial. The study was a two-arm randomised clinical trial (RCT), both arms received the Home Management Booklet.

The aim of this review therefore was to develop a home management booklet that was based on the latest, best evidence from guidelines. In addition, the booklet went through a stakeholder process to ensure the readability and understanding of the content which included text and illustrations.

The stakeholder process and the outcomes from that have been published elsewhere (Rix et al. 2021) (See Chapter 8).

6.3. Methods

6.3.1. Booklet Content Development

Relevant peer-reviewed literature was systematically searched in PubMed, MEDLINE, CINAHL and Web of Science. Search Terms included medical subject headings (MeSH terms) specific to each database and a combination of keywords relevant to guidelines (guidelines, protocols, practice guidelines, clinical guidelines), low back pain (lumbar pain, lumbar spine pain, non-specific low back pain), non-invasive treatment (chiropractic, manual therapy, manipulative therapy). The search period was restricted to 5 years to ensure the latest guidelines were located. This is in keeping with the schedule of updates for Clinical Knowledge Summaries available as NICE guidelines (Clinical Knowledge Summaries 2012). The search dates included publications from

January 2014 to March 2019. A manual review of the articles' reference lists was used as an additional data source.

Titles and abstracts were screened to identify relevant, possibly relevant, and irrelevant studies. Relevant and possibly relevant were then read in full text to determine eligibility. Studies were deemed eligible if they were national or international guidelines for the non-invasive treatment of NSLBP. The future study will specifically explore the biomechanical effects of manual therapy in adult patients suffering from acute NSLBP (LBP without leg pain). In line with the inclusion/exclusion criteria for the study, only guidelines for the treatment of adults were considered, guidelines aimed at special populations such as paediatrics or geriatrics were excluded. Only guidelines available in English were included. This review focused on the treatment of acute NSLBP. Due to the varying definitions of acute, twelve weeks or less were considered acute for the purposes of this summary. Guideline recommendations for radicular pain or LBP with leg symptoms were not included in the data extraction, only recommendations for NSLBP were considered for the purposes of this summary.

Data particularly relating to topics which can be addressed as a Home Management Booklet were extracted from the selected studies. The topics included were patient education and reassurance; staying active/ avoiding bed rest; pharmacological recommendations; the use of heat and cold; and treatment options. While a number of the guidelines included recommendations for the diagnostic process and patient consent, this information was not extracted as it was not relevant to the content of the Home Management Booklet.

Data were tabulated to compare the guideline recommendations. Where guidelines specifically stated recommendations for acute LBP, only these data were tabulated. Where guidelines did not specify duration of LBP, all recommendations were tabulated. Where provided, the original studies used to develop the guidelines were consulted for a deeper understanding of the literature. Wherever most guidelines agreed, this information was prioritised for content of the Home Management Booklet.

A draft version of the Home Management Booklet was produced and discussed within the research team. This resulted in the inclusion of text related to patient safety and the ethical responsibility of the research team towards the participants of the study.

6.3.2. Creating the Home Management Booklet

The booklet aimed to facilitate patient education, as such it was compiled in lay persons' language, the clarity of which was assessed by a stakeholder consultation process. The

stakeholders included members of the public and patients with LBP, chiropractic interns (final year chiropractic students) and qualified experienced chiropractors. The aim was to explore readability and understanding of the booklet content, as well as style (layout, font, font size and line spacing). Stakeholders were also provided with a selection of picture genres and asked to select those which elicited reassurance for the booklet illustrations. The picture genre selection included black and white stick figures, simple black and white diagram, classic cartoon, anime, and photograph. The details of the stakeholder consultation process have been published elsewhere (Rix et al. 2021) (See Chapter 8).

6.4. Results

6.4.1. Booklet Content Development

The literature search identified 301 citations. After removing duplicates and following two phases of screening, seven national and international guidelines met the inclusion and exclusion criteria. No additional guidelines were identified through manual review of references (See Figure 6.1).

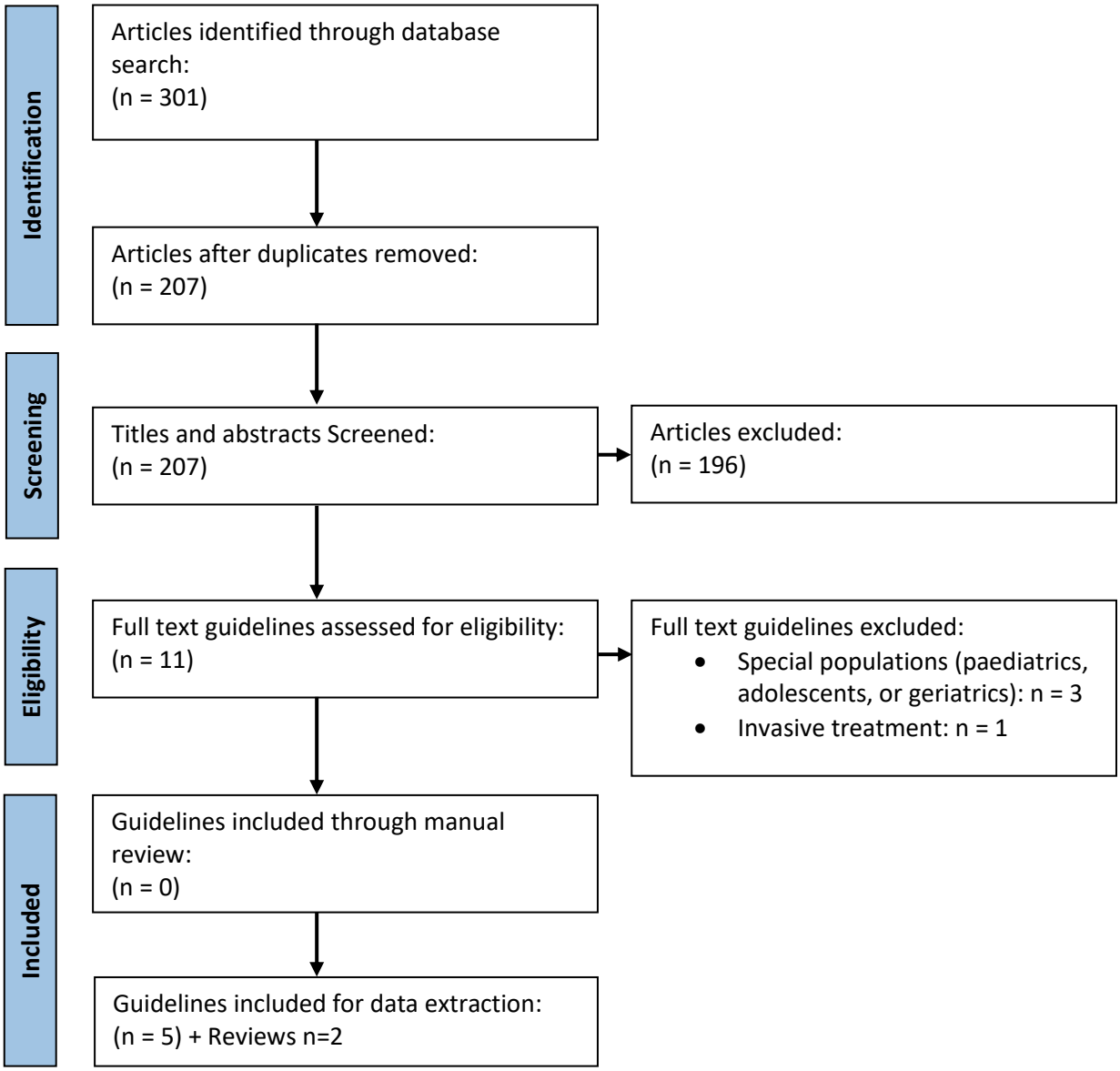

Figure 6.1: PRISMA flow diagram. Flow diagram representing article identification, article screening (which included the removal of articles which were not guidelines), guideline eligibility and guidelines used for data extraction for the Home Management Booklet content.

Five guidelines utilised primary data to support their recommendations (Globe et al. 2016; Qaseem et al. 2017; Bussieres et al. 2018; Stochkendahl et al. 2018; NICE 2019), a summary of which can be seen on Table 6.1a. Two guidelines reviewed previous guidelines to support their recommendations (Wong et al. 2017b; Oliveira et al. 2018), a summary of which can be seen in Table 6.1b. The division of categories used for data extraction were derived from the categories used in the guidelines.

Recommendations specifically relating to acute NSLBP (pain of twelve weeks or less) were obtained. However, NICE (2019) guidelines did not base their recommendations on duration of symptoms. The review by Oliveira et al. (2018) included three guidelines which defined acute as four weeks and less, and two guidelines which defined acute as six weeks and less. Wong et al. (2017b) did not specify how all included guidelines defined acute.

Table 6.1a: Summary guidelines for the recommendations for the non-invasive treatment of acute low back pain (LBP). Where guidelines specifically provide recommendations for acute low back pain, only these recommendations are tabulated. Where no pain duration is mentioned, all recommendations are tabulated. Greyed out blocks indicate subject areas not mentioned in the guidelines.

Authors (year)	**Development of Guidelines**	**Symptom Duration**	**Patient Education and Reassurance**	**Staying active and avoid bed rest**	**Pharmacological Recommendations**	**Superficial Heat and Cold**	**Treatment Options**
(Bussières et al. 2018)	Literature review	Acute (defined as <12 weeks)					Spinal Manipulative Therapy (SMT)
(Globe et al. 2016)	Literature review	Acute and subacute (defined as <12 weeks)					SMT (2 – 3 treatments per week, for 2 – 4 weeks)
(NICE 2019)	Literature review	Not specified	Advice and information should be provided on nature of low back pain	Encouragement to continue with normal activities	Non-steroidal anti-inflammatory drugs (NSAIDs) recommended (take contraindications and risks into consideration); consider weak opioids		Manual therapy recommended, but only as a treatment package including exercise, with or without psychological therapy; Exercises recommended, take

					only if NSAIDs contraindicated, not tolerated or ineffective.; paracetamol not recommended.		patient's needs, preferences, and capabilities into consideration
(Qaseem et al. 2017)	Literature review	Acute and subacute (defined as <12 weeks)	Patient education of generally favourable prognosis and high likelihood for substantial improvement in the first month	Advice to remain as active as tolerated	NSAIDs recommended (pain relief (moderate-quality evidence), function (moderate-quality evidence), beware of risks of NSAID usage; muscle relaxants recommended (pain relief (moderate-quality evidence))	Superficial heat recommended (moderate-quality evidence)	Massage recommended (low-quality evidence with a small to moderate improvement); acupuncture recommended (low-quality evidence with a small effect on function); SMT (low-quality evidence)
(Stochkendahl et al. 2018)	Literature review	Acute (defined as <12 weeks)	Weak recommendation for individualised	Weak recommendation for staying active,	Weak recommendation against the use of		Weak recommendation to offer SMT in addition

			patient education in addition to usual care	rather than bed rest	paracetamol (no short-term effects); weak recommendation against the use of opioids (no short-term effects); Weak recommendation against the use of NSAIDs (no short-term effects)		to usual care; weak recommendation to offer supervised exercises in addition to usual care; weak recommendation against the use of acupuncture (the effect is uncertain);

Table 6.1b: Summary reviews of clinical guidelines for the recommendations for the non-invasive treatment of acute low back pain (LBP). Where guidelines specifically provide recommendations for acute low back pain, only these recommendations are tabulated. Where no pain duration is mentioned, all recommendations are tabulated. Greyed out blocks indicate subject areas not mentioned in the guidelines.

Authors (year)	**Development of Guidelines**	**Symptom Duration**	**Patient Education and Reassurance**	**Staying active and avoid bed rest**	**Pharmacological Recommendations**	**Superficial Heat and Cold**	**Treatment Options**
(Oliveira et al. 2018)	Review of clinical practice guidelines	Acute (majority of guidelines defined acute as <12 weeks. However, 3 guidelines defined acute as <4 weeks and 2 guidelines defined acute as <6 weeks.	10 out of 14 guidelines recommend using patient education and reassurance.	7 out of 11 practice guidelines recommended avoiding bed rest for acute LBP; 7 out of 12 practice guidelines recommended maintaining normal activities	14 out of 15 guidelines recommend the use of NSAIDs; 4 out of 8 guidelines recommend the use of paracetamol, whereas 5 out of 14 guidelines are against the use of paracetamol; 8 out of 13 guidelines recommend the use of opioids, whereas 2 out of 3 studies are against the use of opioids; 8		1 out of 11 guidelines recommend the use of psychological therapy; 3 out of 14 guidelines recommend the use of exercise therapy; 6 out of 9 guidelines recommend the use of SMT, whereas 2 out of 11 are against the use of SMT; 4 out of 8 guidelines recommend the use of acupuncture

					out of 10 guidelines recommend the use of antidepressants, whereas 2 out of 10 guidelines are against the use of antidepressants; 3 out of 6 guidelines recommend the use of muscle relaxants, whereas 5 out of 11 guidelines are against the use of muscle relaxants		
(Wong et al. 2017a)	Review of guidelines	Acute	Patient advice, education and reassurance recommended	Early return to activities, staying active, or avoiding bed rest recommended	Paracetamol or NSAIDs recommended, with advice and considerations of risks; muscle relaxants (short course) alone or in		SMT recommended for patients not improving with self-care or failing to return to normal activities.

					addition to NSAIDs if initial trial of paracetamol or NSAIDs failed to reduce pain; short term use of opioids recommended to control severe pain, long tern use may be associated with tolerance, addiction, or abuse		

6.4.1.1. Patient advice, education, and reassurance

Five of the guidelines recommended patient education and reassurance, as well as staying active and resuming normal activities (Qaseem et al. 2017; Wong et al. 2017b; Oliveira et al. 2018; Stochkendahl et al. 2018; NICE 2019). One guideline specifically recommended avoiding bed rest (Oliveira et al. 2018).

6.4.1.2. Pharmacology

Five of the guidelines included pharmacological recommendations (Qaseem et al. 2017; Wong et al. 2017b; Oliveira et al. 2018; Stochkendahl et al. 2018; NICE 2019). However, their recommendations differed:

Three guidelines did not recommend Paracetamol (Oliveira et al. 2018; Stochkendahl et al. 2018; NICE 2019), while one guideline did (Wong et al. 2017b).

Four guidelines recommended non-steroidal anti-inflammatory drugs (NSAIDs) (Qaseem et al. 2017; Wong et al. 2017b; Oliveira et al. 2018; NICE 2019), while one guideline did not (Stochkendahl et al. 2018).

Two guidelines recommended the use of opioids, particularly if the patient failed to respond to conservative care or NSAIDs (Oliveira et al. 2018; NICE 2019), one recommended their use only to control severe pain (Wong et al. 2017b), one guideline did not recommend opioids (Stochkendahl et al. 2018).

Two guidelines recommended the use of muscle relaxants (Qaseem et al. 2017; Wong et al. 2017b), Oliveira et al. (2018) found three out of six guidelines recommended the use of muscle relaxants and five out of eleven were against the use of muscle relaxants.

One guideline recommended the use of antidepressants (Oliveira et al. 2018), however, the duration of symptoms was not specified.

6.4.1.3. Use of Heat and/ or cold

Only one guideline recommended superficial heat (Qaseem et al. 2017). The use of cold was not discussed in any of the guidelines.

6.4.1.4. Treatment Options

Most guidelines recommend SMT. Five guidelines utilised primary data to support their recommendations (Globe et al. 2016; Qaseem et al. 2017; Wong et al. 2017b; Bussieres et al. 2018; Oliveira et al. 2018; Stochkendahl et al. 2018).

NICE Guidelines (2019) recommended a treatment package of spinal manipulative therapy (SMT) and exercise, with or without psychological therapy.

Oliviera et al. (2018) found that only one out of eleven guidelines recommended psychological therapy.

Oliviera et al. (2018) found that three out of fourteen guidelines recommended exercise therapy, equally Stochkendahl et al. (2018) made a weak recommendation for supervised exercises.

Acupuncture was recommended; however, the evidence was deemed low-quality with a small effect on function (Qaseem et al. 2017). Oliviera et al. (2018) found that four out of eight guidelines recommended acupuncture.

Massage was recommended; however, evidence was low-quality with a small to moderate improvement (Qaseem et al. 2017).

6.4.2. Creating the Home Management Booklet

Using the guideline recommendations, the content of the Home Management Booklet was compiled. The research team discussed the booklet and decided that an additional section consisting of when to contact a healthcare practitioner and who to contact would be an important addition.

The content went through a stakeholder consultation process, both public and patient volunteers as well as the chiropractic intern volunteers provided feedback on additional information which they felt should be added to the existing content. The additional content was particularly related to homemade heat and ice packs, rather than the recommendation of shop bought products. Feedback was also provided on the font and font size of the text. The majority of stakeholders chose a coloured classic cartoon as the picture genre for the Home Management Booklet, it was felt that that this genre of picture best gave the feeling of being reassured and informed about their condition. The details of the results of the stakeholder process have been published (Rix et al. 2021) (See Chapter 8).

The Home Management Booklet was finalised and submitted as part of the REC ethics application. No changes were recommended to the booklet and the study received a favourable opinion from the ethics committee (REC Reference: 20/EE/0001).

6.5. Discussion

Clinical guidelines seek to optimise the quality of patient care and reduce the potential for harm associated with unsafe and ineffective treatment (O'Connell and Ward 2018). As many guidelines

examine the same evidence, it would be understandable to expect a consensus on guideline recommendations. However, this is not necessarily the case. Guidelines are developed using systematic review and quality assessment of literature. It is possible that the quality assessment being used differs between guidelines, thus interpretation of benefit/ harm can be skewed (O'Connell and Ward 2018). Equally, guidelines differ in their interpretation of "effectiveness" (O'Connell and Ward 2018). Some guidelines interpret any positive change in objective or subjective measurements to be effective; some guidelines only consider measurements which reach MCIC to be effective; and some guidelines only consider minimal clinical important difference to be effective. Thus, where unequivocal evidence exists for particular treatments, guidelines have clear agreement. Whereas, where evidence is 'grey' or open to interpretation, guidelines differ in their recommendations. Furthermore, some of the guidelines included were national guidelines. As countries differ in what is available in their healthcare systems it is possible this may have had an influence in the recommendations made.

6.5.1. Patient Advice, Education, and Reassurance

Patient education was defined as education regarding health literacy, competencies, and adaption of behaviour (Vos 2017; Stochkendahl et al. 2018). The World Health Organisation called for more patient education to aid the prevention of chronic disease. This education should be aimed at helping patients to self-manage their conditions; avoid complications and co-morbidities; and improve quality of life (WHO 1998). It is not uncommon for a clinician to assist patients with self-management, this usually includes education regarding exercise (staying active and/ or specific exercises for easing LBP), as well as lifestyle and postural modifications (Globe et al. 2016; Qaseem et al. 2017). Reassurance has been recommended in many of the treatment guidelines (Wong et al. 2017b; Stochkendahl et al. 2018). Patients with acute NSLBP may benefit from a combination of clear information regarding their condition, as well as empathy with cognitive reassurance (Hasenbring and Pincus 2015). Reassurance may have a significant impact on reducing fear avoidance behaviour (Storheim et al. 2003).

A section of the booklet was dedicated to a brief explanation of the condition of NSLBP, as well as a section on lifestyle and postural modifications. Reassurance was provided in both the written content, as well as the illustrations used for the booklet. Illustrations can be linked with particular emotions; this is named photo elicitation (Harper 2002). As part of the stakeholder process, the majority of the stakeholders chose a coloured classic cartoon genre for the images. It was felt that this elicited both reassurance, while still taking the condition seriously (Rix et al. 2021) (See Chapter 8).

6.5.2. Early Return to Activity, Staying Active and Avoid Bed Rest

Staying active was defined as *"maintaining usual levels of daily activity, including work, despite pain"* (Stochkendahl et al. 2018). Staying active was recommended by a number of guidelines (Wong et al. 2017b; Bussieres et al. 2018; Oliveira et al. 2018; Stochkendahl et al. 2018), however, literature is conflicting when looking specifically at acute NSLBP patients. When comparing bed rest to staying active, there was no statistical difference between groups for pain intensity, disability, or vertebral stiffness at seven days (Rozenberg et al. 2002). It should be noted that this study included the use of paracetamol, NSAIDs and muscle relaxants for all participants over seven days which may have influenced the results. When comparing bed rest; staying active; and back extension exercises, Malmivaara et al. (1995) found patients who stayed active had significant reduction in pain intensity and duration of pain, as well as an increased ability to work. Lastly, when staying active was compared to modified activity, Olaya-Contreras et al. (2015) found no difference between groups. Interestingly, when the same evidence was reviewed by Stochkendahl et al. (2018), the working group concluded *"the overall positive effects of staying active outweigh the potential harmful effects which has led to a recommendation in favour of advice to stay active".* None of the literature mentioned harmful effects of staying active, however, there could be some benefit and, on that basis, staying active is advisable (Malmivaara et al. 1995; Rozenberg et al. 2002; Olaya-Contreras et al. 2015). As such, a section of the booklet encouraged patients to stay active and continue with normal activity as much as possible.

6.5.3. Pharmacological Recommendations

6.5.3.1. Paracetamol

The use of Paracetamol in the treatment of acute NSLBP is not recommended (Oliveira et al. 2018; Stochkendahl et al. 2018; NICE 2019). It is suggested that Paracetamol is no more effective than placebo in the treatment of acute NSLBP (Machado Gustavo et al. 2015; Traeger et al. 2019). When Paracetamol was compared to placebo, there was no difference between groups for pain intensity or short-term activity limitations (Williams et al. 2014). Equally, concerns have arisen over the long-term usage of Paracetamol (more than 7 days). There is evidence to suggest that Paracetamol users have an increased risk of cardiovascular events; gastrointestinal bleeds; and renal toxicity, all of which can result in death (Roberts et al. 2016).

6.5.3.2. NSAIDs

The use of NSAIDs in the treatment of acute NSLBP is recommended in some guidelines (Qaseem et al. 2017; Wong et al. 2017b; Oliveira et al. 2018; NICE 2019) and not in others (Stochkendahl et al. 2018). Examining the literature, NSAIDs reduce pain intensity in acute LBP patients more than

placebo. It is suggested NSAIDs reduce pain intensity by approximately 6 points (on a 100-point scale) (Machado et al. 2017; Traeger et al. 2019). However, Machado et al. (2017) suggests MCIC is 10-points and Ostelo et al. (2008) suggests MCIC is 15-points on a 100-point pain intensity scale. As such, the reduction in pain intensity for acute patients does not meet MCIC and may not be a meaningful change for the patient. In addition to this, there was an increased risk of myocardial infarction as well as gastrointestinal and renal effects in the short-term use of NSAIDs (less than 7 days' use) (Traeger et al. 2019).

6.5.3.3. Other Pharmacological Recommendations

The use of muscle relaxants was recommended in some guidelines (Qaseem et al. 2017; Wong et al. 2017b). Muscle relaxants can reduce pain intensity in acute NSLBP patients, more than placebo (Abdel Shaheed et al. 2017). However, there is substantial risk for side effects such as dizziness, drowsiness, and sedation (Qaseem et al. 2017).

Opioids were recommended by one guideline (Oliveira et al. 2018). Some guidelines recommended opioids as an option in LBP patients who have failed to respond to conservative care (Wong et al. 2017b; NICE 2019) and in one guideline specifically looking at opioid use in acute NSLBP, they were not recommended (Stochkendahl et al. 2018). Examining the literature, there is a paucity of literature relating to the use of opioids in acute LBP patients. There is some evidence to suggest that opioids do reduce pain intensity in chronic pain patients and have more of an effect that placebo, however, the effect is approximately 10.1 points (on a 100-point scale) and therefore may not be meaningful for the patient (Abdel Shaheed et al. 2016). Studies using opioids have been accused of overestimating the benefits by only reporting the findings from the patients who benefitted and not from the patients who dropped out due to lack of efficacy or adverse reactions to treatment. It is estimated that up to 50% of study participants drop out of opioid studies for these reasons (Abdel Shaheed et al. 2016; Traeger et al. 2019). It should be noted that what constitutes an adverse reaction to an opioid is not specifically defined in the literature. Risks or complications of opioid use include overdose, abuse, myocardial infarction and sexual dysfunction (Chou et al. 2015; Traeger et al. 2019).

There is a paucity of literature relating to the use of antidepressants in the treatment of acute NSLBP. However, antidepressants do not reduce pain intensity or depression, more than placebo, in chronic LBP patients (Urquhart et al. 2008). The side effects of the medication are increased drowsiness, dizziness, constipation, dry mouth, sexual dysfunction, and nausea (Qaseem et al. 2017).

As most guidelines do recommend NSAIDs, this was recommended in the booklet. Equally, as most guidelines do not recommend Paracetamol, this information was also added to the booklet. However, the section was qualified by requesting patients seek advice from a pharmacist before commencing with any pharmacological interventions. This addition was largely due to the concern for patient safety around side effects of the medication, as well as drug-drug interactions. The recommendations related to muscle relaxants, opioids and antidepressants were not included in the booklet as these medications are not 'over the counter' and would require a prescription from a general practitioner.

6.5.4. Use of Heat and/ or Cold

One guideline recommended superficial heat for pain relief (Qaseem et al. 2017). It is suggested that a heat wrap moderately improves pain at 5 days and disability at 4 days when compared to placebo (French et al. 2006). There is a paucity of literature relating to the use of cold in acute NSLBP patients. Two studies have compared heat and cold (ice massage), the studies were deemed low quality due to small participant numbers and a lack of randomisation. These studies had conflicting conclusions, with one indicating heat was better for pain reduction and the other indicating cold (ice massage) was better for pain reduction (Landen 1967; French et al. 2006).

While there is a paucity of literature relating to use of heat or cold for acute NSLBP, there is some evidence to support their use and very little risk related to the use of this modality. As such, their use was added to the booklet. The section was qualified by instructions on recommended use to prevent heat or cold skin burns. The public and patient group in the stakeholder process felt the booklet recommended shop purchased products and that a cheaper home approach could be valuable. This feedback was taken into consideration and the booklet was altered to include home heat and ice packs, as well as shop bought products.

6.5.5. Treatment Options

The booklet was designed to support the future trial and as part of the consent process for the trial participants would be made aware of treatment option limitations for the duration of the trial. However, the researchers felt that this was an opportunity for patient education as well as supporting participant continuation of care following the trial. As such, treatment options were included in the booklet.

Most guidelines recommended SMT (Globe et al. 2016; Qaseem et al. 2017; Wong et al. 2017b; Bussieres et al. 2018; Oliveira et al. 2018; Stochkendahl et al. 2018). Stochkendahl et al. (2018) defines SMT as *"any manual technique that moves one or more joints within normal ranges of motion and aims at improving joint motion or function (for example mobilisation or spinal*

manipulative therapy (SMT)". Evidence suggests that among patients with acute NSLBP, SMT was associated with moderate improvement in pain (Paige et al. 2017; Stochkendahl et al. 2018) and function (Paige et al. 2017). The Cochrane review investigating SMT for the treatment of LBP concluded that SMT is no more effective than inert interventions, sham SMT, or when added to another intervention (such as exercise) (Rubinstein et al. 2012). However, both Rubinstein et al. (2012) and Paige et al. (2017) indicate that heterogeneity of literature can make comparisons between interventions difficult. Equally, much of the literature is deemed low quality. The decision to use SMT as a treatment should be based upon cost, preference of the clinician and patients and relative safety of manual therapy compared to other treatment options. Spinal manipulation of the lumbar spine and pelvis (Sacroiliac joints) is considered minimal risk. It has been calculated that less than 1 in 3.7 million patients will experience a serious adverse complication, such as worsening disc lesion or cauda equina syndrome (Oliphant 2004). However, mild transient discomfort post-treatment (lasting up to 2 days) is considered common and can occur in 50% - 67% of patients (Oliphant 2004; Paige et al. 2017).

There is much debate within manual therapy professions regarding the definition of manual therapy. The debate revolves around whether manual therapy consists of SMT alone or if additional soft tissue therapy can be included. To standardise treatment provided in the UK Back pain Exercise and Manipulation (UK BEAM) trial, a treatment package of manual therapy was agreed by professions (chiropractic, osteopathy, and physiotherapy) to include spinal manipulative therapy, mobilisation, soft tissue techniques (stretching and massage) and trigger point therapy (Harvey et al. 2003). Massage was a recommended treatment option (Qaseem et al. 2017). NICE Guidelines (2019) recommend manual therapy, but only as a treatment package including exercise, with or without psychological therapy. Exercises were recommended (Stochkendahl et al. 2018; NICE 2019), but the recommendation was more for supervised exercise program or group classes.

The booklet recommended manual therapy as a treatment option, as well as exercise classes (or group exercise). Psychological support was mentioned in the booklet as there is evidence to suggest that cognitive-behavioural training (CBT) is an effective tool to enable back pain patients to follow self-management programs (Gohner and Schlicht 2006). As such, NICE (2019) recommend CBT combined with a physical exercise programme for patients with persistent LBP or patients with significant obstacles to recovery (for example fear avoidance based on inappropriate assumptions about their condition).

The research team thought the addition of when to contact someone and what constitutes an emergency was important for patients to be aware of. Much of the booklet is about reassuring the patient and the research team have no desire to frighten patients. However, there is a responsibility towards the patient of educating what constitutes an emergency and who to contact in this case. This additional information was largely added for patient safety reasons for the participants on the study and signposts the participants to contact the research team if they experience particular symptoms, such as leg pain or numbness, or worsening of their condition.

As recommended in the literature, the completed booklet (Appendix J) was compiled from the latest evidence (Sustersic et al. 2017); provided relevant information on the complaint (Hasenbring and Pincus 2015; NICE 2019), and used language (Storheim et al. 2003), as well as illustrations which were reassuring (Rix et al. 2021) (See Chapter 8). The booklet also provides postural advice, as well as lifestyle advice related to sitting and driving (Globe et al. 2016); pharmacological advice (Machado et al. 2017; Traeger et al. 2019); advice on heat and cold (Landen 1967; French et al. 2006); and advice on treatment options (NICE 2019). Additional information was added for participant safety and to ensure participants know when and where to find help if needed.

The booklet used a Dyslexic friendly style (British Dyslexia Association 2018), and language which was both reading age appropriate for the average adult literacy age in the UK (The National Literacy Trust 2017) and appropriate for a lay person (Flesch 1979; Dixon and Park 1990).

The booklet content not only received feedback from the research team, but also stakeholders such as the members of the public and patients who had experienced LBP, chiropractic interns and experienced chiropractic clinicians (Rix et al. 2021) (See Chapter 8). The booklet forms part of a feasibility study as such ongoing feedback on the booklet may be obtained from participants of the trial.

6.6. Conclusion

An evidence-based Home Management Booklet was developed for the study entitled: Biomechanical Effects of Manual Therapy – A Feasibility Study. The booklet content was compiled using the latest guidelines for acute NSLBP and aimed to complement the face-to-face consultation and aid patient education. Readability and understanding of the booklet were improved through a stakeholder process, equally this process aided the choice of illustration genre.

7. A Public and Patient Consultation Process as an Aid to Design a Person-Centred Randomised Clinical Trial

This chapter was submitted and accepted for publishing:

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(In accordance with the Code of Practice for Research Degrees 2021-22, the lead author contributed at least 75% of the substantive content of the paper)

It was also presented at:

- Joint World Federation of Chiropractic and European Chiropractic Union Conference. 2019. Researchers' Day Presentation:
    - Public, Clinician and Student Involvement in the development of the methodology for the PhD entitled: The Biomechanical Effects of Manual Therapy - A Feasibility Study.
- UK Imaging and Oncology Congress. 2021. Platform Presentation: Patient and Public Involvement in Research.
- World Federation of Chiropractic Conference. 2021:
    - Platform Presentation (online) of unpublished work: Usability Testing as an Aid to Design a Person-Centred Randomised Clinical Trial

7.1. Introduction

This chapter is in the format of a publishable paper and forms part of the methods of the study. During the design phase of the trial, this Patient and Public Involvement Process was carried out to assist in designing a person-centred trial.

7.2. Background

Healthcare, in recent years, has seen a paradigm shift from medical autonomy and disease-based care to a more person-centred approach to care (McCormack and McCance 2010). The principles and concepts of person-centeredness are now commonplace in national (Department of Health 2012; GOV.UK 2015; NHS 2020) and global healthcare policies (World Health Organisation 2015). There are also significant funding investments into providing tools aimed at healthcare professionals designed to improve person-centred care (Planetree 2018; BMJ 2020), as well as independent charities working towards improving care centred around the individual (The King's Fund 2020; The Point of Care Foundation 2020). Healthcare research is following this paradigm shift and significant efforts are being made to design research which takes the person into consideration (Tritter 2009; Mullins et al. 2012; Mullins et al. 2014).

The term 'person-centred' in healthcare is difficult to define, largely due to it being dependent on the care needs, circumstances and preferences of the individual receiving care (The Health Foundation 2016). 'Person-centred' is thought to differ from the term 'patient-centred', as it focuses not only on the individual receiving healthcare (as a patient), but on the person as a whole, living with their condition, in the context of their work, life and family (Starfield 2011). Care which is centred around the person has been demonstrated to be effective in a healthcare setting (Olsson et al. 2013). Involving multidisciplinary teams, including patients, in clinical decision-making as well as increased communication between patient and care provider appear to be more successful (Olsson et al. 2013). However, the heterogeneity of the literature makes the effectiveness of this approach difficult to ascertain. This is partly due to the lack of a definitive definition of person-centred care which results in significantly different study designs in the literature, but also due to a lack of a consistently utilised outcome measure with which to assess effectiveness (Olsson et al. 2013).

Typically, research studies have been designed by researchers with little or no input from the patients or members of the public (Mullins et al. 2012; Mullins et al. 2014). Thus, studies tended to be researcher-driven or researcher-centred (Tritter 2009; Mullins et al. 2012). In recent years, there has been a move from researchers carrying out research "on" or "to" participants, to a more inclusive research design whereby it is carried out "with" participants (Tritter 2009).

Involving patients and members of the public, together with researchers, in decisions about how studies are designed and conducted can create a person-centred study, echoing the changes in healthcare (Mullins et al. 2014).

Participation in research studies can be burdensome on participants. Therefore, when designing a study, the psychological, physical and financial burdens of participation should be recognised and minimised as much as possible (Naidoo et al. 2020). Considerations may include avoiding an overwhelming number of visits to the study site, or burdensome study requirements requiring a large time commitment from participants (Lingler et al. 2014; Gregg et al. 2019). The design may also acknowledge that participants have busy lives and are juggling various work, life, and family commitments (Sharma 2015). Research participants have highlighted the importance of good communication, for example having the researcher clearly express that their participation is valued and ensuring continued care and support from researchers at the end of their participation (Chhatre et al. 2018; Daykin et al. 2018). In developing and designing a study that is based around the participant, these important aspects should be maximised.

It is important to understand the potential participant population (Mullins et al. 2014). One of the ways to achieve this is to involve the people from that population and invite them to provide their input in building the study design and protocol (Sharma 2015; Gregg et al. 2019). There is some discussion in the literature regarding methodology for involving patients and members of the public in research (Kearney et al. 2017a; Hannigan 2018a). INVOLVE (INVOLVE 2017) suggest patient and public involvement may include a consultation, a collaboration or user-led research. A consultation involves patients and the public to advise on either an aspect of the study or throughout the research study; collaboration involves the patients and the public as integral members of the research team; and user-led allows people with the lived experience of the condition to take the lead in study direction and design (Hughes and Duffy 2018). Involvement needs to be flexible to the needs of research studies and research methods, rather than a rigid token addition to a pre-designed study (Kearney et al. 2017a).

Literature suggests that simulations have been used to give patients and members of the public a chance to experience the research study method (Lim et al. 2017). This is not always possible, particularly if the aim is to contribute to the design of a future study, where the study design has not been finalised. Equally, there may be ethical considerations if the study involves potentially invasive investigations or treatment. For this reason, an alternative method of patient and public consultation may need to be considered, such as usability testing. Usability testing is extensively used in computer engineering fields. It was introduced by Lewis (1982) and later refined by

Ericsson and Simon (1984). The aim is to gain an understanding of users and identify the main problems associated with using a system (Nielsen 1994). During the consultation, volunteers are encouraged to keep talking and focus on how they experience the system in their own words, with minimal intervention from the researcher (Georgsson et al. 2019). This differs from other usability tests, such as cognitive walkthroughs which are usually carried out by an analyst or engineer (fellow expert in the field), and not the end stage user. There is a paucity of literature relating to the use of a usability testing as an aid to designing clinical studies, as such this is a novel approach to a patient and public involvement consultation.

This patient and public involvement process utilised a targeted consultation process and involved patients and the public in one aspect of the study design (Hughes and Duffy 2018), to assist in creating a more person-centred study from a pre-existing study method for the RCT entitled: Biomechanical Effects of Manual Therapy – A Feasibility Study. As this was a feasibility study, a targeted consultation process was used, rather than collaboration or user-led involvement as a large group of volunteers could be recruited for maximum feedback on one aspect of the study design.

The resulting RCT will look at biomechanical changes associated with acute NSLBP. As such, patients currently having treatment for NSLBP and members of the public who have had experience of LBP were invited to participate in usability testing of the proposed study method. This was followed by a post-usability test discussion for areas of the method where usability testing could not be utilised.

7.3. Method

7.3.1. Ethics

This Patient and Public Involvement was a consultation process, and not considered research by the NHS (HRA 2017). Following completion of the HRA NHS Review decision tool (HRA 2020c) and under the advice of local ethics, ethical approval was not required.

7.3.2. Recruitment

Adult public and patient volunteers were sought with current or prior experience of LBP. Volunteers were recruited via the university public and patient partnership, as well as an advertisement displayed in the reception of the university's private teaching clinic. Involvement was voluntary, and volunteers were not paid for their time. All interested volunteers were sent an email containing details of the consultation process including:

- The role of the volunteer in the consultation process. Volunteers were being recruited to assist in the design of a research study to make it as participant friendly as possible. Their experience of LBP allowed volunteers to view the study design from the participant's standpoint, which placed them in a unique position to provide valuable feedback.
- What to expect on the day of the consultation process.
- Date and time the consultation processes were taking place. Two dates and time slots were available.

An additional date was arranged with two volunteers as they were unavailable for the proposed dates. No more than five volunteers per time slot, this was largely dictated by the need to minimise disruption in a busy clinic during opening hours. A total of nine interested volunteers responded to the advertisement, all responders took part in the consultation process.

7.3.3. Consultation Process

Volunteers agreed to: Voice recording of the consultation process; future contact for the purposes of discussion clarification; and named acknowledgement in future publications if they wished. The process followed that set out in Figure 7.1.

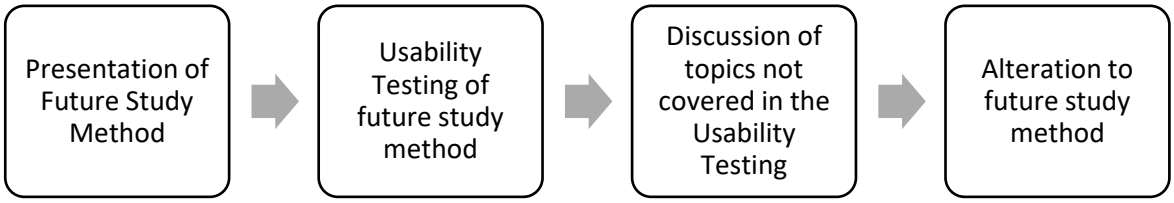

Figure 7.1: Outline of the consultation process aimed at exploring the most person-centred way of carrying out the clinical study.

The aims and objectives of the future study, and how it would contribute to existing knowledge related to LBP were outlined to the volunteers. This provided background information to enable a better understanding of the study. An outline of the proposed study method (Table 7.1) was handed out to support discussion between the researcher and volunteers.

Table 7.1: Outline summary of the future study method. The study is a two-arm randomised clinical trial investigating the biomechanical effects of manual therapy.

Timeline:	**Study Stage:**	**Details of study stage:**	
	Recruitment	Recruitment carried out in private university teaching clinic; Patient identified; Patient eligibility established at the New Patient Examination.	
Day 1	Baseline Measurements:	Participant consented into study; Back pain questionnaires; Pre-fluoroscopy form (pregnancy statement); fluoroscopy (moving video x-rays)	
Day 2 to day 13	Intervention:	Both groups receive a home management booklet.	
		Group 1: Five manual therapy appointments within two weeks	**Group 2:** No treatment appointments
Day 14	Follow up Measurements:	Back pain questionnaires; Pre-fluoroscopy form (pregnancy statement); fluoroscopy (moving video x-ray)	
	Study completion:	Signposting for further treatment once study is complete; Dissemination of results of study	

The consultation process was carried out in two parts, all volunteers took part in both parts.

7.3.3.1. Usability testing

Volunteers were walked through the physical environment of the clinic and what would be expected of study participants in each of the study locations was described (Figure 7.2). Walking the volunteers through the physical environment linked the study expectations to the physical space in which it would take place. Stopping and exploring each room provided insight into the reaction of future participants to the study experience. Volunteers were encouraged to 'think aloud' in each room and respond to the activity description. They were also given a clip board, paper, and a pen to make additional notes.

Clinic Reception: The researcher introduced the volunteers to the reception staff and the reception area. The reception area is the proposed area where future study participants will complete the study consent and questionnaires. At the time of the start of the walkthrough the reception was quiet. This allowed the volunteers to have full access to the area.

The radiology waiting area: The researcher led the volunteers through to the radiology waiting area. This is where the future study participants will complete the pre-radiology questionnaire and consent. Volunteers were shown the radiology changing area (including the patient gowning instructions and gowns to be used) and toilet facilities.

