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The role of fear avoidance beliefs as a risk factor for chronicity in patients with acute or sub-acute non-specific low back pain: a prognostic systematic review.

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Abstract

BACKGROUND CONTEXT: Psychological factors, including fear avoidance beliefs, are believed to influence the development of chronic low back pain (LBP).

PURPOSE: The purpose of this review was to determine the prognostic importance of fear avoidance beliefs for clinically relevant outcomes in patients with nonspecific LBP.

DESIGN/SETTING: The design of this study was a systematic review.

METHODS: In August 2021, the following databases were searched: Ovid/Medline, Cochrane Library, PubMed/Medline, Scopus, and Web of Science. To ensure the completeness of the search, a hand search and a search of bibliographies was conducted and all relevant references included. A total of 742 references were retrieved, leaving 370 references after the removal of duplicates. For 83 references, the full-text was assessed and, finally, 6 studies were included in the analysis.

RESULTS: Six studies, evaluating 1398 patients, were included in this systematic review. Several of these were rated at low/moderate risk of bias. Four studies provided that fear-avoidance beliefs and behavior are a risk for chronicity (pain and disability) in patients with acute and sub-acute low back pain at the 6 and 12 month follow-up. Moreover demographic and historical variables in conjunction and in comparison to fear-avoidence behavior make a contribution to the prediction. In two of six included studies the results did not clearly support that fear-avoidance beliefs are predictive of constant low back pain.

CONCLUSIONS: This systematic review has provided moderate evidence that fear avoidance beliefs and behavior are prognostic for poor outcome in acute and sub-acute LBP, and thus early treatment, including interventions to reduce fear avoidance beliefs, may avoid delayed recovery and chronicity.

Summary

1. Introduction

Low back pain (LBP) is defined as pain on the posterior aspect of the body from the lower margin of the twelfth ribs to the lower gluteal folds, with or without radiation to the knee (but not below the knee), which may cause the inability to do the normal daily activities or which may cause the absence from work (Govannoni et al., 2006).

Most people who experience low back pain have “non-specific low back pain”, a diagnosis of exclusion that includes heterogeneous presentation and symptoms not attributed to a recognizable, known specific pathology (eg, infection, tumor, osteoporosis, fracture, structural deformity, inflammatory disorder, radicular syndrome, or cauda equina syndrome) (Balagué et al., 2012).

Low back pain has a variable clinical course: at 6 months following onset, 16% of patients initially off-work remain off-work, and at 12 months post-onset, 62% of all patients still have pain; within 12 months of onset, recurrences of pain and of work absence are common (Hestbaek et al., 2003).

Several prognostic factors have been associated with persistent low back pain and poor clinical outcomes (Nieminen et al., 2021), including psychological aspects related to fear (Waddell et al., 1993).

Previous systematic reviews (Pincus et al., 2006; Wertli, Rasmussen-Barr, et al., 2014) identified very low to moderate quality of evidence that fear-avoidance beliefs and behavior are associated with high levels of pain intensity and disability in individuals with low back pain, but those reviews indicated that more studies are needed to strengthen the evidence.

Fear-avoidance is an emotional response to an identifiable threat with a behavioral response that prevents an aversive stimulus (Adolphs, 2013). It may be considered a protective behavior for those who have experienced acute or intense pain; however, it may be counterproductive in the long term and cause activity restrictions (Gatchel et al., 2016).

The Fear Avoidance Model is used widely to explain how psychological factors affect the experience of pain, and the development of chronic pain and disability (Linton & Shaw, 2011).

According to this model, negative beliefs about pain and/or negative illness information leads to a catastrophizing response in which the worst possible outcome is imaged; this leads to fear of activity and avoidance, which in turn causes disuse and resultant distress, reinforcing the original negative appraisal in a deleterious cycle (Lethem et al., 1983; Slade et al., 1983). In the long term, the vicious cycle may lead to increased disability (J. W. S. Vlaeyen et al., 1995).

Although the Fear Avoidance Model is generally accepted, it is a matter of debate regarding how and when it is best to assess fear avoidance beliefs in clinical practice. An approach that considers patterns of responses across multiple variables may provide valuable insights into possible underlying mechanisms and the factors associated with low back pain. So this review included not only the studies that measured fear

avoidance beliefs using the two most commonly Fear Avoidance Questionnaire (Waddell et al., 1993) and Tampa Scale of Kinesiophobia (J. Vlaeyen et al., 1995) but also using different fear-avoidance variables.

Previous low back pain prognostic reviews (Chou & Shekelle, 2010; Iles et al., 2008; Kent & Keating, 2008; Pincus et al., 2006; Ramond et al., 2011; Wertli, Rasmussen-Barr, et al., 2014) have also included cohorts with specific LBP and LBP with neurocompressive signs (low back pain with distal radiation below the knee, pins, needles, numbness and weakness). This is the first review that considered only cohorts with non-specific LBP. The sampling of individuals with similar characteristics may provide a better understanding of the clinical presentation and pain-related fear of patients with low back pain.

The aim of this systematic review is twofold: (1) reviewing the existing literature on the role of fear avoidance beliefs as a prognostic factor in patients with acute or sub-acute non-specific LBP; (2) analyzing a case study with non-specific low back pain and fear-avoidance behaviors in the light of the obtained results.

1.1. Patient scenario

This single case study aims to describe the role of psycho-social factors in the development of chronic low back pain after an acute episode.

A 26-year-old female with recurrent episodes (on average two or three times a year) of low back pain since two years was evaluated in a physiotherapy clinic for an acute episode of non-specific low back pain.

She complained asymmetrical left low back and left posterior thigh pain since 10 days. This episode was preceded by a pain-free period of 4 months. The pain arose after a sudden flexion-extension movement of the trunk. She reported that “it was if someone put a knife in her back” while bending forward. The pain was worse following exercise or activity and with prolonged sitting or sleeping (slept on her side and/or back). She rates the pain as 8 out of 10 and reports little improvement with non-steroidal anti-inflammatory drugs.

The patient scored 19 on the Roland Morris Disability Questionnaire. Symptoms impaired the activity of daily living: she walked, got dressed and moved more slowly than usual and they compelled her to ask help of her family.

Moreover she was unable to work so she had to take a sick leave for two weeks. The patient states she is worried about her ability to return to work. She said: “I am a free lancer nurse. It is a stressful work period due to Coronavirus (Covid-19) disease pandemic. My work aggravated my pain because it is too heavy for me. I will never be able to go back to that work”.

On the other hand, she expressed the need to return to work because she had not a private health insurance; so she is inclined to adopt active coping strategies to return to work.

She is avoiding many of her usual activities due to the pain and fear of making her back worse.

The patient scored 19 on the physical activity subscale of fear avoidance beliefs questionnaire (FABQ-PA), 40 on the work subscale of fear avoidance beliefs questionnaire (FABQ-W), 30 on Pain Catastrophizing Scale (PCS), 43 on Tampa Scale of Kinesiophobia (TSK-I).

She also had a history of panic attacks.

Will this patient develop chronic disabling low back pain?

2. Methods

This review was reported according to PRISMA guidelines (Moher et al., 2015), while supplementing as necessary for a prognostic factor systematic review.

It was considered six key steps:

1. Defining the review question
2. Identifying studies
3. Selecting studies
4. Critically appraising studies
5. Collecting data
6. Synthesizing and interpreting results

A focused systematic review was conducted (as opposed to a broad review that investigates evidence on many prognostic factors) to facilitate the most complete assessment and interpretation of the evidence available (Hayden et al., 2009).

