Contemporary Understanding of Prevention of Spinal Pain

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As supervisors of Tarcisio Folly de Campos' doctoral work, we certify that we consider his thesis ***"Contemporary Understanding of Prevention of Spinal Pain"*** to be suitable for examination.

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STATEMENT OF ORIGINALITY

I, Tarcisio Folly de Campos, hereby declare that the work contained within this thesis, ***"Contemporary Understanding of Prevention of Spinal Pain"***, is my own and has not been submitted to any other university or institution, in part or whole, as a requirement of a degree.

I, Tarcisio Folly de Campos, hereby declare that I was the principal researcher of all work included in this thesis, including the work published with multiple authors.

I, Tarcisio Folly de Campos, 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 certify that all information sources and literature are indicated in this thesis.

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PUBLICATIONS, PRESENTATIONS AND MEDIA ARISING FROM THIS THESIS

Some of the work contained in this thesis has been published or submitted to a peer-reviewed journal and/or presented in the following conferences, and social media.

Peer-reviewed published papers

de Campos TF, Maher CG, Steffens D, Fuller JT, Hancock MJ. Exercise programs may be effective in preventing a new episode of neck pain: a systematic review and meta-analysis. *J Physiother*. 2018 Jul;64(3):159-165. doi: 10.1016/j.jphys.2018.05.003

de Campos TF, Maher CG, Clare HA, da Silva TM, Hancock MJ. Effectiveness of McKenzie method-based self-management approach for the secondary prevention of a recurrence of low back pain (SAFE Trial): protocol for a pragmatic randomized controlled trial. *Phys Ther*. 2017 Aug 1;97(8):799-806. doi: 10.1093/ptj/pzx046

Submitted papers under peer-review

de Campos TF, Pocovi NC, Maher CG, Clare HA, da Silva TM, Hancock MJ. An individualised self-management exercise and education program did not prevent recurrence of low back pain, but may reduce care seeking: a randomised, controlled trial. *Submitted to the Journal of Physiotherapy (November 21st 2019).*

de Campos TF, Maher CG, Fuller JT, Steffens D, Attwell S, Hancock MJ. Prevention strategies to reduce future impact of low back pain: a systematic review and meta-analysis. *Submitted to the British Journal of Sports Medicine (November 5th 2019).*

Peer-reviewed published papers during PhD candidature (related topics but not contained within this thesis)

da Silva T, Mills K, Brown BT, Pocovi N, ***de Campos T***, Maher C, Hancock MJ. Recurrence of low back pain is common: a prospective inception cohort study. *J Physiother*. 2019 Jul;65(3):159-165. doi: 10.1016/j.jphys.2019.04.010

Overaas CK, Johansson MS, ***de Campos TF***, Ferreira ML, Natvig B, Mork PJ, Hartvigsen J. Prevalence and pattern of co-occurring musculoskeletal pain and its association with back-related disability among people with persistent low back pain: protocol for a systematic review and meta-analysis. *Syst Rev*. 2017 Dec 16;6(1):258. doi: 10.1186/s13643-017-0656-7

National and international conference/congress presentations

Poster presentations

da Silva T, Mills K, Brown BT, Pocovi N, ***de Campos T***, Maher C, Hancock MJ. Recurrences of low back pain are very common – a prospective inception cohort study. *International Forum for Back and Neck Pain Research in Primary Care – 2019*, Quebec City – Canada; July 2019.

de Campos TF, Maher CG, Steffens D, Fuller JT, Hancock MJ. Prevention of neck pain: a systematic review and meta-analysis. *World Congress on Pain (IASP) – 2018,* Boston – USA; September 2018.

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de Campos TF, Maher CG, Clare HA, da Silva TM, Hancock MJ. Effectiveness of McKenzie method-based self-management approach for the secondary prevention of a recurrence of low back pain (SAFE Trial): protocol for a pragmatic randomized controlled trial. *Back and Neck Pain Forum – 2017,* Oslo – Norway; September 2017.

Oral presentation

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PREFACE

This thesis by publication is arranged in six chapters and written so that each chapter can be read independently of each other. The studies included in this thesis investigate the prevention of low back pain (**Chapters Two to Chapter Four**), and prevention of neck pain (**Chapter Five**). Some of the work presented in **Chapters Two** to **Chapter Five** has been published in peer-reviewed journals. Macquarie University allows published manuscripts that arise from the candidature to be included in the thesis.

The introductory **Chapter One** provides comprehensive background information on the topics that will be presented in the remaining chapters of the thesis. **Chapter Two** is the protocol for a randomised controlled trial describing the rationale and methodology involved in the trial investigating the effectiveness of McKenzie-based self-management approach for the secondary prevention of a recurrence of low back pain. The study protocol is presented as the paper published in *Physical Therapy*. **Chapter Three** is a randomised controlled trial investigating the effectiveness of the McKenzie-based self-management exercise and education program for the secondary prevention of a recurrence of low back pain. The trial is presented as a manuscript submitted to the *Journal of Physiotherapy* and has recently been accepted for publication. **Chapter Four** consists of a systematic review and meta-analysis investigating the evidence for prevention strategies to reduce future impact of low back pain. This study is presented as a manuscript submitted to the *British Journal of Sports Medicine* and has recently been accepted for publication. **Chapter Five** is a systematic review and meta-analysis investigating the evidence for strategies to prevent neck pain. This study is presented as a manuscript published in the *Journal of Physiotherapy*. **Chapter Six** is an overview of the key findings with clinical implications and some future research directions.

Each chapter in this thesis contains its own reference list. Appendices that were published as online supplementary material are included at the end of the relevant chapter. Any other additional appendices and supplementary material not related to individual chapters are included at the end of the thesis. Ethical approval was obtained from Macquarie University Human Research Ethics Committee for the randomised controlled trial (ref number:

5201600187) reported in **Chapter Two** and **Chapter Three**. **Chapter Four** and **Chapter Five** did not require ethical approval. All studies presented in this thesis were prospectively registered. The randomised controlled trial presented in **Chapter Two** and **Chapter Three** was registered with the Australian New Zealand Clinical Trial Registry (ANZCTR): 12616000926437. The systematic review presented in **Chapter Four** was registered in PROSPERO (CRD42018107946). The systematic review presented in **Chapter Five** was also registered in PROSPERO (CRD42017055174).

ABSTRACT

Spinal pain, including low back pain and neck pain, are among the leading causes of disability, affecting over half a billion people around the world. Despite much research over the past three decades devoted to increasing understanding of spinal pain, the burden associated with this condition has failed to reduce. Effective strategies to prevent spinal pain are important to reducing the global burden. Given the recurrent nature of spinal pain, interventions that can reduce the risk of recurrence in those who have previously experienced an episode are particularly important.

The broad aims of the work presented in this thesis were to, (1) investigate the effectiveness of a McKenzie-based self-management exercise and education program, following the Mechanical Diagnosis and Therapy principles, in preventing a recurrence of low back pain (Chapter Two and Chapter Three) and (2) to synthesise the available literature investigating prevention strategies aiming to reduce future impact of low back pain (Chapter Four); as well as, the literature investigating prevention strategies aiming to reduce the risk of neck pain episodes (Chapter Five).

The studies presented in Chapter Two and Chapter Three outline the design and results of a randomised controlled trial evaluating the effectiveness of the McKenzie-based self-management exercise and education program as secondary prevention for a recurrence of low back pain. Findings from this randomised controlled trial suggest that the intervention did not produce a substantial reduction on the risk of a new episode of activity-limiting low back pain when compared to the control group; however, this intervention program may reduce the risk of episodes of low back pain that result in a person seeking care. Although the effect on episodes resulting in care seeking looks promissing, the confidence intervals include no effect so caution is required. We found no substantial effect between groups when assessing the overall personal impact of low back pain over 12-months. In Chapter Four, we systematically reviewed the literature evaluating the effectiveness of prevention strategies to reduce future impact of low back pain. The results of this study indicated that exercise programs can reduce future low back pain intensity, and that exercise combined with education can reduce future disability due to low back pain.

In Chapter Five, the effectiveness of intervention strategies to prevent an episode of neck pain was investigated through a systematic review of the literature. This review showed that exercise programs may be effective in preventing a new episode of neck pain.

In conclusion, findings from the randomised controlled trial (Chapter Three) provided evidence that a McKenzie-based self-management exercise and education program was no more effective than minimal intervention in reducing recurrences of low back pain; however, it may produce a substantial reduction in recurrences resulting in healthcare-seeking. In contrast, the systematic reviews presented in this thesis provided promising results. The evidence from the study in Chapter Four suggests that exercise-based and education interventions may reduce future low back pain intensity and associated disability, while the study in Chapter Five provides evidence that exercise-based programs may be effective in preventing a new episode of neck pain.

CHAPTER ONE

Introduction

1.1 Definitions and classifications of spinal pain

1.1.1 Diagnostic triage classification of spinal pain

Spinal pain is a symptom not a disease and includes pain experienced in the cervical, thoracic and lumbar spine regions. Rarely spinal pain is caused by specific spinal pathology such as fracture, cancer or infection (<1%).[1 2] Spinal pain can also be associated with radicular syndrome (radicular pain and/or radiculopathy) in approximately 5% to 10% of cases.[1 2] However, for the majority of people (90% to 95%) presenting with spinal pain, the nociceptive source of pain cannot be identified, so the term non-specific spinal pain is used to convey the diagnostic uncertainty.[1 2]

1.1.2 Spinal pain can be classified by the location of the pain

Spinal pain can also be classified by the location of the pain. Pain experienced in the cervical spine, most commonly known as neck pain, is defined by The Bone and Joint Decade 2000 – 2010 Task Force on Neck Pain and its Associated Disorders, as pain or discomfort in the posterior neck region from the superior nuchal line down to the spine of the scapula (Figure 1.A), and laterally down to the superior border of the clavicle and the suprasternal notch (Figure 1.B), with or without symptoms referred to the upper limbs.[3 4]

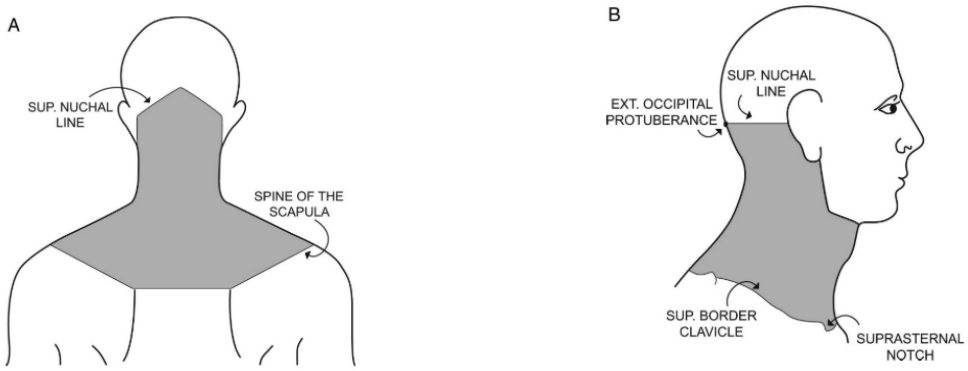

Figure 1. The anatomic region of the neck from the back (A) and the side (B) as defined by The Bone and Joint Decade 2000–2010 Task Force on Neck Pain and its Associated Disorders.[3] (*Image reproduced with permission from Springer Nature – Appendix 1*)

Pain experienced in the thoracic spine, also known as mid-back pain, is defined as pain experienced in the region of the thoracic spine, between the boundaries of the 1st thoracic and 12th thoracic vertebrae and across the posterior aspect of the trunk.[5 6]

Pain experienced in the lumbar region, commonly known as low back pain, is defined as pain and discomfort typically involving the area between the 12th rib and the buttock crease, with or without symptoms referred to the legs.[7 8] This thesis will focus on low back pain and neck pain as these conditions are among the top 10 in terms of Years Lived with Disability (YLDs),[9] and these are the spinal regions where prevention of pain is most important.

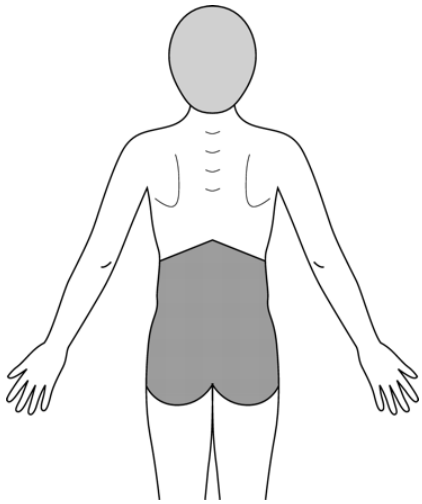

Figure 2. The anatomic region of lower back pain.[10] (*Image reproduced with permission from Springer Nature – Appendix 2*)

1.1.3 Spinal pain is commonly further classified by the duration of symptoms

Spinal pain can also be classified according to symptom duration into acute, subacute and persistent pain. The duration of symptom used to define the transition from an acute to a subacute episode of spinal pain is 6-weeks in most literature, while the transition from a subacute episode to a persistent episode is usually considered to be 3-months.[11 12]

1.2 Prevalence of spinal pain

The estimates of the prevalence of low back pain and neck pain for the adult population vary substantially between studies. This large variability in prevalence estimates is likely due to methodological differences across studies (e.g. variation in case definition, recall period) combined with heterogenous populations in terms of age, sex, culture and geographic location.[13-15]

The global point prevalence of low back pain is reported to range from 12% to 40% while the 1-year prevalence ranges from 10% to 56%.[15] In 2012, Hoy and colleagues conducted a systematic

review of the global prevalence of low back pain.[16] The authors reported a mean point prevalence of 18.3%, and 1-year mean prevalence of 38%. For neck pain, the mean point prevalence across different studies was reported to be 14.4% ranging between 0.4% and 41.5%, and a 1-year mean prevalence of about 26% ranging from 5% to 80%.[14] The best estimate of neck pain prevalence comes from the Global Burden of Disease 2010 study.[17] The authors estimated a global age-standardised point prevalence of neck pain to be around 5%. Prevalence is typically higher in females for both low back pain and neck pain.[14 16-18] The prevalence of pain is also associated with age, typically peaking between 40 to 69 years for low back pain, and 35 to 49 years for neck pain.[14-17] Not all spinal pain is associated with an impact on activities of daily living. The mean point prevalence of activity-limiting low back pain is approximately 12%, and 1-year mean prevalence around 40%.[16 19] For activity-limitation due to neck pain, the 1-year mean prevalence in the general population is estimated to be 11.5%.[20] Spinal pain is a common reason for seeking healthcare. Woodhouse and colleagues estimated the percentage of care-seeking after a new episode of low back pain or neck pain using data from the HUNT Study.[21] The reported estimates of care-seeking due to low back pain and neck pain in the general community was around 45%.

1.3 The global burden and economic cost associated with spinal pain

Spinal pain affects over half a billion people around the world.[22 23] The Global Burden of Disease Study 2016 estimated Years Lived with Disability (YLDs) for 195 countries between 1990 and 2016. In this study, low back pain ranked 1st, neck pain ranked 6th in terms of YLDs, and together they have contributed an estimated 86.6 million (95% CI, 61.3 to 113.6 million) YLDs. The total number of YLDs due to neck pain and low back pain has increased by 19.3% from 2006 to 2016, and this figure is expected to continue to increase due to the ageing and increasing population.[9]

In many countries, the economic costs associated with spinal pain are huge.[24 25] In the United States the estimated direct cost (health care expenditure) and indirect cost (e.g., productivity losses) related to low back pain and neck pain was around US$87 billion in 2013,[26] and in Australia, the total estimated cost related to low back pain was approximately AU$9 billion.[24] A systematic review investigating the costs associated with low back pain in eight different countries reported that the largest proportion of direct medical costs for low back pain was spent on physiotherapy (17%) and inpatient services (17%), followed by pharmacy (13%), and primary care (13%);[27] however direct medical costs represent only a small percentage of the

total low back pain costs. Most of the total estimated costs in these studies are indirect costs resulting from lost work productivity.[27] Data from these studies suggest that effective spinal pain prevention strategies targeting disability and days lost from work have the potential to substantially reduce the economic burden associated with spinal pain conditions.

1.4 The course of spinal pain

The available literature suggests that an acute episode of spinal pain typically has a favourable prognosis, with most people recovered or greatly improved in the first few weeks after onset.[12 28-30] A 2012 systematic review, including a total of 33 cohort studies, investigated the clinical course of pain and disability in patients with acute and persistent low back pain. The pooled mean pain score (0 to 100 pain rating scale), from 15 cohort studies, indicated that most people presenting with acute low back pain improved markedly within the first 6-weeks. The pain reduced from 52 (95% CI, 48 to 57) points at baseline down to 23 (95% CI, 21 to 25) at 6 weeks; however, after 6 weeks improvement slows, and by one year, the mean levels of pain are estimated to be low at 6 (95% CI, 3 to 10) points.[30] In this same study, the course of disability followed a similar course to that of pain.

The course of acute neck pain is also favourable but probably not as good as low back pain. A systematic review of the literature on the prognosis of acute non-specific neck pain and disability was conducted in 2011 by Hush and colleagues.[31] This review included six studies and reported a pooled mean pain score (0 to 100 pain rating scale) of 64 (95% CI, 61 to 67) at onset, 35 (95% CI, 32 to 38) at 6.5-weeks, and 42 (95% CI, 39 to 45) at 12-months. Disability, reduced from a pooled weighted mean score (0 to 100 disability rating scale) at onset of 30 (95% CI, 28 to 32) to 17 (95% CI, 15 to 19) by 6.5 weeks, without further improvement at 12-months. This study used less sophisticated data analysis methods for pooling the data across the studies when compared to the 2012 systematic review on low back pain prognosis,[30] so the less favourable prognosis needs to be treated with some caution.

Focusing on the mean population course, in terms of pain or disability, has been challenged as it does not represent the different courses of many individuals with spinal pain.[32] Therefore, some contemporary studies have turned their focus to investigating and identifying common spinal pain trajectories, which could better reflect the individual variability in the prognosis of spinal pain.

1.4.1 Individual trajectories of spinal pain

In a pioneering 2006 study,[33] Dunn and colleagues identified four different pain trajectories in a sample with low back pain over one-year. These included: *persistent mild pain* (n = 122, 36%); *recovered* (n = 104, 30%); *severe chronic pain* (n = 71, 21%); and, *fluctuating pain* (n = 45, 13%). The long-term trajectory was confirmed after seven-years follow-up for this study.[34] Further, in 2015, Kongsted and colleagues identified low back pain trajectories of 1,082 patients using low back pain intensity measured weekly over a 1-year period.[35] The authors identified eight subgroups of pain trajectories using mean low back pain intensity and the mean number of days with low back pain (latent class cluster model iv). Two of the identified trajectories included complete recovery (*recovery* and *late recovery*; 33% of participants) and one trajectory (*severe on-going*; 6% of participants) included ongoing high levels of pain. Most participants (61%) followed other trajectories that typically involved fluctuation and episodic pain (weeks with pain separated by pain-free periods).

Only a few studies have investigated neck pain trajectories.[36 37] In 2018, Ailliet and colleagues studied the course of both neck pain and low back pain over 26-weeks in patients presenting to chiropractors in Belgium and the Netherlands using latent class growth analysis. Within the neck pain sub-sample, the '*recovering from mild baseline pain'* class was the most prevalent (73.9%) representing those patients who start with mild levels of pain and improve to very low levels throughout the follow-up period. The '*recovering from severe baseline pain'* class was the second most prevalent (16.3%) representing those patients with severe pain at baseline who experience a reduction of pain over the first 6 weeks and then remain at very low levels of pain. The '*severe-chronic'* class (7.2%), represents those patients who had permanently high levels of pain throughout the follow-up period. The '*recovering from mild baseline pain with a flare-up*' class (2.6%) was the least prevalent in this study, representing patients who had a flare-up part-way through the study follow-up.[37] Further, Hallman and colleagues in 2018 identified six distinct neck-shoulder pain trajectory patterns over a 1-year follow-up period for 748 Danish workers.[36] The study found that over 60% of the study participants recovered and about 25% had a fluctuating pattern over the study follow-up period. Results from these studies on pain trajectories suggest that commonly spinal pain episodes are short-lived with a significant proportion of people improving rapidly; however, in the long-term, this condition often has an episodic course or fluctuating pattern.

1.5 The recurrent nature of spinal pain

Despite the favourable prognosis and high initial recovery rates from an episode of low back pain and neck pain, recurrent episodes are believed to be common, and one of the main reasons for the global social and economic burden.[3 14 15 38] Assessing the rates of recurrence for spinal pain has been made difficult by the lack of a standardised definition of recurrence of spinal pain. In a 2011 Delphi study, Stanton and colleagues defined a recurrence of an episode of low back pain as "a return of low back pain lasting at least 24-hours with a pain intensity of >2 on an 11-points numeric rating scale (NRS), following a period of at least 30-days pain-free".[39] A similar definition has been used in the literature for a new episode of neck pain: "an episode of neck pain lasting at least 24 hours, with a pain intensity of greater than 2 on an 11-points NRS and at least 30-days pain-free episode between episodes".[40]

The 1-year rates of recurrence of low back pain reported in the literature range from around 30% to 80%,[41-43] while for neck pain the estimates are from 50% to 85% one to five years later.[44] Likely reasons for the observed variability in estimates of recurrence include lack of standardisation of how recurrence is defined and also the inclusion of both survival cohorts and inception cohorts. Survival cohorts include participants who recovered from their last episode of low back pain or neck pain at different times producing variable and biased estimates of the risk of recurrence.

A recent systematic review of the literature investigating the risk of recurrence of low back pain included eight studies.[45] This review reported that only one study was considered to have an appropriate estimate for rate of a recurrence of low back pain within 1-year as the authors used a short inception period. This study conducted by Stanton and colleagues reported an estimated recurrence rate of 33%.[42] The authors in this review, however, suggested that it was not yet possible to obtain reliable estimates of recurrence proportions as most included studies have small sample sizes, and low methodological quality.

To overcome this gap in the literature Da Silva and colleagues conducted a high-quality prospective inception cohort study in Australia including 250 participants who had recovered from an episode of low back pain within the previous month.[19] This study investigated how commonly low back pain recurrences occur within 1-year of recovering from a previous episode

of low back pain, using three different definitions of low back pain recurrence. The primary outcome in this study was recurrence of low back pain based on the consensus definition published by Stanton and colleagues: "a return of low back pain lasting at least 24-hours with a pain intensity of >2 on an 11-points numeric rating scale".[39] The other two recurrence definitions were: (i) a return of an episode of low back pain lasting at least 24-hours with a pain intensity of >2 on an 11-points numeric rating scale, leading to at least moderate activity-limitation, and ii) a return of an episode of low back pain lasting at least 24-hours with a pain intensity of >2 on an 11-points numeric rating scale, causing care-seeking. The study found that by 1-year, 69% (95% CI, 62 to 74) of participants experienced a recurrence of any episode of low back pain, 40% (95% CI, 33 to 46) of participants had a recurrence of an episode of low back pain leading to at least moderate activity-limitation, and 41% (95% CI, 34 to 46) of participants had a recurrence of low back pain for which healthcare was sought.[19] Results from this study confirmed the high rates of recurrence and the need for effective strategies to prevent recurrences of spinal pain.

1.6 Prevention of spinal pain

Despite the clear evidence that spinal pain is a long term problem characterised by recurrent episodes,[19 32-35 37] there has been very little attention on strategies for the prevention of spinal pain. Over the last two decades, the number of randomised controlled trials investigating interventions for spinal pain has grown rapidly; however, the vast majority have tested interventions to treat spinal pain and very few have investigated prevention strategies.[46 47] Therefore, greater understanding regarding effective strategies to prevent spinal pain represents an important research priority.[17 48 49]

1.6.1 Prevention interventions are commonly classified into three levels

It is important when considering prevention to distinguish the definitions commonly used in the literature. Prevention is typically classified under three levels: primary, secondary, and tertiary prevention.[50] Primary prevention aims to prevent the onset of the condition in people who have never experienced the condition (i.e. preventing the first-ever episode of the disease). Secondary prevention involves identifying people who have experienced the condition; however, are not currently experiencing signs and symptoms of the disease (i.e. preventing the occurrence of a new episode – recurrence). The objective of tertiary prevention is to reduce further complications associated with the condition in those with established disease.[50] In the

context of spinal pain, it could be argued that primary prevention refers to preventing the first-ever episode of spinal pain. Given the available epidemiological data, this would typically include prevention strategies in children as the rates of spinal pain rise rapidly during the teenage years and are comparable to adult rates by the age of 18 years.[51] On the other hand, secondary prevention of spinal pain may involve preventing recurrences of spinal pain in those who have recovered from a previous episode of spinal pain. Given the high rates of recurrence reported in the literature,[19] secondary prevention of recurrent episodes appears particularly important for spinal pain. Tertiary prevention of spinal pain could involve strategies to prevent flare-ups in those with low levels of pain or strategies to reduce the impact of spinal pain such as work absenteeism and loss of function.

1.6.2 Evidence on the prevention of low back pain

Few systematic reviews investigating strategies to prevent low back pain have been published.[46 47 52-54] Of the few available, most have methodological limitations such as inclusion of non-randomised controlled trials,[47] no assessment of the strength of evidence (e.g. using the Grading of Recommendations Assessment, Development, and Evaluation system),[53 54] and not following a pre-specified published protocol.[52 53]

In 2016, Steffens and colleagues[46] published a high-quality systematic review and meta-analysis investigating interventions aiming to prevent a new episode of low back pain. This review included 23 trial reports and found moderate-quality evidence that an exercise program in combination with education reduces the risk of a new episode of low back pain by 45% (RR, 0.55; 95% CI, 0.41 to 0.74), and low-quality evidence that an exercise program alone may reduce the risk by 35% (RR, 0.65; 95% CI, 0.50 to 0.86); however, most other intervention strategies such as education alone, use of back-belts, use of shoe insole, and ergonomic programs either lacked evidence or appeared to be ineffective.

Despite the evidence that prevention programs involving exercise and education are effective in preventing low back pain, most of these trials investigate exercise programs which are relatively costly and time-consuming group-based classes; for example one trial provided 20 exercise sessions over 3 months.[55] In addition to the cost and time, these programs are relatively inflexible and often difficult to access, reducing the likelihood of successful implementation of these prevention programs on a large scale.

1.6.3 Barriers to implementation of current prevention strategies

Despite the evidence for the effectiveness of exercise and education programs for the prevention of spinal pain, these prevention programs do not appear to be widely implemented.[49] Barriers to implementation may include high-cost and time-consuming programs that make these prevention approaches relatively inflexible and inaccessible for many people. Previous studies have investigated possible barriers to adherence and implementation of such programs.[56 57] In a recent randomised controlled pilot study (12 participants) investigating an exercise and education program for preventing recurrence of low back pain, the authors explored the feasibility and acceptability of a physiotherapist-led group exercise and education program delivered over 8 weeks (eight, one-hour session per week) after an initial one-hour assessment session.[57] This study reported that the lack of flexible times to do the sessions, and travel time to locations may impact the acceptability of the intervention program. Barriers such as those reported in this feasibility study are likely to reduce intervention adherence and importantly make it challenging to implement these programs in the community.

1.6.4 Need for flexible, self-management approach for prevention of spinal pain

To overcome some of the barriers to widescale implementation of exercise and education prevention programs it is important to investigate alternative approaches that are still likely effective but are easier to implement. An example is the study by Larsen and colleagues that investigated the effect of a simple exercise program involving passive prone back extensions performed twice daily over ten months, and the McKenzie method-based education, in male military conscripts.[60] In this trial, the authors reported a relative risk reduction of an episode of low back pain of 64% (RR, 0.36; 95% CI, 0.18 to 0.73) when compared to no intervention control group. This trial however recruited a heterogeneous population with and without current low back pain (approximately 25% of participants had pain at the start of the study) and reported fairly high dropout rate (21%). The study provides preliminary evidence that an intervention where people are empowered with skills and knowledge to independently prevent episodes of low back pain may be effective. Interventions of this type are likely to be easier to implement widely than relatively inflexible and expensive exercise programs based on supervised group classes. Moreover, while preventing episodes of low back pain is a clear goal for prevention programs, providing individuals with the skills to self-manage minor recurrences without the

need to seek care is also important. Self-management programs including education and advice seem well suited to providing skills to manage minor recurrences, however, no previous studies have investigated the effectiveness of such an approach.

1.6.5 McKenzie method intervention for the prevention of spinal pain

The McKenzie method of Mechanical Diagnosis and Therapy (MDT), has been widely used by physiotherapists all over the world as an individualised approach for people presenting with musculoskeletal conditions, including spinal pain. This method aims to make people as independent as possible, empowering them with skills that help them self-manage their condition.[58] A systematic review published in 2018 investigated the effectiveness of the McKenzie method for the treatment of pain and disability in people presenting with either acute or chronic low back pain.[59] This review reported that MDT was no more effective when compared to other rehabilitation interventions to reduce pain and disability in people presenting with an acute episode of low back pain; however, for people with chronic low back pain, the MDT method was superior to other rehabilitation interventions for reducing pain and disability.

Despite a large amount of research investigating the McKenzie method for the treatment of spinal pain such as low back pain, there is limited evidence for the use of McKenzie method as an intervention to prevent spinal pain. To date, only one trial, conducted by Larsen and colleagues in 2002, included some elements of the McKenzie approach as part of the experimental intervention to prevent low back pain.[60] This study presented some limitations such as recruiting a mixed population with and without current low back pain, a relatively high drop-out rate around 21% and conducting the study in a military setting. Accordingly, it is important to investigate if a similar self-management intervention for prevention of low back pain recurrence is effective in a broad population sample who have recently recovered from an episode of low back pain. **Chapter Two** and **Chapter Three** in this thesis present the rationale, methodology, and results from a randomised, controlled trial study investigating the effectiveness of the McKenzie-based self-management exercise and education program for the secondary prevention of a recurrence of low back pain.

1.6.6 Evidence for prevention strategies to reduce future low back pain and associated disability

The review by Steffens et al. investigated a traditional approach to prevention including only trials enrolling people asymptomatic at study entry and focussed on preventing new episodes of low back pain.[46] In conditions such as low back pain, where there is commonly a chronic fluctuating pattern, it is also important to prevent future impact or complications of the chronic disease. Therefore, a complementary approach is to explore whether there are trials investigating the effect of interventions evaluating prevention strategies aiming to reduce future back pain or disability. An example is a study by Chaleat-Valayer and colleagues[61] that evaluated the long-term effect of a prevention program to prevent work-related disability among hospital workers. Such studies typically include "mixed populations" (i.e. both asymptomatic and symptomatic patients) at study entry, rather than restricting inclusion only to people without low back pain. These studies provide important information about the potential effect of prevention strategies on reducing future low back pain and associated disability. No previous systematic review has attempted to synthesise the evidence on the effects of prevention strategies aiming to reduce future low back pain and associated disability. Therefore, **Chapter Four** in this thesis presents the results from a systematic review investigating the effectiveness of prevention strategies aiming to reduce future low back pain and associated disability in a mixed population.

1.6.7 Evidence on the prevention of neck pain

Previous systematic reviews have investigated interventions to prevent neck pain.[47 62-65] However, none of these reviews investigating strategies for prevention of neck pain included only randomised controlled trials. Moreover, four of these reviews included studies investigating populations with neck and upper extremity conditions,[62-64 66] so it is difficult to estimate the effectiveness of interventions on neck pain conditions alone. In 2016, Van Eerd and colleagues investigated the evidence of the effect of exercise for preventing upper extremity musculoskeletal disorders, including neck pain.[62] The evidence from this review is that exercise could prevent upper extremity musculoskeletal disorder symptoms. This study, however, included study designs other than randomised controlled trials; which are likely to be biased. Moreover, this review did not differentiate neck pain from shoulder pain when assessing trials for the effectiveness of exercise prevention strategies. A Cochrane review,[66] conducted by Hoe and colleagues in 2012, included 13 randomised controlled trials (2,397

participants). The authors reported that most ergonomic interventions were not effective in preventing work-related upper limb and neck disorders. The evidence of one meta-analysis in this review, including two trials,[67 68] demonstrated that the use of ergonomic equipment may reduce the incidence of neck/shoulder pain. Similarly to Van Eerd's review,[62] this study included reports of studies that did not differentiate neck pain and shoulder pain.

Currently, there is no systematic review of the literature investigating strategies for the prevention of an episode of neck pain including only randomised controlled trials. **Chapter Five** in this thesis therefore presents results from a systematic review and meta-analysis investigating randomised controlled trials evaluating the effectiveness of intervention strategies to prevent a new episode of neck pain.

1.7 Aims of the thesis

The overall aim of this thesis is to investigate the effectiveness of interventions for preventing spinal pain.

Specific aims of this thesis are to:

1. Describe the rationale and methodology involved in the trial investigating the effectiveness of McKenzie-based self-management approach for the secondary prevention of a recurrence of low back pain (**Chapter Two**);
2. Determine the effectiveness of McKenzie-based self-management approach for the secondary prevention of a recurrence of low back pain, by conducting a randomised controlled trial study (**Chapter Three**);
3. Systematically review the current literature on the effectiveness of prevention strategies to reduce future impact of low back pain, by performing a systematic review and meta-analysis of randomised controlled trials (**Chapter Four**);
4. Systematically review the current literature on the effectiveness of interventions to prevent an episode of neck pain, by performing a systematic review and meta-analysis of randomised controlled trials (**Chapter Five**).

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CHAPTER TWO

Effectiveness of McKenzie Method-Based Self-Management Approach for the Secondary Prevention of a Recurrence of Low Back Pain (SAFE Trial): Protocol for a Pragmatic Randomized Controlled Trial

2.1 Preface

In **Chapter One** it was noted that spinal pain is a common condition affecting millions of people globally. Despite many years of investigating the best care and treatment for spinal pain, there is little research focusing on prevention strategies for spinal pain conditions. Current evidence from a 2016 systematic review demonstrates that exercise and education reduce the risk for future episodes of low back pain. However, most of the included trials investigated programs which were relatively costly and time-consuming. **Chapter Two,** therefore, presents the protocol for a randomised controlled trial describing the rationale and methods of a randomised controlled trial investigating a low-cost and less time-consuming exercise and education program based on McKenzie principles for the secondary prevention of a recurrence of low back pain.

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

de Campos TF, Maher CG, Clare HA, da Silva TM, Hancock MJ. Effectiveness of McKenzie method-based self-management approach for the secondary prevention of a recurrence of low back pain (SAFE Trial): protocol for a pragmatic randomized controlled trial. *Phys Ther*. 2017 Aug 1;97(8):799-806. doi: 10.1093/ptj/pzx046

The ethics approval for this trial is presented in **Thesis Appendix 3**, and the trial registration with the Australian New Zealand Clinical Trial Registry (ANZCTR) is presented in **Thesis Appendix 4**. The participant information and consent form is presented in **Thesis Appendix 5**.

2.2 Authorship attribution statement

This statement is to outline the contribution made by Tarcisio Folly de Campos in the preparation and submission of the following manuscript: "***de Campos TF***, Maher CG, Clare HA, da Silva TM, Hancock MJ. Effectiveness of McKenzie method-based self-management approach for the secondary prevention of a recurrence of low back pain (SAFE Trial): protocol for a pragmatic randomized controlled trial. *Phys Ther*. 2017 Aug 1;97(8):799-806". The convention is that the author with the principal contribution to the study is the first author.

Tarcisio Folly de Campos, during his PhD candidature, was responsible for the conception and design of the study protocol, designing the intervention and data collection instruments, drafting the ethics submission and responding to feedback, registering the trial in the Australian New Zealand Clinical Trials Registry (ANZCTR), managing the research project, writing the protocol draft manuscript and subsequent revisions, responding to reviewer's feedback and coordinating submission and publication of the original research protocol manuscript.

The individual roles of co-authors are listed below:

Task	**Co-author's contribution**
Conception and research design	CM, HC, TS, MH
Funding procurement	CM, HC, TS, MH
Data collection	TS, MH
Project management	CM, HC, MH
Drafting of the manuscript	CM, HC, TS, MH
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As supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statement above is correct.

Professor Mark Hancock _____ Date: 28 / 02 /2020

Effectiveness of McKenzie Method–Based Self-Management Approach for the Secondary Prevention of a Recurrence of Low Back Pain (SAFE Trial): Protocol for a Pragmatic Randomized Controlled Trial

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Background. Although many people recover quickly from an episode of low back pain (LBP), recurrence is very common. There is limited evidence on effective prevention strategies for recurrences of LBP.

Objective. The purpose of this study was to determine the effectiveness of a McKenzie method–based self-management approach in the secondary prevention of LBP.

Design. This will be a pragmatic randomized controlled trial.

Setting. Participants will be recruited from the community and primary care, with the intervention delivered in a number of physical therapist practices in Sydney, Australia.

Participants. The study will have 396 participants, all of whom are at least 18 years old.

Intervention. Participants will be randomly assigned to either the McKenzie method–based self-management approach group or a minimal intervention control group.

Measurements. The primary outcome will be days to first self-reported recurrence of an episode of activity-limiting LBP. The secondary outcomes will include: days to first self-reported recurrence of an episode of LBP, days to first self-reported recurrence of an episode of LBP leading to care seeking, and the impact of LBP over a 12-month period. All participants will be followed up monthly for a minimum of 12 months or until they have a recurrence of activity-limiting LBP. All participants will also be followed-up at 3, 6, 9, and 12 months to assess the impact of back pain, physical activity levels, study program adherence, credibility, and adverse events.

Limitations. Participants and therapists will not be masked to the interventions.

Conclusions. To our knowledge, this will be the first large, high-quality randomized controlled trial investigating the effectiveness of a McKenzie method–based self-management approach for preventing recurrences of LBP. If this approach is found to be effective, it will offer a low-cost, simple method for reducing the personal and societal burdens of LBP.

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Low back pain (LBP) is the health condition that carries the greatest burden worldwide accounting for approximately 10.7% of total years lived with disability, according to recent Global Burden of Disease Studies reports.[1-3] The point prevalence of activity-limiting LBP, lasting more than 1 day, is estimated to be 11.9%,[4] and 1-month prevalence of activity-limiting LBP is around 23.2%.[4] Additionally, almost half of the people who experience LBP are expected to seek care.[5] Therefore, the direct and indirect costs related to LBP are enormous: approximately $9 billion annually in Australia[6] and $90 billion in the United States.[7]

The majority of people with an episode of nonspecific LBP improve quickly;[8,9] more than 80% recover within 3 months.[10] However, recurrences of back pain are common, with 12-month recurrence rates reported in the literature ranging from 24% to 80%.[11-13] Thus, the recurrent nature of LBP is one of the major reasons why the condition carries such a large social and economic burden worldwide.

Although thousands of trials have been conducted to investigate treatments for LBP, surprisingly few have investigated interventions to prevent LBP. A 2016 systematic review on prevention of LBP[14] found 21 randomized controlled trials with a total of 30,850 participants. This systematic review showed evidence that both exercise alone and in combination with education were effective in reducing LBP episodes (35% and 45% risk reductions, respectively) for up to one year. However, the trials included in the review had a number of methodological flaws. The trials were typically small and unregistered and did not attend to trial features, such as concealed allocation, masking and intention-to-treat analysis (known to control against bias). Consequently, it is likely that these trials overestimated the prevention effects. Despite the favorable results, these exercise programs are relatively costly and time consuming often requiring people to attend many sessions. For example, in the Soukup et al, randomized controlled trial participants were required to attend 20 group sessions of exercise and education over a period of 13 weeks.[15]

Self-management programs aim to empower patients with skills that help them become more active and responsible in the management of their condition.[16] Previous studies have demonstrated that a self-management program has some beneficial effect on management of a number of conditions, such as asthma, arthritis, diabetes, and chronic LBP.[17,18] Thus, an effective self-management intervention in which the patient/participant is empowered with knowledge and skills to prevent future episodes of LBP would be ideal, reducing the cost and time burden for participants, and increasing the likelihood of large-scale implementation.

The McKenzie method–based self-management approach has several potentially important advantages over traditional group-based exercise approaches in preventing recurrence of LBP. The program involves very simple exercises that are quick to perform and can be done on a daily basis without the need to attend regular exercise classes. Exercises focus on balancing mechanical forces created by the postures or positions used by each individual throughout a typical day (ie, if a person spends most of the time in either a flexed or extended spinal posture, exercises will be focused on the opposite direction). For most people this involves lumbar extension to counteract the large amount of flexion activity typical of most people's lives either in sitting or performing manual tasks. Importantly, the McKenzie method-based self-management approach also provides simple strategies with the aim of allowing management of mild episodes without seeking care.

