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## The Signs and Symptoms of Discogenic Low Back Pain

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Supervisor: Walton, David, *The University of Western Ontario* Co-Supervisor: Birmingham, Trevor, *The University of Western Ontario* Joint Supervisor: Atkinson, Hayden, *The University of Western Ontario* A thesis submitted in partial fulfillment of the requirements for the Doctor of Philosophy degree in Physical Therapy © Joe J. Putos 2024

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#### Abstract

The signs and symptoms of low back pain (LBP) associated with disc herniation (DLBP) and its underlying mechanism(s) are not well supported. One theory proposes that some low back pain (LBP) is the result of a disc herniation compressing adjacent tissues innervated with nociceptors. The theory proposes that spinal manipulation (SM) and/or mobilizations (SMOB) can reduce the size and position of the herniation, and relieve pain and improve range of motion. There is no research to support or negate the theory even though clinical evidence supports its plausibility.

In this three-part study we examined clinical practices that have an anecdotal history of success. Part one consisted of surveying international clinicians in order to determine their perspectives on the signs and symptoms of DLBP. We then compared those views against published literature through a systematic review. The third part of the study used magnetic resonance imaging (MRI) technology to examine for evidence of change in order to test the hypothesis that disc morphology (i.e., the size and position) can be altered through a specific spinal movement or position. Our findings showed that clinicians who screen for DLBP appear to follow what little guidance is available however most rely instead on theory, experience, and intuition. Despite the large numbers of proposed features of DLBP, this study shows that there is a need to develop valid and reliable criteria for its diagnosis. With the exception of the centralization phenomenon, there remains no consensus on referencebased index tests that would help clinicians to identify DLBP. There remains a gap between clinical practice and evidence on the use of spinal manipulative therapy (SMT) for LBP. Currently there is no clear evidence to assist clinicians to determine the subgroup of LBP patients that respond best to SMT. This study demonstrated a reliable method for measuring changes in disc shape. Future studies should focus on understanding these responses in larger and more diverse samples, as well as their clinical relevance in patients with existing discogenic low back pain.

# Keywords

Lumbar, Low Back Pain, Discogenic Low Back Pain, Signs and Symptoms, Disc Herniation, Disc Reduction, Disc Regression, Spinal Manipulative Therapy, Spinal Manipulation, Spinal Mobilization, Disc Morphology

## Summary for Lay Audience

Low back pain is something most people experience. It may be caused by a single incident, such as lifting a heavy object. For others it may be connected to postures such as sitting in uncomfortable positions for long periods of time, or doing repetitive movements at work or at home. People who have low back pain may visit a physiotherapist, a chiropractor or another medical clinician to try to get a diagnosis and treatment for the pain. The clinician will ask questions about symptoms, how they started, what makes them worse or what provides relief. They will then do a physical examination involving different tests and procedures. Currently, there are few guidelines to help clinicians determine the exact cause of low back pain. Our study surveyed clinicians to find out how they determine what is the problem with people suffering low back pain and how they go about treating the symptoms. We then compared what clinicians told us with what the latest research has to say about low back pain. We found some areas of agreement between the literature and what clinicians told us. We suggest that clinicians and researchers work together to develop better guidelines for examining and treating patients with low back pain.

## **Co-Authorship Statement**

Joseph Putos, PhD Candidate

David Walton, Primary Supervisor

Trevor Birmingham, Co-Supervisor

Hayden Atkinson, Data Analysis, Results, Chapter 5

Stephen Ecklin, Data Analysis, Chapter 5

Swati Mehta, 2<sup>nd</sup> Reviewer, Chapter 4

Paul Fenton, Advisory Committee Member

Stuart McGill, Advisory Committee Member

## Acknowledgments

"All pain has a source. Treatment must be directed to the source of pain. It must be the correct treatment." Dr. James Cyriax, M.D.

This dissertation is dedicated to Anthoulis (Tony) Constantinides, Physical Therapist, Fellow of the Society of Orthopedic Medicine (United Kingdom). Anthoulis is a physical therapist who practices in Cyprus. He was trained by Dr. James Cyriax. I met Tony in 1983 when I was a physical therapy student on placement at Kingston General Hospital. He was there completing an internship in order to become licensed to practice in Ontario. It was Anthoulis who introduced me to Dr. James Cyriax and the field of orthopedic medicine. Tony is a passionate clinician and a very good musculoskeletal diagnostician. From him I learned that in order to be an effective clinician, i.e., someone capable of helping patients who present to you, you had to have a passion for reading, studying, researching and reflection. You must remain open to other opinions, discuss and acknowledge what you don't know and, seek out answers to clinical questions no matter where that takes you. By doing so, you increase your chances of gaining more knowledge and as a result become a more effective and useful clinician.

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"Cervantes said, the journey is better than the inn." I like that. I think that is. Sometimes when you get there it's almost a letdown but it's getting there that's the fun. As a basketball coach at UCLA, I liked our practices to be the journey and the game would be the end result....There again, it's getting the players to get self-satisfaction, knowing they made the effort to do the best of which they are capable." Coach John Wooden, UCLA

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### Preface

Low back pain (LBP) continues to be a major health issue with little forward progress at unravelling the underlying mechanisms despite a great deal of effort made by clinicians and basic experimental scientists in fields such as anatomy, biology, biomechanics, surgery, epidemiology and engineering. Identifying practical, feasible, timely and cost-effective treatments could lead to the advancement of the knowledge base around LBP and so a change in the LBP paradigm is in order. This does not necessarily mean a new research direction. Instead, we suggest examining and collating existing knowledge and experiences from clinicians as well as data from basic science studies on the biology and non-linear mechanical behaviours of intervertebral discs. This could generate a number of workable and testable hypotheses which can be assembled and pursued with the collaboration of experimental science.

## Chapter 1

## 1 Introduction

#### 1.1 Purpose of the Dissertation

This dissertation was motivated by my clinical experiences as a physical therapist and a theory proposed by Dr. James Cyriax M.D. more than seventy years ago that some low back pain (LBP) was the result of herniated annular disc material compressing adjacent tissues innervated with nociceptors (Cyriax, 1950). The theory suggested that when LBP is associated with a disc herniation, spinal manipulation (SM) and/or mobilizations (SMOB) could reduce the size and position of the herniation, relieve pain and improve lumbar range of motion. While acknowledged as a clinical entity, there remains no research to support or negate the theory advocated by Cyriax and others, even though clinical evidence supports its plausibility. To date, the signs and symptoms of LBP associated with disc herniation and the underlying mechanism(s) are not well supported or even acknowledged as a potential source of LBP in recent literature (Swanson & Creighton, 2020; R. D. Vining et al., 2019; Zhao et al., 2019).

Consider the case of a patient presenting to a clinician with acute, central or unilateral LBP. A detailed history is taken followed by a thorough physical examination. A provisional diagnosis of mechanical LBP attributable to a single source is made. Treatment is implemented by the clinician, consisting of several therapeutic maneuvers. These may include single or repeated manipulation(s) or sustained and repeated mobilization(s). Within the same session the patient reports significant improvements in pain and lumbar movements. The patient is then instructed on how to maintain the improvements to prevent a recurrence and is scheduled for a follow up appointment within a short time period.

The rapid improvements in signs and symptoms are not adequately accounted for by some of the LBP theories that have been advanced, such as the psychosocial elements of the biopsychosocial model (Mescouto et al., 2022) or by muscular reflexogenic or neurophysiological effects (Goodwin et al., 2021; Gyer et al., 2019). A more plausible

explanation is that the symptoms and signs reflect a biomechanical disorder that improves quickly with specific therapeutic movements targeting the individual's unique clinical presentation (Ikeda & McGill, 2012).

One proposed mechanism to explain the rapid change in symptoms and signs is that an abnormally displaced nucleus pulposus has been reduced by the specific maneuver or series of maneuvers, to a more central position within the intervertebral disc (Chan et al., 2013). This is similar to Cyriax's theory. Both propose that the changes are the result of specific mechanical loading strategies used to reduce a herniation responsible for the symptoms. For this dissertation, pain arising from a symptomatic disc herniation (whether based on the nuclear or annular theory) is referred to as discogenic low back pain (DLBP).

A useful approach to advance the knowledge base around the diagnostic criteria and underlying mechanism(s) of DLBP would be to examine clinical practices that have at least an anecdotal history of success in a subgroup of LBP patients. We set out by first investigating the perspectives of international clinicians on DLBP and then compared those views against published literature through a systematic review. We concluded by testing the hypothesis that disc morphology (i.e., the size and position) can be altered through a specific spinal movement or position by examining for evidence of change using magnetic resonance imaging (MRI) technology.

#### 1.2 Objectives

1. to survey international orthopedic clinicians about their perspectives of the signs and symptoms of DLBP;

2. to conduct a systematic review of the literature to compare clinicians' perspectives from the survey against published research;

3. to investigate the effects of a spinal position commonly used by clinicians to treat low back pain (LBP) on the morphology (i.e., the size and position) of lumbar discs in healthy participants using MRI;

4. to review the literature on the macro and micro anatomy of the intervertebral disc as it relates to its biomechanical response to loads;

5. to propose short-and-medium term goals for future research directions on DLBP

#### 1.3 Scope, Assumptions and Exclusions

This study is part of a larger research program focused on investigating DLBP associated with contained reducible lumbar disc herniations in symptomatic participants (Chan et al., 2013; Petersen et al., 2003).

#### **1.3.1** Assumptions

- The intervertebral disc (IVD) is one source of LBP. Current explanations for DLBP as a result of internal disc derangement (IDD) alone are inadequate to explain clinicians' experiences when treating LBP patients (Kim et al., 2009; Ract et al., 2015; Zhou & Abdi, 2006). For any noxious stimulus to result in discogenic pain, there must be stimulation of nerves in the endplate or the peri-annular region (Fagan et al., 2003);
- The normal IVD is a poorly innervated structure supplied by sensory (mainly nociceptive) and postganglionic sympathetic (vasomotor efferents) nerve fibers (Fagan et al., 2003; García-Cosamalón et al., 2010; Groh et al., 2021). See Figure 1;
- IVD's are biological tissues that display non-linear behaviours in response to mechanical loads (Bezci et al., 2020; Kulak, Belytschko & Schultz, 1976; Marini et al., 2015; Shirazi-adl et al., 1984);
- IVD's can herniate and those same herniations can regress spontaneously (Amin et al., 2017; Autio et al., 2006; Awad & Moskovich, 2006; Chiu et al., 2015; Son et al., 2017; Y. Wang et al., 2020);
- LBP and/or radicular symptoms can be the result of IVD herniations compressing adjacent tissues innervated with nociceptors such as the posterior longitudinal ligament, ventral dura mater and dural nerve root sleeves (Cheung et al., 2009; Cuchanski et al., 2011; Daghighi et al., 2014; Geers et al., 2003; L. G. F. Giles, 2000; Jinkins, 2004; Lee et al., 2018; Ohtori et al., 2015; Sekine et al., 2001; Urits et al., 2019).

#### **1.3.2** Exclusions

This dissertation does not include DLBP as a result of disc sequestrations, infections, tumours, fractures, spinal stenosis, synovial cysts, facet joint derangements, end plate failures or osteophytes.



Figure 1 Schematic representation of the innervation of the intervertebral disc (IVD). Nociceptive sensory fibers originate in the dorsal root ganglia (DRGs) (red) and postganglionic sensory nerve fibers (blue) enter the outer part of the annulus fibrosus. Nerves in the IVD arise from the sinuvertebral nerve, from spinal nerves or from grey rami communicantes. In addition, mechanical nerve fibers originate in the DRGs and coming from the anterior and posterior longitudinal ligament innervate the external layers of the annulus fibrosus of the IVD. (*Reproduced with permission from García-Cosamalón, J., Del Valle, M. E., Calavia, M. G., García-Suárez, O., López-Muñiz, A., Otero, J., & Vega, J. A. (2010). Intervertebral disc, sensory nerves and neurotrophins: who is who in discogenic pain? Journal of anatomy, 217(1), 1-15).* 

# 1.4 Why This Research is Important and What Contribution Does it Make

Currently the diagnosis, treatment and underlying mechanism(s) of LBP remain largely without consensus and supportive evidence. The lack of an empirical evidence base for diagnostic criteria and relevant therapeutic interventions continues to leave clinicians in a quandary (Deane & McGregor, 2016; Ford & Hahne, 2013; Hallegraeff et al., 2009; Keter et al., 2023; Slater et al., 2012).

LBP is commonly believed to be self-limiting in most cases, however, data show that many individuals experience recurrences. (Hoy et al., 2010; Simon et al., 2014). Additionally,10 to 15 percent of patients with acute LBP develop chronic symptoms (Balagué et al., 2012). A better understanding of underlying mechanisms is a prerequisite for reducing recurrences through preventive means and subsequently, lowering the number of patients who go on to develop chronic LBP. Physiologically there is a strong rationale for treating patients with acute LBP. Because afferent inputs can provoke alterations withing the central nervous system leading to central sensitization, treatment of acute conditions should be directed to abolishing both peripheral and central sensitization (Woolf, 1991).

Clinically, with the exception of LBP with radicular symptoms, there are currently no widely-accepted diagnostic criteria (i.e. index tests) supported by reference standards available to clinicians to make a differential diagnosis in LBP patients (Fang et al., 2017; Urits et al., 2019; Vining et al., 2019). For clinicians, establishing an accurate diagnosis with a patient presenting with LBP is made more difficult because of the considerable overlap of pain patterns from potentially different sources all of which are innervated by nociceptors. These include the IVD, facet joints, the sacroiliac joints (SIJ), the hip joints, various ligaments, paravertebral musculature, fascia and internal organs. Some recommended reference standards such as invasive IVD provocation procedures or diagnostic blocks, are not suitable or available for routine use by clinicians (Han et al., 2023). Hence, there is a need for simple reference-based index tests so that clinicians may more accurately determine a diagnosis in LBP patients and then select appropriate treatment options based on the individual patient.

#### 1.5 Terms and Definitions

#### 1.5.1 Low Back Pain

Although the definition of LBP remains without consensus, the most recent Global Burden of Disease studies report defines LBP as pain in the area on the posterior aspect of the body from the lower margin of the twelfth ribs to the lower gluteal folds with or without pain referred into one or both lower limbs that lasts for at least one day (Ferreira et al., 2023). Acute LBP is a period of pain in the lower back lasting for more than 24 hours, preceded and followed by a period of at least one month without low back pain (De Vet et al., 2002; Ferreira et al., 2023).

LBP is typically divided into 3 broad categories. LBP from serious pathology, LBP accompanied with radicular symptoms and non-specific low back pain (NSLBP). The first two categories account for 3 to 5 percent of all LBP cases depending on the author (Gau et al., 2020; J. T. Martin et al., 2022). They may be the result of specific pathologies or underlying systemic disease including infections, tumors, fractures, spinal stenosis, nerve root compression producing radicular symptoms, synovial cysts, facet joint derangements, end plate failures and osteophytes (Atlas & Deyo, 2001; Bardin et al., 2017; Elsharkawy et al., 2019). The third category, NSLBP, for which there is no attributable cause, accounts for up to 90 per cent of LBP cases (Balagué et al., 2012; Ferreira et al., 2023; Koes et al., 2006; Zhang et al., 2009).

#### 1.5.2 Discogenic Low Back Pain

DLBP is often defined as pain initiated from nociceptive activity originating in nerves innervating a dysfunctional or distorted IVD, with a mechanism due to internal disc disruption (IDD) (Bogduk et al., 2013; Fujii et al., 2019; Peng, 2013; Simon et al., 2014; Swanson & Creighton, 2020; Vining et al., 2019; Zhao et al., 2019). To date there remains no widely accepted standard for its definition (Fujii et al., 2019) or its diagnosis. Some authors have attributed DLBP to disc herniation.

#### **1.5.3** Intervertebral Disc Herniations

IVD herniation refers to a localized displacement of nucleus, cartilage, fragmented apophyseal bone, or fragmented annular tissue beyond the IVD space (Fardon et al., 2014; Son et al., 2017). The interspace is defined, cranial and caudad, by the vertebral body endplates (Fardon et al., 2014). References to herniations in this dissertation refer to focal or broad-based protrusions not extrusions or sequestrations.

Herniations are further classified based on the shape of the displaced material and whether they are contained or uncontained. If the herniated material is covered by a thin residual layer of the outer annulus it is "contained" (Castro-Mateos et al., 2014). If not covered, it is "uncontained." (Amin et al., 2017; Bartynski & Rothfus, 2012). A number of different grading systems are used to describe the distribution of herniations in both two and three dimensions. They be central, paracentral, posterolateral, lateral or anterior herniations (Daghighi et al., 2014; Ehrler et al., 2016; Halldin et al., 2009). See Figure 3. A contained herniation that is reversible by specific mechanical loading strategies is referred to as reducible (Petersen et al., 2003; Surkitt et al., 2016). A contained herniation that is not reducible is referred to as irreducible or non-reducible (Chan et al., 2013; Chan et al., 2017; Petersen et al., 2003).

Protrusions are contained herniated IVD material where the distance between the edges of the IVD material beyond the IVD space is less than the distance between the edges of the base when measured in the same plane. Protrusions may be focal or broad based (Amin et al., 2017; Bartynski & Rothfus, 2012). See Figure 2.

Extrusions are herniated IVD material where any one distance between the edges of the IVD material beyond the IVD space is greater than the distance between the edges of the base when measured in the same plane, or when no continuity exists between the IVD material beyond the IVD space and that within the IVD space (Amin et al., 2017; Bartynski & Rothfus, 2012, p. E100). See Figure 2.

Sequestrations are the severest form of IVD herniations. Sequestered IVDs are known as free fragments of IVD tissue that are no longer attached to their respective intervertebral IVD (Macki et al., 2014).



Figure 2. Classification of the five subtypes of disc herniations in the lumbar spine. (*Reproduced with permission from M. Macki et al. / Clinical Neurology and Neurosurgery 120 (2014) 136–141 137).* 



Figure 3. Axial T2-weighted lumbar MRI slice showing the anatomic zones for classifying the location of disc herniation according to the combined task forces of the North American Spine Society, the American Society of Spine Radiology and the American Society of Neuroradiology. This patient has a paracentral herniation (b), a = central; b = paracentral; c = foraminal; d = extraforaminal (*Reproduced with permission from Ehrler, M., Peterson, C., Leemann, S., Schmid, C., Anklin, B., & Humphreys, B. K. (2016). Symptomatic, MRI confirmed, lumbar disc Herniations: a comparison of outcomes depending on the type and anatomical axial location of the* 

hernia in patients treated with high-velocity, low-amplitude spinal manipulation. Journal of manipulative and physiological therapeutics, 39(3), 192-199.

#### 1.5.4 Centralization

Centralization, also referred to as the centralization phenomenon (CP), is defined as progressive resolution, reduction or retreat of pain toward the midline (May & Aina, 2012; Werneke et al., 2008). It was first described by New Zealand physical therapist Robin McKenzie, who developed a method of assessment and treatment for spinal and extremity pain (Wetzel & Donelson, 2003). See Figures 3 and 4.



Figure 4. Centralization is the progressive retreat of the most distal extent of referred or radicular pain toward or to the lumbar midline. Peripheralization is the oppositely directed phenomenon. During this standardized mechanical assessment the most common direction of lumbar testing that centralizes pain (directional preference) is extension, whereas a smaller group will centralize only with laterally directed movements (sidegliding). It is a much smaller group whose pain will centralize and abolish with lumbar flexion only. (*Reproduced with permission from Donelson, R., Aprill, C., Medcalf, R., & Grant, W. (1997). A prospective study of centralization of lumbar and referred pain: a predictor of symptomatic discs and annular competence. Spine, 22(10), 1115-1122).* 

The mechanism underlying this response is described as a reduction of a painful, abnormally displaced nucleus pulposus, to a more central and less pain-provoking position within the lumbar IVD (Chan et al., 2013). Clinical observations have shown that full end range movement is often necessary to achieve complete centralization
(Horton, 2010). Furthermore, combined positions or movements, or interventions such as specific mobilizations, may be needed to facilitate end range to obtain centralization (Donelson et al., 1997; Horton, 2010). See Figure 4.



Figure 5. Commonly used end-range lumbar test movements performed repeatedly in both loaded and unloaded positions will determine the presence of a directional preference based on whether referred pain can be centralized or midline pain abolished. A, Flexion while standing, B, Extension while standing, C, Side-gliding while standing, D, Side-gliding with overpressure, E, Extension while lying, F, Flexion while lying, and G, Flexion/rotation with overpressure. (*Reproduced with permission from Donelson, R., Aprill, C., Medcalf, R., & Grant, W. (1997). A prospective study of centralization of lumbar and referred pain: a predictor of symptomatic discs and annular competence. Spine, 22(10), 1115-1122).* 

#### 1.5.5 Intervertebral Disc Regression/Reduction

Some types of lumbar IVD herniations have shown to regress, that is, reduce in size and position over time (Altun & Yüksel, 2017; Autio et al., 2006; Chiu et al., 2015; Haro, 2014; Masui et al., 2005; Teplick & Haskin, 1986; Wang et al., 2020; Zou et al., 2023). See Figures 5 and 6. The literature reports IVD bulges, protrusions, extrusions and even sequestrations, confirmed by CT or MRI or myelogram, at all lumbar levels, regress at different rates and proportions (Chiu et al., 2015).

Several mechanisms have been proposed to explain IVD regression including, dehydration and shrinkage (Autio et al., 2006; Martínez-Quiñones et al., 2010; Yang et al., 2016), resorption (Çitişli et al., 2015; Haro, 2014; Martínez-Quiñones et al., 2010), retraction (Teplick & Haskin, 1986), enzymatic degradation and phagocytosis of cartilaginous tissue (Kim et al., 2013; Yang et al., 2016).

IVD regression and/or resorption may be a plausible explanation for the relief of NSLPB in some patients. Further support for this comes from studies of conservative interventions including traction and spinal mobilizations or manipulations which have shown association with IVD regression (Guinto et al., 1984; Ozturk et al., 2006; Teplick & Haskin, 1986).



Figure 6. Sequential magnetic resonance imaging of a 66-year-old man demonstrating resorption of the herniated disc. from, Haro, H. (2014). current status of diagnosis and treatment. Journal of Orthopaedic Science, 19(4), 515-520. Reproduced without modification, under a Creative Commons Attribution-NonCommercial-No Derivatives License (CC BY NC ND). https://creativecommons.org/licenses/by-nc-nd/4.0/



Figure 7. The sagittal MRI views of an LDH patient before (A) and after treatment (B). The patient was free of symptoms at 7th month after treatment. The axial MRI views of the same patient before (A) and after treatment (B). *Reproduced without modification from, Altun, I., & Yüksel, K. Z. (2017). Lumbar herniated disc: spontaneous regression. The Korean Journal of Pain, 30(1), 44-50.* an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<u>http://creativecommons.org/licenses/by-nc/4.0/</u>

#### **1.5.6** Spinal Manipulative Therapy

Spinal manipulative therapy (SMT) refers to a group of manual procedures used by clinicians in various disciplines to treat LBP. These range from repetitive oscillations of joints and high velocity low amplitude thrusts to various sorts of soft tissue massage which are neither directed at, nor necessarily involve, joint movement (Zusman, 1986). SMT is typically differentiated by the profession performing it, including physiotherapy, osteopathy, chiropractic, and physicians trained in orthopedic medicine (Zusman, 1986). Each profession has a theoretical body of knowledge peculiar to it, which is biased towards substantiating various hypothesized effects of SMT, as well as the mechanisms believed to be responsible for these effects (Zusman, 1986).

#### **1.5.7** Spinal Manipulation

Spinal manipulation (SM) is a form of spinal manipulative therapy SMT. It is described as, low amplitude, high velocity passive movements within, at the limit of or slightly beyond the passive range of joint motion (Bronfort et al., 2008; Ernst & Canter, 2006; McCarthy et al., 2015). There are many variations of SM, broadly categorized as either short-lever (i.e., the thrust is applied directly to the spine, or long-lever, in which force is not provided directly to the spine, but from rotation of the patient's thigh and/or leg (Bronfort et al., 2012). See Figure 7. While some positive clinical benefits have been demonstrated with SM, the underlying mechanism(s) remain poorly developed. Selection of the appropriate maneuver(s) continues to depend on the judgment and expertise of the clinician based on their interpretation of the patient's signs and symptoms (Kuo, Loh, 1987).



Figure 8. Side-posture 'rotational' lumbar manipulation. (*Reproduced with permission, from Evans, D. W. (2010).* Why do spinal manipulation techniques take the form they do? Towards a general model of spinal manipulation. Manual therapy, 15(3), 212-219).

## 1.5.8 Spinal Mobilization

Spinal mobilizations (SMOB) are defined as low velocity passive oscillatory movements within the passive range of joint motion that does not involve a thrust (Bronfort et al., 2012; Lascurain-Aguirrebeña et al., 2015). They can be labelled using different descriptive terms, take any number of forms and can vary in directionality. SMOB's have been shown to reduce symptoms in some LBP subgroups although the mechanism(s) of action are not clear (Lascurain-Aguirrebeña et al., 2015). As per SM, selection of the appropriate mobilization(s) depends on the clinician's judgment and expertise based on their interpretation of the patient's signs and symptoms (Kuo & Loh, 1987).

## 1.5.9 Nonlinear Behaviour

Biological tissues such as IVD's are complex heterogeneous structures that demonstrate nonlinear behaviours, i.e., behaviors that are difficult to predict. The elastic response of the annulus fibrosus (AF) to mechanical loads is very nonlinear, largely dependent on its structural architecture, specifically its collagen fibers (Kulak, Belytschko & Schultz, 1976; Marini et al., 2015; Shirazi-adl et al., 1984; Sun & Mi, 2023). Differences in response behaviours have been demonstrated in finite element studies of non-degenerated and degenerated IVD models (Bashkuev et al., 2018, 2020; Park et al., 2013). The large variability in the structural architecture of the AF among individuals in both nondegenerated and degenerated cases has implications for unravelling the underlying mechanism(s) of DLBP as well as for clinicians examining and treating patients with DLBP (Kulak, Belytschko & Schultz, 1976).

# 1.6 Background

A majority of people of all ages will experience low back pain (LBP) over their lifetime. Low back pain (LBP) is the primary cause of years lived with disability globally (Ferreira et al., 2023). The lifetime prevalence of NSLBP is reported to be as high as 84 - 90%, and the prevalence of chronic low back pain (CLBP) is about 23%, with 11–12% of the population being disabled by low back pain (Allegri et al., 2016; Balagué et al., 2012).

Recent high-impact systematic reviews indicate considerable gaps in knowledge about LBP (Buchbinder et al., 2020). The underlying mechanism(s) responsible for the symptoms of NSLBP are not yet well understood although various authors have offered theories. These include mechanical, inflammatory, biomechanical, neurovascular, motor and psychological factors, either acting alone or more often, in conjunction with each other (Balagué et al., 2012; Bogduk, 2012; Cavanaugh et al., 1997; Cox, 2012; Cyriax, 1984; Giles & Crawford, 1997; Hallegraeff et al., 2009; Huijbregts, 1998; Krämer, 2010; McCarthy et al., 2015; McGill, 2007; Mescouto et al., 2022; Yang & King, 1984).

Dr. James Cyriax, an English physician, had proffered a theory that conceptualized some LBP as being due to mechanical deformation of innervated paraspinal tissues such as the PLL and the ventral dura mater (VDM) both of which are highly innervated with nociceptors. Cyriax was not the first to propose this mechanism as a cause of LBP. Posterior extrusion of an IVD was identified as a clinical entity associated with acute low back pain as early as 1911 (Goldthwait, 1911).

The early purely biomechanical focus on structural pathoanatomy was insufficient to explain the symptoms of NSLBP, especially in the absence of an identifiable lesion. The technology of the time was insufficient to fully explore this theory. Subsequently, focus shifted from mechanical explanations of LBP to biopsychosocial, neurophysiologic, immune, inflammatory, or even genetic causes (Cavanaugh et al., 1997; Crock, 1986; MacGregor et al., 2004; Mescouto et al., 2022; Twomey, 1992).

This abandonment of mechanical theories may however have been premature, as treatment interventions based on Cyriax's early teachings (Cyriax, 1945, 1950) appeared to be beneficial for at least a subgroup of people with NSLBP (Yates et al., 1969). Subgrouping patients such as those with DLBP based on signs and symptoms as a means of improving treatment outcomes has been recommended by researchers and clinicians (Brennan et al., 2006; Chan et al., 2013; Flynn et al., 2002; Han et al., 2023).

To this end we have chosen to examine clinical practices that have at least an anecdotal history of success in a subgroup of patients with LBP, drawing on tacit knowledge of clinicians to generate new research directions.

# 1.7 Brief Review of the Literature on Discogenic Low Back Pain

Despite the long history in research and practice, DLBP is not well-represented in this discourse (Han et al., 2023). Across the published evidence we find little consensus on the definition of DLBP or its diagnostic criteria (Fujii et al., 2019; Lorio et al., 2023).

While DLBP is often reported as a result of internal disc disruption (IDD), it is common to find only minimal internal disc changes or disruption in patients diagnosed with DLBP (Kim et al., 2009; Ract et al., 2015; Zhou & Abdi, 2006). Additionally, the high rate of false positive results with imaging techniques including MRI, CT-scan or discography as well as that by age 60, the frequency of symptomatic periods drops quickly, challenges the notion that IDD is the primary underlying mechanism for DLBP (Bisschop & Van Ooteghem, 2003). Therefore, there are likely additional mechanisms involving IVDs that may produce LBP in some patients (Brock et al., 1992; Lipson, 1988; Moore et al., 1996; Rajasekaran et al., 2013).

There is adequate literature supporting IVD compression of a nerve sleeve and its root producing radiculopathy symptoms and signs or the more severe effects of spinal cord compression (Beattie et al., 2000; He et al., 2018; Kobayashi et al., 2004; Kreiner et al., 2014; Rhee, Schaufele & Abdu, 2006; Smyth & Wright, 1958; Verwoerd et al., 2014). There is scant literature on the symptoms and signs caused by IVD deformations that do not impact nerve roots or the spinal cord but are theorized to be a mechanism for some

NSLBP. It is not unreasonable to propose such deformations compressing adjacent tissues such as the posterior longitudinal ligament and the ventral dura mater may produce the symptoms of NSLBP.

# 1.8 The Meaningful Gap in the Literature on Discogenic Low Back Pain

The lack of evidence-informed diagnostic criteria for DLBP means patients presenting to clinicians may be misdiagnosed and under-represented in data on incidence and prevalence. Treatments based on misdiagnosis are unlikely to be beneficial. Therefore, there is a need to identify simple diagnostic tests to help clinicians to identify the nociceptive sources of low back pain such as DLBP (Han et al., 2023).

Studies of DLBP seldom include outcome data on lumbar range of motion (ROM) pre and post treatment and whether the movements are limited or full and painful or painless even though painful lumbar movements are typically the initiating reason a patient will seek the help of a clinician. The value of lumbar ROM as an outcome is overlooked. Improvements in ROM have been paired with important reduction in pain and disability scores (Passmore & Descarreaux, 2012).

There remains a limited understanding of DLBP, its pain mechanisms and a lack of reference supported diagnostic criteria. Aside from an expert panel consensus report that DLBP, as a subgroup of LBP, has good concurrent and predictive validity, the clinical features of DLBP have not been validated (Chan et al., 2013). Diagnostic patterns of signs and symptoms from history and physical examination data may help clinicians in unravelling the source of pain and be useful in directing treatment at the painful structure (Petersen et al., 2017).

At present MRI is not useful in detecting IVD herniations compressing the anterior aspect of the PLL in symptomatic versus asymptomatic patients. Studies do refer to the PLL having a role in lumbar IVD herniation (Kilitci et al., 2021; Martin et al., 2002) but there is a lack of evidence and data on the compressive effects of IVD herniations against the anterior aspect of the PLL.

# 1.9 Review of the Anatomy of Structures Involved with Discogenic Low Back

Primary support for the theory of DLBP associated with IVD herniations is based on the anatomy of several key structures that are involved with DLBP associated with IVD herniations impacting adjacent tissues innervated with nociceptors. A comprehensive report on the IVD's structure and function is beyond the scope of this dissertation.

#### 1.9.1 The Intervertebral Disc

The IVD is a heterogeneous, viscoelastic structure that provides spinal stability and mobility while bearing large mechanical loads (Bezci et al., 2020; Broberg, 1983). It is composed of the nucleus pulposus (NP), the end plate cartilage (EPC) and the annulus fibrosis (AF). The structural characteristics of an IVD determines it's behavior to loads (Meakin & Hukins, 2000).

#### **1.9.2** Nucleus Pulposus

The NP consists of a three-dimensional network of collagen fibers enmeshed in a mucoprotein gel that contains various mucopolysaccharides (Smith & Fazzalari, 2009). The proteoglycans of the center absorb and disperse forces allowing the IVD to act as a shock absorber for axial forces (Smith & Fazzalari, 2009). However, it is not the primary load-bearing component. The NP only redistributes applied loads to the more rigid component of the IVD, the AF (Ghannam et al., 2017).

#### 1.9.3 The End Plate Cartilage

The EPC is mainly a hyaline cartilage that forms a 0.5 mm layer separating the proper IVD from adjacent vertebral bodies. The EPC plays a central role in maintaining IVD and vertebral health (Lotz et al., 2013). Its thickness ranges between 0.1 mm and 1.6 mm, greatest adjacent to the nucleus and inner annulus and absent in the outer annulus. It is weakly attached to the cortical bones of adjacent vertebral bodies and strongly attached to the IVD though the AF (Ghannam et al., 2017).

#### 1.9.4 The Annulus Fibrosus

The AF is a complex structure made up of strong fibrocartilaginous tissue that forms the outer ring of the IVD (Vergari et al., 2017). It is subdivided into an outer, middle and inner annulus. The annulus contains the radial bulging of the central nucleus pulposus and distends and rotates, in order to facilitate joint mobility (Briar, 2021; Smith & Fazzalari, 2009; Wagner & Lotz, 2004). It is not a homogeneous structure. The inner AF is cartilaginous with chondrocyte-like cells producing type II collagen and proteoglycans. The outer includes fibroblastic-like cells which produce a predominantly type I collagenrich extracellular matrix (ECM) (Empere et al., 2023). The posterior AF is thin, nearly half as thick as the lateral and anterior AF (Lundon & Bolton, 2001). Collagen fibers are interlaced in the front, left, and right parts of the AF but there are no interlaced fibers near the middle of the posterior AF (Zhu et al., 2008). This variation in collagen fiber content is an inherent weakness and may predispose the posterior parts of the AF to herniate as a result of the various mechanical loads the AF is subjected to (Ghannam et al., 2017).

Elastin makes up approximately 1.7% of the dry weight of both the annulus and the nucleus of human IVDs (Nakagawa et al., 1994). The nonlinear biomechanical responses of the IVD are partially attributable to the distribution pattern of elastic fibers which also play a key role in the rapid recovery of IVD shape after loading (Holzapfel et al., 2005; Z. Sun & Mi, 2023; J. Yu et al., 2002). See Figure 8.

Annular tears, as a result of injury to the IVD, can be seen on MR images and are likely early evidence of IVD degeneration (Gallucci et al., 2011). Annular tears are found in both symptomatic and asymptomatic persons and may or may not be associated with herniations (Milette et al., 1999; Munter et al., 2002). Three types of tears have been identified, including rim lesions, (radial tears at the periphery of the annulus adjacent to the endplates), circumferential tears (ruptures between the annular lamellae (Goel et al., 1995) and radial tears (tears perpendicular to the end-plates and which cut through the annulus layers (Green et al., 2014). The tears can create a channel for migration of the nucleus pulposus out towards the periphery of the disc.



Figure 9. (a) A schematic representation of the intervertebral disc model. (b) an inset of (a) detailing the interstitial fluids and non-fibrillar matrix of the posterolateral region of the annulus fibrosus, (c) a typical crossply arrangement of the of the orientation collagen fibers, and (d) a representative spatial distribution of elastic fibers embedded in the posterolateral annulus fibrosus shown in (a) and (b). In (a), the anterior and posterolateral regions of the annulus fibrosus were colored in gray. Both regions are composed of several inner, middle and outer lamellae. In the right of (c), a red inter-lamella sandwiched by the blue and pink lamellae is shown. The angular coordinate indicates the orientation of collagen fibers and illustrates the principal direction of an elastic fiber family, respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.) (*Reproduced with permission from, Sun, Z., & Mi, C. (2023). On the identification of the ultra-structural organization of elastic fibers and their effects on the integrity of annulus fibrosus. Journal of Biomechanics, 157, 111728).* 

#### 1.9.5 Microstructure of the Annulus Fibrosus – The Lamellae

The mechanical behavior of the AF is determined essentially by the tensile properties of the lamellae, their fiber orientations, and the regional variation of these (Herod & Veres, 2020; Holzapfel et al., 2005). The lamellar structure is much more complex than traditionally described. See Figure 9.



Fig. 2. The intervertebral disk. (From Levin KH, Covington EC, Devereaux MW, et al. Neck and low back pain. Continuum (NY) 2001;7:11; with permission.)



For L2-3 and L5-5 IVDs, the laminate structure is not uniform and more complex than typically described (Marchand & Ahmed, 1990). See Figures 10 and 11. Similar findings have been reported in the L4-5 IVD (Tsuji et al., 1993). See Figures 12 and 13. These reports reveal the lamellae to be discontinuous, in other words, they are not rings running around the entire IVD, but rather bands connecting adjacent endplates (Langlais et al., 2019). This pre-existing non uniformity in lamellar architecture may be symptomless but also may facilitate IVD herniation under certain loading conditions (Brinckmann & Porter, 1994). The many interruptions in the lamellar structure that appear more frequently in the posterolateral and posterior regions offer a plausible explanation for the finding that IVD protrusions are commonly associated with posterior and posterolateral directions (Marchand & Ahmed, 1990; Skaggs, Weidenbaum, Ratcliffe & Mow, 1994).



Figure 11. Incomplete layers creating a Y-shaped pattern on a transverse section. (*Reproduced with permission from Marchand and Ahmed, 1990*).



Figure 12. The frequency of layer interruption is maximum at the posterolateral location of the annulus. Posterolateral lesions may be due to these structural irregularities and well as higher stresses and strains at the posterolateral location. (*Reproduced with permission from Marchand and Ahmed, 1990*).



Figure 13. Polarized microphotographs of the middle anulus of L4-5 disc from a 7-year old girl. The anterior anulus mainly composed of complete lamellar bundles (A), but a predominance of incomplete/discontinuous bundles is demonstrated in the posterior anulus (B) (X10). (*Reproduced with permission from, Tsuji, H., Hirano, N., Ohshima, H., Ishihara, H., Terahata, N., & Motoe, T. (1993). Structural variation of the anterior and posterior anulus fibrosus in the development of human lumbar intervertebral disc. A risk factor for intervertebral disc rupture. Spine, 18(2), 204-210).* 



Figure 14. Polarized microphotographs of L4-5 disc from a 21-year old woman. A, Anterior middle anulus showing a typical arrangement of the lamellar bundles. B. Posterior middle anulus showing irregular and coarse fibre arrangement (X10). (*Reproduced with permission from, Tsuji, H., Hirano, N., Ohshima, H., Ishihara, H., Terahata, N., & Motoe, T. (1993). Structural variation of the anterior and posterior anulus fibrosus in the development of human lumbar intervertebral disc. A risk factor for intervertebral disc rupture. Spine, 18(2), 204-210).* 

#### 1.9.6 Microstructure of the Annulus Fibrosus - The Intralaminar Matrix

The inter-lamellar matrix (ILM) lies between adjacent lamellae in the AF (Tavakoli & Costi, 2018). It consists primarily of elastic fibers but also of collagen type IV, cells, several glycoproteins and matrix (Tavakoli & Costi, 2018). The elastic fibers and crossbridges, likely play a role in providing mechanical integrity of the AF (Tavakoli & Costi, 2018). See Figure 14. The way in which these various components respond to various loads and stabilize adjacent lamellae structure will influence AF tear formation and subsequent herniation (Tavakoli & Costi, 2018).

Any significant degradation of the interconnecting relationships of the ILM will lead to a reduction in annular wall strength and a decreased resistance to bulging and in turn, will lead to increased radial distension with the potential for eventual herniation (Pezowicz et al., 2005). It is plausible that individual variations in the laminate structure of the annulus will affect the restraining function of the annulus to contain loads by leading to an abnormal distribution of pressure resulting in a IVD herniation (Hirsch & Schajowicz, 1952). This may be even more likely with the addition of annular tears that also affect the restraining function of the AF. The implications for clinicians are that responses to both aggravating activities and therapeutic interventions such as spinal manipulations or mobilizations may be influenced by these variations in lamellar architecture and will likely be different for every individual patient.



Figure 15. Macro view of core bridging structure in an oblique slice. Section plane orientation is indicated in the insert. White asterisk, refer to Fig. 3C for high magnification micrograph. (*Reproduced with permission from* 

Schollum, M. L., Robertson, P. A., & Broom, N. D. (2009). A microstructural investigation of intervertebral disc lamellar connectivity: detailed analysis of the translamellar bridges. Journal of anatomy, 214(6), 805-816).

#### 1.9.7 The Posterior Longitudinal Ligament and Ventral Dura Mater

DLBP as defined in this dissertation may be the result of a lumbar IVD herniation compressing adjacent nociceptor innervated tissues such as the PLL and the VDM (Bogduk, 2012; Li et al., 2014; Loughenbury et al., 2006; Raoul et al., 2002; Sekine et al., 2001). The PLL consists of superficial and deep connective tissue layers. The PLL is the first structure impinged upon by an IVD protrusion outside the annulus fibrosus (Groen, Gerbrand & Drukker, 1990). The fibers of the PLL extend as a long band from the anterior margin of the foramen magnum down to the IVD between L3 and L4. The width and thickness of the PLL varies according to level being most developed at the level of L3 and L4, Its width decreases significantly gradually or abruptly from L4 and can be considered as one of the factors favoring the occurrence of IVD herniation at L4–L5 and L5–S1 levels (Lee et al., 2018; Salaud et al., 2018). The deep and superficial layers of the PLL and the VDM are highly innervated and have an intimate anatomical relationship with IVDs (Kojima et al., 1990). See Figures 15 and 16. The dura mater is closely connected to the PLL by ligaments. These ligaments may play a role as a barrier to transverse displacements of herniated material.



Figure 16. Schematic representation of the dorsal segment of a lumbar intervertebral disc with adjacent vertebrae in a paramedian view. Locations of nerve terminals in the PLL (pll) are indicated (stars). cp Capillary plexus; d spinal dura mater; af annulus fibrosus; np nucleus pulposus; hc hyalin cartilage; fc fibrous cartilage; v verte- bra. Bar: 0,5 mm. (*Reproduced with permission from von During, Fricke & Dahlmann, 1995*).



Figure 17. A. Paramedian section showing part of the interverterbral disc, spinal dura mater (d), posterior longitudinal ligament (pll), and annulus fibrosus (af). Capillaries (cp) lie in the ventral part of the PLL. Remak bundles (small arrows) are found in the ventral and dorsal part of the PLL. Semithin section. Bar: 10 µm. B Part of the capillary wall of the capillary plexus (cp) with fenestrations and a smooth muscle cell (smc). Bar: 1 µm (*Reproduced with permission from von During, Fricke & Dahlmann, 1995*).

The myriad vertical and horizontal interconnections of the dense network of nerves and their location with respect to the IVD, the PLL, the VDM and potentially the peridural membrane may provide an explanation of the observed pain patterns associated with DLBP (Ansari et al., 2012; Bosscher et al., 2020; Loughenbury et al., 2006; Nakamura et al., 1996; Takahashi et al., 1996; Wiltse, 2000). See Figure 17.



Figure 18. (a-b). Camera lucida drawings of the superficial nerve network (a) and the deeper nerve network (b). The arrowheads indicate the intervertebral portion. MB, meningeal branch; AB, ascending branch; DB, descending branch; TB, transverse branch; BV, blood vessel (*Reproduced with permission from Kojima, Maeda, Arai & Shichikawa, 1990*).

# 1.9.8 The Role of the Posterior Longitudinal Ligament and the Ventral Dura Mater

The PLL along with the anterior longitudinal ligament (ALL) act to stabilize the IVD and prevent the IVD from bulging (Heuer et al., 2008). The superficial layer of the PLL and the VDM are bound together by fibrous tissue (Nakagawa et al., 1994). Deformation of either or both of these tissues by a mechanical force such as a protruded annular IVD

fragment is possible given the anatomical relationships of these tissues. Adequate deformation of the IVD posteriorly or posterolaterally can lead to deformation of the PLL and the dura mater. Both tissues are highly innervated with nerve fibers that have low conduction velocities and high mechanical thresholds and may act as either nociceptors or mechanoreceptors (von Düring et al., 1995). Given that the prerequisite anatomy is present for pain to be generated it is not unreasonable to propose a scenario where such deformation may stimulate nociceptive afferent fibers.

# 1.9.9 Summary of Several Features of the Lumbar Intervertebral Disc with Implications for Discogenic Low Back Pain

• The behaviour of a lumbar IVD, to loads, movements and postures, is determined by its macro and micro architecture;

• The AF serves as the primary restraining apparatus to the loads applied to the disc;

• The nonlinear mechanical behavior of the AF is determined by the regional variations in, the tensile properties of its lamellae, the non-uniformity of the lamellar structure and collagen fiber orientations, and the variations in the interlaminar matrix;

• Posterior migration of the AF is inhibited by the PLL;

• The PLL is the first structure impinged upon by a posterior IVD herniation outside the AF;

• The PLL is capable of nociception through its extensive network of nociceptive afferent fibers.

# 1.10 Imaging of Lumbar IVDs

## 1.10.1 Conventional MRI

Investigations such as CT, MRI and discography were unavailable until only recently as aiding in determining a diagnosis in LBP. While magnetic resonance imaging (MRI) is a tool frequently used to examine for lumbar IVD herniations, conventional MRI has

significant limitations. Standard supine lying MRI can reveal disc herniations but it does not allow assessment of the spine under loaded or movement conditions (Zou et al., 2008). In one study only 70% of patients who were diagnosed with a lumbar IVD herniation based on clinical examination had a lumbar IVD herniation confirmed by MRI (Tarantino et al., 2013).

#### 1.10.2 Kinetic or Upright MRI

The advance in imaging technology using kinetic MRI (KMRI) allows the imaging of a patient in a weight-bearing position (either standing up or sitting), and in the flexed and extended positions, which can reveal abnormalities missed by a conventional MRI scan. Studies report that upright MRI shows a higher detection rate of missed lumbar IVD herniations than standard recumbent MRI. Weight-bearing MRI may increase the diagnostic sensitivity of IVD herniations in patients suspected of nerve root compression (Botchu et al., 2018; Nguyen et al., 2016; Nordberg et al., 2021; Tarantino et al., 2013). In cases where there are convincing clinical symptoms and signs but conventional MRI shows no significant abnormalities, re-imaging in the upright position with the addition of flexion and extension, is recommended (Alyas et al., 2008).

# 1.11 Outline of Dissertation Studies

The paper is organized as follows: n Chapter 2 we report the results of an international survey on clinicians' perspectives on the signs and symptoms of a subgroup of patients with LBP that have at least an anecdotal history of success drawing on tacit knowledge of clinicians to generate new research directions. In Chapter 3 we report survey findings on clinicians' rationale for performing spinal manipulation. In Chapter 4 we present findings of a systematic review of the signs and symptoms of DLBP associated with IVD herniation. Chapter 5 includes the results of a study on the effects of a commonly used spinal rotation maneuver on the morphology of lumbar IVDs using MRI. Chapter 6, brings together the results of all 3 projects and includes a brief discussion and recommendations for further research directions to advance the knowledge base of the field of LBP.