2.1. Criteria for considering studies for this review

This review includes prognostic study evidence with the definitions of eligible participants (non-specific low back pain), the prognostic factor of interest (fear avoidance beliefs), outcomes and study designs.

Target population

It was selected studies involving any population of adult participants (≥ 18 years), including general populations, occupational and non-surgical clinical populations, with acute (less than four weeks) or sub-acute (less than twelve weeks) non-specific low back pain.

It was excluded studies if they investigated mixed-pain populations (including conditions other than low back pain, such as thoracic pain, neck pain or low back pain with distal radiation below the knee), chronic non-specific low back pain, low back pain caused by specific pathologies (including nerve root impingement, fracture, ankylosing spondylitis, spondyloarthritis, infection, neoplasm, or metastasis) or specific conditions (for example pregnancy).

Some studies used the term sciatica to describe any LBP-associated leg pain and included patients with sciatica in populations with non-specific low back pain. In this review the term sciatica was interpreted as indicating the presence of neurocompressive symptoms; so studies including participants with neurocompressive symptoms were excluded.

Prognostic factor of interest

Studies that assessed fear avoidance beliefs at baseline or an early point in patient management (i.e. at initial consultation) were included.

According to Fear Avoidance Model (Lethem et al., 1983; Slade et al., 1983) research was focus on pain-related fear and on fear of movement or re-injury.

It was included studies of fear avoidance beliefs assessed using any measurement approach: not only Fear-Avoidance Beliefs Questionnaire (FABQ) and Tampa Scale of Kinesiophobia (TSK) but also multidimensional measurement tools.

Types of outcomes

Studies with at least one of the following outcomes were included:

- Pain intensity, measured by Graded Chronic Pain Scale (Von Korff et al., 1992), pain scale such as numerical rating scale (11-point or 5-point NRS) or visual analogue scale (VAS) (Jensen et al., 1998; Wolff et al., 2020) and pain-related disability, measured by Pain Disability Index (PDI) (Tait et al., 1990).
- Functional limitations, measured by a low back pain-specific scale (for example, the Roland-Morris Disability Questionnaire (RMDQ) (Roland & Fairbank, 2000).
- Work status, measured as time on sick leave (Klenerman et al., 1995).
- Course of LBP (Klenerman et al., 1995).

Types of study designs

This review focused on studies with a minimal follow-up of 6 months and it was limited to prospective longitudinal studies and to publications presenting analyses of randomised controlled trials (RCTs), if they reported on the association between fear-avoidance beliefs and low back pain outcomes in the study population. Treatment effect modification evidence was not included in results' syntheses but it was included data about the association between fear-avoidance and low back pain outcomes when available in these studies. Retrospective studies were excluded due to the potential bias in this type of study (Whiting et al., 2004).

2.2. Search methods for identification of studies

The search strategy included electronic searches and additional strategies to retrieve as many relevant publications as possible.

It was conducted a focused electronic search, using indexed terms and free-text words, with no date or language restrictions. The following databases were searched in September 2021: MEDLINE (PubMed and Ovid), Cochrane Library, Scopus and Web of Science.

The search strategy included terms related to non specific low back pain, prognostic factor of interest (fear avoidance beliefs) and prognostic study methods (prognosis sensitive strategy of Wilczynski & Haynes, 2004); see Appendix 1 for the full focused strategies.

For lack of time, it was not conducted a broad search (as suggested by Hayden 2007 and Hayden 2009) that included terms related to low back pain and prognostic study methods, without focused terms related to fear avoidance beliefs.

Recognising potential limitations of electronic search strategies, the focused electronic search was supplemented from other sources: reference searches of relevant reviews, including previously published systematic reviews of variables, based on fear avoidance model, and low back pain (Pincus et al., 2002; Wertli, Eugster, et al., 2014; Wertli, Rasmussen-Barr, et al., 2014), and identified broad systematic reviews of low back pain prognosis or prognostic factors (Chou & Shekelle, 2010; Iles et al., 2008; Kent & Keating, 2008; Ramond et al., 2011).

2.3. Selection of studies

The comprehensive search was executed and downloaded into Mendeley for electronic bibliographic management. An online electronic systematic review software, Rayyan (Ouzzani et al., 2016), was used to organize and track the selection process.

One reviewer screened all 370 references by title and abstract. Full text was reviewed in all studies meeting the predefined eligibility criteria (N=83).

2.4. Data extraction and management

For each included study it was extracted: study design, participant characteristics (sample size, age, gender, inclusion criteria, exclusion criteria and duration of low back pain episode at baseline), setting, main study focus, follow-up period(s), measures assessed, outcomes, statistical analysis used, result, conclusion and limits of study.

2.5. Assessment of risk of bias in included studies

One review author assessed each study's risk of bias using the Quality in Prognosis Studies (QUIPS) tool (Hayden et al., 2013), appropriate for prognostic factor review questions.

Six domains were considered: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting; Appendix 2 presents a copy of the QUIPS tool modified for this review and the description of six domains.

The items of each domain were supported by information and methodological comments and then judged using the QUIPS tool by rating each domain as having high, moderate, or low risk of bias. The reviewer was not blinded to study authors, institution or journal of publication due to feasibility.

3. Results

3.1. Study selection

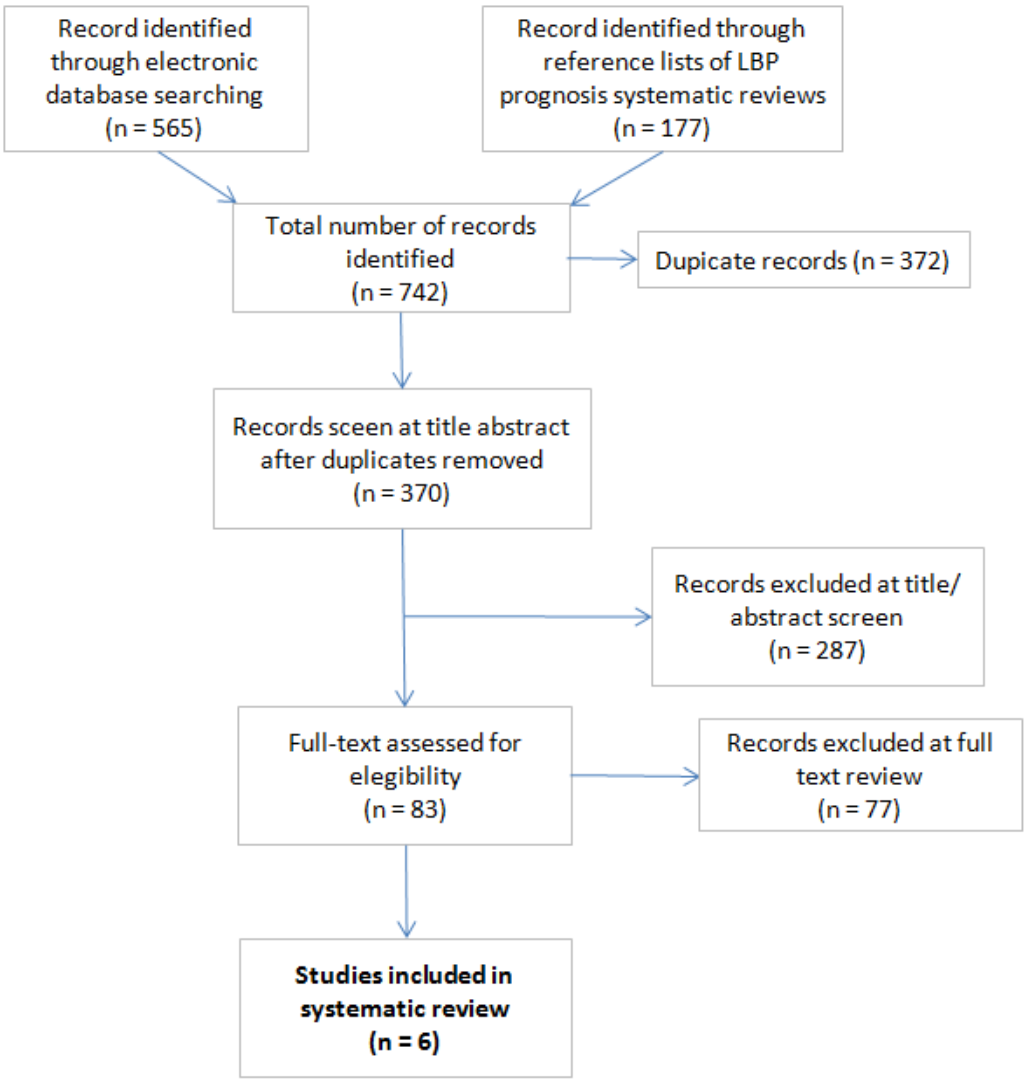
The search and inclusion process is summarized in Figure 1.