The radiology room: The researcher led the volunteers through to the radiology room, where they were introduced to the fluoroscopy operator. The operator demonstrated the fluoroscopy procedure that the future study participants will take part in (the demonstration was done with the fluoroscope switched off, as such no risk of x-ray exposure for volunteers).

Treatment room: The researcher led the volunteers to a treatment room. The clinic has more than 45 treatment rooms which have very similar lay outs, as such the volunteers were shown one treatment room. This is where the future study participants would have their research appointments. A typical treatment was not demonstrated, most volunteers stated they were familiar with manual therapy treatment.

Clinic Reception: The researcher led the volunteers back through the clinic reception area. This was timed to coincide with a busy time in clinic reception to give the volunteers insight into how busy the area can get and the impact on the future study volunteers.

Figure 7.2: Flow diagram of the usability testing.

7.3.3.2. Post-usability Test Discussion

Following the usability testing, a discussion took place in a quiet environment. The researcher-led discussion focused on areas of the study not addressed during the usability testing. The discussion was based on a semi-structured focus group format to ensure all volunteer groups discussed similar topics.

The topics for discussion were:

- Recruitment strategies.
- Participant's willingness to be randomised.
- Treatment schedules for both arms of the randomised clinical study.
- Continuity of patient care once the research study is complete.
- Dissemination of study results to participants.

Discussions lasted a maximum of thirty minutes. Any additional notes taken by the volunteers during the usability testing were collected. At the close, volunteers were thanked for their assistance.

7.3.4. Feedback

Feedback was collated by the researcher who carried out the consultation process and compiled into one document (Microsoft® Word for Microsoft 365, USA). All researchers discussed the feedback from the consultation process and decided which areas of the study required alterations; if any alterations may impact the research questions; and if the alterations to the study were practical and achievable for the clinic layout and resources. Agreed alterations were made to the future study method to create a study which took the individual participants into consideration.

7.4. Results

Three consultation processes took place, with a total of nine volunteers. There were five volunteers in the first while the second and third comprised of two volunteers each. One male and eight females took part in the process, with an age range of 24 – 76 years of age. The ethnic group of all volunteers was white (British).

7.4.1. Usability Testing Recommendations

7.4.1.1. Clinic Reception

It was felt that the waiting room was very busy and noisy and as such other places for the filling out of forms and questionnaires were discussed. A treatment room was thought to be more comfortable for the participant, where it is quiet. Volunteers also felt it was awkward to complete

questionnaires and forms while sitting in a chair with a clipboard. As the participants will be suffering from back pain, volunteers felt they may need a little space to move around if needed.

7.4.1.2. The radiology waiting area

The radiology waiting area is smaller, less noisy, and more private. This was considered by one volunteer group as an area where the consent process, questionnaires and pre-fluoroscopy forms could be completed. The remaining two groups felt that a treatment room would be the best option.

7.4.1.3. The radiology room

The volunteers enjoyed the fluoroscopy demonstration and felt that both the researchers present made them feel comfortable. The volunteers acknowledged that the room contained lots of *"scary looking complicated equipment",* but the personal interaction with the researchers, and demonstration of the equipment made the process of a fluoroscopy less intimidating.

7.4.1.4. The treatment room

As most of the volunteers have had treatment at the university teaching clinic before, it was acknowledged that all rooms are essentially the same. It would be preferable to get a treatment room close to the radiology suite for ease of getting to and from the fluoroscope.

7.4.2. Post-usability Test Discussion

7.4.2.1. Recruitment

Volunteers were interested in discussing additional recruitment strategies:

- Volunteers discussed the option of recruitment via general practitioner (GP) surgeries as a viable option.
- Private practice recruitment was discussed, it was felt that the clinicians may feel that paying patients are being taken away from them and as such the volunteers felt this may not be a viable option.
- Recruitment via hospitals was discussed, the researcher outlined that these patients may not fulfil the inclusion/ exclusion criteria of the future study.

Regarding the approach to potential participants for the study by the researcher, volunteers discussed that potential participants may like time to consider whether to take part in the study or may want someone else present in the room. The researcher informed volunteers that potential participants were given 24 hours to decide whether to take part in the study or not.

7.4.2.2. Randomisation

The researcher led a discussion on what randomisation is, and the two groups of the clinical study. The researcher had concerns regarding willingness of participants to be randomised. The volunteers felt that the information sheet provided to potential future study participants was well written and explained the randomisation process and what would happen to the participant in each group. As such, if potential participants did not want to be randomised, they will not join the study.

7.4.2.3. Appointment schedules for both groups

An in-depth discussion was had by the volunteers regarding the non-manual therapy group. This group will receive fluoroscopy at the first and last research visit, and a Home Management Booklet. One volunteer group discussed that the participants in this group may feel as if they are left on their own to cope and as such have a higher risk of drop out. As a result of the discussion, an additional appointment halfway through the research will be made with participants in the non-manual therapy group (See Table 6.2). While another volunteer group seemed to pick up on the doctoral researchers wording when explaining the two groups and gave feedback that the doctoral researcher could be more encouraging and positive when discussing this study arm. Home management (advice and reassurance) is a recognised form of treatment for LBP, but potentially participants may not view the booklet as that, and it may need to be discussed and explained to the participants. The researcher should try to use wording that evokes participant empowerment (Volunteer Quotes: *"You can control the progress of your back pain"; "you can control your own back pain").*

Regarding the manual therapy group, this group's participation includes a first research visit which includes fluoroscopy (study day 1); followed by five manual therapy appointments (study day 2 – 13); followed by the last research appointment which includes fluoroscopy (study day 14). One volunteer group suggested that when thinking about driving to and from appointments and research load on participants, this was a lot of appointments in two weeks. Could they be cut down? This was discussed at length between researchers, and it was concluded that the first manual therapy treatment would take place at the first research visit (study day 1); followed by three manual therapy appointments (study day 2 – 13) and the fifth manual therapy treatment would take place at the last research visit (study day 14), thus reducing the appointment total from seven to five appointments (See Table 7.2).

Table 7.2: Outline of original proposed appointment schedule and the alterations made following the consultation process for both research groups.

	Group 1: Manual Therapy		**Group 2: Non-manual Therapy**	
Timeline (days)	**Appointment schedule before PPI**	**Appointment schedule after PPI**	**Appointment schedule before PPI**	**Appointment schedule after PPI**
1	Both groups receive a Home Management Booklet			
	Baseline Measurements (fluoroscopy and questionnaires)	Baseline Measurements (fluoroscopy and questionnaires) and first manual therapy appointment	Baseline Measurements (fluoroscopy and questionnaires)	Baseline Measurements (fluoroscopy and questionnaires)
2 – 13	Five manual therapy appointments	Three manual therapy appointments	No appointments	Appointment halfway through the study.
14	Follow up measurements (fluoroscopy and questionnaires)	Final manual therapy appointment and follow up measurements (fluoroscopy and questionnaires)	Follow up measurements (fluoroscopy and questionnaires)	Follow up measurements (fluoroscopy and questionnaires)

7.4.2.4. Continuity of care

Upon completion of the study, participants will be signposted back to the original clinician who completed the New Patient Appointment. The volunteers thought this was an excellent idea, it allows continuity of care for participants. Clinicians will also have access to all research documentation related to the participant, such as treatment notes, fluoroscopy images and completed questionnaires.

7.4.2.5. Dissemination of results

Volunteers thought it was important to provide participants with a summary of the study results as they had a vested interest in the outcome of the study.

7.5. Discussion

All volunteers provided feedback during the consultation process and were willing to enter discussions on trial improvements. As a result of the discussions that took place during the consultation process, several changes will be included in the design of the future trial including recruitment; location for questionnaire completion; the consent process; randomisation; the appointment schedule burden; continued support of participants; continuity of care; and dissemination of results.

7.5.1. Recruitment

The current feasibility study proposes single site recruitment at a university teaching clinic. However, a future fully powered randomised control trial would need to recruit from a larger pool of volunteers to meet the required sample size. During the post-usability test discussion, volunteers provided valuable thoughts on additional potential participant identification and recruitment sites. Recruitment from GP practices in the area, private practices (musculoskeletal health care providers) and hospitals were discussed. Each of these options would require further investigation as to the feasibility of using these additional Participant Identifying Centres, and a Participant Identifying Centre Agreement would need to be completed (IRAS 2021b). While this is not an obstacle, it will require further resources and it is recommended that this should be considered at the proposal stage and not as an amendment or addition to an existing project (HRA 2020a).

Recruitment at the university teaching clinic will take place at the New Patient Appointment. While the New Patient Appointment will be carried out by a student intern (final year chiropractic student), if the patient appears eligible for the study the researcher will then approach them. As means of introduction, they will give a brief outline of the study, and hand out an information sheet. Involving the researcher in recruitment aids development of a trusting relationship with the researcher and opens lines of communication from the outset. All of this is thought to aid person-centred recruitment (Chhatre et al. 2018; Daykin et al. 2018). It will also allow potential participants to ask questions related to the study from a researcher who is better versed in the study method. This facilitates open dialog between the researcher and the potential participant when discussing the option of joining the study (Chhatre et al. 2018). Shared decision making allows the researcher and potential participant to converse about the best course of care for the

individual, which may or may not be the research study (Kunneman and Montori 2017). As the decision to take part in any research study should not be taken lightly, the volunteers in this PPI process felt that potential participants may want to be given the opportunity to have an additional person in the room with them. This is mirrored in the literature where it is suggested that researchers should encourage potential participants to speak to their family members to aid the decision-making process (HRA 2020a).

Volunteers felt that potential participants should not have to decide at the New Patient Appointment as to whether they would like to join the study. This had been considered during the study design by the researchers as it is suggested in the HRA guidance for consent and participant information (HRA 2020a). All potential participants will be asked for permission to be contacted telephonically by the researcher after 24 hours. There is no fixed guidance on the amount of time a potential participant should be given (HRA 2020a), however, the study had an inclusion criteria of patients suffering from acute NSLBP. Due to potential participants being in acute pain, it was thought that 24 hours would be sufficient time for the participant to consider taking part in the study while balanced with receiving care in a timeous manner. While the researcher will contact the potential participant in 24 hours, they may request further time to decide whether they would like to take part in the study.

7.5.2. Consent and Baseline Measurements

Once a study participant decides to take part, a baseline measurement appointment will be scheduled. During this appointment, the information sheet will be discussed and written informed consent will be completed in accordance with the HRA guidance (HRA 2020a). While the content of the information sheet; the consent form; and the questionnaires were subject to a separate stakeholder consultation process (Rix et al. 2021), the location for the consent process and completing questionnaires was discussed. A treatment room was thought to be best option for this activity due to the room being quieter and more private. It is vital that a future study participant understands fully what the study is for; what their involvement will be; the risks involved with taking part; and alternative treatment options, before signing an informed consent (HRA 2020a). It is suggested that an information sheet and consent form, together with a meeting with a research team member for an extended discussion can improve understanding of the study (Flory and Emanuel 2004). It would be difficult to have a private discussion in a busy waiting room, and as such the suggestion of using a treatment room would be the best option. A treatment room would also give the participant the option of a chair and desk to complete the consent and study baseline questionnaires, as well as room to stand and walk around if needed. The volunteers felt that completing paperwork using a clipboard in a busy waiting area would be

uncomfortable, and the option of sitting at a desk with a comfortable chair would be welcomed by participants. As participants will be in acute LBP, it was felt the option of walking around during the appointment would also be welcomed. As majority of the volunteers had or have had episodes of acute LBP, their experience provided invaluable feedback for the creation of an environment which takes participant comfort into consideration.

During the baseline measurement appointment, study participants will have a fluoroscopy investigation of their low back. The radiology suite does have a number of *"scary looking complicated"* machines, as a clinician and researcher working with these machines daily, one forgets how intimidating they can appear (Rix et al. 2021). For the usability testing the fluoroscopy was demonstrated and explained. The volunteers felt that this put them at ease with the equipment and as such recommended a brief explanation of the equipment for the study participants. This contributes towards fully informed consent, whereby it is vital that study participants understand what their involvement entails and potential risks (WMA 2018). As such the brief demonstration will not only contribute to putting the study participants at ease, but ensure they fully understand the investigation they are about to take part, supporting the notion that research should be carried out 'with' the participant and not 'to' the participant (Tritter 2009).

7.5.3. Randomisation

Following baseline measurements, the study participants will be randomised onto one of two groups. While the researcher had reservations about participants willingness to be randomised, the volunteers did not. Volunteers felt that all participants were given adequate detail in the study information sheet as to what the two groups involved. Participants not willing to be randomised would not take part in the study. The future study is a feasibility study and as such, willingness to be randomised will be explored as part of the study and the proposed randomisation process may be refined or altered following the outcome. Potential study participants who do not wish to take part will be asked whether they are willing to give a reason as to why. Information may give further insight into participants willingness to be randomised.

7.5.4. Appointment Schedule

The volunteers were open to discussing the appointment schedules for both groups of the study. They felt that the non-manual therapy group had a chance of 'drop out' as this group was only seen by the researchers for their investigations. The volunteers suggested an additional appointment halfway through the study would be helpful to allow the study participants to make contact with the researcher and gain reassurance and advice if needed. Ongoing communication

fosters a positive relationship and can be reassuring to study participants (Chhatre et al. 2018; Daykin et al. 2018), as such the appointment schedule for this group was altered for the study. Equally, the language used by the researcher may lead to potential drop out in the non-manual therapy group. This highlighted the need to be more cognisant of wording used to describe the trial arms. It is suggested that participants who have a more positive interaction are more likely to view the study more positively (Daykin et al. 2018).

Regarding the manual therapy group, the volunteers felt that the research burden on the study participants was large as there could potentially be seven appointments in two weeks. The literature mirrors the concern of patients regarding overwhelming numbers of appointments or large research burdens on patients (Gregg et al. 2019; Naidoo et al. 2020). Five treatments in two weeks are recommended by treatment guidelines, however as a result of the feedback from the volunteers it was decided that the first treatment would be carried out in the same appointment after the first fluoroscopy, and the last treatment would be carried out in the same appointment before the last fluoroscopy, as such the study participants would only have five research appointments in total, rather than the original seven. Although this would make the first and last appointments longer, participants who may be traveling a distance for the trial would ultimately save time as well as travel costs.

7.5.5. Continuity of Care

Once a participant has completed the study, they will be signposted back to their original clinic intern (final year chiropractic student); thus, they would not have to start again with someone new. The unique experience of the volunteers of having been treated within the university teaching clinic highlighted the importance of continuity of care for the future study participants, which is consistent with the literature (Daykin et al. 2018).

7.5.6. Dissemination of Results

The volunteers felt that if participants had given their time to be a part of the study, they should be informed of the study outcome, which is supported in the literature (Daykin et al. 2018). As such, changes were made to the study consent form to include an additional optional tick box *"I am interested in the overall results of the research. I would like the overall results emailed to me upon completion of the research. I agree to my email address being used for this purpose."*

Interestingly, during the usability testing, volunteers were focused on the physical rooms, although they were introduced to the receptionists and fluoroscope operators. There was very little feedback relating to the people who the future participants will be in contact with. One of the keys to developing a person-centred study is communication and reassurance (Daykin et al.

2018). While much of this will come from the researcher, the whole healthcare team is instrumental in providing this.

This usability test and discussion resulted in changes to the original study method with the aim of producing a more person-centred study design. The method of this consultation process was unique in a healthcare study development setting. Many patient and public involvement processes encourage payment of volunteers for ongoing research collaboration, or expenses reimbursed for a 'one off' involvement (NHS England 2017). During recruitment for this consultation process volunteers were informed that no payment would be provided, which is generally considered poor practice (INVOLVE 2010). However, a reward may be offered which is not necessarily financial and as such volunteers were provided with refreshments during the consultation process and asked whether they would like to be acknowledged in any resulting publications (INVOLVE 2010). Future studies should consider building in a public and patient involvement process into the proposal and budget calculations of a study. The method is most likely more time consuming than a cognitive walkthrough, which would use fellow experts in the field such as fellow clinicians or researchers. However, the benefits of using a participant representative population outweigh the time burden for researchers. There is a growing need for a wider range of voices to be heard in study development and research, such as Black, Asian and minority ethnic populations (BAME) (INVOLVE 2012). This consultation process advertised for, and welcomed, all adults from any ethnic group. However, responses were only obtained from one ethnic group, which is generally considered a weakness as not all voices are heard. For this reason, future public involvement processes should aim to include under-represented groups.

The original study method had already been viewed by the team of researchers; the volunteers were able to view the study through the eyes of a participant. This resulted in recommendations and changes to the study the research team had not considered. As such, this consultation process was invaluable in helping to create a more person-centred study. It should be reiterated that the future study is a feasibility study and as such the alterations suggested by the volunteers can be implemented, reflected upon, and possibly refined before the final study protocol is established.

7.6. Limitations

The age range of the volunteers (24 – 76 years of age) is slightly older than the age range of the future study which is 18 – 65 years of age. Gender representation within the consultation group was skewed as only one of the volunteers was male, the remaining volunteers were female. It is proposed that a gender gap in research participation, especially when voluntary (unpaid), is

influenced by gender roles, responsibilities, and gender specific decision-making processes (Lobato et al. 2014). Females are significantly more likely to volunteer for research based on general altruistic considerations (Lobato et al. 2014). The significant gender gap evident in this consultation process was not thought to influence the outcome of the process.

It is unknown whether the lack of reimbursement influenced who volunteered or the outcome of the consultation. Furthermore, the lack of ethnic diversity on the outcome of the process cannot be discounted.

7.7. Conclusion

The consultation process used the unique method of usability testing, together with a post-usability discussion to aid the design of a more person-centred study. The process resulted in alterations to the future study, including participant recruitment, location of study paperwork completion, study appointment schedule, continuity of care, and informing the participants of the study outcome. It is hoped that these alterations may facilitate making the future study as person-centred as possible.

8. Stakeholder Involvement in the Development of Trial Material for a Clinical Trial.

This chapter was submitted and accepted for publishing:

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(In accordance with the Code of Practice for Research Degrees 2021-22, the lead author contributed at least 75% of the substantive content of the paper)

It was also presented at:

- Joint World Federation of Chiropractic and European Chiropractic Union Conference. 2019. Researchers' Day Presentation:
    - Public, Clinician and Student Involvement in the development of the methodology for the PhD entitled: The Biomechanical Effects of Manual Therapy - A Feasibility Study.
- European Chiropractic Union Conference. 2020. Researchers' Day Presentation (accepted, but due to COVID 19, not presented):
    - Stakeholder Involvement in a Clinical Research and Trial Documentation Development.
- UK Imaging and Oncology Congress. 2021. Platform Presentation: Patient and Public Involvement in Research.
- World Federation of Chiropractic Conference. 2021:
    - Poster Presentation of published work: Stakeholder Involvement in the Development of Trial Material for a Clinical Trial.

8.1. Introduction

This chapter is in the format of a publishable paper and forms part of the methods of the study. Once the study method had been solidified, the participant trial material (including the Home Management Booklet) was compiled. This trial material was sent to stakeholder volunteers to assist with readability and understanding. The volunteers also assisted with the choice of genre for the Home Management Booklet pictures.

8.2. Background

It is suggested that a large quantity of health research in the United Kingdom is avoidably wasted (Chalmers et al. 2014). Some of this research waste has been attributed to failure to publish findings; unclear reporting of findings; and failure of new research studies to systematically review previous work in similar fields, resulting in unnecessary replication (Minogue et al. 2018; Minogue and Wells 2018). Patients and members of the public have an interest in and role to play in research waste reduction (Minogue et al. 2018).

Involving and collaborating with patients and members of the public can improve study design, methods, and relevance of research (Al-Shahi Salman et al. 2014; Minogue et al. 2016). Together with researchers, they can be involved in decisions regarding how studies are prioritised, designed, and conducted (Minogue et al. 2018). This improves research by making it more relevant to the patient (Kearney et al. 2017b; Minogue et al. 2018). Patients and members of the public can also bring different perspectives from those who are conducting the research, such as a lay person's perspective, as well as the lived experience of the condition or caring for someone with the condition (Minogue et al. 2016). Patient and public involvement (PPI) may be used to aid development of trial material for patients which may have an impact in the recruitment and retention of trial participants (Al-Shahi Salman et al. 2014; Kearney et al. 2017b; Hannigan 2018b), as well as the consent process (Brett et al. 2014).

Stakeholder involvement is inclusive participation of all stakeholders in healthcare research, from the grass roots student population to clinicians, and from the public to patient. Each volunteer group brings unique experiences, knowledge and skill sets to the development of healthcare research creating an authentic partnership of self-identified volunteers working towards a common goal (Ahmed and Palermo 2010).

While much of the research carried out and published in the area of stakeholder involvement is centred around PPI, there is only a small amount of literature extending the sphere of collaboration to professional members of the healthcare community who may have an impact on, or be impacted by, the subject under investigation (Ahmed and Palermo 2010). It is suggested

that healthcare professionals may provide personal insight into clinical trial development, as well as a breadth of knowledge relating to clinical trial design and interventions (Gray-Burrows et al. 2018). Equally, healthcare professionals may provide insight into whether the trial would be practical, useful, or usable in a particular setting.

By combining the public and patient experience and perspective, together with the knowledge and personal insight of a healthcare professional, a well-rounded unique view of the study can be obtained and can enhance the development of a clinical trial (Gray-Burrows et al. 2018). Equally, involving patients and members of the public, together with healthcare professionals in research is vital as they are the end-users (Gray-Burrows et al. 2018).

While the primary goal of healthcare research is to generate new knowledge, according to the Declaration of Helsinki, this cannot take precedence over the interests and rights of human research participants (WMA 2018). Informed consent is the cornerstone of ethical research (Nishimura et al. 2013). In healthcare research, when informed consent is given, it indicates an individual has made a fully informed and voluntary decision to take part in the research trial. Therefore, the onus lies with the team conducting the trial to support the consent process by providing the participant with adequate details of the trial reasoning and procedures. This information should provide potential participants with all the materials they require to make an informed decision about their participation in the trial (HRA 2020b). For example, the purpose of the research; potential benefits and risks; the right to refuse or withdraw; and treatment alternatives (WMA 2018). However, the quantity of information given can overwhelm participants (Antoniou et al. 2011; Kirkby et al. 2012) and may lead to a participant's lack of understanding of key aspects of the trial which could be considered crucial information to those who are considering their participation (Griffin et al. 2006; Montalvo and Larson 2014; Innes et al. 2018). This may be due to the information being supplied in a complex way, not designed to support a participant's informed decision process, or using language which is better suited to a medical professional rather than a trial participant or lay person (Krieger et al. 2015; Innes et al. 2018).

An additional complexity in the consent process occurs when potential participants lack adequate literacy to be able to read and understand the information sheet and consent form. The National Literacy Trust (The National Literacy Trust 2017) indicates that the 16.4% of adults in England have "very poor literacy skills" and are defined as functionally illiterate (a reading age at or below the average 11-year-old). Up to 74% of studies relating to informed consent and participant comprehension of research information do not assess participant comprehension, which may contribute to a lack of participant understanding (Montalvo and Larson 2014).

One way to assess comprehension of text is to use readability formulas. These formulas generate automated numerical estimates of readability of a text. The readability formulas focus on the average number of syllables in a word (word length) and the number of words in a sentence (sentence length).

Three readability formulas considered objective measures of text comprehension are:

- The Flesch Reading Ease Formula (Flesch 1948) will output a number ranging from 0 – 100, the higher score indicates easier reading. A score of 90 – 100 can be understood by an average fifth grade student (10 – 11-year-old); 60 – 70 can be understood by an average eighth or ninth grade student (13 – 15-year-old); 0 – 30 can be understood by an average university student (18 – 21-year-old).
- The Flesch-Kincaid Grade Level (Flesch 1979) indicates a school grade level (USA) which the average student in that grade would be able to read.
- The Gunning Fog Formula (Gunning 1952) is a scale that indicates syllable and sentence length. A Fog score of 5 is readable, 10 is hard, 15 is difficult and 20 is very difficult.

However, the formulas may not be an appropriate predictor of comprehension for short question surveys or questionnaires (Lenzner 2014).

In addition, many studies do not consider additional impacts on readability such as layout, appearance, font size, and use of diagrams or pictures (Boulos 2005). According to the British Dyslexia Association (British Dyslexia Association 2018), up to 10% of the British population has some degree of dyslexia. As such, Dyslexia Guidelines should be considered when designing an information sheet or consent form for ease of readability.

The use of pictures in healthcare booklets or information sheets enhances engagement of patients (Delp and Jones 1996) and can facilitate comprehension of the written word (Houts et al. 2006). Patients have indicated that booklets with pictures are easier to read than text alone, even when the written text is identical (Delp and Jones 1996; Thompson et al. 2010). Additionally, photo or picture elicitation has been used in social science research in a variety of ways (Harper 2002). Images can elicit moods or feelings distinct from written text (Harper 2002; Jordan 2009). As such, consideration of the photograph or picture genre can aid understanding or create misunderstanding depending on the genre choice (Jordan 2009). In the case of healthcare research, this could mean the difference between the participant feeling informed and reassured, versus feeling fearful or that their condition is not being taken seriously.

This Stakeholder Involvement Process examined the material for the trial entitled: Biomechanical Effects of Manual Therapy – A Feasibility Study. The trial material examined in this process included the Participant Information Sheet, Participant Consent Form, the trial questionnaires, and the home management booklet for LBP. This process included stakeholders chosen for their unique experience and expertise which would encompass feedback from a layperson's, as well as practitioner's perspective. The layperson brought their experience of the lived experience of LBP, while practitioners brought their wealth of knowledge in the subject area, and their years of experience in practice. Intern students brought their theoretical knowledge, but more importantly their experience of working in the environment where the future trial will take place. The primary aim of this process was to improve the comprehension (through improvements in readability and understanding) of the trial materials for the future participants, equally to contribute towards the development of a comprehensive information sheet. Both contribute towards informed consent for the future trial participants.

8.3. Method

8.3.1. Ethics

A Stakeholder Involvement Process is a collaborative process, and not considered research by the NHS (HRA 2017). Following completion of the HRA NHS Review decision tool (HRA 2020c) and under the advice of local ethical guidelines, ethical approval was not required.

8.3.2. Volunteer Recruitment

Five volunteers were sought from each the following groups, each group was recruited via separate advertising strategies. All advertising and recruitment material specified that taking part was voluntary, unfortunately the project did not have a budget to reimburse volunteers.

- Members of the public who have experienced LBP were recruited via the university public and patient partnership. It was hoped that the public group would be able to give feedback from a lay person's perspective, which would be helpful in ensuring the potential trial participants would be able to read and understand what is involved with taking part in the trial.
- Registered chiropractic clinicians who have been in practice for at least two years were recruited via an advertising email. Emails were sent to Chiropractic Institution tutors who met the relevant criteria. It was expected that the practitioner group would be able to identify areas of missing information or pertinent information not highlighted sufficiently.
- Chiropractic intern students (final year chiropractic student clinicians) were recruited via an advertising email. Emails were sent via the Chiropractic Institution tutors. It was

expected that the intern group would be able to give feedback from their strength in theoretical knowledge. Equally, the intern students work in the same building where the trial will take place, as such it was expected their feedback may highlight practical considerations related to carrying out the trial.

The collaboration process was carried out from the beginning of April 2019 until the end of June 2019.

8.3.3. Collaboration Process

All volunteers were sent the trial documentation, either as an electronic version (by email) or as a paper copy, depending on their preference or level of IT skills. These included the information sheet, consent form, questionnaires, and home management booklet. An additional document which included different genres of pictures for potential use within the home management booklet was also provided. All documents sent to volunteers were single spaced, using the font Calibri in a size 11 (Microsoft® Word for Microsoft Office 365, USA). Volunteers were asked to provide feedback on the documentation, this could be completed either as 'tracked changes' in a Microsoft Word Document or as changes made on a paper copy. The individual documents and requested feedback are outlined below.

8.3.3.1. Participant Information Sheet

The information sheet underpins the participant understanding of the trial, what the purpose of the trial is, what their role in the trial will be, withdrawal process and data management. The Health Research Authority template and the university template was used to complete the information sheet (HRA 2020e).

Feedback was requested on:

- Content:
    - How easy was the wording of the information sheet to read?
    - Was the information sheet clear and easy to understand?
- Style:
    - Was the information sheet easy to read, specifically looking at style layout, font, font size and line spacing?
- Were there any additional changes to the document that volunteers would like to add? These did not necessarily have to be related to readability and understanding. Practitioners and intern students were asked if they felt there was any missing information or additional information which may be helpful to a participant.

8.3.3.2. Participant Consent Form

The consent form is a signed agreement between the researcher and the participant indicating that the participant has read and understood the information sheet and is happy to be a part of the trial. The Health Research Authority template and university template was used to complete the consent form.

Feedback was requested on:

- Content
    - How easy was the wording of the consent form to read?
    - Was the consent form clear and easy to understand?
- Style
    - Was the consent form easy to read, specifically looking at style (layout, font, font size and line spacing)?

8.3.3.3. The Questionnaires

Two questionnaires will be used in the trial, the Bournemouth Questionnaire (Bolton and Breen 1999), and the Roland Morris Disability Questionnaire (Roland and Fairbank 2000). These questionnaires are used as Patient Reported Outcomes Measures (Deyo et al. 1998a) (See Section 4.5.1). As these are validated, the questions cannot be changed without influencing the validity of the questionnaires. Equally, the readability formulas are not very accurate for short questions (Lenzner 2014).

For these reasons, feedback was only requested on style:

- Were the questionnaires easy to read, specifically looking at style (layout, font, font size and line spacing)?

8.3.3.4. The Home Management Booklet

The evidence informed home management booklet was developed and compiled by the research team from recent published guidelines relating to non-invasive treatment of acute NSLBP (See Chapter 5). Volunteers were sent the wording of the booklet, without illustrations.

Feedback was requested on:

- Content:
    - How easy was the wording of the home management booklet to read?
    - Was the home management booklet clear and easy to understand?

- Style:
    - Was the home management booklet easy to read, specifically looking at style (layout, font, font size and line spacing)?

A document which included different genres of pictures was also sent. Volunteers were asked to select the picture which gave the feeling of reassurance, without giving the feeling that the condition of the patient was not being taken seriously. Pictures were divided into two categories, anatomy of the back, and postural and ergonomic pictures. Pictures were organised from most detailed, to least detailed (See Table 8.1). Volunteers were supplied with an example of each genre, however due to copyright, not all pictures could be included in this article. In the category of anatomical pictures, examples of a coloured anatomically correct anime can be seen in Figure 8.1, and a coloured classic cartoon can be seen in Figure 8.2. In the category of postural pictures, examples of a photograph can be seen in Figure 8.3, a coloured classic cartoon can be seen in Figure 8.4, and a black and white stick figure can be seen in Figure 8.5. Volunteers were asked to choose one picture from each category.

Table 8.1: Picture genres to be used in the Home Management Booklet (listed from most detailed picture genre to least detailed picture genre for each category). The picture genres were provided to volunteers for each category.

Categories:	**Picture Genres:**
Anatomy of the back	• Coloured anatomically correct illustration (detailed) Most detailed • Coloured anatomically correct anime • Coloured classic cartoon (detailed cartoon) • Black and white classic cartoon (detailed cartoon) Least detailed
Posture and ergonomics	• Photograph Most detailed • Coloured anime • Black and white anime • Coloured classic cartoon (detailed cartoon) • Black and white classic cartoon (detailed cartoon) • Simple black and white diagram • Black and white stick figure. Least detailed

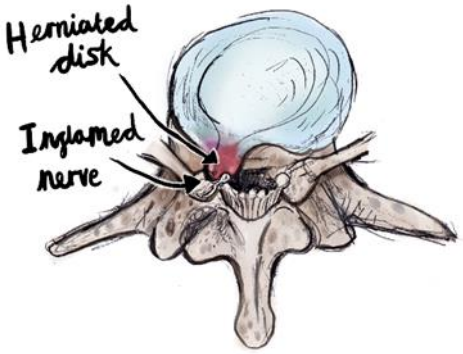


Figure 8.1: Anatomically correct anime

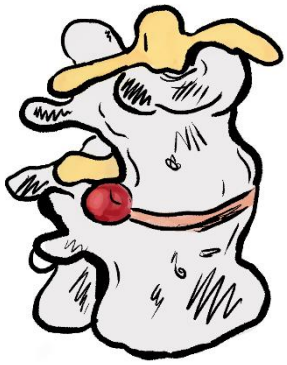
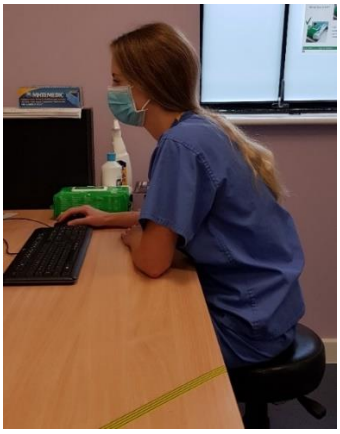


Figure 8.2: Coloured classic cartoon



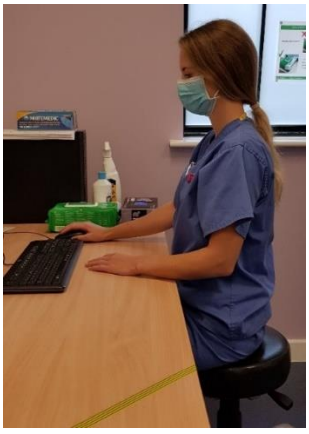


Figure 8.3: Photograph

Figure 8.4: Coloured classic cartoon

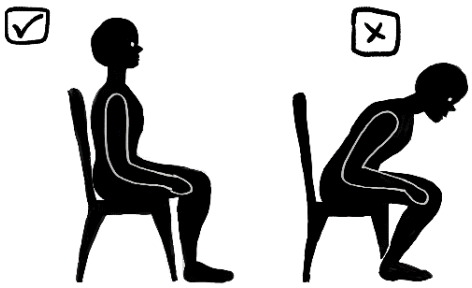


Figure 8.5: Black and white stick figure

8.3.4. Feedback

A thematic framework analysis of the feedback was carried out (Spencer 2014). This is a systematic approach to analysing qualitative data, where commonalities and differences are identified (Gale et al. 2013). Its defining feature is the development of a matrix whereby rows (in this case, each volunteer's feedback) and columns (themes) provide a structure in which to systematically manage data and analyse it by theme and individual (Gale et al. 2013; Spencer 2014). The matrix allowed the researcher to organise the data into the three groups to analyse common themes or common aspects of feedback highlighted by each group (Spencer 2014).

Feedback was combined with the original documents into one Microsoft Word Document (Microsoft® Word for Microsoft Office 365, USA), using 'tracked changes'. The primary researcher made changes to the original documents accordingly. Changes which reduced the sentence length and number of syllables in the wording were made as this may reduce reading age and increase understanding of the documents. For layout, font, font size and spacing, all feedback and comments were considered together with the dyslexia guidelines (British Dyslexia Association 2018). Regarding the pictures, all feedback was collated and the genre which was chosen most frequently was used for the home management booklet. All modified documents were sent to the remaining researchers for feedback and discussion.

8.3.5. Readability Formulas

All documents were tested using the readability formulas of Flesch Reading Ease Formula, Flesch-Kincaid Grade Level, Gunning Fog Formula (Readability Formulas 2020), before and after consultation.

8.4. Results

8.4.1. Demographic Data

A total of fifteen volunteers took part in the process:

- Members of the public: 4 females, 1 male; age range 38 – 73 years.
- Registered Chiropractic Clinicians: 3 females, 2 males; age range 31 – 47 years.
- Chiropractic Intern Students: 4 females, 1 male; age range 23 – 31 years.

8.4.2. Feedback

In general, the public group provided more feedback than the remaining two groups. The thematic framework analysis identified themes within the feedback. Once the thematic matrix was complete, common within group themes were identified (See Table 8.2).

Table 8.2: Thematic framework analysis of common themes within groups and between groups related to content (readability and understanding) and style.

Group / Theme	Public	Chiropractic Practitioners	Chiropractic Interns
Length of Participant Information Sheet:	It was felt by four of the public volunteers that the information sheet was too long, they questioned if all the information outlined was necessary.	No comments	No comments
Length of paragraphs and sentences in the Participant Information Sheet:	Some feedback was given for sentence length, such as "The consent process is a bit wordy, can you simplify it?"	Some feedback was given for paragraph length, such as "Split this paragraph here in two paragraphs, it's really long otherwise"	No comments
Use of language (and medical terms) in all documents:	All five volunteers identified language which they did not understand, such as "can the withdrawal section be made simpler? Instead of withdrawal, can you just say stop participating"; "I don't know what 'randomisation' meant, I had to look it up"; "what do you mean by an 'incidental finding' on x-ray?". The group also felt that the consent form contained "big words" and felt these needed to be simplified.	No comments	No comments
Insufficient information in the Participant Information Sheet:	No Comments	Some feedback given regarding eligibility criteria. It was felt inclusion and exclusion criteria could be elaborated upon. Some feedback was given relating to the incidental x-ray findings as it was felt these	Some feedback was given regarding the possible incidental findings on an x-ray. It was felt that this could be explained better, or a

		could be listed. Alternative treatments available for the same condition were not outlined in the document.	list of possible incidental findings being provided.
Sequence and Flow of the Participant Information Sheet:	No comments	No comment	Four of the chiropractic Interns identified sequence errors in the section related to what the participants would be required to do in the study. Two of the volunteers changed the sequence using 'tracked changes' to create a more logical sequence of events.
The addition of pictures in the Participant Information Sheet:	Some feedback was given by the public group to add photos or pictures of "scary equipment" to give the participants an idea of what to expect particularly relating to fluoroscopy.	No comment	No comment
Data Management sections in the Participant Information Sheet and Participant Consent Form:	The public volunteers struggled to understand both documents. In summary, "I don't understand any of this, basically will you keep my data safe"	No comment	No comment
Home Management Booklet	Some feedback given relating to the hot and cold pack section, can more options be listed or signpost participants to their pharmacy for other options. One participant suggested that I inform participants to speak to their pharmacist before taking any medication for their back	No comment	Two of the five volunteers suggested that an exercise and rehabilitation section be added to the booklet.

	pain. One participant recommended when pictures are added to the booklet, that they reflect a diverse population.		
Font, font size and layout	One comment relating to colour used within documents, “it’s all so black and white, it makes my eyes sore”. It was suggested that the font was quite small and could be made bigger. One person commented that they liked the font in the Information Sheet, but not in the Home Management Booklet. However, the fonts used were all the same across all documents.	It was suggested that the font spacing be 1.5 spaced to allow the reader to read the document more easily.	No comment

The public group had concerns about the length of the information sheet, in contrast, the intern and practitioner groups provided feedback on where they felt there was insufficient information and what could be added to the information sheet. The public group provided feedback on length of sentences and use of language (particularly medical terms). Equally, they felt that the use of pictures may help manage future participants expectations of the trial. Neither the practitioner group, nor the intern student group identified this in their feedback. The public group provided feedback on the data management section of the information sheet, indicating that this section was difficult to understand. Neither the practitioner group, nor the student intern group identified this in their feedback. The intern group provided feedback on the practicalities of running the future trial in the clinic. Neither the practitioner group, nor the public group identified this in their feedback.

Both the public group and the student intern group provided feedback on the home management booklet, suggesting that further information could be added. The practitioner group did not identify this in their feedback.

The public group and practitioner group provided feedback on structure (font and layout), the student intern group did not. Feedback included making the font larger, as well as increasing the spacing between lines. The public group felt the booklet was very black and white and would prefer the addition of colour.

8.4.3. Picture Feedback

8.4.3.1. Images of Back Anatomy

Thirteen of the 15 volunteers chose coloured classic cartoons (detailed cartoon):

- Three out of five volunteers in the public group chose coloured classic cartoon (detailed cartoon) (see Figure 8.2). One participant did not choose a picture, and one participant chose coloured anatomically correct anime (see Figure 8.1).
- Five out of five chiropractic practitioners, as well as five out of five student interns chose coloured classic cartoon (detailed cartoon) (see Figure 8.2). Although volunteers were not asked for further feedback, one volunteer commented that the coloured anatomically correct illustration was quite scary to a lay person and could create more anxiety about their LBP

8.4.3.2. Posture and Ergonomics

Again, thirteen volunteers chose coloured classic cartoon (detailed cartoon):

- Three out of five volunteers in the public group chose coloured classic cartoon (detailed cartoon) (see Figure 8.4). One participant did not choose a picture, and one participant chose stick figures (see Figure 8.5).
- Five out of five chiropractic practitioners, as well as five out of five student interns chose coloured classic cartoon (detailed cartoon) (see Figure 8.4).

8.4.4. Readability Scores

Readability scores for the trial documents, information sheet, consent form, and home management booklet were calculated. The scores before and after the Stakeholder Involvement Process can be seen in Table 8.3. The table includes the participant information sheet readability scores with the data management section removed, as well as the data management section on its own.

Table 8.3: Readability Scores of trial documentation before the Stakeholder Involvement Process and after the Stakeholder Involvement Process.