To our knowledge, there are no published studies that have evaluated the effectiveness of McKenzie method–based self-management approach in secondary prevention of a recurrence of LBP. A previous study by Larsen and colleagues[19] investigated prone extension exercises for the "prevention" of LBP. The study recruited military conscripts and randomized them to education and passive prone extension exercises done daily or a group that received no intervention (control). Significantly fewer people in the intervention group than in the control group reported back problems during the 1-year follow-up (33% and 51%, respectively). The main limitation of this study is that it recruited a heterogeneous population with and without current LBP, so assessment of the effect of the intervention on prevention is difficult, as approximately 25% of participants had pain at the start of the study. The study also had a fairly high dropout rate (21%). We believe it is important to test if the promising findings can be generalized to a broad population sample who have recently recovered from an episode of LBP.

Therefore, the aim of our randomized controlled trial is to compare the effectiveness of the McKenzie method–based self-management and educational approach with that of a minimal intervention control in preventing recurrence of LBP in people recently recovered from an episode of nonspecific LBP. We will also investigate whether the approach reduces the impact of back pain over 1 year, and establish the risk of adverse events during the follow-up period. A safe, low-cost, and effective intervention to prevent recurrences of LBP would be of enormous benefit to individuals and society.

Methods

Design Overview

The SAFE Trial is designed to be a pragmatic randomized controlled trial, where the outcome assessors and the statistician are masked. A total of 396 participants who have recently recovered from an episode of nonspecific LBP will be randomized to either the McKenzie method–based self-management approach or a minimal intervention group control. Participants will be followed-up from the day of randomization for a minimum of 12 months and up to 30 months, depending on when they enter the study. The primary outcome is days from randomization to a self-reported recurrence of activity-limiting LBP. The SAFE Trial design is illustrated in the Figure. The Pragmatic in

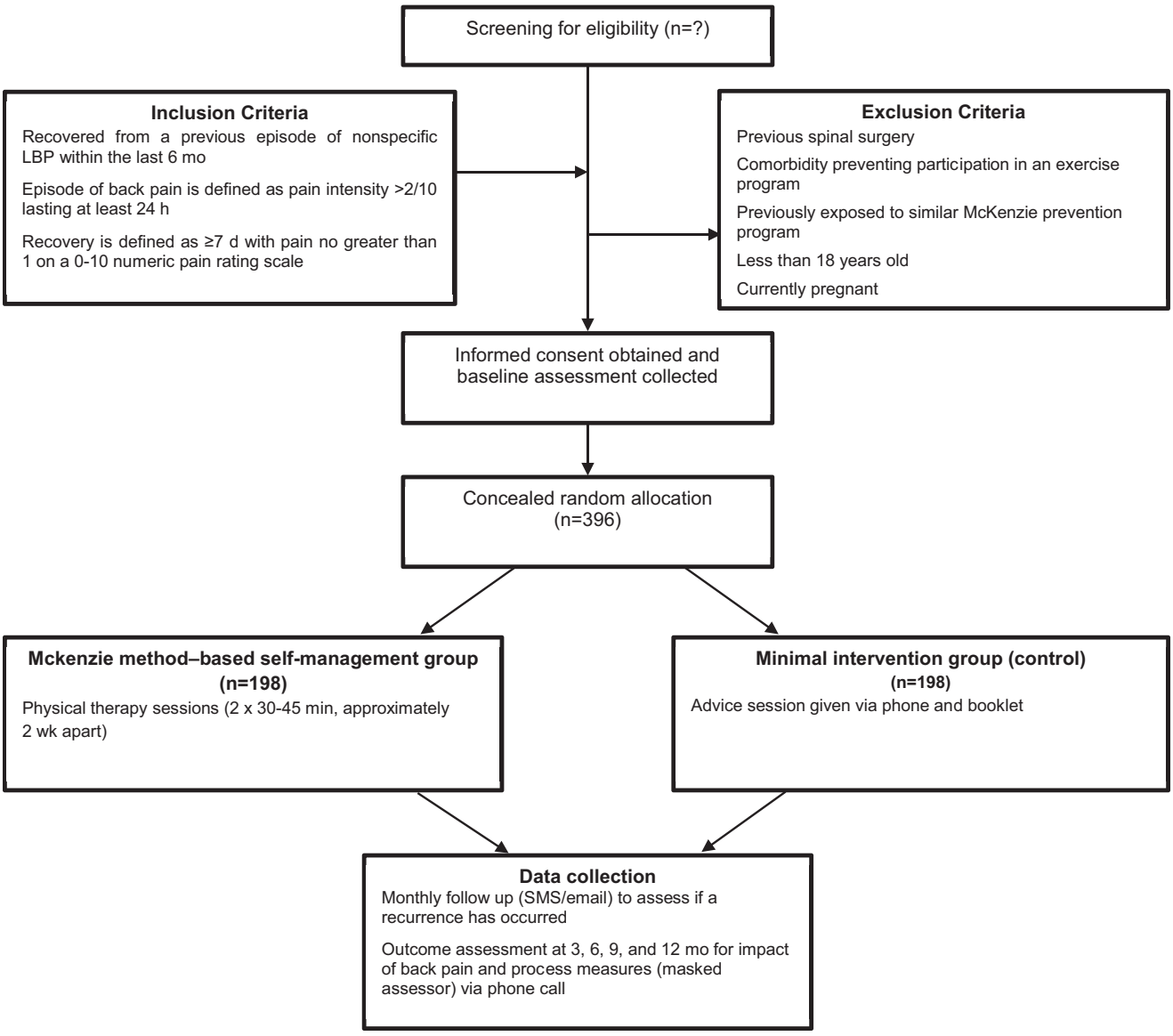

Figure.
Design of SAFE Trial study. LBP = low back pain, SMS = Short Message Service.

design, the SAFE Trial aims to determine the benefit of the intervention in a real-world clinical setting.[20,21] There are limited inclusion and exclusion criteria, treatment is tailored to the individual, and outcomes are directly relevant to participants.

Participant Eligibility and Recruitment

Eligibility. We will include 396 participants who are at least 18 years old and who have recently recovered (within the last 6 months) from an episode of nonspecific LBP (with or without leg pain). Nonspecific LBP is defined as pain in the area between the 12th rib and buttock crease[22] not attributed to a specific diagnosis, such as ankylosing spondylitis or vertebral fracture. Recovery is defined as having occurred after 7 consecutive days with pain no greater than 1 on a numeric pain rating scale (ratings = 0–10). Participants will be excluded if they meet any of the following criteria: previous spinal surgery; comorbidity restricting or preventing safe participation in exercise (eg, traumatic brain injury, psychological illness); inadequate English usage to complete outcome measures; previous exposure to the McKenzie method–based self-management approach as a method of preventing future LBP; or current pregnancy. Participants will be recruited from the community via advertisements (eg, public noticeboards, websites) and from primary care clinics (general practitioner, physical therapist, or chiropractor) in Sydney, Australia.

Recruitment procedure. The trial advertisements will direct members of the community interested in the study to contact the researchers. Also, patients being discharged from primary care clinics on recovery from an episode of nonspecific LBP will be informed about the study by their clinician. People interested in finding out more about the study can either contact the researchers directly (phone or email) or provide verbal consent for the clinician to forward their contact details to the researchers. The participant information and consent form will be posted or emailed to the participant. Potential participants referred to the study will be contacted by phone to explain the study in more detail and answer any questions they have. Potential participants who want to volunteer for the study will be screened to determine if they meet all study eligibility criteria.

Participants will be enrolled into the study over the phone without meeting one of the researchers in person. Therefore, the consent will be a verbal consent. We will gain verbal consent over the phone through the following process. After answering any questions the participant has about the study, the researcher will read the following statement: "By completing this questionnaire, you are indicating that you have read and understood the information in the participant information and consent form provided to you and any questions you have asked have been answered to your satisfaction. You agree to participate in this research, knowing that you can withdraw from further participation in the research at any time without consequence."

Baseline Assessment

After fulfilling the eligibility criteria, agreeing to participate, and providing verbal consent, participants will undergo a standardized baseline assessment over the phone. This will take approximately 10 to 15 minutes and will collect data on demographics, history of LBP and prognostic factors for recurrence. All baseline data will be entered directly onto a hard copy of the baseline assessment questionnaire and then entered into the electronic database at the first available opportunity.

Randomization

Immediately after completing the baseline assessment, participants will be randomly allocated into either the McKenzie method–based self-management approach group or minimal intervention (control) group. The researcher will open the next consecutively numbered, sealed, opaque randomization envelope to ensure concealed allocation. A randomization schedule—incorporating randomly permuted block sizes of 4, 6, and 8—will be generated prior to the commencement of the trial by an independent investigator not involved in participant recruitment, treatment, or follow-up, using a computer program. Randomization will be stratified by history of more than 2 previous episodes of LBP (dichotomised as "yes" or "no") as our previous research showed that this is the only known consistent predictor of recurrence.[13] Study participants will be considered enrolled into the study when the allocation envelope is opened and the participant is assigned to either the McKenzie method–based self-management approach or the minimal intervention group. They will receive a study enrollment number and this will be documented in the participant's clinical trial record and on all study documents.

Masking. Due to the nature of the trial, complete masking will not be possible. In an effort to mask the participants as much as possible to the trial research question, they will be told that the study is comparing 2 methods for preventing future recurrence of back pain, one delivered face-to-face and the other delivered over the phone. Also, it will not be possible to mask the treatment providers to group allocation. The statistician and the outcome assessors will be masked to group allocation.

Study Interventions

Minimal intervention group (control). Participants allocated to the minimal intervention (control) group will receive simple advice that is widely available about how to prevent back pain. This will be delivered over the phone by a physical therapist. The key points in this advice will be maintenance of regular exercise and education about lifting and handling objects safely, taking approximately 10 to 15 minutes. Participants in this group will be posted a copy of the "*Managing Back Pain – Get Back on Track*" booklet,[23] which was developed by Bupa Australia Pty Ltd (private health insurance company). This booklet includes general advice about back pain prevention and self-management. The company has given consent for the booklet to be used in this project. Participants will have the opportunity to contact the physical therapist who delivered the intervention on one further occasion, approximately 2 to 4 weeks after being randomized, by email or phone, if they require further clarification.

McKenzie method–based self-management approach group. Participants allocated to the McKenzie method–based self-management approach group will attend two 30- to 45-minute individual sessions with a trained physical therapist. These sessions will be approximately 2 weeks apart. In the first session, study physical therapists will assess participants using the McKenzie Institute Lumbar Spine Assessment Form.[24] The history will focus on developing a clear understanding of the previous episodes including causal or aggravating factors, and the daily mechanical and postural stresses for each individual. The physical examination will assess habitual postures and their relationship to symptoms, spinal movement loss, and any effect of repeated spinal movements on symptoms and mobility. This assessment will help the therapists to gather information that will guide prescription of an appropriate home prevention exercise program for each particular participant's circumstances. The participant will be provided with and educated about an individualized simple specific exercise program focusing on movements that balance/counteract the postures or positions habitually adopted throughout the day and on improving any existing movement loss. Because the intervention is individualized for each participant, the exercises to be completed at home will vary in frequency and duration, based on the judgment of the assessing physical therapist. Typically exercises

will be performed multiple times per day and be of short duration.

At the follow-up session, the physical therapists will perform a reassessment and obtain feedback from participants on how the program is going and any barriers to adhering to the program. Depending on this reassessment the physical therapist will then modify or progress the home exercise prevention program as needed. The therapist will emphasize the importance of continuing these exercises indefinitely as a prevention strategy for back pain recurrence. For most people the exercise program will involve lumbar extension to counteract the large amount of flexion activity typical of most people's lives (either sitting or performing manual tasks).

Follow-up

Participants will be followed up monthly by email or text message from the day of randomization into the study for at least 12 months and up to 30 months, depending on when they enter the study. To make maximum use of all available data, the usual practice in studies using survival analysis is to follow people until the study concludes. Because people enter the study at different dates, some participants will be followed for only 12 months and some will be followed for as long as 30 months. Participants will be asked whether they have had a recurrence of LBP of intensity greater than 2 on a numeric pain scale (ratings = 0–10) and lasting at least 24 hours within the past 4 weeks or since the last contact from the research team. If participants reply "yes" to this email or text message, a study researcher will contact them via phone call for further information about this recurrence. Participants who have not replied to the first text message or email within 2 days will be sent a second text message or email. Participants not responding to these 2 messages will be then contacted by phone. In addition to the recurrence data, outcome data will be collected at 3, 6, 9, and 12 months from randomization into the study by a phone call at these time points. Follow-ups will be conducted by a researcher masked to group allocation.

Outcome Measures

Primary outcome. The primary outcome will be the number of days from randomization to first self-reported recurrence of an episode of activity-limiting LBP (somewhat or greater activity limitation measured using an adaptation of item PI9 of the PROMIS item bank to measure pain interference).[25] Participants will be followed up for this outcome for between 12 and 30 months post-randomization, depending on when they are randomized into the study.

Secondary outcomes. One secondary outcome will be the number of days from randomization to first self-reported recurrence of an episode of nonspecific LBP (intensity > 2/10 on the numeric pain rating scale and lasting at least 24 hours).[26] Participants will be followed up for this outcome for between 12 and 30 months after randomization, depending on when they are randomized into the study.

Days from randomization to first self-reported recurrence of an episode of LBP leading to care seeking (with consultation to a health care provider) will be another secondary outcome. Participants will be followed up for this outcome for between 12 and 30 months after randomization, depending on when they are randomized into the study.

The personal impact of LBP over the first 12 months after randomization will be determined for all participants in the study. The impact of back pain will be measured with the Impact of Back Pain Questionnaire using 9 items of the 29-item PROMIS short form.[27] This measure was recommended in the recent NIH Task Force report on research standards for LBP.[27] These 9 items cover the domains of pain intensity, pain interference with normal activities, and functional status. The total score on the Impact of Back Pain Questionnaire ranges from 8 (least impact) to 50 (great impact). This outcome will be collected at the 3-, 6-, 9-, and 12-month follow-ups by asking about the impact of back pain over the past 3 months.

Process Measures

Additional process measures will also be collected. These measures will help better understand the study results and include:

Physical activity levels will be measured by the International Physical Activity Questionnaire (IPAQ).[28] This questionnaire estimates a participant's physical activity level over the past week. Physical activity measures will be collected at baseline and at the 3- and 12-month follow-up assessments.

Study program compliance will be monitored by recording attendance at the two physical therapist visits, asking physical therapists to rate their perception of participant compliance to the home exercise program between the participants initial and second visit (2-week period), and asking participants to rate compliance with home program using the Brief Adherence Rating Scale at 3-, 6-, 9-, and 12-month follow-ups.

Credibility/expectancy regarding treatment will be measured with a credibility/expectancy questionnaire modified from Devilly and Brokovec.[29] This questionnaire will provide information on the participant's beliefs about the intervention received. The credibility/expectancy scores will be collected at the 3-month follow-up assessment.

Adverse Events and Use of Co-interventions

Adverse events will be considered to be any health problems or complaint reported by the participants during the study. Adverse events will be collected by self-report at the 3-month and 12-month follow-up assessments after randomization. Data on use of any intervention for treatment or prevention of LBP, apart from the study program, will be collected at all follow-up assessments (3, 6, 9, and 12 months).

Physical Therapist Training and Treatment Fidelity

We will work with a small number of physical therapist clinicians (eg, 8-10),

who have undertaken, at least, training in the McKenzie Method of Mechanical Diagnosis and Therapy, Parts A and B, or are fully credentialed in the McKenzie method, around metropolitan Sydney. All study physical therapists will be trained in the study intervention procedures in a single session lasting approximately 1 hour. H.A.C. will be responsible for ensuring that clinicians are adequately trained to deliver the intervention and for assessing compliance with the study procedures. She will be in regular contact with the participating clinicians, to discuss any issues in delivering the intervention and provide reminders of the study procedures. She will attend some sessions to directly observe the fidelity of the intervention being delivered. Physical therapists will complete standardized assessment and prevention strategy notes for each session that will be collected by researchers after the participants' final sessions.

Data Analysis, Monitoring, and Auditing

Sample size calculation. The sample size was calculated for the primary outcome using PASS statistical software (NCSS Statistical Software, Kaysville, Utah), as described by Lakatos.[30] For a 2-sided log rank test with an alpha value of 0.05 we calculated that a sample size of 198 participants per group will provide 80% power to detect a 40% relative reduction in recurrence rates between the treatment group and the control group. These calculations are based upon 30% recurrence in 1 year in the control group. Higher rates of recurrence typically reported in the literature would increase power. Our sample size calculations are based on an 18-month accrual period and 12-month follow-up period. We have conservatively allowed for 1% loss to follow-up, and 1% treatment nonadherence per month in both groups.

Data integrity and analysis. All study data will be entered into an electronic database as soon as possible after being collected. Access to the data obtained in this research will be restricted to the researchers involved in the collection and analysis of the data. Participant confidentiality will be maintained through secure data storage, during and after the study. Data will be carefully monitored for any errors. We will use descriptive analyses to identify outliers and potential errors. All data being entered manually will be double entered by a second researcher and checked for any data discrepancy.

Data will be analyzed by a statistician who is masked to group status. The primary analyses comparing the groups will follow the intention-to-treat principle.[31] For the primary outcome, a P value of <.05 will be considered statistically significant. For the secondary outcomes, a P value of <.01 will be considered significant.

For the primary outcome analysis, we will assess difference in survival curves (days from randomization to first self-reported recurrence of activity-limiting LBP) using the log-rank statistic. Cox-regression will be used to assess the effect of treatment group on hazard ratios. We have stratified for the only known predictor of recurrence (previous recurrence).[13] We will treat prognostic factors for LBP[32,33] as potential confounders and, if these are unbalanced despite randomization, we will include them as covariates in the analysis. The proportional hazards assumption will be tested using the time-dependent covariate method.

For the secondary outcomes of days from randomization to first self-reported recurrence of either an episode of nonspecific LBP or an episode of LBP leading to care seeking, a survival analysis analogous to that of the primary outcome will be conducted. To investigate whether the intervention will have an influence on the impact of back pain over a 1-year period, we intend to use repeated-measures linear models; however, given that this is a new measure, we will explore the data distribution before making a final decision.

A secondary analysis will assess the presence of a limited number of baseline variables as modifiers of treatment effects. Variables to be investigated include age, body mass index, number of previous episodes, sitting time, perceived risk of recurrence, and frequency of exposure to heavy loads and awkward positions.

Ethics Approval

Ethical approval was obtained from Macquarie University Human Research Ethics Committee in April 2016 (ref. no. 5201600187). The study will be conducted in accordance with the *National Statement on Ethical Conduct in Human Research 2007*.[34] Compliance with these standards provides assurance that the rights, safety and well-being of trial participants are respected. The study protocol will be implemented and reported in line with the SPIRIT statement.[35] Also, the completed clinical trial and its results will be reported according to CONSORT[36,37] and TIDieR[38] guidelines. Study results will be disseminated at research conferences and as published articles in peer-reviewed journals.

Role of the Funding Source

This trial is funded by the International Mechanical Diagnosis and Therapy Research Foundation – USA. The funders will have no role in this study other than to provide funding.

Discussion

Potential Impact and Significance of the Study

Back pain places an enormous burden on individuals and society as demonstrated by the recent Global Burden of Disease Study reports.[2,3] Much of this burden is due to the recurrent nature of LBP. The great majority of trials in the back pain field evaluate treatment rather than prevention. A recent systematic review investigating all interventions for prevention of LBP found low-quality evidence supporting exercise as a strategy for preventing future back pain episodes. The lack of high-quality back pain prevention research limits the ability to provide clinicians and patients with strong recommendations about effective prevention approaches.

To our knowledge, this study will be one of only a few high–quality, large trials evaluating secondary prevention of recurrent LBP and the first evaluating the McKenzie method-based self-management approach, which aims to teach participants simple exercise focused on balancing mechanical forces or positions used during typical daily activities and improving mobility. The identification of a cost-effective method to prevent recurrences of LBP would be a major breakthrough and could make an enormous contribution to global health. If this self-management approach is found to be effective against recurrence of LBP, our research will have the potential to help prevent pain and disability for millions of people worldwide.

Strengths and Weaknesses of the Study

This trial was prospectively registered with the Australian and New Zealand Clinical Trial Registry, and the sample size was preplanned to provide robust evidence. We will use a stratified, blocked randomization process, concealed allocation, masked assessments, and an intention-to-treat analysis. Experienced physical therapists trained by the research team in the study process will be conducting the McKenzie method–based intervention, and the quality of the intervention will be monitored. Due to the nature of the interventions, it is not possible to mask the therapists and participants to the treatment allocation, but outcome assessors and statisticians will be masked.

Recruitment for clinical studies is typically difficult, but, we have designed the study to make this process as easy as possible. We will be recruiting participants for this study primarily through community advertisements, and also through primary care clinicians as needed. The role for the recruiting clinicians will be simply, as they need only pass on the study information to appropriate patients. The time commitment for patients will be relatively small, and all follow-up assessments will be done remotely. However, if we do struggle with these 2 recruitment strategies, we will increase the number of recruiting clinicians and investigate barriers to recruitment from all perspectives.

Contribution to the Physical Therapy Profession

High-quality evidence about prevention of LBP is very important for physical therapy, given that LBP and the associated recurrences are the most common condition presenting to musculoskeletal physical therapists. If we find evidence for the effectiveness of the McKenzie method–based self-management program, then this has the potential to influence the physical therapist management of many patients who could be provided with this program when they recover from an episode of LBP. Physical therapists could offer this program to people in the community who are not currently seeking care but who have recurrent episodes of LBP. The skills and training of physical therapists make them the ideal professionals to deliver evidence-based interventions for prevention of LBP.

Author Contributions and Acknowledgments

Concept/idea/research design: T.F. de Campos, C.G. Maher, H.A. Clare, M.J. Hancock
Writing: T.F. de Campos, C.G. Maher, H.A. Clare, T.M. da Silva, M.J. Hancock
Data collection: T.F. de Campos, T.M. da Silva, M.J. Hancock
Project management: T.F. de Campos, C.G. Maher, H.A. Clare, M.J. Hancock
Fund procurement: C.G. Maher, H.A. Clare, T.M. da Silva, M.J. Hancock
Consultation (including review of manuscript before submitting): T.F. de Campos, C.G. Maher, H.A. Clare, T.M. da Silva, M.J. Hancock
M.J. Hancock, T.F.de Campos, C.G. Maher, and H.A. Clare will form the data management committee.

Funding

This trial is funded by the International Mechanical Diagnosis and Therapy Research Foundation – USA. The funders will have no role in this study other than to provide funding.

Clinical Trial Registration

This study is registered in the Australian and New Zealand Clinical Trial Registry (ANZCTR) (ACTRN12616000926437). Universal Trial Number (UTN): U1111-1184-9436.

Ethics Approval

Ethical approval was obtained from Macquarie University Human Research Ethics Committee on April 2016 (ref. no. 5201600187).

Disclosures

The authors completed the ICJME Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest. C.G. Maher's fellowship is funded by Australia's National Health and Medical Research Council. T.F. de Campos has a PhD scholarship from Macquarie University (Macquarie University Research Excellence Scholarship (MQRES) - Allocation No. 2016221. T.M. da Silva receives a scholarship from CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior), Ministry of Education of Brazil.

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Pages 23-30 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:

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CHAPTER THREE

An individualised self-management exercise and education program did not prevent recurrence of low back pain, but may reduce care seeking: a randomised, controlled trial

3.1 Preface

Chapter Two presented the methods and rationale for a randomised controlled trial aiming to investigate if a low-cost exercise and education approach based on the McKenzie method reduced the risk of a recurrence of low back pain in people recently recovered from a low back pain episode. **Chapter Three** presents the results for the randomised controlled trial investigating the McKenzie method-based self-management approach for the secondary prevention of a recurrence of low back pain. The trial enrolled 262 participants who had recovered from an episode of low back pain within the last six months and followed them for a minimum of 12 months and up to 30 months.

The study presented in **Chapter Three** has been submitted to the Journal of Physiotherapy and has recently been accepted for publication. The manuscript is presented in the format of the accepted manuscript before edits.

The ethics approval for this trial is presented in **Thesis Appendix 3**, and the trial registration with the Australian New Zealand Clinical Trials Registry (ANZCTR) is presented in **Thesis Appendix 4**. The participant information and consent form are presented in **Thesis Appendix 5**.

3.2 Authorship attribution statement

This statement is to outline the contribution made by Tarcisio Folly de Campos in the preparation and submission of the following manuscript: "***de Campos TF***, Pocovi NC, Maher CG, Clare HA, da Silva TM, Hancock MJ. An individualised self-management exercise and education program did not prevent recurrence of low back pain, but may reduce care seeking: a randomised, controlled trial. Submitted to Journal of Physiotherapy (November 21st 2019) and has recently been accepted for publication". The convention is that the author with the principal contribution to the study is the first author.

Tarcisio Folly de Campos, during his PhD candidature, was responsible for the conception and design of the trial, designing the study data collection instruments, drafting the ethics submission and responding to feedback, registering the trial in the Australian New Zealand Clinical Trials Registry (ANZCTR), managing the research project, draftingthe study final manuscript and subsequent revisions, and coordinating submission for publication of the original study manuscript.

The individual roles of co-authors are listed below:

Task	**Co-author's contribution**
Conception and research design	CM, HC, TS, MH
Data collection	NP, TS, MH
Project management	CM, HC, MH
Drafting of the manuscript	MH
Revision and critical comment of manuscript	NP, CM, HC, TS, MH

NP, Natasha Pocovi; **CM**, Chris Maher; **HC**, Helen Clare; **TS**, Tatiane da Silva; **MH**, Mark Hancock

Mr Tarcisio Folly de Campos _____ Date: 28 / 02 /2020

As supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statement above is correct.

Professor Mark Hancock _____ Date: 28 / 02 /2020

Title: An individualised self-management exercise and education program did not prevent recurrence of low back pain, but may reduce care seeking: a randomised, controlled trial

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Footnotes

eAddenda: None.

Ethics approval: Ethical approval for the study protocol was obtained from Macquarie University Human Research Ethics Committee on April 2016 (ref. number: 5201600187). All participants provided verbal informed consent before data collection began.

Competing interests: Mr Tarcisio F. de Campos received an International Mechanical Diagnosis and Therapy Research Foundation (IMDTRF) continuation grant. Helen A. Clare is an International Director of Education and Instructor of the McKenzie Institute. Prof Mark J. Hancock was Keynote speaker at the McKenzie International conference in San Francisco – USA, and travel and accommodation costs were paid.

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Provenance: Not invited. Peer reviewed.

Abstract

Questions: What is the effect of a McKenzie-based self-management exercise and education program on the risk of recurrence of low back pain (LBP), and on the impact of LBP?

Design: Randomised, controlled trial

Participants: 262 adults recently recovered from an episode of LBP.

Intervention: The group receiving McKenzie-based self-management exercise and education program received 2 x 30-45 minutes individual sessions with a physiotherapist, delivered approximately 2 weeks apart. The minimal intervention group received a single over the phone advice session.

Outcome measures: The primary outcome was number of days to first recurrence of an episode of activity-limiting LBP. Secondary outcomes included days to any recurrence of LBP, days to a recurrence causing care-seeking and a composite measure of pain and function ('impact of LBP'). All participants were followed-up monthly for a minimum of 12 months.

Results: The estimate of the experimental intervention's effect on the risk of recurrence of an episode of activity-limiting LBP was HR 1.11 (95% CI, 0.80 to 1.54), on any recurrence of LBP episode was HR 0.95 (95% CI, 0.72 to 1.26), and on LBP episodes for which care was sought was HR 0.69 (95% CI, 0.46 to 1.04). The quarterly estimates of the experimental intervention's effect on impact of LBP and their 95% CIs were all within 4 points above or below zero (no effect) on this scale from 8 to 50.

Conclusion: Our best estimate is that a McKenzie-based self-management exercise and education program does not produce a substantial reduction on the risk of an activity-limiting episode of LBP. It may reduce the risk of care-seeking for a recurrence of LBP, but does not have any substantial effect on the impact of LBP over 12 months.

Trial registration: Australian and New Zealand Clinical Trial Registry (ANZCTR), ACTRN12616000926437.

Introduction

Low back pain (LBP) is a common condition and the leading cause of global disability according to the Global Burden of Disease studies.[1,2] Most people with an episode of LBP improve quickly;[3,4] however, recurrences within a year are common (40% to 69% depending on the definition used).[5,6] The recurrent nature of LBP is one of the major reasons why the condition carries such a large social and economic burden.

Despite the recurrent nature of LBP, few previous trials have investigated prevention strategies. Present evidence on prevention of LBP[7] shows that exercise alone, and in combination with education, is effective in reducing risk of LBP episodes (35% and 45% risk reduction respectively for up to one year); however, the majority of the exercise programs in these trials are relatively costly, inflexible and time-consuming (e.g. 20 sessions over 13 weeks),[8] potentially making uptake of such programs difficult.[9]

To overcome these barriers, we developed a low-cost and flexible exercise and education program, based on McKenzie method and emphasising self-management. The program involves simple, and individualised exercises that require minimal time, and can be done independently on a daily basis. Importantly, this program also provides strategies and education for self-management of mild episodes without seeking care.

Therefore, we aimed to investigate the estimated effect of a McKenzie-based self-management exercise and educational approach compared to a minimal intervention control group, in preventing recurrences of LBP and future care seeking in people recently recovered from an episode of non-specific LBP. We also aimed to investigate if the approach reduces the impact of LBP over 1-year.

The research question for this randomised, controlled trial was:

1. What is the effect of a McKenzie-based self-management exercise and education program on the risk of recurrence of LBP, and on the impact of LBP?

Methods

Design

The SAFE trial is a two group randomised, controlled trial, where the outcome assessors and

the statistician were blinded. This trial was prospectively registered with the Australian and New Zealand Clinical Trial Registry (ANZCTR), number ACTRN12616000926437. The study protocol has been previously published.[10]

In brief, 262 eligible participants, were randomised to either a McKenzie-based self-management exercise and education program, or a minimal intervention control group. Participants were followed for a minimum of 12 months and up to 30 months for the primary outcome of days to first self-reported recurrence of an activity-limiting episode of LBP. The design of the SAFE trial is illustrated in Figure 1. The study is pragmatic in design, investigating the effectiveness of the intervention in a real-world setting.[11,12]

Participants and therapists

Inclusion criteria were adults aged ≥18, recently recovered (within the last 6 months) from an episode of non-specific LBP (with or without leg pain). An episode of non-specific LBP was defined as pain lasting over 24 hours in the area between the 12th rib and buttock crease[13] not attributed to a specific diagnosis (e.g. vertebral fracture or cancer). Recovery was defined as occurring after 7 consecutive days with pain no greater than 1 on a 0-10 numeric pain scale. Exclusion criteria were previous spinal surgery, co-morbidity restricting safe participation in exercise, inadequate English, previously exposed to a McKenzie-based approach as a method of preventing future LBP, and currently pregnant.

Participants were recruited through community advertising (e.g. public noticeboards and social media websites) in Sydney, Australia. All potential participants were screened for eligibility. Eligible participants provided verbal consent and underwent a standardised baseline assessment over the phone.

All study physiotherapists were trained together in the study procedures in a single session. This session was lead by an experienced McKenzie therapist instructor and the senior author who has over 20 years of experience using the Mckenzie approach. The session involved an explanation of the study design and purpose, followed by the step-by-step process of evaluating participants and delivering the intervention. This session lasted approximately 2 hours and included opportunity for clarification of any remaining questions. After this session all therapists were visited on one more occasion by the lead author to ensure they were ready to deliver the intervention as per protocol. During the study regular contact was made with

therapists via study newletters (approximately 3 per year) and one on one meetings, to discuss any issues in delivering the intervention and to provide reminders of the study procedures.

Randomisation

A researcher, not involved in the study, developed a randomisation schedule and produced consecutively numbered sealed opaque envelopes containing the allocation schedule. The randomisation schedule used randomly permuted block sizes of 4, 6 and 8. Randomisation was stratified by history of previous episodes (1 or 2, and over 2),[14] with balanced randomisation (1:1). To ensure allocation was concealed, after collecting baseline data, the blinded researcher opened the next envelope, containing the allocation number. Treatment providers and participants were not blind to group allocation.

Interventions

McKenzie-based self-management approach

Participants allocated to the experimental intervention group attended 2 x 30-45minutes individual sessions, delivered approximately 2 weeks apart, with a physiotherapist trained at least to level A and B of the McKenzie method.

In the first session, participants were assessed using a modification of the McKenzie Lumbar Spine Assessment Form.[15] The history focused on developing a clear understanding of factors associated with previous episodes, and the individual's daily mechanical/postural stresses. The physical examination aimed to assess habitual postures and their relationship to symptoms, spinal movement loss and any effect of repeated spinal movements on symptoms and mobility. This assessment helped the therapists to gather information that guided prescription of an individualised home prevention exercise program. All participants were provided with education and an individualised exercise program focusing on those movements that balance/counteract the daily postures or positions habitually adopted and on improving any existing lumbar spine movement loss. For instance, for some participants the exercise program involved lumbar extension to counterbalance the large amount of flexion activity/posture typical of most people's lives either in performing manual tasks or sitting. Each participant's exercise program varied in frequency and duration based on the therapist's assessment. Typically, exercises were performed multiple times per day and were of short duration.

At the follow-up session, the physiotherapists discussed with participants any barriers to participation in the program. Depending on this re-assessment the physiotherapist modified or progressed the home exercise program as needed. Therapists emphasised the importance of continuing these exercises as a prevention strategy for LBP recurrence.

Minimal intervention

The control group received simple advice on prevention of LBP, delivered over the phone by a single physiotherapist. The key points were to maintain regular exercise, and education about lifting and handling objects safely, taking approximately 10-15 minutes. A copy of the "*Managing Back Pain – Get Back on Track"* booklet,[16] developed by BUPA Australia Pty Ltd, was posted to participants in this group. This booklet includes general advice about back pain prevention and self-management. Participants in the control group had the opportunity to contact the physiotherapist on one further occasion, approximately 2-4 weeks after being randomised, by email or phone, if they required further clarification.

Follow-up

Participants were followed-up monthly, by a blinded researcher, for at least 12 months, or until the study concluded. Participants received a monthly email or text message asking if they had experienced a recurrence of LBP of intensity greater than 2 on a 0-10 pain rating scale lasting at least 24 hours within the past 4 weeks or since the last contact from the research team. Participants who replied "yes" were phoned by a researcher who collected further information about this recurrence, including whether it met the criteria for primary outcome of activity-limitation due to LBP. In addition to the recurrence data, other data were collected on the impact of LBP[17,18] at the 3-, 6-, 9- and 12-month follow-ups by phone or online survey (Qualtrics®).

Outcome measures

Primary outcome

The primary outcome was recurrence of an episode of activity-limiting LBP, defined as the number of days from randomisation to first self-reported recurrence of an episode of activity-limiting LBP (intensity $>$ 2 on 0-10 the numeric pain rating scale, lasting at least 24 hours, and responding that pain interfered with day-to-day activities 'somewhat', 'quite a bit' or 'very

much' using an adaptation of item PI9 of the PROMIS item bank to measure pain interference).[19]

Secondary outcomes

The secondary outcomes were: (i) recurrence of an episode of non-specific LBP defined as the number of days from randomisation to first reported recurrence of an episode of non-specific LBP (intensity > 2/10 on the numeric pain rating scale, lasting at least 24 hours);[20] (ii) recurrence of an episode of care seeking LBP defined as the number of days from randomisation to first reported recurrence of an episode of care seeking (consultation to a healthcare provider) LBP; (iii) the personal impact of LBP. Personal impact was measured using the impact score as recommended by the NIH Task Force, which incorporates 9 items of the 29-item PROMIS short form.[17,18] These items cover the domains of pain intensity, pain interference with normal activities and functional status. The total score ranges from 8 (least impact) to 50 (great impact). This measure was collected at the 3-, 6-, 9- and 12-month follow-ups asking participants about the impact of LBP over the previous 3 months.

Process measures

We collected some additional process measure to help interpret trial results. These process measures included measures of physical activity, treatment compliance and treatment credibility. Physical activity was measured using a modified version of the International Physical Activity Questionnaire (IPAQ) at baseline, 3- and 12-month follow-ups.[21] Treatment compliance was monitored by: a) recording attendance at the two physiotherapy visits, and b) asking participants to rate compliance with home program using the Brief Adherence Rating Scale (BARS) ranging from 0 (not compliant at all) to 10 (very compliant), at the 3-, 6-, 9- and 12-month follow-ups. Treatment credibility was measured by the Credibility Expectancy Questionnaire (CEQ)[22] at the 3-month follow-up assessment.

Adverse Events (AEs) and Co-interventions Utilisation

We monitored AEs and the use of any co-intervention during the study period. We defined AEs as any new medical condition or exacerbation of an existing condition as reported by the participants during the study. Serious adverse events (SAEs) were defined as any event resulting in death or hospital admission. AEs and SAEs were assessed by direct questioning participants at the 3- and 12-month follow-ups ("Have you had a new medical condition or an exacerbation

of an existing condition since the beginning of the study?"). We also collected data, using free-text, on any intervention for treatment or prevention of LBP, apart from the study program, at the 3-, 6-, 9-, and 12-month follow-ups.

Data analysis

Study sample size was calculated using PASS statistical software (NCSS – USA), based upon the method of Lakatos.[23] At the beginning of the study, we estimated a 30% recurrence rate in the control group at 1-year and initially calculated that a sample size of 198 participants per group would give 80% power to detect a 40% relative reduction in recurrence rates between the treatment group and the control group. The sample size calculations were based on a 24-month accrual period and 12-month follow-up period. The study conservatively allowed for 1% loss to follow-up, and 1% treatment non-compliance per month in both groups. However, 20 months after recruitment began (sample size 231), the sample size was re-assessed as, based on a cohort study of a similar population,[5] we suspected the control group recurrence rate was greater than the 30% used in the original calulcations. Using a 40% recurrence rate at 1-year for the study control group (observed rate was 44% at 1-year in control group at this time) the updated calculation indicated a sample size of 131 participants per group would provide 80% power to detect a 40% relative reduction in recurrence rates with a two-sided alpha level of 0.05. This change to the study protocol was updated on the clinical trial registry.

All data were double-entered and analysed using the intention-to-treat principle.[24] For the primary and secondary outcomes, we estimated mean effects with 95% confidence intervals (CIs). We analysed baseline comparability between groups using key prognostic variables to assess for any chance imbalance that may have occurred and added as a confounder variable in the model if needed. We visually inspected the survival curves and used the time-dependent covariate method to check if the proportional hazards assumption was violated.

Cox-regression was used to estimate the effects with 95% CI of experimental intervention group on hazard ratios.[14] For each group, the 25th percentile days to recurrence of activity-limiting LBP (number of days when 25% of participants had experienced a recurrence) was calculated. For the secondary outcomes of first self-reported recurrence of (i) an episode of non-specific LBP and (ii) an episode of care seeking LBP, an analogous survival analysis was conducted to that of the primary outcome. For secondary outcome of the impact of LBP we

estimated effects with 95% CI of the experimental intervention at the 3-, 6-, 9-, and 12-month using repeated measures linear models to estimate the overall effect of the experimental intervention on the impact of LBP over a 1-year period.

We calculated completeness of follow-up using the completeness index.[25] The index quantifies the total observed person-time of follow-up as a percentage of the potential time of follow-up in the study. All analyses and interpretation of the results were done by a blinded researcher. Analyses were performed using the IBM® SPSS® Statistics version 25.

Results

Flow of participants through the study

Recruitment occurred from July 2016 to June 2018 with follow-up ending on the 30th of June, 2019. A total of 670 potential participants were screened for eligibility and 262 entered the study (figure 1). One participant, randomized to the experimental intervention group, was excluded after randomization as the treating physiotherapist identified that the participant had ongoing chronic LBP and should not have been included. Two blinded researchers reviewed the case and recommended the participant be excluded from the analyses. Of the 261 participants, 132 were assigned to the experimental intervention group, and 129 to the control group. 127 participants in the experimental intervention group received the allocated intervention, while 6 participants did not receive allocated intervention (1 post-randomisation exclusion, and 5 could not attend the sessions). 128 participants in the control group received the advice about prevention strategies, while 1 participant could not be contacted to receive the minimal intervention. 246 participants (94%) either reached study primary outcome or were censored at the end of study follow-up period. The remaining 15 participants (5 in the experimental intervention group and 10 in the control group) either were lost to follow-up or withdrew and were censored early. The completeness index was 94% for the study primary outcome.