The search strategy resulted in an initial yield of 742 references: 565 from electronic database searching and 177 from references of other published low back pain prognosis systematic reviews.

There were 370 unique citations, of which we excluded 287 citations at title/abstract screening. A summary of studies excluded at title/abstract screening is presented in Appendix 3.

After screening of 83 the full text articles, 6 studies met inclusion criteria (Klenerman et al., 1995; Klyne et al., 2020; Sieben et al., 2002; Sieben et al., 2005; Swinkels-Meewisse et al., 2006; Wolff et al., 2020). Appendix 4 presents a summary of studies excluded at full text review.

Figure 1: PRISMA flow diagram showing identification and selection of included studies.



3.2. Included study characteristics

Six studies (1398 participants) were included in this review (Table 1: Descriptive summary of included studies).

Five were prospective cohort studies design and one was prospective case series design.

Four studies (67%) were published more than five years ago (before 2016).

The sample size of included studies ranged from 44 (Sieben et al., 2002a) to 555 (Swinkels-Meewisse et al., 2006), with a median of 183 participants (interquartile range (IQR): 136 to 281).

The study populations had similar numbers of men and women (median, 49,8% men; IQR 45% to 51%) and mean age ranged from 18 to 70 years.

All studies investigated patients with acute or sub-acute non-specific LBP; the duration of the LBP episode was less than three month and the onset of LBP was preceded by a pain free period of at least 3 months.

Studies were conducted in the primary care setting (not only general practitioners but also physiotherapists), 3 studies in the Netherlands, 1 study in Germany, 1 study in Australia and 1 in the United Kingdom.

The follow-up was mostly 6 months; the duration of follow-up ranged between 2 weeks and 12 months.

Fear avoidance beliefs were evaluated using Fear-Avoidance Beliefs Questionnaire (FABQ) (Klyne et al., 2020), Tampa Scale for Kinesiophobia (TSK) (Sieben et al., 2002; Swinkels-Meewisse et al., 2006) or using different variables concerning fear-avoidance behavior (Klenerman et al., 1995), fear avoidance model (Sieben et al., 2005) or avoidance-endurance model of pain (Wolff et al., 2020).

In four studies (Klenerman et al., 1995; Klyne et al., 2020; Sieben et al., 2005; Swinkels-Meewisse et al., 2006) fear-avoidance beliefs was tested evaluated in conjunction and in comparison to physical, demographic and historical variables. Only one study (Sieben et al., 2002a) considered the short-term course of pain-related fear during the acute stage of a new low back pain episode and the its role in the development of chronicity. One study (Wolff et al., 2020) evaluated the ability of Avoidance-Endurance Fast-Screening (AE-FS), an instrument based on the avoidance-endurance model (AEM), to predict recurrent or constant low back pain.

Pain and disability were outcomes assessed in most included studies. Pain was measured using Graded Chronic Pain Scale, Numeric Pain Rating Scale (NPRS), Pain Disability Index (PDI); disability using Roland Morris Disability Questionnaire (RMDQ). One study (Klenerman et al., 1995) evaluated also the work status, one study (Swinkels-Meewisse et al., 2006) also participation.

Four of six included studies provided that fear-avoidance beliefs and behavior are a risk factor for poor outcomes.

One study (Wolff et al., 2020) proved that in patients with non-specific sub-acute low back pain fear-avoidance and dysfunctional endurance styles of pain processing were a risk for chronicity (pain and disability) at the 6 month follow-up.

One study (Swinkels-Meewisse et al., 2006) found that fear of movement or (re)injury significantly predicted future perceived disability and, together with several episode specific and demographic variables, contributed to the prediction of future participation in patients with non-specific acute low back pain.

One study (Sieben et al., 2002) shown that patients with rising pain-related fear levels, measured for 14 days following a new episode of non-specific low back pain, were more disabled after one year.

One study (Klenerman et al., 1995) pointed out that fear avoidance variables predict chronicity (pain, disability, sick leave) of low back pain and also that demographic and historical variables in conjunction and in comparison to fear-avoidance behavior make a contribution to the prediction at the 12 month follow-up.

In two of six included studies the results did not clearly support that fear-avoidance beliefs are a risk factor for poor outcomes.

In one study fear avoidance beliefs were measured using not only the Tampa Scale of Kinesiophobia (TSK) but also a measure of avoidance of physical activity and the Pain Catastrophizing Scale. Only negative affect (depression, measured by the Beck Depression Inventory, minus somatic items) predicted outcome (measured on the Graded Chronic Pain Scale) at 3, 6, and 12 months.

Another study (Klyne et al., 2020) revealed that some psychological factors (depressive symptoms, pain catastrophizing, pain self-efficacy) were associated with the transition to persistent or recurrent LBP but not fear-avoidance beliefs, evaluated using Fear-Avoidance Beliefs Questionnaire (FABQ).

Tabella 1: Characteristics of included studies [ordered by study ID]

