The Physiotherapy Management of Lumbar Radicular Syndrome

Does Early Intervention Physiotherapy Improve Outcomes?

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Summary

Physiotherapy for Sciatica; Is earlier better?

Lumbar radiucular syndrome (LRS) carries a significant individual and societal burden. It is often associated with low back pain but is distinct in its presentation, effects and symptom duration. There are varied treatment options for the manangement of LRS, but the optimal timing of interventions is significanlty under-researched. This is a problem for patients suffering with LRS, but also clinicans and service commisioners as it is unclear when it is best to instigate different treatments for LRS.

This PhD aimed to determine the feasibility of undertaking an RCT to determine the effectiveness and cost-effectiveness of early physiotherapy compared to usual care for LRS.

A sytematic review was carried out to determine the optimal timing of commonly used interventions for LRS such as physiotherapy and surgery. From an initial screening of 330 eligible articles, only four studies met the eligibility criteria. Three of the articles were from one study, the original study and two follow-up papers. The results found there was insufficent evidence to suggest the optimal timing of any interventions commonly used for LRS.

The findings of the systematic review provided the foundations for the POLAR mixed methods study, comprising of an external pilot study, stakeholder interviews and a preliminary economic evaluation. 80 participants were recruited in 10 GP practices over 34 weeks, within time and randomised to usual care (n=38) or early intervention physiotherapy within 2 weeks of randomisation (n=42). Both groups received the same individualised physiotherapy approach of up to six treatment sessions over an 8-week period.

All feasibility objectives were achieved including recruitment, attrition and intervention delivery and fidelity. The mean area under the curve (larger values indicating more disability) for the Oswestry Disability Index over the 26 weeks was 16.6 (SD 11.4) in the usual care group and 16.0 (SD 14.0) in the intervention group. A difference of −0.6 (95% CI −0.68 to 5.6) in favour of the intervention group.

Feedback from participants (n=33) through 45 interviews found acceptance of the study processes and intervention. Furthermore, key themes emerged as to participant experiences of LRS and management which will aid future intervention development and research.

The findings from this mixed methods PhD suggest that a full RCT is feasible, within a reasonable time scale and resource envelope in order to determine the optimal timing of physiotherapy for LRS.

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List of Abbreviations

AE	Adverse Event
A&E	Accident and Emergency
AF	Annulus Fibrosus
BAME	Black and Asian minority ethnic
BMI	Body Mass Index
CES	Cauda Equina Syndrome
CFT	Cognitive Functional Therapy
CPPP	Combined Physical and Psychological Programme
CRN	Clinical Research Network
CSP	Chartered Society of Physiotherapists
CI	Chief Investigator
CI	Confidence Interval
CT	Computed Tomography
CVA	Cerebro-Vascular-Accident
DLSS	Degenerative Lumbar Spinal Stenosis
DoH	Department of Health
DNA	Did Not Attend
EEACT	Economic Evaluation Alongside Clinical Trial
EQ5D-5L	EuroQol 5-dimension 5-level questionnaire
GIRFT	Getting It Right First Time
GP	General Practitioner
HTA	Health Technology Assessment
ICER	Incremental Cost Effectiveness Ratio

IVD	InterVetertebral Disc
LBP	Low Back Pain
LDH	Lumbar Disc Herniation
LRS	Lumbar Radicular Syndrome
MCIC	Minimal Clinically Important Change
MCID	Minimal Clinically Important Difference
MMPs	Matrix Metalloproteinase
MMP-7	Matrix Metalloproteinase 7
MRI	Magnetic Resonance Imaging
NBRPP	National Back and Radicular Pain Pathway
NHS	National Health Service
NHSFT	National Health Service Foundation Trust
NIHR	National Institute for Health Research
NP	Nucleus Pulposus
NRS	Numerical Rating Scale
nVAS	numerical Visual Analogue Score
ODI	Oswestry Disability Index
OECD	Organisation for Economic Cooperation and Development
PNE	Pain Neuroscience Education
PI	Principal Investigator
PICOTS	Population, Intervention, Comparison, Outcomes, Setting
POLAR	PhysiOtherapy management of LumbAr Radicular syndrome
PPIE	Patient and Public Involvement and Engagement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta Analyses

PROMS	Patient Reported Outcome Measures
QUALY	Quality Adjusted Life Years
RCT	Randomised Clinical Trial
RMDQ	Rolland-Morris Disability Questionnaire
RTW	Return To Work
SAE	Serious Adverse Event
SBI	Sciatica Bothersomeness Index
SFI	Sciatica Frequency Index
SMD	Standard Mean Difference
STB	StarTBack Screening form
STH	Sheffield Teaching Hospitals
TMG	Trial Management Group
TNFa	Tumour Necrosis Factor alpha
ToC	Theory of Change
TSC	Trial Steering Committee
UK	United Kingdom of Great Britain and Northern Ireland
XSLR	Cross Straight Leg Raise

Chapter 1 Introduction

In this first chapter I will introduce the reader to the clinical entity known as 'Lumbar Radicular Syndrome' (LRS) and to the POLAR study. I will go on to provide the background to the study, its aims and objectives together with a clear rationale for the research. The chapter will then provide an outline of each of the remaining chapters and how they will come together to form the thesis.

1.1 Introduction

Lumbar Radicular Syndrome (LRS) is a painful and often disabling condition, which is usually of benign causation with varying clinical presentation. It presents along a spectrum of severity, ranging from being mildly troublesome and self-limiting without sequelae to extremely painful and debilitating with long-term consequences on both the individual sufferer and to society at large. It is a major cause of disability, work loss and presentation to healthcare (Waddell, 2004; Hartvigsen *et al.*, 2018). Although it often accompanies Low Back Pain (LBP), LRS is a unique entity (B.N. Ong et al. 2011) and requires different approaches to management. Together with LBP it is the number one cause of disability worldwide (Vos *et al.*, 2016).

1.2 Terminology

The descriptive nomenclature associated with lumbar-sacral nerve root dysfunction is extensive, with many different terms used interchangeably. Lumbar radicular syndrome is the preferred collective term for the signs and symptoms associated with compression and or neural inflammation of the lumbosacral nerve roots (Koes, Æ Bart W, van Tulder MW, 2007; Luijsterburg *et al.*, 2007). The most common signs and symptoms associated with LRS are leg pain in an area served by one or more spinal nerve roots, paraesthesia and or aneasthesia in a dermatomal distribution and or weakness in one or more myotomal areas associated with the lumbo-sacral spine (Peul and Koes, 2007). Its clinical presentation is however heterogeneous in terms of severity, area and nature of pain, level of disability, functional restrictions and its effects on the quality of life of the individual.

Sciatica refers to neuropathic pain, signs and or symptoms emanating from the sciatic nerve, the sciatic nerve being made up from the lumbar spinal nerves of L4, L5, S1, S2 and S3 (Standering, 2016). The upper lumbar nerve roots of L2, L3 and L4 supply the femoral nerve which can also be compressed, inflamed or irritated and cause signs and symptoms akin to sciatica on the ventral aspect of the thigh. It is perhaps the definition of LRS and its close,

symbiotic association with sciatica and LBP that makes estimation of the true prevalence difficult. Studies which have attempted to define the prevalence have acknowledged the challenge with estimates ranging from 43% (Konstantinou and Dunn, 2008) who found in their English language literature review of the incidence of sciatica that many estimates were based on patient self-report of symptoms or clinician diagnosis, both methods of which are open to bias and lack of a gold standard definition of what consitutes LRS/sciatica. Other studys have found an incidence of self-reported sciatica in a French occupational cohort of 19.2 % (Tubach, Beauté and Leclerc, 2004) to 1.6 % (Battié *et al.*, 2007) of the population. With the most conservative estimate meaning that over 1 million people a year in the United Kingdom (UK) suffer with LRS/sciatica.

1.3 Causes, diagnosis and management of LRS

LRS has been described over centuries with a miscellany of potential causes proposed and treatments devised, including bloodletting, a practice that spread widely across cultures which has fortunately, not stood the test of time (Missori, 2015). It was not until the 18th century that the herniated lumbar intervertebral disc was proposed as one potential cause of LRS. With this new understanding of causation came new treatments including the surgical removal of the offending disc material, first described in the pioneering work of Mixter and Barr in the 1930s (Truumees, 2015). In the intervening period there has been a plethora of treatment methods advocated for the management of LRS, including bed rest, bracing, traction, injection therapies, chemical ablation, analgesia, muscle relaxants, acupuncture, cognitive and behavioural therapies, exercise therapies and physical therapies. Despite this, the optimum management strategies for LRS remain elusive but commonly include conservative care such as GP management, physiotherapy and if necessary, surgery. There is the potential for the healthcare approaches to add to the significant fiscal burden of LBP/LRS rather than reduce it (Hartvigsen *et al.*, 2018). The diagnosis of LRS is often made clinically, with varying degrees of accuracy as the signs and symptoms readily mimic those of other conditions of the neurological, musculoskeletal and vascular systems. Common examples include peripheral neuropathy, vascular claudication (Gray, 2017),pathologies of the hip (Zibis *et al.*, 2018), and entrapment neuropathies such as piriformis syndrome (Cassidy *et al.*, 2012). Degenerate Lumbar Spinal Stenosis (DLSS) is perhaps most closely clinically associated with LRS as they share symptoms which can include unilateral or bilateral lower limb symptoms including pain, paraesthesia, anaesthesia and weakness on walking and weight bearing (Iversen and Katz, 2001). The onset of DLSS occurs usually after the age of 65 (Comer *et al.*, 2009), whereas the incidence of LRS peaks in the 5th decade (National Insititute for Health and Care Excellence, 2016).

There are many and varied studies exploring the effectiveness of commonly used interventions for LRS, however there remains a clear lack of research into the timing of such

interventions. Further research is required to determine the optimum timing, sequencing and organisation of services for those suffering with LBP and LRS.

1.4 Rationale for the POLAR study

Physiotherapy is widely used in the National Health Service (NHS) of the UK and in these turbulent fiscal times physiotherapy services are being restricted to save money, resulting in grossly restricted or delayed access to services. The POLAR (PhysiOtherapy management of LumbAr Radicular syndrome) study stems from the authors and colleagues clinical experience of patients with LRS having to wait prolonged periods, often several weeks or months before they can access treatment, including physiotherapy, imaging, and surgery, with these waiting times rising due to increased governmental fiscal pressures (CSP, 2010, 2012). The James Lind alliance has identified as physiotherapy priority 1 *'When health problems are developing, at what point is physiotherapy most/least effective for improving patient results compared to no physiotherapy? What factors affect this?'*. This relates directly to musculoskeletal problems, including LRS. This is a call for research investigating the timing of physiotherapy and in particular the optimum timing compared to no physiotherapy. It is known that patients prefer and indeed have improved outcomes in terms of pain, disability with early intervention physiotherapy for LBP (Wand *et al.*, 2004; Lau, Chow and Pope, 2008; Whitfill *et al.*, 2010; Childs *et al.*, 2015). There are recommendations for early administration of advice and education for LBP, although what this advice consists of, when it should be administered, in what form and by whom is not specified in detail in the latest NICE guidelines for the management of LBP and sciatica (National Insititute for Health and Care Excellence, 2016). Previous guidelines for the early management of LBP have suggested a multi-modal approach with advice, education and self-management at the core of treatment for patients with LBP of a duration between 6 weeks and 12 months. Physical activity, manual therapy, acupuncture and a combined physical and psychological programme (CPPP) treatment approach are all advocated but there is no guidance on when in the symptom duration cycle to instigate which or any of these treatments (National Collaborating Centre for Primary Care, 2009). A retrospective survery of patients suffering with LBP in the Republic of Ireland found that those who accessed early physiotherapy in private practice had significantly less number of treatment sessions (2 versus 5) with a significantly decreased duration of treatment (1 week versus 5.5 weeks)(Casserley-Feeney *et al.*, 2008). Early intervention is also more cost-effective than delayed initiation of therapy, with delayed therapy being associated with increased cost and healthcare consumption (Fritz *et al.*, 2012). A literature review carried out by the author found a paucity of evidence surrounding the timing of interventions for LBP and LRS. In particular there is a lack of

Randomised Controlled Trials (RCTs) investigating the timing of physiotherapy for LRS with adequete longitudinal follow-up.

1.4.1 Research question

The overall research questions for this study is, is it feasible to conduct a full scale study to determine whether early intervention physiotherapy can improve outcomes in patients with LRS compared to usual care?

1.4.2 Aim

The overall aim for the study is to investigate the feasibility of undertaking a fully powered, multi-centre RCT to determine the effectiveness and cost-effectiveness of early intervention physiotherapy compared to usual care for patients with LRS.

1.4.3 Objectives

The objectives of the pilot trial fall into two categories. Firstly, process objectives will allow the analysis of the practical and logistical aspects of setting up and running the study such as recruitment, randomisation, the use of outcome measures, and data collection. Secondly, research objectives will provide valuable information as to the delivery and acceptance of the intervention and help inform the sample size for the definitive RCT.

1.4.4 Process Objectives

1. To test the feasibility, practicality, safety and acceptability of the study design and protocol.

2. Demonstrate the ability to set up and recruit in primary care centres.

3. To assess the feasibility of delivering the early intervention within the time parameters (2 weeks for the intervention group, 6 weeks for the usual care group).

4. Demonstrate a recruitment rate of 7 patients per month in a maximum of 14 GP centres, equal to a rate of 0.5 of a participants per centre per month.

5. Demonstrate the ability to organise 75% of physiotherapy appointments within 2 weeks of randomisation.

6. Patient attendance at 66% of individual physiotherapy sessions.

7. 75% of patients randomised to early intervention have their first physiotherapy session within 20 days of randomisation.

8. Patient attrition rate of <25% over the course of the study.

9. Outcome measurement return rate of 80% at 6/52 follow-up.

1.4.5 Research Objectives

1. To determine the acceptability of the intervention to patients and clinicians.

2. Demonstrate the acceptability of the primary and secondary outcome measures to patients and clinicians.

3. To inform the sample size calculation for the definitive trial.

The feasibility of data collection was assessed in terms of the completion rates of the Patient Reported Outcome Measures (PROMS) at baseline, 6,12- and 26-weeks post randomisation. Levels of missing data, completion rates and amounts of missing data at each timepoint were recorded. The fidelity of intervention delivery was assessed utilising digital video recording of the treating physiotherapist in order to determine the level of accepatbility of adherance. The maximum score for 'essential' aspects of fidelity was 15/15 with an acceptable level of fidelity being 10/15 (75%).

A previous iteration of the POLAR intervention was utilised in a pilot study, published in 2016 (Boote *et al.*, 2016). In the study 24 participants in the treatment arm received the multi-modal physiotherapy intervention to good effect. The quantitative results have not been published, however, a key theme emanating from the qualitative element of the study suggested that the intervention was well received. Participants did highlight however, that they would have preferred the treatment earlier in the symptom cycle, rather than waiting almost a year for definitive treatment. The intervention represents what patients and clinicians find useful in managing LBP and LRS and utilises a multi-modal and complex approach to the assessment and management of LRS.
The aim of the POLAR study was to determine the feasibility of progressing to a full-scale RCT with economic evaluation. In particular the study aimed to refine recruitment parameters, the optimal outcome measures, the ability to deliver the intervention at the appropriate time-point with acceptable fidelity, and the acceptance of the intervention by patients and clinicians alike. The study aimed to provide an insight into patients' experiences of LRS and stakeholders views of the intervention and the processes in place to deliver it.
This first chapter has been given over to introducing the POLAR study, a brief history of the diagnosis and management of LRS together with the feasibility and research objectives of the study. The following chapter presents a detailed background to the normal anatomy and function of the lumbar spine, the physiology and pathophysiology of the inter-vertebral disc,

the aetiology, prognosis and management of LRS and the effects of LRS on the individual and society. Chapter 2 also presents the literature review which formed the initial basis of the study and from which the research question and the study was based upon. Chapter 3 sets out the systematic review which was carried out to evaluate the existing literature regarding the timing of commonly used interventions for LRS, including physiotherapy. The systematic review outlines the need for further research. The POLAR study is mixed methods in its design and in order to ensure clarity of presentation, the design and methods are found in their respective chapters, the quantitative in Chapter 4 and the qualitative elements are presented in Chapter 5. The protocol for the pilot trial has also been published and can be found in Appendix 1 or via the following link: https://bmjopen.bmj.com/content/bmjopen/7/3/e014422.full.pdf.

The intervention used in the study has been developed over many years in conjunction with colleagues and patients alike. Although the effectiveness of the intervention is not being formally tested in the study, the iterative nature and background to its development is integral to the study and is described in Chapter 4. A rationale is provided for the use and potential mechanisms of action for each domain and treatment components of the intervention. In keeping with the presentation of the methods, the results are presented in their quantitative form in Chapter 7, which details the findings from the external pilot RCT which recruited and randomised 80 patients. The qualitative aspect of the study consisted of 45 interviews with 33 participants and is detailed in Chapter 8. The benefits of utilising a mixed methods design for the POLAR study are to gain a greater breadth, depth and understanding of the study results, which would not be afforded through exclusive use of quantitative or qualitative methods alone. In this respect, Chapter 9 presents the mixed methods results of the study. Each participant completed health resource use forms at each time point of the study in order to determine the costs of LRS, the results of which are presented in Chapter 10 as a preliminary economic analysis. The final chapter brings together the thesis to discuss its findings, draw appropriate conclusions and make recommendations for future research.

The study has gained favourable ethics approval from the East of Scotland Research Ethics Service (15/ES/0130), see Appendix 2 for the approval letter.

The trial was registered with International Standard Randomised Controlled Trial Number (ISRCTN-25018352) and Clinical Trials.Gov (NCT02618278).

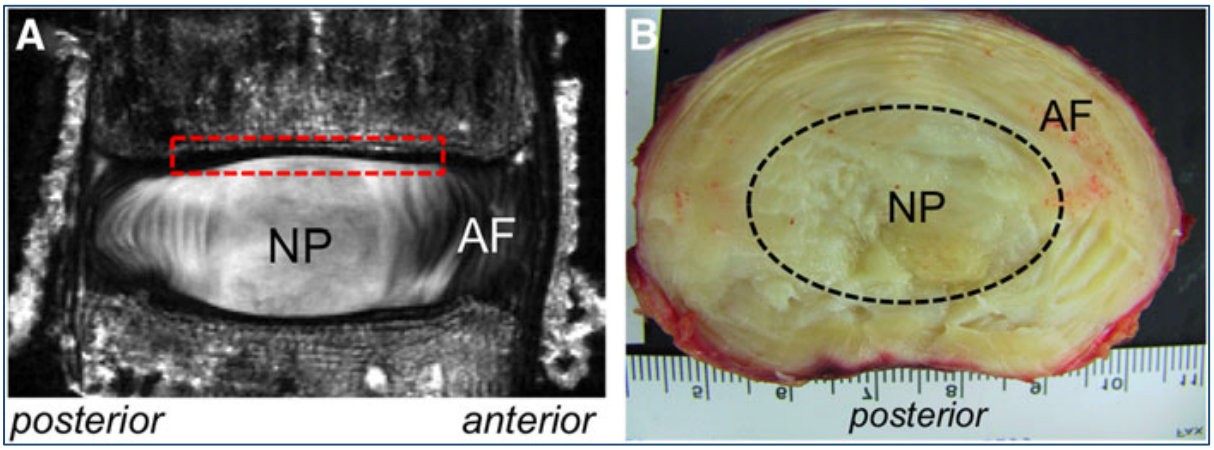
Chapter 2 Background

Chapter 2 expands on the introduction to the study with an overview of the anatomy of the lumbar spine and lumbar Inter-Vertebral Disc structure, physiology and pathophysiology together with its potential role in the development of LRS. The findings of a review of the literature underpin a discussion of the different forms of managing LRS

2.1 Introduction

The human Lumbar spine is comprised of five vertebrae, although there are variants, whose function is to provide stability, motion and protection for the lumbar nerve roots and associated vasculature. The cartilaginous inter-vertebral joints are formed between the vertebral body and the Inter-Vertebral Disc (IVD) anteriorly, and posteriorly lies the synovial superior and inferior facets which form the facet (zygapophysial) joint. The vertebral body, together with the IVD and a complex of ligamentous and muscular attachments, form a motion segment allowing a stable, dynamic structure. The human lumbar IVD is a fibrocartilaginous disc made up of a gel-like, central Nucleus Pulposus (NP) and a fibro-cartilage outer ring known as the Annulus Fibrosus (AF) (Adams *et al.*, 2014). Figure 2.1 illustrates the normal structure of a human IVD. The NP consists of a proteoglycan matrix which is hydrophilic and endows the disc with hydrostatic properties enabling the disc to withstand high mechanical, compressive loads. The function of the IVD is to form an adaptive damping mechanism for the axial spine and skeleton, allowing transmission of mechanical forces.

Figure 2.1 Normal structure of human lumbar intervertebral disc



(A) High-resolution magnetic resonance image (MRI) from the midsagittal slice of a non-degenerated lumbar intervertebral disc. Red dashed box represents a region covered by the cartilaginous end plate, which is located on the superior and inferior end of the disc. (B) Cross-sectional view of healthy non-degenerated lumbar disc. The Nucleus Pulposus (NP) region is outlined by the black dashed oval. Annulus Fibrosus (AF) structure can be identified on both images (O'Connell, Leach and Klineberg, 2015).

2.2 Lumbar Intervertebral disc degeneration

The constituent parts of the IVD are not static, they are routinely degraded by enzymes known as Matrix Metalloproteinases (MMPs) which enable freshly synthesised components for the NP. The degenerative process of the IVD involves cell senescence, a disturbance in the control of MMPs and thus a change in the rate of cellular turnover (Hadjipavlou *et al.*, 2008). This results in the net loss of hydrophilic cells in the NP and consequent loss of the mechanical abilities of the IVD to control and withstand forces transmitted through it. This gradually manifests itself with microscopic tears of the AF which, it is theorised allows the displacement of NP material through the clefts in the AF, potentially causing LRS. This degenerative process is not necessarily symptomatic, with such degenerative changes being present in asymptomatic individuals (Brinjikji *et al.*, 2015).

2.3 Causes of LRS

LRS is a collection of often changing clinical symptoms rather than a specific pathophysiological diagnosis, with the diagnosis being made through clinical examination and if necessary, appropriate imaging. LRS is chararcterised by pain and/or neurological dysfunction in a specific nerve root distrubution. However, it is often difficult to make a clinical differentiation between neuropathic symptoms (true LRS), arising from injury or inflammation in the somatosensory system (nerve) or 'referred pain' (pseudo-LRS) which arises from the nociceptive system. There may be considerable overlap between the two systems (Freynhagen *et al.*, 2008; Mahn *et al.*, 2011). Patients with 'true' LRS are likely to have higher levels of back pain, leg pain, depression and anxiety morbidity than those with nociceptive leg pain (Harrisson *et al.*, 2017). LRS has many potential causes including serious pathologies such as neoplasia (malignant or benign), fracture or infection, although serious pathologies are associated with less than 1% of presentations of LBP and/or LRS (Henschke *et al.*, 2013). The most common cause of LRS is a lumbar disc herniation (LDH) although the presence of an LDH is not always symptomatic. Figure 2.2 shows a normal MRI image of the lumbar spine and Figure 2.3 a lumbar spine with a large disc prolapse.

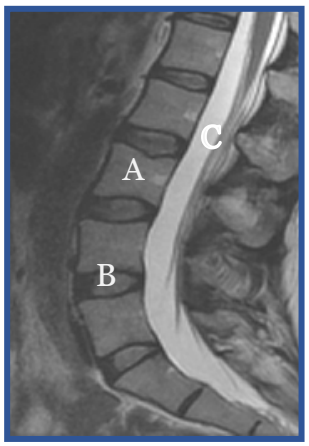
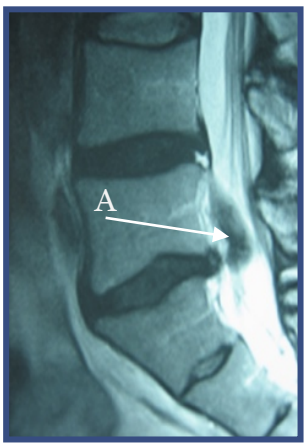


Figure 2.2 *(left)* Shows a 'normal' sagittal view of the lumbar spine using T2 weighted MRI with
A denoting the vertebral body,
B the IVD and
C the nerves of the cauda equina.

Figure 2.3 is also a lumbar spine, sagittal T2 weighted MRI scan.
A shows a large sequestered disc fragment (arrowed).



Degenerative Lumbar Spinal Stenosis (DLSS) is a group of symptoms which are similar to LRS as epitomised by LBP and pain in one or both legs. This is caused by degenerative changes in the IVD, facet joints and buckling of spinal ligaments, in particular the Ligamentum Flavum, which occupy space as the nerves which leave the spinal canal to innervate the lower limbs and in turn increase the pressure within the space, leaving the nerves ischaemic upon walking and weight-bearing.

2.4 The natural history of LRS secondary to LDH

The natural history of a symptomatic herniated IVD is that it is likely to spontaneously absorb over time (Saal, Saal and Herzog, 1990; Bush, 1992; Ellenberg *et al.*, 1993; Matsubara.Y *et al.*, 1995; Komori *et al.*, 1996; Ahn, Ahn and Byun, 2000), which can be closely linked with the level of patient symptoms, if they are symptomatic at the time (R. A. Autio *et al.*, 2006). It is not necessarily the direct compression of the exiting nerve root that causes symptoms, although this does occur (Winkelstein, Weinstein and DeLeo, 2002), symptoms can also be caused by inflammation of the nerve secondary to inflammatory chemicals exuded by the NP (Olmarker, Størkson and Berge, 2002). The disc prolapse initiates the inflammatory process (Doita *et al.*, 2001) with Tumour Necrosis Factor alpha (TNFa) and interleukins stimulating the expression of MMPs which, in turn facilitate the breakdown of collagen 1 & 2. MMP-7 is an important mediator in recruiting macrophages with ensuing phagocytosis of the disc fragment, (Yoshizawa H, 1995; Ito T, Yamada M, Ikuta F, Fukada T, Hoshi S, 1996; Koike *et al.*, 2003; Kobayashi *et al.*, 2009). It is therefore proposed that complex inflammatory processes are instrumental in decreasing the size of the disc fragment, which if concordant with symptomatology, may help decrease those symptoms.

There is no reliable predictive indicator as to how long IVD resorption will take in any individual.

2.5 Clinical presentation and assessment of LRS

The diagnosis of low limb radicular symptoms is often made in the clinical setting based on the clinical characteristics of the patients pain site and spread, nature and severity. In the study this was patients with unilateral radicular-type leg pain and/or parasthesia/anaesthesia in a dermatomal distribution, with leg pain being predominant (see Appendix 3 for GP instructions). There are several classification systems which have been developed in an attempt to identify low back related leg symptoms, including LRS, with varying degrees of quality and relaibility (Stynes, Konstantinou and Dunn, 2016). Recent work to determine a clinical diagnostic model for patients presenting with lower limb radicular pain have suggested four items which are highly predictive of sciatica. These are; pain extending below the knee, leg pain greater than low back pain, positive neural tension (positive SLR/slump tests) and neurological deficit (Stynes *et al.*, 2018). The generalisability of the study findings may be questioned as the cohort of patients presenting to the research group were ones who were willing to participate in research and therefore may not represent the usual sciatica population. The choice of items to include in the diagnostic test groups were a result mainly of consensus, the reliability of which is questionable, as different results may occur with different groups of clinicians. There were 173 patients excluded from the analysis as they did not meet the arbitrary cut off of 80% confidence of a diagnosis of sciatica made by the clinician. The reliability of the clinical methods of assessment appears to have been accepted without validation or explanation. It is unclear whether the results would have been different if these and other patients had not had a MRI (reasons not given) would have affected the results. Other clinical classification criteria for the diagnosis of radicular pain caused by IVD prolapse have been proposed (Genevay *et al.*, 2017). This Delphi study utilised 17 spinal 'experts' from a convenience sample to determine five items which, with a score over 11 suggests radicular pain caused by IVD prolapse. The items are; monoradicular pain, SLR>60, unilateral ankle reflex decrease, unilateral muscle weakness and unilateral patient self-report pain in legs. Although the authors found good face and construct validity, the significant limitation is that of inherent bias of the delphi group.

A Cochrane review of the utility of physical examination tests for lumbar radiculopathy due to disc herniation found that commonly used clinical tests are inaccurate in distinguishing LBP patients with LRS secondary to a LDH (van der Windt *et al.*, 2010). The review does suggest that in surgical populations the SLR test has high sensitivity with variable specicifity, whereas the Cross SLR (XSLR) has high specicifity and low sensitivity. The accuracy of the SLR has however been questioned (Capra *et al.*, 2011). A retrospective review of 2352 patients with sciatica found low predictive value of the SLR when utilising MRI as the gold standard. There is a significant risk of bias in the study; only one neurosurgeon was used to

undertake the SLR, there were no pre-defined diagnostic criteria for sciatica and the study population was heterogenous in terms of clinical presentation and duration of symptoms. Differential diagnosis of LRS from DLSS is often the most common and difficult to elucidate due to the similarity of symptoms. The use of clinical classification criteria have also been proposed for DLSS. The N-CLASS have been found to have utility in independently predicting DLSS symptoms. The criterai are; over 60 years of age, a positive 30 second extension test, negative SLR, bilateral leg pains, pain relieved by sitting and pain relieved by lumbar flexion/leaning forwards (Genevay *et al.*, 2018).

It is important to acknowledge that in the clinical setting the assessment processes are not undertaken to enable a patho-anatomical diagnosis of the cause of the participants symptoms. Moreover, it is important to note that it is the participant and their functional problems and goals which are highlighted as key aims of rehabilitation, rather than correcting any hitherto identified patho-anatomocal dysfunction using imaging. Differentiation of the pathoanatomical cause of a patients LRS is extremely difficult to reliably make clinically and unnecessary unless the patient presents with symptoms of potential serious pathology or is eligible and considering surgery or injection therapy.

2.6 The impact of LRS

LBP and LRS are the biggest causes of disability and years lived with disability in the UK (Murray *et al.*, 2013). The associated costs with this level of disability are significant and are estimated at over 10 billion pounds sterling to society and costs to the NHS of £1.6 billion and rising (Maniadakis and Gray, 2000; Greenhough, 2014). Patients suffering with LRS utilise more healthcare resource than those with LBP alone, they have more time off work or are less likely to be doing their usual duties at work and have a poor quality of life as a result (Hider *et al.*, 2015). The Hider et al. study agrees with others in finding that LRS sufferers are more likely to undergo investigations and surgery than those with LBP alone (Verwoerd *et al.*, 2013). This is however likely to be because there is a potential surgical solution to LRS, there is not for LBP and so extensive investigations and surgery are not warrnated for LBP alone. The facts remain, however that LRS is a distinct entity often with significant pain, disability and significant associated costs.

2.6.1 The impact of LRS on the individual

The impact of LRS on the individual varies enormously from very severe, with loss of function, severe pain and significant effects on work, relationships and social life, to very mild, self-limiting and short-lasting. There are several studies investigating the effects and experiences of LBP on individuals, their families and work (Verbeek *et al.*, 2004; De Souza and Frank, 2011; Scheermesser *et al.*, 2012). There are few studies examining the effects of

LRS on similar domains. The distinctive nature and severity of the pain, sensory disturbance and motor deficits experienced with LRS are quite different to that of LBP and causes great concern for patients (B.N. Ong et al. 2011). The impact and effect of LRS can be very different in terms of pain, duration and disability than LBP and should therefore be treated as a separate entity.

2.7 Treatment options for LRS

Despite the prevalence and impact of LRS there is still significant debate as to how best to manage it (Truumees, 2015). There are many treatment options available, ranging from conservative methods such as analgesia, advice from GP, chiropractic, osteopathy, physiotherapy and acupuncture to more invasive treatment options such as nerve root injections and decompressive surgery. There is a body of research comparing conservative and surgical management of LRS. Further research into treatments for LBP and LRS in terms of implementation of best practice guidelines, changes to clinical pathways, integration of health and occupational management strategies and changes to payment systems and legislation is required (Foster *et al.*, 2018).

2.7.1 Physiotherapy management of LRS

In the UK the mainstay of rehabilitation of patients with LRS is physiotherapy. Physiotherapy for LRS has been advocated but without consensus on the type, duration or timing of intervention (Koes, Æ Bart W, van Tulder MW, 2007; Thomas *et al.*, 2007). Reported success rates of conservative treatment have shown a wide variation (P. Vroomen, de Krom and Knottnerus, 2002; Luijsterburg *et al.*, 2007). The aims of physiotherapy are to promote physical and psychological health for the patient, and in doing so promote and improve optimum function. In light of the evidence to suggest that spontaneous resorption of the disc fragment occurs, physiotherapy provides support and guidance for the patient to manage their symptoms whilst symptom resolution occurs.

There are many schools of physiotherapy which have, historically esposed treatments broadly based on dogma, rather than science. These approaches are slowly changing and a multi-modal, evidence-based approach to physiotherapy management has been proposed (National Insititute for Health and Care Excellence, 2016). The guidelines advocate self-management, pyschological therapies, the use of advice, exercise, manual therapies (mobilisation, manipulation) dependent on the patients individual requirements. Individualised physiotherapy for patients with LBP with or without LRS is better than advice alone and patients with LRS have been found to value an individual physiotherapy intervention, its type, duration and applicability to their needs and goals (Ford *et al.*, 2015;

Boote *et al.*, 2016). Patients who undertake physiotherapy have greater feelings of empowerment and well-being than their surgical counterparts (Svensson, Wendt, Thomeé, & Danielson, 2013).

The costs of surgery for LRS (micro-discectomy and laminectomy) were found to add 5 billion dollars to the overall cost of back pain and LRS in the USA in 2004 (Atlas *et al.*, 2005a; Chiarotto *et al.*, 2015). The cost of physiotherapy for a group of patients who went on to have surgery for LRS accounted for 11% of the total pre-operative costs or on average $379 per patient. The mean cost of imaging alone accounted for 31% of costs or $1067 for each patient (Daffner, Hymanson and Wang, 2010), highlighting the relatively small costs and uptake of physiotherapy compared to other, non-therapeutic costs.

There are no systematically reported side-effects or risks of physiotherapy for patients undergoing physiotherapy rehabilitation for LRS although a transient exacerbation of pain is not uncommon.

2.7.2 Surgical management of LRS

Surgery for LRS is widely practised and effective in the short-term in managing symptoms of LRS secondary to IVD for some patients. However, defining the group that is likely to do well after surgery, who would not have had a good outcome anyway, is without scientific basis at present. Rates of surgery differ greatly, both internationally and nationally (Jacobs *et al.*, 2011; Lequin *et al.*, 2013). The long-term outcomes of patients undergoing surgery have been reported to favour surgery over nonsurgical management (Atlas *et al.*, 2005b). A large prospective trial of patients with sciatica who were randomised to surgery or non-operative care (not defined) found surgery to be most effective (Weinstein *et al.*, 2008).
A significant number of patients never have any substantial relief from surgery (Haugen *et al.*, 2012; Lurie *et al.*, 2013) and there are small but significant risks associated with surgery for LRS. These include new or worsening neurological deficit as a result of surgery, LBP, direct nerve injury, infection and the need for re-operation. Perhaps the most common risk is that symptoms will simply not improve with surgery. The overall, combined rates for these complications in a recent systematic review was 12.5% for 'open' micro-discectomy, this being the most common surgical procedure for LRS secondary to LDH in the UK (Shriver *et al.*, 2015).

2.8 Timing of treatment of LRS

The plethora of research which advocates either conservative or surgical methods have one thing in common, that is the uncertainty as to when to instigate treatment. There is a general consensus among clinicians that a waiting period of at least two months is recommended for patients with LRS, prior to micro-discectomy surgery (P. Vroomen, de Krom and

Knottnerus, 2002; Ng, 2007) as this allows time for disc resorption to begin (Ahn et al., 2000; R. A. Autio et al., 2006). However, early surgery has been advocated in the management of LRS with a trial showing improved outcomes in the first 3-4 months post-operative period compared to the non-operative treatment, in this case GP management unless the patient was kinesiophobic, in which case they recieved physiotherapy (Peul *et al.*, 2007). However, at one, two and five years post randomisation, the improvements are similar in both groups. A 'watch and wait' policy has been advocated for patients with a 'massive' disc herniation with authors finding in 83% of cases sustained improvement without surgery being required (Benson *et al.*, 2010).

The recent work of Rhon (Rhon and Fritz, 2015; Rhon, Miller and Fritz, 2018) and Liu (Liu, X, Hanney WJ, Masaracchio, M, Kolber, MJ, Zhao, M, Spaulding, AC, 2018) have found in their retrospective cohort study of patients presenting with LBP and or LRS over a four year period, that early physiotherapy within 3 days of symptom onset for LBP/LRS was associated with significantly less health care utilisation and cost. These findings are in keeping with those findings of Childs 2015 (Childs *et al.*, 2015) who found that early, guideline adherent treatment had lower costs and improved outcomes compared to non-guideline/delayed treatment, early treatment being defined as within 14 days of presentation to healthcare.

Prognostic indicators for a favourable outcome for patients with LRS are a disease duration of less than 30 days (P. Vroomen, de Krom and Knottnerus, 2002). Prognostic indicators for a less favourable outcome are an episode of LRS in the previous year (Tubach, Beauté and Leclerc, 2004) and duration of symptoms greater than 3 or 6 months (Rihn *et al.*, 2011; Haugen *et al.*, 2012). There is a time period between when surgery is advocated, if necessary, and when physiotherapy is commissioned to begin, in many areas of the UK. The decision as to when to refer patients with LRS has been shaped by the introduction of patient care pathways in many areas in the UK (Greenhough, 2014; National Insititute for Health and Care Excellence, 2016). This varies geographically between service commissioners but ranges from 2 weeks to many months.

There has not been a study to determine the effects of early physiotherapy management of patients with LRS.

Chapter 2 has provided a detailed background to the anatomy, physiology and pathophysiology of the lumbar IVD and its potential to cause LRS, the natural history and its effects on the individual and society as well as the common treatment modalities employed in the UK. The chapter reflects the literature review undertaken, and since updated, as part of the initial stages of the study. Its key findings of a lack of evidence on the timings of interventions for LRS outlined the need for further research and served as a starting point

from which the POLAR study evolved. Chapter 3 will now present the results of the systematic review of the timings of treatment modalities for LRS.

Chapter 3 Systematic Review

What is the optimum timing of interventions for sciatica: a systematic review?

The overview of literature in Chapter 2 outlined the impact which LRS has on an individual and societal basis. The causes and uncertainty regarding optimal management strategies have also been presented. This chapter builds on the literature review by using a systematic review of one particular area of debate: the timing of interventions for LRS.

3.1 Introduction

The widespread and often disabling effects of LRS have been outlined in previous chapters, as have some of the commonly utilised treatment options. It is known that the natural history of LRS is positive, with 75% of LRS sufferers having symptom resolution by 12 weeks (P. C. A. J. Vroomen, de Krom and Knottnerus, 2002). There is however, no reliable predictor of an early recovery, late recovery or no recovery at all. LRS has significant effects on the physical and psychological health of sufferers (Boote *et al.*, 2016) and so it is important to know whether and when to instigate which treatment. The timing of access to treatment services is important to patients, service providers, and employers but, as chapter 2 alluded to, there is a dearth of research in this field. This chapter will systematically review the evidence for the timings of interventions used for the management of LRS.

3.2 Objectives

The objective of this review was to identify and synthesise available evidence regarding the optimal timing of interventions used in developed countries, defined as members of the Organisation for Economic Co-operation and Development (OECD), for the management of LRS. In doing do it was envisaged that recommendations could be made as to the optimum time to initiate treatments. This would guide future research into the optimum timing of treatments for LRS, including a potential full-scale POLAR RCT.

3.3 Methods and Design

A mixed method systematic review of quantitative and qualitative literature reporting the effectiveness of interventions for LRS in specific regard to their timing. The review used established processes for identification of literature and was conducted according to the Cochrane handbook for systematic reviews (Higgins JPT and Green, 2011). The systematic review is reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher *et al.*, 2015) and can be found in Appendix 4 .

The review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) number CRD42018088668.

3.4 Inclusion criteria

The following criteria were used to set the parameters of the review.

3.4.1 Types of studies

Studies using experimental and observational designs were included encompassing: RCTs, cohort studies, systematic reviews and longitudinal (before and after) studies. Studies with a single time point were excluded, and studies described as case series or case studies were excluded. The review included studies using qualitative and mixed methods designs.

3.4.2 Types of participants

The review included studies with participants who have were aged 18 or above with a clinician-confirmed diagnosis of LRS (including Sciatic and/or Femoral nerve signs and symptoms). The diagnosis of LRS could be clinical by means of symptom area and nature of signs and symptoms. This, in practice included clinical findings such as a positive symptom provocation test (slump test or straight leg raise test). The diagnosis could also be made by radiological means by Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) with a report by a suitably qualified radiologist and a check of clinical concordance by a suitably qualified clinician. This could be an initial onset of sciatica or patients with a recurrent or prolonged history of sciatica.

3.4.3 Types of interventions

The review included studies reporting conservative and non-conservative interventions for sciatica that were available within OECD countries. Typically, these included but were not exclusive to GP management, physiotherapy, osteopathy, chiropractic, acupuncture, pain management, injection therapy, pharmacological management and surgery. Studies were not chosen or excluded because of a particular treatment approach or combination of approaches.

3.4.4 Comparator

Studies with comparator groups and studies of no comparator design were included.

3.4.5 Outcomes

Data relating to outcomes of the timing of the delivery of an intervention were required to be included in the study. It was therefore imperative that included studies report the duration

of symptoms and/or define the starting point of treatment and a timed reference point for follow-up. Studies were required to include commonly used and validated PROMS for disability and back and leg pain such as the Oswestry Disability Index (ODI) (Fairbank and Pynsent, 2000), the Roland-Morris Disability Questionnaire (RMDQ) (Roland and Morris, 1983), Sciatica Frequency and Bothersomeness Indices (SFI, SBI) (Patrick *et al.*, 1995) or pain measurements such as the Visual Analogue Scale (VAS). These were reported at least at baseline and after completion of the intervention and could report either the minimally clinically important change (MCIC) or the minimally clinically important difference (MCID)(Ferreira *et al.*, 2012). The review also included data relating to the costs of providing or not providing an intervention such as staffing costs and wider individual and societal economic costs.

3.4.6 Setting or Context

Studies in any healthcare setting within OECD countries, including publicly or privately funded healthcare, primary or secondary care settings were eligible for inclusion.

3.4.7 Other criteria

Studies included in the review were limited to those in the English language, and research from OECD countries, as they are the most relevant to the UK healthcare system. The inclusion of only developed rather than developing countries in a review is common practice, given the very limited applicability of some health settings in the developing world to the UK NHS. The contextual setting of interventions is known to be a key element of implementation, therefore this review aimed to examine evidence of most relevance to the UK to inform the design of future interventions. Research published between 1st January 1997 and 31st December 2017 was included as providing most recent and relevant results.

3.5 Methods for identification of studies

3.5.1 Information sources

A comprehensive electronic search of the following health care databases was carried out:

1. Allied and Complementary Medicine Database (AMED)
2. CINAHL
3. MEDLINE
4. PubMed
5. Physiotherapy Evidence Database (PEDro)
6. Web of Science
7. Cochrane databases
8. Embase

The search terms used for the electronic search strategy can be found in Table 3.1. They were developed in conjunction with an information specialist at the University of Sheffield and after consultation with clinical colleagues. The author conducted a scoping review in order to ensure that the review, or similar had not been conducted before. The results of which found that there was no such review in existence or ongoing as registered with PROSPERO.

Table 3.1 Electronic search strategy

	Search Term	Limited to
1	Sciatica/ or piriformis muscle syndrome/ or pudendal neuralgia	Title & abstract
2	Lumbar Radiculopathy	Title & abstract
3	Lumbar Radicular syndrome	Title & abstract
4	1 or 2 or 3	
5	Early intervention	Title & abstract
6	Early treatment	Title & abstract
7	Early management	Title & abstract
8	Optimal timing	Title & abstract
9	Timing of intervention	Title & abstract
10	Timing of treatment	Title & abstract
11	Treatment timing	Title & abstract
12	5 or 6 or 7 or 8 or 9 or 10 or 11	
13	4 and 12	
14	Delayed treatment	Title & abstract
15	Delayed intervention	Title & abstract
16	Late treatment	Title & abstract
17	Late intervention	Title & abstract
18	Late management	Title & abstract
19	5 or 6 or 7 or 8 or 9 or 10 or 11 or 14 or 16 or 17 or 18	
20	4 and 19	
21	(Prolonged adj3 (treatment or Management or intervention))	Title & abstract
22	19 or 21	
23	4 and 22	
24	"Wait and see"	Title & abstract
25	"Watchful waiting"	Title & abstract
26	Optimal duration	Title & abstract
27	22 or 24 or 25 or 26	
28	4 and 27	

3.5.2 Grey literature

A search of the grey literature in the English language was conducted in the Open Grey database, the ISRCTN register, the UKCRN database and the NHS England website for studies between 1997 and 2017.

3.5.3 Supplementary searching strategies

Citation searching of key papers identified in the initial search was used to identify further studies. Conference proceedings from the society for back pain research, Eurospine and Britspine/British Association of spinal surgeons were searched from 1997-2017. Reference list screening of included papers was also carried out.

3.6 Data management

3.6.1 Study Selection

All studies identified as per the search strategy were retrieved by MR and downloaded to reference management software Mendeley (version 1.19). The studies were initially screened by title using the eligibility criteria and codes applied to indicate potentially relevant papers. Where the title did not enable a decision to be made, then the abstract and where necessary full paper was retrieved and screened against the eligibility criteria. Screening of titles and abstracts was completed by the author. In the event of any ambiguity on decision making on a particular paper, a decision was made with the help of the supervisory team. Papers meeting the inclusion criteria progressed to the next stage of data extraction

3.6.2 Data collection

A data collection form was developed and piloted on studies of varying designs prior to finalisation and use (see Appendix 5). This was based on the Centre for Reviews and Dissemination (CRD), University of York (Centre for Reviews and Dissemination, 2009) data extraction form, and included the following:

1. First author
2. Title of article
3. Type of publication
4. Date of publication
5. Language
6. The design of the study
7. The methodology used, to include the randomisation process, details of blinding if appropriate and if not, why not, rate of dropout from the study, measures of methods to prevent/mitigate bias
8. The study population, age, gender
9. Type of LRS (sciatic or femoral)
10. Time since onset of symptoms
11. Type of intervention
12. Setting of intervention

13. Time to receive definitive treatment
14. Number of participants in groups, numbers analysed, withdrawals, lost to follow-up and exclusions with reasons
15. Results, analyses performed

3.7 Quality appraisal

The Cochrane risk of bias tool was used to assess the risk of bias in RCTs with risk of bias tables produced to display the results (Higgins *et al.*, 2011). The Critical Appraisal Skills Programme (CASP) systematic review, qualitative and cohort study checklists were utilised for quality appraisal of other study designs (Critical Appraisal Skills Programme (CASP), 2013, 2017b, 2017a) with the results being summarised in tabular form.