Characteristics of study participants and therapists

Baseline characteristics of participants included in this trial are presented in Table 1. The mean age was 42 years (SD 13), and approximately half (49%) were female. The median number of previous episodes across both groups was 6 (IQR 3 to 15). Participants in both groups were similar for baseline measures. Nine physiotherapists credentialled in the McKenzie method, delivered the McKenzie-based intervention.

Process measure outcomes

Self-reported intervention compliance was similar across both groups over the 1-year follow-up period (Table 2). Attendance at the two physiotherapy sessions in the intervention group were: 117 (89%) attended 2 sessions, 10 (7%) attended the initial session only, and 5 (4%) did not attend any sessions. Further details of study process measures are presented in Table 2.

Effects of the intervention

Primary outcome

For the primary outcome of number of days from randomisation to first reported recurrence of activity-limiting LBP, the preventive effect of the experimental intervention was estimated as HR 1.11 (95% CI, 0.80 to 1.54). The 25th percentile days from randomisation to activity-limiting recurrence of LBP were 101 (95% CI, 74 to 127) in the experimental intervention group, and 127 (95% CI, 44 to 210) in the control group. Figure 2 presents the Kaplan-Meier survival curves for days to first recurrence of an episode of activity-limiting LBP.

Secondary outcomes

The preventive effect of the experimental intervention on the secondary outcome of any recurrence of LBP was estimated as HR 0.95 (95% CI, 0.72 to 1.26). The 25th percentile days to a recurrence of any episode of LBP were 58 (95% CI, 41 to 75) in the experimental intervention group, and 59 (95% CI, 33 to 85) in the control group. Figure 3 presents the Kaplan-Meier survival curves for days to first recurrence of any episode of LBP.

The preventive effect of the experimental intervention on the secondary outcome of a recurrence of an episode of LBP leading to care-seeking was estimated as HR 0.69 (95% CI, 0.46 to 1.04), indicating a point estimate of 31% reduction in care-seeking in the experimental intervention group compared to control group. The 25th percentile days to a recurrence of LBP leading to care-seeking were 344 (95% CI, 197 to 491) in the experimental intervention group, and 238 (95% CI, 134 to 342) in the control group. Figure 4 presents the Kaplan-Meier survival curves for days to first recurrence of LBP leading to care-seeking.

The experimental intervention did not have a substantial effect on the secondary outcome of impact of LBP over 12-months period. The mean effect sizes and their confidence intervals at 3-

, 6-, 9- and 12-months were all within 4 points above or below zero (no effect) on the scale from 8 to 50 (Table 3).

Discussion

The purpose of this study was to estimate the effect of two sessions of the McKenzie-based self-management exercise and education program in people who have recently recovered from an episode of LBP.

The primary outcome of this study was the risk of recurrence of activity-limiting LBP. The estimate of the effect on this outcome was HR 1.11 (95% CI, 0.80 to 1.54). Our best estimate is that a McKenzie-based self-management exercise and education program does not produce substantial reductions in the risk of an activity-limiting episode of LBP; however, we cannot rule out modestly reduced or moderately increased risk based on the confidence interval. This confidence interval indicates that the true effect of the experimental intervention on this outcome in the general population might be anywhere between increasing the hazard ratio by 54% or decreasing it by 20%. Further research could be undertaken to try to decrease this uncertainty about the effect on activity-limiting LBP.

Similarly, the best estimate suggests that the experimental intervention does not produce substantial reductions in risk for the secondary outcome of any LBP recurrence (HR, 0.95; 95% CI, 0.72 to 1.26). The confidence interval for the secondary outcome of recurrence of any LBP, extended from 0.72 to 1.26, indicating that the experimental intervention might increase the hazard ratio by 26% or decrease it by 28%.

For the secondary outcome of recurrence of LBP causing care-seeking the best estimate is that the experimental intervention may produce substantial reductions in risk for this outcome (HR, 0.69; 95% CI, 0.46 to 1.04). The CI excludes the possibility that the experimental intervention increases the hazard ratio to any important extent (ie, 4% or less) and includes the possibility that the effect is very worthwhile (decrease the HR by 54%).

The experimental intervention had a negligible effect on secondary outcome of the impact of LBP, with effect sizes and their confidence intervals all lying within 4 points above or below zero (no effect) on the scale from 8 to 50.

Current evidence from a systematic review of RCTs on prevention of LBP suggests that exercise in combination with education has a protective effect for up to one year (RR, 0.55; 95% CI, 0.41 to 0.74).[7] Most trials in this review included group-based strength and aerobic exercises that were quite different from our experimental intervention, that primarily included passive range of motion exercises. However, one of the included trials by Larsen et al.[26] investigated the effect of passive prone back extensions performed twice daily, and McKenzie method based education, in male military conscripts. This study reported relative risk reduction of a new LBP episode of around 60% (RR, 0.36; 95% CI, 0.18 to 0.73). In contrast, the best estimates from our trial suggest that a McKenzie-based self-management and education program did not produce substantial reductions in the risk of a recurrence and did not generate precise-enough estimates to confidently recommend whether or not it should be used in preventing recurrences of LBP. Important differences between our RCT and Larsen et al.[26] trial, that could explain the different findings include: different populations (broad community population, compared with male military conscripts); we recruited participants who had recovered from a previous episode of LBP within the past 6 months, while they included a mixed population with and without LBP; and, follow-up period (we followed participants from 12 months up to 30 months, while Larsen and colleagues followed participants for only 10 months).

Strengths of our study include a pre-specified published protocol,[10] regular follow-ups to avoid recall bias and use of 3 definitions of a recurrence. We followed participants for between 12 months and 30 months, and reported very high follow-up rates (completeness index of 94%). A limitation of our trial is that it was not possible to blind clinicians and participants to group allocation due to the nature of the intervention. A single therapist delivered the minimal intervention to the control group, which could impact the generalisability of findings. Participants in both groups received some co-interventions and these may have impacted on the results, especially the secondary outcome impact of low back pain, as most co-interventions were received as a result of the recurrences.

It is unclear why the best estimates from our trial suggest the intervention did not produce substantial reductions in risk of a recurrence while exercise and education interventions have been effective in most previous trials. It is possible this is due to our imprecise estimates, but also suggests future research should investigate whether it is the exercise type, dosage, or both

that determines a protective effect. Our promising findings regarding reduction in care-seeking require further testing in larger RCTs fully powered for this less common but important event.

What should clinicians make of this study's findings? The imprecise estimates on the first few outcomes should not be interpreted as evidence that the experimental intervention is ineffective for those outcomes. Further evidence may clarify that the intervention's effect is beneficial, negligible or harmful. Clinicians should keep an open mind about those outcomes until more precise estimates are available. For the time being, those estimates narrow our idea of what the true average effect of the intervention on those outcomes might be, but not enough to indicate whether we should use the treatment. The estimate of the effect on recurrence of LBP that leads to care-seeking is more promising and does exclude the possibility of any important harm, but it still includes the possibility of no effect, so the study cannot be used to recommend the experimental intervention to prevent care-seeking. Where the study was able to provide clear evidence was on the impact of LBP, with very narrow confidence intervals centred close to zero (ie, no effect). Clinicians can conclude that the experimental approach has a negligible effect on the impact of LBP.

Given the strong trend evident on the 'care-seeking' outcome and the clear indication of negligible effect on the 'impact of LBP', it is interesting to speculate whether a treatment could prevent care-seeking even though it does not affect the impact of LBP. Although both interventions in this study offered strategies for self-management, the more intensive experimental intervention may have reinforced this message more effectively. Perhaps the experimental intervention does not delay the recurrence of LBP, but it does effectively teach patients to self-manage well enough that they don't need to seek care from a healthcare practitioner when the LBP recurs. The experimental intervention specifically aimed to provide participants with skills to become more active and responsible in the management of their condition. Participants were instructed to remain active and to use the exercises taught to manage minor recurrent symptoms.

In conclusion, our best estimate is that a McKenzie-based self-management exercise and education program does not produce a substantial reduction in the risk of an activity-limiting episode of LBP but may produce a substantial reduction in recurrence of an episode of LBP leading to care-seeking. We also found clear evidence that any effect on the impact of LBP over

one year is negligible. Further research is necessary to understand whether the contraditory finding in this trial, when compared to previous trials, is because the experimental intervention was different in terms of the mode and dosage of the exercise or pehaps the different population characteristics. Future research should also investigate the promising trend that this experimental intervention might delay care-seeking when LBP recurs.

What was already known on this topic: Current evidence of randomised, controlled trials (RCTs) suggests exercise combined with education reduces the risk of a new episode of LBP; however, the evidence from these RCTs is mostly based on relatively costly, inflexible and time-consuming exercise programs.

What this study adds: This study provided robust but imprecise estimates about whether a McKenzie-based self-management exercise and education program affects recurrence of LBP, but it provided clear evidence that any effect on the impact of LBP over one year is negligible. Further research should investigate the promising trend that this intervention might prevent people from seeking healthcare when LBP recurs.

Table 1. Baseline characteristics of participants included in the SAFE trial.

Baseline variables	All participants (N=261)	Intervention group (N=132)	Control group (N=129)
Age, *years, mean (SD)*	42.3 (12.7)	40.8 (13.0)	43.8 (12.3)
Women, *n (%)*	129 (49.4)	68 (51.5)	61 (47.3)
Weight, *Kg, mean (SD)*	74.4 (16.1)	73.8 (17.1)	75.0 (15.0)
Height, *cm, mean (SD)*	170.7 (9.4)	170.6 (9.1)	170.8 (9.7)
BMI, *kg/m^2, mean (SD)*	25.5 (5.0)	25.3 (5.2)	25.7 (4.9)
Education level, *n (%)*			
Some secondary school	02 (0.8)	2 (1.5)	0 (0.0)
Completed high school	17 (6.5)	11 (8.3)	6 (4.7)
Some additional training	38 (14.6)	20 (15.2)	18 (14.0)
Undergraduate university	104 (39.8)	47 (35.6)	57 (44.2)
Postgraduate university	100 (38.3)	52 (39.4)	48 (37.2)
Current work status, *n (%)*			
Full time	154 (59.0)	75 (56.8)	79 (61.2)
Part time	53 (20.3)	26 (19.7)	27 (20.9)
Unemployed	11 (4.2)	7 (5.3)	4 (3.1)
Students or homeworkers	17 (6.5)	12 (9.1)	5 (3.9)
Other	26 (10)	12 (9.1)	14 (10.9)
Smoking, *n (%)*			
Never	196 (75.1)	98 (74.2)	98 (76.0)
Used to smoke, but quit	54 (20.7)	28 (21.2)	26 (20.2)
Current smoker	11 (4.2)	6 (4.5)	5 (3.9)
Manual task involving heavy loads, *n (%)*			
Very frequently	18 (6.9)	9 (6.8)	9 (7.0)
Frequently	43 (16.5)	24 (18.2)	19 (14.7)
Occasionally	84 (32.2)	43 (32.6)	41 (31.8)
Rarely	54 (20.7)	28 (21.2)	26 (20.2)
Very rarely	49 (18.8)	20 (15.2)	29 (22.5)
Never	13 (5.0)	8 (6.1)	5 (3.9)
Manual task involving awkward position, *n (%)*			
Very frequently	10 (3.8)	6 (4.5)	4 (3.1)
Frequently	34 (13.0)	20 (15.2)	14 (10.9)
Occasionally	85 (24.9)	30 (22.7)	35 (27.1)
Rarely	65 (32.6)	44 (33.3)	41 (31.8)
Very rarely	48 (18.4)	21 (15.9)	27 (20.9)
Never	19 (7.3)	11 (8.3)	8 (6.2)
General Health, *n (%)*			
Excellent	46 (17.6)	23 (17.4)	23 (17.8)
Very good	111 (42.5)	53 (40.2)	58 (45.0)
Good	93 (35.6)	52 (39.4)	41 (31.8)
Fair	11 (4.2)	4 (3.0%)	7 (5.4)
Number of previous episodes	6 (IQR, 3 to 15)	6.5 (IQR, 3 to 15)	6 (IQR, 3 to 15)
Duration of last episode, *days*	7 (IQR, 3 to 21)	7 (IQR, 3 to 19.5)	7 (IQR, 4 to 21)
Perceived risk of recurrence*, mean (SD)*	6.5 (2.3)	6.6 (2.3)	6.5 (2.3)
Physical activity, *minutes past 7 days*			
Walking	180 (IQR, 90 to 330)	192 (IQR, 92 to 358)	180 (IQR, 90 to 305)
Moderate/Vigorous PA	90 (IQR, 15 to 240)	90 (IQR, 0 to 240)	120 (IQR, 27 to 240)
Time sitting, *hours, mean (SD)*	7.6 (3.2)	7.7 (3.2)	7.5 (3.3)
DASS-21*, mean (SD)*			
Depression	4.4 (5.9)	5.0 (6.8)	3.8 (5.0)
Anxiety	4.0 (4.7)	4.3 (4.9)	3.7 (4.4)
Stress	10.1 (8.3)	10.5 (8.8)	9.7 (7.8)
Sleep quality, *n (%)*			
Very good	55 (21.1)	29 (22.0)	26 (20.2)
Fairly good	144 (55.2)	67 (50.8)	77 (59.7)
Fairly bad	56 (21.5)	31 (23.5)	25 (19.4)
Very bad	6 (2.3)	5 (3.8)	1 (0.8)

Values are mean (SD), n (%) or median (IQR). N, refers to participants included in the analyses; SD, Standard Deviation; n, refers to number of participants scored in each category; IQR, Interquartile Range; BMI, Body Mass Index; PA, Physical Activity.
Perceived risk of recurrence over the next 12-months, scored from 0 (no risk) to 10 (very high risk); Physical activity, self-rated total time spent doing the activity (at least 10 minutes at a time) over the last 7 days; Time sitting, hours spent sitting on an average week-day in the last week; DASS-21, 21 items Depression Anxiety Stress Scale (each domain score range from 0 to 21).

Table 2. Process measures in the SAFE trial.

Measures	Intervention group	Control group
Physical Activity, *minutes past 7 days*		
Walking		
Baseline	192 (IQR, 92 to 358)	180 (IQR, 90 to 305)
3-months	150 (IQR, 90 to 300)	180 (IQR, 82 to 307)
12-months	180 (IQR, 90 to 300)	180 (IQR, 90 to 303)
Moderate/Vigorous PA		
Baseline	90 (IQR, 0 to 240)	120 (IQR, 27 to 240)
3-months	90 (IQR, 40 to 200)	90 (IQR, 17 to 245)
12-months	90 (IQR, 20 to 205)	90 (IQR, 30 to 180)
Program compliance		
Physiotherapy first session only, *n (%)*	10 (7.6)	NA
Physiotherapy both sessions, *n (%)*	117 (88.6)	NA
Home exercise program between sessions (BARS), *mean (SD)*	7.3 (2.1)	NA
Compliance over 12-months (BARS), *mean (SD)*		
3-months	6.8 (2.3)	5.9 (2.5)
6-months	5.5 (2.6)	5.7 (2.8)
9-months	5.2 (2.7)	5.3 (2.8)
12-months	5.1 (2.8)	5.2 (2.8)
Credibility/expectancy	29.5 (6.0)	24.5 (9.0)
Adverse events		
Serious adverse events, *no. of events*	9	6
Adverse events, *no. of events*	29	41
Co-interventions		
Overall, *no. of co-interventions*	153	210
Most common, *no. of co-interventions*		
Physiotherapy	45	57
Chiropractor	24	52
Massage	21	37
Pilates	21	11
Acupuncture	10	17
Yoga	6	9
Others	26	27
Pregnancy	1	3

Values are mean (SD), n (%) or median (IQR). SD, Standard Deviation; n, refers to number of participants scored in each category; IQR, Interquartile Range; PA, Physical Activity; BARS, Brief Adherence Rating Scale - scored from 0 (not compliant at all) to 10 (very compliant).

Physical activity, self-rated total time spent doing the activity (at least 10 minutes at a time) over the last 7 days; Credibility/expectancy, scored from 4 (low credibility/expectancy) to 36 (high credibility/expectancy); Adverse events, number of adverse events reported in the study over 2 time-points (3-, and 12-months follow-ups); Co-intervention, number of additional co-interventions reported in the study over 4 time-points (3-, 6-, 9-, and 12-months follow-ups).

Table 3. Modelled estimates of the Personal Impact of Back Pain over 12-months period.

	Intervention group		Control group		MD (95% CI)*
Time-point	**N**	**Mean (SD)**	**N**	**Mean (SD)**	
Baseline	132	21.71 (8.06)	129	21.66 (8.95)	NA
3-months	129	13.04 (4.72)	125	13.22 (5.76)	-0.12 (-1.76 to 1.51)
6-months	129	12.61 (5.35)	120	13.76 (6.09)	-1.12 (-2.99 to 0.73)
9-months	126	12.99 (5.01)	122	14.48 (7.28)	-1.35 (-3.28 to 0.57)
12-months	125	13.57 (6.80)	117	13.39 (6.21)	0.14 (-1.81 to 2.09)

N, number of participants; SD, Standard Deviation; MD, Mean difference; CI, Confidence Interval; NA, Not Applicable.
*MD between groups based on modelled estimates. A negative value of the MD estimate represents an effect in favour of the intervention group. Personal Impact of Back Pain (9 items of the 29-item PROMIS short form), scored from 8 (least impact) to 50 (great impact).

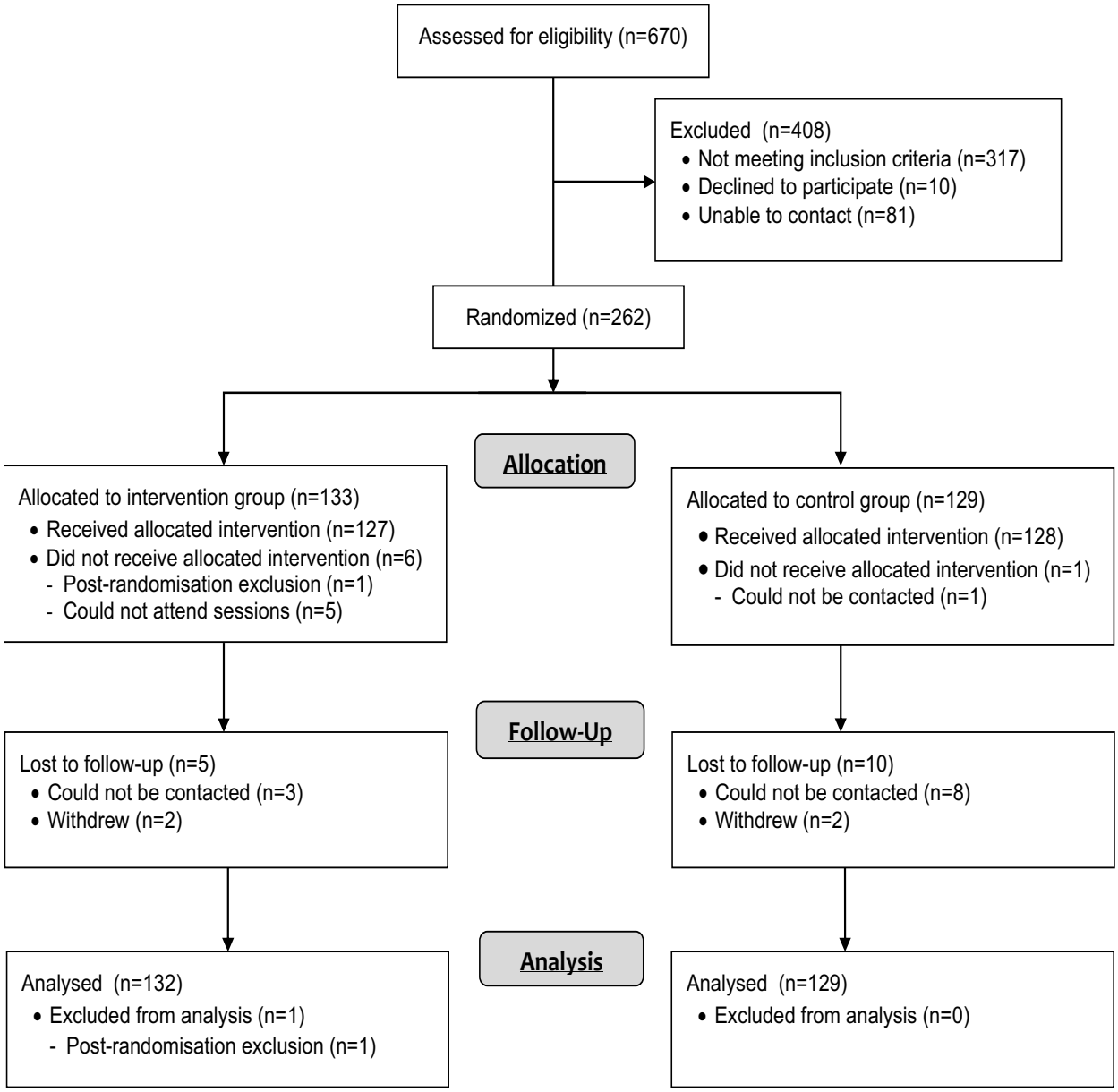
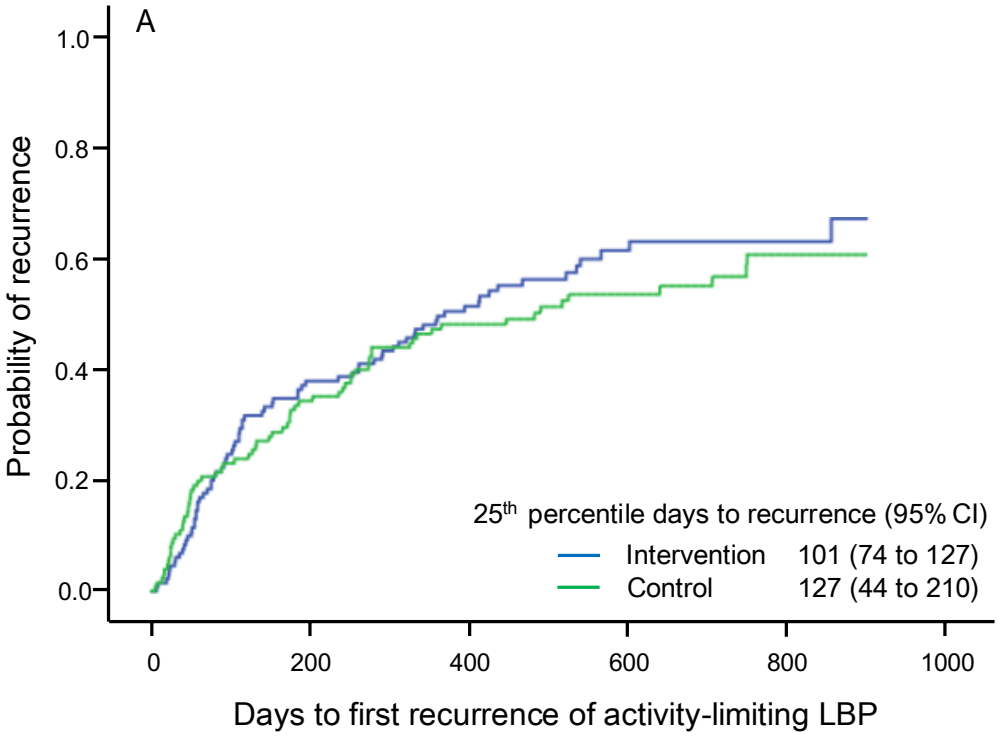
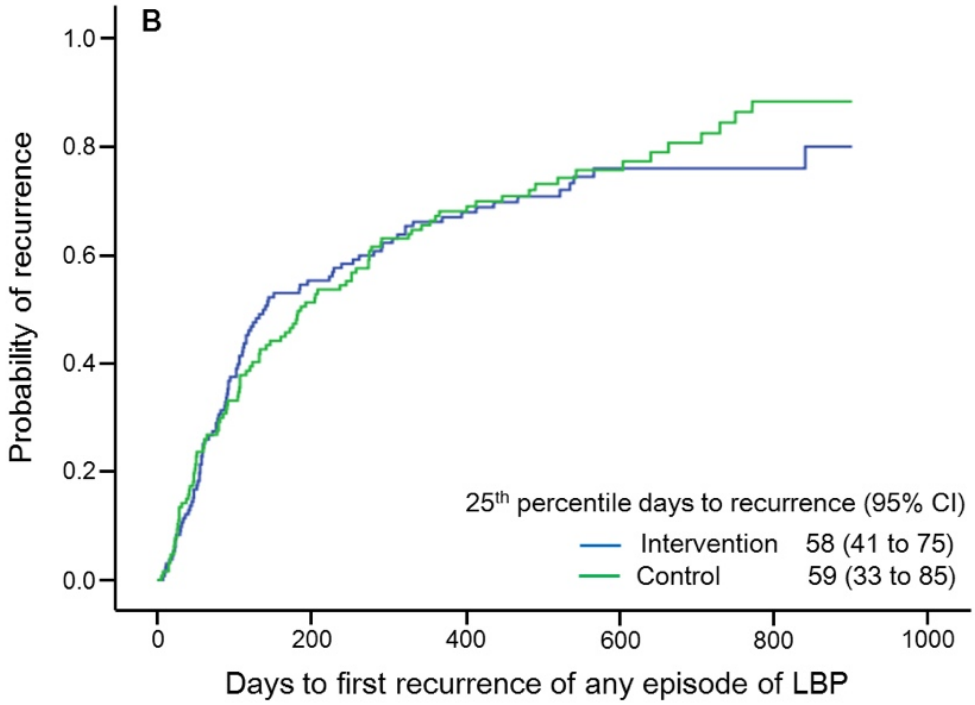


Figure 1. Flow diagram of participants through SAFE trial.



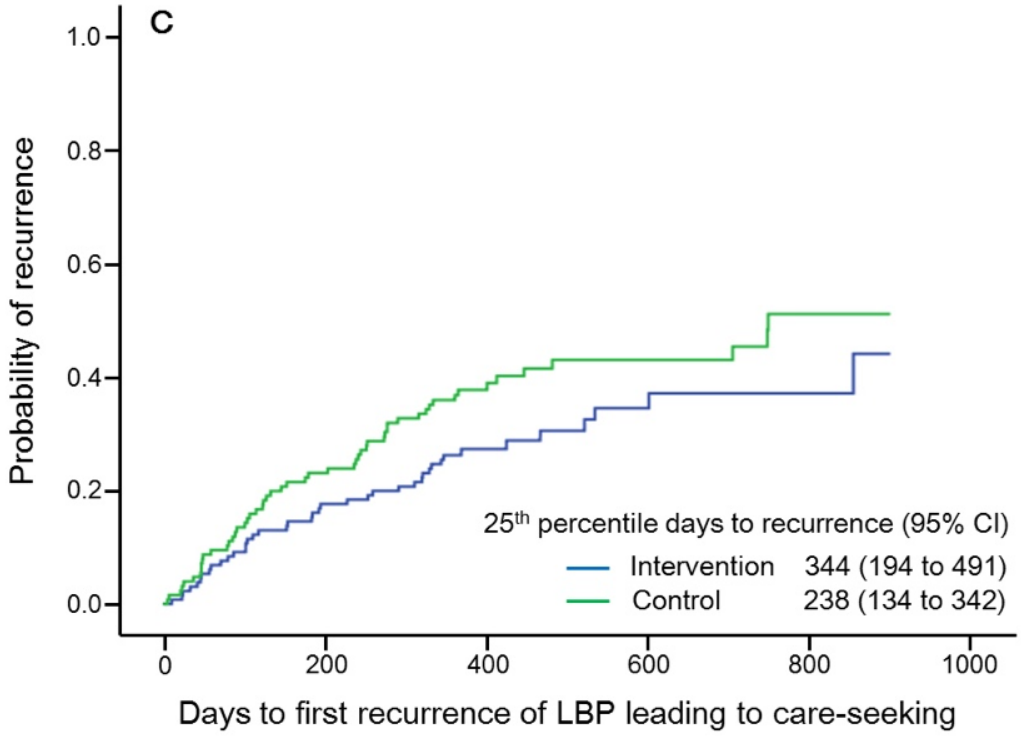
LBP, Low Back Pain; CI, Confidence Interval; Recurrence is defined as a new episode of LBP of intensity >2/10, lasting at least 24 hours.

Figure 2. Kaplan-Meier survival curves for days to first recurrence of an episode of activity-limiting LBP (A).



LBP, Low Back Pain; CI, Confidence Interval; Recurrence is defined as a new episode of LBP of intensity >2/10, lasting at least 24 hours.

Figure 3. Kaplan-Meier survival curves for days to first recurrence of any episode of LBP (B).



LBP, Low Back Pain; CI, Confidence Interval; Recurrence is defined as a new episode of LBP of intensity >2/10, lasting at least 24 hours.

Figure 4. Kaplan-Meier survival curves for days to first recurrence of LBP leading to care-seeking (C).

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CHAPTER FOUR

Prevention Strategies to Reduce Future Impact of Low Back Pain: A Systematic Review and Meta-Analysis

4.1 Preface

The study presented in **Chapter Three** evaluated the effectiveness of an intervention aiming to prevent a new episode of low back pain. Similarly to the study in **Chapter Three**, some of the previous literature investigating prevention strategies for low back pain is based on trials aiming to reduce the risk of a new episode of low back pain. These studies usually recruit asymptomatic participants at study entry. However, other previous trials investigating the prevention of low back pain have recruited a mixed population of people, asymptomatic and symptomatic at study entry, rather than restricting inclusion only to asymptomatic people. These studies provide further important information regarding different outcomes such as future low back pain intensity and associated disability but were not included in previous systematic reviews. To the candidate's knowledge, no previous systematic review has attempted to summarise the evidence on these outcomes. **Chapter Four**, therefore, presents the results for a systematic review that investigated the current literature evaluating the effectiveness of prevention strategies aiming to reduce future impact of low back pain; where impact is measured by low back pain intensity and associated disability.

The study presented in **Chapter Four** has been submitted to the British Journal of Sports Medicine and has been recently accepted for publication. The manuscript is presented in the format of the accepted manuscript before edits.

The systematic review registration with PROSPERO is presented in the **Thesis Appendix 6**.

4.2 Authorship attribution statement

This statement is to stipulate the contribution made by Tarcisio Folly de Campos in the preparation and submission of the following manuscript: "***de Campos TF***, Maher CG, Fuller JT, Steffens D, Attwell S, Hancock MJ. Prevention strategies to reduce future impact of low back pain: a systematic review and meta-analysis. Submitted to British Journal of Sports Medicine (November 5th 2019) and has recently been accepted for publication". The convention is that the author with the principal contribution to the study is the first author.

Tarcisio Folly de Campos, during his PhD candidature, developed the original concept and design of this systematic review, and was responsible for designing the search strategy, data search and data extraction instruments, registering the review in the PROSPERO database, appraising the selected studies for methodological quality and risk of bias, writing the draft manuscript and subsequent revisions, responding to reviewer's feedback and coordinating submission for publication of the original manuscript.

The individual roles of co-authors are listed below:

Task	**Co-author's contribution**
Conception and research design	CM, JF, MH
Data search, study selection, data extraction	JF, DS, SA, MH
Risk of bias and methodological quality assessment	JF, DS, MH
Drafting of the manuscript	MH
Revision and critical comment of manuscript	CM, JF, DS, SA, MH

CM, Chris Maher; **JF**, Joel Fuller; **DS**, Daniel Steffens; **SA**, Stephanie Attwell; **MH**, Mark Hancock

Mr Tarcisio Folly de Campos _____ Date: 28 / 02 /2020

As supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statement above is correct.

Professor Mark Hancock _____ Date: 28 / 02 /2020

Prevention Strategies to Reduce Future Impact of Low Back Pain

A Systematic Review and Meta-analysis

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Keywords: Low back pain; Prevention; Randomised controlled trial; Systematic review; Meta-analysis.

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Word Count: 3,970 words

Abstract

Objective: To evaluate the evidence from randomised, controlled trials (RCTs) on the effectiveness of prevention strategies to reduce future impact of low back pain (LBP) and associated disability.

Design: Systematic review with meta-analysis.

Data Sources: MEDLINE, Embase, CINAHL, PEDro, and The Cochrane (CENTRAL) databases from inception to October 22, 2018.

Eligibility criteria: RCTs evaluating any intervention aiming to prevent future impact of LBP, not restricting recruitment to participants with current LBP, reporting an outcome measure of LBP intensity and/or disability measured at least 3 months post-randomisation, and the intervention group must be compared to a group that received no intervention/placebo or minimal intervention.

Main Outcome(s) and Measure(s): Primary outcome measures were low back pain-intensity and associated disability. Secondary outcome measures were other patient-centered outcomes relevant to LBP such as quality of life (QoL). Where possible data were pooled using random-effects meta-analysis, outcomes were converted to a common 0 to 100 scale to accommodate for differences in trial scales and presented as between-group mean difference (MD) and 95% confidence intervals (CI).

Results: 27 published reports of 25 different trials including a total of 8341 participants fulfilled the inclusion criteria. The pooled results, from three RCTs (612 participants), found moderate-quality evidence that an exercise program can prevent future LBP intensity (MD, -4.50; 95% CI, -7.26 to -1.74). There was moderate-quality evidence from pooling of 4 RCTs (471 participants) that an exercise and education program can prevent future disability due to LBP (MD, -6.28; 95% CI, -9.51 to -3.06). It is uncertain whether prevention programs improve quality of life (QoL) and workability due to the overall low- and very low-quality available evidence.

Conclusions: This review provides moderate-quality evidence that both an exercise program, and a program combining exercise and education, are effective to reduce future LBP intensity and associated disability. It is uncertain whether prevention programs can improve future QoL and workability. Further high-quality RCTs evaluating prevention programs aiming to reduce future impact of LBP are needed.

Introduction

Low back pain (LBP) is the leading cause of global disability and a common reason for work absenteeism, lost productivity and care-seeking.[1-3] Although most people with an episode of LBP improve substantially within 6-12 weeks,[4] most will also experience a recurrence within 12 months.[5] The modern understanding is that LBP is a chronic condition presenting recurrent symptomatic episodes. Effective prevention strategies to reduce future LBP intensity and associated disability have the potential to greatly reduce the burden associated with this condition.

A recent systematic review conducted by Steffens et. al.[6] demonstrated there was moderate-quality evidence that exercise combined with education reduces the risk of a future episode of LBP (RR, 0.55; 95% CI, 0.41 to 0.74), but most other interventions either lacked evidence or appeared to be ineffective. Importantly, this review took a traditional approach to prevention by only including studies where participants did not have LBP at baseline. While this approach works well in acute conditions where the onset and the end of the episode are clear, it has limitations for a chronic recurrent condition like LBP. In chronic fluctuating conditions it is arguably more important to prevent the consequences of the chronic disease (sometimes considered tertiary prevention) than to simply prevent the onset of the initial episode.

Some previous studies have investigated the effectiveness of prevention strategies in terms of reducing future LBP intensity and/or associated disability rather than preventing a new episode of LBP.[7 8] These studies commonly include “mixed populations” (ie, both asymptomatic and symptomatic patients) at study entry, rather than restricting inclusion only to people without LBP. Studies such as these provide important information about the potential effectiveness of prevention strategies on reducing future LBP intensity and associated disability, but were not included in the previous systematic review by Steffens and colleagues.[6] These studies including “mixed populations” are also different from traditional treatment studies that require all participants to have symptoms at study entry. We are unaware of any previous review that has focused on these types of prevention studies.

Therefore, the primary aim of this systematic review was to investigate the effectiveness of prevention strategies aiming to reduce future impact of LBP; where impact is measured by LBP intensity and associated disability.

Methods

Study reporting and protocol registration

The systematic review adhered to the statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions (PRISMA).[9] The review protocol was prospectively registered on PROSPERO (CRD42018107946).

Data sources and searches

A comprehensive search of five electronic databases (MEDLINE via Ovid, EMBASE via Ovid, CINAHL, Physiotherapy Evidence Database (PEDro), and The Cochrane Central Register of Controlled Trials (CENTRAL) via The Cochrane Library for eligible manuscripts was conducted from the date of inception to October 22, 2018. A sensitive search strategy was used based on the recommendations of the Cochrane Back and Neck Group[10] for "Randomised Controlled Trials" and "low back pain", combined with search terms for "prevention". The full search strategy for each database is presented in the online supplementary appendix A. In addition, reference lists of relevant reviews and included randomised controlled trials (RCTs) were manually searched and citation tracking of all included trials was performed. The searches and inclusion criteria were not restricted by language.

Study selection and screening criteria

We included published reports of RCTs, including cluster-RCTs, testing the effectiveness of prevention strategies aiming to reduce future impact of LBP. Impact of LBP was measured by LBP intensity and disability. We excluded RCTs that restricted recruitment to participants with current LBP (treatment studies). Eligible interventions included any approach aiming to prevent or reduce future impact of LBP such as workplace interventions to control risk factors or interventions to make people more fit/healthy/resilient. To be eligible trials needed to compare an intervention group to a group that received no intervention, sham intervention or minimal intervention. We also included RCTs investigating multimodal interventions if the effect of one intervention could be isolated (eg, back exercise and education versus education alone).

Trials needed to report an outcome measure of LBP intensity and/or LBP associated disability measured at least 3 months post-randomisation. Primary outcomes for this review were: a) pain-intensity measured by a self-reported outcome measure (eg, visual analogue scale,

numerical rating scale) and b) disability measured by a self-reported outcome measure (eg, Oswestry Disability Index and Roland-Morris Disability Questionnaire). Other patient-centered outcomes relevant to back pain such as quality of life (QoL) were considered secondary outcomes. Studies that used a quasi-randomised design were excluded.

A three stage screening process was used to select relevant RCTs for this review. In the first-stage, one reviewer (TFC) screened all titles for eligibility and excluded clearly irrelevant studies. In the second-stage, each study title and abstract was independently evaluated by pairs of review authors (TFC, DS, JTF, MJH, SA). In the third-stage, the full-text for each potentially eligible study was assessed against the eligibility criteria by a pair of independent review authors (TFC, DS, JTF, MJH, SA). Disagreements were resolved through discussion. We contacted authors for additional information as necessary.

Data extraction

Data for each included trial were extracted by pairs of independent reviewers (TFC, DS, JTF, MJH, SA) using a standardised data extraction form and discrepancies were resolved through discussion. Extracted data included: study characteristics (eg, source, study design, country, participant's characteristics, outcome measure, description of the intervention/control groups, and follow-up periods), means and measures of variability for all outcomes. When possible, raw mean and standard deviation outcome data for both the intervention group and control group were extracted. We also estimated raw data from graphs in cases where this information was not presented in tables or text. We attempted to contact authors of included RCTs to clarify any relevant information or request additional data when required.

Quality appraisal

Risk of bias was assessed using the PEDro Scale[11-13] by either downloading the available scores from the PEDro database (http://www.pedro.org.au), or by two experienced PEDro raters rating the report when not available online. The total score on the PEDro scale is the addition of "yes" (criterion is clearly satisfied) responses for items 2-11 (item 1 is not used for calculation of the total PEDro scale score because it is more related to external validity) and range from 0 (high risk of bias) to 10 (low risk of bias). There is evidence that the PEDro scale total score has acceptably high reliability and validity[11 12] and Rasch analysis has confirmed that it can be used as a continuous scale.[14]

Quality of evidence assessment

The overall quality of evidence for each intervention contrast was rated as high-, moderate-, low-, or very low-quality as recommended by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.[15] The GRADE classification was downgraded one level per study limitation, from high-quality, if any of the following limitations were present: (i) Design limitation (more than a quarter of participants from studies with low methodological quality [PEDro score <7]); (ii) Inconsistency of results (wide variation of point estimates across individual trials or substantial heterogeneity, I^2 >50%); (iii) Imprecision (based on a threshold of <400 total participants for each pooled outcome estimate). We did not consider the indirectness criterion in this review as we included a specific population with relevant outcomes. When only a single RCT was available, evidence from RCTs with fewer than 400 participants was downgraded for inconsistency and imprecision; however, evidence from single RCTs presenting more than 400 participants was only downgraded for inconsistency. Publication bias was not evaluated due to the small number of trials in each meta-analysis.[16]

A GRADE profile was completed for each pooled estimate and for single RCTs comparing a LBP prevention strategy with a control intervention. Two independent reviewers (TFC and MJH) independently performed GRADE assessments for each treatment contrast and disagreements were resolved by discussion.