ID	First author	Year	Type of study	Population	Setting	Main study focus	Follow-up time	Measure	Outcome	Statistical Analysis	Results	Predictive	Conclusions	Limits
11	Sieben	2005	Prospective cohort study	Sample size: 222, 220 (T1), 180 (T2), 168 (T3), 171-174 (T4) Age, years; mean (SD): 18-60 years; ≤24 years, 5.9%; 25–34 years, 17.6%; 35–44 years, 25.2%; 45–54 years, 38.7%; ≥55 years, 12.6% Gender: Female 43,7% Inclusion criteria: a new episode of non-specific LBP (pain localised below the scapulae and above the gluteal folds; time since pain onset no longer than 3 weeks; after at least 3 months without relevant activity limitations due to LBP) Exclusion criteria: age younger than 18 or older than 60 years; (suspected) specific cause of LBP; major disease or psychiatric disorder; pregnancy; insufficient knowledge of Dutch language to complete a questionnaire Duration of LBP: < 3 weeks	Primary care	The aim of study was to prospectively test the assumption that pain-related fear in acute stages successfully predicts future disability	Follow-up: 3 months (T2); 6 months (T3) and 12 months (T4)	Questionnaire consisted of (a) a set of descriptives such as work status, back pain history and characteristics of the current episode (T1) (b) measures concerning the fear–avoidance model: Pain intensity - Visual Analogue Scale, VAS; Negative affect - Negative Emotionality Scale, NEM; Pain catastrophizing - Pain Catastrophizing Scale, PCS; Pain-related fear - Tampa Scale for Kinesiophobia; Physical disability - Quebec Back Pain Disability Scale, QBPDS; Social interference - Adapted National Health Interview Survey; (Avoidance of) physical activity - The Physical Activity Rating Scale, PARS; Depression - Beck Depression Inventory, BDI (T1, T2, T3, T4)	Graded Chronic Pain Scale (T1, T2, T3, T4)	Regression analysis report with end of study Graded Chronic Pain Scale as a dependent variable and baseline pain-related fear characteristics as independent variables Measure reported: NR	Age, baseline pain intensity, previous LBP history, level of education and negative affect are predictors of end of study Graded Chronic Pain Scale scores. Of the fear–avoidance model variables, only negative affect added to this model; the remaining variable were removed: they don't explain end of study chronic pain grade.	Non Prognostic	The results did not clearly support the fear–avoidance model in explaining the transition from acute LBP to long-term outcome	In–en exclusion criteria were set to explicitly select acute patients consulting with LBP as a primary problem. However, since LBP is known for high comorbidity with other functional disorders and psychiatric symptoms, some degree of "contamination" may have occurred. Using an adapted version instead of Graded Chronic Pain Scale for the secondary measurements in this study The number of participants in this study was expected to be higher
48	Wolff	2020	Prospective cohort study	Sample size: 144 (T1), 124 (T2) Age, years; mean (SD): 18-70 years: 45 years Gender: Female 55% Inclusion criteria: lumbar back pain with or without radiation to the knee; duration of actual pain <12 weeks, preceded by a painfree period of at least 6 months; age >17 years. Exclusion criteria: specific reasons for symptoms, which require immediate medical therapy; known psychiatric disorders; insufficient knowledge of the German language. Duration of LBP: subacute LBP (<3 months)	Primary care	The aim of the study was to develop a short screening method, based on the avoidance-endurance model of pain and to investigate the prognostic validity for pain intensity, disability and physical function.	Follow-up: 6 months (T2)	Avoidance-Endurance Fast-Screening (AE-FS) 9-item, short version of Avoidance-Endurance Screening (AES 37-item, long version)	Pain intensity: 5-point Numeric Pain Rating Scale Pain-related disability: Pain Disability Index (PDI)	Chi-square analysis for prevalence of unfavourable outcome, positive predictive value(PPV) and negative predictive value (NPV), ROC analyses for sensitivity, specificity and area under the curve (AUC) values	By the use of the cut-off value "2" for the outcome pain intensity the 9-item AE-FS had a prevalence of 68%, sensitivity of 82%, specificity of 58%, PPV of 80% and NPV of 61%. By the use of the cut-off value "PDI ≥1" the 9-item AE-FS had a prevalence of 61%, a sensitivity of 44%, a specificity of 85%, PPV of 82% and NPV of 49%. Result AUC: NR	Prognostic	The 9-item AE-FS, based on the avoidance-endurance model (AEM) offers an economic way for an early recognition of a risk for future chronicity in patients with subacute low back pain.	Strenghts: It's the first to investigate the AE-FS 9-item short screening to predict recurrent or constant LBP; a high rate of 86% of the participants stayed for the follow-up period; excluded patients with chronic pain, leading to the advantage of avoiding the overestimation of correctly positive findings. Limits: the use of point by a point survey to assess the outcomes pain intensity and disability; limited follow-up period of 6 months.
74	Klyne	2020	Prospective cohort study	Sample size: N=133 (T1) , N=98 (T2), N=89 (T3), N=84 (T4), N=92 (T5) Age, years; mean (SD): 22-34 years Gender: Female 51.9% Inclusion criteria: ability to understand, speak and read English; within 2 weeks of onset of an acute episode of acute LBP; occurred between the gluteal fold and T12; lasted for >24 hours and remained present at time of study commencement; caused functional limitation; caused participant to seek/seriously consider health intervention; followed a period of at least 1 month without pain; average level of pain (NRS) ≥1 and average level of disability (RMDQ) ≥1 during the week prior to study commencement Exclusion criteria: Refusal to participate; <18 years old, >50 years old; serious spinal pathology; other major diseases/disorders; participants were using corticosteroids, non-steroidal anti-rheumatic drugs, or anti-cytokine therapy; average level of pain (NRS) <1 and average level of disability (RMDQ) <1 during the week prior to study commencement. Duration of LBP: < 2 weeks	Primary care	The aim of the study were evaluate whether promising and potentially modificable biological, psychological, social and behavioural factors, along with their possible interactions, predict LBP outcome after an acute episode; and evaluate the time-course of changes in these factors from LBP onset.	Follow-up LBP population: 3 months (T2); 6 months (T3), 9 months (T4), and 12 months (T5)	Fear-Avoidance Beliefs Questionnaire (FABQ)	Pain (Numeric Pain Rating Scale - NPRS) Disability (Roland Morris Disability Questionnaire - RMDQ)	Unclare t tests (continuous data, normally distributed) Mann–Whitney U tests (continuous data, not normally distributed) Chi squared tests (categorical data)	p-value Fear-Avoidance Beliefs Questionnaire-work (FABQ-W): p = 0.136 (T2); p = 0.223 (T3); p = 0.144 (T4); p = 0.960 (T5) p-value Fear-Avoidance Beliefs Questionnaire-activity (FABQ-PA): p = 0.835 (T2); p = 0.944 (T3); p = 0.686 (T4); p = 0.926 (T5)	Non Prognostic (for Fear Avoidance)	Comparison of baseline characteristics between LBP participants who did and did not follow-up for laboratory based measures at 3, 6 and 9 months, and questionnaire measures at 12 months, revealed that Fear-Avoidance Beliefs are not associated with the transition to persistent/recurrent LBP	The planned sample size (N=217) was not achieved due to strict "acute LBP" inclusion criteria Study measures and follow-up procedures imposed substantial burden and explains the reported attrition Missing data due to attrition was high as is usual in longitudinal cohorts, and statistical approaches