3.8 Data analysis and synthesis

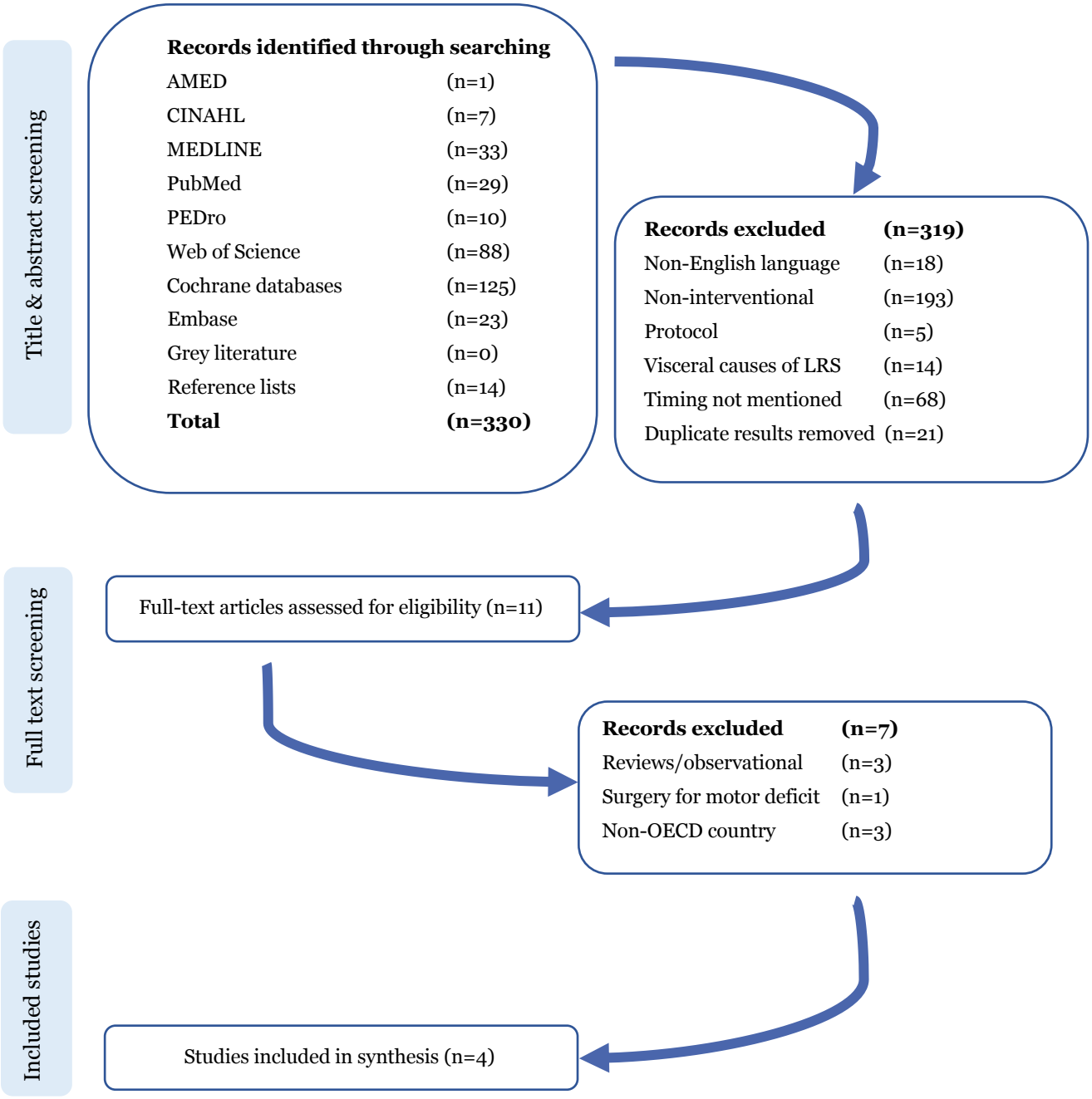
It had been planned that the results of the studies would be summarised with an "effect measure" if the extracted studies were sufficiently similar in terms of PICOTS (Populations, Interventions, Comparators, Outcomes, Time or duration of follow-ups, Setting and study design). If heterogeneity permitted, then the standardised mean difference (SMD) outcomes for each study would be reported alongside associated 95% Confidence Interval (CI) in a series of forest plots. Forest plots would display the study results ordered by publication date; study size and study quality. Following this a decision on whether or not to proceed to a formal meta-analysis would be made. If appropriate a random-effects model would be used to combine or pool the results. The I^2 and heterogeneity statistics would be reported from the model as appropriate. It was anticipated that the studies would be grouped according to the timing of delivery; early intervention <6 weeks after presentation to the treating clinician or >6 weeks after presentation to healthcare. These cut off points to establish the groups were chosen as they represented the clinical situation, patients are not able to access physiotherapy services in the authors locale before six weeks of symptom duration.

If the nature of the studies excluded this analysis, then a narrative synthesis would be carried out to identify key themes including development of typologies, graphs, and the use of graphs such as harvest plots if appropriate. Tabulation of the results would be carried out and descriptive statistics presented together with textual description of the studies. Qualitative research studies would be analysed using thematic synthesis (Harden, 2008) and a matrix would be used to compare and contrast the qualitative and quantitative findings to further explore the data, for example to investigate where the views and perceptions of qualitative study participants could be linked to implementation and outcomes in the quantitative studies (Harden & Thomas 2005; Thomas et al. 2004).

3.9 Results

From a database of 330 potentially eligible articles from title and assessment screening, four studies met the eligibility criteria and were included in the final review. Of the four studies, one had two follow-up studies, the remaining study was unique. The number of studies retrieved from each of the databases together with those studies which were excluded can be found in Figure 3.1. The search was undertaken between August and November 2018. Four papers required a second opinion on their suitability and fit for the search.

Figure 3.1 PRISMA diagram illustrating the process of study selection and exclusion



3.10 Risk of Bias assessment

Three of the four full text articles included in the final analysis were assessed for risk of bias using the Cochrane risk of bias tool in RCTs with tables produced to display the results (Higgins *et al.*, 2011). The risk of bias assessment can be viewed in Table 3.2 for the three RCTS, the cohort study is reviewed separately.

Table 3.2 Assessment of risk of bias for included RCT studies

Study	Components of Risk of Bias							Comments
	1	2	3	4	5	6	7	
Peul et al. 2007 *Peul et al. 2008* *Lequin et al. 2013*	L	H	H	U	L	L	L	Potential recruitment bias from surgical recruiters and significant crossover in both surgical and conservative groups. No evidence of conflict of interest.

Components of risk of bias:

1 Indicates random sequence generation
2 Allocation concealment
3 Blinding of participants, personnel
4 Blinding of outcome assessment
5 Incomplete outcome data
6 Selective outcome reporting
7 Other bias

Levels of risk of bias:

H Indicates high risk of bias
U Unclear risk of bias
L Low risk of bias.

There were no qualitative nor mixed methods studies found in the review. The one included RCT (Peul *et al.*, 2007) and its two subsequent follow-up studies exemplify the difficulty in designing clinical trials whilst blinding participants and clinical personnel to the timing and type of intervention, leading to claims of potential allocation and performance bias. The blinding of outcome assessment was not mentioned in the study text and so it is unclear as to what means were in place to prevent detection bias.

The one cohort study included in the analysis (Quon *et al.*, 2013) was assessed using the CASP checklist for cohort studies (Critical Appraisal Skills Programme (CASP), 2017a). This study focussed on the effects of system-imposed delay in waiting times for lumbar discectomy surgery. This study is a review of patient data from a registry. There is no evidence of consent given for the purposes of the study. The primary means of assessment

was the numerical rating scale, a widely used instrument for patient reported pain. However, a measure of self-reported disability such as the ODI or RMDQ has not been utilised and would be expected in such a study. Analysis was based on a dichotomised cut off point of 12 weeks defined as an inappropriately long wait. Potential confounding factors have been controlled for in the analysis, but not defined. Results reported a 60% reduction in the odds of a worse outcome, defined as comparatively greater intensity of pain, in the group with a history of pain between 6 and 12 weeks. Unfortunately, as the groups were not randomised, and a control group was not in place, the decrease in pain noted in the results may be due to chance or indeed the natural history of the condition. Several questions are left unanswered by the study; Does the decrease in pain lead to a functional improvement? Does the decrease in pain lead to an improved quality of life? What were the consequences and or side effects for the study population of undergoing surgery? Were there any differences in side-effects between groups? Were there cost-implications for the treatment delay? I would conclude that this study is likely to hold a high degree of bias for the reasons aforementioned.

3.11 Study characteristics

A summary of the characteristics of each included study can be found in Table 3.3. The primary outcomes differed between the included studies with the Quon (2013) study utilising the timing of surgery and the Peul et (2007) study using self-rated disability as the primary outcome. Both studies used self-rated pain measurement scales as their secondary outcomes, VAS or Numerical Rating Scale (NRS). The follow-up period of the primary RCT (Peul 2007) was initially 1 year. Subsequent follow-up analyses were published for 2 years (Peul 2008) and 5 years (Lequin 2013). No conflicts of interest were declared. Quon (2013) used a data registry to access data on patients who had undergone lumbar discectomy surgery. The outcomes were analysed and dichotomised into two groups; those waiting less than 12 weeks or greater than 12 weeks. Three of eight authors had potential conflicts of interest having disclosed financial support from surgical device manufacturers and or medical companies.

Table 3.3 Characteristics of included full-text studies

Study	Context	Participants	Intervention	Timing	Outcome measures
Peul et al (2007) [1]Peul (2008) [2]Lequin (2013)	RCT based in Netherlands	n=283 Early surgery n=141 Conservative n=142 18-65 years old	Conservative care=GP management (non-specific-non protocolised). Surgery=microdiscectomy	Early surgery (mean=2.2 weeks) versus prolonged conservative care	Roland-Morris questionnaire score VAS Pain score
Quon (2013)	Ambidirectional cohort study in Canada. Retrospective analysis of waiting list time for surgery.	N=291 43 years (mean)	Lumbar microdiscectomy	Comparison of outcomes between patients with symptom duration 6-12 weeks or >12 weeks.	Symptom duration (6-12 weeks or >12 weeks) Numerical pain scale

[1] 2 year results of Peul (2007) study [2] 5 year results of Peul (2007) study

Seven full-text studies were excluded from the final review. Three were excluded as being from non-OECD countries and so not representative of a similar western healthcare system to the UK, in these cases Egypt, Hong Kong and India. Three studies were excluded as being observational or review of current practice studies and therefore did not meet the eligibility criteria for study design. The final excluded study investigated the effects of surgical timing for motor deficit as a retrospective case review series, although this study did refer to the timing of surgery, it did not refer to treatment for LRS, but for one infrequent element of it (motor deficit). Details of the excluded studies can be found in Table 3.4.

3.12 Context of the included studies

One of the studies (Peul 2007) was conducted in Europe and the other (Quon 2013) in North America. Peul (2007) utilised GPs to deliver the conservative element of the treatment, including advice, education regarding recovery, medication review and referral to a physiotherapist if the patient exhibited kinesiophobic tendencies. How this was determined is not stated, neither is the content, context or duration of the physiotherapy. This was compared with early lumbar microdiscectomy surgery. Quon et al (2013) reviewed a cohort of patients who had undergone lumbar microdiscectomy surgery, then dichotomised the subjects according to their duration of symptoms.

Table 3.4 Excluded full-text articles

Study	Country	Reason for exclusion
Abou-Elroos, D.A. et al., 2017. Prolonged Physiotherapy versus Early Surgical Intervention in Patients with Lumbar Disk Herniation: Short-term Outcomes of Clinical Randomized Trial. *Asian spine journal*, 11(4), pp.531–537. (Abou-Elroos, 2017)	Egypt	Non-OECD country
Akagi, R. et al., 2010. Comparison of early and late surgical intervention for lumbar disc herniation: Is earlier better? *Journal of Orthopaedic Science*, 15(3), pp.294–298.(Akagi *et al.*, 2010)	Japan	Review/observational study
Arts, M.P. & Peul, W.C., 2011. Timing and minimal access surgery for sciatica: A summary of two randomized trials. *Acta Neurochirurgica*, 153(5), pp.967–974.(Arts and Peul, 2011)	Netherlands	Review/observational study
Lau, P.M.-Y., Chow, D.H.-K. & Pope, M.H., 2008. Early physiotherapy intervention in an Accident and Emergency Department reduces pain and improves satisfaction for patients with acute low back pain: a randomised trial. *The Australian journal of physiotherapy*, 54(4), pp.243–9. (Lau, Chow and Pope, 2008)	Hong Kong	Non-OECD country
Petr, O. et al., 2017. Immediate versus Delayed Surgical Treatment of Lumbar Disc Herniation for Acute Motor Deficits: The Impact of Surgical Timing on Functional Outcome. *Spine*, (43).(Petr *et al.*, 2017)	Austria	Surgery for motor deficit not pain Review/observational study
Sabnis, A.B. & Diwan, A.D., 2014. The timing of surgery in lumbar disc prolapse: A systematic review. *Indian Journal of Orthopaedics*, 48(2), pp.127–135.(Sabnis and Diwan, 2014)	India	Non-OECD country
Villavicencio, A.T. et al., 2016. The Timing of Surgery and Symptom Resolution in Patients Undergoing Transforaminal Lumbar Interbody Fusion for Lumbar Degenerative Disk Disease and Radiculopathy. *Clin Spine Surg*, 30(6), pp.765–769. (Villavicencio *et al.*, 2016)	United States of America	Review/observational study

The studies which did not meet the inclusion criteria included one study investigating early surgical treatment for LRS (Abou-Elroos *et al.*, 2017). This is a small study (n=60) with a limited age range of patients with LRS, the oldest patient being 45 years of age. All patients in the study had 4 weeks of physiotherapy and medical management before randomisation of those that had not improved. The findings suggest that the outcomes from early surgery are

similar and not significantly different from prolonged physiotherapy. A comparison of early surgery for LRS in a Japanese observational study found that early surgery for the relief of LRS symptoms was not superior to delayed surgery (Akagi *et al.*, 2010). Both groups had nerve root injections or epidural block, medication (medication type, dose, duration and frequency not noted), a corset and exercise for the back muscles. This regimen does not reflect primary or secondary care conservative management in the UK and due to the number and diversity of the different treatments administered, it is impossible to determine which aspects were in fact therapeutically effective. A limited literature review of the timing of surgery for LRS found that delayed treatment impacted on outcomes (Sabnis and Diwan, 2014). This review lacked methodological rigour in not utlising any independent reviewers, devising an untried and tested scoring system for included papers and only including 2 RCTS in their review. A review of 330 consecutive cases of surgery for moderate/severe motor defict secondary to IVD prolapse in Austria found that surgery within 48 hours of clinical presentation provided superior outcomes (Petr *et al.*, 2017). The study also found that the severity of sciatica symptoms significantly improved with surgery. However, the study was not randomised and was open to significant bias with unblinded and non-independent assessment. An excellent review of the contemporary evidence for surgery or conservative treatment, including timing, is presented in one excluded study (Arts and Peul, 2011). The review suggests that it entirely reasonable to offer early surgery for those patients with severe, disabling LRS. However, prolonged conservative treatment is also reasonable to offer patients with less severe symptoms. An observational study of fusion surgery for LRS found that a shorter duration of symptoms was predictive of a better resolution of radicular leg symptoms (Villavicencio *et al.*, 2016). In this case a shorter duration of symptoms was less than 24 months. Finally, early intervention physiotherapy for LBP in an Accident and Emergency (A&E) department in Hong Kong found was found to be more effective. The intervention group treatment was multi-modal and included advice, reassurance and electrotherapy, the usual care group received advice and walking aids. The inclusion criteria included patients with referred leg pain, but no attempt was made to discern whether this included radicular leg pain/LRS.

3.13 Timing of the interventions

A meta-analysis was unsuitable due to the heterogeneity of the study populations and outcomes, therefore the findings of the review are reported via narrative synthesis. Participants in the early surgery arm of the Peul (2007) received surgery within 2 weeks after randomisation (mean of 1.9 weeks). The mean duration of symptoms in the early surgery group was 9.4 weeks (+/- 2.4 weeks, a range of between 7.0-11.8 weeks) and those in the conservative treatment arm had a symptom duration of 9.5 weeks (+/- 2.1 weeks, a range of between 7.4-11.6 weeks). There was significant crossover between groups with 55 of 142

patients in the conservative care group undergoing surgery at 1 year and 66 of 142 (46%) patients in the conservative care group undergoing surgery at the 5-year follow-up point. The initial results suggest that early surgery is superior to conservative care, however at one-year post randomisation, both groups had similar recovery rates of around 95%.
The duration of wait prior to surgery in the Quon (2013) study was dichotomised as those waiting less than 12 weeks for surgery or longer than 12 weeks. Those in the longer than 12-week group were more likely to have symptoms for more than 6 months and have greater levels of self-report pain.

3.14 Discussion

The objective of this review was to identify and synthesise available evidence regarding the optimal timing of interventions. The limited number of studies found describing the timing of interventions for the management of LRS indicates the need for research into this area. There was a lack of RCTs, qualitative and cohort studies exploring the timings of interventions across all commonly used modalities for the management of LRS, including physiotherapy, and surgery. The one RCT reported (Peul 2007) and the two accompanying follow-up analyses, suggests that patients who undergo surgery between 7 and 12 weeks after symptom onset, have improved outcome initially but at 1, 2 and 5 years there is no significant difference in terms of self-reported disability, leg pain or back pain between groups.

3.14.1 Strengths and limitations of the review

The review benefitted in the development and use of a pre-defined protocol, registered on PROSPERO. The use of the current Cochrane guidelines for systematic reviews and the PRISMA checklist adds strength and transparency to the study. Furthermore, the use of widely utilised and valid tools in the collection and review of data is a key strength of the review. The review was limited in its search to OECD countries and in doing so ensures the search has critical utility in the geographical area it was meant for. Potential limitations of the review were the exclusion, due to pragmatic reasons, of non-English language articles. The initial title and abstract searches found 18 studies which were not in the English language and so were excluded. The other key limitation was the use of only one reviewer (MR) to search, retrieve, catalogue and appraise studies. This was for educational reasons although could still lead to potential risk of bias.

3.15 Conclusion

This systematic review provided information about the optimal timings of interventions commonly utilised in the management of LRS. The review found only one RCT which

recommended surgery within two weeks of randomisation. There are insufficient number of studies to make clear recommendations about the timing of interventions for LRS. This is reflected in clinical practice with uncertainty as to when to instigate any form of treatment. Further research is required to determine the optimal timing for interventions used in the management of LRS. Particularly welcome would be trials with quality longitudinal designs and detailed, protocolised interventions, so as to enable replication in the clinical setting. This chapter has built upon the literature review carried out for Chapter 2. It has highlighted the lack of evidence as to the optimum timing of commonly used modalities for the management of LRS and need for further research. In the next chapter I will outline the quantitative design elements of the study.

Chapter 4 POLAR intervention

An integral part of the POLAR study is the physiotherapy intervention being delivered through a participant-physiotherapist partnership. This chapter provides background to physiotherapy approaches historically used for LBP and LRS and an insight into how the POLAR approach was developed. The current iteration of the POLAR approach used in the study is presented.

4.1 The Intervention

There are many physiotherapy approaches for the management of spinal conditions used in the western world. The uptake of which is often dependent on the individual clinicians undergraduate and postgraduate education, local expectations in individual hospital physiotherapy departments and personal preference. The most common approaches include the Maitland concept (Hengeveld E, 2013), Society of Musculoskeletal Medicine (Cyriax, 1996) and the McKenzie method of mechanical diagnosis and therapy (Mckenzie, 2011). All of these and others have advanced the physiotherapy management of musculoskeletal conditions immeasurably over many years. However, these approaches were developed by clinicians before the advent of independent, autonomous physiotherapy practice, Bachelor's degree courses in physiotherapy and the application of scientific rigour to physiotherapy practice. They have in common, a pathoanatomical approach to treatment which aims to find a pathoanatomical/pathophysiological cause for the patients' symptoms. These approaches, although some having been revised over the years, still tend to address a pathoanatomical cause for pain, be unimodal and reductionist with the aim being to place patients into manageable sub-groups dependent on their symptoms, rather than their wishes, goals and problems. They fail to consider all of the elements which can be part of the 'whole' problem of LBP and LRS in the individual. Problems arise when the intervention is seen as a 'whole' rather than a complex, multiple-part entity with discrete parts (Cresswell, J.W, 2011; Clark, 2013). The adoption of the biopsychosocial model, rather than a biomedical approach, changed physiotherapy treatment from being a didactic, medically driven, mechanistic approach to a more holistic partnership between patient and clinician (Hartvigsen *et al.*, 2018). More contemporary methods have evolved to encompass a patient-focussed, flexible, evidence-based, biopsychosocial approach, such as the Cognitive Functional Therapy (CFT) (O'Sullivan *et al.*, 2018) and the Pain Neuroscience Education (PNE) approaches (Clarke, Ryan and Martin, 2011). These approaches make great strides in addressing the complexities of LBP and draw heavily on the neurosciences and pain sciences with behavioural and cognitive change at their core.

The POLAR approach has a similar reliance on pain and neurosciences, together with a core multi-modal approach encompassing the varied elements of the patient's problems. The POLAR approach is an amalgam of the approaches aforementioned and aims to draw on the key elements of each. The approach has evolved over many years and continues to do so with the author and other clinicians, together with patients driving its development. Key elements pre-date the CFT and PNE approach but has encapsulated key elements of both. The POLAR approach is utilised clinically for LBP but was specifically developed for patients with LRS. The CFT approach filters out patients with disc prolapse, lateral canal stenosis, central stenosis, high grade spondylolisthesis (not specified which grading system) and refers for imaging. There are no robust and reliable clinical tests that would enable the aforementioned diagnoses, so it is questionable how the diagnosis would be made in the absence of MRI/CT scanning. The POLAR approach focusses not on the biomedical diagnosis, for example, lateral recess stenosis but on the patient's functional problems and their goals.

The reporting of interventions in detail enough to render them reproducible is essential with its absence evident across many clinical groups, including physiotherapy. Interventions are often described with a broad stroke such as 'physiotherapy' or 'conservative care', which limits the possibilities to determine the effective component(s) of the intervention (Michie et al. 2011) and its reproducibility. Finally, the POLAR approach has been protocolised in order to improve its robustness, reproducibility and to promote clarity of clinical decision making.

Guidelines have been produced to educate and encourage best practice in the management of LBP and LRS. The European guidelines for the management of CLBP acknowledged the complexity of the problem and that unimodal treatments were unlikely to be effective (Airaksinen *et al.*, 2005). Airaksinen (2005) found modest effect sizes for most treatment approaches for LBP and CLBP and recognised the utility of cognitive therapies which encourage exercise, together with manual therapy, exercise therapy and a multidisciplinary approach. It is important to acknowledge that the guidelines refer to CLBP and do not encompass management of LRS/sciatica. The recommendation not to offer imaging (X-ray, MRI, CT) for CLBP is supported by the European guidelines as well as the primary care guidelines (National Collaborating Centre for Primary Care, 2009). This guidance also promotes a patient-centred approach by giving patients choices of their care, for instance exercise type. The guideline is however reductionist and suggests a unimodal approach to care in promoting an exercise programme or manual therapy or acupuncture.

The clinical effectiveness and cost-effectiveness of management strategies for sciatica has been published (Lewis *et al.*, 2011). This health technologies assessment systematic review provided evidence for the use of non-opioid analgesia, epidural corticosteroid injections and Lumbar disc surgery as well as chemonucleolysis, a seldom used intervention. The review also suggests passive therapies, such as acupuncture. The review supposes a uni-modal

approach to the management of sciatica in a stepwise method. In reality this means starting with the cheapest treatment and only referring onto the next step only when the first has been proven ineffective. This undeniably adds significant time and potential added costs to the processes. This is in contrast to the UK government and NHS targets of 'getting it right first time' (Hutton, 2019). The most contemporary guideline addresses both LBP and LRS/sciatica (National Insititute for Health and Care Excellence, 2016). This comprehensive guideline has extensive recommendations with regards to the management and implementation of management strategies for LBP and sciatica. The guideline suggests that a screening tool be employed to stratify patients with LBP, with or without sciatica at first contact in order to direct treatment. Treatment should then be stratified according to the patients' risk of developing chronicity, with the higher risk and more complex patient presentations receiving more complex treatment. The use of group exercise programmes are presented and, importantly, acknowledging patient's wishes for the type of exercise they undertake. The guidelines also acknowledge the complexity of LBP/sciatica and the utility of offering a multi-modal package of treatment, depending on patients' needs and wishes.
The ongoing improvements to the management of LBP and sciatica through the implementation of guidelines-based evidence have been augmented by the use of evidence-based algorithms and pathways of care. The Sheffield Back pain pathway was introduced in 2008, this aimed to improve the standard and equity of care for people with LBP/sciatica in Sheffield (Hart and Ryton, 2013). Several areas across England have implemented their own versions of the Sheffield backpain pathway and more recently a national back and radicular pain pathway (NBRPP) has been implemented (Services, 2017). The NBRPP aims to ensure that the appropriate assessment and treatment of low back and radicular pain is rapidly referred to the appropriate agency. It aims to expediate treatment, including physiotherapy and surgery and provide effective and timely care for acute LBP/sciatica sufferers in order to reduce disability and costs. This is in keeping with the Getting it right first time (GIRFT) initiative from the department of health (DoH) which aims to improve operational efficiency for spinal patients (Hutton, 2019). The adherence to such guidelines is questionable and they are a source of great debate as is their relevance to clinical practice and patient-centred care (Bishop *et al.*, 2015).

4.2 POLAR intervention development

The POLAR intervention approach has been described in terms of the TIDieR checklist (Hoffmann *et al.*, 2014). The intervention has been developed prior to this study by the author and colleagues, together with the feedback and guidance of patients, students and colleagues over more than 20 years of clinical practice. The approach continues to evolve according to emerging evidence and clinical refinement. The initial drivers for the

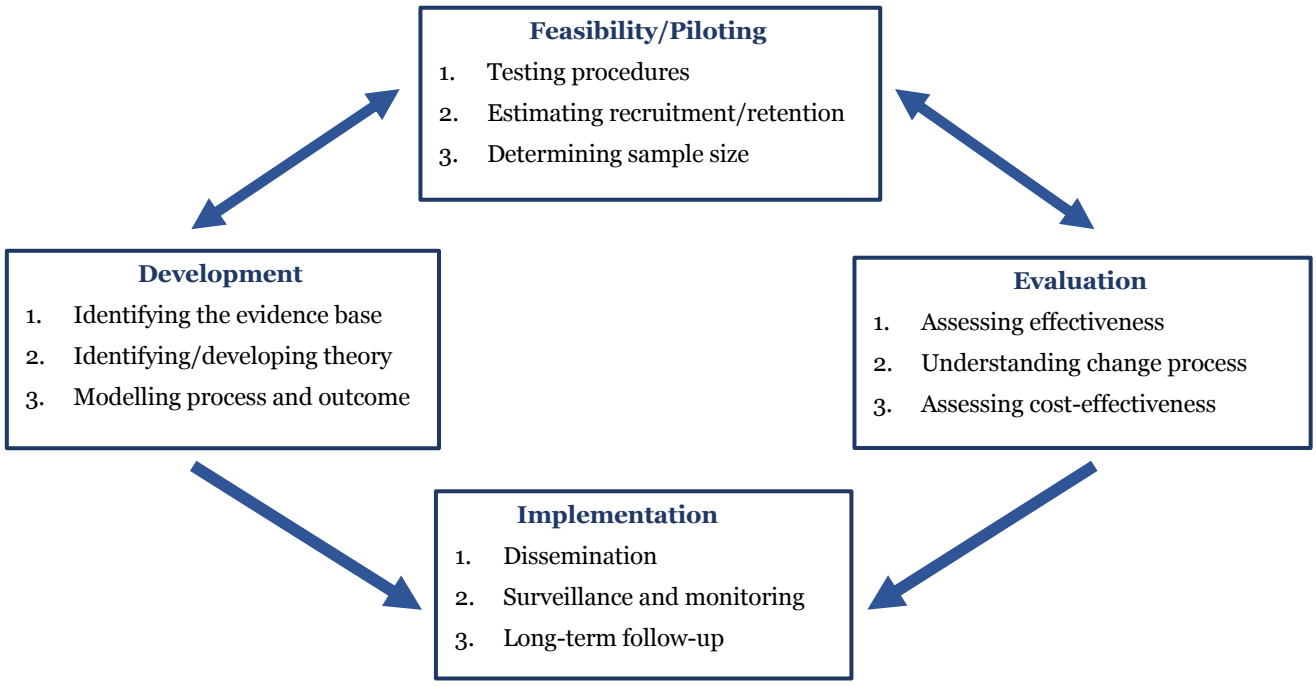
development and use of the approach were two-fold. Firstly, regular feedback from patients regarding their previous or ongoing physiotherapy treatment. The common refrain was of not being listened to, of not being valued as an individual, of the treatment being didactic and not relevant to them and of being given a generic exercise sheet and told to come back in several weeks' time. Secondly, the approach grew from the integration of approaches and techniques usually utilised in the rehabilitation of neurological patients, such as movement analysis and goal-based strategies, which seemed to work with complex LBP and LRS patients.

The pragmatic development of the approach, prior to the onset of the POLAR study, stems from forming an amalgam of the 'best' parts of a variety of commonly used approaches. These treatment components were exposed to a thorough scientific critique of the surrounding literature for that element and refined through discussion and debate as to the component's clinical credibility. Patients were involved from the start of the informal process in these informal critiques and evaluations in person or remotely and continue to provide the most important user-feedback. The results of patient recorded outcome measures which were routinely administered to patients were analysed, the results of which helped to form an opinion on the use of a particular element of the treatment approach.
The approach therefore began its organic growth from clinical experience of what seemed to work for patients with LRS. This approach is somewhat against the theory-driven intervention development espoused by the Medical Research Council (MRC) guidelines (Peter Craig *et al.*, 2008). However, such an approach has been advocated by Miller and Shinn who argue that by finding 'real world' interventions that have already been implemented into local practice, external validity and clinical acceptability is already in place (Miller and Shinn, 2005).
The POLAR intervention was first protocolised for a study (Boote *et al.*, 2016) and utilised the checklist for health service interventions and was well received by patients and physiotherapists (Dorling *et al.*, 2014). Patients valued the individual approach to rehabilitation, pain management, manual therapy, movement re-education, increasing spinal movement and function-biased approach. During the development of the study it became clear that it would be difficult to evaluate which elements of the intervention were effective. If it worked then we would not know why or which elements were key. The complexity of the intervention had continued to grow through its iterations without a solid theoretical framework from which it could evolve. This is a priority for further intervention development.

4.3 Complex intervention development

The POLAR intervention has been utilised in a previous pilot trial for sciatica Boote et al (2015) and no significant changes have been made for this study other than a new training manual. The intervention was widely accepted by patients and clinicians alike, although formal fidelity testing for this study was not undertaken. A logic model has been developed in order to describe and visualise the complex elements of intervention components and study processes. The POLAR approach encompasses several elements of a complex intervention, including a number of interacting components (the assessment and treatment domains), number of organisational levels targeted (study processes), variability of outcomes (varying severity of symptoms in patients, varying clinical presentation) and the flexibility required to deliver the intervention (patient-centred and goal orientated) (P Craig *et al.*, 2008). The emergence of the United Kingdom MRC guidance for developing and evaluating complex interventions has provided guidance for the presentation of the POLAR intervention prior to the study commencing (Sermeus, 2015). The guidance suggests a systematic approach to the development of interventions with careful testing at each stage. However, it was simply not practical, although desirous, to formally develop the intervention for the study due to time and fiscal constraints. Figure 4.1 illustrates the key elements of the development and evaluation of a complex intervention.

Figure 4.1 Key elements of the development and evaluation process
(P Craig *et al.*, 2008)



4.4 POLAR physiotherapy approach

A patient-centred, holistic, multidimensional treatment framework has been developed, prior to this study, to assess and treat the various aspects of the patients' problems arising from their LRS. Some aspects may be contributing considerably to the patients' problems, other elements less so. Some aspects may be responsible for a considerable proportion of the problem, but may not be amenable to physiotherapy, for example financial concerns, bereavement, divorce. Others may be eminently responsive to the multi-modal physiotherapy approach. However, by identifying the complexities of the problems faced by the patient and signposting them to the right element of the treatment regimen, an improvement in quality of life and function will become evident.

The intervention is an amalgam of seven different domains of treatment, including much of what was described in the opening paragraph. The approach is not exhaustive, it is not final and is most importantly, it is iterative. It will change and grow as new evidence emerges. It attempts to reflect patient needs, best current interpretation of evidence, patient preferences and is pragmatic in being developed in the NHS in England and is cognisant of the fiscal restrictions placed on services and commissioners. The approach is by design, multi-modal in order to reflect the multifarious needs of the individual patient.

4.4.1 Behavioural change

An important aspect of the intervention is behavioural change. The abherant behaviours which are most often evident in LRS patients are movement avoidance or adaptive behaviours. These are behaviours or ways of doing things that may be manifest and indeed useful in the acute phase of LRS but can quickly become maladaptive and deleterious to the long-term outcome. It is therefore imperative that a change in maladaptive movement behaviours, rather than simply carrying out daily exercises is undertaken. It is important to first assess the patients' willingness for change, which may involve education as to the nature of the aetiology and prognosis of LRS. This may be affected by other factors such as the patients' levels of fear, their understanding of the problem and levels of pain.

Behavioural change theories have been utilised in the management and self-management of LBP and CLBP (Hurley *et al.*, 2016). However, there do not appear to be any examples in the literature regarding the utilisation of behavioural change theories in the management of LRS. There are many proposed methods of behavioural change, including the behavioral change wheel (Michie, van Stralen and West, 2011), the fear avoidance model. Behavioural change theories have been proposed, however the implementation of those theories is limited in LBP research (Keogh *et al.*, 2015), in this regard it is therefore important to have vehicles to help the implementation process. Two such vehicles are the Capability, Opportunity, Motivation-Behaviour (COM-B) (Michie *et al.*, 2011) and the Theoretical

Domains Framework (TDF) methods (Cane,. O'Connor,D. Michie, 2012). The COM-B components bring together those factors which are necessary to bring about behavioural change. Capability refers to the individuals (or groups) ability to engage in behavioural change physically and psycologically. Opportunity refers to the factors external to the individual which make behaviour possible and Motivation alludes to the habits and emotional responses of the individual towards those behaviours (Mansell, Hall and Toomey, 2016). The TDF aims to make the process of developing behavioural change easier and consists of 14 domains and 84 component constructs. The use of such methods allows the detailed description of the components of behavioural change to be documented and reproduced in the clinical setting.

The therapeutic setting allows for health education and promotion to improve overall health, such as signposting the patient to the appropriate smoking cessation programme.

4.5 Principals of assessment

The aim of the patient assessment is primarily to elicit information from the patient in order to form a management plan to achieve their goals. There are very many ways of doing this, the method advocated for use in the POLAR approach is a patient centred method taking a few of the principles of motivational interviewing (MI) (Hall, Gibbie and Lubman, 2012; Miller and Rollnick, 2013). A review of motivational strategies in the physiotherapeutic domain. Three studies utilising MI were found, only one of which targeted CLBP, with significant differences between groups. No studies were found relating to LRS and therefore no conclusions can be drawn in terms of its utilisation for patients with LRS (McGrane *et al.*, 2015). Increased adherence to chronic pain treatments have been found for those utilising MI tools in a recent systematic review (Alperstein and Sharpe, 2016). The study was however limited to chronic pain patients and, again not specific to those with LRS. The use of MI has been found to strengthen the effects of physiotherapy in a small population of patients with LBP, but not LRS (Cheing *et al.*, 2014). Patients with LBP want an approach that is open, empathetic with validating communication. The basic principles in relation to the POLAR approach are founded on the following:

- A patient centred approach
- Empathic
- Patient/physiotherapeutic partnership
- Clarifying answers
- Open questions
- Non-judgmental
- 'Active' & 'Reflective' listening

- Supportive
- Discursive
- Non-confrontational
- Non-argumentative

It is important to note from this list that effective verbal and non-verbal communication is important. Not just what is said but how it is conveyed. The aim to embody an approach which is logical, structured and step-wise, with a transparent clinical reasoning process that is in partnership with the patient (Parry, 2015).

4.5.1 Utilising the placebo and patient-therapist effect

There are many and varied definitions of what a placebo is, ranging from 'A treatment that has not been proven effective' (Shapiro, A. K. & Shapiro, 1997) to a more nuanced view that 'Placebo effects are beneficial effects that are attributable to the brain-mind responses to the context in which a treatment is delivered rather than the specific actions of the drug (or treatment)' (Wager and Atlas, 2015). There are several physiological systems postulated to be involved in the placebo response (Goebel, 2002; Schedlowski and Pacheco-López, 2010), including the immune (Benedetti *et al.*, 2003) neuroendocrine and autonomic (Meissner, 2011). The descending pain modulating systems are particularly important in terms of the POLAR intervention as they have the potential to reduce nociceptive input (Fields, 2004)..
It is important to acknowledge the presence of the practitioner effect when treatment is being delivered by more than one clinician (Lewis *et al.*, 2010). The perceived effect has been shown in trials of spinal pain and disability as a non-specific effect of treatment. It therefore has implications in study design and sample size calculation.
Interventions which are delivered in a clinical setting are subject to social, environmental and physical cues. There are four factors postulated to have a key influence on the patient-therapist effect, communication and interpersonal skills, practical physiotherapeutic skills, individualised care and organisational and environmental factors (O'Keeffe *et al.*, 2016). They are also subject to the patients' previous experience, pain levels and above all expectations, positive or negative. In order to harness the patient-therapist effect in practice it is important to manipulate these key areas within the clinical environment. These include the immediate environment, is it safe, clean, accessible and comfortable? The social cues involved in the interaction between the patient and clinician, such as verbal and non-verbal communication, a friendly welcome, 'active' listening, eye contact, a friendly tone of voice and the smart appearance of the clinician. The verbal suggestions from the clinician with the patient are important. They should be encouraging, open and non-judgemental, voicing a

clear, understandable diagnosis (if appropriate) and provide the patient with treatment options.

4.5.2 Eradicating the nocebo effect

Whilst the placebo phenomenon is relatively well researched as to its effects, the clinical, psychological and physiological effects of the nocebo effect are less well understood. The nocebo effect is defined as 'the effect that follows the administration of an inert treatment along with verbal suggestions of symptom worsening' (Petersena G.L, Finnerup N.B, Colloca L, Amanzio M, Price D.D, Jensen T.S, 2014). Clinically, it is seen regularly in LBP and LRS patients who have been told that certain activities are dangerous, such as bending, exercising and lifting. The descent into the fear avoidance model can follow. Verbally induced nocebo has been found to increase anxiety in patients suffering with pain, the physiological pathways for which have been postulated to increase hyperalgesia and facilitate pain transmission (Benedetti *et al.*, 2006). Fear of pain has been found to be a useful predictor of nocebo hyperalgesia (Aslaksen and Lyby, 2015). Identifying the source of fear of pain is therefore important in the clinical setting in order to treat, minimise and eradicate the nocebo effect. In the clinical scenario it is important that communication doesn't activate these postulated nocebo pathways. Avoidance of emotive, negative terms is of the highest importance, such as giving an overly negative diagnosis, describing an IVD prolapse as abnormal, and as a permanent entity which will limit activity and will never improve, whereas IVD prolapses are often found in normal in pain-free subjects Another common nocebo inducing clinical scenario is telling patients they shouldn't exercise as it will worsen arthritis and thus accelerate pain and disability. These examples are common in the clinical setting but have no grounds in science.

The commonality between the placebo and nocebo effects is the patient's expectation of pain; pain relief with the placebo effect and heightened pain with the nocebo effect. The POLAR approach aims therefore to harness the placebo phenomenon therapeutically and minimise or eradicate the nocebo effect through clear, concise and factually correct communication.

4.6 Goal Setting

Goal setting is an important aspect of patient care, one which is a high priority for patients with CLBP. Goal setting is a way of finding out what the patient wants from treatment. Common goals are to be able to return to work or look after their children, walk further or take part in sport. Goal setting is inherently linked with self-efficacy (Locke and Latham, 2006) which is important both in helping resolution of the current problem and in self-management of future exacerbations.

However, goal setting in the physiotherapy care of patients with CLBP can be sporadic (Gardner *et al.*, 2018) and significant heterogeneity of patient goals exist (Gardner *et al.*, 2015). Adherence to treatment appears to improve with goal setting for patients with CLBP, but this may not equate to improved outcomes (Levack *et al.*, 2006; Rosewilliam, Roskell and Pandyan, 2011). An important foundation for the POLAR approach is to define specific goals with the patient, goals are dynamic and change according to the participants evolving needs. Goal setting is a complex and sometimes difficult endeavour where agreement between physiotherapist and patient is the primary goal. Goals change with time and change between domains. The most obvious goal which almost all patients want, is to be free of pain. There simply isn't a cure for LRS, whether medicinal, surgical or physiotherapeutic which will make pain disappear. Pain will not disappear instantly but will usually subside in a graded way making life easier step by step.

4.6.1 Develop SMART goals

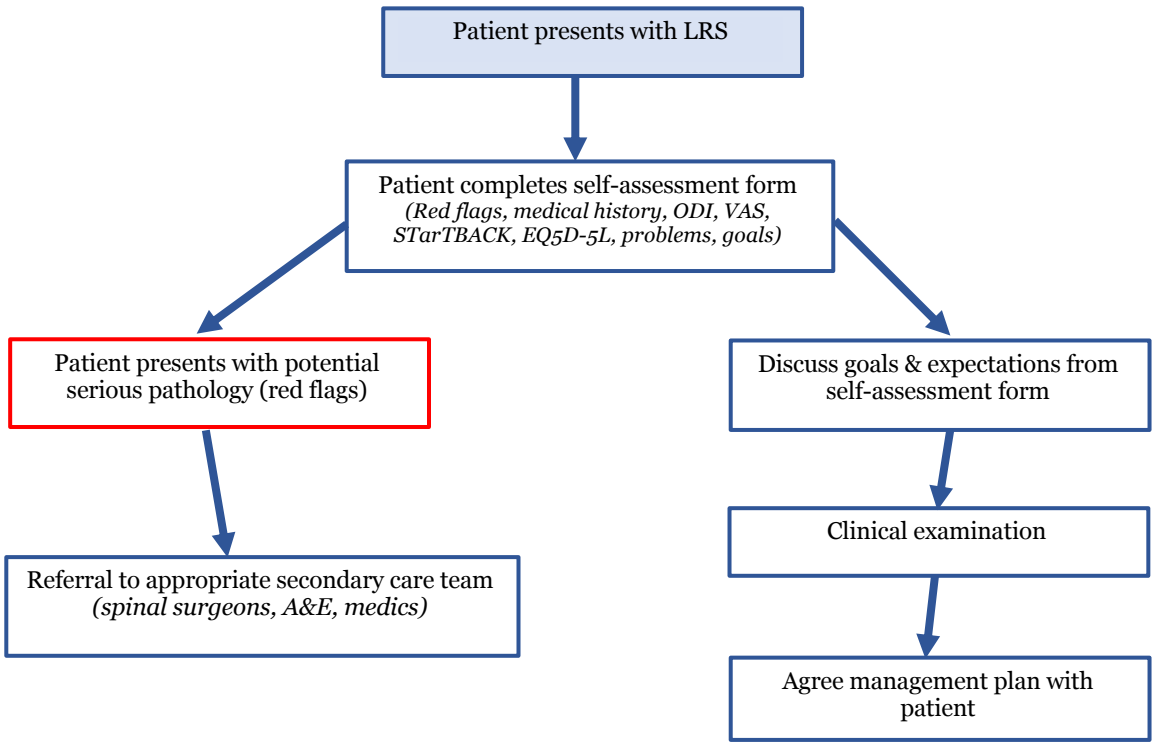
Collaborating with the patient in a supportive and discursive manner to elicit SMART (Specific, Measurable, Achievable, Realistic and Timely) goals is the first step in developing a management plan. Action plans are a useful method of stating the what, when, how and how often of a goal (Bodenheimer and Handley, 2009). This can take the form of a tacit agreement between the patient and clinician. For example, if the patient's goal would be to walk for 45 minutes 5 times a day, the clinician and patient may agree upon an incremental increase in walking time daily, with rests to stretch or relax in between. The development of SMART goals for the POLAR participants will encompass the specific domains within which the participant has identified problems. Therefore, the participant will have several domain specific goals which will encompass the participants overall goal of, for example returning to work.

4.7 Assessment and intervention

The assessment and intervention process for the POLAR approach is illustrated in Figure 4.2. It shows the initial triage process of ensuring that potential serious pathology is excluded or, if suspected the patient is referred for imaging and appropriate medical or surgical consultation. This information is elicited through the patient's self-assessment form and clinical examination. The process continues onto the management plan, encompassing the seven treatment domains. Before the initial assessment, patients are asked to complete a baseline self-assessment, consisting of a section highlighting potentially serious health problems (red flags), psychological health questionnaire (Keele STarTBack), area and nature of pain(s), self-rated disability (ODI), leg and back pain (VAS), general health questionnaire (EQ5D-5L) and what their expectations and goals of physiotherapy are. A thorough clinical

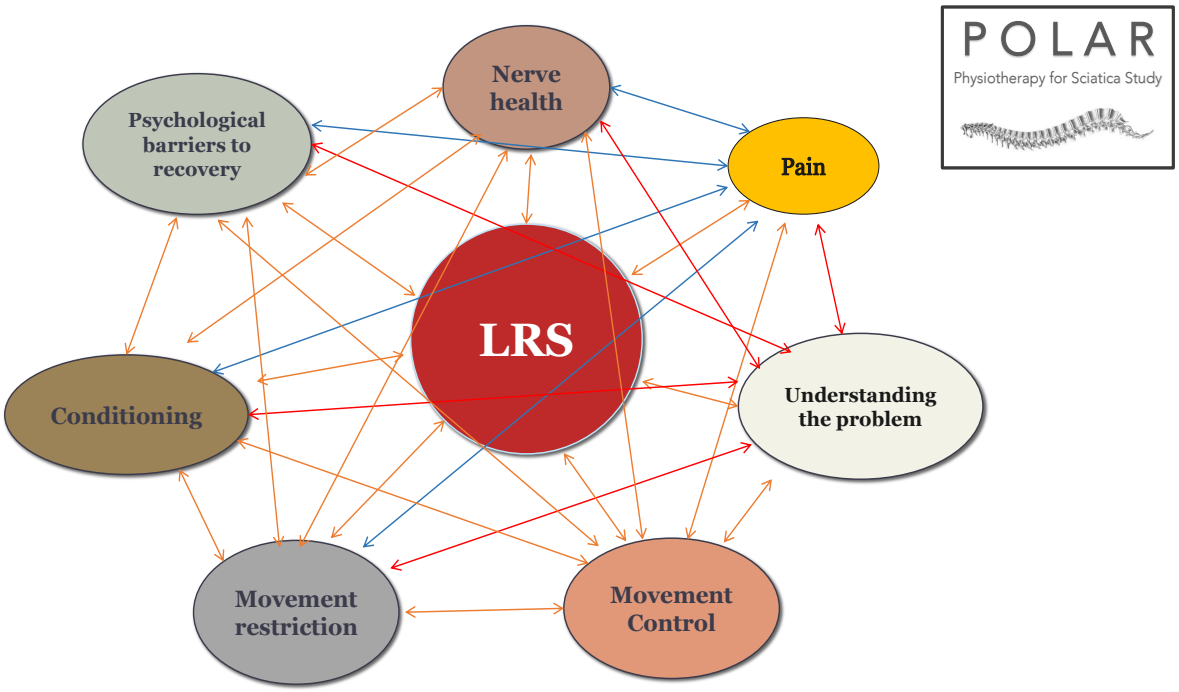
examination of the lumbar spine is carried out based around the information gleaned from the patient responses to the questionnaires and history-taking. The self-assessment forms can be found in Appendix 6.

Figure 4.2 Assessment and treatment process



The intervention framework has been developed, prior to the POLAR study, with colleagues and patients with the use of contemporary evidence from literature. This is based on an amalgam of science, clinical experience and patient feedback in order to deliver the best, patient focussed assessment and management plan possible for the individual. Figure 4.3 presents the seven domains of assessment and treatment and postulates the interactions within the framework.

Figure 4.3 Diagrammatic representation of the intervention domains



The framework advocates a patient-specific, goal-orientated functional approach to physiotherapy. It does not advocate a strict algorithm or recipe book from which to didactically or passively 'treat' a patient, but rather an opportunity to develop a partnership.

The seven domains of the POLAR intervention are described in detail below with their treatment components. The components are key composites of the treatment that will be delivered during the therapeutic interaction. Ten physiotherapists applied to take part in the study and were eligible by being a band 6 or 7. All were interviewed by the author (MR) and a senior manager of the physiotherapy service provider. Four physiotherapists were successful, with three delivering the treatment and one on standby to use as necessary. The fourth physiotherapist was not used during the course of the study. The physiotherapists underwent 21 hours of theory and practical training as well as mentoring through the course of the study. Mentoring was given as required to each physiotherapist throughout the course of the study as per the individuals request. This entailed discussion and clarification of processes, but not discussion or mentoring regarding individual participant management. It is beyond the scope of this thesis to provide an exhaustive description of the depth of the theoretical background for each component. Appendix 7 presents the intervention handbook

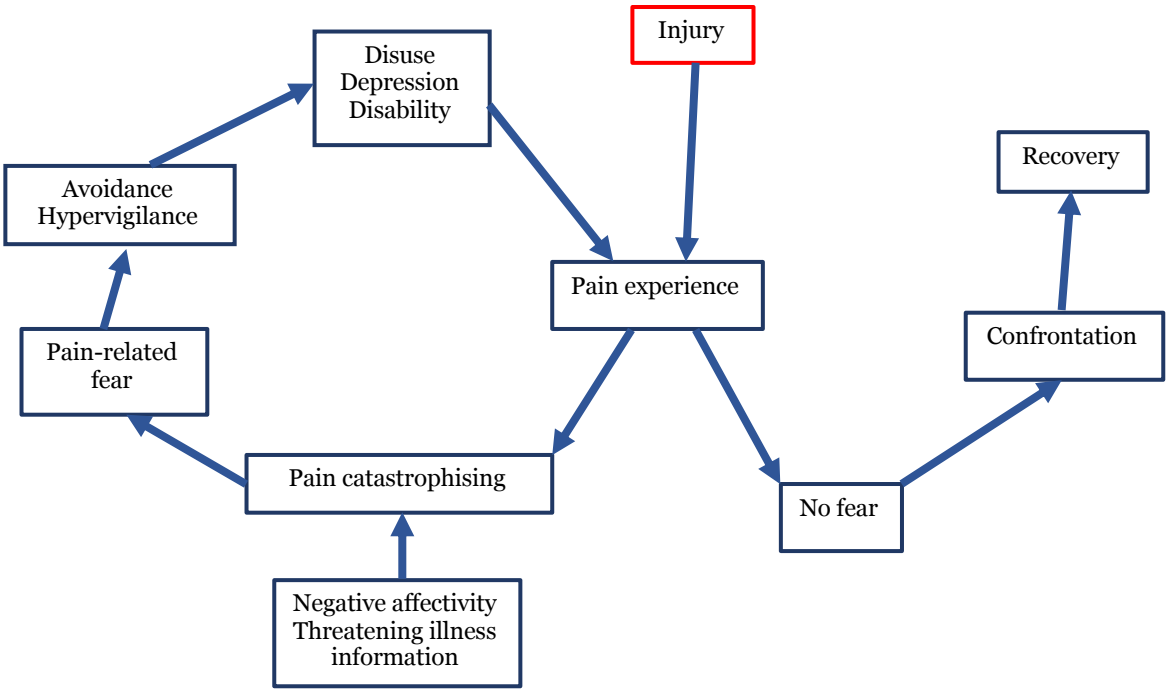
with more practical detail of the intervention domains and descriptions of how to administer each element.

