New insights into recovery and recurrences of non-specific low back pain

Tatiane Mota da Silva

BPhys (Hons), MSc

MACQUARIE
University
SYDNEY·AUSTRALIA

Department of Health Professions
Faculty of Medicine and Health Sciences
Macquarie University
Sydney, Australia

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Supervisors' statement

As supervisors of Tatiane Mota da Silva's doctoral work, we certify that we consider her thesis "New insights into recovery and recurrences of non-specific low back pain" to be suitable for examination.

A/Prof Mark Hancock _____

Department of Health Professions

Faculty of Medicine and Health Sciences Date 10/10/2018

Macquarie University

Dr Kathryn Mills _____

Department of Health Professions

Faculty of Medicine and Health Sciences Date 10/10/2018

Macquarie University

Candidate's statement

I, Tatiane Mota da Silva, hereby declare that the work contained within this thesis, "New insights into recovery and recurrences of non-specific low back pain", is my own and has not been submitted to any other university or institution, in part or in whole, as a requirement of a degree.

I, Tatiane Mota da Silva, hereby declare that I was the principal researcher of all work included in this thesis, including the work published with multiple authors.

I, Tatiane Mota da Silva, hereby declare that this thesis is an original piece of work and it is written by me. Any assistance that I have received in the preparation of this thesis has been appropriately acknowledged. In addition, I also certify that all information sources and literature are indicated in this thesis.

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Tatiane Mota da Silva

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Publications and presentations

Parts of the work presented in this thesis have been published or submitted to a peer-reviewed journal and presented at national and international conferences.

Published papers

- **da Silva T**, Macaskill P, Mills K, Maher C, Williams C, Lin C, Hancock MJ. Predicting recovery in patients with acute low back pain: A Clinical Prediction Model. *Eur J Pain.* 2017 Apr;21(4):716-726. doi: 10.1002/ejp.976.
- **da Silva T**, Mills K, Brown BT, Herbert RD, Maher CG, Hancock MJ. Risk of Recurrence of Low Back Pain: A Systematic Review. *J Orthop Sports Phys Ther*. 2017 May;47(5):305-313. doi: 10.2519/jospt.2017.7415.
- **da Silva T**, Macaskill P, Kongsted A, Mills K, Maher C, Hancock J. Predicting pain recovery in patients with acute low back pain: Updating and validation of a clinical prediction model. *Eur J Pain*. Epub 2018 Aug 24.

Submitted paper under review

- **da Silva T**, Mills K, Brown B, Pocovi N, de Campos T, Maher C, Hancock M. Risk of recurrences among people recently recovered from an episode of low back pain: prospective inception cohort study. *Br J Sports Med*. [2018 Oct 10]

Conference Proceedings

Oral Presentations:

- Predicting recovery in acute low back pain. EnCouRage Research Symposium, Sydney, Australia 2016.
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- Predicting recovery in patients with acute low back pain. International Back and Neck Pain Forum, Oslo, Norway 2017.
- Risk of recurrence of low back pain: a systematic review. International Back and Neck Pain Forum, Oslo, Norway 2017.
- Risk of recurrence of low back pain. Momentum 2017 Physiotherapy Conference, Sydney, Australia 2017.

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With love,

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Preface

This thesis is arranged into seven chapters and is structured so that each chapter can be read independently. The chapters included in this thesis comprise of five studies covering two broad aims. The first aim is to develop and validate a clinical prediction model for recovery of an episode of acute low back pain, and the second aim is to provide a better understanding of recurrences of low back pain and related prognostic factors. Macquarie University allows published papers that arose from the candidature to be included in the thesis. **Chapter Two, Chapter Three** and **Chapter Four** are the PDF files of the published papers, and **Chapter Five** and **Chapter Six** are formatted as per the instructions for authors of the journals where they have been, or will be, submitted.

Chapter One is the introduction of the thesis and provides relevant background information from the literature related to low back pain and forms the rationale of the topics investigated in the following studies. **Chapter Two** is a development study of a clinical prediction model to predict the probability of recovery at three time points in patients who still have low back pain one-week after initially seeking care. **Chapter Three** is a validation study of the developed clinical prediction model. **Chapter Two** and **Chapter Three** are presented as the papers published in *European Journal of Pain*. **Chapter Four** is a systematic review investigating the current evidence on risk of, and prognostic factors for, a recurrence of low back pain in patients who have recovered from a previous episode of low back pain within the last year. It is presented as the paper published in *Journal of Orthopaedic & Sports Physical Therapy*. **Chapter Five** presents an inception cohort study investigating the risk of recurrence and prognostic factors for a recurrence in a cohort of people recently recovered from an episode of low back pain, and it is presented as per the instructions for authors of *British Journal of Sports Medicine* where it has been submitted for publication. **Chapter Six** presents a sub-analysis of the cohort study which assesses the personal impact of recurrences of low back pain, and it is presented as per the instructions for authors of *PAIN* where it will be submitted for publication. **Chapter Seven** presents a summary of the thesis findings and discusses implications of these findings.

Each chapter contains its own reference list. Appendices that were published as online supplementary material are included at the end of the relevant chapter. Additional appendices are included at the end of the thesis. Ethical approval was obtained from the from the Low-risk Ethics Subcommittee for the study reported in **Chapter Three** (#5201700443), and from the Human Research Ethics Committee, Macquarie University (#5201500494) for the studies reported in **Chapters Five** and **Six**. The remaining chapters did not require ethical approval.

Abstract

The broad aims of this thesis are: 1) to develop and validate a clinical prediction model for recovery from an episode of acute low back pain, and 2) to provide a better understanding of recurrences of low back pain and related prognostic factors. **Chapter Two** describes the development of a clinical prediction model to predict the probability of recovery at three different time points in patients with acute low back pain. The study provided evidence that the developed clinical prediction model could predict the likelihood of recovery from an episode of acute low back pain. However, clinical prediction models need to be tested for external validity before being recommended for clinical practice. **Chapter Three** presents a validation study of the developed clinical prediction model described in **Chapter Two**. The study provided evidence that the developed clinical prediction model demonstrated reasonably good external validity when tested in a different population. **Chapter Four** is a systematic review that investigated the risk of, and prognostic factors for, a recurrence of low back pain in patients who have recovered from a previous episode of low back pain within the last year. The main finding was that the available research does not provide robust estimates of the risk of low back pain recurrence and provides little information about factors that predict recurrence in people recently recovered from an episode of low back pain. The review demonstrated the need for a large, well-designed inception cohort study to investigate risk of recurrences and prognostic factors for a recurrence. **Chapter Five** is an inception cohort study investigating the risk of recurrences over the first year after recovering from an episode of low back pain. This study also investigated prognostic factors for a recurrence in a cohort of people recently recovered from an episode of low back pain. The study provided evidence that: 1) the estimate of recurrence is much higher than previously reported, and 2) new prognostic factors for a recurrence of low back pain were identified. **Chapter Six** is a sub-analysis of the inception cohort study aiming to: 1) investigate the personal impact of low back pain over a one-year period in people recently recovered from a previous episode of low back pain; 2) investigate if the personal impact of low back pain is different in people who do and do not experience a recurrence; and 3) investigate the personal impact of low back pain in participants who met three different definitions of a recurrence of low back pain. The study presented evidence that while most people report a recurrence of an episode of low back pain, many recurrences result in little personal impact. In summary, the series of studies described in this thesis have produced new and important information regarding recovery from an episode of low back pain, and recurrences that commonly occur following recovering from an episode of low back pain.

Chapter 1

Introduction

1.1 Definition and classification of low back pain

Low back pain is a symptom rather than a disease, and can result from several different known and unknown diseases.[1,2] Low back pain is defined as pain and discomfort, localised between the lower costal margin and the inferior gluteal folds, with or without referred leg pain.[3-5] Non-specific low back pain is the most common form of low back pain,[2,5] and is defined as symptoms not attributed to a known specific pathology (e.g. infection, tumour, ankylosing spondylitis, fracture, or cauda equina syndrome).[2,3,5] Commonly, low back pain is further classified according to the duration of symptoms. Acute low back pain is usually defined as when the pain persists for less than six weeks, subacute low back pain when the pain persists between six weeks and three months, and chronic low back pain when the pain lasts longer than three months.[3,5,6]

1.2 Prevalence of low back pain

Low back pain is an extremely common symptom affecting most people at some point in their life.[7,8] The estimated mean point prevalence (prevalence at a specific point in time) is 18.3% (standard deviation [SD], ±11.7),[2,4,7,8] the estimated mean one-month prevalence (prevalence anytime in the past month) is 30.8% (SD, ±12.7),[2,7,8] and the estimated mean one-year prevalence (prevalence anytime in the past year) is 38.0% (SD, ±19.4).[4,7,8] Low back pain appears to be more common in people between 40 and 69 years than in other age groups,[2,7,8] and in females when compared to males.[2,7,8] Prevalence appears to be somewhat higher in countries with high-income economies (mean=32.9, SD±19.0) compared with middle-income (mean=25.4, SD±18.3) and low-income economies (mean 16.7, SD±15.7); however, the literature shows no difference in prevalence between urban and rural areas.[2,7]

1.3 Care-seeking behaviour in lower back pain

Although low back pain is extremely common, many people experiencing low back pain do not seek care. A systematic review of 13,486 participants in high income countries reported a pooled estimated prevalence of care-seeking among people with low back pain of 58% (95% confidence

interval [CI]: 32% to 83%).[9] Care-seeking due to low back pain appears to be more common in women, people with a previous history of back pain, patients with poor general health and those with higher pain and disability.[9] Individual studies within the review reported that people with pain of less than two weeks duration,[10] or patients using passive coping strategies to manage pain (e.g. 'avoiding ways to react toward workmates and superiors when in conflict or when feeling one has been treated unjustly')[11] are less likely to seek care.[9] In addition, patients who believe that their pain management is the responsibility of others,[12] who have fear of future job impairment,[13] limited social functioning,[14] and patients involved with sports activities[9] are more likely to seek care.