139	Swinkels Meewisse	2006	Prospective cohort study	Sample size: 555 (T1); 467 (T2); 431 (T3) Age, years; mean (SD): 18-65 years; 42.4 (11.3) Gender: female 42% Inclusion criteria: Acute nonspecific LBP, having been free of LBP 3 months preceding the current episode Exclusion criteria: presence of specific LBP, malignancies, operations in the lumbar area, pregnancy or inability to read and write Duration of LBP: <4 weeks of LBP	Primary care	To investigate prospectively whether pain-related fear predicts future perceived disability and participation in patients with acute low back pain (LBP)	Follow-up: 6 weeks (T2); 6 months (T3)	Self-report questionnaires: Sociodemographic Variables (T1); Follow-up Questionnaire (T2 and T3) Visual Analog Scale (VAS) (T1, T2 and T3) Tampa Scale of Kinesiophobia (TSK) (T1, T2, and T3)	Roland Morris Disability Questionnaire - RMDQ (T1, T2, and T3) 5 questions concerning self-report level of participation derived from the Chronic Pain Grade Questionnaire (T1, T2, and T3)	Multilevel analyses Regression analyses, with perceived disability and participation as dependent variables Measure reported: β	Fear of movement/(re)injury is the most powerful predictor of future perceived disability (β=0.23, p <0.001) and contributed to the prediction of future participation (Fear of movement/(re)injury β= - 0.10, p = 0.011).	Prognostic	Fear of movement/(re)injury significantly predicted future perceived disability and, together with several episode specific and demographic variables, contributed to the prediction of future participation	Population included was quite heterogeneous, consisting of patients with and without previous episodes of LBP The times were chosen based on existing guidelines differentiating between acute, subacute and chronic LBP In the absence of a standardized and well-validated measure of participation, a new measure was developed consisting of 5 items The measures used in the current study were all self-report measures The estimates of the various equations are quite low, resulting in a low overall percentage of explained variance
206	Sieben	2002	Prospective case series	Sample size: N=44 (T1); N=34 (T2); N=33 (T3); N=30 (T4) Age, years; mean (SD): 18–65 years; 42,7 years (SD ˜10,8) Gender: Female 50% (T1); NR (T2, T3, T4) Inclusion criteria: pain localized below the scapulae and above the gluteal folds; duration since time of pain onset no longer than 2 weeks; after a period of at least 3 months without significant activity limitations due to back trouble; 18–65 years of age; sufficient knowledge of Dutch/Flemish language; informed consent. Exclusion criteria: specific cause or strong suspicion of specific cause; pregnancy. Duration of LBP: < 2 weeks	Primary care	The overall aim of this study is to explore the characteristics of pain-related fear during the acute stage of low back pain.	Follow-up: 2 weeks (T2); 3 months (T3); 12 months (T4)	Pain-related fear: Tampa Scale for Kinesiophobia (TSK) Pain catastrophizing: Pain Catastrophizing Scale (PCS) Diary: A single VAS-item; VAS-items derived from the TSK (4 items); VAS-items derived from the PCS (3 items).	Back pain disability: Roland Disability Questionnaire (RDQ) (T1, T2, T3, T4)	Time series analysis (TSA): course of pain-related fear over time Kruskal Wallis tests Chi-squared tests: to determine differences on baseline variables between groups with different patterns MANOVA: to test differences on follow-up outcome Wilcoxon: to determine differences between the levels of pain-related fear and pain catastrophizing before, during and after the peak-day	Those with rising pain-related fear showed significantly lower RMD than those with descending pain related fear at baseline (r = 0.46), but significantly higher RMD than those with descending pain-related fear at 3 months (r = 0.55) and 12 months (r = 0.44); this trend was also present at 2 weeks (r = 0.32) but not significantly so (despite the medium effect size); increases in pain were associated with a rising level of pain-related fear (r = 0.49) and pain catastrophizing (r = 0.35)	Prognostic (rising of pain-related fear during the acute stage)	Patients with rising pain-related fear levels were more disabled after one year	The patterns found in fear and pain are not sufficiently explained. The sensitivity of the method used for sequential analysis can be questioned: use of more sensitive measures and shorter intervals are needed to test sequential relationships (diaries were completed retrospectively; handheld computer diary-methods can probably be helpful). Although a new episode can be properly defined by its occurrence in time, a patient's cognitions accompanying this new episode will inevitably be influenced by any previous back pain experiences.
335	Klenerman	1995	Prospective cohort study	Sample size: N=300 (T1); N=162 (T2); N=196 including attenders N=58 and postal recipients N=138 (T3); N=123 (T1, T2, T3) Age, years; mean (SD): NR Gender: Female 49,67% Inclusion criteria: musculo-skeletal LBP; pain begun not more than 1 week Exclusion criteria: NR Duration of LBP: < 1 week	Primary care	The aim of this study was to test whether physical, demographic and historical variables in conjunction and in comparison to fear-avoidance behavior predict who would develop a chronic low back condition at an earlier stage in its natural history	Follow-up: 2 months (T2); 12 months (T3)	Screening Questionnaire (T1, T2, T3): information on demographic characteristics, previous and present history and severity of LBP; ratings measures of the four fear-avoidance contextual variables (stressful life events - Holmes and Rahe stressful life events scale; personality - Modified Somatic Perception Questionnaire or MSPQ; Previous Pain History; Pain Coping Strategies)	Back pain disability: Roland Disability Questionnaire (RDQ) (T3) Level of pain (T3) Work status (T3) Course of LBP (T3)	Present pain and disability: a series of multiple regression analyses Sick leave and course of LBP: a series of multiple discriminant function analyses	Series of multiple regression analyses used to predict outcome (combined pain and disability): - fear avoidance variables obtained at the acute stage (< 1 week) predict outcome significantly (p= 0.0001) and increase the predictive outcome to 25% (r-square = 0.25) at 2 months - fear avoidance variables obtained at the acute stage (< 1 week) predict outcome significantly (p= 0.0002) and increase the predictive outcome to 14% (r-square = 0.137) at 12 months - fear avoidance variables obtained at the sub-acute stage (2 months) predict outcome significantly (p= 0.0001) and increase the predictive outcome to 23% (r-square = 0.226) at 12 months Series of multiple discriminant function analyses used to predict outcome (sick leave and course of LBP): - fear-avoidance predict sick leave significantly (p value = 0.02) - fear-avoidance alone don't predict course of LBP significantly (p value NS) but the combination of all three sets (demographic, historical and fear-avoidance variables) of acute variables provide the best prediction (chi-square = 33.54; p value = 0.01)	Prognostic (combined pain, disability, sick leave) Predictive in conjunction with demographic and historical variables (course of LBP)	Variables, based on fear avoidance model, predict chronicity of LBP. Demographic and historical variables also make a contribution to the prediction.	Incomplete follow-up rates achived: 41% of subjects were assessed at all three data collection points

3.3. Risk of bias assessment of included studies

Risks of bias were assessed across six domains, using the QUIPS tool for each of six included studies, by a review author.

Appendix 5 presents detailed information about Risk of bias judgements for each included study.

None of studies was rate as having low risk of bias for all of the six domains.

Four studies (67%) were rated at low/moderate risk of bias, with all six domains judged to be at low or moderate risk of bias.

In one study, study attrition was rated at high risk of bias, in another study, study population, attrition and confounding were rated at high risk of bias.

4. Discussion

This systematic review of six observational studies has provided moderate evidence that fear avoidance beliefs are predictive of constant low back pain.

Four studies, three of which were rated at low/moderate risk of bias, found fear avoidance beliefs and behaviors to be prognostic risk factors for poor outcomes in patients with acute or sub-acute non-specific LBP. However, two studies, rated at low/moderate risk of bias, did not find fear avoidance beliefs significant when developing a clinical algorithm to predict poor outcome.

The role of fear avoidance beliefs and behaviors in the transition from acute to chronic pain has been established in the literature but the predictive role of fear avoidance is not clear in the acute stage.

A systematic review, published in 2006, found little evidence to link fear of pain with poor outcome (Pincus et al., 2006), two systematic reviews found moderate evidence that fear avoidance beliefs are predictive of work outcome (Iles et al., 2008; Wertli et al., 2014).

The lack of strong evidence is probably due to an unclear method of measuring fear avoidance beliefs.

In the studies included in this systematic review fear avoidance beliefs were evaluated using Fear-Avoidance Beliefs Questionnaire (FABQ) (Klyne et al., 2020), Tampa Scale for Kinesiophobia (TSK) (Sieben et al., 2002; Swinkels-Meewisse et al., 2006) or using different variables concerning fear-avoidance behavior (Klenerman et al., 1995), fear avoidance model (Sieben et al., 2005) or avoidance-endurance model of pain (Wolff et al., 2020).

The best method of measuring fear avoidance beliefs is using different variables concerning fear-avoidance beliefs and behavior, not only a scale such Tampa Scale for Kinesiophobia (TSK) or questionnaire such as Fear Avoidance Beliefs Questionnaire.