4.7.1 Psychological barriers to recovery

Domain	Method of assessment	Treatment components
Psychological barriers to recovery	Keele STarTBack Clinical interview & history	a. Treatment of Kinesiophobia with graded exposure, education and movement re-education
		b. Treatment of hypervigilance with education, distraction & desensitisation
		c. Treatment of faulty beliefs about pain, LRS, treatment and/or prognosis with education and self-management strategies
		d. Treatment of Iatrogenic beliefs and corresponding avoidance behaviours with education and movement re-education
		e. Treatment of aspects of work as a barrier to recovery and treatment with ergonomic advice and practise
		f. Identification of financial barriers to recovery and signposting e.g. debt management, citizens advice bureau
		g. Identification of emotional barriers to recovery and signposting to appropriate therapy e.g. GP/Psychology

Assessment of psychological barriers to recovery is important as they are key predictors of a negative outcome (Blyth, Macfarlane and Nicholas, 2007; Linton and Shaw, 2011; Nicholas and George, 2011). The fear avoidance model of chronic musculoskeletal pain, including LBP has been widely adopted and is seen in clinical practice as a key barrier to recovery. Figure 4.4 shows the two proposed pathways following a hypothetical injury. The 'normal' pathway on the right-hand aspect shows a 'no fear' response to injury and a routine recovery. The alternative response, on the left, to injury is with the addition of fear. This promotes a cascade, both psychologically and physiologically which leads to worry about the cause of their symptoms (catastrophisation), avoidance of normal behaviours and activities (work, sport, normal daily life, movements) and eventual depression, disuse (de-conditioning, restriction of movement) and a continued cycling of the model (Vlaeyen and Linton, 2000, 2012). This is a common clinical occurrence and can be very difficult to interrupt and divert the maladaptive cycle. The POLAR approach attempts to do so by identifying the specific causative elements of fear and educating the patient appropriately. For example, the patient with LRS who believes or has iatrogenic disability secondary to believing that their pain is due to 'wear and tear', 'arthritis' or a disc has 'popped out' when lifting something. Such terms may seem innocuous, but they often evoke intense fear, kinesiophobia and triggering the fear avoidance cycle. Using education, both in terms of decreasing fear, stress and anxiety through verbal and visual cues but also through movement re-education. By decreasing the causative factors of fear and showing patients that they can function with decreased pain moves the fear avoidance cycle to the right.

Figure 4.4 The fear avoidance model



4.7.2 Neurological (nerve health)

Domain	Method of assessment	Treatment options
Neurological	Clinical assessment	a. Neural interface mobilisation
		b. Functional neurological movement re-education

The nature of LRS suggests a neurological dysfunction somewhere along the neural pathway, which is most commonly attributed to a lumbar IVD prolapse. An appropriate lower motor neurone neurological examination is warranted with symptoms of LRS to assess lower motor neurone neural integrity. An upper motor neurone examination would be carried out if symptoms suggested, such as gait disturbance, loss of fine motor control such as writing, difficulty instigating movement. Once the integrity of the nervous system has been established, the physiotherapeutic aim is to optimise the movement of neural structures within their interfaces. This is done therapeutically by manual mobilisation techniques such as slump stretching (Cleland *et al.*, 2006) and or exercises (Butler, 2000) in order to reduce potential intraneural oedema, improve intraneural fluid dispersion, reduce mechanical hyperalgesia, promote nerve regeneration and decrease immune response to injury (Whitehurst *et al.*, 2001; Song *et al.*, 2006; Adel, 2011; Da Silva *et al.*, 2015; Gilbert *et al.*, 2015). There is equivocal evidence suggesting neural mobilisation and lumbar mobilisation utilised together is effective in improving lumbar radicular pain (Efstathiou *et al.*, 2015; Ridehalgh, Moore and Hough, 2016; Das MS, Dowle P, 2018). Integration of neural

mobilising techniques into normal daily functional is vital. Normal, unhindered, fearless function will mobilise the neural system.

4.7.3 Movement restriction

Domain	Method of assessment	Treatment options
Movement restriction	Clinical assessment	a. Flexion mobilisation (Grade 2-4)
		b. Side-flexion mobilisation (Gr. 2-4)
		c. Extension mobilisation (Gr. 2-4)
		d. Rotation mobilisation (Gr. 2-4)
		e. Flexion+side-flexion mobilisation (Gr. 2-4)
		f. Flexion+side-flexion+rotation mobilisation (Gr. 2-4)
		g. Extension+side-flexion mobilisation (Grade 2-4)
		h. Manipulation (Gr. 5)
		i. Seated Mobilisation With Movement (MWM)
		j. Standing MWM
		k. Mobilisation into functional position
		l. Muscle stretches
		m. Functional movement re-education

Patients presenting with restricted movement in the lumbo-pelvic region on clinical examination or by voicing their problems of 'stiffness', which is deemed to be concordant with an element of their symptoms, are offered the corresponding manual therapy technique to improve movement, in order to facilitate their functional goal. The goal however is not merely to increase multi-segmental mobility in the lumbo-pelvis, but to ensure behavioural adoption of the new-found movement into functionally relevant goals and activities. Mobilisation and manipulative techniques have been adopted from the Maitland approach Manipulation (Bronfort et al. 2014) as part of a multi-modal package of care is superior to advice and exercise alone. The NICE guidelines suggest utilisation of manual therapy techniques (manipulation, mobilisation, soft tissue therapies) as part of a multi-modal treatment package (National Insititute for Health and Care Excellence, 2016).

4.7.4 Understanding the problem

Domain	Method of assessment	Treatment options
Understanding	Clinical assessment Interview	a. Management of erroneous believes relating to LRS provide education to help eradicate these beliefs
		b. Pacing behaviours
		c. Goal attainment
		d. Health Promotion
		e. Identification and treatment of central sensitisation-liaison with GP/pain clinic
		f. Identification and treatment of peripheral sensitisation-liaison with GP/pain clinic

The patient self-assessment form provides some evidence as to their understanding of their problems. From this, the clinical interview delves deeper into the patients understanding, beliefs and cognitions about LRS as well as general health and exercise. Any false beliefs and faulty cognitions can be challenged and reasoned with the patient a part of a larger treatment plan. It is important to identify erroneous beliefs and cognitions regarding LRS to avoid chronicity (Airaksinen *et al.*, 2005; Whitehead, Sully and Campbell, 2014; Otoo, S.K.W, Hendrick, P, Ribeiro, 2015). Pain hypersensitivity as a result of either central processing amplification or peripheral hypersensitisation are identified through clinical examination. Patients with such symptoms as a result of these phenomena are counselled and educated as to the possible causes and perpetuating factors (if identified) and an onwards referral to specialist pain management teams is made if appropriate.

The clinical encounter allows the opportunity for health promotion, in terms of optimising recovery from LRS but also to lead a healthier lifestyle. Identifying behaviours likely to benefit from health promotion such as smoking cessation, weight management and activity and exercise promotion are an integral part of the approach. Participants who smoked tobacco were signposted towards the Yorkshire smoke-free services and Sheffield smoking cessation programme and if they were a council or hospital employee, they were given the details of those specific services. This is in order to facilitate an active lifestyle and regular exercise; participants were given literature on the Sheffield 'Move More' campaign and signposted to the Sheffield 'Aches and Pains' website for information about their problem. For more information on LBP and LRS we have developed Sheffieldbackpain.com which POLAR participants were advised to utilise. Participants who were obese and wished to access services to aid weight loss were asked to see their GP regarding services recommended by the NICE guidance (NICE, 2018).

4.7.5 Conditioning

Domain	Method of assessment	Treatment options
Conditioning	Self-assessment Clinical interview & history	a. Cardiovascular & conditioning exercise relevant to patients' goals
		b. Function specific stretches
		c. Function specific strengthening
		d. Ergonomic advice
		e. Ergonomic practise
		f. Group exercise
		g. Perturbation training

Identifying meaningful patient goals is perhaps most important in relation to conditioning. There needs to be relevance to the patient in their goals, in terms of work, sport or other important activities. This needs to be reflected in the exercise regimens prescribed, rather than adopting a generic approach. Early intervention isometric exercises have been found to be beneficial in patients with LRS (Huber *et al.*, 2011) and may be a useful adjunct to function-specific exercises in some patients. The approach focuses on function-specific conditioning and functional-based exercise (Searle *et al.*, 2015) In practise this may equate to global cardiovascular conditioning for a young footballer or specific pelvic girdle and lower limb strengthening in a sedentary elderly patient with the goal of getting out of their chair easily. There is conjecture regarding the optimum form of exercise for patients with LBP and or LRS. Exercise has been supported in the recent NICE guidelines (National Insititute for Health and Care Excellence, 2016) for the management of LBP and LRS for its potential to effectively help LBP/LRS but also for its potential for other health benefits and concomitant downstream cost-savings.

4.7.6 Movement control

Domain	Method of assessment	Treatment options
Movement control	Clinical assessment	a. Sagittal plane control in functional positions relevant to patients' problems/goals
		b. Coronal plane control in functional positions relevant to patients' problems/goals
		c. Axial plane control in functional positions relevant to patients' problems/goals
		d. Multi-planar control in functional positions relevant to patients' problems/goals
		e. Movement re-education in functional positions relevant to patients' problems/goals

Motor control of movement of the lumbar spine and pelvis gained popularity over the last twenty or so years and has gained recognition as 'core stability' in common parlance. The

spinal stability model suggested that a lack of neuromuscular control around a motion segment resulted in 'instability' around that segment and could lead to pain and spinal dysfunction (M. M. Panjabi, 1992; M. Panjabi, 1992; Panjabi, 2006). The effectiveness of models of stabilising exercises have failed to show any significant improvements in patients with LBP. This may be due to the unimodal approach of strengthening exercises for a multidimensional problem. The POLAR approach supports the use of movement control exercises for a specific functional problem in a functional manner. For example, if the patient lacks coronal control of the lumbo-pelvis whilst lifting a basket, then exercises to strengthen those muscles which control the lumbo-pelvic region in the coronal plan would be carried out. Those exercises would involve lifting the basket, maybe with less weight, until the patient has the strength to do it with less or no pain (O'Sullivan 2005; Luomajoki & Moseley 2011). There are various movement control rehabilitation approaches, one of the most comprehensive guides suggests rather a rigid framework, it does however have its merits in terms of clinical reasoning and exercise prescription (O'Sullivan, 2005; Luomajoki and Moseley, 2011).

Movement re-education is a key component of this domain and involves exposing the patient to potentially highly fearful movements (Alrwaily *et al.*, 2018), which are identified by a kinesiophobic response to movement in the assessment. Treatment involves hands-on support and direction by the physiotherapist in a controlled manner to re-educate the patient that the feared movement is no longer painful (or as painful). Once a movement has changed from being painful to less so, changing movement behaviours from abnormal to normal is practised so as to become habitual. This reinforces normal movement control in an improved pain state, thus decreasing kinesiophobic influence and breaking the fear avoidance behavioural cycle. This approach then introduces the integration of all of the aspects of the approach into the desirous functional movement, or the patient goals.

'Core' stabilisation exercises which have gained increasing popularity in the field of spinal rehabilitation over the last 20 years are not supported by the POLAR approach. Core stabilisation exercises have not been found to be more effective than general exercises in the management of LBP (Vasseljen *et al.*, 2012; Smith, Littlewood and May, 2014).

4.7.7 Pain

Domain	Method of assessment	Treatment options
Pain	ODI VAS back VAS leg Clinical interview & history	a. Analgesic review & advice in liaison with GP/Pharmacist
		b. Pain education
		c. Pain coping strategies
		d. Fear reduction intervention in liaison with psychologist/pain clinic
		e. Stress reduction intervention in liaison with psychologist/pain clinic

Pain is the most common symptom of LRS that patients will present for healthcare with. A thorough assessment of the patients pain using the ODI and VAS back and leg scores and subsequent development of pain management strategies is of the utmost importance (Pinto et al. 2012). The first aspect of pain management is to ensure that the patient is receiving the most appropriate pain relief, in an adequate dose at the appropriate time. This may require liaison with the prescriber of the medication to optimise pain relief in line with the NICE guidance for management of neuropathic pain (National Institute for Health Care and Exellence, 2013). The guidelines suggest giving the patient the choice of either Amitriptyline, Duloxetine, Gabapentin or Pregabalin with the option to trial to try another of the aforementioned if the initial choice is unsuccessful.

The second aspect of pain management is education. Pain education is based on the principals on pain neurophysiology education. The method of pain neurophysiology education described by is advocated for use as a practical and understandable means of relaying sometimes complex concepts. This involves regaining as near normal function and improved quality of life through a thorough understanding of what pain is, what pain is not and what patients and clinicians can do to manage it (Butler, D. Moseley 2013; Moseley, G L 2017; Moseley, G L, Butler D.S, Beames T.B 2012). The use of pain neurophysiology education in the management of pain has shown to decrease self-rated pain, disability and catastrophisation (Moseley, G L, Butler D.S, Beames T.B, 2012; Butler, D. Moseley, 2013; Moseley, G L, 2017). Pain education can also change maladaptive cognitions about pain and the patient's condition, suggesting a state of transition from pain to normalcy rather than to a permanent state of pain (Moseley, 2002, 2003; Clarke, Ryan and Martin, 2011; Louw *et al.*, 2011). By ensuring adequate analgesia and a clear understanding of pain it allows to patient to undergo other elements of the physical rehabilitation as well as return to function.

4.8 Proposed mechanisms of effectiveness

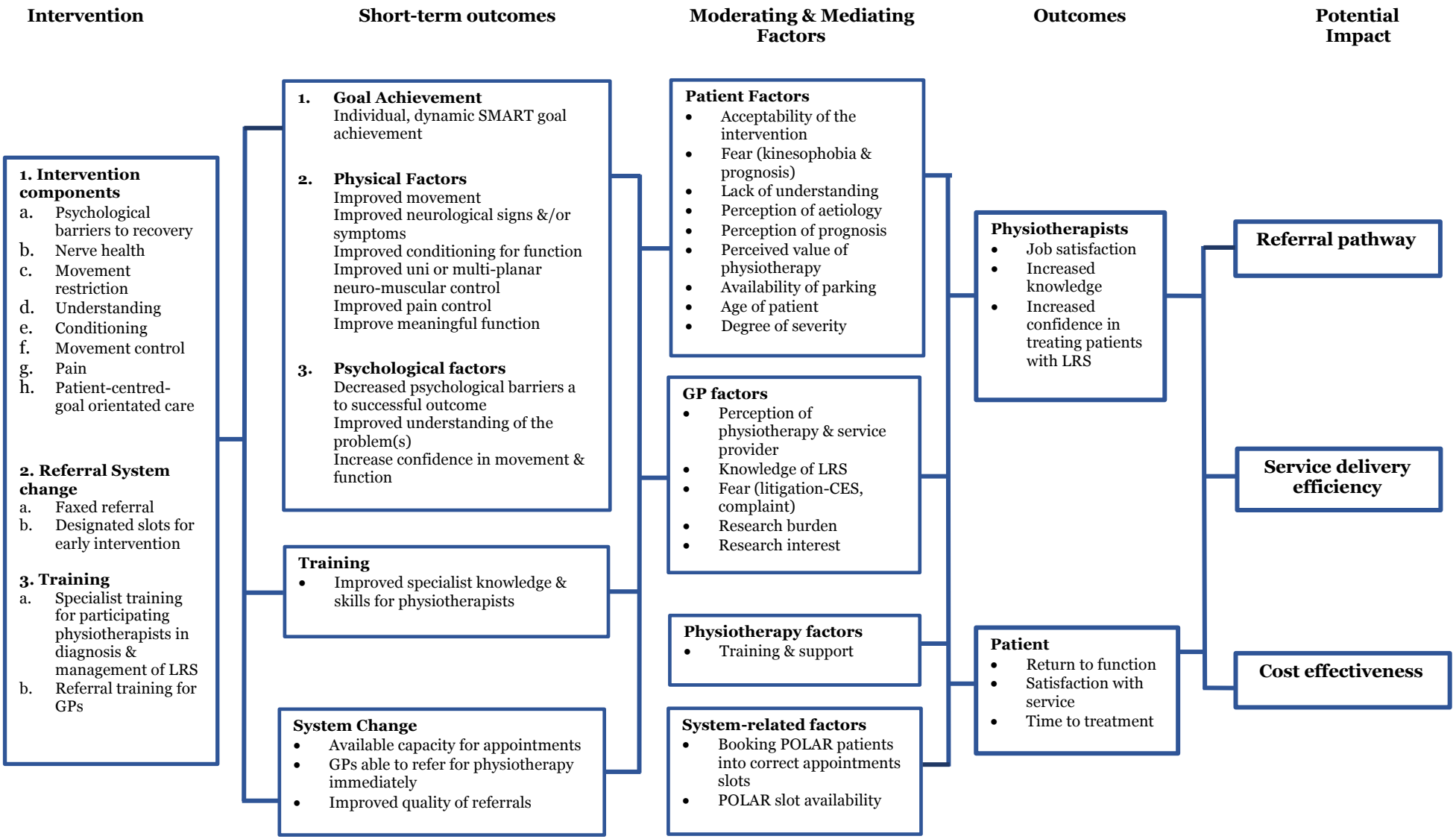
The seven domains of the POLAR study approach have been presented with the theoretical backgrounds for each. The complex intervention is hypothesised to work by identifying with the patient those aspects of pain, disability and lack of function that are deleterious to their recovery. The identification of these elements leads to an associated individual and flexible management plan.

A logic model is a pictorial representation of the process and theory of how an intervention or programme works (W K Kellogg Foundation, 2004). Programme logic models are utilised extensively in business, education, the social sciences and increasingly in healthcare to allow program developers to illustrate how a programme works (Hawe, 2012).

A flexible and iterative logic model has been developed as a means to describe and visualise the complexity of the intervention and the study processes in the POLAR study (Figure 4.5).

The logic model conveys the potential mechanisms of the intervention, the perceived outcomes and impact of those outcomes. In the example in Figure 4.5, the intervention domains on the left of the model are joined by other key elements required for the intervention to work, notably changes to the referral system and training the physiotherapists. The short-term outcomes for these inputs are the beneficial physical and psychological effects on the patient, for example, improved movement and understanding. There may be many moderating factors which will affect the effectiveness of the intervention, for example the perception of physiotherapy by the referring GPs. If the GPs question the worth of the study or the intervention, they may not refer patients. The logic model moves to the right with potential outcomes, it is important to highlight that the intervention will have an output for more than the patient. The treating physiotherapist outputs are likely to include improved knowledge of LRS, increased confidence of treating patients with LRS and potentially greater job satisfaction having taken part in the study.

Figure 4.5 POLAR Logic Model



4.9 Discussion

The intervention has been developed prior to this study by a clinical team, within a clinical environment and continues to be a work in progress. The approach absorbs and refines elements from other approaches and emerging evidence to reflect clinical requirements and has been piloted in a study which found it had acceptable clinical utility.

Following the utilisation of the POLAR approach within the study for the management of LRS, the next step is to utilise intervention development and evaluation theories such as the MRC complex interventions framework, theory of change and intervention mapping (Bartholomew *et al.*, 2001; Anderson *et al.*, 2011) to support its reproducibility in different environments and its robustness to varying clinical scenarios and clinicians. Further adoption of any new clinical and theoretical work would be integrated into the intervention as they become available. For example, the results of the SCOPiC trial (Foster *et al.*, 2017) will guide the effectiveness of elements of this intervention. It would be useful to determine if there are any 'critical' components of the intervention and which key moderating factors need to be addressed and their interaction with the other domains and components. The MRC process evaluation of complex intervention guidance would be utilised in these efforts.

4.10 Conclusion

The POLAR intervention utilised in the study has been described in this chapter. The intervention has been developed clinically and although this has been utilised successfully in two pilot RCTs, it would benefit from re-development using intervention development theories.

This chapter has described the clinical intervention developed prior to the POLAR study and utilised in the study. The intervention and the timing of its delivery is central to the study, the quantitative study design and methods for which are presented in Chapter 5.

Chapter 5 Quantitative study design and methods

The gap in evidence for the timing of physiotherapy for LRS has been illustrated in the previous chapters, supporting the need for more research in this area. In this fifth chapter, the design and methods for the quantitative element of the POLAR study are presented. They include the aims and objectives together with an innovative means of recruitment to solve a pragmatic problem.

5.1 Introduction

A mixed methods design was adopted for the study in order to meet the demands of the complexity of the area being addressed (Cooper *et al.*, 2014). The quantitative aspects of the study will provide evidence as to the feasibility of delivering the study, the intervention and recruitment parameters. The qualitative methodology and design will be presented in Chapter 6 and will explore the experiences of participants and other stakeholders. This chapter describes the methods used in the pilot trial. This pilot trial is an essential preliminary to a definitive RCT assessing the effectiveness and cost effectiveness of early physiotherapy intervention for patients with LRS. The pilot trial will test the protocol, the intervention, the use of outcome measures and the ability to set-up and run the trial to enable refinement of a future definitive RCT. This chapter is based on the protocol for pilot trial published in the BMJ Open (see Appendix 1) and received ethical by the East of Scotland Research Ethics Service (15/ES/0130) on 20th August 2015.

5.2 Methods

5.2.1 Aims and Objectives

The objectives of the pilot trial fall into two categories. Firstly, feasibility objectives allow the analysis of the practical and logistical aspects of setting up and running the study such as recruitment, the use of outcome measures, randomisation and data collection. Secondly, research objectives will provide valuable information as to the delivery and acceptance of the intervention and help inform the sample size for the definitive RCT.

The feasibility objectives for the pilot trial were adapted from examples given in the CONSORT extension for reporting randomised pilot and feasibility trials (Eldridge *et al.*, 2016). The CONSORT guidelines recommend that pilot trials have specific objectives for example:

1. To determine how many patients accept randomisation and early referral to a physiotherapy programme or usual physiotherapy;

2. To determine how many patients participate in early referral to physiotherapist programme;
3. To investigate the uptake of early referral to a physiotherapy programme in relation to subsequent behaviour change and impact on health-related quality of life;
4. To estimate eligibility, consent and recruitment rates, and 3- and 6-months follow-up rates;
5. To estimate key outcome domains for patients and patient reported outcome measures (that is, completion rates, missing data, estimates, variances and 95% confidence intervals for the difference between the control and intervention groups);
6. To synthesize data, on the key outcomes, to inform the sample size of a definitive trial.

Furthermore, designing studies with an external pilot phase may optimise the use of pilot work to inform more efficient randomised controlled trials (RCTs). Avery et al 2017 recommend careful selection of pre-agreed decision or 'progression' criteria at the juncture between the external pilot and main trial phases to provide an opportunity to evaluate the likely success of the main trial and optimise its design or, if necessary, to make the decision not to proceed with the main trial (Avery *et al.*, 2017). However, guidance on the appropriate selection and application of progression criteria is lacking. Therefore, our quantitative feasibility criteria were based on practical and pragmatic grounds rather than a published or recommended guideline. The 25% rate of participant attrition was chosen as a conservative estimate and was within the range of attrition reported elsewhere for RCTs 4% to 28% (Hewitt et al); (Wood, White and Thompson, 2004; Hewitt, Catherine E. Dumville and Kumaravel, BharathyTorgerson, 2010) and is in the range of attrition rates of similar studies in the field of spinal care of 20% and 22% (Bishop *et al.*, 2014, 2017).

5.2.2 Feasibility Objectives

1. Successfully set-up recruitment sites in GP practices.
2. Achieve a recruitment rate of 7 participants per month.
3. Demonstrate the ability to organise 75% of physiotherapy appointments within 2 weeks of randomisation.
4. Provide an appointment within 20 days of randomisation for >75% of participants randomised to the intervention group.
5. Achieve a participant attendance at >66% of physiotherapy appointments.
6. Achieve a participant attrition rate of <25% over the course of the study.
7. Achieve 80% return of Patient Reported Outcome Measures (PROMS) at 6/52 follow-up.

5.2.3 Research Objectives

1. To test the feasibility, practicality, safety and acceptability of the study design and protocol.

2. Demonstrate acceptability of the primary and secondary outcome measures to patients and clinicians.

3. To inform the sample size calculation for the definitive RCT trial.

5.3 Study design and setting

A mixed methods design compliments the study as it extends the understanding of a problem through its use of different methodological perspectives and is well suited to the POLAR study as it allows us to answer different parts of the same question. In this instance the question could be the 'acceptability of the intervention'. The quantitative element to the answer to this question may be the attendance levels at physiotherapy and attrition rates. The qualitative data would provide information as to what the participant found useful or not in the intervention as well as the reasons why they did or did not attend their physiotherapy sessions. Both aspects of the answers to this question would enable adjustments and refinements to the processes of the study and the intervention as necessary, which may not have been possible with uni-modal data.

A particular strength of the quantitative approach in the POLAR study is its ability to show any patterns in the results, for example the comparison between levels of self-reported disability from baseline to 26 weeks. The preliminary analysis using descriptive statistics of outcome data will allow decisions to be made for future studies in this area as to the acceptability of the outcome measures. The quantitative data will be utilised in tandem with the qualitative data to hypothesise potential mechanisms of action for the intervention.

The participants are at the heart of the study and have been from its inception. Their views, experiences and guidance were integral to this pilot study as they allowed iterations and developments of study processes.

5.4 Participants

Twenty GP practices in Sheffield, England were approached to take part in the study, with ten initially agreeing to participate. Towards the end of the second tranche of recruitment it was evident that one practice was recruiting a large number of participants. A decision was made to enrol new recruitment centres in order to decrease the reliance on the one, well performing centre and to see if recruitment was possible and practical elsewhere. Seven further GP practices were therefore approached, with four agreeing to participate. Patients with LRS were referred by their GP for physiotherapy following a clinical diagnosis of LRS.

The onset of symptoms were defined as the date of onset of non-tolerable radicular leg symptoms. GPs were given information and training about the study and posters were placed in clinical areas of recruiting practices (see Appendix 8). The patients were given a POLAR study information sheet (see Appendix 9) and asked to contact the research team if they wish to participate in the study.

Screening for eligibility took place according to inclusion and exclusion criteria, firstly with the GP and secondly when the patient contacted the research team. If the patient met the inclusion criteria, a meeting was arranged to obtain written consent (see Appendix 10). The inclusion criteria were that they have unilateral radicular-like leg pain, could speak and understand the English language and be under 70 years of age.

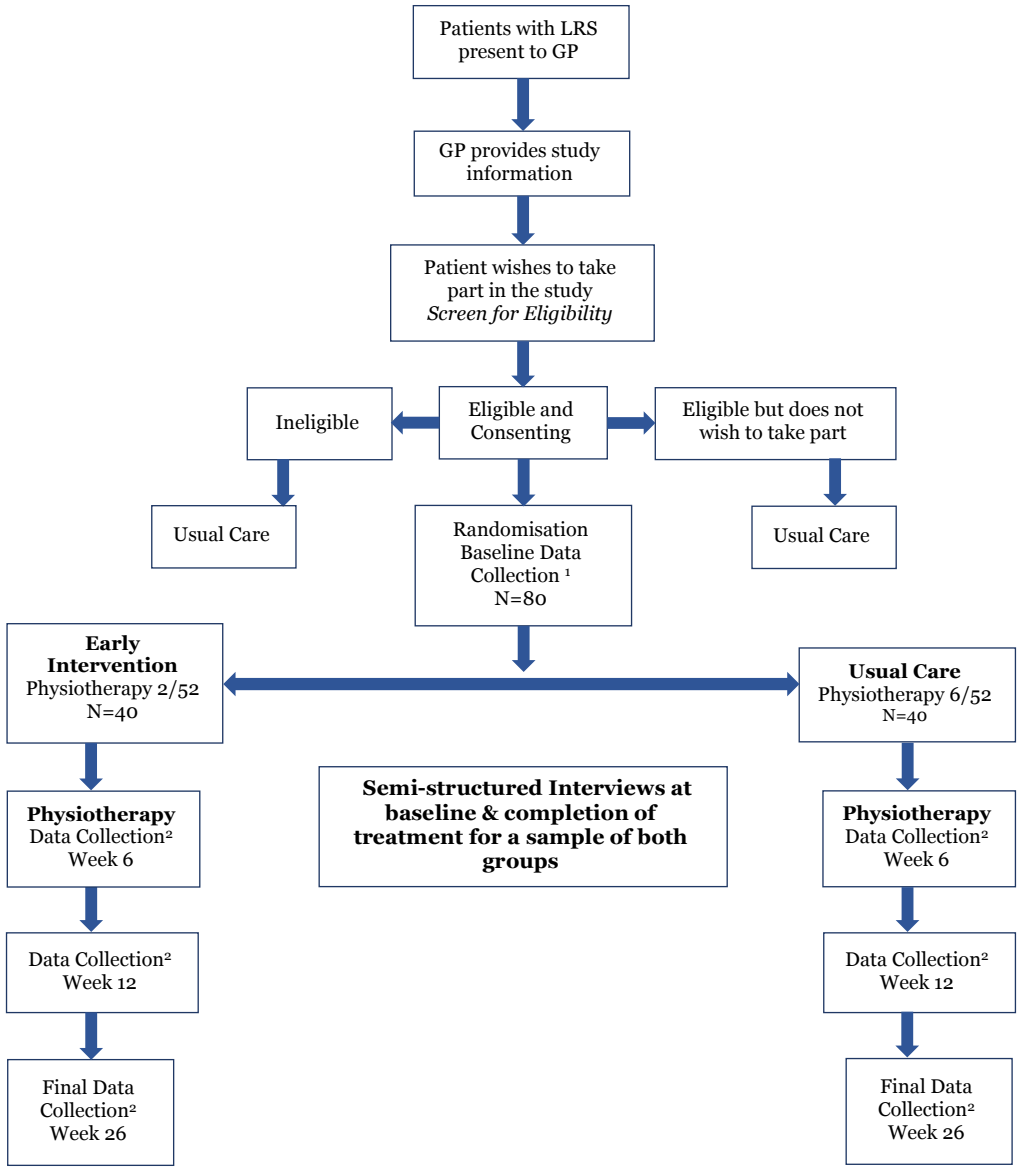
The recruitment, randomisation and patient flow processes are highlighted in Figure 5.1.

5.5 Public and patient involvement and engagement

The use of Public and patient involvement and engagement is central to health research policy and ensures clinical relevance of the research (Boote, Wong and Booth, 2015). INVOLVE define public involvement in research as research being carried out 'with' or 'by' members of the public, rather than 'to' or 'about' them. This is of paramount importance in clinical research such as the POLAR study where the research question was informed directly from patient feedback on physiotherapy services for LRS. Current and past patients who have experienced LRS and current physiotherapy and or surgical services were involved from the study's inception. The initial ideas for the study were garnered from discussions with patients and their experiences of LRS and the services they had received.

The study evolved with the direction of patients, in particular, the study's relevance to patient experience. Formal meetings were arranged during the application process where the research questions, aims and objectives were refined with the help of the patient group members. Further meetings were held following the successful application where at least one representative and usually two were present to discuss a specific agenda regarding the progress of the study. The representatives were influential in gaining ethical approval and in forming the lay summary for the ethics committee. They sat on the TMG and gave feedback on the development of the study design, methods used to collect data from patients and the intervention. The development of the qualitative aspect of the study was aided by the representatives in order to develop the interview transcripts and discuss the importance of allowing the voice of the participants in terms of their experiences of LRS.

Figure 5.1 Flow chart illustrating the recruitment and randomisation process



[1]Data collection to include: Baseline demographics, Medical history, ODI, VAS, STB, EQ5D-5L
[2]Data Collection to include ODI, VAS, EQ5D-5L

5.6 Inclusion and exclusion criteria

Inclusion criteria

1. Patients aged between 18-70 years of age with unilateral LRS defined as pain and or sensory disturbance and or weakness in a dermatomal and or myotmal distribution.

Exclusion criteria

1. Bilateral LRS.
2. Patients with 'red flag' signs and symptoms of potential serious pathology.

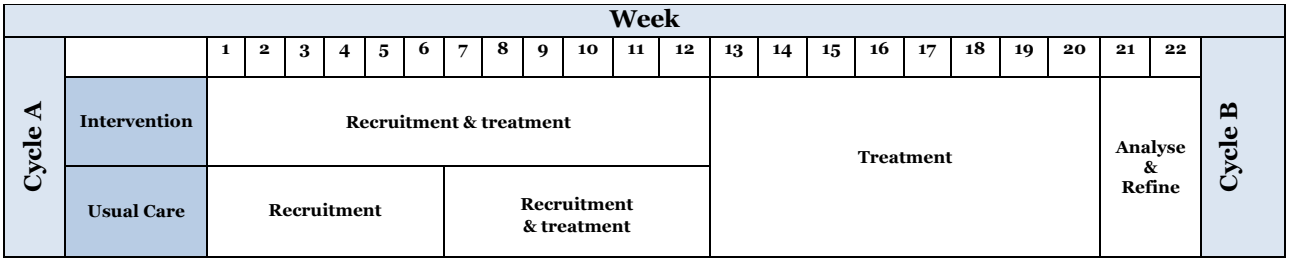
3. Cancer at the time of the study.
4. Proven vascular claudication.
5. Cauda Equina Syndrome (CES).
6. Spinal fracture within the last 3 months.
7. Chronic regional pain syndromes.
8. Recent lower limb fracture.
9. CVA with physical and/or psychiatric disability.
10. Poor English skills (necessitating the use of an interpreter and invalidating outcomes measures (ODI) as well as increasing costs).
11. Other significant physical or psychological co-morbidities preventing regular attendance at physiotherapy clinics.
12. Patients with significant mental health problems for which treatment adherence may be difficult or psychologically disabling, this will be at the discretion of the referring GP.

The initial screen for inclusion and exclusion criteria was carried out by the referring GP in order to determine eligbility. This was augmented by the author (MR) confirming the site and nature of the patients symptoms when contacted by the patient by telephone, in particular if the patients symptoms were unilateral and if they extended to the posterior aspect of the lower limb and distal to the knee. Furthermore, the treating physiotherapist confirmed (or denied) the diagnosis during the initial clinical assessment based on the criterai aforementioned. No inter-rater reliability testing for confirmation of diagnosis was undetaken.

5.7 Recruitment methods

Patient recruitment started on the 1st March 2016 and ended on the 7th November 2016 and took place over 3 cycles as illustrated in in Figure 5.2. Each recruitment cycle lasted for 20 weeks with a 2 week 'washout' period after each cycle for preliminary analysis of the completed interviews and stakeholder feedback. This was to ensure where necessary, reflection and refinement of the intervention and the study processes. This would be potentially problematic in a full RCT as it may make it difficult to replicate the intervention in future trials and may not represent the clinical reality of delivery intervention (Ritchie, J. Ormston, 2014).

Figure 5.2 Participant recruitment



5.8 Factors employed to maximise recruitment

A key feasibility objective was to ensure recruitment occurred within timeframe of patients into the study. To maximise recruitment, all potential stakeholders who may have influence over the study were identified in the planning stages of the study. Stakeholders were identified through a detailed process and stakeholder mapping exercise. This involved each process and sub-process of the participant journey from their initial GP appointment, referral to the study, completion of treatment and return of outcome measures being analysed in detail. These included the GP receptionists and clerks at the individual GP practices, both of which are involved in the provision of appointments and signposting patients towards the study. The GPs are key stakeholders as they are the first to make a clinical diagnosis of LRS and provide the patient with POLAR study information and instructions should they wish to participate. Practice nurses may also encounter potential participants and are therefore stakeholders. The referral to physiotherapy for potential participants in the study was sent by fax or email to a central referral group, staff in the group were stakeholders as they were pivotal in sending the referral onto the treating physiotherapist. Staff responsible for booking appointments for all physiotherapy appointments in Sheffield through the single point of access were important as they had to ensure that POLAR study participants were placed in POLAR study physiotherapy appointment slots. Receptionists at the service provider were also involved in the planning stages as they would be responsible for ensuring follow-up (second-sixth) appointments were made appropriately and with the correct physiotherapist. Process mapping events for each GP practice took place where the process of the patient journey from reception to identification of eligibility and onward referral was determined for each practice. There were mostly similarities between processes and sites, such as the clinical examination and where to send the referral, however there were practical issues which arose for 6 of the practices which involved changes to the study referral processes. In doing so it was envisaged that potential risks to either the success of the processes of the study and or elements of the treatment may be mitigated. Feedback from GPs and Physiotherapists was obtained prior to recruitment starting, to ensure that study processes are as near as possible to usual practise.

5.9 Outcome measures and data collection

Baseline outcome measures were collected at randomisation by either the author or the research nurse associated with the study. Further measures were collected at 6 weeks by the treating physiotherapist or receptionist, 12-week measures were collected either by the author during the post-treatment interviews or post and the 26-week measures were collected by post. The participant completed the outcome measures and forms independently and without aid from the author or research nurse. The research nurse was blinded to the participant allocation. The timings of the clinical assessment and outcome measures can be found in Table 5.1.

5.10 Primary outcome measures

The primary objectives for the POLAR study were the feasibility measures outlined in 5.2.2.

5.11 Secondary Outcomes Measures

The following secondary outcomes were used to reflect the multifarious nature of LRS and are the proposed outcome measures for a definitive, full-scale RCT:

1. Self-report disability was measured by the ODI version 2.1a (Fairbank and Pynsent, 2000). The ODI is a self-rated disability score based on 10 domains, each domain being scored out of 10. The higher the score, the greater the level of disability.
2. Back & leg pain will be measured by completing the Visual Analogue Scale (VAS) for their back and leg pain respectively. The VAS provides a score from 0-10, with 0 representing no pain and 10 the worst pain imaginable.
3. The EQ-5D-5L (EuroQol group) will be used as an overall outcome of health measurement. It comprises of two parts; the EQ5D-5L VAS and weighted health index score, a self-rated score of overall health 0-100, the higher the score, the better the quality of life and the EQ5D-5L Utility score, -0.6 to 1.00 with a higher score representing better quality of life.
4. The participants Return To Work (RTW) was measured by how soon they return after their initial physiotherapy appointment as will the number working days, which have been missed as a consequence of their sciatica.
5. The number of patients going on to have MRI and those who are referred to secondary care was measured and costed through utilisation of the secondary care provider electronic record system.
6. The number of patients undergoing surgery for their LRS was recorded and costed through utilisation of the secondary care provider electronic record system whereby an email would be sent to the author if a patient was listed for surgery.

7. The number of Serious Adverse Events (SAE), an SAE being defined as an event that may result in: (a) death; (b) is life-threatening; (c) requires hospitalisation or prolongation of existing hospitalisation; (d) results in persistent or significant disability or incapacity; and (e) consists of a congenital anomaly or birth defect.
8. Time from randomisation to physiotherapy treatment initiation.

The data collection domains and the methods in which they were collected along with the timepoints at which they are collected are presented in Table 5.1.

Table 5.1 Data collection and time points

Domain	Method of collection	Baseline	6 weeks	12 weeks	26 weeks
Probable primary outcome measure for full RCT					
Participant-rated disability	**Oswestry Disability Index** *0-100. Higher score, higher self-rated disability*				
Secondary outcome measures					
Participant-rated pain	**Visual Analogue Scale (VAS) leg & back pain** 0-10 *Higher score=more pain*				
Quality of life	**EQ5D-5L** *Higher score, better quality of life*				
Risk of persistent problems	**Keele STarT Back** *Total & sub scores determine risk of chronicity*				
Clinical measurements					
Demographics	**Participant self-assessment form**				
Pain location					
Participant goals					
Clinical History	**Patient interview**				
Past medical History					
Neurological status	**Clinical examination**				
Adverse Event **Serious Adverse Event**	**Local research department forms** **Report to ethics service**				

5.12 Screening for risk of chronicity

The STarT Back (STB) screening tool (Hill *et al.*, 2008) was used to analyse the participants risk of developing chronic symptoms. This will be administered before treatment commences and analysed at the end of the participants' treatment. Psychological factors are known to influence recovery from LBP, early intervention for these patients is recommended (Linton and Shaw, 2011; Nicholas and George, 2011).

5.13 Randomisation and allocation concealment

Information from the baseline dataset was used to randomise the participants using a web-based system. The ODI was used as the stratification factor with 3 levels based on ODI severity (Fairbank and Pynsent, 2000); 'mild & moderate' (≤22-40%), 'severe' (>40 to 60%) and 'crippled' (>60 to 80%). A blinded block size was used to minimise predictability. The random allocation sequence and block size stratified by centre and ODI disability score was independently generated by the Sheffield Clinical Trials Research Unit (CTRU).

Participants were informed of their group allocation within 1 working day of their consent and randomisation by either the author or the research nurse. Participants were randomised to physiotherapy treatment at either 2 or 6 weeks post-randomisation. In an effort to minimise bias, both groups of patients received protocolised treatment based on the same assessment and treatment framework at the different time points.

5.14 The intervention and comparator

The protocolised intervention allowed the treating physiotherapist a range of treatment options within each domain, with the selected options recorded electronically for each treatment session. The goal-orientated physiotherapy regimen for both groups were tailored to the individuals' requirements based on the information gathered from the baseline interview data, PROMS and clinical assessment as outlined in Table 5.1. Participants were assessed using a multi-dimensional approach based on seven different elements; psychological barriers to recovery, neurological factors, movement restriction, understanding, conditioning, movement control and pain. Individualised physiotherapy for LBP and LRS is known to be superior and more cost-effective than advice alone (Hahne, Ford, Hinman, *et al.*, 2017; Hahne, Ford, Surkitt, *et al.*, 2017), and the approach is flexible and directly relevant to the individual and their changing needs. The assessment and intervention was delivered by one of three physiotherapists at a single treatment site. The intervention is discussed in detail in Chapter 4.

5.14.1 Intervention

The intervention group received up to 6 sessions of physiotherapy over the maximum of an 8-week period or until the patient has reached their pre-determined goals. Their physiotherapy treatment commenced up to 2 weeks after randomisation. Implementation fidelity refers to "the degree to which the intervention, treatment or program is implemented as intended" (Gearing *et al.*, 2011). In order to address implementation fidelity in the study, the program model constituted the interventions and procedures involved in delivery of the intervention. To this end a logic model was developed, outlining the study and treatment processes. A treatment manual was developed by the clinical team and patient advocates, training was delivered according to the treatment manual.

Limited implementation fidelity testing was carried out in order to assess that the treating clinicians were delivering the intervention as intended by the protocol. This was done by utilising a fidelity checklist, developed for the POLAR study (Appendix 11). An independent assessor reviewed video footage of the physiotherapist and participant session in order to assess implementation fidelity. This involved the assessor viewing the recording, alone in a quiet room and noting whether the physiotherapist achieved each of the items on the fidelity checklist, developed for the POLAR study (Appendix 11). The assessor could spend as long as they required and view the recording as many times as they wished. The checklist has 'essential' and 'desirable' elements to it and the assessor was given guidance on what constituted attainment of the item of fidelity. However, there was no reliability testing of the checklist and only one assessor used. There were no specific thresholds for fidelity item attainment and therefore the assessment was subjective and open to bias. It is however important to address fidelity of intervention implementation in order to ensure that any differences detected (or not) are due to the intervention and not variability of implementation (Bellg *et al.*, 2004; Toomey, Matthews and Hurley, 2017). The wider field of fidelity and in particular implementation fidelity, was out with the time and resources available for this project. There are other aspects of fidelity which require consideration for a future study, such as ensuring that the components are detailed in such a way as to ensure reproducibility and are measurable with fidelity tools. The fidelity of intervention training is important to ensure that those delivering it can do so according to the training manual (Gearing *et al.*, 2011). A particular concern with the POLAR intervention is the complexity of components and their interaction which may be a threat to training fidelity. The monitoring of intervention delivery has already been discussed for the study and relates to unique aspects of the intervention and of the intervention components which are essential to intervention delivery. For instance, the therapeutic approach, aspects of the intervention that are deliverable but not particularly essential and finally those aspects of the intervention that must be avoided as they may be deleterious to the intervention validity. One aspect of

particular concern with the intervention delivery is usually the differentiation between treatments, for instance if one participant group is receiving a wholly different intervention. In the POLAR study however, the differentiation came in terms of the timing of the intervention and not any differentiation between treatment approaches. Finally, the fidelity of treatment receipt measures the extent to which the intervention was received by the participant, who can in turn utilise the intervention as intended (Borrelli, 2011). This was not formally assessed in the quantitative aspect of the study, however, in the qualitative interviews the acceptance and value which participants placed on the intervention was a key theme.

Many of these aspects of fidelity have been addressed in the study protocol and intervention handbook. However, the formal assessment of the different aspects of fidelity need to be addressed in a future trial with specific detail as to the aims of measuring each aspect of fidelity, the tools with which to perform the measurement and a priori standards against which to independently measure.

5.14.2 Training-content

Training had three different but intercalating elements to it. Firstly, the processes of data collection, electronic data input onto the POLAR site and arrangement of appointments required for the smooth running of the study. This involved training clinicians, clerical staff and research staff. Secondly the theoretical and academic aspect of the treatment modalities used for the POLAR study were taught and discussed in order to understand and be able to teach the treatment framework to participants. This was delivered to the treating clinicians and in part, to referring GPs. Third and finally, the practical and clinical skills of assessment and treatment were delivered together with the essential communication approach encapsulated within the seven domains of treatment. The theoretical and practical aspects were delivered solely by the author over three days, each a week apart with the three treating physiotherapists. The details of the training are included in the intervention training handbook (Appendix 7).

5.14.3 Training-assessment of quality

In order to address the receipt and understanding of training, measurements of comprehension included quizzes on what had been taught, role play to enact what had been taught and peer to peer feedback on assessment and treatment techniques undertaken.

5.14.4 Comparator

The usual care group will receive up to 6 sessions of physiotherapy over the maximum of an 8-week period or until the patient has reached their pre-determined goals. Their physiotherapy will begin at 6 weeks following randomisation.

5.15 Data analysis plan

As the trial was a pilot pragmatic parallel group RCT, the final results data were reported and presented according to the CONSORT statement for pilot and feasibility trials (Eldridge *et al.*, 2016). The statistical analyses were performed on an intention-to-treat basis. As a feasibility study the main analysis were mainly descriptive and focussed on confidence interval estimation and not formal hypothesis testing. We reported rates of consent, recruitment and follow-up by centre and by randomised group. Outcome measures were summarised overall and by randomised group, to inform sample size estimation for the main trial. We used the data from this feasibility study to estimate the consent rate, attrition rate, and the variability of the continuous outcomes (e.g. Leg and Back Pain VAS, ODI, EQ-5D) in the trial population and used this information to inform the sample size calculation for the definitive RCT. We also included, as part of the feasibility analysis, estimation of the effect size for the 26-week ODI-pain outcome (the probable primary endpoint for the definitive study) with confidence interval estimates to check that the likely effect is within a clinically relevant range (as confirmation that it is worth progressing with the full trial). This information along with the acceptability of the study design and protocol to patients, therapists and GPs; the safety of the intervention; patient recruitment and consent/retention rates will enable us to determine whether or not the definitive RCT is feasible.
Data was inputted by the treating physiotherapists for the clinical and treatment aspects and by the author, with reliability checks by a supervisor (SW). The data was managed by the Sheffield clinical trials unit and analysed by MR with support from his supervisor SW.

We also reported the number of SAEs overall by randomised group. The time from randomisation to start of physiotherapy will be summarised by randomised group.

The sample size for a feasibility study should be adequate to estimate the uncertain critical parameters (SD for continuous outcomes; consent rates, event rates, attrition rates for binary outcomes) needed to inform the design of the full RCT with sufficient precision. A sample size of 80 patients allows a standard deviation to be estimated to within a precision of approximately ±16% of its true underlying value with 95% confidence. It has been suggested that a sample size of 70 subjects are necessary for an external pilot study (Eldridge *et al.*, 2016). This estimate will be synthesised with standard deviations observed in other published studies and ongoing trials, in the same population, to provide a robust estimate for

use in the sample size calculation for the full trial. Preliminary estimates suggest the definitive RCT would need to have between 350 and 500 patients, in total, to detect a small standardised effect size of 0.35 at conventional levels of power (90%) and significance (5% two-sided). It is expected that recruitment will take around 12 months.

This chapter has detailed the quantitative design and methods utilised for the POLAR study. It has proposed an iterative and reflective approach in order to maximise recruitment and ensure any changes are made during the study in order to improve the outcome. The following chapter will outline the qualitative methods used in the study which, together with this chapter, provide a whole description of this mixed methods study.

Chapter 6 Qualitative study design and methods

The previous chapter has introduced the quantitative design and methods of the study. The nature of the pilot study allows for the exploration of the stakeholders' views and experiences. In this chapter the qualitative element of the POLAR study will be presented, outlining the methodology, and practical methods of recruitment and data collection.