1.4 Burden of low back pain

Low back pain causes an enormous economic burden on individuals, families, communities, industries and governments.[15-17] The 2015 Global Burden of Disease study reported low back pain to be the leading cause of years lived with disability in both developed and developing countries.[18] Low back pain is a common cause of absenteeism from employment due to its high prevalence in working-age individuals.[18] In the United States, low back pain is responsible for more absenteeism than any other work-related musculoskeletal condition.[19] In Australia, low back pain is the chronic disease which forces the highest number of older Australian workers to retire prematurely.[20]

Costs related to low back pain are, in general, reported as direct healthcare costs and indirect costs. Direct healthcare costs commonly include health practitioner consultations, diagnostic and therapeutic procedures, use of drugs, hospitalisations and rehabilitation care.[21,22] Indirect costs commonly include costs related to employment and household productivity and are the largest proportion of costs in most countries.[22] Several studies estimate the indirect costs of low back pain are in the billions of dollars.[22-25] In the United States, the estimated total annual cost of low back pain from a 2006 study was at least $100 billion USD.[22,23] Two-thirds of these were related to indirect costs.[22,23] In Australia, the estimated total annual cost, from a 2003 study, was $9 billion AUD, and about $8 billion of these related to indirect costs.[22,25] In the Netherlands, the estimated total cost (from a 2007 study) was €3.5 billion, and 88% of these related to indirect costs.[24] The data from these studies are from the early 2000s and it is likely that costs have escalated since then.[22-25]

1.4.1 Personal burden due to low back pain

While the burden of low back pain is often described by components such as prevalence, disability and costs, none alone are sufficient in quantifying the overall burden of low back pain from the perspective of the individuals affected. The description of low back pain burden should consider the way in which low back pain affects the lives of individuals with the condition.[15] The degree of burden includes pain and activity limitations, psychological consequences, as well as broader impacts such as participation restrictions, carer burden, use of health-care resources and financial burden to the individual.[15-17] Systematic reviews of qualitative studies have described the experience of living with low back pain.[26-28] Pain experiences are commonly reported as persistent, disruptive and distressing.[27,28] Patients often describe low back pain as a symptom stigmatised by lack of authenticity and legitimacy,[26,27] and as a consequence, they withdraw from social activities to avoid rejection from others.[26,27] Other reasons for social withdrawal include a sense of social invisibility, inability to complete common activities, and irritability as a result of pain.[27] The activities most commonly effected by low back pain are domestic chores,[26,27] and leisure activities.[26,27]

1.5 Course of low back pain

The modern understanding of low back pain suggests it is typically a long-term condition with a variable course.[1] The clinical course of acute low back pain is widely reported to be favorable in terms of pain and disability. A systematic review, of 33 studies from 2012 summarised the clinical course of low back pain by using pain scores on a zero (no pain) to 100 (worst possible pain) scale.[29] Fifteen included cohort studies described the course of acute low back pain. The pooled mean pain score was 52 (95% CI=48 to 57) at baseline, 23 (95% CI=21 to 25) at six weeks, 12 (95% CI=9 to 15) at 26 weeks, and 6 (95% CI=3 to 10) at 52 weeks.[29] A similar improvement was observed in mean disability scores.[29] Recovery was measured in 19 studies, and while the data were not pooled due to heterogeneity between studies, most studies reported that the majority of patients presenting with acute low back pain recovered by 12 weeks.[29] A large inception cohort study (973 consecutive patients) investigating the course of low back pain in patients presenting to primary care in Sydney, Australia, reported a cumulative probability of recovery from pain of 39.9% by six weeks, 58.2% by 12 weeks, and 72.5% by one year.[30] The median time to recovery in terms of pain was described as 58 days (95% CI=53 to 63 days).[30]

In contrast to the favorable prognosis of acute low back pain, chronic low back pain has a poor prognosis. The aforementioned systematic review[29] investigating the course of low back pain

identified six cohort studies describing the course of chronic low back pain. The pooled mean pain score was 51 (95% CI=44 to 59) at baseline, 33 (95% CI=29 to 38) at six weeks, 26 (95% CI=20 to 33) at 26 weeks, and 23 (95% CI=16 to 30) at 52 weeks.[29] Recovery occurred in less than half of the patients.[29] In the Australian inception cohort, from the 406 patients who developed chronic low back pain (defined as pain persisting for more than three months), 47% recovered within twelve months.[31]

Recent studies have investigated the course of low back pain from a different perspective, by characterising pain trajectories over time. Downie et al.[32] in 2016 identified five distinct pain trajectory patterns during a 12-week period for 1,585 patients with acute low back pain. The study found that 36% of patients recovered rapidly, 34% improved more slowly but recovered by 12 weeks, 14% had incomplete recovery by 12 weeks, 11% had fluctuating pain, and 5% had persistent high pain during the 12-week period. Dunn et al.[33] identified different recovery trajectories for patients with low back pain using data over a seven-year period, including: recovery (31%), persistent mild symptoms (37%), constantly fluctuating problems (11%) and severe chronic levels of pain (21%). These studies found a large proportion of people have recurrent or fluctuating low back pain.

1.5.1 The importance of recovery

Within the low back pain field, the concept of recovery is commonly used in studies investigating diagnosis,[34] prognosis,[30] and determining the effect of treatments.[35] The definition of recovery is also important to the measurement of recurrences. An individual becomes at risk of recurrence only after they have recovered from an episode of low back pain.[36,37] Although 'recovery' is a commonly used outcome, there is no broadly accepted definition of what recovery from low back pain means or agreement on how it should be measured. As such, it is often measured and reported in low back pain studies in different ways.[38-40] A systematic review[38] from 2010 reported 66 different measures of recovery from 82 studies; and 59 of the measures did not appear in more than one study. Recovery was measured by different constructs, most often using measurements of pain, disability or function, or a combination of the two.[38]

1.6 Prognostic factors for an episode of low back pain

Prognostic factors are characteristics that are associated with or predict the course of a condition.[41] There is a range of prognostic factors that have been shown to predict poor

outcomes in patients with low back pain. However, the results vary somewhat between studies. A 'review of reviews' from 2009 attempted to summarise the findings of 17 reviews about prognostic factors associated with low back pain.[42] However, the included reviews varied substantially in design and conduct,[42] and only a limited number of prognostic factors were consistently reported including: older age, poor general health, increased psychological or psychosocial stress, poor relations with colleagues, physically heavy work, worse baseline functional disability, sciatica, and the presence of compensation.[42] One review[43] from 2015 investigating the extent to which putative mediators explain the effect of pain on disability in people with low back pain or neck pain identified that self-efficacy (β=0.23, 95% CI=0.10 to 0.34), psychological distress (β=0.10, 95% CI=0.01 to 0.18), and fear (β=0.08, 95% CI=0.01 to 0.14) mediated the relationship between pain and disability, but catastrophising did not (β=0.07, 95% CI=-0.06 to 0.19).[43] The findings of this review should be interpreted with caution, as the risk of confounding must be considered for mediation analysis, and only three studies controlled for the effect of potential confounders.[43] Another review[44] from 2015 investigating clinical findings found that only clinical tests of centralisation and non-organic signs demonstrated a consistent association with at least one of the outcomes.[44] However, associations between the factors and outcomes were often inconsistent between studies, due to the use of the tests in different patient populations and various settings, employing different treatment methods, and using a broad range of definitions of tests and a great variation in definitions of outcome that were often measured in non-standardized ways and with different timing of follow-ups.[44] Identifying prognostic factors is important to understand possible determinants for the course of low back pain; however, no single factor is strongly predictive, so there is a need to look at multiple concurrent factors.

1.7 Clinical Prediction Models

The use of clinical prediction models is a way to identify groups or individual patients who are likely to have a specific outcome based on a cluster of prognostic factors. Clinical prediction models use patient's characteristics such as medical history, physical examination, and test results, to estimate the probability of disease or outcome, for example, providing the likelihood of a patient experiencing an outcome at a specific time point.[45]

There are three phases for studies related to a clinical prediction model. The first phase is the development study which produces the model and performs preliminary testing.[41] The second phase is the validation study which evaluates the performance of the model in a new sample of patients, to ensure that similar results are found in a different sample of patients or a different

health care setting.[41,46-48] The third phase is the impact study which tests the impact of the prediction model when utilised in clinical practice,[41] by identifying if the prediction model produces a change in clinicians' behavior or an improvement in patients' outcomes. After this step the prediction model can be recommended for use in clinical practice.[49]

1.7.1 Clinical prediction models for patients with low back pain

There are existing clinical prediction models for patients with low back pain; however, they have important limitations. A systematic review[50] of studies published prior to 2014 (18 studies) summarised the discrimination of clinical prediction models to identify the prognosis in patients with low back pain of less than three months duration. The review identified seven clinical prediction models that have been developed for patients with low back pain.[50] All clinical prediction models were developed to identify a poor outcome (persistent pain or non-recovery), at a long term time-point (e.g. 12 months).[50] Few previous prediction models provide actual probability estimates of an outcome at specific time points, but rather categorise patients in risk groups (e.g. as being at low or high risk of having the outcome).[50] Few have undergone any validation testing and most lack acceptable discrimination and/or accuracy.[50]

The Orebro Musculoskeletal Pain Screening Questionnaire[51] is one of the few clinical prediction models that has been evaluated in several independent patient samples by multiple research groups. This tool includes 25 items that assess psychosocial factors to identify patients at risk for developing persistent back pain problems. The aforementioned systematic review[50] investigating the discrimination of prognostic clinical prediction models found the Orebro Musculoskeletal Pain Questionnaire has 'excellent' discrimination to predict prolonged absenteeism at six months (pooled AUC=0.83, 95% CI=0.75 to 0.90); 'acceptable' discrimination to predict prolonged absenteeism at 12 months (pooled AUC=0.7, 95% CI=0.64 to 0.78), and disability (polled AUC=0.75, 95% CI=0.69 to 0.82), and 'poor' discrimination to predict pain outcomes (polled AUC=0.69, 95% CI=0.62 to 0.76).[50]

The STarT Back Tool[52,53] is another prediction model that has been tested in different patient samples from different countries. The STarT Back Tool is not only a prognosis tool, but it also has matched treatments and has been tested for improving patient outcomes.[54] It includes nine items (referred leg pain, co-morbid pain, disability (two items), bothersomeness, catastrophising, fear, anxiety and depression), and classifies patients as low, medium or high risk, reflecting the complexity of their back pain problem.[52,53] The aforementioned systematic review[50] investigating the discrimination of the low back pain clinical prediction models found the STarT Back Tool has 'acceptable' discrimination to predict disability (polled AUC=0.74, 95% CI=0.66 to 0.82),

and 'non-informative' discrimination to predict pain outcome (polled AUC=0.59, 95% CI=0.59 to 0.63).[50]

Both the Orebro Musculoskeletal Pain Questionnaire and STarT Back Tool focus on predicting poor outcomes (e.g. persistent pain or non-recovery, disability and work absence) at long-term follow-up (e.g. six and twelve-months). Although this information is useful, this might not be most relevant to clinicians and patients regarding decisions about short and intermediate-term management of patients with acute low back pain. **Chapter Two** of this thesis describes a development study of a new clinical prediction model to predict recovery over the first three months in patients with acute low back pain. **Chapter Three** of this thesis describes a validation study to assess the performance (discrimination and calibration) of the developed clinical prediction model to predict recovery over the first three months in patients with acute low back pain.