Readability Score / Document	Flesch Reading Ease		Flesch-Kincaid Grade Level		Gunning Fog Formula	
	Before	**After**	**Before**	**After**	**Before**	**After**
Participant Information Sheet (Whole document)	39.4 (difficult to read)	39.4 (difficult to read)	12.1 (twelfth grade (17 years-old))	12.1 (twelfth grade (17 years-old))	14 (hard to read)	14 (hard to read)
Participant Information Sheet without Data Management Section	38.0 (difficult to read)	72.0 (13 – 15-years-old)	12.1 (twelfth grade (17 years-old))	7.9 (eighth grade (13 – 14-years-old))	14 (hard to read)	10.5 (hard to read)
Participant Information Sheet, Data Management Section Only	39.8 (difficult to read)	39.8 (difficult to read)	12.1 (twelfth grade (17 years-old))	12.1 (twelfth grade (17 years-old))	14 (hard to read)	14 (hard to read)
Participant Consent Form	45.8 (difficult to read)	45.8 (difficult to read)	12.0 (twelfth grade (17 years-old))	12.0 (twelfth grade (17 years-old))	13.4 (hard to read)	13.4 (hard to read)
Home Management Booklet	70.4 (13 – 15-years-old)	79.2 (11-years-old)	7.7 (eighth grade (13 – 14-years-old))	5.9 (sixth grade (11-years-old))	10.9 (hard to read)	9.4 (fairly easy to read)

8.5. Discussion

The primary aim of this process was to improve the comprehension (through improvements in readability and understanding) of the trial materials for the future participants, as well as to contribute towards the development of a comprehensive information sheet. Both contribute towards informed consent for the future trial participants.

The age range of the public group was 38 – 73 years of age, which is slightly older than the age range for the future trial of 18 – 65 years of age. The location of the clinic where the trial will be taking place is ranked 113th in the Index of Multiple Deprivation, meaning it is in the top 1% of the most deprived areas in England (Corporate Research Team 2013). However, the clinic where the trial will be taking place is a private clinic requiring payment for treatment. Equally, this process did not collect socioeconomic status or level of education from the volunteers. A chiropractic student Intern is completing a Masters (UK) and as such is completing a level 7 qualification, equally qualified chiropractic practitioners would have completed a level 7 qualification at the very least. However, the student intern and practitioner groups were included for their clinical expertise, and not their experience of LBP. The public group contained current clinic patients, which indicates that the public group is representative of the future trial population who will be recruited from the clinic. Ethnic data was not collected from volunteers, which is a weakness of this stakeholder process. There is a growing need for a wider range of voices to be heard in research and trial development, as such stakeholder processes should consider recruitment of under-represented groups such as Black, Asian and minority ethnic (BAME) populations.

Few studies related to readability and understanding of trial documentation calculate readability scores (Montalvo and Larson 2014). In the UK, the Health Research Authority encourage researchers to calculate readability and to ensure that trial documentation is readable for the average person in the UK. The Flesch Reading Ease Formula and Flesch-Kincaid Grade Level are valid between the ages of 10 and 16. They correlate with Fry and Simple Measures of Gobbledygook readability formulas (Meade and Smith 1991), as well as the Cloze Comprehension Test (Taylor 1953). However, readability formulas are not without limitations. Readability scores are calculated by readability formulas which are mathematical calculations based on word length, number of words per sentence and number of syllables per word. The formulas may not be able to tell the difference between a heading, a table, or a figure and as these have short sentences this may result in a lower score. Equally, the software program being used may see each full stop as the end of a sentence and may not take into account abbreviations or decimals in numbers which may result in a lower score. Not

all multisyllabic words are difficult to understand, for example “cucumber” is not considered difficult to read or difficult to understand (Jindal and MacDermid 2017).

The readability scores of the information sheet and consent form were higher than the level at which the average person in the United Kingdom would be able to read comfortably. Even when changes were made to the documentation in response to the Stakeholder Involvement Process, such as sentence length and paragraph length, the readability scores did not decrease. Interestingly, when the data management section was removed from the information sheet, the average readability age of the information sheet before feedback changes were made was 17-years-old. Once changes were made in response to the feedback the readability improved greatly with a readability age of 13 – 14-years-old. The data management section is predominantly a templated section, which cannot be altered. This was mirrored in the comments from the public group related to the Data Management Section of the information sheet whereby one volunteer stated they did not understand any of it and essentially would like to be reassured that their data is safe. One possible reason for the high reading age in this section may be the use of legal language and jargon related to data management and data protection. Neither the practitioner group, nor the intern group raised comments related to the level of the language in the Data Management section. As the template cannot be altered, this is a limitation of this process. The consent form also largely contains templated wording, which may result in the readability age being so high. The results of this stakeholder process may provide the template authors with incentive to go through a similar process to reduce the reading age of the templates and increase understanding and comprehension.

Readability formulas can only give a reading level, it does not provide feedback on layout (font style, font size, spacing, colour) (Jindal and MacDermid 2017), style of writing (context and appropriateness) (Jindal and MacDermid 2017), difficulty of concept (Heydari 2012), prior knowledge (Heydari 2012) or coherence of text (Heydari 2012). Nor does it provide feedback on whether the medical language being used is understandable to the reader (Jindal and MacDermid 2017). As such, the stakeholder involvement process examined these potential issues.

It was felt by the public group that the information sheet was very long and questioned whether all information was necessary. This is supported in the literature whereby the volume of information provided to participants may exceed their preference (Antoniou et al. 2011; Kirkby et al. 2012). Neither the practitioner group nor the intern group raised comments relating to the length of the information sheet. Conversely, the practitioner group and the intern group suggested additional information could be added to the information sheet.

Use of language (and medical terms) in the information sheet and consent form was a theme of feedback which was common from all five volunteers in the public group. A lack of understanding of medical words may be a barrier to participants understanding the information sheet (Innes et al. 2018). The use of medical terms was not identified in the comments from the practitioner group or intern group, which indicates that they do not feel the language is an issue. This highlights the need for public involvement in the development of trial documentation. The additional information that the practitioner group and intern group felt was required would essentially increase the medical language used. A high level of medical language can increase participant fear (Derevianchenko et al. 2018) and potentially decrease recruitment. However, taking all comments on board related to additional information and the use of medical language, changes were made to the section relating to 'incidental examination findings' in a way that is hoped to decrease participant fear and increase understanding.

The comments related to readability and understanding of the information sheet and consent form begs the question, is full informed consent taking place? Participants should have an opportunity to ask questions before signing the consent form, however by simply asking the participant "do you have any questions?", this may not be sufficient to reveal whether the participant understands the trial or are signing full informed consent. This Stakeholder Involvement Process revealed that there is potentially a lack of understanding of the information sheet and consent form. To improve patient understanding interventions have been identified, such as person-to-person interactions with an extended discussion to complement the information sheet; multimedia interventions (including video presentation of the trial); enhanced consent forms (Flory and Emanuel 2004). Multimedia interventions and enhanced forms can be expensive and time consuming, equally the literature does not reflect that there is an increased understanding. Literature suggests that a standard format information sheet and consent form, together with a meeting with a research team member for an extended discussion can improve understanding and is inexpensive while using minimal resources (Flory and Emanuel 2004). An extended discussion may consist of a thirty-minute telephone discussion or a two-hour face-to-face counselling session, there is no strict guideline on this to allow the complexity of the trial to guide the amount of time spent with a prospective participant. It is suggested that an extended discussion whereby participants are quizzed or asked to explain their understanding of the trial back to the researcher is beneficial for trial understanding (Bossert and Strech 2017). A lack of a definitive definition of 'understanding' exists in the literature, which can make it difficult to ascertain whether understanding has taken place. What the literature can agree on is that further empirical research is required in the area of informed consent (Bossert and Strech 2017; Rempala et al. 2020). Reflecting upon feedback from this collaboration process, an extended

discussion with participants in the future trial should include the meaning and implications of randomisation, what will happen to the participant during the trial, and data management.

Volunteers were also asked if there was anything they would like to add to the information sheet. The public group suggested the use of pictures, particularly relating to *"scary"* medical equipment mentioned in the section related to what will happen to the participant during the trial. Additional pictures were added to the information sheet to aid understanding of the process, as well as managing participant expectations of trial procedures. The intern group suggested changes were made to the sequence and flow of the procedure participants will go through during the trial, this will make the future trial process smoother and more logical for the participants. It will also reduce the participant time burden during the trial.

For the home management booklet, the public group were quick to think of other options for home management, particularly related to how to make a hot or cold pack at home. These were incredibly creative, and generally were not added to the booklet as it would increase the length of the booklet considerably. Equally, some of the more creative ideas may increase risk of injury. However, the booklet does now suggest that other heat and cold packs can be used. There was a concern that participants may take over the counter pain medication without speaking to their pharmacist. It should be noted that the section relating to medication already urged all participants to consult their pharmacist before starting to take pain medication, as such no further changes were made. The suggestion from the intern group to include rehabilitation exercises was not considered as this may add an additional confounding variable to the trial, however, a link (web address) to the NHS website was provided which does have information on basic stretches for LBP.

It has been established in the literature that pictures can complement the written word to increase understanding (Houts et al. 2006). Volunteers were asked to choose the genre of pictures which best elicits the feeling of reassurance, and that the condition is being taken seriously. The majority of volunteers chose coloured classic cartoons for the illustrations for the home management booklet. An understanding of why most volunteers chose the same genre is unclear. However, the use of coloured cartoons can be used to entertain and persuade children and adults alike (Leiner et al. 2004). Cartoons can cross barriers of culture, age and literacy which can add to the effectiveness of the communication tool. In line with this, pictures for the book were commissioned to reflect a diverse population as recommended by our public consultation group. An example of one of the illustrations can be seen in Figure 8.4.

Regarding fonts, font size and layout feedback was in line with the Dyslexia Guidelines (British Dyslexia Association 2018). As a result of the feedback, the font remained as Calibri, a standard font

which is sans serif which makes the font more readable. Italics and underlining were removed, with bold being used for emphasis. Font size was increased from 11 to 12, letter spacing was increased by 20% and line spacing was adjusted to 1.5. The paper used was thicker to ensure that wording on the back of the page cannot be seen through the page.

The altered trial material was not sent back to the volunteers for further feedback. This was largely due to time constraints to this doctoral project, which is not an uncommon issue related to doctoral research (Heydari 2012). The altered material was however viewed by the research team for further feedback. The altered material was submitted, together with an ethical application for the future trial to a NHS Research Ethics Committee, which included lay members.

Volunteers were not paid for their time due to budget limitations. This is considered poor practice; however budgetary limitations are not uncommon in doctoral research and can be a limitation in carrying out stakeholder involvement processes (Coupe and Mathieson 2020). Future studies should consider building in a stakeholder process into the proposal and budget calculations of a study.

8.6. Conclusion

The Stakeholder Involvement Process was an invaluable exercise that aided the development of the trial documentation. Each group of volunteers made a unique contribution to the study design, the readability and understanding of trial documentation, and the development of the home management booklet. This in turn feeds back into the informed consent process contributing towards fully informed consent by participants in the future trial.

9. A retrospective study of the potential pool of research participants with non-specific low back pain at an outpatient manual therapy clinic pre- and post-Covid 19. A parallel study to 'Biomechanical Effects of Manual Therapy - A Feasibility Study'

9.1. Introduction

This chapter is in the format of a publishable paper and forms part of the results of the study. As most of the trial took place during Covid-19, the pandemic introduced limitations and alterations to the trial. For this reason, it was not possible to explore the feasibility of conducting a full-scale trial outside of the Covid-19 pandemic. For this reason, a retrospective data analysis of clinic files was conducted to explore the potential pool of eligible patients and whether they differed between the Covid-19 era and pre-Covid-19.

9.2. Background

A substantial amount of public funding is spent on health care research each year. Reportedly, the National Institute for Health Research (NIHR) spends one billion pounds from the Department of Health and Social Care on Research every year (NIHR 2022b). However, in the first quarter of 2021-2022, only 51.8% of trials met their time and recruitment target (NIHR 2022a).

Recruitment is vital to the success of a trial. Failing to recruit a planned sample size within a defined time frame in clinical trials leads to costly delays of outcomes (Chaudhari et al. 2020). Failure to recruit the planned sample size for a clinical trial could result in, at best an inconclusive or underpowered outcome, or at worst an abandoned trial (King et al. 2020). For this reason, exploration of recruitment rates, and realistic time frames is paramount when designing a trial. This is one of the parameters which can be explored in a feasibility study (NIHR 2019a).

The clinical trial for the study entitled: Biomechanical Effect of Manual Therapy - A Feasibility Study opened to recruitment on 10 February 2020, just as the Covid-19 pandemic took hold in the United Kingdom. The primary objective of the study was to assess the feasibility of carrying out a full-scale trial. The trial collected data such as the number of new patients visits; number of new patients who presented with LBP; and how many of these met the inclusion/ exclusion criteria. However, much of the trial took place during the Covid-19 era and was halted and restarted numerous times due to Covid-19 restrictions. As much of the data for the trial was collected in the Covid-19 era, it would have been very difficult to explore the feasibility of carrying out the trial outside of the pandemic.

Equally, it was unknown whether the characteristics of the patients presenting to the AECC UC Clinic would differ between the Covid-19 era and outside of Covid-19. Most people who are infected with Covid-19 experience mild to moderate respiratory illness, however, some will become seriously ill and may require hospitalisation (WHO 2021). During National Lockdown One, risk factors for becoming seriously ill from Covid-19 were explored. At the time, there was evidence to suggest that people over the age of fifty were more at risk, particularly males (Mallapaty 2020). High risk included people with conditions such as long-term lung conditions (severe asthma, chronic obstructive pulmonary disease), long-term heart of blood conditions (congenital heart disease, peripheral artery disease), long-term kidney, liver or spleen conditions, diabetes, and severe obesity (BMI of 40 or more) (NHS 2021). Those considered high risk were encouraged to stay at home and shield (NHS 2021). For this reason, there was an expectation that those patients with high risk factors would not attend the AECC UC Clinic during the pandemic. Additionally, those with common symptoms of Covid-19 (high temperature, continuous cough, loss of taste or smell) were required to self-isolate (BBC News 2020a). This was extended to those who had been in contact with someone with Covid-19. Between those shielding and those self-isolating, a decrease in overall patients attending the clinic was expected. However, other than a general decrease in patient numbers, it was unknown whether the pandemic would result in different characteristics, or signs and symptoms, in LBP patients, thus affecting potential recruitment for a full-scale trial.

Due to the virus being highly infectious, during National Lockdown One, the British Chiropractic Association recommended a move towards telehealth appointments only, and to cease all face-to-face consultations (British Chiropractic Association 2020a). Telehealth is the use of telephone or online video consultation to support patient care remotely (HealthIT.gov 2017). When face-to-face appointments could no longer be carried out, it was suggested patients thought telehealth was helpful, addressed their concerns, and provided a safe method of obtaining advice and care (Green et al. 2020). When National Lockdown One eased, the British Chiropractic Association moved from telehealth only, to telehealth plus a return to risk assessed face-to-face appointments (British Chiropractic Association 2021). Telehealth was maintained at the AECC UC Clinic as a pre-new patient history taking appointment. This system was implemented for three reasons, firstly to triage patients who may not be appropriate for chiropractic treatment or management and advised on the best place to find help. By doing this, these patients' exposure to Covid-19 would be reduced as they would not need to attend the clinic to gain this information. Secondly, to reduce the time that an intern and patient were in the room together during the New Patient examination, theoretically reducing the exposure time. Although, the estimated critical exposure time is 15 minutes which is much less than the one hour the intern and patient are in the room together (GOV.UK 2021). Thirdly,

to provide limited management over the telephone to patients who were unable to attend the clinic due to shielding or self-isolation. Equally, as National Lockdown One eased, the British Chiropractic Association, in line with government guidelines, issued guidance on the use of personal protection equipment (PPE), Covid-screening, social distancing and working 'bubbles', additional cleaning, and disposal of clinical waste (British Chiropractic Association 2020b). With the requirement of thorough cleaning of the treatment room, as well as reception, appointment times were made longer to accommodate this.

Due to Covid-19, a number of changes were made to the way the Clinic functioned, and as such, the potential effect of these changes on recruitment were explored. This retrospective study aimed to explore the potential pool of participants in the Covid-19 era and outside of Covid-19. A comparison of characteristics, signs and symptoms of LBP patients were explored utilising the trials inclusion and exclusion criteria between patients in the Covid-19 era and those outside of Covid-19.

9.3. Methods

The study entitled: Biomechanical Effect of Manual Therapy - A Feasibility Study received NREC ethical favourable opinion, however, this only included data captured during the time the trial was open. As such additional local Bournemouth University and AECC UC Ethics favourable opinion were sought and received for the period before Covid-19 (pre-Covid-19), as well as the dates the trial was temporary halted (Appendix K and L). A Bournemouth University Risk Assessment was carried out and approval of off-site research was received (Appendix M).

Data were collected via patient records for pre-Covid-19 from 1 August 2019 to 20 March 2020 (inclusive), and in the Covid-19 era from 1 August 2020 to 20 March 2021 (inclusive). The AECC UC Clinic was closed from 20 March 2020 until 1 August 2020 due to National Lockdown One, and as such no comparative data were available during this time. Retrospective data capture took place in February and March 2021.

Covid-19 restrictions resulted in the following operational changes at the AECC UC Clinic: opening hours, available rooms (some rooms during Covid-19 were used to store PPE and clinical waste), availability of clinic interns, telehealth and appointment duration. As such the way the clinic operated pre-Covid-19 and in the Covid-19 era was compared to assess the potential effect on the feasibility of a full-scale trial.

As a demonstration of difference in treatment capacity, maximum treatment capacity for one week was calculated. The clinic opening hours used for the Covid-19 era were the September 2020 to March 2021 opening hours (See Table 9.1). The clinic opening hours were defined as the number of

hours treatment could take place and does not include the hours that only reception was operational in the clinic. Maximum treatment capacity was calculated as:

Maximum Treatment Capacity = Clinic opening hours / treatment duration x number of rooms

Retrospective data from clinic files were collected to match new patients who presented to the AECC UC Clinic against the trial's inclusion/ exclusion criteria (See Table 5.1, page 99) to assess whether they would have been eligible for the trial.

Data collected included:

- Number of new patients presenting to the clinic
- Did the New Patient present with LBP or lumbopelvic pain (yes/ no)? If so, the following data was collected. This data relates to the inclusion/ exclusion criteria of the trial (Patients between the age of 18 – 65, with a pain scale of less than 8, having pain more than 10 but less than 28 days and answer no to the remaining questions)
    - Age (in years)
    - Numerical Pain Rating Scale (number between 0 and 10)
    - Pain duration (in weeks)
    - Pregnant (yes/ no)
    - Lumbar surgery (yes/ no)
    - Diagnosed scoliosis (yes/ no)
    - Diagnosed osteoporosis (yes/ no)
    - Recent trauma to the low back (yes/ no)
    - Absolute Contraindication to SMT (yes/ no) (See section 2.7.1)
    - Ionising radiation exposure greater than 8mSv within the last six months (yes/ no)
    - Pain down the legs further than mid-thigh (yes/ no)
    - Body mass index above 30 (yes/ no)
    - Diagnosed (within the last 12 months) and medicated for anxiety or depression (yes/ no)
    - Written English too limited to understand Participant Information Sheet, or if 'interpreter required' was written in the clinic notes in the clinic file (yes/ no)

9.3.1. Data Analysis

The Kolmogorov-Smirnov test was used to determine the distribution of data (Field 2018). Scale data of age, NRS and pain duration were normally distributed, as such an unpaired t-test was used to compare independent samples (pre-Covid-19 vs. Covid-19).

Chi-Squared test was used for the analysis of the categorical data of eligibility criteria of new patients presenting with LBP.

9.4. Results

9.4.1. Operational Changes

Changes were made to the operation of the AECC UC Clinic in the Covid-19 era to accommodate telehealth, the formation of intern student and chiropractic clinician 'bubbles', increased cleaning between patients, and Covid-19 screening (Appendix N). Additionally, there was a decrease in the numbers of existing patients and new patients who made appointments during the Covid-19 era, for this reason the clinic operated reduced hours (See Table 9.1).

The maximum treatment capacity of the AECC UC Clinic was much reduced in the Covid-19 era (See Table 9.1). Maximum treatment capacity in the Covid-19 era was 43% of pre-Covid-19 treatment capacity.

Pre-Covid-19, telehealth appointments were not taking place and new patients could telephone the Clinic to make an appointment for a New Patient Examination. However, in the Covid-19 era, telehealth was carried out as an additional screening appointment before the New Patient Examination, however, only ten telehealth appointments could be carried out each day due to resources. This led to a delay between the first telephone call from a new patient to make a telehealth appointment, to the telehealth appointment being carried out. This data was not collected by the AECC UC Clinic and as such could not be objectively quantified. There was a further delay between the telehealth appointment and the New Patient Examination and on average the delay between the telehealth appointment and the New Patient Examination was 5.3 days (range 1 – 46 days). There was an attrition rate of 40% between telehealth and the New Patient Examination.

Table 9.1: Summary of operational changes made to the way AECC UC Clinic operated in Covid-19 versus pre-Covid-19.

	Pre-Covid-19 (1 August 2019 – 20 March 2020)	**Covid-19 (1 August 2020 – 20 March 2021)**
Clinic Opening Hours	Monday to Friday, 11:00 – 19:00; Saturday 09:00 – 12:00.	4 August: Tuesday to Friday; 10:00 – 14:00. 17 August: Tuesday to Friday, 09:00 – 15:00. September - March: Monday to Friday, 10:30 – 17:00
Available rooms	43	40
Number of Interns available for patient appointments	130 interns available, each intern was able to work up to four full days a week.	4 August: 32 interns started on 4 August; each intern was able to work two two-hour shifts a week. 17 August: A further 32 interns started; each intern was able to work two three-hour shifts a week. September - March: The remainder of the interns entered the clinic (total of 140 interns); each intern was able to work two three-hour shifts a week.
Telehealth	Not Applicable	Required
Covid Screening	Not Applicable	Required
Appointment times	New Patient exam: 2 hours Report of Findings (and treatment): 1 hour Treatment visit: 30 mins	New Patient exam: 1 hour and 30 mins Treatment visit: 45 mins All appointment times included 10 minutes for cleaning between patients.
Intern absence	No information available	Due to government guidelines on shielding and isolation, as well as those who contracted Covid-19 several interns were unable to attend their clinic shifts.
Maximum Treatment Capacity	3698 hours/ week	1600 hours/ week

9.4.2. New Patient Data

A comparison of new patient data collected between Covid-19 and pre-Covid-19 can be seen in Table 9.2. Total number of new patients were reduced during Covid-19 at 73% that of the new patients which presented pre-Covid-19. Pre-Covid-19, 42% of new patients were suffering from LBP, whereas in Covid-19 only 30% of new patients were suffering from LBP. Pre-Covid-19 (9.8%) and within the Covid-19 era (10.8%) would have been eligible for the trial.

Table 9.2: Comparison of New Patient data in the Covid-era versus pre-Covid-19.

	Pre-Covid-19 (1 August 2019 – 20 March 2020)	**Covid-19 (1 August 2020 – 20 March 2021)**
Total number of new patients	2450	1794
Number of missing files	15	0
Total number of new patients with LBP	1024	546
Total number of new patients who met eligibility criteria	100	59

9.4.3. Eligibility Data

Eligibility data were explored to ascertain if the new LBP patients in the Covid-era differed from those in the pre-Covid-19 era. This can be seen in Table 9.3. As is evident from the table, there is a general trend of LBP presenting in patients aged mid to late forties with chronic LBP. A significant percentage of LBP patients presented with pain below mid-thigh (36.1% – 37.8%). Although not significantly different, patients waited longer to attend the clinic as seen by the difference in mean weeks of pain. The only significant difference between the groups was the percentage of LBP patients who had a BMI of 30.0 or more (p=0.003).

Table 9.3: Comparison of eligibility criteria of LBP new patients in the Covid-era versus pre-Covid-19 (* = Chi-Squared p<0.005).

	Pre-Covid-19 (1 August 2019 – 20 March 2020)	**Covid-19 (1 August 2020 – 20 March 2021)**
Mean Age in years (SD)	49.8 (±18.4)	45.4 (±18.5)
Mean NRS Score (SD)	5.0 (±2.6)	5.4 (±2.6)
Mean pain duration in weeks (SD)	19.5 (±21.1)	22.2 (±21.7)
Pregnant (%)	1.2	1.1
Lumbar or pelvic surgery (%)	1.3	2.2
Diagnosed scoliosis or osteoporosis (%)	1.5	2.9
Recent trauma to the Low back or pelvis (%)	2.4	5.3
Absolute contraindications to SMT (%)	5.8	7.5
Ionising radiation of greater than 8mSv recently (%)	0	0
Patients with leg pain below mid-thigh (%)	37.8	36.1
BMI above 30 (%)	19.3 *	4.8 *
Diagnosed with, or medicated for, depression or anxiety (%)	2.7	2.0
Limited English (%)	0.1	0.7

9.5. Discussion

9.5.1. Operational Changes

The changes made to the operation of the AECC UC Clinic influenced the maximum treatment capacity of the clinic. The maximum treatment capacity of the clinic was affected by the reduced opening hours, the increased treatment times to accommodate additional cleaning, and the reduced number of available rooms. The maximum capacity for treatment during Covid-19 was less than half of what it was pre-Covid-19 (43%). However, the actual capacity would have been further reduced during Covid-19 due to number of interns working at any one time due to working 'bubbles', as well as increased staff and intern absence due to shielding and self-isolating. This data was not collected but would likely have contributed to the additional lowering of maximum treatment capacity. Interestingly, while maximum treatment capacity was reduced by 57%, new patients presenting in

Covid-19 were only reduced by 27% when compared to pre-Covid-19 numbers. When looking at new patient numbers in the context of maximum treatment capacity, there were double the number of new patients presenting to the AECC UC Clinic during Covid-19. This may reflect the change in type or amount of activity during National Lockdowns (Constandt et al. 2020; Ding et al. 2020).

The additional step of telehealth in the new patient process meant that patients waited between the first telephone call for an appointment and their telehealth consultation, then waited again until their intern was available for their New Patient Examination. It is possible this waiting time led to a large attrition rate. However, it is equally possible that with the increasing Covid-19 infection rates at the time, the attrition rate reflects self-isolation or the reluctance to attend a busy clinic during Covid-19. It should be noted that reasons for New Patient non-attendance were not obtained and as such it is unknown to what extent the waiting time played a role in the attrition rate.

9.5.2. New Patient Data

Pre-Covid-19, 42% of all new patients presented to the clinic with LBP, whereas 30% of all new patients during Covid-19 presented to the clinic with LBP. The reason for this difference is unknown and potentially an exploration of this during the time of the National Lockdowns would have been helpful in identifying possible reasons for this. Possibly patients with LBP do not see their complaint as serious or requiring immediate treatment and as such did not want to increase their Covid-19 risk by presenting to a large clinic such as the AECC UC Clinic. Or possibly during Lockdown lifestyle changes resulted in less LBP or alternatively, an increase in different complaints presenting to the AECC UC Clinic. Both pre-Covid-19 and within the Covid-19 era, approximately 10% of patients presenting with LBP were eligible for the trial. With this being constant, feasibility of carrying out a full-scale trial can be explored assuming 10% of the LBP population will be eligible, no matter when the trial takes place.

9.5.3. Eligibility Data

When eligibility criteria were explored pre-Covid-19 and in the Covid-19 era, there were no significant differences, other than BMI, indicating that the characteristics of LBP patients presenting to an outpatient private musculoskeletal clinic had not changed. It was expected that characteristics of LBP patients in the Covid-19 era may differ in age, as being over 50 years of age may increase the patient's risk of severity of illness from Covid-19 (Mallapaty 2020; NHS 2021). Equally, it was expected that the characteristics of LBP patients may differ in severity of pain, and that only patients in severe pain would increase their risk of contracting Covid-19 by attending a large chiropractic clinic. Neither theory was supported by the data obtained in this parallel study. Although not significant, patients waited longer to attend the clinic, this was evident by the mean number of

weeks with pain being longer in the Covid-19 era. Again, it would have been helpful to explore this further at the time of the Covid-19 pandemic.

The trial could only include LBP patients who had a BMI of less than 30 (See Table 5.1, page 99). The NHS suggests that people with a BMI of over 35 are at a medium risk, and over 40 are at a higher risk of severe of illness from Covid-19 (NHS 2021). It was thought that people with a higher BMI may not attend the AECC UC Clinic as it would increase their risk of contracting Covid-19. The data in this parallel study appears to support this theory, however the data may not be accurate. During Covid-19 the weight and height stations in the AECC UC Clinic were removed as the potential risk of multiple people using the stations outweighed the benefit of collecting this data from the patient. For this reason, objective weight and height measurements were not obtained for all patients (missing data). Self-reported height and weight were included in some patient files; however, Bowring et al. (2012) suggest that only 34% accurately self-report weight, with 52% under-reporting their weight; and 52% accurately self-report height, with 30% under-reporting it. As such, during Covid-19 it appears that there were few patients with a BMI of over 30.

Although not significant, there was increase in patients who had previous lumbopelvic surgery, diagnosed osteoporosis/ scoliosis, and lumbar trauma reported during the pandemic. The reason for this is unclear, however the comparative rise in trauma may be due to the change in exercise and lifestyle during the pandemic (Constandt et al. 2020; Ding et al. 2020).

While it was thought that the LBP population characteristics would differ pre-Covid-19 and within the Covid-19 era, this was not the case. The LBP populations were comparable and as such whether the future trial takes place in the Covid-19 era or not, the sample is likely to be representative of the LBP population.

9.6. Limitations

As this parallel study utilised patient files to obtain data, there is a risk that not all information is recorded in the file, or there is potential for inaccurate reporting. Literature indicates that levels of accuracy vary, depending on the clinical setting and the data being collected (Hogan and Wagner 1997). It is unknown to what extent patient file accuracy may have influenced the data collected in this parallel study.

It was not possible to explore to what extent working 'bubbles' and intern absenteeism effected the number of new patients seen in the clinic or maximum treatment capacity of the clinic during Covid-19. Equally, whether telehealth led to the large attrition rate, or whether it was other Covid-19 related reasons. Additionally, it was not possible to explore the reason as to why patients appeared

to wait longer to attend the clinic for their LBP. It would have been helpful to explore this data during the Covid-19 era.

Potentially, the results of the study are not generalisable as the study was carried out in a single manual therapy clinic and as such implications for low back pain researchers or manual therapists may be limited. The results of this study suggest that the characteristics of low back pain patients in the pandemic were similar to those outside of the pandemic. This could mean that clinical management of patients both within and outside of the pandemic was similar. However, there were fewer patients in general attending the clinic during the pandemic, as well as a reduced proportion of patients with low back pain, as such the implications for low back pain researchers were that increased time would have been required for recruitment during the pandemic.

9.7. Conclusion

Not only were there fewer patients who presented to the clinic, the proportion of new patients presenting with LBP was also reduced compared to pre-Covid-19. However, the characteristics of those LBP patients presenting were comparable to the pre-Covid-19 population.

10. Primary Objectives: Biomechanical Effects of Manual Therapy in Patients with Acute Non-specific Low Back Pain – A Feasibility Study

10.1. Introduction

This chapter is in the format of a publishable paper and forms part of the results of the study. This chapter explores the primary outcome of the study of whether a full-scale trial is feasible.

10.2. Background

For scientific background and rationale for the study, please see Chapter 1, 2 and 4.

This study was a feasibility study and as such the primary objective of the study was to determine if a full-scale trial would be feasible, and if so, would the proposed method answer the research questions of:

- In patients with acute non-specific low back pain, does lumbar intervertebral movement change following a course of manual therapy?
- In patients with acute non-specific low back pain, do those who respond to manual therapy (established by PROMs) have different intervertebral movement to those who do not?

Previous research has demonstrated a difference in intervertebral motion between patients with chronic NSLBP and pain-free patients (Mellor et al. 2014a). In an observational study of neck pain patients, changes in intervertebral motion were not related to patient reported outcomes (Branney 2014). Intervertebral motion has not been investigated in patients with acute NSLBP, nor has the relationship between intervertebral motion and PROMs been explored in this population. For this reason, a feasibility study was carried out to explore whether a full-scale trial was feasible in a population of acute NSLBP patients.

A feasibility study can be utilised to identify and understand parameters which may affect the implementation and execution of a full-scale trial (NIHR 2019a). A feasibility study may generate data on the outcome of interest, but analysis of the outcome of interest is not the primary aim (NIHR 2019a).

The aim of this chapter is to explore the feasibility parameters of (NIHR 2019a):

- An exploration of participant recruitment (such as, whether the recruitment strategies are sufficient, as well as whether the participant identification strategies are sufficient)
- Number of eligible patients, as well as conversion to consenting participants

- Willingness of participants to be randomised
- Time needed to recruit and carry out the trial for a full-scale trial

The remaining feasibility parameters will be explored in Chapter 11, these include (NIHR 2019a):

- Practicality of obtaining baseline and trial measurements in the proposed setting
- Appropriateness of outcome measures to answer the research question
- Standard deviation of the outcome measure, which is needed to estimate sample size for a full-scale trial

10.3. Methods

For detailed methods, please see Chapter 5.

10.3.1. Trial Duration

See Section 5.4 for detailed trial duration and Section 5.5 for detailed sample size.

Due to Covid-19, equipment failure, and the Christmas Holiday closure, the trial opened and temporarily halted four times. The trial was open from 10 February 2020 – 20 March 2020, 4 August 2020 – 18 August 2020, 16 September 2020 – 10 December 2020, and 19 January 2021 – 2 April 2021. Only data collected while the trial was open was utilised.

Data collected included:

- Number of new patients presenting to the AECC University College Clinic.
- Number of new patients who presented with LBP.
- Number of LBP patients who were eligible for the trial.
- Number of eligible patients who consented onto the trial. Those who chose not to join the trial, the reasons for doing so.
- Participant withdrawal by the researcher (and reason), as well as if the participant withdrew themselves (and reason).
- Missing data (and reason).

Time needed to recruit and complete the future trial will be explored utilising calculated sample size (See Section 11.4.5, page 231). Taking into consideration the amount of time required for the baseline and follow up measurements, as well as intervention appointments.

10.4. Results

Figure 10.1 presents the number of patients who were screened, enrolled, randomised, and completed the trial. During the trial, 33% of new patients presenting to the AECC UC Clinic presented with LBP. 10% of patients with LBP were eligible for the trial. Twenty-eight patients were invited to participate in the study. Twenty-four participants verbally consented to receiving a Patient Information Booklet.

Pre-Covid-19 the trial was open from 10 February 2020 until 20 March 2020. During this time, four patients were approached, three verbally consented to discuss the trial and accept the Patient Information Sheet, of which one patient consented onto the trial. The patient who did not verbally consent to discuss the trial chose not to give a reason for their decision. The two who declined the trial were nervous about the use of ionising radiation.

During the time the trial was open in the Covid-19 era (4 August 2020 – 18 August 2020, 16 September 2020 – 10 December 2020, 19 January 2021 – 2 April 2021), 24 eligible new patients were approached, 22 (92%) of which verbally consented to discuss the trial and accepted the Patient Information Sheet. The two patients who did not verbally consent to discuss the trial chose not to give a reason for their decision. Of those who verbally consented to discuss the study, 15 (68%) consented onto the trial. The reasons given for the seven patients who declined the trial included three who were nervous about the use of ionising radiation, one who contracted Covid-19 between the New Patient appointment and the first research appointment, one who had transport issues getting to the clinic for multiple appointments, one who did not wish to be randomised into the non-manual therapy group, and one who did not want to be randomised into the manual therapy group.

During the time the trial was open, 16 participants consented onto the trial and were randomised into the manual therapy group or the non-manual therapy group. In the manual therapy group, eight participants began the trial, and all participants completed the trial. There were no participants who withdrew, nor were withdrawn, however one participants QF data was missing due to the breakdown of the fluoroscope. In the non-manual therapy group, eight participants began the trial, and seven completed the trial. One participant withdrew after the baseline data had been captured due to Covid-19. No participants were withdrawn, nor was there any missing data.

There were no adverse events or serious adverse events during the trial.

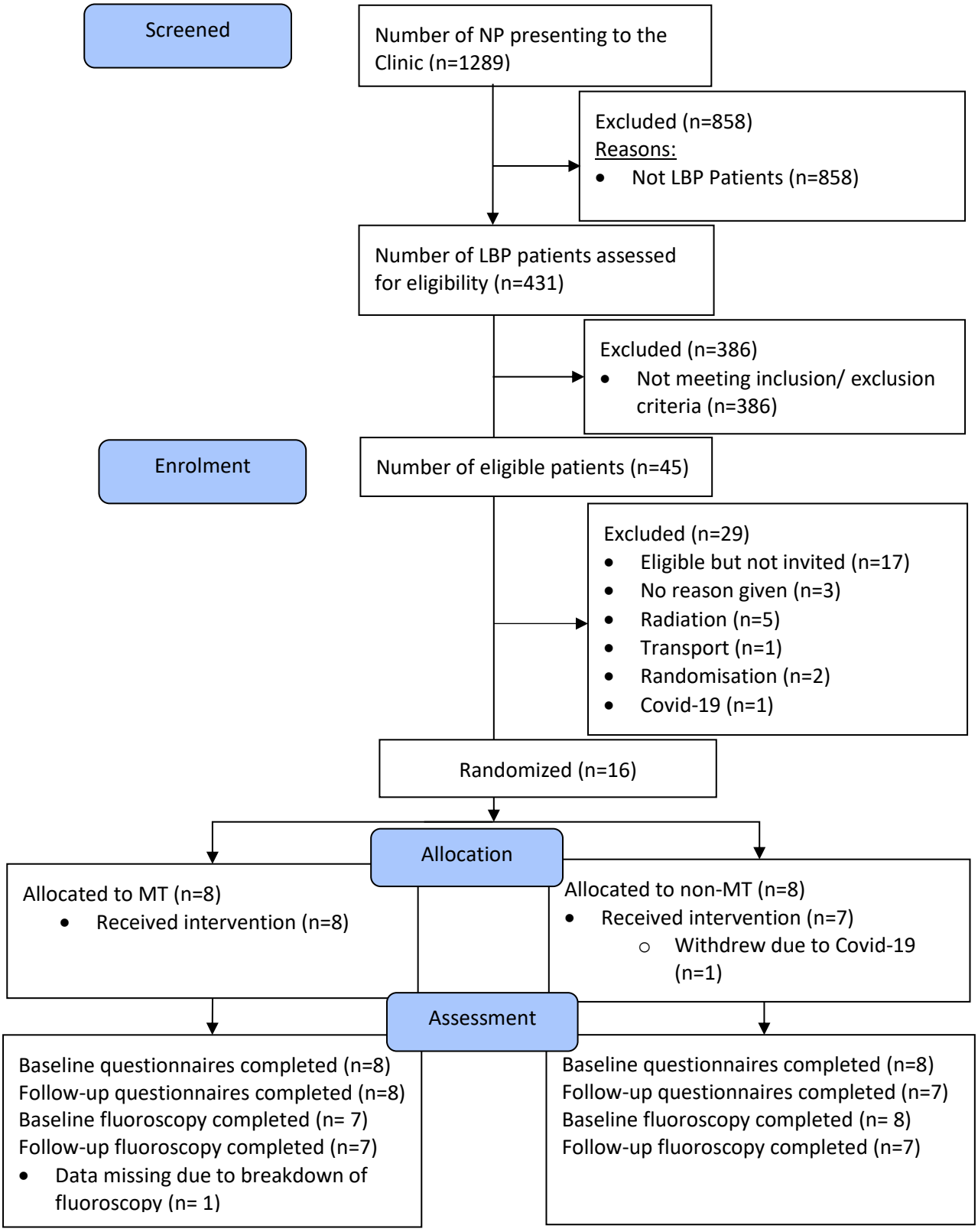


Figure 10.1: Flow diagram presenting the number of patients screened, enrolled, randomised and completed the feasibility trial (Modified from Eldridge et al. (2016))

Demographic data for the manual therapy and non-manual therapy groups can be seen in section 11.4.1 (Page 206).

Utilising the data from the parallel study (See Chapter 9), together with the data from the time the trial was open, the number of eligible patients per week has been calculated (See Table 10.1).

Table 10.1: Number of eligible patients presenting to the AECC UC Clinic per week.

	Pre-Covid-19 (Parallel Study)	**Covid-19 (Parallel Study)**	**Trial open**
Total number of new patients	2450	1794	1289
Total number of new patients with LBP	1024 (42%)	546 (30%)	431 (33%)
Total number of new patients who met eligibility criteria	100 (9.8%)	59 (10.8%)	45 (10.4%)
Number of weeks of data capture	31 weeks	31 weeks	30 weeks
Total number of eligible patients presenting to the clinic per week	3.2 patients/ week	1.9 patients/ week	1.5 patients/ week

Time needed to recruit and complete a full-scale trial has been calculated utilising the sample size calculated for MSI and MSV of 262 (328 including 20% for withdrawal), as well as the maximum sample size of 66492 (83115 including 20% for withdrawal) (See Section 11.4.5, page 231). Time needed to recruit has been calculated for both within Covid-19 and outside of the Covid-19 pandemic (See Table 10.2), assuming a single centre, single researcher trial design.

Table 10.2: Time needed to recruit and carry out a future full-scale trial, both within Covid-19 pandemic and outside of Covid-19 pandemic.

	Without Covid-19	**Covid-19**
Clinic treatment hours	Monday to Friday, 11:00 – 19:00; Saturday 09:00 – 12:00. **Total 43 hours.**	Monday to Friday, 10:30 – 17:00. **Total 32.5 hours.**
Fluoroscope availability	11:00 – 13:00, three days a week; 11:00 – 19:00, two days a week. **Total 22 hours.**	10:30 – 13:00, three days a week; 10:30 – 17:00, two days a week. **Total 20.5 hours.**
Amount of time for a baseline/ follow up measurement appointment	1.45 hours	2 hours
Maximum number of baseline/ follow up measurements per week	11	9
Number of weeks to collect data for a sample size of 262	47.8 weeks	58.4 weeks
Number of weeks to collect data for a sample size of 328	59.6 weeks	72.9 weeks
Number of weeks to collect data for a sample size of 66492	12090 weeks	14776 weeks

10.5. Discussion

Pre-Covid-19, the trial was open to recruitment for five weeks and recruited one participant. This data does not accurately reflect five weeks of recruitment. When the trial opened on 10 February 2020, the doctoral researcher was assisting on a different project and training as a fluoroscopy operator during AECC UC Clinic opening hours. As such, patients who were eligible for the trial were not approached or invited, and much active recruitment time was lost. Once the project was complete and the doctoral researcher was fully trained, Covid-19 was declared a global pandemic by the WHO and the AECC UC Clinic was closed. However, once the trial reopened in August 2020, the doctoral researcher utilised all clinic opening hours for recruitment for the trial.