6.1 Introduction

There is an increasing body of qualitative research exploring the effects and experiences of LBP on individuals, their families and its effects on work (Verbeek *et al.*, 2004; De Souza and Frank, 2011; Scheermesser *et al.*, 2012). There are however, few studies detailing the effects of LRS on individuals lives. LBP and LRS are distinct clinical entities which often co-exist, which often leads to the terms being used synonymously. The complexity of the clinical presentation of LRS, the multi-faceted nature of the intervention, and the need for the study to analyse in depth the processes underpinning implementation, necessitate an approach robust enough to accommodate these demands. A mixed methods design was therefore adopted to gather data from an external pilot trial and in-depth qualitative data from participants interviews. This approach aimed to allow in-depth exploration of data, which would not have been possible using quantitative or qualitative methods alone. It was anticipated that the collection, analysis and comparison of both quantitative and qualitative data would provide greater depth of understanding from the patients' experiences, views and expectations of physiotherapy and LRS (Rolfe, Mcevoy and Richards, 2006; B. N. Ong *et al.*, 2011). The experiences of participants and other stakeholders were also sought to provide information regarding implementation, acceptability and feasibility during this external pilot study. An iterative, cyclical, learning approach to improve and refine the intervention and study processes was utilised to ensure any barriers or facilitators could be identified and addressed to ensure the smooth running of the study.

A qualitative study of patients awaiting lumbar microdiscectomy for LRS highlighted how disruptive LRS was on their quality of life (Boote *et al.*, 2016). The same study highlighted key themes from patient interviews, including the value they placed on individualised, multi-modal physiotherapy. The disruption to everyday life highlighted in the Boote (2016) study is echoed in other work, findings of despair and uncertainty were voiced by a small group of individuals with LBP who were concerned about the impact of LBP on their futures (Corbett, Foster and Ong, 2007). The value of a thorough clinical assessment and diagnosis was a key expectation found in a study of the expectations and experiences of patients with sciatica

(Hopayian and Notley, 2014). Another key finding of this study was the importance of personalised care, in particular involvement in decision-making and tailoring care to and with the patient. Personliased care and putting the patient at the heart of decision-making is a commonality in the Boote and Hopayian studies and also in the qualitative study of patients experiences of sciatica (B. B. N. Ong *et al.*, 2011). The qualitative aspect of the POLAR study aimed to build upon this work by investigating the participants experiences of the physiotherapy approach and the study processess in order to gain further insight into participants views on physiotherapy for LRS.

6.2 Methodology

The nature of the condition (LRS), the physiotherapeutic intervention, the intervention components, the interaction between each component and the interpretation of those components by the participant and the physiotherapist reflect the complexity of the clinical scenario. The ontology of critical realism is well suited to the exploration of clinical complexity, espousing not one mechanistic cause with an effect, but one in which many causal mechanisms may co-exist to bring about outcomes in different individuals in differing social contexts (Rolfe, Mcevoy and Richards, 2006). The critical realist approach attempts to gain an understanding of any number of causal mechanisms underpinning an intervention, within their social contexts. Causation or effect may be attributable to different combinations of an intervention in different contexts utilising different methodologies (Blackwood, O'Halloran and Porter, 2010). It is proposed by critical realist theorists that it is the inter-dependence of causal elements that bring about causation and that when those critical elements are presented in a necessary amount for that person in that social context, change (effect) occurs (Fletcher *et al.*, 2016). Any change in the amount of parts delivered by the intervention may account for a wholly different effect (Modell, 2009). This approach lends itself to the evolving nature of the POLAR intervention in which the complex nature and the complicatedness of the intervention and importantly its timing, will change according to the participants needs and wishes and the participants randomisation. Critical realism is also well suited as an underpinning ontology to mixed methods designs, recognising that different approaches can complement each other by gaining an understanding of the same phenomena from different realities. Critical realism informed the dual approach to data analysis in to creating themes inductively from the literature but also deductively from prior literature.

In order to maximise the utility of the qualitative element of this mixed methods study, the guidance advocated by O'Cathain was implemented (O'Cathain *et al.*, 2015). In particular the importance of initial design and planning of sampling together with the support of a qualitative researcher has not been overlooked.

6.3 Design and methods

6.3.1 Aims

1. The aim of the qualitative phase of the study was to compare and contrast the experiences of patients in both the intervention and control groups of the pilot trial, in order to ascertain the perceived value of the intervention, the physiotherapy service and both study and service processes. The study aimed to explore the acceptability and feasibility of the intervention from a patient's perspective.
2. The second aim was to determine the acceptability and feasibility of delivering the intervention by the physiotherapists and support staff with their views being valuable in refining the study.

6.3.2 Inclusion and exclusion criteria

Patients who had already consented to participate in the pilot trial aspect of the POLAR study were given information regarding the qualitative part of the study. The pilot trial and qualitative parts shared inclusion and exclusion criteria.

6.3.3 Recruitment and sampling strategy

A sample of patients who had already consented to participate in the pilot trial aspect of the POLAR study were asked to participate in the qualitative element of the study. There was no expectation that a participant in the quantitative element of the study would also take part in the qualitative study and no coercion took place. A purposive sampling method was used to ensure a maximal variation in age, gender and severity of symptoms in order to contribute to wider applicability of the findings. It was envisaged that around 8-10 interviewees will be required per study arm, per cycle. Recruitment ceased when it was judged that data saturation had been reached with no new themes emerging. Strategies to enhance retention included a phone call or text message to the participant, with their consent at the time the outcome measures were due. The participants were also able to contact the research team to discuss non-clinical issues.

6.3.4 Data collection

Semi-structured interviews were used to obtain the views and experiences of patients with LRS having received physiotherapy in either the intervention or usual care arms. The broad issues which were addressed included, but were not exclusive to the patients experience of LRS, how LRS affected their daily lives, their experiences of the management of LRS (including GP and physiotherapy), how the timing of the intervention affected them and their experiences of being involved in the trial. The information gathered from the interviews was used to inform the ongoing research process. It was an iterative and collaborative

process involving not only the recipients of the treatment (participants) but the people delivering the intervention (physiotherapists) and those referring the patients for treatment (GPs). In this way it was hoped that the implementation of the intervention and acceptance to stakeholders of the intervention would be optimised.

Semi-structured interviews were used to explore the views and perceptions of participants. The semi-structured nature allowed the flexibility of being able to change the order and nature of questions in relation to interviewees answers whilst providing an a priori guide to the questions (Green and Thorogood, 2014). Each participant interview was undertaken in a location chosen by the participant, that was convenient to the participant and in all cases this was the participant's home. Interviews with the physiotherapists took place in their respective workplaces. All interviews were recorded with the interviewees consent.

Interviews were based around an interview topic guide, which was developed by the study team, including the patient representatives (Appendix 12). The interview guide was tested in five pilot interviews with a patient undergoing physiotherapy treatment for LRS to evaluate usability, and following this, questions were refined where necessary. The interview topic guide was also adjusted in later interviews, in order to explore areas that emerged from earlier interviews.

6.4 Interviewer

The male first author had met each participant on at least one previous occasion when taking consent and had discussed the study at length. During the initial meeting the reasons for undertaking the interviews were discussed as was the relationship of the first author to the study (doctoral fellowship). The author had previous experience of undertaking participant interviews and had attended an in-depth interview course prior to beginning the study interviews. The interviewer was also the principal investigator and the holder of the research fellowship. These factors are all potential causes of bias. In order to mitigate against these, the initial interview topic guides were developed with PPIE representatives, clinicians and academic supervisors. Regular supervisory meetings took place (at least monthly) where data from both the quantitative and the qualitative elements were subject to scrutiny from the supervisory team and the trials unit. During the initial data analysis phase, iterative themes were generated, which were done in conjunction with the qualitative supervisor. Similarly, the final analysis was done with close supervision and checking from the supervisor.

6.5 Data analysis

Interviews were recorded and transcribed verbatim, with any potentially identifying information removed. Interviews were transcribed by the first author and were uploaded to

Atlas Ti software (version 8.2.1), which was used to support data storage, and retrieval and to assist in achieving a systematic approach to coding of the data. Each interview was initially read to become familiarised with the data and provide a broad overview. Each transcribed interview was then further examined line by line using a thematic analysis approach (Guest G, MacQueen KM, 2012). Recurring themes within the data were identified by means of recognising regularities, recurrences, varying views, similarities, discordance and relationships (Ryan and Bernard, 2003). The coding framework was agreed with the qualitative supervisor (SB) and was utilised during regular meetings to examine sections of data in order to achieve consensus.

6.6 Interview methods

Each interview was undertaken by the author in the home of the participant, at their request. All interviews were securely recorded, with the interviewees consent. A reflexive diary was kept for each interview, noting the environment, people present and non-verbal responses to questions. The duration of interviews ranged from 8 minutes to 65 minutes. Interviews were transcribed by the first author, a copy of which was sent to each in order to check participant validation (Birt *et al.*, 2016). A follow-up telephone call to check the participants response to the transcript was carried out by the first author. Respondent validation was utilised to minimise bias, although this has been called into question as it is unlikely that interpretation by the researcher will have the same meaning as the interviewees, individually or as a group. There were no objections to the transcripts.

6.7 Qualitative analysis

Atlas Ti software (version 8.2.1) was used to support storage, aid retrieval and ensure a systematic approach to the coding of the data. Each transcribed interview was analysed, line by line by the author using a thematic analysis approach. Each interview was initially analysed to familiarise the data and provide a broad overview.

6.7.1 Ethical considerations

Participants were provided with a detailed information sheet prior to recruitment to the qualitative phase of the study, which they were given time to consider before deciding whether or not to take part. Participants were asked to complete and sign a consent form prior to the interviews being carried out (Appendix 13). Ethical approval for the study as a whole was granted by the East of Scotland Research Ethics Service (15/ES/0130) on 20th August 2015. There was a potential safety risk for the qualitative researcher conducting the interviews in the participant's home. To minimise this risk, the researcher let another member of the research team know the time and location of each interview and took a

mobile phone with him to each interview site. At the end of each interview, he phoned the other member of the research team to let them know that he was safe. If the interviewee showed any signs of physical or psychological distress the interviewee was given the option to terminate the interview or have a break, or to re-arrange the interview at a later date. Any data from the physiotherapist interviews which may have enabled identification were anonymised.

6.7.2 Public and patient involvement and engagement

The research question was informed directly from patient feedback on physiotherapy services for LRS. Current and past patients who have experienced LRS and current physiotherapy and or surgical services were involved from the study's inception. Two patient representatives were involved in the qualitative study in the first instance by helping to generate the initial set of interview schedules. Their insight and experiences of LRS helped form the initial questions as well as contributing to the iterative nature of question and thematic development.

The qualitative design, methodology and methods have been presented in this chapter. Both the qualitative and quantitative aspects of the study have now been presented and an overview of the study can be appreciated. The following two chapters will present the results from both the quantitative and qualitative elements of the study.

Chapter 7 Quantitative results

The intervention development has been discussed in the previous chapter, completing the design and methods of the POLAR study. The results of the external POLAR pilot study will be presented in this chapter. A brief review of the objectives of the study will be outlined and the results of both the feasibility and research objectives will be described.

7.1 Introduction

The quantitative results of the POLAR external pilot trial are presented in this chapter in line with the consolidated standards of reporting trials (CONSORT) extension for reporting pilot and feasibility trials (Eldridge *et al.*, 2016). The CONSORT checklist can be found in Appendix 14. This is an extended version of the POLAR pilot trial results paper published in BMJ Open (2018, Vol 8, issue 7, pages e021631) and can be found in Appendix 15. The recruitment of fourteen GP practices in Sheffield, England was greatly aided by the use of a Clinical Research Network (CRN) of research ready practices. The recruitment processes were process mapped for each recruiting GP practice. The generic participant recruitment process flowchart can be found in Figure 7.1. with the flow chart of the participant journey for the POLAR study can be viewed in Figure 7.2. Ninety potential participants contacted the research team after being given details of the study by their respective GPs. Ten were excluded as they either did not meet the inclusion criteria or refused to be randomised, with eighty going on to be randomised from ten different primary care GP practices. Four practices, although enrolled in the study, failed to recruit. Table 7.1 illustrates the feasibility targets for the study.

Table 7.1 The feasibility objectives

Feasibility Parameter	Target
Set up recruitment sites in primary care	Successful site set-up n=14
Recruitment rate	7 participants/month
Organise physiotherapy appointments	75% of physiotherapy appointments made within 2 weeks of randomisation.
The feasibility of intervention delivery	75% of participant in early group have appointment within 20 days of randomisation
Participant attendance	Attendance at >66% of treatment sessions
Participant attrition	Attrition rate <25%
Outcome measures	80% of PROMS returned at 6/52

Figure 7.1 Participant recruitment processes

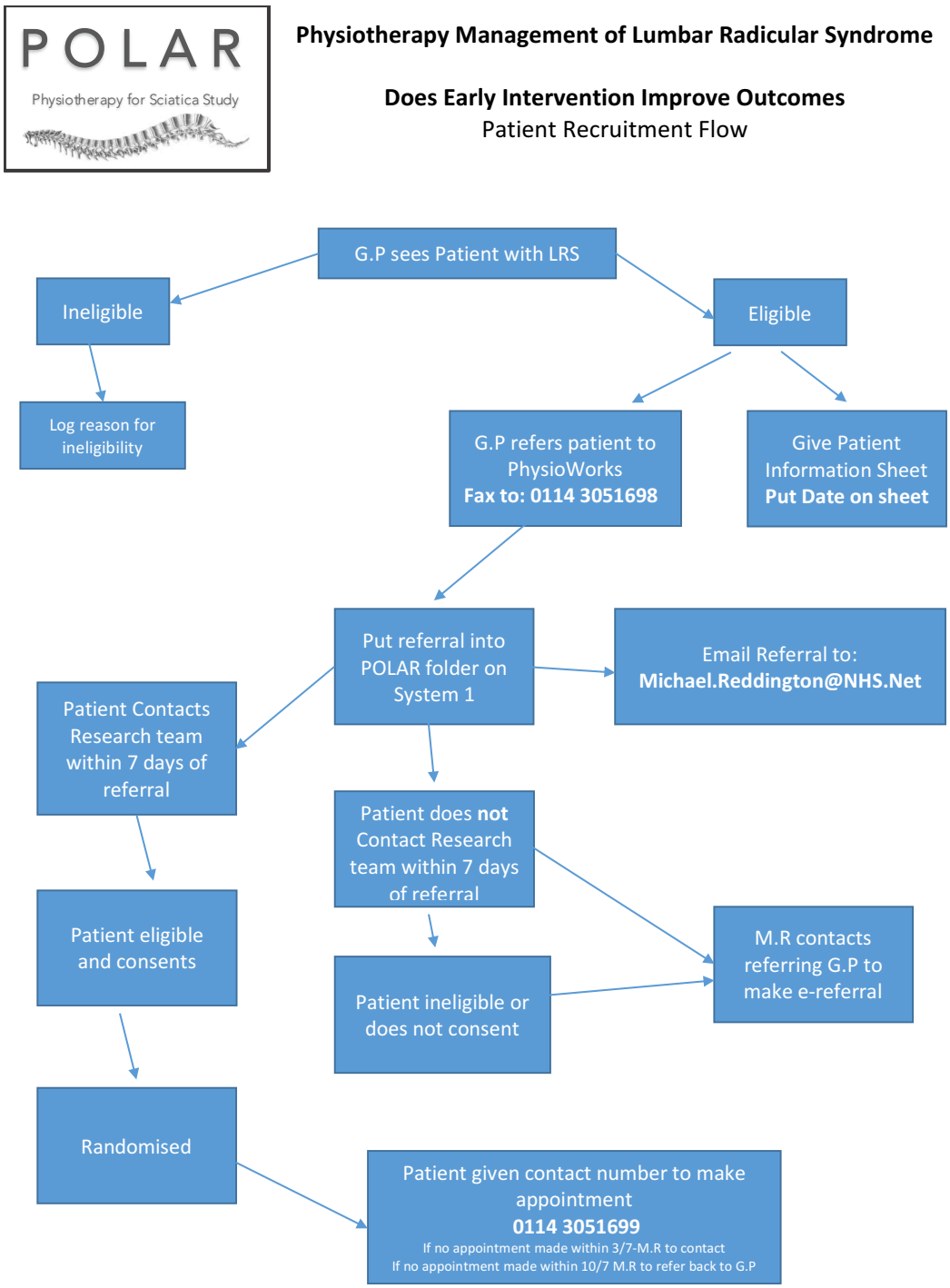
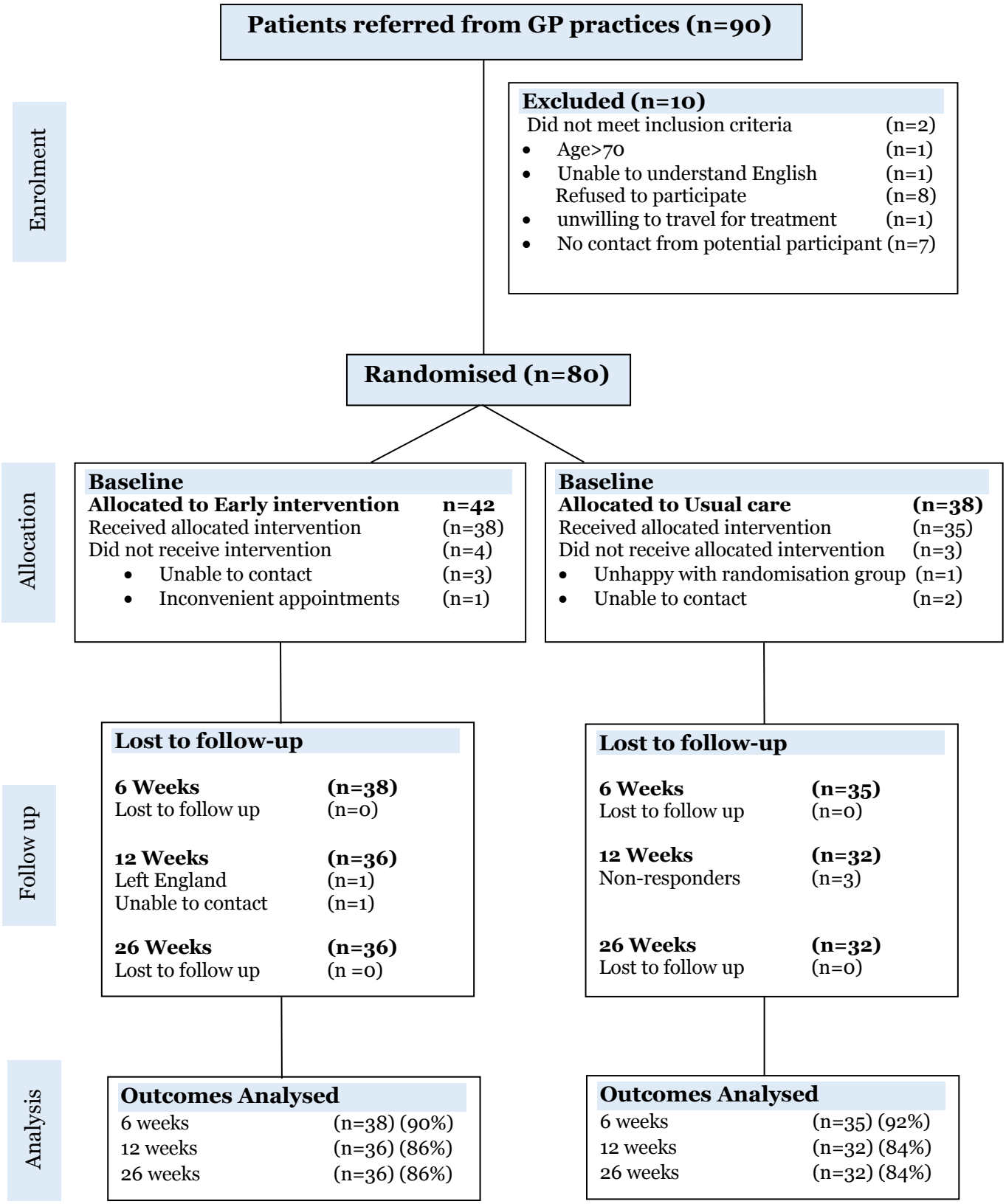


Figure 7.2 Participant flow through the POLAR study



7.2 Baseline characteristics

The baseline characteristics of all participants, by group can be found in Table 7.2. This illustrates the comparability of the two arms with no evidence of selection bias. The groups were well matched for demographic factors such as age, gender and BMI as well as levels of self-reported disability, leg and back pain, risk of chronicity and general health status. The early intervention physiotherapy group had longer symptom duration going into the study due to one outlier with a symptom duration of over three years. There was evidence of a small baseline difference in the EQ-5D utility scores which is attributable to chance as all participants were randomised.

Table 7.2 Baseline characteristics of POLAR participants

	Early Intervention physiotherapy			**Usual Care**			**Total**		
	N	%		N	%		N	%	
Female	21	50		18	47		39	49	
White British	38	90		33	87		71	89	
	N	**Mean**	**SD**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Age (years)	42	47	14	38	47	13	80	47	13
Height (CM)	42	172.1	10.7	38	172.1	9.8	80	171.7	10.2
Weight (KG)	39[1]	81.5	14.8	38	80.6	15.7	77	81	15.2
BMI	39[1]	27.7	4.6	38	27.3	5.6	77	27.5	5.1
ODI score (%)	42	44.6	19.5	38	45.2	17.4	80	44.9	18.4
Leg Pain	42	7.2	1.8	38	6.9	2.3	80	7	2.1
Back pain	42	5.4	3.3	38	6	2.6	80	5.7	3.0
EQ5D-5L VAS	42	63.8	20.6	38	64.6	18.9	80	64.1	19.7
EQ5D-5L Utility score	42	0.44	0.29	38	0.52	0.25	80	0.48	0.27
Keele STarT-Back	42	5.7	2.0	38	5.7	1.8	80	5.7	1.9
Keele STarT-Back Sub-score	42	2.0	1.5	38	2.7	1.3	80	2.8	1.4
Low risk	6	14.3		2	5.3		8	10.0	
Medium risk	19	45.2		25	65.8		44	55.0	
High risk	17	40.5		11	28.9		28	35.0	
Time to treatment (days)[2]	38	11.1	10.5	31	43.6	8.9	69	25.7	19.0
	N	**Median**	**IQR**	**N**	**Median**	**IQR**	**N**	**Median**	**IQR**
Symptoms duration (days)	42	92	276	38	61	51	80	77	203
Nerve root level									
L2	0			1			1		
L3	1			1			2		
L4	0			2			2		
L5	13			14			27		
S1	27			19			46		

[1] 3 missing values

[2] Time between randomisation and first scheduled treatment session

7.3 Process results

The POLAR study was an external pilot trial, outlined below are the results of the feasibility objectives.

7.3.1 Set-up of recruitment sites in primary care

The original recruitment site was a secondary care hospital and their primary care arm, which comprised one physiotherapy service provider. They had initially agreed to be the main sites of recruitment and delivery of the physiotherapy intervention. However, due to unexpected, long-term, sickness leave and the pressure to fulfil and deliver contracts to provide patient contacts, they were unable to service their own contracted work and therefore, reluctantly withdrew from the study. Another primary care physiotherapy service provider, who was known to the author and research team was approached to deliver the physiotherapy intervention and kindly agreed. The Yorkshire and Humber primary care CRN steering group for division 5 provided access to research-ready GPs. Twenty GP practices were initially approached to take part in the study, with ten initially agreeing to participate. Towards the end of the second tranche of recruitment it was evident that one practice was recruiting a large number of participants. A decision was made to enrol new recruitment centres in order to decrease the reliance on the one, well performing centre and to see if recruitment was possible and practical elsewhere. Seven further GP practices were therefore approached, with four agreeing to participate. Participants were recruited from the different GP practices participating in the study and from individual GPs within those practices. GPs recruited into both arms of the study, GPs and their practices did not unilaterally recruit into one arm exclusively. The physiotherapy intervention was delivered by one of the three treating physiotherapists in the same primary care site, a council-managed sports centre. The physiotherapists had a mean age of 36 years (range 34–40 years) and a mean of 10 years post-graduate experience (range 7–12 years). All of the physiotherapists were educated in England and all three physiotherapists had postgraduate experience at MSc level, having undertaken modules in musculoskeletal physiotherapy management, including the clinical management of musculoskeletal disorders. All had attended a variety of postgraduate clinical courses, including courses on pain, manual therapy and exercise therapy. The physiotherapists utilised the POLAR treatment approach for both groups, with each physiotherapist seeing only their own patients for the duration of their treatment.

7.3.2 Recruitment rate

Eighty participants were recruited during the period between the 1st March 2016 and the 7th of November 2016, a recruitment rate of 2.4 participants per week or 9.6 participants per month which enabled recruitment to end earlier than anticipated. This compares favourably

when compared with a review of publicly funded RCTs in the UK who had a median recruitment rate of 0.92 recruits per centre, per month (Walters *et al.*, 2017). Forty-two participants were randomised into the early intervention group and 38 in the usual care group. The weekly recruitment rate and cumulative recruitment rate by site is shown in Figure 7.3. The recruitment rate by centre is presented in Table 7.3. This shows that one centre Woodseats recruited 38% (30/80) of the trial participants. Four centres failed to recruit a single participant due to unforeseen circumstances during the period of recruitment, for example prolonged staff sickness absence. The recruitment rates have been calculated in Table 7.3, with and without the four non-recruiting sites. Recruitment rates for each site were collated on a weekly basis and e-mailed to the recruiting sites. Figure 7.4 illustrates the weekly and cumulative recruits required together with the number attained. The trends in recruitment rates can be seen with the significant dips in weeks 10-12 and 19-21 being attributable to school holidays.

Figure 7.3 Recruitment rates by site and cumulative rate

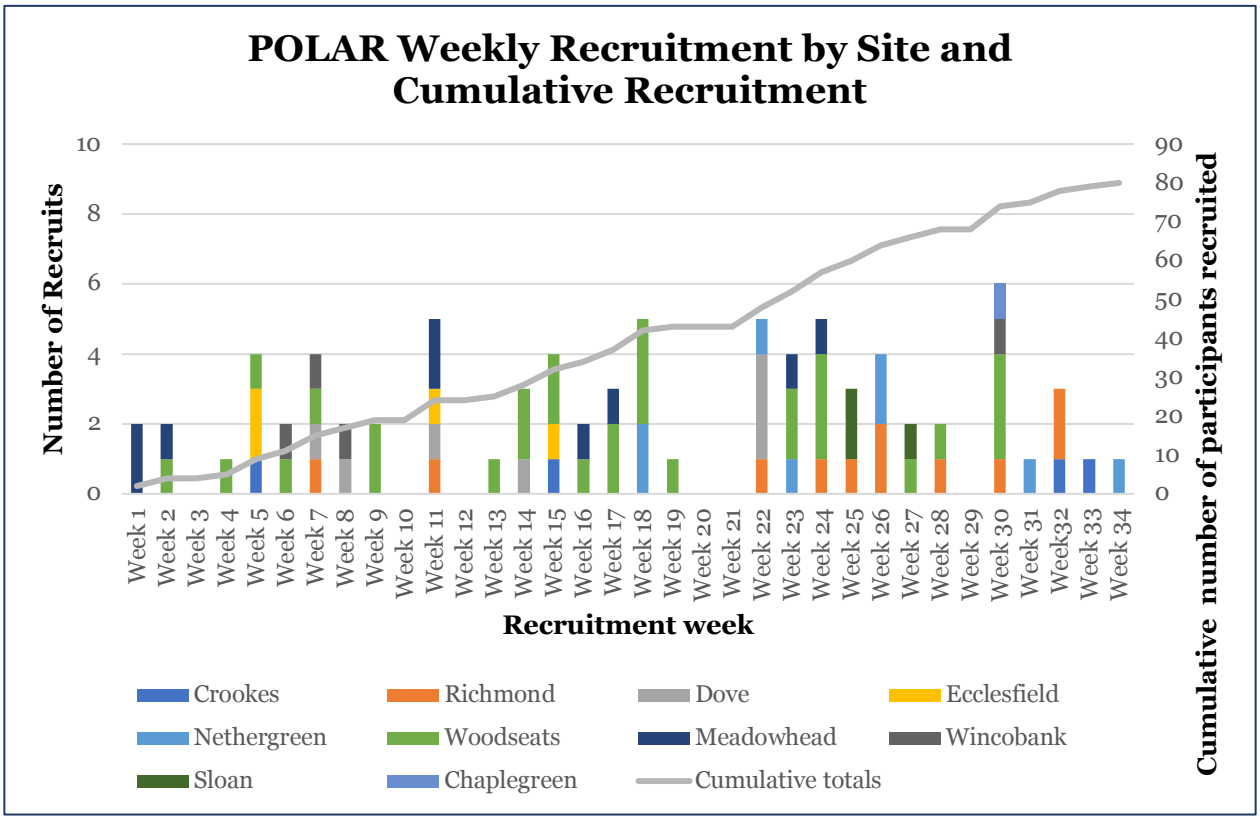
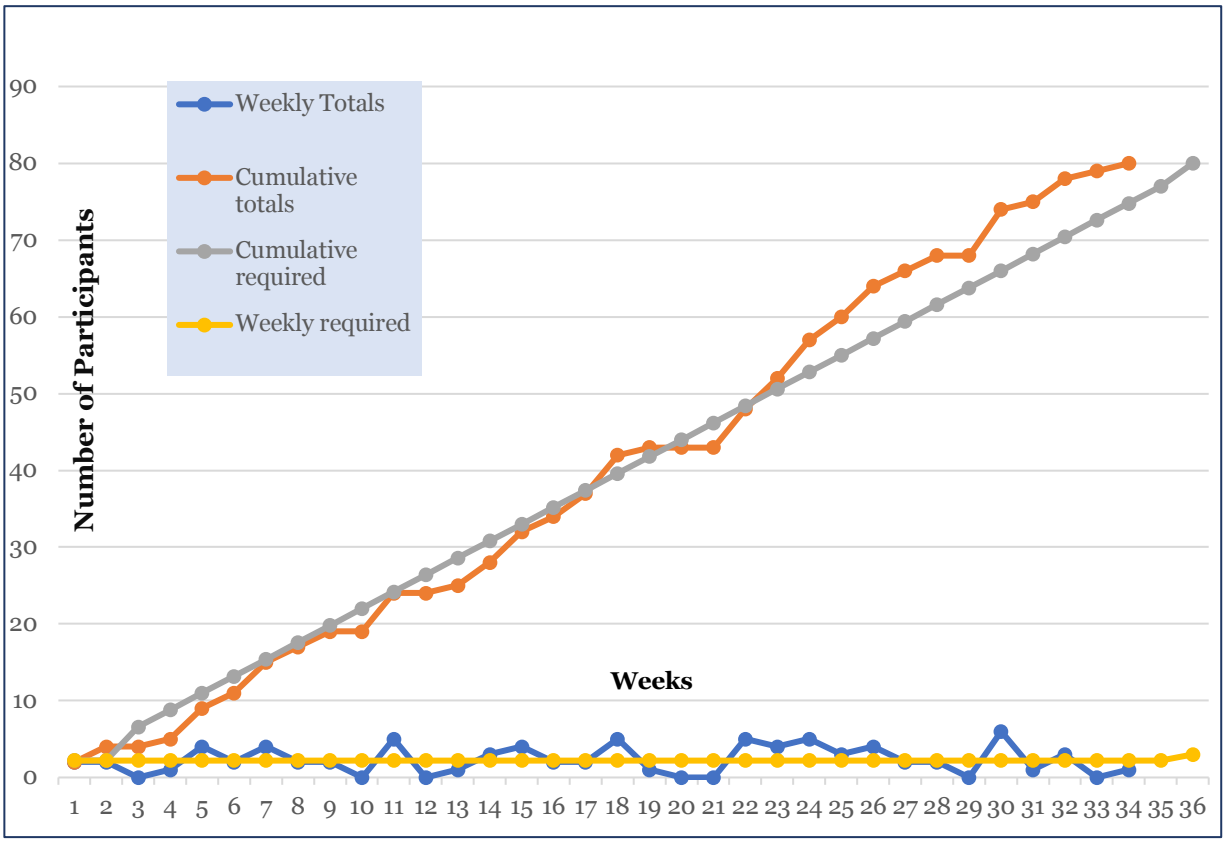


Table 7.3 Recruitment rates per centre

GP Practice	Number of weeks recruiting	Number recruited	Recruitment rate (per week)
Wincoback	34	4	0.12
Crookes	34	3	0.09
Richmond	34	11	0.32
Ecclesfield	34	5	0.15
Nethergreen	34	8	0.23
Woodseats	34	30	0.88
Meadowhead	34	8	0.23
Dove	34	7	0.20
Chapelgreen	6	1	0.17
Sloan	34	3	0.09
Dore	6	0	0
Sothall	6	0	0
Woodhouse	34	0	0
Birley	6	0	0
Total	**364**	**80**	**0.22**
Without centres <1 recruit	*312*	*80*	*0.27*

Figure 7.4 Cumulative recruitment over the course of the POLAR study



7.3.3 Organisation of physiotherapy appointments

The target of 75% of physiotherapy appointments being made within two weeks of randomisation was surpassed in both groups. 100% (42/42) (95% CI: 92% to 100%) of early intervention physiotherapy participants received their appointment within 20 days of randomisation and 38/38 (95% CI:91% to 100%) in the usual care group. This illustrates the feasibility of making appointments for participants at short notice.

7.3.4 The feasibility of intervention delivery

A key feasibility parameter was the ability for at least 75% of early intervention physiotherapy participants to be seen by a physiotherapist within 20 days of randomisation. 100% (42/42) (95% CI 92% to 100%) of participants reached this target, with a mean of 14.1 days between randomisation and first treatment session.

7.3.5 Participant treatment session attendance

The mean attendance rate for physiotherapy appointments in both groups was 92.6% (SD 16.2), 93.8% (SD 12.6) for the intervention group physiotherapy and 91.1% (SD 19.8) in the usual care group. All surpassed the a priori target of greater than 66% attendance.

7.3.6 Participant attrition

Eighty participants agreed to take part in the study with 12 participants withdrawing in equal numbers from both groups. Table 7.4 displays the reasons why participants withdrew from the study, the most common reason being that the research team were unable to make contact. The intervention group attrition rate was 14% (6/42) (95% CI: 7% to 28%) and in the usual care group it was 16% (6/38) (95% CI 7% to 30%) at 26 weeks follow-up. The overall attrition rate for drop out of participants was 15% (95% CI 9% to 24%), all within the a priori limit set at 25% and was relatively symmetrical between groups. This is slightly higher than the attrition rate of 10% found in a study of publicly funded RCTs in the UK (Walters *et al.*, 2017), but lower than similar studies in the field (Atlas *et al.*, 2001; Lequin *et al.*, 2013) The validity of outcomes from RCTs has been called into question if attrition rates are higher than 20% (Schulz and Grimes, 2002) and it has been suggested that studies should move away from simply using a percentage attrition rate as the key metric (Amico, 2009).

Table 7.4 Reasons for participant withdrawal from the study

Screening number	Group	Reason	Time point (0,6,12,26)
S03/002	Early	No contact	0
S02/001	Early	No contact	0
S10/002	Early	No contact	0
S05/006	Early	Unable to attend due to times of appointments	0
S02/004	Early	Left England	6
S02/014	Early	No contact	12
S09/001	Usual Care	No contact	0
S06/007	Usual Care	No contact	0
S03/001	Usual Care	No contact	12
S09/003	Usual Care	No contact	12
S02/011	Usual Care	Left England	0
S07/005	Usual Care	No contact	12

7.3.7 Outcome measure return

The outcome measure return rates surpassed expectations of 80% at six weeks and were as follows: 38/42 (91; 95% CI: 78% to 96%) at six weeks post randomisation for the intervention group and 35/38 (92%; 95% CI 79% to 97%) for the usual care group. At twelve weeks the return rates were 36/42 (86%) for the intervention group and 32/38 (84%) for the usual care groups and finally at twenty-six weeks they were 36/42 (86%) and 32/38 (84%) for the intervention and usual care groups respectively.

Table 7.5 provides a summary of the feasibility results, illustrating the attainment of all a priori targets.

Table 7.5 Summary of feasibility results

Feasibility Parameter	Target	Results
Set up recruitment sites in primary care	Successful site set-up	10 centres actively recruited
Recruitment rate	7 participants/month	9 participants/month recruited
Organise physiotherapy appointments	75% of physiotherapy appointments made within 2 weeks of randomisation	100% of physiotherapy appointments were made within 2 weeks of randomisation
The feasibility of intervention delivery	75% of participant in early group have appointment within 20 days of randomisation	100% of participants in the early group reached the target
Participant attendance	Attendance at >66% of treatment sessions	A mean attendance of 92.6% for both groups, 93.8% in the intervention group and 91.1% in the usual care group
Participant attrition	Attrition rate <25%	The attrition rate for both groups was 15%, 14% in the intervention group and 16% in the usual care group
Outcome measures	80% of PROMS returned at 6/52	91% return rate (complete data)

7.3.8 Refinement of the study processes and the intervention

The iterative methods of recruitment ensured that any changes to either the study processes or the intervention itself could be made between recruitment cycles. The appropriate approval of the Trial Management Group (TMG) and/or ethics approval through protocol amendments were sought before any changes were instigated.

Advice from stakeholders provided solutions to problems identified in the first weeks of recruitment and treatment. Outlined below are examples of these:

1. Completion of the treatment log and its components by the treating physiotherapist was sporadic in the first weeks of the study. The clinicians often forgot or were unsure how to access the log on the computer system. The solution came from the clinicians identifying a functionality of the appointment software where a reminder could be placed for the clinician to carry out the task of logging treatment.
2. Clinicians were expected to collect the 6-week outcome measures from the patients at the physiotherapy appointment. They often forget to administer the questionnaire during a busy clinical day. The solution to this came from the reception staff who would be e-mailed (securely) a list of participants for each week who would require

the administration of outcome measures that week. The reception staff would then administer and collect the appropriate measures.

3. The problem of potential participants not contacting the research team after seeing their GP was an intermittent problem. Some potential participants were told by their GP that the study team would contact them, however ethics approval forbid this. Occasionally the study team were expecting a call from the potential participant. A solution came in a weekly e-mail to GPs re-iterating the need for potential recruits to contact the study team. The booking clerks, who would contact the patient to make a physiotherapy appointment would remind the patient about the study, when calling them to make a routine appointment, to contact the research team if they were interested in taking part in the study.
4. Another common problem voiced by recruiting GPs was that rather than electronically sending a physiotherapy referral, the POLAR referral had to be faxed in order to be expeditiously screened. The fax number and the POLAR study symbol, together with clear instructions were placed on the physiotherapy referral forms.
5. A protocol amendment was made after discussion with GPs and clinical supervisors about the original age limit for the study. The age limit for the first 2 weeks of the study was 70. This was changed to reflect the need for patients over 70 with LRS to be given the opportunity to participate in the study.

There were no changes proposed for the intervention from feedback from patients, GPs, other stakeholders or the treating physiotherapists.

7.4 Research results

7.4.1 Analysis of key clinical outcomes

The self-rated disability score (ODI) and leg pain scores are likely to be the primary outcome measures for a definitive RCT. Tables 7.6 and 7.7 together with Figures 7.4 and 7.5 show the leg pain and ODI scores, for participants with all 4 assessments completed. Testing for statistical significance was not carried out as it was not appropriate for pilot studies according to the CONSORT statement for pilot and feasibility trials (Eldridge *et al.*, 2016). The blue line illustrates the increased rate of recovery in the early intervention physiotherapy group up to 6 weeks. At the point the usual care group begins their physiotherapy (six weeks) the rate of recovery assimilates and by 12 weeks and both groups have very similar scores.

Leg pain is the most common symptom which distinguishes LRS from LBP and is the symptom which is most bothersome to LRS sufferers. The baseline levels of leg pain between groups shows a slightly higher pain score in the early physiotherapy group (Table 7.6). Leg pain scores decrease in the early intervention group up to six weeks, however the usual care

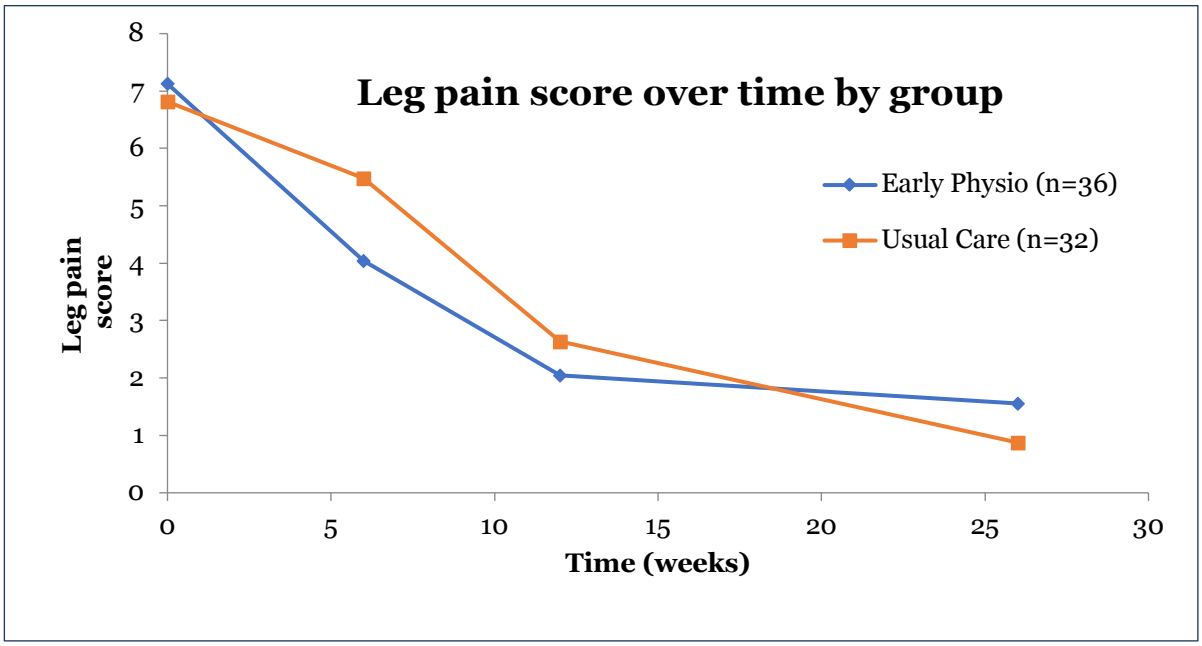
group who had been waiting for their physiotherapy to begin, also had a decrease in symptoms over this period. This is illustrated in Figure 7.5 where the gap widens between the groups at six weeks then narrows, before the usual care groups symptoms improve further towards the 26-week point.

Table 7.6 Leg pain scores* over time by group for participants with all 4 assessments

	Early Intervention			Usual Care		
	N	Mean	SD	N	Mean	SD
Baseline	36	7.12	1.86	32	6.82	2.22
6 Weeks	36	4.04	2.99	32	5.55	2.81
12 weeks	36	2.04	2.48	32	2.64	2.85
26 weeks	36	1.56	2.17	32	0.87	2.17

* Measured using the Visual Analogue Scale 0-10, higher score=higher self-report pain

Figure 7.5 Leg pain scores over time by group for participants with all 4 assessments



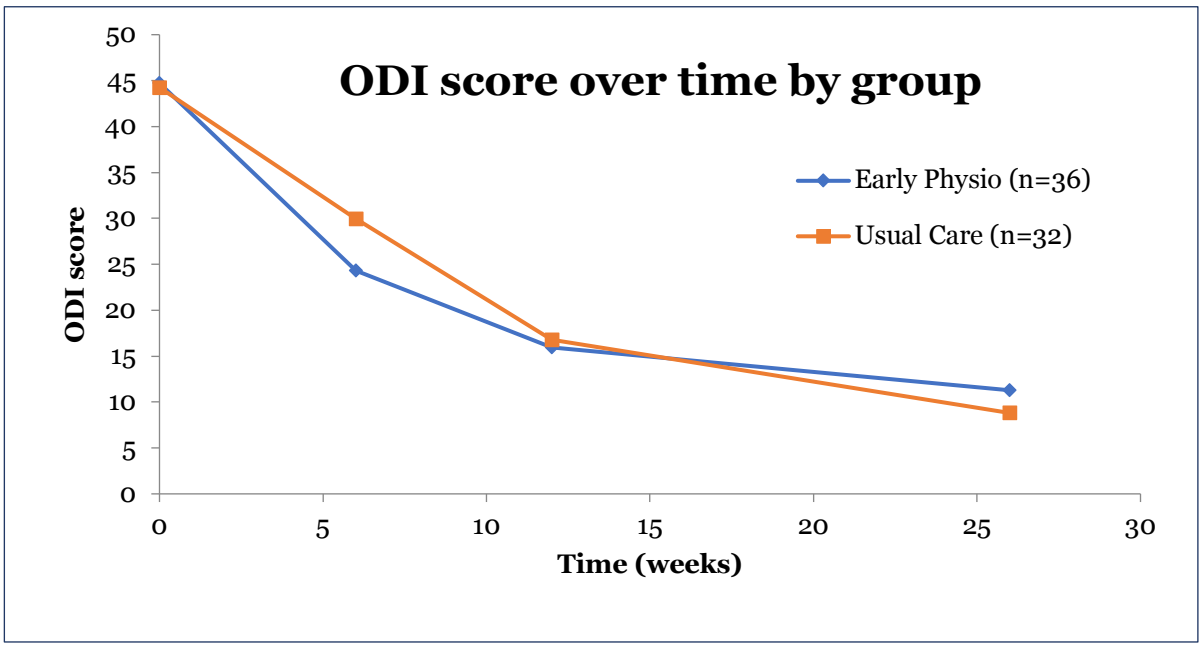
The levels of self-rated disability across the four timepoints can be seen can be seen in Table 7.7. The baseline levels in both groups signify a severe level of disability (Fairbank, JC. Couper, J. Davies, JB. O'Brien, 1980) which shows a clinically significant level of improvement in both groups over the ensuing 12 weeks. By 12 weeks the levels of disability in both groups has dropped below a significant level, with this trend continuing to the end of the study at 26 weeks. This is illustrated in Figure 7.6 with the convergence of scores at 12 weeks being prominent.

Table 7.7 ODI* score over time by group for participants with all 4 assessments

	Early Intervention				Usual Care			
	N	Mean	SD	Std. Error mean	N	Mean	SD	Std. Error mean
Baseline	36	44.72	19.98	3.33	32	44.25	17.73	3.13
6 Weeks	36	24.31	19.06	3.18	32	29.97	16.23	2.86
12 weeks	36	15.97	19.04	3.17	32	16.81	19.19	3.39
26 weeks	36	11.28	15.53	2.58	32	8.81	11.28	1.99

*Oswestry Disability Index (ODI) 0-100, higher score=higher level of self-rated disability

Figure 7.6 ODI score over time by group for participants with all 4 assessments



Within group changes are provided for each group in Tables 7.8 and 7.9

Table 7.8 Early intervention group changes from baseline to 26 weeks

Outcome	Baseline			26 weeks			Paired differences		95% Confidence Intervals	
	Mean	N	SD	Mean	N	SD	Mean	SD	Lower	Upper
ODI	44.7	36	20.0	11.3	36	15.5	-33.4	19.3	-40.0	-26.9
Backpain VAS	5.2	36	3.3	2.0	36	2.2	-3.2	3.7	-4.5	-1.9
Leg pain VAS	7.1	36	1.9	1.6	36	2.2	-5.6	2.5	-6.4	-4.7
EQ5D utility	0.45	36	0.29	0.86	36	0.19	0.42	0.27	0.32	0.51
EQ5D VAS	64.5	36	20.0	79.61	36	16.3	15.1	17.5	9.2	21.0

Table 7.9 Usual care group changes from baseline to 26 weeks

Outcome	Baseline			26 weeks			Paired differences		95% Confidence Intervals	
	Mean	N	SD	Mean	N	SD	Mean	SD	Lower	Upper
ODI	44.3	32	17.7	8.8	32	11.3	-35.4	18.5	-42.1	-28.8
Backpain VAS	6.1	32	2.5	2.1	32	2.1	-4.0	2.7	-5.0	-3.0
Leg pain VAS	6.8	32	2.2	0.9	32	2.2	-5.9	3.3	-7.1	-4.7
EQ5D utility	0.53	32	0.26	0.92	32	0.12	0.39	0.25	0.30	0.48
EQ5D VAS	65.7	32	18.1	81.7	32	12	15.9	19.2	9.0	22.9

7.4.2 The feasibility, practicality, safety and acceptability of the study design and protocol

The potential feasibility of the study has been suggested by the results of the feasibility parameters. There were several adjustments made to the processes of the study which were made possible by the breaks in recruitment. These included a brief weekly email to all participating GPs to remind them of the study and improve the clarity of inclusion and exclusion criteria. A change to the process of administering the six-week outcome measures was necessary, after the physiotherapists reported it too time consuming to administer. There were no changes made to the intervention, which appeared to be well received by both participants and clinicians alike. There were no adverse events or serious adverse events associated with the intervention or the study processes.

7.4.3 Harms

There was one Serious Adverse Event (SAE) during the course of the study in the early intervention physiotherapy group. The SAE rate was 2% (1/42) in the early intervention physiotherapy group and 0% (0/38) in the usual care group, a difference of 2% (95% CI -7% to 12%). The participant was hospitalised after suffering a Cerebro-Vascular-Accident (CVA) related to pre-existing vascular hypertension. The participant had completed their physiotherapy intervention two weeks prior and made a complete recovery within 6 months. This was reported to the ethics committee and TMG.