1.8 Recurrences of low back pain

Although previous literature demonstrates that most individuals with acute low back pain recover within six- to 12-weeks;[29,30] it is widely believed that recurrences are common.[8,55] Previous systematic reviews attempted to identify how commonly a recurrence of low back pain occurs; however, substantial variability between studies is reported. One systematic review from 2003 (15 studies) studied the course and prognostic factors of acute low back pain and sciatica, and also described estimates of recurrence at three and 12 months.[56] The cumulative risk of at least one recurrence within three months was 26% (95% CI=19% to 34%); however, this finding was drawn from a single study of 135 participants.[56] The cumulative risk of at least one recurrence within 12 months varied from 66% to 84%.[56]

Another systematic review from 2014 (45 studies) studied estimates and prognostic factors for first-time low back pain and "transition to low back pain" in people who were pain free at baseline.[57] The summary pooled estimate of "transition to low back pain" (based on three studies) was 27% (95% CI=18% to 35%).[57] However, the pooled estimate was based on studies with long and variable inception periods (i.e. participants who had been pain free for any time duration), and follow-up periods ranging from six to 36 months.[57] The findings of previous reviews need to be interpreted with caution due to the substantial limitations of all previous primary studies.

Producing accurate estimates of how commonly a recurrence occurs is challenging due to 1)

methodological issues,[58] and 2) different definitions of recurrence.[8,59-61] To produce an unbiased estimate, studies should include an inception cohort (i.e. include all patients at a similar, well-defined point in the course of their disease)[58,62] of people who have recently recovered from a previous episode of low back pain and, therefore, are at risk of having a recurrence. This is important because the risk of recurrence for people who recovered a long time ago is likely to be different from the risk of recurrence for people who have just recovered. Previous studies investigating recurrence of low back pain reported long and variable inception periods.[56,57] Another methodological issue when investigating how commonly a recurrence occurs is the duration and frequency of the follow-ups. Participants must be followed for sufficient duration for the recurrence to occur and regularly enough, to avoid recall bias. Previous studies have typically suffered from infrequent follow-ups (e.g. one year after study entry) and are therefore, likely to produce biased estimates of recurrence.[37,63]

The second challenge when investigating how commonly a recurrence occurs is the definition of recurrence used. A systematic review from 2010 (43 studies) summarised definitions of recurrence (and related recovery definitions) used in the literature. The review found that from 53 included studies, only 32% described an explicit definition of recurrence[64] and less than 10% of studies used a common definition of recurrence.[64] Stanton et al.[65] in 2011 used a modified Delphi approach to create a consensus definition for a 'recurrence of an episode of low back pain'. A consensus definition was reached with 95% of panel members supporting the definition as 'return of low back pain lasting at least 24 hours with a pain intensity of greater than two points on an 11-point numeric rating scale (or >20mm on a 100mm visual analogue scale) following a period of at least 30 days pain-free'.[65] Understandably, recurrence estimates will vary depending on the definition used.

Chapter Four of this thesis presents a systematic review of the best available literature summarising the risk of a recurrence of low back pain in patients who have recovered from a previous episode of low back pain within the last year. **Chapter Five** describes the findings of an inception cohort study designed to address the limitations from previous studies investigating the risk of recurrences of low back pain.

1.8.1 Prognostic factors for a recurrence of low back pain

While there are a number of systematic reviews investigating a range of prognostic factors associated with poor outcomes from an episode of low back pain, there is little information about the prognostic factors exploring who will experience a recurrence of low back pain. The only

consistently reported prognostic factor for a recurrence is the number of previous episodes.[37,63] However, no studies have investigated a wide range of potential prognostic factors in a high-quality inception cohort study. **Chapter Four** of this thesis presents a systematic review summarising the prognostic factors for a recurrence of low back pain in patients who have recovered from a previous episode of low back pain within the last year. **Chapter Five** describes the findings of a high-quality inception cohort study that investigated a range of prognostic factors for a recurrence of low back pain in a cohort of people recently recovered from an episode of low back pain.

1.8.2 Personal impact of recurrences low back pain

Despite the importance of investigating how commonly a recurrence occurs and related prognostic factors, little is known about how much impact is associated with a recurrence. No study has investigated the personal impact (pain intensity, pain interference, and physical function)[66] associated with a recurrence of low back pain. Additionally, the personal impact associated with a recurrence of low back pain will likely be influenced by how a recurrence is defined. It is unclear if people experiencing a recurrence of an episode of low back pain experience substantial impact or not. It is possible that definitions of a recurrence which require some associated activity limitation or care-seeking may result in more significant impact. **Chapter Six** describes a sub-analysis study that used the measure of "personal impact of low back pain" recommended by the National Institutes of Health task force on research standards for low back pain[66] to 1) investigate the personal impact of low back pain over a one-year period in people recently recovered from a previous episode of low back pain; 2) investigate if the personal impact of low back pain is different in people who do and do not experience a recurrence; and 3) investigate the personal impact of low back pain in participants who met three different definitions of a recurrence of low back pain.

1.9 Aims of the thesis

1) To develop a clinical prediction model to predict the probability of recovery at three time points in patients with acute low back pain (**Chapter Two**).
2) To validate the developed clinical prediction model for predicting the probability of recovery at three time points in patients with acute low back pain (**Chapter Three**).
3) To investigate how commonly recurrences of low back pain occur and prognostic factors for a recurrence of low back pain in patients who have recovered from a previous episode of low back pain within the last year (**Chapter Four**).
4) To provide robust estimates for the risk of a recurrence of low back pain over the first year; and identify prognostic factors for a recurrence of low back pain in a cohort of people recently recovered from an episode of low back pain (**Chapter Five**).
5) To investigate the personal impact of recurrences of low back pain over a one-year period (**Chapter Six**), more specifically:
    - to investigate the impact of low back pain in people recently recovered from a previous episode of low back pain;
    - to investigate if the impact of low back pain is different in people who do and do not experience a recurrence; and
    - to investigate the impact of low back pain in participants who met three different definitions of a recurrence of low back pain.

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Chapter 2

Predicting recovery in patients with acute low back pain: A Clinical Prediction Model

2.1 Preface

Despite the favourable average clinical course of an episode of acute low back pain, there is substantial individual variability. The ability to identify the individual likelihood of recovery by key time points would be valuable to better inform patients and decisions about care. **Chapter Two** presents a study that developed a clinical prediction model to predict the probability of recovery at 1-week, 1-month and 3-months after 1-week review in patients who still have low back pain 1-week after initially seeking care.

The study presented in **Chapter Two** has been published as:

da Silva T, Macaskill P, Mills K, Maher C, Williams C, Lin C, Hancock MJ. Predicting recovery in patients with acute low back pain: A Clinical Prediction Model. Eur J Pain. 2017 Apr; 21(4): 716-726. doi: 10.1002/ejp.976. Epub 2017 Jan 20.

An erratum of this paper is presented at the end of the manuscript.

2.2 Co-authors' statement

The co-authors of the paper: "da Silva T, Macaskill P, Mills K, Maher C, Williams C, Lin C, Hancock MJ. Predicting recovery in patients with acute low back pain: A Clinical Prediction Model. Eur J Pain. 2017 Apr;21(4):716-726" confirm that Tatiane Mota da Silva has made the following contributions:

- Conception and design of the study
- Prepared and cleaned the data
- Interpretation of findings
- Writing the first draft of the manuscript and incorporating suggestions from other authors

Mark Hancock _____ Date: 05/10/2018

Petra Macaskill _____Date: 05/10/2018

Kathryn Mills _____Date: 05/10/2018

Christopher Maher _____Date: 05/10/2018

Christopher Williams _____Date: 05/10/2018

Christine Lin _____Date: 05/10/2018

da Silva, T., Macaskill, P., Mills, K., Maher, C., Williams, C., Lin, C., & Hancock, M. J. (2017). Predicting recovery in patients with acute low back pain: a clinical prediction model. European Journal of Pain (United Kingdom), 21(4), 716-726.

DOI: 10.1002/ejp.976

Chapter 3

Predicting pain recovery in patients with acute low back pain: Updating and validation of a clinical prediction model

3.1 Preface

Model validation studies evaluate the performance of the original model using data from a different sample to investigate if similar results are found. **Chapter Three** presents a validation study of the developed clinical prediction model described in **Chapter Two**. Some variables were initially re-categorized in the developmental dataset to enable validation testing of the model in the validation dataset.

The study presented in **Chapter Three** has been published as:

“da Silva T, Macaskill P, Kongsted A, Mills K, Maher CG, Hancock MJ. Predicting pain recovery in patients with acute low back pain: Updating and validation of a clinical prediction model. Eur J Pain. 2018;1–13.”

The ethics approval for this study is presented in the **Thesis Appendix 1**.

Amendment

There is an error in the DPF file on page xx of published manuscript: "From the 1,643 participants in the Danish cohort study, 756 met all the inclusion criteria and were included in the study", should read: "From the 1,169 participants in the Danish cohort study, 756 met all the inclusion criteria and were included in the study."

3.2 Co-authors' statement

The co-authors of the paper: "da Silva T, Macaskill P, Kongsted A, Mills K, Maher CG, Hancock MJ. Predicting pain recovery in patients with acute low back pain: Updating and validation of a clinical prediction model. Eur J Pain" confirm that Tatiane Mota da Silva has made the following contributions:

- Conception and design of the study
- Prepared and cleaned the data
- Interpretation of findings
- Writing the first draft of the manuscript and incorporating suggestions from other authors

Mark Hancock _____ Date: 05/10/2018

Petra Macaskill _____Date: 05/10/2018

Alice Kongsted _____Date: 05/10/2018

Kathryn Mills _____Date: 05/10/2018

Christopher Maher _____Date: 05/10/2018

Pages 33-45 of this thesis have been removed as they contain published material. Please refer to the following citation for details of the article contained in these pages.

da Silva, T., Macaskill, P., Kongsted, A., Mills, K., Maher, C. G., & Hancock, M. J. (2019). Predicting pain recovery in patients with acute low back pain: updating and validation of a clinical prediction model. *European Journal of Pain (United Kingdom)*, *23*(2), 341-353.

DOI: 10.1002/ejp.1308

Chapter 4

Risk of Recurrence of Low Back Pain: A Systematic Review

4.1 Preface

Previous literature demonstrates that most individuals with acute low back pain recover within 6-12 weeks; however, it is widely believed that recurrences are common. There are, to date, no widely accepted estimates of the risk of recurrences of low back pain and very little is known about prognostic factors for a recurrence of low back pain. **Chapter Four** presents a systematic review which investigated the risk of, and prognostic factors for a recurrence of low back pain. The review included longitudinal studies of adults who had recovered from a previous episode of low back pain within 12 months.

The study presented in **Chapter Four** has been published as:

da Silva T, Mills K, Brown BT, Herbert RD, Maher CG, Hancock MJ. Risk of Recurrence of Low Back Pain: A Systematic Review. J Orthop Sports Phys Ther. 2017 May;47(5):305-313. doi: 10.2519/jospt.2017.7415. Epub 2017 Mar 29. Reprinted with permission from J Orthop Sports Phys Ther.