Statistical analysis

The between-groups mean difference (MD) and 95% confidence intervals (CIs) were calculated using the mean final score for the intervention and control groups. We used final scores rather than within group change scores as only one study reported change scores.[16] When possible, we combined results in a meta-analysis using random-effects models. Negative values of the mean difference estimate represent an effect in favour of the intervention group. To accommodate the different scales used for study outcomes, we converted, whenever possible, outcomes to a common 0 to 100 scale. If conversion was not possible due to the nature of outcome (eg, categorical or ordinal), we did not convert the results but instead presented them as a narrative synthesis. If information regarding standard deviations was missing, we calculated these from CIs, standard errors or P-values; however, if no measure of variability was

presented, we estimated the standard deviation from the most similar and high-quality trial in the review as recommended by *The Cochrane Collaboration*.[16]

Outcome assessment data were extracted for two time periods: short-term follow-up (collected at <12-months post-randomisation); long-term follow-up (collected at ≥12-months post-randomisation). When studies presented multiple follow-up time-points that fell within the same category, we used the time-point that was closest to 6-months for short-term follow-up and one closest to 12-months for long-term follow-up. For RCTs including multiple treatment arms, we extracted data for each comparison that met the inclusion criteria and adjusted the numbers per group as recommended by *The Cochrane Handbook for Systematic Review of Interventions*.[16]

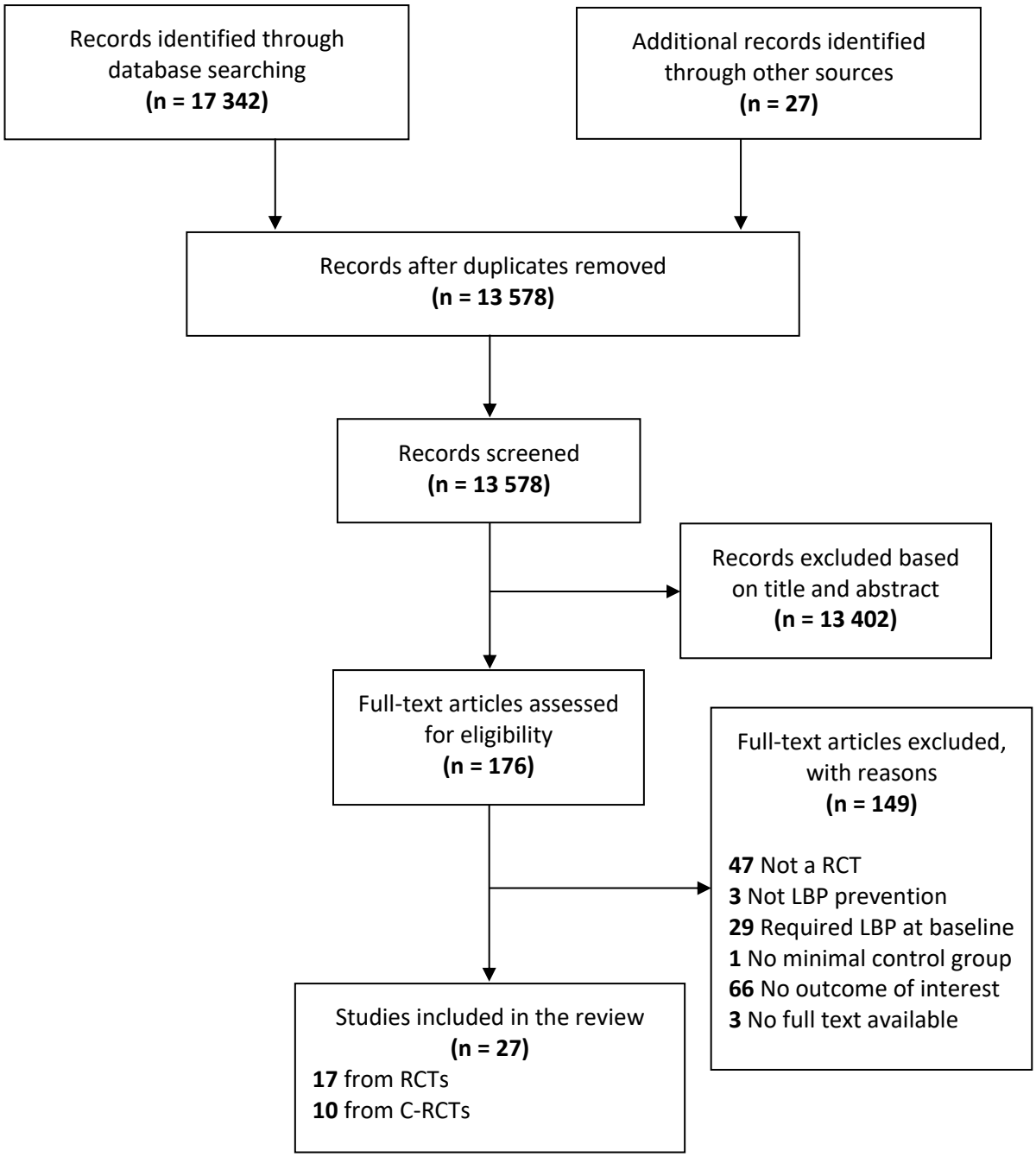
Trials considered homogeneous were grouped, when possible, according to the population (eg, children, pregnant women), intervention strategy, outcome measure, and outcome assessment time-points (short-term and long-term). For RCTs not reporting the sample size at the follow-up time-point, we adopted the baseline sample size.

Where we considered study interventions to be sufficiently similar to be combined in meta-analyses, we assessed heterogeneity of treatment effects by visual inspection of effect size with 95% CI and by using the I^2 statistic. We used Comprehensive Meta-analysis, version 2.2.064 (Biostat) for all analyses.

Results

Of the 17 342 identified records, 176 were considered potentially eligible and we reviewed full-text manuscripts. Of these, twenty-seven published reports (25 different RCTs including 8 341 participants) met the inclusion criteria and were deemed eligible for this review.[7 8 17-41] The 25 RCTs included ten cluster-RCTs[7 17 20 28 30 34 35 39-41]. Two RCTs were reported in four published manuscripts reporting different follow-up time-points.[25 32 36 37] An outline of the screening and selection process is provided in Figure 1.

Figure 1. Flow diagram of study selection



Abbreviations: RCT, Randomised Controlled Trial; C-RCT, Cluster Randomised Controlled Trial; LBP, Low Back Pain

The included studies investigated three different populations: general adults, pregnant women, and children. Most trials recruited participants who were employees at a hospital (32%) or company (40%) setting while only two trials (8%) recruited people from the general community. Most included trials (8 269 participants) examined a working-age population with the mean age of 45.1 years and majority female (75.9%). Six different LBP prevention strategies were investigated: exercise, exercise and education, education, ergonomics, ergonomics and education, and lumbar support. Two trials investigated LBP prevention strategies in a population of pregnant women,[21 23] while one trial investigated a sample of primary school children.[22] Eight trials presented two intervention contrasts (3 arms).[7 17 19 29 31 35 40 41] Table 1 and online supplementary appendix B provide details of the characteristics of each included trial.

Table 1. Characteristic of RCTs included in the systematic review of prevention strategies to reduce future impact of low back pain

Source	Study design	Country	Participants	Outcome measure	Study Groups	Time and frequency of Interventions	Follow-up period
Barene et al,[17] (2014)	C-RCT	Norway	118 hospital employees; mean (SD) age, 45.8 (9.3) y; female (91%)	LBP Intensity LBP Duration	I1: Exercise - Soccer I2: Exercise - Zumba C: No intervention	Two-three 1-h sessions per wk over 40 wks for both intervention groups	10 months
Chaleat-Valayer et al,[8] (2016)	RCT	France	342 healthcare workers from ten hospitals; mean (SD) age, 47.2 (8.5) y; female (77%)	LBP Intensity (VAS) Disability (QBPDS)	I: Education and Exercise training sessions C: No intervention	Single 2-hrs education session and 5 weekly 90-min group exercise sessions	18 months
Donaldson et al,[18] (1993)	RCT	Canada	172 hospital employees; mean (SD) age NR; sex NR	LBP Intensity (MPQ)	I: Education course (classes) C: No intervention	9 classes, 1.5-hrs each	12 months
Donchin et al,[19] (1990)	RCT	Israel	142 hospital employees; mean (SD) age, 46.0 (NR) y; female (66%)	LBP (Painful months)	I1: Exercise - Calisthenics I2: Exercise - Back school C: No intervention	I1: 45-min sessions, bi-weekly, for 3 mo I2: 4x 90-min sessions during a 2-wks	12 months
Driessen et al,[20] (2011)	C-RCT	Netherlands	3047 workers from 4 Dutch companies; mean (SD) age, 42.0 (10.95) y; female (41%)	LBP Intensity (VAS) LBP Duration	I: Ergonomics program C: Minimal intervention	I: Use the ergonomics program while on duty C: 3 short education videos	12 months
Eggen et al,[21] (2012)	RCT	Norway	257 healthy pregnant women before gestation week 20; mean (SD) age, 30.3 (4.8) y; female (100%)	LBP Intensity (VAS) Disability (RMDQ)	I: Exercise - Group classes and home exercises C: No intervention	1x /wk 1-hr group exercise session for 16 to 20 wks	4 months
Fanucchi et al,[22] (2009)	RCT	South Africa	72 children in Grade 6 and Grade 7 primary school; mean (SD) age, 12.3 (0.7) y; female (46%)	LBP Intensity (VAS)	I: Education and exercise sessions C: No intervention	8x classes 40-45min each over 8 wks	6 months
Garshasbi et al,[23] (2005)	RCT	Iran	212 pregnant women (17-22nd weeks of gestation); mean (SD) age, 26.4 (4.6) y; female (100%)	LBP Intensity (KQ)	I: Exercise training C: No intervention	3x /wk for 60min each for 12 wks	3 months
Gatty et al,[24] (2004)	RCT	USA	16 clerical and office workers; mean (SD) age, NR; female (100%)	LBP Intensity (VAS) LBP Duration	I: Ergonomics - Implementation of individualized work injury prevention program (WIPPs) C: No intervention	1-hr session over 4 wks period (4 sessions)	9 months
Glomsrod et al,[25] (2001)	RCT	Norway	81 community and participants referred from primary care clinicians; mean (SD) age, 39.4 (6.8) y; female (54%)	LBP Intensity (VAS) Disability (VAS)	I: Exercise and education C: No intervention	2 Sessions per wk for 7 wks; 1 session per wk for 6 wks; each session 60min	36 months
Gundewall et al,[26] (1993)	RCT	Sweden	69 hospital nurses/nurse's aides; mean (SD) age, 37.5 (10.5) y; female (98%)	LBP Duration	I: Exercise - Back muscle exercises C: No intervention	6x monthly sessions of 20min each	13 months
Haufe et al,[27] (2017)	RCT	Germany	226 workers from 3 medium-sized companies; mean (SD) age, 42.7 (10.2) y; female (40%)	LBP Intensity (VAS) Disability (ODI)	I: General exercise training and individual counselling/supervision sessions C: Continue their current lifestyle	I: 20-min non-supervised general exercise session 3x per wk. 5x once monthly counselling session	5 months

Table 1. (Continuation)

Source	Study design	Country	Participants	Outcome measure	Study Groups	Time and frequency of Interventions	Follow-up period
Ijzelenberg et al,[28] (2007)	C-RCT	Netherlands	489 workers performing physically demanding jobs in companies; mean (SD) age, 41.3 (9.7) y; female (3%)	LBP Intensity (NRS) Disability (RMDQ)	I: Education and ergonomics adjustments C: Usual care - health care for LBP	3x group training sessions. Unclear frequency	12 months
Irvine et al,[29] (2015)	RCT	USA	597 workers from 4 companies also general work population; mean (SD) age, NR; female (60%)	LBP Intensity LBP Duration LBP Functionality	I1: Education - FitBack website program I2: Education - Alternative care C: No intervention	I: Weekly emails and unlimited access to online material during study period	4 months
Jensen et al,[7] (2006)	C-RCT	Denmark	210 home care workers, nurses, and nurse's aides; mean (SD) age, 44.3 (8.9) y; female (100%)	LBP Intensity (NRS)	I1: Education - Transfer Technique Intervention (TTI) I2: Education - Stress Management Intervention (SMI) C: No intervention	I1: 2x 4-hrs classes and 30-hours site education (6 mo) I2: Group sessions every 2 wks for 2-hrs (20 wks)	24 months
Kamioka et al,[30] (2011)	C-RCT	Japan	88 female caregivers from 4 nursing homes in Tokyo; mean (SD) age, 38.15 (13.75) y; female (100%)	LBP Intensity (VAS)	I: Education lecture and stretching exercise C: No intervention	Single lecture of 30min; 1-hr exercises. Daily stretching (6min)	3 months
Ketola et al,[31] (2002)	RCT	Finland	109 office workers; mean (range) age, 48.0 (29 to 59) y; female (60%)	LBP Discomfort	I1: Intensive ergonomics I2: Ergonomics education C: No intervention	I1: Around 2-hrs of implementation I2: a single 1-hr session	10 months
Lonn et al,[32] (1999)	RCT	Norway	81 community and participants referred from primary care clinicians; mean (SD) age, 39.4 (6.8) y; female (54%)	LBP Intensity (VAS) Disability (VAS)	I: Exercise and education C: No intervention	2 Sessions per wk for 7 wks; 1 session per wk for 6 wks; each session 60min	12 months
Menzel et al,[33] (2006)	RCT	USA	31 registered nurses and nursing aides; mean (SD) age, 41.94 (9.0) y; female (97%)	LBP Intensity (VAS) Disability (ODI)	I: Education - Psychoeducational sessions for stress and pain management C: No intervention	6x 1.5-hrs group-discussion session	3 months
Pedersen et al,[34] (2013)	C-RCT	Denmark	537 laboratory technicians; mean (SD) age, 42.0 (10.5) y; female (85%)	LBP Intensity (VAS)	I: Exercise training sessions C: No intervention	3x weekly for 20min each over 5 mo	5 months
Pedersen et al,[35] (2009)	C-RCT	Denmark	549 office workers; mean (SD) age, 45.1 (9.4) y; female (64%).	LBP Duration	I1: Specific Resistance Training (SRT) I2: All-round Physical Exercise (APE) C: Reference group (REF): group discussion to improve knowledge on health and working conditions	I1: 3x/wk for 20min 12 mo I2: 1x introductory session at worksite; 1-hr per wk	12 months
Soukup et al,[37] (2001)	RCT	Norway	77 community and primary care participants; mean (SD) age, 37.7 (8.0) y; female (53%).	LBP Intensity (VAS) Disability (VAS)	I: Mensendieck exercises and ergonomics C: No intervention	20 Sessions for 60min over a period of 13 wks	36 months

Table 1. (Continuation)

Source	Study design	Country	Participants	Outcome measure	Study Groups	Time and frequency of Interventions	Follow-up period
Soukup et al,[36] (1999)	RCT	Norway	77 community and primary care participants; mean (SD) age, 37.7 (8.0) y; female (53%).	LBP Intensity (VAS) Disability (VAS)	I: Mensendieck exercises and ergonomics education C: No intervention	20 Sessions for 60min over a period of 13 wks	12 months
Tuchin et al,[38] (1998)	RCT	Australia	61 employees of a large mailing house; mean (SD) age NR; sex NR.	Disability (ODI)	I: A comprehensive spinal pain education lecture including advice on effective exercises C: Advice on stretching procedures used for sports "warm-up"	I: Single 120min lecture session. C: Daily over 6 mo period.	6 months
van Poppel * et al,[39] (1998)	C-RCT	Netherlands	312 airline company workers; mean (SD) age, 35.1 (7.8) y; sex NR.	LBP Duration	I1: Lumbar Support + Education I2: Lumbar Support only I3: Education only C: No intervention	Lumbar Support: Wear for 6 mo (work hours) Education (lifting instructions): 1x 2-hrs; 2x 1.5-hs; 3x (12 wks) C: No intervention	6 months
Warming et al,[40] (2008)	C-RCT	Denmark	181 hospital nurses; mean (SD) age, 35.2 (10.5) y; female (90%).	LBP Intensity (NQ) Disability (RS)	I1: Education - transfer technique (TT) I2: Education and physical training (TTPT) C: No intervention	I1: 2x 6 wks sessions I2: 2x/wk for 1-hr (8 wks)	12 months
Yassi et al,[41] (2001)	C-RCT	Canada	346 staff performing patient lifts and transfers (nurses and unit assistants); mean (SD) age NR; sex NR.	LBP Discomfort Disability (ODI)	I1: Arm B – Education - Safe Lifting program I2: Arm C – Education - No Strenuous Lifting program C: Arm A – Usual practice.	I1 and I2: 3-hrs single session	12 months

Abbreviations: RCT, Randomised Controlled Trial; C-RCT, Cluster Randomised Controlled Trial; LBP, Low Back Pain; SD, Standard Deviation; VAS, Visual Analog Scale; QBPDS, Quebec Back Pain Disability Scale; MPQ, McGill Pain Questionnaire; RMDQ, Roland Morris Disability Questionnaire; KQ, KEBK Questionnaire; ODI, Oswestry Disability Index; NRS, Numeric Rating Scale; NQ, Nordic Questionnaire; RS, Rating Scale; I, Intervention group; C, Control group; NR, Not Reported.

* van Poppel et al[39] study was analysed as a 2x2 factorial design (ie, 4 groups) with the following intervention contrasts: Lumbar Support versus No Lumbar Support, and Education versus No Education.

Risk of bias scores for twenty-four[7 8 17-28 30-32 34-37 39-41] of the included studies were found on the PEDro database website. The other three studies[29 33 38] were assessed by two raters. The mean (SD) PEDro score was 5.4 (1.2) with blinding, concealed allocation, intention-to-treat analysis and adequate follow-up being the main items scored as high risk of bias in 92%, 63%, 55% and 52% of included studies, respectively. The PEDro scale ratings for individual items and the total score for each included RCT are available in online supplementary appendix C.

Raw final scores data for intervention and control groups were available for 23 of the 25 included trials. For the remaining two trials, we used the reported MD (95% CI).[17 28] For six trials[21 31 34-36 39] we calculated standard deviation (SD) and for two trials[20 38] we imputed data from similar studies. Study design, follow-up time-point, outcome measure, sample size, raw MD and standard deviation for each intervention, and between-groups MD (95% CIs) for all included trials are presented in online supplementary appendix D (primary outcomes) and online supplementary appendix E (secondary outcomes). Trials were grouped according to the prevention strategy, outcomes, follow-up time-point (short- or long-term) and population. Table 2, online supplementary appendix F (primary outcomes) and online supplementary appendix G, online supplementary appendix H (secondary outcomes) provide a summary of the findings and the quality of evidence (GRADE) rating.

Table 2. Summary of findings for primary outcome and quality of evidence assessment (GRADE)[a]

Outcome	Follow-up time point	Number of participants	MD [95% CI][b]	GRADE
General Population				
Exercise vs. Control				
Pain intensity	Short-term	612[17 27 34]	-4.50 [-7.26 to -1.74]	Moderate-quality
Disability	Short-term	189[27]	-2.36 [-7.11 to 2.39]	Very Low-quality[c]
Exercise and Education vs. Control				
Pain intensity	Short-term	184[30 32 36]	-1.95 [-10.09 to 6.18]	Low-quality
Pain intensity	Long-term	471[8 32 36 40]	-4.37 [-9.16 to 0.43]	Moderate-quality
Disability	Short-term	150[32 36]	-4.94 [-12.78 to 2.90]	Low-quality
Disability	Long-term	471[8 32 36 40]	-6.28 [-9.51 to -3.06]	Moderate-quality
Education vs. Control				
Pain intensity	Short-term	777[18 29 33]	-1.81 [-4.68 to 1.07]	Moderate-quality
Pain intensity	Long-term	126[7 40]	1.71 [-6.14 to 9.56]	Low-quality
Disability	Short-term	804[29 33 38 41]	-2.59 [-6.15 to 0.96]	Moderate-quality
Disability	Long-term	176[40 41]	-0.29 [-4.87 to 4.30]	Low-quality
Ergonomics vs. Control				
Pain intensity	Short-term	552[20]	1.40 [-3.28 to 6.08]	Low-quality[c]
Pain intensity	Long-term	538[20]	2.00 [-2.74 to 6.74]	Low-quality[c]
Ergonomics and Education vs. Control				
Pain intensity	Short-term	192[28]	1.00 [-6.93 to 8.93]	Very Low-quality[c]
Pain intensity	Long-term	266[7 28]	0.00 [-6.70 to 6.70]	Low-quality
Disability	Short-term	192[28]	2.08 [-1.87 to 6.03]	Very Low-quality[c]
Disability	Long-term	184[28]	1.25 [-3.08 to 5.58]	Very Low-quality[c]
Pregnant Population				
Exercise vs. Control				
Pain intensity	Short-term	452[21 23]	-2.70 [-6.56 to 1.17]	High-quality
Disability	Short-term	240[21]	-2.91 [-7.06 to 1.24]	Low-quality[c]
Children Population				
Exercise and Education vs. Control				
Pain intensity	Short-term	70[22]	0.00 [-11.68 to 11.68]	Very Low-quality[c]

Abbreviations: GRADE, Grading of Recommendations Assessment, Development and Evaluation; MD, Mean Difference; CI, Confidence Interval.

[a] Only studies providing results that could be converted to a 0-100 scale are presented.

[b] Value presented on 0-100 scale.

[c] Quality of evidence assessment based on a single trial.

A negative value of the mean difference estimate represents an effect in favour of the intervention group.

Short-term indicates follow-up assessment of less than 12-months.

Long-term indicates follow-up assessment of 12-months or more.

Effectiveness of interventions for primary outcomes

Exercise

Three trials (612 participants) investigated the short-term effects of exercise programs on prevention or reduction of future LBP intensity and associated disability.[17 27 34] The pooled results of three trials (four intervention contrasts) provided moderate-quality evidence that exercise is effective for preventing future LBP intensity (MD, -4.50; 95% CI, -7.26 to -1.74) (Table 2 and Table 3).

For prevention of associated disability due to LBP, a single trial (189 participants) provided very low-quality evidence of no short-term effect of exercise programs (MD, -2.36; 95% CI, -7.11 to 2.39) (Table 2 and Table 4).[27]

Table 3. Individual study results and pooled effects for primary outcome of pain-intensity[a]

Source	Study design	Follow-up time point	Number of participants	MD [95% CI][b]	Weight, %
		General Population			
Exercise vs. Control (short-term)					
Haufe et al,[27] (2017)	RCT	5-months	189	-6.6 [-13.38 to 0.18]	15.08
Barene et al,[17] (2014) (soccer)	C-RCT (6 clusters)	3-months	43	-1.0 [-10.70 to 8.70]	7.70
Barene et al,[17] (2014) (zumba)	C-RCT (6 clusters)	3-months	46	2.0 [-6.75 to 10.75]	9.38
Pedersen et al,[34] (2013)	C-RCT (57 cluster)	5-months	334	-5.33 [-7.94 to -2.72]	67.84
Pooled effect: I^2 = 1.78%				**-4.50 [-7.26 to -1.74]**	
Exercise and Education vs. Control (short-term)					
Lonn et al,[32] (1999)	RCT	5-months	81[c]	-8.0 [-14.84 to -1.16]	41.83
Soukup et al,[36] (1999)	RCT	5-months	69	-1.0 [-8.79 to 6.79]	38.42
Kamioka et al,[30] (2011)	C-RCT (4 clusters)	3-months	34	9.0 [-5.95 to 23.95]	19.75
Pooled effect: I^2 = 10.23%				**-1.95 [-10.09 to 6.18]**	
Exercise and Education vs. Control (long-term)					
Chaleat-Valayer et al,[8] (2016)	RCT	18-months	280	-0.50 [-5.42 to 4.42]	43.76
Glomsrod et al,[25] (2001); Lonn et al,[32] (1999)	RCT	12-months	73	-11.00 [-20.18 to -1.82]	20.44
Soukup et al,[37] (2001); Soukup et al,[36] (1999)	RCT	12-months	69	-6.00 [-15.97 to 3.97]	18.01
Warming et al,[40] (2008) (TTPT)	C-RCT (11 clusters)	12-months	49	-4.60 [-14.64 to 5.44]	17.80
Pooled effect: I^2 = 0%				**-4.37 [-9.16 to 0.43]**	
Education vs. Control (short-term)					
Donaldson et al,[18] (1993)	RCT	3-months	172[c]	-1.54 [-5.97 to 2.89]	24.49
Irvine et al,[29] (2015) (FitBack program)	RCT	4-months	288	-4.20 [-7.04 to -1.36]	37.15
Irvine et al,[29] (2015) (alternative care)	RCT	4-months	294	-0.90 [-4.16 to 2.36]	33.30
Menzel et al,[33] (2006)	RCT	3-months	23	8.50 [-3.72 to 20.72]	5.07
Pooled effect: I^2 = 17.04%				**-1.81 [-4.68 to 1.07]**	
Education vs. Control (long-term)					
Jensen et al,[7] (2006) (SMI)	C-RCT (19 clusters)	24-months	78	2.00 [-8.93 to 12.93]	48.41
Warming et al,[40] (2008) (TT)	C-RCT (11 clusters)	12-months	48	1.40 [-9.88 to 12.68]	51.59
Pooled effect: I^2 = 0%				**1.71 [-6.14 to 9.56]**	
Ergonomics vs. Control (short-term)					
Driessen et al,[20] (2011)	C-RCT (37 clusters)	6-months	552	**1.40 [-3.28 to 6.08]**	100
Ergonomics vs. Control (long-term)					
Driessen et al,[20] (2011)	C-RCT (37 clusters)	12-months	538	**2.00 [-2.74 to 6.74]**	100
Ergonomics and Education vs. Control (short-term)					
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	6-months	192	**1.00 [-6.93 to 8.93]**	100
Ergonomics and Education vs. Control (long-term)					

Table 3. (Continuation)

Source	Study design	Follow-up time point	Number of participants	MD [95% CI][b]	Weight, %
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	12-months	184	0.00 [-8.38 to 8.38]	63.82
Jensen et al,[7] (2006) (TTI)	C-RCT (19 clusters)	24-months	82	0.00 [-11.14 to 11.14]	36.18
Pooled effect: I^2 = 0%				**0.00 [-6.70 to 6.70]**	
	Pregnant Population				
Exercise vs. Control (short-term)					
Eggen et al,[21] (2012)	RCT	8-months	240	-3.00 [-9.36 to 3.36]	36.92
Garshasbi et al,[23] (2005)	RCT	3-months	212	-2.52 [-7.38 to 2.34]	63.08
Pooled effect: I^2 = 0%				**-2.70 [-6.56 to 1.17]**	
	Children				
Exercise and Education vs. Control (short-term)					
Fanucchi et al,[22] (2009)	RCT	6-months	70	**0.00 [-11.68 to 11.68]**	100

Abbreviations: MD, Mean Difference; CI, Confidence Interval; RCT, Randomised Controlled Trial; C-RCT, Cluster-Randomised Controlled Trial; TTPT, Transfer Technique and Physical Activity; TT, Transfer Technique; SMI, Stress Management Intervention; TTI, Transfer Technique Intervention.

[a] Only studies providing results that could be converted to a 0-100 scale are presented.

[b] Value presented on 0-100 scale.

[c] Only baseline data was available.

A negative value of the mean difference estimate represents an effect in favour of the intervention group.

Short-term indicates follow-up assessment of less than 12-months.

Long-term indicates follow-up assessment of 12-months or more.

Table 4. Individual study results and pooled effects for primary outcome of disability[a]

Source	Study design	Follow-up time point	Number of participants	MD [95% CI][b]	Weight, %
		General Population			
Exercise vs. Control (short-term)					
Haufe et al,[27] (2017)	RCT	5-months	189	**-2.36 [-7.11 to 2.39]**	100
Exercise and Education vs. Control (short-term)					
Lonn et al,[32] (1999)	RCT	5-months	81[c]	-9.00 [-17.91 to -0.09]	49.28
Soukup et al,[36] (1999)	RCT	5-months	69	-1.00 [-9.70 to 7.70]	50.72
Pooled effect: I^2 = 0%				**-4.94 [-12.78 to 2.90]**	
Exercise and Education vs. Control (long-term)					
Chaleat-Valayer et al,[8] (2016)	RCT	18-months	280	-4.60 [-8.37 to -0.83]	52.69
Glomsrod et al,[25] (2001); Lonn et al,[32] (1999)	RCT	12-months	73	-15.00 [-25.56 to -4.44]	8.89
Soukup et al,[37] (2001); Soukup et al,[36] (1999)	RCT	12-months	69	-6.00 [-16.85 to 4.85]	8.43
Warming et al,[40] (2008) (TTPT)	C-RCT (11 clusters)	12-months	49	-6.74 [-12.14 to -1.34]	30.00
Pooled effect: I^2 = 3.41%				**-6.28 [-9.51 to -3.06]**	
Education vs. Control (short-term)					
Irvine et al,[29] (2015) (FitBack program)	RCT	4-months	288	-7.10 [-11.98 to -2.22]	25.21
Irvine et al,[29] (2015) (alternative care)	RCT	4-months	294	-4.30 [-9.33 to 0.73]	24.47
Menzel et al,[33] (2006)	RCT	3-months	24	2.00 [-4.72 to 8.72]	17.68
Tuchin et al,[38] (1998)	RCT	6-months	61	-5.60 [-15.11 to 3.91]	10.81
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	6-months	68	2.80 [-6.79 to 12.39]	10.67
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	6-months	69	1.80 [-7.52 to 11.12]	11.15
Pooled effect: I^2 = 0%				**-2.59 [-6.15 to 0.96]**	
Education vs. Control (long-term)					
Warming et al,[40] (2008) (TT)	C-RCT (11 clusters)	12-months	48	0.18 [-6.12 to 6.47]	50.04
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	12-months	63	0.60 [-9.30 to 10.50]	21.44
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	12-months	65	-2.00 [-11.08 to 7.08]	25.52
Pooled effect: I^2 = 0%				**-0.29 [-4.87 to 4.30]**	
Ergonomics and Education vs. Control (short-term)					
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	6-months	192	**2.08 [-1.87 to 6.03]**	100
Ergonomics and Education vs. Control (long-term)					
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	12-months	184	**1.25 [-3.08 to 5.58]**	100

Table 4. (Continuation)

Source	Study design	Follow-up time point	Number of participants	MD [95% CI][b]	Weight, %
		Pregnant Population			
Exercise vs. Control (short-term)					
Eggen et al,[21] (2012)	RCT	8-months	240	**-2.91 [-7.06 to 1.24]**	100

Abbreviations: MD, Mean Difference; CI, Confidence Interval; RCT, Randomised Controlled Trial; C-RCT, Cluster-Randomised Controlled Trial; TTPT, Transfer Technique and Physical Activity; TT, Transfer Technique.
[a] Only studies providing results that could be converted to a 0-100 points scale are presented.
[b] Value presented on 0-100 scale.
[c] Only baseline data was available.
A negative value of the mean difference estimate represents an effect in favour of the intervention group.
Short-term indicates follow-up assessment of less than 12-months.
Long-term indicates follow-up assessment of 12-months or more.

Exercise and Education

Three trials (184 participants) investigated the effectiveness of an exercise and education prevention program on reducing future LBP intensity at short-term follow-up,[30 32 36] and four trials[8 32 36 40] (471 participants) at long-term follow-up. The pooled results of the three trials provided low-quality evidence that an exercise and education program is not effective at short-term follow-up (MD, -1.95; 95% CI, -10.09 to 6.18). The long-term results are based on pooling for the four trials and provided moderate-quality evidence of no long-term effect (MD, -4.37; 95% CI, -9.16 to 0.43) (Table 2 and Table 3).

For prevention of future disability due to LBP, two trials (150 participants) investigated short-term follow-up,[32 36] and four trials[8 32 36 40] (471 participants) long-term follow-up. Pooled results of the two trials provides low-quality evidence of no short-term effect of an exercise and education program on reducing future disability associated with LBP (MD, -4.94; 95% CI, -12.78 to 2.90). For long-term follow-up, four trials were pooled and provided moderate-quality evidence that exercise and education program is effective to reduce future disability associated with LBP (MD, -6.28; 95% CI, -9.51 to -3.06) (Table 2 and Table 4).

Education

The short-term effect of an education program on preventing future LBP intensity was investigated in four trials,[18 29 31 33] while two trials[7 40] reported results on long-term effects. The pooled results of three trials (777 participants)[18 29 33] provided moderate-quality evidence that education programs do not prevent future LBP intensity at short-term follow-up (MD, -1.81; 95% CI, -4.68 to 1.07). One trial (57 participants)[31] was not included in the meta-analysis as it was not possible to convert data to a 0-100 scale. The long-term results are based on pooling of the two trials (126 participants)[7 40] and provide low-quality evidence of no effect (MD, 1.71; 95% CI, -6.14 to 9.56) (Table 2 and Table 3).

For prevention of LBP associated disability, four trials (804 participants)[29 33 38 41] reported short-term data, and two trials (176 participants)[40 41] reported long-term data. The pooled results of the four trials provide moderate-quality evidence of no short-term effect (MD, -2.59; 95% CI, -6.15 to 0.96), while pooling of the two trials provide low-quality evidence of no long-term effect (MD, -0.29; 95% CI, -4.87 to 4.30) (Table 2 and Table 4).

Ergonomics intervention

Three trials[20 24 31] investigated the effectiveness of an ergonomics program on prevention of future LBP intensity at short-term follow-up (619 participants), and a single trial[20] at long-term follow-up (538 participants). It was not possible to pool estimates for the three trials investigating short-term follow-up as we could not convert two trials[24 31] to a 0-100 scale. The results from one trial[20] on short-term (552 participants) (MD, 1.40; 95% CI, -3.28 to 6.08), and long-term (538 participants) (MD, 2.00; 95% CI, -2.74 to 6.74) follow-ups provides low-quality evidence of no effect on preventing future LBP intensity (Table 2 and Table 3).

Ergonomics intervention and Education

The effectiveness of an ergonomics and education program for preventing future LBP intensity (short-term) and LBP associated disability (short- and long-term) was investigated in a single trial.[28] The results from one trial on short-term (192 participants) effect for either prevention of future LBP intensity (MD, 1.00 [95%CI, -6.93 to 8.93]) or disability due to LBP (MD, 2.08 [95%CI, -1.87 to 6.03]), and long-term (184 participants) effect for disability due to LBP (MD, 1.25 [95%CI, -3.08 to 5.58]) provide very low-quality evidence of no preventive effect.[28] The long-term effect on preventing future LBP intensity was investigated in two trials (266 participants)[7 28] and provide low-quality evidence of no effect (MD, 0.00 [95%CI, -6.70 to 6.70]) (Table 2, Table 3 and Table 4).

Effectiveness of interventions for primary outcomes in special populations

Three trials investigated the short-term effect of two different strategies to prevent future LBP intensity and associated disability in pregnant women and children.[21-23] Pooling of two trials (452 participants) provides moderate-quality evidence that an exercise program was not effective for prevention of future LBP intensity (MD, -2.70; 95% CI, -6.56 to 1.17) at short-term follow-up in pregnant women.[21 23] In addition, one trial (240 participants) provides low-quality evidence of no preventive effect on future disability due to LBP (MD, -2.91; 95% CI, -7.06 to 1.24) in pregnant women.[21]

Furthermore, a single trial (70 participants) shows very low-quality evidence that an exercise and education program has no effect on preventing future LBP intensity (MD, 0.00; 95% CI, -11.68 to 11.68) in children at short-term follow-up.[22] Results are presented in Table 2, Table 3 and Table 4.

Effectiveness of interventions for secondary outcomes

Four secondary outcome measures (QoL, workability, pain duration, and duration of sick leave) were investigated in 18 included trials;[8 17 19-22 24-30 32 35-39 41] however, only two outcomes (QoL, and workability) were included in the meta-analysis as we could convert data to a 0-100 scale. Overall, we found the evidence was low- or very low-quality with intervention contrasts suggesting no prevention effect on either QoL or workability at short- and long-term follow-ups. Results for secondary outcomes are presented in online supplementary appendix G and online supplementary appendix I.

Discussion

The key findings of this review were that there is moderate-quality evidence based on three trials (612 participants) (4 intervention contrasts) that exercise alone can reduce future LBP intensity (MD, -4.50; 95% CI, -7.26 to -1.74) at short-term follow-up. We found no studies that investigated the long-term effect of exercise. Furthermore, moderate-quality evidence from four trials (471 participants) indicates that exercise and education programs can reduce future disability associated with LBP (MD, -6.28; 95% CI, -9.51 to -3.06) at long-term follow-up. In addition, although not statistically significant, the evidence for exercise and education suggests that at short-term it may reduce future disability associated with LBP (MD, -4.94; 95% CI, -12.78 to 2.90), and at long-term it may reduce future LBP intensity (MD, -4.37; 95% CI, -9.16 to 0.43). It is uncertain whether education, ergonomics, and ergonomics combined with education or interventions delivered in special populations (ie, pregnant women and children), can reduce future LBP intensity and associated disability due to very low- to low-quality of evidence found. Moreover, it is uncertain if a prevention program can reduce the impact of LBP on QoL and workability due to very low- to low-quality evidence presented in investigated intervention contrasts.

Few previous systematic reviews have investigated prevention strategies for LBP.[6 42-46] Of these, a recently published high-quality systematic review and meta-analysis included 23 reports and found moderate-quality evidence that exercise programs alone or in combination with education reduce the risk of a new episode of LBP.[6] While our review investigated different outcomes (pain-intensity and disability rather than episodes of LBP) and different populations (including some people with current LBP) than Steffens et al,[6] results from our study are

reasonably consistent with findings from Steffens and colleagues,[6] supporting the evidence that exercise alone and in combination with education can also reduce future LBP intensity and associated disability.

Although our review found evidence that both exercise and exercise combined with education program can reduce future LBP intensity and associated disability respectively, the evidence was of moderate-quality which means further high-quality RCTs are needed. In addition, the absolute effect sizes for exercise and exercise combined with education appear small. However, these effects must be considered in the context of LBP prevention. As relative effects and across large populations the preventative benefits may be important. For instance, when we look at the long-term outcome of disability for exercise combined with education we found a 20% relative reduction.

Some of the strengths of this study include the use of a pre-specified protocol registered on PROSPERO; no inclusion restriction on populations, settings, and age; sensitive search strategy using multiple electronic databases with supplementary hand searching, following the PRISMA recommendations; the use of the GRADE system to appraise the overall quality of the evidence; and the use of PEDro scale to assess risk of bias of included trials.

The following limitations should be considered when interpreting our results. Despite our best efforts, authors could not be contacted to gather information for one potentially eligible RCT;[47] some standard deviations were not presented in included publications and had to be estimated from a similar included trial as recommended by *The Cochrane Collaboration;*[16] nine cluster-RCTs (18 intervention contrasts) required adjustment for clustering; only a small number of trials were included for most intervention contrasts; and some outcome measures (eg, pain duration and duration of sick leave) could not be pooled together due to the heterogeneity in measurements. In addition, for some of the included trials, the limited descriptions of the experimental intervention and minimal intervention made it difficult to be certain if the control group met our criteria for minimal intervention control. As an example, the control group in the Tuchin et al[38] study did some exercises, however, these were limited and appeared to be very broad and not specific to spinal pain ("warm-up stretching program for sports"). Furthermore, there was an exercise component in the intervention group, so we felt this study had an appropriate minimal intervention control for the education contrast. Inspection of data from

included trials suggested that some data were likely skewed (mean/SD <2).[48] We, therefore, conducted unplanned sensitivity analyses on the study's primary outcomes of pain intensity and disability using the log-transformation methods recommended by Higgins and colleagues,[49] and have included these as Appendix J and Appendix K, respectively. Between-group differences on the log-transformed scale were then back-transformed producing effects as ratios with the 95% CI (see Appendix J and Appendix K), enabling comparison with the original effects from raw data. The results of these sensitivity analyses were consistent with the original analyses using raw data in terms of effect direction, size and statistical significance, other than the short-term effect on the disability outcome of the intervention contrast comparing education with control, which changed from a small, non-significant, beneficial effect when using original raw data to a small, significant, beneficial effect when using the log-transformed data (see Appendix K table). Most studies included in our review had sample sizes greater than 50 participants, and therefore inferences based on means are less problematic due to the central limit theorem.[49 50]

Conclusion

Currently, there is moderate-quality evidence indicating that an exercise program can reduce future LBP intensity at short-term follow-up and that exercise in combination with education can reduce future disability due to LBP at long-term follow-up. On the other hand, there is very low- to low-quality of evidence that interventions including education alone, ergonomics, and ergonomics combined with education or interventions for specific populations (ie, pregnant women and children), do not seem to reduce future LBP intensity and associated disability. The impact of prevention programs on future QoL and workability is unclear due to the low- to very low-quality of available evidence.