7.4.4 Acceptability of the primary and secondary outcome measures to patients and clinicians

The examination of acceptability of the outcome measures, processes and the intervention was a key area of investigation for this mixed methods study. The qualitative element to explore these aspects can be found in Chapter 8. In summary, the key processes necessary for implementation and evaluation of the study were reported to be acceptable by all stakeholders.

7.4.5 Fidelity

The fidelity of intervention delivery as it is intended is essential in order to establish internal validity, intervention replicability and for credibility of outcomes (Keogh, Matthews and Hurley, 2018). Physiotherapists electronically recorded the components of their treatment sessions at each patient encounter in order to enhance and measure treatment fidelity. Participants in the early intervention physiotherapy group had a mean of 4 treatment sessions and those participants in the usual care group 3 sessions. There were 269 physiotherapy sessions carried out as part of the POLAR study with 1267 component parts, 36 (3%) of which were outside the protocolled treatment framework. Table 8.0 details each domain and treatment component. The components outside the protocol consisted of three sessions of acupuncture and exercises other than those in the protocol. Video analysis was carried out independently on a purposive sample of 5 treatment sessions with five different participants at different time points during that participants treatment journey. For example, two initial assessment and treatment sessions were recorded, and the remainder were recorded later on in the treatment programme. The fidelity assessment tool was developed by the lead author, clinical colleagues and public and PPIE representatives (see Appendix 11). The tool addressed one limited aspect of implementation fidelity, in order to capture the fidelity of intervention delivery and was carried out during the treatment phase of the study. Participants gave their written consent and were not identifiable from the videos. The maximum score for ‘essential’ aspects of fidelity was 15/15. The median score for the videos was 14/15 (93%) with a range of 13-15 (87-100%).

Table 7.10 Frequency of physiotherapy intervention components

Domain	No. of participants receiving component N=69	Method of assessment	Treatment options	Frequency of component used	%
Psychological barriers to recovery	47 (68%)	Keele STarTBack Clinical interview & history	a. Treatment of Kinesiophobia with graded exposure, education and movement re-education	16	1.3
			b. Treatment of hypervigilance with education, distraction & desensitisation	17	1.4
			c. Treatment of faulty beliefs about pain, LRS, treatment and/or prognosis with education and self-management strategies	38	3.2
			d. Treatment of Iatrogenic beliefs and corresponding avoidance behaviours with education and movement re-education	3	0.2
			e. Treatment of aspects of work as a barrier to recovery and treatment with ergonomic advice and practise	15	1.2
			f. Identification of financial barriers to recovery and signposting e.g. debt management	15	1.2
			g. Identification of emotional barriers to recovery and signposting to appropriate therapy e.g. GP/Psychology	57	4.7
Neurological	39 (58%)	Clinical assessment	a. Neural interface mobilisation	98	8.1
			b. Functional neurological movement re-education	7	0.6
Movement restriction	59 (86%)	Clinical assessment	a. Flexion mobilisation (Grade 2-4)	68	5.6
			b. Side-flexion mobilisation (Gr. 2-4)	5	0.4
			c. Extension mobilisation (Gr. 2-4)	15	1.2
			d. Rotation mobilisation (Gr. 2-4)	41	3.4
			e. Flexion+Side-flexion mobilisation (Gr. 2-4)	11	0.9
			f. Flexion+Side-flexion+rotation mobilisation (Gr. 2-4)	62	5.2
			g. Extension+Side-flexion mobilisation (Grade 2-4)	0	0
			h. Manipulation (Gr. 5)	0	0
			i. Seated Mobilisation With Movement (MWM)	16	1.3
			j. Standing MWM	16	1.3
			k. Mobilisation into functional position	14	1.2
			l. Muscle stretches	61	5.1
			m. Functional movement re-education	7	0.6

Understanding	66 (96%)	Clinical assessment and interview	a. Management of erroneous believes relating to LRS provide education to help eradicate these beliefs	57	4.7
			b. Pacing behaviours	53	4.4
			c. Goal attainment	58	4.8
			d. Health Promotion	80	6.6
			e. Identification and treatment of central sensitisation-liaison with GP/pain clinic	8	0.7
			f. Identification and treatment of peripheral sensitisation-liaison with GP/pain clinic	7	0.6
Conditioning	63 (91%)	Self-assessment answers, clinical interview & history	a. Cardiovascular & conditioning exercise relevant to patients' goals	83	6.9
			b. Function specific stretches	39	3.2
			c. Function specific strengthening	62	5.2
			d. Ergonomic advice	14	1.2
			e. Ergonomic practise	6	0.5
			f. Group exercise	0	0.0
			g. Perturbation training	7	0.6
Movement control	33 (48%)	Clinical assessment	a. Sagittal plane control in functional positions relevant to patients' problems/goals	24	2.0
			b. Coronal plane control in functional positions relevant to patients' problems/goals	15	1.2
			c. Axial plane control in functional positions relevant to patients' problems/goals	1	0.1
			d. Multi-planar control in functional positions relevant to patients' problems/goals	6	0.5
			e. Movement re-education in functional positions relevant to patients' problems/goals	18	1.5
Pain	52 (75%)	ODI VAS back & leg Clinical interview & history	a. Analgesic review & advice in liaison with GP/Pharmacist	23	1.9
			b. Pain education	60	5.0
			c. Pain coping strategies	20	1.7
			d. Fear reduction intervention in liaison with psychologist/pain clinic	12	1.0
			e. Stress reduction intervention in liaison with psychologist/pain clinic	32	2.7
Totals				1267	99.8%[1]

[1]0.2% or 1 component of missing data

The number of participants treated by each of the three physiotherapists is presented in Table 7.11

Table 7.11 Treating physiotherapist treatment numbers

Treating Physiotherapist	Early Intervention		Usual Care		Total (%)
	no. of patients	% Within group	no. of patients	% Within group	
1	13	31.0	9	23.7	22 (27.5)
2	17	40.5	19	50.0	36 (45.0)
3	12	28.5	10	26.3	22 (27.5
Total	42	100	38	100	80 (100)

The utilisation of the seven treatment domains components in both arms of the study is provided in Table 7.12.

Table 7.12 Treatment domains utilised according to group

Treatment component	Early Intervention		Usual Care		Total	
	n	%	n	%	n	%
Movement restriction	34	89%	25	81%	59	86%
Neurological	26	68%	13	42%	39	57%
Psychological	26	68%	21	68%	47	68%
Understanding	37	97%	29	94%	66	96%
Conditioning	36	95%	27	87%	63	91%
Movement control	20	53%	13	42%	33	48%
Pain	32	84%	20	65%	52	75%

The utilisation of treatment domains delivered by each individual physiotherapist, according to group is provided in Table 7.13. The domains of Understanding and Conditioning are the most commonly delivered intervention domains for all three treating physiotherapists. The domain of Movement control being the least commonly delivered element of the intervention for all physiotherapists. This is in keeping with the data from Table 8.2 where the

understanding and Conditioning domains are the most commonly delivered and Movement control the least commonly delivered domain.

Table 7.13 Treatment domains delivered by physiotherapists

Physiotherapist	Treatment component	Early Intervention		Usual Care	
		Number of patients	%	Number of patients	%
1	**Movement restriction**	11	100%	7	88%
	Neurological	5	45%	4	50%
	Psychological	7	64%	5	63%
	Understanding	11	100%	7	88%
	Conditioning	11	100%	7	88%
	Movement control	5	45%	3	38%
	Pain	8	73%	1	13%
2	**Movement restriction**	11	73%	9	64%
	Neurological	11	73%	5	36%
	Psychological	11	73%	9	64%
	Understanding	14	93%	13	93%
	Conditioning	14	93%	14	100%
	Movement control	8	53%	5	36%
	Pain	13	87%	11	79%
3	**Movement restriction**	12	100%	9	100%
	Neurological	10	83%	4	44%
	Psychological	8	67%	7	78%
	Understanding	12	100%	9	100%
	Conditioning	11	92%	6	67%
	Movement control	7	58%	5	56%
	Pain	11	92%	8	89%

Tables 7.14.1, 7.14.2 and 7.14.3 show the participant PROMs for each of the three treating physiotherapists. The tables show the similarities between baseline score for disability and pain levels, together with similar mean differences between baseline and 26-week scores.

Table 7.14.1 Patient reported outcomes for physiotherapist 1

							Paired differences		95% Confidence intervals of difference	
Outcome	**Baseline mean**	**N**	**SD**	**26 weeks mean**	**N**	**SD**	**Mean**	**SD**	**Lower**	**Upper**
ODI (0-100)	45.0	20	19.7	11.7	20	12.0	-33.3	17.6	-41.5	-25.1
Back pain	4.8	20	3.4	2.3	20	2.3	-2.5	3.9	-4.3	-0.7
Leg pain	7.2	20	1.6	1.8	20	2.5	-5.4	3.0	-6.8	-4.0
EQ5D Utility	0.44	20	0.27	0.84	20	0.17	0.40	0.26	0.28	0.52
EQ5D VAS	61.7	20	18.7	77.7	20	15.1	16	19.9	6.7	25.3

Table 7.14.2 Patient reported outcomes for physiotherapist 2

							Paired differences		95% Confidence intervals of difference	
Outcome	**Baseline mean**	**N**	**SD**	**26 weeks mean**	**N**	**SD**	**Mean**	**SD**	**Lower**	**Upper**
ODI (0-100)	45.6	27	16.807	9.3	27	10.0	-36.4	18.1	-43.5	-29.2
Back pain	6.2	27	2.4189	2.1	27	2.2	-4.1	2.8	-5.2	-3.0
Leg pain	6.6	27	2.3317	1.1	27	2.1	-5.5	3.4	-6.8	-4.1
EQ5D Utility	0.47	27	0.30	0.90	27	0.11	0.43	0.29	0.32	0.55
EQ5D VAS	66.9	27	19.6	81.2	27	13.2	14.3	18.8	6.9	21.7

Table 7.14.3 Patient reported outcomes for physiotherapist 3

							Paired differences		95% Confidence intervals of difference	
Outcome	**Baseline mean**	**N**	**SD**	**26 weeks mean**	**N**	**SD**	**Mean**	**SD**	**Lower**	**Upper**
ODI (0-100)	42.6	21	21.1	9.8	21	18.8	-32.9	21.5	-42.6	-23.1
Back pain	5.8	21	3.1	1.8	21	1.9	-4.0	3.2	-5.4	-2.5
Leg pain	7.3	21	1.9	0.9	21	1.8	-6.5	2.2	-7.4	-5.5
EQ5D Utility	0.55	21	0.26	0.92	21	0.20	0.37	0.23	0.27	0.47
EQ5D VAS	66.0	21	19.0	82.52	21	15.3	16.5	16.5	9.0	24.0

7.4.6 Sample size calculation for the definitive RCT trial

For the definitive RCT I propose the primary outcome is the ODI at 26-weeks post-randomisation as the ODI has shown to be acceptable to patients and is a commonly used measurement of self-rated disability. In this pilot trial, we observed a difference in means of 2.5 points (95% CU: -4.5 to 9.1) between the randomised groups (with the usual care group having the better quality of life/lower level of disability) and a SD of 16points at 26 weeks. There is a lack of consensus regarding the MCID for the ODI, with suggestions ranging from 6 to 30 points (Fritz and Irrgang J.J, 2001; Ostelo, Deyo, *et al.*, 2008). Table 7.15 shows a range of sample sizes for varying target differences in the ODI. If we assume a target difference of five-points on the ODI scale, then with 217 patients per group (434 in total) we would have 90% power to detect a five-point difference or more as statistically significant at the 5% (two-sided level). This is equivalent to standardised effect size of 0.31 between the randomised groups. An standardised effect size of 0.3 is the average target effect size for trials published in the Health Technology Assessment Journal and so is a reasonable target (Rothwell, Julious and Cooper, 2018). Allowing for a conservative estimate of 20% attrition (we observed 15% in this pilot) we would need to recruit and randomise 272 per group (544 in total).

Table 7.16.1 details the number of recruitment centres required for a given recruitment rate and study duration supposing a target difference of 5 on the ODI. Table 7.16.2b provides the same data but for a target difference of 2.5 points on the ODI.

In this pilot trial, we observed a difference in means of 2.5 points (95% CI: -4.5 to 9.1) between the randomised groups (with the usual care group having the better quality of life/lower level of disability). There is considerable uncertainty in the estimated treatment effect from this pilot trial and the results are compatible with a wide range of treatment effects with a 4.5-point difference favouring early physiotherapy arm to a 9.1-point difference favouring usual care; and the point estimate of 2.5–points favouring usual care. There is a lack of consensus regarding the MCID for the ODI, with suggestions ranging from 6 points to 30 points (Keogh, Matthews and Hurley, 2018). The DELTA^2 guidance on choosing the target difference and undertaking and reporting the sample size calculation for an RCT recommends the target difference for a definitive trial should be one considered to be important to at least one key stakeholder group. The target difference does not necessarily have to be the minimum value that would be considered important if a larger difference is considered a realistic possibility or would be necessary to alter practice. The DELTA^2 guidance also recommends a sensitivity analyses, which consider the effect of uncertainty around key inputs, for example, the target difference used in the sample size calculation,

should be carried out; and that a pilot trial can be used to inform the choice of the standard deviation value for a continuous outcome along with other relevant inputs such as the amount of missing outcome data (Cook *et al.*, 2018).

The required sample size is very sensitive to the target difference. Halving the target difference quadruples the sample size. If we assume a target difference of 2.5-points on the ODI scale, then with 862 patients per group (1724 in total) we would have 90% power to detect a 2.5-point difference or more. This is equivalent to standardised effect size of 0.16 between the randomised groups. Bell et al 2018 also recommend that *"target effect size must also be realistic, and the estimated effect size and confidence interval (CI) from the pilot can give some evidence here i.e. whether there is any indication that the intervention is effective and important differences might be obtained in the main trial. The small sample size of a pilot makes estimation uncertain, so caution must be exercised."*. Furthermore, they "*strongly stress that preliminary efficacy evidence from a pilot study should not be overstated, and researchers should avoid temptation to forgo the main trial."* (Bell, Whitehead and Julious, 2018).

Table 7.15 Sample sizes for main RCT for a range of target mean differences with a primary outcome of the ODI score at 26-weeks post-randomisation

Significance Level	Power	SD	Target Mean Difference	Standardised Effect Size	Number in each group	Total Sample Size (N)	Total sample size Dropout	
							15%	20%
5%	90%	16	2	0.13	1346	2692	3168	3366
5%	90%	16	2.5	0.16	862	1724	2030	2156
5%	90%	16	3	0.19	599	1198	1410	1498
5%	90%	16	3.5	0.22	441	882	1038	1104
5%	90%	16	4	0.25	338	676	796	846
5%	90%	16	4.5	0.28	267	534	630	668
5%	90%	16	5	0.31	217	434	512	544
5%	90%	16	5.5	0.34	179	358	422	448
5%	90%	16	6	0.38	151	302	356	378
5%	90%	16	6.5	0.41	129	258	304	324
5%	90%	16	7	0.44	111	222	262	278
5%	90%	16	7.5	0.47	97	194	230	244
5%	90%	16	8	0.50	86	172	204	216
5%	90%	16	8.5	0.53	76	152	180	190
5%	90%	16	9	0.56	68	136	160	170
5%	90%	16	9.5	0.59	61	122	144	154
5%	90%	16	10	0.63	55	110	130	138

Table 7.16.1 Required recruitment rate, duration and number of recruiting centres calculation for RCT with a 5-point target difference

Recruitment rate Patient-centre-month	Significance level	Power	SD	Target mean difference	Standardised effect size	Number in each group	Total sample size (N)	Sample size with 20% dropout	Recruitment rate duration (months)	Number of centres
0.9	5%	90%	16	5	0.31	217	434	544	12	51
0.9	5%	90%	16	5	0.31	217	434	544	18	34
0.9	5%	90%	16	5	0.31	217	434	544	24	26
0.9	5%	90%	16	5	0.31	217	434	544	30	21
1	5%	90%	16	5	0.31	217	434	544	12	46
1	5%	90%	16	5	0.31	217	434	544	18	31
1	5%	90%	16	5	0.31	217	434	544	24	23
1	5%	90%	16	5	0.31	217	434	544	30	19
1.5	5%	90%	16	5	0.31	217	434	544	12	31
1.5	5%	90%	16	5	0.31	217	434	544	18	21
1.5	5%	90%	16	5	0.31	217	434	544	24	16
1.5	5%	90%	16	5	0.31	217	434	544	30	13
2	5%	90%	16	5	0.31	217	434	544	12	23
2	5%	90%	16	5	0.31	217	434	544	18	16
2	5%	90%	16	5	0.31	217	434	544	24	12
2	5%	90%	16	5	0.31	217	434	544	30	10

Table 7.16.2 Required recruitment rate, duration and number of recruiting centres calculation for RCT with a 2.5 –point target difference

Recruitment rate Patient-centre-month	Significance level	Power	SD	Target mean difference	Standardised effect size	Number in each group	Total sample size (N)	Sample size with 20% dropout	Recruitment rate duration (months)	Number of centres
0.9	5%	90%	16	2.5	0.16	862	1724	2156	12	200
0.9	5%	90%	16	2.5	0.16	862	1724	2156	18	134
0.9	5%	90%	16	2.5	0.16	862	1724	2156	24	100
0.9	5%	90%	16	2.5	0.16	862	1724	2156	30	80
1	5%	90%	16	2.5	0.16	862	1724	2156	12	180
1	5%	90%	16	2.5	0.16	862	1724	2156	18	120
1	5%	90%	16	2.5	0.16	862	1724	2156	24	90
1	5%	90%	16	2.5	0.16	862	1724	2156	30	72
1.5	5%	90%	16	2.5	0.16	862	1724	2156	12	120
1.5	5%	90%	16	2.5	0.16	862	1724	2156	18	80
1.5	5%	90%	16	2.5	0.16	862	1724	2156	24	60
1.5	5%	90%	16	2.5	0.16	862	1724	2156	30	48
2	5%	90%	16	2.5	0.16	862	1724	2156	12	90
2	5%	90%	16	2.5	0.16	862	1724	2156	18	60
2	5%	90%	16	2.5	0.16	862	1724	2156	24	45
2	5%	90%	16	2.5	0.16	862	1724	2156	30	36

The descriptive statistics for all participants by group and time point can be found in Table 7.17. This represents all data collected from participants, including those who were lost to follow-up from the study. As this was a pilot trial, significance testing was not undertaken (Eldridge *et al.*, 2016). The direction of travel appeared to be in favour of the early intervention physiotherapy group in the short-term (0-12 weeks). In particular the self-rated disability scores (ODI), the back and leg pain score (VAS) and EQ5D-5L VAS score were all in favour of the early intervention physiotherapy group. At the 26 week point it appears that the early improvement in the early intervention group has plateaued, with the usual care group reversing the trend and having slightly less self-rated disability, pain and a slightly better quality of life as measured by the EQ5D-5L.

Participants completed the Keele STarT Back screening questionnaire in order to determine their risk of chronicity. The majority of participants were in the medium or high-risk groups. The highest ODI and leg pain scores were found in the high risk STarT Back group and the lowest ODI and leg pain scores in the lowest risk groups. However, this did not appear to affect their response to treatment, with participants in all risk groups showing significant improvements in ODI and leg pain scores across all timepoints. Table 7.18 shows the results of the ODI and VAS leg pain for each group at the four timepoints according to risk group.

Table 7.17 Descriptive statistics for outcome measures at each time point

Outcome	Baseline		6 Weeks		12 Weeks		26 weeks		Area Under the Curve*				
											Difference 95% CI		
	Control *n=38*	Intervention *n=42*	Control *n=35*	Intervention *n=38*	Control *n=32*	Intervention *n=36*	Control *n=32*	Intervention *n=36*	Control *n=32*	Intervention *n=36*	Mean	Lower	Upper
ODI[1](SD)	45.2(17.4)	44.6 (19.5)	29.1(16.1)	24.0(18.7)	16.8(19.2)	16.0(19.0)	8.8(11.3)	11.3(15.5)	16.6 (11.4)	16.0 (14.0)	-0.6	-6.8	5.6
VAS Back[2] (SD)	6.0(2.6)	5.4(3.3)	4.6(2.7)	3.7(2.6)	3.1(2.5)	2.6(2.5)	2.1(2.1)	2.7(2.2)	1.8 (0.8)	1.5 (1.0)	-0.3	-0.7	0.1
VAS Leg[2] (SD)	6.9(2.3)	7.2(1.8)	5.2(2.9)	4.1(3.0)	2.6(2.9)	2.0(2.5)	0.9(2.2)	1.6(2.2)	1.7 (0.9)	1.5 (1.0)	-0.2	-0.6	0.3
EQ5D-5L VAS (SD)	64.6(18.9)	63.8(20.6)	68.9(16.4	72.7(17.7)	73.2(22.9)	79.6(17.5)	81.7(12)	79.6(16.3)	36.8 (7.1)	38.1 (7.8)	1.4	-2.2	5.0
EQ5D-5L Utility score (SD)	0.52(0.25)	0.44(0.29)	0.7(0.26)	0.74(0.22)	0.83(0.23)	0.85(0.22)	0.92(0.12)	0.86(0.19)	0.39 (0.09)	0.39 (0.10)	0.00	-0.05	0.04

[1]Oswestry Disability Index (ODI) 0-100, higher score=higher level of self-rated disability. For the ODI a larger AUC represents a greater level of disability over the 26 weeks. A negative difference means the Early Intervention Physiotherapy group has the better outcome (lower levels of disability) over the 26-weeks follow-up.

[2]Visual Analogue Scale 0-10, higher score=higher self-report pain. For the VAS back pain and leg pain outcomes a larger AUC represents a higher level of pain over the 26 weeks. A negative difference means the Early Intervention Physiotherapy group has the better outcome (lower levels of pain) over the 26-weeks follow-up.

[3] EQ5D-5L VAS score, 0-100, self-rated health. the higher the score, the better the quality of life. For the EQ5D-5L VAS score a larger AUC represents a higher level of quality of life over the 26 weeks. A positive difference means the Early Intervention Physiotherapy group has the better outcome (higher levels of quality of life) over the 26-weeks follow-up.

[4] EQ5D-5L Utility score, -0.6 to 1.00 with a higher score representing better quality of life. For the EQ5D-5L Utility score a larger AUC represents a higher level of quality of life over the 26 weeks. A positive difference means the Early Intervention Physiotherapy group has the better outcome (higher levels of quality of life) over the 26-weeks follow-up.
*When calculating the AUC time was classified in years e.g. 26 weeks = 0.5 years.

Table 7.18 Outcomes according to Keele STarT Back stratified risk score

		Keele STarT Back risk group at baseline																	
		Low risk						Medium risk						High risk					
		Early intervention			Usual care			Early intervention			Usual care			Early intervention			Usual care		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
ODI[1]	**Baseline**	21.3	12.8	6	13.9	7.1	2	42.3	17.7	19	46.2	16.9	25	55.5	15.3	17	48.9	14.4	11
	6 weeks	11.8	10.4	6	17.0	18.4	2	22.5	17.7	17	27.9	15.7	23	30.7	20.3	15	34.1	16.7	10
	12 weeks	10.4	6.2	5	2.0	2.8	2	13.4	16.6	17	14.6	14.3	22	21.1	24.0	14	26.5	28.9	8
	26 weeks	8.0	5.1	5	2.0	2.8	2	9.1	10.1	17	9.6	11.1	22	15.1	22.1	14	8.2	13.4	8
	AUC	9.6	5.6	5	5.0	5.4	2	13.9	11.4	17	15.8	10.0	22	20.7	17.7	14	21.7	14.1	8
VAS Leg pain[2]	**Baseline**	5.9	1.7	6	5.0	0.0	2	6.7	1.9	19	7.0	2.3	25	8.1	1.3	17	7.0	2.3	11
	6 weeks	3.3	2.0	6	5.0	4.2	2	4.2	3.1	17	4.9	2.9	23	4.2	3.2	15	6.0	2.8	10
	12 weeks	3.0	2.0	5	0.5	0.7	2	1.5	2.2	17	2.2	2.2	22	2.4	2.9	14	4.3	4.0	8
	26 weeks	1.8	2.7	5	0.0	0.0	2	1.3	1.8	17	0.8	2.1	22	1.8	2.6	14	1.3	2.8	8
	AUC	1.6	0.7	5	1.0	0.4	2	1.3	0.9	17	1.5	0.7	22	1.6	1.2	14	2.2	1.2	8

[1] Oswestry Disability Index (ODI) 0-100, higher score=higher level of self-rated disability. For the ODI a larger AUC represents a greater level of disability over the 26 weeks.

[2]Visual Analogue Scale 0-10, higher score=higher self-report pain.

The severity of back pain experienced by participants in both groups at baseline were less than their levels of reported leg pain. Figure 7.7 shows the levels of decreasing back pain in both groups running parallel until week 12 when there is a greater improvement in symptoms in the usual care group. The usual care group had greater levels of back pain at baseline than the early intervention group but by 26 weeks the degree of pain had converged, as illustrated in Table 7.19.

Figure 7.7 Back score VAS score over time by group for participants with all 4 assessments

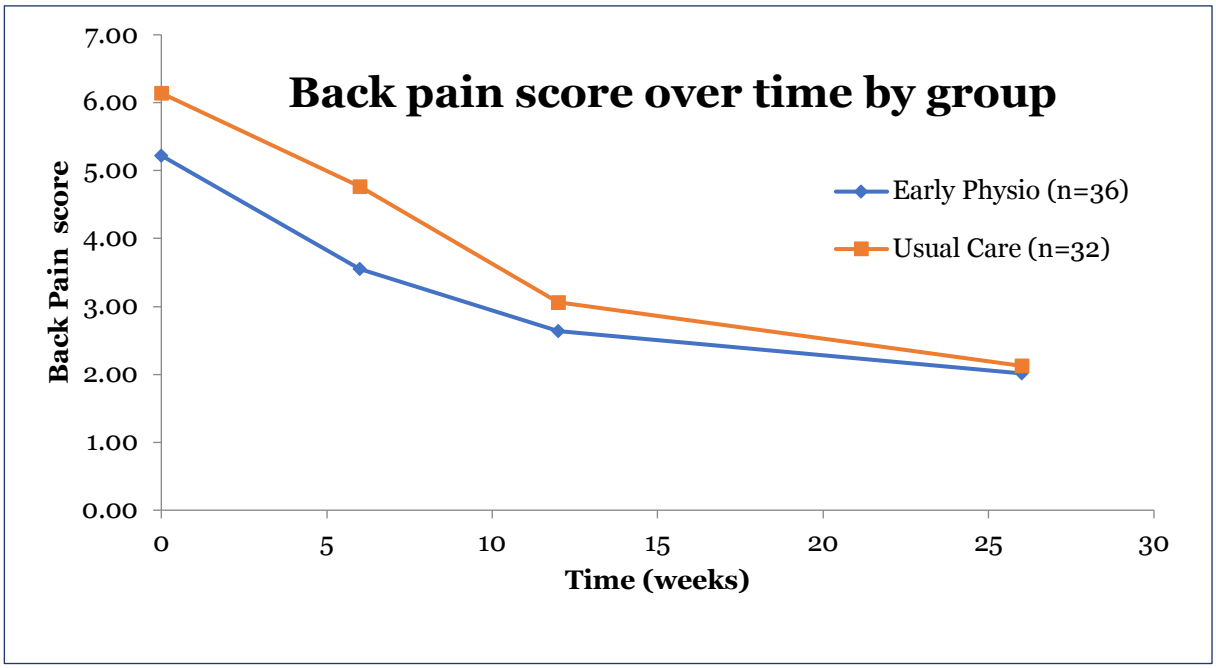


Table 7.19 Back pain score* over time by group for participants with all 4 assessments

	Early Intervention			Usual Care		
	N	Mean	SD	N	Mean	SD
Baseline	36	5.22	3.30	32	6.14	2.46
6 Weeks	36	3.56	2.60	32	4.77	2.77
12 weeks	36	2.64	2.51	32	3.06	2.46
26 weeks	36	2.01	2.16	32	2.12	2.09

* Measured using the Visual Analogue Scale 0-10, higher score=higher self-report pain

The baseline EQ-5D-5L scores between groups were very similar before any intervention as is seen in Figure 7.8. The early intervention physiotherapy group had a greater rate of improvement in overall self-rated health after the initiation of treatment. This difference continued until around week 22 when the two groups converged and at week 26 the usual care group reported slightly higher self-rated health. Table 7.20 presents this data in detail.

Figure 7.8 EQ-5D VAS score over time by group for participants with all 4 assessments

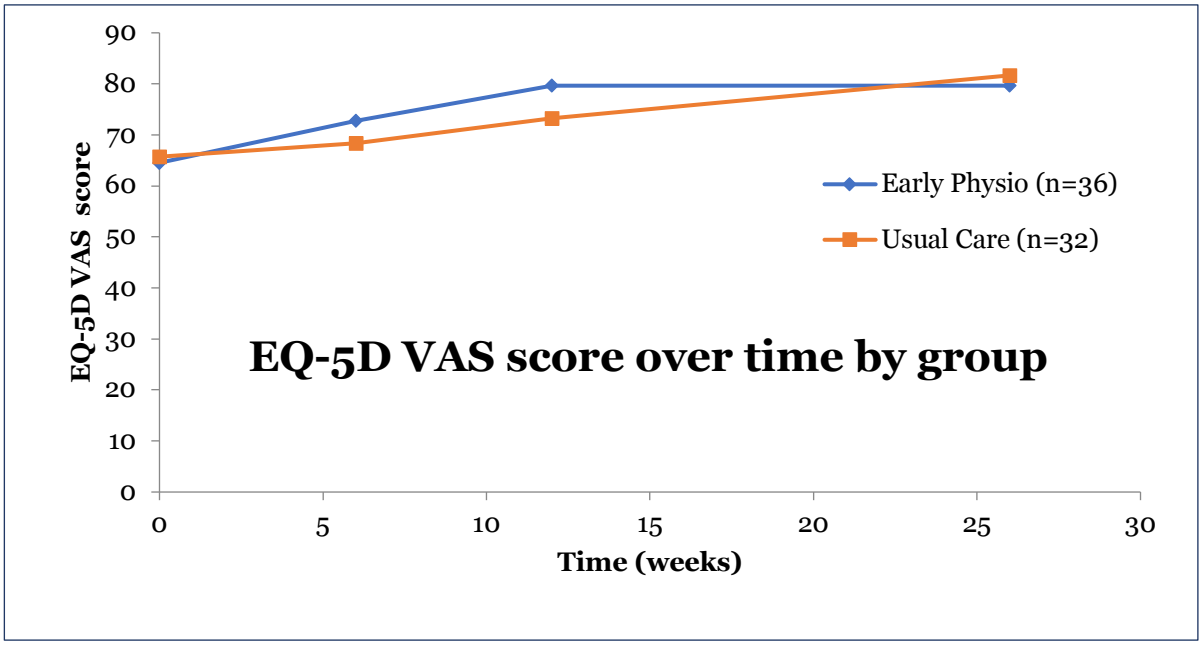


Table 7.20 EQ-5D VAS* score over time by group for participants with all 4 assessments

	Early Intervention			Usual Care		
	N	Mean	SD	N	Mean	SD
Baseline	36	64.53	20.01	32	65.72	18.09
6 Weeks	36	72.69	18.23	32	68.34	16.94
12 weeks	36	79.64	17.47	32	73.22	22.86
26 weeks	36	79.61	16.29	32	81.66	11.96

* EQ5D-5L VAS score, 0-100, self-rated health. the higher the score, the better the quality of life

The scores for the EQ-5D-5L utility scores follow those of the EQ-5D-5L VAS score over the 26-week course. There was a evidence of a baseline difference between the groups with the early intervention physiotherapy group having a lower quality of life which was quickly reversed after the initiation of treatment, as seen in Figure 7.9 and table 7.21. The baseline difference is attributable to chance as individuals were exposed to the same randomisation processes.

Figure 7.9 EQ-5D utility score over time by group for participants with all 4 assessments

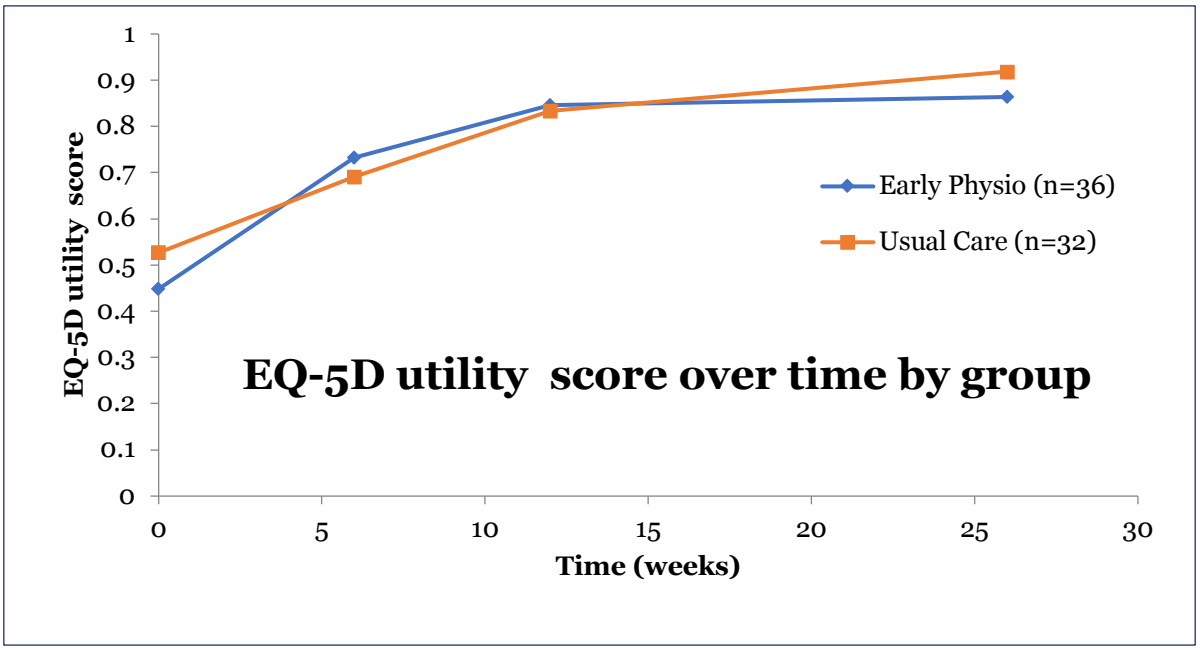


Table 7.21 EQ-5D-5L* utility score over time by group for participants with all 4 assessments

	Early Intervention			Usual Care		
	N	Mean	SD	N	Mean	SD
Baseline	36	0.45	0.29	32	0.52	0.25
6 Weeks	36	0.73	0.22	32	0.69	0.26
12 weeks	36	0.84	0.22	32	0.83	0.23
26 weeks	36	0.86	0.19	32	0.91	0.12

*EQ5D-5L Utility score, -0.6 to 1.00 with a higher score representing better quality of life.

7.5 Discussion

This external pilot study is the first to explore the role of early intervention physiotherapy for LRS. The study aimed to determine the feasibility of carrying out a full-scale RCT to determine the effectiveness and cost-effectiveness of early physiotherapy for LRS.

There are significant strengths of the study, including the successful recruitment of GPs, physiotherapists and successful delivery of the intervention. The return rate of PROMS at the definitive 6-week post randomisation point was 91% was encouraging as was the 26-week return rate of 84%. The attrition of participants in the study was similar in both groups, with 14% attrition rate in the early intervention group and 16% rate in the usual care group. However, the utility of pilot trial recruitment data to inform rates of recruitment for a full RCT have recently been called into question (Cooper *et al.*, 2018) and these estimates should be treated with caution. Furthermore, all of the feasibility parameters were found to be acceptable, including the set-up of 14 GP centres to recruit participants. The recruitment of participants was achieved within time despite a series of challenges, including GPs uncertainty as to the referral process and patient's uncertainty regarding contacting the research team to participate in the study. The recruitment of 80 participants within time is a significant success for the study. A recent review of the recruitment and retention rates of NIHR Health Technology Assessment funded studies found that the recruitment target was only achieved in 56% of studies (Walters *et al.*, 2017). and the retention of 85% of participants at 26 weeks was slightly below the 89% retention in HTA studies. Although 90 patients contacted the research team and 80 were successfully randomised, it is difficult to determine, with any degree of certainty the number of patients with LRS who were eligible but did not receive study information from the GP and or did not contact the research team. It would be useful to have this data for planning of a future study and in particular the reasons why GPs failed to provide potentially eligible patients the study information as well as the reasons why, if at all that eligible patients who were given the study information didn't contact the research team.

Both groups received the intervention at the appropriate time, within 2 weeks of randomisation for the early intervention physiotherapy group and after 6 weeks for the usual care group. The acceptance of the intervention, judged by the rate of attendance by participants at their treatment sessions, was better than anticipated and an improvement on usual rates of attendance seen in the physiotherapy provider service. This is potentially due to the group of participants involved in the study. It may be that they are better motivated in seeking healthcare and participating in a research study than other groups of patients with LRS. The acceptance of the intervention may also be attributable to the therapeutic relationship developed between the participant and physiotherapist and which is at the heart of the study. The individualised nature of the intervention is another important factor in

participants acceptance of the intervention. We know that patients with LRS prefer the individualised physiotherapeutic approach and do not like a generic, exercise sheet driven approach (Boote *et al.*, 2016).

The research results suggest early improvements in pain and disability with early intervention physiotherapy, for an initial period during which the intervention is delivered to the early group. The usual care group rate of recovery lags behind the early intervention group until they begin treatment at 6 weeks post-randomisation. At this point the outcome scores begin to converge. These results are however from a pilot study and not appropriately powered to detect effectiveness, therefore these are broad, non-specific indicators and so judgement regarding the effectiveness of the intervention should be withheld for a definitive RCT.

There were some limitations to this study. Although recruitment was satisfactory and ahead of time, the GPs involved in the study were well motivated and supportive of the study, in a city with a proven track-record of GP involvement in service development. This may not be the case across the country and further afield. The uneven rate of recruitment is a limitation of the study and factors to mitigate against this were introduced within the study in terms of recruiting new centres. For a full-scale RCT it would be useful to identify strategies to ensure adequate recruitment within each site, such as group and individual incentives, ensuring recruitment needs are met in different phases and to ensure communication channels between recruiters and trial managers are open (Campbell *et al.*, 2007; Brueton *et al.*, 2013). Similarly, the support of the service provider clinical, administrative and management staff was a key factor in the success of the study, a factor which may not be reproducible in other centres. This may be mitigated against with the use of the regional CRNs to harness the 'research ready' GPs and the utilisation of clear, concise and service-related processes and outcomes, as realised in this work. Our recommendations about recruitment also suggest including a wider geographical spread of GP centres to help meet the proposed recruitment rates. Site selection would need to consider current physiotherapy service provision and the ability to deliver the intervention in settings that are convenient and accessible to patients.

Patients self-referred into the study after an introduction from their GP (a pre-requisite for ethics approval) and so this group of patients may not be representative of a wider population of people with LRS. The POLAR group of participants were motivated, in the first instance to seek healthcare for their problem and secondly to contact the research team to discuss participation. This relies on a worthy level of confidence, self-organisation and communication skills, which other people with LRS may not possess. These factors need to be taken in account when planning a definitive study, and as such we have taken a more conservative view of attrition in the definitive sample size calculation (Rothwell, Julious and

Cooper, 2018). The recruitment may be made easier and negate the need for the aforementioned requisite communication skills and confidence by use of web-based recruitment processes, in different languages in order to mitigate against the low number of BAME found in this study.

The measure of implementation fidelity relates to the degree to which the components of the intervention have been delivered in relation to the protocol (Gearing *et al.*, 2011). The measurement of implementation fidelity in the POLAR study was made in a limited fashion with the use of an independent assessor to determine whether the intervention had been delivered, by the treating physiotherapist as per protocol. There are several limitations to this method, including the low number of physiotherapist/participant encounters analysed, the use of a newly developed measurement tool and the lack of clearly defined fidelity parameters as to what constitutes 'good' fidelity. It is acknowledged, however that assessing fidelity in its entirety, is expensive and time consuming (Perepletchikova and Kazdin, 2005). Although an attempt has been made to address one aspect of fidelity, assessment of fidelity in its entirety is outside of the remit of the study.

There are other aspects of fidelity which require consideration for a future study. These include the design of the intervention and the trial to ensure that the components are detailed in such a way as to ensure reproducibility (Bellg *et al.*, 2004; Borrelli, 2011). Other aspects of fidelity which require development prior to a full RCT include the fidelity of intervention training, intervention delivery and intervention receipt by the participant. A more detailed analysis of key aspects of the intervention such as the therapeutic approach and aspects of the intervention that are deliverable but not particularly essential and finally those aspects of the intervention that must be avoided as they may be deleterious to the intervention validity (Waltz *et al.*, 1993).

Many of these aspects of fidelity have been addressed in the study protocol and intervention handbook. However, the formal assessment of the different aspects of fidelity need to be addressed in a future trial with specific detail as to the aims of measuring each aspect of fidelity, the tools with which to perform the measurement and a priori standards against which to independently measure.

The nature and duration of participants symptoms were assessed during the baseline data collection phase. The initial onset of the patient's symptoms was not used in a way to define absolute duration of their LRS. Instead the point at which they sought healthcare assistance was used as a marker of onset. A future full scale RCT would need to have a clear definition of the onset of non-tolerable radicular leg pain as the defining date of onset. Methods to ensure recruitment of these patients at the time of onset of non-tolerable symptoms will be formulated and include a measure of time from onset to non-tolerability.

This was a pragmatic study in a clinical setting, using clinical staff and available resources and as such represents the real world of the NHS. It also represents research which stems from patients suffering with LRS and the problems they encountered with access to, and quality of physiotherapy. We demonstrated that the study is feasible and the potential of early intervention physiotherapy to improve patient care.

7.6 Conclusions

The POLAR study results indicate that a full RCT is potentially feasible within a reasonable timescale and resource envelope. There is a gap in evidence about how and when to treat this population, I conclude that a definitive trial is needed to help inform clinical practice.
The quantitative results of the POLAR study have been presented in this chapter, outlining the success in study set-up, recruitment and follow-up of participants. The following chapter will augment this by providing the results and reflections of participants and other stakeholders in the qualitative results.

Chapter 8 Qualitative results

The results of the quantitative element of the POLAR study have been presented in chapter 7, finding that the feasibility and research objectives were all met. The results suggest that a full-scale trial would be potentially feasible. This being a mixed methods study, Chapter 8 builds on these positive findings with the qualitative results, providing meaning, depth and an understanding behind the quantitative results.

8.1 Introduction

The qualitative aspect of the POLAR study aimed to gain experiences and feedback from all stakeholders in the study regarding processes of recruitment, content, and delivery of the intervention. The design of the qualitative aspect of the study can be found in Chapter 5. The results of the qualitative element of the POLAR study will be presented in this chapter. The interviews carried out with participants were illuminating, humbling and insightful, offering practically useful insights into the study and intervention processes, as well as the often-emotional reflections of patients on the effects of LRS on their lives and the lives of others. The interviews provided a rich seam of data, from which key emergent themes and their potential impacts are proposed. The results are presented in line with the consolidated criteria for reporting qualitative studies (COREQ) and the checklist found in Appendix 16 (Tong, Sainsbury and Craig, 2007).

8.2 Data collection and the role of the researcher

An initial interview guide was developed with input from the patient representatives, clinical and academic colleagues and was piloted in five interviews with patients undergoing physiotherapy treatment for LRS to evaluate usability and utility. Several changes to the wording of the questions in the topic guides were made after the pilot interviews together with clarification of some of the questions surrounding function. Interviews were carried out by the author who was a qualified and chartered physiotherapist, working as an extended scope spinal physiotherapist. His qualifications included BSc (hons), MSc, member of the musculoskeletal association of chartered physiotherapists and a PhD candidate. He was undertaking in depth interviews for the first time and had attended the national centre for social research (NATCEN) in depth interview course prior to the interviews. A telephone call to establish the interview parameters and help develop a relationship with each participant was undertaken prior to each interview by the author. During the telephone conversation the nature of the research being a PhD and clinical academic fellowship was discussed with each participant. The interviews lasted between 12 and 65 minutes (mean 38 minutes) and were

audio recorded with the consent of the interviewee. And field notes were made for each interview. All interviews with patient participants were carried out in their homes, at their request and at a convenient time, between 10am and 5pm, Monday to Friday. Several of the patient interviewees had family members present who remained outside of the narratives but helped frame them before and after the interviews. All interviews were relaxed and conversational, often with refreshments provided by the interviewee. The physiotherapist interviews took place in their respective workplaces during normal working hours, in privacy and away from their normal work rooms so as to avoid interruptions. Data was primarily analysed by MR with checks by one supervisor (SB) during the course of the interviews in order to utilise key emergent themes in subsequent interviews. It is important to consider the role of the researcher during data collection and interpretation.

8.3 Characteristics of participants

Of the 80 patients who took part in the main feasibility study, 33 participants were recruited into the qualitative element of the study with a total of 45 interviews being carried out. The number of interviews carried out exceeded the expected number for two reasons. Primarily the interviewees were generating new data regarding the acceptance of the intervention and the study processes. Secondly, during the interviews, it was evident that the participants were keen to voice the effects of LRS on their lives. Thirteen participants were interviewed before and after their physiotherapy programme, six participants were interviewed only at the pre-treatment stage and thirteen only at the post-treatment stage. Four participants who had undertaken pre-treatment interviews were not available for post-treatment interviews due to constraints such as work commitments. Two of these participants had dropped out of the study (S03/001 and S02/014). Thirteen participants could only be interviewed post-treatment due to an inability to schedule pre-treatment interviews at a time to suit the participant prior to the intervention commencing. There were nineteen female and fourteen male participants with a mean age of 51 years of age (32-71 years range). They had a pre-treatment mean ODI of 45% (range 8-80%) and a post-treatment ODI of 11% (range 0-86%). See Table 8.1 for details of patient participant characteristics.

All three physiotherapist participants who delivered the intervention consented to be interviewed. The physiotherapists had a mean age of 36 years (range 34–40 years) and a mean of 10 years post-graduate experience (range 7–12 years).

Recruiting GPs were invited to participate in the interviews, but they declined due to limitations on their time. Feedback from GPs were gathered using email with three responses, all of which provided positive encouragement regarding the study.

Table 8.1 Characteristics of Interviewees

Recruitment cycle	Screening number	Age	Group[1]	Gender	Pre-treatment Interview	Pre-treatment ODI[2] %	Pre-treatment Pain score[3]		Keele STarT Back score[4]	Post-treatment ODI %[2]	Post treatment Pain score		Post-treatment Interview
							Leg	Back			Leg	Back	
1	**S03/001**	56	UC	M	Yes	38	8	9	5/3	14	1	3	No
	S06/012	52	UC	M	Yes	48	6	7	5/3	8	1	1	No
	S07/004	45	UC	F	Yes	28	8	10	6/2	4	0	4	Yes
	S07/005	34	UC	M	Yes	42	9	6	9/5	34	4	4	No
	S06/011	46	UC	F	Yes	51	8	6	7/4	2	1	2	Yes
	S04/001	63	Early	F	Yes	58	7	0	8/5	2	2	0	Yes
	S06/003	48	Early	F	No	28	5	7	2/1	10	3	6	Yes
	S06/006	56	Early	M	Yes	38	5	7	7/4	10	3	6	No
	S07/001	67	Early	F	Yes	10	3	0	4/1	0	0	2	Yes
	S03/004	61	Early	M	No	68	8	4	6/4	24	7	2	Yes
2	**S02/003**	65	UC	M	Yes	80	9	9	6/3	0	1	1	Yes
	S04/005	51	Early	F	No	51	9	7	6/4	6	0	2	Yes
	S03/005	62	UC	F	Yes	32	9	3	5/2	8	0	2	Yes
	S05/003	51	UC	M	Yes	38	2	7	4/1	10	2	3	Yes
	S06/022	23	UC	M	Yes	66	6	8	6/2	30	9	8	Yes
	S06/024	38	UC	M	Yes	8	5	7	2/1	0	0	0	Yes
	S07/009	68	UC	F	Yes	27	9	0	4/2	0	0	0	Yes
	S01/002	52	UC	F	No	66	9	1	6/2	4	0	1	Yes
	S06/017	32	Early	F	No	40	9	8	8/4	4	0	1	Yes
	S06/016		Early	F	No	72	8	9	8/4	6	0	2	Yes
	S06/021	46	Early	M	No	62	10	8	6/4	0	0	0	Yes
	S05/001	61	Early	F	No	12	6.5	8	2/0	8	0	3	Yes
	S06/013	63	Early	F	No	60	4	9	6/3	6	0	2	Yes
	S06/018	30	Early	M	No	22	8	2	5/3	2	0	0	Yes
3	**S10/003**	50	UC	F	Yes	52	9	7	7/4	12	0	2	No
	S06/026	48	UC	F	Yes	30	8	8	6/2	2	0	0	Yes
	S02/014	40	Early	M	Yes	58	8	9	8/5	Lost to follow-up			
	S05/008	71	UC	F	Yes	38	7	9	4/2	9	0	2	Yes
	S02/006	56	UC	M	Yes	32	8	0	6/4	0	0	0	Yes
	S06/030	54	UC	F	Yes	32	3	7	6/3	42	0	7	No
	S01/003	42	Early	F	No	42	7	4	6/3	0	0	0	Yes
	S06/027	37	Early	M	No	80	10	8	9/5	86	7.5	8	Yes
	S05/007	61	UC	F	No	74	9.5	7	5/1	9	0	1	Yes

[1] Early=Early intervention physiotherapy UC=Usual Care physiotherapy [2] Oswestry Disability Index (ODI) 0-100, higher score=higher level of self-rated disability

[3] Visual Analogue Scale 0-10, higher score=higher pain [4]Keele STarT Back screening tool. Total score 3 or less=low risk of chronicity, Sub-score 3 or less=medium risk, 4 or more=high risk

8.4 Presentation of data

In the following section the results of data analysis are presented as key themes and subthemes, providing insights into the perceptions and experiences of patients and treating physiotherapists. The initial section outlines data which relate to acceptability and implementation of study processes and the intervention components. These data provide insight into the feasibility of delivering a full-scale trial of POLAR.