The final strategy of all databases is presented in **Thesis Appendix 2**.

4.2 Co-authors' statement

The co-authors of the paper: "da Silva T, Mills K, Brown BT, Herbert RD, Maher CG, Hancock MJ. Risk of Recurrence of Low Back Pain: A Systematic Review. J Orthop Sports Phys Ther. 2017 May;47(5):305-313" confirm that Tatiane Mota da Silva has made the following contributions:

- Conception and design of the study
- Data search, study selection, data extraction, assessment of risk of bias
- Interpretation of findings
- Writing the first draft of the manuscript and incorporating suggestions from other authors

Mark Hancock _____ Date: 05/10/2018

Kathryn Mills _____Date: 05/10/2018

Benjamin Brown _____Date: 05/10/2018

Robert Herbert _____Date: 05/10/2018

Christopher Maher _____Date: 05/10/2018

Da Silva, T., Mills, K., Brown, B. T., Herbert, R. D., Maher, C. G., & Hancock, M. J. (2017). Risk of recurrence of low back pain: a systematic review. *Journal of Orthopaedic and Sports Physical Therapy*, *47*(5), 305-313.

DOI: 10.2519/jospt.2017.7415

Chapter 5

Risk of recurrences of low back pain: A prospective inception cohort study

5.1 Preface

The systematic review presented in **Chapter Four** demonstrated the need for a large, well-designed inception cohort study to investigate risk of recurrences and prognostic factors for a recurrence. **Chapter Five** presents an inception cohort study designed to address the limitations of previous studies investigating the risk of recurrences of low back pain and related prognostic factors. The study enrolled 250 patients recovered from an episode of low back pain within one month and followed them monthly for one year.

The study presented in **Chapter Five** has been submitted to *British Journal of Sports Medicine* and is presented in the format of the submitted manuscript. The ethics approval of this study is presented in **Thesis Appendix 3**, and the participant information consent form is presented in **Thesis Appendix 4**. Instructions for authors of the *British Journal of Sports Medicine* are presented in **Thesis Appendix 5**.

5.2 Co-authors' statement

The co-authors of the manuscript: "da Silva T, Mills K, Brown BT, Pocovi N, de Campos T, Maher CG, Hancock MJ. Risk of recurrences of low back pain: A prospective inception cohort study" confirm that Tatiane Mota da Silva has made the following contributions:

- Conception and design of the study
- Data collection, data entry, and data analysis
- Interpretation of findings
- Writing the first draft of the manuscript and incorporating suggestions from other authors

Mark Hancock _____ Date: 05/10/2018

Kathryn Mills _____Date: 05/10/2018

Benjamin Brown _____Date: 05/10/2018

Natasha Pocovi _____Date: 05/10/2018

Tarcisio de Campos _____Date: 05/10/2018

Christopher Maher _____Date: 05/10/2018

da Silva, T., Mills, K., Brown, B. T., Pocovi, N., de Campos, T., Maher, C., & Hancock, M. J. (2019). Recurrence of low back pain is common: a prospective inception cohort study. *Journal of Physiotherapy*, *65*(3), 159-165.

DOI: 10.1016/j.jphys.2019.04.010

Chapter 6

What is the impact of recurrences of low back pain? Sub analysis of an inception cohort study

6.1 Preface

Despite the findings in **Chapter Five** providing strong evidence that recurrences are very common, little is known about how much impact is associated with recurrences. In addition, it is unclear how much the definition of a recurrence influences the associated personal impact. **Chapter Six** describes a study that used the multidimensional measure of "personal impact of low back pain" recommended by the National Institutes of Health task force on research standards for low back pain to: 1) investigate the personal impact of low back pain over a one-year period in people recently recovered from a previous episode of low back pain; 2) investigate if the personal impact of low back pain is different in people who do and do not experience a recurrence; and 3) investigate the personal impact of low back pain in participants who met three different definitions of a recurrence of low back pain.

The study presented in **Chapter Six** is formatted for submission to the journal *PAIN*. However, it has not yet been submitted as it contains some details of the results of the study presented in **Chapter Five.** It will be submitted immediately after that paper is accepted for publication. Instructions for authors of *PAIN* are presented in **Thesis Appendix 6**.

6.2 Co-authors' statement

The co-authors of the manuscript: "da Silva T, Mills K, Kongsted A, Maher C, Hancock M. What is the impact of recurrences of low back pain? Sub analysis of an inception cohort study" confirm that Tatiane Mota da Silva has made the following contributions:

- Conception and design of the study
- Data collection, data entry, and data analysis
- Interpretation of findings
- Writing the first draft of the manuscript and incorporating suggestions from other authors

Mark Hancock _____ Date: 05/10/2018

Kathryn Mills _____Date: 05/10/2018

Alice Kongsted _____Date: 05/10/2018

Christopher Maher _____Date: 05/10/2018

What is the impact of recurrences of low back pain? Sub-analysis of an inception cohort study

Tatiane da Silva, PhD candidate, Department of Health Professions, Macquarie University, Sydney, NSW, Australia
Kathryn Mills, PhD, Department of Health Professions, Macquarie University, Sydney, NSW, Australia
Alice Kongsted, PhD, Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark + Nordic Institute of Chiropractic and Clinical Biomechanics
Christopher G Maher, PhD, Sydney School of Public Health, The University of Sydney, Sydney, NSW/Australia
Mark Hancock, PhD, Department of Health Professions, Macquarie University, Sydney, NSW, Australia

Correspondence to: Tatiane da Silva
Contact address: Department of Health Professions, Ground Floor, 75 Talavera Rd, Macquarie University, NSW 2109, Australia
Email address: tatiane.mota-da-silva@students.mq.edu.au

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Abstract

The aims of this cohort study were to: investigate the personal impact of low back pain (LBP) over a one-year period in people recently recovered from a previous episode of LBP; investigate if the personal impact differs in people who do and do not experience a LBP recurrence; and investigate the personal impact of LBP based on three definitions of a recurrence of LBP. This inception cohort study included 250 participants, recently recovered from an episode of LBP. The average personal impact of LBP (eight-50 scale) over the previous three-months was assessed at three-, six-, nine- and 12-months. Participants were contacted monthly to determine if a recurrence of LBP had occurred. Recurrence was defined as: recurrence of an episode of LBP; recurrence of activity-limiting LBP; and recurrence of LBP causing care-seeking. The personal impact of LBP over one year was calculated by the mean of measures of impact. Generalised estimating equations compared the personal impact in participants who did and did not have a recurrence, and the relationship between the three definitions of a recurrence and personal impact. The median personal impact score over one year was 11.5 points (IQR=9.5 to 14.8). The impact was 15.2 points (95% CI=13.9 to 16.3) for those who reported any recurrence, whereas for those without any recurrence it was 11.1 points (95% CI=10.6 to 11.5). When comparing the definitions of recurrence, those who had a recurrence of an episode of LBP which did not cause moderate activity limitation or result in care seeking, had an overall impact of 12.7 points (95% CI=11.6 to 13.8). Participants who had recurrences of activity-limiting LBP, but who did not seek care, had an overall impact of 15.5 points (95% CI=13.5 to 17.6), and those who had recurrences causing care seeking had an overall impact of 16.9 points (95% CI=15.3 to 18.4).

1. Introduction

Recent evidence suggests that low back pain (LBP) is the leading global cause of years lived with disability.[6] LBP is one of the most prevalent musculoskeletal complaints and affects most people at some point in their life.[8; 9] The initial prognosis is favourable, with the majority of patients recovering quickly.[2] However, recurrences are common and may be responsible for much of the cost and disability associated with LBP.[9; 16] Despite the potential burden resulting from recurrences of LBP, no study has investigated the personal impact (pain intensity, pain interference, and physical function)[3] associated with recurrences of LBP.

The personal impact associated with recurrences of LBP will likely be influenced by how a recurrence is defined. A recent consensus definition of a recurrence of LBP defined a recurrence as "return of LBP lasting at least 24 hours with a pain intensity of >two on a 11-point numerical rating scale".[17] However, the validity of this definition has not been tested and it is unclear if people experiencing a recurrence according to this definition experience substantial impact or not. It is possible that definitions of a recurrence which require some associated activity limitation or care-seeking may be more strongly associated with important recurrences resulting in significant impact.

The National Institutes of Health task force on research standards for LBP recently proposed a multidimensional measure of "personal impact of LBP".[3] This measure was developed to classify patients with LBP according to the impact of the back pain given the challenges with classifying LBP according to the causes of pain. The measure combines nine items from the Patient Reported Outcome Measurement Information System (PROMIS) short form, and covers the domains of pain intensity, pain interference with normal activities and functional status.[3] Previous research demonstrated the discriminatory and prognostic importance of these items.[1; 4; 11; 13; 18] This multidimensional measure can be used to investigate the impact associated with recurrences of LBP and how this varies depending on the definition of a recurrence. Therefore, the aims of this study were:

1. To investigate the personal impact of LBP over a 1-year period in people recently recovered from an episode of LBP.
2. To investigate if the personal impact of LBP is different in people who do and do not experience a recurrence, during the first year after recovering from a previous episode of LBP.

3. To investigate the personal impact of LBP in participants who met three different definitions of a recurrence of LBP.

2. Methods

2.1. Study design overview

This study is a pre-planned sub analysis using data from a cohort study investigating estimates of recurrences of LBP and related prognostic factors in people recently recovered from a previous episode of LBP. The details and results of this study have been published elsewhere.

2.2. Participants

The prospective inception cohort study recruited 250 patients, aged over 18 years, who were discharged from primary care practices (physiotherapy and chiropractic) having recovered from an episode of non-specific LBP within the previous month. Non-specific LBP was defined as pain in the area between the 12th rib and buttock crease not attributed to a specific diagnosis (e.g. ankylosing spondylitis, vertebral fracture).[19] Recovery was defined as a score of zero or one on a 11-point numerical rating scale for at least seven consecutive days. Exclusion criteria were: previous spinal surgery, and/or inadequate English comprehension to complete outcome measures. Ethical clearance was granted by the Human Research Ethics Committee (Medical Sciences), Macquarie University (#5201500494).

2.3. Study variables

2.3.1. Outcome - Personal Impact of LBP

The “personal impact of low back pain” measure covers the domains of pain intensity, pain interference with normal activities and functional status.[3] Pain intensity is assessed by a 11-point numerical rating scale. The domains of pain interference with normal activities and functional status are assessed by four items each with response options provided by a five-option Likert scale (ranging between one=’not at’ all and five=’very much’). The final score is produced by the sum of all items, and it can range from eight (least impact) to 50 (greatest impact). **Appendix 1** presents the personal impact of LBP questionnaire. The questionnaire was administered at baseline, three-, six-, nine- and 12-month follow-ups through a telephone interview and the questions were related to the previous three months. Participants also had the possibility of answering the questions using an online survey if they preferred.