# Chapter 2

# 2 Results of an International Survey of Orthopedic Clinicians to Capture Perspectives on Diagnostic Indicators for Discogenic Low Back Pain

# 2.1 Introduction

Low back pain remains the leading cause of years lived with disability (YLDs) globally with more than half a billion prevalent cases of low back pain reported worldwide (Ferreira et al., 2023). Recent high-impact systematic reviews indicate considerable gaps in knowledge about the condition (Buchbinder et al., 2020). Clinicians from disciplines including physical therapy, medicine, chiropractic with and osteopathic medicine often encounter patients with complaints of low back pain (LBP). Although some risk factors associated with the onset of LBP have been identified (Manchikanti et al., 2014) its origin is unclear in more than 80% of patients leading to the term, non-specific low back pain (NSLBP) (Koes et al., 2006; Videman & Battié, 2012; Zhang et al., 2009). NSLBP is an umbrella term to describe symptoms not attributable to an obvious pathological process or lesion (Ardakani, Leboeuf-Yde, & Walker, 2018; Balagué, Mannion, Pellisé, & Cedraschi, 2012; Dewitte et al., 2018). While data suggest that intervertebral disc pathology is the most common structural source of symptoms in NSLBP (Petersen et al., 2003) there are no widely-accepted reference based diagnostic criteria available to clinicians for determining it's diagnosis.

Given the lack of evidence-based explanations for NSLBP, the assertion that a specific symptom profile might be required to predict the underlying mechanism is a framework that seems a reasonable and appropriate strategy to add to the knowledge base of NSLBP (Baron, 2006). A useful approach to identifying mechanisms underlying NSLBP could be to examine clinical practices that have at least an anecdotal history of success in a subgroup of patients with acute low back pain. One such subgroup has been referred to as discogenic low back pain (DLBP) which has been further divided into "reducible discogenic low back pain" (RDLBP) and irreducible low back pain (IRDLBP) (Surkitt et al., 2016; Petersen et al, 2003).

# 2.2 Purposes of the Survey

Currently, there are no gold standard clinical tests, imaging or other procedures to assist clinicians with identifying DLBP (Petersen, Laslett, & Juhl, 2017; Goertz, Pohlman, Vining, Brantingham, & Long, 2012) and few clear frameworks for treatment decisions when it is identified. Across the published evidence we currently find little consensus on what proportion of NSLBP is due to DLBP as diagnosed by experienced clinicians, possibly being less than 30% of all back pain cases (Zhang et al., 2009). As a first step towards an updated clinical decision-making pathway, we have surveyed clinician beliefs and practice patterns when evaluating and treating suspected DLBP. The primary purpose of this survey was to obtain information on clinicians' perspectives on the signs and symptoms that they believe are more common in people with DLBP. A secondary purpose, reported in a separate chapter, was to explore clinician decision-making regarding the use and mechanisms of specific manual therapy intervention for DLBP.

# 2.3 Methodology

#### 2.3.1 Design

This study used a mixed methods approach involving the collection and analysis of quantitative and qualitative data. A voluntary internet-based survey of international health clinicians likely to treat patients with LBP was conducted between May 2014 and February 2016. The 20-item survey was developed by the authors and was pretested on four experienced manual therapy clinicians to elicit feedback on the appropriateness and clarity of the questions, its usability and technical functionality before wider dissemination. Feedback was incorporated into the final version of the survey.

The survey was created and distributed through the SurveyMonkeyTM survey platform (https://www.surveymonkey.com). A letter of information accompanied the survey. See Appendix O-1. Survey questions were a combination of quantitative ratings and openended qualitative questions and were neither randomized nor mandatory.

The survey consisted of two parts. In Part 1, participants responded to questions capturing the proportion of patients they see with LBP, their beliefs about the

mechanisms of LBP, the types of LBP seen in their practice. In addition, respondents were asked questions about how they screen patients for manipulation and their beliefs about the mechanisms of manipulation. These responses are reported in a second manuscript. Respondent characteristics (sex, years in practice, discipline, geographic region, post-graduate training) were captured in Part 2. The primary open-ended questions pertained to evidence or key information from the patient history and the key clinical tests or observations that would lead practitioners to suspect DLBP. See Appendix 0-2.

Eligible respondents were from of one of 30 professional associations in 22 countries with members who may perform direct patient care activities that would likely include spinal manual therapy for LBP. The survey link was distributed through administrative assistants who were asked to distribute the survey to current members either by direct email or posting a notification of the survey on their website. Organization-specific web links were provided to track responses from each. A target of 1% of all eligible respondents was set, equating to 200 to 300 surveys.

#### 2.3.2 Data Cleaning

Duplicate responses from the same internet protocol identification address were identified and reviewed. In cases that were identified as being completed by the same user, the more complete version was retained.

#### 2.3.3 Data Analysis

#### 2.3.3.1 Quantitative Data

Quantitative data were analyzed using descriptive statistics (mean, median), frequency tables, and counts. All complete and partial responses were analyzed. Participants with missing data for specific questions were removed for that analysis only but retained for other analyses where data were available.

#### 2.3.3.2 Qualitative Data

A qualitative description (QD) approach was chosen to analyze the qualitative data collected. The Standards for Reporting Qualitative Research (SRQR) was employed to assist with reporting this data (O'Brien et al., 2014). QD is a useful method for focusing on the concrete daily experiences of professionals and when there is a need for straight description of data that is not highly interpretive (Neergaard et al., 2009; Sandelowski, 2010). It is founded in "existing knowledge, thoughtful linkages to the work of others in the field and clinical experience of the research-group" (Neergaard et al., 2009). The analysis was done using NVivo 11 (https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home) software.

As a descriptive analysis, no a priori theoretical framework was selected, rather, the two researchers were themselves trained and embedded within orthopedic musculoskeletal physiotherapy for more than 20 years and so approached the data from the perspectives and language of use in that field. The researchers independently reviewed the responses and created a code book, grouping like responses together to create sub-themes, then grouping like sub-themes together to create themes. They met several times over two months to compare and discuss their findings and agree upon a final structure of themes and sub-themes. Frequencies of responses informing each theme were tracked for descriptive purposes and to frame the results but was not a primary focus of this analysis.

#### 2.4 Results

Fifteen of 31 contacted organizations agreed to distribute the survey to their members. See Table 1. They represented 10 countries and 15,346 potential participants. A total of 200 (full and partially completed) survey responses were received between June 2014 and February 2016. This was 1.3% of potentially eligible respondents. Of those, 65.2% were male and 90% identified as physiotherapists. A majority (87%) reported spending more than 16 hours/week providing direct patient care with 84% working in private practice. Notably, 65% indicated having completed post-graduate training in manual spinal therapy. Most (89.4%) attributed 'discogenic' mechanisms to less than 50% of patients with LBP. See Appendix 0-3 for respondents' demographics.

	Country	Association	Agreed to Distribute Survey	No. of Members
1	Australia	Musculoskeletal Physiotherapy Australia		
2	Austria	Austrian Association of Orthopaedic Manual Therapy	Х	72
3	Belgium	Belgische Vereniging van Manueeo Therapeuten	Х	180
4	Belgium	European Teaching Group Orthopedic Medicine (Cyriax)	Х	4
5	Canada	Canadian Academy of Manipulative Physical Therapists	Х	573
6	Canada	Orthopedic Division Canadian Physiotherapy Association	Х	4492
7	Canada	Canadian Association of Orthopedic Medicine	Х	55
8	Canada	Canadian Chiropractic Association		7100
9	Denmark	Danish Musculoskeletal Physiotherapy Association		
10	Germany	German Federal Association of Manual Therapists		
11	Greece	The Scientific Manual Therapy Group of the Panhellenic Physiotherapists' Association Hong Kong Physiotherapy Association Manipulative Therapy		
12	Hong Kong	Specialty Group		
13	Ireland	Chartered Physiotherapists in Manipulative Therapy	Х	3023
14	Italy	Gruppo di Terapia Manuale	Х	200
15	Japan	Japanese Orthopaedic Manual Therapy Association		
16	Netherlands	Nederlandse Vereniging voor Manuele Therapie		110
17	New Zealand	New Zealand Manipulative Physiotherapists Association		410
18	Norway	Manuell Terapi Norway		
19	Portugal	Portuguese Manual Therapy Interest Group		
20	South Africa	Orthopaedic Manipulative Physiotherapy Group	Х	689
21	Spain	OMT Spain		
22	Sweden	Sektionen for Ortopedisk Manuell Terapi	X	1500
23	Switzerland	Schweizerischer Verband Orthopadischer Manipulativer Physiotherapie	Х	500
24	United Kingdom	Members of Society of Orthopedic Medicine	Х	500
25	United Kingdom	Chartered Society of Physiotherapy		
26	United Kingdom	Musculoskeletal Association of Chartered Physiotherapists		
27	United States	American Academy of Orthopaedic Manual Physical Therapy	Х	2305
28	United States	American Osteopathic Association	Х	1134
29	United States	American Physical Therapy Association		
30	United States	American Chiropractic Association		
31	United States	California Orthopedic Manual Physical Therapy Special Interest Group	Х	119

Table 1. Associations contacted and that agreed to distribute the international survey on low back pain.

## 2.4.1 Information from Patient History Clinicians use to Identify Discogenic Low Back Pain

One hundred and thirty-seven (68.5%) respondents replied to the open-ended question *List the key evidence or information from the patient history/interview that would lead you to suspect discogenic low back pain.* After verbatim extraction and cleaning, the two independent reviewers reached consensus on 8 themes and 16 sub-themes. The themes (in order of reporting frequency) were: Behavior of Symptoms, Location of Symptoms, Mechanism of Onset, Neurological Symptoms, Age, Past History, Pain Descriptors, Investigations and an "uncategorized" category. See Table 2.

## 2.4.1.1 Behaviour of Symptoms

Behaviours related to the ways in which symptoms fluctuated with movements or throughout the day. Two subthemes were identified: *aggravating factors* and *relieving factors*. Aggravating factors included specific movements, postures, diurnal fluctuations, and procedures thought to increase intrathecal pressure. Examples were "symptoms aggravated with sitting or walking or bending forward' and 'pain with sneezing or coughing." Samples of relieving factors included: "extension eases back pain' and 'pain improved with standing." While not explicitly stated, the responses seemed to indicate that the more of these specific aggravating and easing factors present, the more likely was LBP to be attributed to a discogenic mechanism.

#### Location of Symptoms

Responses indicated that DLBP could be at least partly identified based on the location (i.e., body regions) in which patients described symptoms. Radiation of symptoms beyond the back was the primary indicator, though respondents were split on whether radicular symptoms are positive or negative for DLBP. Some respondents endorsed "*pain in the leg*" as an indicator of DLBP, while others endorsed "*central low back pai*n" as an indicator.

# 2.4.1.2 Mechanism of Injury

Respondents indicated that DLBP was more likely when the onset of symptoms could be traced to a discrete precipitating event (trauma) such as an "*awkward lift or twist*, or '*repetitive bending*" while it was less likely if the mechanism was attributed to "*degenerative processes*' or '*slow onset over time*." The existence of an easily identifiable *event* or *injury* as the precursor to pain onset appeared to support the diagnosis of DLBP.

# 2.4.1.3 Neurological Symptoms

Patient descriptions of neurological symptoms were reported as indicators of DLBP. Responses evenly distributed amongst *"impaired sensation*", *'weakness"* and other paroxysmal symptoms (e.g., bowel/bladder disturbance, absent or altered reflexes).

## 2.4.1.4 Age

Nearly half of the responses tended to indicate that younger or middle-aged patients are more likely than older patients to have DLBP.

## 2.4.1.5 Past History

A prior history of multiple or repeated episodes of LBP was noted by a majority of the respondents as an indicator of DLBP. Not all responders agreed. One respondent noted that "history assists with understanding lesion behavior, but cannot elicit centralization and therefore no clear historical factor can be used to say the anatomical source of pain is discogenic."

# 2.4.1.6 Pain Descriptors

Respondents indicated that certain qualifiers or pain descriptors used by patients could indicate likely DLBP. These included "*deep pain in the middle of the spine*' and '*severe*' *low back pain*."

	Theme	Sub-themes	Total Responses	Sample Response
1	Behaviour of Symptoms		188	
	Aggravating Factors		133	
		Movements	45	Pain with movements involving lumbar flexion
		Postures	43	pain with prolonged sitting
		Time of Day	24	morning stiffness and pain
		Intrathecal	21	pain on coughing/sneezing
	Relieving Factors		40	
		Extension	14	Pain decreased or centralized by prolonged extension
		Postures	12	relieved by lying down or standing
		Walking	9	moderate walking makes pain less
		Other	5	specific spinal unloading position of pain relief
	Other		15	Truth is I don't "diagnose" people with "bulged discs" but rather recognize a clinical pattern that is often attributed to discs - but the presence of an actual disc bulge is not relevant to me.
2	Location of Symptoms		89	
	Radiation		73	Description of neuropathic leg/buttock pain as well as low back pain
	Other		16	deep pain in the middle of the spine
3	Mechanism of Injury		40	mechanism of injury being flexion movement or chronic flexion posture / repeated flexion
4	Neurological Symptoms		37	
	Sensation		14	Pins and needles / numbness
	Weakness		13	profound weakness in a myotome
	Other		10	Bladder / Bowel disturbance
5	Demographics		13	younger age 25-55yo.

Table 2. Emergent themes and sub-themes based on analysis of open-ended responses to the question, List the key evidence or information from the patient history/interview that would lead you to suspect discogenic low back pain. (n= 137)

6	Past Hx	8	History assists with understanding lesion behavior, but can not elicit centralization and therefore no clear historical factor can be used to say the anatomical source of pain is discogenic.
7	Pain Descriptors	4	severe LBP
8	Investigations	3	MRI evidence although not ever considered conclusive

# 2.4.2 Information from Clinical Testing That Clinicians use to Identify Discogenic Low Back Pain

One hundred and thirty-six respondents (68.0%) replied to the open-ended question *List the key clinical tests or observations that would lead you to suspect discogenic low back pain.* Two independent reviewers reached consensus on 7 main themes and 34 subthemes. The main themes in order or reporting were: Lumbar Movements, Neurodynamic Tests, Neurological Symptoms, Pain Patterns, Anatomical Deviations Observed, Special Tests, Uncategorized, and Investigations. See Table 3.

#### 2.4.2.1 Lumbar Movements

Lumbar movements were the most frequent reported clinical test used for differentiating discogenic from other forms of LBP though the precise direction of movements that would be considered *positive* varied widely. The pattern of painful movements that would suggest DLBP in order of reporting were: flexion, repeated movements, extension, non-classified, rotation, combined movements and side flexion

Together, flexion and repeated movements accounted for more than half (64%) of the lumbar movement findings that would suggest DLBP. In general, responses indicated that lumbar flexion may or may not be limited, but should be painful or lead to the peripheralization phenomenon of symptoms while extension should be less painful and lead to the centralization phenomenon. One respondent wrote, "*There are no reasonable objective tests for discogenic low back pain. Rather there is a clinical pattern of flexion dominant pain with an extension directional preference that is often described as discogenic.*"

## 2.4.2.2 Neurodynamic Tests

Specific neurodynamic tests were grouped into 8 sub-themes. In order of reporting they were: straight leg raise, slump test, crossed straight leg raise, Braggard's test, Bowstring sign, prone knee bend and reverse straight leg raise. Fifty percent of responses indicated that a positive result on a straight leg raise test would be indicative of DLBP. Sample responses included, "*slump test can indicate neural irritation*', '*positive cross straight leg* 

*raise*' and '*reduced neural dynamics* (e.g., *prone knee bend or PKB*)." Responses did not include information on what a positive test entailed, how the test was actually conducted, or whether clinicians use a threshold angle of the straight leg raise at which pain is experienced to indicate a *positive* test.

#### 2.4.2.3 Neurological Signs

Seven neurological sub-themes were identified from survey responses. These were: nonclassified, reflexes, myotomes, weakness, dermatomes, sensation and intrathecal signs.

Non-classified signs had the largest number of responses, albeit many being one-off responses that did not fit meaningfully into any specific sub-theme. These included "*hard neuro signs*, +/- *neuro scan* and *positive conduction signs*." The presumed intention in each of these, based on the phrasing of the question, was that DLBP was more likely to be the diagnosis when findings of lower extremity neurological examination revealed some kind of nerve conduction or mobility deficit.

The remaining sub-themes were signs typically characteristic of nerve root or thecal compression. Sample responses included, "diminished patellar or Achilles DTR, weakness in muscle associated with suspected nerve root, abnormal dermatomal sensation and positive Valsalva."

#### 2.4.2.4 Pain Patterns

Pain patterns were divided into 6 sub-themes: relieving activities, centralization, peripheralization, radiation, location and directional preference. The most reported sub-themes, were, relieving activities (as a result of repeated extension), centralization (symptoms moved centrally with lumbar extension) and peripheralization (symptoms moved away from the centre with flexion movements. The descriptions implicate a lumbar structure capable of being influenced by movements that result in increasing or decreasing symptoms.

## 2.4.2.5 Observed Anatomical Deviations

Tied with pain patterns, observed anatomical deviations that would lead to suspicion of DLBP were, "a shift or deviation or list observed at rest or during lumbar movements, antalgic or unequal weight bearing during standing or walking, loss of lumbar lordosis and standing with a flexed knee."

# 2.4.2.6 Special Tests

Several special tests that would indicate DLBP included: accessory movements, compression/distraction and Milgram's test. Accessory movements, either "*central or unilateral posterior/anterior mobilizations*" were used to '*elicit or localize pain*', '*detect hypomobility*' and '*determine end feel*". Pain on vertical spinal compression was reported as a special test that would lead respondents to suspect DLBP. A sample response was "*pain with loaded postures, i.e. prolonged sitting or standing*". A single respondent reported using the "*Milgram's test*" to determine disc pathology.

#### 2.4.2.7 Uncategorized

A group of 21 uncategorized and wide-ranging findings were reported such as, "restricted Schober measurement of less than 2 cm', 'prone instability test', 'pain zone', 'absence of specific facet symptoms' and 'confirmation of subjective symptoms." One response reflected a different approach to the issue of a clinical diagnosis. The respondent reported, "I focus on impairments of movement and finding strategies to manage the problem rather than being overly diagnostic."

#### 2.4.2.8 Investigations

"

A single respondent reported that "positive radiological findings would be used along with clinical findings to help determine a diagnosis."

	Theme	Response Count	Sample Response
1	Lumbar Movements	136	
	Flexion	42	pain worse with forward flexion
	Repeated Movements	32	worse with repeated flexion
	Extension	22	reduced extension in lumbar spine
	Non-Classified	20	decreased lumbar motion
	Rotation	9	pain with rotary stress
	Combined Movements	7	painful quadrant
	Side Flexion	4	Pain on lumbar spine AROM (side or forward flexion)
2	Neurodynamic	108	
	Straight Leg Raise	56	positive SLR
	Slump Test	19	slump test can indicate neural irritation
	Crossed Straight Leg Raise	16	contralateral SLR
	Non-Classified	6	positive neuro dynamics
	Braggard's	4	braggards
	Bowstring	4	bowstring
	Prone Knee Bend	2	reduced neural dynamics (PKB)
	Reverse Straight Leg Raise	1	reverse straight leg rising
3	Neurological Signs	107	
	Non-classified	26	hard neuro signs
	Reflexes	22	diminished patellar or Achilles DTR
	Myotomes	15	myotome weakness
	Weakness	13	decreased strength in lower lumbar or sacral myotomes
	Dermatomes	12	radiating leg pain in a specific dermatomal/myotomal pattern
	Sensation	9	abnormal dermatomal sensation)

Table 3. Emergent themes and sub-themes based on analysis of open-ended responses to the question, List the key clinical tests or observations that would lead you to suspect discogenic low back pain. (n=136)

	Intrathecal		9	thecal sign are positive findings almost always
4	Pain Patterns	59		
	Relieving Activity	21		
	McKenzie		9	McKenzie rescue positions centralizing pain after testing into flexion
	Traction		8	relief with lumbar traction
	Position		4	preference to stand versus sit
	Centralization	14		centralization with repeated extension.
	Peripheralization	12		peripheralization of symptoms with repeated flexion
	Radiation	8		radicular dermatomal pain pattern
	Location	2		Classic: Patient shows pain location by sweeping two fingers laterally across back near belt-line.
	Directional Preference	2		directional preference with movements
5	Observed Anatomical	59		lateral trunk shift
6	Deviations Special Tests	34		
	Accessory Movements	2	22	centralization with CPAs or UPAs
	Compression/Distraction	1	13	pain with loaded postures, i.e. prolonged sitting or standing
	Miligram's		1	miligram test
7	Uncategorized	21		I focus on impairments of movement and finding strategies to manage the problem rather than being overly diagnostic
8	Investigations	1		positive radiological

# 2.5 Discussion

The purpose of this survey was to obtain information on the clinical decision making and differential diagnosis process of clinicians who treat people with LBP, with a specific focus on signs and symptoms that clinicians believe are more common in people with pain of discogenic origin. In a separate paper we report on the rationale for spinal manipulation/mobilization/adjustment to manage suspected DLBP. While the survey responses were rich and provided ample opportunity for analysis, perhaps the most relevant finding is the wide variety of tests with inconsistent indicators of a 'positive' result across clinicians when making a diagnosis of DLBP

# 2.5.1 Key Information from Patient History Clinicians use to Identify Discogenic Low Back Pain

While terminology in classifying symptoms among studies may vary and includes a wider variety of descriptors than the 8 themes and 16 sub-themes identified in this study, the cluster of symptoms reported by respondents is supported in the available literature seeking to explore the causes or mechanisms of DLBP. It appears that a cluster of information from the patient, along with clinical findings may provide a more exact clinical picture to determine a source of pain pathology (Billis et al., 2013; Chan et al., 2013; Hancock et al., 2007; Shultz et al., 2015). The following are examples from our survey of a patient's history that would suggest DLBP which have been identified in previous studies (Vroomen et al., 2002).

- pain localized to the low back/midline of the spine;
- chronic deep dull, axial pain low back pain;
- sharp, stabbing, pulsating, shooting pain;
- symptoms worse with sitting/less with standing;

# 2.5.2 Key Information from Clinical Findings Clinicians Use to Identify Discogenic Low Back Pain

Clinical findings reported by respondents that would lead to suspicion of DLBP were organized into 8 themes and 34 sub-themes. With the exception of centralization (CP), no one clinical finding has been shown to be demonstrative for DLBP (Wetzel & Donelson, 2003). The following are examples from our survey of clinical findings which have also been proposed by other authors as suggestive of DLBP. None of these features have been validated.

- CP and pain when rising from sitting to standing;
- antalgic posture: clear shift/tilt in posture or with forward flexion;
- provocation in response to combined movement testing;
- range of motion often reduced in flexion but may be reduced in all planes because of pain;
- pain/symptom provocation with repeated flexion, whereas extension results in pain reduction;

In our study, centralization as a feature of DLBP was reported as a symptom by only 4 respondents and as a clinical finding by 14 respondents. CP was the most reported pain relieving pattern while peripheralization was the most aggravating pain pattern. In the literature, CP is the only feature rated as diagnostic for discogenic pain (Aina et al., 2004; Alexander et al., 2007; Hancock et al., 2007; Laslett et al., 2005; Petersen et al., 2017; Vining et al., 2013; Wetzel & Donelson, 2003; Zhang et al., 2009)

Research evidence to support the value of history-taking and clinical examination in making a diagnosis is inconclusive. While supported in most clinical guidelines, the history-taking and clinical exam process has had little formal scientific assessment of its validity regarding diagnosis and outcomes for LBP (Balagué et al., 2012). To date, with the arguable exception of the centralization phenomenon (Cook & Hegedus, 2011;
Petersen et al., 2017; Tessitore et al., 2015; Werneke et al., 2011), the majority of test characteristics for diagnosing DLBP have yet to be empirically evaluated (Kallewaard et al., 2011). Our findings suggest that one or two of the more frequent responses might be worthy of further empirical research to determine if they can be included as part of a cluster of history/clinical indicators to identify DLBP.

Furthermore, this study revealed that respondents use a combination of key information from a patient's history and clinical examination findings to reach a presumed diagnosis of DLBP. Hancock (Hancock et al., 2011) in a study of patients with sciatica due to disc herniations at lower lumbar levels concluded that that the diagnostic accuracy of a combination of index tests was slightly superior to the most informative individual test. Our respondents attributed LBP to a protruded disc in less than 50% of patients. This is similar to what is reported in the literature where the prevalence of DLBP has been estimated to be between 39.0% and 43.0% (Amirdelfan et al., 2014; Hancock et al., 2007). Chan and colleagues (A. Chan et al., 2013) conducted a Delphi survey of expert panelists and achieved only 50% consensus on indicators of DLBP. These findings are in alignment with those of our survey, and appear to highlight an ongoing critical lack of agreement on diagnostic indicators of DLBP. Without a clear consensus, the reported prevalence of DLBP may be underrepresented. Research in the field seems to offer little to clinicians in terms of clear guidance for diagnostic and treatment decisions (Maher et al., 2017). Of note, some respondents appear to disagree with the concept that DLBP is even a true clinical entity but did not elaborate further. The lack of a gold standard for DLBP adds to the critical gap in how clinicians make sense of patient's presenting with LBP. Equally important is that without clear reference standards for diagnosis, the true prevalence of DLBP cannot be ascertained.

#### 2.6 Limitations and Weaknesses

The low response rate (1.3%, n=200) to our survey may give rise to sampling bias (Draugalis & Plaza, 2009), may not be representative of the populations of clinicians who treat patients with LBP and the results cannot be generalized to the larger population of clinicians. Similar surveys of clinicians' practice patterns resulted in response rates of

28.8% (Bill et al., 2020), 33.9% (Allee et al., 2005), and 49.1% (Adams et al., 2018) for osteopaths and allopaths; (25% (n=720) (Webster et al., 2005) and 48% (n=87) (Di Iorio et al., 2000) for physicians; 36% (Keating et al., 2016), 38% (Carlesso et al., 2014) and 82.2% (Carlesso et al., 2013) for physiotherapists; 60% (Axén et al., 2008), 88% (Malmqvist & Leboeuf-Yde, 2008) and 37% (n=743) (Walker et al., 2011) for chiropractors.

Survey results included partial item-level responses and incomplete responses both of which are characteristic limitations of online web-based surveys. The thematic analysis approach used to analyze the data in this study has advantages and disadvantages. It is a flexible method that can be used and applied to a wide range of study questions, designs and sample sizes (Kiger & Varpio, 2020). This flexibility though may be viewed as lacking rigor (Kiger & Varpio, 2020). A more detailed audit trail as evidence of the decisions and choices made by the two independent researchers would benefit other researchers to clearly follow a decision trail (Nowell et al., 2017).

More detailed elaborations of open-ended response questions could have been used. For example, we could have asked respondents to describe the procedures used if it was determined that SM would be beneficial. For the question, *Of those patients who present to your practice with low back pain what percentage do you attribute to having a bulged or protruded disc(s)* we could have asked, *In those patients who you think do not have a bulged or protruded disc(s) what pathology(ies) would you attribute the symptoms to?* 

The lack of consensus regarding the signs and symptoms of DLBP among survey respondents may be due to our use of a single open-ended question format canvassing for information. A more detailed list of signs and symptoms may have been obtained had we asked respondents to elaborate their responses. To assist them we could have provided a more comprehensive list of items as identified by expert panel opinion in the literature (Chan et al., 2013; Cid et al., 2015; Kent, Keating, & Taylor, 2009; McCarthy et al., 2006).

By separating the survey questions into indicators from the history and those from the clinical exam, it is difficult to determine how clinicians may integrate information from

these different sources into a broader tacit practice of pattern recognition. Prior work has shown that single diagnostic tests are unlikely to be fruitful, but at least in the diagnosis of sacroiliac joint dysfunction, (Hancock et al., 2007) found that a cluster of tests interpreted together provides greater diagnostic accuracy. This clinical reasoning has some support from more recent studies (Chan et al., 2013; Cid et al., 2015; Dewitte et al., 2018; McCarthy et al., 2006) and it would be interesting to supplement this survey research with individual qualitative interviews to explore ways that clinicians make decisions about likely diagnoses.

As this was anonymous survey research, we had no ability to pose follow-up or probing questions where clarity was needed. As a result, several of the responses were too ambiguous to be clearly assigned to a specific sub-theme, resulting in a large proportion of 'unclassified' responses that were clearly associated with one of the broader themes but were missing more specific information.

## 2.7 Conclusion

Clinicians use a combination of key information from a patient's history as well as clinical examination findings to determine a diagnosis of DLBP. Clinicians who screen for DLBP appear to follow what guidance is available but that appears to be very little, relying instead on theory, experience, and intuition.

## 2.8 Ethical Approval

The study was approved by Western University's Health Science Research Board.

## 2.9 Funding

Through the Pain and Quality of Life Integrative Research Lab, Faculty of Health Sciences, Western University, London, ON

## 2.10 Conflicts of Interest

There are no conflicts of interest.

## 2.11 What is Already Known on this Topic

NSLBP patients make up a large heterogeneous group of LBP patients. There are no widely-accepted reference based diagnostic criteria available to clinicians for determining these subgroups. Research evidence on the value of history-taking and clinical examination to make a diagnosis of DLBP is inconclusive. Subgroups of NSLBP patients could be more effectively treated if they could be allocated to homogeneous subgroups on the basis of valid diagnostic criteria.

## 2.12 What This Study Adds

Clinicians use a combination of key information from a patient's history as well as clinical examination findings to determine a diagnosis of DLBP. There is insufficient evidence that the clinical community identifies DLBP from a disc herniation as a true clinical entity. We recommend the development and undertaking of a series of high-quality and well-designed observational studies to with the goal of developing valid and reliable criteria for diagnosing DLBP based on using subgroups as classified by Petersen (Petersen et al., 2003).

# Chapter 3

# 3 Results of an International Survey of Orthopedic Clinicians to Capture Perspectives on the Rationale for Using Spinal Manipulation

# 3.1 Introduction

This study is part of a larger research project investigating the theory that discogenic low back pain (DLBP) may be the result of a displaced fragment of disc compressing adjacent innervated tissues. Chapter 2 of this dissertation provided the results of a survey of clinicians' perspectives on the diagnostic criteria (i.e., signs and symptoms) of DLBP. Accordingly, in this study we have reported the second part of the results of the international survey focusing specifically on clinician beliefs about the mechanisms of action of spinal manipulation and spinal mobilization.

In developing this research program, we see value in starting with a large-scale international survey of clinician practice patterns and beliefs about clinical signs and symptoms as well as treatment indications and mechanisms from which a new clinical decision pathway can be developed. While survey data can be difficult to interpret and provides no opportunity for further investigation or clarification of responses, the open-ended questions provide a rich dataset to explore from which subsequent steps in this research program might be developed. Generating a hypothesis to do with a specific treatment effect identified from a subgroup analysis, even in an individual study, is an acceptable approach when investigating subgroup interventions (Sun et al., 2010, p. 63).

# 3.2 Background

Low back pain (LBP) is the primary cause of years lived with disability globally (Ferreira et al., 2023). A majority of LBP, is referred to as non-specific low back pain (NSLBP) and according to some, has no known attributable cause (Balagué et al., 2012; Ferreira et al., 2023; Koes et al., 2006; Zhang et al., 2009). Others hold that diagnosing NSLBP based on anatomical structures is possible (Bogduk, 2012; Laslett et al., 2005; McGill, 2016; Petersen et al., 2017).

Although recent research has generally focused and on the psychosocial drivers of the biopsychosocial model as well as some subgroups of NSLBP, there remains a need for better understanding of biological drivers for clinicians treating patients with NSLBP for two reasons.

1. The variety of potential pain-generating structures has been suggested as a primary reason that randomized-controlled trials involving interventions for NSLBP have failed to show consistent treatment effects (Chan et al., 2013; Fersum et al., 2010).

2. Presumably, certain subgroups of patients with NSLBP originating from different structures will respond to different interventions (Petersen et al., 2017).

Subclassification is based on the assumption that NSLBP patients make up a large heterogeneous group and would more effectively be treated if they could be allocated to more homogeneous subgroups on the basis of valid criteria (Bialosky et al., 2018; Hebert et al., 2008; Petersen et al., 2003). Although several classification systems, mostly based on treatment-based physical examination approaches, have been proposed to subdivide NSLBP, there is little to no evidence to demonstrate consistent superiority of any one approach over others (Kreiner et al., 2020; Maher et al., 2017; Petersen et al., 2003).

Petersen proposed a classification system based on a pathoanatomic basis of known pain producing structures (Petersen et al., 2003, p. 222). The underlying rationale for this is that diagnostic reasoning with a structural or pathoanatomical emphasis is common among clinicians and is recognized as an essential component of the biopsychosocial model (Petersen et al., 2017). Petersen's first group (Category 1) is disc syndrome, based on the fact that data suggests that intervertebral disc pathology, (referring largely to studies of disc degeneration) is the most common structural source of symptoms in NSLBP (Petersen et al., 2003). This category is further separated into 3 subcategories; reducible disc, non-reducible disc and non-mechanical disc disorders. For the purpose of this study, reducible disc syndrome will be referred to as DLBP.

Among the various treatments for DLBP is spinal manipulative therapy (SMT). SMT includes various forms including spinal manipulation (SM) spinal mobilization (SMOB)

and spinal manipulation with rotation (SRM). See Appendix 0-4. The choice of the form of SMT is at the discretion of the clinician. Despite widespread use of SMT by physiotherapists, chiropractors, osteopathic doctors and medical physicians, the actual mechanism of action remains largely underdeveloped, tending to rely on anecdote and theory (Carnes et al., 2010; Nim et al., 2021). While some positive clinical effects have been demonstrated with SMT (Mourad et al., 2022; Paige et al., 2017; Rubinstein et al., 2019), a stronger understanding of the mechanism of action would contribute to evidence-based practice (Bialosky et al., 2018; Mourad et al., 2022; Stanton, 2016). In the absence of a gold standard to guide the use of SMT, survey research can provide initial evidence to probe the clinical decision-making strategies of clinicians who treat DLBP and to collect first-hand information on practice patterns and decision-making processes..

## 3.3 Purpose of the Study

The purpose of this survey was to collect opinions from these clinicians about the mechanism of action of one type of SMT as a treatment for DLBP.

## 3.4 Methodology

#### 3.4.1 Design

This study used a mixed methods approach involving the collection and analysis of quantitative and qualitative data. A voluntary internet-based survey of international health clinicians likely to treat patients with LBP was conducted between May 2014 and February 2016. The 20-item survey was developed by the authors and was pretested on four experienced manual therapy clinicians to elicit feedback on the appropriateness and clarity of the questions, its usability and technical functionality before wider dissemination. Feedback was incorporated into the final version of the survey.

The survey was created and distributed through the SurveyMonkeyTM survey platform (https://www.surveymonkey.com/). Survey questions were a combination of quantitative

ratings and open-ended qualitative questions and were neither randomized nor mandatory.

The survey consisted of two parts. In Part 1, respondent characteristics (gender, years in practice, discipline, country of practice, post-graduate training, etc.) were captured. Questions related to treatment decisions are reported in Chapter 2. Relevant to this chapter were questions related to the proportion of patients with suspected DLBP, beliefs about mechanisms of DLBP, and signs and symptoms clinicians use to identify suspected DLBP. A video demo of the SRM technique was included in the survey.

Eligible respondents were from of one of 30 professional associations in 22 countries with members who may perform direct patient care activities that would likely include spinal manual therapy for LBP (see Table 4). The survey link was distributed through administrative assistants who were asked to distribute the survey to current members either by direct email or posting a notification of the survey on their website. Organization-specific web links were provided to track responses from each. A target of 1% of all eligible respondents was set, equating to an estimated 200 to 300 surveys.

## 3.4.2 Data Cleaning

Duplicate responses from the same internet protocol identification address were identified and reviewed. In cases that were identified as being completed by the same user, the more complete version was retained.

#### **3.4.3** Data Analysis

#### 3.4.3.1 Quantitative Data

Quantitative data were analyzed using descriptive statistics (mean, median), frequency tables, and counts. All complete and partial responses were analyzed. Participants with missing data for specific questions were removed for that analysis only but retained for other analyses where data were available.

#### 3.4.3.2 Qualitative Data

A qualitative description (QD) approach was chosen to analyze the qualitative data collected. The Standards for Reporting Qualitative Research (SRQR) was employed to assist with reporting the qualitative data (O'Brien et al., 2014). QD is a useful method for focusing on the concrete daily experiences of professionals and when there is a need for straight description of data that is not highly interpretive (Neergaard et al., 2009; Sandelowski, 2010). It is founded in "existing knowledge, thoughtful linkages to the work of others in the field and clinical experience of the research-group" (Neergaard et al., 2009, p. 2). The analysis was done using NVivo 11 (https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home) software.

As a descriptive analysis, no a priori theoretical framework was selected, rather, the two researchers were trained and embedded within orthopedic musculoskeletal physiotherapy for more than 20 years and so approached the data from the perspectives and language of use in that field. The researchers independently reviewed the responses and created a code book, grouping like responses together to create sub-themes, then grouping like sub-themes together to create themes. They met several times over two months to compare and discuss their findings and agree upon a final structure of themes and sub-themes. Frequencies of responses informing each theme were tracked for descriptive purposes and to frame the results but was not a primary focus of this analysis. Descriptive themes were then tested against a group of independent experienced manual therapy clinicians to ensure interpretability and meaning, as a means to improve rigor of the findings.

#### 3.5 Results

Fifteen of the 31 organizations contacted agreed to distribute the survey to their members. The 15 represented 15,346 potential respondents based on membership information provided by each participating organization. Four organizations declined to participate. No responses were received from twelve (See Table 4). A total of 200 full and partial survey responses were received (a 1.3% response rate) between June 2014 and February 2016. Of those, eight (4 pairs) were identified as having duplicate internet protocol (IP) addresses. We determined that 3 of the 4 pairs of responses with the same IP address were sufficiently different to be included in the final tally. Presumably, respondents in the 3 pairs used the same computer to submit the surveys independently of one another. Therefore, a total of 199 surveys were used for data analysis.

Country	Association	Agreed to Distribute Survey	No. of Members
Australia	Musculoskeletal Physiotherapy Australia		
Austria	Austrian Association of Orthopaedic Manual Therapy	Х	72
Belgium	Belgische Vereniging van Manueeo Therapeuten	Х	180
Belgium	European Teaching Group Orthopedic Medicine (Cyriax)	Х	4
Canada	Canadian Academy of Manipulative Physical Therapists	Х	573
Canada	Orthopedic Division Canadian Physiotherapy Association	Х	4492
Canada	Canadian Association of Orthopedic Medicine	Х	55
Canada	Canadian Chiropractic Association		7100
Denmark	Danish Musculoskeletal Physiotherapy Association		
Germany	German Federal Association of Manual Therapists The Scientific Manual Therapy Group of the Panhellenic		
Greece	Physiotherapists' Association		
Hong Kong	Specialty Group		
Ireland	Chartered Physiotherapists in Manipulative Therapy	Х	3023
Italy	Gruppo di Terapia Manuale	Х	200
Japan	Japanese Orthopaedic Manual Therapy Association		
Netherlands	Nederlandse Vereniging voor Manuele Therapie		
New Zealand	New Zealand Manipulative Physiotherapists Association		410
Norway	Manuell Terapi Norway		
Portugal	Portuguese Manual Therapy Interest Group		
South Africa	Orthopaedic Manipulative Physiotherapy Group	Х	689
Spain	OMT Spain		
Sweden	Sektionen for Ortopedisk Manuell Terapi	X	1500
Switzerland	Schweizerischer Verband Orthopadischer Manipulativer Physiotherapie	Х	500
United Kingdom	Members of Society of Orthopedic Medicine	Х	500
United Kingdom	Chartered Society of Physiotherapy		
United Kingdom	Musculoskeletal Association of Chartered Physiotherapists		

Table 4. Associations contacted and that agreed to distribute the international survey on low back pain.

United States	American Academy of Orthopaedic Manual Physical Therapy	Х	2305
United States	American Osteopathic Association	Х	1134
United States	American Physical Therapy Association		
United States	American Chiropractic Association California Orthopedic Manual Physical Therapy Special Interest	Х	119
United States	Group		

Respondents came from 20 countries with the majority from Canada (n=57), the United States (n=31), Ireland (n=22) and Switzerland (n=15). Other countries included, Australia, Austria, Belgium, Germany, Hong Kong, India, Italy, Liechtenstein, New Zealand, Pakistan, Poland, Saudi Arabia, Singapore, Spain, the United Kingdom and the United Emirates (See Table 5 for respondents' demographics).

Of the 141 who identified their sex, 65.2% were male (n=92) and 34.8% were female (n=49). The modal professional designation was physiotherapist (90.0%, n=140), 3.6% (n=5) were chiropractors, 3.6% (n=5) as osteopaths, 2.9% (n=4) as physicians and 10 as "Others". Thirty-seven respondents identified themselves as practicing under more than one designation. The majority (84.0%) worked in a private for-pay clinic. A majority (87.0%) indicated they had completed some form of professionally-relevant post-graduate training in manual spinal therapy (Table 5). Eighty-seven percent (n=112) reported spending more than 16 hours per week providing direct patient care. Average years of practice experience was 15 (range 1 to 44 years).

Spinal mobilization was used as a treatment by 92.9% (n= 177) of respondents. Spinal manipulation was used by 84.9% (n=163) and 15.1% (n=29) used spinal adjustments. These three treatments had been used by respondents (n=135) for an average of 12.5 years with a range between 1 and 35 years. Patient with LBP comprised at least 50% of the clinical caseload for only 28.2% of respondents. A standardized assessment protocol for LBP was used by 75.7% while the remaining 24.3% reported no standardized protocol when assessing patients with LBP. Amongst those who did indicate a standardized protocol, 37 different approaches were described. See Appendix 0-19.

The majority of respondents (71.8%) indicated that disc bulge or protrusion was the primary pain mechanism in less than half of all patients with LBP.

Demographic	Respondents	Response Count	Response Percentage
Gender (n-141)	male	92	65.2%
Gender (II=1+1)	female	49	34.8%
Clinical Designation (choose all that apply) (n=140)			54.07
	Physiotherapist or Physical Therapist	127	90.7%
	Physician	4	2.9%
	Osteopath	5	3.6%
	Chiropractor	5	3.6%
	Other	10	
Place(s) of work (choose all that apply) (n=133)			
	Hospital	20	15.0%
	Private Practice	112	84.2%
	Family/Community Health Centre	6	4.5%
	Industry	3	2.3%
	University/College	19	14.3%
	Other *	13	9.8%
Hours/week providing direct patient care (n=142)			
	<u>&lt;</u> 15	17	12%
	16-30	49	35%
	31-44	59	42%
	<u>≥</u> 45	14	10%
Number of years qualified in respective discipline (n=142)			
	Mean	15	
	Median	14	
	Mode	20	

#### Table 5. Demographics of Survey Respondents

Min	1
Max	44
SD	9.5

If you practice under more than one designation, please list all designations. Describe the designation in full and list how long you have been qualified in each discipline (n=37)	Respondents cited various certifications but within the same field of practice. E.g., PT, MD, DO, DC. Only 2 respondents indicated they practiced under more than one clinical designation.	
	Acupuncturist/Chiropractor	1
	Athletic Therapist/PT	1
	Diplomierter Assistent für Physikalische Medizin 10y Diplomierter Physiotherapeut 5y Physiotherapeut	1
	Certified Strength and Conditioning Specialist, Certified Acupuncture Provider	1
	Certified Strength and	
	Conditioning Specialist, Certified	1
Country of current registration as a practitioner (If more than one country, include all that apply (n=136)	Acupalicale Hovider	
(II-150)	Australia	1
	Austria	2
	Belgium	1
	Canada	57
	Germany	3
	Hong Kong	1
	India	3
	Ireland	22
	Italy	1
	Liechtenstein	1
	New Zealand	1
	Pakistan	2
	Poland	1
	Saudi Arabia	1
	Singapore	1
	Spain	1
	Switzerland	15
	United Kingdom	2
	United Arab Emirates	1
	USA	31

Post-graduate training in manual spinal treatments (n=130)*	*some respondents included multiple types of post graduate training		Sample Response
	Master Degree	33	Masters in Orthopaedic Manual Physical Therapy
	Manual Therapy Certification	30	CAMPT/FCAMPT program
	Continuing Education Courses	30	Neuromuscular Stabilization (Prague school of rehabilitation)
	Graduate Program	17	Diploma of advanced studies in manual therapy
	Fellowship Program	8	2 year Fellowship in Manual Therapy at Institute of Orthopedic Manual Physical Therapy
	Residency Program	7	Hayward residency program
	Chiropractic College	3	Chiropractic college
	Doctorate Program	2	Evidence in Motion doctorate of physical therapy
Do you use ony of the	Board Certification	1	Board certified in family practice / osteopathic manipulative treatment as well as neuromusculoskeletal medicine/ osteopathic manipulative medicine
Do you use any of the following treatments? (choose all that apply) (n=192)			
	spinal manipulation	163	84.9%
	spinal mobilization	177	92.2%
	spinal adjustment	29	15.1%
Number of years using these treatments (n=135)			
	Mean	12.5	
	Median	10	
	Mode	10	
	Min	1	
	Max	35	
	SD	8.7	

<5%	3	2.1%
5 - 25%	44	30.3%
26 - 50%	57	39.3%
51 - 75%	33	22.8%
>75%	8	5.5%
Yes	109	75.7%
No	35	24.3%
Curiaz	30	35 5%
	57	55.570
Maitland	73	66.4%
McKenzie	65	59.1%
Mulligan	38	34.5%
Muscle Energy	26	23.6%
Myofascial Techniques	39	35.5%
Kaltenborn	35	31.8%
Chiropractic	11	10.0%
Osteopathic	23	20.9%
Other	31	
Applied kinesiology Biomechanical Assessment as taught by the Orthopedic Division of the Canadian Physiotherapy Association Clinical patterns as described by Hamilton Hall Combo of biomechanics and psychosocial with some neuroscience Conventional medical approach Diagnostic injections of local anaesthetic Dunning: Spinal Manipulation Institute Dynamic Neuromuscular Stabilization or DNS (Prague School) Evidence on motion General musculoskeletal assessment		
	Maitland McKenzie Mulligan Muscle Energy Myofascial Techniques Kaltenborn Chiropractic Osteopathic Other Applied kinesiology Biomechanical Assessment as taught by the Orthopedic Division of the Canadian Physiotherapy Association Clinical patterns as described by Hamilton Hall Combo of biomechanics and psychosocial with some neuroscience Conventional medical approach Diagnostic injections of local anaesthetic Dunning: Spinal Manipulation Institute Dynamic Neuromuscular Stabilization or DNS (Prague School) Evidence on motion	Maitland73McKenzie65Mulligan38Muscle Energy26Myofascial Techniques39Kaltenborn35Chiropractic11Osteopathic23Other31Applied kinesiology31Biomechanical Assessment as taught by the Orthopedic Division of the Canadian Physiotherapy Association

	Movement Control Test Battery from Luomajoki		
	Movement System Impairment syndromes		
	Muscle Balance		
	Muscle controle		
	Nwugarian Technique		
	Orthopedic Manual Physiotherapy		
	Orthopedic Medicine		
	O'Sullivan classifcation system (CLBP)		
	Patient response		
	Primitive reflex integration (PRRT) (Masgutova method)		
	Sahrmann,		
	Selective Functional Movement Assessment (SFMA)		
	Treatment based classification		
	Test Battery from Luomajoki		
	Zero Balancing		
	I don't use "protocols" for assessment or treatment. I use the techniques and or theories of assessment based upon what I checked. The goal is reproduction of pain or the comparable sign and to find joint hyper/hypomobility. To me "protocol" is a standardized, checklist approach to treating a patient, such like a CPR- clinical prediction rule		
Percentage of low back			
pain patients attributed to having a protruded disc (n=142)			
· /	a. <5%	33	23.2%
	b. 5 - 25%	60	42.3%
	c. 26 - 50%	34	23.9%
	d. 51 - 75%	9	6.3%
	e. >75%	6	4.2%
Of the patients with low back pain symptoms that you believe are discogenic, what percentage would be treated using a treatment similar to the one demonstrated in the video (n=140)			
	<5%	80	57%
	5 - 25%	18	12.8%

26 - 50%	11	7.8%
51 - 75%	1	.7%
>75%	6	4.2%

#### 3.5.1 Rationale for the Use of Spinal Rotary Manipulation

There were 80 responses to the question, *If you do use a treatment similar to the one demonstrated in the video, please describe your rationale for using it as a treatment for low back pain.* Sixty-one respondents indicated they use the same or a similar technique to the one shown in the video. Fourteen respondents reported they did not use this technique. Thematic analyses revealed four primary themes: mechanical benefits (n=43), neurophysiological effects (n=28), decisions based on experience and risk (n=23) and decisions based on empirical evidence (4). There were 11 sub-themes identified within the four primary themes. In general, respondents indicated that using SRM was based on proper patient selection, specific techniques, and associated risks.