Three eligible participants chose not to verbally agree to hear about the trial. This occurred after the doctoral researcher introduced themselves and indicated the reason, they were in the treatment room. These patients chose not to hear about the trial or obtain further information from the Participant Information Sheet. None of the patients were willing to provide a reason as to why this was the case.

Both pre-Covid-19 and in the Covid-19 era, five eligible participants chose not to participate in the trial due to the perceived risks associated with ionising radiation. At the time it was thought that this may have been partly the doctoral researchers' error as during the trial discussion the word "radiation" was used. For this reason, the trial discussion language used was altered to replace the word "radiation" with "x-ray". Following this there were no eligible participants who chose not to participate for this reason. It should be emphasised that the Participant Information Sheet remained unchanged which utilised the word "radiation" and outlined the risks to the participant.

Prior to the trial, it was thought that eligible patients may not want to be randomised to the non-manual therapy group as patients presenting to a chiropractic clinic expect hands on treatment. However, during the PPI consultation process (See Chapter 7), patients and members of the public felt that this would not be an issue if potential participants were well informed of what involvement in the trial would involve. Interestingly, one eligible patient did not want to take the chance at being randomised into the non-manual therapy group, and one eligible patient did not want to take the chance at being randomised into the manual therapy group. As such, willingness to be randomised was a concern for two eligible participants (7% of approached eligible participants), but in opposite directions. As the trial sample size was small, potentially the extent to which participants may not take part due to randomisation is difficult to estimate but should be recognised as a potential issue for a future full-scale trial.

One eligible patient was not able to take part due to transport issues, which was unforeseen and not something the doctoral researcher could accommodate. Should the eligible patient have been randomised to the non-manual therapy group, they may have been able to cope with the trial time burden, however eligible patients needed to verbally consent to the trial before finding out which group they were randomised to and for this reason the patient chose not to take part. This may indicate future issues in a full-scale trial with the appointment burden for the MT group, however, current data does not indicate this will become a hinderance to completing a full-scale trial.

While Covid-19 played a role in the general decrease in new patient numbers, only one participant made a first research appointment and had to cancel due to contracting the virus. Although the participant was willing to return to the trial once the isolation period (at the time 14 days) was

complete, this would have pushed them beyond the inclusion criteria of no more than 28 days of pain. As the Covid-19 pandemic becomes more manageable, this is not thought to be a problem for a future full-scale trial.

Seven of the eight participants in the non-MT group completed the trial. One participant withdrew following the first research appointment due to Covid-19. As the pandemic becomes more manageable, this may no longer be a problem for a future full-scale trial. All eight participants in the MT group completed the trial, however, due to the breakdown of the fluoroscope, there is QF data from seven participants only. During the trial there were no adverse events or serious adverse events recorded.

The risk of breakdown of equipment is clearly an issue for a full-scale trial. The AECC UC Clinic has one fluoroscope and as such, if the machine should require repairs the trial is halted and therefore time is lost to recruitment, but more importantly data is missing for participants already consented onto the trial. It was suggested by the repair company that repairs of the fluoroscope are prioritised to machines on a maintenance plan, of which the AECC UC Clinic machine was not. As such, at the very least the machine should be on a maintenance plan prior to any future full-scale trial. It is not feasible to suggest a second machine is purchased for the purposes of a full-scale trial due to cost and the lack of storage facility. It may be possible that a multi-site, or a site with multiple fluoroscopes (such as a hospital), could be utilised in a full-scale trial to mitigate against the risk of fluoroscope breakdown.

Pre-Covid-19 42% of all new patients presented with LBP, and within the Covid-19 era 30% of all new patients presented with LBP. During the trial, 33% of new patients presenting to the AECC UC Clinic presented with LBP. The trial took place in both the pre-Covid-19 era, as well as the Covid-19 era, and as such, it is logical that the percentage of new patients presenting with LBP would be between pre-Covid-19 and Covid-19 levels. Similar to the data obtained from the Parallel Study, 10.4% of patients who presented with LBP were eligible for the trial. This strengthens the premise that approximately 10% of all new patients presenting to the AECC UC Clinic with LBP will be eligible for the trial. As the trial was open for 30 weeks, there were approximately 14 new patients presenting with LBP per week, of which between 1 – 2 new patients would have been eligible for the trial per week. As the Covid-19 impact on a future full-scale trial is unknown, using the Parallel Study data it is estimated that between 1-4 eligible patients may present to the AECC UC Clinic per week.

Time needed to recruit and complete a full-scale trial is a challenge to estimate. In a single centre, single researcher full-scale trial utilising all biomechanical variables, potentially between 12090 and 14776 weeks would be required to complete the trial. This is not feasible nor desirable, however,

potentially the most useful measurements are MSI and MSV (See Chapter 11). As such, in a single centre, single researcher full-scale trial utilising MSI and MSV only, potentially a maximum of 72.9 weeks would be required to complete the trial. However, these figures are based upon maximum trial capacity (between 4 and 6 eligible patients per week, who all consent to take part in the trial) of the AECC UC Clinic. For this reason, it is not entirely realistic. Firstly, between 1 – 4 eligible patients attend the AECC UC Clinic per week. Secondly, 28 patients were approached to take part in the trial, 24 of which verbally agreed to discuss information on the trial, and only 16 agreed to participate in the trial. As such, only 57% of all patients approached consented onto the trial. Resulting in a more realistic figure which is approximately four times the calculated time required to complete the trial. Thus, it is possible that the trial at the AECC UC Clinic only could take in excess of five years to complete.

The current number of eligible patients presenting to the AECC UC Clinic are less than the weekly capacity of one researcher in terms of recruitment and research appointments. However, the time required to mark up the fluoroscopy images is approximately four hours per participant (two hours for baseline and two hours for follow up fluoroscopy sequences). For this reason, a research team would be required to carry out the trial at a single site. It is possible that part of the team could carry out recruitment and research appointments, while the remaining research team mark up the fluoroscopy sequences. This would result in potentially only a small amount of additional time required to complete the trial.

Further time would be required to carry out the data analysis, a detailed data analysis strategy has been suggested in Chapter 11. Equally, further time would need to be allocated to report and present the findings of the trial. Thus, as a single-site full-scale trial at the AECC UC Clinic utilising a team of researchers, the study could take as long as six - seven years to complete.

The number of weeks calculated in this chapter represent number of weeks the trial would need to be open. What is not considered in this calculation is research team absence due to illness or annual leave. This may affect the number of weeks needed to carry out the trial, or alternatively additional research team members will be required to compensate for this. This would need to be considered whether a future full-scale trial took place within the Covid-19 era or not.

It is possible that the trial may be more feasible if additional identifying sites were used in the area of the AECC UC Clinic, such as GP practices. This would increase the potential pool of participants consenting onto the trial to maximise the capacity available at the AECC UC Clinic. This option was not explored in this feasibility study and as such, the practicalities of the process of additional identifying sites (IRAS 2021b), or the willingness of local general practitioners to participate in the

area is unknown. Equally, it is possible the trial would be more feasible if it was a multi-site trial. The exploration of additional sites which have both the equipment and the qualified staff to complete the trial was not within the scope of this feasibility study. For this reason, whether there are appropriate sites which can be utilised to carry out the trial is unknown.

10.6. Conclusion

Ten percent of all LBP patients presenting to the AECC UC Clinic would be eligible for a full-scale trial. The number of eligible patients presenting to the clinic may be insufficient to complete a full-scale trial timeously. Equally, only 57% of all eligible patients consented to join the trial. For this reason, the trial may not be feasible as a single-site trial, but potentially more feasible as a multi-site trial or with additional local participant identifying sites.

11. Secondary Objectives: Biomechanical Effects of Manual Therapy in Patients with Acute Non-specific Low Back Pain – A Feasibility Study

11.1. Introduction

This chapter is in the format of a publishable paper and forms part of the results of the study. This chapter explores the secondary objectives of the feasibility study, however, as the sample size was small, the focus was shifted to providing a blueprint of the methods, data analysis and objective measures for a full-scale trial.

11.2. Background

Based on numerous systematic reviews SMT and mobilisation have been shown to reduce pain and dysfunction in at least some patients with LBP. However, the mechanism behind this clinical effect remains uncertain. It is thought that the clinical effects might be due to an effect on intervertebral motion, but evidence for this is largely from animal or cadaveric studies (See Section 3.1). In the past it has been difficult to measure intervertebral motion *in vivo*, however, with the development of QF, this is now possible (See Section 4.2). QF can be utilised to calculate intervertebral motion variables including IV-ROM, disc height, translation, initial attainment rate (IAR), motion sharing inequality (MSI) and motion sharing variability (MSV) (See Section 4.4.2). An exploration of the effects of manual therapy on these intervertebral motion variables has not been carried out in patients with acute NSLBP. Neither has an exploration of whether changes in the intervertebral motion variables could explain why some patients report a reduction in pain and dysfunction and others do not.

For a detailed literature review, please see literature review chapter (see Chapter 3 and 4).

This study was a feasibility study and as such its primary objective was to determine if a full-scale trial would be feasible, and if so, would the proposed method answer the research questions:

- In patients with acute non-specific low back pain, does lumbar intervertebral movement change following a course of manual therapy?
- In patients with acute non-specific low back pain, do those who respond to manual therapy (established by PROMs) have different intervertebral movement to those who do not?

The aim of this chapter is to present a blueprint of the potential data analysis method for a future full-scale study and not to evaluate the outcome of interest (Eldridge et al. 2016; NIHR 2019a). This chapter will look back to the study proposal and explore whether changes should be made for a full-

scale trial. This chapter will also explore the process of fluoroscopy image acquisition with participants; the choice of motion sequences and biomechanical variables for a future trial; the data analysis strategy for a future trial; and lastly sample size calculations for a future full-scale trial.

11.3. Methods

The detailed feasibility study method can be seen in Chapter 5. This methods section outlines the data analysis strategy for the QF data, as well as the PROMs data. It also includes the calculation of a sample size for a future full-scale trial.

11.3.1. Data Analysis

Data collected from the feasibility study were analysed to inform the data analysis strategy. It should be noted that the sample size was very small (*n*=7 per group) and as such, it is not appropriate to interpret or make inferences based upon the results due to the risk of Type I and Type II data errors (Field 2018). A Type I error occurs when there is a statistically significant effect in the study population, when in reality, there is not (false positive). A Type II error occurs when there is no statistically significant effect in the study population, when in reality, there is (false negative) (Field 2018). For this reason, data presented in the results section includes descriptive statistics and interpretations with the purpose of developing a blueprint for a future trial.

11.3.1.1. Normal Distribution of Data (homogeneity of variances)

A normal distribution of a continuous data (or scale data) is advantageous. It allows conclusions to be drawn beyond just the study sample (Field 2018). Outliers can affect the distribution of continuous data and result in a distribution that is not normal, which can introduce bias (Field 2018). For this reason, normally distributed data is analysed differently to non-normally distributed data (Field 2018).

There is some debate in the literature around how to best determine normal distribution of data. The Kolmogorov-Smirnov test is thought to be more accurate for samples of more than *n*=50, whereas the Shapiro-Wilk test is thought to be more accurate for samples of less than *n*=50 (Mishra et al. 2019).

Equally, the minimum number required for normality testing to be accurate is also debatable. It is widely accepted that a sample size of at least *n*=30 is sufficient to determine normal distribution of data. However, in a distribution where outliers are rare, a sample size of *n*=20 may be sufficient (Field 2018). But a distribution where outliers are common, *n*=100 or *n*=160 may be necessary (Field 2018). Yap and Sim (2011) indicate that the Shapiro-Wilk test can be used for any *n* in the range 3<*n*<5000. However, Field (2018) suggests that small sample sizes with outliers should be treated as

non-parametric data to avoid Type II errors. As the study sample was small (*n*=7 per group), and there are outliers, all data were treated as non-parametric.

For completeness, the data of this study was tested for normal distribution of data using the following data analysis strategy as outlined by Field (2018):

- Descriptive Stats: P-P plots; frequency.
- Shapiro-Wilk tests
- Levene's Test

For a future full-scale trial, normally distributed continuous data should be analysed using parametric tests. The parametric test for between groups is the unpaired t-test, and for within groups is the paired t-test. As the data for this trial was not normally distributed, the analysis outlined will focus on non-parametric tests.

11.3.1.2. Demographic Data

The data were analysed using non-parametric testing:

- Mann-Whitney U Test for comparison of independent samples (MT group vs. non-MT group) were used for age, weight, height, and Body Mass Index (BMI). It should be noted that the Mann-Whitney U test has very little power for small sample sizes. The smaller the sample size, the greater risk of Type II errors (Field 2018).
- Chi-Squared Test can be used for the analysis of categorical data (MT group vs. non-MT group), such as sex (Male: Female). It should be noted that the sample size in this study is too small for this test as the count in three of the four categories are 5 or less (categories include MT male; MT female; non-MT male and non-MT female), and as such, there is a profound reduction in test power (Field 2018). For this reason, Chi-Squared Test is better for larger sample sizes. However, Fisher's exact test can be used on smaller sample sizes and as such, it has been used to analyse the difference between categorical data (such as sex) between the MT and non-MT groups. However, caution should be used when interpreting the data as even Fisher's exact test may not be accurate for the very small sample size in this study (Field 2018).

11.3.1.3. Quantitative Fluoroscopy Data

11.3.1.3.1. Intervertebral motion variables

Figure 11.1 is a summary of the analysis strategy for the data obtained using QF, including the indicative tests used. In order to answer the research question: **"In patients with acute non-specific**

low back pain, does lumbar intervertebral movement change following a course of manual therapy?" potentially the independent samples test of the change between baseline and follow up (subtract baseline measurement from follow up) in the MT group versus the non-MT group would best answer the question.

Statistical significance indicates the observed difference between groups is due to chance. If the p-value is greater than 0.05 (the chosen alpha level), any observed difference may be due to sampling variability. With a sufficiently large sample, a statistical test may demonstrate significance, however when coupled with a small effect size, may be clinically meaningless (Sullivan and Feinn 2012; Field 2018). For this reason, significant tests were coupled with effect size (Pearson's r) to explore meaningful effects. An r-value of ±0.1 indicates a small effect; ±0.3 indicates a medium effect; and ±0.5 indicates a large effect (Field 2018). A negative relationship indicates that as one variable increases, the other decreases. A positive relationship indicates that as one variable increases, as does the other (Field 2018).

Baseline Data		**Follow Up Data**
MT Group	Within Group Related Samples Test: Wilcoxon Signed-rank Test →	MT Group

↓ Between Group Independent Samples Test: Mann-Whitney U Test	Change between Baseline and follow up of MT group (calculated by subtracting baseline from follow up measurements), and change between baseline and follow up of non-MT group:
	• Independent Samples Test: Mann-Whitney U Test
	• Calculate Minimal Detectable Change (MDC): Is the change between baseline and follow up greater than MDC?
	  ○ Calculate Intraclass Correlation Coefficient (ICC) for each group baseline vs. follow up
	  ○ Calculate Standard Error of Measurement (SEM) using the equation: SEM = SD x √(1-ICC)
	  ○ Calculate MDC using the equation: MDC = z-score (95% CI) x SEM x √2 (z-score is 1.960 for 95% CI)
	• Correlation statistics between variables: Spearman's rho or Kendall's Tau
		↓ Between Group Independent Samples Test: Mann-Whitney U Test

Non-MT Group	Within Group Related Samples Test: Wilcoxon Signed-rank Test →	Non-MT Group

Figure 11.1: Data analysis strategy for data obtained using QF.

An essential requirement of outcome measures is that they are valid and reproducible. Repeated measures may differ due to day-to-day or time of day biological variations in a patient, variations in the measurement tool, or variations in the circumstances or environment the measurement takes place in. Reproducibility is the umbrella term for agreement and reliability (de Vet et al. 2006). Agreement assesses how close the scores are for repeated measures of continuous data and is concerned with measurement error (Standard Error of Measurement (SEM)), whereas reliability is how well patients can be distinguished from each other despite measurement errors (intra class correlation (ICC)) (de Vet et al. 2006).

Reliability relates the measurement error to the variability between study participants (de Vet et al. 2006). ICC is a ratio ranging in value between 0 (totally unreliable) and 1 (perfect reliability). ICC in this study was calculated using SPSS (SPSS statistics 28, IBM, USA). ICC of less than 0.5 is considered poor reliability, values between 0.5 and 0.75 indicate moderate reliability, values between 0.75 and 0.9 indicate good reliability, and values greater than 0.9 indicate excellent reliability (Koo and Li 2016).

There are a number of ways to calculate SEM. SEM agreement considers systematic errors between different measurement operators, whereas SEM consistency does not. As there was only one operator in this trial, the formula for SEM consistency was utilised, where SD is represented by the pooled Standard Deviation ($\sqrt{(SD_{Baseline}^2 + SD_{Follow\ up}^2)}$) (de Vet et al. 2006).

$SEM = SD \times \sqrt{(1-ICC)}$

The SEM can be utilised to calculate the Minimal Detectable Change (MDC) which is the minimal change that can be detected outside of the measurement error (Turner et al. 2010; Dontje et al. 2018). MDC was calculated using the formula:

MDC = z-score (95% CI) x SEM x √2 (z-score is 1.960 for 95% CI)

A previous normative population study calculated MDC using baseline and a six week follow up (Breen et al. 2019b). This study involved acute NSLBP participants with a two-week follow up. The difference in the population, as well as the follow up time gap, may affect the MDC (de Vet et al. 2006; Dontje et al. 2018). However, MDC should be calculated utilising a group which does not change due to an intervention (de Vet et al. 2006; Stokes 2010; Dontje et al. 2018). For this reason, MDC was calculated utilising the non-MT data. Where appropriate comparisons to the normative population study were made.

There is some debate in the literature regarding whether MDC can only be utilised when data are normally distributed. Indeed, it is more common for MDC to be calculated for data which are

normally distributed and as such this would need to be recalculated in a future full-scale trial. By calculating MDC using non-parametric data, which is highly variable, the SD of the measurements is large, this in turn influences the SEM which is used to calculate MDC. For this reason, MDC may appear large and is potentially inaccurate.

11.3.1.3.2. Correlation between variables

Based on previous research, the following relationships were explored:

- Age and sex affect lumbar flexibility (Arshad et al. 2019a) and may correlate with total ROM (See Section 2.7.2)
- Translation and IAR are both considered to be related to joint instability and as such, may correlate with each other (Widmer et al. 2019) (See Section 2.7.1 and 2.7.3)
- A reduction in disc height may be negatively related to translation or IAR when intervertebral motion is increased (joint hypermobility or instability) or positively related to translation or IAR when intervertebral motion is decreased (joint hypomobility) (Kirkaldy-Willis and Bernard 1999). Equally, a loss of disc height affects the intervertebral movement and as such, may correlate with MSI and MSV (Kirkaldy-Willis and Bernard 1999; Widmer et al. 2019) (See Section 2.7.4).
- Disc height tends to decrease with increased age and increased weight (Bogduk 2012) (See Section 2.7.4).
- MSI and MSV indicate aberrant motion, but do not indicate what caused the motion. For this reason, potentially correlation with translation and IAR may indicate if motion segments are moving too much or too little (See Section 2.7.5).

Correlation analysis was carried out between variables. If the data were not normally distributed, Spearman's Rho or Kendall's Tau was used. Kendall's Tau is best for small data sets, or data sets with outliers (Field 2018). But again, due to the small sample size in this study, outcomes should be interpreted with caution.

11.3.1.4. Patient Reported Outcome Measures (PROMs)

Correlation analysis (Kendall's Tau) was used to explore the relationship between PROMs (NRS, BQ and RMDS-24) and the intervertebral motion variables.

In order to address the research question: **"In patients with acute non-specific low back pain, do those who respond to manual therapy (established by PROMs) have different intervertebral movement to those who do not?"** data needed to be dichotomised into those participants who responded and those who did not based on those who did or did not exhibit a Minimally Clinical

Important Change (MCIC) for their PROMs. The MCIC for patients with acute LBP is 26 points for the BQ (Hurst and Bolton 2004), and 4 points for the RMDS-24 (Kamper et al. 2010). Using an independent samples test (Mann-Whitney U Test), the change in biomechanical variables could be compared between responders and non-responders to MT. In the context of this study, this statistical analysis was not pursued due to the study being underpowered (n=7 in the MT group).

11.3.1.5. Sample Size Calculation

A study utilising QF and PROMs data in an acute NSLBP population has not been carried out before. As such, it is impossible to perform a sample size calculation in the absence of previous studies. Equally, as the intervertebral motion variables have not been explored in acute NSLBP patients, the primary or most useful variables have not been explored or established. This study aimed to identify the most useful intervertebral motion variables to utilise in a future full-scale, fully powered study, as well as calculate the sample size required for such a randomised clinical trial. A fully powered study suggests that the study is probably able to identify a difference, if it exists, between the two groups (Field 2018).

Sample size calculations were performed for each intervertebral motion variable using the commonly used, free software G*Power (Universitat Duesseldorf) which offers the ability to calculate power using a variety of tests (Kang 2021). If the intervertebral motion variables had large standard deviations, a larger sample would be needed to detect a difference between the MT group and the non-MT group. Equally, if the intervertebral motion variables had a small effect size, a large sample would be required to detect a difference between the MT group and non-MT group (Kadam and Bhalerao 2010).

It was not possible to statistically analyse the intervertebral motion variables between responders in this study. Without this data it was not possible to calculate sample size needed for a full-scale and as such a future full-scale trial should consider this.

11.4. Results

The MT group recruited eight participants, with QF data for seven participants. The non-MT group recruited eight participants, however, due to one withdrawal, there is follow up data on seven participants (See table 11.1).

Table 11.1: Visual representation of sample size obtained for the MT and non-MT group at baseline and follow up.

	MT		Non-MT	
Baseline (day 0)	PROMs (*n*=8)	QF (*n*=7)	PROMs (*n*=8)	QF (*n*=8)
Follow Up (day 14)	PROMs (*n*=8)	QF (*n*=7)	PROMs *(n*=7)	QF (*n*=7)

The mean radiation dose for all four fluoroscopy sequences (flexion weight bearing, extension weight bearing, flexion recumbent and extension recumbent) at baseline was 0.67 mSv, and at follow up was 0.69 mSv, resulting in a total mean radiation dose of 1.36mSv.

11.4.1. Demographic Data

The MT group consisted of more males than females and were generally taller and had greater mass than the non-MT group. The demographic data for the two groups can be seen in table 11.2.

Table 11.2: Demographic data for the MT and non-MT group.

Variable	**MT (*n*=8)**	**Non-MT (*n*=8)**
	Median (Range)	**Median (Range)**
Age (yrs)	32 (23 – 47)	36 (20 – 57)
Mass (kg)	77.0 (63.5 - 91.4)	63.0 (40.2 - 82.0)
Height (m)	1.78 (1.6 - 1.89)	1.62 (1.52 - 1.75)
BMI	25.3 (24 - 27.8)	25.7 (16.1 - 28.6)
Variable	**Ratio (Male: Female)**	**Ratio (Male: Female)**
Sex	5:3	1:7

11.4.2. Radiographic Incidental Findings

There were no radiographic incidental findings on the fluoroscopy images. Although considered a normal anatomical variant, five out of the fifteen (33%) participants who had baseline fluoroscopy images had lumbosacral transitional vertebra. As the fluoroscopy images were lateral views only, it was not possible to suggest the type of lumbosacral transitional vertebra according to the Castelli Classification (Castellvi et al. 1984).

11.4.3. Quantitative Fluoroscopy Data

11.4.3.1. Angular Intervertebral Range of Motion (IV-ROM):

Total median ROM (L2 – S1) and range can be seen in Table 11.3 for the four fluoroscopy sequences. Although not significant, there was a difference between the groups for flexion weight bearing baseline. In the MT group, all total ROM increased in the follow up measurements, except for extension weightbearing. Whereas in the non-MT group, all total ROM increased in the follow up measurements, except for extension recumbent.

Table 11.3: Mean and range (measured in degrees) for the total ROM (L2 – S1) for all four fluoroscopy sequences. 'WB' represents weight bearing and 'Rec' represents recumbent. Positive values indicate movement into flexion, and negative values indicate movement into extension.

	MT		**Non-MT**	
	Median (range) Baseline	**Median (range) Follow Up**	**Median (range) Baseline**	**Median (range) Follow Up**
Flexion WB	26.13 (10.16– 43.33)	28.23 (15.49- 32.62)	34.36 (28.56- 39.40)	39.95 (29.47- 44.92)
Flexion Rec	20.13 (15.88 – 24.59)	23.24 (16.31 – 27.49)	20.63 (18.71 – 30.07)	22.10 (19.74 – 28.83)
Extension WB	-8.37 (-2.96 - -16.39)	-7.78 (-0.69 - -16.39)	-6.95 (-0.58 - -14.20)	-7.29 (-1.40 - -13.92)
Extension Rec	-19.35 (-13.80 - -23.84)	-19.61 (-11.45 - -24.16)	-19.29 (-10.87 - -25.84)	-15.82 (-6.33 - -25.39)

A visual representation of flexion weight bearing IV-ROM data can be seen in Figure 11.2. The figure presents the angular ROM at each level, grouped into one column to demonstrate total angular ROM of the lumbar spine. Note JR002 (missing) and JR003 (withdrawal) data has not been included. Where IV-ROM are represented as negative, this means that the segment has moved into extension or demonstrated paradoxical motion at L5-S1. Five in the MT group and two in the non-MT group demonstrate paradoxical motion at L5-S1. Baseline (_BL) and follow up (_FU) are presented next to each other for each participant for ease of comparison. Three of the seven participants demonstrate

increased overall ROM and four demonstrate a decrease in ROM following MT, whereas all participants demonstrate an increased overall ROM in the non-MT group. Figure 11.3 represents the difference in ROM between baseline and follow up. Where segments are represented as negative, this means that ROM at follow up was less than ROM at baseline. There is greater change in overall ROM graph in the MT group, however, much of this change is negative or a reduction in motion.

Exploring angular ROM between those with lumbosacral transitional vertebrae and those without, there appears to be no discernible pattern. Three of the five demonstrate an increase in ROM, two of the five demonstrate a decrease in ROM, and one demonstrates paradoxical motion.

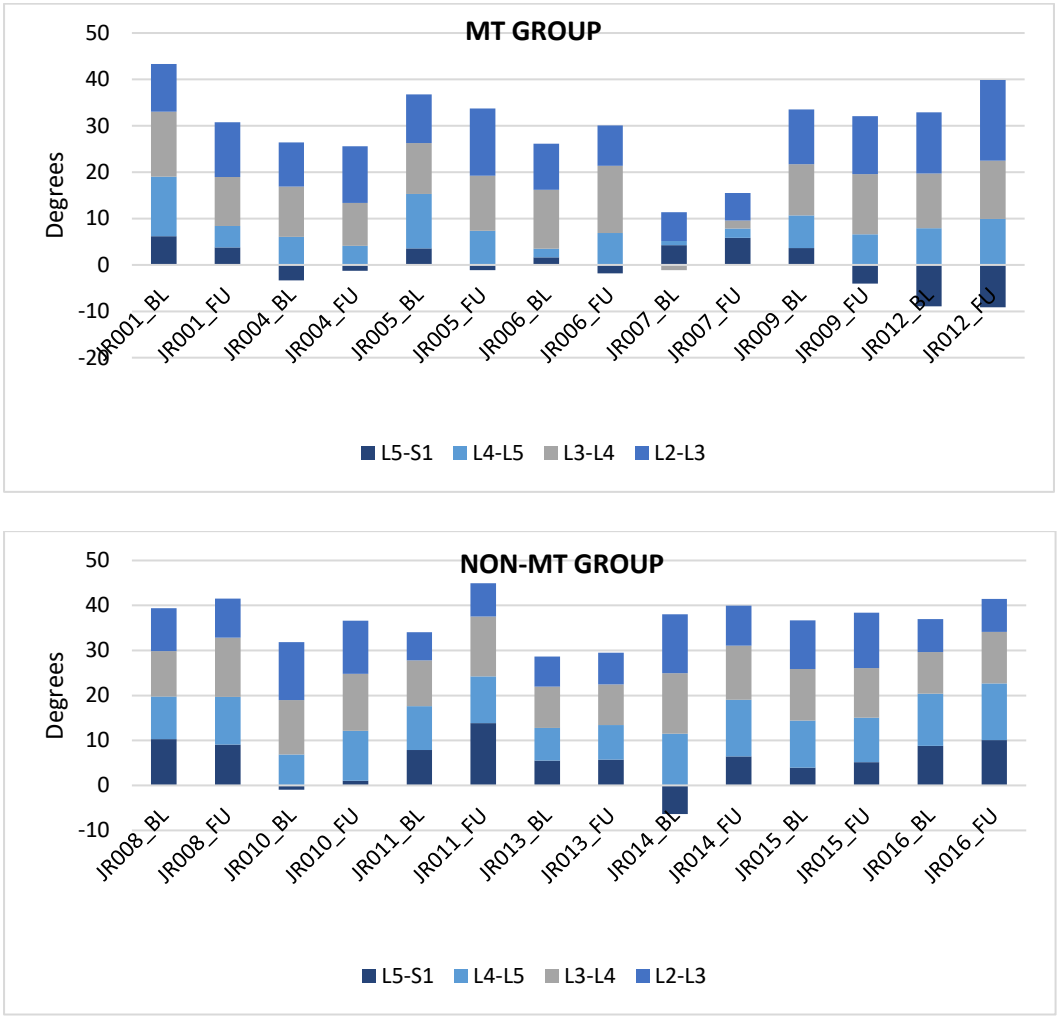


Figure 11.2: Visual representation of the MT group and non-MT group Range of Motion (ROM) during flexion weight bearing.

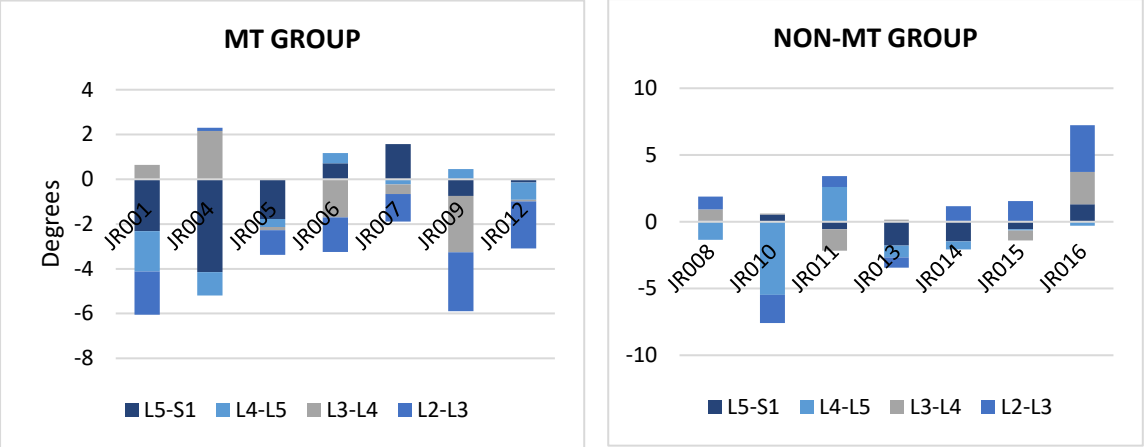


Figure 11.3: Visual representation of the difference between baseline and follow measurements for the MT and non-MT group during flexion weight bearing.

A visual representation of flexion recumbent IV-ROM data can be seen in Figure 11.4. As can be seen in the figure three of the participants demonstrate increased overall ROM and four participants demonstrate an overall decrease in ROM following MT, whereas all participants demonstrate an increased overall ROM in the non-MT group. Figure 11.5 represents the difference in ROM between baseline and follow up.

Figure 11.4: Visual representation of the MT group and non-MT group Range of Motion (ROM) during flexion recumbent.

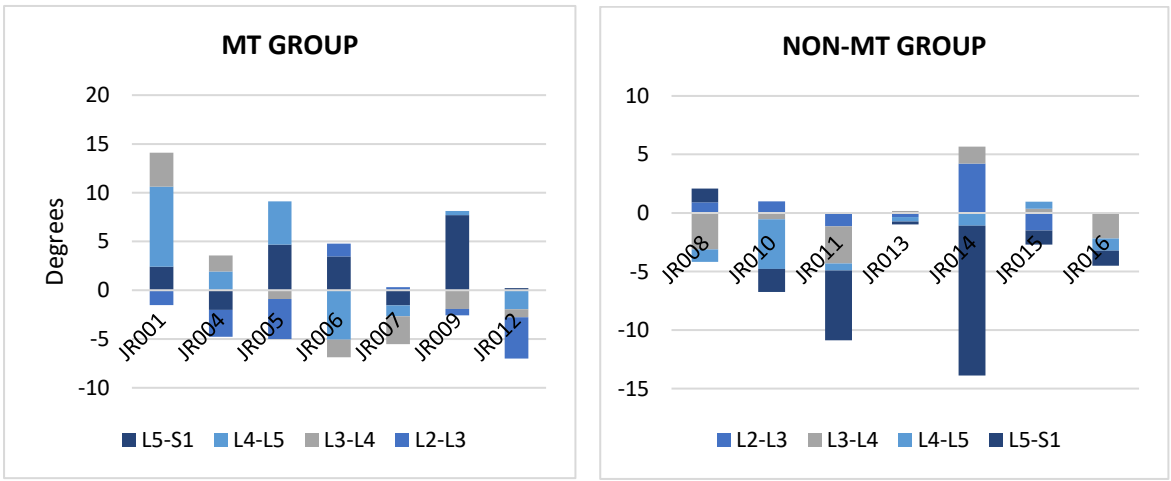


Figure 11.5: Visual representation of the difference between baseline and follow measurements for the MT and non-MT group during flexion recumbent.

In the MT group it appears that there is a greater difference in motion in L2-L3 and L5-S1 during weightbearing flexion, while in the non-MT group the greater difference is only in L2-3. In recumbent flexion the greater difference is seen in L4-5 and L5-S1 in the MT group, but only in L5-S1 in the non-MT group.

Extension weight bearing and extension recumbent data have not been compared visually. This is partly due to the lack of significant differences found in extension, but mostly due to the ROM that the participants are guided to during extension weight bearing (20 degrees) and as such, each segments contribution to ROM is so small that a meaningful visual comparison was not possible. Examining the data numerically, a very small increase in total extension weight bearing ROM was detected in four of the MT group participants, and six of the non-MT group participants. A very small increase in total extension recumbent ROM was detected in three of the MT group participants, and seven of the non-MT group participants.

At baseline, there were no significant differences between the groups for flexion and extension weightbearing or recumbent. In the MT group, there was one significant difference between the baseline and follow up variables (Flexion recumbent increased at L2-L3 IV-ROM ($p=0.028$; $r=-0.830$). In the non-MT group, there were two significant differences between baseline and follow up variables (Flexion weight bearing increased at L4-L5 IV-ROM ($p=0.043$; $r=-0.767$); Flexion weight bearing increased at L5-S1 IV-ROM ($p=0.043$; $r=-0.767$). When analysing the change between baseline and follow up between the groups, there were no significant differences between the groups.

Correlation statistical analyses were carried out (Kendall's Tau) between IV-ROM, total ROM, age, and sex. There were no significant findings.

Following the calculation of ICC and MDC for each variable, few participants reached the MDC (See Table 11.4.). As evidenced from the table, nine out of twenty variables demonstrate poor reliability (ICC of less than 0.5), eight out of the nine were related to extension weight bearing and recumbent.

Table 11.4: MDC (calculated from non-MT group data) and the number of participants who reached MDC (in degrees) IV-ROM for each group. 'WB' represents weight bearing, 'Rec' represents recumbent. ICC with values of less than 0.5 indicate poor reliability and have been highlighted in grey.

Variable	MDC (Degrees)	ICC	No. that reached MDC	
			MT (n=7)	Non-MT (*n*=7)
Weight bearing				
Flexion				
Flex WB L2-L3	2.54	0.848	3	1
Flex WB L3-L4	3.28	0.424	1	0
Flex WB L4-L5	2.50	0.721	2	0
Flex WB L5-S1	7.48	0.664	0	0
Flex WB L2 – S1	7.46	0.589	1	2
Extension				
Ext WB L2-L3	7.32	0.009	0	1
Ext WB L3-L4	3.61	0.3	0	1
Ext WB L4-L5	5.26	0.662	0	1
Ext WB L5-S1	5.06	0.29	2	0
Ext WB L2 – S1	9.87	0.347	1	1
Recumbent				
Flexion				
Flex Rec L2-L3	2.91	0.491	0	1
Flex Rec L3-L4	1.75	0.724	2	1
Flex Rec L4-L5	4.00	0.683	0	1
Flex Rec L5-S1	1.62	0.891	2	1
Flex Rec L2 – S1	6.41	0.616	0	2
Extension				
Ext Rec L2-L3	8.51	0.007	0	0
Ext Rec L3-L4	8.31	0.227	0	0
Ext Rec L4-L5	3.52	0.651	0	1
Ext Rec L5-S1	5.96	0.269	0	1
Ext Rec L2 – S1	11.36	0.402	0	1

11.4.3.2. Translation and Initial Attainment Rate (IAR)

A visual representation of total weight bearing translation for the MT group and non-MT group can be seen in figure 11.6. and recumbent can be seen in figure 11.7. The figure combines the measurements of flexion weight bearing and extension weight bearing to produce total translation at each segment (measured in equivalent mm). Baseline (_BL) and follow up (_FU) are presented next to each other for each participant for ease of comparison. According to Leone et al. (2007) a 4mm intervertebral translation, which when coupled with the clinical picture can be an indication for surgery for intervertebral instability. The 4mm cut off is indicated by the red dashed line on the graph. According to Posner et al. (1982) the cut off for intersegmental instability should be 8% of the vertebral body unit (VBU), which when using the standard VBU of 35mm is only 2.8mm. This is represented by the green line on the graph. Most evident is the change between baseline and follow up measurements for most participants. Equally, it is evident that some participants, depending on the definition of instability used, display translation which may be categorised as intervertebral instability.