2.3.2. Recurrence definitions

Recurrence was defined in three ways: 1) recurrence of an episode of LBP, 2) recurrence of activity-limiting LBP and 3) recurrence of LBP causing care-seeking. *Recurrence of an episode* of LBP was defined using the definition from a previous expert consensus as "return of LBP lasting at least 24 hours with a pain intensity of >two on a 11-point numerical rating scale".[17] *Recurrence of activity-limiting LBP* was defined as recurrence of an episode of LBP with moderate or greater activity limitation measured using an adaptation of Item eight of the SF36 ('during the recurrence, how much did LBP interfere with your normal work, including work both outside the home and housework?').[20] *Recurrence of LBP causing care-seeking* was defined as a recurrence of an episode of LBP resulting in consultation to a health care provider.

Participants were contacted monthly by email or text message (based on the participants' preference) for 12 months to determine if a recurrence had occurred. Participants were asked if they had a recurrence of an episode of LBP lasting at least 24 hours, with a pain intensity of >two on a scale from 11-point numerical rating scale where zero is no pain and ten is the worst possible pain within the last month (first definition). If a participant reported a recurrence, they were contacted by telephone to obtain a detailed description of the episode, including whether the recurrence met the criteria for a recurrence of activity-limiting LBP (second definition) and recurrence of LBP causing care-seeking (third definition). Participants not responding to monthly email or text messages within 48 hours were contacted by telephone.

2.4. Sample size calculation

We did not complete a formal power calculation as this was not the primary purpose of this cohort study. However, sample size was most critical for aims two and three, and the sample size available of 250 participants was expected to produce relatively precise estimates of the association between recurrences and personal impact given the outcome variable was continuous, and we expected at least 20% of the sample to be in the smallest group. In our model we adjusted for 11 baseline covariates, and had more than 20 participants per variable exceeding common recommendations.[14; 15]

2.5. Statistical Analysis

The personal impact of LBP over one year for each participant regardless of whether they had a recurrence or not (aim one) was assessed by taking a mean of the four measures of impact from the three-, six-, nine- and 12-month follow-up. Participants missing two or more measures of the four time points were excluded from this analysis. In cases of participants who had impact of LBP

scores for three of the four time points, the mean was taken considering only three measures. We did not use imputation of data since few cases had missing data. Medians and interquartile ranges (IQR) were used to describe the personal impact of LBP over one year and for each time period.

To investigate if the personal impact of LBP is different in people who do and do not experience a recurrence (aim two) and the personal impact of LBP in participants who met the three different definitions of a recurrence of LBP (aim three) we used generalised estimating equations (GEE) with autoregressive correlation structure and robust assumptions. These analyses were conducted using four windows of time for each participant. We divided the 12-month follow-up into four-time epochs (baseline to three months, three to six months, six to nine months, and nine to 12 months). To assess if the personal impact of LBP was different in people who experienced and did not experience a recurrence, we coded each participant based on the dichotomous option (no recurrence, any recurrence) within each epoch. If a recurrence spanned more than one epoch it was coded as a recurrence in all relevant epochs. We considered only the first two recurrences reported by any participant within the 12-months as data about duration of recurrences were not available on any additional recurrences. Any epochs after the first two recurrences for an individual were not used in the analysis. First, we ran a GEE analysis investigating the association between the definitions of recurrence and the impact score without any covariates. The second GEE was an adjusted analysis investigating whether this relationship was influenced by baseline covariates. The following variables were measured at baseline and considered to be potential confounders: age, gender, exposure to heavy loads, exposure to awkward posture, physical activity, number of previous episodes, duration of previous episode, general health, depression, anxiety and stress.

To investigate the personal impact of LBP for the three definitions of recurrence (aim 3) we coded each participant based on a categorical option within each epoch. Participants who did not experience a recurrence were the reference group. Participants who experienced a recurrence were coded so they could only meet one of the three recurrence definitions. Participants were coded as having a *recurrence of low back pain* if they had a recurrence but did not report it as meeting the definition for recurrence of activity-limiting LBP or recurrence of LBP causing care-seeking. Participants were coded as having a *recurrence of activity-limiting LBP* if they met this definition but did not seek care. Participants were coded as having a *recurrence of LBP causing care-seeking* care seeking if they reported a recurrence causing care seeking regardless of the degree of activity limitation reported. All epochs after the first two recurrences were considered to be missing values in the analysis. The first GEE for this analysis investigated the unadjusted association between the

definitions of recurrence and the impact score and the second GEE was an adjusted analysis that investigated whether this relationship was influenced by baseline covariates. All analyses were performed with IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp.).[10]

3. Results

3.1. Participants

The demographic and clinical characteristics of the participants are presented in **Table 1**. The mean age of participants was 49.7 years (SD, ±15.1), 50% were men, and 79.2% were referred from a physiotherapist. The median duration of recovery at the time of study entry was 14 days (IQR=7 to 27.5). The median number of previous episodes was 5 episodes (IQR=2 to 18.5), and the median duration of the previous episode was 14 days (IQR=5 to 40.5). The median personal impact of LBP during the previous three-months at baseline was 19 points (ranging from 8 to 49). Of the 250 participants, 68% had a recurrence of LBP, and 32% had no recurrence over the 12-month period.

3.2. Personal impact of LBP in people who recently recovered from an episode of LBP

The average personal impact of LBP over one year in people who recently recovered from an episode of LBP was based on 238 participants as there were 12 participants with missing data for the outcome at more than one time point. The median personal impact of LBP over one year in people who recently recovered from an episode of LBP (regardless of having a recurrence or not) was 11.5 points (IQR=9.5 to 14.8). Throughout the study period the median and IQR for personal impact of LBP was relatively stable as shown in **Figure 1**.

3.3. Personal impact of LBP in people who do and do not experience a recurrence

For the GEE analyses, the percentage of missing data across the four follow-up time points for the outcome of impact of LBP was very low (4.9%), and the missing data for the variable of recurrence was about 13% (approximately 10% related to the criteria of considering the data after two recurrences as missing). As a result, of the 1,000 possible assessment epochs (250 participants with four epochs each) we included 846 (84.6%) in the analysis.

As shown in **Table 2**, results from the GEE analysis demonstrated that the estimate of the personal impact for people who had no recurrence was 11.1 points (95% CI=10.6 to 11.5). Overall, having a recurrence increased the personal impact of LBP by 4.1 points (95% CI=3.3 to 4.8) when compared to the reference group (no recurrence). This means that over a three-month period, the

personal impact for people who experienced a recurrence of LBP was 15.2 points (95% CI=13.9 to 16.3). The results from the adjusted model were similar to the unadjusted model.

3.4. Personal impact of LBP associated with three definitions of recurrence

Of the 68% participants who had a recurrence of LBP, 14.4% only had a recurrence of an episode of LBP (definition one), 14.0% had a recurrence of activity-limiting LBP but no care-seeking (definition two), and 39.6% had a recurrence of LBP causing care-seeking (definition three). The results from the GEE analysis demonstrated that the estimate of the personal impact for people who had no recurrence was 11.1 points (95% CI=10.7 to 11.5). Overall, having a recurrence of an episode of LBP (definition one) increased the personal impact of LBP by 1.6 points (95% CI=0.9, 2.3), having a recurrence of activity-limiting LBP (definition two) increased the personal impact of LBP by 4.4 points (95% CI=2.8 to 6.1), and having a recurrence of LBP causing care-seeking (definition three) increased the personal impact of LBP by 5.8 points (95% CI=4.6 to 6.9), when compared to the reference group (no recurrence). This means that over a 3-month period, the personal impact for people who experienced a recurrence of an episode of LBP (definition one) was 12.7 points (95% CI=11.6 to 13.8), for people who experienced a recurrence of activity-limiting LBP (definition two) was 15.5 points (95% CI=13.5 to 17.6), and for people who experienced a recurrence of LBP causing care-seeking (definition three) was 16.9 points (95% CI=15.3 to 18.4). The results from the adjusted model were similar with the unadjusted model. **Figure 2** presents the estimates of the personal impact over each three-month period for each definition.

4. Discussion

4.1. Summary of main findings

This study found that participants who had recently recovered from an episode of LBP on average experienced minimal impact due to LBP over the following year. The personal impact due to LBP was higher in those who had experienced a recurrence, but the magnitude was relatively small on average and dependent on the definition of recurrence used. Those who had a recurrence but did not report it as meeting definitions for recurrence of activity-limiting LBP or recurrence of LBP causing care-seeking had only minor increases in impact. The group of people having a recurrence that resulted in care-seeking reported the greatest personal impact (16.9 points in a scale ranging between eight and 50) due to LBP.

4.2. Strengths and limitations of the study

This study provides the first evaluation of the influence of recurrences of LBP on the average personal impact of LBP. The data for this study came from a large inception cohort of consecutive patients recently recovered from an episode of LBP. We investigated the influence of three different definitions of recurrence on the personal impact. To do this, we used a multidimensional measure of the personal impact of LBP recently recommended by the National Institutes of Health task force for LBP. The measure covers the important domains of pain intensity, pain interference, and physical function. The study also has some limitations. First, we collected the measure of personal impact related to the previous three-months. We acknowledge that the results may be affected by recall. However, previous studies investigating recall over three-months in working-age adults with musculoskeletal complains indicate that patients are able to accurately recall specific measures for up to three-months.[7; 12] Additionally, we collected the average personal impact over three-months, which may hide some shorter periods (e.g. one week) with much higher impact. Secondly, to date, there are no studies describing the clinimetric properties of the personal impact of LBP questionnaire, nor are there published thresholds of low, moderate or high impact; however, this measure includes well established items,[1; 4; 11; 13; 18] and is recommended by the National Institutes of Health task force for LBP. Our study provides some important data on this new measure. Finally, for the analysis investigating different definitions of a recurrence we considered only the first two recurrences reported by any participant within the 12-months. The decision was made because data about the start and end date of additional recurrences were not collected.

4.3. Meaning of the study: implications for clinicians and future research

The findings of this study have important implications for clinicians and patients. The results demonstrate that despite recurrences being very common in the first year after recovering from an episode of LBP, the average personal impact is quite low even in those patients who do report a recurrence, given that the measure ranges from eight to 50. So, while clinicians should educate patients about the likelihood of recurrences, they should also reassure them that many recurrences will have little impact. Given we also found the impact scores were only a little higher in those who sought care, further research is needed to understand the drivers of care seeking in patients who have a recurrence of LBP. Although care-seeking due to LBP appears to be more common in patients with higher pain and disability,[5] there are no studies investigating factors associated with care seeking in patients who have a recurrence of LBP.