One study (Klyne et al., 2020), included in this systematic review, found that different psychological factors, concerning fear avoidance behavior such as depression, pain catastrophizing, pain self-efficacy, predict LBP outcome after an acute episode of non-specific low back pain but not fear avoidance beliefs, measured using Fear Avoidance Beliefs Questionnaire (FABQ). This questionnaire was the most commonly used measurement tool, but this method combines a mixture of psychosocial constructs (Waddell et al., 1993). For example, the work subscale includes constructs of fear avoidance, injury compensation and recovery expectation. Psychosocial constructs are often difficult to isolate using questionnaires as many constructs have some overlap, underlining the importance of using appropriate tools to limit potential bias when measuring prognostic factors (Hayden et al., 2006).

Instead, another two studies (Klenerman et al., 1995; Swinkels-Meewisse et al., 2006) found that fear of movement and (re)injury predicted chronicity of LBP in conjunction with demographic and historical variables.

Another critical aspect to consider is method of outcome measurement including the different components of biopsychosocial model of health.

In a study (Sieben et al., 2005), judged to be at low risk of bias for using a good method of measuring fear avoidance beliefs, only negative affect (depression) predicted outcome. However, in this study, chronicity of low back pain was evaluated using only an adapted version of Graded Chronic Pain Scale.

On the other hand, two studies (Klenerman et al., 1995; Swinkels-Meewisse et al., 2006) considered as outcome not only pain and disability but also work status and participation.

4.1. Strength and limitations

This systematic review has numerous strengths but also a number of limitations.

The study design was planned a priori with clearly-defined selection criteria.

The conducted literature search was comprehensive enough: focused electronic search and reference searches of other low back pain prognostic factor systematic reviews were used but not a broad search of low back pain prognosis studies; so "positive study" bias could be included in review search strategy (Hayden et al., 2009).

Only six article were include in this systematic review. It's mainly related to the sampling of the evidence available. In mostly low back pain prognostic factor studies, population included both non-specific and specific low back pain, in particular low back pain with distal radiation below the knee. In this systematic review only studies of non-specific low back pain population were included.

4.2. Scenario resolution

A patient with an acute non-specific low back pain was introduced at the beginning of this review. She had decreased baseline function and described behaviors consistent with fear avoidance (avoidance of work, movement or other activities due to fear that they will damage or worsen the back) and pain catastrophizing.

In accordance with results of this systematic review, fear avoidance beliefs and behaviors were evaluated throught the patient's history and measured by several scales (Fear-avoidance Beliefs Questionnaire, Pain Catastrophizing Scale, Tampa Scale of Kinesiophobia). Work-related aspects were also considered because they can adversely affect the outcomes. The treatment based particularly on education: the patient is counseled that usual activities will not hurt her back, that she is likely to recover from this episode and that she should remain active and return to work as soon as possible. In this regard some exercises were

suggested. It is also explained to her that extensive treatments or additional diagnostic tests are not necessary at this time.

A decrease in fear avoidance beliefs led to improvement of outcome and prevent the transition to persistent/recurrent LBP. In fact, no more episodes of low back pain occurred within a year.

Appendices

Appendix 1. Search strategies for focused search, using population (Low Back Pain), exposure (psychological factors: Fear-avoidance beliefs) and study design (prognosis) terms.

Database: MEDLINE (Pubmed)

<table>
<tr><th colspan="4">POPULATION</th></tr>
<tr><th>Term</th><th>Major Heading</th><th>Keywords</th><th>Search Text</th></tr>
<tr><td>Acute</td><td>/</td><td>/</td><td rowspan="4">(Acute OR Sub-acute OR "Sub Acute")
AND
("Low Back Pain"[Mesh] OR "Back Pain"[Mesh] OR "Back Pain"[tw] OR Backache[tw] OR "Low Back Pain*"[tw] OR "Lower Back Pain*"[tw] OR "Low Back Ache*"[tw] OR Lumbago[tw])
NOT
("Intervertebral Disc Displacement"[Mesh] OR "Intervertebral Disk Displacement"[tw] OR "Intervertebral Disc/surgery"[Mesh] OR "Intervertebral Disc Displacement/surgery"[Mesh] OR Diskectomy[Mesh] OR Diskectomy[tw] OR Infections[Mesh] OR Infection*[tw] OR Neoplasms[Mesh] OR Neoplas*[tw] OR Tumor*[tw] OR Cancer*[tw] OR Arthritis[Mesh] OR Arthritis[tw] OR "Spine Osteoarthritis"[tw] OR Spondylarthropath*[tw] OR "Psoriasis Arthritic"[tw] OR Fibromyalgia[Mesh] OR Fibromyalgia[tw] OR "Fractures, Bone"[Mesh] OR "Broken Bone*"[tw] OR "Bone Fracture*"[tw] OR Osteoporosis[Mesh] OR Osteoporos*[tw] OR Pregnancy[Mesh] OR Pregnancy[tw])</td></tr>
<tr><td>Subacute</td><td>/</td><td>/</td></tr>
<tr><td>Low Back Pain</td><td>Back Pain

Low Back Pain</td><td>Back Pain, Backache, Low(er) Back Pain, Low Back Ache(s), Lumbago, Non-specific Low Back Pain</td></tr>
<tr><td>Specific Disease</td><td colspan="2">Intervertebral disk displacement, Diskectomy, Infection, Neoplasm, Neoplasm metastasis, Arthritis, Fibromyalgia, Fractures-Bone, Osteoporosis, Pregnancy</td></tr>
</table>

<table>
<tr><th colspan="4">EXPOSURE: Kinesiophobia + Fear-avoidance beliefs</th></tr>
<tr><th>Term</th><th>Major Heading</th><th>Keywords</th><th>Search Text</th></tr>
<tr><td rowspan="8">Fear-avoidance beliefs</td><td rowspan="8">Fear</td><td>Fear avoidance</td><td rowspan="8">(("Fear" [Mesh:NoExp] OR "Fear" [tw]) AND ("Avoidance Learning"[Mesh] OR "Avoidance Learning"[tw])) OR "Kinesiophobia"[tw] OR "Fear of Movement"[tw] OR "Fear of Pain" [tw] OR "Fear of movement-related pain"[tw] OR "Fear of Injur*"[tw] OR "Fear of Re-injur*"[tw] OR "Fear of Reinjur*"[tw] OR "Fear-avoidance belie*"[tw] OR "Fear-avoidance behavior"[tw] OR "Pain belie*"[tw] OR "Pain-related fear"[tw]</td></tr>
<tr><td>Fear-avoidance belief(s) questionnaire</td></tr>
<tr><td>Kinesiophobia</td></tr>
<tr><td>Tampa Scale Kinesiophobia</td></tr>
<tr><td>Fear of Movement, Pain, Injury, Re-injury</td></tr>
<tr><td>Fear-avoidance belief(s)</td></tr>
<tr><td>Fear-avoidance behavior</td></tr>
</table>

		Pain belief(s)	
		Pain-related fear	

PROGNOSIS SEARCH STRATEGY
More sensitive search strategy for identifying potentially prognosis articles
(Prospective Studies [MeSH] OR incidence[MeSH] OR mortality[MeSH] OR follow up studies[MeSH] OR prognos*[tw] OR predict*[tw] OR course*[tw])
Wilczynski 2004 modified according to the present study design

Database: MEDLINE (Ovid)