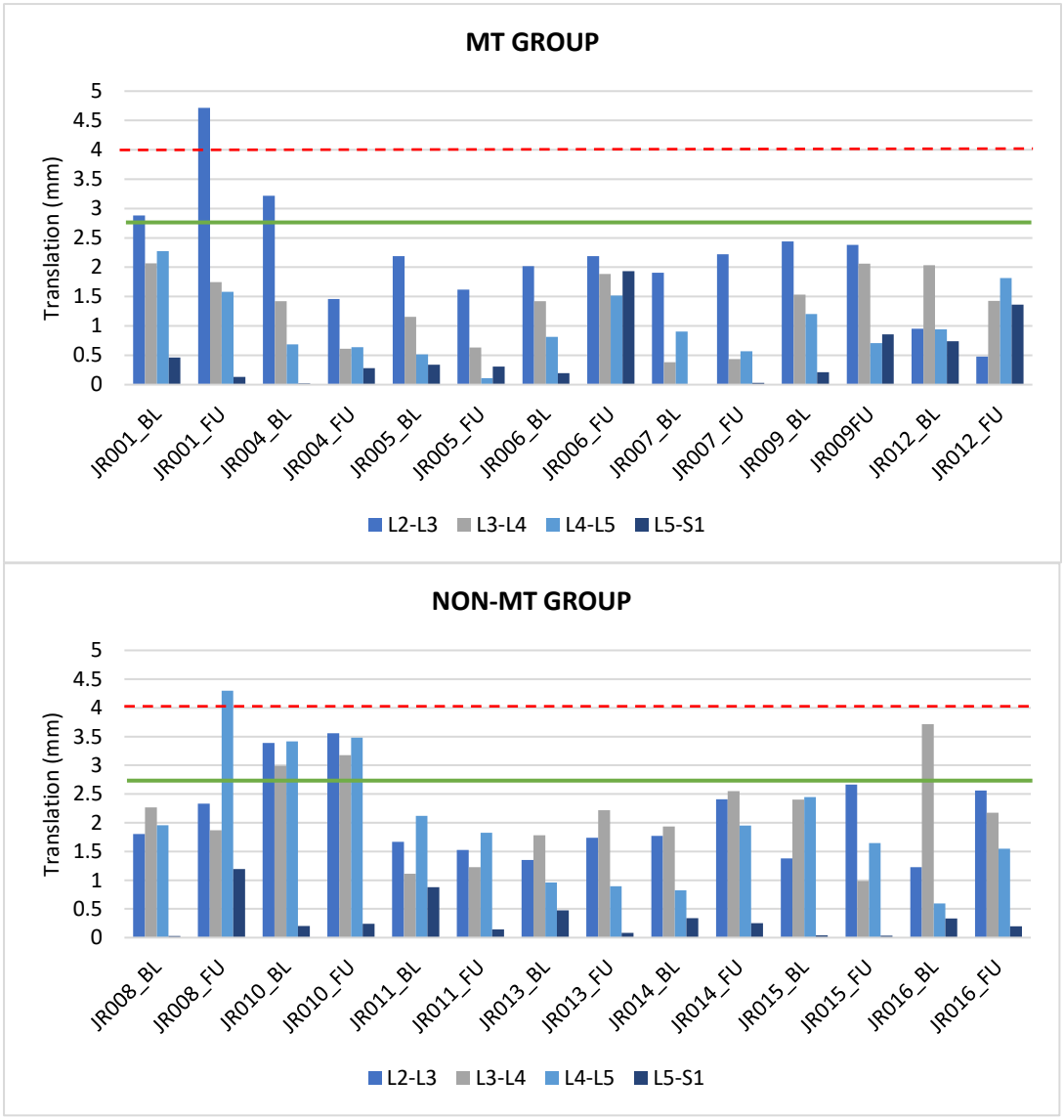
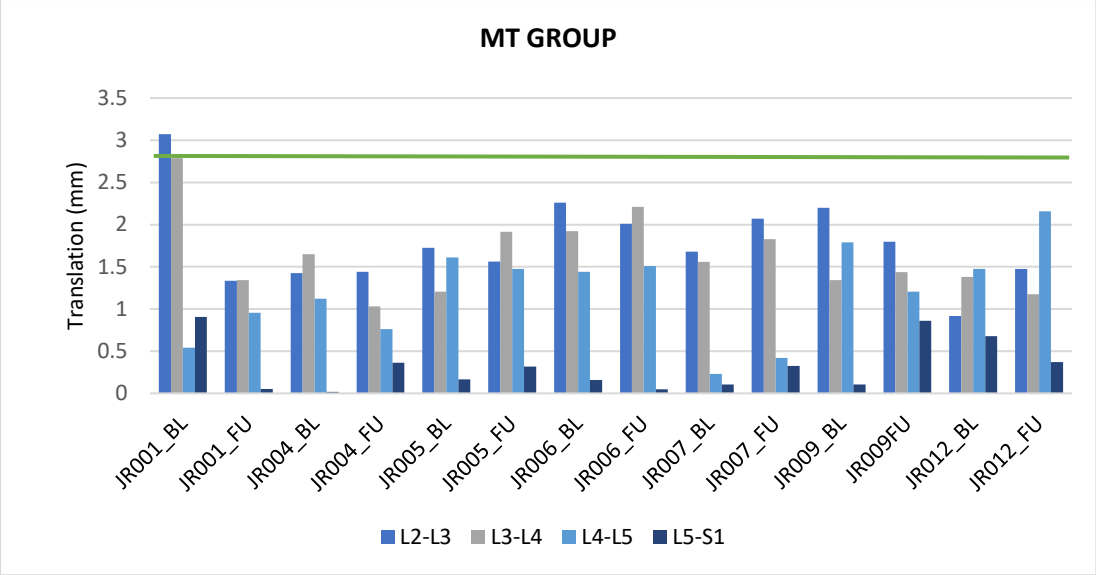


Figure 11.6: Visual representation of translation during weight bearing flexion and extension (in equivalent millimetres). The red dashed line indicates the 4mm cut off; the green solid line indicates the 2.8mm cut off.



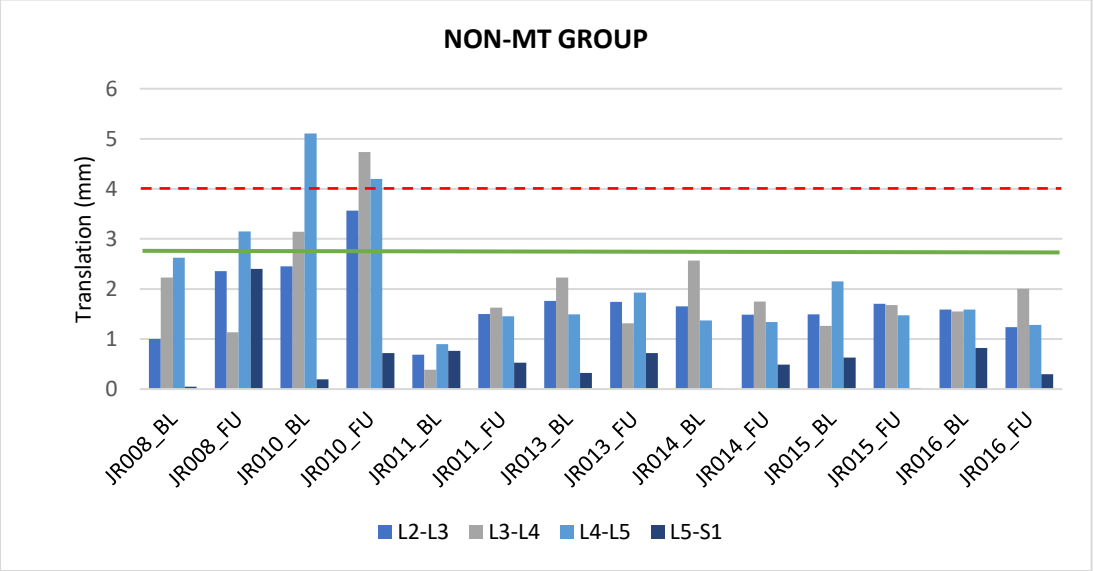
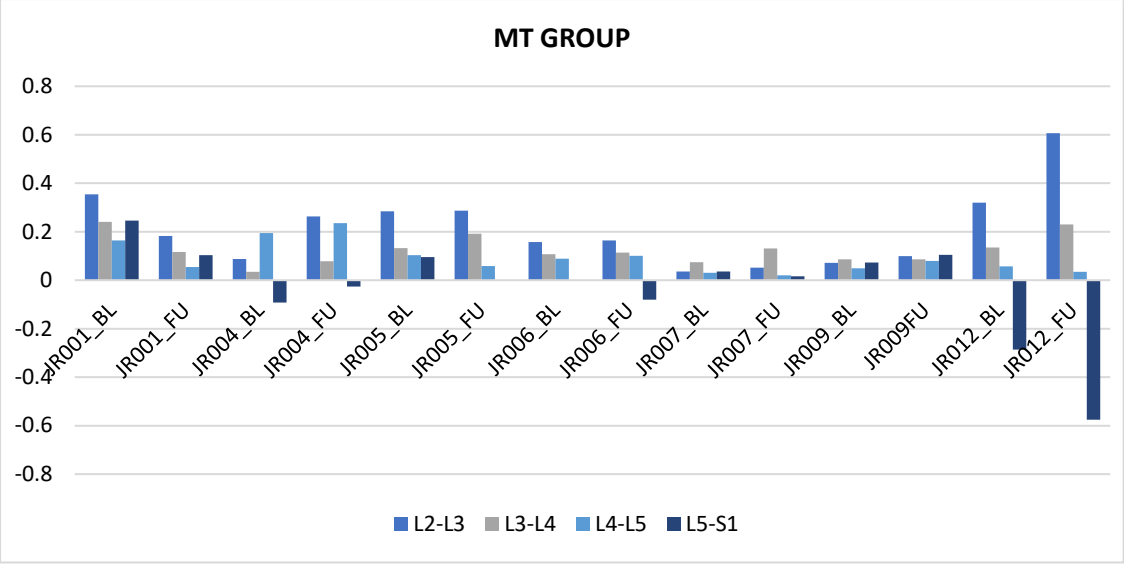


Figure 11.7: Visual representation of translation during recumbent flexion and extension (in equivalent millimetres). The red dashed line indicates the 4mm cut off; the green solid line indicates the 2.8mm cut off.

Figure 11.8 is a visual representation of IAR during flexion weight bearing and figure 11.9 is a visual representation of IAR for flexion recumbent for each group. Baseline (_BL) and follow up (_FU) are presented next to each other for each participant for ease of comparison. No pattern was observed between baseline and follow up measurements in the MT group and the non-MT group in weight bearing or recumbent flexion.



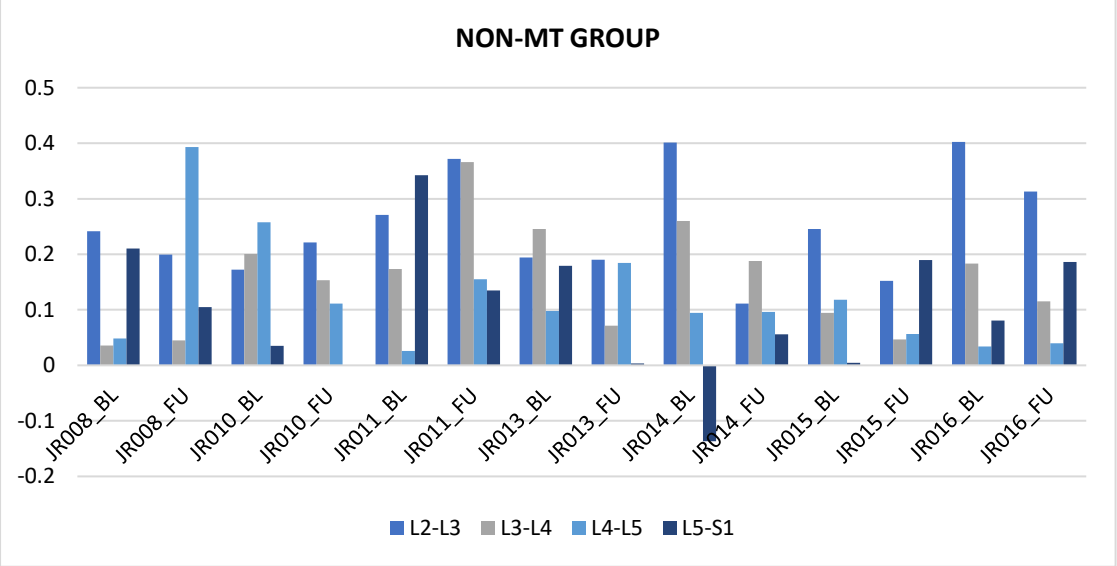


Figure 11.8: Initial Attainment Rate (measured in Vertebral Body Units) during flexion weight bearing for the MT and non-MT groups.

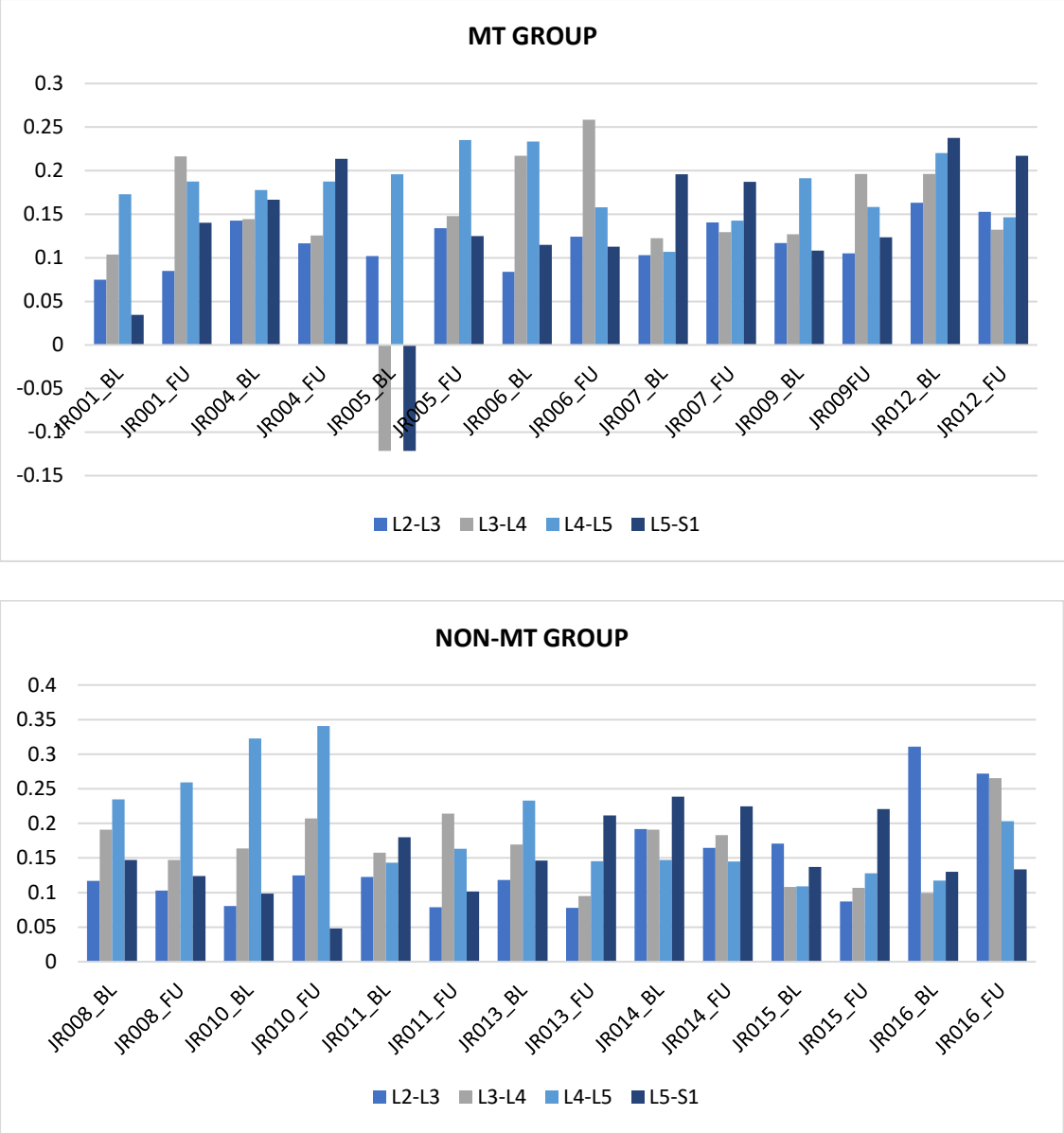


Figure 11.9: Initial Attainment Rate (measured in Vertebral Body Units) during flexion recumbent for the MT and non-MT groups.

At baseline, there were no significant differences in translation or IAR between the groups for flexion and extension weightbearing or recumbent. In the MT group, there were no significant differences between the baseline and follow up variables. In the non-MT group, there were two significant differences between baseline and follow up variables (Extension weight bearing decreased in L4-L5 IAR ($p = 0.043$; $r=-0.766$); Flexion weight bearing increased in L2-L3 translation ($p = 0.018$; $r=-0.894$)). When analysing the change between baseline and follow up, there were three significant differences between the groups (Extension weight bearing L5-S1 IAR was significantly higher in the non-MT

group (p = 0.011; r=0.666); Extension recumbent L4-L5 IAR was significantly higher in the non-MT group (p = 0.038; r=0.563); Extension recumbent L3-L4 translation was significantly higher in the non-MT group (p = 0.017; r=0.632)).

Correlation statistical analysis was carried out between IAR and translation for each level. There was only one significant finding: Extension weight bearing L2-L3 IAR and translation at baseline (τ = -0.406, p = 0.037, CI95% -0.676 - -0.040).

Following the calculation of ICC and MDC for each variable, the number of participants who reached MDC were counted for each group. Translation can be seen in Table 11.5 and IAR can be seen in Table 11.6. While change was measured between baseline and follow up, in many instances they were not sufficient to meet MDC. ICC of less than 0.5 has been highlighted in grey to indicate poor reliability. Seven out of the sixteen variables demonstrated poor reliability for translation, with five out of seven being related to extension weight bearing and recumbent. Whereas five out of sixteen variables demonstrated poor reliability for IAR, with three of the five being related to extension.

Table 11.5: Translation MDC (calculated from the non-MT group) and the number of participants who reached MDC (in millimetres) per variable for each group. ICC with values of less than 0.5 indicate poor reliability and have been highlighted in grey.

Variable	MDC (equivalent mm)	ICC	No. that reached MDC	
			MT (n=7)	Non-MT (*n*=7)
Weight bearing				
Flexion				
Flex WB L2-L3	0.31	0.781	0	2
Flex WB L3-L4	0.21	0.901	0	1
Flex WB L4-L5	0.43	0.37	1	2
Flex WB L5-S1	0.31	0.558	2	0
Extension				
Ext WB L2-L3	0.50	0.026	1	0
Ext WB L3-L4	1.43	0.355	0	0
Ext WB L4-L5	2.21	0.029	1	1
Ext WB L5-S1	0.63	0.357	1	0
Recumbent				
Flexion				
Flex Rec L2-L3	0.69	0.541	0	1
Flex Rec L3-L4	0.43	0.709	1	1
Flex Rec L4-L5	0.58	0.9	1	3
Flex Rec L5-S1	0.41	0.386	0	1
Extension				
Ext Rec L2-L3	1.38	0.304	0	1
Ext Rec L3-L4	1.46	0.675	0	1
Ext Rec L4-L5	0.55	0.899	1	2
Ext Rec L5-S1	2.24	0.814	0	0

Table 11.6: IAR ICC and MDC and the number of participants who reached MDC per variable for each group. ICC with values of less than 0.5 indicate poor reliability and have been highlighted in grey.

Variable	MDC	ICC	No. that reached MDC	
			MT (*n*=7)	Non-MT (*n*=7)
Flex WB L2-L3	0.23	0.094	1	1
Flex WB L3-L4	0.18	0.531	1	1
Flex WB L4-L5	0.35	0.581	1	0
Flex WB L5-S1	0.28	0.182	1	0
Ext WB L2-L3	0.29	0.544	0	1
Ext WB L3-L4	0.30	0.862	1	0
Ext WB L4-L5	0.27	0.623	0	1
Ext WB L5-S1	0.47	0.039	1	0
Flex Rec L2-L3	0.06	0.897	1	1
Flex Rec L3-L4	0.17	0.619	1	0
Flex Rec L4-L5	0.07	0.888	0	2
Flex Rec L5-S1	0.09	0.683	1	1
Ext Rec L2-L3	0.23	0.511	1	1
Ext Rec L3-L4	0.07	0.732	2	1
Ext Rec L4-L5	0.16	0.189	1	0
Ext Rec L5-S1	0.31	0.033	2	0

In previous literature (Breen et al. 2019b) intervertebral levels have been pooled for translation and IAR, in order to compare MDC this has been carried out with the data from this study (see Table 11.7). The pooling of data consists of putting together all data obtained for all the levels, in other words, rather than L2-L3 (*n*=7), L3-L4 (*n*=7), L4-L5 (*n*=7), L5-S1 (*n*=7); the levels are pooled to obtain *n*=28. In many variables the MDC are similar, with the exception of flexion weight bearing translation, extension recumbent translation and extension recumbent IAR.

Table 11.7: Translation and IAR MDC calculated using pooled levels to compare to existing literature (Breen et al. 2019b).

Variable	**MDC for Non-MT group (*n*=28)**	**Healthy volunteers (Breen et al. 2019b)**	
		n	**MDC**
Flex WB translation	1.17	216	2.10
Flex Rec translation	1.24	219	1.39
Ext WB translation	1.17	218	1.12
Ext Rec translation	1.24	216	1.67
Flex WB IAR	0.33	208	0.37
Flex Rec IAR	0.17	213	0.18
Ext WB IAR	0.35	171	0.32
Ext Rec IAR	1.78	208	0.19

11.4.3.3. Disc Height

A graphical representation of the comparison between baseline and follow up disc height for both the MT group and the non-MT group during weight bearing can be seen in Figure 11.10, and during recumbent in Figure 11.11. Disc height for each level has been calculated by subtracting minimum anterior disc height in full flexion from maximum anterior disc height in full extension, to calculate the change in disc height for each level. As evident from both figures, there are changes between baseline and follow up measurements, however, the difference is less than 0.1 VBU. There are several outliers represented on the figures as asterisk or circles. According to SPSS (SPSS statistics 28, IBM, USA) circles represent outliers, and the asterisk represents extreme outliers. An outlier is calculated as 3rd quartile + (1.5 x interquartile range) or 1st quartile – (1.5 x interquartile range); an extreme outlier is calculated as 3rd quartile + (3 x interquartile range) or 1st quartile – (3 x interquartile range).

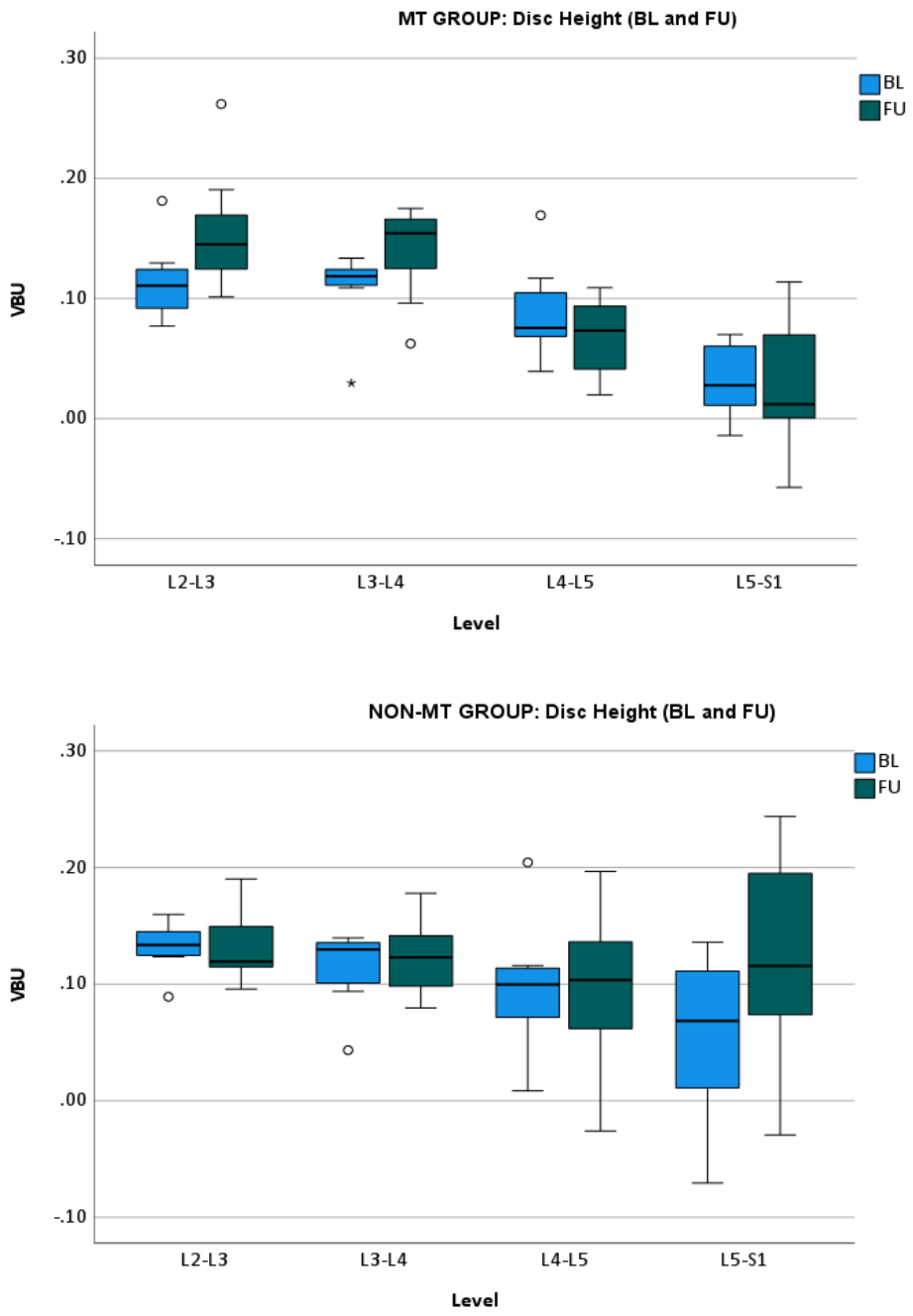
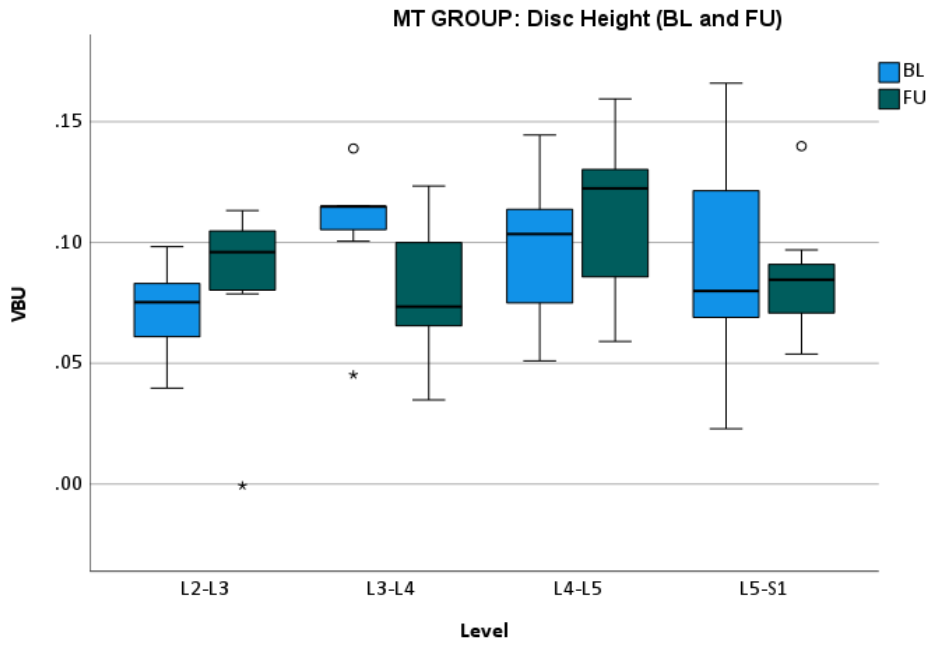


Figure 11.10: Visual representation of the MT and non-MT groups weight bearing change in disc height baseline versus follow up for each level. A circle represents an outlier, an asterisk represents an extreme outlier. Vertebral Body Units is represented by the label 'VBU' on the y-axis; BL represents baseline; and FU represents follow up.



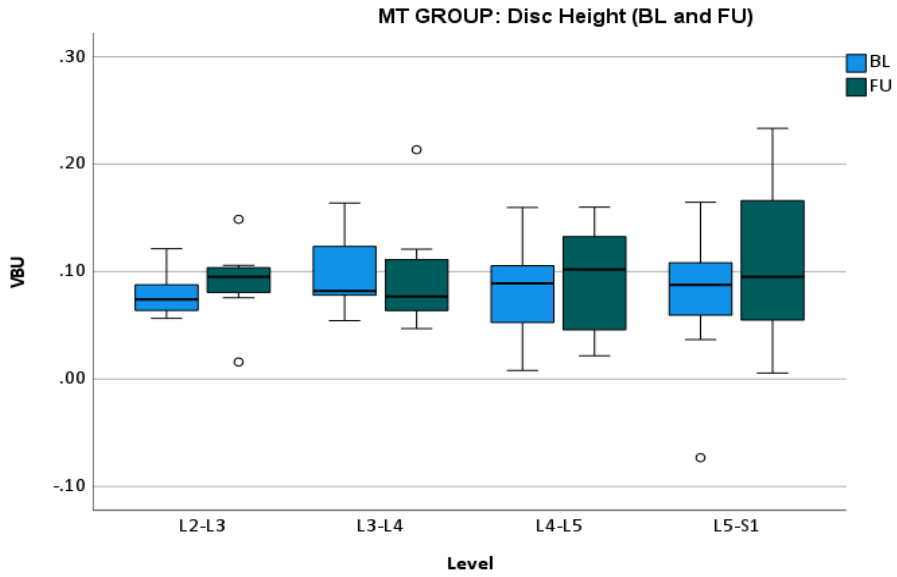


Figure 11.11: Visual representation of the MT and non-MT groups recumbent change in disc height baseline versus follow up for each level. A circle represents an outlier, an asterisk represents an extreme outlier. Vertebral Body Units is represented by the label 'VBU' on the y-axis; BL represents baseline; and FU represents follow up.

At baseline, there were no significant differences between the two groups. In the MT group, there were no significant differences between the baseline and follow up variables. In the non-MT group,

there were no significant differences between baseline and follow up variables. When analysing the change between baseline and follow up, there were no significant differences between the groups.

Correlations were analysed between each disc height level, the same levels translation and IAR, as well as MSI and MSV. The significant correlation outcomes between disc height and translation, IAR, MSI and MSV can be seen in Table 11.8. Nine out of the sixty-four correlation calculations carried out were statistically significant. Correlation between disc height, age and weight were carried out, however, there were no significant differences.

Table 11.8: Statistically significant correlations between disc height and translation, MSI, MSV and IAR.

Variables	**τ**	**p-value**	**CI 95% lower**	**CI 95% higher**
Flexion recumbent disc height L3-L4_BL and flexion recumbent L3-L4 translation_BL	0.672	0.040	0.031	0.822
Extension weight bearing disc height L2-L3_FU and extension weight bearing L2-L3 translation_FU	-0.606	0.022	-0.860	-0.111
Flexion weight bearing disc height L2-L3_FU and flexion weight bearing MSV_FU	-0.582	0.004	-0.792	-0.251
extension weight bearing disc height L5-S1_FU and extension weight bearing MSI_FU	0.656	0.011	0.193	0.880
flexion recumbent disc height L4-L5_BL and flexion recumbent MSI_BL	0.665	0.031	0.062	0.832
extension recumbent disc height L3-L4_BL and extension recumbent MSI_BL	0.587	0.021	0.107	0.845
extension recumbent disc height L5-S1_BL and extension recumbent MSI_BL	-0.607	0.016	-0.854	-0.137
Flexion recumbent disc height L2-L3_BL and flexion recumbent IAR L2-L3_BL	0.448	0.020	0.091	0.703
Extension recumbent disc height L2-L3_BL and extension recumbent IAR L2-L3_BL	-0.390	0.042	-0.666	-0.022

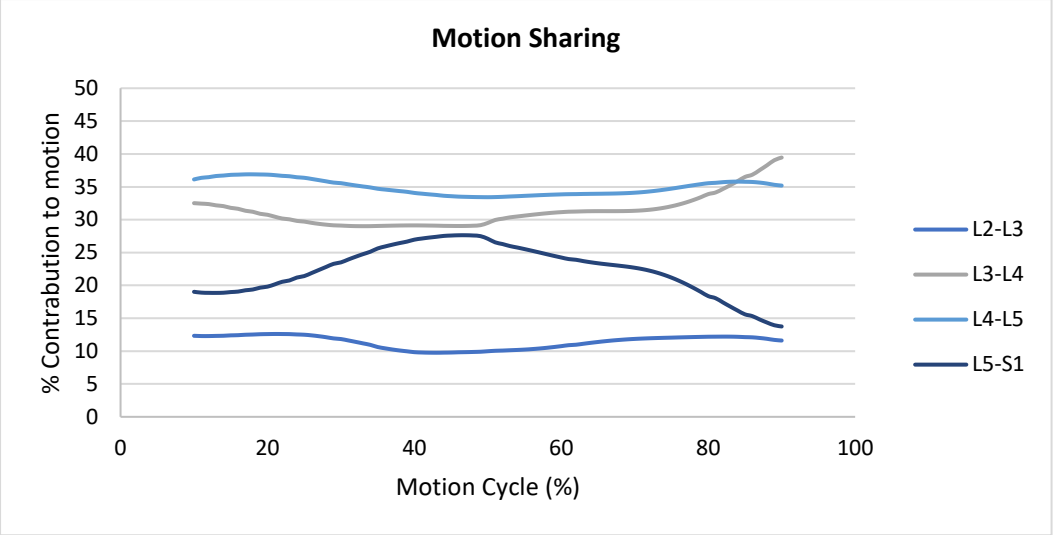
Following the calculation of ICC and MDC for each variable, the number of participants who reached MDC were counted for each group (See Table 11.9). As evident from the table, very few participants reached MDC. Four out of eight variables demonstrated poor reliability, which were split evenly between flexion and extension.

Table 11.9: Disc height MDC (in Vertebral Body Units) and the number of participants who reached MDC per variable for each group. Note that disc height for each level has been calculated by subtracting minimum anterior disc height in full flexion from maximum anterior disc height in full extension to calculate the change in disc height for each level. ICC with values of less than 0.5 indicate poor reliability and have been highlighted in grey.

Variable	**MDC**	**ICC**	**No. that reached MDC**	
			MT (*n*=7)	**Non-MT (*n*=7)**
WB L2-L3	0.07	0.035	0	0
WB L3-L4	0.07	0.593	0	0
WB L4-L5	0.10	0.684	0	0
WB L5-S1	0.24	0.059	0	1
Rec L2-L3	0.08	0.132	0	0
Rec L3-L4	0.08	0.602	0	0
Rec L4-L5	0.12	0.301	1	1
Rec L5-S1	0.14	0.622	0	1

11.4.3.4. Motion Sharing Inequality (MSI) and Motion Sharing Variability (MSV):

Figure 11.12 is a participant's graphical representation of flexion recumbent MSI and MSV and demonstrates a high MSI (0.237), and as can be seen in the figure each motion segment contribution is quite different to the other. However, each motion segments contribution is relatively constant and as such the MSV is low (0.010). Figure 11.13 is a participant's graphical representation of flexion recumbent MSI and MSV and demonstrates a low MSI (0.083). As can be seen in the figure each motion segment contribution is relatively similar to the other. However, each motion segment contribution is variable and as such the MSV is relatively high (0.044).



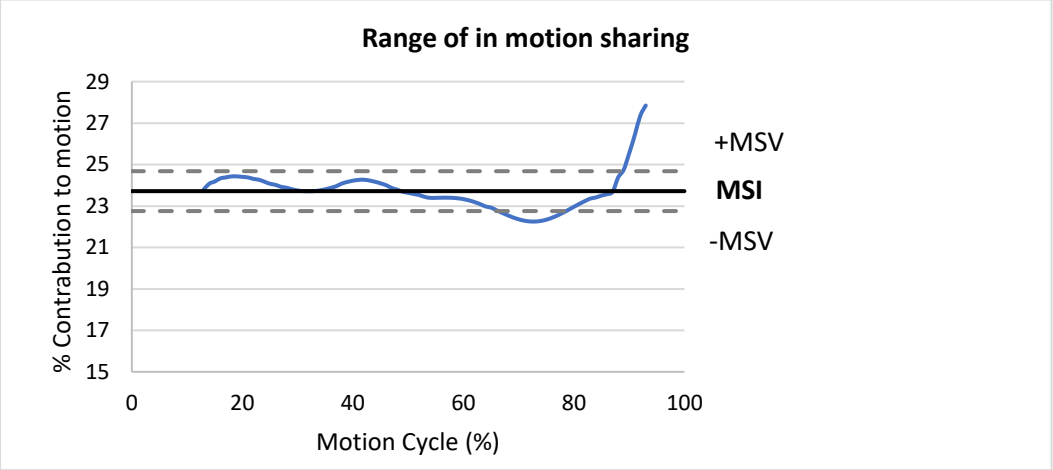
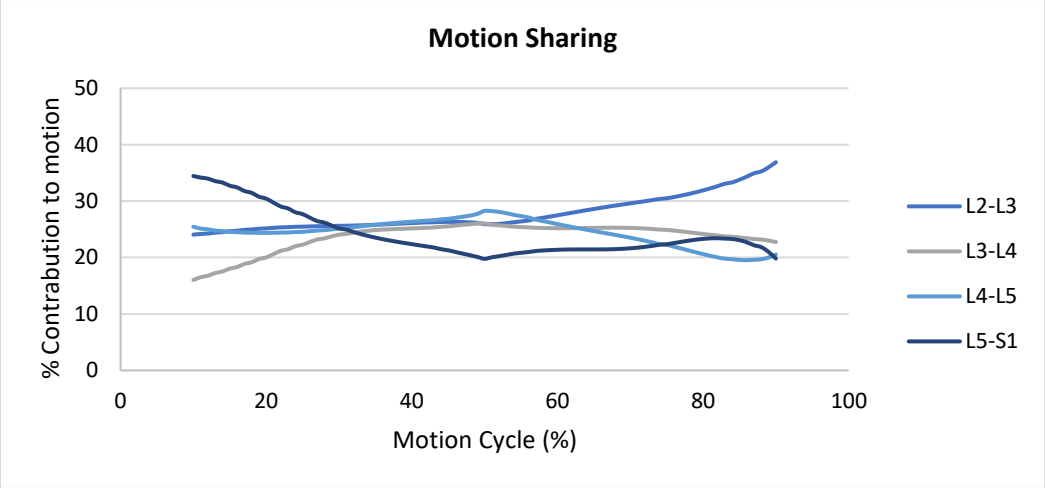


Figure 11.12: MSI and MSV for flexion recumbent representing a high MSI (Motion Sharing) and low MSV (Range of in motion sharing).



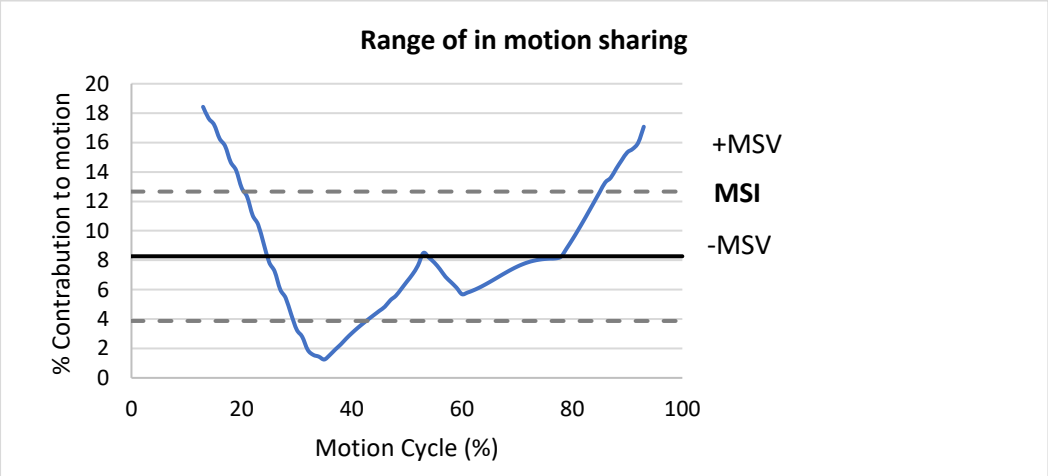


Figure 11.13: MSI and MSV for flexion recumbent representing a low MSI (Motion Sharing) and a relatively high MSV (Range of in motion sharing).

At baseline, there were no significant differences between the two groups for MSI and MSV. In the MT group, there were no significant differences between the baseline and follow up variables. In the non-MT group, there were three significant differences between baseline and follow up variables (Flexion weight bearing MSV decreased ($p = 0.028$; $r=-0.830$); Extension weight bearing MSV increased ($p = 0.043$; $r=-0.766$); Flexion recumbent MSI decreased ($p = 0.028$; $r=-0.830$)). When analysing the change between baseline and follow up, there were no significant differences between the groups, however five out of the eight variables measured demonstrated medium to large effect sizes (See Table 11.10)

Table 11.10: Change between baseline and follow up between groups for MSI and MSV. The table includes significance values (p-values), as well as effect sizes (Pearson's r values).

Variables	**p-value**	**r**	**relationship**
Flex WB L2-S1 MSV	0.128	-0.427	As MT reduced, non-MT increased
Flex WB L2-S1 MSI	0.097	-0.461	As MT reduced, non-MT increased
Ext WB L2-S1 MSV	0.620	0.154	As MT increased, non-MT increased
Ext WB L2-S1 MSI	0.710	0.119	As MT increased, non-MT increased
Flex Rec L2-S1 MSV	0.456	-0.222	As MT reduced, non-MT increased
Flex Rec L2-S1 MSVI	0.097	-0.461	As MT reduced, non-MT increased
Ext Rec L2-S1 MSV	0.209	0.359	As MT increased, non-MT increased
Ext Rec L2-S1 MSI	0.073	0.495	As MT increased, non-MT increased

The statistically significant correlations between MSI and MSV, as well as translation and IAR, can be seen in Table 11.11. As evident in the table there twenty-one out of a total of one hundred and twenty-eight correlation calculations reached a p-value of less than 0.05.

Table 11.11: Statistically significant correlations between MSI, MSV and translation and IAR.

Variables	**τ**	**p-value**	**CI 95% lower**	**CI 95% higher**
Flexion weight bearing MSV_BL and Flexion weight bearing L2-L3 translation_BL	-0.714	0.013	-0.913	-0.243
Flexion weight bearing MSI_BL and flexion weight bearing L2-L3 translation_BL	0.714	0.013	0.243	0.913
Flexion weight bearing MSV_FU and Flexion weight bearing L2-L3 translation _FU	-0.718	0.004	-0.904	-0.303
Flexion weight bearing MSI_FU and Flexion weight bearing L2-L3 translation _FU	-0.589	0.027	-0.853	-0.086
Extension weight bearing MSV_FU and Extension weight bearing L3-L4 translation_FU	-0.570	0.033	-0.845	-0.057
Extension weight bearing MSI_FU and Extension weight bearing L3-L4 translation_FU	-0.577	0.031	-0.848	-0.068
Extension weight bearing MSV_FU and Extension weight bearing L4-L5 translation_FU	-0.907	<0.001	-0.970	-0.725
Extension weight bearing MSI_FU and Extension weight bearing L4-L5 translation_FU	-0.912	<0.001	-0.972	-0.738
Flexion recumbent MSV_BL and flexion recumbent L2-L3 translation_BL	0.570	0.027	0.081	0.838
Flexion recumbent MSI_BL and flexion recumbent L3-L4 translation_BL	0.555	0.032	0.060	0.831
Extension recumbent MSI_BL and extension recumbent L3-L4 translation_BL	-0.607	0.016	-0.854	-0.137
Extension recumbent MSI_BL and extension recumbent L4-L5 translation_BL	-0.568	0.027	-0.837	-0.079

Table 11.11 cont.: Statistically significant correlations between MSI, MSV and translation and IAR.