Our findings suggest that the consensus definition of a recurrence[17] includes recurrences that appear to have little personal impact. This raises questions about whether this definition of a recurrence is ideal for assessing the effect of interventions aiming to prevent recurrences. While it would be ideal to prevent all recurrences, this is probably not realistic and our results provide some support for using a definition such as recurrence causing at least moderate impact on activities of daily living, given we found higher levels of personal impact when this definition was used. Additionally, future studies need to investigate clinimetric properties of the personal impact of LBP questionnaire, and possible thresholds describing the levels of impact (e.g. low, moderate or high impact).

5. Conclusion

In summary, despite recurrences of LBP being common, on average, people have minimal impact due to LBP over the following year. The personal impact due to LBP is higher in those who experience a recurrence of moderate activity-limiting LBP or a recurrence of LBP causing care-seeking.

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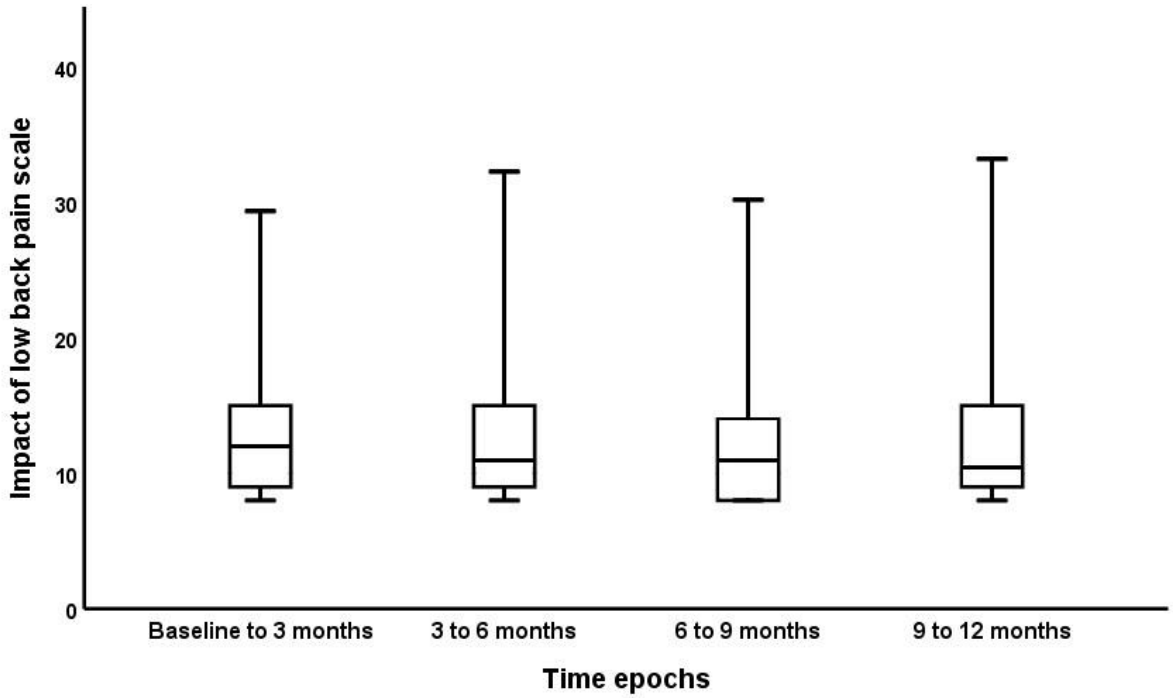

Figure 1. Personal impact of LBP over one year considering each time epochs in people recently recovered from an episode of LBP. Values are presented according to median and interquartile range.

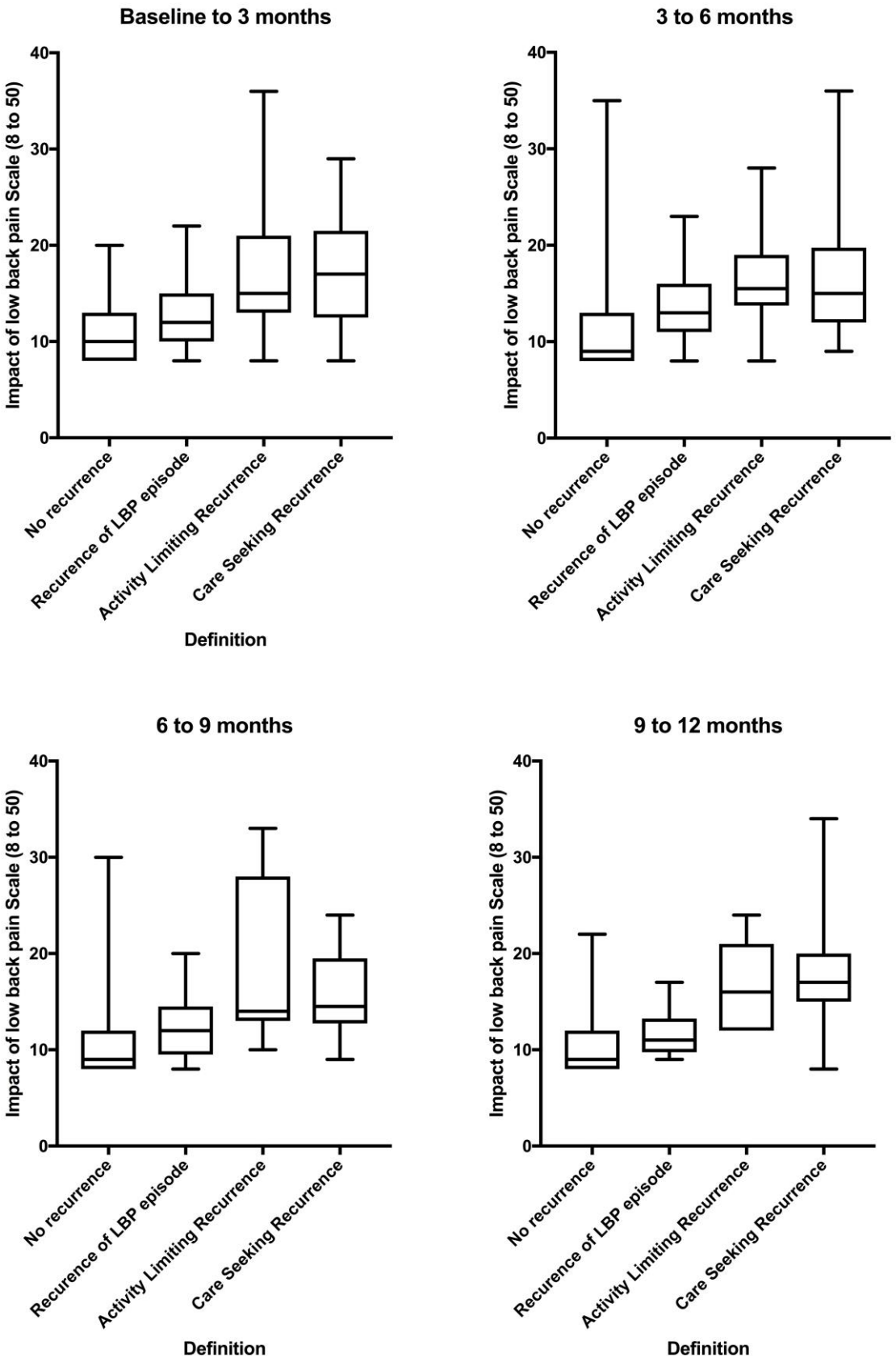

Figure 2. Personal impact of LBP for participants meeting each definition over each 3-month epoch. Graphs based on raw data.

Table 1. Baseline characteristics of the study participants. Values are numbers (percentages) unless stated otherwise

Variable	Participants
Mean (SD) age mean years	49.7 (15.1)
Gender	
Male	125/250 (50.0)
Manual task involving heavy loads	
Rarely (rarely, very rarely or never)	100/250 (40.0)
Occasionally	84/250 (33.6)
Frequently (frequently or very frequently)	66/250 (26.4)
Manual task involving awkward position	
Rarely (rarely, very rarely or never)	110/250 (44.0)
Occasionally	74/250 (29.6)
Frequently (frequently or very frequently)	66/250 (26.4)
Physical activity	
Vigorous	124/250 (49.6)
Moderate	56/250 (22.4)
Low	70/250 (28.0)
General Health	
Excellent (excellent or very good)	128/250 (51.2)
Good	99/250 (39.6)
Poor (fair or poor)	23/250 (9.2)
Number of previous episodes	
1-2 episodes	70/250 (28.0)
3-10 episodes	93/250 (37.2)
More than 10 episodes	87/250 (34.8)
Duration of last episode	
<2 weeks	146/250 (58.4)
2-6 weeks	51/250 (20.4)
>6 weeks	53/250 (21.2)
Perceived risk of recurrence	
0-5 points	125/250 (50.0)
>5 points	125/250 (50.0)
Depression	
Normal (normal or mild)	215/250 (86.0)
≥Moderate (moderate, severe or extremely severe)	35/250 (14.0)
Anxiety	
Normal (normal or mild)	206/250 (82.4)
≥Moderate (moderate, severe or extremely severe)	44/250 (17.6)
Stress	
Normal (normal or mild)	204/250 (81.6)
≥Moderate (moderate, severe or extremely severe)	46/250 (18.4)
Recurrence of LBP	
Yes	170/250 (68%)
No	80/250 (32%)

Data were measured at baseline assessment. SD, standard deviation. LBP, low back pain.

Table 2. Effect of recurrences on personal impact of LBP scores, using a GEE model with an exchangeable correlation

	β coefficient (95% CI)
Aim 2: No recurrence comapred to recurrence (unajusted)*	
No recurrence	Reference
Recurrence of an episode of LBP	4.1 (3.3, 4.8)
Intercept (mean of reference group)	11.1 (10.6, 11.5)
Aim 2: No recurrence compared to recurrence (ajusted)**	
No recurrence	Reference
Recurrence of an episode of LBP	4.0 (3.3, 4.8)
Intercept (mean of reference group)	8.0 (6.5, 9.4)
Aim 3: No recurrence compared to different recurrence definitions (unadjusted)†	
No recurrence	Reference
Recurrence of an episode of LBP	1.6 (0.9, 2.3)
Recurrence of activity limiting	4.4 (2.8, 6.1)
Recurrence of care-seeking	5.8 (4.6, 6.9)
Intercept (mean of reference group)	11.1 (10.7, 11.5)
Aim 3: No recurrence compared to different recurrence definitions (adjusted)††	
No recurrence	Reference
Recurrence of an episode of LBP	1.5 (0.8, 2.3)
Recurrence of activity limiting	4.4 (2.8, 6.0)
Recurrence of care-seeking	5.7 (4.6, 6.8)
Intercept (mean of reference group)	8.1 (6.7, 9.5)

GEE, generalised estimating equation; LBP, low back pain; 95% CI, confidence interval.

*Dependent variable: personal impact of LBP; Independent variable: recurrence definition (as no recurrence, recurrence of LBP).