#### 3.5.1.1 Mechanical Benefits

Mechanical benefits was the most frequent theme (n=43) reported by respondents who employed SRM for suspected DLBP. There were 8 subthemes identified. These included normalizing or restoring facet joint mobility (n=13), increasing range of motion (n=12), improving segmental joint motion (n=6), improving intervertebral '*space*' (distance between vertebral bodies) (n=5), non-classified (n=3), reducing pressure on nerve roots (n=1) and correcting of postural deviation (n=1). One respondent indicated that the maneuver may have its effect through reducing the size of the disc bulge. See Table 6.

#### 3.5.1.2 Neurophysiological Effects

The second most frequent theme (n=28) suggested clinicians expected a beneficial "neurophysiological effect" as a result of the SRM. Four subthemes were identified including pain relief (n=14), presumably through some alteration in the transmission of action potentials through ascending/descending nociceptive pathways, reducing local muscle tone/spasm through direct effects on muscle proprioceptors (n=10), improving circulation/neurological function through reducing constriction on local vessels or nerves

(n=3), and reduced local inflammation (n = 1) though no additional mechanistic information was provided in that response. Examples of respondents' explanations for proposed effects include, "possible afferent barrage of nociceptive input mediating longterm potentiation of c-fiber pain via stimulation of a-delta fibers possibly causing longterm depression', 'facilitating increased descending inhibition of ascending nociceptive signals', 'a short sharp stretch may overcome muscle guarding and perhaps the afferent information from the affected tissues allows the nervous system to conclude that it is ok to switch off the muscle guarding' and, 'decrease efferent signals in spinal stabilizing muscles." See Table 7.

#### **3.5.1.3** Clinical Reasoning Based on Experience and Risk

The third theme indicated that clinicians chose to apply an SRM maneuver out of what might be defined as "heuristics", or tacit knowledge gained through experience with the technique. Responses were unique and did not fit into any particular subthemes. The impression here was that some respondents were able to synthesize the available information about the patient and their perceived knowledge of empirical evidence to arrive at a decision of whether SRM was appropriate based on prior similar presentations weighted against the potential risks of the maneuver. Where risk or safety were cited, respondents indicated that they considered the maneuver to be of low risk, suggesting that their threshold for anticipated risk/benefit was not hard to exceed and that even if it was not effective, it was unlikely to result in an adverse outcome. See Table 8.

#### **3.5.1.4** Decisions Driven by Empirical Evidence

A minority of respondents (n=6) indicated that their motivations for using an SRM maneuver were driven less by a firm expectation of a particular effect or action, and more by available empirical evidence indicating when to use the technique. Some cited a specific approach such as the Treatment Based Classification System of (Alrwaily et al., 2016), while others made more generic statements such as, "*I practice in an evidence-based manner, research shows manipulation is helpful for treating discogenic back pain.*" See Table 8.

### 3.5.1.5 Do Not Use SRM

Within the responses were some (n=14) that indicated they would not use SRM for DLBP. Exploration of responses revealed little clarity about the reasons for not performing the maneuver. A representative response here was "*I do not use spinal manipulation with patients when I suspect discogenic LB*." Further information was not provided. See Table 8.

Facet or Sacroiliac Joint (n=14)	Range of Motion (n=9)	Segmental Mobility (n=9)	Joint Space (n=6)	Joint Mobility (n=3)	Not Classified (n=3)	Correction of Observed Deviations (n=1)	Nerve Root Pressure (n=1)
this technique normalizes the facet joint motion and treats any restriction in the facets and helps ease the movements most commonly. only a fraction of patients report more pain after this	increase joint range of motion	mobilize the spinal segments	improve space and circulation to the bulge	improving movement/mobilit y	directional preference rotation (MDT). posterior-lateral derangement	correct shift	decrease pressure off nerve root
facet impingement or SI	improving movement/mobility	hypomobility noted with PA testing	distract joint space	it often times improves mobility and relieves pain.	reduction bulging		
when facet is affected as secondary impairment, a lumbar rotation down glide or up glide can restore improved movement after discogenic lesion	decreased rotational range of movement,	lbp is never discogenic alone, there are always somatic dysfunctions causing most of the pain. and as there is very little movement in the treater segment it's absolutely safe!	opening up the compressed structure	facilitate joint mobility in a position that is not likely to irritate symptom presentation	to release joint tension		

Table 6. Sample responses for biomechanical rationale for using a spinal rotation manipulation.

		with a more specific variation	
open up facets distract joint space	to increase rom	first I never manipulate from a dorsal position, second I adjust in these cases the axis of movement. so mostly not on the painful segment when DH is the case	potentially could cause a slight 'opening' of foramen.
facet joint hypomobility	when properly applied, it restores restricted motion to the lumbar or ls facet on the patient's left.	if the disc appears stable enough, then I would use spinal facet joint manipulation to improve the segmental joint mobility. this allows for more effective extension exercises at the level of injury to reduce discal pressure	improvement of room within foraminal space
different technique to video if facet joint closing was sensitive	I use a side lying mobilization to treat discogenic pain. disc side is placed down. rotational mobilization can help to improve patient's extension and side bending	stiff facet in sup glide can cause aberrant forces on the disc during flexion - so restoration of stiff facet in sup glide can improve mechanics of segment and ease pressure on disc.	opening technique

i would use it if I suspected the pain to be due to a facet being stuck in its range of motion, and even then only when other techniques have first been exhausted

When properly applied, it restores restricted motion to the lumbar or LS facet on the patient's left.

i would use a shorter lever, more controlled technique for nondiscogenic lbp - facet dysfunction, local muscle guarding

facet joint problem

stiff facet in sup glide can cause aberrant forces on the disc during flexion - so restoration of stiff facet in sup glide can improve mechanics of segment and ease pressure on disc

decreased mobility in arom movements that does not improve with repeated I use locking whenever possible and use a level specific technique in order to restore motion

limited rotation, no

leg pain, no night

pain

get rid of any residual stiffness in range of motion.

68

movement towards direction of preference, without neurological findings, muscular hypertonicity

for a fixated/locked facet joint or a joint compressed from excessive muscle tone. I would not usually use manipulation for a true discogenic problem

for sacroiliac joint pain

Pain (n=14)	Muscle (n=10)	Other (n=3)	Inflammation (n=1)
Release endorphins for pain			
relief	decrease muscle tension	improve neurological function	Decrease inflammation
Possible afferent barrage of nociceptive input mediating long-term potentiation of c- fiber pain via stimulation of a- delta fibers possibly causing long-term depression	relax the muscles (only if the position is comfortable and only adjusting the segments above or below the suspected lesion	improve space and circulation to the bulge	
pain relief	decrease efferent signals in spinal stabilizing muscles	Non-specific, neurophysiological effects	
pain relief descending inhibition	trigger points lumbar extensors		
Mechanical LPB	a short sharp stretch may overcome muscle guarding and perhaps the afferent information from the affected tissues allows the nervous system to conclude that it is ok to switch off the muscle guarding		
It often times improves mobility and relieves pain	Patients who report stiffness in the lower back who do not exhibit neurological symptoms or any 'red flags'		
Neurophysiological effects, such as facilitating increased descending inhibition of ascending nociceptive signals	I would use a shorter lever, more controlled technique for non- discogenic LBP - facet dysfunction, local muscle guarding		

#### Table 7. Sample responses for neurophysiological rationale for using a spinal rotation manipulation.

Worsening of decreased spasm/pain, asymmetrical/unilateral improved motor control symptoms following exhaustion of sagittal plane forces and elicitation of centralization or clear functional/mechanical improvement after performing Long lever not common For a fixated/locked facet technique in my practice joint or a joint compressed however if I were to use a nonfrom excessive muscle specific technique as above, it tone. would be on an individual that did not have radiating symptoms and symptoms were not worse or reproduced in that position pre-manipulation. I would use this to get the individual moving and then progress to exercise as quickly as I could First, I never manipulate from a Stretched muscles dorsal position. Second I adjust in these cases the axis of movement. So mostly not on the painful segment when a DH is the case To activate GABA for reducing local deep pressure/tension in surrounding tissues and reducing pain

Clinical Reasoning Based on Experience and Risk (n=20)	Not Used (n=14)	Decisions Driven by Empirical Evidence (n=6)
Patients who report stiffness in the lower back who do not exhibit neurological symptoms or any 'red flags'	Do not use this technique	I practice in an Evidence based manner, research shows manipulation is helpful for treating discogenic back pain and carries very low risks
absence of hard motor signs	I do not use spinal manipulation with patients when I suspect discogenic LBP	it has been proven effective via clinical prediction rule to reduce pain and symptoms
if I were to use a non-specific technique as above, it would be on an individual that did not have radiating symptoms and symptoms were not worse or reproduced in that position pre-manipulation.	I don't use rotation impulse for discogenic diagnosis	Evidence based Clinical prediction rules
limited rotation no leg pain no night pain	I do not	Clinical prediction rules and the clinical practice guidelines recommend its use in a subset of LBP patients.
decreased mobility in AROM movements that does not improve with repeated movement towards direction of preference, without neurological findings, muscular hypertonicity	None	According to treatment based classification manipulation is effective in acute stage < 16 days,
Patients who report stiffness in the lower back who do not exhibit neurological symptoms or any 'red flags'	don't use with discogenic patients	Maitland recommended technique for discogenic back pain
Patient may receive manipulative treatment if: no sx distal to knee, shorter duration of $sx < 3$ wks, hypomobility noted with PA testing		
I am on the other side of the body but yes I do once severity and irritability are low enough	Non specific and too much rotation: never used	
Depends on the patient. Primarily will do a rotary type adjustment of the lumbar spine/pelvis. If patient is unable to tolerate that position a prone adjustment with a drop piece will be utilized.	None	

# Table 8. Sample responses for Clinical Reasoning Based on Experience and Risks Not Used and Decisions Driven by Empirical Evidence Rationales for using spinal manipulation.

I don't use manipulation on patient I suspect of having discogenic pain if there are overt signs of radiculopathy	I do not
This looks like a "sham" manipulation. I'm doing manipulation on lumbar spine, with a "body drop" and not with the Hands. I'm standing in front of the patient an fixing the segment, that I want to manipulate. The kind of manipulation I do is a HVLA.	Would not do this on my pet cow if you paid me
In acute episodes of LBP and symptoms no below knee, this can be a useful technique if done lying on the correct side. I would likely do the treatment as mobilization 1st to see it's effects.	Non specific and too much rotation: never used
depends on clinical presentation	virtually never now, used to in past, particularly with sports teams when requested!
For patients who have symptoms symptoms above the knee (either at onset or who have centralized) and progress has plateaued with repeated motions and spinal mobilization,	to global
May also use a similar technique for assessment purposes to better understand lesion behavior	technique is horrid and non- specific in the video, so I would say 0% treated as such, but know what you are getting at.
I use a side lying mobilization to treat discogenic pain. Disc side is placed down. Rotational mobilization can help to improve patients extension and side bending.	no uncontrolled multilevel techniques
If force progression according to McKenzie do not work, my final force progression is a the manipulation according to Cyriax (Lumbar Stretch Maneuver)	
Treatment is based on diagnosis. If the technique shown on the video was done without a diagnosis of the somatic dysfunction, then it should not be done (answer to #10 would be zero). If a somatic dysfunction in the lumbar spine L5RRSL was present, then the video technique could be employed. After the manipulative technique, the patient would be re-	

evaluated for improvement of motion.

I would apply only on under 55year-old with no symptoms beyond knee who was not frightened of bending but rather couldn't - like they were jammed up or locked

LBP is never discogenic alone, there are always somatic dysfunctions causing most of the pain.

I would face the patient, closer to patient, do pre manip testing, aka progressive mobilization

I did not get to see the video as my hospital computer blocked it but by looking at the picture I would use this technique with a bolster under the downward hip as described in S-1 by Paris for positional distraction, a gait belt can be used where the practioners R hand is placed

Same or better results with weaker (longer during) technique

## 3.6 Discussion

In this study we have reported the second part of the results of an international survey of clinicians focusing specifically on clinician beliefs about the mechanisms of action of SRM. The respondent demographics and practice settings indicated that the respondents were well-targeted to the purpose of the survey, evidenced by the majority of respondents who use SMOB and/or SM in clinical practice and have done so for an average of over 12 years.

In our study spinal mobilization was used as a treatment by 92.2% (n= 177). Spinal manipulation was used by 84.9% (n=163) and 15.1% (n=29) used spinal adjustments. In comparison, a survey of physiotherapists by Hendrick (2013) with a 17% response rate (n=170/1029) reported a 92.9% use of spinal mobilization and 33.5% use of spinal manipulation. The frequency of spinal mobilization use is almost identical between the two studies, indicating that this is a nearly universal strategy for treatment of NSLBP. The much higher rate of spinal manipulation use in our study may reflect the targeted recruitment strategy we used in that we were specifically seeking participants who would

be most likely to use such a technique in routine practice. Choice of intervention is likely dependent on several factors including professional discipline, educational background, post graduate musculoskeletal specialization, years of clinical experience, and the use of clinical prediction rules and guidelines (Mourad et al., 2022).

#### **3.6.1** Rationale for the Use of Spinal Rotary Manipulation

Four themes emerged from the thematic analysis of responses to the question, If you do use a treatment similar to the one demonstrated in the video, please describe your rationale for using it as a treatment for low back pain. The largest reported theme was mechanical benefits. The 4 largest mechanical benefit subthemes were, normalizing or restoring facet joint mobility, increasing range of motion (ROM), improving segmental joint motion, improving intervertebral "space" (distance between vertebral bodies). Respondents were not specifically asked to elaborate on their responses although some did provide more information.

#### **3.6.1.1** Facet Joints

The largest subtheme was that SRM could be used to normalize, "*open up*" or restore altered facet joint mechanics, described variously as, locked, fixated, stiff or hypomobile. No details were provided as to how the hypomobility was determined. Similar findings were reported from a survey of certified Canadian manipulative physiotherapists which revealed that the top two reasons for choosing to manipulate rather than mobilize were that the spinal joint is fixated or stuck and to improve joint mobility (Carlesso et al., 2013). The two top reasons for choosing to mobilize rather than manipulate were that manipulation is contraindicated and the patient's condition is too irritable for manipulation. There is no current research supporting the proposed effect that SMT normalizes or restores facet joint mobility. There is evidence of a mechanical gapping of the facet joints during manipulation, however, the clinical significance remains unknown (McCarthy et al., 2006).

#### 3.6.1.2 Range of Motion

Respondents reported that SRM could improve/increase/restore lumbar ROM without further explanation as to the underlying pathology or mechanism at work. One respondent did offer a rationale. "I use a side lying mobilization to treat discogenic pain. disc side is placed down. rotational mobilization can help to improve patient's extension and side bending." Another offered this explanation. "I use locking whenever possible and use a level specific technique in order to restore motion." In the literature, ROM is less commonly reported as an outcome in studies of the effects of SMT (Almeida et al., 2023; Chiarotto et al., 2015; Donelson et al., 2012; Millan et al., 2012). It may seem counter intuitive that studies of movement invoked pain, rarely include ROM as an outcome measure (Bialosky et al., 2018) given that research demonstrates that the mobility of the lumbar spine in people with LBP is significantly lower (Shum et al., 2013). Notable authors and clinicians, within the field of manual therapy, have strongly advocated for the use of within-session reassessment of ROM to evaluate the effect of treatment and to guide ongoing intervention (Hahne et al., 2004). Patients whose pain and ROM improved within-session, are considerably more likely to demonstrate betweensession improvements (Hahne et al., 2004). While there are reports of significant differences for some outcome measures, before and after spinal mobilization (Shum et al., 2013), the efficacy of SMT on ROM remains conflicting (Aoyagi et al., 2019; Hahne et al., 2004; Millan et al., 2012).

#### **3.6.1.3** Segmental Joint Motion and Intervertebral Space

Respondents reported that SRM could improve segmental joint mobility, mechanics, reduce hypomobility and "open up" space for a bulge or a compressed structure. For the most part few details were provided as to what makes up a segmental joint nor how to assess and determine problems with segmental motion are present. Contrary opinions were offered by two respondents with one stating, "LBP is never discogenic alone, there are always somatic dysfunctions causing most of the pain. and as there is very little movement in the treater segment it's absolutely safe, with a more specific variation', and another stated, 'if the disc appears stable enough, then I would use spinal facet joint manipulation to improve the segmental joint mobility. This allows for more effective

*extension exercises at the level of injury to reduce discal pressure.*" To date there is no credible evidence that SMT results in a lasting vertebral positional change or improves intervertebral space, i.e., the distance between vertebral bodies (Gyer et al., 2019; Lascurain-Aguirrebena et al., 2016).

#### **3.6.1.4** Neurophysiological Effects

The second most frequent theme from our analysis was beneficial neurophysiological effects as a result of the SRM. These include pain relief possibly through some alteration in the transmission through ascending/descending nociceptive pathways, reducing local muscle tone/spasm, improving circulation/neurological function and reduced local inflammation. Examples of respondents' explanations for proposed effects include, "possible afferent barrage of nociceptive input mediating long-term potentiation of cfiber pain via stimulation of a-delta fibers possibly causing long-term depression', 'facilitating increased descending inhibition of ascending nociceptive signals', 'a short sharp stretch may overcome muscle guarding and perhaps the afferent information from the affected tissues allows the nervous system to conclude that it is ok to switch off the muscle guarding' and, 'decrease efferent signals in spinal stabilizing muscles." Similar to our survey results, studies of the effects of SMT on asymptomatic and symptomatic subjects have reported responses on the autonomic nervous system including, spinal reflexes, proprioception, functional brain connectivity, hypoalgesia, muscle responses and pain intensity and processing (Bialosky et al., 2010; Coronado et al., 2012; Currie et al., 2016; Pickar & Bolton, 2012; Wirth et al., 2019). Ohers have reported effects on the immune and endocrine systems (Colombi & Testa, 2019), visceral responses (Bolton & Budgell, 2012) and changes in biochemical markers (Kovanur-Sampath et al., 2017). Evidence suggests that SMT results in various short term neurophysiological effects such as, hypoalgesia, sympatho-excitation, and improved muscle function (Lascurain-Aguirrebena et al., 2016) however, the quality of evidence is very low (Goodwin et al., 2021; Gyer et al., 2019). A recent systematic literature review, found no consistent and meaningful or hypoalgesic effects from either SM of SMOB in pain-free individuals and patients with musculoskeletal disorders (Jung et al., 2023). In summary, the evidence to

date suggests that the effects of SMT are beyond biomechanical changes but that evidence remains limited (Gyer et al., 2019).

#### **3.6.1.5** Clinical Reasoning Based on Experience and Risk

The third theme that came out of our analysis is clinical reasoning (CR) or clinical decision making (CDM). CR refers to the thinking process associated with the clinical examination and management of a patient (Karvonen et al., 2017; Riley et al., 2021; Sniderman et al., 2013). Responses from our survey indicated clinicians choose to apply an SRM maneuver based on the tacit knowledge gained through their own clinical experience which would also likely be influenced by differences in professional education, post graduate training and the way in which research findings are interpreted (Kent, Keating, & Buchbinder, 2009). The impression here was that some respondents were able to synthesize the available information about the patient and their perceived knowledge of empirical evidence to arrive at a decision of whether SRM was appropriate based on prior similar presentations weighted against the potential risks of the maneuver. Where risk or safety were cited, respondents indicated that they considered the maneuver to be of low risk, suggesting that their threshold for anticipated risk/benefit was not hard to exceed and that even if it was not effective, it was unlikely to result in an adverse outcome. CR of experienced clinicians differs from entry level clinicians. Respondents in our survey had been in their respective discipline an average of 15 years (range of 1-44years) and had been using SMT as a treatment for an average of 12.5 years (range of 1 - 1) 35 years). (Mourad et al., 2022) reported that Italian physiotherapists with more than five years of clinical experience and who were familiar with clinical prediction rules were more comfortable with and perceived SM as safe. It is clear from our survey responses that clinicians consider using manipulation after screening for contraindications.

#### **3.6.1.6** Decisions Driven by Empirical Evidence

Several respondents indicated that their motivations for using an SRM maneuver were driven less by a firm expectation of a particular effect or action, and more by available empirical evidence indicating when to use the technique. Several cited CPR's, including one respondent who stated "*SM is effective in the acute stage*", i.e., < 16 days onset,

which is one of a number of variables reported, that increase the likelihood of success with SM from 45% to 95% (Flynn et al., 2002). Other variables include, duration of symptoms <16 days, Fear Avoidance Belief Questionnaire Work subscale score <19, at least one hip with >35 degrees of internal rotation range of motion, hypomobility in the lumbar spine, and no symptoms distal to the knee. Interestingly, (Learman et al., 2014) in a study that used the clinical prediction rule proposed by Flynn, and using data from a larger RCT, concluded that patients who satisfied Flynn's prescriptive CPR for lumbar spinal manipulation benefited as much from non-thrust manipulation as from thrust manipulation (Learman et al., 2014). A single respondent referred to clinical practice guidelines (CPG's) in making decisions without offering further details. Some respondents specifically identified an approach such as the Treatment Based Classification System (Alrwaily et al., 2016), while others made more generic statements such as, "*I practice in an evidence-based manner, research shows manipulation is helpful for treating discogenic back pain*."

Within the responses were some that indicated they would not use SRM for DLBP. Exploration of these responses revealed the reasons for not preforming a maneuver as demonstrated on the video were not due to any belief in the effectiveness (or lack thereof) of the technique, but that the respondents did not use such a maneuver or that the maneuver was not employed in the case of patients with DLBP. Representative responses included "*I do not use spinal manipulation with patients when I suspect discogenic LBP*." Empirical evidence for the use of SRM or SM on DLBP is largely confined to studies of the centralization phenomenon (CP) and directional preference (DP) (Apeldoorn et al., 2016; May et al., 2018; Simon et al., 2014). DP as a biomechanical effect of SRM was reported by one survey respondent while another stated it could reduce a bulging disc. A recent systematic review concluded that the importance of centralization and DP as prognostic factors is "probably overwhelming; whether they indicate a particular management pathway is not clear" (May et al., 2018, p. 61).

Prior studies have found, a significant number of clinicians who manage people with acute LBP do not follow or are non-compliant with evidence-based recommendations or clinical guidelines (Di Iorio et al., 2000; Walker et al., 2011; Webster et al., 2005;

Williams et al., 2010). Webster (Webster et al., 2005) reported that in patients without sciatica and with sciatica, 26.9% and 4.3% of physicians fully complied with published guidelines, respectively, and the odds of noncompliance increased 1.03 times for each year in practice. Clinicians report that while they believe in the principles of evidence-based practice and its relevance to clinical practice, clinical guidelines are outdated, unrealistic and idealistic, challenge clinician autonomy, and lack relevance and specificity (Adams et al., 2018; Bill et al., 2020; Di Iorio et al., 2000; Parr & May, 2014).

#### **3.6.1.7** Implications for Clinicians and Researchers

The influence of manual therapy is not purely biomechanical but there is clearly more than neurophysiology to consider. Questions remain about clinical decisions to do with the force, amplitude, and direction of manipulative interventions (Swanson & Creighton, 2020).

#### 3.7 Limitations and Weaknesses

Online web-based surveys have a number of potential limitations (Draugalis & Plaza, 2009) including low response rates, non-response bias, incomplete responses, misrepresentation of identity, age, gender, level of education and other variables. This study included a low overall response rate (1.3%), as well as partial item-level responses.. Although we received a relatively small sample size, our results are in keeping with other studies that examined practitioner views on signs and symptoms of low back pain (LBP), non-specific low back pain (NSLBP) and DLBP. A low response rate can give rise to sampling bias (Draugalis & Plaza, 2009). The results of a study with a low response rate are not representative of a larger population. Although a higher response bias is to occur. Finally, as this was anonymous survey research, we had no ability to pose follow-up or probing questions where clarity was needed. As a result, several of the responses were too ambiguous to be clearly assigned to a specific sub-theme, resulting in a large proportion of unclassified responses that were clearly associated with one of the broader themes but were missing more specific information.

Thematic analysis as used to analyze the data in this study has advantages and disadvantages. There is a lack of substantial literature on thematic analysis compared with that of grounded theory, ethnography and phenomenology (Nowell et al., 2017). One method to establish trustworthiness in the data analysis is to use criteria such as credibility, transferability, dependability and confirmability which are comparable to the concepts of validity and reliability used in conventional quantitative research. See (Nowell et al., 2017) for a more detailed explanation of these criteria. We could have used a more detailed audit trail that would have provided evidence of the decisions and choices made by the two independent researchers, used a reflective journal to document the logistics of the data analysis as other researchers would benefit from being able to clearly follow a decision trail (Nowell et al., 2017).

Given the responses to survey question 7, *Of those patients who present to your practice with low back pain what percentage do you attribute to having a bulged or protruded disc(s)?* we could have included a subsequent question such as, *In those patients who you think do not have a bulged or protruded disc(s) what pathology(ies) would you attribute the symptoms to?* In addition to open-ended response questions, we could have included requests for more detailed elaborations of open-ended response questions with prompts for example, following the question SM rationale, "*Please describe the procedures you use if you determine that SM would be beneficial.*"

## 3.8 Conclusion

There remains a gap between clinical practice and evidence on the use of SMT. Studies reporting the largest benefits of SMT used clinical criteria to select patients as more likely to benefit. Currently, there is no clear evidence to assist clinicians determine the subgroup that responds best to SMT.

## 3.9 Ethical Approval

The study was approved by Western University's Health Science Research Board.

## 3.10 Funding

Through the Pain and Quality of Life Integrative Research Lab, Faculty of Health Sciences, Western University, London, ON

## 3.11 Conflicts of Interest

There are no conflicts of interest.

## 3.12 What is Already Known on this Topic

SMT is commonly used as a treatment for patients with NSLBP. Some positive clinical effects have been demonstrated with SMT for treating some subgroups of NSLBP. There is no clear evidence to assist clinicians in determining the subgroup that responds best to SMT or the specifics of any SMT that would be effective for the subgroups.

## 3.13 What This Study Adds

Mechanical benefits is the most reported rationale for using SMR. Clinician decisionmaking regarding the use and mechanisms of specific manual therapy intervention for DLBP remains critical in the absence of standards and explanations for the underlying causes of DLBP. Findings from clinicians' perspectives offer valuable insights for the development of high-quality and well-designed observational studies of subgroups of NSLBP that demonstrate positive clinical effects from SMT.
# Chapter 4

# 4 The clinical signs and symptoms of discogenic low back pain (DLBP) associated with lumbar disc herniations. A systematic review

# 4.1 Rationale for the Study

Non-specific low back pain (NSLBP) makes up the largest proportion of patients with acute low back pain (LBP) with estimates as high as 90% (Balagué et al., 2012; Ferreira et al., 2023; Han et al., 2023; Videman & Battié, 2012). Intervertebral disc derangement (IDD) has been reported as a significant structural source of symptoms in NSLBP patients and is frequently referred to as, discogenic low back pain (DLBP) (Fujii et al., 2019; Lorio et al., 2023; Peng, 2013). It is common, however, to find only minimal internal disc changes in patients diagnosed with DLBP (Kim et al., 2009; Ract et al., 2015; Zhou & Abdi, 2006). Moreover, the high rate of false positive results with imaging techniques including MRI, CT-scan or discography, as well as that by age 60, the frequency of symptomatic episodes drops quickly, challenges the notion that IDD is the primary underlying mechanism for DLBP (Bisschop & Van Ooteghem, 2003). Therefore, there are likely additional mechanisms involving intervertebral discs (IVDs) that may produce LBP in some patients (Brock et al., 1992; Lipson, 1988; Moore et al., 1996; Rajasekaran et al., 2013). One possible mechanism is disc herniation with and without nerve root involvement (Chan et al., 2013; Cyriax, 1950; Petersen et al., 2003, 2017).

DLBP remains without widely accepted standards or agreement on its terminology, clinical signs and symptoms or treatment, leaving practitioners in a quandary as to its diagnosis and what to choose as an effective intervention (Fujii et al., 2019; Kreiner et al., 2020). Estimates of the prevalence of DLBP vary, depending on how it is defined or whether it is acute, subacute, recurring acute episodes or persistent chronic pain. The lack of agreed upon standards for its definition and diagnostic criteria likely affects prevalence rates and so DLBP is possibly under-reported as a clinical entity.

Expert panel studies have reported several clinical features of DLBP associated with disc herniation, however, the level of consensus was low (Chan et al., 2013; Cid et al., 2015;

Dewitte et al., 2018). The results of the international survey described in Chapters 2 and 3 of this dissertation on the perspectives of international practitioners regarding the signs and symptoms of DLBP revealed some common features with those reported by expert panelists, however both results have yet to be evaluated against published literature.

The purpose of this systematic review was to investigate the quantity, level and quality of evidence in the published literature on the clinical signs and symptoms of DLBP associated with disc herniation and to compare the results with the views reported by international clinicians.

# 4.2 Objectives

1. Identify the clinical signs and symptoms of DLBP associated with disc herniation as reported in the literature.

2. Identify and report on reference standards and diagnostic measures associated with the clinical signs and symptoms.

3. Examine the quality and level of evidence of studies reporting clinical signs and symptoms.

# 4.3 Methods

## 4.3.1 Study Design

A systematic review was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines for Reporting Systematic Reviews (Page et al., 2021). We followed the PRISMA 2020 statement as well as the PRISMA item checklist in completing the review (Page et al, 2021).

## 4.3.2 Concept Map

A concept map based on the research question was developed using a framework from the P.I.E.C.E.S. excel workbook, a planning tool for conducting systematic reviews (<u>https://guides.lib.utexas.edu/pbh/reviews</u>). Five primary concepts were identified including discogenic, low back pain, signs, symptoms and diagnosis.

Alternative terms, including medical subject headings (i.e., MESH) and key words for each primary concept were then identified (Table 9). This was done in collaboration with three experienced librarians from Western University, London, Ontario, Canada.

Concept	Thesaurus term such as MESH heading	Keywords
lumbar	lumbar; lumbar vertebrae;	back symptoms; lumbosacral; lumbar spine
disc	disc; disk; intervertebral disc;	internal disc disruption;
herniation	herniat; bulg; protrusion; extrusion; sequest*; disrupt; displace; prolapse; intervertebral disc displacement/	intervertebral disc herniation; nucleus pulposus deformation; intervertebral disc prolapse;
symptoms and signs	clinical finding; diagnosis/; features; symptoms; signs; clinical sign; clinical symptoms; histor; test; assess; eval; physical; exam	history taking; mechanical diagnosis and treatment; back symptoms: diagnostic criteria; clinical reasoning; classification of low back pain; evaluation; classification; diagnostic accuracy; diagnostic validity; clinical reasoning; clinical patterns; evaluation; diagnostic criteria; outcome measures; clinical decision making/; diagnostic techniques and procedures*/
discogenic pain	pain; low back pain; axial pain; non specific low back pain; discogenic low back pain	
exclude	not radiculopathy; not cervical	
limit to English; limit to human	spine,	

#### Table 9. Concept Map.

# 4.3.3 Eligibility Criteria

Studies had to meet the following inclusion and exclusion criteria to be included in the review.

# 4.3.3.1 Inclusion criteria

Peer reviewed studies of participants of any age with low back pain due to herniated or prolapsed lumbar disc(s) that included;

- history and/or physical examination data on participants of any age with low back pain with/without radiculopathy due to herniated or prolapsed lumbar disc(s);
- ii) history and/or physical examination data against a reference standard including but not limited to plain radiograph, magnetic resonance imaging (MRI), computed tomography (CT) and/or ultrasound (US);
- iii) diagnostic accuracy measures for some or all the reference standards if reported.

# 4.3.3.2 Exclusion Criteria

- i) Commentaries, reviews and editorials;
- Studies reporting results of surgical outcomes without referencing pre surgical signs and symptoms,
- iv) Studies published in a language other than English;
- v) Animal studies.

# 4.3.4 Information Sources

# 4.3.4.1 Electronic searches

The following databases were searched. MEDLINE (Ovid), EMBASE, and CINAHL (all publications <1946 to September 22, 2021). Search alerts following September 22, 2021 up to the present were checked regularly for updated retrievals.

# 4.3.4.2 Other Resources

Hand searching had been conducted prior to the formal search to scan the literature based on the concept map.

## 4.3.5 Search Strategy

Several iterations of the search strategy were trialed before the final version was determined.

The search strategy for Medline (Ovid) included key terms combined with the extensions mp. and tw,kf. See Table 10. When the broader search using the extension mp was compared with the results of the narrower search using the extension tw.kf, there were a number of articles unique to each search, therefore both extensions were used to avoid missing relevant articles. Search strategies were then customized for EMBASE, and CINAHL (EBSCO). See Appendix 0-5 for Cinahl (EBSCO) search strategy terms.

#### Table 10. Search strategy for Medline Ovid

- 1. lumbar Vertebrae/ or lumbar.mp.
- 2. lumbar spine.mp.
- 3. lumbosacral Region/ or lumbosacral.mp.
- 4. back symptoms.mp.
- 5. 1 or 2 or 3 or 4
- 6. disc.mp. or exp Intervertebral Disc/
- 7. disk.mp.
- 8. discogenic.mp.
- 9. internal disc disruption.mp.
- 10. intervertebral disk disruption.mp. or Longitudinal Ligaments/
- 11. intervertebral disc disruption.mp.
- 12. 6 or 7 or 8 or 9 or 10 or 11
- $13. \hspace{0.1 cm} prolapse.mp. \hspace{0.1 cm} or \hspace{0.1 cm} Prolapse/$
- 14. intervertebral disc displacement.mp. or Intervertebral Disc Displacement/
- 15. herniation.mp.
- 16. bulge.mp.
- 17. protrusion.mp.
- 18. extrusion.mp.
- 19. sequestration.mp.
- 20. disruption.mp.
- 21. displacement.mp.
- 22. nucleus pulposus/ or nucleus pulposus deformation.mp.
- 23. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
- (Diagnosis or Diagnosis, Differential or diagnosis).mp. [mp=title, abstract, original title, name of substance word,
   subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- 25. clinical history.mp.
- 26. (medical history taking or Medical History Taking).mp. [mp=title, abstract, original title, name of substance
- word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept

word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

- 27. physical examination.mp. or Physical Examination/
- 28. clinical symptoms.mp.
- 29. clinical signs.mp.
- 30. clinical assess\*.mp.
- 31. clinical test\*.mp.
- 32. clinical finding\*.mp.

(clinical reasoning or Clinical Reasoning or Clinical Decision-Making).mp. [mp=title, abstract, original title,

- name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- 34. clinical pattern\*.mp.
- 35. clinical featur\*.mp.
- 36. clinical presentat\*.mp.
- 37. clinical evaluat\*.mp.
- 38. diagnostic criteria.mp.

(diagnostic technique\* or diagnostic procedure\*).mp. [mp=title, abstract, original title, name of substance word, 39. subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word,

- protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (classification or Classification).mp. [mp=title, abstract, original title, name of substance word, subject heading
- 40. word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- 41. mechanical diagnosis.mp.
- 42. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41
- 43. low back pain.mp. or Low Back Pain/
- 44. lumbar pain.mp.
- 45. axial low back pain.mp.
- 46. acute low back pain.mp.
- 47. non specific low back pain.mp.
- 48. acute non specific low back pain.mp.
- 49. discogenic low back pain.mp.
- 50. 43 or 44 or 45 or 46 or 47 or 48 or 49
- $51. \hspace{0.2cm} 5 \hspace{0.1cm} and \hspace{0.1cm} 12 \hspace{0.1cm} and \hspace{0.1cm} 23 \hspace{0.1cm} and \hspace{0.1cm} 42 \hspace{0.1cm} and \hspace{0.1cm} 50 \hspace{0.1cm}$
- 52. limit 51 to english language
- 53. 52 not (exp animals/ not humans/)
- 54. (lumbar or Lumbar Vertebrae).tw,kf.
- 55. lumbar spine.tw,kf.
- 56. (lumbosacral or Lumbosacral region).tw,kf.
- 57. back symptoms.tw,kf.
- 58. 54 or 55 or 56 or 57
- 59. (disc or Intervertebral Disc).tw,kf.
- 60. disk.tw,kf.
- 61. discogenic.tw,kf.
- 62. internal disc disruption.tw,kf.
- 63. (intervertebral disk disruption or Longitudinal Ligaments).tw,kf.
- 64. intervertebral disc disruption.tw,kf.
- 65. 59 or 60 or 61 or 62 or 63 or 64
- 66. (prolapse or Prolapse).tw,kf.
- 67. herniation.tw,kf.
- 68. bulge.tw,kf.
- 69. protrusion.tw,kf.

- 70. extrusion.tw,kf.
- 71. sequestration.tw,kf.
- 72. disruption.tw,kf.
- 73. displacement.tw,kf.
- 74. (Nucleus Pulposus or nucleus pulposus deformation).tw,kf.
- 75. (intervertebral disc displacement or Intervertebral Disc Displacement).tw,kf.
- 76. 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75
- 77. (Diagnosis or Diagnosis, Differential or diagnosis).tw,kf.
- 78. clinical history.tw,kf.
- 79. (medical history taking or Medical History Taking).tw,kf.
- 80. (physical examination or Physical Examination).tw,kf.
- 81. clinical symptoms.tw,kf.
- 82. clinical signs.tw,kf.
- 83. clinical assess\*.tw,kf.
- 84. clinical test\*.tw,kf.
- 85. clinical finding\*.tw,kf.
- 86. (clinical reasoning or Clinical Reasoning or Clinical Decision-Making).tw,kf.
- 87. clinical pattern\*.tw,kf.
- 88. clinical featur\*.tw,kf.
- 89. clinical presentat\*.tw,kf.
- 90. clinical evaluat\*.tw,kf.
- 91. diagnostic criteria.tw,kf.
- 92. (diagnostic technique or diagnostic procedure\*).tw,kf.
- 93. (classification or Classification).tw,kf.
- 94. mechanical diagnosis.tw,kf.
- 95. 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94
- 96. (low back pain or Low Back Pain).tw,kf.
- 97. lumbar pain.tw,kf.
- 98. axial low back pain.tw,kf.
- 99. acute low back pain.tw,kf.
- 100. non specific low back pain.tw,kf.
- 101. acute non specific low back pain.tw,kf.
- 102. discogenic low back pain.tw,kf.
- 103. 96 or 97 or 98 or 99 or 100 or 101 or 102
- 104. 58 and 65 and 76 and 95 and 103
- 105. limit 104 to english language
- 106. 105 not (exp animals/ not humans/)
- 107. 53 not 106

#### **4.3.6** Selection Process

Covidence, a web-based software program for conducting systematic reviews available through Western University's libraries, was used in this review. Full text articles identified through the searches of the three databases were imported into Covidence software. Duplication of articles was done through the deduplication function in Covidence. Once duplicates were removed the screening process was initiated beginning with titles and abstracts followed by screening of full text articles that met the eligibility criteria.

One reviewer (JP) excluded titles that were clearly unrelated to the research question. Two reviewers (JP, SM) independently screened abstracts for relevance using the inclusion criteria. Disagreements were resolved through discussion. The two reviewers then independently screened full texts based on the inclusion criteria.

At the stage of the full text review, the original inclusion and exclusion criteria were found to be too broad resulting in a number of marginal papers being included. To conduct a more focused review based on the research question, the inclusion criteria were modified following discussions between the two reviewers (JP, SW).

#### 4.3.7 Amended Inclusion Criteria

The amended inclusion criteria would include peer reviewed studies of participants of any age with low back pain due to herniated or prolapsed lumbar disc(s) that included;

- i) a research question;
- ii) history and/or physical examination data against a comparable reference standard including but not limited to plain radiograph, magnetic resonance imaging (MRI), computed tomography (CT) and/or ultrasound (US);
- iii) diagnostic accuracy measures for some or all the reference standards if reported.

Two reviewers (JP, SW) screened full text articles using the amended inclusion criteria. A third reviewer (DW) was available in the case of disagreement between the two reviewers (JP, SW).

## 4.3.8 Data Collection Process

## 4.3.8.1 Data Extraction

A study specific data extraction form relevant to the review question and based on the inclusion criteria was developed following discussions between two reviewers (JP, SW). The form was created using resources including the checklists from the Critical Appraisal Skills Programme (Uk, 2019), Cochrane Collaboration's Data Collection form for RCT's and non-RCT's (Bossuyt et al., 2013), and guidelines from Covidence software, 6. Data Extraction - Knowledge Synthesis: Systematic & Scoping Reviews - Research Guides at Western University. The form was piloted using sample articles prior to its final content being determined.

# 4.3.8.2 Data Items

The data extraction form sought to capture study details in four areas: author and publication details; study methodology items, such as the research question, study design, method of participant enrollment/recruitment, eligibility criteria, and participants' description; data regarding diagnostic tests; and any reported measures of diagnostic accuracy such as sensitivity, specificity, predictive values, likelihood and odds ratios. See Table 11. Missing items were labelled as such. Study characteristics and diagnostic data were collated and presented in tabular form for further analysis.

# Table 11. List of Data Extraction Items \*\*Most important for inclusion to risk of bias and compatibility assessment.

Data extractor
Date of extraction
Covidence extraction reference number
Study title
Author(s)
Year
Aim, Type, Study Design **
Level of evidence **
Inclusion criteria **
Exclusion criteria **
Is there a clear and focused question? **
Is there a comparison with an appropriate reference standard? **
Is it worth continuing?
Participant enrollment, random or consecutive? **
Participant's characteristics **
Did participants constitute a representative sample of those presenting with a diagnostic dilemma? **
Country study conducted in
Blinding **

List of symptoms reported **
Reference standard for symptoms **
Sensitivity reported for symptoms or signs/tests **
Specificity reported for symptoms or signs/tests **
Predictive values +ve/-ve for symptoms or signs/tests **
List of signs/tests/diagnostic items **
Reference standard for signs/tests/items **
Likelihood ratios +ve/-ve reported **
Odds ratios reported
Did all participants get the same diagnostic test and reference standard? **
Could the results of the test been influenced by the results of the reference standard? Were those interpreting the test
and reference standard blind to the other results? **
Is the disease status of the tested population clearly described? **
Were the methods for performing the test described in sufficient detail? **
What are the results? **
How sure are we about the results? Consequences and cost of alternatives performed? **
Can the results be applied to all patients/the population of interest? **
Were all outcomes important to the individual or population considered?
Conclusions **

# 4.3.9 Risk of Bias Assessment

Two reviewers (JP, SW) independently conducted the risk of bias (RoB) and applicability assessment on the final papers using the Quality Assessment of Diagnostic Accuracy Studies 2 tool (QUADAS-2) (Cuchanski et al., 2011). See Appendix 0-6. The tool consists of four key domains: patient selection, index test, reference standard and flow and timing. Each domain is assessed in terms of RoB and only the first three in terms of concerns regarding applicability. The tool is applied in four phases:

- 1. Summarize the review question.
- 2. Tailor the tool to the review and produce review-specific guidance.
- 3. Construct a flow diagram for the primary study.
- 4. Assess RoB and concerns regarding applicability.

The QUADAS-2 RoB assessment allows for a decision of 'high', 'low' or 'unclear' for each individual item. A summary judgement enables a rating of 'at risk' or 'low risk'. A study is rated 'at risk' if it has one or more 'unclear' and/or 'high' judgements. The applicability assessment allows for a judgement of 'with concerns' or 'no concerns'. A study is rated 'with concern' if it has one or more 'unclear' and/or 'low' judgements. The two reviewers conducted initial training using a sample study to ensure understanding of and agreement on the individual items of the tool. Differences were resolved through discussions. A third reviewer (DW) was available to mediate disagreements.

The QUADAS-2 website provides templates for displaying results of the RoB and applicability concerns <u>https://www.bristol.ac.uk/population-health-</u><u>sciences/projects/quadas/quadas-2/</u>

# 4.4 Results

A search of relevant electronic databases and a hand search resulted in a total of 2434 articles identified. Following the removal by automation of 569 duplicates, 1865 articles were screened by title and abstract, leaving 127 for full text review. One paper could not be located leaving 126. Two reviewers independently reviewed each of the final studies for risk of bias and applicability concerns using the Quadas-2 tool (Whiting et al., 2011). See Figure 18. Differences in agreement between the two reviewers at each stage of the screening process were discussed. There was 100% agreement between the 2 independent reviewers at each stage of screening as well as in the final review.

# 4.4.1 PRISMA Flow Diagram



Figure 19. PRISMA Flow Diagram.

#### 4.4.2 Excluded Studies

Of the 126 full text articles identified, 120 were excluded based on amended inclusion criteria. One paper was excluded because it involved a single patient (Deyo & Mirza, 2016), one did not include descriptions of the index tests used (Janardhana et al., 2010), and one paper did not report reference standards or diagnostic accuracy measures (Walsh & Hall, 2009). See Appendix 0-7.

#### 4.4.3 Study Characteristics

Three studies matched the eligibility criteria and were included in the final pool of papers for review (Hancock, 2011; Laslett, 2005; Vroomen et al., 2002). All 3 reported on several radicular clinical signs and symptoms of DLBP associated with disc herniation. It was unclear if the Laslett study included non-radicular DLBP. There were differences among the 3 studies in patient characteristics, index tests, diagnostic test items, and diagnostic accuracy measures. The implications of this for generalizability of findings are discussed in section 4.5. Study characteristics are summarized in Table 12.

Study (Year)	Subject Characteristics	Index Standard	Reference Standard	Diagnostic Test Items	SN/SP (95%CI) PPV, NPV, OR (95%CI)	Conclusions
Hancock, M. J., Koes, B., Ostelo, R., & Peul, W. (2011). Diagnostic accuracy of the clinical examination in identifying the level of herniation in patients with sciatica. <i>Spine</i> , 6(11), E712- E719.	283 patients with sciatica from a previously published randomized controlled trial Received diagnosis from neurologist of lumbosacral radicular syndrome (dermatomal pain pattern with signs of nerve root compression) lasting 6 to 12 weeks, 18 to 65 years of age, and had a radiologically confirmed dise herniation.	One of 68 neurologists performed a clinical examination of patients before the MRI. The neurologist was free to perform whatever tests they felt were appropriate however, this typically involved a range of nonspecific tests to determine if a disc herniation was likely to be the cause of the sciatica. Individual neurologic examinations were performed by one of six research nurses following a standardized protocol. They were specifically trained by a neurologist and neurosurgeon and started independently examining patients only after passing tests concordant with the training of residents of neurology.	MRI	Pain/dermatome location Reflex tests (ankle & knee) Sensory loss testing (L4, L5, S1) Motor strength/weakness (quadriceps, tibialis anterior, peroneals, extensor hallucis longus, triceps surae/calf	Sensitivity, Specificity Area Under the Curve	The current study did not find evidence to support the accuracy of individual tests from the neurological examination in identifying the level of disc herniation demonstrated on MRI. A neurologist's overall impression was moderately accurate in identifying the level of disc herniation engaged in shared decision making regarding surgery,
Laslett, M., McDonald, B., Tropp, H., Aprill, C. N., & Öberg, B. (2005). Agreement between diagnoses reached by clinical examination and available reference standards: a prospective study of 216 patients with lumbopelvic pain. <i>BMC musculoskeletal</i> <i>disorders</i> , 6(1), 1-10.	216 consecutive chronic and distressed LBP patients who attended clinic between May 2001 and October 2002 were recruited through a clinical examination. Nearly 30% had a history of lumbar spinal surgery with persistent or recurrent pain.	The examination method used was the McKenzie assessment augmented by provocation stress tests of the SIJ . A specific reasoning process using the McKenzie examination to exclude symptomatic disc pathology was applied to minimise false positives enabling an improved ability to differentiate between SIJ and non-SIJ cases. Study of these papers will give the reader sufficient information to understand the method.	Provocation discography (Fluoroscopy guided radiographic imaging)	Ipsilateral SLR Contralateral SLR Weakness ankle dorsiflexion Weakness EHL Ankle reflex weak Sensory loss Patellar reflex weak weakness] Ankle PF weakness Centralization or Peripheralization	Sensitivity, specificity	Using available reference standard technique, two thirds of patients received a pathoanatomic diagnosis with multiple pain generators identified in 10% of cases. Diagnoses of the tissue origin of chronic LBP or referred lower
Vroomen, P. C. A. J., De Krom, M. C. T. F. M., Wilmink, J. T., Kester, A. D. M., & Knottnerus, J. A. (2002). Diagnostic value of history and physical examination in patients suspected of lumbosacral nerve root compression. <i>Journal of Neurology,</i> <i>Neurosurgery &amp; Psychiatry</i> , 72(5), 630-634.	Cross sectional study of 274 patients presenting to a primary care physician with a new episode of pain radiating into the leg. 18 – 61 years of age. Have had symptoms from < 14 to 48 days.	Clinical findings were then established in a standardised fashion based on good clinical practice, standard textbook sections, and published reports. The methods and interobserver consistency of the history and physical examination have been reported elsewhere. 16	The gold standard in all patients was MR imaging of the lumbar spine within 24 hours after the clinical examination.	Decreased lordosis; Antalgia; Vertebral percussion tenderness; Paravertebral hypertonia; Disturbed walking on heels; Disturbed walking on toes; Disturbed kneebending; Paresis; Extensor hallucis longus; Peroneii; Anterior tibial; Gastrocnemius; Sensory loss; Hypesthesia; Hypalgesia; Reflex differences; Ankle tendon; Knee tendon; Absent reflexes; Ankle tendon reflex; Knee tendon; Absent pain; Any pain in the leg on; SLR lower than; Positive straight leg raising; Typically dermatomal pain; Any pain in the leg on; SLR lower than; Positive; Positive reversed Lase' gue; If SLR is positive; Positive reversed Lase' gue; If SLR is positive; Positive reversed Lase' gue; Sign; Positive Naffziger sign	Odd's ratios, Adjusted odd's ratios	The main component in the diagnosis of sciatica caused by disc herniation is the history. Few physical signs add useful additional information or result in alteration of a diagnosis made on the basis of the history. extremity symptoms by experienced physiotherapy clinicians agreed with available reference standard diagnoses 19–24% over and above expected chance agreement.