POPULATION			
Term	**Major Heading**	**Keywords**	**Search Text**
Acute	/	/	((Acute or Sub-acute or Subacute).mp.) AND (exp Low Back Pain/ OR exp Back Pain/ OR Low Back Pain*.mp. OR Lower Back Pain*.mp. OR Backache.mp. OR Low Back Ache*.mp. OR Lumbago.mp.) NOT (exp Spinal Diseases/ OR "Intervertebral Disc Displacement".mp. OR "Intervertebral Disc Degeneration".mp. OR "Spinal Stenosis".mp. OR Spondylitis.mp. OR Spondylosis.mp. OR exp Infections/ OR Infection*.mp. OR exp Rheumatic Diseases/ OR Spondylarthr*.mp. OR Arthrit?s.mp. OR "Spine Osteoarthritis".mp. OR Fibromyalgia.mp. OR "Psoriasis Arthritis".mp. OR exp Neoplasms/ OR Neoplas*.mp. OR Tumor*.mp. OR Cancer*.mp. OR exp Fractures, Bone/ OR Broken Bone*.mp. OR Bone Fracture*.mp. OR exp Osteoporosis/ OR Osteoporos?s.mp. OR exp Pregnancy/ OR Pregnancy.mp.)
Subacute	/	/	
Low Back Pain	Back Pain Low Back Pain	Back Pain, Backache, Low(er) Back Pain, Low Back Ache(s), Lumbago, Non-specific Low Back Pain	
Specific Disease	Intervertebral disk displacement, Diskectomy, Infection, Neoplasm, Neoplasm metastasis, Arthritis, Fibromyalgia, Fractures-Bone, Osteoporosis, Pregnancy		

EXPOSURE			
Term	**Major Heading**	**Keywords**	**Search Text**
Fear-avoidance beliefs	Fear	Fear avoidance	((*Fear/ OR fear.mp) AND (exp Avoidance Learning/ or avoidance.mp)) OR Kinesiophobia.mp. OR (Fear adj3 (Movement or Pain or Injury or Re$injury)).ti,ab,kf. OR Fear-avoidance belief*.mp. OR Fear-avoidance behavior.mp. OR (Pain adj3 belie*).ti,ab,kf. OR ((Fear and (Movement or Pain or Avoidance or Injury or Re$injury)) adj3 (Questionnaire or Measure)).ti,ab,kf.
		Kinesiophobia	
		Fear of Movement, Pain, Injury, Re-injury	
		Fear-avoidance belief(s)	
		Fear-avoidance behavior	
		Pain belief(s)	

		Measure/ Questionnaire	

PROGNOSIS SEARCH STRATEGY
More sensitive search strategy for identifying potentially prognosis articles
exp follow-up studies/ or exp prospective studies/ OR exp mortality/ OR incidence.sh. OR prognos*.tw. OR predict*.tw. OR course*.tw.
Wilczynski 2004 modified according to the present study design

Database: Cochrane Library

<table>
<tr><th colspan="4">POPULATION</th></tr>
<tr><th>Term</th><th>Major Heading</th><th>Keywords</th><th>Search Text</th></tr>
<tr><td>Acute</td><td>/</td><td>/</td><td rowspan="4">(Acute OR “Subacute” OR "Sub-acute")
AND
(MeSH descriptor: [Low Back Pain] explode all trees) OR ("Low Back Pain") OR ("Lower Back Pain") OR ("Low Back Ache") OR ("Low Backache") OR ("Lumbago")
NOT
MeSH descriptor: [Spinal Diseases] explode all trees OR (“Intervertebral Disk Displacement”) OR ("Intervertebral Disk Degeneration") OR ("Spinal Stenosis") OR ("Spondylitis") OR ("Spondylosis") OR MeSH descriptor: [Infections] explode all trees OR ("Infection*") OR MeSH descriptor: [Neoplasms] explode all trees OR (Neoplasm*) OR (Cancer*) OR (Tumor*) OR MeSH descriptor: [Neoplasm Metastasis] explode all trees OR (Metastas?s) OR MeSH descriptor: [Arthritis] explode all trees OR ("Arthritides") OR ("Arthritis") OR ("Osteoarthritis") OR (Spondylarthritis) OR ("psoriatic arthritis") OR MeSH descriptor: [Fibromyalgia] explode all trees OR ("Fibromyalgia") OR MeSH descriptor: [Fractures, Bone] explode all trees OR ("Bone Fractures") OR MeSH descriptor: [Osteoporosis] explode all trees OR (Osteoporos?s) OR OR MeSH descriptor: [Pregnancy] explode all trees OR ("Pregnancy") OR ("Pregnancies")</td></tr>
<tr><td>Subacute</td><td>/</td><td>/</td></tr>
<tr><td>Low Back Pain</td><td>Back Pain

Low Back Pain</td><td>Low(er) Back Pain(s), Low Back Ache(s), Low Backache, Mechanical Low Back Pain, Lumbago</td></tr>
<tr><td>Specific Disease</td><td colspan="2">Spinal Diseases,
Intervertebral disk displacement,
Intervertebral disk degeneration,
Spinal Stenosis, Spondylitis,
Spondylosis
Infection
Neoplasm, Neoplasm metastasis,
Arthritis, Fibromyalgia,
Fractures-Bone,
Osteoporosis,
Pregnancy</td></tr>
</table>

<table>
<tr><th colspan="4">EXPOSURE</th></tr>
<tr><th>Term</th><th>Major Heading</th><th>Keywords</th><th>Search Text</th></tr>
<tr><td rowspan="3">Fear-avoidance beliefs</td><td rowspan="3">Fear</td><td>Fear avoidance</td><td rowspan="3">(MeSH descriptor: [Fear] this term only OR “Fear”) AND (MeSH descriptor: [Avoidance Learning] explode all trees OR “avoidance”) OR Kinesiophobia OR (Fear NEAR/3 (Movement or Pain or Injur* or Reinjur*)) OR</td></tr>
<tr><td>Kinesiophobia</td></tr>
<tr><td>Fear of Movement, Pain, Injury, Re-injury</td></tr>
</table>

		Fear-avoidance belief(s)	(Fear-avoidance NEXT belief*) OR ("Fear-avoidance behavior") (Pain NEXT belief*) OR ((Fear and (Movement or Pain or Avoidance or Injur* or Reinjur*)) NEAR/3 (Questionnaire or Measure))
		Fear-avoidance behavior	
		Pain belief(s)	
		Measure/ Questionnaire	

PROGNOSIS SEARCH STRATEGY
More sensitive search strategy for identifying potentially prognosis articles
MeSH descriptor: [Incidence] this term only OR MeSH descriptor: [Mortality] explode all trees OR MeSH descriptor: [Follow-Up Studies] explode all trees OR MeSH descriptor: [Prospective Studies] explode all trees OR (prognos*) OR (predict*) OR (course*)
Wilczynski 2004 modified according to the present study design

Database: Web of Science

POPULATION			
Term	**Major Heading**	**Keywords**	**Search Text**
Acute	/	/	TS=(Acute OR Subacute OR Sub-acute) AND TS=("Low Back Pain*" OR "Lower Back Pain*" OR "Low Back Ache" OR "Low Backache" OR Lumbago) NOT TS=("Intervertebral Disk Displacement" OR "Intervertebral Disk Degeneration" OR Diskectomy OR "Spinal Stenosis" OR Spondylitis OR Spondylosis OR Infection* OR Neoplasm* OR Cancer OR Tumor OR Metastas?s OR Arthritis OR Osteoarthrit?s OR Spondylarthropath* OR Spondylarthritis OR "Psoriatic Arthritis" OR Fibromyalgia OR "Bone Fracture*" OR "Broken Bone*" OR Osteoporos?s OR Pregnanc*)
Subacute	/	/	
Low Back Pain	Low Back Pain	Low(er) Back Pain(s), Low Back Ache(s), Low Backache, Lumbago	
Specific Disease	Intervertebral disk displacement, Diskectomy, Infection, Neoplasm, Neoplasm metastasis, Arthritis, Fibromyalgia, Fractures-Bone, Osteoporosis, Pregnancy		