**Dependent variable: personal impact of LBP; Independent variables: recurrence definition, age, gender, exposure to heavy loads, exposure to awkward posture, physical activity level, general health, number of previous episodes, duration of previous episode, depression, anxiety, and stress.

†Dependent variable: personal impact of LBP; Independent variable: recurrence definition (as no recurrence, recurrence of an episode of LBP, recurrence of activity limiting LBP, and recurrence of care-seeking).

††Dependent variable: personal impact of LBP; Independent variables: recurrence definition, age, gender, exposure to heavy loads, exposure to awkward posture, physical activity level, general health, number of previous episodes, duration of previous episode, depression, anxiety, and stress.

Appendix 1. Personal impact of low back pain questionnaire

In the past 3 months, how would you rate your low back pain on average? 0 means no pain and 10 means the worst imaginable pain

0	1	2	3	4	5	6	7	8	9	10

Considering the last **3 months** please select one option for each question below:

	Not at all	A little bit	Somewhat	Quite a bit	Very much
How much did pain interfere with your day-to-day activities?	□	□	□	□	□
How much did pain interfere with work around the home?	□	□	□	□	□
How much did pain interfere with your ability to participate in social activities?	□	□	□	□	□
How much did pain interfere with your household chores?	□	□	□	□	□

Considering the last **3 months** please select one option for each question below:

	Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
Are you able to do chores such as vacuuming or yard work?	□	□	□	□	□
Are you able to go up and down stairs at a normal pace?	□	□	□	□	□
Are you able to go for a walk of at least 15 minutes?	□	□	□	□	□
Are you able to run errands and shop?	□	□	□	□	□

Chapter 7

Discussion

7.1 Preface

The broad aims of this thesis were: 1) to develop and validate a clinical prediction model for recovery of an episode of acute low back pain, and 2) to provide a better understanding of the course of recurrences of low back pain and related prognostic factors. The first chapter of this thesis presents an overview of the existing low back pain literature and the topics investigated in the following studies. The first two studies of the thesis (**Chapter Two** and **Chapter Three)** present the results of studies that aimed to develop (**Chapter Two**) and validate (**Chapter Three**) a clinical prediction model to predict recovery from an episode of acute low back pain at three different time points. The study presented in **Chapter Four** is a systematic review that synthesised the current literature on estimates of recurrences of low back pain and related prognostic factors. The study presented in **Chapter Five** continues this theme, using an inception cohort study to investigate how commonly recurrences occur, and prognostic factors for a recurrence. The study presented in **Chapter Six** describes the personal impact of recurrences of low back pain. The current chapter summarises the thesis findings, and implications of these findings. The implications section covers both clinical implications and implications for future research.

7.2 Summary of thesis findings

7.2.1 Predicting recovery of an episode of acute low back pain

Despite the favorable average clinical course of an episode of acute low back pain, there is substantial individual variability.[1-3] The ability to identify the individual likelihood of recovery by key time points would be valuable to better inform patients and decisions about care. **Chapter Two** presented a study that developed a clinical prediction model to predict the probability of recovery at one-week, one-month and three-months after one-week review in patients who still have low back pain one-week after initially seeking care. The final model included duration of current episode, number of previous episodes, depressive symptoms, pain intensity at one-week, and change in pain over the first week after seeking care. Depending on an individual's scores for each of these five predictor variables, the probability of recovery at one-week, one-month and three-months after one-week review ranged from 4% to 59%, 19% to 91% and 30% to 97%, respectively. The model had good discrimination (C-statistic=0.76) and calibration. **Chapter two** provided evidence that the developed clinical prediction model was

able to predict the likelihood of recovery from an episode of acute low back pain at three time points. However, clinical prediction models need to be tested for external validity before being recommended for clinical practice, as many prediction models do not generalise when tested in new populations.[4]

Model validation studies evaluate the performance of the original model using data from a different sample to investigate if similar results are found.[5] **Chapter Three** presented a validation study of the developed clinical prediction model described in **Chapter Two**. Some variables were initially re-categorised in the development dataset to enable validation testing of the model in the new dataset. The performance of the clinical prediction model with re-categorised variables in the development dataset was good (C-statistic=0.76). The discrimination of the model using the validation dataset was also good (C-statistic=0.71). The calibration for the validation sample was acceptable at one-month. However, the predicted probabilities within quintiles tended to overestimate the observed recovery proportions at one-week and underestimate them at three-months. This needs to be considered if the tool is used for guiding decisions about care. For example, at one-week the model over-predicted the numbers of patients recovered, and this should be considered if recommending no extra intervention due to a good prognosis. **Chapter Three** provided evidence that the developed clinical prediction model demonstrated reasonably good external validity when tested in a different population.

7.2.2 Risk, prognostic factors and personal impact of recurrences of low back pain

Previous literature demonstrates that most individuals with acute low back pain recover within six- to 12-weeks;[2,6] however, it is widely believed that recurrences are common.[7,8] To date, there are no widely accepted estimates of the risk of a recurrence of low back pain and very little is known about prognostic factors for a recurrence of low back pain. **Chapter Four** presented a systematic review, which investigated the risk of and prognostic factors for a recurrence of low back pain. The review included longitudinal studies of adults who had recovered from a previous episode of low back pain within 12-months. Only one included study[9] was considered to have an adequately short inception period (i.e. less than six-weeks) to provide unbiased results. The study reported an estimate of a recurrence of an episode of low back pain of 24% within one year, however, this result was based on a one-year recall period. When recurrence was defined as recall of recurrence at one-year or pain reported at the three- or 12-month follow-up (even if participants failed to report a recurrence at 12 months), the recurrence estimate increased to 33%. A history of previous episodes of low back pain prior to the most recent episode was the only significant predictor of recurrence of low back pain in the two included studies,[9,10] which

investigated prognostic factors. The available limited evidence showed that there are no robust estimates of the risk of a recurrence of low back pain and related prognostic factors. **Chapter Four** demonstrated the need for a large, well-designed inception cohort study to investigate risk of recurrences and prognostic factors for a recurrence.

Chapter Five presented an inception cohort study, designed to address the limitations from previous studies[9-16] investigating the risk of recurrences of low back pain and related prognostic factors. The study enrolled 250 patients who had recovered from an episode of low back pain within the past month and followed them monthly for one year. Within one year, 69% of participants experienced a recurrence of an episode of low back pain, and approximately 40% experienced a recurrence of activity limiting low back pain or a recurrence of low back pain causing care seeking. Frequent exposure to awkward postures, longer time spent sitting, and greater than two previous episodes of low back pain increased the risk of a recurrence of an episode of low back pain. **Chapter Five** provided evidence that: 1) the estimate of recurrence is much higher than previously reported, and 2) novel prognostic factors for a recurrence of low back pain were proposed.

Despite the findings in **Chapter Five** providing strong evidence that recurrences are very common, little is known about how much impact is associated with recurrences. In addition, it is unclear how much the definition of a recurrence influences the associated personal impact. **Chapter Six** described a study that used the measure of "personal impact of low back pain" recommended by the National Institutes of Health task force on research standards for low back pain[17] to: 1) investigate the personal impact of low back pain over a one-year period in people recently recovered from a previous episode of low back pain; 2) investigate if the personal impact of low back pain is different in people who do and do not experience a recurrence; and 3) investigate the personal impact of low back pain in participants who met three different definitions of a recurrence of low back pain. The study found that participants who have recently recovered from an episode of low back pain have minimal levels of personal impact due to low back pain over the following year. The personal impact due to low back pain was higher in those who had experienced a recurrence when compared with those who had no recurrence, but the magnitude of impact was dependent on the definition of recurrence used. Those who had a recurrence but did not report moderate activity-limitation or care-seeking had only minor increases in impact. Participants who had recurrences of low back pain causing care-seeking reported the greatest personal impact (16.9 points in a scale ranging between 8 and 50). **Chapter Six** reported evidence that while most people report a recurrence of an episode of low back pain, many recurrences result in little personal impact.

7.3 Clinical and research implications

7.3.1 Predicting recovery of an episode of acute low back pain

Chapter Two provided evidence that a clinical prediction model using five variables was able to predict the likelihood of recovery from an episode of acute low back pain at three time points, and **Chapter Three** provided evidence that the developed clinical prediction model demonstrated reasonably good external validity when tested in a different population. The different nature of the source of samples could influence the accuracy of the rule, due to predictors be specific to particular populations.[18] However, confirmative results in the validation study with a different patient population and from different clinicians provides evidence that the prediction model can be generalized to new patients.[18]

This tool can provide important information to patients and clinicians and may help clinical decision making. For example, a patient with a favourable prognosis and high likelihood of recovery by one-week and one-month, may be reassured and decide to continue simple baseline care rather than receive additional intervention. Alternatively, a patient with low probability of recovery by three-months may be more likely to decide to receive additional intervention. Although there is a need to test the clinical and cost effectiveness of the use of this clinical prediction model in future impact studies, previous clinical prediction models have demonstrated usefulness in clinical practice.[19-21]

Easy to use clinical prediction models, such as the short-form Orebro Musculoskeletal Pain Questionnaire[21] and the STarT Back Tool,[20,22] are recommended[23,24] to identify patients likely to have poor outcomes and thus help when making clinical decisions. Our clinical prediction model can potentially be used as well as, or instead of, the previous clinical prediction models, and may be more relevant to some patients with acute low back pain. Both the Orebro Musculoskeletal Pain Questionnaire and the STarT Back Tool were designed to predict poor outcomes (e.g. persistent pain or disability) at intermediate and long-term follow-up (e.g. six- and 12-months), and may therefore be more relevant for patients with chronic low back pain, while our clinical prediction model provides estimates of likely time to recovery of patients at short-term follow-up (<three months), and may be more relevant to patients with acute low back pain.

The use of our clinical prediction model may also help to reinforce the recommendations of recent guidelines[24,25] for the management of low back pain, in respect to advice and education about the prognosis of low back pain. The guidelines recommend that early management should include advice and education about the course of low back pain; reassurance that low back pain is not a serious disease and that the symptoms will improve over time; as well as encouragement to stay active.[24,25] Early supervised exercise therapy can be considered if recovery is slow or for

patients in a higher risk group for persistent disabling pain.[25,26]

There are also some important research implications related to the findings of the development and validation studies of this clinical prediction model. Most importantly, there is a need for future studies to investigate if the use of the clinical prediction model improves health outcomes and costs associated with acute low back pain. While the clinical prediction model has potential to reduce unnecessary care in patients who have a good prognosis, this needs to be tested in future studies. A randomised controlled trial investigating the clinical and economic benefits of using the stratified approach of the STarT Back Tool compared with current practice found better outcomes and less costs when minimal care was provided in patients with a good prognosis.[20] The use of our clinical prediction model should be tested in a randomised controlled trial to assess if its use reduces costs. Other study design options for testing the clinical value of the prediction model include a "before-after" impact study which measures the outcome before, during, and after using the clinical prediction model, and an "on-off" impact study which measures the outcome at different time points when the clinical prediction model is or is not utilised.[27]

Our clinical prediction model has demonstrated reasonably good discrimination for recovery from pain but has not been tested for predicting disability. The Orebro Musculoskeletal Pain Questionnaire has 'acceptable' discrimination to predict disability (polled AUC=0.75, 95% CI=0.69 to 0.82), and 'poor' discrimination to predict pain outcomes (polled AUC=0.69, 95% CI=0.62 to 0.76).[28] The StarT Back Screening Tool has an 'acceptable' discrimination to predict disability (polled AUC=0.74, 95% CI=0.66 to 0.82) 'non-informative' discrimination to predict pain outcome (polled AUC=0.59, 95% CI=0.59 to 0.63).[28] Future studies should test the performance of our clinical prediction model for prediction of disability.