#### Table 12. Study characteristics of final 3 papers included in systematic review.

#### 4.4.4 Risk of Bias in Studies

Only one paper (Vroomen et al., 2002) was deemed to have a low RoB and applicability concerns. The study by (Laslett et al., 2005) was found to be lacking in clarity for 5 of 7 different areas. One paper (Hancock et al., 2011) was enabled with a high RoB for Flow and Timing. See Table 13. Details of the RoB and applicability concerns for each study by the reviewers can be found in the Appendices. See Appendix 0-08 for Vroomen, Appendix 0-09 for Laslett and Appendix 0-10 for Hancock.

		RISK O	F BIAS	APPLICA	BILITY CO	ONCERNS	
Study PA SEL	TIENT I ECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Hancock	Low	Low	Low	High	Low	Low	Low
Laslett U	nclear L	Jnclear	Low	Unclear	Unclear	Unclear	Low
Vroomen	Low	Low	Low	Low	Low	Low	Low

Table 13. Summary of QUADAS-2 results

## 4.4.5 Results of Individual Studies

Of the 3 final studies, one was rated as low risk of bias (Vroomen et al., 2002). It reported on both signs and symptoms related to nerve root compression. They compared clinical findings in n = 274 participants presenting with severe leg pain with MRI confirming nerve root compression. Grading criteria for the MR images included evidence of a protruding annulus or extruded nucleus material, lateral recess narrowing and flattening, and compression of the ventrolateral dural sac or emerging nerve root sleeve. Vroomen reported odds ratios and area under the curve values for some history and physical examination variables. See Table 14. They found a significant association between MR images, three clinical symptoms and four clinical signs. See Appendices 0-12, 0-13, 0-14, 0-15, 0-16. An association was also found between MR images and patient age, the duration of symptoms, and having an occupation with a predominance of standing, walking and lifting. Symptoms associated with positive MR findings were increased pain with a cough/sneeze or strain, a dermatomal pattern of pain distribution and reports of coldness in the leg. Signs associated with MR images were paresis, a finger-floor

distance of > 25 cm, absence of quadriceps/achilles reflex and a positive straight leg raise. Sensory loss was not significantly diagnostic. The Vroomen study was the only one to report on symptoms associated with DLBP and concluded that history is the main factor in the diagnosis of radicular symptoms (i.e., sciatica, i.e., symptoms related to nerve root compression) with few clinical signs adding valuable information. These results pertained to a sample of patients with severe leg pain symptoms and so they may not be generalizable to the broader population of patients variations of nerve root compression.

The paper by Laslett (Laslett et al., 2005) was found to have 5 of 7 RoB features 'unclear'. A low score for RoB and applicability concerns was assigned for reference standards. It was a prospective blinded validity study (n = 216) of chronic and distressed patients in which nearly 30% had a history of lumbar spinal surgery with persistent or recurrent pain. Clinical diagnoses were determined by a physiotherapist and compared against diagnoses by a radiologist who identified the tissue origin of symptoms based on imaging and responses to diagnostic injections. Reported clinical signs were largely to do with radicular DLBP. Discogenic pain was reported as the sole diagnosis in 27% (n = 59) of patients. In the case where more than one source of pain was identified, discogenic origin was reported in 39% (n = 85) of patients. A significant association was found for centralization, ipsilateral straight leg raise and discography. See Appendix 0.11.

The paper by Hancock (Hancock et al., 2011) was rated high RoB for flow and timing. See section 4.4.5 Certainty of Evidence for further details. The study investigated the relationship between the level and location of disc herniation identified on MRI against clinical examination findings in a cross sectional study of n = 283 patients with sciatica and confirmed disc herniation. Clinical signs but not symptoms were reported. The diagnostic accuracy of a combination of tests was found to be slightly better than the results of individual tests but remained inferior to the overall impression from the neurologist. See Appendix 0.17.

Consistent signs of DLBP across all 3 studies were: patellar tendon hyporeflexia, Achille's hyporeflexia, weakness or paresis, and sensory loss. Looking across the results for these tests only, two reported that the straight leg raise, deep tendon reflex changes and myotomal weakness were able to significantly discriminate between participants with and without radiographically-confirmed disc herniation (Laslett et al., 2005; Vroomen et al., 2002). These apply only to DLBP with radicular symptoms. With the possible exception of the report of centralization in the Laslett paper, signs and symptoms of DLBP without radicular symptoms were not reported. The general findings from these 3 papers are:

- diagnostic accuracy increases with the use of multiple testing procedures;
- neurodynamic tests lack diagnostic accuracy, and,
- there is no consensus on the diagnostic accuracy of neurological tests to detect disc herniation resulting in nerve root compression.

# 4.4.6 Certainty of Evidence

Part of the rationale for Hancock's study was based on the premise that clinicians can confidently provide patients with an explanation for their leg pain only if clinical findings correlate strongly with MRI findings. We chose to keep Hancock's paper in the final pool because it included some of the same diagnostic clinical tests for weakness, sensation and reflexes reported by (Laslett et al., 2005; Vroomen et al., 2002).

Hancock's paper was deemed to have a high RoB for Flow and Timing. As per the Quadas-2 tool, all patients received the same reference standard. However, our confidence in the results is low for the following reasons: not all patients were included in the analysis; it is unclear if there was an appropriate interval between index tests and reference standards; one of 68 neurologists was free to perform whatever index tests they felt were appropriate so that there was not standard index text protocol and description of which index tests were conducted; and it's uncertain if the same index test was administered to all patients.

Test	Adjusted	95% CI
	diagnostic OR	
History		
Age (years)		
41–50 v 16–40	1.8	1.3 to 2.6
51–81 v 16–40	2.8	1.9 to 4.2
Duration of disease (days)		
15–30 v <15	2.2	1.5 to 3.3
>30 v <15	0.8	0.6 to 1.1
Paroxysmal pain	1.8	1.3 to 2.5
Pain worse in leg than in back	4.5	3.3 to 6.2
Typical dermatomal distribution	3.2	2.2 to 4.7
Pain worse on		
coughing/sneezing/straining	2	1.4 to 2.7
Physical examination		
Finger-floor distance (cm)		
5-24 v 0-4	1.1	0.7 to 1.6
>25 v 0-4	2.8	1.9 to 4.3
Missing v 0–4	1	0.4 to 2.1
Paresis	5.2	3.3 to 11.6
Intercept -3.511		
Vroomen et al. (2002). Diagnostic value of l	nistory and physical	examination in patients
Psychiatry, 72(5), 630-634.	ession. Journal of Ne	eurology, Neurosurgery &
CI, confidence interval; OR, odds ratio.		

Table 14. Predictors of nerve root compression on magnetic resonance imaging: results of multiple logistic regression analysis.

# 4.5 Discussion

DLBP remains without consensus or standards for its clinical signs and symptoms and treatment. The purpose of this systematic review was to investigate the quantity, level and quality of evidence in the published literature on the clinical signs and symptoms of DLBP with and without radicular symptoms that are supported with reference standards. Only a few studies met the eligibility criteria of the review. Not withstanding that the criteria may have been overly narrow, unfocused or too broad, the few findings we

reported on in this review are not surprising given the current state of the knowledge base of diagnosing patients with NSLBP or DLBP.

Our review found a total of 7 themes of DLBP symptoms and 4 signs that are in agreement with clinical experiences reported by survey respondents in Chapters 2 and 3 including sudden onset or an incident associated with flexion/rotation and compression, a paroxysmal pattern, pain made worse by sitting, repeated flexion, sitting, postures, coughing/sneezing/straining, symptoms relieved by extension, lying down and subjective reports of centralization of symptoms. See Table 15 for further details. The centralization phenomenon (CP) is the only reference supported clinical sign that is diagnostic for non-radicular and some variations of nerve root pain as a result of DLBP (Laslett et al., 2005; Petersen et al., 2017). Signs include centralization and peripheralization of symptoms in response to movements or mechanical loading strategies, ipsilateral and crossed leg straight leg raise, altered patellar and Achille's reflexex, myotomal weakness and sensory loss.

The results of the Laslett study (Laslett et al., 2005) which included distressed chronic pain patients with nearly 30% having a history of lumbar spinal surgery with persistent or recurrent pain are not necessarily generalizable to acute and subacute LBP populations which make up a larger proportion of patients with DLBP. Index or clinical tests used in the Laslett study were based on the McKenzie system of examination techniques employing repeated lumbar movements. The McKenzie system at the time of the study was perhaps the most widely used system among therapists in North America for examining and treating LBP patients (Laslett et al., 2005). In our survey, clinicians reported the use of 38 different protocols. See Appendix 0-I9. While the McKenzie been formally studied for inter-examiner reliability with satisfactory results among trained clinicians and for validity different results may have been obtained with the use of an alternate physical examination protocol.

More recent studies have not added additional information on diagnostic criteria other than to affirm DLBP is characterized by axial midline low back pain, sitting intolerance, pain with flexion, positive provocation with sustained hip flexion, absence of motor/sensor/reflex change, and positive discography although not all degenerated discs exhibit DLBP (Fujii et al., 2019; Lorio et al., 2023). There remains conflicting evidence for the usefulness of most clinical findings assisting with diagnoses, with the exception of centralization and non-organic signs (May et al., 2018). See Table 16.

There is some support for Vroomen's conclusion on the value of history taking as well as various tests for diagnosing nerve root compression using a reference standard. The general findings were; that while diagnostic accuracy increases with the use of multiple testing procedures, there is no consensus on the diagnostic accuracy of neurological tests to detect disc herniation resulting in nerve root compression; individual test results have no clinical utility; and neurodynamic tests lack diagnostic accuracy (Al Nezari et al., 2013; de los Monteros et al., 2020; Ekedahl et al., 2018; Tawa et al., 2017; Verwoerd et al., 2016). See Appendix 0-18.

In the absence of new information on the diagnostic criteria for DLBP, it is worthwhile to revisit the results of expert panels research reports. To that end, we matched the results from the expert panels against the known results from the systematic review and the survey respondents. See Table 15. There was agreement on six themes of symptoms. Features of DLBP that show some agreement include :

- Mechanism of injury: an incident associated with flexion/rotation or compression;
- Behaviour of symptoms: pain worse at night;
- Aggravating activities: flexion, sitting, pain provoked by postures;
- Intrathecal symptoms: increased pain on coughing/sneezing/straining;
- Pain pattern: centralization of symptoms in response to movements or mechanical loading strategies and peripheralization of symptoms in response to movements or loading strategies;

#### Table 15. Symptoms and signs of DLBP from survey respondents, systematic review and expert panels.

Chergy         No.         These         Symplex         Reference         Statistical Narway         Symplex in the local of with index to the parameter in the parame				Key X = agreement on DLBP features								
Non-matched and exclusion graphing         1         Matched model matter conversion and comparison of the matched model in and the matched in the matched model in and comparison of the matched model in andin an	Category	No.	Theme	Symptoms	Reference Standard	Statis	tical Measure		Survey Respondents <sup>a</sup> (n=200)	Systematic Review <sup>b</sup> (n=2)	Expert Panels (n=3)	
<ul> <li>1 Non-Interface of problem of the interval of the</li></ul>						Odds Ratio (95% CI)	%Sensitivity	%Specificity	(11-200)	(11-2)	( <b>n</b> -5)	
Image and the set of	<ol> <li>Nonradicular and radicular symptoms</li> </ol>	1	Mechanism of injury	incident associated with flexion/rotation and/or compression a, b, c	MRI	0.8(0.5 to 1.3)**			Х	х	х	
1 Industor of symple matrix and algo when any of the symple set				sudden onset <sup>a, b</sup> known cause <sup>b</sup>	MRI	0.9 (0.6 to 1.5)** 0.8(0.5 to 1.3)**			Х	X X		
intervalue of the sector of t		2	Behviour of symptom	s pain worse at night <sup>a, b, c</sup>	MRI	0.9(0.5 to 1.4)**			х	х	х	
1 Agenetic and set of the set o				paroxysmal pattern a, b	MRI	1.3(0.8 to 2.0)**			х	Х		
3. Again of again of again of again of a set of a				pain worse at night a, b, c	MRI	0.9(0.5 to 1.4)**			х	х	х	
1     Note: Note		3	Aggravating activities	flexion <sup>a, b, c</sup>					х	х	х	
<ul> <li>second with add companys h<sup>1</sup></li> <li>second with</li></ul>				pain/symptom provocation with repeated flexion and flexion/rotation <sup>a, c</sup>					х		х	
<ul> <li>1 Non-Radicalar in the interpretation of relationships in the interpretation of rel</li></ul>				worsens with axial compression 8, 0					x		x	
A second				sitting <sup>a,b,c</sup>	MRI	0.9 (0.6 to 1.5)**			x	x	x	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				pain behaviour provoked and relieved by		015 (010 (0 110))			**			
<ul> <li>1 Relating actions by long down hand and and actions or adapt has a methodic position "actions position" actions of a social distribution of the position of the</li></ul>				movements or postures a, b, c					х	х	х	
<ul> <li>subset of walking ***</li> <li>sub</li></ul>		4	Relieving activities	lying down <sup>a, b, c</sup>	MRI	1.1 (0.7 to 1.9)**			х	Х	х	
<ul> <li>a unicoding position<sup>1</sup></li> <li>notard preference e.g., shacked vs. arect position<sup>2</sup></li> <li>presence of a. lateral shift<sup>2</sup></li> <li>presence of a. lateral shift<sup>2</sup></li></ul>				standing or walking a, b	MRI	0.9 (0.5 to 1.7)**			х	Х		
$ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$				unloading position <sup>a</sup>					х			
s Poture's potential of the potentia				extension <sup>8, c</sup>					х		х	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		5	Postures	postural preference e.g., slouched vs. erect					х		х	
1  intradiced intradiced intradices intervalues i				posture ","							v	
2 Nov Radicular Signt 12 Curtain large in the low ranks 1 and 1 for		6	Intrathecal	pain worsening on cough speeze strain a, b, c	1 101				37	37	~	
$ \begin{tabular}{l l l l l l l l l l l l l l l l l l l $		-		pair worschnig on cough, siecze, stain	MKI	2.1 (1.3 to 3.4)^^			X	X	X	
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$ 1 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ $				region and/or the lower limb °							х	
$ 1 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ $				nein chenging sides of the lumber spine <sup>6</sup>								
$ \begin{array}{ c c c c c } & Pain Pattern & entilization $^{h,h^{-0}} & & & X & X & X & X & X & X & X & X &$				pair charging sides of the future spine							А	
$ \begin{array}{c c c c c c c } & Pain Fauch & certification $^{h,0}$ (certification $^{h$		0	Doin Battarn	pain worse in leg than back	MRI	5.5(3.2 to 9.4)**			37	X	37	
$ 1 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ $		0	r alli r aucili	centralization a b c					X	X	A V	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				directional professional <sup>8</sup> , <sup>b</sup> , <sup>c</sup>					×	X V	X V	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				dermatomal distribution <sup>8,b</sup>	MRI	3 8(2 f) to 7 3)**			v	x	л	
$ \begin{array}{ c c c } 10 & Sensation &$		9	Symptom descriptors	dermatomal cold sensations <sup>8, b</sup>	MRI	1.8(1.0 to 3.2)**			x	x		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		10	Sensation	subjective sensory loss <sup>8, b</sup>	MRI	0.9(0.6 to 1.5)**			x	x		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				dermatomal paraesthesia <sup>a, b</sup>	MRI	0.7(0.5 to 1.2)**			x	x		
11History previous solade pain epbisode $^{h,b}$ previous sciatica $^{h}$ hc indicator contraistion a coording to investigater $^{h}$ MRI $0.80.5 to 1.2)^{**}$ $X$ X2Non Radicular Signs12Centralization $h^{h,c}$ Discography $0.94^{*}$ $X$ XX3Peripheralization investigater $^{h,h,c}$ Discography $0.92^{*}$ $0.64^{*}$ XXX3Peripheralization investigater $^{h,h,c}$ $0.69^{*}$ $0.64^{*}$ XXXX3Peripheralization investigater $^{h,h,c}$ $0.69^{*}$ $0.64^{*}$ XXXX3Radicular signs14Neurodyamnicfinger to floor distance $^{h}$ contraliateral $^{h}$ MRI $2.4(1.4 \text{ to } 0.9^{**})$ $88 \cdot 100^{**}$ XX3Radicular signs14Neurodyamnicfinger to floor distance $^{h}$ contraliateral $^{h}$ MRI $2.3(2.6 \text{ to } 3.7)^{**}$ XX4Neurodyamnicguadriceps/ahle (not differentiate between the two) $^{h}$ MRI $2.3(2.6 \text{ to } 3.7)^{**}$ XX4Myotomal weaknessankle dorsiflexion $^{h}$ $0.64^{*}$ XXX4Marki filterin filterin filterin $^{h}$ $X$ XX5Deep tendor reflex quadriceps $^{h,h}$ $X$ $X$ XX4Marki filterin filterin filterin filterin filterin $^{h}$ $X$ XX5Deep tendor reflex quadriceps $^{h,h}$ $0.64^{*}$ $0.95$				subjective muscle weakness *, b	MRI	0.6(0.4 to 1.0)**			х	х		
$ 2 \ Non Radicular Signs \\ 2 \ Non Radicular Signs \\ 2 \ Non Radicular Signs \\ 12 \ Centralization \\ begin beraization \\ beg$		11	History	previous back pain epbisode a, b	MRI	1.3(0.7 to 2.1)**			х	х		
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3 Radicular signs 14 Neurodyamic $\frac{14}{15}$ $\frac{14}{1$		10	renpiiorumation	finger to floor dictance b	MRI	2 4 (1 4 to 4 0)**	0.09	0.04	л	v	л	
$ \begin{array}{cccc} & & & & & & & & & & & & & & & & & $	3 Radicular signs	14	Neurodyanmic	Insilateral <sup>a b</sup>	1	2.4 (1.4 to 4.0)	76 - 97*	11 - 45*	x	X		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				contralateral b			23 - 27*	88 - 100*		x		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				crossed/reversed a, b					х	х		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				SLR unclear if ipsilaleral, contralateral,	MDI	2.2 (2.6 +- 2.7)88			X	N		
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Intervol     Mail     Mail     Mail     Mail     Mail     Mail       quadriceps     ankle     40 - 70*     93 - 97*     X     X       ankle     ankle     50 - 52*     62 - 63*     X     X       l6     Myotomal weakness     ankle dorsiflexion     50 - 52*     62 - 63*     X     X       ankle plantarflexion     0.6*     0.95*     X     X       quadriceps     0.6*     0.95*     X       quadriceps     0.1*     0.99*     X       paresis (unspecified)     NRI     5.2 (2.4 to 11.7)**     X       17     Sensory loss     sensory loss     0.66*     0.51*     X       hypesthesia     MRI     0.8 (0.5 to 1.3)**     X     X		15	Deep tendon reflex	quadriceps/ankle (not differentiated between	MRI	2.4 (1.0 to 5.6)**				x		
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ankle **     50 - 52*     62 - 63*     X     X       16     Myotomal weakness     ankle dorsiflexion <sup>b</sup> 20 - 49*     54 - 82*     X       ankle plantarflexion <sup>b</sup> 0.6*     0.95*     X       extensor hallucis longus <sup>b</sup> 0.37*     0.71*     X       quadriceps <sup>b</sup> 0.1*     0.99*     X       paresis (unspecified) * <sup>b</sup> MRI     5.2 (2.4 to 11.7)**     X       17     Sensory loss     sensory loss * <sup>b</sup> 0.66*     0.51*     X       hypesthesia <sup>b</sup> MRI     0.8 (0.5 to 1.3)**     X     X				quadriceps a, b			40 - 70*	93 - 97*	Х	Х		
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quartneps $0.1^{-1}$ $0.99^{-8}$ X           paresis (unspecified) * <sup>b</sup> MRI         5.2 (2.4 to 11.7)**         X         X           17         Sensory loss * <sup>b</sup> $0.66^{+*}$ $0.66^{+*}$ $0.51^{+*}$ X           hypesthesia <sup>b</sup> MRI $0.8 (0.5 to 1.3)^{**}$ X         X				extensor hallucis longus			0.37*	U./I*		X		
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hypotusatu MRI 12 (6 6 to 2 1)** V			,	hypesthesia <sup>b</sup>	MRI	0.8 (0.5 to 1.3)**	0.00	0.21	~~	x		
				hymalthesia <sup>b</sup>	MRI	1.2 (0.6 to 2.1)**				x		

\*\* Vroomen et al, (2002). Diagnostic value of history and physical examination in patients suspected of lumbosacral nerve root compression. Journal of Neurology, Neurosurgery & Psychiatry, 72(5), 630-634.

Values in **bold** indicate significant effect Chan et al, (2013). Preliminary evidence for the features of non-reducible discogenic low back pain: survey of an international physiotherapy expert panel with the Delphi technique. Physiotherapy, 99(3), 212-220. Cid et al, (2015). A modified Delphi survey on the signs and symptoms of low back pain: indicators for an interventional management approach. Pain Practice, 15(1), 12-21.

Table	16.	Recent	studies	examining	accuracy	of clinical	tests for	nerve roo	t compression.
T HOIC	<b>T</b> O.	neccuit	brautos	v.a.	accuracy	or chineur	101	1101 / 0 1 00	compression.

Author and Year	Study	Study Purpose	Test	Reference Standard	Diagnositc Outcome Measures	Conclusion
Tawa, N., Rhoda, A., & Diener, I. (2017).	Accuracy of clinical neurological examination in diagnosing lumbo- sacral radiculopathy: a systematic literature review. <i>BMC</i> <i>musculoskeletal</i> <i>disorders</i> , 18(1), 1-11.	Analysed accuracy of index tests for diagnosing lumbo-sacral radiculopathy (sensory, motor, reflex and neuro-dynamic) comparing to MR imaging, electro-diagnostics or intra- operative findings	Sensory, Motor, Reflexes, Femoral n. stretch, Straight leg raise	MRI	Sensitiity, specificity including 95% confidence intervals	Scarcity of studies on diagnostic accuracy of clinical neurological testing able to detect disc hernation. Did not consider disc herniation as the cause of nerve root impingement and subsequent radiculopathy
González Espinosa de los Monteros, F. J., Gonzalez-Medina, G., Ardila, E. M. G., Mansilla, J. R., Expósito, J. P., & Ruiz, P. O. (2020).	Use of neurodynamic or orthopedic tension tests for the diagnosis of lumbar and lumbosacral radiculopathies: study of the diagnostic validity. International Journal of Environmental Research and Public Health, 17 (19), 7046.	Aim was of estimating the diagnostic validity of the following orthopedic stress tests and/or neurodynamic tests (performed individually, in combination and in parallel	Straight leg raise, Bragard test & combined tests of both, Fajersztajn test, Sicard test, and the combined tests of both, the Passive Neck Flexion test, the Kernig test and combinned tests of both, the Slump test, the Dejerine's triad and the test combining both	MRI	Sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios, and diagnostic odds ratios (DORs)	Tests havng no clinical utility when performed individually: Passive Neck Flexion test, the Dejerine's triad, the Straight Leg Raise test, the Bragard test, the Fajersztajn test, the Slump test, the Sicard test and the Kernig test. Combined tests - Slump test, Dejerine's triad, Straight Leg Raise, Bragard test sow validity (internal and external).
Ekedahl, H., Jönsson, B., Annertz, M., & Frobell, R. B. (2018)	Accuracy of Clinical Tests in Detecting Disk Herniation and Nerve Root Compression in Subjects With Lumbar Radicular Symptoms	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), 726-735.	Slump test, SLR, femoral n. test, radiculopathy I* and II**, sensory, tendon reflexes, muscle weakness* one neurologic signs was present and corre sponded to the nerve root of the planned steroid injection **2 neurologic signs (sensory deficit or reflex impairment or muscle weakness) were present and corresponded to the specific nerve root of the planned steroid injection	MRI	Sensitivity, specificity, and receiver operating characteristics analysis with area under the curve including 95% confidence intervals, and secondarily evaluated using positive and negative predictive values, positive and negative likelihood ratios, and diagnostic odds ratios	Investigated neurodynamic tests for radiculopathy lacked diagnostic accuracy. The slump test was the most sensitive test, while radiculopathy II was the most specific test. Most interestingly, no relationship was found between any neurodynamic test and foraminal nerve compression (foraminal stenosis) as visualized on MRI.
Al Nezari, N. H., Schneiders, A. G., & Hendrick, P. A. (2013).	Neurological examination of the peripheral nervous system to diagnose lumbar spinal disc herniation with suspected radiculopathy: a systematic review and meta-analysis. <i>The Spine</i> <i>Journal</i> , <i>13</i> (6), 657-674.	To review the scientific literature to evaluate the diagnostic accuracy of the neurolog- ical examination to detect lumbar disc herniation with suspected radiculopathy.	octor ajector	MRI	Sensitivity, specificity, pos and neg likelihood ratios, diagnostic odds ratio	Ability of neurological testing procedures to detect either a disc herniation or the level of herniation was poor
Verwoerd, A. J., Peul, W. C., Willemsen, S. P., Koes, B. W., Vleggeert-Lankamp, C. L., el Barzouhi, A., & Verhagen, A. P. (2014)	Diagnostic accuracy of history taking to assess lumbosacral nerve root compression. <i>The Spine</i> <i>Journal</i> , <i>14</i> (9), 2028-2037.	To assess the diagnostic accuracy of history taking for the presence of lumbosacral nerve root compression or disc herniation on magnetic resonance imaging in patients with sciatica.	History items pre-selected from the literature (age, gender, pain worse in leg than in back, sensory loss, muscle weakness, and more pain on coughing/sneezing/straining	MRI	Odds Ratios	For now, the diagnostic accuracy of history taking in assessing humbosacral nerve root compression and disc herniation on MRI seems to be more limited than previously assumed. This may cause difficulty in distinguishing between specific symptoms and nonspecific symptoms

# 4.6 Conclusions

While some informative diagnostic tests (i.e., ones with a likelihood ratio  $\geq 2.0$  or  $\leq 0.5$ ) may assist in diagnosing disc related symptoms (Han et al., 2023) with the exception of the centralization phenomenon, there remains no general consensus on reference-based index tests that would help clinicians to identify DLBP without and only a few for DLBP with radicular symptoms.

# 4.7 Registration and Protocol

The review was not registered. A protocol was prepared and submitted to PROSPERO in anticipation of registering the review. We had already started data extraction prior to registering the review. Due to a change in criteria for registering reviews with PROSPERO in which a review is not eligible for registration if data extraction has begun, the review could not be registered.

# 4.8 Support

This review did not receive financial or non-financial support.

# 4.9 Competing Interests

There are no competing interests.

# 4.10 Availability of Data, Code and Other Materials

Search results for Embase and CINAH, the Quadas 2 Tool, data collection tool, data extracted from the final 3 included studies are found in the Appendices.

# 4.11 What is Already Known on this Topic

Discogenic low bac pain associated with disc herniation remains without widely accepted standards or agreement on its terminology, clinical signs and symptoms or treatment, leaving practitioners in a quandary as to its diagnosis.

# 4.12 What This Study Adds

While some informative diagnostic tests (i.e., ones with a likelihood ratio  $\geq 2.0$  or  $\leq 0.5$ ) may assist in diagnosing disc related symptoms (Han et al., 2023) with the exception of the centralization phenomenon, there remains no general consensus on reference-based index tests that would help clinicians to identify DLBP without and only a few for DLBP with radicular symptoms.

# Chapter 5

# 5 The effects of a unilateral side lying spinal rotation position of lumbar disc morphology.

# 5.1 Introduction

Almost 80% of the global population will experience low back pain (LBP) at least once during their lifetime, potentially bringing with it significant disability and a high economic burden to individuals and society (Amin et al., 2017; Geurts et al., 2018; Urits et al., 2019). It is the leading cause of years lived with disability (YLD's) (Ferreira et al., 2023) . In the majority of cases no attributable cause can be identified and is termed non-specific low back pain (NSLBP) (Hartvigsen et al., 2018) although others believe a cause can be identified (Bogduk et al., 2013; McGill, 2016). Not entirely without controversy, intervertebral disc degeneration is often cited as being strongly associated with NSLBP leading to degenerative disc disease (DDD) and potentially, lumbar disc herniation (LDH) (Petersen et al., 2003). Not all herniation is a result of DDD, as spinal overloading can lead to symptomatic herniations (Amin et al., 2017). Current treatment options for symptomatic herniations are surgery or conservative treatment (Yu et al., 2022). Patients who fail conservative treatment may need surgical removal of the offending disc fragment, however, recurrent herniation with symptoms after surgery is common, affecting 2% to 25% of patients (Hornung et al., 2023).

There appears to be a subgroup of LBP patients with and without radiculopathy in which herniations and symptoms regress (also referred to as, retract, resorb or reduce) spontaneously over time without surgical or conservative interventions. The rate of regression, can range from less than 2 months to 12 months (Autio et al., 2006; Chiu et al., 2015; Hornung et al., 2023). Several factors that may increase the likelihood of regression include, the initial size of the herniation or sequestration, the percentage of rim enhancement on initial magnetic resonance imaging (MRI), the composition of cellular and inflammatory mediators present, and the involvement of the posterior longitudinal ligament (Hornung et al., 2023).

Three mechanisms have been proposed to explain spontaneous regression including, inflammation and neovascularization, disk dehydration, and mechanical traction (Yu et al., 2022). Mechanical traction is thought to retract disk fragments because of tension from the posterior longitudinal ligament (PLL) but only as long as the annulus fibrosus is contained and disk fragments are not extruded or sequestrated (Teplick & Haskin, 1986). Another means of regression or reduction was proposed by Dr. James Cyriax, an English physician (Cyriax, 1950). Instead of mechanical traction as put forward by Teplick and Haskin, Cyriax maintained that when LBP is associated with a herniated or displaced fragment of annulus fibrosus (AF), spinal manipulation (SM) could reduce the size and position of the herniation or fragment. Cyriax demonstrated this clinically, however, aside from myelography, there was no other technology available at the time that could show evidence of the proposed effects. In order for the theory to be plausible, the shape or morphology of the intervertebral (IVD) herniation should demonstrate some measure of change before and after the treatment.

The emergence of magnetic resonance imaging (MRI) (Plewes & Kucharczyk, 2012) has allowed a more detailed observation of IVD behaviour in vivo (Foltz et al., 2017; Haro, 2014; Hebelka et al., 2018; Menon et al., 2021) and so allows for further exploration of the theory proposed by Cyriax. Studies have reported changes in lumbar disc morphology in response to specific spinal positions in one or two lumbar disc segments in nondegenerated IVD's of asymptomatic participants (Fazey et al., 2006, 2013; Kolber & Hanney, 2009; Nazari et al., 2012; Takasaki et al., 2010). The advantages of using MRI are twofold. It is a non-invasive imaging technology that allows for an accurate visualization of soft tissues such as the IVD. Secondly, it is an appropriate technology to obtain 3 dimensional (3D) reconstructions of IVD's (Chevrefils et al., 2007, p. 1017) using a method such as segmentation.

A number of methods for quantifying lumbar disc morphology from MR images have been reported (Baswaraj et al., 2012; Castro-Mateos et al., 2014; Chan & Neu, 2014; Jiang et al., 2012; Koh et al., 2012; Matos et al., 2023; Neubert et al., 2013; Nordberg et al., 2021; Passias et al., 2011; Saal, Saal, 1990; Violas et al., 2005) While no one method has yet to be universally endorsed as a gold standard, it has been demonstrated that it is possible to reliably quantify directional deformation of lumbar IVD nucleus pulposus (NP) in response to rotated postures (Fazey et al., 2006). Regardless of the method used, obtaining precise measures of tissue morphology or changes in morphology from MR images is technically challenging (Chan & Neu, 2014; Menon et al., 2021).

Despite heterogeneity among participant characteristics, recent studies demonstrate consistent changes in lumbar disc morphology in response to specific spinal positions including flexion, extension and rotation (Alexander et al., 2007; Byrne et al., 2019; Fazey et al., 2013; Kim et al., 2017; Kolber & Hanney, 2009; McCarthy et al., 2015; Takasaki et al., 2010; Xu et al., 2022). It has been observed that in asymptomatic participants, the NP at L1–2 and L4–5 deforms predictably away from offset compressive load in positions of flexion and extension (Fazey et al., 2013). Kinetic magnetic resonance imaging (KMRI) which permits scans in weight bearing, has demonstrated similar changes in disc herniations with different spinal positions (Zou et al., 2009).

As to the effects of rotation positions, which are commonly used by practitioners who treat LBP patients, deformation direction was more variable however, there was a trend to right migration with left trunk rotation, although not all discs behaved in that pattern (Fazey et al., 2013).

By studying the responses to spinal positions commonly used in the treatment of LBP patients, insight into healthy disc biomechanical responses may contribute to further understanding of the mechanism at work in discogenic LBP (DLBP). This can lead to more effective treatment intervention guidelines for practitioners (Wilson et al., 2021; Xu et al., 2022b).

Measuring normal in vivo IVD function is critical to understanding back pain (Martin et al., 2022). The purpose of this proof-of-concept study is to use 3T MRI to investigate the change in volume and shape of lumbar intervertebral discs (IVD's) to a spinal rotation

position commonly used as an intervention for patients with LBP. The results from this study may provide further understanding of the response of the IVD with direction-specific interventions, and potentially stem further research to examine the effects of other spinal positions or movements on patients with different clinical presentations but also with suspected DLBP.

We hypothesize that there will be no change in lumbar disc morphology between the two baseline timepoints 1 and 2. We expect a change in disc morphology to be apparent between the baseline timepoints and the post-rotation timepoint, as measured by volumetrics, statistical shape modeling, or both.

# 5.2 Methodology

# 5.2.1 Participants

A convenience sample of 5 healthy participants (4 male and 1 female) between the ages of 20 and 30 with no recent history of low back pain or sciatica and no back pain within 24 hours of the scan who met normal inclusion criteria for MRI scanning, were recruited from a group of university students. Participants completed a health history questionnaire, and read and signed an informed consent form approved by the Western University's Research Ethics Board.

# 5.2.2 Pre-Scanning Procedures

Upon arrival at the Centre for Functional and Metabolic Mapping at the Robarts Research Institute in London, Canada, participants were seated for 20 minutes to reduce acute or accumulated effects of load on the spine. Each participant was provided with a numerical pain rating scale to complete. An assessment of each participant's active lumbar range of motion was conducted by an experienced physical therapist. Lumbar range of motion was noted along with any reports of pain. Both were recorded to ensure that only healthy controls with full and painless lumbar range of motion were used as participants in the study.

#### 5.2.3 Imaging Protocol

Participants underwent three separate scans including high resolution midsagittal T1 and T2 weighted 3 dimensional (3D) images and axial T2 weighted 3D images using standard clinical acquisition sequences of their lumbar spines at three time points. A 3.0 Tesla Siemens Magnetom Trio Magnet with a surface spine coil was used for all three scans. Sequence parameters are presented in Table 17.

#### Table 17. MRI Protocol.

Sequence	TR (ms)	TE	FOV (mm)	Matrix Size	Slice Thickness (mm)	Slice Gap (mm)	Scan time (mins)	Variables of interest
T1 VIBE Dixon Sagittal	5.8	2.46, 3.69	300x 282	320x290	0.9	0.2	10:46	IVD Shape
T2 3D SPACE Sagittal	1500	144	300x 300	320x320	0.94		5:57	

TR = repetition time, TE = echo time, TSE = turbo spin echo, FOV = field of view, ms = milliseconds, VIBE = volumetric interpolated breath-hold examination, SPACE = sampling perfection with application optimized contrasts with flip angle evolutions.

The T1 VIBE sequence was repeated a total of three times, twice for the baseline/reliability measures, and a third time following the rotation

## 5.2.4 Participant Position for the Three Time Points

The scan for timepoint 1 was conducted immediately after the 20 minutes of unloading. The positioning protocols for time points 1 and 2 were identical. Participants were positioned supine in the scanner with knees comfortably flexed to approximately 20 degrees, supported by a pillow, with the spine coil against their lower back (Figure 19a). Between time points 1 and 2, participants remained on the table after it was retracted from the scanner. After two minutes the table was placed back into the scanner. The identical scanning protocol was repeated for timepoint 2. The purpose for two scans with no change in position of the participant was to provide two timepoints without any intervention to allow for assessment of test-retest reliability of the measurement of lumbar IVD shape, and determine if any changes in disc shape occurred with the passage of time simply in supine-lying.

Prior to the third scan, the table was again retracted. Participants were repositioned in a standardized side lying posture similar to what patients receiving lumbar manipulation would adopt (Figure 19b). The patient was instructed to lie on their right side with the right leg (bottom leg) straight and the left leg (top leg) flexed to 90 degrees at the hip and knee. The left foot was left resting on the inside of the right knee. They were then asked to rotate their thorax to the left until both shoulders were in contact with the table. No overpressure was applied. Participants were asked to relax. This position was maintained for 2 minutes. Participants were then repositioned into the original supine lying posture and inserted into the scanner a third time to repeat the scanning protocol.



Figure 20. Standardized participant positioning for scans at timepoints 1 and 2 supported under the head and knees with a pillow. The collapsible spine coil rests between the lumbar spine and the bed.

Figure 21. Depiction of the rotated position patients maintained for two minutes prior to returning to the supine position in figure 19a. Adapted from (Cramer et al., 2002).

# 5.3 Data Analysis

# 5.3.1 Image Segmentation

Each intervertebral disc, i.e. from L1-L2 to L5-S1 was manually segmented from the <sup>b</sup> VIBE MR images using ITKSnap 3.6.0 (Yushkevich et al., 2006) by one of the authors (JP). Segmentation was done with JP blinded to participant and timepoint. JP had been trained to segment by an imaging specialist with the Robarts Research Centre at Western University, London, Ontario, Canada. MR images were segmented using views from all three planes to ensure accuracy. See Figures 20 and 21 for examples of the segmentation output.



Figure 22. Sagittal (left), and coronal (middle) view of segmented discs L1-L5, an axial view (right) of L4 disc.



Figure 23. Sagittal 3D view of completed segmentation for a single participant.

# 5.3.2 Reliability Analysis

We assessed test-retest reliability of intervertebral disc measurements by conducting an ICC(2,1) using statistical shape data, specifically the top five principal component scores for each disc at timepoint 1 and timepoint 2. This was done to determine the repeatability and test-retest reliability of the statistical shape measures under the condition of repeated supine lying with no applied rotation.

## 5.3.3 Volumetric Analysis

The volume of each disc, obtained via segmentation, was compared at all three timepoints. The two baseline timepoints were combined as a mean volume to provide increased power to detect differences in volume. Dependent samples t-tests were conducted for each segment to assess significant changes in IVD volumes.

## 5.3.4 Statistical Shape Modeling

We used ShapeWorks Studio to process statistical shape modeling analyses (Cates et al., 2017). For the primary analysis, segmented images of each lumbar intervertebral disc of all 5 participants were used to analyze overall changes in shape across all intervertebral discs between the first timepoint (resting in supine lying), second timepoint (repeated resting in supine lying) and the third timepoint (resting in supine lying following positioning in left-side lying and right trunk rotation).

#### 5.3.5 Parameters

We applied a Laplacian smoothing filter with 100 iterations for the analysis of all intervertebral discs, and 50 iterations for the analysis of individual disc segments. After smoothing, we created a mesh using 256 automatically placed particles, evenly spaced across the surface of the intervertebral disc mesh to enable standardized measurement of changes in magnitude and direction of disc shape. We used a Generalized Procrustes Analysis to control for disc size, and centered the discs to a common origin in 3D space. This allowed us to eliminate differences in disc size or orientation as a statistical shape variable, allowing us to identify true changes in shape as the primary outcome.

# 5.3.6 Primary Statistical Shape Analysis

Principal component analysis was performed to identify the top 10 principal components with respect to changes in shape between each condition, inclusive of all patients' intervertebral discs. We used paired T-tests to compare principal component scores for the first condition against the second condition for each of the top ten identified principal components to determine if any significant differences in shape were observed. For the primary analysis, we included all five lumbar intervertebral discs (L1-L2 to L5-S1) from each participant at all three timepoints in the analysis, for a total of 75 intervertebral discs, computing the mean of the two baseline timepoints as one averaged timepoint to compare to the post-rotation timepoint.

# 5.3.7 Secondary Statistical Shape Analysis

Principal component analysis was also used to identify the top 10 principal components with respect to changes in shape between each condition independently, for each intervertebral disc, analyzed across the sample (i.e.: all L1-L2 discs, all L2-L3 discs,...all L5-S1 discs). We used paired T-tests to compare principal component scores for the first condition against the second condition for each of the top ten identified principal components to determine if any significant differences in shape were observed using paired T-tests. For this analysis, we included all five participants at all three timepoints, for a total of 15 discs per segment. The same approach with regards to combining the two baseline timepoints was used for the secondary analysis.

# 5.4 Results

Test-retest reliability of the top five principal component scores, analyzing the mathematical shape feature of each disc in repeated supine lying was excellent, with a mean of 0.89, ranging between 0.80 to 0.98, indicating that there is little to no change in the shape of the disc in the absence of a change in posture. As a result, we combined the two baseline timepoints of 5 participants into one sample of 10 data points for the statistical shape analyses, providing greater power to detect differences in shape following the applied rotation.

# 5.4.1 Volumetric Analysis

Results of the volumetric analysis are outlined in Table 18. We observed no differences in IVD volume between the averaged baseline timepoint in comparison to the postrotation timepoint.

Segment	Baseline 1	Baseline 2	Baseline Average	Post-Rotation	Change	p-value
L1-L2	11,579.9 ± 5729.9	11,368.2 ± 4878.6	11,474.1 ± 5018.2	12,448.7 ± 6,999.8	974.6 ± 1806.3	0.9
L2-L3	13,402.3 ± 5551.8	13,438.20 ± 4143.1221	13,420.3 ± 4397.0	13,759.3 ± 4917.6	339.0 ± 838.1	0.4
L3-L4	15,277.1 ± 3945.9	15,125.74 ± 3697.64592	15,201.4 ± 3606.0	15,279.7 ± 4176.6	78.3 ± 762.7	0.2
L4-L5	15,492.7± 5633.5	15,553.78 ± 4776.23484	15,523.2 ± 4620.0	15,660.8 ± 5120.0	137.5 ± 542.7	0.8
L5-S1	12,483.8 ± 3168.3	12,050.6 ± 3577.0	12,267.2 ± 3193.8	13,180.2 ± 3479.1	913.0 ± 526.7	0.3

Table 18. Volumetric analysis of IVD disc segments at each timepoint.

# 5.4.2 Statistical Shape Modeling: Principal Component Analysis – Primary

PCA identified significant changes in disc shape for 2 of the top 10 modes in the primary analysis (evaluating all discs simultaneously) between the two conditions (Table 19). These two principal components represented changes in shape in a reciprocal and opposite direction (Figure 22) and in a lateral direction towards the right (Figure 22).

# 5.4.3 Statistical Shape Modeling: Magnitude of Shape Changes – Primary

Significant changes in shape were observed in mode 4 and 7 (Table 19). Mode 4 demonstrates rotational differences in shape that represent between -1.7% (shrinking) to 2.5% (expansion) of the disc in an ellipsoid pattern, representative of the anatomical areas of the disc being compressed and relieved with the applied rotation positioning (Figure 22 below).

	Participant								
	1	2	3	4	5	Mean & Mean			
PC Mode						Difference (95%CI)			
1 - Pre	-19.45	3.22	-28.37	-28.44	59.20	-2.77			
1-Post	-22.34	7.05	1.18	-24.26	66.07	5.54			
Difference	-2.88	3.83	29.56	4.18	6.86	8.32 (-2.63; 19.26)			
2-Pre	-8.14	1.74	3.22	-0.38	4.70	0.23			
2- Post	-7.60	-0.97	0.28	0.88	5.09	-0.46			
Difference	0.53	-2.72	-2.94	1.27	0.38	-0.69 (-7.21; 5.82)			
3-Pre	11.28	4.42	-9.27	8.36	-19.74	-0.99			
3-Post	10.50	-1.61	3.80	12.36	-15.15	1.97			
Difference	-0.78	-6.03	13.08	3.99	4.59	2.97 (-1.61; 7.55)			
4-Pre	-0.47	-6.33	-5.42	10.24	6.33	0.86			
4-Post	0.59	-5.75	-7.94	7.96	-3.52	-1.73			
Difference	1.06	0.57	-2.51	-2.28	-9.85	-2.60 (-4.79; -0.41)			
5-Pre	0.06	2.66	-3.10	2.48	-4.80	-0.53			
5-Post	-1.49	5.26	-3.67	3.22	2.06	1.07			
Difference	-1.55	2.59	-0.56	0.74	6.86	1.62 (-0.79; 4.02)			
6-Pre	-2.05	4.70	-3.28	0.79	1.22	0.27			
6-Post	-4.13	2.22	-2.59	-0.26	1.99	-0.55			
Difference	-2.08	-2.47	0.68	-1.05	0.76	-0.83 (-2.87; 1.21)			
7-Pre	-6.19	3.47	3.00	3.03	-0.80	0.50			
7-Post	-5.99	0.91	2.23	1.63	-3.82	-1.00			
Difference	0.19	-2.55	-0.76	-1.40	-3.01	-1.51 (-2.65; -0.37)			
8-Pre	0.73	0.95	-0.47	-0.88	-0.36	-0.00			
8-Post	1.23	-0.72	-0.53	-0.07	0.15	0.01			
Difference	0.50	-1.68	-0.06	0.81	0.51	0.02 (-0.80; 0.83)			
9-Pre	0.02	0.43	0.33	1.20	-0.07	0.38			
9-Post	-0.78	0.32	0.45	-2.25	-1.61	-0.77			
Difference	-0.81	-0.11	0.12	-3.45	-1.53	-1.16 (-2.69; 0.37)			
10-Pre	-0.03	-0.29	0.62	-0.22	1.39	0.29			
10-Post	1.08	-0.45	-0.33	-0.51	-2.70	-0.58			
Difference	1.11	-0.16	-0.96	-0.29	-4.09	-0.88 (-2.23; 0.47)			
Mean scores o repositioning s difference are	f the entire cores are a presented	e group pr averaged. in the righ	esented ir Group me tmost col	n the right eans, mea umn. Sign	-most colu an differen iificant diff	mn. The two pre- ces, and 95%CI of the erences are bolded.			