Competing interests

The authors have no competing interest to declare.

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Contributorship

Mr de Campos and Dr Hancock had full access to all the data in this systematic review and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: de Campos, Maher, Fuller, Steffens, Hancock.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: de Campos, Maher, Hancock.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: de Campos, Maher, Fuller, Hancock.

Administrative, technical, or material support: de Campos, Fuller, Steffens, Attwell, Hancock.

Study supervision: de Campos, Maher, Hancock.

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4.9 Published supplementary material

Summary Box

What is already known?

- The available research suggests exercise combined with education reduces the risk of a future episode of low back pain; however, it is unclear if effective prevention strategies exist to reduce future low back pain intensity and associated disability.

What are the new findings?

- We found moderate-quality evidence supporting the effectiveness of exercise as a prevention strategy to reduce future low back pain intensity at short-term follow-up and that exercise combined with education can reduce future disability associated with low back pain at long-term follow up.
- We are uncertain whether prevention strategies can positively impact quality of life or workability owing the low- to very low-quality evidence found.

Appendix A. Database specific search strategies

MEDILINE via Ovid
1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. comparative study.pt.
4. clinical trial.pt.
5. pragmatic clinical trial.pt.
6. randomized.ab.
7. placebo.ab,ti.
8. drug therapy.fs.
9. randomly.ab,ti.
10. trial.ab,ti.
11. groups.ab,ti.
12. or/1-11
13. (animals not (humans and animals)).sh.
14. 12 not 13
15. dorsalgia.ti,ab.
16. backache.ti,ab.
17. (lumbar adj pain).ti,ab.
18. coccyx.ti,ab.
19. coccydynia.ti,ab.
20. sciatica.ti,ab.
21. spondylosis.ti,ab.
22. lumbago.ti,ab.
23. back disorder$.ti,ab.
24. Low Back Pain/
25. Back Pain/
26. sciatic neuropathy/
27. or/15-26
28. prevent$.mp.
29. prophylactic.mp.
30. recur$.mp.
31. relapse.mp.
32. reappearance$.mp.
33. reoccurrence$.mp.
34. return.mp.
35. exp recurrence/
36. exp relapse/
37. primary prevention/
38. secondary prevention/
39. or/28-38
40. 14 AND 27 AND 39

Embase via Ovid

1. randomized controlled trial.mp.
2. controlled clinical trial.mp.
3. comparative study.mp.
4. clinical trial.mp.
5. pragmatic clinical trial.mp.
6. randomized.ab.
7. placebo.ab,ti.
8. drug therapy.fs.
9. randomly.ab,ti.
10. trial.ab,ti.
11. groups.ab,ti.
12. or/1-11
13. (animals not (humans and animals)).sh.
14. 12 not 13
15. dorsalgia.ti,ab.
16. backache.ti,ab.
17. (lumbar adj pain).ti,ab.
18. coccyx.ti,ab.
19. coccydynia.ti,ab.
20. sciatica.ti,ab.
21. spondylosis.ti,ab.
22. lumbago.ti,ab.
23. back disorder$.ti,ab.
24. Low Back Pain/
25. Back Pain/
26. sciatic neuropathy/
27. or/15-26
28. prevent$.mp.
29. prophylactic.mp.
30. recur$.mp.
31. relapse.mp.
32. reappearance$.mp.
33. reoccurrence$.mp.
34. return.mp.
35. exp recurrence/
36. exp relapse/
37. primary prevention/
38. secondary prevention/
39. or/28-38
40. 14 AND 27 AND 39

CINAHL via EBSCO

S1. “back pain”
S2. “back strain”
S3. “low back pain”
S4. “low back syndrome”
S5. “low back dysfunction”
S6. “low back disorder”
S7. “dorsalgia”
S8. “backache”
S9. “radiculopathy”
S10. “lumbago”
S11. “sciatica”
S12. “coccyx”
S13. “coccydynia”
S14. (MH “Low Back Pain”)
S15. (MH “Back Pain”)
S16. (MH “Sciatica”)
S17. (MH “Coccyx”)
S18. (MH “Lumbar Vertebrae”)
S19. (MH “Spondylolisthesis”)
S20. (MH “Spondylolysis”)
S21. (MH “Radiculopathy”)
S22. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21
S23. (MH “Clinical Trials+”)
S24. “randomi?ed controlled trial”
S25. “clinical W3 trial”
S26. “single-blind”
S27. “double-blind”
S28. “triple-blind”
S29. S23 OR S24 OR S25 OR S26 OR S27 OR S28
S30. (MH “Placebo Effect”)
S31. (MH “Placebos”)
S32. “placebo*”
S33. “random*”
S34. S30 OR S31 OR S32 OR S33
S35. (MH “Random Sample+”)
S36. (MH “Comparative Studies”)
S37. (MH “Evaluation Research+”)
S38. (MH “Prospective Studies+”)
S39. S35 OR S36 OR S37 OR S38
S40. “follow-up stud*”
S41. “followup stud*”
S42. “control”
S43. “prospectiv*”
S44. “volunteer*”
S45. S40 OR S41 OR S42 OR S43 OR S44
S46. S29 OR S34 OR S39 OR S45
S47. (MH “Animals”)
S48. S46 not S47
S49. “prevent*”
S50. “prophyla*”
S51. “recur*”
S52. “relaps*”
S53. “reappearance*”
S54. “reoccur*”
S55. “return*”
S56. (MH “Preventive trials”)
S57. (MH “Recurrence”)
S58. S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57
S59. S22 AND S48 AND S58

Physiotherapy Evidence Database (PEDro)
#1. prevent* in <Abstract & Title> field
#2. pain in <Problem> field
#3. “lumbar spine, sacro-iliac joint or pelvis” in <Body Part> field
#4. musculoskeletal in <Subdiscipline> field
#5. clinical trial in <Method> field
#6. Match all search terms (AND) in <When Searching> field

The Cochrane Central Register of Controlled Trials (CENTRAL) via Cochrane Library

#1. low back pain
#2. backache
#3. back strain
#4. back injur*
#5. low back syndrome
#6. low back dysfunction
#7. low back disorder
#8. back pain
#9. lumbar pain
#10. lumbago
#11. sciatica
#12. MeSH descriptor: [Low Back Pain] explode all trees
#13. MeSH descriptor: [Back Pain] explode all trees
#14. MeSH descriptor: [Lumbar Vertebrae] explode all trees
#15. MeSH descriptor: [Sciatica] explode all trees
#16. MeSH descriptor: [Sciatic Nerve] explode all trees
#17. MeSH descriptor: [Radiculopathy] explode all trees
#18. {or #1- #17}
#19. Randomized controlled trial
#20. controlled clinical trial
#21. clinical trial
#22. random*
#23. placebo*
#24. Trial
#25. MeSH descriptor: [Comparative Study] explode all trees
#26. MeSH descriptor: [Placebos] explode all trees
#27. MeSH descriptor: [Random Allocation] explode all trees
#28. MeSH descriptor: [Single-Blind Method] explode all trees
#29. MeSH descriptor: [Double-Blind Method] explode all trees
#30. MeSH descriptor: [Evaluation Studies as Topic] explode all trees
#31. MeSH descriptor: [Controlled Clinical Trials as Topic] explode all trees
#32. MeSH descriptor: [Clinical Trials as Topic] explode all trees
#33. MeSH descriptor: [Follow-Up Studies] explode all trees
#34. {or #19- #33}
#35. animal*
#36. #34 not #35
#37. MeSH descriptor: [Primary Prevention] explode all trees
#38. MeSH descriptor: [Secondary Prevention] explode all trees
#39. MeSH descriptor: [Recurrence] explode all trees
#40. prevent*
#41. prophyla*
#42. recur*
#43. relaps*
#44. reappearance*
#45. reoccur*
#46. return*
#47. {or #37 - #46}
#48. #18 and #36 and #47

Appendix B. Detailed characteristic of RCTs included in the systematic review of prevention strategies to reduce future impact of low back pain

Source	Study design	Country	Participants	Outcome measure	Study Groups	Time and frequency of Interventions	Follow-up period
Barene et al,[17] (2014)	C-RCT	Norway	118 hospital employees (nurses, healthcare assistant, and other professions, mainly bioengineers and social educators); mean (SD) age, 45.8 (9.3) y; female (91%).	LBP Intensity LBP Duration	I1: Soccer training: performed soccer training sessions supervised by an instructor. I2: Zumba training: The Zumba sessions consisted of continuous dance-movements with varying intensity level throughout the sessions. C: No intervention.	Two-three 1-hour sessions per week over 40 weeks for both intervention groups.	10 months
Chaleat-Valayer et al,[8] (2016)	RCT	France	342 healthcare workers from ten hospitals; mean (SD) age, 47.2 (8.5) y; female (77%).	LBP Intensity (VAS) Disability (QBPDS)	I: Three steps: a single education session; Exercise training sessions in the work place delivered by a Physio (8-10 participants); home-based self-managed exercise program (booklet). C: No intervention.	Single 2-hours education session and 5 weekly 90-min group exercise training sessions.	18 months
Donaldson et al,[18] (1993)	RCT	Canada	172 employees from hospital in the regional health care aging population facilities in Drumheller Region; mean (SD) age NR; sex NR.	LBP Intensity (MPQ)	I: Education course (classes) on how to use information from the "Back to Balance" booklet to prevent back injury, delivered by two experienced instructors. C: No intervention.	9 classes per instructor. The classroom presentation lasted approximately one and a half hours.	12 months
Donchin et al,[19] (1990)	RCT	Israel	142 hospital employees from the various clinical, administrative and technical professions; mean (SD) age, 46.0 (NR) y; female (66%).	LBP (Painful months)	I1: Calisthenics training: Exercises aiming at strengthening the abdominal muscles, expanding spinal forward flexion, and rectifying the general posture. They were supervised by an physical education instructor. I2: Back school training: Instruction in proper body mechanics as well in exercises for the back and abdominal muscles. Sessions led by a physiotherapist. C: No intervention	I1: 45-min sessions, bi-weekly, for 3 months, in groups of 10 to 12 participants. I2: 4x 90-min sessions during a 2-week period in groups of 10 to 12 participants plus a fifth session after 2 months.	12 months
Driessen et al,[20] (2011)	C-RCT	Netherlands	3047 workers from 4 Dutch companies; mean (SD) age, 42.0 (10.95) y; female (41%).	LBP Intensity (VAS) LBP Duration	I: Ergonomic program: implementation of ergonomic program (evaluation and prioritise the risk factors and ergonomic measures to prevent LBP). C: Minimal intervention: short educational movies about prevention of LBP.	I: Use the ergonomic program while on duty (first 3 months to implement the ergonomic measures). C: 3 short (45s) educational movies on back pain prevention.	12 months

Appendix B. (Continuation)

Source	Study design	Country	Participants	Outcome measure	Study Groups	Time and frequency of Interventions	Follow-up period
Eggen et al,[21] (2012)	RCT	Norway	257 health pregnant women before gestation week 20; mean (SD) age, 30.3 (4.8) y; female (100%).	LBP Intensity (VAS) Disability (RMDQ)	I: Exercises, including ergonomic advice, in groups and advise to do home exercises. Goal of the exercises was to achieve efficient motor control and the ability to dynamically control and stabilize the lumbo-pelvic region during daily activities. Sessions supervised by a physiotherapist. C: No intervention.	1x/week 1-hour group exercise session for 16 to 20 weeks.	4 months
Fanucchi et al,[22] (2009)	RCT	South Africa	72 children in Grade 6 and Grade 7 primary school; mean (SD) age, 12.3 (0.7) y; female (46%).	LBP Intensity (VAS)	I: Education session on the importance of exercise for LBP. Exercise classes at school and weekly home exercise program. C: No intervention.	8x classes 40-45min each over 8 weeks	6 months
Garshasbi et al,[23] (2005)	RCT	Iran	212 pregnant women (17-22nd weeks of gestation); mean (SD) age, 26.4 (4.6) y; female (100%).	LBP Intensity (KQ)	I: Exercise training aiming to strength the abdominal-pelvic region, including 5 min of slow walking, 5 min of extension movements, and 10 min of general warming up, 15 min of anaerobic exercise, 20 min of specific exercise and 5 min to cool down. C: No intervention.	3x per week for 60min each for 12 weeks.	3 months
Gatty et al,[24] (2004)	RCT	USA	16 clerical and office workers; mean (SD) age, NR; female (100%).	LBP Intensity (VAS) LBP Duration	I: Implementation of individualized work injury prevention program (WIPPs). The program combined approaches which incorporate various strategies or components, such as education, workstation redesign, and task modification. C: No intervention.	1-hour session over 4 weeks period (4 sessions). Intervention continuous during study period.	9 months
Glomsrod et al,[25] (2001)	RCT	Norway	81 community and participants referred from primary care clinicians; mean (SD) age, 39.4 (6.8) y; female (54%).	LBP Intensity (VAS) Disability (VAS)	I: Exercise and education: active back school-didactic session; practical session included bending the knee and hip joints, while keeping the lumbar segments near mid-position and using short lever arms during functional exercises and obstacle course simulations; strength training and some stretching exercises. C: No intervention.	2 Sessions per week for 7 weeks; 1 session per week for 6 weeks; each session 60 min.	36 months
Gundewall et al,[26] (1993)	RCT	Sweden	69 nurses and nurse's aides at a geriatric hospital; mean (SD) age, 37.5 (10.5) y; female (98%).	LBP Duration	I: Back muscle exercises to increase endurance, isometric strength and functional coordination. C: No intervention.	6x monthly sessions of 20 min each.	13 months

Appendix B. (Continuation)

Source	Study design	Country	Participants	Outcome measure	Study Groups	Time and frequency of Interventions	Follow-up period
Haufe et al,[27] (2017)	RCT	Germany	226 workers from 3 medium-sized companies; mean (SD) age, 42.7 (10.2) y; female (40%).	LBP Intensity (VAS) Disability (ODI)	I: Monthly individual counselling/supervision sessions with a physiotherapist. Also, general training for the trunk and shoulder muscles. C: Participants were asked to continue their current lifestyle.	I: 20-min non-supervised general exercise session 3x per week. 5x once monthly counselling session.	5 months
Ijzelenberg et al,[28] (2007)	C-RCT	Netherlands	489 workers performing physically demanding jobs in 9 large companies; mean (SD) age, 41.3 (9.7) y; female (3%).	LBP Intensity (NRS) Disability (RMDQ)	I: Education, training, and ergonomic adjustments: individually tailored education and training, immediate treatment of acute LBP, and advice on ergonomic adjustment of the workplace. C: Usual care - Dutch guidelines for the health care of patients with LBP.	3x group training sessions. Unclear frequency.	12 months
Irvine et al,[29] (2015)	RCT	USA	597 workers from 4 companies (trucking, manufactoring, technology, and a corporate headquarters), also general work population; mean (SD) age, NR; female (60%).	LBP Intensity LBP Duration LBP Functionality	I1: FitBack website program: Online education and behavioral strategies encouraging users to adopt appropriate strategies for prevention of LBP. I2: Alternative care: received 8 email with links to 6 websites with general information about LBP. C: No intervention	I: Weekly emails and unlimited access to online material during study period.	4 months
Jensen et al,[7] (2006)	C-RCT	Denmark	210 home care workers, nurses, and nurse's aides from 3 separate eldercare wards; mean (SD) age, 44.3 (8.9) y; female (100%).	LBP Intensity (NRS)	I1: Transfer Technique Intervention (TTI): Based on the Stockholm training concept, which aims to reduce the biomechanical load on the back, minimize work in asymmetric postures, and prevent sudden unexpected loads. Practical classroom education and instruction at the work site I2: Stress Management Intervention (SMI): Developed to address the work stress in health care with particular attention to prevention of burnout and development of strategies for stress management. C: No intervention	I1: 2x 4-hours classes and 30-hours site education delivered over 6 months period. I2: Group sessions every 2 weeks for 2-hours, over 20 weeks period.	24 months

Appendix B. (Continuation)

Source	Study design	Country	Participants	Outcome measure	Study Groups	Time and frequency of Interventions	Follow-up period
Kamioka et al,[30] (2011)	C-RCT	Japan	88 female caregivers from 4 nursing homes in Tokyo; mean (SD) age, 38.15 (13.75) y; female (100%).	LBP Intensity (VAS)	I: A lecture and stretching exercise. The lecture contained information on risk factors, biomechanics of care-movement, treatment, and recommended exercise. Daily stretching exercises aiming to prevent LBP based on William and McKenzie exercises. C: No intervention.	Single lecture of 30min; 1-hour instruction on stretching exercises. Daily stretching for about 6min.	3 months
Ketola et al,[31] (2002)	RCT	Finland	109 office workers; mean (range) age, 48.0 (29 to 59) y; female (60%).	LBP Discomfort	I1: Intensive ergonomics: Ergonomic checklist emphasizing the layout and environmental conditions of the workroom, adjustments of the workstation, and breaks during work under guidance of a physiotherapist. I2: Ergonomic education: Training session in ergonomics in groups of 2 to 6 persons plus advice pauses during work. C: No intervention	I1: Around 2-hours of implementation. I2: a single 1-hour session.	10 months
Lonn et al,[32] (1999)	RCT	Norway	81 participants recruited through media advertisement and referred from primary care clinicians; mean (SD) age, 39.4 (6.8) y; female (54%).	LBP Intensity (VAS) Disability (VAS)	I: Exercise and education: active back school-didactic session; practical session included bending the knee and hip joints, while keeping the lumbar segments near mid-position and using short lever arms during functional exercises and obstacle course simulations; strength training and some stretching exercises. C: No intervention.	2 Sessions per week for 7 weeks; 1 session per week for 6 weeks; each session 60 min.	12 months
Menzel et al,[33] (2006)	RCT	USA	31 registered nurses and nursing aides; mean (SD) age, 41.94 (9.0) y; female (97%).	LBP Intensity (VAS) Disability (ODI)	I: Psychoeducational sessions for stress and pain management. C: No intervention.	6x 1.5-hours group-discussion session.	3 months
Pedersen et al,[34] (2013)	C-RCT	Denmark	537 industrial laboratory technicians; mean (SD) age, 42.0 (10.5) y; female (85%).	LBP Intensity (VAS)	I: Exercise training sessions for the shoulder, neck and arm with dumbbells, supervised by an experienced instructor. C: No intervention.	3x weekly for 20min each over 5 months.	5 months

Appendix B. (Continuation)

Source	Study design	Country	Participants	Outcome measure	Study Groups	Time and frequency of Interventions	Follow-up period
Pedersen et al,[35] (2009)	C-RCT	Denmark	549 office workers recruited from a Danish public administration authority, from 12 offices in geographically different locations in the eastern part of Denmark; mean (SD) age, 45.1 (9.4) y; female (64%).	LBP Duration	I1: Specific Resistance Training (SRT): Exercise training sessions for the shoulder, neck and arm with dumbbells, supervised by an experienced instructor. I2: All-round Physical Exercise (APE): consisted of various types of physical activities at the worksite plus 8-minute CD-based exercise program for aerobic fitness and general strength. C: Reference group (REF): Encouraged to form groups with the purpose of improving their knowledge on health and working conditions.	I1: 3x weekly for 20min each over 12 months. I2: 1x introductory session at worksite; 1-hour per week	12 months
Soukup et al,[37] (2001)	RCT	Norway	77 community and primary care participants; mean (SD) age, 37.7 (8.0) y; female (53%).	LBP Intensity (VAS) Disability (VAS)	I: Mensendieck exercises and biomechanical/ ergonomic, back anatomy, pain mechanisms, and working posture education. C: No intervention.	20 Sessions for 60 min over a period of 13 weeks.	36 months
Soukup et al,[36] (1999)	RCT	Norway	77 community and primary care participants; mean (SD) age, 37.7 (8.0) y; female (53%).	LBP Intensity (VAS) Disability (VAS)	I: Mensendieck exercises and biomechanical/ ergonomic, back anatomy, pain mechanisms, and working posture education. C: No intervention.	20 Sessions for 60 min over a period of 13 weeks.	12 months
Tuchin et al,[38] (1998)	RCT	Australia	61 employees of a large mailing house; mean (SD) age NR; sex NR.	Disability (ODI)	I: A comprehensive lecture detailing spinal structures, an explanation about back pain, correct lifting techniques, treatments for back problems, effective exercises, ergonomics, and specific relationship of back pain to occupation and tasks involved. C: A series of daily exercises. The exercises consisted of a routine series of stretching procedures used as “warm up” program for sports.	I: Single 120min lecture session. C: Daily over 6 months period.	6 months
van Poppel * et al,[39] (1998)	C-RCT	Netherlands	312 airline company workers whose jobs included manual material handling; mean (SD) age, 35.1 (7.8) y; sex NR.	LBP Duration	I1: Lumbar Support + Education: Back belts with adjustable elastic side pulls with Velcro fasteners and flexible stays + Education on lifting. I2: Lumbar Support only: Back belts with adjustable elastic side pulls with Velcro fasteners and flexible stays I3: Education only: education on lifting C: No intervention.	Lumbar support: Wear for 6 mo (work hours) Education (lifting instructions): 1x 2-hrs; 2x 1.5-hs; 3x (12 wks) C: No intervention	6 months

Appendix B. (Continuation)

Source	Study design	Country	Participants	Outcome measure	Study Groups	Time and frequency of Interventions	Follow-up period
Warming et al,[40] (2008)	C-RCT	Denmark	181 hospital nurses; mean (SD) age, 35.2 (10.5) y; female (90%).	LBP Intensity (NQ) Disability (RS)	I1: Education: patient transfer technique based on the law of physics and the natural movement pattern of moving 1 body part at a time. I2: Exercise and education: physical fitness training - aerobic fitness and strength training and transfer technique (TTPT). C: No intervention.	I1: 2x 6 weeks sessions. I2: 2x weekly for 1-hour over 8 weeks period.	12 months
Yassi et al,[41] (2001)	C-RCT	Canada	346 staff performing patient lifts and transfers (nurses and unit assistants); mean (SD) age NR; sex NR.	LBP Discomfort Disability (ODI)	I1: Arm B - Safe Lifting program. Intensive training in back care, patient assessment, and handling techniques used to improve patient handling techniques using manual equipment. I2: Arm C - No Strenuous Lifting program. Intensive training in back care, patient assessment, and handling techniques aimed to eliminate manual patient handling through use of additional mechanical and other assistive equipment. C: Arm A – Usual practice.	I1 and I2: 3-hours single session	12 months

Abbreviations: RCT, Randomised Controlled Trial; C-RCT, Cluster Randomised Controlled Trial; LBP, Low Back Pain; SD, Standard Deviation; VAS, Visual Analog Scale; QBPDS, Quebec Back Pain Disability Scale; MPQ, McGill Pain Questionnaire; RMDQ, Roland Morris Disability Questionnaire; KQ, KEBK Questionnaire; ODI, Oswestry Disability Index; NRS, Numeric Rating Scale; NQ, Nordic Questionnaire; RS, Rating Scale; I, Intervention group; C, Control group; NR, Not Reported.

* van Poppel et al[39] study was analysed as a 2x2 factorial design (ie, 4 groups) with the following intervention contrasts: Lumbar Support versus No Lumbar Support, and Education versus No Education.

Appendix C. PEDro scores of included Randomised Controlled Trials

Source	Eligibility criteria	Random allocation	Concealed allocation	Baseline comparability	Blind subjects	Blind therapists	Blind assessors	Adequate follow-up	Intention-to-treat analysis	Between-group comparisons	Point estimates and variability	Total score
Haufe[27] (2017)	Yes	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	6
Chaleat-Valayer[8] (2016)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Irvine[29] (2015)	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5
Barene[17] (2014)	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	5
Pedersen[34] (2013)	Yes	Yes	No	Yes	No	No	No	No	Yes	Yes	Yes	5
Eggen[21] (2012)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7
Kamioka[30] (2011)	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	5
Driessen[20] (2011)	Yes	Yes	No	Yes	No	No	No	No	Yes	Yes	Yes	5
Pedersen[35] (2009)	Yes	Yes	No	No	No	No	Yes	No	Yes	Yes	Yes	5
Fanucchi[22] (2009)	Yes	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	6
Warming[40] (2008)	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	6
Ijzelenberg[28] (2007)	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	6
Menzel[33] (2006)	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4
Jensen[7] (2006)	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4
Garshasbi[23] (2005)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7
Gatty[24] (2004)	No	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4
Ketola[31] (2002)	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	6
Yassi[41] (2001)	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5
Soukup[37] (2001)	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Glomsrod[25] (2001)	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Soukup[36] (1999)	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5
Lonn[32] (1999)	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5
van Poppel[39] (1998)	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7

Appendix C. (Continuation)

Source	Eligibility criteria	Random allocation	Concealed allocation	Baseline comparability	Blind subjects	Blind therapists	Blind assessors	Adequate follow-up	Intention-to-treat analysis	Between-group comparisons	Point estimates and variability	Total score
Tuchin[38] (1998)	No	Yes	No	No	No	No	No	No	No	Yes	Yes	3
Gundewall[26] (1993)	No	Yes	No	No	No	No	No	Yes	No	Yes	Yes	4
Donaldson[18] (1993)	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4
Donchin[19] (1990)	Yes	Yes	No	Yes	No	No	No	No	Yes	Yes	No	4

Abbreviation: PEDro, Physiotherapy Evidence Database.

Appendix D. Results from all included studies – Primary Outcomes

Source	Study design	Follow-up time point	Outcome measure (range)	Intervention[a]			Contrast[a]			MD [95% CI][b]
				Total	Mean	SD[c]	Total	Mean	SD[c]	
			General Populations							
Exercise vs. Control (short-term)										
Pain Intensity										
Haufe et al,[27] (2017)	RCT	5-months	VAS (0-10)	92	1.88	2.24	97	2.54	2.5	-6.6 [-13.38 to 0.18]
Barene et al,[17] (2014) (soccer)	C-RCT (6 clusters)	3-months	Nordic Q. - VAS (0-10)	28	NR	NR	15	NR	NR	-1.0 [-10.70 to 8.70]
Barene et al,[17] (2014) (zumba)	C-RCT (6 clusters)	3-months	Nordic Q. - VAS (0-10)	30	NR	NR	16	NR	NR	2.0 [-6.75 to 10.75]
Pedersen et al,[34] (2013)	C-RCT (57 cluster)	5-months	Nordic Q. - VAS (0-9)	157	1.13	1.13[d]	177	1.61	1.06[d]	-5.33 [-7.94 to -2.72]
Disability										
Haufe et al,[27] (2017)	RCT	5-months	ODI (0-50)	92	7.69	8.08	97	8.87	8.57	-2.36 [-7.11 to 2.39]
Exercise and Education vs. Control (short-term)										
Pain Intensity										
Lonn et al,[32] (1999)	RCT	5-months	VAS (0-10)	43[e]	1.8	1.46[f]	38[e]	2.6	1.68[f]	-8.0 [-14.84 to -1.16]
Soukup et al,[36] (1999)	RCT	5-months	VAS (0-100)	34	23	16	35	24	17	-1.0 [-8.79 to 6.79]
Kamioka et al,[30] (2011)	C-RCT (4 clusters)	3-months	VAS (0-10)	22	5.0	1.9	12	4.1	2.5	9.0 [-5.95 to 23.95]
Disability										
Lonn et al,[32] (1999)	RCT	5-months	VAS LBP function (0-10)	43[e]	7	1.95[f]	38[e]	6.1	2.14[f]	-9.0 [-17.91 to -0.09]
Soukup et al,[36] (1999)	RCT	5-months	VAS LBP function (0-100)	34	60	15.95[f]	35	61	20.58[f]	-1.0 [-9.70 to 7.70]
Exercise and Education vs. Control (long-term)										
Pain Intensity										
Chaleat-Valayer et al,[8] (2016)	RCT	18-months	VAS (0-100)	139	36.2	21	141	36.7	21	-0.50 [-5.42 to 4.42]
Glomsrod et al,[25] (2001); Lonn et al,[32] (1999)	RCT	12-months	VAS (0-10)	38	2.2	1.9	35	3.3	2.1	-11.00 [-20.18 to -1.82]
Soukup et al,[37] (2001); Soukup et al,[36] (1999)	RCT	12-months	VAS (0-100)	34	26	19	35	32	23	-6.00 [-15.97 to 3.97]
Warming et al,[40] (2008) (TTPT)	C-RCT (11 clusters)	12-months	Nordic Q. - VAS (0-10)	28	1.17	1.49	21	1.63	2.1	-4.60 [-14.64 to 5.44]
Disability										
Chaleat-Valayer et al,[8] (2016)	RCT	18-months	QBPDS (0-100)	139	19.8	15.8	141	24.4	16.4	-4.60 [-8.37 to -0.83]
Glomsrod et al,[25] (2001); Lonn et al,[32] (1999)	RCT	12-months	VAS LBP function (0-10)	38	6.7	2.3	35	5.2	2.3	-15.00 [-25.56 to -4.44]
Soukup et al,[37] (2001); Soukup et al,[36] (1999)	RCT	12-months	VAS LBP function (0-100)	34	58	23	35	52	23	-6.00 [-16.85 to 4.85]
Warming et al,[40] (2008) (TTPT)	C-RCT (11 clusters)	12-months	Disability Quest. (0-38)	28	3.29	2.79	21	5.85	4.52	-6.74 [-12.14 to -1.34]
Education vs. Control (short-term)										
Pain Intensity										
Donaldson et al,[18] (1993)	RCT	3-months	McGill Pain Quest. (0-78)	86[e]	10.7	11.2	86[e]	11.9	12.2	-1.54 [-5.97 to 2.89]
Irvine et al,[29] (2015) (FitBack program)	RCT	4-months	VAS (0-10)	190	0.56	1	98	0.98	1.43	-4.20 [-7.04 to -1.36]
Irvine et al,[29] (2015) (alternative care)	RCT	4-months	VAS (0-10)	196	0.89	1.3	98	0.98	1.43	-0.90 [-4.16 to 2.36]
Ketola et al,[31] (2002) (ergonomics education)	RCT	10-months	Pain score (1-5)	31	2.7	1.11[d]	26	2.6	1.01[d]	0.10 [-0.45 to 0.65][g]
Menzel et al,[33] (2006)	RCT	3-months	VAS (0-100)	12	25.9	14	11	17.4	15.9	8.50 [-3.72 to 20.72]

Appendix D. (Continuation)

Source	Study design	Follow-up time point	Outcome measure (range)	Intervention[a]			Contrast[a]			MD [95% CI][b]
				Total	Mean	SD[c]	Total	Mean	SD[c]	
Disability										
Irvine et al,[29] (2015) (FitBack program)	RCT	4-months	VAS (1-10)	190	3.03	1.88	98	3.74	2.22	-7.10 [-11.98 to -2.22]
Irvine et al,[29] (2015) (alternative care)	RCT	4-months	VAS (1-10)	196	3.31	2	98	3.74	2.22	-4.30 [-9.33 to 0.73]
Menzel et al,[33] (2006)	RCT	3-months	ODI (0-50)	13	15.1	3.8	11	14.1	4.6	2.00 [-4.72 to 8.72]
Tuchin et al,[38] (1998)	RCT	6-months	ODI (0-50)	34	7.1	9.5	27	9.9	9.3	-5.60 [-15.11 to 3.91]
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	6-months	ODI (0-50)	46	7.2	9.5	22	5.8	9.3	2.80 [-6.79 to 12.39]
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	6-months	ODI (0-50)	48	6.7	9	21	5.8	9.3	1.80 [-7.52 to 11.12]
Education vs. Control (long-term)										
Pain Intensity										
Jensen et al,[7] (2006) (SMI)	C-RCT (19 clusters)	24-months	VAS (0-10)	35	2	2.1	43	1.8	2.7	2.00 [-8.93 to 12.93]
Warming et al,[40] (2008) (TT)	C-RCT (11 clusters)	12-months	Nordic Q. VAS (0-10)	27	1.77	1.88	21	1.63	2.1	1.40 [-9.88 to 12.68]
Disability										
Warming et al,[40] (2008) (TT)	C-RCT (11 clusters)	12-months	Disability Quest. (0-38)	27	5.92	3.93	21	5.85	4.52	0.18 [-6.12 to 6.47]
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	12-months	ODI (0-50)	43	6.7	8.7	20	6.4	10.6	0.60 [-9.30 to 10.50]
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	12-months	ODI (0-50)	45	5.4	7.6	20	6.4	10.6	-2.00 [-11.08 to 7.08]
Ergonomic vs. Control (short-term)										
Pain Intensity										
Gatty et al,[24] (2004)	RCT	4-months	Pain score (1-4)	6	2.3	0.82	7	1.9	1.21	0.40 [-0.74 to 1.54][g]
Ketola et al,[31] (2002) (intensive ergonomics)	RCT	10-months	Pain score (1-5)	28	2.5	1.05[d]	26	2.6	1.01[d]	-0.10 [-0.65 to 0.45][g]
Driessen et al,[20] (2011)	C-RCT (37 clusters)	6-months	VAS (0-10)	256	1.62	2.8	296	1.48	2.8	1.40 [-3.28 to 6.08]
Ergonomic vs. Control (long-term)										
Pain Intensity										
Driessen et al,[20] (2011)	C-RCT (37 clusters)	12-months	VAS (0-10)	252	1.63	2.8	286	1.43	2.8	2.00 [-2.74 to 6.74]
Ergonomic and Education vs. Control (short-term)										
Pain Intensity										
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	6-months	VAS (0-10)	101	1.9	2.8	91	1.8	2.8	1.00 [-6.93 to 8.93]
Disability										
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	6-months	RMDQ (0-24)	101	1.7	3.7	91	1.2	2.9	2.08 [-1.87 to 6.03]
Ergonomic and Education vs. Control (long-term)										
Pain Intensity										
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	12-months	VAS (0-10)	95	1.9	2.9	89	1.9	2.9	0.00 [-8.38 to 8.38]
Jensen et al,[7] (2006) (TTI)	C-RCT (19 clusters)	24-months	VAS (0-10)	38	1.8	2.4	44	1.8	2.7	0.00 [-11.14 to 11.14]
Disability										
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	12-months	RMDQ (0-24)	95	1.7	4	89	1.4	3.1	1.25 [-3.08 to 5.58]

Appendix D. (Continuation)

Source	Study design	Follow-up time point	Outcome measure (range)	Intervention[a]			Contrast[a]			MD [95% CI][b]
				Total	Mean	SD[c]	Total	Mean	SD[c]	
			Pregnant Population							
Exercise vs. Control (short-term)										
Pain Intensity										
Eggen et al,[21] (2012)	RCT	8-months	VAS (0-10)	116	1.9	2.47[f]	124	2.2	2.55[f]	-3.00 [-9.36 to 3.36]
Garshasbi et al,[23] (2005)	RCT	3-months	VAS (0-100)	107	30.48	15.46	105	33	20.39	-2.52 [-7.38 to 2.34]
Disability										
Eggen et al,[21] (2012)	RCT	8-months	RMDQ (0-24)	116	2.4	3.57[f]	124	3.1	4.25[f]	-2.91 [-7.06 to 1.24]
			Children Population							
Exercise and Education vs. Control (short-term)										
Pain Intensity										
Fanucchi et al,[22] (2009)	RCT	6-months	VAS (0-10)	38	1.5	2.7	32	1.5	2.2	0.00 [-11.68 to 11.68]

Abbreviations: SD, Standard Deviation; MD, Mean Difference; CI, Confidence Interval; RCT, Randomised Controlled Trial; C-RCT, Cluster-Randomised Controlled Trial; NR, Not Reported; RMDQ, Rolland Morris Disability Questionnaire; VAS, Visual Analogue Scale; Nordic Q., Nordic Musculoskeletal Questionnaire; ODI, Oswestry Disability Index; LBP, Low Back Pain; QBPDS, Quebec Back Pain Disability Scale.

[a] Values presented in the original scale as measured.

[b] Value presented on 0-100 scale unless otherwise indicated.

[c] Value presented as standard deviation unless otherwise indicated.

[d] SD obtained from standard error following Cochrane Handbook recommendations.

[e] Only baseline data was available.

[f] SD obtained from 95% Confidence Interval following Cochrane Handbook recommendations.

[g] Value presented on study original scale.

A negative value of the mean difference estimate represents an effect in favour of the intervention group.

Short-term indicates follow-up assessment of less than 12-months.

Long-term indicates follow-up assessment of 12-months or more.