Variables	**τ**	**p-value**	**CI 95% lower**	**CI 95% higher**
Extension recumbent MSV_BL and extension recumbent L5-S1 translation_BL	-0.535	0.040	-0.822	-0.031
Extension recumbent MSV_FU and extension recumbent L5-S1 translation_FU	-0.815	<0.001	-0.939	-0.501
Flexion weight bearing MSI_BL and flexion weight bearing IAR L5-S1_BL	-0.562	0.004	-0.772	-0.240
Flexion weight bearing MSI_FU and flexion weight bearing IAR L5-S1_FU	-0.641	0.001	-0.824	-0.336
Extension weight bearing MSI_FU and extension weight bearing IAR L5-S1_FU	0.707	<0.001	0.440	0.859
Flexion recumbent MSI_BL and flexion recumbent IAR L2-L3	0.524	0.006	0.189	0.750
Flexion recumbent MSI_BL and flexion recumbent IAR L5-S1_BL	0.543	0.005	0.214	0.761
Flexion recumbent MSI_FU and flexion recumbent IAR L4-L5_FU	-0.538	0.007	-0.766	-0.190
Extension recumbent MSI_FU and extension recumbent IAR L4-L5_FU	0.473	0.019	0.103	0.727

Following the calculation of ICC and MDC for each variable, the number of participants who reached MDC were counted for each group (see Table 11.12). As evident from the table, very few participants reached MDC. Four out of the eight variables demonstrated poor reliability, with all four being related to extension weight bearing and recumbent. The table includes a comparison to previous literature MDC (Breen et al. 2019b). It is evident from the table that there the MDC calculated in this study differs greatly from the MDC calculated in the previous literature.

Table 11.12: MSV and MSI MDC and the number of participants who reached MDC per variable for each group. Including comparison with existing literature (Breen et al. 2019b). ICC with values of less than 0.5 indicate poor reliability and have been highlighted in grey.

Variable	**MDC (*n*=7)**	**ICC**	**No. that reached MDC**		**Healthy volunteers (Breen et al. 2019b)**			
			MT (*n*=7)	**Non-MT (*n*=7)**	***n***	**MDC**	**No. that reached MDC**	
							MT (*n*=7)	**Non-MT (*n*=7)**
Flex WB MSV	0.36	0.547	0	0	52	0.23	0	0
Flex WB MSI	0.12	0.717	3	1	52	0.31	1	1
Ext WB MSV	0.39	0.147	0	0	53	0.37	0	0
Ext WB MSI	1.91	0.099	0	0	53	0.59	0	0
Flex Rec MSV	0.04	0.754	3	1	54	0.12	1	0
Flex Rec MSI	0.05	0.977	4	1	54	0.31	0	0
Ext Rec MSV	0.72	0.27	0	0	52	0.20	0	1
Ext Rec MSI	0.23	0.188	1	2	52	0.39	0	0

11.4.4. Patient Reported Outcomes Measures (PROMs)

Seven of the eight participants in the MT group, and all participants in the non-MT group, improved clinically but not necessarily achieving a MCIC. A data summary from the PROMs for each group can be seen in Table 11.13, including the number of participants who improved with a MCIC. In the non-MT group, five participants reached MCIC in the NRS and three participants reached MCIC in the BQ and RMDS-24. As such they demonstrated a greater clinical change when compared to the MT group in which four participants reached MCIC in the NRS and one participant in the BQ and RMDS-24. However, this difference was not significant between the groups.

Table 11.13: Data summary for the clinical change in the participants for each group (* No range reported as only one participant reached MCIC).

		NRS	BQ	RMDS-24
MT	**Median difference between baseline and follow up** **No. who reached MCIC (% change score range)**	2 4 (57% – 66%)	9 1 (69%)*	3 1 (89%)*
Non-MT	**Median difference between baseline and follow up** **No. who reached MCIC (% change score range)**	2 5 (40% - 86%)	13 3 (64% - 79%)	3 3 (78% - 92%)

11.4.4.1. Correlation of biomechanical variables to PROMs in the MT group

Two variables correlated with NRS, extension weight bearing L3-L4 laxity ($\tau = 0.720$, $p = 0.028$, CI 95% 0.158 – 0.930) and flexion recumbent L4-L5 translation ($\tau = 0.720$, $p = 0.028$, CI 95% 0.158 – 0.930). One variable correlated with RMDS-24, extension recumbent L4-L5 IV-ROM ($\tau = 0.781$, $p = 0.015$, CI 95% 0.291 – 0.946).

11.4.4.2. Correlation of biomechanical variables to PROMs in the Non-MT group

One variable correlated with the BQ, extension weight bearing L4-L5 laxity ($\tau = 0.781$, $p = 0.020$, CI 95% 0.291 – 0.946). One variable correlated with RMDS-24, flexion recumbent L3-L4 IV-ROM ($\tau = 0.781$, $p = 0.015$, CI 95% 0.291 – 0.946).

11.4.5. Sample Size Calculation

The sample size was calculated for each intervertebral motion variable using the change between baseline and follow up, taking into account effect size (see Appendix O). The maximum sample size calculated was 66492 participants (83115 including 20% for drop out) for flexion weight bearing IAR L2-L3. When calculating sample size for MSI and MSV only, the largest sample size is 262 (328 including 20% for drop out).

11.5. Discussion

The aim of this chapter was to explore the study protocol and outcomes to produce a blueprint for a future full-scale trial. The achieved sample size for this feasibility study was small (*n*=7 per group), largely due to the impact of Covid 19 on recruitment (see Chapter 5). This could result in underpowered statistical analysis increasing the risk of Type I and Type II errors. There was great variation in demographic data with the MT group being heavier and taller, and the non-MT group being majority female. As such, it is possible that this difference could account for differences in the

outcomes alone. Furthermore, with the large number of variables being analysed, it is possible that some outcomes show statistical significance by chance alone. With this in mind, it is not appropriate to make assumptions or inferences from the data. Descriptive statistical analysis and visual trends were used to explore the data to inform recommendations on motion sequences and intervertebral motion variables of interest for a future full-scale trial.

This study used a standardised fluoroscopy protocol for flexion weight bearing, extension weight bearing, flexion recumbent and extension recumbent (Breen et al. 2012a). The mean effective radiation dose for all four fluoroscopy sequences at baseline was 0.67 mSv; and the mean effective radiation dose for all four fluoroscopy sequences at follow up was 0.69 mSv. This was in keeping with a previous normative population study, using the same protocol, the mean effective radiation dose was 0.77mSv. This study resulted in a total mean effective radiation dose for baseline and follow up of 1.36mSv. This is similar to the typical effective dose for a single lumbar x-ray examination of 1.3mSv (Public Health England 2008).

Something which was considered in the protocol was the impact of level of pain on the fluoroscopy acquisition with participants. The trial protocol exclusion criteria stated *"Patients with a numeric pain scale of 8 or more, or 2 or less, taken at the New Patient Examination Appointment"* would be excluded, however, a pain scale is subjective. It was hoped that patients with a pain scale of 7 or less would be able to complete the ROM required for the four fluoroscopy motion sequences, however, this was not the case. In the case of JR008 baseline measurement, they were unable to complete the full 60 degrees of flexion weight bearing due to pain but were able to complete the motion during follow up. Despite this, the changes between baseline and follow up were negligible. However, if only participants who can reach the full ROM are selected, this would exclude a section of the population who would arguably most benefit from this investigation. But by including these participants, the heterogeneity of the population increases, with the addition of confounding variables. As the intervertebral motion variables are highly variable themselves, there is a need to keep the protocol as consistent as possible to make comparison possible. As a compromise, participants who are unable to complete the ROM during weight bearing could be asked to move as far as they are able, while using a goniometer to record their maximum ROM. This would enable the same ROM to be carried out in the follow up measurement. The alteration to the data analysis may need to include percentage change or relative change, rather than absolute change to incorporate these participants.

An additional consideration is the impact of the fluoroscopy sequence acquisition on the participant's pain. Some participants reported an increase in pain following acquisition of their

fluoroscopy motion sequences, however, it should be noted that those reporting increased pain stated that the increase was small but noteworthy. The addition of a NRS following the fluoroscopy procedure may be beneficial for a future full-scale trial to explore the impact of the fluoroscopy acquisition on the participants. To what extent the increase in pain may have had on the outcome of the study is unknown. In a future full-scale trial, the change in pain scale could be analysed to explore correlation with changes in biomechanical variables.

While the results and discussion sections present the biomechanical variables individually, it should be noted that the variables interact with each other extensively.

11.5.1. Demographics

Demographically, there were significant differences between the two groups. The MT group consisted of considerably more male participants, which may have resulted in the significant difference of height and weight between the two groups. While the ages of the two groups were not significantly different, of note is the difference in age range. The MT group consisted of a more even spread throughout the age range of 23 – 47; whereas the non-MT group consisted of four participants above the age of 45 and the remaining three participants below 23. The effect of these demographic differences on the biomechanical variables will be discussed throughout this Discussion section.

11.5.2. Lumbosacral Transitional Vertebra

Thirty three percent of the study population had lumbosacral transition vertebra. It is suggested that in the global general population prevalence is between 4% - 30%, demonstrating that the population in this study is just above the normal prevalence (Konin and Walz 2010). While there are four types of lumbosacral transitional vertebra, to investigate the type further in this study would have required further anterior to posterior imaging. As this was not the focus of the study, further imaging was not carried out. It is suggested that type III and type IV sacralisations may alter the biomechanics of the spine by putting more pressure on the L4-L5 motion segment, however, there is little literature to substantiate this suggestion (Quinlan et al. 2006). Visually, within this trial there were no trends or patterns in the intervertebral motion of participants with transitional vertebrae. Due to the additional radiation for an additional anterior to posterior view, together with a paucity in literature, to suggest it could alter the intervertebral motion. Further investigation of the impact of lumbosacral transitional vertebrae on intervertebral motion is not recommended for a future full-scale trial.

11.5.3. Angular Intervertebral Range of Motion (IV-ROM)

Three of the seven participants demonstrate increased overall ROM (L2 – S1) following MT. An increase in IV-ROM is one of the goals of manual therapy (Bergmann and Petersen 2011) as such it would be easy to assume that increase in either IV-ROM or overall ROM in the manual therapy group is desired. However, a systematic review suggests that there is no relationship between SMT and an increase in regional ROM (Millan et al. 2012). Potentially a more important goal of manual therapy is a return to 'normal' IV-ROM for the patient (Triano 2001), but it is difficult to determine 'normal' in a measure that is subject to natural variation. Total lumbar flexion ROM in pain free participants measured using x-ray has been reported as 51° on average (Pearcy et al. 1985) and by goniometer 56.4° (Van Herp et al. 2000). However, both these studies measured from L1 – S1 and allowed pain free participants to actively go to their full flexion ROM, whereas this study measured from L2 – S1 and limited flexion recumbent to 40° and flexion weight bearing to 60° and as a result, a like-for-like comparison cannot be made.

All seven of the non-MT group increased their overall ROM. This brings to question whether an increase in overall ROM in the two groups is simply a reflection of the natural progression of the disorder or decrease in pain (Itz et al. 2013). Itz et al. (2013) indicates that patients who still experience pain after two weeks are less likely to improve without treatment, as such, it was hoped that the inclusion criteria of *"patients who have experienced pain for more than two weeks, but less than four weeks"* may reduce the number of participants in the study who would have improved symptomatically without intervention. Although not all participants reached MCIC in reduction of pain, all participants with QF data did demonstrate a reduction in pain. There is evidence to suggest that there is a negative correlation between regional ROM and pain (Vaisy et al. 2015).

There is an assumption that females are more flexible than males, however, a recent systematic review concluded that young females (age 20 – 39) showed significantly greater lumber lordosis and ROM in extension, whereas young males (age 20 – 39) showed a greater regional ROM in flexion (Arshad et al. 2019a). The same systematic review explored the effect that age has on regional ROM and noted regional ROM decreased with age (Arshad et al. 2019a). This present study explored correlations between IV-ROM (L2-S1), individual level IV-ROM, sex and age and found no significant relationship. It is possible this was due to the small sample size and as such it would be beneficial to explore this relationship in a full-scale trial. As there is evidence to suggest that age and sex do effect ROM, it would be prudent to control these variables in a future full-scale study by age and sex matching participants between the groups. Equally, ROM increases throughout the day (Ensink et al.

1996) and for this reason, it would be prudent to collect baseline and follow up data at the same time of day for participants.

Paradoxical motion is defined as motion opposite to the intended motion (Panjabi and White 1980). Five participants in the MT group demonstrated paradoxical motion at L5-S1 during weight bearing flexion (See Figure 11.2). Paradoxical motion is thought to be associated with instability (Panjabi and White 1980) and as such, it would have been useful to compare intervertebral motion variables of those with paradoxical motion (IAR and translation) to the remaining participants. As this would further divide the MT group into paradoxical motion (n=5) and those without (n=2), statistical analysis was not appropriate. However, an exploration of this would be of interest in future research.

When analysing the change between baseline and follow up between the groups, there were no significant differences between the groups in IV-ROM at any levels (L2-S1). Previous literature has compared chronic NSLBP patients to pain-free persons and found no significant differences in IV-ROM (Mellor et al. 2014a). There is an expectation that if there is no significant difference between chronic NSLBP patients and pain-free controls, that it would be less likely to be one between two groups of acute NSLBP patients. Additionally, very few participants had changes in IV-ROM which met the MDC. The difference in baseline demographics may have contributed to the variability of IV-ROM. The variability of the data contributed to the large standard deviation, which in turn contributes towards the large SEM. The SEM is used to calculate MDC and as such the MDC is large. There is a concern that the MDC is so large that theoretically the change between baseline and follow up would need to be more than the ROM the lumbar spine is capable of. For this reason, very few participants would be capable of reaching MDC or beyond purely based on the anatomical limit of the lumbar spine ROM. However, the larger the sample size, the more homogenous the data may potentially become, and this could decrease the danger of this occurring (Field 2018).

11.5.4. Translation and Initial Attainment Rate (IAR)

NSLBP has been linked to intervertebral instability and alteration in muscle control of the trunk (van Dieën et al. 2019). The general understanding is that muscle activity increases in NSLBP patients as a way of stabilising or guarding the spine, which may result in a decrease in IAR. However, in pain free patients muscle activity or guarding is reduced, which may result in an increased IAR. In other words, when NSLBP patients pain improves, there may be less muscle activation during forward bending leading to a decrease in stabilisation resulting in a higher IAR measurement (or more lax) (du Rose et al. 2018). As such, participants in acute LBP could potentially have increased muscle guarding, and decreased IAR, during their baseline measurements, but as they improve clinically the muscle

activity decreases leading to an increased IAR. The previous research was carried out on weight bearing lumbar flexion only. In order to test the theories, a relationship between PROMs and IAR were analysed in weight bearing lumbar flexion in both groups, there were no significant findings. There was, however, one significant finding in extension weight bearing, a reduction in L3-L4 IAR correlated with a reduction in NRS in the MT group. This does not support the theory that when pain decreases, IAR increases.

An alternative theory is related to compensation in the lumbar spine, as some of the joints become more stiff (less lax), the remaining lumbar spine joints become more lax to compensate (du Rose and Breen 2016a). Whether this moves towards explaining the change in the IAR between baseline and follow up is unknown. It is evident from the data that at some segments IAR increase, and others decrease between baseline and follow up in the same participant. There is a paucity of literature relating to what is considered a 'normal' measurement or range for IAR. This is a promising area to explore in a full-scale trial.

Another measurement of instability is translation. Literature suggests that there is 'cut off' point for stable translation, with Leone et al. (2007) suggesting a 4mm cut off for translation (together with the clinical picture), and Posner et al. (1982) suggesting the cut off should be 8% of the vertebral body unit (VBU), which when using the standard VBU of 35mm is 2.8mm. However, both cut off points were acquired at the end of the participant ROM, whereas the QF protocol was restrained and guided motion. It is suggested that free bending results in approximately 0.5mm greater translation than controlled weight bearing flexion to 60° (Breen et al. 2012a). As such, there are participants who demonstrate instability according to the literature. However, as mentioned by Leone et al. (2007), it is also dependant on the clinical picture, as such, a relationship between PROMs and translation were analysed. A reduction in flexion recumbent L4-L5 translation from baseline to follow up correlated with a reduced NRS in the MT group.

To allow for the data being collected in this trial to be compared to Leone et al. (2007) and Posner et al. (1982), total translation from full extension to full flexion were used for weight bearing and recumbent. This required the data from flexion to be added to the data from extension. A potential issue with this is it assumes that the starting neutral point will be the same in both sequences, which may not be the case. As such, this may introduce a measurement error into the calculated total translation. It should be noted that Posner et al. (1982) and Leone et al. (2007) measure total translation in the same way.

JR010 demonstrated translation that would be considered unstable at L2-L3, L3-L4 and L4-L5, however, this participant was also a competing national rhythmic gymnast until two years prior to

taking part in the study. Whether this alone contributes towards both the high translation and IAR measurements is unknown. Interestingly, the IV-ROM and regional ROM do not appear to be higher than the remaining participants which may be as a result of the restrained pelvis and limitation of torso ROM in the study protocol.

Comparing MDC to previous literature (Breen et al. 2019b), this study appeared to have lower MDC for most of the variables and particularly flexion weight bearing translation. The previous literature consisted of pain free volunteers, with six weeks between baseline and follow up measurements, and used the identical fluoroscopy sequence acquisition to this study. This study demonstrating similar or lower MDC means that the error in the measurement method is similar for pain free volunteers as for patients with acute NSLBP. Thus, potentially this study population did not introduce additional errors in the measurement, equally, nor did the relatively inexperienced researcher carrying out the fluoroscopy sequence acquisition and image processing.

While it is possible not to calculate MDC and simply utilise the previous normative study data (Breen et al. 2019b), this may not be appropriate. Firstly, MDC can differ between populations, for example, patients in acute pain may introduce small errors in the measurements, such as positioning and altered movement due to pain (de Vet et al. 2006). Secondly, the time between baseline and follow up measurements are different, which can affect MDC (Dontje et al. 2018). Thirdly, the previous study pooled the intervertebral levels to obtain a larger sample size. What this assumes is that all levels move the same magnitude, and thus will not introduce variability which will have a knock-on effect by increasing the SD. However, literature suggests that levels move differently and reach a different maximum (Widmer et al. 2019). As such to pool the data may result in inaccurate calculations of MDC.

11.5.5. Disc Height

There is very little literature to support the measurement of disc height in isolation. However, theoretically it could be useful when coupled with other measurements to create a clearer biomechanical understanding of a lumbar segment. According to Kirkaldy-Willis and Bernard (1999), it is possible that in phase two of degeneration, a decrease in disc height could negatively correlate with IAR and translation. Or in the case of phase three of degeneration, a decrease in disc height could positively correlate with IAR and translation. However, previous literature consisting of ten healthy volunteers (pain free) with early to moderate disc degeneration found no correlation between disc degeneration, translation, and IAR (Breen et al. 2020).

This study did not assess for disc or joint degeneration, however, this study did have some significant findings: flexion recumbent disc height L3-L4 and flexion recumbent L3-L4 translation at baseline

positively correlated; extension weight bearing disc height L2-L3 and extension weight bearing L2-L3 translation at follow up negatively correlated; flexion recumbent disc height L2-L3 and flexion recumbent IAR L2-L3 at baseline positively correlated; and extension recumbent disc height L2-L3 and extension recumbent IAR L2-L3 at baseline negatively correlated. The relationship between disc height, MSI and MSV was also explored and there were a number of correlations, pointing toward the relationship between disc height and aberrant movement of the spine. With the number of correlations, even in such a small sample size, it may suggest that this is a relationship worth investigating further in a full-scale trial.

11.5.6. MSI and MSV

While there are no previous studies in patients with acute NSLBP to compare to, in a study comparing chronic non-specific LBP patients with pain free controls, the patients with LBP had significantly greater flexion recumbent MSI values than the pain free controls (Breen et al. 2018).

MSI and MSV are measurements which explore abnormal or aberrant motion of the lumbar spine. Arguably, the indication of aberrant motion is useful both scientifically and clinically in isolation. However, to explore the cause or underlying pathomechanics the addition of investigating the relationship between MSI, MSV and the remaining intervertebral motion variables is even more useful. As is evident from table 11.8 and discussed in section 11.2.1.3. there is a relationship between MSI, MSV and disc height. As is evident from table 11.10, there is a relationship between MSI, MSV, translation and IAR. Even with the small sample size, there is a strong indication that these relationships will be worth investigating further in a full-scale trial.

Not many participants reached MDC. When this study's MDC was compared to previous literature (Breen et al. 2019b), the values are similar for most of the variables. Again, demonstrating consistency with previous literature.

11.5.7. PROMs

In order to address the research question: **"In patients with acute non-specific low back pain, do those who respond to manual therapy (established by PROMs) have different intervertebral movement to those who do not?"** the MT group would have had to be further divided into those who reached MCIC and those who did not for comparison. This would have made both groups too small for any sub-analysis to be meaningful and as such was not carried out.

In the MT group and the non-MT group, some intervertebral motion variables do correlate with PROMs. Whether this is a genuine correlation is unknown, partly due to the randomness of the relationships which could point towards the odds of finding a statistically significant finding in 144

variables, and partly due to the small sample size. In an observational study of changes in cervical intervertebral motion and the relationship with PROMs in patients undergoing manual therapy for neck pain, there was no relationship between PROMs and IV-ROM (Branney 2014), nor was there a relationship between PROMs, MSI or MSV (Branney et al. 2021). However, whether there is a relationship between PROMs and these variables in LBP patients has yet to be explored.

11.5.8. Sample Size

A sample size should adequately represent the population of patients with acute NSLBP, so that true inferences about the population can be made from the results obtained (Kadam and Bhalerao 2010). As evidenced from the table in Appendix O, the sample size for a full-scale trial utilising all intervertebral motion variables is very large. However, potentially, the most useful variables are MSI and MSV as they explore aberrant motion in the lumbar spine. When change between baseline and follow up between groups were explored for MSI and MSV, there were no significant findings, however five of the eight variables explored demonstrated medium to large effect sizes. The larger the effect size, the smaller the sample size required for the future study (Sullivan and Feinn 2012). As such, when looking at only these variables, the sample size is 262 (131 per group; 328 including 20% for drop out).

As the sample size was very small for this study, with outliers, this would affect standard deviation and as a result effect the sample size calculation. To what extent the sample size calculation was affected by a small sample size or type I/II data errors is not known.

Due to the small sample size, a division of the MT group into responders versus non-responders was not carried out. As such, it is not possible to calculate the sample size needed for this aspect of the study. Should a full-scale trial be carried out, this will need to be investigated.

11.5.9. General

Almost half of the IV-ROM, translation, IAR, MSI and MSV measurements demonstrated poor reliability. Interestingly, most measurements with poor reliability were related to extension weight bearing and recumbent. This is not mirrored in the normative study whereby very few intervertebral motion variables demonstrated poor reliability (Breen et al. 2019b). As an indicator of test-retest reliability, having poor reliability is an issue as it indicates that there is difference between baseline and follow up measurements. However, in the context of this study, it may be an indicator that the non-MT group changed sufficiently within the two-week gap to decrease the reliability. This is not unexpected as acute NSLBP patients can improve over time due to the natural progression of the disorder. What this does indicate is that additional test-retest reliability testing is required in this

population to increase reliability, and potentially the time gap between baseline and follow up should be much reduced. This should be considered for additional future research.

This trial is underpowered, and it is not possible to make inferences from the data. Which means that it is not possible to suggest alterations to the proposed fluoroscopy sequences to be utilised in a future full-scale trial. As such, while it would appear that extension weight bearing and recumbent are less reliable, this may be due to the natural progression of the disorder and not a fault with the measurement. Equally, while potentially extension weight bearing may have caused an increase in pain in some participants and appears to provide less valuable information, it is not possible to suggest that this sequence is not used in a full-scale trial as not all participants mentioned an increase in pain, and this trial is so underpowered. When examining benefit of utilising all four sequences versus the risk of radiation, there is no more radiation than a normal lumbar spine x-ray sequence which is considered low risk. On balance, it is recommended that all four sequences (flexion weight bearing and recumbent, extension weight bearing and recumbent) be carried out in a future full-scale trial.

It is recommended that the primary outcome measure be MSI and MSV, however there is value to correlations between MSI and MSV, with IV-ROM, translation, IAR and disc height. Equally, these variables can be measured without additional radiation or resources and as such can be collected and analysed easily. Although correlations between IV-ROM, and sex and age, as well as disc height, and age and weight did not demonstrate significant relationships, there is literature to suggest these relationships may exist and as such should be explored in a full-scale trial. This would assist in answering the research question: "**In patients with acute non-specific low back pain, does lumbar intervertebral movement change following a course of manual therapy?"**

Although not carried out in this trial due to the small sample size, comparing intervertebral motion in those that respond to manual therapy and those who do not, could provide valuable information regarding responders versus non-responders. Thus, answering the second research question: **"In patients with acute non-specific low back pain, do those who respond to manual therapy (established by PROMs) have different intervertebral movement to those who do not?"**

11.6. Conclusion

The aim of this chapter was to provide a blueprint for a future full-scale trial. Due to the small sample size the study was underpowered and as such inferences from the data analysis should not be made. However, some recommendations for a future trial can be made.

There is insufficient evidence to substantiate altering the fluoroscopy sequences to be carried out. However, there is evidence to suggest that MSI and MSV be the primary outcome measure, with IV-ROM, IAR, translation and disc height as secondary measurements mostly utilised to explore correlation. This would mean that a future full-scale trial would require 328 participants (including 20% for drop out).

There is insufficient evidence to substantiate altering the PROMs being utilised. It is suggested that a secondary analysis be carried out during a full-scale trial to allow the sample size for a full-scale trial to include a responder analysis.

As a suggestion for future research, test-retest in an acute NSLBP population should be explored with a shorter time gap between measurements. As an alternative the non-MT group could be utilised to calculate ICC, SEM and MDC. In a fully powered, full-scale trial the data may be more reliable.

12. Discussion

12.1. Introduction

This is the first study to explore the feasibility of conducting a fully powered, full-scale, trial exploring the effects of manual therapy on intervertebral motion variables as measured by QF in acute NSLBP patients. The full-scale trial is designed to answer the following research questions:

- In patients with acute non-specific low back pain, does lumbar intervertebral movement change following a course of manual therapy?
- In patients with acute non-specific low back pain, do those who respond to manual therapy (established by PROMs) have different intervertebral movement to those who do not?

This feasibility study explored parameters such as appropriateness of the objective measurements to answer the research questions, as well as sample size and time required to complete a full-scale trial. These parameters have been explored extensively in Chapters 10 and 11. A further discussion of these parameters, as well as an exploration of the study methods, results, limitations, and generalisability are presented in this chapter. The chapter concludes with the unique contributions to knowledge made by this study.

12.2. Background

Eldridge et al. (2016) developed an extension to the CONSORT 2010 statement for the reporting of parallel group randomised trials (Schilz et al. 2010). The extension is specifically designed for randomised pilot and feasibility trials (Eldridge et al. 2016). The extension was designed to improve the quality and transparency of reporting pilot and feasibility studies. This extension included a checklist of information to include when reporting a pilot or feasibility trial. The completed checklist can be seen in Table 12.1. As demonstrated in the table, all the recommended information to be included in the reporting of a feasibility trial has been included in this thesis.

Table 12.1: CONSORT checklist of information included in this feasibility study (Modified from Eldridge et al. (2016)).

Section/Topic	Item No	Checklist item	Reported location
Title and abstract			
	1a	Identification as a pilot or feasibility trial in the title	Title Page
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	Pg 3
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	Rationale Chapter 1 Background and literature review Chapters 2,3 and 4
	2b	Specific objectives or research questions for pilot trial	Section 1.3
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	Section 5.2
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	Covid-19 Sections 5.13.7 and Chapter 9
Participants	4a	Eligibility criteria for participants	Section 5.7
	4b	Settings and locations where the data were collected	Section 5.4
	4c	How participants were identified and consented	Section 5.9
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Table 5.2 and Section 5.11
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	Table 5.2 and Section 5.10
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	N/A
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	Chapter 10 and 11 – Background sections

Sample size	7a	Rationale for numbers in the pilot trial	Section 5.6
	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	Section 5.9.2
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	Section 5.9.2
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	Section 5.15.1
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Section 5.9.2 and 5.15.1
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Section 5.15.1
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	Chapters 10 and 11 – methods sections
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	Section 10.4 (incl. Figure 10.1)
	13b	For each group, losses, and exclusions after randomisation, together with reasons	Section 10.4 (incl. Figure 10.1)
Recruitment	14a	Dates defining the periods of recruitment and follow up	Section 5.5 and 10.3.1
	14b	Why the pilot trial ended or was stopped	Section 5.4 and 5.5
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Section 11.4.1 (incl. Table 11.2)
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	Table 11.4 (*n* has been included in all

			tables of objective outcomes)
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	Section 11.4
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	Chapter 9, 10 and 11.
Harms	19	All-important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Section 10.4 (No AE or SAE)
	19a	If relevant, other important unintended consequences	N/A
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	Section 12.7.2
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	Section 12.7.1
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	Chapter 12
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	Chapter 12
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	Section 5.12
Protocol	24	Where the pilot trial protocol can be accessed, if available	Section 5.12 (ClinicalTrails.gov)
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Pg 15
	26	Ethical approval or approval by research review committee, confirmed with reference number	Section 5.12 and 9.3

12.3. Minor Considerations for a Full-scale Trial

12.3.1. Inclusion/ Exclusion Criteria

The trial included patients who experienced pain for more than two weeks, but less than four weeks. There are multiple definitions of acute, subacute and chronic pain, in terms of length of time. The research team chose the definition supported by the World Health Organisation (WHO) stating that acute pain was defined as less than four weeks. However, it is possible to include patients with pain less than six weeks, as defined by the European Guidelines for Acute Low Back Pain. Whether this inclusion would alter the outcome of the full-scale study is not clear. However, the natural progression of the disorder must be considered. It is suggested that at least 33% of patients spontaneously recover within the first three months (Itz et al. 2013). As such, if patients with pain of up to three months were included, the outcomes may be due to the natural progression of the disorder and not from manual therapy.

The trial included patients who were experiencing acute low back pain for the first time, as well as recurrent back pain sufferers, provided they had not received treatment for this current episode of back pain. There is a paucity of literature to suggest that first time low back pain sufferers demonstrate different biomechanics than patients with recurrent back pain. For this reason, it is recommended that the full-scale trial continue to include both subsets of low back pain patients. However, this may be something to explore with sub-group analysis.

12.3.2. Recruitment and Consent

While recruitment of participants onto a study is important, retaining their participation is key to the success of a trial. Upon reflection, there were changes which could be made to a future full-scale trial to improve recruitment and retention. Equally, there were areas that were positive and should be carried forward into a full-scale trial.

Building a relationship between participants and researchers positively contributes towards both recruitment and retention (Chhatre et al. 2018; Daykin et al. 2018). For this reason, a member of the research team carried out recruitment in person with all eligible patients to start building the relationship from the start of participant contact. All communication during the trial was carried out by the research team ensuring that this relationship continued throughout the trial, including dissemination of study results. It was also positive to have a member of the research team involved in recruitment to enable swift answers to potential participant questions to prevent delays. Equally, a member of the research team will potentially be more dedicated to recruitment than if it was being done by the student Intern carrying out the New Patient appointment.

It was clear during the trial discussion with eligible patients that the use of language played an important role in potential participants deciding whether to join the trial or not. Five participants chose not to join the trial due to the use of the word “radiation”. It is possible that the word “radiation” is more associated with Chernobyl, and less with x-ray. When the researcher altered the script to substitute the word “radiation” with “x-ray”, there were no further eligible patients who rejected the trial. It should be noted that the Participant Information Sheet remained unchanged in the description of what fluoroscopy involves, as well as the risks associated with it.

Allowing potential participants to have someone with them during the trial discussion and decision-making process, as well as time to decide whether to take part in the trial or not is recommended by the HRA (2020a) and was reinforced in the trial usability testing to create a person-centred trial (See Chapter 7). It should be utilised in a future full-scale trial.

There were a small percentage of eligible participants who were unable to take part in the trial due to lack of understanding of spoken and written English (0.1 – 0.7% of LBP patients (See Table 9.3)). As this percentage is small, it was not thought to be a large enough problem to warrant the investigation of translating the Participant Information Sheet into other languages. Equally, due to the small percentage, other appropriate languages were not explored. Should the future full-scale trial be multi-centred, with additional participant identifying sites, the translation of the Participant Information Sheet and Consent Form may need to be considered, as well as the use of translators or recruitment of multi-lingual research team members.

The Participant Information Sheet and the Consent Forms were modified through the stakeholder process to be more readable and better understood (See Chapter 8). This is extremely important for ensuring full informed consent is obtained from participants. Following the outcome of the stakeholder process, an additional trial discussion was had with the participants prior to signing the consent form to ensure they understood the trial. This took longer than originally anticipated and as such a little extra time should be added to the first research appointment to accommodate this. Originally one hour and 45 minutes were allocated for the first appointment, but potentially this should be extended up to two hours to ensure a relaxed conversation regarding the trial can be had.

12.3.3. Block Randomisation

Block randomisation using blocks of the same size can increase the risk that the allocation process may be predictable (Efird 2011). For this reason, it is suggested that variable block sizes should be used in a full-scale trial to reduce the chance of prediction.

12.3.4. Fluoroscopy

All participants were required to complete a pre-fluoroscopy form, included in this was a pregnancy statement for female participants. Female participants of childbearing age (15 – 49 years of age) were required to carry out a pregnancy test prior to their fluoroscopy investigation. It is normal practice for female patients requiring NHS examinations with ionising radiation to complete a pregnancy statement signing that they are not knowingly pregnant at the time of the investigation, it is not common practice for these patients to asked to complete a pregnancy test. This addition to this trial was made on the recommendation of the Research Ethics Committee (REC). The reasoning was that participants would not require a fluoroscopy as part of usual care, and as such it was being carried out for research purposes only. This required further reassurance that the participant was not pregnant at the time of the fluoroscopy. The requirement of the pregnancy test was listed in the Participant Information Sheet, and for majority of participants this was not a problem. However, it was suggested by some females of childbearing age that it was unnecessary as they were *"definitely not pregnant".* The pregnancy test did, however, reduce further invasive and potentially embarrassing questioning as to why they felt they were *"definitely not pregnant",* as this discussion became null and void. However, it increased the potential that a previously unaware participant may have to be told by the researcher that they were pregnant. For this reason, the researcher underwent training in mental health first aid. As the use of the pregnancy test will most likely remain for a full-scale trial, it should be thought of during the trial budget calculations to include the purchase of pregnancy testing kits.

Prior to the participant taking part in their baseline fluoroscopy, they were introduced to the *"scary"* (as quoted by a Public and Patient Consultation volunteer) equipment and what would occur during the investigation. This was introduced into the trial following the outcome of the PPI usability testing of the trial method (See Chapter 7). During this process, the participants were introduced to the research team, which continues the theme of continued communication throughout the trial, as well as putting the participants at ease during the investigation.

Part of the fluoroscopy set up with participants was the utilisation of lead shielding for gonads, breast, and thyroid. However, there is a growing argument that patient contact shielding is not generally required in diagnostic radiology (British Institute of Radiology 2020). It is thought that shielding can lead to an increase of patient radiation dose by not letting the radiation scatter leave the body, essentially trapping the scatter inside the patient's body (Frantzen et al. 2012; British Institute of Radiology 2020; Jeukens et al. 2020). For this reason, a future full-scale trial should review the need to use lead contact shielding.

During the investigation itself, not all participants were able to reach the ROM desired during flexion and extension weight bearing at the baseline appointment due to pain, however, were able to reach the desired ROM at the follow up appointment. During the feasibility study, the participant was not withdrawn from the study and the data was included in the analysis. Upon analysis of the data, it appeared that the effect on the data was negligible. This could potentially become an additional confounder to the results and would need to be declared in a future full-scale trial. What may be possible is to include a goniometer reading in degrees at the baseline appointment to ensure the same amount of ROM is carried out at the follow up appointment. This would need to be declared in the results of a full-scale trial; however, this would prevent the loss of the participant if they were withdrawn from the trial.

The fluoroscopy investigation caused some increase in pain in some participants. To what extent the pain increased is unknown, however, it would be prudent to investigate this in a future full-scale trial by introducing a post-fluoroscopy NRS. This could assess whether the increase in pain reaches MCIC or not. It is not thought that the increase in pain effected the outcome measures of the trial as the participants mentioned the increase in pain being a result of the weight bearing sequences which were carried out last. The potential of an increase in pain from the fluoroscopy investigation needs to be added to the Participant Information Sheet and included in the trial ethics as a potential trial risk. Whether the increase in pain may affect recruitment or retention is unknown. There were no participants during this feasibility trial who withdrew for this reason. However, it may be an issue in the non-MT group who do not receive treatment following the baseline fluoroscopy investigation and may be left in increased pain. This would need to be kept in mind during a full-scale study.

There were no incidental findings on fluoroscopy imaging during the trial. However, there were a significant number of participants with lumbosacral transitional vertebrae which are considered normal anatomical variances. It has been suggested that majority of lumbosacral transitional vertebrae are genetic and as a result the percentage of the population with lumbosacral transitional vertebrae are increased in particular geographic areas (Barnes 1994; Drew and Kjellström 2021). This could account for the proportionally high percentage of lumbosacral transitional vertebrae in this study. It appears that the presence of a lumbosacral transitional vertebra does not affect the intervertebral motion outcome measured. This should be explored in a full-scale, fully powered trial to determine if the presence of a transitional lumbosacral vertebrae does affect outcome measures.

This study resulted in a total mean effective radiation dose for baseline and follow up of 1.36mSv. This is similar to the typical effective dose for a single lumbar x-ray examination of 1.3mSv (Public Health England 2008). Due to the mean effective radiation dose for the trial, it would be unethical for additional fluoroscopy investigations to be added to the study. Equally, the use of fluoroscopy as a long-term monitoring investigation is not advised due to the radiation dose.

12.3.5. PROMs and Analgesia Diary

The RMDS-24 is a valid and reliable questionnaire which measures physical function (Chiarotto et al. 2018c). It is potentially the best questionnaire to assess physical function in acute LBP participants (Hush et al. 2010). The BQ assesses NRS and health related quality of life, together with two questions related to physical functioning and is valid and reliable (Hurst and Bolton 2004). Potentially, it could be replaced by the two questionnaires of NRS (Chiarotto et al. 2018b) and SF-12 (Chiarotto et al. 2018d). The NRS would cover the core outcome of pain intensity, the SF-12 would cover the core outcome of health-related quality of life, and the RMDS-24 would cover the core outcome of physical function. The SF-12 was derived from the SF-36. There is little literature relating to the SF-12 use in acute LBP studies, partly due to it being relatively new. However, the SF-36 is a valid and reliable method of measuring health related quality of life in acute LBP patients (Chiarotto et al. 2018d). The BQ was already in use at the AECC UC Clinic as an outcome measure which meant there was a reduction in trial burden for the participants, which was one of the main reasons it was used in the trial. Equally, this meant that once the trial was complete and the participant returned to their original intern, the trial BQ questionnaires could be compared to intern treatment BQ questionnaires. Potentially, if a full-scale trial was to be multi-site, the use of the BQ could be reassessed as to whether it should be replaced by the NRS and SF-12.

The trial method included the use of an analgesia diary for participants, however, the data from the participants diaries were not utilised. The primary reason for this was the lack of recording of analgesia usage by the participants and as such while some participants wrote down all the analgesia taken during the trial, others did not write down anything and attempted to estimate days, medication, and dosage. The lack of participant compliance, as well as lack of accuracy of the reported data, is a recognised problem in research (Drieling et al. 2016). The primary reason for the inclusion of the analgesia diary was to gain an understanding if the medication usage changed throughout the trial. Prescription analgesia (such as opioids) can influence PROMs as the participant perceives that they are in less pain and as such it effects NRS (Tucker et al. 2020). As the participant perceives less pain, they may be more willing to be physically active (thus effecting

physical function questionnaires) and may perceive an improved health related quality of life. As such, the analgesia diary was to potentially see how many participants were taking prescription analgesia during the time of the trial or started prescription analgesia once the trial had begun. Other than a potential influence on PROMs, potentially if participants were perceiving less pain, they would be more willing to move during the fluoroscopy sequences or their movement quality may be altered, thus effecting intervertebral motion variables. For these reasons, the analgesia diary should be continued in a full-scale trial. However, either better instructions need to be provided on how to use the analgesia diary, or alternatively a better alternative to written data collection should be considered, such as an App which notifies participants to complete daily.

12.3.6. Interventions

During recruitment, two eligible patients decided not to take part in the study based upon the chance they would be randomised to a group they did not want to be in. One eligible patient did not want to take the chance of being randomised into the non-MT group, whereas the other did not want to be randomised into the MT group. During the trial, there were no participants who indicated they were unhappy with the intervention they received or wished they could change groups. As such, while the treatment options for each group may be a barrier to recruitment, it did not have an effect on retention.

Due to Covid-19 there was a mid-trial alteration to the original trial protocol for the non-MT group. This change allowed for the interim check-up appointment to be carried out online via Zoom (Zoom Video Communications Inc., USA) if the participant so wished. There was no evidence to suggest that this should not be carried forward into a full-scale trial. Equally, it reduces the time and travel burden on the non-MT group, which may contribute towards a person-centred trial, thus aiding participant retention. It is not possible to implement this change for the MT group as they receive hands treatment from a clinician.