 Table 19. Combined PC scores of all discs (L1-L2 to L5-S1) of each participant before and after 2 minutes of rotation.

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Mode 7 demonstrates an expansion of the disc away from the compressed side. Differences in shape that represent between -0.8% (shrinking) to 1.5% (expansion) of the disc in an anterolateral expansion pattern, and importantly, a regression in volume away from the posterior horn of the disc, representative of the anatomical areas of the disc being compressed and relieved with the applied rotation positioning (Figure 22 below).



Figure 24. Visual representation of significant differences in disc shape as per Principal Component Mode 4 with all IVD's included in the model (red = growing, blue = shrinking), posterior-anterior view. Scale on right indicates the magnitude of shape change for the colour-coded vectors in the figure (change of 2.5 indicates a 2.5% growth in the direction of the vector, relative to the size of the disc).

#### 5.4.4 Statistical Shape Modeling: Principal Component Analysis – Secondary

When we analyzed each individual disc across the entire group of participants, significant changes in shape were observed in one of the top ten principal components for the L1-L2 (Mode 3, Table 20), and L2-L3 intervertebral discs (Mode 4, Table 21), consistent with similar changes in shape observed with the primary analysis. PCA did not identify any

significant changes in shape for the top ten principal components for the remaining intervertebral discs (L3-L4, L4-L5, L5-S1). See Appendix 0-23.

## 5.4.5 Statistical Shape Modeling: Magnitude of Shape Changes – Secondary

Significant changes in shape were observed in mode 3 for the L1-L2 discs (Table 20) and mode 4 in the L2-L3 discs (Table 21). Both observed differences in shape were characteristic of similar rotational differences in shape observed in the primary analysis (compare shape vectors of Figure 23 to Figure 24, and 25) that represent between -1.4 to - 1.8% (shrinking) to 1.3 to 1.9% (expansion) of the disc in an ellipsoid pattern, representative of the anatomical areas of the disc being compressed and relieved with the applied rotation position (Figures 23 and 24 below).



Figure 25. Visual representation of significant differences in disc shape as per Principal Component Mode 7 from the primary analysis, with all IVDs included in the model (red = growing, blue = shrinking), superior-inferior view. Scale indicates the magnitude of shape change for the colour-coded vectors in the figure (change of 1.5 indicates 1.5% growth in the direction of the vector, relative to disc size).



Figure 26. Visual representation of significant differences in disc shape as per Principal Component Mode 3 from the secondary analysis, with all L1-L2 discs included in the model (red = growing, blue = shrinking), posterior-anterior view. Scale on right indicates the magnitude of shape change for the colour-coded vectors in the figure (change of 1.3 indicates a 1.3% growth in the direction of the vector, relative to the size of the disc).

	Participant							
PC Mode	1	2	3	4	5	Mean & Mean Difference		
						(95%CI)		
1 - Pre	-33.69	8.70	-13.76	-35.91	74.46	-0.04		
1-Post	-44.82	14.13	-14.02	-44.00	89.11	0.08		
Difference	-11.13	5.43	-0.26	-8.09	14.65	0.12 (-12.81; 13.05)		
2-Pre	7.68	-23.62	7.52	-2.36	2.85	-1.59		
2- Post	8.57	-18.63	6.01	3.57	16.33	3.17		
Difference	0.89	4.99	-1.51	5.93	13.48	4.76 (-2.37; 11.88)		
3-Pre	-8.81	-2.69	8.57	8.76	4.63	2.09		
3-Post	-13.29	-7.37	3.45	4.76	-8.47	-4.18		
Difference	-4.48	-4.68	-5.12	-4.00	-13.10	-6.28 (-11.03; -1.51)		
4-Pre	6.81	-1.04	-5.97	0.11	3.50	0.68		
4-Post	-0.44	-0.35	-9.36	6.78	-3.46	-1.37		
Difference	-7.25	0.69	-3.39	6.67	-6.96	-2.05 (-9.30; 5.21)		
5-Pre	0.50	1.22	3.19	-2.27	3.53	1.23		
5-Post	8.36	-2.63	0.16	-10.46	-7.81	-2.48		
Difference	7.86	-3.85	-3.03	-8.19	-11.34	-3.71 (-12.76; 5.34)		
6-Pre	-2.61	-1.15	-1.04	-2.01	4.61	-0.44		

Table 20. PC Scores of each L1-L2 disc before and after 2 minutes of rotation.

6-Post	2.84	0.74	-1.88	7.95	-5.23	0.88
Difference	5.45	1.89	-0.84	9.96	-9.84	1.32 (-7.91; 10.56)
7-Pre	-4.59	0.90	-2.12	0.84	-0.91	-1.18
7-Post	5.17	-1.31	2.84	3.01	2.03	2.35
Difference	9.76	-2.21	4.96	2.17	2.94	3.52 (-1.89; 8.93)
8-Pre	1.63	0.30	-3.72	3.08	2.43	0.74
8-Post	0.17	-4.68	-1.06	-0.97	-0.91	-1.49
Difference	-1.46	-4.98	2.66	-4.05	-3.34	-2.23 (-5.99; 1.52)
9-Pre	-2.09	-1.99	-1.42	2.28	0.42	-0.56
9-Post	4.27	2.10	0.96	-1.99	0.25	1.12
Difference	6.36	4.09	2.38	-4.27	-0.17	1.68 (-3.41; 6.76)
10-Pre	0.29	0.26	0.51	-2.13	0.95	-0.02
10-Post	0.99	-0.48	1.39	0.30	-1.96	0.05
Difference	0.7	-0.74	0.88	2.43	-2.91	0.07 (-2.42; 2.56)
Units are Principal Component Scores, indicating the degree of difference of each individual disc from the average disc shape of the sample at each respective timepoint. The two pre-repositioning scores are averaged. Group means, mean differences, and 95%CI of the difference are presented in the rightmost column. Significant differences are bolded.						

Table 21. PC Scores of each L2-L3 disc before and after 2 minutes of rotation.

	Participant						
PC Mode	1	2	3	4	5	Group Mean & Mean	
						Difference (95%Cl)	
1 - Pre	-32.97	9.03	-11.44	-34.47	65.83	-0.80	
1-Post	-32.16	8.59	-8.87	-30.04	70.34	1.56	
Difference	0.81	-0.44	2.57	4.43	4.51	2.36 (-0.34; 5.05)	
2-Pre	2.63	-11.85	-6.62	10.62	7.55	0.47	
2- Post	0.54	-14.10	-3.20	6.29	5.79	-0.94	
Difference	-2.09	-2.25	3.42	-4.33	-1.76	-1.40 (-4.98; 2.17)	
3-Pre	2.93	0.53	-2.80	2.10	-0.86	0.38	
3-Post	0.95	13.32	-19.34	-0.53	1.79	-0.76	
Difference	-1.98	12.79	-16.54	-2.63	2.65	-1.14 (-14.29; 12.01)	
4-Pre	-8.75	2.64	5.73	5.51	1.68	1.36	
4-Post	-10.24	1.00	2.89	0.34	-7.60	-2.72	
Difference	-1.49	-1.64	-2.84	-5.17	-9.28	-4.08 (-8.13; -0.04)	
5-Pre	-1.30	-3.93	1.04	0.94	-3.34	-1.32	
5-Post	-4.39	7.71	2.67	1.45	5.74	2.64	
Difference	-3.09	11.64	1.63	0.51	9.08	3.95 (-3.71; 11.62)	
6-Pre	-1.51	3.99	-7.15	2.66	-0.78	-0.56	
6-Post	-1.13	2.77	1.39	2.62	-0.05	1.12	
Difference	0.38	-1.22	8.54	-0.04	0.73	1.68 (-3.17; 6.53)	

7-Pre	-2.61	0.58	0.72	3.35	-1.20	0.17	
7-Post	1.13	-2.64	-1.06	-1.46	2.35	-0.34	
Difference	3.74	-3.22	-1.78	-4.81	3.55	-0.50 (-5.40; 4.39)	
8-Pre	-1.12	0.29	-1.06	1.12	2.04	0.25	
8-Post	0.76	1.52	-0.70	0.20	-4.32	-0.51	
Difference	1.88	1.23	0.36	-0.92	-6.36	-0.76 (-4.86; 3.34)	
9-Pre	1.17	-2.17	-1.24	-0.77	1.23	-0.36	
9-Post	-0.86	2.05	4.12	0.27	-2.02	0.71	
Difference	-2.03	4.22	5.36	1.04	-3.25	1.07 (-3.60; 5.73)	
10-Pre	2.54	0.74	0.60	0.43	0.14	0.89	
10-Post	-6.39	-1.59	-1.91	1.22	-0.23	-1.78	
Difference	-8.93	-2.33	-2.51	0.79	-0.37	-2.67 (-7.34; 2.00)	
Units are Principal Component Scores, indicating the degree of difference of each individual disc from the							
average disc shape of the sample at each respective timepoint. The two pre-repositioning scores are averaged.							
Group means, mean differences, and 95%CI of the difference are presented in the rightmost column. Significant							
differences are bolded.							



Figure 27. Visual representation of significant differences in disc shape with all L2-L3 discs included in the model (red = growing, blue = shrinking), posterior-anterior view. Scale on right indicates the magnitude of shape change for the colour-coded vectors in the figure (change of 1.9 indicates a 1.9% growth in the direction of the vector, relative to the size of the disc).

#### 5.5 Discussion

This proof-of-concept study investigated the response of lumbar intervertebral discs (IVD's) in five healthy asymptomatic participants to a sustained unilateral spinal rotation position commonly used as an intervention for patients with LBP. Based on clinical experience and observations of patients with DLBP without radicular symptoms and who respond to specific sustained spinal mobilizations, we hypothesized that there would be no change in lumbar disc morphology between times 1 and 2 and that there would be a change in disc morphology between the calculated mean of baseline times 1 and two and the and following rotation mobilization. Investigating and quantifying the effects of a common treatment intervention for LBP on a potential source and mechanism of DLBP is important as it advances the field of knowledge in a manner that up to now has not been widely studied.

Despite a small sample size, results revealed a general change in disc morphology following the rotation position in (i.e., time 3) but no changes between times 1 and 2 as hypothesized. The most prominent morphological changes were demonstrated in the upper lumbar segments of L1 - L2 and L2 - L3. No statistically significant changes in disc morphology were observed in the lower lumbar segments. Wang (Wang et al., 2009) in a study of disc deformation under-weight bearing with no rotation, reported that L2-3, L3-4 and L4-5 discs demonstrated different deformation patterns. This may suggest the role of other potential influencing factors. One of these factors may be that IVD's have different geometric features at different segmental levels, growing increasingly larger towards the lumbar spine (Zhong et al., 2014). The kinematic properties of the facets of the upper lumbar spine (L2-L3 and L3-L4) are similar but different from that of the lower lumbar spine (L4-L5) allowing less range of motion in the more caudal segments (Kozanek et al., 2009; Wachowski et al., 2009), The axial rotation response of an intervertebral motion segment is likely influenced individually and as a system by the stiffness properties of the disc, ligaments and facet joints (Ahmed et al., 1990). Finally, as a result of many of these aforementioned factors, variations in the location of the centre (axis) of rotation (COR) among lumbar vertebrae within and between participants (Alapan et al., 2014), potentially leading to different responses of the IVD to rotation.

Our findings are supported by other studies of deformation patterns of lumbar discs subjected to rotation positions in healthy participants. Xu (Xu et al., 2022, 2022) used CT imaging to infer changes in disc morphology based on changes in vertebral positions under a rotated position. They demonstrated that a left rotation resulted in greater compression of the right lateral and posterior aspects of the L3-4 and L4-L5 IVD's, and a right rotation resulted in greater compression of the left lateral and posterior aspects of the L3-4 and L4-L5 IVD's, and a right rotation resulted in greater compression of the left lateral and posterior aspects of the L3-4 and L4-L5 IVD's. Fazey (Fazey et al., 2013) reported the NP at L1-2 and L4-5 deformed away from the offset compressive load in positions of flexion and extension. They found the direction of deformation following left rotation in flexion and extension was less predictable. Kolber (Kolber & Hanney, 2009) concluded the non-degenerated disc has a predictable pattern of NP migration. Small sample sizes in these studies, however, reduce the power and generalizability of the results which are inclined to support the notion that disc deformation exhibits direction specificity based on the applied change in position.

The underlying rationale for the effect of the unilateral side lying spinal rotation position is that hydrated discs behave as a hydrostatic mechanism and as such deform towards an area of least load. Despite differences in study characteristics, others have reported that deformation of the IVD shows direction specificity concluding that the compressive force is greater on the side of concavity, and that deformation is towards the side of convexity (Fazey et al., 2013; Xu et al., 2022). The coupled lateral flexion that inevitably occurs concurrently with ipsilateral rotation has the ability to impart asymmetrical loading on the intervertebral disc and influence NP deformation direction (Fazey et al., 2006). For this behavior to occur, the annulus must be intact, and the hydrostatic mechanism of the intervertebral disc (IVD) must be functioning (Kolber & Hanney, 2009).

Further evidence of the effect of a rotation position comes from a study of healthy men and women which quantified lumbar zygapophyseal joint (i.e., facet joint) space separation or gapping in LBP subjects after spinal manipulative therapy (SMT) or a sideposture position (SPP) using MRI (Cramer et al., 2013). The SPP, that involved a rotation, appeared to have additional therapeutic benefit regarding pain reduction and Z joint gapping (Cramer et al., 2013) other than what had been hypothesized and that continuation of the side-posture position after manipulation should be considered.

This is the first investigation that we are aware of, that examined the effects of a sustained (2 minute) unilateral spinal rotation position, commonly used as a treatment for LBP, on the morphology of lumbar discs. Investigating and establishing baseline characteristics of changes in the morphology of lumbar IVD's in healthy participants using SRM has important implications for the understanding of the underlying mechanism of DLBP as proposed by several authors (Cyriax, 1950; Diwan & Melrose, 2023; Geers et al., 2003; L. G. Giles, 2000). Similar SMT maneuvers are used by clinicians when treating some patients with LBP. When a patient's symptoms are changed and relocated to a more central area of the lumbar spine, and may also be accompanied by a reduction in pain intensity, following the application of similar maneuver(s), the centralization phenomenon (CP) has occurred. CP is a progressive resolution, reduction or retreat of pain toward the midline (Werneke et al., 2008). CP supports the notion of reducible discogenic low back pain (RDLBP), one of three broad categories of disc syndrome (Petersen et al., 2003) as a cause of LBP. Complementing this has been Donelson's work on the dynamic disc model (Kolber & Hanney, 2009).

Importantly, we scanned our participants in a supine resting position after the application of the 2-minute rotation positioning. The changes observed in the present study suggests that the morphologic changes are sustained, at the very least for a brief period of time. Adding support to the notion that spinal manipulative treatment (SMT) can alter a disc deformation are studies by Takasaki (Takasaki et al., 2010) and (Scannell & McGill, 2009). Takasaki reported the results from a study of the L4-5 disc in a single patient with right sided LBP and right buttock pain. The patient was treated with self-mobilization's based on the McKenzie management strategy. Initially the MRI showed a portion of the NP displaced right and posteriorly towards the side of pain and an overall NP position in the coronal plane shifted to the left. Repeat MRI one month later showed the displaced portion of NP was no longer present and the left shifted NP was centrally located. Future studies should evaluate repeated imaging to discern if the timeline of regression of the disc back to its resting position has a temporal association with the change in symptoms to better understand the relationship between disc morphology and therapeutic effect. Scannell and McGill demonstrated that repeated or combined extension after disc prolapse was found to redirect displaced portions of the nucleus pulposus back centrally in a number of discs which matches clinical observation that the McKenzie approach can be effective with some patients with herniated discs but not with others (Scannell & McGill, 2009). They showed that loss of disc height distinguished between specimens that responded to reversal testing and those that did not respond (Scannell & McGill, 2009). This is noteworthy information for clinicians using the McKenzie treatment protocol.

#### 5.6 Strengths and Limitations

Strengths of the study include the use of 3T MRI to acquire representative morphological changes of the intervertebral disc to best understanding the structural response to the effect of repositioning. Additionally, the use of statistical shape modeling in conjunction with morphologic measurements provides both general and specific understanding of the changes in shape as well as the specific directions that these changes presented. Using this approach made it possible to understand the general trends, but also the variation among the sample. Additionally, our methods were supported by the demonstrated test-retest reliability indicated by no change between disc shapes in the first two control timepoints.

This study has limitations. Primarily, the small sample size made for a limited ability to make generalizations about each individual disc. It is possible that each disc responded similarly, and that there was simply a lack of data to support this. As a result, we took several approaches to best explain the potential phenomena, by analyzing the entire group at each segment, as well as combining all of the segments to understand the general response of a lumbar intervertebral disc, regardless of the specific segment. Future research should include a larger sample size. Additionally, due to restrictions with scanner booking time, only left side rotation was assessed. Bilateral rotation studies with the same or a larger cohort would be valuable to better test the assumption of symmetry of direction-specific coupled motion responses in IVD deformation. Finally, with image

segmentation, there is always inherent subjective bias in interpretation of the anatomy, particularly with determining which pixel intensities represent the anatomy of interest for segmentation. We controlled for this to the best of our ability by having the reader trained by an expert and blinding the reader to participant and timepoint.

#### 5.7 Future Directions

Our study needs to be repeated using a calculated larger sample size to ensure high power testing of the hypothesis. The long-term purpose of our research project is to use MRI pre and post treatment to examine a subgroup of patients who have been diagnosed with RDLBP as participants. As Takasaki (Takasaki et al., 2010) has recommended, there is value in conducting repeat MRIs in patients with LBP, immediately before and after centralization and/or abolition of symptoms. This type of study would be more convincing evidence of a link between centralization and changes to disc morphology. Additional important questions worth answering include understanding the dose-response relationship related to repositioning, such as the time exposed or the amount of rotation applied, as well as understanding if there are limits at which there may be diminishing returns or potential harm involved with the application of sustained rotation. Additionally, understanding for how long these effects are sustained, and for patients with RDLBP, how long these sustained effects contribute to symptom modification. Also, while we demonstrated segment specific differences in the magnitude of response, a larger sample size would provide the opportunity to verify if these are differences in disc behaviour, or if we simply lacked the signal to identify this.

#### 5.8 Conclusion

Using 3T MRI, we observed changes in lumbar disc morphology in response to a unilateral side lying rotation position commonly used in the treatment of LBP. The most prominent morphological changes were demonstrated in the upper lumbar segments of L1 - L2 and L2 - L3. No statistically significant changes in disc morphology were observed in the lower lumbar segments in this sample. Our study also demonstrated that this method is reliable for measuring changes in disc shape, as there was good reliability between the first and second control conditions. Future studies should focus on

understanding these responses in larger and more diverse samples, as well as their clinical relevance in patients with existing discogenic low back pain.

#### 5.9 Ethical Approval

The study was approved by Western University's Health Science Research Board.

## 5.10 Funding

Through the Pain and Quality of Life Integrative Research Lab, Faculty of Health Sciences, Western University, London, ON

## 5.11 Conflicts of Interest

There are no conflicts of interest.

## 5.12 What is Already Known on this Topic

MRI studies report changes in lumbar disc morphology in response to specific spinal positions in non-degenerated IVD's of asymptomatic participants. MRI is a non-invasive imaging technology that allows for an accurate visualization of changes in disc morphology.

## 5.13 What this Study Adds to this Topic

In spite of the very small sample in this study, lumbar IVD morphology is affected in a predictable fashion by a side lying trunk rotation position. This adds to the credibility of pursuing further research using variations of positions that mimic particular SMT forms used by clinicians to treat DLBP in larger samples of asymptomatic participants and subsequently, to symptomatic participants presenting with the signs and symptoms of DLBP.

#### Chapter 6

#### 6 Conclusion

#### 6.1 Introduction

In this dissertation we have sought to investigate the signs and symptoms of a subgroup of patients with non-specific low back pain (NSLBP) and to examine changes in lumbar disc morphology in response to a side lying rotation position commonly used as a treatment for patients with low back pain (LBP). The subgroup of patients has been categorized as having discogenic low back pain (DLBP) associated with a disc herniation that is reducible using mechanical loading strategies (Petersen et al., 2017). This description provides a plausible explanation of the mechanism involved in the centralization phenomenon (CP) reported by researchers and clinicians (Laslett et al., 2005; May et al., 2018; Werneke et al., 2008).

We found that in patients with DLBP, there were several clinical symptoms and signs reported associated with disc herniations. Clinical symptoms include: a sudden onset of low back pain or an incident associated with flexion/rotation and compression; aggravating activities such as pain increased by sitting, repeated flexion or slouched postures, coughing/sneezing/straining; and, relieving activities including lumbar extension, lying down as opposed to standing or walking and subjective reports of centralization of symptoms. Clinical signs include: centralization and peripheralization of symptoms in response to movements or mechanical loading strategies; ipsilateral and crossed leg straight leg raise; altered patellar and Achille's reflexes; myotomal weakness; and, sensory loss. Findings from our investigation of changes in disc morphology reported on in Chapter 5, demonstrated changes in lumbar disc morphology in response to a unilateral side lying rotation position commonly used in the treatment of LBP. Summary of the results of the three dissertation projects are found in Figure 26.



Figure 28. Summary of results of the three dissertation projects.

We also found that despite the large body of published evidence that the intervertebral disc (IVD) can be a potential pain generator, there remains no consensus on the various definitions, classifications, diagnostic criteria or treatment of DLBP (Fujii et al., 2019; Lorio et al., 2023). In fact, there are no International Classification of Diseases (ICD-10-CM) coding sub-terms for "discogenic" back pain (Lorio et al., 2023). We agree with Lorio that the term DLBP needs to be redefined. DLBP should include non-radicular pain from a disc herniation. While research continues to focus on internal disc derangement, little progress has been made towards a deeper understanding of the complicated nature and treatment of DLBP. Since the clinical examination is the basis upon which management of DLBP is based on, and that poor pre-procedure selection and diagnosis is

a major contributing factor to treatment failure, there remains a critical need to develop valid and reliable criteria for diagnosing DLBP (Laslett et al., 2005).

Given the evidence we have presented in this dissertation, there is coherence between anecdotal clinical evidence, changes in lumbar disc morphology and the theory that some DLBP may be a result of disc herniation. Evidence supporting this comes from studies that concluded the origin of DLBP in some patients may be the result of contained lumbar disc herniations compressing adjacent innervated paraspinal tissues such as the posterior longitudinal ligament, the dura mater and the sleeved dural nerve roots; and that the degree of back or leg pain caused by an acute disc herniation may depend in part on the degree of dural or nerve root compression (Chan et al., 2013; Cyriax, 1950; Giles, 2000; Laslett, 1987; Summers et al., 2005). These conclusions are restricted to patients presenting with acute back pain and not chronic back pain (Summers et al., 2005).

While there remains different, and some would say, competing explanations for the underlying mechanisms of DLBP, as well as its treatment, we suggest there are more symmetries than differences. The diagnostic process is a complicated series of decisions and for DLBP, it has not yet been sufficiently developed to allow clinicians to determine whether the diagnosis is present or not (Croft et al., 2015). In attempting to unravel the underlying mechanism(s) of DLBP, it might be useful to keep in mind the principle behind Occam's razor, the notion that when faced with competing explanations, choosing the simplest that fits the facts may be appropriate (McFadden, 2023).

While randomized-controlled trials (RCT's) and meta-analysis have often been used in LBP research particularly for investigations of the effects of spinal manipulative therapy, and remain the main tools of evidence-based medicine (EBM), it is research into clinical practices that will help generate new knowledge to fill the gap that currently exists with respect to the diagnosis and treatment of DLBP (Horn & Gassaway, 2007). A paradigm shift to alternative research designs in the field of DLBP appears necessary, or at the very least should be trialed. Toward that end, we recommend further research into existing clinical practices that have a strong association with good outcomes. The lack of sufficient direct evidence to support the proposed mechanism of DLBP as a result of disc

herniation could be overcome with a methodical series of well-designed research projects. To show cause-and-effect, we can use the Bradford-Hill criteria to frame future studies (Shimonovich et al., 2021). Otherwise known as Hill's criteria for causation, they are a group of minimal conditions necessary to provide adequate evidence of a causal relationship between two variables. The list of the criteria includes strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment and analogy. Each criterion can be assessed for strength, consistency and specificity. We have shown that there is a small field of evidence from different researchers who have demonstrated that some posterior lumbar disc protrusions impinge on and deform the posterior longitudinal ligament, the dura mater and spinal nerve roots. Advances in imaging technology, now allow accurate visualization and quantification of the magnitude of change in disc morphology and deformation of these tissues. This data will allow direct correlation between rigorously-quantified deformations or other parameters of disc morphology and clinical signs and symptoms to a degree not previously possible. The temporality criterion would be conceptually more difficult, requiring accurate demonstration that the cause (bulging disc) precedes the effect of the symptoms of DLBP. This could theoretically be accomplished through population-based studies in which symptom and bulge-free individuals are radiologically assessed at regular intervals until such time as DLBP occurs. Evidence of no bulge, or at least no pressure on mechanosensitive tissues, in the asymptomatic phase followed by evidence of pressure in the symptomatic phase would satisfy this criterion. Reversibility would also support a temporal relationship; that is, removal of the cause should lead to subsequent and proportional reduction of the effect.

To that end and included in our list of recommendations for further research, a first step to further exploration of DLBP, is the creation and development of a clinical decision support system for clinicians from the various disciplines who treat patients with LBP. We have outlined a list of short-term goals below. Potential medium, and, long term goals may be found in Appendix 0-25.

- 1. Begin to develop a clinical decision support system for clinicians with the long-term goal of creating reference-based standards for diagnosing patients with DLBP;
- 2. Develop standard clinical terminology for DLBP;
- Undertake goals 1 and 2 using a collaborative approach with clinicians from physiotherapy, chiropractic, osteopathic, medicine disciplines, basic and experimental scientists;
- 4. Repeat the MRI project reported on in Chapter 5 of this dissertation with a larger sample of healthy asymptomatic participants;
- Repeat a revised on line survey as reported on in Chapters 2 and 3 to update the results and take measures to incentivize a higher response rate to between 30 and 40%
- Create a well-designed MRI project using participants with suspected DLBP to examine the correlation of clinical and MRI findings of disc morphology in patients pre and post spinal manipulation therapies using the Bradford-Hill criteria.

## 6.3 What is Already Known about Discogenic Low Back Pain Associated with Disc Herniation

- There are no gold standards for the majority of the index (i.e. clinical tests) tests used for physical examination of patients suspected of DLBP;
- There is no consensus of the mechanism(s) underlying DLBP;
- There is no consensus on effective treatment(s) for DLBP;
- There is no consensus on the use of or the mechanism of action of spinal manipulation or mobilization as a treatment for DLBP or LBP;
- We are not able to identify responders based on history alone but in conjunction with clinical testing, those that demonstrate the centralization phenomenon (CP), fall into the category of having a contained reducible disc herniation;
- A common clinical feature of DLBP is centralization, defined as the proximal movement and/or abolition of distal symptoms originating from the spine in response to the application of mechanical loading strategies (MLS), such as repeated movements.

# 6.4 What this Dissertation adds to What is Known about Discogenic Low Back Pain

- Clinicians use a combination of key information from a patient's history as well as clinical examination findings to determine a diagnosis of DLBP, however, there is little consensus among clinicians;
- Symptoms and signs of DLBP have not been validated although findings from our systematic review support the findings;
- The use of single clinical tests appears to be less useful than clusters of tests which is more closely in line with clinical decision making;
- Symptoms of DLBP include, sudden onset or an incident associated with lexion/rotationand compression, a paroxysmal painpattern, symptoms aggravated by sitting, repeated flexion, sitting, postures, coughing/sneezing/straining; symptoms relieved by extension, lying down and subjective reports of centralization of symptoms;
- The centralization phenomenon (CP) is the only reference supported clinical symptom sign that is diagnostic for non-radicular and some variations of nerve root pain as a result of DLBP;
- Signs of DLBP include include centralization and peripheralization of symptoms in response to movements or mechanical loading strategies, ipsilateral and crossed leg straight leg raise, altered patellar and Achille's reflexex, myotomal weakness and sensory loss;
- Centralization has high sensitivity and moderate specificity and is the only reference based sign of non-radicular DLBP;
- Radicular signs including straight leg raise, weakness, reflex changes and sensory changes are supported with reference standards;
- While clinical experience suggests that spinal manipulation is effective for at least some patients with LBP, spinal manipulative therapy (SMT) (including spinal manipulation and spinal mobilization) remain a secondary or adjunctive treatment for DLBP;
- There remains a gap between clinical practice and evidence on the use of SMT;
- There is lack of evidence regarding the effects of specific types, different grades and variations in duration of SMT.

### 7 References

- Adams, J., Sibbritt, D., Steel, A., & Peng, W. (2018). A workforce survey of Australian osteopathy: Analysis of a nationally-representative sample of osteopaths from the Osteopathy Research and Innovation Network (ORION) project. *BMC Health Services Research*, 18(1), 1–7. https://doi.org/10.1186/s12913-018-3158-y
- Ahmed, Duncan, & Burke. (1990). The effect of facet geometry on the axial torquerotation response of lumbar motion segments. *Spine*, *15*(5), 391–401.
- Aina, A., May, S., & Clare, H. (2004). The centralization phenomenon of spinal symptoms - A systematic review. *Manual Therapy*, 9(3), 134–143. https://doi.org/10.1016/j.math.2004.03.004
- Al Nezari, N. H., Schneiders, A. G., & Hendrick, P. A. (2013). Neurological examination of the peripheral nervous system to diagnose lumbar spinal disc herniation with suspected radiculopathy: A systematic review and meta-analysis. *Spine Journal*, *13*(6), 657–674. https://doi.org/10.1016/j.spinee.2013.02.007
- Alapan, Y., Sezer, S., Demir, C., Kaner, T., & Inceoğlu, S. (2014). Load sharing in lumbar spinal segment as a function of location of center of rotation: Laboratory investigation. *Journal of Neurosurgery: Spine*, 20(5), 542–549. https://doi.org/10.3171/2014.1.SPINE13426
- Alexander, L. A., Hancock, E., Agouris, I., Smith, F. W., & MacSween, A. (2007). The response of the nucleus pulposus of the lumbar intervertebral discs to functionally loaded positions. *Spine*, 32(14), 1508–1512. https://doi.org/10.1097/BRS.0b013e318067dccb
- Allee, B. A., Pollak, M. H., & Malnar, K. F. (2005). Survey of osteopathic and allopathic residents' attitudes toward osteopathic manipulative treatment. *Journal of the American Osteopathic Association*, 105(12), 551–561. https://doi.org/10.7556/jaoa.2005.105.12.551
- Allegri, M., Montella, S., Salici, F., Valente, A., Marchesini, M., Compagnone, C., Baciarello, M., Manferdini, M. E., & Fanelli, G. (2016). Mechanisms of low back pain: A guide for diagnosis and therapy [version 1; referees: 3 approved]. *F1000Research*, 5(PG-1-11), 1–11. https://doi.org/10.12688/F1000RESEARCH.8105.1

Almeida, M. O., Narciso Garcia, A., Menezes Costa, L. C., van Tulder, M. W., Lin, C.

W. C., & Machado, L. A. C. (2023). The McKenzie method for (sub)acute nonspecific low back pain. *Cochrane Database of Systematic Reviews*, 2023(4). https://doi.org/10.1002/14651858.CD009711.pub2

- Alrwaily, M., Timko, M., Schneider, M., Stevans, J., Bise, C., Hariharan, K., Delitto, A., Alrwaily, M., Timko, M., Schneider, M., Delitto, A., Virginia, W., Timko, M., Schneider, M., Stevans, J., Bise, C., Hariharan, K., & Delitto, A. (2016). Treatment-Based Classification System for Low Back Pain: Revision and Update. *Phys Ther*, 96(7), 1057–1066. https://academic.oup.com/ptj/article/96/7/1057/2864925
- Altun, I., & Yüksel, K. Z. (2017). Lumbar herniated disc: Spontaneous regression. Korean Journal of Pain, 30(1), 44–50. https://doi.org/10.3344/kjp.2017.30.1.44
- Alyas, F., Connell, D., & Saifuddin, A. (2008). Upright positional MRI of the lumbar spine. *Clinical Radiology*, 63(9), 1035–1048. https://doi.org/10.1016/j.crad.2007.11.022
- Amin, R. M., Andrade, N. S., & Neuman, B. J. (2017). Lumbar Disc Herniation. *Current Reviews in Musculoskeletal Medicine*, 10(4), 507–516. https://doi.org/10.1007/s12178-017-9441-4
- Amirdelfan, K., McRoberts, P., & Deer, T. R. (2014). The differential diagnosis of low back pain: A primer on the evolving paradigm. *Neuromodulation*, *17*(S2 PG-11-17), 11–17. https://doi.org/10.1111/ner.12173
- Ansari, S., Heavner, J. E., McConnell, D. J., Azari, H., & Bosscher, H. A. (2012). The Peridural Membrane of the Spinal Canal: A Critical Review. *Pain Practice*, 12(4), 315–325. https://doi.org/10.1111/j.1533-2500.2011.00510.x
- Aoyagi, K., Heller, D., Hazlewood, D., Sharma, N., & dos Santos, M. (2019). Is spinal mobilization effective for low back pain?: A systematic review. *Complementary Therapies in Clinical Practice*, 34(November 2018), 51–63. https://doi.org/10.1016/j.ctcp.2018.11.003
- Apeldoorn, A. T., Van Helvoirt, H., Meihuizen, H., Tempelman, H., Vandeput, D., Knol, D. L., Kamper, S. J., & Ostelo, R. W. (2016). The influence of centralization and directional preference on spinal control in patients with nonspecific low back pain. *Journal of Orthopaedic & Sports Physical Therapy*, *46*(4 PG-258–269), 258–269.
- Ardakani, E. M., Leboeuf-Yde, C., & Walker, B. F. (2018). Failure to define low back pain as a disease or an episode renders research on causality unsuitable: Results of a

systematic review. *Chiropractic and Manual Therapies*, 26(1), 1–10. https://doi.org/10.1186/s12998-017-0172-9

- Atlas, S. J., & Deyo, R. A. (2001). Evaluating and managing acute low back pain in the primary care setting. *Journal of General Internal Medicine*, 16(2), 120–131. https://doi.org/10.1046/j.1525-1497.2001.91141.x
- Autio, R. A., Karppinen, J., Niinimäki, J., Ojala, R., Kurunlahti, M., Haapea, M., Vanharanta, H., & Tervonen, O. (2006). Determinants of spontaneous resorption of intervertebral disc herniations. *Spine*, *31*(11), 1247–1252. https://doi.org/10.1097/01.brs.0000217681.83524.4a
- Awad, J. N., & Moskovich, R. (2006). Lumbar disc herniations: Surgical versus nonsurgical treatment. *Clinical Orthopaedics and Related Research*, 443, 183–197. https://doi.org/10.1097/01.blo.0000198724.54891.3a
- Axén, I., Rosenbaum, A., Eklund, A., Halasz, L., Jørgensen, K., Lövgren, P. W., Lange, F., & Leboeuf-Yde, C. (2008). The Nordic maintenance care program - Case management of chiropractic patients with low back pain: A survey of Swedish chiropractors. *Chiropractic and Osteopathy*, *16*, 1–7. https://doi.org/10.1186/1746-1340-16-6
- Balagué, F., Mannion, A. F., Pellisé, F., & Cedraschi, C. (2012). Non-specific low back pain. *The Lancet*, *379*(9814 PG-482–491), 482–491. https://doi.org/10.1016/S0140-6736(11)60610-7
- Bardin, L. D., King, P., & Maher, C. G. (2017). Diagnostic triage for low back pain: A practical approach for primary care. *Medical Journal of Australia*, 206(6), 268–273. https://doi.org/10.5694/mja16.00828
- Baron, R. (2006). Mechanisms of disease: Neuropathic pain A clinical perspective. *Nature Clinical Practice Neurology*, 2(2), 95–106. https://doi.org/10.1038/ncpneuro0113
- Bartynski, W. S., & Rothfus, W. E. (2012). Peripheral disc margin shape and internal disc derangement: Imaging correlation in significantly painful discs identified at provocation lumbar discography. *Interventional Neuroradiology*, *18*(2 PG-227– 241), 227–241. https://doi.org/10.1177/159101991201800217
- Bashkuev, M., Reitmaier, S., & Schmidt, H. (2018). Effect of disc degeneration on the mechanical behavior of the human lumbar spine: a probabilistic finite element study.

Spine Journal, 18(10), 1910–1920. https://doi.org/10.1016/j.spinee.2018.05.046

- Bashkuev, M., Reitmaier, S., & Schmidt, H. (2020). Relationship between intervertebral disc and facet joint degeneration: A probabilistic finite element model study. *Journal of Biomechanics*, 102, 109518. https://doi.org/10.1016/j.jbiomech.2019.109518
- Baswaraj, D., Govardhan, A., & Premchand, P. (2012). Active contours and image segmentation: The current state of the art. *Global Journal of Computer Science and Technology*, *12*(11-F).
- Beattie, P. F., Meyers, S. P., Stratford, P., Millard, R. W., & Hollenberg, G. M. (2000). Associations between patient report of symptoms and anatomic impairment visible on lumbar magnetic resonance imaging. *Spine*, 25(7), 819–828. https://doi.org/10.1097/00007632-200004010-00010
- Bezci, S. E., Lim, S., & O'Connell, G. D. (2020). Nonlinear stress-dependent recovery behavior of the intervertebral disc. *Journal of the Mechanical Behavior of Biomedical Materials*, 110. https://doi.org/10.1016/j.jmbbm.2020.103881
- Bialosky, J. E., Beneciuk, J. M., Bishop, M. D., Coronado, R. A., Penza, C. W., Simon, C. B., & George, S. Z. (2018). Unraveling the mechanisms of manual therapy: Modeling an approach. In *Journal of Orthopaedic and Sports Physical Therapy* (Vol. 48, Issue 1, pp. 8–18). Movement Science Media. https://doi.org/10.2519/jospt.2018.7476
- Bialosky, J. E., Bishop, M. D., Robinson, M. E., & George, S. Z. (2010). The Relationship of the Audible Pop to Hypoalgesia Associated With High-Velocity, Low-Amplitude Thrust Manipulation: A Secondary Analysis of an Experimental Study in Pain-Free Participants. *Journal of Manipulative and Physiological Therapeutics*, 33(2), 117–124. https://doi.org/10.1016/j.jmpt.2009.12.008
- Bill, A. S., Dubois, J., Pasquier, J., Burnand, B., & Rodondi, P. Y. (2020). Osteopathy in the French-speaking part of Switzerland: Practitioners' profile and scope of back pain management. *PLoS ONE*, *15*(5), 1–14. https://doi.org/10.1371/journal.pone.0232607
- Billis, E., McCarthy, C. J., Roberts, C., Gliatis, J., Papandreou, M., Gioftsos, G., & Oldham, J. A. (2013). Sub-grouping patients with non-specific low back pain based on cluster analysis of discriminatory clinical items. *Journal of Rehabilitation Medicine*, 45(2), 177–185.

- Bisschop, P., & Van Ooteghem, P. (2003). Low Back Pain : Clinical Evidence for " the Dural Concept ." *Spine*, 72, 1–12.
- Bogduk, N. (2012). *Clinical and Radiological Anatomy of the Lumbar Spine* (E-Book). Elsevier Health Sciences.
- Bogduk, N., Aprill, C., & Derby, R. (2013a). Lumbar discogenic pain: State-of-the-art review. *Pain Medicine (United States)*, 14(6), 813–836. https://doi.org/10.1111/pme.12082
- Bogduk, N., Aprill, C., & Derby, R. (2013b). Lumbar Discogenic Pain: State-of-the Art Review. *Pain Medicine*, 14, 813–836. https://academic.oup.com/painmedicine/article/14/6/813/1858109
- Bolton, P. S., & Budgell, B. (2012). Visceral responses to spinal manipulation. In *Journal* of *Electromyography and Kinesiology*. https://doi.org/10.1016/j.jelekin.2012.02.016
- Bosscher, H. A., Grozdanov, P. N., Warraich, I. I., MacDonald, C. C., & Day, M. R. (2020). The anatomy of the peridural membrane of the human spine. *Anatomical Record*, 304(March), 1–15. https://doi.org/10.1002/ar.24476
- Bossuyt, P., Davenport, C., Deeks, J., Hyde, C., Leeflang, M., & Scholten, R. (2013). Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy Chapter 11 Interpreting results and drawing conclusions. 1–31. http://srdta.cochrane.org/.
- Botchu, R., Bharath, A., Davies, A. M., Butt, S., & James, S. L. (2018). Current concept in upright spinal MRI. *European Spine Journal*, 27(5), 987–993. https://doi.org/10.1007/s00586-017-5304-3
- Brault, J. S., Driscoll, D. M., Laakso, L. L., Kappler, R. E., Allin, E. F., & Glonek, T. (1997). Quantification of Lumbar Intradiscal Deformation During Flexion and Extension, by Mathematical Analysis of Magnetic Resonance Imaging Pixel Intensity Profiles. *Spine*, 22(18), 2066–2072.
- Brennan, G. P., Fritz, J. M., Hunter, S. J., Thackeray, A., Delitto, A., & Erhard, R. E. (2006). Identifying subgroups of patients with acute/subacute "nonspecific" low back pain: results of a randomized clinical trial. *Spine*, *31*(6), 623–631. https://doi.org/10.1097/01.brs.0000202807.72292.a8 [doi]
- Briar, K. (2021). *The impact of combined flexion and compression on the mechanical integrity of the annulus fibrosus.*

- Brinckmann, P; Porter, R. (1994). A Laboratory Model of Lumbar Disc Protrusion. *Spine*, *19*(2), 228–235.
- Broberg, K. B. (1983). On the mechanical behaviour of intervertebral discs. *Spine*, 8(2), 151–165.
- Brock, M., Patt, S., & Mayer, H. M. (1992). The form and structure of the extruded disc. *Spine*, *17*(12), 1457–1461.
- Bronfort, G., Haas, M., Evans, R., Kawchuk, G., & Dagenais, S. (2012). No Title. In *Evidence-based management of low back pain* (pp. 229–247). Elsevier Health Sciences.
- Bronfort, G., Haas, M., Evans, R., Kawchuk, G., & Dagenais, S. (2008). Evidenceinformed management of chronic low back pain with spinal manipulation and mobilization. In *Spine Journal*. https://doi.org/10.1016/j.spinee.2007.10.023
- Buchbinder, R., Underwood, M., Hartvigsen, J., & Maher, C. G. (2020). The Lancet Series call to action to reduce low value care for low back pain: an update. *Pain*, 161(9), S57–S64. https://doi.org/10.1097/j.pain.000000000001869
- Byrne, R. M., Aiyangar, A. K., & Zhang, X. (2019). A Dynamic Radiographic Imaging Study of Lumbar Intervertebral Disc Morphometry and Deformation In Vivo. *Scientific Reports*, 9(1), 1–12. https://doi.org/10.1038/s41598-019-51871-w
- Carlesso, L. C., MacDermid, J. C., Gross, A. R., Walton, D. M., & Santaguida, P. L. (2014). Treatment preferences amongst physical therapists and chiropractors for the management of neck pain: Results of an international survey. *Chiropractic and Manual Therapies*, 22(1), 1–15. https://doi.org/10.1186/2045-709X-22-11
- Carlesso, L. C., Macdermid, J. C., Lina Santaguida, P., Thabane, L., Giulekas, K., Larocque, L., Millard, J., Williams, C., Miller, J., & Chesworth, B. M. (2013).
  Beliefs and practice patterns in spinal manipulation and spinal motion palpation reported by Canadian manipulative physiotherapists. *Physiotherapy Canada*, 65(2), 167–175. https://doi.org/10.3138/ptc.2012-11
- Carnes, D., Mars, T. S., Mullinger, B., Froud, R., & Underwood, M. (2010). Adverse events and manual therapy: a systematic review. *Manual Therapy*, *15*(4), 355–363.
- Castro-Mateos, I., Pozo, J. M., Eltes, P. E., Rio, L. Del, Lazary, A., & Frangi, A. F. (2014). 3D segmentation of annulus fibrosus and nucleus pulposus from T2-

weighted magnetic resonance images. *Physics in Medicine and Biology*, 59(24), 7847–7864. https://doi.org/10.1088/0031-9155/59/24/7847

- Cates, J., Elhabian, S., & Whitaker, R. (2017). Chapter 10 ShapeWorks: Particle-Based Shape Correspondence and Visualization Software. In *Statistical Shape and Deformation Analysis* (pp. 257–298). Academic Press.
- Cavanaugh, Ozaktay, Yamashita, Avramov, Getchell, & King. (1997). Mechanisms of low back pain A neurophysiologic and neuroanatomic study.pdf.
- Chan, A., Ford, J. J., McMeeken, J. M., & Wilde, V. E. (2013). Preliminary evidence for the features of non-reducible discogenic low back pain: survey of an international physiotherapy expert panel with the Delphi technique. *Physiotherapy*, 99(3), 212– 220. https://doi.org/10.1016/j.physio.2012.09.007
- Chan, A. Y. P., Ford, J. J., Surkitt, L. D., Richards, M. C., Slater, S. L., Davidson, M., & Hahne, A. J. (2017). Individualised functional restoration plus guideline-based advice vs advice alone for non-reducible discogenic low back pain: a randomised controlled trial. *Physiotherapy*, 103(2), 121–130. https://doi.org/S0031-9406(16)30043-8 [pii]
- Chan, D. D., & Neu, C. P. (2014). Intervertebral disc internal deformation measured by displacements under applied loading with MRI at 3T. *Magnetic Resonance in Medicine*, 71(3), 1231–1237.
- Cheung, K. M. C., Karppinen, J., Chan, D., Ho, D. W. H., Song, Y. Q., Sham, P., Cheah, K. S. E., Leong, J. C. Y., & Luk, K. D. K. (2009). Prevalence and pattern of lumbar magnetic resonance imaging changes in a population study of one thousand fortythree individuals. *Spine*, *34*(9), 934–940. https://doi.org/10.1097/BRS.0b013e3181a01b3f
- Chevrefils, C., Chériet, F., Grimard, G., & Aubin, C.-E. C. E. (2007). Watershed segmentation of intervertebral disk and spinal canal from MRI images. *International Conference Image Analysis and Recognition*, 4633 LNCS(3), 1017–1027. https://doi.org/10.1007/978-3-540-74260-9\_90
- Chiarotto, A., Deyo, R. A., Terwee, C. B., Boers, M., Buchbinder, R., Corbin, T. P., Costa, L. O. P., Foster, N. E., Grotle, M., Koes, B. W., Kovacs, F. M., Lin, C. W. C., Maher, C. G., Pearson, A. M., Peul, W. C., Schoene, M. L., Turk, D. C., van Tulder, M. W., & Ostelo, R. W. (2015). Core outcome domains for clinical trials in nonspecific low back pain. *European Spine Journal*, 24(6), 1127–1142.