The second section outlines data collected which relate to the experiences of patients living with LRS. While not relating specifically to feasibility and delivery of a future trial, the data provide valuable insights into the lives of people living with LRS, and potentially their motives and needs for engaging with interventions. These data will be considered in regard to what they tell us about elements of optimal interventions, and potential indicators of effectiveness.

In the following sections the strategy for participant quote selection was made on the basis of illustrating variation of response, particularly indicating where there was dissonance or consensus in the findings.

8.5 Acceptability and feasibility of study processes and intervention components

8.5.1 Patient views of referral processes into the study

Recruitment was central to the success of the pilot study and the feasibility of a future, full-scale RCT. I met with each GP group practice to refine and optimise the recruitment process for that practice. Each GP had a study pack, including patient information and posters for their clinic and waiting rooms. Patients were given the POLAR study details by their GP and asked to contact the research team. Overall, the participants' experience of the study processes were favourable and planned referral methods had worked well:

"Both GPs were very good, you never have enough time, but I've never got a bad word to say about them" S06/012

"*Getting to the study, the doctor said straightaway there is a study about this do you want to go on it and I said yes I do and phoned and got it all sorted*" S02/014

8.5.2 Waiting for physiotherapy treatment

Those participants in the early intervention physiotherapy group were universally positive towards their group allocation. Fifteen of the participants stressed the importance of being in

the early group both in terms of their physical symptoms but more noticeably their ability to cope with the psychological effects of LRS:

"I was really glad because I don't think I would have coped like that for another six weeks. I don't know what I would have done if I didn't get something that quick you know. I would dread to think especially because of the depression and things." S06/27

"As I said earlier, I don't think I would have managed having to wait six weeks or even three weeks with the pain I was in. Getting to see someone so soon really helped get back on my feet mentally as well as physically." S06/018

"It is excruciating. Life changing at such a fast pace. Unbelievable. The effect it has physically is terrible, but the effect on my mental health was even worse. Having to wait another 6 weeks would have been bad for me physically, but mentally it would have devastated me," S02/003

Whilst the experiences of those participants randomised to the early intervention physiotherapy group were positive, they could appreciate the potential negative effects that waiting could have had. The participants in the usual care group all understandably had less favourable views about having to wait for their treatment to begin:

"Well you know I prefer to be in the other group can get things sorted quickly" S02/006

"I'll be honest, by the time I was ready to see the physio at six weeks I was certainly no better and probably quite a bit worse in terms of, you know would I have been better in the early group? Definitely." S06/022

Managing the concerns and possible reluctance of future participants randomised to the control arm of an intervention will be important to consider during a future full trial. It will be important to convey to participants in the usual care group of any future study, that they are not receiving an inferior service but the same approach, at a different timepoint.

8.5.3 Patient views of study processes

The study processes were well-received by patients. These participants however, did have suggestions for improvements regarding the physiotherapy appointments:

"Well the appointments are quite short and only about half an hour, so I think with more time I could have got more out of it" S06/027

"It would be great if there were more appointment times not during work hours" S06/022

Acknowledgement of the difficulties faced in the NHS in terms of treatment optimisation and organisation of appointments were acknowledged:

"I would be much better with a week's wait rather than two weeks but I know that's never going to happen on the NHS but you know that would be even better" S06/017

"I think it would have been useful to have two or three extra sessions at the end…just in case, because getting back to see the GP and organise normal physio will be a nightmare" S06/018

"Well you come to expect these things in the NHS don't you? I don't want to moan…but I would prefer to be seen sooner rather than later." S05/008

Participants recognised the challenges inherent in delivering NHS services and were generally reluctant to be critical. New interventions (such as the one in this study) which have potential to improve NHS capacity or reduce waiting times are positively viewed as overcoming NHS resourcing limitations, with this potentially supporting achieving required rates of patient recruitment for a full-scale trial.

8.5.4 Patient views of the intervention

The physiotherapy intervention was designed to reflect participant needs, depending on their problems, goals and clinical findings. This focus was reflected in the range of positive comments, the most recurrent being the positive effect of the clarity of individualised advice:

"The advice was really useful I think in the first instance, knowing that it was safe to go swimming for instance is what I needed really because I didn't really know" S06/018

"Some bits were really useful like advice, it just shows people don't know what (they are) doing because of the mixed messages." S01/002

These quotes highlight that the use of self-management may be an important component of the management of LBP and LRS, and may be a particular contributor to positive intervention outcomes reported in this feasibility study:

"The physios are definitely given me methods and techniques to enable me to get on with things and manage them better." S06/022

Fourteen interviewees voiced their appreciation of aspects of the treatment approach such as being listened to, given enough time to explain their symptoms and the individualised nature of their care:

"I felt that I was respected as an individual, I felt like he had time to listen to me and was obviously a specialist in his field and definitely knew what he was talking about." S04/005

"With this I felt listened, I felt like a person, listened to how it had affected my life" S07/009

Exercises were widely used as part of the intervention with 91% of participants receiving exercise therapy. Participants experiences supported the use of exercises in helping manage their symptoms:

"*The exercises were certainly useful*" S06/011

"*the most useful thing being exercise that he gave me we used to do exercise there and then I used to do them here (at home) and I'm positive that it really has helped me to get better*." S07/001

Movement re-education involves challenging patients on how they move and correcting any movement dysfunctions or aberrant movement patterns which can arise during episodes of pain. Movement re-education can take many forms, and participant reports indicate that it was a well-accepted component of the intervention:

"for instance, not using my hands to stand up out of a chair, using my legs and I now feel my legs are much stronger as a result and as a result of that I can now go up and down stairs normally" S03/005

Manual therapies to relieve movement restriction were used as a treatment option in 86% of treatment sessions, with patient participants reporting that this was particularly valuable in providing relief from symptoms:

"I really liked the kneading and the pulling and stretching and oh I felt about six inches taller after those and that really helped give me confidence that I can get back doing things" S07/009

The intervention used an individual goal-orientated approach to ensure that each participant received the best possible intervention mix for them. There were several suggestions from participants in both groups as to how to improve this aspect of the intervention further:

"probably a bit more information about what I can do to help, what I can do at home rather than what I can do there" S04/001

"I don't know I think, more actual gym work and more exercises and really getting going would I think of been useful." S03/005

Qualitative data indicated the value of the multi-modal, goal orientated, individualised treatment approach, with reports that all elements of the intervention were positively received. Patient views regarding the relative importance of the different treatment components varied, there were suggestions regarding how to improve the goal-setting element, the exercise component and the provision of information. Overall the intervention was found to be acceptable and perceived as effective by patients.

8.5.5 Physiotherapist views of the study and its processes

The interviews with the three physiotherapists who had delivered the intervention explored the acceptability of the study processes for themselves and the service. They reported that they found participation overall to be a positive experience:

"Really positive, a really good experience, really good for the patients and really good for me"

Two of the physiotherapists reported difficulty in completing the electronic treatment log in the first few weeks:

"There were loads of treatment components and so it was difficult to remember where everything fit"

They did however suggest solutions which can be integrated into the intervention training for a full trial:

"More training on the live database, filling out the treatment stuff would have helped"

"Having another meeting, training after we started to iron out things like that would've been good"

All three physiotherapists had 'ring-fenced' time within their normal diaries for study participants. They voiced difficulties in ensuring that this time wasn't used for non-study patients:

"I, we often found that they had put non-POLAR patients in those slots. It was a pain to sort out"

This suggests therefore, that it is important for a full trial to ensure that treatment time-slots for participants are kept separate from the treating physiotherapists other treatment slots for non-study patients. Adequate funding for the study time slots is essential in this regard.

8.5.6 Physiotherapist views of the intervention

The insights gained from interviews with the physiotherapists prior to their training allowed for planning of delivery of the intervention in terms of content and style. Learning styles of the physiotherapists were explored and refinements were made to the theoretical and practical aspects of the training. Feedback during and after the physiotherapists had completed treating participants provided significant information for the subtle, but key iterations during the study.

The physiotherapists underwent around twenty hours of face-face training in preparation for the study, including both theory, clinical reasoning and hands-on practise, which they found prepared them well:

"The training in the seven or eight domains of treatment was really good, compartmentalising the different aspects made a lot of sense to me"

The intervention was protocolised, paper and electronic copies of the protocol were given to each physiotherapist, as well as two simple aide-memoires, one explaining the study processes and the other the treatment domains:

"I thought it was really good to go through the study processes initially and the crib sheet really helped during the study"

"I found the intervention really helpful as it focussed me on what I needed to look at-the individual"

The physiotherapists were asked how the POLAR intervention was similar or different to their usual practice:

"I don't really think it's that different really…what it does is make me think differently, more focussed really"

"It helped me focus, reflect and look at the different parts of the patients' problems"

"It allowed me to concentrate on what their goals were and how we were going to achieve them by going, by saying we need to do this, this and this"

The treating physiotherapists were given thirty minutes for each follow-up appointment, an increase of ten minutes on their usual time allowance in order to enter the treatment components on the computer system. They reacted positively to having more time:

"*Having the extra time really helped, helped having the time to sit and explain things better, without rushing"*

"Giving the patient time to discuss their problems and what difficulties they were having led to a more patient-centred approach than usual"

The patient-centred focus was a cornerstone of the treatment approach, and patient data which highlighted the value of individualising intervention was echoed by the treating physiotherapists. The physiotherapist participants described positive views of the motivational interview approach, which was able to provide time for patients to express their feelings:

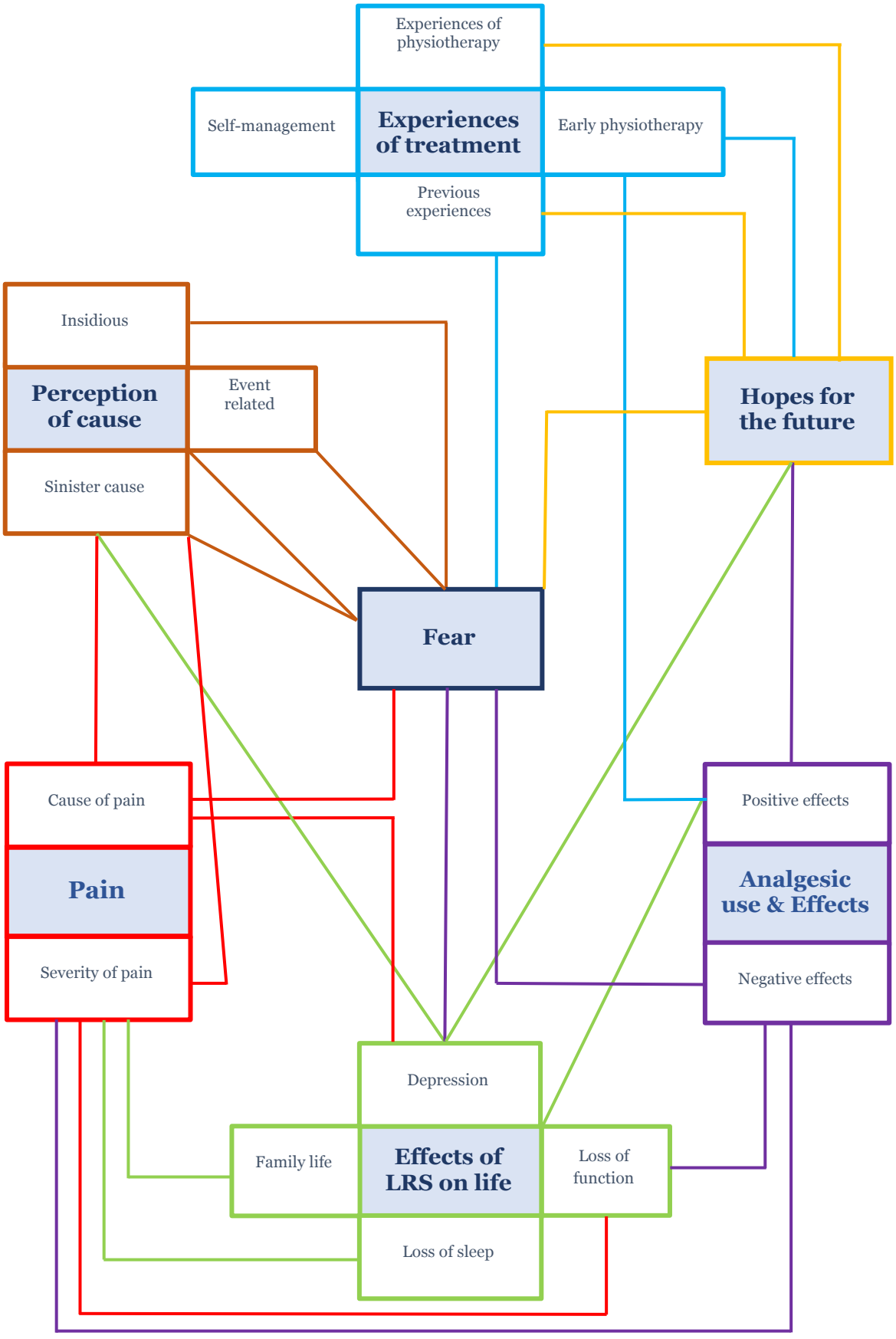
"Giving the patient time to discuss their problems and what difficulties they were having led to a more patient-centred approach than usual"

Physiotherapist views regarding the preparation for and delivery of the interventions were therefore overwhelmingly positive, suggesting that the intervention would be feasible and acceptable to deliver within a larger scale full trial. The framework element of the intervention appeared to be a key component of it, which was reported to differ from usual practice. In an echo of the patient data, the individualised nature of the approach was reported to be a central feature of the intervention, suggesting that this may be a key contributor to effectiveness.

8.6 Patient participant experiences of LRS

Whilst the interviews primarily explored the intervention, implementation and study processes, the data also contained insights into patient participant wider views and perceptions of their condition, the potential causes, concerns and experiences. The following section explores these data and considers how these perceptions of people living with LRS may inform the design, delivery and outcomes of interventions. Figure 8.1 provides a summary of the themes and subthemes and their relationships developed from the interview data.

Figure 8.1 Thematic representation of the relationship between emergent themes



8.6.1 Perception of the cause of LRS

The clinical assessment process explored participant perceptions of the cause of their symptoms. Thirteen interviewees were unable to identify a specific causative event:

"*Well the pain just started for no reason really, it's not like I did something to cause it, you know like lift something.*" S06/018

"*I have absolutely no idea. I feel a bit confused about all of that, I presume it was because of being sedentary and possibly falling asleep on couch on Sunday afternoon.*" S06/26

"*There was nothing to cause it, I mean I didn't do anything that I can remember, and you would remember, wouldn't you*?" S05/008

These quotes provide an insight into the difficulty participants faced in making sense of their symptoms, with attempts to justify what they perceived to be normal, innocuous causative events such as lifting or falling asleep, suggesting the need for interventions to explore potential causation with patients.

There were ten participants who reported that they could identify specific incidents as being the causative event:

"This happened when I twisted it at work it was when I had my foot down I twisted my leg behind me I felt my back go. I knew I'd done it straightaway." S02/006

"So, I was reaching down to pick up my son out of his travel cot and I felt a twinge in my back and then it got a bit worse and then went down my leg." S02/003

"I bent a little obscurely to put a box onto a shelf at work and my back went" S02/014

Others perceived an innocuous cause:

"I was sat on the toilet and I have a bad habit of either playing games or. . . when I tried to get up I felt my back collapse and I had terrible pain in the back and leg." S06/030

"I think I guess just the daily routine of work habits and sitting marking on a computer, I hate typing, sitting meetings sitting in armchairs." S06/012

"I think I was sitting in a car in a traffic jam in London for five hours, I was very uncomfortable." S05/003

The severe nature of nine participants symptoms caused them to worry about a possible serious cause:

"I don't know, you hear things don't you, like cancer or a fracture. Osteoporosis and things." S06/027

"Honestly, I think I've probably got something like a hairline fracture of the pelvis or I dislocated my hip, so yeah I think they've probably missed something serious" S02/006

"Well actually if I'm being honest and I think we all think this when we get something going wrong that I've got an underlying cancer or something nasty like that that was causing all this pain." S05/008

"I don't know, I was a bit worried at the time because with pain like that at my age I was a bit concerned that it might be something serious." S05/001

These varying perceptions of causation indicate the importance of treating clinicians exploring any underlying perceptual mis-matches between the participants' thoughts pertaining to the cause of their symptoms, and the reality. These mismatches were common in patient participant interviews. These data suggest that it is important to establish the participants perception of the cause of their symptoms from which to base the educational element of treatment on, and this may have been a key element of the intervention delivered.

8.6.2 The effects of LRS on the participants life

LRS manifests itself differently in individuals, in terms of the severity of pain, disability, location, frequency and the duration of symptoms. The assessment process trialled has been designed to encompass as many different aspects of the symptoms as possible, whilst ensuring that a goal-orientated framework is utilised. The effect LRS has on an individual's life and their quality of life encompasses many different elements and was reflected in the frequency with which LRS had affected their lives (119 individual quotes):

"Getting about is really affected. My motivation is ground zero due to pain and the lack of sleep. I'm hardly able to do anything" S06/027

This snapshot of how LRS affects many aspects of an individual illustrates the severe impact that LRS can have on a person, severely limiting their ability to function. The inability 'to do anything' clearly has had an effect on their motivation, and the lack of sleep exacerbates and perpetuates this cycle. This highlights the importance of including examination of patient priorities and goals during assessment, and of developing an intervention that addresses multiple elements of the patients' problems.

Loss of function

The effect of LRS on quality of life was exemplified in the comments of 26 participants regarding function. Function relates to an individuals' ability to carry out activities relevant and desirous to them. During the assessment process, functional goals were agreed upon between the participant and physiotherapist, from which the treatment plan was devised. There were a range of responses beginning with an overwhelming sense of LRS taking over their lives:

"*Totally more or less, I've not driven, I've not done owt (anything) really. I can't sleep, cook, clean-the housework's' suffered because I have to do it*" S02/003

Other participants found their symptoms had a lesser effect on their day to day function, but found it annoying that their symptoms were interfering with sport:

"*I can't go to badminton, I can't ride the bike, it's really, really annoying me.*" S02/006

These two quotes exemplify the importance of an individualised assessment and goal-orientated treatment approach. The goals of these two participants were dramatically different, highlighting that individualising treatment may be important in achieving effectiveness.

Loss of sleep

A common theme (27 quotes) between both groups of participants was the effect that LRS had on their ability to sleep. Sleep is essential for health and wellbeing, the lack of sleep reported by the participants had a significantly deleterious effect on their lives:

"I'm only sleeping for about three hours a night; I know why they use it for torture now sleep deprivation. Try to keep positive you know but other days I just want a bullet." S06/27

"Sleep was really affected; if I could get a couple of hours sleep I was really lucky. Just really tough to try and find a position to sleep and really, really affected most things." S06/022

Many participants attempted to find their own ways of ensuring they slept. Most used prescribed analgesia, exercise and heat with many finding these ineffective, others relied on illicit drugs and alcohol:

"I can only sleep if I was drugged up……. I was having to do that three or four times a week-completely hammered because that's the only way I could sleep. Just to knock me out" S06/021

"I know I'm not supposed to drink on these tablets but having a glass of wine helps" S06/12

Assessing sleep patterns was not part of the 'formal' assessment for the intervention trialled however, the data suggest that this will be a useful element to add in a future evaluation.

Family life

Participants with families voiced their concerns, fears and feelings of guilt about how their problems were impacting on family life:

"It really affected the wife and the kids, and you don't know if you can get better and we can't live like that, you know with the wife and the kids it was horrible for everybody" S06/021

"I don't really trust it-me back, I don't trust myself. I don't bend down to pick up my son because I don't want that twinge when picking him" S02/003

"I can't go around and do normal things like run around and play with my daughter and go camping and things like that." S05/003

Although this wasn't an anticipated part of the assessment or treatment, the responses from participants highlight that LRS has a dramatic effect on family life. Many participants set goals in the assessment around functional elements of family life, such as playing with and caring for their children, indicating that this aspect may be important to include in interventions, and potentially may be helpful to add as part of an evaluation tool.

Depression

The interview data illustrate the effects that LRS has on depression, particularly in those participants with ongoing depressive symptoms. Data outlined how LRS was curtailing their ability to function, in particular activities involving walking. This made it difficult to leave the house, which was then having a secondary effect of instilling a feeling of isolation and worsening depression:

"(LRS) Is restricting me a bit because that doesn't help with the depression because I'm not getting out so that's getting worse" S06/027

'There was a point where I said to a friend I really don't think I can go on like this. I could never contemplate suicide, but I could see how pain affects your life and really takes over." S05/003

"I didn't work. I was in bed most of the time I was becoming depressed. I don't think people realise how bad it is." S03/005

The diversity of responses as to how LRS affects sufferers highlights the importance of capturing the individuals own problems, goals, fears and expectations of treatment during the initial phases, with this potentially influencing intervention outcomes. The study intervention approach aims to do this by gathering data in several ways, including patient interviews, patient examination, patient reported clinical history, patient reported outcome measures for pain, disability and quality of life. These data also suggest that these elements may be important to include in future evaluation of the intervention.

Pain

Pain is the symptom which usually motivates people to seek healthcare assistance. The effects of pain have been discussed in section 8.6.2 and are echoed in the participants descriptions of the severity and nature of their pain. One key theme to emerge from the participant interviews was the severity of pain. The severity of pain was a significant concern for participants:

"The pain when I'm walking is really unbearable, and I'm really worried about getting out" S07/001

"It was so severe so deep and over such a large part of your body, for me it was the whole leg but particularly from the knee right up the hip so it felt like a massive part of my body" S03/001

The severity of pain experienced by participants covered a wide range, from mild to severe. The nature of pain was also heterogenous, with some complaining of the 'achey' nature of their pain to others describing a 'burning' type-pain:

"…it was a searing pain and burning pain it was the worst pain I've ever known" S05/003

"It felt like someone had taken a knife and cut around the top of my leg and was peeling my skin down like you take off a stocking it was burning all the way down" S05/008

"*It's just really achey, like a constant toothache that just nags and nags"* S07/001

The severity and inability to cope with the pain were often linked with fears of a sinister cause of symptoms, thus highlighting the importance of gaining an understanding of what participants perceive the cause to be. The use of analgesia was often the first attempt at self-management of symptoms, some participants self-medicated using 'over the counter' pain relief or for the more severe levels of pain, prescription medication. Although the prescribed medication was not always prescribed for the patient but for other family members or friends.

8.6.3 Analgesic use

The use of analgesia was discussed 27 times in interviews, with its use in both groups extensive. Every participant used a range of opioid, non-opioid and/or neurological pain modulating medication. The effects and reaction to the use of analgesia was not uniform. Despite the widespread use of various forms of analgesia within the participant groups, only three participants described positive opinions relating to their use to relieve symptoms:

"there's only one thing that helped me so far and that's tramadol, tramadol and Ibuprofen and paracetamol all mixed but I don't like because it makes you feel groggy" S07/005

The difficult decisions patients make when faced with the choice of managing pain effectively and enduring the side effects are highlighted here. For this individual, the side-effects were preferable to the pain.

Participants negative feelings towards analgesia were common, with twenty-four interviewees discussing the negative effects of the drugs and how they made them feel. They were concerned about their ability to carry out normal day to day tasks such as childcare, work and driving because of the side-effects of the drugs:

"They were very strong and powerful, the strongest ones did work but they make me feel totally out of it, the drugs really didn't work." S05/003

"They gave me some tablets but they really upset me really made me feel out of it, bloated and not really myself so couldn't have them and work" S06/027

"Taking all those drugs I hated, it affects your whole, you know your metabolism, your gastric, the whole of you just doesn't feel like you and you get a bit low in mood" S07/009

The qualitative findings suggest that, in some patients who aren't coping well with their symptoms despite medication, methods to optimise the effects of medication should be sought. The effectiveness of the commonly prescribed anti-neuropathic pain medication, Pregabalin has been questioned. A recent high quality study found that Pregabalin was not effective in relieving sciatica (Mathieson *et al.*, 2017). This is in keeping with the findings of a recent systematic review which found that patients were unhappy with the pharmacological management of LBP. Alternatives to medication were utilised by participants who found the side-effects too onerous. Alternative pain-relieving drugs and optimising drug regimens together with non-medicinal alternatives and self-management strategies should be investigated further and form an integral part of future intervention development. Improvements in pain relief should enable improved function and adherence to rehabilitation. In order to facilitate this, optimal communication between therapists and the clinician prescribing the pain-relieving medication (usually the GP) should be sought. The results of Chapter 7 suggest that the POLAR treatment approach in both groups significantly helped to decrease the levels of back and leg pain.

8.7 Treatment

8.7.1 Self-management

Most participants had attempted to self-manage their LRS symptoms in some way before seeking professional healthcare assistance. Often the participants expected their symptoms to ease in the short-term, with some waiting a few days, others several weeks before going to their GP for treatment. Thirty-eight participants outlined a range of self-management methods which they had utilised:

"(what) I usually do is get in the bath or the shower, warm myself up and do some stretches while I'm in there" S02/006

"But the thing that helps take the pain away consistently is laying down, I feel laying down with my bad leg twisted over my good leg really helps" S02/14

Participants who found self-management strategies gave insufficient symptom relief sought help from their GP. This re-iterates the importance of effective communication between clinicians and the exploration of the effectiveness of pain-relieving modalities at each treatment session.

8.7.2 Previous experiences of treatment

There was reluctance in several participants to being referred for physiotherapy due to their past experiences. Past experiences of physiotherapy for other conditions or previous LRS, were reported to have shaped the views and expectations of 29 of the participants. One participant felt that physiotherapy for a previous episode of back pain made them worse:

"Seeing that physio was the worst point for me in the whole thing, she was afraid to touch me because I was crying and in so much pain, she didn't know what to do." S05/003

For others the process of beginning physiotherapy was onerous:

"The whole thing took too long, too long. I needed an intervention much quicker, I felt alone." S07/009

This was one of twelve responses to the slow process of being referred into the physiotherapy system. These, and other participants were attracted to the study due to the 'early' nature of the treatment, so suggesting that timeliness of care may have been an important factor in the high rates of participant uptake of the offer of intervention. Only one participant dropped out of the study because they were randomised to the usual care group.
Nine participants complained about the nature and content of previous physiotherapy they had experienced:

"I didn't like physiotherapy, the problem I've had with that in the past is that of being given a program, an exercise sheet and they just send you away" S03/001

These particular experiences of a generic approach to physiotherapy treatment resonate, as they are a common complaint in clinical practice and are a key reason for the development of the POLAR study. The participants concerns were allayed after discussing with them the nature of the POLAR intervention and the differences between it and their experiences of physiotherapy. A future RCT needs to address these potential issues in order to maximise recruitment. This could be done through the patient information sheets which potential participants receive, together with ensuring the consenting team-member being able to differentiate the POLAR approach from others.

8.8 Pre-treatment expectations and post-treatment experiences

Participants were interviewed before treatment began with regard to their expectations. Twelve of the thirteen participants who were interviewed pre and post-treatment were optimistic:

"Suppose my expectation is we can get better than we are at present. You know the back pain is there, the sciatica is there so really I don't want to go back." S05/003

"*Well I'm hoping to get back to something like normal.*" S02/006

Their optimism was well founded, all twelve participants had a positive outcome in terms of both function, pain and attainment of their individual goals:

"Yes, I would say psychologically it's had a massive effect" S05/003

"I feel great hundred percent from what I was a can now walk all the way down to town with no pain no problems. He's done a great job I'm really happy." S02/006

Other participants in their pre-treatment were not so optimistic pre-treatment with a fear that treatment may exacerbate their symptoms and prevent them from returning to function:

"Very unconfident. I'm frightened of hurting it even more and going back to square one and having it in the four weeks and not getting back to work." S02/014

The participants lack of confidence was misplaced, when interviewed after completion of their treatment programme they reported life being back to normal:

"I'm just getting on with life you know I still got a very, very slight pain there but it's rare that that comes" S02/014

The POLAR treatment approach is centred upon working towards individual goals and improving function and quality of life. This is often difficult for both the patient and the physiotherapist as the main concern is often pain, and traditionally the physiotherapist has been taught to help patients manage their pain. These tensions were exhibited in some participants before treatment:

"Well probably a little bit unrealistic because of course I wanted to be cured, immediately without delay" S05/001

Although post-treatment the participant made significant improvements:

"I wouldn't say I'm a hundred percent but I'm certainly back to something like normal despite the odd twinge here and there" S05/001

8.9 Hopes for the future

Participants were asked what their hopes were for the future after they had completed their physiotherapy treatment. 31/32 (97%) interviewees were optimistic that they would continue to be relatively symptom-free with life continuing as normal:

"I hope that I don't get it again, but I don't know whether I will or not. I hope not. I think I'll be alright now apart from the odd twinge, which I can live with." S04/005

"So, I think now I'll be all right, I know want to do, got the exercises to do and if you get a niggle I give it a stretch and it goes." S02/003

"I expect, I really believe I'll be where I am now-able to do anything without any pain and the same for six months. I can't see me going back." S07/001

These optimistic thoughts about the patient participants' future suggest that a follow-up period for a future RCT of greater six months will enable exploration of longer-term treatment effects.

8.10 Fear

A recurring theme which echoed through many of the other themes was that of fear.

Fear was in itself a key theme from the interviews with participants, but it was also an integral sub-theme for several other main themes. Fear was pervasive in terms of fear of a potential serious cause of LRS, fear of the future with LRS, fear for family life and fear of never improving.

"I was in the mental state where I was really frightened to leave the house. I didn't dare go out of the house because if it got bad, I was worried that I wouldn't make it home again." S01/002

"I've not done anything because I'm scared of bending down scared of doing things. I can bend down for a bit but we really does hurt and so I avoid it" S06/030.

The fear induced by pain has led the participant to avoid activities in this case, Lumbar flexion for fear of causing harm. Kinesiophobia was assessed during the initial physical assessment due to its importance as a prognostic indicator of a poor outcome.

A small number of participants expressed a high level of fear and anxiety of the pain never improving:

"I'm sure most people get better but for me I was scared I'd have a lifetime of it" S05/003

"You know I had doubts that it was ever going to get better, you feel you getting better and then it gets worse" S03/005

The fear of the pain returning was elicited from seven participants, despite them returning back to full function, with little or no pain reported, they still voiced significant fear:

"I am still afraid of it coming back because it's frightening. I'm scared of having an operation that doesn't work, I'm afraid of the sciatica coming back as it did before." S05/003

"I'm frightened of hurting it even more and going back to square one. I'm really scared then I don't know what's going to happen with work. You know long-term" S02/014

The most common cause of LRS is a prolapsed IVD, there are however other potential causes, including serious pathology, such as cancer, benign tumours, infection and fracture. These concerns have been presented in 8.6.1.

The participants responses support the importance of establishing the presence of fear and if so, the nature of any fear. This is a key focus of the POLAR treatment approach as it allows clinicians to provide a treatment approach to help assuage those fears. The approach also allowed time for the participants to explore their fears and discuss methods to curb them.

8.11 Discussion

The aim of the POLAR pilot study was to determine the feasibility of carrying out a full RCT to determine the effectiveness of early-intervention physiotherapy for LRS. It was therefore of importance to explore the views and perceptions of participants regarding acceptance and delivery of study processes and intervention elements during this study in both arms. In addition to elements of feasibility, the data also contained insights into the optimal content of the intervention and elements that might be useful to evaluate in a future trial.

The experiences of participants in both arms of the pilot trial were overwhelmingly positive, with the only discernible difference between groups being that the usual care group would have preferred to have started their physiotherapy earlier. Both groups of participants and the physiotherapists welcomed the longer treatment duration compared to the usual length in primary care. The importance of 'ring-fencing' treatment time-slots for participants was highlighted by the physiotherapists and must be a priority when designing the processes for a full-scale trial.

A key distinguishing feature of the POLAR approach was its focus on the improvement of function, and with-it quality of life, rather than the traditional physiotherapy approaches which emphasise the therapeutic pain-relieving effects. The data suggest that this may be a key element underpinning intervention effectiveness. The acceptability and feasibility of delivering the intervention was established within the interviews with physiotherapists before and after the study. They found the approach to be logical, easy to interpret and useful in both assessment and treatment planning. Both groups valued the individualised aspects of the treatment which enabled them to focus on achieving their own goals and was in contrast to some participants previous experience of physiotherapy.
A qualitative study investigating the experiences of patients waiting for lumbar microdiscectomy surgery found several key themes. First among them was the impact of sciatica on the patient's quality of life, in terms of activities of daily living such as dressing. The POLAR approach aims to address functional issues, directed from the patient as key goals. The significant effect on the patient's quality of life cause by sciatica included a significant deleterious effect on their psychological health. Participants in both studies found the significant levels of pain and disability, together with social exclusion and inability to

work had a negative effect on their psychological health. Another theme of the Boote et al (2015) study was the appreciation of the multi-modal physiotherapeutic approach. The tailoring of the approach to the individual was appreciated in both groups in both the Boote (2015) and POLAR studies.

Personalised care has previously been found to be of importance to patients with LBP and or LRS, including shared decision-making and the tailoring of treatment to the individual (Chou, Ranger, Peiris, Cicuttini, Urquhart, Sullivan, M. Seneviwickrama, *et al.*, 2018). The participants preference for individualised treatment extended to them feeling valued and being listened to as an individual. This echoes previous insights into patients experiences of physiotherapy treatment of sciatica and the importance of listening to a patients' narrative and providing a thorough examination, diagnosis and treatment plan with the patient (Hopayian and Notley, 2014; Chou, Ranger, Peiris, Cicuttini, Urquhart, Sullivan, K. Seneviwickrama, *et al.*, 2018). It is suggested that it is communicated to potential recruits for a full-scale trial, that the physiotherapy will be individualised and not merely infrequent treatment sessions and an exercise sheet, in order to overcome any pre-existing negative opinions of physiotherapy and optimise recruitment and outcomes.

The study is the first to find that people with LRS valued early physiotherapy treatment. A previous study of patients awaiting lumbar microdiscectomy surgery for LRS found that patients valued the content of the POLAR physiotherapy intervention prior to surgery, but the intervention was delivered at an advanced stage of symptomology (mean 49 weeks) (Boote *et al.*, 2016). A study of physiotherapy treatment of LRS has been found to increase 'feelings of well-being' among sufferers, empowering them to remain active with or without symptoms (Limbäck Svensson *et al.*, 2013).
The number of interviews exceed that which was expected in order to achieve the stated aims of the qualitative element of the study. This was due to the emergent participant data regarding their experiences of LRS in their daily life, family and work. The paper presents for the first-time, participant concerns regarding a sinister cause of LRS. Participants voiced their fears that their symptoms may be due to cancer, infection or fracture, which in some cases led to fear avoidance behaviours. Pain related fear has been found to be a factor in the delayed recovery of patients with LRS within the fear avoidance model (Haugen *et al.*, 2016). The model suggests fear as a result of pain leads to the avoidance of activity, increased pain, weakness and a persistent cycling of symptoms. Fear was an integral factor between several themes described by participants, fear of the pain never going away, of the pain returning or of there being a serious cause of symptoms. A fear for what the future holds was evident in interview responses and has been previously highlighted in work investigating patients with

LBP and/or LRS as being predictive of outcome at six months post symptom onset (Henschke *et al.*, 2009). Although the participants fears were real, the incidence of serious pathologies presenting as LBP and or LRS is less than 1% of cases in primary care. The severity of symptoms in some cases of LRS leads to the perception by patients and healthcare professionals that there must be a 'serious' cause. It is therefore imperative during clinical examination that the clinician gains an insight into the patients understanding as to the likely cause of their symptoms, and treatment provides an opportunity to explore these fears in depth in order for a management plan to be instigated and this potential barrier to outcomes is addressed.

The cause of LRS is often impossible to determine but is nevertheless important for some patients in order for them to make sense of their symptoms (Aldrich and Eccleston, 2000). A small number of participants believed that further investigation with MRI was necessary (Espeland, Baerheim and Albrektsen, 2001). Legitimacy of symptoms can be sought by seeking investigations to provide a definitive diagnosis for the patients symptoms A feeling of relief in the patient is often felt when the investigation results are concordant with symptoms, however disappointment and frustration can emerge if no such concordance is evident (Ryan and Roberts, 2018). The cost, lack of predictive value and lack of specificity of MRI (Wassenaar *et al.*, 2012; Brinjikji *et al.*, 2015; Steffens *et al.*, 2015) makes investigation in all who present to healthcare with LRS unnecessary in the short-term.

The severity of pain varied significantly between participants; the side-effects of the analgesic medication were common. Most participants were prescribed medication recommended for use with LRS, a mix of opioids, anti-neuropathic pain medication and anti-inflammatory drugs. Finding a balance of effective pain relief with minimal or no side-effects is a challenge but is important if optimal outcomes for an individual from treatment are to be achieved. The study has highlighted the role of close communication between a GP and physiotherapist in order that analgesic intervention is appropriately tailored to other concurrent treatment.

The effects of LRS differed greatly between individuals. However, two key themes emerged; the effects of LRS on sleep and on family life. Difficulty sleeping as a result of LRS was commonly reported in this study and this is the first study to do so. Sleep has been reported to be troublesome for patients with LRS in a previous study, but was not demonstrated as a key theme in interviews with 21 patients awaiting surgery for their LRS (Boote *et al.*, 2016). This is in keeping with the work of Karp et al (2014) who found that sleep disturbance and negative affect (undefined) was related to a negative outcome of epidural steroid injections

in patients with LBP and/or LRS (Karp *et al.*, 2014). In this work, it was a key theme which participants felt had a significant effect on their levels of pain, mood and ability to cope, likening sleep deprivation to torture. Sleep is essential for life and health as well as being important in the foundations of memory (Feld and Born, 2017). Impaired or disturbed sleep reduces the immune systems' ability to fight disease as well as increasing inflammation, potentially being associated with an increased risk of cardiovascular disease and cancer (Irwin, 2015). In a systematic review of the association between CLBP and sleep, it was found that CLBP has a significant effect on several elements of sleep. These include sleep disturbance, poorer day time function, such as work and patients with CLBP may have difficulty initiating sleep (Kelly *et al.*, 2011). The quality of sleep has been found to have a negative effect on pain intensity, patients suffering with LBP have been found to have increased pain if their sleep had been affected (Alsaadi *et al.*, 2014). Feelings of guilt, helplessness and fear for the future were reported by participants concerned about the effects of LRS on family life. It is therefore proposed to address the issue of sleep during history taking, clinical examination and subsequent appointments to measure the effectiveness of this element of treatment.

Several participants had a history of psychological distress, including depression and anxietous disorders. These were identified during the clinical history-taking and utilising the Keele STarT Back screening tool (Hill *et al.*, 2008) as the presence of depression/anxietous disorders, catastrophising and fear avoidance is in patients with LRS been found to be a predictor of heightened symptoms, decreased physical function, ongoing disability and poor outcome (Edwards *et al.*, 2007; Pinheiro *et al.*, 2016). This was reflected in the frequency of physiotherapy components utilised, with 68% of the participants receiving one or more elements of treatment to help their psychological barriers to recovery.
Rigour and trustworthiness of qualitative research are the equivalent to validity and reliability in quantitative research. In mixed methods research, the term 'legitimacy' (Onwuegbuzie, A., J. & Johnson, B., 2006) is often used, as is 'credibility' (Lincoln, Y.S, Guba, 1984), which refers to 'confidence in the truth of the findings. Transparency of process is critical in order to maintain rigour, trustworthiness, legitimacy and credibility of the research. It is therefore imperative that during the qualitative part of the POLAR study efforts were made to acknowledge personal and professional biases and to ensure avoidance of any overt personal agenda. The personal bias which is most evident is that this work is extremely important to me as a career changing shift from experienced clinician to clinical academic with the fellowship award. The pressure to succeed is therefore overt. Further potential points of bias are the intervention used, which is again a piece of work which has taken many years of my life and that of colleagues to develop. A particular bias in

interviewing was evident when, as a clinician with vast experience of clinically interviewing patients, it was difficult to not to utilise the therapeutic, adaptive and responsive interviewing techniques I use clinically. The bias was to help the participant rather than interview them. It is important however, to acknowledge that the researcher is of course integral to the qualitative research process and it is with my 'lens' that the macroscopic and microscopic views of the research is viewed (Spencer *et al.*, 2003). Attempts to acknowledge and mitigate potential bias, where appropriate started at the very beginning with the development of the research questions. The supervisory team were involved in refining the research question, which had already been developed with three patient representatives and clinical and academic colleagues. The PPIE were particularly important in this regard in ensuring the relevance of the question to them and the wider patient population. The PPIE representatives were also pressed into action in developing the primary interview transcripts, helping to define both the questions and length and number of questions. In doing so the PPIE together with the academic and clinical teams helped to mitigate against potential bias at this stage.

Another potential point of bias in qualitative research and in the POLAR study is the recruitment sample. Although a research nurse was employed to recruit and consent potential participants, the author recruited the majority of the participants. All participants in the pilot trial element of the POLAR study were also asked if they would consent to be interviewed as part of the qualitative element. Most participants chose not to participate in the interviews (47/80) which can be interpreted that no coercion by the author took place to force participation. It is of course impossible to determine whether the participants' views and themes generated would differ with a different sample. However, in order to mitigate against potential bias during the analysis phase, analysis was done primarily by the author but with support and verification of themes by the qualitative supervisor and PPIE representatives. The COREQ checklist (Tong, Sainsbury and Craig, 2007) was used both during the set-up of the qualitative element of the study and during the analysis as a guide and aide memoir. Whilst the COREQ and other checklists are useful in the evaluation of utility and relevance, they do not ensure utility or relevance (Morse *et al.*, 2002).

There is a postscript to this exploration of how my personal and professional biases may have affected the development and analysis of the study. The term bias is suffused with negative connotations, however put in another, less pejorative way, it may be argued that bias is inherent and made up of my wealth of experiences and views and as such is innate (Guest G, MacQueen KM, 2012).

8.12 Conclusions

The study processes and intervention were well-received by participants and physiotherapists alike and the results suggest a number of areas of refinement for a full-scale RCT. Primarily, the study highlights the importance of listening to the patient narrative and providing a goal-orientated, individualised treatment plan for participants and a treatment framework for the physiotherapists. Planning for a full trial should ensure that there are adequate ring-fenced appointment times for participants.

The qualitative component of the POLAR study has provided valuable insight into the feelings and experiences of patients who have LRS. The results provide new evidence as to the importance patients place on early intervention physiotherapy for LRS, the significant deleterious effects of LRS on sleep and the role which fear holds for those sufferers. The findings of the POLAR study suggest that further development and evaluation of interventions such as POLAR which include management strategies to help with optimising sleep and pain management are required. The data indicate that individualised multiple-element complex interventions may be effective for patients with LRS, and that interventions which include these elements have potential and should be evaluated rigorously.

The POLAR study is a mixed methods study and as such the integration of both the Quantitative and Qualitative elements can be found in Appendix 17. In the appendix a mixed methods matrix is utilised, alongside clinically relevant case-studies to illustrate the relationship between the quantitative and qualitative findings. This enables new meanings to emerge as well as giving depth and consolidation to other findings.

Chapter 9 Preliminary economic evaluation

The previous chapters have presented both the quantitative, qualitative and mixed methods results of the POLAR study. The results have shown the feasibility of a full-scale study and found that the intervention and its timing agreeable to participants. This chapter reports the results of the preliminary economic evaluation conducted alongside the POLAR RCT (EEACT).

9.1 Introduction

It is important to consider the costs associated with the effectiveness of any intervention in order to ensure greatest benefit for tax-funded healthcare (Walters, 2009). The cost of LBP and LRS is a significant burden to society, which appears to be rising and is now the largest cause of years lived with disability (Hoy *et al.*, 2014). It is a great enterprise in attempting to determine the cost of LBP and LRS, which makes it difficult to find reliable and comparable data. A recent Swedish study evaluating the societal costs of LBP found that total the lifetime economic burden for all patients clinically presenting is €8.8bn (Olafsson *et al.*, 2017). They also calculated that the economic burden including quality adjusted life years (QUALYs) lost was €35.3bn, a combined total of €44.1bn. The direct health costs of LBP in the UK were estimated at £1,632million twenty years ago (Maniadakis and Gray, 2000). Although not an insignificant sum, it pales when compared to the costs of informal care and production losses which were estimated at £10,668 million in the same study. The heterogenous nature of cost data collection and methodology to analyse it leaves comparisons between countries and different time-points problematic. It has been estimated that costs in the USA for LBP are between $19.6 and $118.8 billion annually, including direct and indirect costs (Dagenais, Caro and Haldeman, 2008). These sums are significant for any economy to bear and at a time of fiscal conservatism in the UK, it is important to ensure value for money for any intervention.

The purpose of the economic evaluation embedded within the pilot study was to assess the feasibility of collecting resource use data and quality-of-life outcomes (particularly the EQ-5D) together with any variations in the reporting of resource use and intervention costings.

9.2 Methods

This exploratory analysis is from an NHS perspective, although it could be argued that a societal perspective could equally be assumed as significant elements of the costs are societal, such as sickness work absence and loss of productivity. Data collection was carried

out by the main author (MR) as was the analysis with help and support from the supervisory team (SW) and guidance from a health economist based in the health economics and decision science section of ScHARR, University of Sheffield.

Some quality of life (QoL) instruments have been designed to measure the utility or preference for, or desirability of, a specific level of health status. Utilities can be measured or valued for various possible health states. This can be done by questioning patients who are in that particular health state at the time of measurement and asking them to value or express a preference for the particular health state. Alternatively, you can describe the health states to subjects who may or may not have had personal experience of the health state being measured and asking them to value or express a preference for the particular health state. The health state utility or preference value is usually a number between 0.0 which would equate to death and 1.0, which would mean full health or functioning with no adverse symptoms. There are three main methods for valuing or assessing the preferences of subjects for health states: the visual analogue rating scale, the time trade-off method and the standard gamble method (Brazier JE, Ratcliffe J, 2007). Examples of preference based QoL instruments include the quality of well-being scale, health utilities index, EQ-5D and SF-6D. Since health is a function of both length of life and quality of life the QALY (Quality-adjusted life year) has been developed in an attempt to combine the value of these attributes into a single index number. Health state utilities, such as those measured by the EQ5D, do not have units. If utilities are multiplied by the amount of time spent in that particular health state, then they become QALYs (and are measured in units of time). The POLAR trial used the EQ-5D-5L to measure utility at baseline, 6 weeks, 12 weeks and 26 weeks post-randomisation. Costs and effects were evaluated over a short term 26 week or 6 months' time horizon. As this was a pilot study, long term follow-up of participants was not practical and no attempt to explore cost-effectiveness between groups was undertaken.

9.2.1 Costs

Patient reported health resource utilisation was collected using a questionnaire completed by participants at baseline, 6, 12- and 26-weeks post randomisation (Appendix 18). A range of healthcare costs were collected, including any previous or ongoing treatment, any medication for LRS, hospital visits and any investigations, such as X-ray or MRI scan for this episode of LRS. A full list of healthcare activities can be found in Table 1. The source of costs found in Table 9.1 are attributed below the table.

Table 9.1 POLAR health resource use costs 2015-16

Activity	Unit cost
GP consultation[1]	£45
Private physiotherapy/session[2]	£40
Private Osteopathy/session[2]	£45
Private Chiropractic/session[2]	£45
Private Acupuncture/session[2]	£39
A&E consultation[3] (no investigation, no treatment)	£63
Paramedic consultation[3]	£40
Ambulance to A&E[3]	£254
Consultant Surgeon consultation[3]	£277.90
Cost of Spinal surgery/unit (Lumbar decompression/microdiscectomy)	£3002.70
Cost of spinal injection/unit	£542
MRI scan (spine) including reporting NHS	£136
MRI scan (spine) including reporting private[4]	£450
Lumbar Spine X-ray private[4]	£250
Walk in centre	£75

[1] Sheffield CCG

[2] A sample of 10 private service providers were sampled in Sheffield in July 2016. A mean value was obtained for each service, including an initial visit and follow-up

[3] Source: https://improvement.nhs.uk/resources/national-tariff-1719/

[4] Aspen healthcare UK

9.3 Results

This evaluation has been presented in line with the consolidated health economic evaluation reporting standards (CHEERS) statement and the checklist can be found in Appendix 19 (Husereau *et al.*, 2013).