The appointment schedule was emphasised during recruitment, and eligible patients were asked to pay particular attention to the appointment schedule section of the Participant Information Sheet. There were no eligible patients who chose not to take part in the trial due to the appointment schedule, however, one did decide not to take part due to transport difficulties. Potentially if the eligible patient was in the non-MT group, they could have joined the trial as it involved less travel. However, participants were required to consent to the trial before finding out which group they were in. As such, the appointment schedule was not a barrier to recruitment and retention.

Regarding compliance to the appointment schedule for the MT group, only one participant did not complete the trial within two weeks. The participant did, however, complete the trial within two weeks and two days, this was not thought to impact the participants outcomes. Regarding compliance to the appointment schedule for the non-MT group, all participants completed the trial within two weeks. It is important for a person-centred trial to be somewhat flexible for participants, however, often flexibility cannot be built into the trial method as it may affect the outcomes being collected. In the context of this trial, it is not thought that an additional day or two to complete the trial would affect the outcome measure to such an extent it would require the participant to be withdrawn or the data withdrawn from the trial. As such, a future full-scale trial should include a buffer of two days for participants to complete the trial. More than a two-day buffer may result in changes in intervertebral motion due to the natural progression of the condition and not necessarily the intervention (Itz et al. 2013).

At the completion of the first research appointment, the researcher encouraged participants to book all their research appointments. This may have contributed to the compliance of the participants to the appointment schedule. The appointment schedule was printed onto a business card, which included contact details in case cancellation, or rescheduling was required. As the trial took place in a busy and large multi-intern clinic, there was a concern that participants would not be able to contact the research team if needed, as such, the researcher acquired a mobile phone for the purposes of the trial only. The mobile phone was utilised by the doctoral researcher to notify participants about changes to the trial due to Covid-19 or equipment failure. Equally, participants were able to contact the doctoral researcher during lockdown when the AECC UC Clinic was closed. The researcher also had access to the AECC UC Clinic booking software to schedule or change appointments for participants if needed, without having to go through the clinic reception team.

Access to the AECC UC Clinic was given to the research team outside of formal opening hours to see trial participants. This meant that participants were able to book appointments from 08:00 until 18:00 (extended hours). This allowed participants to continue with their job during working hours, with trial appointments taking place either before or after the workday. This is supported in the literature whereby patients attending GP practices during extended hours were more satisfied with their care due to appointments that fit in with their family and work life (Cowling et al. 2017). There is a lack of literature related to extended opening hours and manual therapists. Three out of the seven participants in the MT group, and one out of the non-MT group had one or more trial appointments outside of normal AECC UC Clinic opening hours. It is likely that being accommodating to participants schedules did positively impact recruitment and retention.

All manual therapy appointments were carried out by a single, experienced chiropractor (the doctoral researcher), as such the researcher was able to standardise treatments between participants. However, in a full-scale trial it may not be possible for all treatment appointments to be carried out by one practitioner, as such standardisation of treatment will need to be considered.

There were no recorded adverse events (AE) or serious adverse events (SAE) during the trial. SMT of the spine and sacroiliac joints are considered minimal risk with less than 1 in 3.7 million patients experiencing serious adverse complications (Oliphant 2004). As such, a serious adverse event was not expected during the trial. However, mild transient discomfort post-treatment is common and occurs in approximately 50% - 67% of patients (Oliphant 2004; Paige et al. 2017). None of the MT group participants mentioned that they had experienced discomfort post-treatment when asked.

12.4. Major Considerations for a Full-scale Trial

This study was a feasibility study to explore the effects of manual therapy on the intervertebral motion of acute NSLBP patients. In order to explore this, the trial recruited acute NSLBP patients and divided them (randomly) into two groups, one with the intervention of manual therapy and a home management booklet, and one with the home management booklet only.

The trial utilised QF to measure intervertebral motion in the motion sequences of flexion (weight bearing and recumbent) and extension (weight bearing and recumbent). Flexion and extension in the lumbar spine are pure movements requiring very little intervertebral axial rotation or lateral flexion. Equally, there is relatively more movement between the vertebra during flexion and extension. Together these make the sagittal plane movement of flexion and extension more accurate to measure. The trial also utilised weight bearing and recumbent motion sequences. Recumbent movement assume no (or very little) muscular or motor influence and provide an understanding of the passive elements of the FSU, whereas weight bearing movement involves the simultaneous function of the passive elements, active spinal musculature, and motor control (Mellor et al. 2009; Breen et al. 2012b). Due to the trial being underpowered, there was insufficient evidence to recommend alterations to fluoroscopy motion sequences for a full-scale trial and as such, it is recommended that flexion (weight bearing and recumbent) and extension (weight bearing and recumbent) are carried out in a full-scale trial.

This trial explored the intervertebral motion variables of intervertebral angular range of motion (IV-ROM), initial attainment rate (IAR), translation, disc height, motion sharing inequality (MSI) and motion sharing variability (MSV). The results of this feasibility study were utilised to explore

whether these intervertebral motion variables were the optimum variables for a future full-scale trial.

Potentially the best way to answer the research question of biomechanical effects of manual therapy is to compare the change in intervertebral motion between the two groups. Assuming there is a change, the difference between baseline and follow up would need to be compared to the MDC to ascertain if the change is more than the measurement error. When exploring IV-ROM, IAR, translation and disc height, issues arise:

- IV-ROM: Although underpowered, very few participants met the MDC. Potentially, the MDC is so large (approximately a sixth of L2-S1 IV-ROM) that for a participant to exceed the MDC they would need to move more than their anatomical limit.
- IAR and translation: Both measurements are used to indicate the stability of a joint. There is a paucity of literature relating to what is normal translation or IAR for a FSU, as such, a comparison the 'normal' cannot be made. The MDC in this trial when calculated per vertebral level, while large, should still be within most participants anatomical limits. However, when pooled and compared to healthy volunteers (Breen et al. 2019b), the MDC is larger. There is an expectation that translation and IAR should not change drastically in a patient due to treatment, as either joints are becoming too unstable or developing a large amount of stability quite quickly, and as such, the difference in translation and IAR reaching MDC is unlikely.
- Disc height: Very few participants reached the MDC for disc height change between groups. However, a large change in disc height was not expected and nor should it be. A sudden large change in disc height from baseline to follow up within a two-week trial would indicate that a participant had changed anatomically very quickly which is generally not a good sign and could constitute a medical emergency if supported clinically.

With their being measurement problems with IV-ROM, translation, IAR and disc height in terms of agreement and reliability, potentially a future full-scale trial might not discover a difference between baseline and follow up measurements between groups, not because they are not there, but because there is a fault with the measuring tool. However, until a more reproducible way of measuring intervertebral motion can be developed, fluoroscopy remains the gold standard.

For the reasons stated above, there is evidence to support altering the intervertebral motion variables to be explored in a future full-scale trial. It is recommended that the primary outcome measure be MSI and MSV, which as suggested, is the most useful in exploring aberrant motion (Breen et al. 2018). However, to enable an understanding of what is aberrant about the motion,

correlations with IV-ROM, IAR, translation and disc height would be useful. Equally, as IV-ROM is influenced by age and sex; and disc height is influenced by age and weight, these correlations could add to the understanding of aberrant motion. As the calculation of MSI is closely related to the measurement of IV-ROM, and IV-ROM is affected by age and sex, it is recommended that the groups of MT and non-MT are age and sex matched. Equally, as ROM increases throughout the day, it is recommended that baseline and follow up measurements for each participant are carried out at the same time of day.

The research question assumes that there will be a change in intervertebral motion following manual therapy. Some studies support this assumption; however, the relationship is not that simple. Much of the literature surrounding intervertebral motion following SMT and mobilisation is related to immediate effects. The immediate effects are influenced by force of thrust, speed and acceleration, contact site, angle of contact, and patient positioning. There is little literature relating to short-term or long-term effects of SMT or mobilisation on intervertebral motion. Clinically, SMT and mobilisation have similar short-term (up to five hours) neurophysiologic effects (Coronado et al. 2010). Immediate clinical effects of SMT on cervical ROM can lead to the effects lasting between treatment sessions, however, literature suggests that these effects may not have any influence on long-term outcomes (Tuttle et al. 2006; Wright et al. 2010; Garrison et al. 2011). The intervention for this trial for the MT group was five MT appointments in two weeks as supported in the literature (Globe et al. 2016). To ensure the greatest opportunity of finding any biomechanical effects of manual therapy, the final treatment took place directly prior to the follow up fluoroscopy. Thus, potentially including both long-term effects (over two weeks) and short-term effects (within five hours). For this reason, it is not possible to decipher whether intervertebral motion differences between baseline and follow up could be attributed to short-term or long-term effects only. As the exploration of short-term and long-term effects of manual therapy are not the focus of the research questions, a change in method is not warranted.

Some patients respond to manual therapy, and some do not. It has been suggested that clinical responders to SMT demonstrate less spinal stiffness than their non-responding counterparts (Wong et al. 2015). For this reason, it is possible that responders to manual therapy may have different intervertebral differences between baseline and follow up to their non-responding counterparts. The difficulty is in defining responders. Where some literature indicating a response is any positive change to their condition (Andersson 1999; van Tulder et al. 2006); some indicating a MCIC (Itz et al. 2013; Kongsted et al. 2016); and some indicating a total resolution to their condition (Itz et al. 2013). For the purposes of this trial, responders were those who reached a MCIC on their PROMs questionnaires. Due to the small sample size, dichotomising the MT group

would not have provided meaningful outcomes. It is recommended that this be carried out in a full-scale trial.

During this trial, both groups demonstrated some improvement (but not necessarily a MCIC) in their PROMs questionnaires. As both groups improved similarly, it is possible that it demonstrates the natural progression of pain reduction in patients with acute NSLBP. Acute NSLBP patients can improve without treatment within the first four weeks, however, the most improvement takes place within the first two weeks (Itz et al. 2013). For this reason, the inclusion criteria sought participants who had experienced pain for at least two weeks, but no more than four weeks. It is possible that week's three and four the non-MT group demonstrate a positive natural progression of the disorder at the same rate as the MT group. This very real possibility could result in no difference between the MT group and the non-MT groups intervertebral motion variables in a full-scale trial.

12.5. Is the Trial Feasible?

It was the decision of the research team to carry out a randomised feasibility study. While it is acknowledged that many of the parameters explored in this feasibility study could have been explored using a manual therapy group alone, there was a concern that in effectively running half the trial outcome measures may not be fully explored. Willingness to be randomised was explored somewhat in the Public and Patient Involvement process, indicating that randomisation of participants would be accepted. Whereas, during the trial, randomisation was an issue for two eligible patients who rejected the trial. The research team felt that a full run through of the trial, with both groups, exploring the practicalities of carrying out a trial would inform a full-scale trial. It provided information on not only patient uptake, and the execution of the trial, but perceived positive or negative effects on the AECC University College Clinic as well.

Utilising the sample size calculated for MSI and MSV only, 262 complete data sets would be required. Assuming the full-scale trial was to take place at the AECC UC Clinic, as a single site, single researcher, with only onsite participant identification, the trial is not feasible. As a single site, with only onsite participant identification but a team of researchers (fluoroscopy operator, manual therapist, QF MATLAB operator, statistician), the total time required for a full-scale study would be approximately six years. That is assuming there is no breakdown of equipment or other trial delays.

The trial becomes more feasible as a single site, research team, with additional identifying centres, such as GP practices. The suitability of a GP practice and acceptance of participation by GPs will need to be further explored as it was not within the scope of this feasibility study.

Guidance on additional identifying sites is provided by the HRA (HRA 2022). Equally, the trial would be most feasible as a multi-site (more than one clinic or hospital), each site with their own research team (fluoroscopy operator, manual therapist), with additional participant identifying centres (local GP practices or manual therapy clinics). This would much reduce the amount of time the trial would take; however, additional trial sites were not explored as part of this feasibility study and as such whether suitable sites exist is unknown.

With a trial of this magnitude, the budget would need to be carefully thought out. Assuming multi-site, multi-research team, with additional participant identifying sites, the following budget items will need to be considered:

- Payment to AECC UC Clinic for the use of their premises. Equally, additional trial sites will need to be compensated for hosting the trial. Whether the site fee includes disposables, cleaning and washing of patient gown needs to be established to allow for additional budget to be allocated if not included.
- Payment of research Principal Investigator, together with the research team of fluoroscope operator (and team); QF MATLAB analyst; manual therapist; and statistician. At least a fluoroscope operator and manual therapist will be required at each site.
- Payment for a fluoroscope maintenance plan (or contribution towards). Equipment on a maintenance plan is prioritised for repair and any loss of time needs to be minimised.
- Payment for any additional equipment required such as the recumbent and weight bearing moving platforms.
- Recruitment, and administration costs (including printing of participant trial material and advertising).
- Purchasing of pregnancy tests (depending on if required by the REC).
- Publishing costs (open access) and conference presentation costs.

12.6. Is a Full-Scale Trial Worth Pursuing?

Potentially, the answer to this question lies in whether the research questions for a full-scale trial are worth answering. Upon personal reflection, this can be explored in two ways. Firstly, from the point of view of furthering the understanding of NSLBP, and secondly from the point of view of furthering the understanding of manual therapy.

Low back pain is one of the major global public health problems (Buchbinder et al. 2018). For this reason, any research into the understanding of the disorder is worth pursuing. As the name implies, NSLBP is a diagnosis of exclusion, which is a diagnosis reached by eliminating all other

possible causes of LBP. NSLBP is not solely an anatomical or biomechanical problem, there are psychological and social aspects to consider as well, however for the purposes of this thesis, the biological aspect of NSLBP were explored. Anatomically, structures in the lumbar spine contain nociceptors, which when stimulated can be interpreted as pain by the brain. The nociceptors can be stimulated by chemical or physical (compression or stretching) stimulation. Through imaging of patients with NSLBP, what are thought to be abnormalities in structure may be found, however, in pain-free person these same structural differences may also be found. For this reason, the focus has turned towards understanding the biomechanics of NSLBP. It is difficult to understand the biomechanics of the lumbar spine through static imaging of neutral, flexion and extension. This only provides information of the end of the range of motion, and not on what occurs from beginning to end. Fluoroscopic image sequences can be used to provide information on continuous motion throughout the range of motion. While it is easier to measure flexion and extension intervertebral motion variables, it is possible to measure lateral flexion motion variables as well, which should not be discounted. There is also an assumption that weightbearing and recumbent imaging is necessary to explore active (using motor control and active muscle recruitment) and passive (passive restraint system), however, there is little literature exploring the differences in intervertebral motion variables between the two positions. However, there are electromyography (EMG) studies which indicate that muscle activation only occurs in the weightbearing sequences (du Rose 2017). Upon reflection, the clinician might argue that the fluoroscopy protocol, with the restraint of the pelvis and limitation of full torso range of motion, is not representative of the way a patient would move and, as such, is not exploring the patient *in situ*. However, the researcher might argue that people move differently, and without pelvic restraint and a standard image acquisition protocol participants will move too differently and make comparisons of data difficult, or the participant may move out of the fluoroscope field entirely. Equally, there is evidence to suggest that the fluoroscopic intervertebral motion variable measurement errors are large (SEM and MDC). While both these arguments are correct, there is no other imaging modality which is able to gather continuous motion data at the intervertebral level and as such is the best imaging modality at this time. Potentially combining fluoroscopy with EMG or fMRI may provide a better understanding of spinal biomechanics than fluoroscopy alone.

Little research has been conducted relating to the intervertebral motion differences between pain-free persons and acute NSLBP patients. However, previous literature has demonstrated a difference between pain-free persons and chronic NSLBP patients (Mellor et al. 2014a; Breen et al. 2018). According to Breen et al. (2018), chronic NSLBP patients have greater motion sharing inequality (MSI) values, however, initial attainment rate (IAR), translation and motion sharing

variability (MSV) were no different than pain-free controls. The exploration of the intervertebral motion differences between acute NSLBP patients and pain-free controls would be a useful prequel study. If there is a difference in intervertebral motion variables between pain-free persons and patients with acute NSLBP, then it would make logical sense to explore whether manual therapy effects intervertebral motion in patients with acute NSLBP. If there are no differences in intervertebral motion variables between pain-free persons and patients with acute NSLBP, why would changes in intervertebral motion variables be expected in patients with acute NSLBP following a course of manual therapy? Alternatively, potentially manual therapy could create the same intervertebral changes in both the symptomatic and asymptomatic populations, which reduces the clinical value of the investigation. For this reason, the question arises, is the exploration of biomechanical effects of manual therapy putting the cart before the horse? As such, potentially a full-scale trial is not worth pursuing at this time.

The second area to consider is developing a better understanding of manual therapy. There is evidence to suggest that manual therapy creates immediate changes in biomechanics, but short-term and long-term effects are still being explored. A full-scale trial will explore the intervertebral effects of manual therapy both short-term and long term, which has not been done before. There is also evidence to suggest that manual therapy is associated with pain reduction and improvement in function, however, exploration into how manual therapy achieves this is still under investigation. A full-scale study will be able to explore this at an intervertebral level, *in vivo*, which has also not been done before. Some patients respond to manual therapy and others do not, and the reason for this is still under investigation. A full-scale study will be able to gain insight into this perplexing area. For this reason, exploring the intervertebral biomechanical effects of manual therapy, as well as differences between responders and non-responders, is worth exploring. Potentially, if there is improved understanding of this area, it may assist with identifying patients who would respond to manual therapy, which could contribute to preventing acute NSLBP from becoming chronic.

12.7. Limitations

12.7.1. Generalisability

The study was designed to assess the feasibility of carrying out a full-scale trial at the AECC UC Clinic. However, the proposed future full-scale trial could take place at any musculoskeletal clinic which had the appropriate equipment and trained staff members. As the sample size calculated for a future full-scale trial is large, it is recommended that if the study were to take place, it would be a multi-site, multi-research team trial, potentially also requiring multiple identifying sites.

However, other appropriate sites for participant identification, recruitment, and the trial were not explored during this feasibility study.

This trial is underpowered, as such, no inferences or outcomes can be made from the data analysis. Equally, the trial recruited a total of 16 NSLBP participants out of a total of 45 eligible patients. For this reason, the outcome of the trial is not representative of the NSLBP population (local or global), nor is it generalisable (Kukull and Ganguli 2012).

12.7.2. Bias

Bias describes a systematic error introduced into a trial (usually unconsciously) which can have an effect on the outcome of the trial (Delgado-Rodríguez and Llorca 2004; Probst et al. 2016). The CONSORT Statement for reporting parallel group randomised trials defined the following domains of bias: randomisation; blinding of participants and personnel; and blinding of outcomes assessment, among others (Schulz et al. 2010; Probst et al. 2016).

The study utilised the online randomisation website Sealed Envelope™ (Sealed Envelope Ltd, UK) to generate the randomisation list. The list was held by the researcher, and participants were assigned their group following the list consecutively. It was not possible to blind the participants to the intervention, the reason for this was the two group's interventions were explicitly described in the Participant Information Sheet and as such, each participant knew what group they were assigned to. Nor was it possible to blind the researcher to the intervention as the researcher was carrying out the interventions for both groups.

Each participant was assigned a unique study number, and all identifying data was removed from the PROMs questionnaires and QF image sequences and replaced with the unique study number. However, the researcher carried out the outcome's measures, as well as the data capture and analysis of the outcomes. It is very difficult for the researcher to introduce bias into the questionnaire data, or the QF data, however not impossible. For this reason, in a future full-scale trial, separate researchers to carry out the intervention, the outcome measures, and the data capture and analysis would be advisable.

The study was carried out at the AECC UC Clinic, which is a manual therapy clinic. As such, patients attend the clinic expecting to receive manual therapy, and potentially have some prior knowledge of what manual therapy entails. For this reason, eligible patients may have been more enthusiastic and willing to take part in a study which included manual therapy treatment. It is possible that eligible patients recruited from other centres not specialising or offering manual

therapy may have a different recruitment outcome, and as a result a different study outcome. This is termed selection bias (Delgado-Rodríguez and Llorca 2004; Kukull and Ganguli 2012).

It is possible that participants tried to provide PROMs questionnaire answers that the researcher wanted to see. This is known as reporting bias, whereby the participant reports what they think the researcher wants (Delgado-Rodríguez and Llorca 2004). In attempt to prevent this from occurring, questionnaires were filled in two weeks apart, and participants were not provided with the outcome of the questionnaires, nor allowed to see the completed baseline questionnaires before completing the follow up questionnaires.

12.8. Contribution to Knowledge

This body of work has made the following significant contributions to knowledge:

- This thesis systematically reviewed the literature on intersegmental motion in the lumbar spine in live symptomatic and asymptomatic humans following SMT and mobilisation. A systematic review of this literature has not been carried out in the past and as such amalgamating the literature into one systematic review is a unique contribution to knowledge.
- This thesis reviewed the literature on the most effective PROMs measure for patients with acute NSLBP, while still fulfilling the core outcome set suggested by Chiarotto et al. (2015). The literature review supported the use of RMDS-24 as a physical function questionnaire, however, either the BQ or SF-12 could have been utilised for the trial. The decision to utilise the BQ was largely based upon reduction of trial burden on participants as it was already in use at the AECC UC Clinic.
- A Home Management Booklet was produced for the trial based upon current guidelines for the non-invasive management of acute LBP in adults (above 16 years of age). The content was derived from a scoping review of the latest guidelines for the non-invasive management of NSLBP. Through the stakeholder process, the readability and comprehension of the booklet was improved. The stakeholder process also assisted in choosing the illustrations for the booklet. The booklet produced is not just for the trial but could be utilised for all acute NSLBP patients. The production of the booklet and the booklet itself was a unique contribution to knowledge.
- A Patient and Public Involvement Process (PPI) was carried out to assist with creating a more person-centred randomised controlled trial. The PPI utilised the unique method of usability testing and post-usability discussion. The method was published and presented

as a proof of concept and was a unique contribution to the PPI field. Equally, the PPI altered the trial method to be more person-centred.

- A stakeholder process was carried out utilising patients and members of the public, as well as clinicians and student interns to improve the content, readability and understanding of the trial material. The utilisation of all three groups within a stakeholder process had not been carried out before and as such, the method makes a unique contribution to knowledge. The paper was published, contributing to the literature pool of PPI and stakeholder consultations.
- The feasibility study explored whether the trial method was suitable to answer the research questions in a future full-scale trial. This study solidified the method, assessed the outcome measures to be utilised and calculated the sample size needed for a full-scale trial. The final contribution to knowledge was the development of a robust future full-scale trial protocol which is aimed at improving the understanding of an important societal problem, acute NSLBP.

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Appendix A: PEDro Scale

- eligibility criteria were specified
- subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)
- allocation was concealed
- the groups were similar at baseline regarding the most important prognostic indicators
- there was blinding of all subjects
- there was blinding of all therapists who administered the therapy
- there was blinding of all assessors who measured at least one key outcome
- measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups
- all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by “intention to treat”
- the results of between-group statistical comparisons are reported for at least one key outcome
- the study provides both point measures and measures of variability for at least one key outcome

The PEDro scale is based on the Delphi list developed by Verhagen and colleagues at the Department of Epidemiology, University of Maastricht (Verhagen AP et al (1998). The Delphi list: a criteria list for quality assessment of randomised clinical trials for conducting systematic reviews developed by Delphi consensus. Journal of Clinical Epidemiology, 51(12):1235-41). The list is based on "expert consensus" not, for the most part, on empirical data. Two additional items not on the Delphi list (PEDro scale items 8 and 10) have been included in the PEDro scale. As more empirical data comes to hand it may become possible to "weight" scale items so that the PEDro score reflects the importance of individual scale items.

The purpose of the PEDro scale is to help the users of the PEDro database rapidly identify which of the known or suspected randomised clinical trials (i.e., RCTs or CCTs) archived on the PEDro database are likely to be internally valid (criteria 2-9) and could have sufficient statistical information to make their results interpretable (criteria 10-11). An additional criterion (criterion 1) that relates to the external validity (or “generalisability” or “applicability” of the trial) has been retained so that the Delphi list is complete, but this criterion will not be used to calculate the PEDro score reported on the PEDro web site.

The PEDro scale should not be used as a measure of the “validity” of a study’s conclusions. In particular, we caution users of the PEDro scale that studies which show significant treatment effects, and which score highly on the PEDro scale do not necessarily provide evidence that the

treatment is clinically useful. Additional considerations include whether the treatment effect was big enough to be clinically worthwhile, whether the positive effects of the treatment outweigh its negative effects, and the cost-effectiveness of the treatment. The scale should not be used to compare the "quality" of trials performed in different areas of therapy, primarily because it is not possible to satisfy all scale items in some areas of physiotherapy practice.

Notes on administration of the PEDro scale:

All criteria Points are only awarded when a criterion is clearly satisfied. If on a literal reading of the trial report it is possible that a criterion was not satisfied, a point should not be awarded for that criterion.

Criterion 1 This criterion is satisfied if the report describes the source of subjects and a list of criteria used to determine who was eligible to participate in the study.

Criterion 2 A study is considered to have used random allocation if the report states that allocation was random. The precise method of randomisation need not be specified. Procedures such as coin-tossing and dice-rolling should be considered random. Quasi-randomisation allocation procedures such as allocation by hospital record number or birth date, or alternation, do not satisfy this criterion.

Criterion 3 Concealed allocation means that the person who determined if a subject was eligible for inclusion in the trial was unaware, when this decision was made, of which group the subject would be allocated to. A point is awarded for these criteria, even if it is not stated that allocation was concealed, when the report states that allocation was by sealed opaque envelopes or that allocation involved contacting the holder of the allocation schedule who was “off-site”.

Criterion 4 At a minimum, in studies of therapeutic interventions, the report must describe at least one measure of the severity of the condition being treated and at least one (different) key outcome measure at baseline. The rater must be satisfied that the groups’ outcomes would not be expected to differ on the basis of baseline differences in prognostic variables alone, by a clinically significant amount. This criterion is satisfied even if only baseline data of study completers are presented.

Criteria 4, 7-11 Key outcomes are those outcomes which provide the primary measure of the effectiveness (or lack of effectiveness) of the therapy. In most studies, more than one variable is used as an outcome measure.

Criterion 5-7 Blinding means the person in question (subject, therapist, or assessor) did not know which group the subject had been allocated to. In addition, subjects and therapists are only considered to be "blind" if it could be expected that they would have been unable to distinguish between the treatments applied to different groups. In trials in which key outcomes are self-reported (e.g., visual analogue scale, pain diary), the assessor is considered to be blind if the subject was blind.

Criterion 8 This criterion is only satisfied if the report explicitly states both the number of subjects initially allocated to groups and the number of subjects from whom key outcome measures were obtained. In trials in which outcomes are measured at several points in time, a key outcome must have been measured in more than 85% of subjects at one of those points in time.

Criterion 9 An intention to treat analysis means that, where subjects did not receive treatment (or the control condition) as allocated, and where measures of outcomes were available, the analysis was performed as if subjects received the treatment (or control condition) they were allocated to. This criterion is satisfied, even if there is no mention of analysis by intention to treat, if the report explicitly states that all subjects received treatment or control conditions as allocated.

Criterion 10 A between-group statistical comparison involves statistical comparison of one group with another. Depending on the design of the study, this may involve comparison of two or more treatments, or comparison of treatment with a control condition. The analysis may be a simple comparison of outcomes measured after the treatment was administered, or a comparison of the change in one group with the change in another (when a factorial analysis of variance has been used to analyse the data, the latter is often reported as a group × time interaction). The comparison may be in the form hypothesis testing (which provides a "p" value, describing the probability that the groups differed only by chance) or in the form of an estimate (for example, the mean or median difference, or a difference in proportions, or number needed to treat, or a relative risk or hazard ratio) and its confidence interval.

Criterion 11 A point measure is a measure of the size of the treatment effect. The treatment effect may be described as a difference in group outcomes, or as the outcome in (each of) all groups. Measures of variability include standard deviations, standard errors, confidence intervals, interquartile ranges (or other quantile ranges), and ranges. Point measures and/or measures of variability may be provided graphically (for example, SDs may be given as error bars in a Figure) as long as it is clear what is being graphed (for example, as long as it is clear whether error bars represent SDs or SEs). Where outcomes are categorical, this criterion is considered to have been met if the number of subjects in each category is given for each group.

Appendix B: Participant Eligibility Checklist

Name of participant/ File number:

Inclusion Criteria	**Y/N**	**notes**
Patients with acute NSLBP, without leg pain, of at least 2 weeks duration, but no more than 4 weeks duration		
Patients between the ages of 18 and 65		
Exclusion Criteria		
Patients who cannot understand written English and unable to provide full informed consent.		
Patients who are currently involved in another research study		
Patients with a BMI over 30 (less likely to obtain the required information from the images)		
Pregnancy or potentially pregnant		
Previous ionising radiation exposure within the last 6 months greater than 8mSv.		
Previous lumbar spine surgery, as well as recent abdominal or pelvic surgery (within the last 12 months).		
Scoliosis or positive Adams forward Bending Test for Scoliosis.		
Diagnosed Osteoporosis (Bone Density Scan)		
Patients with a numeric pain scale of 8 or more, or 2 or less, taken at the New Patient Examination Appointment.		
Manual therapy already received for this episode of NSLBP		
Litigation or compensation pending		
Diagnosis of depression (by a medical doctor) within the last 12 months.		

Appendix C: Participant Information Sheet

REC Reference: 20/EE/0001

Version: 2.0

Date: 23.01.2020

Participant Information Sheet

The title of the research study

The Biomechanical Effects of Manual Therapy - A Feasibility Study.

Invitation to take part

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Who is organising/funding the research?

The research is being organised by Jacqui Rix. Jacqui is a qualified chiropractor, as well as a PhD student at Bournemouth University. The research is jointly funded by Bournemouth University and the AECC University College.

Who has reviewed the research?

The research has been reviewed by experts in the area and approved by the NHS Research Ethics Committee (East of England – Cambridge Central). The methods, as well as the trial documentation have been reviewed through a public involvement process.

What is the purpose of the project?

The majority of people with low back pain are diagnosed with non-specific low back pain (NSLBP). This means that the pain is unlikely to be due to a serious cause. NSLBP is

thought to be at least partly due to abnormal spinal movement. New technology has enabled us to look at spinal movement with the use of motion x-ray or quantitative fluoroscopy. To date, quantitative fluoroscopy has been used to help us understand spinal movement in people who do not have back pain, and in people who have had back pain for longer than 12 weeks. This study will be looking at spinal movement in people who have had pain for four weeks or less. Specifically, we will investigate whether spinal movement changes after a course of manual therapy. We would also like to compare spinal movement in people who get a positive outcome from manual therapy to those who do not. This study is a feasibility study which means we are exploring how best to carry out a large-scale study with more participants to gain a better understanding of spinal movement in people with low back pain for four weeks or less.

The study forms part of a three-year PhD project.

Why have I been chosen?

You have been chosen because you have non-specific low back pain; you have been in pain for at least 10 days (but no more than 4 weeks;) and you are aged between 18 and 65. This study would like to recruit 30 participants.

Please note that you will be unable to participate in the study if you have a body mass index (BMI) of over 30 (as the fluoroscopy images may not be clear enough to see spinal movement); if you are pregnant (or potentially pregnant); if you have had a x-rays of your lower back or abdomen within the last 6 months; or you have had lumbar spine surgery or recent abdominal surgery.

Do I have to take part?

It is up to you to decide whether to take part, or not. If you decide to take part, you will be given this information sheet to keep and be asked to sign an informed Consent Form. You can withdraw from participation at any time and without giving a reason. If you decide to withdraw, we will usually remove any data collected about you from the study. Once the trial has finished you may still be able to withdraw your data up to the point where the data is analysed and incorporated into the research findings or outputs. At this point your data will become anonymous, so your identity cannot be determined, and it

may not be possible to identify your data within the anonymous dataset. Withdrawing your data at this point may also adversely affect the validity and integrity of the research.

If you decide not to take part or decide to withdraw from the study, this will not impact upon your clinical management and treatment at the AECC University College Clinic.

What would taking part involve?

First Appointment: (Approximately 90 minutes)

You will be invited to attend the AECC University College Clinic at a time convenient to you. I will meet you and go through this Participant Information Sheet with you and answer any questions you may have. If you are happy to proceed you will be asked to sign an informed Consent Form. You will be given a copy of this form to take home with you.

You will then be taken through to the x-ray department. Here you will be given the following to complete:

- A pre-study participant form which will include a consent form to consent to x-ray. You will be given a copy of this form to take home with you.
- A pregnancy statement (female patients only).
- A set of questionnaires examining pain and physical functioning.

Females of childbearing age (18 – 49 years of age) will need to undertake a pregnancy test (urine dipstick). This is because x-rays may harm an unborn child and we would like to do ensure that both you and your unborn child are protected.

You will then be shown to a changing room and asked to change into a gown. When you return, the radiographer will show you how the x-ray equipment works. Quantitative Fluoroscopy uses specially designed motion tables and low dose video x-rays.

First you will be asked to lie on one motion table. The upper half of the table will swing slowly from side to side and video x-rays will be taken showing the movement of your vertebrae as you bend (see picture 1). Then you will be asked to move to an upright motion table and stand against it. Again, the table will slowly swing while you bend, following a moving arm rest, while the x-rays are taken simultaneously (see picture 2).

Before we take the x-rays we will find the range of bending that you are comfortable with.

Picture 1

Picture 2

During examinations, your lower abdomen will be covered with a lead apron to protect the reproductive organs. You will also be provided with a button that will allow you to stop the table should you begin to feel pain or discomfort.

Once complete you will be shown to a changing room to change back into your clothes. I will then take you back to clinic reception to arrange further appointments.

This type of study is called a randomised clinical trial. As such you will be randomly placed into one of two groups. A computer program designed for this purpose will assign you to one of the following groups:

Group 1:

You will be invited to attend five treatment appointments over two weeks. The first treatment appointment will occur directly after your first trial appointment (first Fluoroscopy). The last treatment appointment will occur directly before your final follow up appointment (second fluoroscopy). Each appointment will last up to 30 minutes and will include manual therapy which may consist of spinal manipulation, spinal mobilisation,

trigger point therapy (a way of reducing tension in muscles) and light massage. You will be asked to sign a consent form to consent to the intervention. I will be carrying out the treatment.

You will also be given a pamphlet of useful evidence-informed information to help you self-manage your pain between appointments.

At the end of the second week you will be invited to attend the clinic for your final follow up appointment.

Group 2:

You will be given a booklet of evidence-informed information to help you manage your back pain at home. You will be asked to sign a consent form to consent to the intervention.

After one week, you will be invited to attend the clinic for a 30-minute appointment to discuss your back pain and how you are doing with the home management program. It is important to note that this is an advice appointment only, no physical treatment will be offered. I will be carrying out the appointment.

At the end of the second week you will be invited to attend the clinic for your final follow up appointment.

Final Follow up Appointment: (Approximately 90 minutes):

This appointment will be the same as your first appointment. You will be invited to attend the AECC University College Clinic at a time convenient to you. You will then be taken through to the x-ray department. Here you will be given the following to complete:

- A pregnancy form (female patients only).
- A set of questionnaires examining pain and physical functioning.

You will then be shown to a changing room and asked to change into a gown. When you return, the radiographer will take your video x-rays and return you to the changing room to change back into your clothes. I will then take you back to clinic reception.

If you would like a copy of your video x-rays, we will arrange this for you. You will be able to pick up your copy from AECC University College Clinic reception.

You have now completed the research trial. We cannot pay you for your participation, however during the trial period all appointments will be free of charge. We cannot reimburse you for travel costs associated with your participation in the research trial. Once the trial is complete, should you wish to continue care at the AECC University College Clinic, you are most welcome to do so at your own cost. You can do this by booking in with your original intern at clinic reception. The intern will have access to all clinical notes taken during the trial.

What are the advantages and possible disadvantages or risks of taking part?

Risk of x-rays:

If you take part in this study, you will have quantitative fluoroscopy (video x-rays). These will be extra to those that you would have if you did not take part. These procedures use ionising radiation to form images of your body. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. Therefore, it is important you understand the risks and benefits of taking part.

We are all at risk of developing cancer during our lifetime. The normal risk is that this will happen to 1 in 2 people at some point during their life. The radiation dose from this examination is roughly the same amount of naturally occurring background radiation you would receive in the UK over an 8-month period. Experts agree that it is very difficult to determine the risk of inducing cancer from such low doses, however it is estimated that there is a 1 in 13 000 extra chance of getting cancer from this examination. You may wish to consider this risk in relation to some more familiar events as in table 1. There is no direct benefit to you from the radiation dose; however, the risk is seen as minimal.

Table 1: Risk in relation to familiar events

Some familiar risks	**Chance they will happen**
Getting four balls in the UK national lottery (Lottery.co.uk/lotto/odds)	1 in 2 180
Dying from Sunstroke (https://www.statista.com/chart/16647/the-lifetime-odds-of-dying-from-selected-causes/ 2017)	1 in 8 912
Dying from Canoeing (National Center for Health Statistics 2018)	1 in 10 000
Dying from Mountain Hiking (National Center for Health Statistics 2018)	1 in 15 700
Dying at a Dance Party (National Center for Health Statistics 2018)	1 in 100 000
Getting five balls in the UK national lottery (Lottery.co.uk/lotto/odds)	1 in 144 415

There is also a chance that an 'incidental' finding will be seen on your video x-ray. An incidental finding is one that is discovered unintentionally. To date, over 500 patients have undergone this examination and there have been no significant incidental findings. As a trained chiropractor I am trained to interpret these examinations and if necessary, they will be reviewed by a chiropractor with specialised training in interpreting x-rays. In the event of an incidental finding you will be referred to your GP if that is what you would like. Your GP will be able to help you receive further tests if necessary. Such detection has the benefit of starting treatment early but in a small number of cases may have implications for future employment and insurance.

Risk of spinal manipulative therapy:

Around 50 – 67% of people treated with any type of manual therapy (for example spinal manipulation, joint mobilisation, massage, and trigger point muscle therapy) can expect mild temporary increased discomfort after treatment. This might include mild bruising from trigger point muscle therapy or tenderness related to spinal manipulation or mobilisation.

Spinal manipulation of the lower back is considered very low risk. It has been calculated that the possibility of a serious reaction to spinal manipulation happens in less than 1 in 1

million – 128 million manipulations. In the event of a serious reaction to spinal manipulation, I will ensure that you receive appropriate advice, treatment, or care.

Benefits of taking part:

Both home management as well as spinal manipulative therapy have been shown to be effective for short-term pain relief. There may not be any direct benefit to you from this study, but it is hoped that the information received might help improve the diagnosis and treatment of patients with low back pain in the future.

What type of information will be sought from me and why is the collection of this information relevant for achieving the research project's objectives?

1. Access to your AECC University College Clinic file. This file contains details of your medical history which you supplied at your New Patient Examination at the AECC Clinic, as well as the notes taken by your intern from the chiropractic examination. Your interns' notes give details of what examinations have been done and their findings. This will help me to determine if you are eligible for the trial or not. It is possible that if some examinations are too painful for you to perform, you may not be able to complete the trial. The researcher will be adding your trial notes to your Clinic file notes to allow continuation of care after you have completed the trial.
2. You will be asked to complete pre-study participations forms. These forms help me to ensure that it is appropriate and safe for you to have a moving x-ray taken of your spine.
3. You will be asked to complete a physical functioning questionnaire and a pain questionnaire. These questionnaires are called outcomes measures and are used to assess if you are getting better or not. They are done once at the beginning of the trial and once at the end of the trial to look at your progress.
4. The motion x-rays will be taken of your lower back to assess movement of your spine. They will be done once at the beginning of the trial and once at the end of the trial to compare changes to the movement of your spine.

How will my information be kept?

All the information we collect about you during the course of this research will be kept strictly in accordance with EU General Data Protection Regulation or GDPR. Research is a task that we perform in the public interest, as part of our core function as a university. Bournemouth University (BU) is a Data Controller of your information which means that we are responsible for looking after your information and using it appropriately. BU's Research Participant Privacy Notice sets out more information about how we fulfil our responsibilities as a data controller and about your rights as an individual under the data protection legislation. We ask you to read this Privacy Notice (https://intranetsp.bournemouth.ac.uk/documentsrep/Research%20Participant%20Privacy%20Notice.pdf) so that you can fully understand the basis on which we will process your information. This notice is available as a hard copy.

In Summary, the Privacy Notice says BU must:

- Take steps to ensure your data is accurate and up to date
- Keep your data secure (please see sections below for how we will keep your data secure and how long we will hold identifiable data)
- Use your data only for the specific purposes described to you in this Participant Information Sheet

Publication

You will not be able to be identified in any reports or publications about the research without your specific consent. Otherwise, your information will only be included in these materials in an anonymous form, i.e., you will not be identifiable.

Research results will be published in peer-reviewed scientific journals and presented at national and international research conferences. Overall results will be available to all participants by email once the study is complete.

Security and access controls

BU and AECC will hold the information we collect about you in hard copy in a secure location, and on a BU and AECC password protected secure network where held electronically.

Except where it has been anonymised your personal information will be accessed and used only by appropriate, authorised individuals and when this is necessary for the purposes of the research, or another purpose identified in the Privacy Notice. This may include giving access to BU staff or others responsible for monitoring and/or audit of the study, who need to ensure that the research is complying with applicable regulations.

During recruitment for the trial and the trial itself, I will be accessing and adding the trial notes to your AECC University College Clinic file. During this time, your data will not be anonymised, and you will be identifiable. However, your clinic file will not leave the premises of the AECC University College Clinic and will be stored securely. Once your participation in the trial is complete, your trial questionnaires and moving x-rays will be saved to a password protected secure network using a unique trial number and you will no longer be identifiable. This anonymous data will be transferred to an AECC University College password protected secure network for analysis of your motion x-rays and questionnaires.