https://doi.org/10.1007/s00586-015-3892-3

- Chiu, C. C., Chuang, T. Y., Chang, K. H., Wu, C. H., Lin, P. W., & Hsu, W. Y. (2015). The probability of spontaneous regression of lumbar herniated disc: A systematic review. *Clinical Rehabilitation*, 29(2), 184–195. https://doi.org/10.1177/0269215514540919
- Cid, J., Calle, J. L., López, E., Del Pozo, C., Perucho, A., Acedo, M. S., Bedmar, D., Benito, J., De Andrés, J., Díaz, S., De La Calle, J. L., López, E., Del Pozo, C., Perucho, A., Acedo, M. S., Bedmar, D., Benito, J., De Andrés, J., Díaz, S., ... Díaz, S. (2015). A modified Delphi survey on the signs and symptoms of low back pain: indicators for an interventional management approach. *Pain Practice*, *15*(1), 12–21. https://doi.org/10.1111/papr.12135
- Çitişli, V., İbrahimoğlu, M., Veli, Ç., Muhammet, İ., Çitişli, V., & İbrahimoğlu, M. (2015). Spontaneous Remission of a Big Subligamentous Extruded Disc Herniation: Case Report and Review of the Literature. *Korean Journal of Spine*, *12*(1), 19. https://doi.org/10.14245/kjs.2015.12.1.19
- Colombi, A., & Testa, M. (2019). The effects induced by spinal manipulative therapy on the immune and endocrine systems. *Medicina (Lithuania)*, 55(8). https://doi.org/10.3390/medicina55080448
- Cook, C., & Hegedus, E. (2011). Diagnostic utility of clinical tests for spinal dysfunction. *Manual Therapy*, *16*(1), 21–25. https://doi.org/10.1016/j.math.2010.07.004
- Coronado, R. A., Gay, C. W., Bialosky, J. E., Carnaby, G. D., Bishop, M. D., & George, S. Z. (2012). Changes in pain sensitivity following spinal manipulation: A systematic review and meta-analysis. *Journal of Electromyography and Kinesiology*, 22(5), 752–767. https://doi.org/10.1016/j.jelekin.2011.12.013
- Cox, J.M. (2012). *Low back pain: Mechanism, diagnosis and treatment*. Lippincott Williams & Wilkins.
- Cramer, G. D., Cambron, J., Cantu, J. A., Dexheimer, J. M., Pocius, J. D., Gregerson, D., Fergus, M., McKinnis, R., & Grieve, T. J. (2013). Magnetic resonance imaging zygapophyseal joint space changes (gapping) in low back pain patients following spinal manipulation and side-posture positioning: A randomized controlled mechanisms trial with blinding. *Journal of Manipulative and Physiological Therapeutics*, 36(4), 203–217. https://doi.org/10.1016/j.jmpt.2013.04.003

- Cramer, G. D., Gregerson, D. M., Knudsen, J. T., Hubbard, B. B., Ustas, L. M., & Cantu, J. A. (2002). The effects of side-posture positioning and spinal adjusting on the lumbar Z joints: A randomized controlled trial with sixty-four subjects. *Spine*, 27(22), 2459–2466. https://doi.org/10.1097/00007632-200211150-00008
- Crock, H. V. (1986). Internal disc disruption A challenge to disc prolapse fifty years on. *Spine*, *11*(650–653).
- Croft, P., Altman, D. G., Deeks, J. J., Dunn, K. M., Hay, A. D., Hemingway, H.,
  LeResche, L., Peat, G., Perel, P., Petersen, S. E., Riley, R. D., Roberts, I., Sharpe,
  M., Stevens, R. J., Van Der Windt, D. A., Von Korff, M., & Timmis, A. (2015). The science of clinical practice: Disease diagnosis or patient prognosis? Evidence about "what is likely to happen" should shape clinical practice. *BMC Medicine*, *13*(1), 1–8. https://doi.org/10.1186/s12916-014-0265-4
- Cuchanski, M., Cook, D., Whiting, D. M., & Cheng, B. C. (2011). Measurement of occlusion of the spinal canal and intervertebral foramen by intervertebral disc bulge. SAS Journal, 5(1), 9–15. https://doi.org/10.1016/j.esas.2010.09.004
- Currie, S. J., Myers, C. A., Durso, C., Enebo, B. A., & Davidson, B. S. (2016). The Neuromuscular Response to Spinal Manipulation in the Presence of Pain. *Journal of Manipulative and Physiological Therapeutics*, 39(4), 288–293. https://doi.org/10.1016/j.jmpt.2016.02.011
- Cyriax, J. (1945). Lumbago Mechanism of Dural Pain. The Lancet, 246(6371), 427–429.
- Cyriax, J. (1950). The Treatment of Lumbar Disk Lesions. *British Medical Journal*, 2(4694), 1434–1438. https://doi.org/10.1136/bmj.2.4693.1378
- Cyriax, J. (1984). Textbook of orthopedic medicine, volume 1. Baillière Tindall.
- Daghighi, M. H., Pouriesa, M., Maleki, M., Fouladi, D. F., Pezeshki, M. Z., Mazaheri Khameneh, R., & Bazzazi, A. M. (2014). Migration patterns of herniated disc fragments: A study on 1,020 patients with extruded lumbar disc herniation. *Spine Journal*, 14(9), 1970–1977. https://doi.org/10.1016/j.spinee.2013.11.056
- de los Monteros, F. J. G. E., Gonzalez-Medina, G., Ardila, E. M. G., Mansilla, J. R., Expósito, J. P., & Ruiz, P. O. (2020). Use of neurodynamic or orthopedic tension tests for the diagnosis of lumbar and lumbosacral radiculopathies: Study of the diagnostic validity. *International Journal of Environmental Research and Public Health*, 17(19), 1–12. https://doi.org/10.3390/ijerph17197046

- De Vet, H. C. W., Heymans, M. W., Dunn, K. M., Pope, D. P., Van der Beek, A. J., Macfarlane, G. J., Bouter, L. M., & Croft, P. R. (2002). Episodes of low back pain: A proposal for uniform definitions to be used in research. *Spine*, 27(21), 2409–2416. https://doi.org/10.1097/00007632-200211010-00016
- Deane, J. A., & McGregor, A. H. (2016). Current and future perspectives on lumbar degenerative disc disease: A UK survey exploring specialist multidisciplinary clinical opinion. *BMJ Open*, 6(9), 1–11. https://doi.org/10.1136/bmjopen-2016-011075
- Dewitte, V., De Pauw, R., De Meulemeester, K., Peersman, W., Danneels, L., Bouche, K., Roets, A., & Cagnie, B. (2018). Clinical classification criteria for nonspecific low back pain: A Delphi-survey of clinical experts. *Musculoskeletal Science and Practice*, 34(January), 66–76. https://doi.org/10.1016/j.msksp.2018.01.002
- Deyo, R. A., & Mirza, S. K. (2016). CLINICAL PRACTICE. Herniated Lumbar Intervertebral Disk. *The New England Journal of Medicine*, 374(18 PG-1763–72), 1763–1772. https://doi.org/https://dx.doi.org/10.1056/NEJMcp1512658
- Di Iorio, D., Henley, E., & Doughty, A. (2000). A survey of primary care physician practice patterns and adherence to acute low back problem guidelines. *Archives of Family Medicine*, 9(10), 1015–1021. https://doi.org/10.1001/archfami.9.10.1015
- Diwan, A. D., & Melrose, J. (2023). Intervertebral disc degeneration and how it leads to low back pain. *JOR Spine*, *6*(1), 1–23. https://doi.org/10.1002/jsp2.1231
- Donelson, R., Aprill, C., Medcalf, R., & Grant, W. (1997). A prospective study of centralization of lumbar and referred pain: A predictor of symptomatic discs and anular competence. *Spine*, 22(10), 1115–1122. https://doi.org/10.1097/00007632-199705150-00011
- Donelson, R., Long, A., Spratt, K., & Fung, T. (2012). Influence of Directional Preference on Two Clinical Dichotomies: Acute Versus Chronic Pain and Axial Low Back Pain Versus Sciatica. *PM and R*, 4(9), 667–681. https://doi.org/10.1016/j.pmrj.2012.04.013
- Draugalis, J. L. R., & Plaza, C. M. (2009). Best practices for survey research reports revisited: Implications of target population, probability sampling, and response rate. *American Journal of Pharmaceutical Education*, 73(8), 2–4. https://doi.org/10.5688/aj7308142

- Ehrler, M., Peterson, C., Leemann, S., Schmid, C., Anklin, B., & Kim Humphreys, B. (2016). Symptomatic, MRI Confirmed, Lumbar Disc Herniations: A Comparison of Outcomes Depending on the Type and Anatomical Axial Location of the Hernia in Patients Treated with High-Velocity, Low-Amplitude Spinal Manipulation. *Journal of Manipulative and Physiological Therapeutics*, *39*(3), 192–199. https://doi.org/10.1016/j.jmpt.2016.02.013
- Ekedahl, H., Jönsson, B., Annertz, M., & Frobell, R. B. (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), 726–735. https://doi.org/10.1016/j.apmr.2017.11.006
- Elsharkawy, A. E., Hagemann, A., & Klassen, P. D. (2019). Posterior epidural migration of herniated lumbar disc fragment: a literature review. *Neurosurgical Review*, *42*(4), 811–823. https://doi.org/10.1007/s10143-018-01065-1
- Empere, M., Wang, X., Prein, C., Aspberg, A., Moser, M., Oohashi, T., Clausen-Schaumann, H., Aszodi, A., & Alberton, P. (2023). Aggrecan governs intervertebral discs development by providing critical mechanical cues of the extracellular matrix. *Frontiers in Bioengineering and Biotechnology*, 11(March), 1–19. https://doi.org/10.3389/fbioe.2023.1128587
- Ernst, E., & Canter, P. H. (2006). A systematic review of systematic reviews of spinal manipulation. In *Journal of the Royal Society of Medicine*. https://doi.org/10.1258/jrsm.99.4.192
- Fagan, A., Moore, R., Roberts, B. V., Blumbergs, P., & Fraser, R. (2003). ISSLS Prize Winner: The Innervation of the Intervertebral Disc: A Quantitative Analysis. In SPINE (Vol. 28, Issue 23). http://journals.lww.com/spinejournal
- Fang, C., Zhang, W., Chen, L., & Li, H. (2017). The correlation between the highintensity zone on a T2-weighted MRI and positive outcomes of discography: A meta-analysis. *Journal of Orthopaedic Surgery and Research*, 12(1), 1–6. https://doi.org/10.1186/s13018-017-0523-1
- Fardon, D. F., Williams, A. L., Dohring, E. J., Murtagh, F. R., Gabriel Rothman, S. L., Sze, G. K., Rothman, S. L. G., Sze, G. K., Gabriel Rothman, S. L., Sze, G. K., Rothman, S. L. G., & Sze, G. K. (2014). Lumbar disc nomenclature: Version 2.0 Recommendations of the combined task forces of the North American Spine Society, the American Society of Spine Radiology and the American Society of Neuroradiology. *Spine Journal*, *14*(11), 2525–2545.

https://doi.org/10.1016/j.spinee.2014.04.022

- Fazey, P. J., Song, S., Mønsås, Åshild, Johansson, L., Haukalid, T., Price, R. I., & Singer, K. P. (2006). An MRI investigation of intervertebral disc deformation in response to torsion. *Clinical Biomechanics*, 21(5), 538–542.
- Fazey, P. J., Song, S., Price, R. I., & Singer, K. P. (2013). Nucleus pulposus deformation in response to rotation at L1–2 and L4–5. *Clinical Biomechanics*, *28*(5), 586–589.
- Fennell, A. J., Jones, A. P., & Hukins, D. W. (1996). Migration of the nucleus pulposus within the intervertebral disc during flexion and extension of the spine. *Spine*, 21(23), 2753–2757.
- Ferreira, M. L., De Luca, K., Haile, L. M., Steinmetz, J. D., Culbreth, G. T., Cross, M., Kopec, J. A., Ferreira, P. H., Blyth, F. M., Buchbinder, R., Hartvigsen, J., Wu, A. M., Safiri, S., Woolf, A. D., Collins, G. S., Ong, K. L., Vollset, S. E., Smith, A. E., Cruz, J. A., ... March, L. M. (2023). Global, regional, and national burden of low back pain, 1990–2020, its attributable risk factors, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021. *The Lancet Rheumatology*, 5(6), e316–e329. https://doi.org/10.1016/S2665-9913(23)00098-X
- Fersum, K. V. (2011). Classification and targeted treatment of patients with Non Specific Chronic Low Back Pain. *Rehabilitation*.
- Fersum, K. V, Dankaerts, W., O'Sullivan, P. B., Maes, J., Skouen, J. S., Bjordal, J. M., & Kvale, A. (2010). Integration of subclassification strategies in randomised controlled clinical trials evaluating manual therapy treatment and exercise therapy for nonspecific chronic low back pain: a systematic review. *British Journal of Sports Medicine*, 44(14), 1054–1062. https://doi.org/10.1136/bjsm.2009.063289 [doi]
- Flynn, T., Fritz, J., Whitman, J., Wainner, R., Magel, J., Rendeiro, D., Butler, B., Garber, M., & Allison, S. (2002). A clinical prediction rule for classifying patients with low back pain who demonstrate short-term improvement with spinal manipulation. *Spine*. https://doi.org/10.1097/00007632-200212150-00021
- Foltz, M. H., Kage, C. C., Johnson, C. P., & Ellingson, A. M. (2017). Noninvasive assessment of biochemical and mechanical properties of lumbar discs through quantitative magnetic resonance imaging in asymptomatic volunteers. *Journal of Biomechanical Engineering*, 139(11), 1–7. https://doi.org/10.1115/1.4037549
- Ford, J. J., & Hahne, A. J. (2013). Complexity in the physiotherapy management of low

back disorders: Clinical and research implications. *Manual Therapy*, *18*(5), 438–442. https://doi.org/10.1016/j.math.2013.01.007

- Fujii, K., Yamazaki, M., Kang, J. D., Risbud, M. V., Cho, S. K., Qureshi, S. A., Hecht, A. C., & Iatridis, J. C. (2019). Discogenic Back Pain: Literature Review of Definition, Diagnosis, and Treatment. *JBMR Plus*, 3(5), 1–11. https://doi.org/10.1002/jbm4.10180
- Gallucci, M., Anselmi, M., Di Sibio, A., & Gregori, L. M. (2011). Annular tears, fissures or HIZ? *Neuroradiology*, 53 Suppl 1, 161–165. https://doi.org/10.1007/s00234-011-0933-4
- García-Cosamalón, J., del Valle, M. E., Calavia, M. G., García-Suárez, O., López-Muñiz, A., Otero, J., & Vega, J. A. (2010). Intervertebral disc, sensory nerves and neurotrophins: who is who in discogenic pain? *Journal of Anatomy*, 217(1), 1–15. https://doi.org/10.1111/j.1469-7580.2010.01227.x
- Gau, K., Schmidt, C. S. M., Urbach, H., Zentner, J., Schulze-Bonhage, A., Kaller, C. P., & Foit, N. A. (2020). Accuracy and practical aspects of semi- and fully automatic segmentation methods for resected brain areas. *Neuroradiology*, 62(12), 1637–1648. https://doi.org/10.1007/s00234-020-02481-1
- Geers, C., Lecouvet, F. E., Behets, C., Malghem, J., Cosnard, G., & Lengelé, B. G. B. G. (2003). Polygonal deformation of the dural sac in lumbar epidural lipomatosis:
  Anatomic explanation by the presence of meningovertebral ligaments. *American Journal of Neuroradiology*, 24(7), 1276–1282. http://www.ajnr.org/content/24/7/
- Geurts, J. W., Willems, P. C., Kallewaard, J. W., Van Kleef, M., & Dirksen, C. (2018).
  The Impact of Chronic Discogenic Low Back Pain: Costs and Patients' Burden. *Pain Research and Management*, 2018. https://doi.org/10.1155/2018/4696180
- Ghannam, M., Jumah, F., Mansour, S., Samara, A., Alkhdour, S., Alzuabi, M. A., Aker, L., Adeeb, N., Massengale, J., Oskouian, R. J., & Shane Tubbs, R. (2017). Surgical anatomy, radiological features, and molecular biology of the lumbar intervertebral discs. *Clinical Anatomy*, 30(2), 251–266. https://doi.org/10.1002/ca.22822
- Giles, L. G. (2000). Mechanisms of Neurovascular Compression Within the Spinal and Intervertebral Canals. *Journal of Manipulative and Physiological Therapeutics*, 23(2), 107–111.
- Giles, L. G. F. (2000). Mechanisms of neurovascular compression within the spinal and

intervertebral canals. *Journal of Manipulative and Physiological Therapeutics*, 23(2), 107–111. https://doi.org/10.1016/S0161-4754(00)90077-0

- Giles, L. G. F., & Crawford, C. M. (1997). Shadows of the truth in patients with spinal pain: A review. *Canadian Journal of Psychiatry*, 42(1), 44–48. https://doi.org/10.1177/070674379704200106
- Goel, V. K., Monroe, B. T., Gilbertson, L. G., & Brinckmann, P. (1995). Interlaminar shear stresses and laminae separation in a disc. Finite element analysis of the L3-L4 motion segment subjected to axial compressive loads. *Spine*, 20(6), 689–698.
- Goertz, C. M., Pohlman, K. A., Vining, R. D., Brantingham, J. W., & Long, C. R. (2012). Patient-centered outcomes of high-velocity, low-amplitude spinal manipulation for low back pain: A systematic review. *Journal of Electromyography and Kinesiology*, 22(5), 670–691. https://doi.org/10.1016/j.jelekin.2012.03.006
- Goodwin, P. C., Al Muslem, W., Hodson-Tole, E., & Hindle, J. (2021). The sympathetic and hypoalgesic effects of spinal mobilisations: A systematic review. *Physiotherapy*, *113*, e191. https://doi.org/10.1016/j.physio.2021.10.205
- Green, E. M., Mansfield, J. C., Bell, J. S., & Winlove, C. P. (2014). The structure and micromechanics of elastic tissue. *Interface Focus*, 4(2). https://doi.org/10.1098/rsfs.2013.0058
- Groen, Gerbrand, Drukker, B. (1990). Nerves and nerve plexuses of the human vertebral column. *American Journal of Anatomy*, 188(3), 282–296. https://doi.org/10.1002/aja.1001880307
- Groh, A. M. R., Fournier, D. E., Battié, M. C., & Séguin, C. A. (2021). Innervation of the Human Intervertebral Disc: A Scoping Review. *Pain Medicine (United States)*, 22(6), 1281–1304. https://doi.org/10.1093/pm/pnab070
- Guinto, F. C., Hashim, H., & Stumer, M. (1984). CT demonstration of disk regression after conservative therapy. *American Journal of Neuroradiology*, 5(5), 632–633.
- Gyer, G., Michael, J., Inklebarger, J., & Tedla, J. S. (2019). Spinal manipulation therapy: Is it all about the brain? A current review of the neurophysiological effects of manipulation. *Journal of Integrative Medicine*, 17(5), 328–337. https://doi.org/10.1016/j.joim.2019.05.004

Hahne, A. J., Keating, J. L., & Wilson, S. C. (2004). Do within-session changes in pain

intensity and range of motion predict between-session changes in patients with low back pain? *Australian Journal of Physiotherapy*, *50*(1), 17–23. https://doi.org/10.1016/S0004-9514(14)60244-0

- Halldin, K., Lind, B., Rönnberg, K., Göthlin, J., Gadeholt-Göthlin, G., Zoëga, B., & Brisby, H. (2009). Three-dimensional radiological classification of lumbar disc herniation in relation to surgical outcome. *International Orthopaedics*, *33*(3), 725–730. https://doi.org/10.1007/s00264-008-0519-x
- Hallegraeff, H., de Greef, M., Winters, J., & Lucas, C. (2009). Manipulative Therapy and Clinical Prediction Criteria in Treatment of Acute Nonspecific Low Back Pain. *Perceptual and Motor Skills*, 108, 196–208.
- Han, C. S., Hancock, M. J., Sharma, S., Sharma, S., Harris, I. A., Cohen, S. P., Magnussen, J., Maher, C. G., & Traeger, A. C. (2023). Low back pain of disc, sacroiliac joint, or facet joint origin: a diagnostic accuracy systematic review. *EClinicalMedicine*, 59. https://doi.org/10.1016/j.eclinm.2023.101960
- Hancock, M. J., Koes, B., Ostelo, R., & Peul, W. (2011). Diagnostic accuracy of the clinical examination in identifying the level of herniation in patients with sciatica. *Spine*, *36*(11 PG-712–719), E712–E719. https://doi.org/http://dx.doi.org/10.1097/BRS.0b013e3181ee7f78
- Hancock, M. J., Maher, C. G., Latimer, J., Spindler, M. F., McAuley, J. H., Laslett, M., & Bogduk, N. (2007). Systematic review of tests to identify the disc, SIJ or facet joint as the source of low back pain. *European Spine Journal*, *16*(10 PG-1539–1550), 1539–1550. https://doi.org/10.1007/s00586-007-0391-1
- Haro, H. (2014). Translational research of herniated discs: Current status of diagnosis and treatment. *Journal of Orthopaedic Science*, 19(4), 515–520. https://doi.org/10.1007/s00776-014-0571-x
- Hartvigsen, J., Hancock, M. J., Kongsted, A., Louw, Q., Ferreira, M. L., Genevay, S., Hoy, D., Karppinen, J., Pransky, G., Sieper, J., Smeets, R. J., Underwood, M., Buchbinder, R., Cherkin, D., Foster, N. E., Maher, C. G., van Tulder, M., Anema, J. R., Chou, R., ... Woolf, A. (2018). What low back pain is and why we need to pay attention. *The Lancet*, *391*(10137), 2356–2367. https://doi.org/10.1016/S0140-6736(18)30480-X
- He, A., Wang, W. Z., Qiao, P. F., Qiao, G. Y., Cheng, H., & Feng, P. Y. (2018). Quantitative Evaluation of Compressed L4-5 and S1 Nerve Roots of Lumbar Disc

Herniation Patients by Diffusion Tensor Imaging and Fiber Tractography. *World Neurosurgery*, *115*, e45–e52. https://doi.org/10.1016/j.wneu.2018.03.134

- Hebelka, H., Torén, L., Lagerstrand, K., & Brisby, H. (2018). Axial loading during MRI reveals deviant characteristics within posterior IVD regions between low back pain patients and controls. *European Spine Journal*, 27(11), 2840–2846. https://doi.org/10.1007/s00586-018-5774-y
- Hebert, J., Koppenhaver, S., Fritz, J., & Parent, E. (2008). Clinical Prediction for Success of Interventions for Managing Low Back Pain. *Clinics in Sports Medicine*, 27(3), 463–479. https://doi.org/10.1016/j.csm.2008.03.002
- Herod, T. W., & Veres, S. P. (2020). ISSLS PRIZE IN BASIC SCIENCE 2020: Beyond microstructure—circumferential specialization within the lumbar intervertebral disc annulus extends to collagen nanostructure, with counterintuitive relationships to macroscale material properties. *European Spine Journal*, 29(4), 670–685. https://doi.org/10.1007/s00586-019-06223-7
- Heuer, F., Schmidt, H., & Wilke, H. J. (2008). The relation between intervertebral disc bulging and annular fiber associated strains for simple and complex loading. *Journal* of *Biomechanics*, 41(5), 1086–1094. https://doi.org/10.1016/j.jbiomech.2007.11.019
- Hirsch, C., & Schajowicz, F. (1952). Studies on structural changes in the lumbar annulus fibrosus. Acta Orthopaedica, 22(1–4), 184–231. https://doi.org/10.3109/17453675208989006
- Holzapfel, G. A., Schulze-Bauer, C. A. J., Feigl, G., & Regitnig, P. (2005). Single lamellar mechanics of the human lumbar anulus fibrosus. *Biomechanics and Modeling in Mechanobiology*, 3(3), 125–140. https://doi.org/10.1007/s10237-004-0053-8
- Horn, S. D., & Gassaway, J. (2007). Practice-based evidence study design for comparative effectiveness research. *Medical Care*, 45(10 SUPPL. 2), 50–57. https://doi.org/10.1097/mlr.0b013e318070c07b
- Hornung, A. L., Baker, J. D., Mallow, G. M., Sayari, A. J., Albert, H. B., Tkachev, A., An, H. S., & Samartzis, D. (2023). Resorption of Lumbar Disk Herniation. *JBJS Reviews*, 11(1), 1–12. https://doi.org/10.2106/jbjs.rvw.22.00148
- Horton, S. (2010). *Disc prolapse: Evidence of reversal with repeated extension*. *38*(March), 2010.

- Hoy, D., Brooks, P., Blyth, F., & Buchbinder, R. (2010). The Epidemiology of low back pain. *Best Practice and Research: Clinical Rheumatology*, 24(6), 769–781. https://doi.org/10.1016/j.berh.2010.10.002
- Huijbregts, P. A. (1998). Fact and fiction of disc reduction: A literature review. *Journal of Manual and Manipulative Therapy*, 6(3), 137–143. https://doi.org/10.1179/jmt.1998.6.3.137
- Ikeda, D. M., & McGill, S. M. (2012). Can altering motions, postures, and loads provide immediate low back pain relief: A study of 4 cases investigating spine load, posture, and stability. *Spine*, 37(23), 1469–1475. https://doi.org/10.1097/BRS.0b013e31826c97e5
- Janardhana, A. P., Rajagopal, Rao, S., & Kamath, A. (2010). Correlation between clinical features and magnetic resonance imaging findings in lumbar disc prolapse. *Indian Journal of Orthopaedics*, 44(3), 263–269. https://doi.org/10.4103/0019-5413.65148
- Jiang, H., Qi, W., Liao, Q., Zhao, H., Lei, W., Guo, L., & Lu, H. (2012). Quantitative evaluation of lumbar disc herniation based on MRI image. *Lecture Notes in Computer Science (Including Subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics)*, 7029 LNCS, 91–98. https://doi.org/10.1007/978-3-642-28557-8\_12
- Jinkins, J. R. (2004). The anatomic and physiologic basis of local, referred and radiating lumbosacral pain syndromes related to disease of the spine. *Journal of Neuroradiology*, 31(3), 163–180. https://doi.org/10.1016/s0150-9861(04)96988-x
- Joel E. Goldthwait, M.D., B. (1911). Origi Articles nal. *Boston Medical and Surgical Journal*, *CLXIV*(II), 365–372.
- Jung, A., Adamczyk, W. M., Ahmed, A., Van Der Schalk, L., Poesl, M., Luedtke, K., & Szikszay, T. M. (2023). No Sufficient Evidence for an Immediate Hypoalgesic Effect of Spinal Manual Therapy on Pressure Pain Thresholds in Asymptomatic and Chronic Pain Populations: A Systematic Review and Meta-Analysis. In *Physical Therapy* (Vol. 103, Issue 3). Oxford University Press. https://doi.org/10.1093/ptj/pzad003
- Kallewaard, J. W., Terheggen, M. A. M. B., Groen, G. J., Sluijter, M. E., Derby, R., Kapural, L., Mekhail, N., & van Kleef, M. (2011). Discogenic Low Back Pain. *Evidence-Based Interventional Pain Medicine: According to Clinical Diagnoses*, *November*, 107–122. https://doi.org/10.1002/9781119968375.ch15

- Karvonen, E., Paatelma, M., Laitinen-Väänänen, S., & Piirainen, A. (2017). Clinical reasoning and critical reflection in physiotherapists' examinations of patients with low back pain in its early phase: a qualitative study from physiotherapists' point of view. *European Journal of Physiotherapy*, 19(4), 185–193. https://doi.org/10.1080/21679169.2017.1316311
- Keating, J. L., McKenzie, J. E., O'Connor, D. A., French, S., Walker, B. F., Charity, M., Page, M. J., & Green, S. E. (2016). Providing services for acute low-back pain: A survey of Australian physiotherapists. *Manual Therapy*, 22, 145–152. https://doi.org/10.1016/j.math.2015.11.005
- Kent, P. M., Keating, J. L., & Buchbinder, R. (2009). Searching for a conceptual framework for nonspecific low back pain. *Manual Therapy*, *14*(4), 387–396.
- Kent, P. M., Keating, J. L., & Taylor, N. F. (2009). Primary care clinicians use variable methods to assess acute nonspecific low back pain and usually focus on impairments. *Manual Therapy*, 14(1), 88–100. https://doi.org/10.1016/j.math.2007.12.006
- Keter, D. L., Bent, J. A., Bialosky, J. E., Courtney, C. A., Esteves, J. E., Funabashi, M., Howarth, S. J., Injeyan, H. S., Mazziari, A. M., Glissmann Nim, C., & Cook, C. E. (2023). An international consensus on gaps in mechanisms of forced-based manipulation research: findings from a nominal group technique. *Journal of Manual and Manipulative Therapy*, *00*(00), 1–7. https://doi.org/10.1080/10669817.2023.2262336
- Kiger, M. E., & Varpio, L. (2020). Thematic analysis of qualitative data: AMEE Guide No. 131. *Medical Teacher*, 42(8), 846–854. https://doi.org/10.1080/0142159X.2020.1755030
- Kilitci, A., Asan, Z., Yuceer, A., Aykanat, O., & Durna, F. (2021). Comparison of the histopathological differences between the disc material and posterior longitudinal ligament in patients with lumbar disc herniation: A focus on the etiopathogenesis. *Annals of Saudi Medicine*, 41(2), 115–120. https://doi.org/10.5144/0256-4947.2021.115
- Kim, H. G., Shin, D. A., Kim, H. I., Yoo, E. A., Shin, D. G., & Lee, J. O. (2009). Clinical and radiological findings of discogenic low back pain confirmed by automated pressure-controlled discography. *Journal of Korean Neurosurgical Society*, 46(4), 333–339. https://doi.org/10.3340/jkns.2009.46.4.333
- Kim, S. G., Yang, J. C., Kim, T. W., & Park, K. H. (2013). Spontaneous Regression of Extruded Lumbar Disc Herniation: Three Cases Report. *Korean Journal of Spine*, 10(2), 78. https://doi.org/10.14245/kjs.2013.10.2.78
- Kim, Y. H., Kim, S. I., Park, S., Hong, S. H., & Chung, S. G. (2017). Effects of Cervical Extension on Deformation of Intervertebral Disk and Migration of Nucleus Pulposus. *PM and R*, 9(4), 329–338. https://doi.org/10.1016/j.pmrj.2016.08.027
- Kobayashi, S., Yoshizawa, H., & Yamada, S. (2004). Pathology of lumbar nerve root compression Part 2: Morphological and immunohistochemical changes of dorsal root ganglion. *Journal of Orthopaedic Research*, 22(1), 180–188. https://doi.org/10.1016/S0736-0266(03)00132-3
- Koes, B. W., van Tulder, M. W., & Thomas, S. (2006). Diagnosis and treatment of low back pain. *British Medical Journal*, 332(7555), 1430–1434. https://doi.org/10.1016/s0300-7073(08)70669-8
- Koh, J., Chaudhary, V., & Dhillon, G. (2012). Disc herniation diagnosis in MRI using a CAD framework and a two-level classifier. *International Journal of Computer Assisted Radiology and Surgery*, 7(6), 861–869. https://doi.org/10.1007/s11548-012-0674-9
- Kojima, Y., Maeda, T., Arai, R., & Shichikawa, K. (1990). Nerve supply to the posterior longitudinal ligament and the intervertebral disc of the rat vertebral column as studied by acetylcholinesterase histochemistry. I. Distribution in the lumbar region. *Journal of Anatomy*, 169, 237–246.
- Kolber, M. J., & Hanney, W. J. (2009). The dynamic disc model: a systematic review of the literature. *Physical Therapy Reviews*, 14(3), 181–189. https://doi.org/10.1179/174328809X452827
- Kovanur-Sampath, K., Mani, R., Cotter, J., Gisselman, A. S., & Tumilty, S. (2017). Changes in biochemical markers following spinal manipulation-a systematic review and meta-analysis. *Musculoskeletal Science and Practice*, 29, 120–131. https://doi.org/10.1016/j.msksp.2017.04.004
- Kozanek, M., Wang, S., Passias, P. G., Xia, Q., Lee, G., Bono, C. M., Wood, K. B., & Li, G. (2009). Range of motion and orientation of the lumbar facet joints in vivo. *Spine*, 34(19), 689–696. https://doi.org/10.1097/BRS.0b013e3181ab4456

Krämer, J. (Ed.). (2010). Intervertebral disk diseases: Causes, diagnosis, treatment and

prophylaxis. Jürgen Krämer.

- Kreiner, D. S., Hwang, S. W., Easa, J. E., Resnick, D. K., Baisden, J. L., Bess, S., Cho, C. H., Depalma, M. J., Dougherty, P., Fernand, R., Ghiselli, G., Hanna, A. S., Lamer, T., Lisi, A. J., Mazanec, D. J., Meagher, R. J., Nucci, R. C., Patel, R. D., Sembrano, J. N., ... Toton, J. F. (2014). An evidence-based clinical guideline for the diagnosis and treatment of lumbar disc herniation with radiculopathy. *Spine Journal*, *14*(1 PG-180–191), 180–191. https://doi.org/10.1016/j.spinee.2013.08.003
- Kreiner, D. S., Matz, P., Bono, C. M., Cho, C. H., Easa, J. E., Ghiselli, G., Ghogawala, Z., Reitman, C. A., Resnick, D. K., Watters, W. C., Annaswamy, T. M., Baisden, J., Bartynski, W. S., Bess, S., Brewer, R. P., Cassidy, R. C., Cheng, D. S., Christie, S. D., Chutkan, N. B., ... Yahiro, A. M. (2020). Guideline summary review: an evidence-based clinical guideline for the diagnosis and treatment of low back pain. In *Spine Journal* (Vol. 20, Issue 7, pp. 998–1024). Elsevier Inc. https://doi.org/10.1016/j.spinee.2020.04.006
- Kulak T B Belytschko, R. F., & Schultz, A. B. (1976). NONLINEAR BEHAVIOR OF THE HUMAN INTERVERTEBRAL DISC UNDER AXIAL LOAD\*.
- Kuo, P. P. F., & Loh, Z. C. (1987). Treatment of lumbar intervertebral disc protrusions by manipulation. *Clinical Orthopaedics and Related Research*, No. 215, 47–55.
- Langlais, T., Desprairies, P., Pietton, R., Rohan, P. Y., Dubousset, J., Meakin, J. R., Winlove, P. C., Vialle, R., Skalli, W., & Vergari, C. (2019). Microstructural characterization of annulus fibrosus by ultrasonography: a feasibility study with an in vivo and in vitro approach. *Biomechanics and Modeling in Mechanobiology*, *18*(6), 1979–1986. https://doi.org/10.1007/s10237-019-01189-3
- Lascurain-Aguirrebena, I., Newham, D., & Critchley, D. J. (2016). Mechanism of action of spinal mobilizations a systematic review. *Spine*, 41(2), 159–172. https://doi.org/10.1097/BRS.00000000001151
- Lascurain Aguirrebeña, I., Newham, D., & Critchley, D. (2015). The mechanism of action of spinal mobilisations: a systematic review. *Physiotherapy*, 101(May), e835. https://doi.org/10.1016/j.physio.2015.03.1651
- Laslett. (1987). The use of manipulative therapy for mechanical pain of spinal origin.pdf.
- Laslett, M. (2005). Diagnostic accuracy of the clinical examination compared to available reference standards in chronic low back pain patients. *Health (San Francisco), Xxx*

*PG-1-126*, 1–126.

- Laslett, M., McDonald, B., Tropp, H., Aprill, C. N., & Öberg, B. (2005). Agreement between diagnoses reached by clinical examination and available reference standards: A prospective study of 216 patients with lumbopelvic pain. *BMC Musculoskeletal Disorders*, 6. https://doi.org/10.1186/1471-2474-6-28
- Learman, K., Showalter, C., O'halloran, B., Donaldson, M., & Cook, C. (2014). No differences in outcomes in people with low back pain who met the clinical prediction rule for lumbar spine manipulation when a pragmatic non-thrust manipulation was used as the comparator. *Physiotherapy Canada*, 66(4), 359–366. https://doi.org/10.3138/ptc.2013-49
- Lee, S. B., Chang, J. C., Lee, G. S., Hwang, J. C., Bae, H. G., & Doh, J. W. (2018). Morphometric study of the lumbar posterior longitudinal ligament. *Journal of Korean Neurosurgical Society*, 61(1), 89–96. https://doi.org/10.3340/jkns.2017.0257
- Li, J., Gu, T., Yang, H., Liang, L., Jiang, D. jie, Wang, Z. chao, Yuan, W., & Wang, X. wei. (2014). Sympathetic nerve innervation in cervical posterior longitudinal ligament as a potential causative factor in cervical spondylosis with sympathetic symptoms and preliminary evidence. *Medical Hypotheses*, 82(5), 631–635. https://doi.org/10.1016/j.mehy.2014.02.029
- Lipson, S. J. (1988). Metaplastic proliferative fibrocartilage as an alternative concept to herniated intervertebral disc. *Spine*, *13*(9), 1055–1060.
- Lorio, M. P., Beall, D. P., Calodney, A. K., Lewandrowski, K. U., Block, J. E., & Mekhail, N. (2023). Defining the Patient with Lumbar Discogenic Pain: Real-World Implications for Diagnosis and Effective Clinical Management. *Journal of Personalized Medicine*, 13(5). https://doi.org/10.3390/jpm13050821
- Lotz, J. C., Fields, A. J., & Liebenberg, E. C. (2013). The Role of the Vertebral End Plate in Low Back Pain. *Global Spine Journal*, *3*(3), 153–163. https://doi.org/10.1055/s-0033-1347298
- Loughenbury, P. R., Wadhwani, S., & Soames, R. W. (2006). The posterior longitudinal ligament and peridural (epidural) membrane. *Clinical Anatomy*, 19(6), 487–492. https://doi.org/10.1002/ca.20200
- Lundon, K., & Bolton, K. (2001). Structure and Function of the Lumbar Intervertebral Disk in Health, Aging, and Pathologic Conditions. *Journal of Orthopaedic and*

Sports Physiotherapy, 31(6), 291–306. https://doi.org/10.1081/TXR-120014407

- Luoma, K., Riihimäki, H., Luukkonen, R., Raininko, R., Viikari-Juntura, E., & Lamminen, A. (2000). Low back pain in relation to lumbar disc degeneration. *Spine*, 25(4), 487–492.
- MacGregor, A. J., Andrew, T., Sambrook, P. N., & Spector, T. D. (2004). Structural, Psychological, and Genetic Influences on Low Back and Neck Pain: A Study of Adult Female Twins. *Arthritis Care and Research*, 51(2), 160–167. https://doi.org/10.1002/art.20236
- Macki, M., Hernandez-Hermann, M., Bydon, M., Gokaslan, A., McGovern, K., & Bydon, A. (2014). Spontaneous regression of sequestrated lumbar disc herniations: Literature review. *Clinical Neurology and Neurosurgery*, *120*, 136–141. https://doi.org/10.1016/j.clineuro.2014.02.013
- Maher, C., Underwood, M., & Buchbinder, R. (2017). Non-specific low back pain. *The Lancet*, *389*(10070), 736–747. https://doi.org/10.1016/S0140-6736(16)30970-9
- Malmqvist, S., & Leboeuf-Yde, C. (2008). Chiropractors in Finland A demographic survey. *Chiropractic and Osteopathy*, 16, 1–5. https://doi.org/10.1186/1746-1340-16-9
- Manchikanti, L., Singh, V., Falco, F. J. E., Benyamin, R. M., & Hirsch, J. A. (2014). Epidemiology of low back pain in adults. *Neuromodulation: Technology at the Neural Interface*, 17(S2), 3–10.
- Marchand, F., & Ahmed, A. M. (1990). Investigation of the laminate structure of lumbar disc anulus fibrosus. *Spine*, 15(5), 402–410. https://doi.org/10.1097/00007632-199005000-00011
- Marini, G., Huber, G., Püschel, K., & Ferguson, S. J. (2015). Nonlinear dynamics of the human lumbar intervertebral disc. *Journal of Biomechanics*, 48(3), 479–488. https://doi.org/10.1016/j.jbiomech.2014.12.006
- Martin, J. T., Oldweiler, A. B., Kosinski, A. S., Spritzer, C. E., Soher, B. J., Erickson, M. M., Goode, A. P., & DeFrate, L. E. (2022). Lumbar intervertebral disc diurnal deformations and T2 and T1rho relaxation times vary by spinal level and disc region. *European Spine Journal*, *31*(3), 746–754. https://doi.org/10.1007/s00586-021-07097-4

- Martin, M. D., Boxell, C. M., & Malone, D. G. (2002). Pathophysiology of lumbar disc degeneration: a review of the literature. *Neurosurgical Focus*, 13(2), 1–6. https://doi.org/10.3171/foc.2002.13.2.2
- Martínez-Quiñones, J. V., Aso-Escario, J., Consolini, F., & Arregui-Calvo, R. (2010). Regresión espontánea de hernias discales intervertebrales. A propósito de una serie de 37 casos. *Neurocirugia*, 21(2), 108–117. https://doi.org/10.1016/S1130-1473(10)70065-8
- Masui, T., Yukawa, Y., Nakamura, S., Kajino, G., Matsubara, Y., Kato, F., & Ishiguro, N. (2005). Natural history of patients with lumbar disc herniation observed by magnetic resonance imaging for minimum 7 years. *Journal of Spinal Disorders and Techniques*, 18(2), 121–126. https://doi.org/10.1097/01.bsd.0000154452.13579.b2
- Matos, R., Fernandes, P. R., Matela, N., & Castro, A. P. G. (2023). Lumbar intervertebral disc segmentation for computer modeling and simulation. *Computer Methods and Programs in Biomedicine*, 230. https://doi.org/10.1016/j.cmpb.2023.107337
- May, S., & Aina, A. (2012). Centralization and directional preference: a systematic review. *Manual Therapy*, 17(6), 497–506. https://doi.org/10.1016/j.math.2012.05.003
- May, S., Runge, N., & Aina, A. (2018). Centralization and directional preference: An updated systematic review with synthesis of previous evidence. *Musculoskeletal Science and Practice*, 38(September), 53–62. https://doi.org/10.1016/j.msksp.2018.09.006
- McCarthy, C., Bialoskiy, J., Rivett, & D. (2015). Spinal manipulation 4th Edition. In Spinal manipulation. Grieve's Modern Musculoskeletal Physiotherapy. https://doi.org/10.1136/bmj.2.3700.1065-a
- McCarthy, C. J., Rushton, A., Billis, V., Arnall, F., & Oldham, J. A. (2006). Development of a clinical examination in non-specific low back pain: A Delphi technique. *Journal of Rehabilitation Medicine*, 38(4), 263–267. https://doi.org/10.1080/16501970600632768
- McFadden, J. (2023). *Razor sharp : The role of Occam 's razor in science*. 8–17. https://doi.org/10.1111/nyas.15086
- McGill, S. (2007). *Low back disorders : evidence-based prevention and rehabilitation*. Human Kinetics.

McGill, S. (2016). There is No Such Thing as "Non -Specific Back P ain ." 1–2.

- Meakin, J. R., & Hukins, D. W. L. (2000). Effect of removing the nucleus pulposus on the deformation of the annulus fibrosus during compression of the intervertebral disc. *Journal of Biomechanics*, 33(5), 575–580. https://doi.org/10.1016/S0021-9290(99)00215-8
- Menon, R. G., Zibetti, M. V. W., Pendola, M., & Regatte, R. R. (2021). Measurement of Three-Dimensional Internal Dynamic Strains in the Intervertebral Disc of the Lumbar Spine With Mechanical Loading and Golden-Angle Radial Sparse Parallel-Magnetic Resonance Imaging. *Journal of Magnetic Resonance Imaging*, 54(2), 486– 496. https://doi.org/10.1002/jmri.27591
- Mescouto, K., Olson, R. E., Hodges, P. W., & Setchell, J. (2022). A critical review of the biopsychosocial model of low back pain care: time for a new approach? *Disability and Rehabilitation*, 44(13), 3270–3284. https://doi.org/10.1080/09638288.2020.1851783
- Milette, P. C., Fontaine, S., Lepanto, L., Cardinal, E., & Breton, G. (1999). Differentiating lumbar disc protrusion, disc bulge,.pdf. *Spine*, *4*(1).
- Millan, M., Leboeuf-Yde, C., Budgell, B., & Amorim, M. A. (2012). The effect of spinal manipulative therapy on experimentally induced pain: A systematic literature review. *Chiropractic and Manual Therapies*, 20. https://doi.org/10.1186/2045-709X-20-26
- Moore, R. J., Vernon-Roberts, B., Fraser, R. D., Osti, O. L., & Schembri, M. (1996). The origin and fate of herniated lumbar intervertebral disc tissue. *Spine*, 21(18), 2149– 2155.
- Mourad, F., Yousif, M. S., Maselli, F., Pellicciari, L., Meroni, R., Dunning, J.,
  Puentedura, E., Taylor, A., Kerry, R., Hutting, N., & Kranenburg, H. A. (2022).
  Knowledge, beliefs, and attitudes of spinal manipulation: a cross-sectional survey of
  Italian physiotherapists. *Chiropractic and Manual Therapies*, 30(1).
  https://doi.org/10.1186/s12998-022-00449-x
- Munter, F. M., Wasserman, B. A., Wu, H. M., & Yousem, D. M. (2002). Serial MR imaging of annular tears in lumbar intervertebral disks. *American Journal of Neuroradiology*, 23(7), 1105–1109.