The number of participants unable to work who are employed or self-employed at baseline due to their LRS can be seen in Table 9.2. This illustrates a similar number of participants in work at baseline. The type of work for each participant is presented in Table 9.3, with 30% of participants not employed at the time of the study. The data available does not provide detail as to why the participant was not in employment and whether this related to their LRS.

Table 9.4 shows that mean number of days off work at baseline is higher in the intervention group due to an outlier who had already had 324 days absent from work at baseline. The cost of the days absent from work in the intervention group is therefore significantly higher at £11,157.11 (SD 10,651.01) compared with £6,406.40 (SD 7,747.91) for the usual care group.

Table 9.4 provides details as to the total costs of the physiotherapy treatment per group. The physiotherapy costs per group at six months were £785.02 (SD 753.04) for the early intervention group and £715.54 (SD 1013.74) for usual care. The difference of £69.47 (95%

CI -359.86 to 498.82) in costs favour of the usual care group are primarily due to a higher number of treatments in the early intervention group, a mean of 4.3 treatments in the early intervention group and 3.3 in the usual care group.

Table 9.2 Participants work status at baseline

Time off work?	Early Intervention		Usual care	
	N	%	N	%
No	19	61	18	64
Yes	12	39	10	36
Total	31	100	28	100

Table 9.3 Participants work type at baseline

Work type	Early intervention		Usual care		Total (%)
	Count	% of group	Count	% of group	
I am not in employment	15	35.7	9	24.3	24 (30.4)
I spend most of my time at work sitting	12	28.6	10	27.0	22 (27.8)
I spend most of my time at work standing or walking. However, my work does not require much intense physical effort	2	4.8	8	21.6	10 (12.7)
My work involves definite physical effort including handling of heavy objects and use of tools	12	28.6	7	18.9	19 (24.1)
My work involves vigorous physical activity including handling of very heavy objects	1	2.4	3	8.1	4 (5.1)
Totals	**42**		**42**		**79 (100)**

The use of summary descriptive events/utilities in the period of the study for both groups are reported in tables 9.4.

Table 9.4 Summary statistics of resource use per group

	Early intervention						Usual Care					
	N	Mean	Median	SD	Min	Max	N	Mean	Median	SD	Min	Max
No. days off work (baseline)	14	107.3	76.0	102.4	18	324	15	61.6	29.0	74.5	2	252
Cost of days off (£)	14	11157.11	7904	10651.01	1872	33696	15	6406.40	3016	7747.91	208	26208
No. X-rays	10	1.3	1.0	0.5	1	2	8	1.5	1.0	0.8	1	3
No. of MRI	11	1.8	2.0	0.9	1	3	7	1.6	1.0	0.8	1	3
Cons referrals	36	0.4	0.4	0.7	0	3	32	0.3	0.0	0.7	1	3
Surgery	36	0.0	0.0	0.2	0	1	32	0.1	0.0	0.2	0	3
Treatment sessions attended	36	4.3	4.3	1.2	2	7	30	3.3	3.0	1.7	1	6

9.4 Discussion

The results of this exploratory economic analysis has provided valuable information which will be of use in designing a definitive economic analysis on the future.

The study found that the intervention arm of the study was more costly by £69.47 compared to the usual care group which was caused by the higher number of treatment sessions in that group. It is not clear from the data why the early intervention group had more treatment sessions, with associated costs. It would be useful to determine, in future work whether this has an effect of the speed of return to work, resource use and overall cost-effectiveness.

Due to a large amount of missing data on the specific medication type, dose and frequency, it was not possible to determine any differences between analgesic use and associated costs at baseline and 6,12- and 26-weeks post randomisation between groups. The nature of reliance on participants to recall the specific names, doses and frequencies of analgesia they had been taking made the data incomplete. The number of days absent from work in the early intervention group was significantly higher due to an outlier having had 324 days of absence at baseline. This is a limitation of the POLAR trial, in not having a specific cut-off point for symptom onset in order to define 'early' or usual care. A further limitation of this analysis is the potential for bias, in particular recall bias in terms of the participant remembering their previous state as better or worse than it actually was (Blome and Augustin, 2015). It is suggested that different methods of collecting such data are trialled with patients suffering with LRS to determine the most effective and robust method. The use of self-reported medication use with patient-clinician confirmation by checking on the GP computer system is currently being used in the clinical setting and may be of use in future research.

A further potential limitation regards the lack of sensitivity of the EQ5D-5L in determining the patients or patient population reason for a change in health status (Walters, 2009). For example, a decrease in health status measured with the EQ5D-5L in one POLAR participant was due to cholecystitis rather than LRS, nevertheless health related quality of life decreased. The convergent validity of HRQoL measures has been questioned (Mokkink *et al.*, 2010) as there is an inherent difficulty and lack of a gold standard in defining what quality of life is.

Both the early intervention group and the usual care group received the same intervention but at different time points. Therefore, the differences in cost are most likely to be seen in the period between and shortly after the early intervention group have received treatment and the usual care group are waiting for treatment to begin. Unfortunately, the amount of missing data at these timepoints make appropriate analyses impossible. A future economic analysis should ensure that data is collected in this key period and that strategies are developed to ensure adequate data collection during this period.

9.5 Conclusions

The results from this preliminary economic analysis has provided key insights into the challenges of designing a future full-scale economic analysis in this patient group. Efforts to improve economic data collection should be a priority to enable accurate data analysis and interpretation of the results.

This chapter has built upon the results of the POLAR pilot trial, qualitative and mixed methods results by providing the results of a preliminary economic analysis. The following chapter will draw the study to a close with a reflection of the study findings and conclusions drawn, together with suggesting future directions for research alongside the findings with a discussion of the results and suggesting appropriate conclusions.

Chapter 10 Discussion and Conclusions

This final chapter draws together the results from the quantitative, qualitative and mixed methods analysis and will discuss the key findings. The chapter will summarise the results and their implications for this and future research, as well as drawing on the work to make clear and concise conclusions.

10.1 Introduction

This PhD thesis has presented the background, methods and results from the POLAR study. The thesis has outlined the problems faced by sufferers of LRS, the potential causal mechanisms, together with treatment options. A literature review provided an overview of existing work in the field, and results of this then formed the basis of a systematic review investigating evidence specifically related to timing of interventions in LRS. Examination of the available research evidence informed analysis of the quantitative and qualitative data collected.

In this final chapter I will draw together the thesis with key findings, conclusions and directions for future research resulting from this study. The beginning of the thesis provided the rationale for the POLAR study together with the research question, aims and objectives as outlined in Chapter 1. The burden of LBP and LRS can be significant with long-term consequences to the individual and society in fiscal terms. These were presented in Chapter 2 alongside the function, anatomy and physiology of the lumbar spine and IVD in order to provide the reader with an understanding of the area being studied. Within Chapter 2 the potential pathophysiology of an IVD prolapse was introduced as a potential causative means of LRS alongside other potential causes. There are a plethora of treatment options available for LRS, the more commonly utilised modalities were also discussed in Chapter 2. The dearth of literature on the subject of timing of physiotherapy for LRS was contextualised and investigated more formally in the systematic review which was carried out and presented in Chapter 3. This was the first mixed methods systematic review of its kind investigating the timing of commonly used treatments, including physiotherapy and surgery. This systematic review provided information about the optimal timings of interventions commonly utilised in the management of LRS. The review found only one RCT which recommended surgery within two weeks of randomisation. There are insufficient number of studies to make clear recommendations about the timing of interventions for LRS. This is reflected in clinical practice with uncertainty as to when to instigate any form of treatment. Further research is required to determine the optimal timing for interventions used in the management of LRS.

Particularly welcome would be trials with quality longitudinal designs and detailed, protocolised interventions, so as to enable replication in the clinical setting.

The clear lack of studies investigating the optimum timing of interventions for the management of LRS provided the rationale for the POLAR mixed methods study. The presentation of the POLAR intervention were the basis of Chapter 4 which also provided detail of the treatment domains and their components. Following the development and utilisation of the POLAR approach to the management of LRS, the next step is to utilise intervention development and evaluation theories such as the MRC complex interventions framework, theory of change and intervention mapping (Bartholomew *et al.*, 2001; Anderson *et al.*, 2011). Development of the theoretical basis of the intervention components and the potential mechanisms of action would be a priority for further research. It would be useful to determine if there are any 'critical' components of the intervention, without which would significantly affect the interventions effectiveness and which key moderating factors need to be addressed and their interaction with the other domains and components. The MRC process evaluation of complex intervention guidance would be utilised in order to identify and clarify causal mechanisms of treatment, mechanisms of impact and the implementation processes (P Craig *et al.*, 2008; Moore *et al.*, 2015).

The quantitative and qualitative study methods have been presented in Chapters 5 and 6, which focussed on an iterative recruitment design in order to learn from patients and other stakeholders' experiences as the study progressed. The quantitative findings were presented in Chapter 7. The POLAR study results indicate that a full RCT is potentially feasible within a reasonable timescale and resource envelope. There is a gap in evidence about how and when to treat this population and therefore a definitive trial is needed to help inform clinical practice. The qualitative findings were presented in Chapter 8. The study processes and intervention were well-received by participants and physiotherapists alike and the results suggest a number of areas of refinement for a full-scale RCT. Primarily, the study highlights the importance of listening to the patient narrative and providing a goal-orientated, individualised treatment plan for participants and a treatment framework for the physiotherapists. Planning for a full trial should ensure that there are adequate ring-fenced appointment times for participants. The qualitative component of the POLAR study has provided valuable insight into the feelings and experiences of patients who have LRS. The results provide new evidence as to the importance patients place on early intervention physiotherapy for LRS, the significant deleterious effects of LRS on sleep and the role which fear holds and mediates experience for those sufferers. The findings of the study suggest that further development and evaluation of interventions such as POLAR which include management strategies to help with optimising sleep and pain management are required. The data indicate that individualised multiple-element complex interventions may be

effective for patients with LRS, and that interventions which include these elements have potential and should be evaluated rigorously.
A preliminary analysis of economic data was the subject of Chapter 9, although definitive analysis was not possible due to incomplete participant data. The findings will prove useful for planning a future economic analysis as part of a wider RCT. In particular the need to develop tools and processes to ensure adequate completion of baseline and follow-up work absenteeism and drug usage.

10.2 Aims of the thesis

The overarching aim of this thesis was to highlight the clinically important yet little researched area of the timing of physiotherapy for LRS. Furthermore, the work aimed to bring new knowledge to the area and in doing so generate further research ideas to enrich patient care. LRS is a significant personal and societal problem with a significant financial burden. LRS patients are often grouped with patients with LBP. However, they are a distinct clinical group who suffer more severe pain, higher levels of disability and have more time off work as a result of their symptoms (Miranda, H; Viikari-Juntura, E, Martikainen, R; Takala, E; Riihimäki, 2002; Grotle *et al.*, 2005; Konstantinou *et al.*, 2015). The prognosis of LRS is generally favourable, however there are no prognostic indicators for a good outcome or when that outcome is likely to occur. The aim of the POLAR study was to determine whether it would be feasible to carry out a full-scale RCT to determine the effectiveness and cost-effectiveness of early physiotherapy for patients suffering with LRS.

10.3 Review of objectives

The objectives of the study were presented in terms of process and research objectives. These are presented below to serve as a reminder and provide a point of reference for the summary of findings.

10.3.1 Process objectives

1. To test the feasibility, practicality, safety and acceptability of the study design and protocol.

2. Demonstrate the ability to set up and recruit in primary care centres.

3. To assess the feasibility of delivering the early intervention within the time parameters (2 weeks for the intervention group, 6 weeks for the usual care group).

4. Demonstrate a recruitment rate of 7 patients per month in a maximum of 14 GP centres, equal to a rate of 0.5 of a participants per centre per month.

5. Demonstrate the ability to organise 75% of physiotherapy appointments within 2 weeks of randomisation.

6. Patient attendance at 66% of individual physiotherapy sessions.

7. 75% of patients randomised to early intervention have their first physiotherapy session within 20 days of randomisation.

8. Patient attrition rate of <25% over the course of the study.

9. Outcome measurement return rate of 80% at 6/52 follow-up.

10.3.2 Research objectives

1. To determine the acceptability of the intervention to patients and clinicians.

2. Demonstrate acceptability of the primary and secondary outcome measures to patients and clinicians.

3. To inform the sample size calculation for the definitive trial.

10.4 Summary of findings

10.4.1 Feasibility findings

The POLAR study was a mixed methods design with an external pilot study and embedded qualitative interviews. The pilot RCT results suggest that a full scale RCT would be feasible within a reasonable timescale and resource envelope. This is the first study of its kind to explore the feasibility of carrying out an RCT to determine the effectiveness of early physiotherapy compared to usual care for the treatment of LRS in primary care. The primary feasibility objectives of finding and setting up GP recruiting sites and recruiting 80 participants were key in realising the aims of the study. The recruitment rate of participants per month, per centre for participants in the POLAR study was 9.6, which is favourable when compared to that of the median number of participants recruited per centre, per month of 0.92 in a review of publicly funded RCTs in the UK (Walters *et al.*, 2017).

These feasibility objectives were met in full and were augmented by the qualitative findings. Data from the 45 interviews with 33 participants found high levels of acceptability of the POLAR intervention as well as the study processes. The participants provided key insights into their lived experiences of LRS. Thematic analysis established several key themes, including the deleterious effects of LRS on daily life, sleep, depression and function. Participant's perceptions of the cause of their symptoms were worrying for many with this

theme among many being mediated by fear. The importance of fear as a key mediating factor was prevalent throughout all themes which emerged.

10.4.2 Research findings

The findings of the study indicate that early intervention physiotherapy can potentially improve outcomes for patients with LRS, in terms of pain, disability and health-related quality of life in the earliest stages of recovery from 0-12 weeks. Although the observed estimates (and confidence intervals) were consistent with no effect, as this was a pilot study and these estimates should be interpreted cautiously; as this trial was not designed (and powered) to assess effectiveness.

This echoes recent findings that early physiotherapy for a military cohort enjoyed improved outcomes at 1-month post-randomisation, although this study also found no difference in outcomes at 1-year (Rhon, Miller and Fritz, 2018). These findings are nonetheless important for patients and employers, such as the military, who want recovery as soon in order to maintain productivity or readiness for military combat. Patients and employers do not want to have the speed of recovery limited by system-imposed delays such as delayed access to treatment. A retrospective cohort review of patients with acute low back pain similarly found that in those patients who required physiotherapy, those that received physiotherapy within three days had better long-term healthcare utilisation and some cost measures (Liu, X, Hanney WJ, Masaracchio, M, Kolber, MJ, Zhao, M, Spaulding, AC, 2018). Both of these recent studies were based in the American military or insurance-based healthcare systems, therefore generalisability of these findings for patients in the UK is therefore uncertain. A future study to determine the effectiveness of early physiotherapy compared to usual care (standard physiotherapy) for the treatment of LRS in the UK is therefore required.

10.5 Strengths and limitations of the study

10.5.1 Strengths

The main strength of the study was that it drew on the real-life experiences and perceptions of patients and healthcare staff of living with LRS and treating patient with LRS. Patients complained of not being able to access expeditious physiotherapy at the onset of their symptoms, believing this to be deleterious to their long-term outcome. The study therefore stems from real patient problems, not a clinical or systems interpretation of those problems. The use of guidelines from which to base the development and planning of each aspect of the study are a key strength. Guidelines such as the CONSORT extension for pilot and feasibility trials, the PRISMA guidance for the development of systematic reviews, the COREQ guidelines for qualitative research and the CHEERS guidance for the reporting of economic evaluations have all been essential in ensuring the rigour of the POLAR study.

The iterative nature of the mixed methods design and recruitment ensured that, as far as possible, potential barriers and limitations to the study could be identified and ameliorated before the start of the study. This involved process mapping the recruitment processes for each recruitment centre to ensure optimum recruitment for each centre. This forward planning ensured that recruitment was a significant success, with participants being recruited within time. This was due, in part to the commitment of a group of research active GPs who see the value in their participation in clinical studies to bring about improvements in patient care.

A problem found in some studies comparing conservative care or physiotherapy with other treatment options, is that they do not specify or protocolise what the conservative care or physiotherapy consists of (Ostelo, Hoogen, *et al.*, 2008; Weinstein *et al.*, 2008; Wilco C. Peul *et al.*, 2008). A real strength of this work is that the intervention has been developed with patient guidance and has been utilised in a previous pilot study with good effects (Boote *et al.*, 2016). A logic model was developed for the study to describe the components and potential mechanisms underpinning change processes. The reproducibility of the study was enhanced by the protocolised intervention and the intervention handbook. No exceptional resources were available for the study, which utilised NHS patients, physiotherapists and clinics and therefore the study should be reproducible in any NHS setting. The value of the therapeutic relationship is acknowledged and harnessed in the intervention as an active part of the intervention.

10.5.2 Limitations

A potential limitation of the study was that the secondary clinical-related outcomes did not include a sciatica specific outcome score. An opportunity existed during the set-up phases of the study to determine the utility of different outcome measures such as the sciatica bothersomeness and sciatica frequency index (SBFI) (Patrick *et al.*, 1995; Grøvle *et al.*, 2010). The SBFI is a sciatica specific outcome measure, completed by the patient who rates the bothersomeness and frequency of those symptoms and signs. The patient with sciatica reports the intensity of their symptoms, any numbness or tingling in the lower limb, any weakness in the lower limb and back and leg pain when sitting and a composite score is calculated. The utility SBFI was not undertaken due to the late change in service provider for delivery of physiotherapy for the study. The service provider did not use the SBFI and was reluctant to change the outcome measures utilised within the service. This was a pragmatic decision, made in conjunction with the service provider and does reflect the outcome measures commonly used in the UK. This would have provided data as to the most appropriate primary outcome measure for a full RCT. The ODI is widely utilised and accepted as a valid and reliable measure of self-reported disability. Similarly, the VAS back

and leg pain scores are widely used in the clinical setting and the scores do represent the patient's main concerns i.e. pain. However, the main objective of the study was to determine the feasibility of the timing of physiotherapy for LRS and so the utilisation of timing as the primary outcome measure for a future RCT would be most appropriate.

Although recruitment was satisfactory and ahead of time, the GPs involved in the study were well motivated and supportive of the study, in a city with a proven track record of GP involvement in service development and research. This may not be the case across the England and further afield. Similarly, the support of the service provider, clinical, administrative and management staff was a key factor in the success of the study, a factor which may not be reproducible in other centres. The use of optimisation strategies will be integrated to allow for the consideration of contextual change between recruitment, population, treatment centres and geographical area (Levati *et al.*, 2016). The risk of having a structured, rigid optimisation strategy is that it may make the approach less adaptable and responsive to on the ground change.

A prerequisite for ethics approval meant that patients had to contact the research team to discuss involvement. This may have introduced an element of self-selection bias and so this group of patients may not be representative of a wider population who choose not to engage in research activity (Friedman, Furberg and DeMets, 2010). In order to mitigate against this in the future, it is hoped that any future study would be able to contact potential participants directly. The results of the qualitative aspects of the study will be used to make this argument, if necessary, for future ethics board approval. The intervention and study processes, including recruitment were well received by participants, with no negative feedback received.

The reliance on a clinical diagnosis of LRS made by the GP and physiotherapists is a potential limitation, although a reflection of the clinical reality. The limitation being that there is likely to be a degree of diagnostic heterogeneity within the sample using a pathoanatomical model of care. There is, therefore, potential that participants with LRS in the study may have symptoms from something other than nerve root inflammation, including pseudoradicular symptoms, somatic or visceral referred symptoms. However, patients exhibiting signs or symptoms of LRS should not routinely be given MRI scans (National Insititute for Health and Care Excellence, 2016). In practice the pathoanatomical cause of the patient's symptoms, other than serious pathology, does not affect the treatment process, which is goal orientated and specific to the individual.

The selection of patients with a specific pathoanatomical diagnosis for the study was purposefully avoided. This was primarily because it reflects the clinical reality for clinicians in primary care. It is also because of the severely limited clinical accuracy of detecting specific pathoanatomical conditions and diseases in the spine (Hancock *et al.*, 2011; Ekedahl

et al., 2018) which lends itself to diagnostic inaccuracy and unavoidable heterogeneity of the study population. This is most often seen between a pathoanatomical diagnosis of a lumbar IVD and DLSS. The lack of an accurate pathoanatomical diagnosis also represents the clinical reality in primary care, where LBP and LRS patients are primarily managed. The gold standard tool for the pathoanatomical diagnosis of LRS is MRI scanning and this is not readily available, and nor should it be available in primary care (National Insititute for Health and Care Excellence, 2016). The diagnosis is therefore made on clinical history and examination and is likely to be pathoanatomically inaccurate. Therefore, in keeping with maintaining the patient as the main source and driver for the management of their symptoms, the focus on the recruitment of patients is of their clinical presentation and their symptoms and goals of treatment, rather than a potential pathoanatomical entity. Recent work to determine a clinical diagnostic model for patients presenting with lower limb radicular pain have suggested four items which are highly predictive of sciatica. These are; pain extending below the knee, leg pain greater than low back pain, positive neural tension (positive SLR/slump tests) and neurological deficit (Stynes *et al.*, 2018). Despite limitations with this and other similar models, it is proposed in a future study that a clinical diagnostic model is utilised.

The target population for the study was anyone over 18 with symptoms of unilateral radicular dysfunction. The geographical areas of the study encompassed several areas of significant deprivation with a large population of black and Asian minority ethnic (BAME) groups. However, the recruited population included only 4 participants (5%) of BAME origin. The reasons for this are not immediately apparent. A potential reason may be that an inclusion criterion stipulated that participants should be able to speak and have an understanding of written English. A full RCT would include non-English speakers and work to discern the best ways to recruit and retain BAME patients would be undertaken prior to an RCT.

One element of the study which was potentially key to its success was the researcher. This was his study, with significant personal time, money, effort and career risks invested. In Chapter 8 the risk of bias from the researcher was discussed with ways suggested to control or acknowledge these in a future study. The challenge of designing, funding and setting up a study relies on the skills, both soft and technical in order to make the project a success. The development of a robust protocol, involving key stakeholders and allowing for site-specific modifications, will help mitigate the need for one individual's soft skills to make the project a success. Similarly, the set-up and development of training for treating physiotherapists will be made as part of a team and not one individual.

These limitations need to be taken into account when planning a definitive study and have underpinned a conservative view of attrition in the definitive sample size calculation.

Caution should be used when estimating randomisation and attrition rates from external pilot studies as there is high variability between pilot and full trials (Cooper *et al.*, 2018). A wider geographical spread of GP centres to meet the proposed recruitment rates would be advisable in order to improve generalisability. Site selection would need to consider current service provision and the ability to deliver the intervention in settings that are convenient and accessible to patients.

Methods to ensure reliability of respondent PROM returns will be developed for a future study, utilising web-based technology including mobile applications whereby automatic reminders are used, with a web link to remind participants to complete their PROMs.

10.6 Recommendations for future research

The feasibility objectives of the study have all been met, with patients assigning utility to the intervention. The next step is therefore to perform the full-scale RCT to determine the effectiveness and cost-effectiveness of early physiotherapy compared to usual physiotherapy for treating people suffering with LRS.

There are several opportunities for further research which have arisen as part of the work of this thesis, these will be explored in turn.

The development of a full-scale RCT affords an opportunity to refine the intervention utilising the MRC complex interventions framework (P Craig *et al.*, 2008). A criticism of the MRC complex interventions framework is that it does not provide guidance on theory driven evaluation methods. The POLAR intervention would benefit from the development of a means of both theory development and evaluation, potentially utilising the theoretical domains framework (TDF) (Francis, O'Connor and Curran, 2012). French et al (2012) have suggested a four-step method to guide the intervention development (French *et al.*, 2012). Integration of a theory of change (ToC) approach (De Silva *et al.*, 2014) would enable future evaluation and monitoring of change. The development of theory will be enhanced with the utilisation of intervention mapping (IM) (Bartholomew, Parcel and Kok, 1998; Hurley *et al.*, 2016; Kok *et al.*, 2016). The integration of these theory-based approaches for the refinement of the intervention will be augmented by the continued work with patient experts. It is important that a complex therapeutic intervention does not become too complex and difficult to clinically deliver into practice. The importance of fear as a mediating factor for participants experiences of LRS is one area which would benefit from further investigation. Qualitative research into the cause of patients' fears and the factors that precipitate and or perpetuate fear is warranted. The development of intervention tools to address fear-related aspects of the participants problem is a research opportunity.

The use of stratified care in the management of LBP is the focus of ongoing research with encouraging results (Hill *et al.*, 2011; Foster *et al.*, 2014). Stratification of treatment allows

for the use of finite fiscal resources to be targeted on those patients who would gain the most benefit. Patients with LBP who develop chronic or persistent symptoms incur the greatest costs and can be recalcitrant to treatment. The use of the stratified care approach affords an opportunity for further research with patients suffering with symptoms of LRS. The complexity of the POLAR intervention allows for patients to receive different elements of the intervention, which compliments the stratified care approach in allowing the utilisation of different aspects of the intervention for those patients with varying needs according to the stratification model.

The traditional and currently used model of healthcare delivery in the UK NHS is for a patient with a health complaint to make an appointment to physically visit their GP who will deliver an episode of healthcare. The waiting times for GP appointments are frustratingly rising, leading to potential delays in treatment and patient dissatisfaction. Alternatives to this model of delivery are being fashioned, including the use of multidisciplinary teams, telephone interactions, web and application (app) based approaches. This could include at first consultation with the GP, the clinic nurse or online as has been previously highlighted. These alternative approaches offer new ways of delivering information for clinicians but also different options for patients as to when and how they access their healthcare. The most commonly utilised components in the POLAR treatment approach were elements to improve the patients understanding of LRS and to decrease psychological distress. An alternative to a face to face delivery of this component may be a telephone or video conversation.

Finally, a recent observational study examining early physiotherapy for a range of musculoskeletal conditions, including LBP has found that early intervention decreases opioid use at one year (Sun et al. 2018). This is an interesting finding and one that suggests an opportunity for further research into the role of early intervention physiotherapy for LRS and its effects on longer term analgesic and in particular opioid use.

10.7 Conclusions

For any given intervention to be effective there needs to be the appropriate therapy, at the appropriate dose at the right time. If any of these input variables are not optimised, then there is a real threat to the effectiveness of that intervention. This is the situation in which physiotherapy finds itself in the management of LBP and LRS. As a profession we have guidelines as to what some of the appropriate therapies are for LBP and LRS and an idea as to the optimum dose/frequency of the therapy. We do not have any evidence as to when the most effective time is to instigate these therapies. This is a clear challenge to the effectiveness of the therapeutic intervention and to the commissioning of those services that deliver the therapy.

The burden of LRS is significant on an individual and population level. This thesis has outlined the significance of this burden and the lack of research into the timing of delivery of physiotherapy interventions to treat LRS. The findings of the study have provided new evidence for the acceptance of a complex physiotherapy intervention for the management of LRS. It has been demonstrated that a full RCT is feasible, within a reasonable time scale and resource envelope, to determine the effectiveness of early intervention physiotherapy compared to usual physiotherapy to treat LRS.

References

Abou-Elroos, D. A. (2017) 'Prolonged Physiotherapy versus Early Surgical Intervention in Patients with Lumbar Disk Herniation: Short-term Outcomes of Clinical Randomized Trial.', *Asian spine journal*, 11(4), pp. 531–7.

Abou-Elroos, D. A. D. A. *et al.* (2017) 'Prolonged Physiotherapy versus Early Surgical Intervention in Patients with Lumbar Disk Herniation: Short-term Outcomes of Clinical Randomized Trial.', *Asian spine journal*, 11(4), pp. 531–7. doi: 10.4184/asj.2017.11.4.531.

Adams, M. a. *et al.* (2014) 'Why do some intervertebral discs degenerate, when others (in the same spine) do not?', *Clinical Anatomy*, 204(April 2014), pp. 195–204. doi: 10.1002/ca.22404.

Adel, S. M. (2011) 'Efficacy of Neural Mobilizations in Treatment of Low Back Dysfunctions', *Journal of American Science*, 7(3), pp. 566–573. doi: 10.1017/CBO9781107415324.004.

Ahn, S. H., Ahn, M. W. and Byun, W. M. (2000) 'Effect of the transligamentous extension of lumbar disc herniations on their regression and the clinical outcome of sciatica.', *Spine*, 25(4), pp. 475–80. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10707394.

Airaksinen, O. *et al.* (2005) 'European guidelines for the management of chronic low back pain', *Manual Therapy*, 2005(November 2004), pp. 1–207.

Akagi, R. *et al.* (2010) 'Comparison of early and late surgical intervention for lumbar disc herniation: Is earlier better?', *Journal of Orthopaedic Science*, 15(3), pp. 294–298. doi: 10.1007/s00776-010-1457-1.

Albaladejo,C. Kovacs,F.M. Royuela, A. del Pino, R. Z. J. (2010) 'The Efficacy of a Short Education Program and a Short Physiotherapy Program for Treating Low Back Pain in Primary Care A Cluster Randomized Trial', *Spine*, 35(5), pp. 483–496. doi: 10.1097/BRS.0b013e3181b9c9a7.

Aldrich, S. and Eccleston, C. (2000) 'Making Sense of Everyday Pain', *Social Science and Medicine*, 50, pp. 1631–1641.

Alperstein, D. and Sharpe, L. (2016) 'The efficacy of motivational interviewing in adults with chronic pain: A meta-analysis and systematic review', *Journal of Pain*. Elsevier Inc, 17(4), pp. 393–403. doi: 10.1016/j.jpain.2015.10.021.

Alrwaily, M. *et al.* (2018) 'Treatment-based Classification System for Patients With Low Back Pain: The Movement Control Approach', *Physical Therapy*, 97(12), pp. 1147–1157.

Alsaadi, S. M. *et al.* (2014) 'Poor Sleep Quality Is Strongly Associated With Subsequent Pain Intensity in Patients With Acute Low Back Pain', *Arthritis & Rheumatology*, 66(5), pp. 1388–1394. doi: 10.1002/art.38329.

Amico, K. R. (2009) 'Percent total attrition: A poor metric for study rigor in hosted intervention designs', *American Journal of Public Health*, 99(9), pp. 1567–1575. doi: 10.2105/AJPH.2008.134767.

Anderson, L. M. *et al.* (2011) 'Using logic models to capture complexity in systematic reviews', *Research Synthesis Methods*, 2(1), pp. 33–42. doi: 10.1002/jrsm.32.
Arts, M. P. and Peul, W. C. (2011) 'Timing and minimal access surgery for sciatica: A summary of two randomized trials', *Acta Neurochirurgica*, 153(5), pp. 967–974. doi: 10.1007/s00701-011-0983-8.
Aslaksen, P. M. and Lyby, P. S. (2015) 'Fear of pain potentiates nocebo hyperalgesia', *Journal of Pain Research*, 8, pp. 703–710. doi: 10.2147/JPR.S91923.
Atlas, S. J. *et al.* (2001) 'Surgical and nonsurgical management of sciatica secondary to a lumbar disc herniation: five-year outcomes from the Maine Lumbar Spine Study.', *Spine*, 26(10), pp. 1179–87. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11413434.
Atlas, S. J. *et al.* (2005a) 'Long-term outcomes of surgical and nonsurgical management of lumbar spinal stenosis: 8 to 10 year results from the maine lumbar spine study.', *Spine*, 30(8), pp. 936–43. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15834339.
Atlas, S. J. *et al.* (2005b) 'Long-term outcomes of surgical and nonsurgical management of sciatica secondary to a lumbar disc herniation: 10 year results from the maine lumbar spine study.', *Spine*, 30(8), pp. 927–35. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15834338.
Autio, R. A. *et al.* (2006) 'Determinants of Spontaneous Resorption of Intervertebral Disc Herniations', *Spine*, 31(11), pp. 1247–1252.
Autio, R. a *et al.* (2006) 'Determinants of Spontaneous Resorption of Intervertebral Disc Herniations', *Spine*, 31(11), pp. 1247–1252. doi: 10.1097/01.brs.0000217681.83524.4a.
Avery, K. N. L. *et al.* (2017) 'Informing efficient randomised controlled trials: Exploration of challenges in developing progression criteria for internal pilot studies', *BMJ Open*, 7(2). doi: 10.1136/bmjopen-2016-013537.
Bartholomew, L. . *et al.* (2001) *Intervention Mapping*. 1st edn. Mayfield Publishing co. Mountain View, USA.
Bartholomew, L. K., Parcel, G. S. and Kok, G. (1998) 'Intervention Mapping: A Process for Developing Theory- and Evidence-Based Health Education Programs', *Health Education and Behavior*, 25(5), pp. 545–563. doi: 10.1177/109019819802500502.
Battié, M. C. *et al.* (2007) 'Heritability of low back pain and the role of disc degeneration.', *Pain*, 131(3), pp. 272–80. doi: 10.1016/j.pain.2007.01.010.
Bell, M. L., Whitehead, A. L. and Julious, S. A. (2018) 'Guidance for using pilot studies to inform the design of intervention trials with continuous outcomes', *Clinical Epidemiology*, 10, pp. 153–157. doi: 10.2147/CLEP.S146397.
Bellg, A. J. *et al.* (2004) 'Enhancing treatment fidelity in health behavior change studies: Best practices and recommendations from the NIH Behavior Change Consortium', *Health Psychology*, 23(5), pp. 443–451. doi: 10.1037/0278-6133.23.5.443.

Benedetti, F. *et al.* (2003) 'Conscious expectation and unconscious conditioning in analgesic, motor, and hormonal placebo/nocebo responses.', *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 23(10), pp. 4315–4323. doi: 23/10/4315 [pii].
Benedetti, F. *et al.* (2006) 'The biochemical and neuroendocrine bases of the hyperalgesic nocebo effect.', *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 26(46), pp. 12014–22. doi: 10.1523/JNEUROSCI.2947-06.2006.
Benson, R. T. *et al.* (2010) 'Conservatively treated massive prolapsed discs: a 7-year follow-up.', *Annals of the Royal College of Surgeons of England*, 92(2), pp. 147–53. doi: 10.1308/003588410X12518836438840.
Birt, L. *et al.* (2016) 'Member Checking: A Tool to Enhance Trustworthiness or Merely a Nod to Validation?', *Qualitative Health Research*, 26(13), pp. 1802–1811. doi: 10.1177/1049732316654870.
Bishop, A. *et al.* (2014) 'Rationale, design and methods of the Study of Work and Pain (SWAP): A cluster randomised controlled trial testing the addition of a vocational advice service to best current primary care for patients with musculoskeletal pain (ISRCTN 52269669)', *BMC Musculoskeletal Disorders*, 15(1), pp. 1–11. doi: 10.1186/1471-2474-15-232.
Bishop, A. *et al.* (2017) 'STEMS pilot trial: A pilot cluster randomised controlled trial to investigate the addition of patient direct access to physiotherapy to usual GP-led primary care for adults with musculoskeletal pain', *BMJ Open*, 7(3), pp. 1–11. doi: 10.1136/bmjopen-2016-012987.
Bishop, F. L. *et al.* (2015) '"lovely pie in the sky plans": A qualitative study of clinicians' perspectives on guidelines for managing low back pain in primary care in England', *Spine*, 40(23), pp. 1842–1850. doi: 10.1097/BRS.0000000000001215.
Blackwood, B., O'Halloran, P. and Porter, S. (2010) 'On the problems of mixing RCTs with qualitative research: The case of the MRC framework for the evaluation of complex healthcare interventions', *Journal of Research in Nursing*, 15(6), pp. 511–521. doi: 10.1177/1744987110373860.
Blome, C. and Augustin, M. (2015) 'Measuring change in quality of life: Bias in prospective and retrospective evaluation', *Value in Health*. Elsevier, 18(1), pp. 110–115. doi: 10.1016/j.jval.2014.10.007.
Blyth, F. M., Macfarlane, G. J. and Nicholas, M. K. (2007) 'The contribution of psychosocial factors to the development of chronic pain: the key to better outcomes for patients?', *Pain*, 129(1–2), pp. 8–11. doi: 10.1016/j.pain.2007.03.009.
Bodenheimer, T. and Handley, M. a. (2009) 'Goal-setting for behavior change in primary care: An exploration and status report', *Patient Education and Counseling*, 76(2), pp. 174–180. doi: 10.1016/j.pec.2009.06.001.

Boote, J. *et al.* (2016) 'Physiotherapy for Patients with Sciatica Awaiting Lumbar Micro-discectomy Surgery: A Nested, Qualitative Study of Patients' Views and Experiences', *Physiotherapy Research International*, 22(3), p. e1665. doi: 10.1002/pri.1665.
Boote, J., Wong, R. and Booth, A. (2015) '"Talking the talk or walking the walk?" A bibliometric review of the literature on public involvement in health research published between 1995 and 2009', *Health Expectations*, 18(1), pp. 44–57. doi: 10.1111/hex.12007.
Borrelli, B. (2011) 'The assessment, monitoring, and enhancement of treatment fidelity in public health clinical trials', *Journal of Public Health Dentistry*, 71(SUPPL. 1). doi: 10.1111/j.1752-7325.2011.00233.x.
Brazier JE, Ratcliffe J, T. A. & S. J. (2007) *Measuring and Valuing Health Benefits for Economic Evaluation*. Oxford: Oxford University Press.
Brinjikji, W. *et al.* (2015) 'Systematic Literature Review of Imaging Features of Spinal Degeneration in Asymptomatic Populations', *Am J Neuroradiology*, 36, pp. 811–816.
Brueton, V. C. *et al.* (2013) 'Strategies to improve retention in randomised trials.', *The Cochrane database of systematic reviews*, 12(12), p. MR000032. doi: 10.1002/14651858.MR000032.pub2.
Bush, K. (1992) 'The Natural history of sciatica associated with disc pathology', pp. 1205–1212.
Butler, D. Moseley, M. L. (2013) *Explain Pain*. 2nd edn. Adelaide: NOI Group Publications.
Butler, D. (2000) *The Sensitive Nervous System*. 1st edn. NOI Group Publications.
Campbell, M. *et al.* (2007) 'Recruitment to randomised trials: strategies for trial enrolment and participation study. The STEPS study HTA Health Technology Assessment NHS R&D HTA Programme www.hta.ac.uk Feedback', *Health Technology Assessment*, 11(48). Available at: http://www.hta.ac.uk.
Cane,. O'Connor,D. Michie, S. (2012) 'Validation of the theoretical domains framework for use in behaviour change...: EBSCOhost', *Implementation Scicence*, 7(37), pp. 1–17.
Caneiro, Anne Smith, Martin Rabey, G. Lorimer Moseley, P. O. *et al.* (2017) 'Process of Change in Pain-Related Fear: Clinical Insights From a Single Case Report of Persistent Back Pain Managed With Cognitive Functional Therapy', *Journal of Orthopaedic & Sports Physical Therapy*, 47(9), pp. 637–651. doi: 10.2519/jospt.2017.7371.
Capra, F. *et al.* (2011) 'Validity of the straight-leg raise test for patients with sciatic pain with or without lumbar pain using magnetic resonance imaging results as a reference standard', *Journal of Manipulative and Physiological Therapeutics*. National University of Health Sciences, 34(4), pp. 231–238. doi: 10.1016/j.jmpt.2011.04.010.
Casserley-Feeney, S. N. *et al.* (2008) 'Physiotherapy for low back pain: Differences between public and private healthcare sectors in Ireland-A retrospective survey', *Manual Therapy*, 13(5), pp. 441–449. doi: 10.1016/j.math.2007.05.017.

Cassidy, L. *et al.* (2012) 'Piriformis syndrome: implications of anatomical variations, diagnostic techniques, and treatment options.', *Surgical and radiologic anatomy : SRA*, 34(6), pp. 479–86. doi: 10.1007/s00276-012-0940-0.
Centre for Reviews and Dissemination, U. of Y. (2009) *Systematic reviews: CRDs guidance for Undertaking reviews in health care*. University of York.
Cheing, G. *et al.* (2014) 'Testing a Path-Analytic Mediation Model of How Motivational Enhancement Physiotherapy Improves Physical Functioning in Pain Patients', *Journal of Occupational Rehabilitation*, 24(4), pp. 798–805. doi: 10.1007/s10926-014-9515-8.
Chiarotto, A. *et al.* (2015) 'Core outcome domains for clinical trials in non-specific low back pain.', *European Spine Journal*, 24, pp. 1127–1142. doi: 10.1007/s00586-015-3892-3.
Childs, J. D. *et al.* (2015) 'Implications of early and guideline adherent physical therapy for low back pain on utilization and costs.', *BMC health services research*, 15, p. 150. doi: 10.1186/s12913-015-0830-3.
Chou, L., Ranger, T. A., Peiris, W., Cicuttini, F. M., Urquhart, D. M., Sullivan, K., Seneviwickrama, M., *et al.* (2018) 'Patients' perceived needs for medical services for non-specific low back pain: A systematic scoping review', *PLoS ONE*, 13(11), pp. 1–29. doi: 10.1371/journal.pone.0204885.
Chou, L., Ranger, T. A., Peiris, W., Cicuttini, F. M., Urquhart, D. M., Sullivan, K., Seneviwickrama, K., *et al.* (2018) 'Patients' perceived needs of health care providers for low back pain management: a systematic scoping review', *Spine Journal*. Elsevier Inc., 18(4), pp. 691–711. doi: 10.1016/j.spinee.2018.01.006.
Clark, A. M. (2013) 'What are the components of complex interventions in healthcare? Theorizing approaches to parts, powers and the whole intervention', *Social Science and Medicine*. Elsevier Ltd, 93, pp. 185–193. doi: 10.1016/j.socscimed.2012.03.035.
Clarke, C. L., Ryan, C. G. and Martin, D. J. (2011) 'Pain neurophysiology education for the management of individuals with chronic low back pain: A systematic review and meta-analysis', *Manual Therapy*. Elsevier Ltd, 16(6), pp. 544–549. doi: 10.1016/j.math.2011.05.003.
Cleland, J. A. *et al.* (2006) 'Slump stretching in the management of non-radicular low back pain: A pilot clinical trial', *Manual Therapy*, 11(4), pp. 279–286. doi: 10.1016/j.math.2005.07.002.
Comer, C. M. *et al.* (2009) 'Assessment and management of neurogenic claudication associated with lumbar spinal stenosis in a UK primary care musculoskeletal service: a survey of current practice among physiotherapists.', *BMC musculoskeletal disorders*, 10, p. 121. doi: 10.1186/1471-2474-10-121.
Cook, A. *et al.* (2018) 'DELTA2 guidance on choosing the target difference and undertaking and reporting the sample size calculation for a randomised controlled trial', *Trials*. doi:

10.1186/s13063-018-2884-0.
Cooper, C. *et al.* (2014) 'Conducting qualitative research within Clinical Trials Units: Avoiding potential pitfalls', *Contemporary Clinical Trials*. Elsevier B.V., 38(2), pp. 338–343. doi: 10.1016/j.cct.2014.06.002.
Cooper, C. L. *et al.* (2018) 'Are pilot trials useful for predicting randomisation and attrition rates in definitive studies: A review of publicly funded trials', *Clinical Trials*, 15(2), pp. 189–196. doi: 10.1177/1740774517752113.
Corbett, M., Foster, N. E. and Ong, B. N. (2007) 'Living with low back pain - stories of hope and despair', *Social Science and Medicine*, 65(8), pp. 1584–1594. doi: 10.1016/j.socscimed.2007.06.008.
Craig, P *et al.* (2008) *Developing and Evaluating Complex Interventions: New Guidance, Medical Research Council*. doi: http://dx.doi.org/10.1136/bmj.a1655.
Craig, Peter *et al.* (2008) 'Developing and evaluating complex interventions: the new Medical Research Council guidance.', *BMJ (Clinical research ed.)*, 337(September), p. a1655. doi: 10.1136/bmj.a1655.
Cresswell, J.W, P. C. V. . (2011) *Designing and Conducting Mixed Methods Research*. 2nd edn. Thousand Oaks, California: Sage.
Critical Appraisal Skills Programme (CASP) (2013) *CASP Systematic Reviews Checklist, CASP*. Available at: http://media.wix.com/ugd/dded87_951541699e9edc71ce66c9bac4734c69.pdf.
Critical Appraisal Skills Programme (CASP) (2017a) 'CASP checklist for Cohort studies'. Available at: http://www.casp-uk.net/checklists.
Critical Appraisal Skills Programme (CASP) (2017b) *CASP Qualitative Research Checklist*. Available at: http://www.casp-uk.net/checklists.
CSP (2010) 'A Survey of NHS Physiotherapy Waiting Times and Musculoskeletal Workload and Caseload in England', *Chartered Society of Physiotherapy Information paper*, (0), p. 31.
CSP (2012) 'An audit of physiotherapy services in England', *Chartered Society of Physiotherapy*, (January).
Cyriax, J. (1996) *Cyriax's Illustrated Manual of Orthopaedic Medicine*. 3rd edn. Butterworth-Heinemann.
Daffner, S. D., Hymanson, H. J. and Wang, J. C. (2010) 'Cost and use of conservative management of lumbar disc herniation before surgical discectomy', *Spine Journal*. Elsevier Inc, 10(6), pp. 463–468. doi: 10.1016/j.spinee.2010.02.005.
Doita, M. *et al.* (2001) 'Influence of Macrophage Infiltration of Herniated Disc Tissue on the Production of Matrix Metalloproteinases Leading to Disc Resorption', *Spine*, 26(14), pp. 1522–1527.

Dorling, H. *et al.* (2014) 'Developing a checklist for research proposals to help describe health service interventions in UK research programmes: a mixed methods study.', *Health research policy and systems / BioMed Central*. Health Research Policy and Systems, 12(1), p. 12. doi: 10.1186/1478-4505-12-12.
Edwards, R. R. *et al.* (2007) 'Symptoms of distress as prospective predictors of pain-related sciatica treatment outcomes', *Pain*, 130(1–2), pp. 47–55. doi: 10.1016/j.pain.2006.10.026.
Efstathiou, M. A. *et al.* (2015) 'Effectiveness of neural mobilization inpatients with spinal radiculopathy: Acritical review', *Journal of Bodywork and Movement Therapies*. Elsevier Ltd, 19(2), pp. 205–212. doi: 10.1016/j.jbmt.2014.08.006.
Ekedahl, H. *et al.* (2018) 'Accuracy of Clinical Tests in Detecting Disk Herniation and Nerve Root Compression in Subjects With Lumbar Radicular Symptoms', *Archives of Physical Medicine and Rehabilitation*, 99(4), pp. 726–735. doi: 10.1016/j.apmr.2017.11.006.
Eldridge, S. M. *et al.* (2016) 'CONSORT 2010 statement: extension to randomised pilot and feasibility trials', *Pilot and Feasibility Studies*, 2(1), p. 64. doi: 10.1186/s40814-016-0105-8.
Ellenberg, M. R. *et al.* (1993) 'Prospective evaluation of the course of disc herniations in patients with proven radiculopathy', *Archives of Physical Medicine and Rehabilitation*, 74(1), pp. 3–8. doi: 0003-9993(93)90374-J [pii].
Espeland, A., Baerheim, A. and Albrektsen, G. (2001) 'Patients ' Views on Importance and Usefulness of Plain Radiography for Low Back Pain', 26(12), pp. 1356–1363.
Fairbank, JC. Couper, J. Davies, JB. O'Brien, J. (1980) 'The Oswestry low back pain disability questionnaire', *Physiotherapy (London)*, 66(8), pp. 271–3.
Fairbank, J. C. and Pynsent, P. B. (2000) 'The Oswestry Disability Index.', *Spine*, 25(22), pp. 2940–52; discussion 2952. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11074683.
Feld, G. B. and Born, J. (2017) 'Sculpting memory during sleep: concurrent consolidation and forgetting', *Current Opinion in Neurobiology*. Elsevier Ltd, 44, pp. 20–27. doi: 10.1016/j.conb.2017.02.012.
Ferreira, M. L. *et al.* (2012) 'A critical review of methods used to determine the smallest worthwhile effect of interventions for low back pain', *Journal of Clinical Epidemiology*. Elsevier Inc, 65(3), pp. 253–261. doi: 10.1016/j.jclinepi.2011.06.018.
Fields, H. (2004) 'State-dependent opioid control of pain', *Nature Reviews Neuroscience*, 5(7), pp. 565–575. doi: 10.1038/nrn1431.
Fletcher, A. *et al.* (2016) 'Realist complex intervention science: Applying realist principles across all phases of the Medical Research Council framework for developing and evaluating complex interventions', *Evaluation*, 22(3), pp. 286–303. doi: 10.1177/1356389016652743.
Ford, J. J. *et al.* (2015) 'Individualised physiotherapy as an adjunct to guideline-based advice for low back disorders in primary care : a randomised controlled trial', *BJSM*, 50(4), p. bjsports-2015-095058-. doi: 10.1136/bjsports-2015-095058.