Appendix E. Results from all included studies – Secondary Outcomes

Source	Study design	Follow-up time point	Outcome measure (range)	Intervention[a]			Contrast[a]			MD [95% CI][b]
				Total	Mean	SD	Total	Mean	SD	
			General Populations							
Exercise vs. Control (short-term)										
Quality of Life										
Haufe et al,[27] (2017)	RCT	5-months	SF-36 Physical (0-100)	92	51.7	7.4	97	50.7	7.7	-1.00 [-3.15 to 1.15]
Haufe et al,[27] (2017)	RCT	5-months	SF-36 Mental (0-100)	92	49.8	8.3	97	49.2	9.3	-0.60 [-3.12 to 1.91]
Workability										
Haufe et al,[27] (2017)	RCT	5-months	WAI (7-49)	92	40.5	5.1	97	39.6	5.1	-1.84 [-4.81 to 1.13]
Barene et al,[17] (2014) (soccer)	C-RCT (6 Clusters)	3-months	WAI (0-10)	28	NR	NR	15	NR	NR	-1.00 [-7.79 to 5.79]
Barene et al,[17] (2014) (zumba)	C-RCT (6 Clusters)	3-months	WAI (0-10)	30	NR	NR	16	NR	NR	-5.00 [-11.52 to 1.52]
Pain Duration (days)										
Barene et al,[17] (2014) (soccer)	C-RCT (6 Clusters)	3-months	Days past 3mo (0-90)	28	NR	NR	15	NR	NR	-5.80 [-15.31 to 3.71][f]
Barene et al,[17] (2014) (zumba)	C-RCT (6 Clusters)	3-months	Days past 3mo (0-90)	30	NR	NR	16	NR	NR	-3.00 [-11.75 to 5.75][f]
Exercise vs. Control (long-term)										
Duration of sick leave (days)										
Gundewall et al,[26] (1993)	RCT	13-months	Days past 13mo (0-395)	28	1	0.189	32	4.84	9.26	-3.84 [-7.27 to -0.41][f]
Pain Duration (days)										
Donchin et al,[19] (1990) (calisthenics program)	RCT	12-months	Painful months (0-12)	46[c]	4.5	14	25[c]	7.4	14	-2.90 [-9.72 to 3.92][f]
Donchin et al,[19] (1990) (back school program)	RCT	12-months	Painful months (0-12)	46[c]	7.3	14	25[c]	7.4	14	-0.10[-6.92 to 6.72][f]
Gundewall et al,[26] (1993)	RCT	13-months	Days past 13mo (0-395)	28	53.9	99	32	94.3	109.9	-40.40 [-93.64 to 12.84][f]
Pedersen et al,[35] (2009) (SRT)	C-RCT (9 Clusters)	12-months	Days past 3mo (0-90)	47	8.41	10.55[d]	23	11.12	8.67[d]	-2.71 [-7.69 to 2.27][f]
Pedersen et al,[35] (2009) (APE)	C-RCT (9 Clusters)	12-months	Days past 3mo (0-90)	47	9.23	10.55[d]	23	11.12	8.67[d]	-1.89 [-6.87 to 3.09][f]
Exercise and Education vs. Control (short-term)										
Quality of Life										
Lonn et al,[32] (1999)	RCT	5-months	COOP-WONCA (7-35)	43[c]	10.3	2.6	38[c]	11.2	3.6	-2.58 [-6.45 to 1.29]
Kamioka et al,[30] (2011)	C-RCT (4 Clusters)	3-months	SF-8 Physical (0-100)	22	32.5	11.7	12	32.3	9.8	-0.20 [-8.00 to 7.60]
Kamioka et al,[30] (2011)	C-RCT (4 Clusters)	3-months	SF-8 Mental (0-100)	22	37.9	8.6	12	41.1	9	-3.20 [-9.35 to 2.95]
Exercise and Education vs. Control (long-term)										
Quality of Life										
Chaleat-Valayer et al,[8] (2016)	RCT	18-months	SF-12 Physical (0-100)	139	47.4	7.7	141	45.1	8.3	-2.30 [-4.18 to -0.42]
Chaleat-Valayer et al,[8] (2016)	RCT	18-months	SF-12 Mental (0-100)	139	45.8	11.7	141	44	11	-1.80 [-4.46 to 0.86]
Glomsrod et al,[25] (2001); Lonn et al,[32] (1999)	RCT	12-months	COOP-WONCA (7-35)	38	10.8	3.6	35	12.5	4.6	-4.86 [-10.25 to 0.53]
Soukup et al,[37] (2001)	RCT	12-months	COOP-WONCA (7-35)	39[c]	14.5	5.6	38[c]	15.3	5.6	-2.29 [-9.44 to 4.86]
Duration of sick leave (days)										
Glomsrod et al,[25] (2001)	RCT	36-months	Days past 12mo (0-365)	31	14.4	12.7	35	63.9	76.3	-49.50 [-76.71 to -22.29][f]

Appendix E. (Continuation)

Source	Study design	Follow-up time point	Outcome measure (range)	Intervention[a]			Contrast[a]			MD [95% CI][b]
				Total	Mean	SD	Total	Mean	SD	
Lonn et al,[32] (1999)	RCT	12-months	Days past 12mo (0-365)	38	10.4	9.3	35	37.8	28	-27.40 [-36.82 to -17.98][f]
Soukup et al,[37] (2001)	RCT	36-months	Days past 12mo (0-365)	31	52.4	97.9	35	63.9	76.3	-11.50 [-53.60 to 30.60][f]
Soukup et al,[36] (1999)	RCT	12-months	Days past 12mo (0-365)	34	29.9	55.2	35	37.8	28	-7.90 [-28.46 to 12.66][f]
Education vs. Control (short-term)										
Quality of Life										
Irvine et al,[29] (2015) (FitBack program)	RCT	4-months	Dartmouth CO-OP (9-45)	190	18.84	5.39	98	20.65	5.64	-4.02 [-6.98 to -1.05]
Irvine et al,[29] (2015) (alternative care)	RCT	4-months	Dartmouth CO-OP (9-45)	196	19.42	5.26	98	20.65	5.64	-2.73 [-5.63 to 0.17]
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	6-months	SF-36 Physical (0-100)	46	50.7	8.3	22	51.5	8.3	-0.80 [-5.02 to 3.42]
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	6-months	SF-36 Physical (0-100)	48	51.5	8.1	21	51.5	8.3	0.00 [-4.18 to 4.18]
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	6-months	SF-36 Mental (0-100)	46	45.4	9.4	22	49.2	7.5	-3.80 [-8.29 to 0.69]
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	6-months	SF-36 Mental (0-100)	48	46.8	9.3	21	49.2	7.5	-2.40 [-6.91 to 2.11]
Duration of sick leave (days)										
Tuchin et al,[38] (1998)	RCT	6-months	Days past month (0-30)	34	2.69	4.2	27	3.8	5.6	-1.11 [-3.57 to 1.35][f]
van Poppel et al,[39] (1998)	C-RCT (36 Clusters)	6-months	Days past month (0-30)	106	0.5	2	104	0.3	2	0.20 [-0.34 to 0.74][f]
Workability										
Irvine et al,[29] (2015) (FitBack program)	RCT	4-months	WLQ (NR)	190	4.26	0.72	98	4.14	0.74	-0.12 [-0.30 to 0.06][f]
Irvine et al,[29] (2015) (alternative care)	RCT	4-months	WLQ (NR)	196	4.23	0.75	98	4.14	0.74	-0.09 [-0.27 to 0.09][f]
Pain Duration (days)										
van Poppel et al,[39] (1998)	C-RCT (36 Clusters)	6-months	Days past month (0-30)	106	1.7	15.6	104	2.2	15.6	-0.50 [-4.72 to 3.72][f]
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	6-months	VAS (0-100)	46	36.2	27.9	22	32.7	31.4	3.50 [-11.26 to 18.26]
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	6-months	VAS (0-100)	48	28.1	24.2	21	32.7	31.4	-4.60 [-18.22 to 9.02]
Education vs. Control (long-term)										
Quality of Life										
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	12-months	SF-36 Physical (0-100)	43	49.9	7.8	20	51.6	8.3	-1.70 [-5.92 to 2.52]
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	12-months	SF-36 Physical (0-100)	45	50.9	8.1	20	51.6	8.3	-0.70 [-5.00 to 3.60]
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	12-months	SF-36 Mental (0-100)	43	47.5	8.9	20	49.6	7.6	-2.10 [-6.62 to 2.42]
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	12-months	SF-36 Mental (0-100)	45	49.3	9	20	49.6	7.6	-0.30 [-4.83 to 4.23]
Pain Duration (days)										
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	12-months	VAS (0-100)	43	29.8	24.2	20	30.2	29.4	-0.40 [-14.16 to 13.36]
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	12-months	VAS (0-100)	45	31.7	27.6	20	30.2	29.4	1.50 [-13.33 to 16.33]
Ergonomic vs. Control (short-term)										
Pain Duration (days)										
Gatty et al,[24] (2004)	RCT	4-months	Days per week (0-7)	6	2.7	1.75	7	1.7	2.36	1.00 [-1.29 to 3.29][f]
Driessen et al,[20] (2011)	C-RCT (37 Clusters)	6-months	Days past 3mo (0-90)	256	8.5	36.3	296	9.03	36.3	-0.53 [-6.60 to 5.54][f]

Appendix E. (Continuation)

Source	Study design	Follow-up time point	Outcome measure (range)	Intervention[a]			Contrast[a]			MD [95% CI][b]
				Total	Mean	SD	Total	Mean	SD	
Ergonomic vs. Control (long-term)										
Pain Duration (days)										
Driessen et al,[20] (2011)	C-RCT (37 Clusters)	12-months	Days past 3mo (0-90)	252	8.9	36.3	286	7.52	36.3	1.38 [-4.77 to 7.53][f]
Ergonomic and Education vs. Control (short-term)										
Quality of Life										
Ijzelenberg et al,[28] (2007)	C-RCT (18 Clusters)	6-months	SF-12 Physical (0-100)	101	NR	NR	91	NR	NR	-0.40 [-2.09 to 1.29]
Ijzelenberg et al,[28] (2007)	C-RCT (18 Clusters)	6-months	SF-12 Mental (0-100)	101	NR	NR	91	NR	NR	-0.40 [-1.99 to 1.19]
Ergonomic and Education vs. Control (long-term)										
Quality of Life										
Ijzelenberg et al,[28] (2007)	C-RCT (18 Clusters)	12-months	SF-12 Physical (0-100)	95	NR	NR	89	NR	NR	-0.5 [-2.14 to 1.14]
Ijzelenberg et al,[28] (2007)	C-RCT (18 Clusters)	12-months	SF-12 Mental (0-100)	95	NR	NR	89	NR	NR	0.0 [-1.84 to 1.84]
Lumbar support vs. Control (short-term)										
Duration of sick leave (days)										
Van Poppel et al,[39] (1998)	C-RCT (36 Clusters)	6-months	Days past month (0-30)	100	0.4	0	110	0.4	0	0.00 [0.00 to 0.00][f]
Pain Duration (days)										
Van Poppel et al,[39] (1998)	C-RCT (36 Clusters)	6-months	Days past month (0-30)	100	1.7	36.3	110	2.1	36.3	-0.40 [-10.23 to 9.43][f]
Pregnant Population										
Exercise vs. Control (short-term)										
Quality of Life										
Eggen et al,[21] (2012)	RCT	8-months	SF-8 Physical (0-100)	116	43.3	9.3	124	41.1	9	-2.20 [-4.52 to 0.12]
Eggen et al,[21] (2012)	RCT	8-months	SF-8 Mental (0-100)	116	49.5	7.7	124	50	7.7	-0.50 [-2.45 to 1.45]
Children Population										
Exercise and Education vs. Control (short-term)										
Quality of Life										
Fanucchi et al,[22] (2009)	RCT	6-months	MHI-5 (5-30)	38	24	5	32	22	4	-6.67 [-13.83 to 0.49]

Abbreviations: SD, Standard Deviation; MD, Mean Difference; CI, Confidence Interval; RCT, Randomised Controlled Trial; C-RCT, Cluster-Randomised Controlled Trial; NR, Not Reported; mo, month; SF-8, 8-Item Short Form Health Survey; SF-12, 12-Item Short Form Health Survey; SF-36, 36-Item Short Form Health Survey; WAI, Work Ability Index; COOP-WONCA, Functional Status Assessment Chart; Dartmouth CO-OP, Dartmouth Primary Care Cooperative Information Project scale; WLQ, Work Limitations Questionnaire; EQ5D, Euro Quality of Life 5 Dimensions; WPAI, *Work Productivity and Activity Impairment* Questionnaire; MHI-5, Mental Health Inventory.

[a] Values presented in the original scale as measured.

[b] Value presented on 0-100 scale unless otherwise indicated.

[c] Only baseline data was available.

[d] SD obtained from standard error following Cochrane Handbook recommendations.

[e] SD obtained from 95% Confidence Interval following Cochrane Handbook recommendations.

[f] Value presented on study original scale.

A negative value of the mean difference estimate represents an effect in favour of the intervention group.

Short-term indicates follow-up assessment of less than 12-months.

Long-term indicates follow-up assessment of 12-months or more.

Appendix F. Quality of evidence assessment (GRADE) for the primary outcome

Outcome	Follow-up time point	Study Limitation	Inconsistency	Imprecision	Overall quality
		General Population			
Exercise vs. Control					
Pain intensity[17,27,34]	Short-term	-1	None	None	Moderate-quality
Disability[27]	Short-term	-1	-1	-1	Very Low-quality[a]
Exercise and Education vs. Control					
Pain intensity[30,32,36]	Short-term	-1	None	-1	Low-quality
Pain intensity[8,32,36,40]	Long-term	-1	None	None	Moderate-quality
Disability[32,36]	Short-term	-1	None	-1	Low-quality
Disability[8,32,36,40]	Long-term	-1	None	None	Moderate-quality
Education vs. Control					
Pain intensity[18,29,33]	Short-term	-1	None	None	Moderate-quality
Pain intensity[7,40]	Long-term	-1	None	-1	Low-quality
Disability[29,33,38,41]	Short-term	-1	None	None	Moderate-quality
Disability[40,41]	Long-term	-1	None	-1	Low-quality
Ergonomic vs. Control					
Pain intensity[20]	Short-term	-1	-1	None	Low-quality[a]
Pain intensity[20]	Long-term	-1	-1	None	Low-quality[a]
Ergonomic and Education vs. Control					
Pain intensity[28]	Short-term	-1	-1	-1	Very Low-quality[a]
Pain intensity[7,28]	Long-term	-1	None	-1	Low-quality
Disability[28]	Short-term	-1	-1	-1	Very Low-quality[a]
Disability[28]	Long-term	-1	-1	-1	Very Low-quality[a]
		Pregnant Population			
Exercise vs. Control					
Pain intensity[21,23]	Short-term	None	None	None	High-quality
Disability[21]	Short-term	None	-1	-1	Low-quality[a]
		Children Population			
Exercise and Education vs. Control					
Pain intensity[22]	Short-term	-1	-1	-1	Very Low-quality[a]

Abbreviations: GRADE, Grading of Recommendations Assessment, Development and Evaluation.

[a] Quality of evidence assessment based on a single trial.

The quality of evidence was downgraded one level (-1) if the study did not comply with each GRADE criteria.

Short-term indicates follow-up assessment of less than 12-months.

Long-term indicates follow-up assessment of 12-months or more.

Appendix G. Summary of findings for secondary outcome and quality of evidence assessment (GRADE)[a]

Outcome	Follow-up time point	Number of participants	MD [95% CI][b]	GRADE
General Population				
Exercise vs. Control				
Quality of Life (SF-36 Physical)	Short-term	189[27]	-1.00 [-3.15 to 1.15]	Very Low-quality[c]
Quality of Life (SF-36 Mental)	Short-term	189[27]	-0.60 [-3.12 to 1.91]	Very Low-quality[c]
Workability (WAI)	Short-term	278[17,27]	-2.19 [-4.70 to 0.31]	Low-quality
Exercise and Education vs. Control				
Quality of Life (SF-8 Physical)	Short-term	34[30]	-0.20 [-8.00 to 7.60]	Very Low-quality[c]
Quality of Life (SF-8 Mental)	Short-term	34[30]	-3.20 [-9.35 to 2.95]	Very Low-quality[c]
Quality of Life (COOP-WONCA)	Short-term	81[32]	-2.58 [-6.45 to 1.29]	Very Low-quality[c]
Quality of Life (SF-12 Physical)	Long-term	280[8]	-2.30 [-4.18 to -0.42]	Low-quality[c]
Quality of Life (SF-12 Mental)	Long-term	280[8]	-1.80 [-4.46 to 0.86]	Low-quality[c]
Quality of Life (COOP-WONCA)	Long-term	150[32,37]	-3.93 [-8.23 to 0.37]	Low-quality
Education vs. Control				
Quality of Life (Dartmouth CO-OP)	Short-term	582[29]	-3.36 [-5.44 to -1.29]	Low-quality[c]
Quality of Life (SF-36 Physical)	Short-term	137[41]	-0.40 [-3.37 to 2.57]	Very Low-quality[c]
Quality of Life (SF-36 Mental)	Short-term	137[41]	-3.10 [-6.29 to 0.08]	Very Low-quality[c]
Quality of Life (SF-36 Physical)	Long-term	128[41]	-1.21 [-4.22 to 1.80]	Very Low-quality[c]
Quality of Life (SF-36 Mental)	Long-term	128[41]	-1.20 [-4.40 to 2.00]	Very Low-quality[c]
Ergonomic and Education vs. Control				
Quality of Life (SF-12 Physical)	Short-term	192[28]	-0.40 [-2.09 to 1.29]	Very Low-quality[c]
Quality of Life (SF-12 Mental)	Short-term	192[28]	-0.40 [-1.99 to 1.19]	Very Low-quality[c]
Quality of Life (SF-12 Physical)	Long-term	184[28]	-0.50 [-2.14 to 1.14]	Very Low-quality[c]
Quality of Life (SF-12 Mental)	Long-term	184[28]	0.00 [-1.84 to 1.84]	Very Low-quality[c]
Pregnant Population				
Exercise vs. Control				
Quality of Life (SF-8 Physical)	Short-term	240[21]	-2.20 [-4.52 to 0.12]	Low-quality[c]
Quality of Life (SF-8 Mental)	Short-term	240[21]	-0.50 [-2.45 to 1.45]	Low-quality[c]
Children Population				
Exercise and Education vs. Control				
Quality of Life (MHI-5)	Short-term	70[22]	-6.67 [-13.83 to 0.49]	Very Low-quality[c]

Abbreviations: GRADE, Grading of Recommendations Assessment, Development and Evaluation; MD, Mean Difference; CI, Confidence Interval.

[a] Only studies providing results that could be converted to a 0-100 points scale are presented.

[b] Value presented on 0-100 scale.

[c] Quality of evidence assessment based on a single trial.

A negative value of the mean difference estimate represents an effect in favour of the intervention group.

Short-term indicates follow-up assessment of less than 12-months.

Long-term indicates follow-up assessment of 12-months or more.

Appendix H. Quality of evidence assessment (GRADE) for the secondary outcome

Outcome	Follow-up time point	Study Limitation	Inconsistency	Imprecision	Overall quality
		General Population			
Exercise vs. Control					
Quality of Life (SF-36 Physical)[27]	Short-term	-1	-1	-1	Very Low-quality[a]
Quality of Life (SF-36 Mental)[27]	Short-term	-1	-1	-1	Very Low-quality[a]
Workability (WAI)[17,27]	Short-term	-1	None	-1	Low-quality
Exercise and Education vs. Control					
Quality of Life (SF-8 Physical)[30]	Short-term	-1	-1	-1	Very Low-quality[a]
Quality of Life (SF-8 Mental)[30]	Short-term	-1	-1	-1	Very Low-quality[a]
Quality of Life (COOP-WONCA)[32]	Short-term	-1	-1	-1	Very Low-quality[a]
Quality of Life (SF-12 Physical)[8]	Long-term	None	-1	-1	Low-quality[a]
Quality of Life (SF-12 Mental)[8]	Long-term	None	-1	-1	Low-quality[a]
Quality of Life (COOP-WONCA)[32,37]	Long-term	-1	None	-1	Low-quality
Education vs. Control					
Quality of Life (Dartmouth CO-OP)[29]	Short-term	-1	-1	None	Low-quality[a]
Quality of Life (SF-36 Physical)[41]	Short-term	-1	-1	-1	Very Low-quality[a]
Quality of Life (SF-36 Mental)[41]	Short-term	-1	-1	-1	Very Low-quality[a]
Quality of Life (SF-36 Physical)[41]	Long-term	-1	-1	-1	Very Low-quality[a]
Quality of Life (SF-36 Mental)[41]	Long-term	-1	-1	-1	Very Low-quality[a]
Ergonomic and Education vs. Control					
Quality of Life (SF-12 Physical)[28]	Short-term	-1	-1	-1	Very Low-quality[a]
Quality of Life (SF-12 Mental)[28]	Short-term	-1	-1	-1	Very Low-quality[a]
Quality of Life (SF-12 Physical)[28]	Long-term	-1	-1	-1	Very Low-quality[a]
Quality of Life (SF-12 Mental)[28]	Long-term	-1	-1	-1	Very Low-quality[a]
		Pregnant Population			
Exercise vs. Control					
Quality of Life (SF-8 Physical)[21]	Short-term	None	-1	-1	Low-quality[a]
Quality of Life (SF-8 Mental)[21]	Short-term	None	-1	-1	Low-quality[a]
		Children Population			
Exercise and Education vs. Control					
Quality of Life (MHI-5)[22]	Short-term	-1	-1	-1	Very Low-quality[a]

Abbreviations: GRADE, Grading of Recommendations Assessment, Development and Evaluation.

[a] Quality of evidence assessment based on a single trial.

The quality of evidence was downgraded one level (-1) if the study did not comply with each GRADE criteria.

Short-term indicates follow-up assessment of less than 12-months.

Long-term indicates follow-up assessment of 12-months or more.

Appendix I. Individual study results and pooled effects for secondary outcomes[a]

Source	Study design	Follow-up time point	Number of participants	MD [95% CI][b]	Weight, %
		General Population			
Exercise vs. Control (short-term)					
Quality of life (SF-36 Physical)					
Haufe et al,[27] (2017)	RCT	5-months	189	**-1.00 [-3.15 to 1.15]**	100
Quality of life (SF-36 Mental)					
Haufe et al,[27] (2017)	RCT	5-months	189	**-0.60 [-3.12 to 1.91]**	100
Workability (WAI)					
Haufe et al,[27] (2017)	RCT	5-months	189	-1.84 [-4.81 to 1.13]	71.53
Barene et al,[17] (2014) (soccer)	C-RCT (6 clusters)	3-months	43	-1.00 [-7.79 to 5.79]	13.64
Barene et al,[17] (2014) (zumba)	C-RCT (6 clusters)	3-months	46	-5.00 [-11.52 to 1.52]	14.83
Pooled effect: I^2 = 0%				**-2.19 [-4.70 to 0.31]**	
Exercise and Education vs. Control (short-term)					
Quality of life (SF-8 Physical)					
Kamioka et al,[30] (2011)	C-RCT (4 clusters)	3-months	34	**-0.20 [-8.00 to 7.60]**	100
Quality of life (SF-8 Mental)					
Kamioka et al,[30] (2011)	C-RCT (4 clusters)	3-months	34	**-3.20 [-9.35 to 2.95]**	100
Quality of life (COOP-WONCA)					
Lonn et al,[32] (1999)	RCT	5-months	81[c]	**-2.58 [-6.45 to 1.29]**	100
Exercise and Education vs. Control (long-term)					
Quality of life (SF-12 Physical)					
Chaleat-Valayer et al,[8] (2016)	RCT	18-months	280	**-2.30 [-4.18 to -0.42]**	100
Quality of life (SF-12 Mental)					
Chaleat-Valayer et al,[8] (2016)	RCT	18-months	280	**-1.80 [-4.46 to 0.86]**	100
Quality of life (COOP-WONCA)					
Glomsrod et al,[25] (2001); Lonn et al,[32] (1999)	RCT	12-months	73	-4.86 [-10.25 to 0.53]	63.76
Soukup et al,[37] (2001)	RCT	12-months	77	-2.29 [-9.44 to 4.86]	36.24
Pooled effect: I^2 = 0%				**-3.93 [-8.23 to 0.37]**	
Education vs. Control (short-term)					
Quality of Life (Dartmouth CO-OP)					
Irvine et al,[29] (2015) (FitBack program)	RCT	4-months	288	-4.02 [-6.98 to -1.05]	48.96
Irvine et al,[29] (2015) (alternative care)	RCT	4-months	294	-2.73 [-5.63 to 0.17]	51.04
Pooled effect: I^2 = 0%				**-3.36 [-5.44 to -1.29]**	
Quality of life (SF-36 Physical)					
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	6-months	68	-0.80 [-5.02 to 3.42]	49.61
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	6-months	69	0.00 [-4.18 to 4.18]	50.39
Pooled effect: I^2 = 0%				**-0.40 [-3.37 to 2.57]**	

Appendix I. (Continuation)

Source	Study design	Follow-up time point	Number of participants	MD [95% CI][b]	Weight, %
Quality of life (SF-36 Mental)					
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	6-months	68	-3.80 [-8.29 to 0.69]	50.25
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	6-months	69	-2.40 [-6.91 to 2.11]	49.75
Pooled effect: I^2 = 0%				**-3.10 [-6.29 to 0.08]**	
Education vs. Control (long-term)					
Quality of life (SF-36 Physical)					
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	12-months	63	-1.70 [-5.92 to 2.52]	50.90
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	12-months	65	-0.70 [-5.00 to 3.60]	49.10
Pooled effect: I^2 = 0%				**-1.21 [-4.22 to 1.80]**	
Quality of life (SF-36 Mental)					
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	12-months	63	-2.10 [-6.62 to 2.42]	50.14
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	12-months	65	-0.30 [-4.83 to 4.23]	49.86
Pooled effect: I^2 = 0%				**-1.20 [-4.40 to 2.00]**	
Ergonomic and Education vs. Control (short-term)					
Quality of life (SF-12 Physical)					
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	6-months	192	**-0.40 [-2.09 to 1.29]**	100
Quality of life (SF-12 Mental)					
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	6-months	192	**-0.40 [-1.99 to 1.19]**	100
Ergonomic and Education vs. Control (long-term)					
Quality of life (SF-12 Physical)					
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	12-months	184	**-0.5 [-2.14 to 1.14]**	100
Quality of life (SF-12 Mental)					
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	12-months	184	**0.0 [-1.84 to 1.84]**	100
Pregnant Population					
Exercise vs. Control (short-term)					
Quality of life (SF-8 Physical)					
Eggen et al,[21] (2012)	RCT	8-months	240	**-2.20 [-4.52 to 0.12]**	100
Quality of life (SF-8 Mental)					
Eggen et al,[21] (2012)	RCT	8-months	240	**-0.50 [-2.45 to 1.45]**	100

Appendix I. (Continuation)

Source	Study design	Follow-up time point	Number of participants	MD [95% CI][b]	Weight, %
		Children Population			
Exercise and Education vs. Control (short-term)					
Quality of Life (MHI-5)					
Fanucchi et al,[22] (2009)	RCT	6-months	70	**-6.67 [-13.83 to 0.49]**	100

Abbreviations: MD, Mean Difference; CI, Confidence Interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; RCT, Randomised Controlled Trial; C-RCT, Cluster-Randomised Controlled Trial.
[a] Only studies providing results that could be converted to a 0-100 scale are presented.
[b] Value presented on 0-100 scale.
[c] Only baseline data was available.
A negative value of the mean difference estimate represents an effect in favour of the intervention group.
Short-term indicates follow-up assessment of less than 12-months.
Long-term indicates follow-up assessment of 12-months or more.

Appendix J. Individual study results and pooled effects log-transformed and back-transformed for primary outcome of pain-intensity

Source	Study design	Follow-up time point	Number of participants	Log MD [95% CI][a]	Exp MD [95% CI][b]
		General Population			
Exercise vs. Control (short-term)[c]					
Haufe et al,[27] *(2017)*	RCT	5-months	189	-0.40 [-0.89 to 0.09]	0.67 [0.41 to 1.09]
Pedersen et al,[34] *(2013)*	C-RCT (57 cluster)	5-months	334	-0.52 [-0.75 to -0.28]	0.59 [0.47 to 0.76]
Pooled effect				**-0.50 [-0.71 to -0.28]**	**0.61 [0.49 to 0.76]**
Exercise and Education vs. Control (short-term)					
Lonn et al,[32] *(1999)*	RCT	5-months	81[d]	-0.45 [-0.78 to -0.12]	0.64 [0.46 to 0.89]
Soukup et al,[36] *(1999)*	RCT	5-months	69	-0.04 [-0.37 to 0.29]	0.96 [0.69 to 1.34]
Kamioka et al,[30] *(2011)*	C-RCT (4 clusters)	3-months	34	0.29 [-0.08 to 0.66]	1.34 [0.92 to 1.94]
Pooled effect				**0.07 [-0.49 to 0.34]**	**0.93 [0.62 to 1.40]**
Exercise and Education vs. Control (long-term)					
Chaleat-Valayer et al,[8] *(2016)*	RCT	18-months	280	-0.02 [-0.16 to 0.12]	0.98 [0.85 to 1.12]
Glomsrod et al,[25] *(2001); Lonn et al,*[32] *(1999)*	RCT	12-months	73	-0.51 [-0.88 to -0.14]	0.60 [0.41 to 0.87]
Soukup et al,[37] *(2001); Soukup et al,*[36] *(1999)*	RCT	12-months	69	-0.21 [-0.56 to 0.14]	0.81 [0.57 to 1.15]
Warming et al,[40] *(2008) (TTPT)*	C-RCT (11 clusters)	12-months	49	-0.32 [-1.77 to 1.13]	0.73 [0.17 to 3.10]
Pooled effect				**-0.20 [-0.46 to 0.06]**	**0.82 [0.63 to 1.06]**
Education vs. Control (short-term)					
Donaldson et al,[18] *(1993)*	RCT	3-months	172[d]	-0.12 [-0.55 to 0.31]	0.89 [0.58 to 1.36]
Irvine et al,[29] *(2015) (FitBack program)*	RCT	4-months	288	-0.71 [-2.02 to 0.60]	0.49 [0.13 to 1.83]
Irvine et al,[29] *(2015) (alternative care)*	RCT	4-months	294	-0.10 [-1.02 to 0.82]	0.90 [0.36 to 2.27]
Menzel et al,[33] *(2006)*	RCT	3-months	23	0.57 [-0.14 to 1.28]	1.77 [0.87 to 3.58]
Pooled effect				**0.01 [-0.41 to 0.43]**	**1.01 [0.66 to 1.53]**
Education vs. Control (long-term)					
Jensen et al,[7] *(2006) (SMI)*	C-RCT (19 clusters)	24-months	78	0.32 [-1.03 to 1.67]	1.28 [0.51 to 3.22]
Warming et al,[40] *(2008) (TT)*	C-RCT (11 clusters)	12-months	48	0.19 [-1.06 to 1.44]	1.21 [0.35 to 4.24]
Pooled effect				**0.25 [-0.67 to 1.17]**	**1.28 [0.51 to 3.22]**
Ergonomic vs. Control (short-term)					
Driessen et al,[20] *(2011)*	C-RCT (37 clusters)	6-months	552	**0.16 [-1.17 to 1.49]**	**1.17 [0.31 to 4.45]**
Ergonomic vs. Control (long-term)					
Driessen et al,[20] *(2011)*	C-RCT (37 clusters)	12-months	538	**0.23 [-1.22 to 1.68]**	**1.26 [0.30 to 5.37]**
Ergonomic and Education vs. Control (short-term)					
Ijzelenberg et al,[28] *(2007)*	C-RCT (18 clusters)	6-months	192	**0.09 [-1.14 to 1.32]**	**1.09 [0.32 to 3.76]**

Appendix J. (Continuation)

Source	Study design	Follow-up time point	Number of participants	Log MD [95% CI][a]	Exp MD [95% CI][b]
Ergonomic and Education vs. Control (long-term)					
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	12-months	184	0.00 [-1.27 to 1.27]	1.00 [0.28 to 3.58]
Jensen et al,[7] (2006) (TTI)	C-RCT (19 clusters)	24-months	82	0.08 [-1.47 to 1.63]	1.08 [0.23 to 5.09]
Pooled effect				**0.03 [-0.95 to 1.02]**	**1.03 [0.39 to 2.76]**
		Pregnant Population			
Exercise vs. Control (short-term)					
Eggen et al,[21] (2012)	RCT	8-months	240	-0.22 [-0.81 to 0.37]	0.80 [0.45 to 1.44]
Garshasbi et al,[23] (2005)	RCT	3-months	212	-0.03 [-0.19 to 0.13]	0.97 [0.83 to 1.14]
Pooled effect				**-0.04 [-0.19 to 0.11]**	**0.96 [0.82 to 1.12]**
		Children			
Exercise and Education vs. Control (short-term)					
Fanucchi et al,[22] (2009)	RCT	6-months	70	**-0.15 [-2.95 to 2.65]**	**0.86 [0.05 to 14.20]**

Abbreviations: Log, Logarithm; MD, Mean Difference; CI, Confidence Interval; Exp, Exponential; RCT, Randomised Controlled Trial; C-RCT, Cluster-Randomised Controlled Trial; TTPT, Transfer Technique and Physical Activity; TT, Transfer Technique; SMI, Stress Management Intervention; TTI, Transfer Technique Intervention.

[a] A negative value of the log mean difference estimate represents an effect in favour of the intervention group.

[b] Exp values were generated using the exponential of the log MD and represent the treatment effect as a ratio. Values below 0 represents an effect in favour of the intervention group.

[c] Barene et al,[17] (2014) was not included in this meta-analysis using log values as raw data was only presented as a mean difference 95% CI.

[d] Only baseline data was available.

Short-term indicates follow-up assessment of less than 12-months.

Long-term indicates follow-up assessment of 12-months or more.

Appendix K. Individual study results and pooled effects log-transformed and back-transformed for primary outcome of disability

Source	Study design	Follow-up time point	Number of participants	Log MD [95% CI][a]	Exp MD [95% CI][b]
		General Population			
Exercise vs. Control (short-term)					
Haufe et al,[7] (2017)	RCT	5-months	189	**-0.19 [-0.58 to 0.20]**	**0.83 [0.56 to 1.22]**
Exercise and Education vs. Control (short-term)					
Lonn et al,[32] (1999)	RCT	5-months	81[c]	-0.16 [-0.30 to -0.02]	0.85 [0.74 to 0.98]
Soukup et al,[36] (1999)	RCT	5-months	69	0.00 [-0.14 to 0.14]	1.00 [0.87 to 1.15]
Pooled effect				**-0.08 [-0.24 to 0.08]**	**0.92 [0.79 to 1.08]**
Exercise and Education vs. Control (long-term)					
Chaleat-Valayer et al,[8] (2016)	RCT	18-months	280	-0.27 [-0.45 to -0.09]	0.76 [0.64 to 0.91]
Glomsrod et al,[25] (2001); Lonn et al,[32] (1999)	RCT	12-months	73	-0.29 [-0.47 to -0.11]	0.75 [0.63 to 0.89]
Soukup et al,[37] (2001); Soukup et al,[36] (1999)	RCT	12-months	69	-0.13 [-0.33 to 0.07]	0.88 [0.72 to 1.07]
Warming et al,[40] (2008) (TTPT)	C-RCT (11 clusters)	12-months	49	-0.61 [-1.10 to -0.12]	0.54 [0.33 to 0.89]
Pooled effect				**-0.26 [-0.37 to -0.14]**	**0.77 [0.69 to 0.87]**
Education vs. Control (short-term)					
Irvine et al,[29] (2015) (FitBack program)	RCT	4-months	288	-0.22 [-0.36 to -0.08]	0.80 [0.70 to 0.92]
Irvine et al,[29] (2015) (alternative care)	RCT	4-months	294	-0.13 [-0.27 to 0.01]	0.88 [0.77 to 1.01]
Menzel et al,[33] (2006)	RCT	3-months	24	0.09 [-0.14 to 0.32]	1.09 [0.87 to 1.38]
Tuchin et al,[38] (1998)	RCT	6-months	61	-0.53 [-1.61 to 0.55]	0.59 [0.20 to 1.73]
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	6-months	68	0.35 [-1.98 to 2.68]	1.42 [0.14 to 14.61]
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	6-months	69	0.27 [-2.10 to 2.64]	1.31 [0.12 to 14.04]
Pooled effect				**-0.13 [-0.24 to -0.02]**	**0.88 [0.79 to 0.98]**
Education vs. Control (long-term)					
Warming et al,[40] (2008) (TT)	C-RCT (11 clusters)	12-months	48	0.06 [-0.37 to 0.49]	1.06 [0.69 to 1.63]
Yassi et al,[41] (2001) (Arm B)	C-RCT (9 clusters)	12-months	63	0.21 [-2.46 to 2.88]	1.23 [0.09 to 17.74]
Yassi et al,[41] (2001) (Arm C)	C-RCT (9 clusters)	12-months	65	-0.06 [-2.80 to 2.68]	0.94 [0.06 to 14.64]
Pooled effect				**0.06 [-0.36 to 0.48]**	**1.06 [0.70 to 1.62]**
Ergonomic and Education vs. Control (short-term)					
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	6-months	192	**0.44 [-4.93 to 5.81]**	**1.55 [0.01 to 333.62]**
Ergonomic and Education vs. Control (long-term)					
Ijzelenberg et al,[28] (2007)	C-RCT (18 clusters)	12-months	184	**0.14 [-5.05 to 5.33]**	**1.15 [0.01 to 207.27]**

Appendix K. (Continuation)

Source	Study design	Follow-up time point	Number of participants	Log MD [95% CI][a]	Exp MD [95% CI][b]
		Pregnant Population			
Exercise vs. Control (short-term)					
Eggen et al,[21] *(2012)*	RCT	8-months	240	**-0.31 [-1.23 to 0.61]**	**0.73 [0.29 to 1.84]**

Abbreviations: Log, Logarithm; MD, Mean Difference; CI, Confidence Interval; Exp, Exponential; RCT, Randomised Controlled Trial; C-RCT, Cluster-Randomised Controlled Trial; TTPT, Transfer Technique and Physical Activity; TT, Transfer Technique.

[a] A negative value of the log mean difference estimate represents an effect in favour of the intervention group.

[b] Exp values were generated using the exponential of the log MD and represent the treatment effect as a ratio. Values below 0 represents an effect in favour of the intervention group.

[c] Only baseline data was available.

Short-term indicates follow-up assessment of less than 12-months.

Long-term indicates follow-up assessment of 12-months or more.

CHAPTER FIVE

Exercise programs may be effective in preventing a new episode of neck pain: a systematic review and meta-analysis

5.1 Preface

Previous systematic reviews have summarised the evidence for interventions to prevent neck pain. However, none of those reviews has investigated prevention strategies including only randomised controlled trials and trials recruiting asymptomatic participants at study entry. **Chapter Five** in this thesis presents the results for a systematic review that investigated prevention strategies to reduce the risk of an episode of neck pain.

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

de Campos TF, Maher CG, Steffens D, Fuller JT, Hancock MJ. Exercise programs may be effective in preventing a new episode of neck pain: a systematic review and meta-analysis. *J Physiother*. 2018 Jul;64(3):159-165. doi: 10.1016/j.jphys.2018.05.003

The systematic review registration with PROSPERO is presented in the **Thesis Appendix 7**.

5.2 Authorship attribution statement

This statement is to outline the contribution made by Tarcisio Folly de Campos in the preparation and submission of the following manuscript: "***de Campos TF***, Maher CG, Steffens D, Fuller JT, Hancock MJ. Exercise programs may be effective in preventing a new episode of neck pain: a systematic review and meta-analysis. *J Physiother*. 2018 Jul;64(3):159-165". The convention is that the author with the principal contribution to the study is the first author.

Tarcisio Folly de Campos, during his PhD candidature, developed the original concept and design of this systematic review, and was responsible for designing the search strategy, data search and data extraction instruments, registering the review in the PROSPERO database, appraising the selected studies for methodological quality and risk of bias, writing the draft manuscript and subsequent revisions, responding to reviewer's feedback and coordinating submission for publication of the original manuscript.

The individual roles of co-authors are listed below:

Task	**Co-author's contribution**
Conception and research design	CM, MH
Data search, study selection, data extraction	DS, JF, MH
Risk of bias and methodological quality assessment	JF, MH
Drafting of the manuscript	MH
Revision and critical comment of manuscript	CM, DS, JF, MH

CM, Chris Maher; **DS**, Daniel Steffens; **JF**, Joel Fuller; **MH**, Mark Hancock

Mr Tarcisio Folly de Campos _____ Date: 28 / 02 /2020

As supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statement above is correct.

Professor Mark Hancock _____ Date: 28 / 02 /2020

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Research

Exercise programs may be effective in preventing a new episode of neck pain: a systematic review and meta-analysis

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KEY WORDS

Neck pain
Prevention
Randomised controlled trial
Systematic review
Meta-analysis

ABSTRACT

Question: What is the effectiveness of interventions that aim to prevent a new episode of neck pain? **Design**: Systematic review and meta-analysis of randomised, controlled trials. **Participants**: People without neck pain at study entry. **Intervention**: Any intervention aiming to prevent a future episode of neck pain. **Outcome measures**: New episode of neck pain. **Results**: Five trials including a total of 3852 individuals met the inclusion criteria. The pooled results from two randomised, controlled trials (500 participants) found moderate-quality evidence that exercise reduces the risk of a new episode of neck pain (OR 0.32, 95% CI 0.12 to 0.86). One of the meta-analysed trials included some co-interventions with the exercise. There was low-quality evidence from three randomised, controlled trials (3352 participants) that ergonomic programs do not reduce the risk of a new neck pain episode (OR 1.00, 95% CI 0.74 to 1.35). **Conclusion**: This review found moderate-quality evidence supporting the effectiveness of an exercise program for reducing the risk of a new episode of neck pain. There is a need for high-quality randomised, controlled trials evaluating interventions to prevent new episodes of neck pain. **Registration**: PROSPERO CRD42017055174. **[de Campos TF, Maher CG, Steffens D, Fuller JT, Hancock MJ (2018) Exercise programs may be effective in preventing a new episode of neck pain: a systematic review. *Journal of Physiotherapy* 64: 159–165]**

Introduction

Neck pain is one of the most significant health problems worldwide.[1] It has been ranked the fourth leading cause of years lived with disability, according to the Global Burden of Disease Study.[2] Mean lifetime prevalence is estimated to be 48.5% and is expected to increase due to the ageing population.[2,3] The natural course of an episode of neck pain is favourable;[4] however, recurrence rates are reported to be high,[5] which contributes to the high global social and economic burden. The Global Burden of Disease studies[1,2] and Task Forces[6] worldwide have called for prevention strategies for neck and back pain. Recent clinical practice guidelines for neck pain lack recommendations for prevention.[7] Consequently, a comprehensive, high-quality systematic review of the literature is required to examine the effectiveness of prevention strategies for neck pain.

A number of systematic reviews that examined the effectiveness of interventions for preventing neck pain have been published.[8–12] However, these systematic reviews have important limitations. Some were published > 10 years ago,[8,9] some did not publish a pre-specified study protocol,[10,12] some included non-randomised studies,[10–12] and some included studies recruiting symptomatic participants at study entry.[9,11] There has been no systematic review investigating strategies for prevention of neck pain including only randomised, controlled trials (randomised, controlled trials) and asymptomatic participants at baseline.

Therefore, the research question for this systematic review was:

What is the effectiveness of interventions that aim to prevent a new episode of neck pain?

Method

This systematic review adhered to the statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions (PRISMA).[13]

Identification and selection of studies

A comprehensive search of five electronic databases (MEDLINE via Ovid, EMBASE via Ovid, CINAHL, Physiotherapy Evidence Database (PEDro), and The Cochrane Central Register of Controlled Trials (CENTRAL) via The Cochrane Library) was conducted from the earliest records published to 27 April, 2018. A sensitive search strategy was used based on the recommendations of the Cochrane Back and Neck Group[14] for 'randomised controlled trials' and 'neck pain', combined with search terms for 'prevention'. The detailed search strategy for each database is presented in Appendix 1 (see eAddenda for Appendix 1). In addition, reference lists of relevant reviews and included randomised, controlled trials were manually searched for additional randomised, controlled trials, and citation tracking of all included trials was performed. Non-English language studies were

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Box 1. Inclusion criteria.