Nakagawa, H., Mikawa, Y., & Watanabe, R. (1994). Elastin in the human posterior

longitudinal ligament and spinal dura: A histologic and biochemical study A histologic and biochemical study. *Spine*, *19*(19), 2164–2169. https://doi.org/10.1097/00007632-199410000-00006

- Nakamura, S. I., Takahashi, K., Takahashi, Y., Yamagata, M., & Moriya, H. (1996). The afferent pathways of discogenic low-back pain. Evaluation of L2 spinal nerve infiltration. *Journal of Bone and Joint Surgery - Series B*, 78(4), 606–612. https://doi.org/10.1302/0301-620X.78B4.0780606
- Nazari, J., Pope, M. H., & Graveling, R. A. (2012). Reality about migration of the nucleus pulposus within the intervertebral disc with changing postures. *Clinical Biomechanics*, 27(3), 213–217. https://doi.org/10.1016/j.clinbiomech.2011.09.011
- Neergaard, M. A., Olesen, F., Andersen, R. S., & Sondergaard, J. (2009). Qualitative description-the poor cousin of health research? *BMC Medical Research Methodology*, 9(1), 1–5. https://doi.org/10.1186/1471-2288-9-52
- Neubert, A., Fripp, J., Engstrom, C., Walker, D., Weber, M. A., Schwarz, R., & Crozier, S. (2013). Three-dimensional morphological and signal intensity features for detection of intervertebral disc degeneration from magnetic resonance images. *Journal of the American Medical Informatics Association : JAMIA*, 20(6), 1082– 1090. https://doi.org/10.1136/amiajnl-2012-001547 [doi]
- Nguyen, H. S., Doan, N., Shabani, S., Baisden, J., Wolfla, C., Paskoff, G., Shender, B., & Stemper, B. (2016). Upright magnetic resonance imaging of the lumbar spine: Back pain and radiculopathy. *Journal of Craniovertebral Junction and Spine*, 7(1), 31–37. https://doi.org/10.4103/0974-8237.176619
- Nim, C. G., Downie, A., O'Neill, S., Kawchuk, G. N., Perle, S. M., & Leboeuf-Yde, C. (2021). The importance of selecting the correct site to apply spinal manipulation when treating spinal pain: Myth or reality? A systematic review. *Scientific Reports*, *11*(1), 1–13. https://doi.org/10.1038/s41598-021-02882-z
- Nordberg, C. L., Boesen, M., Fournier, G. L., Bliddal, H., Hansen, P., & Hansen, B. B. (2021). Positional changes in lumbar disc herniation during standing or lumbar extension: a cross-sectional weight-bearing MRI study. *European Radiology*, *31*(2), 804–812. https://doi.org/10.1007/s00330-020-07132-w
- Nowell, L. S., Norris, J. M., White, D. E., & Moules, N. J. (2017). Thematic Analysis: Striving to Meet the Trustworthiness Criteria. *International Journal of Qualitative Methods*, 16(1), 1–13. https://doi.org/10.1177/1609406917733847

- O'Brien, B. C., Harris, I. B., Beckman, T. J., Reed, D. A., & Cook, D. A. (2014). Standards for reporting qualitative research: A synthesis of recommendations. *Academic Medicine*, 89(9), 1245–1251. https://doi.org/10.1097/ACM.00000000000388
- Ohtori, S., Inoue, G., Miyagi, M., & Takahashi, K. (2015). Pathomechanisms of discogenic low back pain in humans and animal models. *The Spine Journal : Official Journal of the North American Spine Society*, 15(6), 1347–1355. https://doi.org/10.1016/j.spinee.2013.07.490 [doi]
- Ozturk, B., Gunduz, O. H., Ozoran, K., & Bostanoglu, S. (2006). Effect of continuous lumbar traction on the size of herniated disc material in lumbar disc herniation. *Rheumatology International*, *26*(7), 622–626. https://doi.org/10.1007/s00296-005-0035-x
- Page et al. (2021). The PRISMA 2020 Expanded Checklist. *The BMJ*, 372. https://doi.org/10.1136/bmj.n71
- Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., ... Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. In *International Journal of Surgery* (Vol. 88, Issue March). https://doi.org/10.1016/j.ijsu.2021.105906
- Paige, N. M., Miake-Lye, I. M., Booth, M. S., Beroes, J. M., Mardian, A. S., Dougherty, P., Branson, R., Tang, B., Morton, S. C., & Shekelle, P. G. (2017). Association of spinal manipulative therapy with clinical benefit and harm for acute lowback pain systematic review and meta-Analysis. *JAMA - Journal of the American Medical Association*, *317*(14), 1451–1460. https://doi.org/10.1001/jama.2017.3086
- Park, W. M., Kim, Y. H., & Lee, S. (2013). Effect of intervertebral disc degeneration on biomechanical behaviors of a lumbar motion segment under physiological loading conditions. *Journal of Mechanical Science and Technology*, 27(2), 483–489. https://doi.org/10.1007/s12206-012-1264-z
- Parr, S., & May, S. (2014). Do musculoskeletal physiotherapists believe the NICE guidelines for the management of non-specific LBP are practical and relevant to their practice? A cross sectional survey. *Physiotherapy (United Kingdom)*, 100(3), 235–241. https://doi.org/10.1016/j.physio.2013.09.004

- Passias, P. G., Wang, S., Kozanek, M., Xia, Q., Li, W., Grottkau, B., Wood, K. B., & Li, G. (2011). Segmental lumbar rotation in patients with discogenic low back pain during functional weight-bearing activities. *Journal of Bone and Joint Surgery -Series A*, 93(1), 29–37. https://doi.org/10.2106/JBJS.I.01348
- Passmore, S. R., & Descarreaux, M. (2012). Performance based objective outcome measures and spinal manipulation. *Journal of Electromyography and Kinesiology*, 22(5), 697–707. https://doi.org/10.1016/j.jelekin.2012.02.005
- Peng, B. G. (2013). Pathophysiology, diagnosis, and treatment of discogenic low back pain. World Journal of Orthopedics, 4(2), 42–52. https://doi.org/10.5312/wjo.v4.i2.42 [doi]
- Petersen, T., Laslett, M., & Juhl, C. (2017). Clinical classification in low back pain: bestevidence diagnostic rules based on systematic reviews. *BMC Musculoskeletal Disorders*, 18(1 PG-188), 188. https://doi.org/http://dx.doi.org/10.1186/s12891-017-1549-6
- Petersen, T., Laslett, M., Thorsen, H., Manniche, C., Ekdahl, C., Jacobsen, S., & Petersen, T., Laslett, M., Thorsen, H., Manniche, C., Ekdahl, C., & Jacobsen, S. (2003). Diagnostic classification of non-specific low back pain. A new system integrating patho-anatomic and clinical categories. *Physiotherapy Theory and Practice*, 19(4), 213–237. https://doi.org/10.1080/09593980390246760
- Pezowicz, C. A., Robertson, P. A., & Broom, N. D. (2005). Intralamellar relationships within the collagenous architecture of the annulus fibrosus imaged in its fully hydrated state. *Journal of Anatomy*, 207(4), 299–312. https://doi.org/10.1111/j.1469-7580.2005.00467.x
- Pickar, J. G., & Bolton, P. S. (2012). Spinal manipulative therapy and somatosensory activation. *Journal of Electromyography and Kinesiology*, 22(5), 785–794. https://doi.org/10.1016/j.jelekin.2012.01.015
- Plewes, D. B., & Kucharczyk, W. (2012). Physics of MRI: A primer. Journal of Magnetic Resonance Imaging, 35(5), 1038–1054. https://doi.org/10.1002/jmri.23642
- Ract, I., Meadeb, J.-M. M., Mercy, G., Cueff, F., Husson, J.-L. L., & Guillin, R. (2015). A review of the value of MRI signs in low back pain. *Diagnostic and Interventional Imaging*, 96(3), 239–249. https://doi.org/10.1016/j.diii.2014.02.019

Rajasekaran, S., Bajaj, N., Tubaki, V., Kanna, R. M., & Shetty, A. P. (2013). ISSLS Prize

winner: The anatomy of failure in lumbar disc herniation: an in vivo, multimodal, prospective study of 181 subjects. *Spine*, *38*(17), 1491–1500. https://doi.org/10.1097/BRS.0b013e31829a6fa6 [doi]

- Raoul, S., Faure, A., Robert, R., Rogez, J. M., Hamel, O., Cuillère, P., & Le Borgne, J. (2002). Role of the sinu-vertebral nerve in low back pain and anatomical basis of therapeutic implications. *Surgical and Radiologic Anatomy*, 24(6), 366–370. https://doi.org/10.1007/s00276-002-0084-8
- Rhee, J. M., Schaufele, M., & Abdu, W. A. (2006). Radiculopathy and the herniated lumbar disc: controversies regarding pathophysiology and management. 2069– 2080.
- Riley, S. P., Swanson, B. T., & Cleland, J. A. (2021). The why, where, and how clinical reasoning model for the evaluation and treatment of patients with low back pain. *Brazilian Journal of Physical Therapy*, 25(4), 407–414. https://doi.org/10.1016/j.bjpt.2020.12.001
- Rubinstein, S. M., De Zoete, A., Van Middelkoop, M., Assendelft, W. J. J., De Boer, M. R., & Van Tulder, M. W. (2019). Benefits and harms of spinal manipulative therapy for the treatment of chronic low back pain: Systematic review and meta-analysis of randomised controlled trials. *BMJ (Online)*, *364*. https://doi.org/10.1136/bmj.1689
- Saal, Saal, H. (1990). The natural histroy of lumbr intervertebral disc extrusions treated nonoperatively. *Spine*, *15*(7), 683–686.
- Salaud, C., Ploteau, S., Hamel, O., Armstrong, O., & Hamel, A. (2018). Morphometric study of the posterior longitudinal ligament at the lumbar spine. *Surgical and Radiologic Anatomy*, 40(5), 563–569. https://doi.org/10.1007/s00276-017-1964-2
- Sandelowski, M. (2010). What's in a name? Qualitative description revisited. *Research in Nursing & Health*, *33*(1), 77–84. https://doi.org/10.1002/nur.20362
- Scannell, J. P., & McGill, S. M. (2009). Disc prolapse: Evidence of reversal with repeated extension. *Spine*, 34(4), 344–350. https://doi.org/10.1097/BRS.0b013e31819712a6
- Sekine, M., Yamashita, T., Takebayashi, T., Sakamoto, N., Minaki, Y., & Ishii, S. (2001). Mechanosensitive afferent units in the lumbar posterior longitudinal ligament. *Spine*, 26(14), 1516–1521. https://doi.org/10.1097/00007632-200107150-00003

- Shimonovich, M., Pearce, A., Thomson, H., Keyes, K., & Katikireddi, S. V. (2021). Assessing causality in epidemiology: revisiting Bradford Hill to incorporate developments in causal thinking. *European Journal of Epidemiology*, 36(9), 873– 887. https://doi.org/10.1007/s10654-020-00703-7
- Shirazi-adl, Shrivastava, & Ahmend\_. (1984). Stress analysis of the lumbar disc-body unit in compression. *Spine*, *9*(2), 120–134.
- Shultz, S., Averell, K., Eickelman, A., Sanker, H., & Donaldson, M. B. (2015). Diagnostic accuracy of self-report and subjective history in the diagnosis of low back pain with non-specific lower extremity symptoms: A systematic review. *Manual Therapy*, 20(1), 18–27. https://doi.org/10.1016/j.math.2014.08.002
- Shum, G. L., Tsung, B. Y., & Lee, R. Y. (2013). The immediate effect of posteroanterior mobilization on reducing back pain and the stiffness of the lumbar spine. *Archives of Physical Medicine and Rehabilitation*, 94(4), 673–679. https://doi.org/10.1016/j.apmr.2012.11.020
- Simon, J., McAuliffe, M., Shamim, F., Vuong, N., & Tahaei, A. (2014). Discogenic low back pain. *Physical Medicine and Rehabilitation Clinics of North America*, 25(2), 305–317. https://doi.org/10.1016/j.pmr.2014.01.006 [doi]
- Skaggs, D. L., Weidenbaum, M., Ratcliffe, A., & Mow, V. C. (1994). Regional Variation in Tensile Properties and Biochemical Composition of the Human Lumbar Anulus Fibrosus.
- Slater, S. L., Ford, J. J., Richards, M. C., Taylor, N. F., Surkitt, L. D., & Hahne, A. J. (2012). The effectiveness of sub-group specific manual therapy for low back pain: A systematic review. *Manual Therapy*, *17*(3 PG-201–212), 201–212. https://doi.org/10.1016/j.math.2012.01.006
- Smith, L. J., & Fazzalari, N. L. (2009). The elastic fibre network of the human lumbar anulus fibrosus: Architecture, mechanical function and potential role in the progression of intervertebral disc degeneration. *European Spine Journal*, 18(4), 439–448. https://doi.org/10.1007/s00586-009-0918-8
- Smyth, M. J., & Wright, V. J. (1958). Sciatica and the intervertebral disc. *Journal of Bone and Joint Surgery*, *40*(6), 1401–1418.
- Sniderman, A. D., LaChapelle, K. J., Rachon, N. A., & Furberg, C. D. (2013). The necessity for clinical reasoning in the era of evidence-based medicine. *Mayo Clinic*

Proceedings, 88(10), 1108–1114. https://doi.org/10.1016/j.mayocp.2013.07.012

- Son, E. S., Kim, D. H., Jung, J. W., & Lee, D. (2017). Analysis of Migration Patterns of Disk Fragments and Contributing Factors in Extruded Lumbar Disk Herniation. *PM* and R, 9(1), 15–20. https://doi.org/10.1016/j.pmrj.2016.06.007
- Stanton, T. R. (2016). Clinical prediction rules that don't hold up Where to go from here? *Journal of Orthopaedic and Sports Physical Therapy*, 46(7), 502–505. https://doi.org/10.2519/jospt.2016.0606
- Summers, B., Malhan, K., & Cassar-Pullicino, V. (2005). Low back pain on passive straight leg raising: The anterior theca as a source of pain. *Spine*, 30(3), 342–345. https://doi.org/10.1097/01.brs.0000152378.93868.c8
- Sun, X., Briel, M., Walter, S. D., & Guyatt, G. H. (2010). Is a subgroup effect believable? Updating criteria to evaluate the credibility of subgroup analyses. In *BMJ (Online)* (Vol. 340, Issue 7751, pp. 850–854). https://doi.org/10.1136/bmj.c117
- Sun, Z., & Mi, C. (2023). On the identification of the ultra-structural organization of elastic fibers and their effects on the integrity of annulus fibrosus. *Journal of Biomechanics*, 157. https://doi.org/10.1016/j.jbiomech.2023.111728
- Surkitt, L. D., Ford, J. J., Chan, A. Y. P., Richards, M. C., Slater, S. L., Pizzari, T., & Hahne, A. J. (2016). Effects of individualised directional preference management versus advice for reducible discogenic pain: A pre-planned secondary analysis of a randomised controlled trial. *Manual Therapy*, 25, 69–80. https://doi.org/10.1016/j.math.2016.06.002
- Swanson, B. T., & Creighton, D. (2020a). Handwashing, degenerative discs, and other heresies. *Journal of Manual and Manipulative Therapy*, 28(4), 189–190. https://doi.org/10.1080/10669817.2020.1804145
- Swanson, B. T., & Creighton, D. (2020b). The degenerative lumbar disc: not a disease, but still an important consideration for OMPT practice: a review of the history and science of discogenic instability. *Journal of Manual and Manipulative Therapy*, 28(4), 191–200. https://doi.org/10.1080/10669817.2020.1758520
- Takahashi, Y., Morinaga, T., Nakamura, S. I., Suseki, K., Takahashi, K., & Nakajima, Y. (1996). Neural connection between the ventral portion of the lumbar intervertebral disc and the groin skin. *Journal of Neurosurgery*, 85(2), 323–328. https://doi.org/10.3171/jns.1996.85.2.0323

- Takasaki, H., May, S., Fazey, P. J., & Hall, T. (2010). Nucleus pulposus deformation following application of mechanical diagnosis and therapy: a single case report with magnetic resonance imaging. *Journal of Manual & Manipulative Therapy*, 18(3), 153–158. https://doi.org/10.1179/106698110X12640740712455
- Tarantino, U., Fanucci, E., Iundusi, R., Celi, M., Altobelli, S., Gasbarra, E., Simonetti, G., Manenti, G., & Manenti;, T. F. I. C. A. G. S. (2013). Lumbar spine MRI in upright position for diagnosing acute and chronic low back pain: Statistical analysis of morphological changes. *Journal of Orthopaedics and Traumatology*, 14(1), 15– 22. https://doi.org/10.1007/s10195-012-0213-z
- Tavakoli, J., & Costi, J. J. (2018). New findings confirm the viscoelastic behaviour of the inter-lamellar matrix of the disc annulus fibrosus in radial and circumferential directions of loading. *Acta Biomaterialia*, 71, 411–419. https://doi.org/10.1016/j.actbio.2018.03.015
- Tawa, N., Rhoda, A., & Diener, I. (2017). Accuracy of clinical neurological examination in diagnosing lumbo-sacral radiculopathy: A systematic literature review. *BMC Musculoskeletal Disorders*, 18(1), 1–11. https://doi.org/10.1186/s12891-016-1383-2
- Teplick, J. G., & Haskin, M. (1986). Spontaneous regression of herniated nucleus pulposus. AJR. American Journal of Roentgenology, 146(4), 882–883. https://doi.org/10.2214/ajr.146.4.882
- Tessitore, E., Molliqaj, G., Schatlo, B., & Schaller, K. (2015). Clinical evaluation and surgical decision making for patients with lumbar discogenic pain and facet syndrome. *European Journal of Radiology*, 84(5 PG-765–770), 765–770. https://doi.org/10.1016/j.ejrad.2014.03.016
- Tsuji, H., Hirano, N., Ohshima, H., Ishihara, H., Terahata, N., & Motoe, T. (1993).
  Structural variation of the anterior and posterior anulus fibrosus in the development of human lumbar intervertebral disc. *Spine*, *18*(2), 204–210.
- Twomey, L. T. (1992). A rationale for the treatment of back pain and joint pain by manual therapy. *Physical Therapy*, 72(12), 885–892. https://doi.org/10.1093/ptj/72.12.885
- Uk, C. (2019). Critical Appraisal Skills Programme Diagnostic Study Checklist (online).
- Urits, I., Burshtein, A., Sharma, M., Testa, L., Gold, P. A., Orhurhu, V., Viswanath, O., Jones, M. R., Sidransky, M. A., Spektor, B., & Kaye, A. D. (2019). Low Back Pain,

a Comprehensive Review: Pathophysiology, Diagnosis, and Treatment. *Current Pain and Headache Reports*, 23(3), 1–10. https://doi.org/10.1007/s11916-019-0757-1

- Vergari, C., Chan, D., Clarke, A., Mansfield, J. C., Meakin, J. R., & Winlove, P. C. (2017). Bovine and degenerated human annulus fibrosus: a microstructural and micromechanical comparison. *Biomechanics and Modeling in Mechanobiology*, *16*(4), 1475–1484. https://doi.org/10.1007/s10237-017-0900-z
- Verwoerd, A. J. H., Mens, J., el Barzouhi, A., Peul, W. C., Koes, B. W., & Verhagen, A. P. (2016). A diagnostic study in patients with sciatica establishing the importance of localization of worsening of pain during coughing, sneezing and straining to assess nerve root compression on MRI. *European Spine Journal*, 25(5), 1389–1392. https://doi.org/10.1007/s00586-016-4393-8
- Verwoerd, A. J. H., Peul, W. C., Willemsen, S. P., Koes, B. W., Vleggeert-Lankamp, C. L. A. M., El Barzouhi, A., Luijsterburg, P. A. J., & Verhagen, A. P. (2014).
  Diagnostic accuracy of history taking to assess lumbosacral nerve root compression. *Spine Journal*, *14*(9), 2028–2037. https://doi.org/10.1016/j.spinee.2013.11.049
- Videman, T., & Battié, M. C. (2012). Commentary: Back pain epidemiology—the challenge of case definition and developing new ideas. *The Spine Journal*, 12(1), 71–72.
- Vining, R. D., Shannon, Z. K., Minkalis, A. L., & Twist, E. J. (2019). Current Evidence for Diagnosis of Common Conditions Causing Low Back Pain: Systematic Review and Standardized Terminology Recommendations. In *Journal of Manipulative and Physiological Therapeutics* (Vol. 42, Issue 9, pp. 651–664). Elsevier Inc. https://doi.org/10.1016/j.jmpt.2019.08.002
- Vining, R., Potocki, E., Seidman, M., & Morgenthal, A. P. (2013). An evidence-based diagnostic classification system for low back pain. *The Journal of the Canadian Chiropractic Association*, 57(3), 189–204.

Violas, P., Estivalèzes, E., Pédrono, A., De Gauzy, J. S., Sévely, A., & Swider, P. (2005). A method to investigate intervertebral disc morphology from MRI in early idiopathic scoliosis: a preliminary evaluation in a group of 14 patients. *Magnetic Resonance Imaging*, 23(3), 475–479.

<sup>\</sup> 

- von Düring, M., Fricke, B., & Dahlmann, A. (1995). Topography and distribution of nerve fibers in the posterior longitudinal ligament of the rat: an immunocytochemical and electron-microscopical study. *Cell & Tissue Research*, 281(2), 325–338. https://doi.org/10.1007/BF00583401
- Vroomen, P. C. A. J., De Krom, M. C. T. F. M. Wilmink, J. T., Kester, A. D. M., & Knottnerus, J. A. (2002). Diagnostic value of history and physical examination in patients suspected of lumbosacral nerve root compression. *Journal of Neurology Neurosurgery and Psychiatry*, 73(5), 604–605. https://doi.org/10.1136/jnnp.73.5.604
- Wachowski, M. M., Mansour, M., Lee, C., Ackenhausen, A., Spiering, S., Fanghänel, J., Dumont, C., Kubein-Meesenburg, D., & Nägerl, H. (2009). How do spinal segments move? *Journal of Biomechanics*, 42(14), 2286–2293. https://doi.org/10.1016/j.jbiomech.2009.06.055
- Wagner, D. R., & Lotz, J. C. (2004). Theoretical model and experimental results for the nonlinear elastic behavior of human annulus fibrosus. *Journal of Orthopaedic Research*, 22(4), 901–909. https://doi.org/10.1016/j.orthres.2003.12.012
- Walker, B. F., French, S. D., Page, M. J., O'Connor, D. A., McKenzie, J. E., Beringer, K., Murphy, K., Keating, J. L., Michie, S., Francis, J. J., & Green, S. E. (2011).
  Management of people with acute low-back pain: A survey of Australian chiropractors. *Chiropractic and Manual Therapies*, *19*(i), 1–7. https://doi.org/10.1186/2045-709X-19-29
- Walsh, J., & Hall, T. (2009). Agreement and Correlation Between the Straight Leg Raise and Slump Tests in Subjects With Leg Pain. *Journal of Manipulative and Physiological Therapeutics*, 32(3), 184–192. https://doi.org/10.1016/j.jmpt.2009.02.006
- Wang, S., Xia, Q., Passias, P., Wood, K., & Li, G. (2009). Measurement of geometric deformation of lumbar intervertebral discs under in-vivo weightbearing condition. *Journal of Biomechanics*, 42(6), 705–711. https://doi.org/10.1016/j.jbiomech.2009.01.004
- Wang, Y., Dai, G., Jiang, L., & Liao, S. (2020). The incidence of regression after the non-surgical treatment of symptomatic lumbar disc herniation: A systematic review and meta-analysis. In *BMC Musculoskeletal Disorders* (Vol. 21, Issue 1). BioMed Central Ltd. https://doi.org/10.1186/s12891-020-03548-z

Webster, B. S., Courtney, T. K., Huang, Y. H., Matz, S., & Christiani, D. C. (2005). Brief 169

Report: Physicians' initial management of acute low back pain versus evidencebased guidelines. Influence of sciatica. *Journal of General Internal Medicine*, 20(12), 1132–1135. https://doi.org/10.1111/j.1525-1497.2005.0230.x

- Werneke, M. W., Hart, D. L., Cutrone, G., Oliver, D., McGill, M. T., Weinberg, J., Grigsby, D., Oswald, W., & Ward, J. (2011). Association between directional preference and centralization in patients with low back pain. *Journal of Orthopaedic and Sports Physical Therapy*, *41*(1 PG-22–31), 22–31. https://doi.org/10.2519/jospt.2011.3415
- Werneke, M. W., Hart, D., Resnik, L., Stratford, P. W., & Reyes, A. (2008). Centralization: Prevalence and effect on treatment outcomes using a standardized operational definition and measurement method. *Journal of Orthopaedic and Sports Physical Therapy*, 38(3), 116–125. https://doi.org/10.2519/jospt.2008.2596
- Wetzel, F. T., & Donelson, R. (2003). The role of repeated end-range/pain response assessment in the management of symptomatic lumbar discs. *Spine Journal*, 3(2), 146–154. https://doi.org/10.1016/S1529-9430(02)00565-X
- Whiting, P. F., Reitsma, J. B., Leeflang, M. M. G., Sterne, J. A. C., Bossuyt, P. M. M., Rutjes, A. W. S. S., Westwood, M. E., Mallet, S., Deeks, J. J., Reitsma, J. B., Leeflang, M. M. G., Sterne, J. A. C., & Bossuyt, P. M. M. (2011). QUADAS-2: A Revised Tool for the Quality Assessment of Diagnostic Accuracy Studies. *Annals of Internal Medicine*, *155*(4), 529–536. https://doi.org/10.7326/0003-4819-155-8-201110180-00009
- Williams, C. M., Maher, C. G., Hancock, M. J., McAuley, J. H., McLachlan, A. J., Britt, H., Fahridin, S., Harrison, C., & Latimer, J. (2010). Low back pain and best practice care a survey of general practice physicians. *Archives of Internal Medicine*, 170(3), 271–277. https://doi.org/10.1001/archinternmed.2009.507
- Wilson, R. L., Bowen, L., Kim, W., Cai, L., Schneider, S. E., Nauman, E. A., & Neu, C. P. (2021). In vivo intervertebral disc deformation: intratissue strain patterns within adjacent discs during flexion–extension. *Scientific Reports*, 11(1), 1–13. https://doi.org/10.1038/s41598-020-77577-y
- Wiltse, L. L. (2000). Anatomy of the extradural compartments of the lumbar spinal canal: Peridural membrane and circumneural sheath. *Radiologic Clinics of North America*, 38(6), 1177–1206. https://doi.org/10.1016/S0033-8389(08)70003-4

Wirth, B., Gassner, A., De Bruin, E. D., Axén, I., Swanenburg, J., Humphreys, B. K., &

Schweinhardt, P. (2019). Neurophysiological Effects of High Velocity and Low Amplitude Spinal Manipulation in Symptomatic and Asymptomatic Humans: A Systematic Literature Review. *Spine*, *44*(15), E914–E926. https://doi.org/10.1097/BRS.000000000003013

- Woolf, C. J. (1991). Generation of acute pain: Central mechanisms. *British Medical Bulletin*, 47(3), 523–533. https://doi.org/10.1093/oxfordjournals.bmb.a072490
- Xu, H., Wen, W., Zhang, Z., Bai, J., Kou, B., & Miao, J. (2022a). Correction: Investigation of geometric deformations of the lumbar disc during axial body rotations. *BMC Musculoskeletal Disorders*, 23(1), 22–23. https://doi.org/10.1186/s12891-022-05654-6
- Xu, H., Wen, W., Zhang, Z., Bai, J., Kou, B., & Miao, J. (2022b). Investigation of geometric deformations of the lumbar disc during axial body rotations. *BMC Musculoskeletal Disorders*, 23(1), 1–10. https://doi.org/10.1186/s12891-022-05160-9
- Yang, K. H., & King, A. I. (1984). Mechanism of facet load transmission as a hypothesis for low-back pain. In *Spine* (Vol. 9, Issue 6, pp. 557–565). https://doi.org/10.1097/00007632-198409000-00005
- Yang, X., Zhang, Q., Hao, X., Guo, X., & Wang, L. (2016). Spontaneous regression of herniated lumbar discs: Report of one illustrative case and review of the literature. *Clinical Neurology and Neurosurgery*, 143, 86–89. https://doi.org/10.1016/j.clineuro.2016.02.020
- Yates, M. and, Matthews, Y., Yates, M. and, & Matthews, Y. (1969). Reduction of lumbar disc prolapse by manipulation. *British Medical Journal, September*, 694– 697.
- Yu, J., Peter, C., Roberts, S., & Urban, J. P. G. (2002). Elastic fibre organization in the intervertebral discs of the bovine tail. *Journal of Anatomy*, 201(6), 465–475. https://doi.org/10.1046/j.1469-7580.2002.00111.x
- Yu, P., Mao, F., Chen, J., Ma, X., Dai, Y., Liu, G., Dai, F., & Liu, J. (2022). Characteristics and mechanisms of resorption in lumbar disc herniation. *Arthritis Research and Therapy*, 24(1), 1–18. https://doi.org/10.1186/s13075-022-02894-8
- Yushkevich, P. A., Piven, J., Hazlett, H. C., Smith, R. G., Ho, S., Gee, J. C., & Gerig, G. (2006). User-guided 3D active contour segmentation of anatomical structures:

significantly improved efficiency and reliability. *NeuroImage*, 31(3), 1116–1128.

- Zhang, Y. G., Guo, T. M., Guo, X., & Wu, S. X. (2009). Clinical diagnosis for discogenic low back pain. *International Journal of Biological Sciences*, 5(7 PG-647–658), 647– 658. NS -
- Zhao, L., Manchikanti, L., Kaye, A. D., & Abd-Elsayed, A. (2019). Treatment of Discogenic Low Back Pain: Current Treatment Strategies and Future Options—a Literature Review. *Current Pain and Headache Reports*, 23(11). https://doi.org/10.1007/s11916-019-0821-x
- Zhong, W., Driscoll, S. J., Wu, M., Wang, S., Liu, Z., Cha, T. D., Wood, K. B., & Li, G. (2014). In vivo morphological features of human lumbar discs. *Medicine (United States)*, 93(28), e333. https://doi.org/10.1097/MD.00000000000333
- Zhou, Y., & Abdi, S. (2006). Diagnosis and minimally invasive treatment of lumbar discogenic pain--a review of the literature. *The Clinical Journal of Pain*, 22(5), 468– 481. https://doi.org/10.1097/01.ajp.0000208244.33498.05 [doi]
- Zhu, D., Gu, G. S., Wu, W., Gong, H., Zhu, W. M., Jiang, T., & Cao, Z. L. (2008). Micro-structure and mechanical properties of annulus fibrous of the L4-5 and L5-S1 intervertebral discs. *Clinical Biomechanics*, 23(SUPLL.1), 74–82. https://doi.org/10.1016/j.clinbiomech.2008.04.007
- Zou, J., Yang, H., Miyazaki, M., Morishita, Y., Wei, F., McGovern, S., & Wang, J. C. (2009). Dynamic bulging of intervertebral discs in the degenerative lumbar spine. *Spine*, 34(23), 2545–2550. https://doi.org/10.1097/BRS.0b013e3181b32998 [doi]
- Zou, J., Yang, H., Miyazaki, M., Wei, F., Hong, S. W., Yoon, S. H., Morishita, Y., & Wang, J. C. (2008). Missed lumbar disc herniations diagnosed with kinetic magnetic resonance imaging. *Spine*, 33(5 PG-E140-4), E140-4. https://doi.org/https://dx.doi.org/10.1097/BRS.0b013e3181657f7e
- Zou, T., Liu, X. Y., Wang, P. C., Chen, H., Wu, P. G., Feng, X. M., & Sun, H. H. (2023). (2023). Incidence of spontaneous resorption of lumbar disc herniation: a metaanalysis. *Clinical Spine Surgery*, 10, 1097. https://doi.org/10.36076/ppj.2017.1.e45
- Zusman, M. (1986). Spinal Manipulative Therapy: Review of Some Proposed Mechanisms, and a New Hypothesis. *Australian Journal of Physiotherapy*, 32(2), 89–99. https://doi.org/10.1016/S0004-9514(14)60645-0

# Appendices

Appendix 0-1. Letter of information regarding international survey



Health and Rehabilitation Sciences

4 March, 2014

A survey of health practitioners who treat patients with low back pain

Principal Investigator: Dr. David M. Walton PhD, Western University, Canada Co- Investigator: Joe Putos PhD (Student) Western University Canada, Dr. Trevor Birmingham PhD Western University Canada, Dr. Paul Fenton, Queen's University Canada

### 1. Invitation to Participate

You are being invited to participate in a survey intended to evaluate health providers' practice patterns and beliefs about spinal manual and manipulative therapy for low back pain.

### 2. Purpose of the Letter

The purpose of this letter is to provide you with information required for you to make an informed decision regarding participation in this survey.

### 3. Why is this study being done?

Low back pain (LBP) is the most common musculoskeletal pain complaint seen in primary care. LBP can arise from dysfunction in a variety of systems, which has led to a large variety of treatment approaches and techniques. One common approach to non-pharmacological management of low back pain is spinal manipulation or adjustment. Despite widespread use of the technique by physiotherapists, chiropractors, osteopathic doctors and medical physicians, the actual mechanism of action of spinal manipulation remains largely underdeveloped, tending to rely on anecdote and theory. While some positive clinical effects have been demonstrated with spinal manipulation, a stronger understanding of the mechanism of action is an important component of evidence-based practice and can influence policy and practice. The current study is part of a larger program that seeks to provide a better understanding of the mechanisms that explain benefit from spinal manipulation.

### 4. What is the purpose of this study?

This research program represents a new direction for research into the mechanisms underlying spinal manipulation. One of the first steps of a new research program is to gauge the importance of the question by collecting information on the degree to which

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Participant Initials

the technique under study is used clinically, and to appreciate the ways in which those who actually use the technique understand its effects. The purpose of this survey is to collect information about clinical practices for patients with low back pain and opinions on the mechanisms of spinal manipulation for low back pain management from various health disciplines in different countries.

### 5. What is involved?

If you volunteer to participate in the study, you will be asked to answer an internetbased survey on what you are currently doing to treat patients with low back pain in your usual clinical practice.

The survey consists of two parts. In Part 1 you will be asked to respond to fourteen (14) questions (choose a response or short answer) about practice matters for assessing and treating patients with low back pain. In Part 2, you will be asked six (6) general questions about you including your gender, professional designation, years qualified as a practitioner, place of work, country of registration and post graduate training.

Part 1 of the survey will take 15 - 20 minutes to complete. Part 2 will take 3 - 5 minutes to complete. Upon study completion all registrants, whether they complete the survey or not, will be entered into a draw to win a \$50 Amazon gift card.

### 6. How many people will be in this study?

We are anticipating 200 to 300 survey responses.

### 7. What are the possible risks?

There are no foreseeable risks associated with this study. You may feel worried about your responses and the security of your data. As this is an opinion-based survey there are no right or wrong answers. Your responses will remain anonymous, we are not collecting personal identifiers like your name or email address on this survey.

### 8. What are the possible benefits?

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Participant Initials

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It is not expected that you will directly benefit from participation in this study. The results of this study may benefit society and the scientific community in combination with planned future research on improving understanding of the mechanisms and treatment of low back pain.

### 9. What will happen to my personal information?

All information will remain confidential. The internet-based questionnaire is on a secure website. Your data will only be accessible to the investigators and web administrators. Your data will be submitted anonymously and you will only be identified by an ID code in the database. The only personal information we are collecting from you is your sex, years of practice and geographic region of practice. Your email address will be used by you for registration purposes. It will not become part of the database that is used for analysis. All data are stored on a secure server located in the United States with industry-standard software and physical security measures in place. The name of the hosting platform is Survey Monkey (https://www.surveymonkey.com/). Once the data are downloaded from the Survey Monkey servers we will request they be deleted. Local data are stored on a password-protected computer accessible only to the members of the research team and local computer administrators.

### 10. Can participation end early?

Your participation is voluntary and you may withdraw at any time without requiring an explanation. If you choose to withdraw, you have the option of contributing the data collected prior to your withdrawal, or removing all your information completely from the study. You will need to provide us your unique participant ID in order for us to identify and remove your data.

### 11. Contact Information

If you have any concerns or questions about your involvement you may contact the lead researcher, Dr. David Walton, at Western University (London, Canada) if you require any further clarification. His contact information can be found below. If you have any questions about your rights as a research participant or the conduct of the study you may contact the Office of Research Ethics at or by email at

If you wish to receive a summarized copy of the results nlease indicate this by sending a separate email to Mr. Joe Putos at

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Participant Initials

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Dr. David Walton Assistant Professor School of Physical Therapy University of Western Ontario

I understand the terms of registration as outlined above and by clicking on the Agree button below I am giving my consent to participate in the study.

Agree and submit

Page 4 of 4

Version April 30, 2013

Participant Initials

4

### **Appendix 0-2. Survey Questionnaire**

A survey of health practitioners who use manual treatments for a sub-group of patients with low bac  $% \left( {{{\mathbf{x}}_{i}}} \right)$ 

### Introduction

#### February 20, 2014.

#### A survey of health practitioners who treat patients with low back pain

Principal Investigator: David Walton, B.Sc., M.Sc., PhD, University of Western Ontario

Co- Investigator: Joe Putos, B.P.E., B.Ed., B.Sc. PT, M. Ed., PhD (Student), University of Western Ontario

#### Invitation to Participate

You are being invited to participate in a survey that is part of a research study looking at treatment of low back pain by health practitioners who use spinal manipulation.

#### Purpose of the Letter

The purpose of this letter is to provide you with information required for you to make an informed decision regarding participation in this research.

#### Why is this study being done?

Low back pain (LBP) is the most common musculoskeletal pain complaint seen in primary care. LBP can arise from dysfunction in a variety of systems, which has led to a large variety of treatment approaches and techniques. One common approach to non-pharmacological management of low back pain is spinal manipulation or adjustment. Despite widespread use of the technique by physiotherapists, chiropractors, osteopathic doctors and medical physicians, the actual mechanism of action of spinal manipulation remains largely underdeveloped, tending to rely on anecdote and theory. While some positive clinical effects have been demonstrated with spinal manipulation, a stronger understanding of the mechanism of action is an important component of evidence-based practice and can influence around policy and practice. The current study is part of a larger program that seeks to provide a better understanding of the mechanisms that explain benefit from spinal manipulation.

#### What is the purpose of this study?

This research program represents a new direction for research into the mechanisms underlying spinal manipulation. One of the first steps of a new research program is to gauge the importance of the question by collecting information on the degree to which the technique under study is used clinically, and to appreciate the ways in which those who actually use the technique understand its effects. The purpose of this survey is to collect information about clinical practices on patients with low back pain and opinions on the mechanisms of spinal manipulation for low back pain management from various health disciplines in different countries.

#### What is involved?

If you volunteer to participate in the study, you will be asked to answer an internet-based survey on what you are currently doing to treat patients with low back pain in your usual clinical practice.

The survey consists of two parts. In Part 1 you will be asked to respond to fourteen (14) questions (choose a response or short answer) about practice matters for assessing and treating patients with low back pain. In Part 2, you

will be asked six (6) questions about personal details including, gender, professional designation, years qualified as a practitioner, place of work, country of registration and post graduate training.

Part 1 of the survey will take 15 – 20 minutes to complete. Part 2 will take 3 – 5 minutes to complete. Upon study completion all registrants, whether they complete the survey or not, will be entered into a draw to win a \$50 Amazon gift card.

How many people will be in this study?

We are anticipating 200 to 300 survey responses.

What are the possible risks?

There are no foreseeable risks associated with this study. You may feel worried about Your responses. There are no right or wrong answers and you will be completing the survey anonymous

A survey of health practitioners who use manualtreatments for a sub-group of patients with low bac

#### What are the possible benefits?

You may not directly benefit from participation in this study. The results of this study may benefit society and the scientific community in combination with planned future research on improving our understanding of the mechanisms and treatment of low back pain.

#### What will happen to my personal information?

All information will remain confidential. The internet-based questionnaire is on a secure website. Your data will only be accessible to the investigators and web administrators. Your data will be submitted anonymously and you will only be identified by an ID code in the database. The only personal information we are collecting from you is your sex, years of practice and geographic region of practice. Your email address will be used by you for registration purposes. It will not become part of the database that is used for analysis. All data are stored on a secure server located in the United States with industry-standard software and physical security measures in place. The name of the hosting platform is Survey Monkey (https://www.surveymonkey.com/).

#### Can participation end early?

Your participation is voluntary and you may withdraw at any time without requiring an explanation. If you choose to withdraw, you have the option of contributing the data collected prior to your withdrawal, or removing all your information completely from the study (you will need to provide us your unique participant ID in order for us to identify and remove your data.

#### Contact Information

This study has been reviewed and approved by the Western University Health Sciences Research Ethics Board. If you have any concerns or questions about your involvement you may contact the lead researcher, Dr. David Walton, at Western University (London, Canada) if you require any further clarification. His contact information can be found below. If you have any questions about your rights as a research participant or the conduct of the study you may contact the Office of Research Ethics at research or by email at research ethics.

Dr. David Walton Assistant Professor School of Physical Therapy University of Western Ontario Room\_\_\_\_\_ Elborn
College Phone:\_\_\_\_\_

 $\ast$  1. I understand the terms of registration as outlined above and by clicking on the Agree button below I am giving my consent to participate in the study.

◯ Agree and submit

A survey of health practitioners who use manualtreatments for a sub-group of patients with low bac

2. Do you use any of the following treatments for patients with low back pain? Please check all applicable treatments that reflect your practice. If you do not use any of the following treatments go to Question 12.

	a.	Spinal	manipulation
$\square$	b.	Spinal	mobilisation

$\square$	c.	Spinal	adjustment	;

A survey of health practitioners who use manualtreatments for a sub-group of

3. How many years have you used these treatments?

4. Approximately what percentage of your active caseload is made up of patients with low back pain?

- 🔵 a. <5%
- 🔵 b. 5 25%
- 🔿 c. 26 50%
- 🔵 c. 51 75%
- 🔿 d. >75%

5. Do you use a defined or standardized protocol(s) for assessing a patient with lumbar spine pain as a means of identifying the source of the lesion, the nature of the pathology or the most appropriate intervention?

Some examples of assessment protocols include the following (this list is not meant to be exhaustive):

Osteopathic Cyriax McKenzie Chiropractic

🔵 a. Yes 🔵 b. No

6. If Yes, please check off the protocols you use. Check off as many as you use in practice. If the protocol you use is not listed, use the Other box to provide a brief description of the protocol(s) you use.

a. Cyriax			
b. Maitland			
c. McKenzie			
🗌 d. Mulligan			
e. Muscle Er	nergy		
f. Myofascia	l Techniques		
g. Kaltenbor	'n		
h. Chiroprac	tic		
i. Osteopath	ic		
Other (please spec	:ify)		

7. <u>Of those patients who present to your practice with low back pain</u> what percentage do you attribute to having a bulged or protruded disc(s)?

a. <5%</li>
b. 5 - 25%
c. 26 - 50%
d. 51 - 75%
e. >75%

8. List the key evidence or information from the patient history/interview that would lead you to suspect discogenic low back pain.

9. List the key clinical tests or observations that would lead you to suspect discogenic low back pain.

This will take you to a short video demonstrating a type of spinal manipulation. Click the link to the video and then go to question 10. <u>CLICK HERE</u>

10. Of the patients with low back pain symptoms that you believe are discogenic, what percentage would be treated using a treatment similar to the one demonstrated in the video?

11. If you do use a treatment similar to the one demonstrated in the video, please describe your rationale for using it as a treatment for low back pain.

A survey of health pr	actitioners who	use manualtreatments	for a sub-group of
patients with low bac			

About you

The following questions are intended to provide the researchers with general information about you and the nature of your practice.

12.	Sex

🔵 a. Male 🔵 b. Female

13. Clinical Designation (choose all that apply)

a. Physiotherapist or Physical Therapist (P.T.)

- b. Physician (M.D.)
- c. Osteopath (D.O)
- d. Chiropractor (D.C.)
- Other (please specify)

14. Place(s) of work: (choose all that apply)
a. Hospital
b. Private Practice
c. Family/Community Health Centre
d. Industry
e. University/College
Other (please specify)

15. Approximately how many hours per week do you provide direct patient care?

16. Number of years qualified within your respective discipline:

A survey of health practitioners who use manualtreatments for a sub-group of patients with low bac  $% \left( {{{\mathbf{x}}_{i}}} \right)$ 

More then 1 designation?

### if you practice under more than a single designation go to question 16.

17. If you practice under more than one designation please list all designations. Describe the designation in full and list how long you have been qualified in each discipline.

18. Country of current registration as a practitioner. (If more than one country, include all that apply.

19. Have you undergone any formal post-graduate training in manual spinal treatments. If yes, please briefly describe below. Do not use abbreviations.

20. Thank you for your participation.

If you would like to receive a summarized version of the survey results, please send an email to \_\_\_\_\_\_ indicating as much, and you will receive a copy upon completion of this study.



Demographic	Respondents	Response Count		Response Percentage
Gender (n=141)	male	92	65.2%	
	female	49	34.8%	
Clinical Designation (choose all that apply) (n=140)				
	Physiotherapist or Physical Therapist	127	90.7%	
	Physician	4	2.9%	
	Osteopath	5	3.6%	
	Chiropractor	5	3.6%	
	Other	10		
Place(s) of work (choose all that apply) (n=133)				
	Hospital	20	15.0%	
	Private Practice	112	84.2%	
	Family/Community Health Centre	6	4.5%	
	Industry	3	2.3%	
	University/College	19	14.3%	
	Other *	13	9.8%	
Hours/week providing direct patient care (n=142)				
,,	<15	17	100/	
	<u>&lt;</u> 15 16-30	10	35%	
	31-44	49 59	42%	
	>45	14	10%	
	210	17	1070	
Number of years qualified in respective discipline (n=142)				
	Mean	15		
	Median	14		
	Mode	20		
	Min	1		
	Max	44		
	SD	9.5		

# Appendix 0-3. Demographics of survey respondents.

If you practice under more than one designation, please list all designations. Describe the designation in full and list how long you have been qualified in each discipline (n=37)	Respondents cited various certifications but within the same field of practice. E.g., PT, MD, DO, DC. Only 2 respondents indicated they practiced under more than one clinical designation.	
	Acupuncturist/Chiropractor	1
	Athletic Therapist/PT	1
	Diplomierter Assistent für Physikalische Medizin 10y Diplomierter Physiotherapeut 5y Physiotherapeut	1
	Conditioning Specialist, Certified Acupuncture Provider Certified Strength and	1
	Conditioning Specialist, Certified Acupuncture Provider	1
Country of current registration as a practitioner (If more than one country, include all that apply $(n=136)$		
	Australia	1
	Austria	2
	Belgium	1
	Canada	57
	Germany	3
	Hong Kong	1
	India	3
	Ireland	22
	Italy	1
	Liechtenstein	1
	New Zealand	1
	Pakistan	2
	Poland	1
	Saudi Arabia	1
	Singapore	1
	Spain	1
	Switzerland	15
	United Kingdom	2
	United Arab Emirates	1
	USA	31
Post-graduate training in manual spinal treatments (n=130)*	*some respondents included multiple types of post graduate training	
	Master Degree	33
	Manual Therapy Certification	30
	Continuing Education Courses	30

# Sample Response

Masters in Orthopaedic Manual Physical The	erapy
CAMPT/FCAMPT program	

Dynamic Neuromuscular Stabilization (Prague school or rehabilitation)

	Graduate Program	17	Diploma of advanced studies in manual therapy
	Fellowship Program	8	2 year Fellowship in Manual Therapy at Institute of Orthopedic Manual Physical Therapy
	Residency Program	7	Hayward residency program
	Chiropractic College	3	Chiropractic college
	Doctorate Program	2	Evidence in Motion doctorate of physical therapy
	Board Certification	1	Board certified in family practice / osteopathic manipula treatment as well as neuromusculoskeletal medicine/ osteopathic manipulative medicine
Do you use any of the following treatments? (choose all that apply) (n=192)			
	spinal manipulation	163	84.9%
	spinal mobilisation	177	92.2%
	spinal adjustment	29	15.1%
Number of years using these treatments (n=135)			
	Mean	12.5	
	Median	10	
	Mode	10	
	Min	1	
	Max	35	
	SD	8.7	
Percentage of caseload made up of patients with low back pain (n=145)			
	<5%	3	2.1%
	5 - 25%	44	30.3%
	26 - 50%	57	39.3%
	51 - 75%	33	22.8%
	>75%	8	5.5%
Standardized protocol used when assessing patients with lumbar spine pain (n=144)			
()	Yes	109	75.7%
	No	35	24.3%
Assessment protocol used			
(choose all that apply) (n=110)	Cyriax	39	35.5%
. ,	Maitland	73	66.4%
	McKenzie	65	59.1%
	Mulligan	38	34.5%
	Muscle Energy	26	23.6%
	Myofascial Techniques	39	35.5%
	•		

Kaltenborn	35	31.8%
Chiropractic	11	10.0%
Osteopathic	23	20.9%
Other	31	
Applied kinesiology		
Biomechanical Assessment as taught by the Orthopedic Division of the Canadian Physiotherapy Association Clinical patterns as described by Hamilton Hall Combo of biomechanics and psychosocial with some neuroscience Conventional medical approach Diagnostic injections of local anaesthetic Dunning: Spinal Manipulation Institute		
Stabilization or DNS (Prague		
Evidence on motion		
General musculoskeletal		
IMS (not defined by respondent)		
Lumbar scan		
Mixture of many		
Movement Controll Test Battery from Luomajoki		
Movement System Impairment syndromes		
Muscle Balance		
Muscle controle		
Nwugarian Technique		
Orthopedic Manual Physiotherapy		
Orthopedic Medicine O'Sullivan classifcation system (CLBP)		
Patient response Primitive reflex integration (PRRT) (Masgutova method)		
Sahrmann, Selective Functional Movement Assessment (SFMA)		
Treatment based classification		
Test Battery from Luomajoki		
Zero Balancing I don't use "protocols" for assessment or treatment. I use the techniques and or theories of assessment based upon what I checked. The goal is reproduction of pain or the comparable sign and to find joint		

Percentage of low back pain	hyper/hypomobility. To me "protocol" is a standardized, checklist approach to treating a patient, such like a CPR- clinical prediction rule		
a protruded disc (n=142)			
	a. <5%	33	23.2%
	b. 5 - 25%	60	42.3%
	c. 26 - 50%	34	23.9%
	d. 51 - 75%	9	6.3%
	e. >75%	6	4.2%
Of the patients with low back pain symptoms that you believe are discogenic, what percentage would be treated using a treatment similar to the one demonstrated in the video (n=140)			
	<5%	80	
	5 - 25%	18	
	26 - 50%	11	
	51 - 75%	1	
	>75%	6	

# Appendix 0-4. Terms and definitions of manipulation and mobilization

# Spinal Manipulation

Spinal manipulation has been described as low amplitude, high velocity passive movements within, at the limit of or slightly beyond the passive range of joint motion (McCarthy, Bialosky, & Rivett, 2015; Bronfort et al. 2012; Ernst & Canter, 2006). There are many variations of SM broadly categorised as either short-lever (i.e., the thrust is applied directly to the spine, or long-lever in which force is not provided directly to the spine directly, but from rotation of the patient's thigh and/or leg (Bronfort et al. 2012). specific HVLA techniques available to practitioners of SMT, which can also be modified according to patient need. This type of SMT has also been termed short-lever SMT, because the thrust is applied directly to the spine (Figure 17-2). It is distinguished from long-lever SMT, originally from the osteopathic tradition, in which

Fig. 1. Side-posture 'rotational' lumbar manipulation. Reproduced with permission, from Evans, D. W. (2010). Why do spinal manipulation techniques take the form they do? Towards a general model of spinal manipulation. Manual therapy, 15(3), 212-219.