7.3.2 Risk, prognostic factors and personal impact of recurrences of low back pain

Chapter Five provided evidence that the estimate of recurrence of low back pain is much higher than previously reported,[9,14] but **Chapter Six** found that many recurrences result in little personal impact. There are some important clinical implications of these findings. First, it is important for clinicians to inform patients with low back pain that recurrences are very common and occur in approximately two-thirds of patients within one year. This may help to set realistic expectations of patients about the risk of having recurrences after recovering from an episode of low back pain. However, the findings in **Chapter Six** mean that clinicians can also reassure patients that many recurrences will usually produce little personal impact. Information provided by the clinician may potentially impact on patients' expectations.[29]

A second clinical implication of the high estimate of recurrences identified is the potential use and importance of secondary prevention strategies for patients after they recover from an episode of low back pain. Current guidelines for management of low back pain typically lack recommendations for secondary prevention of low back pain,[30,31] reflecting the limited available evidence and potential lack of focus on prevention in this field. A recent systematic review investigating the effectiveness of interventions for prevention of an episode of low back pain found moderate-quality evidence that exercise combined with education reduces the short-term risk of an episode of low back pain by 45% (95% CI=26% to 59%).[32] Importantly, most of the studies included in the review recruited patients who had experienced previous low back pain. By doing so, the studies provided evidence on the effectiveness of secondary prevention, which is particularly relevant given the high recurrence proportion found in this thesis.[25]

There are also important research implications related to the high proportions of recurrences identified and the findings of relatively low impact of most recurrences. Prevention of recurrences, especially those producing substantial impact, has the potential to greatly reduce the burden of low back pain. Despite the recent systematic review demonstrating that exercise and education reduces the risk of an episode of low back pain, the programmes were typically quite intensive (e.g., 20 one-hour sessions of supervised exercise),[32] and this likely limits the broad implementation of this approach.[33] Therefore, an area of important future research is to examine whether interventions which are more flexible, cheaper and less time consuming can also have similar prevention benefits. An example is a recent study protocol describing a trial testing whether two sessions of McKenzie based therapy aiming to teach patients a self-management approach are effective for prevention of recurrences of low back pain.[34]

A second research implication of the findings in **Chapter Five** and **Chapter Six** is the need to further investigate the ideal definition of a recurrence of low back pain. The results of our study suggest that the consensus definition of a recurrence of an episode of low back pain[35] appears to include recurrences that have little personal impact. Future studies investigating the effect of interventions to prevent recurrences should consider using a definition of a recurrence causing at least moderate impact on activities of daily living, given the higher levels of personal impact associated with this definition.

There is also a need for future studies to investigate clinimetric properties of the personal impact of low back pain questionnaire and possible thresholds describing the levels of impact (e.g. low, moderate or high impact). This multidimensional questionnaire covers important domains of pain intensity, pain interference with normal activities and functional status,[17] and has potential to classify patients with low back pain according to its impact. However, interpretation is limited by lack of strong data on the clinimetric properties. Given the tool is recommended by the

National Institutes of Health task force on research standards for low back pain further research on its properties should be a priority.

Chapter Five proposed new prognostic factors for a recurrence of low back pain. There are some important clinical implications related to this finding. First, this may help clinicians identify patients who are at greatest risk of having a recurrence and who are, therefore, even stronger candidates for the use of prevention strategies. The second implication is that clinicians could advise patients about potentially avoiding factors that place them at higher risk of a recurrence, such as high exposure to awkward posture and longer time spent sitting, as these are modifiable factors. However, the studies included in this thesis do not provide any evidence that targeting prevention to those at higher risk or addressing these prognostic factors will result in reduced risk of recurrences. Future research needs to test these hypotheses. The findings from the systematic review of prevention of an episode of low back pain found low-quality evidence of no preventative benefit from ergonomic interventions,[32] however, these did not explicitly address the prognostic factors of awkward postures and long periods of sitting identified in **Chapter Five**.

There are important research implications related to the prognostic factors for recurrence that we propose. First, two of the three prognostic factors proposed in our study are modifiable factors (e.g. exposure to awkward posture and longer time spent sitting), that may be potential targets for the development of new prevention strategies. Future studies need to investigate whether modifying these prognostic factors reduces the risk of recurrences. A challenge for these future studies would be finding practical ways to modify exposure to the prognostic factors. For example, spending less time sitting may be difficult for people who work for long hours and have a primarily seated job. No studies have investigated if the use of stand-up desks or taking regular breaks from sitting reduces the risk of recurrences. Future high-quality randomised controlled trials are needed to investigate this.

The second implication is the need of future studies to validate the prognostic factors for a recurrence. While previous studies have investigated the association of exposure to awkward postures and low back pain, the systematic review in **Chapter Two** and another systematic review[36] have struggled to find consistency between studies. A case-crossover study reported that manual tasks involving awkward postures were associated with an eight-fold (95% CI=5.5 to 11.8) increase in odds of the onset of low back pain,[37] but did not investigate recurrences of back pain. Two other studies that did investigate prognostic factors for a recurrence of low back found exposure to awkward postures was not a significant predictor,[10,14] however, in one of the studies exposures to awkward postures demonstrated a trend towards an important relationship but the analysis was underpowered.[10] In light of the findings in **Chapter Five**, the evidence

regarding the predictive value of awkward postures is somewhat conflicting. This may be due to numerous factors including differences in study design, population studied and study duration. To resolve this issue, clearly defined populations and well designed, fully powered studies are needed.

7.4 Conclusion

In summary, the series of studies described in this thesis have produced new and important information about the recovery from an episode of low back pain, and recurrences that commonly occur after recovering from an episode of low back pain. The findings of the thesis showed that a new developed and validated clinical prediction model is able to predict the likelihood of recovery from an episode of acute low back pain at three time points. Additionally, the estimate of recurrence of low back pain is much higher than previously reported, though many recurrences result in little personal impact. New prognostic factors for a recurrence of low back pain were proposed. Some of the findings have immediate relevance to clinical practice, while others provide preliminary hypotheses that require further testing prior to recommending changes to clinical practice.

7.5 References

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Appendices

Appendix 1: Ethics approval (#5201700443) Chapter Three

Appendix 2: Search strategy used in Chapter Four

Appendix 3: Ethics approval (#5201500494) Chapter Five and Chapter Six

Appendix 4: Participant Information and Consent Form – Chapter Five

Appendix 5: *British Journal of Sports Medicine* instructions for authors

Appendix 6: *PAIN* instructions for authors

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Search strategy on each database of the systematic review - Chapter Four

MEDLINE: 4199 titles - Final search: 16/02/2016

1	dorsalgia.ti,ab.	61
2	exp back pain/	31315
3	backache.ti,ab.	1993
4	exp low back pain/	16230
5	(lumbar adj pain).ti,ab.	1092
6	coccyx.ti,ab.	506
7	coccydynia.ti,ab.	73
8	sciatica.ti,ab.	3305
9	sciatic neuropathy/	1643
10	spondylosis.ti,ab.	2400
11	lumbago.ti,ab.	1117
12	back disorder$.ti,ab.	478
13	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12	40099
14	exp cohort studies/	1491804
15	incidence/	199415
16	follow-up studies/	533561
17	prognos$.mp.	591194
18	predict$.mp.	1001784
19	course.mp.	420347
20	survival.mp.	840262
21	14 or 15 or 16 or 17 or 18 or 19 or 20	3508901
22	exp recurrence/	156014
23	recur$.mp.	511550
24	relaps$.mp.	125250
25	reappearance$.mp.	3970
26	reoccurence$.mp.	10
27	return.mp.	74851
28	episode$.mp.	148687
29	onset.mp.	353124
30	inciden$.mp.	680610

31	new case$.mp.	20938
32	risk.mp.	1640012
33	22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32	2938968
34	**13 and 21 and 33**	**4199**

Embase: 9697 titles - Final search: 16/02/2016

1	dorsalgia.mp.	117
2	back pain.mp.	64443
3	exp low back pain/	41377
4	exp backache/	78939
5	(lumbar adj pain).mp.	1780
6	coccyx.mp.	887
7	coccydynia.mp.	127
8	sciatica.mp.	5089
9	spondylosis.mp.	7940
10	lumbago.mp.	1634
11	back disorder$.ti,ab.	610
12	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11	99631
13	exp cohort studies/	230709
14	incidence/	242847
15	follow-up studies/	552207
16	prognos$.mp.	803325
17	predict$.mp.	1468671
18	course.mp.	876243
19	survival.mp.	1171536
20	13 or 14 or 15 or 16 or 17 or 18 or 19	4254504
21	exp recurrence/	141777
22	recur$.mp.	740225
23	relaps$.mp.	229968
24	reappearance$.mp.	5141
25	reoccurence$.mp.	35
26	return.mp.	109507

27	episode$.mp.	231930
28	onset.mp.	530481
29	inciden$.mp.	998578
30	new case$.mp.	29591
31	risk.mp.	2606119
32	21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31	4488693
33	**12 and 20 and 32**	**9697**

CINAHL: 1061 titles - Final search: 16/02/2016

1	dorsalgia	9
2	back pain	25460
3	low back pain	15909
4	lumbar adj pain	16
5	coccyx	199
6	coccydynia	44
7	sciatica	1459
8	sciatic neuropathy	58
9	spondylosis	692
10	lumbago	54
11	back disorder	504
12	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11	27435
13	cohort studies	42539
14	incidence	98692
15	follow-up studies	13340
16	prognos$	803325
17	predict$	43578

18	course	63675
19	survival	92726
20	13 or 14 or 15 or 16 or 17 or 18 or 19	4316972
21	recurrence	53414
22	recur$	866
23	relaps$	9
24	reappearance$	171
25	return	18445
26	episode$	22384
27	onset	46983
28	inciden$	7
29	new case$.mp.	4685
30	risk.mp.	512342
31	21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30	615901
32	**12 and 20 and 31**	**1061**

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