Design
- Randomised, controlled trials

Participants
- People not meeting the study's definition of an episode of neck pain at study entry

Intervention
- Any intervention aiming to prevent a new episode of neck pain

Outcome measures
- A new episode of neck pain
- A new episode of neck pain leading to care seeking, activity limitation or work loss
- Measures of pain or disability over the follow-up period

Comparisons
- The intervention group must be compared to no intervention/placebo or minimal intervention
- Studies investigating the additional benefit of a treatment (eg, exercise + education versus exercise alone)

included if an appropriate translation could be obtained; otherwise, they were noted but excluded from analyses.

Randomised, controlled trials assessing the effectiveness of prevention strategies for neck pain were included if they met the inclusion criteria listed in Box 1. A three-stage screening process was used to select relevant randomised, controlled trials for this review. In the first stage, one reviewer (TFC) screened all titles for eligibility and excluded clearly irrelevant studies. In the second stage, each study title and abstract was independently evaluated by two reviewers (TFC and DS or JTF). In the third stage, the full text for each potentially eligible study was retrieved and assessed against the eligibility criteria by two independent reviewers (TFC and DS or JTF). In cases of disagreement, a third reviewer (MJH or CGM) was consulted.

Assessment of characteristics of studies

Risk of bias

Risk of bias was assessed using the PEDro Scale[15,16] by downloading the available scores from the PEDro database. If a study had not been rated on the website, two experienced PEDro raters scored the study. The total score on the PEDro scale is the addition of 'yes' (criterion is clearly satisfied) responses for Items 2 to 11 (Item 1 is not used for calculation of the total PEDro scale score because it is more related to external validity) and range from 0 (high risk of bias) to 10 (low risk of bias). There is evidence that the PEDro scale total score has acceptably high reliability and validity[15,16] and Rasch analysis has confirmed that it can be used as a continuous scale.[17]

Participants

Randomised, controlled trials were included if the participants did not have neck pain at study entry or did not meet all of the study's criteria for an episode of neck pain at baseline. For example, if a small proportion of participants had mild neck pain at study entry but all were working, and the study outcome was a new episode of work absence due to neck pain, then the study would be considered eligible.

Intervention

To be eligible for inclusion, trials had to evaluate an intervention aiming to prevent a future episode of neck pain. The experimental group had to be compared to a group that received no intervention, sham intervention or minimal intervention. Randomised, controlled trials investigating multimodal interventions were also included.

Outcome measures

To be eligible for inclusion, trials had to report an outcome measure of a new episode of neck pain (eg, number of participants experiencing a new episode of neck pain, or number of participants taking sick leave due to a new episode of neck pain), or a measure of neck pain or disability over the follow-up period (pain or disability measures at a single point in time did not satisfy this criterion).

Data extraction and analysis

Data for each included trial were extracted by two independent reviewers (TFC and MJH or JTF) using a standardised data extraction form and discrepancies were resolved by discussion with a third author (CGM). Extracted data included the characteristics of the trial (eg, demographic characteristics of the participants, description of the interventions, duration of treatment, and description of the outcomes) and outcome data. Whenever possible, raw outcome data (number of participants having a new episode of neck pain and total number of participants) in both the intervention group and control group were extracted. Treatment effect estimates were calculated using methods recommended in the Cochrane Handbook for Systematic Review of Interventions.[18] Attempts were made to contact authors of included trials to clarify any relevant information or request additional data, when required.

The overall quality of evidence was assessed for each intervention contrast and rated as high, moderate, low, or very low, as recommended by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.[19] The GRADE classification was downgraded one level per study flaw, from high quality, if any of the following flaws were present: design limitation (more than a quarter of participants from studies with high risk of bias, PEDro score < 7); inconsistency of results (substantial heterogeneity, $I^2 > 50\%$); and imprecision (based on a threshold of < 400 participants for each pooled outcome, and also observation of the 95% CIs in cases of dichotomous outcomes). This review did not consider the indirectness criterion because the eligibility criteria ensured a specific population with relevant outcomes. In addition, the review did not assess publication bias due to insufficient study numbers. Two reviewers (TFC and MJH or DS or JTF) independently performed GRADE assessments for each treatment contrast.

Trials considered homogeneous were grouped into the same prevention strategy category. Odds ratios (ORs) and 95% CIs were calculated and a random-effects model was used to pool estimates using commercial meta-analysis software[a]. For randomised, controlled trials that did not report the sample size at the end of the follow-up period, the OR (95% CI) was calculated using the baseline sample size. Outcome data on short-term follow-up ($\leq$ 12 months) and long-term follow-up ($>$ 12 months) were assessed. Statistical heterogeneity was assessed visually and using the I^2 statistic.

Results

Flow of studies through the review

Overall, the comprehensive database search strategy identified 12 725 records. After screening articles by title and abstract, 114 potentially eligible studies were identified, and their full texts were retrieved. In total, five trials (3852 participants) met the inclusion criteria and were included in the review.[20–24] The included studies were three randomised, controlled trials[20,22,24] and two cluster-randomised, controlled trials.[21,23] An outline of the screening and reviewing process can be seen in Figure 1.

Characteristics of studies

Risk of bias

Risk of bias scores for four of the randomised, controlled trials[20,21,23,24] were found on the PEDro database website. The fifth

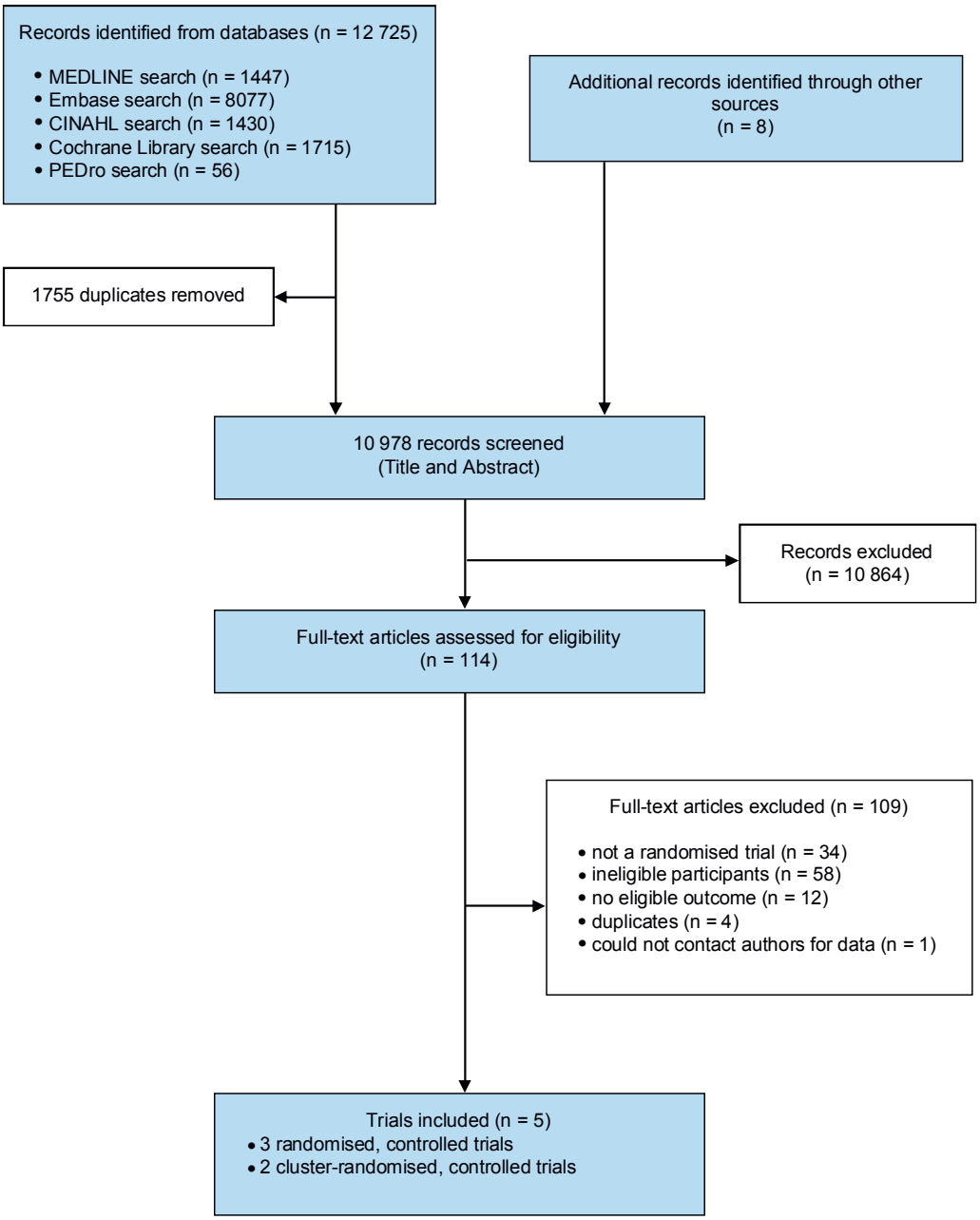

Figure 1. Flow of studies through the review.

study[22] was independently assessed and scored by two experienced PEDro raters. The mean PEDro score was 6.2 (SD 1.3) with blinding, concealed allocation, and adequate follow-up being the main items scored as high risk of bias. The PEDro scale responses for individual items and the total score for each included randomised, controlled trial are available in Table 1.

Participants

All of the included trials (3852 participants) examined a working-age population with the mean age around 40 years, about 42% of whom were female. Four trials investigated prevention strategies in a population of office workers,[20–23] while one trial investigated a sample of nursing personnel.[24] Table 2 provides details about the characteristics of each trial.

Intervention

The included trials investigated the effect of two neck pain prevention strategies: ergonomic programs[20–22] and exercise programs.[23,24] The three trials[20–22] assessing ergonomic programs used multiple prevention strategies: adjustment of workstation,[20,22] ergonomic redesign or modification,[20–22] evaluation of participant posture while performing daily tasks,[22] manual handling aids,[21] and job rotation.[21] One of the two trials investigating exercise programs[23] evaluated neck muscle stretching and endurance training. This was delivered at work twice a day for each working day and twice a week at home over the 12-month study period. The second trial investigating exercise[24] evaluated a generalised aerobic program, including: body awareness and aerobic, strengthening, stabilising and stretching exercises, supplemented by health information/stress management training, and a practical examination of the workplace. The exercise program was delivered in 1-hour sessions, three times per week for 9 months, and the health information/stress management component was delivered in 1-hour sessions, once per week for 4 months.

Outcome measures

Raw data on the number of new events (eg, neck pain episodes) and number of participants were available for four[20,22–24] of the five trials. For these four studies, ORs (95% CI) were calculated. For the remaining study,[21] an OR with 95% CI and *p*-value was provided, but raw data on the number of new events were not presented. No eligible trials were identified that reported outcome data on the number of new episodes of neck pain leading to care

Table 1
PEDro scores of included trials.

Study	Eligibility criteria and source	Random allocation	Concealed allocation	Baseline comparability	Blind subjects	Blind therapists	Blind assessors	Adequate follow-up	Intention-to-treat analysis	Between-group comparisons	Point estimates and variability	Total score *(0 to 10)*
Pillastrini et al (2007)[22]	N	Y	N	Y	N	N	Y	Y	Y	Y	Y	7
Conlon et al (2008)[20]	Y	Y	N	Y	N	N	Y	N	Y	Y	Y	6
Tveito et al (2009)[24]	N	Y	Y	Y	N	N	N	N	N	Y	Y	5
Driessen et al (2011)[21]	Y	Y	N	Y	N	N	N	N	Y	Y	Y	5
Sihawong et al (2014)[23]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8

N = no, PEDro = Physiotherapy Evidence Database, Y = yes.

Table 2
Characteristics of the included trials.

Study	Participants[a]	Outcome definition	Experimental group	Control group	Time and frequency of interventions	Follow-up period
Pillastrini et al (2007)[22]	n = 99 Mean age = 42 yrs Gender = 71% females Administrative personnel of the city's Town Hall	Neck pain episode: Indicated the presence of neck pain on a pain drawing. Outcome assessed at 5 months' follow-up.	Ergonomic intervention: workstation evaluation and adjustments, and postural evaluation while performing daily tasks, by a physiotherapist.	No intervention	Exp: One ergonomic intervention session of 30 mins for each operator, with twice a month supervision and consultation of 5 to 10 mins.	5 months
Conlon et al (2008)[20]	n = 206 Mean age = 43 yrs Gender = 28% females Office workers (engineers)	Neck pain episode: A neck disorder diagnosed on the physical examination if neck discomfort > 5/10 reported at weekly assessment.	Ergonomic program (implementation of an adapted workstation): (i) an alternative mouse; (ii) a conventional mouse + forearm support board; (iii) an alternative mouse + forearm support board – aimed to prevent musculoskeletal disorders.	Minimal intervention: workstation with a conventional mouse	Exp/Con: Participants were asked to use the work station while on duty.	12 months
Driessen et al (2011)[21]	n = 3047 Mean age = 42 yrs Gender = 41% females Participants recruited through four Dutch companies	Neck pain episode: Presence of neck pain at least 3 on a 4-point scale (DMQ). Outcome assessed every 3 months.	Ergonomic program: implementation of Stay@Work participatory ergonomic program (evaluation and prioritise the risk factors and ergonomic measures to prevent neck pain).	Minimal intervention: educational movies about prevention of neck pain	Exp: Participants were asked to use the ergonomic program while on duty (first 3 months to implement the ergonomic measures) Con: 3 × 45 s educational movies.	12 months
Tveito et al (2009)[24]	n = 40 Mean age = N/S Gender = 100% females Employees (nursing personnel) in a nursing home for older people in Norway	Neck pain episode: Severity was scored on a 4-point scale (0 = no complaint to 3 = severe complaints); no cut-off point.	Integrated Health Program: physical exercise (based on a standardised aerobic dancing program) to improve physical capacity, strength and flexibility, including: body awareness, aerobic, strength, stabilising and stretching exercises. Supplemented by health information/stress management training and a practical examination of the work place.	No intervention	Exp: Aerobic program 3 × week for 1 hour for 9 months. A total of 15 hours of information (1 hour/week for 3 months) on stress, coping, health and lifestyle and a workplace practical examination.	9 months
Sihawong et al (2014)[23]	n = 567 Mean age = 37 yrs Gender = 50% females Office workers with lower neck flexion range and muscle endurance, from 12 large-scale enterprises in Bangkok	Neck pain episode: An incident episode was defined as having pain > 30 mm on a 100-mm visual analogue scale and had no weakness or numbness in the upper limb. Outcome assessed using a diary.	Exercise program: stretching exercises and endurance exercises for the neck muscles. Included daily reminder messages for the first 3 months.	No intervention	Exp: Neck muscles stretching exercise twice daily for each working day, and muscle endurance training ten times, twice per wk, during the 12-mth study period.	12 months

Con = control group, DMQ = Dutch Musculoskeletal Questionnaire, Exp = experimental group, N/S = not stated.
[a] Participants with no neck pain at baseline.

seeking, activity limitation, or days lost from work. All trials followed participants for ≤ 12 months (short-term follow-ups). The number of new events, sample size and ORs (95% CIs) for the included randomised, controlled trials are presented in Figure 2 on the eAddenda. A summary of the findings and quality of evidence assessment (GRADE) are presented in Table 3.

Effect of ergonomic programs on preventing neck pain

Three randomised, controlled trials[20–22] (3352 participants) were included in the meta-analysis investigating the effect of ergonomic programs compared to no or minimal intervention. One randomised, controlled trial[20] had four intervention arms. The minimal intervention arm was used as the control group. Each of

Table 3
Summary of findings and quality of evidence assessment.

Prevention strategy	Summary of findings			Quality of evidence assessment (GRADE)			
	Trials (n)	Participants (n)	OR (95% CI)	Study limitation	Inconsistency	Imprecision	Overall quality
Ergonomic program	3	3352[20–22]	1.00 (0.74 to 1.35)	−1	−1	None	Low
Exercise	2	500[23,24]	0.32 (0.12 to 0.86)	None	None	−1[a]	Moderate

GRADE = Grading of Recommendations Assessment, Development and Evaluation.
The quality of evidence was downgraded one level (−1) if the study did not comply with each GRADE criteria.
[a] Downgraded one level (−1) due to wide CI of pooled effect.

three pairwise comparisons were separately included, with the number of events and participants in the control group divided out evenly among the comparisons, as recommended in the Cochrane Handbook for Systematic Reviews.[18] The pooled results for ergonomic programs provided low-quality evidence of no protective effect (OR 1.00, 95% CI 0.74 to 1.35) when compared to no or minimal intervention in preventing new episodes of neck pain (Figure 3, Table 3). See Figure 2 in the eAddenda for a detailed forest plot.

Effect of exercise programs on preventing neck pain

Two randomised, controlled trials[23,24] (500 participants) were included in the meta-analysis investigating the effect of exercise programs compared to no intervention control. In one randomised, controlled trial[23] the intervention was restricted to exercise, while in the other randomised, controlled trial,[24] exercise was the primary intervention, supplemented by health information/stress management training, and a practical examination of the workplace. The pooled results provided moderate-quality evidence of reduced risk of a future neck pain episode (OR 0.32, 95% CI 0.12 to 0.86) (Figure 4, Table 3). See Figure 2 in the eAddenda for a detailed forest plot.

Discussion

Five randomised, controlled trials investigating two intervention strategies to prevent neck pain were deemed eligible to be included in this systematic review. The review found moderate-quality evidence that an exercise program substantially reduces the risk of a new episode of neck pain (OR 0.32, 95% CI 0.12 to 0.86). This evidence was derived from two trials that included 500 participants.[23,24] Pooled results from three trials[20–22] with 3352 participants produced low-quality evidence that ergonomic programs do not reduce the risk of a new episode of neck pain (OR 1.00, 95% CI 0.74 to 1.35).

The strengths of this systematic review included the use of a pre-specified protocol registered on PROSPERO, sensitive search strategy using multiple electronic databases with supplementary hand searching, following the PRISMA recommendations, and the use of the GRADE system to appraise the overall quality of the evidence. The risk of bias of included trials was assessed using the PEDro scale, which has acceptably high reliability and validity,[15,16] and can be used as a continuous scale for measuring risk of bias in randomised, controlled trials.[17]

This systematic review and meta-analysis had some limitations. A small number of trials were included, despite the comprehensive search strategy. The majority of the trials[20–23] evaluated the effectiveness of the intervention in office workers; thus, the generalisability of these findings to other populations is unclear. Authors could not be contacted to gather information for one potentially eligible trial.[25] Some included trials were not registered,[20,22,24] and did not present a pre-specified published protocol,[20,22,24] leading to potential reporting bias. The two trials[23,24] evaluating exercise had different approaches to exercise: in one trial,[23] the program was confined to neck exercises, whereas the other trial[24] evaluated a generalised whole body exercise program, supplemented by health information/stress management training, which means there is uncertainty about which approach to recommend.

It is believed that the current systematic review with meta-analysis is the first to have included only randomised, controlled trials evaluating prevention strategies for neck pain that have included asymptomatic participants at baseline (or at least participants that did not meet all of the study's criteria for an episode of neck pain at baseline). Previous systematic reviews that have investigated the effectiveness of interventions to prevent neck pain have included trials with symptomatic participants at study entry.[8–12] Some are also out of date,[8–10] and some include sub-optimal study designs (such as non-randomised trials or quasi-experimental studies).[9,10]

A recent review[12] investigated the effectiveness of exercise for preventing upper extremity musculoskeletal disorders, including neck pain.[12] That review found evidence of limited to strong quality that exercise could prevent upper extremity symptoms; however, it included studies with symptomatic participants at baseline (ie, the studies evaluated treatment, not prevention), and also included study designs other than randomised, controlled trials. Furthermore, that review did not differentiate neck pain from other body regions (eg, neck/shoulder) when assessing trials for

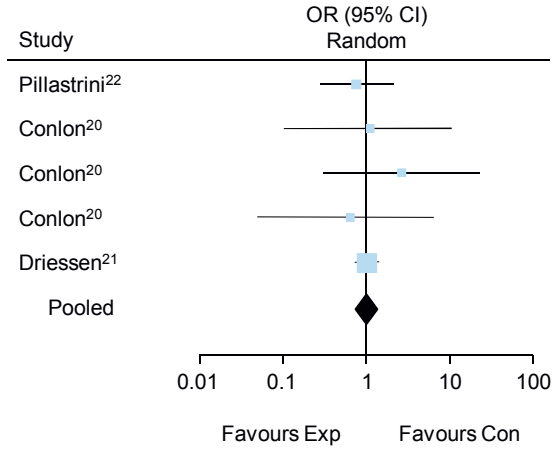

Figure 3. Odds ratio for neck pain episode in trials of ergonomic programs, estimated by pooling data from three trials (n = 3352).
Exp = experimental group, Con = control group.

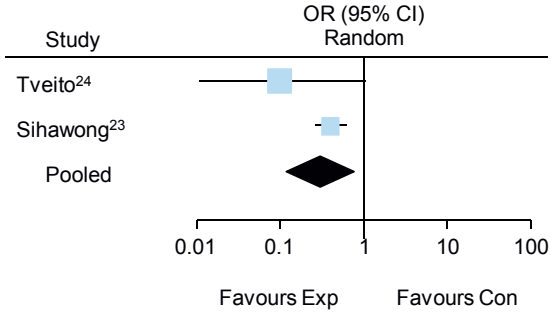

Figure 4. Odds ratio for neck pain episode in trials of exercise, estimated by pooling data from two trials (n = 500). Note that one study[24] administered exercise supplemented by health information/stress management training, and a practical examination of the workplace.
Exp = experimental group, Con = control group.

the effectiveness of exercise prevention strategies. As a result of the stricter inclusion criteria, the current review identified a substantially smaller number of randomised, controlled trials.

A Cochrane review[26] (with 13 randomised, controlled trials involving 2397 workers) reported that most ergonomic interventions were not effective in preventing work-related upper limb and neck musculoskeletal disorders, which is in line with the results from the current review. However, one meta-analysis in the Cochrane review, including two randomised, controlled trials,[20,27] found moderate-quality evidence that the use of ergonomic equipment may reduce the incidence of neck/shoulder pain. The difference in inclusion criteria, especially the inclusion of studies that did not differentiate neck and shoulder pain, and studies of participants with pain at study entry, may explain the somewhat different conclusions between the Cochrane review and the current systematic review and meta-analysis.

The results of the present systematic review on prevention of neck pain are similar to the results of a recently published systematic review on prevention of low back pain.[28] Steffens and colleagues also found that an exercise program alone (RR 0.65, 95% CI 0.50 to 0.86) or in combination with education (RR 0.55, 95% CI 0.41 to 0.74) are effective for preventing low back pain. For a more direct comparison with the result of the Steffens review, the current meta-analysis for the exercise intervention was recalculated as RR (instead of OR as in Figures 2 and 4). Exercise reduced the risk of a new episode of neck pain by 53% (RR 0.47, 95% CI 0.32 to 0.68). The calculation for the pooled RR result for the exercise intervention contrast is presented in Figure 5 on the eAddenda.

Although the current systematic review found that exercise programs are likely to roughly halve the risk of a new episode of neck pain, the quality of the evidence is moderate and further high-quality randomised, controlled trials are needed. One randomised, controlled trial[24] evaluating exercise provided participants with health information/stress management training and a workplace assessment as part of the intervention, which means there is uncertainty about the effectiveness of the exercise alone. The durations of the exercise programs were quite long – 9 months[24] and 12 months[23] – which needs to be borne in mind when considering this therapy. Additionally, there are no outcomes beyond 12 months, so the long-term effect is unknown. Furthermore, high-quality randomised, controlled trials are needed to investigate the potential benefit of interventions to prevent episodes of neck pain leading to care seeking, activity limitation, and days lost from work.

In conclusion, the results of this review found moderate-quality evidence that an exercise program reduces the risk of a new episode of neck pain. Ergonomic strategies do not appear to prevent neck pain. Additional trials with longer-term follow-up would more clearly establish the public health implications of this result.

What was already known on this topic: Neck pain is common, but clinical practice guidelines lack recommendations regarding prevention. Past systematic reviews of preventive interventions for neck pain have had important flaws such as the inclusion of non-randomised studies.
What this study adds: Exercise programs substantially reduce the risk of a new episode of neck pain. The evidence for this is of moderate quality and one of the included trials included some co-interventions with the exercise. Ergonomic programs do not appear to significantly reduce the risk of a new episode of neck pain, but the evidence for this is of low quality.

Footnote: [a] Comprehensive Meta-analysis, version 2.2.064, Biostat, Englewood, NJ, USA.

eAddenda: Appendix 1, Figures 2 and 5 can be found online at https://doi.org/10.1016/j.jphys.2018.05.003

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Conflict of interest: Nil.

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Websites

PEDro www.pedro.org.au

5.9 Published eAddenda material

Appendix 1. Database specific search strategy

Medline via Ovid
#1. Neck pain.mp.
#2. neckache.mp.
#3. neck strain.mp.
#4. neck injur*.mp.
#5. neck syndrome.mp.
#6. neck dysfunction.mp.
#7. neck disorder.mp.
#8. cervical pain.mp.
#9. cervicodynia.mp.
#10. cervicalgia.mp.
#11. radiculopathy.mp.
#12. brachialgia.mp.
#13. brachial neuritis.mp.
#14. brachial neuralgia.mp.
#15. brachial plexus neuropath*.mp.
#16. brachial plexus neuritis.mp.
#17. whiplash.mp.
#18. cervico brachial neuralgia.mp.
#19. cervicobrachial neuralgia.mp.
#20. Neck/
#21. Neck Pain/
#22. exp neck injuries/
#23. Radiculopathy/
#24. exp Brachial Plexus Neuropathies/
#25. exp whiplash injuries/
#26. or/1-25
#27. Randomized controlled trial.pt.
#28. controlled clinical trial.pt.
#29. clinical trial.pt.
#30. random*.tw.
#31. placebo*.mp.
#32. trial.ab,ti.
#33. exp Randomized Controlled Trial as Topic/
#34. Controlled Clinical Trial/
#35. Comparative Study/
#36. Follow-Up Studies/
#37. evaluation studies/
#38. exp Clinical Trial/
#39. Random Allocation/
#40. Placebos/
#41. Single-Blind Method/
#42. Double-Blind Method/
#43. or/27-42
#44. (animals not (humans and animals)).sh.
#45. 43 not 44
#46. Prevent*.mp.
#47. prophyla*.mp.
#48. recur*.mp.
#49. relaps*.mp.
#50. reappearance*.mp.
#51. reoccur*.mp.
#52. return*.mp.
#53. Exp Recurrence/
#54. Primary prevention/
#55. Secondary prevention/
#56. or/46-55
#57. 26 and 45 and 56

EMBASE via Ovid

#1. Neck pain.mp.
#2. neckache.mp.
#3. neck strain.mp.
#4. neck injur*.mp.
#5. neck syndrome.mp.
#6. neck dysfunction.mp.
#7. neck disorder.mp.
#8. cervical pain.mp.
#9. cervicodynia.mp.
#10. cervicalgia.mp.
#11. radiculopathy.mp.
#12. brachialgia.mp.
#13. brachial neuritis.mp.
#14. brachial neuralgia.mp.
#15. brachial plexus neuropath*.mp.
#16. brachial plexus neuritis.mp.
#17. whiplash.mp.
#18. cervico brachial neuralgia.mp.
#19. cervicobrachial neuralgia.mp.
#20. Neck/
#21. Neck Pain/
#22. exp Brachial Plexus Neuropathies/
#23. exp neck injuries/
#24. exp whiplash injuries/
#25. Radiculopathy/
#26. or/1-25
#27. Randomi#ed controlled trial.mp.
#28. controlled clinical trial.mp.
#29. clinical trial.mp.
#30. random*.tw.
#31. placebo*.mp.
#32. trial.ab,ti.
#33. Controlled Clinical Trial/
#34. Comparative Study/
#35. exp Clinical Trial/
#36. Randomized Controlled Trial/
#37. Placebo/
#38. Single Blind Procedure/
#39. Double Blind Procedure/
#40. Random Allocation/
#41. Evaluation Studies/
#42. Follow-Up Studies/
#43. or/27-42
#44. Limit 43 to human
#45. Prevent*.mp.
#46. prophyla*.mp.
#47. recur*.mp.
#48. relaps*.mp.
#49. reappearance*.mp.
#50. reoccur*.mp.
#51. return*.mp.
#52. Primary prevention/
#53. Secondary prevention/
#54. Exp Recurrence/
#55. or/45-54
#56. 26 and 44 and 55

CINAHL via Ebsco

S1. “neck pain”
S2. “neck strain”
S3. “neck injur*”
S4. “neck syndrome”
S5. “neck dysfunction”
S6. “neck disorder”
S7. “cervical pain”
S8. “cervicalgia”
S9. “radiculopathy”
S10. “brachialgia”
S11. “brachial neuritis”
S12. “brachial neuralgia”
S13. “brachial plexus neuropath*”
S14. “brachial plexus neuritis”
S15. “whiplash”
S16. (MH “Neck”)
S17. (MH “Neck Pain”)
S18. (MH “Brachial Plexus Neuropathies+)
S19. (MH “Neck Injuries+”)
S20. (MH “Whiplash Injuries”)
S21. (MH “Radiculopathy”)
S22. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21
S23. (MH “Clinical trials+”)
S24. “randomi?ed controlled trial”
S25. “clinical W3 trial”
S26. “single-blind”
S27. “double-blind”
S28. “triple-blind”
S29. S23 OR S24 OR S25 OR S26 OR S27 OR S28
S30. (MH “Placebo Effect”)
S31. (MH “Placebos”)
S32. “placebo*”
S33. “random*”
S34. S30 OR S31 OR S32 OR S33
S35. (MH “Random Sample+”)
S36. (MH “Comparative Studies”)
S37. (MH “Evaluation Research+”)
S38. (MH “Prospective Studies+”)
S39. S35 OR S36 OR S37 OR S38
S40. “follow-up stud*”
S41. “followup stud*”
S42. “control”
S43. “prospectiv*”
S44. “volunteer*”
S45. S40 OR S41 OR S42 OR S43 OR S44
S46. S29 OR S34 OR S39 OR S45
S47. (MH “Animals”)
S48. S46 not S47
S49. “prevent*”
S50. “prophyla*”
S51. “recur*”
S52. “relaps*”
S53. “reappearance*”
S54. “reoccur*”
S55. “return*”
S56. (MH “Preventive trials”)
S57. (MH “Recurrence”)
S58. S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57
S59. S22 AND S48 AND S58

PEDro (https://www.pedro.org.au/ **)**
#1. prevent* in <Title & Abstract> field
#2. Pain in <Problem> field
#3. “head or neck” in <Body Part> field
#3. clinical trial in <Method> field
#4. Match all search term (AND) in <When Searching> field

The Cochrane Library via Wiley
#1. neck pain
#2. neckache
#3. neck strain
#4. neck injur*
#5. neck syndrome
#6. neck dysfunction
#7. neck disorder
#8. cervical pain
#9. cervicodynia
#10. cervicalgia
#11. radiculopathy
#12. brachialgia
#13. brachial neuritis
#14. brachial neuralgia
#15. brachial plexus neuropath*
#16. brachial plexus neuritis
#17. whiplash
#18. cervico brachial neuralgia
#19. cervicobrachial neuralgia
#20. [Neck] explode all trees
#21. [Neck Pain] explode all trees
#22. [Brachial Plexus Neuropathies] explode all trees
#23. [Neck Injuries] explode all trees
#24. [Whiplash Injuries] explode all trees
#25. [Radiculopathy] explode all trees
#26. or #1 - #25
#27. Randomized controlled trial
#28. controlled clinical trial.
#29. clinical trial
#30. random*
#31. placebo*
#32. trial
#33. [Clinical Trials as Topic] explode all trees
#34. [Comparative Study] explode all trees
#35. [Placebos] explode all trees
#36. [Random Allocation] explode all trees
#37. [Single-Blind Method] explode all trees
#38. [Double-Blind Method] explode all trees
#39. [Evaluation Studies as Topic] explode all trees
#40. [Follow-up Studies] explode all trees
#41. or #27 - #40
#42. animal*
#43. #41 not #42
#44. prevent*
#45. prophyla*
#46. recur*
#47. relaps*
#48. reappearance*
#49. reoccur*
#50. return*
#51. [Primary prevention] explode all trees
#52. [Secondary prevention] explode all trees
#53. [Recurrence] explode all trees
#54. or #44 - #53
#55. #26 and #43 and #54

Figure 2. Odds ratio for neck pain episode in randomised, controlled trials on effectiveness of neck pain prevention strategies.

Study	Exp [a] Events (n)	Exp [a] Participants (n)	Con [a] Events (n)	Con [a] Participants (n)	OR (95% CI)	Weight, %	GRADE rating
Ergonomic program versus control							
Pillastrini et al (2007)[22]	7	46	10	53	0.77 (0.27 to 2.22)	8	
Conlon et al (2008)[20]	3	52 [b]	1	18 [b, c]	1.04 (0.10 to 10.69)	2	
Conlon et al (2008)[20]	7	51 [b]	1	18 [b, c]	2.70 (0.31 to 23.66)	2	
Conlon et al (2008)[20]	2	51 [b]	1	18 [b, c]	0.69 (0.06 to 8.15)	1	
Driessen et al (2011)[21]	NR	1472 [b]	NR	1575 [b]	1.01 (0.73 to 1.39)	87	
Pooled effect: I^2 = 0%					1.00 (0.74 to 1.35)		⊕⊕◯◯ Low
Exercise versus control							
Tveito et al (2009)[24]	1	12	8	17	0.10 (0.01 to 0.98)	16	
Sihawong et al (2014)[23]	32	225	72	246	0.40 (0.25 to 0.64)	84	
Pooled effect: I^2 = 0%					0.32 (0.12 to 0.86)		⊕⊕⊕◯ Moderate

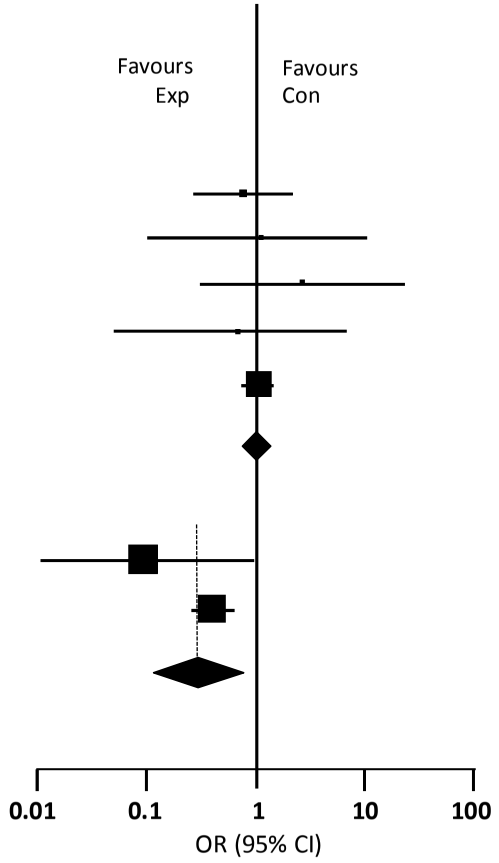

Figure 2. Odds ratio for neck pain episode in randomised, controlled trials on effectiveness of neck pain prevention strategies.

Con = control group, Exp = experimental group, GRADE = Grading of Recommendations Assessment, Development and Evaluation, NR = not reported.

Studies ordered chronologically within prevention strategy category.

[a] Participants with no neck pain at baseline.

[b] Only the baseline sample size was available.

[c] Approximately one third of participants in control group.

Figure 5. Relative risk for neck pain episode in randomised controlled trials investigating exercise strategies.

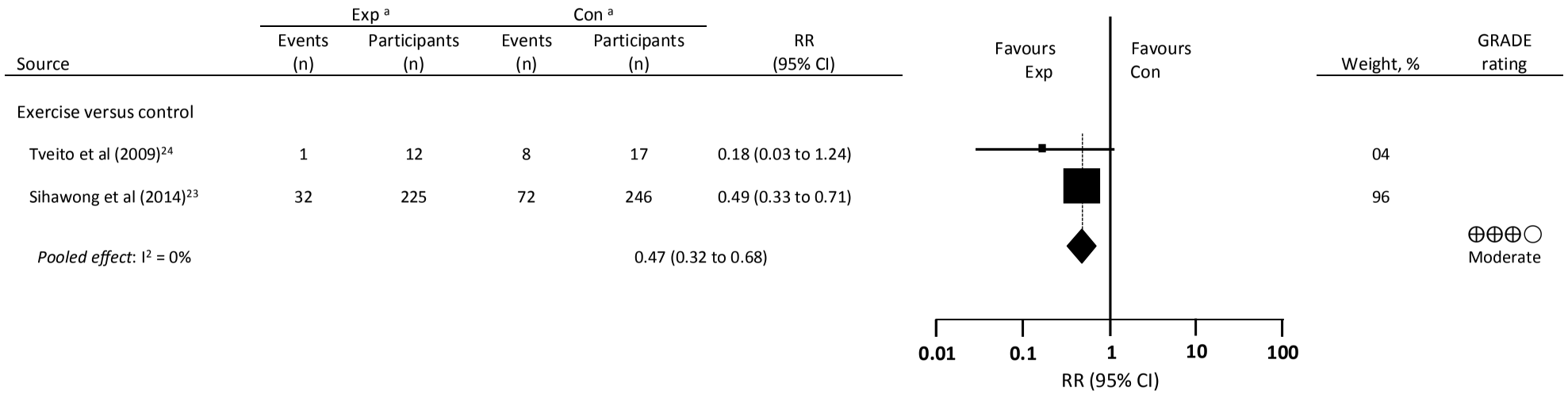

Figure 5. Relative risk for neck pain episode in randomised controlled trials investigating exercise strategies.

Con = control group, Exp = experimental group, GRADE = Grading of Recommendations Assessment, Development and Evaluation.
Studies ordered chronologically within exercise prevention strategy category.
[a] Participants with no neck pain at baseline.

CHAPTER SIX

Discussion and conclusion

6.1 Preface

The work presented in this thesis provides novel data that contribute to the contemporary understanding of effective intervention strategies to prevent spinal pain. The primary aim of this thesis was to investigate the effect of a low-cost and flexible exercise and education program based on the McKenzie method for the prevention of a recurrence of low back pain. **Chapter Two** described the rationale and methods for this study, while **Chapter Three** reported the results from this study. To further explore the effectiveness of prevention strategies to reduce the burden of spinal pain, this thesis also investigated the evidence for prevention strategies aiming to reduce future impact of low back pain (**Chapter Four**), and the evidence for prevention strategies to reduce the risk of an episode of neck pain (**Chapter Five**). The current chapter (**Chapter Six**) provides an overview of the key findings and implications and then discusses future research directions.

6.2 Main findings and implications

6.2.1 The McKenzie-based self-management approach does not appear to reduce risk of back pain recurrences, unlike most previously investigated exercise and education approaches

Despite the current evidence from a systematic review[1] reporting that exercise combined with education can reduce the risk of low back pain, the structure of the programs offered in most of the included trials (e.g. 20 x 1-hour face-to-face sessions) may not be scalable and acceptable. Thus, an effective low-cost, less time-consuming intervention would be ideal, reducing the burden for people seeking healthcare, and increasing the likelihood of large-scale implementation. The randomised controlled trial presented in **Chapter Three,** therefore, provides the first investigation of the effectiveness of the McKenzie-based self-management exercise and education program in the general population for the secondary prevention of a recurrence of low back pain. The trial recruited 262 adults who recently recovered from an episode of low back pain within the last six months. Differently from most previous trials, this study followed participants for a minimum of 12 months and up to 30 months for the primary outcome of a recurrence of low back pain limiting daily activities. The findings from this trial indicate that the experimental intervention is unlikely to reduce the risk of recurrence of low back pain. This is in contrast with a recent systematic review[1] which reported that exercise in combination with education reduces the risk of an episode of low back pain by 45% for up to one year (RR, 0.55; 95% CI, 0.41 to 0.74). The trial findings are also in contrast with a recent

network meta-analysis[2] which summarised the comparative effectiveness of low back pain prevention strategies. The authors of this network meta-analysis review also found exercise and education was effective in preventing low back pain recurrence.

There are important differences between the trial reported in **Chapter Three** and previous exercise and education prevention trials that may help explain the contradictory findings and have implications for clinicians delivering interventions aiming to prevent low back pain. These include differences in the study intervention and population and are discussed below.