# Spinal Mobilisation

Spinal mobilisations are defined as low velocity passive oscillatory movements within the passive range of joint motion that does not involve a thrust (Aguirrebeña, Newham & Critchley, 2015; Bronfort et al. 2012). They can be labelled using different descriptive terms, take a number of forms and vary in directionality. Mobilisations have been shown to reduce symptoms in some LBP subgroups although the mechanism(s) of action are not clear (Aguirrebeña, Newham & Critchley, 2015). Selection of the appropriate maneuver(s) continues to depend on the judgment and expertise of the clinician based on their interpretation of the patient's signs and symptoms (Kuo & Loh, 1987).

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S87	limit to humans	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display	
S86	38 not (radiculopath* or cervi*).	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display	
S85	38 not (radiculopath* or cervi*).	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display	
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	S77	deriv*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display
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S66	clinical sign*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display
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S64	diagnos*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display
S63	clinical finding*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display
S62	S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display
S61	"intervertebral disc displacement"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced	Display

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S39 38 not radiculopath*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display
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S20	featur*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display
S19	diagnos*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display
S18	clinical finding*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display
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S16	"intervertebral disc displacement"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display
S15	herniat*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced	Display

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S14	prolapse*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display
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12/24/23, 8:44 PM F		Print Search Histo	Print Search History: EBSCOhost		
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S3	"lumbar vertebrae"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display	
S2	low back*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	Display	
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Appendix 0-6. Appendix 0 7. Quadas-2 Tool Template.

# QUADAS-2

#### Phase 1: State the review question:

Patients (setting, intended use of index test, presentation, prior testing):

Index test(s):

Reference standard and target condition:

### Phase 2: Draw a flow diagram for the primary study

#### Phase 3: Risk of bias and applicability judgments

QUADAS-2 is structured so that 4 key domains are each rated in terms of the risk of bias and the concern regarding applicability to the research question (as defined above). Each key domain has a set of signalling questions to help reach the judgments regarding bias and applicability.

#### DOMAIN 1: PATIENT SELECTION A. Risk of Bias

Describe methods of patient selection:

Was a consecutive or random sample of patients enrolled?

Was a case-control design avoided?

Did the study avoid inappropriate exclusions?

Yes/No/Unclear Yes/No/Unclear Yes/No/Unclear

Could the selection of patients have introduced bias? RISK: LOW/HIGH/UNCLEAR

#### B. Concerns regarding applicability

Describe included patients (prior testing, presentation, intended use of index test and setting):

Is there concern that the included patients do not match CONCERN: LOW/HIGH/UNCLEAR the review question?

DOMAIN 2: INDEX TEST(S)			
If more than one index test was used, please complete for each test.			
A. Risk of Bias			
Describe the index test and how it was conducted and inter	preted:		
<ul> <li>Were the index test results interpreted without knowledge of the results of the reference standard?</li> <li>If a threshold was used, was it pre-specified?</li> <li>Could the conduct or interpretation of the index test have introduced bias?</li> </ul>	Yes/No/Unclear Yes/No/Unclear RISK: LOW /HIGH/UNCLEAR		
B. Concerns regarding applicability			
Is there concern that the index test, its conduct, or interpretation differ from the review question?	CONCERN: LOW /HIGH/UNCLEAR		

DOMAIN 3: REFERENCE STANDARD		
A. Risk of Bias		
Describe the reference standard and how it was conducted	and interpreted:	
Is the reference standard likely to correctly classify to condition?	he target	Yes/No/Unclear
Were the reference standard results interpreted wirk knowledge of the results of the index test?	thout	Yes/No/Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	RISK: LOW /HIGH	/UNCLEAR
B. Concerns regarding applicability		
Is there concern that the target condition as defined by the reference standard does not match the review question?	CONCERN: LOW /	HIGH/UNCLEAR

DOMAIN 4: FLOW AND TIMING	
A. Risk of Bias	
Describe any patients who did not receive the index test(s) and/or reference were excluded from the 2x2 table (refer to flow diagram):	ence standard or who
Describe the time interval and any interventions between index test(s) a	nd reference standard:
Was there an appropriate interval between index test(s) and reference standard?	Yes/No/Unclear
Did all patients receive a reference standard?	Yes/No/Unclear
Did patients receive the same reference standard?	Yes/No/Unclear
Were all patients included in the analysis?	Yes/No/Unclear
Could the patient flow have introduced bias? RISK: LOW	/HIGH/UNCLEAR

### Appendix 0-7. Summary of studies excluded.

Study (Year)	Subject Characteristics	Diagnsotic Test Items	Reference Standard	Diagnostic Accuracy Measures	Conclusions
Deyo, R. A., & Mirza, S. K. (2016). Herniated lumbar intervertebral disk. <i>New England Journal of Medicine</i> , 374 (18), 1763-1772.	Single patient vignette.	Pain (dermatome) Numbness Motor weakness Screening examination for L4, L5, S1 (e.g. squatting and rising, walking on heels, walking on toes Reflexes	MRI Surgical Findings	Only estimates of accuracy of history and physical examination findings	This is not a primary study rather a review with clinical recommendations. Ccontains only estimates of accuracy of history and physical examination findings
Janardhana, A. P., Rao, S., & Kamath, A. (2010). Correlation between clinical features and magnetic resonance imaging findings in lumbar disc prolapse. Indian journal of orthopaedics, 44(3), 263-269.	119 clinically diagnosed patients with lumbar disc prolapse	No description of index tests. The clinical criteria used a) low backache with radiation to the lower limb, b) radicular pain along a specific dermatome, c) nerve root tension signs like straight leg raising test (SLRT) and d) presence of neurological symptoms and signs.	MRI	Sensitivity, positive and negative predictive values, odds ratios	Clinical findings correlate well with MRI findings, but all MRI abnormalities need notave a clinical significance. The presence of centrolateral disc protrusion and extrusions with gross neural foramen compromise is invariably associated with clinical signs and symptoms. Disc bulges with thecal sac compromise or central protrusions and extrusions without significant neural foramen compromise are clinically insignificant. The presence of neural foramen compromise is more important in determining the clinical signs and symptoms while the type of disc hermition (bulge, protrusion, or extrusion) correlates poorly with clinical signs and symptoms. Whenever there are multiple level disc keisns with neural foramen compromise, patients are likely to have objective neurological deficits.
Walsh, J., & Hall, T. (2009). Agreement and correlation between the straight leg raise and slump tests in subjects with leg pain. Journal of manipulative and physiological therapeutics, 32(3), 184-192.	45 patients with unilateral leg pain recruited from an outpatient Back Pain Screening Clinic at a large teaching hospital in Ireland	SLR;, slump test	No reference standard	Only ICC	In a population of patients with low back and leg pain, when reproduction of presenting symptoms that were intensified by ankle dorsiflexion was interpreted as a positive finding, the SLR and slump tests were highly reliable.

Appendix 0-8. Quadas 2 tool findings for risk of bias and applicability. Vroomen et al. 2002.

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B. Concern regarding applicability	Is there concern that the target condition as defined.	1 - <b>1479</b> 	Leve
BOMAIN & FLOW AND TIMING	Describe any patient who dataset is centre the indexts (t)) and the principal of a who ways can index if from the 2 X 2 table is for the two set in dest from the 2 X 2 table is for the two set.	In d. 200 yokur van adami for in fingerie rwiy. Deyriver van enheld (2) barre - in ditter pie od 17 berne of partie vynde wanyer enhelderten v III. henne Die die wartigelen van enhel of in IV yekan.	(b) (2) Hitpeten wan adami its in fastaseta subjectiventy flaty it wann outblack(3) haar of neuflicant pointed. It because of parameter spin-lengage as a stabilities in a 323 mapsing. Day the inner spin-lengameter matching spinor.
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Nace 1: State the variant question:	What are the clinical class and symptoms of disconsision back nois	SW	JP The current environment to compare disperses derived from a detailed clinical
			examination by a physiotherapist, with expert diagnoses obtained using available reference
			standards for diagnosis of discogenic, facetogenic, SU, hip joint, nerve root pain and symptomatic spinal stenosis.
	Patients (setting, intended use of index test, presentation, prior testing/:	chronic LBP patients through a clinical examination.	296 patients were invited to participate. 53 were excluded. 216 patients were included. Of those .95 were identified as having disc related low back pain.
	Index test(s):	Clinical examination by a physiotherapist.	p. 4. "The clinical reasoning by which the physiotherapist reached a diagnosis has been
			presented elsewhere in defait [18,19]. Discogene pain was concluded when centralisation peripheralisation [20-22] or directional preference were reported by the patient during an
			examination with repeated standardised end range test movements [24], or if the dominant primary pain was located in the exact midline of the lumbar spine. (reference 18) Laslett M
			Wijmen P: Low back and referred pain: diagnosis and a proposed new system of classifica
			NZ Journal of Physiotherapy 1999, 27:5-14. Quote taken from the paper; (p. 8) In this paper it is not possible to give details of the physical examination method uses
			differentiate between disc, SIJ and ZJ pain. The paper by Donekon, R. et al. (1997) gives excellent summary of the McKenzie method of examination that was used in their study.
			study comparing diagnostic judgements from the physical examination and injection into th
			(Young, S. et al. 1998) demonstrates that a good level of diagnostic power was achieved." examination method used was the McKenzie assessment augmented by provocation stress
			of the SIJ (Laslett, M. & Williams, M. 1994). A specific reasoning process using the McK
			enabling an improved ability to differentiate between SU and non-SU cases. Study of these
			papers will give the reader sufficient information to understand the method. (reference 19 Petersen T, Laslett M, Thorsen H, Manniche C, Ekdahl C, Jacobsen S: Diagnostic classifi
			of non-specific low back pain. A new system integrating patho-anatomic and clinical catego
	Reference standard and tarnet condition	Imaging based on flagsroomically mided disputcies injections for the target	Reference Standard Procedures: Discourseby n= 118: ZI Blocks n= 150: SII Blocks n=
		condition of chronic low back pain	Hip joint blocks n= 8; Epidurals n= 30; Other procedures: bone harvest site n= 1; pedicle
			Iracture n= 1; myelogram n= 1; guiteat bursa: n= 2; Discography + ZJ + SIJ Blocks n= 80 Reference Standard Diagnoses: Disc n =83; ZJ n =22; SIJ n = 6; NR n =28; Stenosis n
			Hip n = 7; Illness Beh n =58; Indeterminate n =63; Instability n = 2; Other n = 4
ase 2: Draw a flow diagram for the primary study			
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		100000000 + 2 (0000 + 1	Table 1 - 2 (Table 1 - 4
hase 3: Risk of bias and applicability judgments			
OMAIN 1: PATIENT SELECTION	Describe methods of patient selection:	Consecutive chronic LBP patients who attended clinic between May 2001 and	No description of how the original 1219 patients were identified.
. Risk of Bias	Was a consecutive or random sample of patients enrolled?	October 2002 were recruited.	Yar
	Was a case-control design avoided?	Yes	No
	Did the study avoid inappropriate exclusions? Could the selection of notionst have introduced blac?	Unclear	Unclear
	Courd the selection of particle nave infloated bass.	UBAR	UIKAR
: Concerns regarding applicability	Describe included patients (prior testing, presentation, intended use of index test and catting):	The aim was to investigate the diagnostic performance of clinical examination for diagnosis of LBP. Participants included those seen at a pain clinic to receive	The patients in this sample were referred for invasive diagnostic testing and were typically chronic with hish levels of distress and disability. Most patients had failed multiple attempt
	tons appa motorey.	a block. Prior radiographic testing was conducted to provide a diagnosis. No	treatment, and many had seen a number of general and specialist clinicians without a satisf
	ters and senange	where he has a market a second s	I discussed a balance second and "This second and a second second as a second second second second second second
	ters and minings.	other information on prior testing or presentation of patients was provided.	diagnosis being provided. This was anticipated prior to commencement of the data collectia phase of the project, and it was accepted that psychosocial distress would impact on the ab
	wa and wang).	other information on prior testing or presentation of patients was provided.	diagnosis being provided. This was anticipated prior to commencement of the data collecti phase of the project, and it was accepted that psychosocial distress would impact on the ab of physiotherapy and reference standard elinicians to make a tissue specific diagnosis
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#### Appendix 0-9. Quadas 2 tool findings of risk of bias and applicability. Laslett et al. 2005.

#### Appendix 0-10. Quadas 2 tool findings for risk of bias and applicability. Hancock et al. 2011.

	Hancock, M. J., Koes, B., Ostelo, R., & Peul, W. (2011).	Diagnostic accuracy of the clinical examination in identifying the i	level of herniation in patients with sciatica. Spine, 36(11), E712-E71	9.
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Appendix 0-11. Summary of diagnostic accuracy of key clinical tests used in the study available at the commencement of the study. Laslett et al. 2005.

commencement o	f the study.			
Disorder	Test / Sign / Variable	%Sensitivity	%Specificity	References
Lumbar HNP	Ipsilateral SLR	76-97	11-45	[71] [72] [73]
	Contralateral SLR	23-27	88-100	[71] [72] [74] [73]
	Weakness ankle dorsiflexion	20-49	54-82	(71] [72]
	Weakness EHL	0.37	0.71	[72]
	Ankle reflex weak	50-52	62-63	[71] [72]
	Sensory loss	0.66	0.51	[73]
	Patellar reflex weak	40-70	93-97	[71] [72]
	Quads weakness	0.1	0.99	[72]
	Ankle PF weakness	0.6	0.95	[72]
LSP disc /positive discography	Centralization or peripheralisation	0.94	0.52	[22,75] [22](calculations based on data provided)
	Centralization	0.92	0.64	
	Peripheralization	0.69	0.64	[22](calculations based on data provided)

Laslett, 2005 Summary of diagnostic accuracy of key clinical tests used in the study available at the commencement of the study.

#### Appendix 0-12. Details of history taking and physical examination techniques. Vroomen et al. 2000.

Vroomen, P. C., de Krom, M. C., & Knottnerus, J. A. (2000). Consistency of history taking an	d physical examination in patients with suspected lumbar nerve root involvement. Spine, 25(1), 91.

and the work of the set of the set of the
Appenaix II: Technique of the Physical Examination
Appendix II: Technique of the Physical Examination The reference numbers indicate the original descriptions. of the investigation techniques. With the patient standing erect and firmly on both feet with the arms along the body: Decreased lumbar lordosis (yes, no): A decrease in lumbar curvature was assessed. Antalgic posture (yes, no): While the epatient attained the most comfortable standing posture, it was determined whether there was a convex scollosis and a flexed knee on the afflicted side. Lumbar scollosis (yes, no): If there was a deviation in the coronal plane, the convexity of the scollosis was denominated. Lumbar anteflexity (yes, no): The level of the sacrolliac joint and a level 10 cm cranial to this level were marked. Then, with the patient trying to reach the floor with the extended fingers of both hands without bending the knees, the increase in distance between the two marks was noted in millimeters. This was labeled the Scho: ber (P4). The distance between the floor and the third digit was measured (finger floor distance). A goniometer, the plurimeter-V, was used to measure the degrees of thoracal and sacral flexion.9 Tenderness on percussion over the lumbar vertebrae (yes, with radicular radiation; yes, pinful without radicular radiation; yes, but not painful; no): The paravertebral musculature was plapeted for indurations. Kemp's sign (no pain, ipsilateral pain to the leg, contralateral pain to the back, ipsilateral pain in the back, contralateral pains the back was hyperextended and sinu na naih. Both interval is was were were site was envireed was an one pain the pain numbar neosyly lateroflexed by the observer. The lovation of the envirential and was creative and the envirence and the envirence and the envirence and the environs of the environs of the environs of the environs of the environs of the environs of the environs of the environs of the environs of the environs of the environs of the environs of the environs of the environs of the environs of the environs of the environs of the en
location of eventual pain was registered. Naftziger's sign (typical pain in the leg, nontypical pain, no pain). Both internal jugular veins were compressed manually for a minimum duration of JO seconds. The patient was asked whether a blushing or pressure sensation in the head occurred. If so, the patient was tasked to describe any other sensations. Head flexion symptom (no pain, pain in the back, pain in the leg): Pain in the leg on head flexion is noted (also referred to as Hyndham sign) Walking on heels (undisturbed, disturbed): This is disturbed when any part of the foot other than the heel touches the floor with the patient walking on his or her heels. Walking on the toes (undisturbed): This is disturbed when the heel touches the floor with the patient walking on his or her toes. Knee bending (undisturbed, disturbed): The patient was asked to stand on one leg and bend the knee (90°). Any flexion failure was registered as disturbed. With the patient suppone on a flat investigation table with a single pillow: Decreased or painful mobility of the hip: The leg was flexed (90) Ta the knee and the hip and then passively endo- and exorotated at the hip. And hen passively endo- and exorotated at the hip. Pain and/or decreased mobility of the hip was noted. Straight leg raising (SLR) test (negative, pain in the back only, pain in the leg in a nondermatomal distribution, pain in the leg in a dermatomal distribution, pain in the l

#### Appendix 0-13. Diagnostic accuracy measures of the history. Vroomen et al. 2002.

Vroomen, P. C. A. J., De Krom, M. C. T. F. M., Wilmink, J. T., Kester, A. D. M., & Knottnerus, J. A. (2002). *Diagnostic value of history and physical examination in patients suspected of lumbos acral nerve root compression. Journal of Neurology, Neurosurgery & Psychiatry, 72(5), 630-634.* 

Table 2 Diagnostic accuracy of the history (n=274)				
Characteristic	MRI+ (n=152)	MRI- (n=122)	Odds ratio (95% CI)	
Pain worse in leg than in back	125	56	5.5 (3.2 to 9.4)	
Typically dermatomal distribution	136	84	3.8 (2.0 to 7.3)	
Pain worse on coughing/sneezing/				
straining	76	40	2.1 (1.3 to 3.4)	
Dermatomal cold sensations in leg	47	24	1.8 (1.0 to 3.2)	
More pain on sitting	82	69	0.9 (0.6 to 1.5)	
Less pain standing or walking	31	26	0.9 (0.5 to 1.7)	
Less pain on lying down	91	69	1.1 (0.7 to 1.9)	
Sudden onset	60	51	0.9 (0.6 to 1.5)	
Paroxy smal pattern	67	47	1.3 (0.8 to 2.0)	
Pain worse at night	47	42	0.9 (0.5 to 1.4)	
With known cause	38	37	0.8 (0.5 to 1.3)	
Subjective muscle weakness	41	46	0.6 (0.4 to 1.0)	
Subjective sensory loss	60	51	0.9 (0.6 to 1.5)	
Dermatomal paraesthesiae	78	72	0.7 (0.5 to 1.2)	
Previous back pain episodes	113	85	1.3 (0.7 to 2.1)	
Previous sciatica	55	52	0.8 (0.5 to 1.2)	
History indicating root compression				
according to investigator	118	64	3.1 (1.9 to 5.3)	
Values in bold indicate significant effect.				
CI, confidence interval; MRI+/-, magnetic resonance				

#### Appendix 0-14. Diagnostic accuracy measures of the physical examination. Vroomen et al. 2002.

Vroomen, P. C. A. J., De Krom, M. C. T. F. M., Wilmink, J. T., Kester, A. D. M., & Knottnerus, J. A. (2002). *Diagnostic value of history and physical examination in patients suspected of lumbosacral nerve root compression. Journal of Neurology, Neurosurgery & Psychiatry, 72(5), 630-634.* 

Table 3 Diagnostic accuracy of the physical examination (n=274)				
Characteristic	MRI+ (n=152)	MRI- (n=122)	Odds ratio (95% CI)	
Paresis	41	8	5.2 (2.4 to 11.7)	
Finger-floor distance >25 cm	68	32	2.4 (1.4 to 4.0)	
Absence of ankle/knee tendon reflex	22	8	2.4 (1.0 to 5.6)	
Positive SLR	97	53	2.3 (1.4 to 3.7)	
Sensory loss				
Hypesthesia	48	42	0.8 (0.5 to 1.3)	
Hypalgesia	26	19	1.2 (0.6 to 2.1)	
History and examination indicating root				
compression according to investigator	123	59	4.5 (2.6 to 7.8)	
Values in bold indicate significant effect.				
CL confidence interval: MRI+/- magnetic resonance	e imaging positive or	negative: SLR_straig	nt leo raise	

Appendix 0-15. Predictors of nerve root compression on magnetic resonance imaging: results of multiple logistic regression analysis. Vroomen et al. 2002.

Vroomen, P. C. A. J., De Krom, M. C. T. F. M., Wilmink, J. T., Kester, A. D. M., & Knottnerus, J. A. (2002). Diagnostic value of history and physical examination in patients suspected of lumbosacral nerve root compression. Journal of Neurology, Neurosurgery & Psychiatry, 72(5), 630-634.

# Table 4 Predictors of nerve root compression on magnetic resonance imaging: results of multiple logistic regression analysis (n=274)

Test	Adjusted	95% CI
	diagnostic OR	
History		
Age (years)		
41–50 v 16–40	1.8	1.3 to 2.6
51–81 v 16–40	2.8	1.9 to 4.2
Duration of disease (days)		
15–30 v <15	2.2	1.5 to 3.3
>30 v <15	0.8	0.6 to 1.1
Paroxysmal pain	1.8	1.3 to 2.5
Pain worse in leg than in back	4.5	3.3 to 6.2
Typical dermatomal distribution	3.2	2.2 to 4.7
Pain worse on		
coughing/sneezing/straining	2	1.4 to 2.7
Physical examination		
Finger-floor distance (cm)		
5-24 v 0-4	1.1	0.7 to 1.6
>25 v 0-4	2.8	1.9 to 4.3
Missing v 0–4	1	0.4 to 2.1
Paresis	5.2	3.3 to 11.6
Intercept -3.511		
CI, confidence interval; OR, odds ra	tio.	

Appendix 0-16. Area under the curve: diagnostic evaluation of history and physical examination. Vroomen et al. 2002.



# Appendix 0-17. Diagnostic accuracy of the clinical examination in identifying the level of herniation in patients with sciatica. Hancock et al. 2011.

Hancock, M. J., Koes, B., Ostelo, R., & Peul, W. (2011). Diagnostic accuracy of the clinical examination in identifying the level of herniation in patients with sciatica. Spine, 36(11), E712-E719.

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ccccc									
Predictor		L3/4 Disc Hemiation		L4	5 Disc Hemiation			L5/81 Disc Herniati	on
	Sens	Spec	AUC	S ens	Spec	AUC	Sens	S pec	AUC
Knee reflex	0.5	0.83	0.64	0.19	0.82	0.49	0.16	0.787	0.48
	(0.21-0.79)	(0.78-0.87)	(0.46-0.82)	(0.12-0.27)	(0.75-0.88)	(0.42-0.56)	(0.11-0.23)	(0.69-0.85)	(0.41-0.55)
Ankle reflex	0.27	0.64	0.46	0.16	0.49	0.34	0.48	0.83	0.66
	(0.06-0.61)	(0.58-0.70)	(0.29-0.63)	(0.10-0.24)	(0.41-0.57)	(0.27-0.40)	(0.40-0.56)	(0.75-0.90)	(0.59-0.72)
Sensory loss L4	0.42	0.74)	0.56 (0.38–74)	0.33	0.79	0.55	0.23	0.68	0.47
	(0.15-0.72)	(0.69-0.79	(0.69-0.79	(0.25-0.42)	(0.72-0.85)	(0.48-0.62)	(0.17-0.30)	(0.59-0.77)	(0.400.54)
Sensory loss L5	0.5	0.48	0.47	0.6	0.54	0.57	0.48	0.4	0.44 (0.37-0.51)
	(0.21-0.79)	(0.41-0.54)	(0.30-0.64)	(0.51-0.69)	(0.45-0.62)	(0.50-0.64)	(0.400.56)	(0.31-0.50)	(0.31-0.50)
Sensory loss Sl	0.33	0.48	0.38	0.44	0.43	0.42	0.59	0.6	0.6
	(0.10-0.65)	(0.41-0.54)	(0.22-0.54)	(0.35-0.54)	(0.35-0.50)	(0.36-0.50)	(0.51-0.66)	(0.50-0.69)	(0.53-0.67)
Quadriceps weakness	0.67	0.4	0.52	0.64	0.42	0.52	0.61	0.39	0.51
	(0.35-0.90)	(0.34-0.46)	(0.35-0.69)	(0.55-0.72)	(0.34-0.50)	(0.45-0.59)	(0.53-0.68)	(0.30-0.49)	(0.44-0.58)
Tibialis anterior weakness	0.5	0.64	0.56	0.46	0.7	0.58	0.32	0.56	0.44
	(0.21-0.79)	(0.58-0.70)	(0.38-0.73)	(0.37-0.55)	(0.63-0.77	(0.51-0.65)	(0.25-0.40)	(0.46-0.66)	(0.37-0.51)
Peroneals weakness	0.58	0.61	0.59	0.5	0.68	0.59	0.34	0.51	0.43
	(0.28-0.85)	(0.55-0.67)	(0.41-0.76)	(0.41-0.59)	(0.60-0.75)	(0.52-0.66)	(0.27-0.42)	(0.42-0.61)	(0.360.50)
EHL weakness	0.5	0.57	0.52	0.54	0.64	0.59	0.38	0.47	0.43
	(0.21-0.790)	(0.50-0.63)	(0.34-0.69)	(0.44-0.63)	(0.56-0.72)	(0.52-0.66)	(0.30-0.46)	(0.38-0.57)	(0.36-0.50)
Calfweakness	0.42	0.67	0.53	0.39	0.72	0.55	0.3	0.63	0.47
	(0.15-0.72)	(0.61-0.73)	(0.35-0.70)	(0.30-0.48)	(0.64-0.79)	(0.48-0.62)	(0.23-0.38)	(0.53-0.72)	(0.40-0.54)
									1
Shaded cells represent the	he optimal test in ea	ich category (refle	x, sensation, and	strength) for ea	achlumbar di	sc if AUC is	> 0.55.		
Values in each cell are e	stimate and 95% co	onfidence interval	s.						
Sens indicates sensitivit	v: spec. specifi citv	AUC, area under	curve.						

#### Appendix 0-18. Recent studies on diagnostic accuracy of tests for nerve root compression.

Author and Year	Study	Study Purpose	Test	Reference Standard	Diagnositc Outcome Measures	Conclusion
Tawa, N., Rhoda, A., & Diener, I. (2017).	Accuracy of clinical neurological examination in diagnosing lumbo- sacral radiculopathy: a systematic literature review. <i>BMC</i> <i>musculoskeletal</i> <i>disorders</i> , 18(1), 1-11.	Analysed accuracy of index tests for diagnosing lumbo-sacral radiculopathy (sensory, motor, reflex and neuro-dynamic) comparing to MR imaging, electro-diagnostics or intra- operative findings	Sensory, Motor, Reflexes, Femoral n. stretch, Straight leg raise	MRI	Sensitiity, specificity including 95% confidence intervals	Scarcity of studies on diagnostic accuracy of clinical neurological testing able to detect disc hernation. Did not consider disc hermiation as the cause of nerve root impingement and subsequent radiculopathy
González Espinosa de los Monteros, F. J., Gonzalez-Medina, G., Ardila, E. M. G., Mansilla, J. R., Expósito, J. P., & Ruiz, P. O. (2020).	Use of neurodynamic or orthopedic tension tests for the diagnosis of humbar and lumbosacral radiculopathise: study of the diagnosic validity. International Journal of Environmental Research and Public Health, 17(19), 7046.	Aim was of estimating the diagnostic validity of the following orthopedic stress tests and/or neurodynamic tests (performed individually, in combination and in parallel	Straight leg raise, Bragard test & combined tests of both, Fajersztajn test, Sicard test, and the combined tests of both, the Passive Neck Flexion test, the Kernig test and combinned tests of both, combinned tests of both, Dejerine's triad and the test combining both	MRI	Sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios, and diagnostic odds ratios (DORs)	Tests haveg no clinical utility when performed individually: Passive Neck Flexion test, the Dejerine's triad, the Straight Leg Raise test, the Bragard test, the Fajerstratjn test, the Shump test, the Sicard test and the Kernig test. Combined tests - Shump test, Dejerine's triad, Straight Leg Raise, Bragard test sow validity (internal and external).
Ekedahl, H., Jönsson, B., Annertz, M., & Frobell, R. B. (2018)	Accuracy of Clinical Tests in Detecting Disk Hernitation and Nerve Root Compression in Subjects With Lumbar Radicular Symptoms	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), 726-735.	Slump test, SLR, femoral n. test, radiculopathy 1* and II**, sensory, tendon refixess, muscle weakness* one neurologic signs was present and corre sponded to the nerve root of the planned steroid injection **2 neurologic signs (sensory deficit or reflex impairment or muscle weakness) were present and corresponded to the specific nerve root of the planned steroid injection	MRI	Sensitivity, specificity, and receiver operating characteristics analysis with area under the curve inchafung 95% confidence intervals, and secondarity evaluated using positive and negative predictive values, positive and negative likelihood ratios, and diagnostic odds ratios	Investigated neurodynamic tests for radiculopathy lacked diagnostic accuracy. The slump test was the most sensitive test, while radiculopathy II was the most specific test. Most interestingly, no relationship was found between any neurodynamic test and foraminal nerve compression (foraminal stenosis) as visualized on MRI.
Al Nezari, N. H., Schneiders, A. G., & Hendrick, P. A. (2013).	Neurological examination of the peripheral nervous system to diagnose lumbar spinal disc hemiation with suspected radiculopathy: a systematic review and meta-analysis. <i>The Spine</i> <i>Journal</i> , <i>13</i> (6), 657-674.	To review the scientific literature to evaluate the diagnostic accuracy of the neurolog- ical examination to detect lumbar disc herniation with suspected radiculopathy.	Motor testing for function, atrophy and for weakness/paresis, sensory testing, Achilles and patellar reflexes	MRI, surgical findings, computed tomography, and myelography	Sensitivity, specificity, pos and neg likelihood ratios, diagnostic odds ratio	Ability of neurological testing procedures to detect either a disc hemiation or the level of hemiation was poor
Verwoerd, A. J., Peul, W. C., Willemsen, S. P., Koes, B. W., Vleggeert-Lankamp, C. L., el Barzouhi, A., & Verhagen, A. P. (2014)	Diagnostic accuracy of history taking to assess lumbosacral nerve root compression. <i>The Spine</i> <i>Journal</i> , <i>14</i> (9), 2028-2037.	To assess the diagnostic accuracy of history taking for the presence of lumbosacral nerve root compression or disc herniation on magnetic resonance imaging in patients with sciatica.	History items pre-selected from the literature (age, gender, pain worse in leg than in back, sensory loss, muscle weakness, and more pain on coughing/sneezing/straining	MRI	Odds Ratios	For now, the diagnostic accuracy of history taking in assessing lumbosacral nerve root compression and disc herniation on MRI seems to be more limited than previously assumed. This may cause difficulty in distinguishing between specific symptoms and nonspecific symptoms

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	Currier		25 500/							
			25.50%							
	Myofascial Techniques		35.50%							
	Mulligan	38	34.50%							
	Kaltenborn	35	31.80%							
	Muscle Energy	26	23.60%							
	Osteopathic	23	20.90%							
	Chiropractic	11	10.00%							
	Other	31								
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	Biomechanical Assessment as taught by the Orthopedic Division of the									
	Canadian Physiotherapy P	Association								
	Clinical patterns as descrit			•						
	Combo of biomechanics and psychosocial with some neuroscience									
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	Patient response									
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#### Appendix 0-19. Physical examination protocols reported to be used by survey respondents.

Appendix 0-20. Volumetric comparisons between three time points following initial segmentation.

Time:	41		49			90			
		$(mm^2)$	Change			Cha	Change		
<u>Disc</u>	voi (mms)	voi (mms)	mm3	%	voi (mm3)	mm3	%		
1	9,898.0	10,700.4	802.4	8.1	9,995.2	97.2	1.0		
2	12,987.7	14,156.5	1,168.8	9.0	13,329.5	341.8	2.6		
3	14,184.4	14,554.8	370.4	2.6	13,573.5	- 610.9	- 4.3		
4	12,470.2	14,098.5	1,628.3	13.1	12,467.7	- 2.5	- 0.0		
5	9,869.1	11,285.1	1,416.0	14.3	10,619.8	750.7	7.6		
Total	59,409.4	64,795.3	5,385.9	9.1	59,985.7	576.3	1.0		

Participant S1559

Participant S1632

Time:	11	28			55			
	$\lambda = (mm^2)$	$(mm^2)$	Change			Change		
<u>Disc</u>	voi (mms)	voi (mms)	mm3	%	voi (mms)	mm3	%	
1	10,347.8	10,581.6	233.8	2.3	12,074.9	1,727.1	16.7	
2	11,504.2	11,504.5	0.3	0.0	12,741.0	1,236.8	10.8	
3	14,277.5	15,120.1	842.6	5.9	14,856.4	578.9	4.1	
4	14,925.2	14,623.1	- 302.1	- 2.0	15,109.1	183.9	1.2	
5	14,291.6	13,273.2	- 1,018.4	- 7.1	14,589.9	298.3	2.1	
Total	65,346.3	65,102.5	- 243.8	- 0.4	69,371.3	4,025.0	6.2	

Participant S4296

Time:	48	65			83			
	$\lambda = (mm^2)$	$(mm^2)$	Change		Vol (mm2)	Change		
<u>Disc</u>	voi (mms)	voi (mms)	mm3	%	voi (mms)	mm3	%	
1	7,157.6	6,520.2	- 637.4	- 8.9	6,474.0	- 683.6	- 9.6	
2	10,193.4	11,057.9	864.5	8.5	9,820.5	- 372.9	- 3.7	
3	13,472.0	12,648.6	- 823.4	- 6.1	12,456.5	- 1,015.5	- 7.5	
4	13,370.2	12,379.1	- 991.1	- 7.4	13,268.2	- 102.0	- 0.8	

5	11,521.3	9,056.4	- 2,464.9	- 21.4	11,590.5	69.2	0.6
Total	55,714.5	51,662.2	- 4,052.3	- 7.3	53,609.7	- 2,104.8	- 3.8

Participant	S5383
-------------	-------

Time:	51	59			62			
	Vol (mm2)	$(mm^{2})$	Change			Change		
<u>Disc</u>	voi (mms)	V0I (IIIII3)	mm3	%	voi (mms)	mm3	%	
*1	8,903.4	9,480.9	577.5	6.5	11,540.6	2,637.2	*29.6	
2	9,997.8	10,123.5	125.7	1.3	10,730.6	732.8	7.3	
3	12,264.2	11,985.4	- 278.8	- 2.3	12,936.7	672.5	5.5	
4	12,409.3	12,733.8	324.5	2.6	12,821.9	412.6	3.3	
5	9,656.5	9,022.9	633.6	- 6.6	10,452.1	795.6	8.2	
Total	53,231.2	53,346.5	115.3	0.2	58,481.9	5,250.7	9.9	

\* Time 62 for disc 0001 changed by 29.6% volume compared to Time 51. All other initial disc volumetric comparisons showed variations of less than 9%.

Particip	Jani 30025				-			
Time:	37	69			99			
		$(mm^{2})$	Cha	nge	Vol (mm2)	Cha	inge	
<u>Disc</u>	voi (mm3)	voi (mm3)	mm3	%	voi (mm3)	mm3	%	
1	21,592.8	19,558.1	- 2,034.7	- 9.4	24,445.6	2,852.8	13.2	
2	22,328.5	20,348.6	- 1,979.9	- 8.9	22,174.8	- 153.7	- 0.7	
3	22,187.4	21,319.8	- 867.6	- 3.9	22,575.3	387.9	1.7	
4	24,288.8	23,934.4	- 354.4	- 1.5	24,637.1	348.3	1.4	
5	17,080.4	17,615.5	535.1	3.1	18,648.7	1,568.3	9.2	
Total	107,477.9	102,776.4	- 4,701.5	- 4.4	112,481.5	5,003.6	4.7	

## Participant S6625

Appendix 0-21. Error in initial segmentation for participant S5383. A. Initial segmentation error indicated by arrow. B. Segmentation error corrected.



Appendix 0-22. Volumetric comparison of participant S5383 following segmentation correction.

Time:	51		59			62			
		(mm2) /(al (mm2)		nge		Cha	nge		
<u>Disc</u>	voi (mms)	voi (mm3)	mm3	%	VOI (IIIII3)	mm3	%		
*1	8,903.4	9,480.9	577.5	6.5	9,253.8	350.4	*3.9		
2	9,997.8	10,123.5	125.7	1.3	10,730.6	732.8	7.3		
3	12,264.2	11,985.4	-278.8	-2.3	12,936.7	672.5	5.5		
4	12,409.3	12,733.8	324.5	2.6	12,821.9	412.6	3.3		
5	9,656.5	9,022.9	-633.6	-6.6	10,452.1	795.6	8.2		
Total	53,231.2	53,346.5	115.3	0.2	56,195.1	2,963.9	5.6		

Participant S5383

Appendix 0-23. Combined PC scores of all discs (L1-L2 to L5-S1) of each participant before and after 2 minutes of right rotation, with mean scores of the entire group presented in the right-most column. The two pre-repositioning scores are averaged. Group means, mean differences, and 95%CI of the difference are presented in the right most column. Significant differences are bolded.

	Participa	nt				
	1	2	3	4	5	Mean & Mean Difference (95%Cl)
Mode						
1 - Pre	-19.454	3.22	-28.378	-28.448	59.206	-2.7708
1-Post	-22.34	7.056	1.184	-24.264	66.074	5.542
Difference	-2.886	3.836	29.562	4.184	6.868	8.32 (-2.63; 19.26)
2-Pre	-8.14	1.744	3.226	-0.384	4.708	0.2308
2- Post	-7.602	-0.978	0.286	0.888	5.09	-0.4632
Difference	0.538	-2.722	-2.94	1.272	0.382	-0.69(-7.21; 5.82)
3-Pre	11.286	4.422	-9.276	8.366	-19.748	-0.99
3-Post	10.504	-1.616	3.804	12.36	-15.154	1.9796
Difference	-0.782	-6.038	13.08	3.994	4.594	2.97(-1.61; 7.55)
4-Pre	-0.474	-6.33	-5.428	10.242	6.33	0.868
4-Post	0.59	-5.756	-7.942	7.96	-3.522	-1.734
Difference	1.064	0.574	-2.514	-2.282	-9.852	-2.60(-4.79; -0.41)
5-Pre	0.064	2.668	-3.108	2.48	-4.802	-0.5396
5-Post	-1.492	5.262	-3.676	3.226	2.066	1.0772
Difference	-1.556	2.594	-0.568	0.746	6.868	1.62(-0.79; 4.02)
6-Pre	-2.052	4.704	-3.282	0.792	1.226	0.2776
6-Post	-4.136	2.228	-2.598	-0.262	1.99	-0.5556

Difference	-2.084	-2.476	0.684	-1.054	0.764	-0.83(-2.87; 1.21)
7-Pre	-6.192	3.472	3.002	3.038	-0.804	0.5032
7-Post	-5.994	0.918	2.234	1.632	-3.822	-1.0064
Difference	0.198	-2.554	-0.768	-1.406	-3.018	-1.51(-2.65; -0.37)
8-Pre	0.73	0.958	-0.472	-0.884	-0.364	-0.0064
8-Post	1.234	-0.722	-0.536	-0.072	0.15	0.0108
Difference	0.504	-1.68	-0.064	0.812	0.514	0.02(-0.80; 0.83)
9-Pre	0.028	0.438	0.336	1.204	-0.078	0.3856
9-Post	-0.784	0.326	0.456	-2.252	-1.61	-0.7728
Difference	-0.812	-0.112	0.12	-3.456	-1.532	-1.16(-2.69; 0.37)
10-Pre	-0.036	-0.29	0.628	-0.228	1.39	0.2928
10-Post	1.082	-0.452	-0.336	-0.518	-2.706	-0.586
Difference	1.118	-0.162	-0.964	-0.29	-4.096	-0.88(-2.23; 0.47)

Appendix 0-24. Flow diagram of summary of three dissertation projects.



Appendix 0-25. Clinical support system long term research goals, potential research questions and proposed study topics.

Clinical Support System Long Term Research Goals, Potential Research Questions and Proposed Study Topics

- 1. Identify homogeneous subgroups of patients with NSLBP based on clusters of symptoms and signs (Kent et al., 2009);
- 2. What are the signs and symptoms of a reducible lumbar disc herniation (RDLBP)?
- 3. Can the signs and symptoms of a reducible lumbar disc herniation be validated?
- 4. Are there subgroups of reducible disc herniations and if so, what are their clinical characteristics?
- 5. If there are subgroups of RDLBP, are there differences in effects on the subgroups with various forms of spinal manipulative therapies using MRI?
- 6. What are the kinds of herniations observed using MRI on patients with suspected RDLBP in a large sample?
- 7. What are the mechanisms of regression for RDLBP herniations and non-reducible herniations?
- 8. Use magnetic resonance imaging (MRI) technology to explore and evaluate the association between the centralization phenomenon (CP) and the quantification of disc morphology in patients with suspected RDLBP;

The unique structural architecture of the disc among individuals likely means that treatment has to be tailored to each individual based on the clinical presentation of symptoms and signs and responses to mechanical loading strategies. (i.e., the non-linear response of a disc means the magnitude and direction of the effects of mechanical loading strategies will be unique to patients with different clinical presentations of RDLBP herniations).

9. Investigate the effects of force, amplitude, direction, number of repetitions and length of application time of various spinal manipulative therapies on disc morphology (*There are few guidelines to clinicians outlining the steps to achieve centralization based on the clinical presentation of the signs and symptoms of RDLBP herniations using mechanical loading strategies*).

There is a need to focus on understanding the mechanisms that are involved in acute NSLBP from paraspinal tissues beginning with a careful investigation of the cellular and molecular mechanisms of nociception and mechansensitivity in paraspinal tissues comparable in scope to what is known from cutaneous tissue studies. This data would help to define primary afferents associated with specific modalities and provide useful genetic tools with which to analyze the pathways activated by functionally distinct neuronal populations and transmitters (Lagerström et al., 2011). Ideally to study the pathways involved in the process of nociception from paraspinal tissues, a preparation of isolated nociceptors is needed (Fein, 2012). Fein reports that the free nerve endings of nociceptors are extremely fine and embedded in a tissue matrix, which if dissected to isolate the nociceptors, would release the very molecules that the nociceptor nerve terminal is meant to detect. Because of this lack of accessibility, it is not currently possible to directly study the nociceptor transduction machinery both in an unstimulated state and in its' normal native environment. Instead, the following two research projects are proposed in items 10 and 11 below.

- 10. The first study proposes to identify the type of proteins in nociceptor and mechanosensitive afferents in the IVD, PLL and the ventral aspect of the dura mater using an enzyme linked immunosorbent assay (ELISA). Specifically using 2 dimensional poly acrylamide gel electrophoresis (2D-PAGE) to determine the proteins of greatest relative abundance in the human disc, posterior longitudinal ligament and ventral dura mater.
- 11. In a second study, the use of immunohistochemistry to analyze the proteins of relative abundance found in Study 1 will be conducted.
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#### Appendix 0-38. Ethics approval letter for survey.

Principal Investigator: Dr. Dave Walton         Department & Institution: Health Sciences/Physical Therapy, Western University         INERE File Number: 105100         Study Title: A survey of practice beliefs and patterns of health practitioners who use manual treatments for patients withow back pain         Sponsor:         HSREB Amendment Approval Date: October 22, 2014         HSREB Expiry Date: February 28, 2015         Documents Approved and/or Received for Information:         Document Name       Comments         Version Date         The Western University Health Science Research Ethics Board (HSREB) has reviewed and approve the amendment to the above named study, as of the HSREB Amendment Approval Date noted above, condition to timely submission and acceptance of HSREB Continuing Ethics Review. If an Updated Approval Notice is required prior to the HSREB Expiry Date noted above, condition to tomely submission and acceptance of HSREB Continuing Ethics Review. If an Updated Approval Notice is required prior to the HSREB Expiry Date, the Principal Investigator is responsible for completing and submitting an HSREB Updated Approval Form in a timely fashion.         The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice (TCH E6 R1), the Ontario Personal Health Informati Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations of Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulatio	100000101	L Western University Health So HSREB Amendme	cience Research Ethics I nt Approval Notice	Board
HSREB File Number: 105100         Study Title: A survey of practice beliefs and patterns of health practitioners who use manual treatments for patients will low back pain         Sponsor:         HSREB Amendment Approval Date: October 22, 2014         HSREB Expiry Date: February 28, 2015         Document Name       Comments         Revised Study End Date         Connents Name       Comments         Revised Study End Date         The Western University Health Science Research Ethics Board (HSREB) has reviewed and approve the amendment to the above named study, as of the HSREB Amendment Approval Date noted above, condition to timely submission and acceptance of HSREB Continuing Ethics Review. If an Updated Approva Notice is required prior to the HSREB Expiry Date, the Principal Investigator is responsible for completing and submitting an HSREB Updated Approval Form in a timely fashion.         The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice Practices (ICH E6 R1), the Ontario Personal Health Informati Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada         Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada         Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada <td>Principal Investigator: Department &amp; Institut</td> <td>Dr. Dave Walton ion: Health Sciences\Physical Therap</td> <td>y,Western University</td> <td></td>	Principal Investigator: Department & Institut	Dr. Dave Walton ion: Health Sciences\Physical Therap	y,Western University	
HSREB Amendment Approval Date: October 22, 2014         HSREB Expiry Date: February 28, 2015         Documents Approved and/or Received for Information:         Document Name       Comments         Version Date         The Western University Health Science Research Ethics Board (HSREB) has reviewed and approvent the amendment to the above named study, as of the HSREB Amendment Approval Date noted above the amendment to the above named study, as of the HSREB Expiry Date noted above, condition to timely submission and acceptance of HSREB Continuing Ethics Review. If an Updated Approval Notice is required prior to the HSREB Expiry Date, the Principal Investigator is responsible for completing and submitting an HSREB Updated Approval Form in a timely fashion.         The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice Practices (ICH E6 R1), the Ontario Personal Health Informati Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.         Members of the HSREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.         The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.         cer, on behalf of Dr. Joseph Gilbert, HSREB Chair         Ethics Officer to Contact	HSREB File Number: Study Title: A survey o low back pain Sponsor:	105100 If practice beliefs and patterns of healt	h practitioners who use manua	I treatments for patients with
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Document Name       Comments       Version Date         Revised Study End Date	Documents Approved	and/or Received for Information:		
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# Curriculum Vitae

Name:	Joseph Putos
Post-secondary Education and Degrees:	University of Ottawa Ottawa, Ontario, Canada 1974-1978 B.P.H.E.
	Queens University Kingston, Ontario, Canada 1978-1979 B.Ed.
	Queens University Kingston, Ontario, Canada 1981-1985 B.Sc. PT
	Queens University Kingston, Ontario, Canada 2003-2009 M.Ed.
	Western University London, Ontario, Canada 2012-2024 PhD.
	Trainee, Collaborative Training Program in Musculoskeletal Health Western University London, Ontario, Canada 2012 - 2024
Honours and Awards:	Nan Phillipson Award for Excellence in Teaching Western University London, Ontario, Canada 2015 & 2016
Related Work Experience:	Teaching Assistant The University of Western Ontario 2012-2016
	Academic Assistant Queens University Kingston, Ontario, Canada 2010-2012

Adjunct Queens University Kingston, Ontario, Canada 2009-2010

#### **Publications:**

1. Walton, D. M., Beattie, T., Putos, J., & MacDermid, J. C. (2016). A Rasch analysis of the Brief Pain Inventory Interference subscale reveals three dimensions and an age bias. *Journal of Clinical Epidemiology*.

2. Walton, D. M., Putos, J., Beattie, T., & MacDermid, J. C. (2016). Confirmatory factor analysis of 2 versions of the Brief Pain Inventory in an ambulatory population indicates that sleep interference should be interpreted separately. *Scandinavian Journal of Pain*.

#### **Monographs:**

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