Sharing and further use of your personal information

As well as BU staff and AECC University College staff working on the research project, we may also need to share personal information in non-anonymised for with your GP, but only with your permission.

The information collected about you may be used in an anonymous form to support other research projects in the future and access to it in this form will not be restricted. It will not be possible for you to be identified from this data. Anonymised data will be added to BU's Data Repository (https://research.bournemouth.ac.uk/research-environment/research-data-management/) (a central location where data is stored) and which will be publicly available. This notice is available as a hard copy, please ask me for a copy.

Retention of your data

All personal data collected during the study related to your chiropractic examination, treatment of your back pain and completed questionnaires will be added to your AECC University College Clinic file. This clinic file will be held in accordance with the AECC

University College Patient Privacy Notice (https://www.aecc.ac.uk/media/5190/patient-privacy-notice-updated-may-2018.pdf).

All data collected during the study for research analysis (questionnaire data and motion x-ray data) will be anonymised and stored on a secure networked, password protected computer.

Although published research outputs are anonymised, we need to retain underlying data collected for the study in a non-anonymised form until all participants have completed the trial and the PhD is complete (September 2022) to enable the research to be audited and/or to enable the research findings to be verified.

Contact for further information

If you have any questions or would like further information, please contact Jacqui Rix (rixj@bournemouth.ac.uk). Alternatively, you can contact Jacqui via the AECC University College Clinic reception 01202 436 222.

Supervisory Team:

Lead supervisor: Dr Philip Sewell, Head of Department of Design and Engineering, psewell@bournemouth.ac.uk

AECC University College Director of Clinic:

Dr Neil Osborne, nosborne@aecc.ac.uk

In case of complaints

Any concerns about the study should be directed to the primary supervisor, Philip Sewell. If you concerns have not been answered by, you should contact Professor Tiantian Zhang, Deputy Dean for Research & Professional Practice, Faculty of Science and Technology, Bournemouth University by email to researchgovernance@bournemouth.ac.uk.

Finally, if you decide to take part, you will be given a copy of the information sheet and a signed participant agreement form to keep.

Thank you for considering taking part in this research project.

Appendix D: Consent Form

AECC University College
Transforming lives through Health Sciences

Bournemouth University

IRAS number: 271970

Version: V1.0

Date: 31.10.2019

Consent Form

Full title of project: The Biomechanical Effects of Manual Therapy - A Feasibility Study.

Name, position and contact details of researcher: Jacqueline Rix, PhD student (rixj@bournemuth.ac.uk)

Name, position and contact details of supervisor: Dr Philip Sewell, Head of Department of Design and Engineering, psewell@bournemouth.ac.uk, 01202 961294.

Section A: Agreement to participate in the study

You should only agree to participate in the study if you agree with all of the statements in this table and accept that participating will involve the listed activities.

	Initial boxes to agree
I have read and understood the Participant Information Sheet (Version 2.0 date: 23.01.2020) and have been given access to the BU Research Participant Privacy Notice which sets out how we collect and use personal information (https://www1.bournemouth.ac.uk/about/governance/access-information/data-protection-privacy).	
I have had an opportunity to consider the Participant Information Sheet, ask questions and have had these answered satisfactorily.	
I understand that my participation is voluntary. I am free to withdraw from research activities at any time without giving a reason, without my medical care or legal rights being affected.	

I understand that the Chief Investigator (Jacqueline Rix) may access my AECC University College Clinic file. I give permission for these individuals to have access to my records.	
I understand that taking part in the research will include the following activity/activities as part of the research: • Attending a first appointment during which a motion x-ray will be taken, and questionnaires will be filled in. • Participate in one of the randomly assigned groups • Attending a final appointment during which a motion x-ray will be taken, and questionnaires will be filled in.	
I understand that, if I withdraw from the study, I will also be able to withdraw my data from further use in the study **except** where my data has been anonymised (as I cannot be identified) or it will be harmful to the project to have my data removed.	
I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from Bournemouth University where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
I understand that my data will be included in an anonymised form within a dataset to be archived at BU's Online Research Data Repository (BORDaR).	
I understand that my data may be used in an anonymised form by the research team to support other research projects in the future, including future publications, reports or presentations.	

	Initial box to agree
I agree to take part in the project on the basis set out in the Participant Information Sheet (V2.0 date: 23.01.2020)	

Section B: The following parts of the study are optional

You can decide about each of these activities separately. Even if you do not agree to any of these activities you can still take part in the study. If you do not wish to give permission for an activity, do not initial the box next to it.

	Initial boxes to agree
I would like the researcher to contact my GP and inform them that I am taking part in this research trial.	
I agree that BU researchers may contact my GP as described in the Participant Information Sheet with reference to incidental radiographic findings.	
I am interested in the overall results of the research. I would like the overall results emailed to me upon completion of the research. I agree to my email address being used for this purpose. • My email address is: _____	
I am interested in my motion x-ray (quantitative fluoroscopy). I would like a copy of all my motion x-rays taken during the time of the research. I agree to be contacted by the researcher to arrange collection or delivery of my motion x-rays. I would prefer a DVD/ memory stick (please delete as applicable).	

I confirm my agreement to take part in the project on the basis set out above.

Name of participant (BLOCK CAPITALS)	Date (dd/mm/yyyy)	Signature
Name of researcher (BLOCK CAPITALS)	Date (dd/mm/yyyy)	Signature

Appendix E: Pre-Fluoroscope Consent Form

AECC University College
Transforming lives through Health Sciences

Bournemouth University

PRE-FLUOROSCOPY CONSENT (Baseline Data Collection)

First Name: _____ Surname: _____

Telephone (home)_____mobile: _____

Email: _____

Date of Birth: (DD/MM/YYYY) _____Sex: (M/F)_____

Height: _____Weight: _____BMI: _____

Please answer the following questions:

	Yes	No
Have you had abdominal or pelvic surgery in the last year?		
Have you ever had low back surgery?		
Have you had a CT scan of your chest, abdomen, or pelvis in the last 2 years?		
Have you had an interventional procedure under radiological control (such as an angiograph) in the last two years?		
Do you have a scoliosis or sideways bending of the spine?		
Are you participating in any other research study at the moment?		

FEMALE PARTICIPANTS ONLY

If you are pregnant, or think you might be, it is best to avoid radiation exposure unless your practitioner or doctor decides it is very urgent.

Advice from the Health protection Agency and the Royal College of Radiologists requires us to establish if there is any possibility of pregnancy before this examination is undertaken. This MUST be established in female patients between the ages of 10 to 55years. We therefore require that you sign below to state that you have understood the statement above and that to the best of your knowledge you are not pregnant.

	Yes	No
Are you, or is there any possibility you could be pregnant?		
Is your menstrual period overdue?		

If you would like the opportunity to discuss this with a clinical member of staff or Jacqui Rix please ask to do so before your examination.

I consent to a fluoroscopic investigation as outlined in the Participant Information Sheet.

Participant's signature_____Date_____

Radiologist/ CI signature _____Date_____

PRE-FLUOROSCOPY CONSENT (Follow Up Data Collection)

FEMALE PARTICIPANTS ONLY

If you are pregnant, or think you might be, it is best to avoid radiation exposure unless your practitioner or doctor decides it is very urgent.

Advice from the Health protection Agency and the Royal College of Radiologists requires us to establish if there is any possibility of pregnancy before this examination is undertaken. This MUST be established in female patients between the ages of 10 to 55years. We therefore require that you sign below to state that you have understood the statement above and that to the best of your knowledge you are not pregnant.

	Yes	**No**
Are you, or is there any possibility you could be pregnant?		
Is your menstrual period overdue?		

If you would like the opportunity to discuss this with a clinical member of staff or Jacqui Rix, please ask to do so before your examination.

I consent to a fluoroscopic investigation as outlined in the Participant Information Sheet.

Participant's signature_____ Date_____

Radiologist/ CI signature _____ Date_____

AECC University College
Transforming lives through Health Sciences

Bournemouth University

PRE-TREATMENT QUESTIONNAIRES: | STUDY NUMBER: DATE:

PART 1: BOURNEMOUTH QUESTIONNAIRE (PRE-TREATMENT SCREENING VISIT)

Instructions: Put an "X" in ONE box for EACH of the following statements that best describes your painful complaint and how it is affecting you. Please read each question carefully before answering. Thank you.

Q1 Over the last few days, on average, how would you rate your pain on a scale where "0" is "no pain" and "10" is the "worst pain possible"?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Q2 Over the past few days, on average, how much has your complaint interfered with your normal daily activities (housework, washing, dressing, lifting, walking, reading, driving, climbing stairs, getting in/out of bed/chair, sleeping) on a scale where "0" is "no interference" and "10" is "completely unable to carry on with normal daily activities"?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Q3 Over the past few days, on average, how much has your painful complaint interfered with your normal social routine including recreational, social and family activities, on a scale where "0" is "no interference" and "10" is "completely unable to participate in any social and recreational activity"?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Q4 Over the past few days, on average, how anxious ("uptight", tense, irritable, difficulty in relaxing/concentrating) have you been feeling, on a scale where "0" is "not at all anxious" and "10" is "extremely anxious"?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Q5 Over the last few days, how depressed (ie "down-in-the-dumps", sad, "in low spirits", pessimistic, lethargic) have you been feeling, on a scale where "0" is "not at all depressed" and "10" is "extremely depressed"?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Q6 Over the past few days, how do you think your work (both inside the home and/or employed work) has affected your painful complaint, on a scale where "0" is "makes it no worse" and "10" is "makes it very much worse"?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Q7 Over the past few days, on average, how much have you been able to control (help/reduce) and cope with your pain on your own, on a scale where "0" is "I can control it completely" and "10" is "I have no control whatsoever"?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

PART 2: THE ROLAND-MORRIS DISABILITY QUESTIONNAIRE

When your back hurts, you may find it difficult to do some of the things you normally do. This list contains sentences that people have used to describe themselves when they have back pain. When you read them, you may find that some stand out because they describe you today.

As you read the list, think of yourself today. **When you read a sentence that describes you today, put a tick against it**. If the sentence does not describe you, then leave the space blank and go on to the next one. Remember, only tick the sentence if you are sure it describes you today.

	Tick the box if the sentence applies to you
I stay at home most of the time because of my back	
I change position frequently to try and get my back comfortable.	
I walk more slowly than usual because of my back.	
Because of my back I am not doing any of the jobs that I usually do around the house.	
Because of my back, I use a handrail to get upstairs.	
Because of my back, I lie down to rest more often.	
Because of my back, I have to hold on to something to get out of an easy chair.	
Because of my back, I try to get other people to do things for me.	

I get dressed more slowly than usual because of my back.	
I only stand for short periods of time because of my back.	
Because of my back, I try not to bend or kneel down.	
I find it difficult to get out of a chair because of my back.	
My back is painful almost all the time.	
I find it difficult to turn over in bed because of my back.	
My appetite is not very good because of my back pain.	
I have trouble putting on my socks (or stockings) because of the pain in my back.	
I only walk short distances because of my back.	
I sleep less well because of my back.	
Because of my back pain, I get dressed with help from someone else.	
I sit down for most of the day because of my back.	
I avoid heavy jobs around the house because of my back.	
Because of my back pain, I am more irritable and bad tempered with people than usual.	
Because of my back, I go upstairs more slowly than usual.	
I stay in bed most of the time because of my back.	

PART 3: MEDICATION

1. Have you been taking any analgesics (pain killers) for your low back pain?

If you have answered 'yes' to question 1, please fill in the table below:

Medication name	What dose are you taking and how often are you taking this dose per day?

AECC University College
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Bournemouth University

POST-TREATMENT QUESTIONNAIRES:

STUDY NUMBER: DATE:

PART 1: BOURNEMOUTH QUESTIONNAIRE (POST-TREATMENT SCREENING VISIT)

Instructions: Put an "X" in ONE box for EACH of the following statements that best describes your painful complaint and how it is affecting you. Please read each question carefully before answering. Thank you.

Q1 Over the last few days, on average, how would you rate your pain on a scale where "0" is "no pain" and "10" is the "worst pain possible"?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Q2 Over the past few days, on average, how much has your complaint interfered with your normal daily activities (housework, washing, dressing, lifting, walking, reading, driving, climbing stairs, getting in/out of bed/chair, sleeping) on a scale where "0" is "no interference" and "10" is "completely unable to carry on with normal daily activities"?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Q3 Over the past few days, on average, how much has your painful complaint interfered with your normal social routine including recreational, social and family activities, on a scale where "0" is "no interference" and "10" is "completely unable to participate in any social and recreational activity"?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Q4 Over the past few days, on average, how anxious ("uptight", tense, irritable, difficulty in relaxing/concentrating) have you been feeling, on a scale where "0" is "not at all anxious" and "10" is "extremely anxious"?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Q5 Over the last few days, how depressed (ie "down-in-the-dumps", sad, "in low spirits", pessimistic, lethargic) have you been feeling, on a scale where "0" is "not at all depressed" and "10" is "extremely depressed"?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Q6 Over the past few days, how do you think your work (both inside the home and/or employed work) has affected your painful complaint, on a scale where "0" is "makes it no worse" and "10" is "makes it very much worse"?

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Q7 Over the past few days, on average, how much have you been able to control (help/reduce) and cope with your pain on your own, on a scale where "0" is "I can control it completely" and "10" is "I have no control whatsoever"?

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Q8 Since beginning your treatment at this clinic, how would you describe the change (if any) in ACTIVITY LIMITATIONS, SYMPTOMS, EMOTIONS, and OVERALL QUALITY OF LIFE, related to your painful condition:

No change (or condition has worsened)		Moderately better and a slight but noticeable difference	
Almost the same, hardly any change at all		Better and a definite improvement that has made a real and worthwhile difference	
A little better, but no noticeable change		Great deal better and a considerable improvement that has made all the difference	
Somewhat better, but the change has not made any real difference			

PART 2: THE ROLAND-MORRIS DISABILITY QUESTIONNAIRE

When your back hurts, you may find it difficult to do some of the things you normally do. This list contains sentences that people have used to describe themselves when they have back pain. When you read them, you may find that some stand out because they describe you today.

As you read the list, think of yourself today. **When you read a sentence that describes you today, put a tick against it**. If the sentence does not describe you, then leave the space blank and go on to the next one. Remember, only tick the sentence if you are sure it describes you today.

	Tick the box if the sentence applies to you
I stay at home most of the time because of my back.	
I change position frequently to try and get my back comfortable.	
I walk more slowly than usual because of my back.	
Because of my back I am not doing any of the jobs that I usually do around the house.	
Because of my back, I use a handrail to get upstairs.	
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Because of my back, I have to hold on to something to get out of an easy chair.	
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I get dressed more slowly than usual because of my back.	
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Because of my back, I try not to bend or kneel down.	
I find it difficult to get out of a chair because of my back.	
My back is painful almost all the time.	
I find it difficult to turn over in bed because of my back.	
My appetite is not very good because of my back pain.	
I have trouble putting on my socks (or stockings) because of the pain in my back.	
I only walk short distances because of my back.	

I sleep less well because of my back.	
Because of my back pain, I get dressed with help from someone else.	
I sit down for most of the day because of my back.	
I avoid heavy jobs around the house because of my back.	
Because of my back pain, I am more irritable and bad tempered with people than usual.	
Because of my back, I go upstairs more slowly than usual.	
I stay in bed most of the time because of my back.	

PART 3: MEDICATION

1. Have you been taking any analgesics (pain killers) for your low back pain?

If you have answered 'yes' to question 1, please fill in the table below:

Medication name	What dose are you taking and how often are you taking this dose per day?

Appendix G: Sponsorship

Bournemouth University

To: NHS RESEARCH ETHICS COMMITTEE

Project Title: The Biomechanical Effects of Manual Therapy – A Feasibility Study

As Project Sponsor, Bournemouth University agrees to ensure:

- The research proposal respects the dignity, rights, safety and well-being of participants
- The research proposal is worthwhile and of high scientific quality
- Arrangements proposed for the research are consistent with the UK Policy Framework for Health and Social Care Research
- That organisations and individuals involved in the research have or will agree the division of responsibilities between them

Signature of authorised signatory on behalf of Bournemouth University: .....

Name: Mrs Julie Northam

Role: Head, Research Development & Support

Date: 18/10/2019

Melbury House
1-3 Oxford Road
Bournemouth, BH8 8ES
United Kingdom

01202 961200
www.bournemouth.ac.uk

VAT Reg. No. GB 504 4921 66

Appendix H: REC Favourable Opinion

NHS
Health Research Authority

East of England - Cambridge Central Research Ethics Committee
Royal Standard Place
Nottingham
NG1 6FS

06 February 2020

Mrs Jacqueline Rix
Bournemouth University
PGR student postbox, P519 Poole House, Fern Barrow
Poole
BH12 5BB

Dear Mrs Rix

Study title:	**The Biomechanical Effects of Spinal Manipulation - A Feasibility Study**
REC reference:	**20/EE/0001**
Protocol number:	**n/a**
IRAS project ID:	**271970**

Thank you for your letter of 28 January 2020, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Alternate Vice-Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

It is a condition of the REC favourable opinion that **all clinical trials are registered** on a publicly accessible database. For this purpose, 'clinical trials' are defined as the first four project categories in IRAS project filter question 2. Registration is a legal requirement for clinical trials of investigational medicinal products (CTIMPs), except for phase I trials in healthy volunteers (these must still register as a condition of the REC favourable opinion).

Registration should take place as early as possible and within six weeks of recruiting the first research participant at the latest. Failure to register is a breach of these approval conditions, unless a deferral has been agreed by or on behalf of the Research Ethics Committee (see here for more information on requesting a deferral:
https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/

As set out in the UK Policy Framework, research sponsors are responsible for making information about research publicly available before it starts e.g. by registering the research project on a publicly accessible register. Further guidance on registration is available at:
https://www.hra.nhs.uk/planning-and-improving-research/research-planning/transparency-responsibilities/

You should notify the REC of the registration details. We will audit these as part of the annual progress reporting process.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

After ethical review: Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study, including early termination of the study
- Final report

The latest guidance on these topics can be found at
https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/.

Ethical review of research sites

NHS/HSC sites

The favourable opinion applies to all NHS/HSC sites listed in the application subject to confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or management permission (in Scotland) being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS/HSC sites

I am pleased to confirm that the favourable opinion applies to any non-NHS/HSC sites listed in the application, subject to site management permission being obtained prior to the start of the study at the site.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering letter on headed paper [Cover letter]		01 November 2019
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Sponsor Insurance Confirmation]		31 October 2019
GP/consultant information sheets or letters [GP trial participation letter]	Version 1.0	31 October 2019
Letter from sponsor [Confirmation of Sponsorship]		31 October 2019
Other [J Branney (supervisor) CV]		31 October 2019
Other [A Breen (supervisor) CV]		31 October 2019
Other [S Docherty (supervisor) CV]		31 October 2019
Other [Home Management Back Pain Booklet]	Version 1.0	04 November 2019
Other [Cover Letter and Reviewer Response]		27 January 2020
Other [Research Proposal (tracked changes)]	Version 2.0	27 January 2020
Other [Research Proposal PDF]	Version 2.0	27 January 2020
Other [BU Research Participant Privacy Notice]		27 January 2020
Participant consent form [Consent Form]	Version 1.0	31 October 2019
Participant information sheet (PIS) [Participant Information Sheet (tracked changes)]	Version 2.0	27 January 2020
Participant information sheet (PIS) [Participant Information Sheet PDF]	Version 2.0	27 January 2020
REC Application Form [REC_Form_28012020]		28 January 2020
Summary CV for Chief Investigator (CI) [Jacqueline Rix CV]		31 October 2019
Summary CV for supervisor (student research) [Philip Sewell (lead supervisor) CV]		31 October 2019
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Methods flow diagram]	Version 1.0	31 October 2019
Validated questionnaire [Forms and Questionnaires (tracked changes)]		27 January 2020
Validated questionnaire [Forms and Questionnaires PDF]		27 January 2020

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at:
https://www.hra.nhs.uk/planning-and-improving-research/learning/

20/EE/0001	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

pp

Revd Dr Derek Fraser
Alternate Vice Chair

Email: NRESCommittee.EastofEngland-CambridgeCentral@nhs.net

Copy to: Mrs Julie Northam

Appendix I: Approval for Continuation of Research (Feasibility Study)

Bournemouth University

14th July 2020

REQUEST TO RESUME RESEARCH ACTIVITIES: Biomechanical Effects of Manual Therapy – A Feasibility Study.

Dear Jacqui,

Many thanks for adhering to the Return to Research Process.

I can confirm that we are in receipt of the documentation as follows:

- Risk assessments, including how the Covid-19 associated risks will be minimised, which have been approved by your Faculty Director of Operations.
- Return to research form, which has been endorsed by your Faculty Deputy Dean for Research & Professional Practice.
- Approval from our partners at AECC to restart as articulated
- Confirmation that ethics re-approval is not required.

Therefore, this project can now resume with immediate effect.

Can I take this opportunity to remind you of the importance of adhering to any updated guidance with regards to Covid-19 precautionary measures from both the University and government. It is your responsibility to ensure your activities are fully compliant at all times.

My colleagues within RDS will be in-touch on a regular basis to review activity.

Thank you again for your due consideration and I trust the remainder of this research goes as planned. We will await with interest on news of the results!

Yours sincerely,

Dr Rebecca Edwards
Research Programme Manager, Research Development and Support

Melbury House, M406,
1-3 Oxford Road,
Bournemouth, Dorset BH8 8ES
United Kingdom

Tel: +44 (0) 1202 961538
Email: jnortham@bournemouth.ac.uk
Web: www.bournemouth.ac.uk

VAT Reg No. GB 504 4921 66

Bournemouth University

5th November 2020

REQUEST TO RESUME RESEARCH ACTIVITIES: Biomechanical Effects of Manual Therapy – A Feasibility Study.

Dear Jacqui,

Many thanks for adhering to the updated Return to Research Process.

I can confirm that we are in receipt of the documentation as follows:

- An updated risk assessment, including how the Covid-19 associated risks will be minimised, which has been approved by your Faculty Health and Safety Advisor.
- Approval from the Faculty's Executive Dean that the research may continue during this new lockdown period.
- Approval from our partners at AECC to continue the research. This is in line with government guidelines part 3, item 47 (Health Protection (Coronavirus Restrictions) (England) 2020.

This project may continue with immediate effect.

Can I take this opportunity to remind you of the importance of adhering to any updated guidance with regards to Covid-19 precautionary measures from both the University and government. It is your responsibility to ensure your activities are fully compliant at all times.

My colleagues within RDS will be in-touch on a regular basis to review activity.

Thank you again for your due consideration and I trust the remainder of this research goes as planned. We will await with interest on news of the results!

Yours sincerely,

Suzy Wignall
Clinical Governance Advisor, Research Development and Support

Melbury House, M406,
1-3 Oxford Road,
Bournemouth, Dorset BH8 8ES
United Kingdom

Tel: +44 (0) 1202 961538
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VAT Reg No. GB 504 4921 66

Bournemouth University

12th January 2021

REQUEST TO RESUME RESEARCH ACTIVITIES: Biomechanical Effects of Manual Therapy – A Feasibility Study.

Dear Jacqui,

Many thanks for adhering to the updated Return to Research Process following the start of a third UK lockdown.

I can confirm that we are in receipt of the documentation as follows:

- A risk assessment, including how the Covid-19 associated risks will be minimised, which has been approved by your Faculty Health and Safety Advisor.
- Approval from the Faculty's Deputy Dean for Research & Professional Practice that the research may continue during this new lockdown period.
- Approval from our partners at AECC to continue the research which is operating under Public Health England guidelines.

This project may continue with immediate effect.

Can I take this opportunity to remind you of the importance of adhering to any updated guidance with regards to Covid-19 precautionary measures from both the University and government. It is your responsibility to ensure your activities are fully compliant at all times.

My colleagues within RDS will be in-touch on a regular basis to review activity.

Thank you again for your due consideration and I trust the remainder of this research goes as planned. We will await with interest on news of the results!

Yours sincerely,

Suzy Wignall
Clinical Governance Advisor, Research Development and Support

Melbury House, M406,
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VAT Reg No. GB 504 4921 66

Appendix J: Home Management Booklet

BACK PAIN BOOKLET

This booklet forms part of the treatment protocol for participants enrolled onto the study entitled: The Biomechanical Effects of Manual Therapy - A Feasibility Study.

IRAS number: 271970

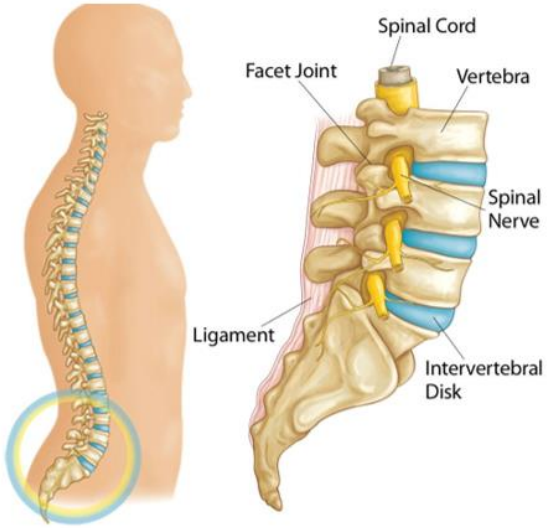
REC Reference: 20/EE/0001

Contents:

Your Back:

Your back is very strongly built. It is made up of a column of bones called vertebrae. At the top of this column is the skull and at the bottom of the column is the pelvis. There are 24 individual vertebrae which make up the spinal column. There are seven vertebrae in the neck or cervical spine; twelve vertebrae in the torso or thoracic spine; and five vertebrae in the lower back or lumbar spine.

Between the vertebrae is a disc, which has a jelly-like centre and is surrounded by strong cartilage, as well as two small joints or facets. The vertebrae are held together by very strong ligaments and surrounded by strong muscles which help the bones to move.



Back Pain:

Back pain or discomfort is not usually due to a serious cause. Most back pain is coming from your muscles, ligaments and joints in your back not working as they should, which can cause discomfort and stiffness. It is surprisingly difficult to cause damage to your spine. Most people with back pain do not have any damage to their spine. Most x-ray findings of people with back pain may have normal changes that occur with age. This is not necessarily arthritis, but is considered normal, just like grey hair. Very few people have a 'slipped disc' or a trapped nerve.

There is no instant fix or answer to your back pain. You may have good days and bad days for a while, which is completely normal. Although it can be difficult, it helps to stay optimistic and know that your back pain should get better in time.

The following information will help you to manage your back pain when it does occur and look at preventing back pain in the future.

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Stay Active!

In most people, back pain settles quickly and reduces enough to get on with normal life. It can be uncomfortable, and you may need to reduce some of the activities you are doing for a short while when your back pain is bad, but it is best not to rest completely.

Bed rest is not very good for bad backs. You may need to have a day or two in bed in the beginning when your back pain is very bad, but it is good for you to get moving again as soon as you are able to. People who remain active are more likely to recover quicker. Build up your activity level gradually.

Regular physical activity can help keep your back strong and flexible and may prevent recurrent episodes of back pain. Activities such as walking, swimming, exercise bike and Pilates are popular choices. This type of exercise can be done even

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when your back is sore, without putting too much stress on your back.

Managing your back pain:

Medication:

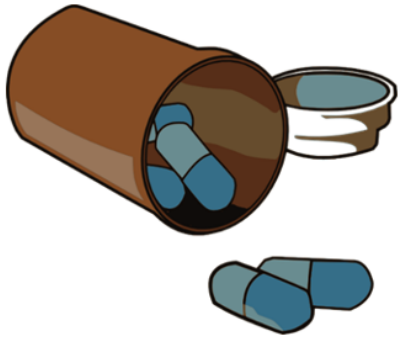
Ibuprofen:

- Non-steroidal anti-inflammatory drug (NSAID) tablets, such as ibuprofen, can help relieve back pain. Many types are available to buy from pharmacies or supermarkets without a prescription.
- NSAIDs are not suitable for everyone. Please check the box or leaflet to see whether you can take the medicine first or speak to a pharmacist if you are not sure.

Paracetamol:

- Paracetamol, on its own, is not recommended for back pain as it may not reduce your pain. It can be used together with ibuprofen or a painkiller prescribed

by your doctor. Please check the box or leaflet to see whether you can take the medicine first or speak to a pharmacist if you are not sure.



Hot and cold packs:

Some people find heat or cold packs help to ease their back pain. There are lots of brands of heat packs and cold packs available from the pharmacy, but it is also easy to make them at home

How to make a heat pack:

1. Fill a hot water bottle with hot water and wrap it in a towel.
2. Place the heat pack on your lower back for 15 – 20 minutes.

How to make a cold pack:

1. Wrap a frozen bag of vegetables or some ice blocks in a tea towel.
2. Place the cold pack on your lower back for 15 – 20 minutes.

Take care when using heat or cold packs as they can burn the skin if they are too hot or too cold, or if they are left in place for longer than the recommended time.

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Some ways to help your back pain:

Poor posture can put strain on ligaments and muscles in your back. Practicing good posture can help prevent back pain.

Sitting:

- Sit with your bottom well back in the chair. The chair should help support your lower back. If your chair does not support your lower back properly, use a cushion or rolled towel in the curve of your lower back.
- Your feet should be flat on the floor. If your feet do not reach the floor, try to adjust the height of the seat or use a footrest.
- Try not to sit for too long at home or at work. Getting up and walking around at least once an hour will keep your back moving.

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At Work:

If you sit at a desk for most of the day:

- Try to stand up or walk around regularly. Try to take your coffee break or lunch away from your desk.
- Make sure you have plenty of leg room under the desk to stretch your legs out and move your legs around regularly.
- Arrange your workspace to make sure your computer screen is directly in front of you and you are not twisted when looking at the screen or using your keyboard and mouse.
- If you use the telephone a lot, you may want to invest in a headset. It is not good for your neck to hold the telephone between your ear and shoulder.
- Ask for advice or an assessment of your workstation or workplace.

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Driving:

- Sit with your bottom well back in the car seat. The car seat should help support your lower back. If your car seat does not support your lower back properly, use a cushion or rolled towel in the curve of your lower back.
- Sit a comfortable distance from the foot pedals and steering wheel.
- If you are driving long distance, take regular breaks to walk around.

Lifting and bending:

It is important to think about your back when lifting objects up off the floor. Here are some handy tips for safe lifting:

- Lift only what you feel you can lift safely.
- Use available equipment to help you. For example, if you are gardening, use a wheelbarrow to move heavy objects.
- Bend your hips and knees to help you lift with your legs, not your back.

- Keep the object close to your body when lifting it and carrying it.
- When turning around, move your feet instead of twisting your body.

Treatment options:

Exercise classes:

Back strengthening exercise and stretching exercises can help reduce back pain. These exercises can be given to you by a chiropractor, osteopath or physiotherapist. The NHS provides some simple back exercises and stretches on their website to help improve strength and flexibility of your lower back (https://www.nhs.uk/live-well/exercise/lower-back-pain-exercises/).

Manual therapy:

Manual therapy is the name for a group of treatments where a therapist uses their hands to move, massage and apply careful force to the muscles, bones and joints in and around your spine. It is usually carried out by a chiropractor, osteopath or physiotherapist. Manual therapy can help reduce your back pain.

Psychological support:

Therapies such as cognitive behavioural therapy (CBT) can help you manage your back pain better by changing how you think about your condition. While the pain in your back is very real, how you think and feel about your condition can make it worse. This is particularly helpful when you have been in pain for a long time, education about pain and the psychology of pain may be offered by your local NHS trust.

When to seek help from your GP or medical professional:

Back pain is rarely being caused by something serious, do not let the following information worry or scare you too much. It is important that you know when to seek help and from whom on the rare chance your back pain is being caused by something serious.

If you have severe back pain which is getting worse over a couple of weeks instead of better, or you are feeling unwell with your back pain, you should go to see your general practitioner (GP).

There are a few symptoms which are extremely rare, but if you do develop any of these with your back pain you should seek help from a

medical professional straight away (your GP or local A and E department):

- Difficulty passing urging or controlling your bladder.
- Numbness around your genital area or back passage.
- Numbness, pins and needles or weakness in both legs.
- Unsteadiness on your feet.

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Further Questions?

If at any time you have questions about this booklet or questions about the study, please contact Jacqui Rix at the AECC University College Clinic (01202 436222).

Written by Jacqueline Rix

Illustrated by Jess Fitzpatrick Illustration

Appendix K: Bournemouth University Research Ethics (Parallel Study)

Bournemouth University

Research Ethics Checklist

About Your Checklist	
Ethics ID	35507
Date Created	13/01/2021 10:45:12
Status	Approved
Date Approved	25/01/2021 18:54:59
Date Submitted	25/01/2021 16:12:57
Risk	Low

Researcher Details	
Name	Jacqui Rix
Faculty	Faculty of Science & Technology
Status	Postgraduate Research (MRes, MPhil, PhD, DProf, EngD, EdD)
Course	Postgraduate Research - FST
Have you received funding to support this research project?	No
Please list any persons or institutions that you will be conducting joint research with, both internal to BU as well as external collaborators.	AECC University College

Project Details	
Title	A retrospective study of the potential pool of research participants with non-specific low back pain at an outpatient manual therapy clinic pre- and post-Covid 19. A parallel study to the 'Biomechanical Effects of Manual Therapy - A Feasibility Study
Start Date of Project	08/01/2021
End Date of Project	01/04/2021
Proposed Start Date of Data Collection	01/02/2021
Original Supervisor	Philip Sewell
Approver	Yi Huang

Appendix L: AECC University College Research Ethics (Parallel Study)

Jacqueline Rix

From: Jane Sutherland
Sent: 03 February 2021 09:13
To: Jacqueline Rix
Cc: David Newell (EX)
Subject: RE: AECC Ethics Application

Dear Jacqui

Thanks for submitting the ethics application and decision you have gained from BU University for your study 'A re**trospective study of the potential pool of research participants with non-specific low back pain at an outpatient manual therapy clinic pre- and post-Covid 19. A parallel study to the 'Biomechanical Effects of Manual Therapy - A Feasibility Study'**

I note that ethical approval has been given by BU University and in accordance with our existing Ethics Policy under section 7.2 (see below), I am happy to grant approval for this project.

Page 9, AECC University College Research Ethics Policy and Procedures:
NHS/ external ethical approval: Projects which require NHS or another external ethical approval, the researcher submits their application to the relevant body. Research involving the NHS, including patients (see 8.3), carers or data must gain ethical approval from NRES. The approval document must be submitted to the RESC via the Chair as evidence for auditing purposes

Jane (on behalf of Dave Newell)

Jane Sutherland
Course Administrator
msc@aecc.ac.uk

AECC University College

Appendix M: Approval for Continuation of Research (Parallel Study)

Bournemouth University

26th January 2021

REQUEST TO RESUME RESEARCH ACTIVITIES: *A retrospective study of the potential pool of research participants with non-specific low back pain at an outpatient manual therapy clinic pre- and post-Covid 19. A parallel study to the 'Biomechanical Effects of Manual Therapy - A Feasibility Study*

Dear Jacqui,

Many thanks for adhering to the Return to Research Process.

I can confirm that we are in receipt of the documentation as follows:

- Risk assessments, including how the Covid-19 associated risks will be minimised, which have been approved by your Faculty Health and Safety Adviser.
- Return to research form, which has been endorsed by your Faculty Deputy Dean for Research & Professional Practice.
- Approval from our partners at AECC to restart as articulated
- Bournemouth University research ethics favourable opinion (approved by Faculty Ethics Champion).

Therefore, this project can now resume with immediate effect.

Can I take this opportunity to remind you of the importance of adhering to any updated guidance with regards to Covid-19 precautionary measures from both the University and government. It is your responsibility to ensure your activities are fully compliant at all times.

My colleagues within RDS will be in-touch on a regular basis to review activity.

Thank you again for your due consideration and I trust the remainder of this research goes as planned. We will await with interest on news of the results!

Yours sincerely,

Suzy Wignall
Clinical Governance Advisor, Research Development and Support

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VAT Reg No. GB 504 4921 66

Appendix N: Covid-19 Screening Questionnaire

Covid-19 face-to-face appointment screening questionnaire

PATIENT NAME: PRACTITIONER NAME:

DATE: FILE NUMBER:

TIME of APPOINTMENT:

During the last 14 days, have you or any of your household had any Symptoms of Covid-19? (details if yes):
(e.g. New continuous cough, High Temperature (>37.8deg C), Unusual/excessive fatigue, Loss of taste and/or smell, Tightness in chest/Shortness of breath)

Yes / No

Patients temperature within normal range (<37.8deg C) Yes / No

Are you part of an increased-risk group? Yes / No

Practitioner Decision – Patient OK to proceed into clinic? Yes / No

Practitioner signature: .....

During the past 14 days, have you and your household engaged with all local Covid-19 guidance

Yes / No

Can you confirm that if you do develop symptoms of Covid-19 **OR** are in close contact with someone who does, you will cancel your appointment and advise the Clinic.

Yes / No

Can you confirm that you understand that there are new procedures in place to maintain a safe environment but that a risk remains. Do you accept that the risk has been mitigated as much as possible by these procedures, and that you will adhere to the instructions provided?

Yes / No

Patient Signature: .....

Date: .....

Id: Clinic\Private Domain\CLINIC ADMIN\Forms (Copy from Management Admin)\Car Park COVID-19 questionnaire – Jan 2021

Appendix O: Table of Sample Size Calculations

Variable	Sample Size	n1	n2	20% for drop out
Flex WB L2-L3 Vert Ang. RoM	150	75	75	187.5
Flex WB L3-L4 Vert Ang. RoM	480	240	240	600
Flex WB L4-L5 Vert Ang. RoM	54	27	27	67.5
Flex WB L5-S1 Vert Ang. RoM	4358	2179	2179	5447.5
Flex WB L2-L3 Laxity	66492	33246	33246	83115
Flex WB L3-L4 Laxity	150	75	75	187.5
Flex WB L4-L5 Laxity	66	33	33	82.5
Flex WB L5-S1 Laxity	176	88	88	220
Flex WB L2-L3 Translation	766	383	383	957.5
Flex WB L3-L4 Translation	21762	10881	10881	27202.5
Flex WB L4-L5 Translation	240	120	120	300
Flex WB L5-S1 Translation	220	110	110	275
Flex WB MSV	82	41	41	102.5
Flex WB MSI	262	131	131	327.5
Ext WB L2-L3 Vert Ang. RoM	346	173	173	432.5
Ext WB L3-L4 Vert Ang. RoM	76	38	38	95
Ext WB L4-L5 Vert Ang. RoM	40	20	20	50
Ext WB L5-S1 Vert Ang. RoM	1332	666	666	1665
Ext WB L2-L3 Translation	110	55	55	137.5
Ext WB L3-L4 Translation	44	22	22	55
Ext WB L4-L5 Translation	78	39	39	97.5
Ext WB L5-S1 Translation	1066	533	533	1332.5
Ext WB L2-L3 Laxity	794	397	397	992.5
Ext WB L3-L4 Laxity	116	58	58	145
Ext WB L4-L5 Laxity	52	26	26	65
Ext WB L5-S1 Laxity	22	11	11	27.5
Ext WB MSV	134	67	67	167.5
Ext WB MSI	182	91	91	227.5
DH Dif L2-L3 WB	108	54	54	135
DH Dif L3-L4 WB	590	295	295	737.5
DH Dif L4-L5 WB	88	44	44	110
DH Dif L5-S1 WB	168	84	84	210
Flex Rec L2-L3 Vert Ang. RoM	8	4	4	10
Flex Rec L3-L4 Vert Ang. RoM	668	334	334	835
Flex Rec L4-L5 Vert Ang. RoM	114	57	57	142.5
Flex Rec L5-S1 Vert Ang. RoM	94	47	47	117.5
Flex Rec L2-L3 Translation	7846	3923	3923	9807.5
Flex Rec L3-L4 Translation	1160	580	580	1450
Flex Rec L4-L5 Translation	546	273	273	682.5
Flex Rec L5-S1 Translation	1766	883	883	2207.5

Flex Rec L2-L3 Laxity	1216	608	608	1520
Flex Rec L3-L4 Laxity	344	172	172	430
Flex Rec L4-L5 Laxity	154	77	77	192.5
Flex Rec L5-S1 Laxity	606	303	303	757.5
Flex rec MSV	116	58	58	145
Flex rec MSI	46	23	23	57.5
Ext Rec L2-L3 Vert Ang. RoM	214	107	107	267.5
Ext Rec L3-L4 Vert Ang. RoM	140	70	70	175
Ext Rec L4-L5 Vert Ang. RoM	148	74	74	185
Ext Rec L5-S1 Vert Ang. RoM	240	120	120	300
Ext Rec L2-L3 Translation	242	121	121	302.5
Ext Rec L3-L4 Translation	26	13	13	32.5
Ext Rec L4-L5 Translation	204	102	102	255
Ext Rec L5-S1 Translation	124	62	62	155
Ext Rec L2-L3 Laxity	58	29	29	72.5
Ext Rec L3-L4 Laxity	1312	656	656	1640
Ext Rec L4-L5 Laxity	32	16	16	40
Ext Rec L5-S1 Laxity	72	36	36	90
Ext rec MSV	58	29	29	72.5
Ext rec MSI	36	18	18	45
DH Dif L2-L3 Rec	368	184	184	460
DH Dif L3-L4 Rec	448	224	224	560
DH Dif L4-L5 Rec	160	80	80	200
DH Dif L5-S1 Rec	70	35	35	87.5
Maximum	**66492**	**33246**	**33246**	**83115**