Foster, N. E. *et al.* (2014) 'Effect of Stratified Care for Low Back Pain in Family Practice (IMPaCT) Back): A Prospective Population-Based Sequential Comparison', *Annals of Family medicine*, 12(2), pp. 102–111. doi: 10.1370/afm.1625.INTRODUCTION.
Foster, N. E. *et al.* (2017) 'The clinical and cost-effectiveness of stratified care for patients with sciatica: the SCOPiC randomised controlled trial protocol (ISRCTN75449581).', *BMC musculoskeletal disorders*, 18(1), p. 172. Available at: http://linker2.worldcat.org/?rft.institution_id=130182&spage=172&pkgName=UKPMCFT&issn=1471-2474&linkclass=to_article&jKey=434&issue=1&provider=NLM&date=2017-04&aulast=Foster%2C+Nadine+E%3B+Konstantinou%2C+Kika%3B+Lewis%2C+Martyn%3B+Ogollah%2C+Reuben%3B+Du.
Foster, N. E. *et al.* (2018) 'Prevention and treatment of low back pain : evidence , challenges , and promising directions', *Lancet*, 6736(18), pp. 1–16. doi: 10.1016/S0140-6736(18)30489-6.
Francis, J. J., O'Connor, D. and Curran, J. (2012) 'Theories of behaviour change synthesised into a set of theoretical groupings: introducing a thematic series on the theoretical domains framework', *Implementation Science*, 7(1). doi: 10.1186/1748-5908-7-35.
French, S. D. *et al.* (2012) 'Developing theory-informed behaviour change interventions to implement evidence into practice: a systematic approach using the Theoretical Domains Framework', *Implementation Science*, 7(1), p. 1. doi: 10.1186/1748-5908-7-38.
Freynhagen, R. *et al.* (2008) 'Pseudoradicular and radicular low-back pain - A disease continuum rather than different entities? Answers from quantitative sensory testing', *Pain*, 135(1–2), pp. 65–74. doi: 10.1016/j.pain.2007.05.004.
Friedman, L. ., Furberg, C. . and DeMets, D. . (2010) *Fundamentals of Clinical Trials*. 4th editio. Springer New York.
Fritz, J. M. *et al.* (2012) 'Primary care referral of patients with low back pain to physical therapy: impact on future health care utilization and costs.', *Spine*, 37(25), pp. 2114–21. doi: 10.1097/BRS.0b013e31825d32f5.
Fritz, J. M. and Irrgang J.J (2001) 'A Comparison of a Modified Oswestry Low Back Pain Disability Questionnaire and the Quebec Back Pain Disability Scale', *Physical Therapy*, 81(2), pp. 776–788.
Gardner, T. *et al.* (2015) 'Patient led goal setting in chronic low back pain-What goals are important to the patient and are they aligned to what we measure?', *Patient Education and Counseling*, 98(8), pp. 1035–1038. doi: 10.1016/j.pec.2015.04.012.
Gardner, T. *et al.* (2018) 'Goal setting practice in chronic low back pain. What is current practice and is it affected by beliefs and attitudes?', *Physiotherapy Theory and Practice*. Taylor & Francis, 34(10), pp. 795–805. doi: 10.1080/09593985.2018.1425785.
Gearing, R. E. *et al.* (2011) 'Major ingredients of fidelity: A review and scientific guide to

improving quality of intervention research implementation', *Clinical Psychology Review*. Elsevier Ltd, 31(1), pp. 79–88. doi: 10.1016/j.cpr.2010.09.007.
Genevay, S. *et al.* (2017) 'Clinical classification criteria for radicular pain caused by lumbar disc herniation: the radicular pain caused by disc herniation (RAPIDH) criteria', *Spine Journal*. Elsevier Inc., 17(10), pp. 1464–1471. doi: 10.1016/j.spinee.2017.05.005.
Genevay, S. *et al.* (2018) 'Clinical classification criteria for neurogenic claudication caused by lumbar spinal stenosis. The N-CLASS criteria', *Spine Journal*. Elsevier Inc., 18(6), pp. 941–947. doi: 10.1016/j.spinee.2017.10.003.
Gilbert, K. K. *et al.* (2015) 'Effects of simulated neural mobilization on fluid movement in cadaveric peripheral nerve sections: implications for the treatment of neuropathic pain and dysfunction', *Journal of Manual & Manipulative Therapy*, 23(4), pp. 219–225. doi: 10.1179/2042618614Y.0000000094.
Goebel, M. U. (2002) 'Behavioral conditioning of immunosuppression is possible in humans', *The FASEB Journal*, 16(14), pp. 1869–1873. doi: 10.1096/fj.02-0389com.
Gray, J. C. (2017) 'Diagnosis of Intermittent Vascular Claudication in a Patient With a Diagnosis of Sciatica', *Physical Therapy*, 79(6), pp. 582–590. doi: 10.1093/ptj/79.6.582.
Green, J. and Thorogood, N. (2014) 'In Depth Interviews', in *Qualitative Methods for Health Research*. 3rd editio. Sage, London, pp. 95–125.
Greenhough, C. (2014) 'Pathfinder Back Pain and Radicular Pain', *NHS Pathfinder projects*, (December 2014).
Grotle, M. P. T. *et al.* (2005) 'Clinical Course and Prognostic Factors in Acute Low Back Pain: Patients Consulting Primary Care for the First Time. [Miscellaneous Article]', *Spine April 15, 2005*, 30(8), pp. 976–982.
Grøvle, L. *et al.* (2010) 'The bothersomeness of sciatica: patients' self-report of paresthesia, weakness and leg pain.', *European spine journal*, 19(2), pp. 263–9. doi: 10.1007/s00586-009-1042-5.
Guest G, MacQueen KM, N. E. (2012) 'Introduction to applied thematic analysis', in *Applied Thematic Analysis*, pp. 3–20.
Hadjipavlou, a G. *et al.* (2008) 'The pathophysiology of disc degeneration: a critical review.', *The Journal of bone and joint surgery. British volume*, 90(10), pp. 1261–70. doi: 10.1302/0301-620X.90B10.20910.
Hahne, A. J., Ford, J. J., Hinman, R. S., *et al.* (2017) 'Individualized functional restoration as an adjunct to advice for lumbar disc herniation with associated radiculopathy. A preplanned subgroup analysis of a randomized controlled trial', *Spine Journal*. Elsevier Inc., 17(3), pp. 346–359. doi: 10.1016/j.spinee.2016.10.004.
Hahne, A. J., Ford, J. J., Surkitt, L. D., *et al.* (2017) 'Individualized Physical Therapy Is Cost-Effective Compared With Guideline-Based Advice for People With Low Back Disorders',

Spine, 42(3), pp. E169–E176. doi: 10.1097/BRS.0000000000001734.
Hahne, A. J., Ford, J. J. and McMeeken, J. M. (2010) 'Conservative management of lumbar disc herniation with associated radiculopathy: a systematic review.', *Spine*, 35(11), pp. E488-504. doi: 10.1097/BRS.0b013e3181cc3f56.
Hall, K., Gibbie, T. and Lubman, D. (2012) 'Motivational interviewing techniques', *Australian Family Physician*, 41(9), pp. 660–667.
Hancock, M. J. *et al.* (2011) 'Diagnostic accuracy of the clinical examination in identifying the level of herniation in patients with sciatica', *Spine*, 36(11). doi: 10.1097/BRS.0b013e3181ee7f78.
Harden, A. and Thomas, J. (2005) 'Methodological issues in combining diverse study types in systematic reviews', *International Journal of Social Research Methodology: Theory and Practice*, 8(3), pp. 257–271. doi: 10.1080/13645570500155078.
Harden, J. T. A. (2008) 'Methods for the thematic synthesis of qualitative research in systematic reviews', *BMC Medical Research Methodolology*, 8(45). doi: 10.1186/1471-2288-8-45.
Harrisson, S. A. *et al.* (2017) 'Neuropathic Pain in Low Back-Related Leg Pain Patients: What Is the Evidence of Prevalence, Characteristics, and Prognosis in Primary Care? A Systematic Review of the Literature', *The Journal of Pain*, 18(11), pp. 1295–1312. doi: 10.1016/j.jpain.2017.04.012.
Hart, O. and Ryton, B. A. (2013) 'Sheffield spinal pathway audit cycle - Pathways, mountains and the view from the top', *British Journal of Pain*, 8(1), pp. 43–48. doi: 10.1177/2049463713504387.
Hartvigsen, J. *et al.* (2018) 'Series Low back pain 1 What low back pain is and why we need to pay attention', *Lancet*, 6736(18). doi: 10.1016/S0140-6736(18)30480-X.
Haugen, A. J. *et al.* (2012) 'Prognostic factors for non-success in patients with sciatica and disc herniation.', *BMC musculoskeletal disorders*, 13(1), p. 183. doi: 10.1186/1471-2474-13-183.
Haugen, A. J. *et al.* (2016) 'Pain-related fear and functional recovery in sciatica: Results from a 2-year observational study', *Journal of Pain Research*, 9, pp. 925–931. doi: 10.2147/JPR.S115003.
Hawe, P. (2012) 'Lessons from Complex Interventions to Improve Health', *Annual Review of Public Health*, 36(1), p. 150112150436006. doi: 10.1146/annurev-publhealth-031912-114421.
Hengeveld E, B. K. (2013) *Maitlands' Vertebral Manipulation*. 8th edn. Churchill Livingstone, Edinburgh.
Henschke, N. *et al.* (2009) 'Prevalence of and screening for serious spinal pathology in patients presenting to primary care settings with acute low back pain', *Arthritis and Rheumatism*, 60(10), pp. 3072–3080. doi: 10.1002/art.24853.

Henschke, N. *et al.* (2013) 'Red flags to screen for malignancy in patients with low-back pain (Review)', *Cochrane Library*, (2), pp. 1–40. doi: 10.1002/14651858.CD008686.pub2.www.cochranelibrary.com.
Hewitt, Catherine E. Dumville, J. C. and Kumaravel, BharathyTorgerson, D. J. (2010) 'Assessing the impact of attrition in randomized controlled trials', *Journal of Clinical Epidemiology*. Elsevier Inc, 63(11), pp. 1264–1270. doi: 10.1016/j.jclinepi.2010.01.010.
Hider, S. L. *et al.* (2015) 'Pain location matters : the impact of leg pain on health care use , work disability and quality of life in patients with low back pain', *Eur Spine J24*, pp. 444–451. doi: 10.1007/s00586-014-3355-2.
Higgins, J. P. T. *et al.* (2011) 'The Cochrane Collaboration's tool for assessing risk of bias in randomised trials.', *BMJ (Clinical research ed.)*, 343, p. d5928. doi: 10.1136/bmj.d5928.
Higgins JPT and Green, S. (2011) 'Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0', *The Cochrane Collaboration*.
Hill, J. C. *et al.* (2008) 'A primary care back pain screening tool: identifying patient subgroups for initial treatment.', *Arthritis and rheumatism*, 59(5), pp. 632–41. doi: 10.1002/art.23563.
Hill, J. C. *et al.* (2011) 'Comparison of stratified primary care management for low back pain with current best practice (STarT Back): A randomised controlled trial', *The Lancet*. Elsevier Ltd, 378(9802), pp. 1560–1571. doi: 10.1016/S0140-6736(11)60937-9.
Hoffmann, T. C. *et al.* (2014) 'Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide.', *BMJ (Clinical research ed.)*, 348(mar07_3), p. g1687. doi: 10.1136/bmj.g1687.
Hopayian, K. and Notley, C. (2014) 'A systematic review of low back pain and sciatica patients' expectations and experiences of health care.', *The spine journal : official journal of the North American Spine Society*. Elsevier Inc, 14(8), pp. 1769–1780. doi: 10.1016/j.spinee.2014.02.029.
Hoy, D. *et al.* (2014) 'The global burden of low back pain: estimates from the Global Burden of Disease 2010 study', *Annals of the Rheumatic Diseases*, 73(6), pp. 968–974. doi: 10.1136/annrheumdis-2013-204428.
Huber, J. *et al.* (2011) 'The effect of early isometric exercises on clinical and neurophysiological parameters in patients with sciatica: An interventional randomized single-blinded study.', *Isokinetics & Exercise Science*. IOS Press, 19(3), pp. 207–214.
Hurley, D. A. *et al.* (2016) 'Using intervention mapping to develop a theory-driven, group-based complex intervention to support self-management of osteoarthritis and low back pain (SOLAS)', *Implementation Science*. Implementation Science, 11(1). doi: 10.1186/S13012-016-0418-2.
Husereau, D. *et al.* (2013) 'Consolidated Health Economic Evaluation Reporting Standards

(CHEERS) statement', *European Journal of Health Economics*, 14(3), pp. 367–372. doi: 10.1007/s10198-013-0471-6.
Hutton, M. (2019) 'Spinal Services GIRFT Programme National Speciality Report', *GIRFT*, (January).
Irwin, M. R. (2015) 'Why Sleep Is Important for Health: A Psychoneuroimmunology Perspective', *Annual Review of Psychology*, 66(1), pp. 143–172. doi: 10.1146/annurev-psych-010213-115205.
Ito T, Yamada M, Ikuta F, Fukada T, Hoshi S, K. Y. (1996) 'Histologic Evidence of Absorption of Sequestration Type Herniated Disc', *Spine*, 21(2), pp. 230–234.
Iversen, M. D. and Katz, J. N. (2001) 'Examination findings and self-reported walking capacity in patients with lumbar spinal stenosis.', *Physical therapy*, 81(7), pp. 1296–306. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11444993.
Jacobs, W. C. H. *et al.* (2011) 'Surgery versus conservative management of sciatica due to a lumbar herniated disc: a systematic review.', *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, 20(4), pp. 513–22. doi: 10.1007/s00586-010-1603-7.
Karp, J. F. *et al.* (2014) 'Negative affect and sleep disturbance may be associated with response to epidural steroid injections for spine-related pain', *Archives of Physical Medicine and Rehabilitation*. Elsevier Ltd, 95(2), pp. 309–315. doi: 10.1016/j.apmr.2013.09.007.
Kelly, G. A. *et al.* (2011) 'The association between chronic low back pain and sleep: A systematic review', *Clinical Journal of Pain*, 27(2), pp. 169–181. doi: 10.1097/AJP.0b013e3181f3bdd5.
Keogh, A. *et al.* (2015) 'A review of behaviour change theories and techniques used in group based self-management programmes for chronic low back pain and arthritis', *Manual Therapy*. doi: 10.1016/j.math.2015.03.014.
Keogh, A., Matthews, J. and Hurley, D. A. (2018) 'An assessment of physiotherapist's delivery of behaviour change techniques within the SOLAS feasibility trial', *British Journal of Health Psychology*, 23(4), pp. 908–932. doi: 10.1111/bjhp.12323.
Kobayashi, S. *et al.* (2009) 'Ultrastructural Analysis on Lumbar Disc Herniation Using Surgical Specimens Role of Neovascularization and Macrophages in Hernias Table 1 . Summary of Clinical Data in 73 Patients With Lumbar Disc Herniation', *Spine*, 34(7), pp. 655–662.
Koes, Æ Bart W, van Tulder MW, P. W. (2007) 'The diagnosis and treatment of sciatica.', *British Medical Journal*, 334, pp. 1313–1317. doi: 10.1136/bmj.39223.428495.BE.
Koike, Y. *et al.* (2003) 'Angiogenesis and inflammatory cell infiltration in lumbar disc herniation.', *Spine*, 28(17), pp. 1928–33. doi: 10.1097/01.BRS.0000083324.65405.AE.

Kok, G. *et al.* (2016) 'A taxonomy of behaviour change methods: an Intervention Mapping approach', *Health Psychology Review*. Taylor & Francis, 10(3), pp. 297–312. doi: 10.1080/17437199.2015.1077155.
Komori, H. *et al.* (1996) 'The natural history of herniated nucleus pulposus with radiculopathy', *Spine*, 21(2), pp. 225–229. Available at: http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:The+Natural+History+of+Herniated+Nucleus+Pulposus+With+Radiculopathy#0 (Accessed: 6 November 2013).
Konstantinou, K. *et al.* (2015) 'Characteristics of patients with low back and leg pain seeking treatment in primary care: baseline results from the ATLAS cohort study', *BMC Musculoskeletal Disorders*. BMC Musculoskeletal Disorders, 16(1), p. 332. doi: 10.1186/s12891-015-0787-8.
Konstantinou, K. and Dunn, K. M. (2008) 'Sciatica Review of Epidemiological Studies and Prevalence Estimates', *Spine*, 33(22), pp. 2464–2472.
Lau, P. M.-Y., Chow, D. H.-K. and Pope, M. H. (2008) 'Early physiotherapy intervention in an Accident and Emergency Department reduces pain and improves satisfaction for patients with acute low back pain: a randomised trial.', *The Australian journal of physiotherapy*, 54(4), pp. 243–9. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19025504.
Lequin, M. B. *et al.* (2013) 'Surgery versus prolonged conservative treatment for sciatica: 5-year results of a randomised controlled trial.', *BMJ open*, 3(5), pp. 1–10. doi: 10.1136/bmjopen-2012-002534.
Levack, W. M. M. *et al.* (2006) 'Is goal planning in rehabilitation effective? A systematic review', *Clinical Rehabilitation*, 20(9), pp. 739–755. doi: 10.1177/0269215506070791.
Levati, S. *et al.* (2016) 'Optimisation of complex health interventions prior to a randomised controlled trial: A scoping review of strategies used', *Pilot and Feasibility Studies*. Pilot and Feasibility Studies, 2(1). doi: 10.1186/s40814-016-0058-y.
Lewis, M. *et al.* (2010) 'Measuring practitioner/therapist effects in randomised trials of low back pain and neck pain interventions in primary care settings', *European Journal of Pain*. European Federation of International Association for the Study of Pain Chapters, 14(10), pp. 1033–1039. doi: 10.1016/j.ejpain.2010.04.002.
Lewis, R. *et al.* (2011) 'The clinical effectiveness and cost-effectiveness of management strategies for sciatica: systematic review and economic model.', *Health technology assessment (Winchester, England)*. NETSCC, 15(39), pp. 1–578. doi: 10.3310/hta15390.
Limbäck Svensson, G. *et al.* (2013) 'Patients' experience of health three years after structured physiotherapy or surgery for lumbar disc herniation.', *Journal of rehabilitation medicine : official journal of the UEMS European Board of Physical and Rehabilitation Medicine*, 45(3), pp. 293–9. doi: 10.2340/16501977-1105.
Lincoln, Y.S, Guba, E. . (1984) *Naturlistic Enquiry*. Sage.

Linton, S. J. and Shaw, W. S. (2011) 'Impact of psychological factors in the experience of pain.', *Physical therapy*, 91(5), pp. 700–11. doi: 10.2522/ptj.20100330.
Liu, X, Hanney WJ, Masaracchio, M, Kolber, MJ, Zhao, M, Spaulding, AC, G. M. (2018) 'Immediate Physical Therapy Initiation in Patients With Acute Low Back Pain Is Associated With a Reduction in Downstream Health Care Utilization and Costs', *Physical Therapy*, 98(5), pp. 336–347. doi: 10.1089/tmj.2010.0074.
Locke, E. A. and Latham, G. P. (2006) 'New Directions in Goal-Setting Theory', *Current directions in psychological science*, 15(5), pp. 265–268.
Louw, A. *et al.* (2011) 'The effect of neuroscience education on pain, disability, anxiety, and stress in chronic musculoskeletal pain', *Archives of Physical Medicine and Rehabilitation*. Elsevier Inc., 92(12), pp. 2041–2056. doi: 10.1016/j.apmr.2011.07.198.
Luijsterburg, P. A. J. *et al.* (2007) 'Cost-Effectiveness of Physical Therapy and General Practitioner Care for Sciatica', *Spine*, 32(18), pp. 1942–1948.
Luomajoki, H. and Moseley, G. L. (2011) 'Tactile acuity and lumbopelvic motor control in patients with back pain and healthy controls.', *British journal of sports medicine*, 45(5), pp. 437–440. doi: 10.1136/bjsm.2009.060731.
Lurie, J. D. *et al.* (2013) 'Surgical Versus Non-Operative Treatment for Lumbar Disc Herniation: Eight-Year Results for the Spine Patient Outcomes Research Trial (SPORT).', *Spine*, 39(1), pp. 3–16. doi: 10.1097/BRS.0000000000000088.
Mahn, F. *et al.* (2011) 'Sensory symptom profiles and co-morbidities in painful radiculopathy', *PLoS ONE*, 6(5), pp. 1–7. doi: 10.1371/journal.pone.0018018.
Maniadakis, N. and Gray, A. (2000) 'The economic burden of back pain in the UK', *Pain*. Elsevier, 84(1), pp. 95–103. doi: 10.1016/S0304-3959(99)00187-6.
Mansell, G., Hall, A. and Toomey, E. (2016) 'Behaviour change and self-management interventions in persistent low back pain', *Best Practice and Research: Clinical Rheumatology*, pp. 994–1002. doi: 10.1016/j.berh.2017.07.004.
Mathieson, S. *et al.* (2017) 'Trial of Pregabalin for Acute and Chronic Sciatica', *New England Journal of Medicine*, 376(12), pp. 1111–1120. doi: 10.1056/NEJMoa1614292.
Matsubara.Y *et al.* (1995) 'Serial changes on MRI in lumbar disc herniations treated conservatively', *Neuroradiology*, 37, pp. 378–383.
McGrane, N. *et al.* (2015) 'Addition of motivational interventions to exercise and traditional Physiotherapy: A review and meta-analysis', *Physiotherapy (United Kingdom)*. The Chartered Society of Physiotherapy, 101(1), pp. 1–12. doi: 10.1016/j.physio.2014.04.009.
McIntosh A, S. C. F. M. (2003) 'Barriers to patient information provision in primary care: patients' and general practitioners' experiences and expectations of information for low back pain.', *Health expectations : an international journal of public participation in health care and health policy*, 6(1), pp. 19–29. Available at:

http://www.ncbi.nlm.nih.gov/pubmed/12603625.
Mckenzie, R. (2011) *Treat Your Own Back*. 9th edn. Orthopedic Physical Therapy & Rehabilitation Products.
Meissner, K. (2011) 'The placebo effect and the autonomic nervous system: Evidence for an intimate relationship', *Philosophical Transactions of the Royal Society B: Biological Sciences*, 366(1572), pp. 1808–1817. doi: 10.1098/rstb.2010.0403.
Michie, S. *et al.* (2011) 'A refined taxonomy of behaviour change techniques to help people change their physical activity and healthy eating behaviours: the CALO-RE taxonomy.', (July 2015). doi: 10.1080/08870446.2010.540664.
Michie, S., van Stralen, M. M. and West, R. (2011) 'The behaviour change wheel: A new method for characterising and designinMichie, Susan, Maartje M. van Stralen, and Robert West. 2011. "The Behaviour Change Wheel: A New Method for Characterising and Designing Behaviour Change Interventions." Implementatio', *Implementation Science*, 6(1). doi: 10.1186/1748-5908-6-42.
Miller, R. L. and Shinn, M. (2005) 'Learning from communities: Overcoming difficulties in dissemination of prevention and promotion efforts', *American Journal of Community Psychology*, 35(3–4), pp. 169–183. doi: 10.1007/s10464-005-3395-1.
Miller, W. R. and Rollnick, S. (2013) *Motivational Interviewing*. 3rd edn. The Guilford Press, New York.
Miranda, H; Viikari-Juntura, E, Martikainen, R; Takala, E; Riihimäki, H. (2002) 'Individual Factors, Occupational Loading, and Physical Exerc... : Spine', *Spine*, 27(10), pp. 1102–1108.
Missori, P. (2015) 'Bloodletting from the Ankle Vein to Treat Sciatic Pain', *Pain Medicine*, 16, pp. 30–36.
Modell, S. (2009) 'In defence of triangulation: A critical realist approach to mixed methods research in management accounting', *Management Accounting Research*, 20(3), pp. 208–221. doi: 10.1016/j.mar.2009.04.001.
Moher, D. *et al.* (2015) 'Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement', *Systematic Reviews*, 4(1), p. 1. doi: 10.1186/2046-4053-4-1.
Mokkink, L. B. *et al.* (2010) 'The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes', *Journal of Clinical Epidemiology*. Elsevier Inc, 63(7), pp. 737–745. doi: 10.1016/j.jclinepi.2010.02.006.
Moore, G. F. *et al.* (2015) 'Process evaluation of complex interventions: Medical Research Council guidance', *Bmj*, 350(mar19 6), pp. h1258–h1258. doi: 10.1136/bmj.h1258.
Morse, J. M. *et al.* (2002) 'Verification Strategies for Establishing Reliability and Validity in Qualitative Research', *International Journal of Qualitative Methods*, 1(2), pp. 13–22. doi:

10.1177/160940690200100202.
Moseley, G L, Butler D.S, Beames T.B, G. T. . (2012) *The Graded Motor Imagery Handbook*. Adelaide: Noigroup Publications.
Moseley, G L, B. D. S. (2017) *Explain Pain Supercharged*. 1st edn. NOI Group Publications.
Moseley, G. L. (2003) 'A pain neuromatrix approach to patients with chronic pain', *Manual Therapy*, 8(3), pp. 130–140. doi: 10.1016/S1356-689X(03)00051-1.
Moseley, L. (2002) 'Combined physiotherapy and education is efficacious for chronic low back pain', *Australian Journal of Physiotherapy*. Australian Physiotherapy Association, 48(4), pp. 297–302. doi: 10.1016/S0004-9514(14)60169-0.
Das MS, Dowle P, I. R. (2018) 'Effect of Spinal Mobilization with Leg Movement as an Adjunct to Neural Mobilization and Conventional Therapy in Patients with Lumbar Radiculopathy: Randomized Controlled Trial', *Journal of Medical Science And clinical Research*, 6(4), pp. 11–19. doi: 10.18535/jmscr/v6i4.59.
Murray, C. J. L. *et al.* (2013) 'Articles UK health performance : fi ndings of the Global Burden of Disease Study 2010', *The Lancet*. Elsevier Ltd, 381(9871), pp. 997–1020. doi: 10.1016/S0140-6736(13)60355-4.
National Collaborating Centre for Primary Care (2009) 'Low back pain Early management of persistent non-specific low back pain', *National Institute for Health and Clinical Excellence*, (May).
National Insititute for Health and Care Excellence (2016) *Low back pain and sciatica in over 16s: assessment and management*, *Https://Www.Nice.Org.Uk/Guidance/Ng59*. Available at: https://www.nice.org.uk/guidance/ng59.
National Institute for Health Care and Exellence (2013) 'Neuropathic pain in adults : pharmacological management in non- specialist settings', *NICE Guideline*, (November 2013), pp. 1–36.
Ng, L. C. L. (2007) 'The effect of duration of symptoms on standard outcome measures in the surgical treatment of spinal stenosis', *European Spine Journal*, pp. 199–206. doi: 10.1007/s00586-006-0078-z.
NICE (2018) 'Weight management: lifestyle services for overweight or obese adults PH53', (May 2014). Available at: https://www.nice.org.uk/terms-and-.
Nicholas, M. K. and George, S. Z. (2011) 'Psychologically informed interventions for low back pain: an update for physical therapists.', *Physical therapy*, 91(5), pp. 765–76. doi: 10.2522/ptj.20100278.
Nijs, J. *et al.* (2011) 'How to explain central sensitization to patients with "unexplained" chronic musculoskeletal pain: Practice guidelines', *Manual Therapy*. Elsevier Ltd, 16(5), pp. 413–418. doi: 10.1016/j.math.2011.04.005.
Nijs, J., Van Houdenhove, B. and Oostendorp, R. a B. (2010) 'Recognition of central

sensitization in patients with musculoskeletal pain: Application of pain neurophysiology in manual therapy practice.', *Manual therapy*, 15(2), pp. 135–41. doi: 10.1016/j.math.2009.12.001.
O'Cathain, A. *et al.* (2015) 'Maximising the impact of qualitative research in feasibility studies for randomised controlled trials: guidance for researchers', *Pilot and Feasibility Studies*. Pilot and Feasibility Studies, 1(1), p. 32. doi: 10.1186/s40814-015-0026-y.
O'Connell, G. D., Leach, J. K. and Klineberg, E. O. (2015) 'Tissue Engineering a Biological Repair Strategy for Lumbar Disc Herniation', *BioResearch Open Access*, 4(1), pp. 431–445. doi: 10.1089/biores.2015.0034.
O'Keeffe, M. *et al.* (2016) 'What Influences Patient-Therapist Interactions in Musculoskeletal Physical Therapy? Qualitative Systematic Review and Meta-Synthesis', *Physical Therapy*, 96(5), pp. 609–622. doi: 10.2522/ptj.20150240.
O'Sullivan, P. (2005) 'Diagnosis and classification of chronic low back pain disorders: maladaptive movement and motor control impairments as underlying mechanism.', *Manual therapy*, 10(4), pp. 242–55. doi: 10.1016/j.math.2005.07.001.
O'Sullivan, P. B. *et al.* (2018) 'Cognitive Functional Therapy: An Integrated Behavioral Approach for the Targeted Management of Disabling Low Back Pain', *Phys Ther*, 98(5), pp. 408–423.
Olafsson, G. *et al.* (2017) 'A health economic lifetime treatment pathway model for low back pain in Sweden', *Journal of Medical Economics*. Informa UK Ltd., 20(12), pp. 1281–1289. doi: 10.1080/13696998.2017.1372252.
Olmarker, K., Størkson, R. and Berge, O.-G. (2002) 'Pathogenesis of sciatic pain: a study of spontaneous behavior in rats exposed to experimental disc herniation.', *Spine*, 27(12), pp. 1312–7. doi: 00007632-200206150-00013 [pii].
Ong, B. B. N. *et al.* (2011) 'Patients' own accounts of sciatica: a qualitative study.', *Spine*. Lippincott Williams & Wilkins, 36(15), pp. 1251–6. doi: 10.1097/BRS.0b013e318204f7a2.
Ong, B. N. *et al.* (2011) 'Patients' own accounts of sciatica: a qualitative study.', *Spine*, 36(15), pp. 1251–6. doi: 10.1097/BRS.0b013e318204f7a2.
Onwuegbuzie, A., J. & Johnson, B., R. (2006) 'The Validity Issue in Mixed Research Anthony J . University of South Alabama', *Research in the Schools*, 13(1), pp. 48–63.
Ostelo, R. W. J. G., Deyo, R. A., *et al.* (2008) 'Interpreting Change Scores for Pain and Functional Status in Low Back Pain', *Spine*, 33(1), pp. 90–94.
Ostelo, R. W. J. G., Hoogen, Æ. H. J. M. M. Van Den, *et al.* (2008) 'Physical therapy plus general practitioners ' care versus general practitioners ' care alone for sciatica : a randomised clinical trial with a 12-month follow-up', *European Spine Journal*, pp. 509–517. doi: 10.1007/s00586-007-0569-6.
Otoo, S.K.W, Hendrick, P, Ribeiro, D. . (2015) 'he comparative effectiveness of

advice/education compared to active physiotherapy (manual therapy and exercise) in the management of chronic non-specific low back pain', *Physical Therapy Reviews*, 20(1), pp. 16–26.
Panjabi, M. (1992) 'The Stabilizing System of the Spine Part I', *Jouurnal of Spinal Disorders*, 5(4), pp. 383–389. doi: 5:383-389.
Panjabi, M. M. (1992) 'The Stabilizing System of the Spine. Part II. Neutral Zone and INstability Hypothesis', *Journal of Spinal Disorders*, 5(4), pp. 390–7.
Panjabi, M. M. (2006) 'A hypothesis of chronic back pain: ligament subfailure injuries lead to muscle control dysfunction.', *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, 15(5), pp. 668–76. doi: 10.1007/s00586-005-0925-3.
Parry, R. (2015) 'Communicating With Patients', in Jull, G. et al. (eds) *Grieves Modern Musculoskeletal Physiotherapy*. 4th edn. Edinburgh: Elsevier, pp. 250–4.
Patrick, D. . *et al.* (1995) 'Assessing Health-Related Quality of Life in Patients with Sciatica', *Spine*, 20(17), pp. 1899–1909.
Perepletchikova, F. and Kazdin, A. E. (2005) 'Treatment integrity and therapeutic change: Issues and research recommendations', *Clinical Psychology: Science and Practice*, 12(4), pp. 365–383. doi: 10.1093/clipsy/bpi045.
Petersena G.L, Finnerup N.B, Colloca L, Amanzio M, Price D.D, Jensen T.S, V. L. (2014) 'The magnitude of nocebo effects in pain: A meta-analysis', *Pain*, 155(8), pp. 1426–1434. doi: 10.2217/nnm.12.167.Gene.
Petr, O. *et al.* (2017) 'Immediate versus Delayed Surgical Treatment of Lumbar Disc Herniation for Acute Motor Deficits: The Impact of Surgical Timing on Functional Outcome', *Spine*, (43). doi: 10.1097/BRS.0000000000002295.
Peul, W. C. *et al.* (2007) 'Surgery versus prolonged conservative treatment for sciatica', *New England Journal of Medicine*. Mass Med Soc, 356(22), p. 2245. Available at: http://content.nejm.org/cgi/content/abstract/356/22/2245.
Peul, Wilco C. *et al.* (2008) 'Improving prediction of "inevitable" surgery during non-surgical treatment of sciatica.', *Pain*, 138(3), pp. 571–6. doi: 10.1016/j.pain.2008.02.011.
Peul, Wilco C *et al.* (2008) 'Prolonged conservative care versus early surgery in patients with sciatica caused by lumbar disc herniation: two year results of a randomised controlled trial.', *BMJ (Clinical research ed.)*, 336(7657), pp. 1355–8. doi: 10.1136/bmj.a143.
Peul, W. C. and Koes, Æ. B. W. (2007) 'Effectiveness of conservative treatments for the lumbosacral radicular syndrome : a systematic review', *European Spine Journal*, pp. 881–899. doi: 10.1007/s00586-007-0367-1.
Pinheiro, M. B. *et al.* (2016) 'Symptoms of depression as a prognostic factor for low back

pain: A systematic review', *Spine Journal*. Elsevier Inc., 16(1), pp. 105–116. doi: 10.1016/j.spinee.2015.10.037.
Quon, J. A. *et al.* (2013) 'The effect of waiting time on pain intensity after elective surgical lumbar discectomy', *Spine Journal*. Elsevier Inc, 13(12), pp. 1736–1748. doi: 10.1016/j.spinee.2013.05.038.
Rhon, D. and Fritz, J. (2015) 'COMParative Early Treatment Effectiveness between physical therapy and usual care for low back pain (COMPETE): study protocol for a randomized controlled trial.', *Trials*. Trials, 16(1), p. 423. doi: 10.1186/s13063-015-0959-8.
Rhon, D., Miller, R. and Fritz, J. (2018) 'Effectiveness and Downstream Healthcare Utilization for Patients that Received Early Physical Therapy Versus Usual Care for Low Back Pain', *Spine*, 43(19), p. 1. doi: 10.1097/BRS.0000000000002619.
Ridehalgh, C., Moore, A. and Hough, A. (2016) 'The short term effects of straight leg raise neurodynamic treatment on pressure pain and vibration thresholds in individuals with spinally referred leg pain', *Manual Therapy*, 23. doi: 10.1016/j.math.2015.12.013.
Rihn, J. A. *et al.* (2011) 'Duration of Symptoms Resulting from Lumbar Disc Herniation: Effect on Treatment Outcomes', *The Journal of Bone & Joint Surgery*, 93-A(20), pp. 1906–1914. doi: 10.2106/JBJS.J.00878.
Ritchie, J. Ormston, R. (2014) 'The Applications of Qualitative Methods to Social Research', in Ritchie, J, Lewis J. Mcnaughton Nicholls, C. Ormston, R. (ed.) *Qualitative research practice. A guide for social science students and researchers*. 2nd edn. London: Sage, London, pp. 39–44.
Roland, M. and Morris, R. (1983) 'A Study of the Natural History of Low-Back Pain', *Spine (Phila Pa 1976)*, 8(2), pp. 145–50.
Rolfe, G., Mcevoy, P. and Richards, D. (2006) 'A critical realist rationale for using a combination of quantitative and qualitative methods', *Journal of Research in Nursing*, 11(1), pp. 66–78. doi: 10.1177/1744987106060898.
Rosewilliam, S., Roskell, C. A. and Pandyan, A. D. (2011) 'A systematic review and synthesis of the quantitative and qualitative evidence behind patient-centred goal setting in stroke rehabilitation', *Clinical Rehabilitation*, 25(6), pp. 501–514. doi: 10.1177/0269215510394467.
Rothwell, J. C., Julious, S. A. and Cooper, C. L. (2018) 'A study of target effect sizes in randomised controlled trials published in the Health Technology Assessment journal'. Trials, pp. 1–13. doi: 10.1186/s13063-018-2886-y.
Ryan, C. and Roberts, L. C. (2018) 'Investigations for radiculopathy: The patient perspective. A qualitative, interpretative inquiry', *Musculoskeletal Science and Practice*. Elsevier, 33(August 2017), pp. 71–76. doi: 10.1016/j.msksp.2017.11.005.
Ryan, G. W. and Bernard, H. R. (2003) 'Techniques to Identify Themes', *Field Methods*, 15(1), pp. 85–109. doi: 10.1177/1525822X02239569.

Saal, J. A., Saal, J. S. and Herzog, R. J. (1990) 'The natural history of lumbar intervertebral disc extrusions treated nonoperatively', *Spine*, 15(7), pp. 683–686. doi: 10.1097/00007632-199007000-00013.
Sabnis, A. B. and Diwan, A. D. (2014) 'The timing of surgery in lumbar disc prolapse: A systematic review', *Indian Journal of Orthopaedics*. India: Medknow Publications & Media Pvt Ltd, 48(2), pp. 127–135. doi: 10.4103/0019-5413.128740.
Schedlowski, M. and Pacheco-López, G. (2010) 'The learned immune response: Pavlov and beyond', *Brain, Behavior, and Immunity*. Elsevier Inc., 24(2), pp. 176–185. doi: 10.1016/j.bbi.2009.08.007.
Scheermesser, M. *et al.* (2012) 'A qualitative study on the role of cultural background in patients' perspectives on rehabilitation.', *BMC musculoskeletal disorders*. BioMed Central Ltd, 13(1), p. 5. doi: 10.1186/1471-2474-13-5.
Schulz, K. F. and Grimes, D. A. (2002) 'Sample size slippages in randomised trials: Exclusions and the lost and wayward', *Lancet*, 359(9308), pp. 781–785. doi: 10.1016/S0140-6736(02)07882-0.
Searle, a. *et al.* (2015) 'Exercise interventions for the treatment of chronic low back pain: A systematic review and meta-analysis of randomised controlled trials', *Clinical Rehabilitation*, 12, pp. 1155–67. doi: 10.1177/0269215515570379.
Sermeus, W. (2015) 'Modelling Process and Outcomes In Complex Interventions', in Richards, D. and Hallberg, I. R. (eds) *Complex Interventions in Health An overview of research methods*. 1st edn. Routledge, London, pp. 111–120.
Services, S. (2017) 'National Back Pain and Radicular Pain Pathway 1 Third Edition 3.0 30', *National Back Pain and Radicular Pain Pathway Report*, 3rd editio.
Shapiro, A. K. & Shapiro, E. ((1997) 'The placebo: Much ado about nothing?.', in *The Placebo Effect*. Cambridge MA: Harvard University Press, pp. 12–36.
Shriver, M. F. *et al.* (2015) 'Lumbar microdiscectomy complication rates: a systematic review and meta-analysis', *Neurosurgical focus*, 39(October), pp. 1–11. doi: 10.3171/2015.7.FOCUS15281.
Da Silva, J. T. *et al.* (2015) 'Neural mobilization promotes nerve regeneration by nerve growth factor and myelin protein zero increased after sciatic nerve injury', *Growth Factors*, 33(1), pp. 8–13. doi: 10.3109/08977194.2014.953630.
De Silva, M. J. *et al.* (2014) 'Theory of Change: A theory-driven approach to enhance the Medical Research Council's framework for complex interventions', *Trials*, 15(1). doi: 10.1186/1745-6215-15-267.
Smith, B. E., Littlewood, C. and May, S. (2014) 'An update of stabilisation exercises for low back pain : a systematic review with meta-analysis', *BMC Musculoskeletal Disorders15*, 416, pp. 1–21. doi: 10.1186/1471-2474-15-416.

Song, X. J. *et al.* (2006) 'Spinal manipulation reduces pain and hyperalgesia after lumbar intervertebral foramen inflammation in the rat', *Journal of Manipulative and Physiological Therapeutics*, 29(1), pp. 5–13. doi: 10.1016/j.jmpt.2005.10.001.
De Souza, L. and Frank, A. O. (2011) 'Patients' experiences of the impact of chronic back pain on family life and work.', *Disability and rehabilitation*, 33(4), pp. 310–8. doi: 10.3109/09638288.2010.490865.
Spencer, L. *et al.* (2003) 'Quality in Qualitative Evaluation A framework for assessing research evidence', *Cabinet office. National Centre for Social Research*.
Standering, S. (ed) (2016) 'Spinal cord and Spinal nerves: Gross anatomy', in Standering, S. (ed.) *Grays Anatomy*. 41st edn. Elsevier, p. 766.
Steffens, D. *et al.* (2015) 'Do MRI findings identify patients with low back pain or sciatica who respond better to particular interventions? A systematic review', *European Spine Journal*. doi: 10.1007/s00586-015-4195-4.
Stynes, S. *et al.* (2018) 'Clinical diagnostic model for sciatica developed in primary care patients with low back-related leg pain', *PLoS ONE*, 13(4), pp. 1–14. doi: 10.1371/journal.pone.0191852.
Stynes, S., Konstantinou, K. and Dunn, K. M. (2016) 'Classification of patients with low back-related leg pain: a systematic review', *BMC Musculoskeletal Disorders*. BMC Musculoskeletal Disorders. doi: 10.1186/s12891-016-1074-z.
Thomas, James; Harden, Angela; Oakley, Ann; Oliver, Sandy; Sutcliffe, Katy; Rees, Rebecca; Brunton, Ginny; Kavanagh, J. (2004) 'Integrating qualitative research with trials in systematic reviews', *BMJ : British Medical Journal*, 328(7446), pp. 1010–1012. doi: 10.1136/bmj.328.7446.1010.
Thomas, K. C. *et al.* (2007) 'Outcome Evaluation of Surgical and Nonsurgical Management of Lumbar Disc Protrusion Causing Radiculopathy', *Spine*, 32(13), pp. 1414–1422.
Tong, A., Sainsbury, P. and Craig, J. (2007) 'Consolidated criterio for reporting qualitative research (COREQ): a 32- item checklist for interviews and focus group', *International Journal of Qualitative in Health Care*, 19(6), pp. 349–357. doi: 10.1093/intqhc/mzm042.
Toomey, E., Matthews, J. and Hurley, D. A. (2017) 'Using mixed methods to assess fidelity of delivery and its influencing factors in a complex self-management intervention for people with osteoarthritis and low back pain', *BMJ Open*, 7(8). doi: 10.1136/bmjopen-2016-015452.
Truumees, E. (2015) 'A History of Lumbar Disc Herniation From Hippocrates to the 1990s', *Clinical Orthopaedics and Related Research*. Springer US, 473(6), pp. 1885–1895. doi: 10.1007/s11999-014-3633-7.
Tubach, F., Beauté, J. and Leclerc, A. (2004) 'Natural history and prognostic indicators of sciatica.', *Journal of clinical epidemiology*, 57(2), pp. 174–9. doi: 10.1016/S0895-4356(03)00257-9.

Vasseljen, O. *et al.* (2012) 'Effect of core stability exercises on feed-forward activation of deep abdominal muscles in chronic low back pain: a randomized controlled trial.', *Spine*, 37(13), pp. 1101–8. doi: 10.1097/BRS.0b013e318241377c.
Verbeek, J. *et al.* (2004) 'Patient Expectations of Treatment for Back Pain', *Spine*, 29(20), pp. 2309–2318. doi: 10.1097/01.brs.0000142007.38256.7f.
Verwoerd, a J. H. *et al.* (2013) 'Systematic review of prognostic factors predicting outcome in non-surgically treated patients with sciatica.', *European journal of pain (London, England)*, 17(8), pp. 1126–37. doi: 10.1002/j.1532-2149.2013.00301.x.
Villavicencio, A. T. *et al.* (2016) 'The Timing of Surgery and Symptom Resolution in Patients Undergoing Transforaminal Lumbar Interbody Fusion for Lumbar Degenerative Disk Disease and Radiculopathy', *Clin Spine Surg*, 30(6), pp. 765–769. doi: 10.1097/BSD.0000000000000392.
Vlaeyen, J. and Linton, S. (2000) 'Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art', *Pain*, 85(3), pp. 317–332.
Vlaeyen, J. W. S. and Linton, S. J. (2012) 'Fear-avoidance model of chronic musculoskeletal pain: 12 years on', *Pain*. International Association for the Study of Pain, 153(6), pp. 1144–1147. doi: 10.1016/j.pain.2011.12.009.
Vos, T. *et al.* (2016) 'Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015', *The Lancet*, 388(10053), pp. 1545–1602. doi: 10.1016/S0140-6736(16)31678-6.
Vroomen, P. C. A. J., de Krom, M. and Knottnerus, J. A. (2002) 'Predicting the outcome of sciatica at short-term follow-up.', *The British journal of general practice : the journal of the Royal College of General Practitioners*, 52(475), pp. 119–123. Available at: http://linker2.worldcat.org/?rft.institution_id=130182&spage=119&pkgName=UKPMC&issn=0960-1643&linkclass=to_article&jKey=474&issue=475&provider=NLM&date=2002-02&aulast=Vroomen%2C+Patrick+C+A+J%3B+de+Krom%2C+M+C+T+F+M%3B+Knottnerus%2C+J+A&atitle=Predicting+.
Vroomen, P., de Krom, M. and Knottnerus, J. (2002) 'Predicting the outcome of sciatica at short-term follow-up.', *The British journal of general practice : the journal of the Royal College of General Practitioners*, 52(475), pp. 119–23. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11887877.
W K Kellogg Foundation (2004) 'W.K. Kellogg Foundation Logic Model Development Guide', *Development*, p. 71.
Waddell, G. (2004) *The Back Pain Revolution*. 2nd editio. Churchill Livingstone, Edinburgh.
Wager, T. D. and Atlas, L. Y. (2015) 'The neuroscience of placebo effects: Connecting context, learning and health', *Nature Reviews Neuroscience*. Nature Publishing Group, 16(7), pp.

403–418. doi: 10.1038/nrn3976.
Walters, S. (2009) *Quality of life outcomes in clinical trials and health care-evaluation*. Chichester: Wiley-Blackwell.
Walters, S. J. *et al.* (2017) 'Recruitment and retention of participants in randomised controlled trials: A review of trials funded and published by the United Kingdom Health Technology Assessment Programme', *BMJ Open*, 7(3). doi: 10.1136/bmjopen-2016-015276.
Waltz, J. *et al.* (1993) 'Testing the Integrity of a Psychotherapy Protocol: Assessment of Adherance and Competence', *Journal of Consulting and Clinical Psychology*, 61(4), pp. 620–630.
Wand, B. M. *et al.* (2004) 'Early Intervention for the Management of Acute Low Back Pain Education , Manual Therapy , and Exercise', *Spine*, 29(21), pp. 2350–2356.
Wassenaar, M. *et al.* (2012) 'Magnetic resonance imaging for diagnosing lumbar spinal pathology in adult patients with low back pain or sciatica: A diagnostic systematic review', *European Spine Journal*, 21(2), pp. 220–227. doi: 10.1007/s00586-011-2019-8.
Weinstein, J. N. *et al.* (2008) 'Surgical versus nonoperative treatment for lumbar disc herniation: four-year results for the Spine Patient Outcomes Research Trial (SPORT).', *Spine*, 33(25), pp. 2789–800. doi: 10.1097/BRS.0b013e31818ed8f4.
Whitehead, A. L., Sully, B. G. O. and Campbell, M. J. (2014) 'Pilot and feasibility studies: Is there a difference from each other and from a randomised controlled trial?', *Contemporary Clinical Trials*. Elsevier Inc., 38(1), pp. 130–133. doi: 10.1016/j.cct.2014.04.001.
Whitehurst, M. *et al.* (2001) 'Functional mobility performance in an elderly population with lumbar spinal stenosis.', *Archives of physical medicine and rehabilitation*, 82(4), pp. 464–7. doi: 10.1053/apmr.2001.20828.
Whitfill, T. *et al.* (2010) 'Early intervention options for acute low back pain patients: A randomized clinical trial with one-year follow-up outcomes', *Journal of Occupational Rehabilitation*, 20(2), pp. 256–263. doi: 10.1007/s10926-010-9238-4.
van der Windt, D. A. *et al.* (2010) 'Physical examination for lumbar radiculopathy due to disc herniation in patients with low-back pain. [Review] [69 refs]', *Cochrane Database of Systematic Reviews*, (2), p. CD007431. doi: 10.1002/14651858.CD007431.pub2.www.cochranelibrary.com.
Winkelstein, B. a, Weinstein, J. N. and DeLeo, J. a (2002) 'The role of mechanical deformation in lumbar radiculopathy: an in vivo model.', *Spine*, 27(1), pp. 27–33. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11805632.
Wood, A. m., White, I. r. and Thompson, S. g. (2004) 'Are missing outcome data adequately handled? A review of published randomized controlled trials in major medical journals', *Clinical Trials*, 1(4), pp. 368–376. doi: 10.1191/1740774504cn032oa.
Yoshizawa H, K. S. M. T. (1995) 'Chronic Nerve Root Compression', *Spine*, 20(4), pp. 397–

407.
Zibis, A. H. *et al.* (2018) 'Great trochanter bursitis vs sciatica, a diagnostic–anatomic trap: differential diagnosis and brief review of the literature', *European Spine Journal*. Springer Berlin Heidelberg, 27(7), pp. 1509–1516. doi: 10.1007/s00586-018-5486-3.