6.2.1.1 Nature and dosage of exercise program

The exercise approach investigated in **Chapter Three** was quite different from the approach used in most previous low back pain prevention trials, including the ones reported in the previous systematic reviews[1 2] and **Chapter Four** review, in both the nature of the exercise and the dosage. The experimental intervention in **Chapter Three** involved a simple exercise program that aimed to balance the mechanical forces resulting from the postures or positions used throughout the day by the individual person. For instance, if a person spent most of the day in a flexed posture or position (e.g. sitting), exercise was focused on the opposite direction (i.e. back extensions). Exercises were typically passive movements or stretches and did not aim to increase muscular strength or endurance. The exercise program was taught over only 2 x 30-45 minutes sessions by a physiotherapist. The exercises prescribed varied according to the physiotherapist's initial assessment in terms of frequency, duration, and direction of movement, as this was an individualised intervention program. This typically involved short sessions (e.g. 10 to 15 repetitions) multiple times per day. In contrast, most of the exercise and education programs in previous prevention trials, included a mix of strengthening, co-ordination and aerobic exercises, delivered in multiple sessions per week over a few months. For instance, in the trial by Lonn and colleagues[3] the active back school (experimental intervention) was delivered in 20 sessions over 13 weeks. Each session lasted 60 minutes with exercise comprising: (i) ergonomic principles of bending the knee and hip joints, while keeping the lumbar segments in a neutral position when performing functional exercises and obstacle course simulations; (ii) strength training of legs, pelvis and upper body muscles; (iii) stretching exercises for the calf muscles, hamstrings, rectus femoris, and hip flexors.

Although, most previous studies have investigated exercise programs that include a mix of aerobic and strengthening exercises, unlike the exercise program investigated in **Chapter Three**, a previous study by Larsen and colleagues[4] investigated an experimental intervention with some similarities to that investigated in **Chapter Three**. Their experimental intervention included 15 repetitions of passive prone back extensions performed twice daily, and a single session of the McKenzie method-based education (40 minutes). The Larsen et al[4] study reported a risk reduction of around 60%. Some differences between the experimental intervention in **Chapter Three** and Larsen's study[4] include individualisation of the program based on an examination by a physiotherapist, variability of the direction of exercises (e.g. trunk flexion, prone extension, side gliding) and different dosage of exercises, all based on the need of each individual participant. In contrast, in the Larsen study, there was no individualisation of the experimental intervention, which means all participants were asked to perform the same exercises (i.e. 15 passive prone back extensions) two times per day in group sessions during the study period.

Based on the study in **Chapter Three** and the previous literature, it remains unclear what the optimal exercise mode is for the prevention of low back pain, and which underlying mechanisms contribute to the reduction in the risk of an episode of low back pain. Given most previous trials reporting benefits used a mix of strengthening, coordination and aerobic exercises, clinicians should consider including these when prescribing exercises to prevent low back pain. Most previous trials also delivered the exercises in a group setting so the available literature suggests this approach may be more effective than exercises performed independently as per the study in **Chapter Three**.

6.2.1.2 Different study populations

A further possible reason that could help explain the difference in results between the study presented in **Chapter Three** and previous exercise and education prevention trials is recruitment from different populations. While the trial presented in **Chapter Three** recruited a broader population sample, previous trials have targeted a more specific population group.

The study presented in **Chapter Three** recruited an adult population presenting about half male and half female with a mean age of 42.3 (SD 12.7) years from Sydney in Australia. On the other hand, Larsen et al[4] recruited a specific group of young male military conscripts, with a mean age

of 21 (SD 1.5) years. One possible reason why the intervention may have been more effective in a military population is better compliance with the exercises compared to the compliance in the study population in **Chapter Three**. Although Larsen and colleagues[4] did not provide specific data on compliance with the experimental intervention, the authors reported that this military setting produced greater compliance within the first 3 months where the experimental intervention was supervised by the responsible sergeants and officers. Recruitment from homogeneous populations that potentially optimise the likelihood of a favourable trial outcome, may however limit the ability to generalise the findings to a broader population as demonstrated in **Chapter Three.**

Another study population characteristic that could explain the different results between the trial in **Chapter Three** and previous trials is the restricting of recruitment to people who had previously experienced at least one episode of low back pain. Previous studies report that a history of previous episodes of low back pain is the only significant predictor of recurrence of low back pain.[5 6] In 2008, Stanton and colleagues estimated the 1-year incidence of recurrence of low back pain in subjects recently recovered from acute non-specific low back pain; and determined factors that could predict low back pain recurrence within 1 year.[6] The authors concluded that a previous episode of low back pain increased the odds of a recurrence within the next 12 months by 1.8 to 2.0 times. Similarly, a recent systematic review by da Silva et al[7] concluded that previous episodes of low back pain is the only consistent predictor of a recurrence of low back pain. In many previous studies investigating exercise and education for prevention of low back pain, it is not clear whether participants had experienced a previous episode of low back pain or not, so these studies could have included a mixed population of people who had never experienced an episode of low back pain and people with a history of previous episodes of low back pain. It is possible that the effectiveness of exercise and education is different in people who have and have not experienced previous episodes of low back pain. However, some previous studies[3 8] that limited inclusion to people who had experienced at least one previous episode of low back pain, similar to **Chapter Three**, did find positive effects of exercise and education interventions.

While the study in **Chapter Three** enrolled an inception cohort of people who have recovered from a recent episode of low back pain within the past six months, no previous trial restricted inclusion to participants recently recovered from an episode of low back pain. This may also

contribute to the different findings with the risk of recurrence highest soon after recovering from an episode.[9]

6.2.2 Despite not reducing low back pain recurrence rates, the McKenzie-based approach for prevention of low back pain may reduce care seeking

Spinal pain symptoms are commonly reported in the general population globally and often result in health care utilisation.[9-11] A 2016 Norwegian study investigating the determinants of healthcare contact over a one-year period in a general population reported over 40% of people with either low back pain or neck pain sought health care at least once throughout the one-year follow-up. Similarly, a prospective inception cohort study published in 2019 reported that in the 12-month period after people recover from an episode of low back pain, about 40% will seek care for a recurrence of low back pain.[9] It is therefore important to investigate if programs to prevent spinal pain can also assist people in the self-management of recurrences and reduce the need to seek care.

The study presented in **Chapter Three** reported that, despite not providing a substantial reduction in recurrence of low back pain, the experimental intervention in this trial may produce a substantial reduction in healthcare use. However, the confidence intervals include no effect so caution is required. While this finding may initially seem somewhat surprising, the experimental intervention did specifically aim to provide participants with skills that support them to become more active and responsible in the management of their condition. Participants were instructed to remain active and to use the exercises taught to manage minor recurrent symptoms. Previous low back pain prevention trials and neck pain prevention trials (**Chapter Five**) have not explicitly aimed to empower people with skills to self-manage recurrences or collected data on whether the intervention reduced care seeking. This finding suggests clinicians should incorporate strategies and advice for patients on self-management of future recurrences of spinal pain if they do occur when providing prevention programs.

6.2.3 Exercise and education programs can reduce future low back pain intensity and associated disability

Previous studies investigating prevention of spinal pain, including the work presented in **Chapter Three** and **Chapter Five**, typically focus on the prevention of an episode of spinal pain and therefore include people without current spinal pain symptoms at study entry. A focus on

prevention of a new episode works well in conditions where the onset and end of the episode are clear; however, it has some limitations for chronic fluctuating conditions such as spinal pain. Given many people present with mild ongoing or fluctuating spinal pain patterns, it can be argued that it is also important to investigate prevention of the future consequences due to spinal pain. Some previous studies[12 13] have evaluated the effect of prevention interventions aiming to reduce future low back pain intensity and/or associated disability, and have included a mixed population at baseline (i.e. asymptomatic and symptomatic participants). These studies provide important information on prevention of spinal pain; however, due to population inclusion criteria in previous prevention reviews,[1 2] studies such as these were not included. To date, there is no systematic review of the literature investigating the evidence for prevention strategies to reduce future low back pain intensity and associated disability.

The systematic review presented in **Chapter Four** provides new data on the evidence for prevention strategies aiming to reduce future low back pain intensity and associated disability. The review included only published reports of randomised controlled trials. To differentiate prevention trials from treatment trials we excluded trials that restricted recruitment to only participants with current low back pain. The key findings from this review suggest that exercise programs are likely to reduce future low back pain intensity in the short-term and exercise programs when combined with education can potentially reduce future low back pain-related disability in the long-term.

Despite the systematic review in **Chapter Four** suggesting prevention strategies including exercise can reduce future low back pain intensity and related disability, there are some important considerations. Some of the trials included in the meta-analyses in **Chapter Four** include somewhat different experimental interventions. For example, three trials[14-16] (four intervention contrasts) were included in the meta-analyses for the intervention contrast exercise versus control. The 2014 trial by Barene and colleagues[15] evaluated a generalised exercise program involving activities such as soccer and zumba dancing while the other two trials[14 16] focused more on exercises targeting the back muscles. The study in **Chapter Four** did not directly compare the effectiveness of different exercise approaches, so it remains unclear which exercise approaches are most effective. In addition, the causal mechanisms (e.g. improved muscular strength, co-ordination, or increase aerobic capacity), that are most

important in helping people to prevent future consequences of back pain, cannot be determined from the available literature.

The studies included in the review in **Chapter Four** may be more representative of the broader population than prevention studies that only include people who currently do not have LBP; however, some caution is required when interpreting the results in these heterogenous populations. Some included studies likely include people who have never experienced spinal pain, people with previous spinal pain and others with ongoing spinal pain. The preventative effect of the interventions on future pain and disability may vary across these populations, but this cannot be determined from the included studies, or the analyses conducted in **Chapter Four**.

Despite the review in **Chapter Four** taking a different approach to prevention of spinal pain, an interesting finding was that exercise and education appears to be effective, which is similar to the two recent reviews[1 2] focusing on prevention of an episode of low back pain and the review in **Chapter Five**, investigating prevention of neck pain. These findings suggest clinicians can consider using exercise and education approaches for preventing both future episodes and the future impacts of spinal pain. The findings also suggest these exercise approaches may be effective in people with and without current or previous spinal pain; however, further investigation of this is needed as discussed previously.

6.2.4 The current evidence suggests that exercise programs may also reduce the risk of neck pain

To further enhance understanding of the prevention of spinal pain, **Chapter Five** presents a systematic review on the prevention of neck pain. No previous systematic review has investigated only randomised controlled trials and included trials recruiting only people asymptomatic at study entry. Thus, **Chapter Five** investigated the evidence for interventions aiming to reduce the risk of a new episode of neck pain. It appears that exercise programs are likely to prevent neck pain episodes. This is an interesting finding as what seems to reduce future low back pain intensity (**Chapter Four**) is also what helps to prevent neck pain episodes (**Chapter Five**). Only two trials were pooled in the meta-analysis for the exercise intervention contrast.[17 18] Similarly to the findings in **Chapter Four,** the included trials in the study in **Chapter Five** investigated different approaches to the exercise. For example, Sihawong and colleagues[17]

investigated an exercise program involving stretching and endurance exercises restricted to the muscles within the neck region, while the trial by Tveito and colleagues[18] evaluated an integrated health program comprising a generalised whole-body exercise program. Consequently, the most effective exercise program to reduce future neck pain episodes remains unclear. Therefore, clinicians should consider patient preference and their clinical judgement of the individual requirements when selecting an exercise program to help an individual in preventing neck pain.

6.2.5 Defining prevention of spinal pain is complex

Typically, prevention strategies are defined in three different levels: primary prevention, secondary prevention, and tertiary prevention.[19] However, given the current understanding that spinal pain is a lifelong complex condition commonly presenting with recurrent episodes, or mild ongoing pain with intermittent flare-ups, defining the stages of spinal pain prevention is complex.[20-22]

The studies presented in **Chapter Three** and **Chapter Five** would commonly be considered secondary prevention studies. They included people at baseline who had little or no current spinal pain, and in some cases had experienced previous episodes of pain. The study presented in **Chapter Four** was purposely conducted to include a wider range of studies including those that enrolled a mixed population with and without current pain symptoms, which are more representative of the general population. This review (**Chapter Four**) investigated the effectiveness of prevention strategies on the future consequences of low back pain using the outcomes of pain intensity and disability, as opposed to the dichotomous outcome of a new episode of low back pain used in **Chapter Three**, as it cannot be used in those who currently experience back pain. The studies in this thesis collectively provide an insight into the complexity of defining prevention of spinal pain, particularly in terms of the relevant populations and outcomes.

Owing to the complexity of the definition of spinal pain prevention, rather than defining spinal pain prevention studies using traditional terms of primary, secondary and tertiary prevention, it may be more appropriate and useful, when designing future prevention studies, to clearly define the population and the outcomes of interest. For example, a workplace study targeting all employees and aiming to prevent spinal pain from impacting employees' workability in the

future, could include, primary prevention (those who have never experienced spinal pain symptoms), secondary prevention (those who have had previous episodes but are currently asymptomatic) and tertiary prevention (those with ongoing low levels of pain) but who are currently working. Importantly, this hypothetical study would likely not be included in many systematic reviews such as that by Steffens et al[1] or that in **Chapter Five** of the thesis, despite providing important information on prevention strategies for future consequences of this condition. Therefore, clinicians must search for evidence on prevention approaches that best matches the population and outcomes of interest to them and their patients, and not presume that all prevention is the same. That said, the available evidence, including that provided in **Chapter Four** and **Chapter Five** of this thesis, suggests that exercise alone and/or exercise combined with education may be effective for the prevention in different populations and for different outcomes.

Given the often fluctuating nature of spinal pain, the distinction between prevention and treatment is not as clear as it might be for many other conditions. In people with ongoing mild pain that does not substantially impact on their activities of daily living, a focus on prevention of flare-ups may be optimal. This thesis did not provide any evidence on interventions aiming to specifically prevent flare-ups of mild pain as these studies would have been excluded from both the reviews in **Chapter Four** and **Chapter Five**.

6.3 Research implications and future directions

The work in this thesis has implications for future research and helps identify priorities for future studies investigating the prevention of spinal pain. The first research implication is that while the majority of existing literature suggests exercise interventions can help reduce spinal pain, some approaches such as that tested in **Chapter Three** are not effective and the best exercise approach and dosage are unclear. Future trials investigating head-to-head comparisons of different exercise interventions to prevent spinal pain are required to clarify which exercise approaches are most effective and for which individuals. Investigation of mediators within these trials may also improve understanding of the causal mechanisms involved in effective spinal pain prevention programs. This body of work would enable clinical practice guidelines to provide stronger and more informed recommendations on the prevention of spinal pain. Currently, most guidelines do not provide recommendations regarding the prevention of spinal pain.

The second research implication from this thesis is that the included populations vary greatly across the existing prevention studies and may contribute to the variability in results. The generalisability of some previous studies, such as the Larsen et al[4] study in army recruits, is limited due to the specific population and setting. Thus, future high-quality trials investigating prevention strategies for spinal pain should ideally recruit a broad population, such as those included in the study in **Chapter Three**, to enhance the generalisability of the findings.

The third research implication is the need for more work to better define what is meant by prevention of spinal pain and determine what types of prevention studies are most important. As discussed in this thesis, prevention can include participants who have never experienced spinal pain, those who have had previous episodes (either recently or a long time in the past), and those with current low levels of pain. The focus of prevention studies can be on preventing future episodes of spinal pain, preventing flare-ups in those with current mild pain, or preventing future pain and disability. It is unclear if prevention interventions are equally effective for these different populations and outcomes. Future studies that include mixed populations such as those with and without a previous history of spinal pain, or those with and without current mild pain, could investigate whether these factors are moderators for the effectiveness of interventions aiming to prevent spinal pain.

The fourth research implication is that, despite the promising results in **Chapter Three** in terms of preventing future healthcare, the trial was not adequately powered to answer this question. This outcome is important and future prevention studies should investigate whether the prevention program can reduce healthcare seeking related to spinal pain. In addition, qualitative studies would help understand what aspects of the prevention program are most important in helping reassure patients to self-manage minor recurrences of low back pain without seeking healthcare. Furthermore, there is a lack of high-quality studies investigating the impact of prevention strategies for spinal pain on other important outcomes such as quality of life, workability, and days lost from work.

6.4 Conclusions

In summary, the body of research presented in this thesis includes important findings from randomised controlled trials and systematic reviews investigating prevention strategies to

reduce the burden of spinal pain. The findings from the studies presented in **Chapter Four** and **Chapter Five** demonstrate that prevention strategies investigating exercise alone and exercise combined with education may reduce future low back pain intensity and associated disability (**Chapter Four**), and reduce the risk of an episode of pain in the neck (**Chapter Five**). The findings from these studies are similar to the results of two recently reported systematic reviews.[1 2] However, the study reported in **Chapter Three**, which investigated an exercise and education program based on the McKenzie method did not provide a substantial benefit for prevention of a new episode of low back pain. Therefore, future research is important to understand whether the different finding is because the experimental intervention presented in **Chapter Three** is different in terms of, the mode and dosage of the exercise or the different population characteristics. Thus, future research is necessary to address these uncertainties.

6.5 References

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APPENDICES

Appendix 1: Copyright license for figure 1 - introduction (Chapter One)

Appendix 2: Copyright license for figure 2 - introduction (Chapter One)

Appendix 3: Ethical and scientific approval (Chapter Three)

Appendix 4: Trial registration (Chapter Three)

Appendix 5: Participant Information and Consent Form (Chapter Three)

Appendix 6: PROSPERO registration (Chapter Four)

Appendix 7: PROSPERO registration (Chapter Five)

Appendix 8: Media coverage - Physiotherapy InMotion online (Chapter Five)

Pages 156-162 ("Appendix 1: Copyright license for figure 1 - introduction (Chapter One)" and "Appendix 2: Copyright license for figure 2 - introduction (Chapter One)") of this thesis have been removed as they contain copyright material.

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MACQUARIE University
SYDNEY·AUSTRALIA

21 April 2016

Dear Prof Hancock

Reference No: 5201600187

Title: *SAFE - Secondary prevention of a recurrence of low back pain.*

Thank you for submitting the above application for ethical and scientific review. Your application was considered by the Macquarie University Human Research Ethics Committee (HREC (Medical Sciences)).

I am pleased to advise that ethical and scientific approval has been granted for this project to be conducted at:

- Macquarie University

This research meets the requirements set out in the *National Statement on Ethical Conduct in Human Research* (2007 – Updated May 2015) (the *National Statement*).

Standard Conditions of Approval:

1. Continuing compliance with the requirements of the *National Statement,* which is available at the following website:

http://www.nhmrc.gov.au/book/national-statement-ethical-conduct-human-research

2. This approval is valid for five (5) years, subject to the submission of annual reports. Please submit your reports on the anniversary of the approval for this protocol.

3. All adverse events, including events which might affect the continued ethical and scientific acceptability of the project, must be reported to the HREC within 72 hours.

4. Proposed changes to the protocol and associated documents must be submitted to the Committee for approval before implementation.

It is the responsibility of the Chief investigator to retain a copy of all documentation related to this project and to forward a copy of this approval letter to all personnel listed on the project.

Should you have any queries regarding your project, please contact the Ethics Secretariat on 9850 4194 or by email ethics.secretariat@mq.edu.au

The HREC (Medical Sciences) Terms of Reference and Standard Operating Procedures are available from the Research Office website at:

http://www.research.mq.edu.au/for/researchers/how_to_obtain_ethics_approval/human_research_ethics

The HREC (Medical Sciences) wishes you every success in your research.

Yours sincerely

Professor Tony Eyers
Chair, Macquarie University Human Research Ethics Committee (Medical Sciences)

This HREC is constituted and operates in accordance with the National Health and Medical Research Council's (NHMRC) *National Statement on Ethical Conduct in Human Research* (2007) and the *CPMP/ICH Note for Guidance on Good Clinical Practice*.

Details of this approval are as follows:

Approval Date: 15 April 2016

The following documentation has been reviewed and approved by the HREC (Medical Sciences):

Documents reviewed	Version no.	Date
Macquarie University Ethics Application Form		Received 9/03/2016
Correspondence responding to the issues raised by the HREC (Medical Sciences)		Received 6/04/2016
Protocol	1	10/02/2016
MQ Participant Information and Consent Form (PICF) entitled '*SAFE: Secondary Prevention of a Recurrence of Low Back Pain*'	1	1/03/2016
Participant Assessment Questionnaire – Baseline Questionnaire (including DASS 21 and Impact of back pain questionnaire)	1	9/03/2016
Follow-up Assessment Questionnaire (including Physical activity questionnaire – 3 & 12 months, Impact of back pain questionnaire – 3, 6, 9 & 12 months and Credibility expectance questionnaire (CEQ) – 3 months)	1	6/04/2016
Advertising Flyer	1	9/03/2016

***If the document has no version date listed one will be created for you. Please ensure the footer of these documents are updated to include this version date to ensure ongoing version control.**

Your ACTRN (registration number): ACTRN12616000926437

From: info@actr.org.au [mailto:info@actr.org.au]
Sent: Tuesday, 12 July 2016 10:31 AM
To: Mark Hancock <mark.hancock@mq.edu.au>
Subject: Your ACTRN (registration number): ACTRN12616000926437

Dear Mark Hancock,

Re: SAFE – Effectiveness of Mckenzie based self-management for the secondary prevention of a recurrence of low back pain.

Thank you for submitting the above trial for inclusion in the Australian New Zealand Clinical Trials Registry (ANZCTR).

Your trial has now been successfully registered and allocated the ACTRN: ACTRN12616000926437

Web address of your trial: http://www.ANZCTR.org.au/ACTRN12616000926437.aspx
Date submitted: 5/07/2016 8:51:59 AM
Date registered: 12/07/2016 10:30:44 AM
Registered by: Mark Hancock
Principal Investigator: Mark Hancock

If you have already obtained Ethics approval for your trial, please send a copy of at least one Ethics Committee approval letter to info@actr.org.au or by fax to (+61 2) 9565 1863, attention to ANZCTR.

Note that updates should be made to the registration record as soon as any trial information changes or new information becomes available. Updates can be made at any time and the quality and accuracy of the information provided is the responsibility of the trial's primary sponsor or their representative (the registrant). For instructions on how to update please see http://www.anzctr.org.au/Support/HowToUpdate.aspx.

Please also note that the original data lodged at the time of trial registration and the tracked history of any changes made as updates will remain publicly available on the ANZCTR website.

The ANZCTR is recognised as an ICMJE acceptable registry (http://www.icmje.org/faq.pdf) and a Primary Registry in the WHO registry network (http://www.who.int/ictrp/network/primary/en/index.html).

If you have any enquiries please send a message to info@actr.org.au or telephone +61 2 9562 5333.

Kind regards,
ANZCTR Staff

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Email: mark.hancock@ mq.edu.au

Chief Investigator's / Supervisor's Name & Title: A/Professor Mark Hancock

Participant Information and Consent Form

Name of Project: SAFE: Secondary Prevention of a Recurrence of Low Back Pain

You are invited to participate in a research study comparing the effectiveness of two different approaches which aim to prevent recurrences of low back pain in people who have recently recovered from an episode of low back pain. One approach involves receiving advice from a physiotherapist over the phone and also a booklet to read. The other approach involves meeting with a physiotherapist in person on two occasions to be shown some exercises and given advice. The purpose of this study is to investigate which of the two approaches is better at preventing or delaying future recurrences of low back pain.

The study is being conducted by Mr Tarcisio Folly de Campos (ph: (02) 9850 6617, email: tarcisio.decampos@mq.edu.au), a student in the Department of Health Professions to meet the requirements of a PhD under the supervision of Associate Professor Mark Hancock (ph: (02) 98506622, email: mark.hancock@mq.edu.au) of the Department of Health Professions.

If you decide to participate, you will be asked to complete a baseline questionnaire over the phone. This will take approximately 10 minutes to complete and asks about demographic characteristics, general health, work status, history of back pain, physical activity levels, and psychological factors. You will then be randomly allocated (like the flip of a coin) to one of the two prevention approaches (advice over the phone and a booklet, or 2 face to face sessions). You will have a 50% chance of being allocated to either approach. You will not be able to choose the treatment group you are allocated to. The study is conducted this way to ensure that the information obtained is reliable.

Participants allocated to the phone advice and booklet group will receive education from a physiotherapist over the phone on strategies to avoid future back pain. This will last approximately 15 minutes depending on how many questions participants have. Participants in this group will also be posted a booklet on managing back pain and can contact the physiotherapist on one additional occasion if they have any further questions.
Participants allocated to the two face to face sessions with a physiotherapist will be required to attend a physiotherapist clinic in the community for 2 sessions of 30-40 minutes approximately 2 weeks apart. The physiotherapist will ask some questions about daily activities and previous back pain, do a simple examination (e.g. look at our flexibility, strength and posture) and then provide a home program and advice which aim to prevent future back pain.

All participants will then be contacted each month by email or text message (based on your preference) and asked if they have had a recurrence of low back pain. Responding to this should take only 1 minute. The monthly follow-ups will continue either until you have a recurrence of back pain, or for between 12 months and 30 months depending on when you entered the study (the first participant enrolling in the study will be followed for up to 30 months while the last participant will be followed for 12 months). If you do not respond to monthly email or text messages within 48 hours, you will be contacted by phone. If you do

report a recurrence a researcher will then, contact you to obtain a description of this new episode of low back pain. This will take less than 5 minutes. At 3, 6, 9 and 12 months after entering the study you will be asked to complete a short questionnaire about any impact back pain has had on your life over the previous 3 months. This can either be done as an online survey or over the phone depending on your preference and will take approximately 5 minutes to complete.

The known risks of this study are minimal. The intervention in both groups may encourage moderate physical activity, gentle stretches and changes to posture. Before enrolling you in the study the physiotherapist will ask you some questions to make sure you are appropriate for the study. While the existing knowledge suggests these interventions are positive for general health, and may reduce the risk of future back pain, it is possible that some participants may experience some temporary soreness or a recurrence of low back pain. You will not be paid to participate in the study; however, the interventions from the physiotherapist will be free to you.

Any information or personal details gathered in the course of the study are confidential, except as required by law. No individual will be identified in any publication of the results. The data collected in this study may be made available to other researchers, in a de-identified form, for future Human Research Ethics Committee approved research projects. A summary of the results of the data can be made available to you on request. If you would like to be provided with this summary, please email Mr Tarcisio Folly de Campos (email: tarcisio.decampos@mq.edu.au).

Participation in this study is entirely voluntary: you are not obliged to participate and if you decide to participate, you are free to withdraw at any time without having to give a reason and without consequence.

I, _____ have read or had read to me, and understand the information above and any questions I have asked have been answered to my satisfaction. I agree to participate in this research, knowing that I can withdraw from further participation in the research at any time without consequence. I have been given a copy of this form to keep.

Participant's Name:_____
(Block letters)

Participant's Signature: _____ Date:_____

Investigator's Name:_____
(Block letters)

Investigator's Signature: _____ __ Date:_____

The ethical aspects of this study have been approved by the Macquarie University Human Research Ethics Committee. If you have any complaints or reservations about any ethical aspect of your participation in this research, you may contact the Committee through the Director, Research Ethics & Integrity (telephone (02) 9850 7854; email ethics@mq.edu.au). Any complaint you make will be treated in confidence and investigated, and you will be informed of the outcome.

(PARTICIPANT'S COPY)

PROSPERO
International prospective register of systematic reviews

NHS National Institute for Health Research

The effectiveness of interventions for prevention of low back pain and associated disability: a systematic review and meta-analysis protocol.

Tarcisio Folly de Campos, Mark Hancock, Chris Maher, Daniel Steffens, Joel Fuller

Citation

Tarcisio Folly de Campos, Mark Hancock, Chris Maher, Daniel Steffens, Joel Fuller. The effectiveness of interventions for prevention of low back pain and associated disability: a systematic review and meta-analysis protocol.. PROSPERO 2018 CRD42018107946 Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018107946

Review question

What is the effectiveness of interventions for prevention of low back pain and associated disability?

Searches

Electronic searches of MEDLINE via Ovid, EMBASE via Ovid, CINAHL, Physiotherapy Evidence Database (www.pedro.org.au), and The Cochrane Central Register of Controlled Trials (CENTRAL) via The Cochrane Library will be performed to identify potential studies.
A sensitive search strategy will be based on the recommendations of the Cochrane Back and Neck Group[1] for “randomised controlled trials” and “low back pain”, combined with search terms for “prevention”[2].
The reference lists of relevant systematic reviews and randomised, controlled trials will be screened for additional studies and we will also use citation tracking of all included trials.
One reviewer (TFC) will screen all titles and exclude only clearly irrelevant studies. The titles and abstracts of the remaining studies will be reviewed by two independent reviewers (TFC and DS or JTF). For each potentially eligible study, reviewers will obtain the full-text article which will be assessed against the inclusion and exclusion criteria by two independent reviewers (TFC and DS or JTF). In cases of disagreement, a third reviewer will be consulted if consensus cannot be reached (CGM or MJH).
Non-English language studies will be included if an appropriate translation can be obtained. Otherwise such studies will be noted but excluded from analysis. This review will have no restrictions on publication date.
[1]. Furlan DA, et al. Spine. 2015;40(21):1660-1673.
[2]. Burton AK, et al. European Spine Journal. 2006;15(2):s136-s168.

Types of study to be included

Only randomised, controlled trials will be included. Studies that used a quasi-randomised design will be excluded.

Condition or domain being studied

Prevention of low back pain.

Participants/population

Studies recruiting people of any age and from community or occupational settings. Studies must not present an inclusion criterion of participants with current low back pain because this review is not including primary treatment studies.

Intervention(s), exposure(s)

Studies investigating any intervention aiming to prevent/reduce the impact of low back pain and/or low back pain related-disability (e.g. workplace interventions to control risk factors for low back pain, interventions to make the person more fit/healthy/resilient, education on a healthy lifestyle to reduce risk of low back pain) will be included. We will also include intervention groups that are composed of one or more interventions combined (e.g. exercise and education).

Comparator(s)/control
The experimental group had to be compared to a group that received no intervention, sham intervention or minimal intervention.

Context
Studies looking at low back pain prevention strategies aiming to reduce the impact of low back pain in the community or occupational setting. Studies recruiting from populations presenting for treatment (care seeking) due to an episode of low back pain will be excluded.

Primary outcome(s)
To be included, studies need to report an outcome measure of low back pain intensity and/or low back pain related-disability measured at least 3 months post randomisation.
Primary outcome(s)
- Pain intensity measured by a self-reported outcome measure (e.g. visual analogue scale or numerical rating scale).
- Disability measured by a self-reported outcome measure (e.g. Oswestry Disability Index, Roland-Morris Disability Questionnaire).

Secondary outcome(s)
Secondary outcome(s)
Other patient centered outcomes relevant to back pain such as quality of life.

Data extraction (selection and coding)
Relevant data will be independently extracted by two reviewers (TFC and DS or JTF) using a standardised form, which will be piloted before use. In case of disagreement, a third reviewer will be consulted. The data extraction form will collate the following information: population characteristics; trial characteristics, description of interventions; the comparison characteristics; and point estimates and measures of variability for outcomes. Authors will be contacted for additional information if needed.

Risk of bias (quality) assessment
Risk of bias will be assessed using the Physiotherapy Evidence Database Scale[3], [4] by downloading the available scores from the PEDro database (http://www.pedro.org.au). If scores are not available online, two independent reviewers will assess the methodological quality of the trials (TFC and DS or JTF). A third independent reviewer will resolve any disagreement (CGM or MJH). Methodological quality is not an inclusion criterion.
The overall quality of evidence will be assessed for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.[5],[6] The GRADE classification will be downgraded one level per study flaw, from high quality, if any of the following flaws are present: (i) Design limitation (>25% of participants from studies with low methodological quality – PEDro score <7); (ii) Inconsistency of results (wide variation of point estimates across individual trials); (iii) Imprecision (this limitation will be considered present whenever a pooled outcome is based on <400 total participants).
[3]. Macedo LG, et al. J Clin Epidemiol. 2010;63(8):920-925.
[4]. Maher CG, et al. Phys Ther. 2003;83(8):713-721.
[5]. Atkins D, et al. BMJ. 2004;328(7454):1490.
[6]. Guyatt GH, et al. BMJ. 2008;336(7650):924-926

Strategy for data synthesis
If studies are considered sufficiently homogeneous, according to their population, prevention strategy, outcome measure and follow-up time point, results will be pooled in a random-effects meta-analysis. To accommodate the different scales used for outcome measures, we will convert outcomes to a common 0 to 100 scale. The I^2 statistics will be used to assess what proportion of the observed variance reflects differences in the true effect sizes rather than sampling error.

Analysis of subgroups or subsets

Subgroup analyses will separate studies for analysis according to shared characteristics and outcomes to determine if this explains differences in effect estimates between studies. If data permit, we will analyse studies separately based on the following:
(i) Characteristics of population (e.g. pregnant or adolescent cohorts);
(ii) Characteristics of prevention strategies (e.g. exercise or ergonomic interventions);
(iii) Follow-up period (e.g. short- and long-term follow-ups).

Contact details for further information

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Department of Health Professions, Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia.
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Assistant/Associate Professor Mark Hancock. Macquarie University
Professor Chris Maher. The University of Sydney
Dr Daniel Steffens. Surgical Outcomes Research Centre (SOuRCe)
Dr Joel Fuller. Macquarie University

Anticipated or actual start date

01 September 2018

Anticipated completion date

01 June 2019

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None

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None known

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English

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Australia

Stage of review

Review_Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Disabled Persons; Humans; Low Back Pain; Pain Measurement

Date of registration in PROSPERO

10 September 2018

Date of publication of this version

10 September 2018

Details of any existing review of the same topic by the same authors

Stage of review at time of this submission

The review has not started

Stage	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Versions

10 September 2018

UNIVERSITY of York
Centre for Reviews and Dissemination

NHS
National Institute for
Health Research

PROSPERO International prospective register of systematic reviews

Prevention of neck pain: a systematic review of randomised controlled trials

Tarcisio F. de Campos, Chris G. Maher, Daniel Steffens, Joel Fuller, Mark J. Hancock

Citation

Tarcisio F. de Campos, Chris G. Maher, Daniel Steffens, Joel Fuller, Mark J. Hancock. Prevention of neck pain: a systematic review of randomised controlled trials. PROSPERO 2017:CRD42017055174 Available from http://www.crd.york.ac.uk/PROSPERO_REBRANDING/display_record.asp?ID=CRD42017055174

Review question(s)

What is the effectiveness of interventions for prevention of neck pain?

Searches

Electronic searches of MEDLINE via Ovid, EMBASE via Ovid, CINAHL, Physiotherapy Evidence Database (PEDro) (www.pedro.org.au), and The Cochrane Central Register of Controlled Trials (CENTRAL) via The Cochrane Library will be performed to identify potential studies.

A sensitive search strategy will be used based on the recommendations of the Cochrane Back and Neck Group [1] for “randomised controlled trials” and “neck pain”, as well as with search terms for “prevention”.

The reference lists of relevant reviews and randomized trials will be screened for additional studies and we will also use citation tracking of all included trials.

One reviewer (TFC) will screen all titles and exclude clearly irrelevant studies. The abstracts of the remaining studies will be reviewed by two independent reviewers (TFC and DS or JF). For each potentially eligible study, reviewers will obtain the full-text article which will be assessed against the inclusion and exclusion criteria by two independent reviewers (TFC and DS or JF). In cases of disagreement, a third reviewer will be consulted if consensus cannot be reached (MJH or CGM).

Non-English language studies will be included if an appropriate translation can be obtained. Otherwise such studies will be noted but excluded from analysis. This review will have no restrictions on publication date.

Reference:

[1]. Furlan DA, Malmivaara GA, Chou AR, et al. 2015 Updated Method Guideline for Systematic Reviews in the Cochrane Back and Neck Group. An Internationl journal for the study of the spine. 2015;40(21):1660-1673.

Types of study to be included

Only randomised controlled trials (RCTs) will be included. Studies that used a quasi-randomised design will be excluded. Trials comparing two prevention strategies will be also excluded.

Condition or domain being studied

Effectiveness of prevention strategies for neck pain.

Participants/ population

To be included, studies need to include participants without current neck pain at study entry or at least one outcome was not present at baseline (e.g. some participants had mild neck pain, but all were working and the study outcome was an episode of work absence due to neck pain.

Intervention(s), exposure(s)

Studies using any intervention aimed to prevent future episode of neck pain will be included. We will also include intervention groups that are composed of one or more interventions combined (e.g. exercise and education).

Comparator(s)/ control

The intervention group must be compared to no intervention/placebo or minimal intervention. Studies investigating the additional benefit of a treatment (e.g. exercise + education versus exercise alone) will be also included.

Context

No restriction will be placed on the setting or context of the included studies.

Outcome(s)

Primary outcomes

The primary outcome is a new episode of neck pain.

Secondary outcomes

The secondary outcomes include a new episode of neck pain leading to care seeking, activity-limitation or work loss. Measures of pain or disability over the follow-up period will also be secondary outcomes.

Data extraction, (selection and coding)

Relevant data will be independently extracted by two reviewers (TFC and DS or JF) using a standardised form, which will be piloted before use. In cases of disagreement, a third reviewer (MJH or CGM) will be consulted and a decision will be made by consensus. The extraction form will include the following criteria: participant characteristics, trial characteristics, description of interventions and point estimates and measures of variability for outcomes. Authors will be contacted for additional information if needed.

Risk of bias (quality) assessment

Risk of bias will be assessed using the Physiotherapy Evidence Database Scale (PEDro) [2, 3] by either downloading the available scores from the PEDro database (http://www.pedro.org.au) or rating the trial ourselves. If scores are not available two independent reviewers (TFC and DS or JF) will assess the quality of the trials. A third independent reviewer (MJH or CGM) will resolve any disagreement. Methodological quality is not an inclusion criterion.

The overall quality of evidence will be assessed for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [4]. The GRADE classification will be downgraded one level per study flaw, from high quality, if any of the following flaws are present: (i) Design limitation (>25% of participants from studies with low methodological quality – PEDro score <7); (ii) Inconsistency of results (wide variation of point estimates across individual trials); (iii) Imprecision (this will be based on a threshold of <400 participants for each pooled outcome, and also observation of the 95% confidence intervals in cases of dichotomous outcomes).

The quality of evidence will be defined as: (i) High quality - further research is unlikely to change our confidence in the estimate of effect. There are no known or suspected reporting biases; all domains fulfilled; (ii) Moderate quality - Further research is likely to have an important impact on our confidence in the estimate of effect and might change the estimate; one of the domains not fulfilled; (iii) Low quality - Further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; two of the domains not fulfilled; Very low quality - We are uncertain about the estimate; three of the domains not fulfilled.[5]

References:

[2]. Macedo LG, Elkins MR, Maher CG, Moseley AM, Herbert RD, Sherrington C. There was evidence of convergent and construct validity of Physiotherapy Evidence Database quality scale for physiotherapy trials. Journal of Clinical Epidemiology. 2010;63(8):920-925.

[3]. Maher CG, Sheerington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. (Research Report).(Physiotherapy Evidence Database). Physical Therapy. 2003;83(8):713.

[4]. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. BMJ (Clinical research ed.). 2004;328(7454):1490.

[5]. Tulder M, Koes B, Malmivaara A. Outcome of non-invasive treatment modalities on back pain: an evidence-based review. European Spine Journal. 2006;15(1):S64-S81.

Strategy for data synthesis
If studies are considered sufficiently homogenous, results will be pooled. The I-squared statistics will be used to assess the heterogeneity between-trials, and random effects model will be used among trials. A meta-analysis will be conducted where studies are considered homogeneous with regards to the prevention strategy, outcome measure, and follow-up time point.

Analysis of subgroups or subsets
We will analyse studies separately based on the following: (i) Primary or secondary prevention; (ii) Types of prevention strategies. Trials that included a mixed sample (i.e. people with or without previous neck pain episodes) will be considered primary prevention if =50% of the sample has no previous neck pain history. Trials reporting <50% of the sample without previous neck pain episodes will be considered as secondary prevention.

Dissemination plans
The results of this review will be submitted to a peer-reviewed journal for publication as well as presented at national and international conferences.

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Stage of review at time of this submission	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Pages 178-179 of this thesis ("Appendix 8: Media coverage - Physiotherapy InMotion online (Chapter Five)") have been removed as they contain published material. Please refer to the following citation for details of the article contained in these pages:

de Campos TF. A closer look at the research - Interventions to prevent neck pain. *InMotion* August 2018: 51-52. InMotion Archives: https://australian.physio/inmotion