EXPOSURE			
Term	**Major Heading**	**Keywords**	**Search Text**
Fear-avoidance beliefs	Fear	Fear avoidance	TS=((Fear AND Avoidance) OR (Kinesiophobia) OR (Fear NEAR/3 (Movement OR Pain OR Injury OR Re-injur*)) OR (“Fear-avoidance belief*”) OR ("Fear-avoidance behavior") OR (“Pain belief*”) OR ((Fear SAME avoidance) near/3 (Questionnaire OR Measure)) OR ((Fear
		Kinesiophobia	
		Fear of Movement, Pain, Injury, Re-injury	
		Fear-avoidance belief(s)	

		Fear-avoidance behavior	SAME movement) near/3 (Questionnaire OR Measure)) OR ((Fear SAME pain) near/3 (Questionnaire OR Measure)) OR ((Fear SAME injur*) near/3 (Questionnaire OR Measure)) OR ((Fear SAME re-injur*) near/3 (Questionnaire OR Measure)))
		Pain belief(s)	
		Measure/ Questionnaire	

PROGNOSIS SEARCH STRATEGY
More sensitive search strategy for identifying potentially prognosis articles
TS=("Prospective Stud*" OR incidence OR mortality OR "follow up stud*" OR prognos* OR predict* OR course*)
Wilczynski 2004 modified according to the present study design

Database: Scopus

POPULATION			
Term	**Major Heading**	**Keywords**	**Search Text**
Acute	/	/	TITLE-ABS-KEY ((Acute OR Subacute OR Sub-acute) AND ("Low Back Pain*" OR "Lower Back Pain*" OR "Low Back Ache" OR "Low Backache" OR Lumbago) AND NOT ("Intervertebral Disk Displacement" OR "Intervertebral Disk Degeneration" OR Diskectomy OR "Spinal Stenosis" OR Spondylitis OR Spondylosis OR Infection* OR Neoplasm* OR Cancer* OR Tumor* OR Metastas?s OR Arthrit* OR Osteoarthrit?s OR Spondylarthropath* OR Spondylarthrit?s OR "Psoriatic Arthritis" OR Fibromyalgia OR "Bone Fracture*" OR "Broken Bone*" OR Osteoporos?s OR Pregnanc*))
Subacute	/	/	
Low Back Pain	Low Back Pain	Low(er) Back Pain(s), Low Back Ache(s), Low Backache, Lumbago	
Specific Disease	Spinal Diseases, Intervertebral disk displacement, Intervertebral disk degeneration, Spinal Stenosis, Spondylitis, Spondylosis Infection Neoplasm, Neoplasm metastasis, Arthritis, Fibromyalgia, Fractures-Bone, Osteoporosis, Pregnancy		

EXPOSURE: Kinesiophobia + Fear-avoidance beliefs			
Term	**Major Heading**	**Keywords**	**Search Text**
Fear-avoidance beliefs	Fear	Fear avoidance	TITLE-ABS-KEY((Fear PRE/2 Avoidance) OR Kinesiophobia OR (Fear W/3 (Movement OR Pain OR Injur* OR Re-injur*)) OR "Fear-avoidance belie*" OR "Fear-avoidance behavior" OR "Pain belie*")
		Fear-avoidance belief(s) questionnaire	
		Kinesiophobia	
		Tampa Scale Kinesiophobia	
		Fear of Movement, Pain, Injury, Re-injury	

		Fear-avoidance belief(s)	
		Fear-avoidance behavior	
		Pain belief(s)	

PROGNOSIS SEARCH STRATEGY
More sensitive search strategy for identifying potentially prognosis articles
TITLE-ABS-KEY("Prospective Stud*" OR incidence OR mortality OR "follow up stud*" OR prognos* OR predict* OR course*)
Wilczynski 2004 modified according to the present study design

Appendix 2. Modified QUIPS tool

A version of the QUIPS tool modified for this prognostic factor review was presented below.

QUIPS identifies issues to consider for judging the overall risk of bias for a study. These issues will guide your thinking and judgement about the risk of bias within each of six domains. Some 'issues' may not be relevant to the specific study or the review research question. These issues are taken together to inform the overall judgement of potential bias for each of the six domains. Provide comments or text excerpts in the boxes below, as necessary, to facilitate the consensus process that will follow. Rate the adequacy of reporting for each applicable item as yes, partial, no or unsure, then (at the bottom of the page) rate potential risk of bias for each of the six domains as High, Moderate, or Low, considering all relevant issues.

Bias: study participation

The study participation domain addresses whether the study sample is representative of the population of interest. A study will be considered as having high risk of bias if the participation rate is low, a very selective rather than consecutive sample of eligible low back pain (LBP) individuals was recruited, or the study sample has a very different demographic and LBP characteristic distribution from our population of interest. Conversely, studies with high participation of eligible and consecutively-recruited LBP individuals who have characteristics similar to those in the source population would have low risk of bias.

Study Participation			
The study sample adequately represents the population of interest			
Issues to consider for judging overall rating of risk of bias		**Study methods and comments**	**Rating of reporting**
Source of target population	The source population or population of interest is adequately described, including who the target population is (e.g. is the desired target population all workers? individuals filing compensation claims?), when (time period of study), where (location), and how (description of recruitment strategy).		
	Comprehensive description would include characteristics of: individual (e.g. age, sex, depression), back pain (history of LBP, current functioning), work (type and characteristics of work environment), treatment (type and extent of care received) and social context (compensation status).		
Method used to identify population	The sampling frame and recruitment (e.g. newspaper advertisement, presentation to a health clinic, or captured from a claims database) are adequately described, including methods to identify the sample sufficient to limit potential bias (number and types used, e.g. referral patterns in health care)		
Recruitment period	Period of recruitment is adequately described.		
Place of recruitment	Place of recruitment (setting and geographic location) are adequately described.		

Inclusion and exclusion criteria	Inclusion and exclusion criteria are adequately described and should define a discreet group with LBP (e.g. the study may include physician diagnosis or explicit diagnostic codes).		
Adequate study participation	There is adequate participation in the study by eligible individuals.		
Baseline characteristics	The baseline study sample (i.e. individuals entering the study) is adequately described. Comprehensive description would include characteristics of: individual (e.g. age, sex, depression), back pain condition (history of LBP, current functioning), work (type and characteristics of work environment), treatment (type and extent of care received) and social context (compensation status).		
Summary study participation	**The study sample represents the population of interest on key characteristics, sufficient to limit potential bias of the observed relationship between fear avoidance beliefs and outcome.**		

Bias: study attrition

The study attrition domain addresses whether participants completing the study (i.e. with follow-up data) represent the baseline sample.

A study will be considered to have high risk of bias if it is likely that persons who completed the study differ from those lost to follow-up in a way that distorts the association between fear avoidance beliefs and LBP outcome. Conversely, studies with complete follow-up, or evidence that participants lost to follow-up are likely to be missing at random, will have low risk of bias.

Study Attrition			
The study data available (i.e., participants not lost to follow-up) adequately represent the study sample			
Issues to consider for judging overall rating of risk of bias		**Study methods and comments**	**Rating of reporting**
Proportion of baseline sample available for analysis	Response rate (i.e. proportion of study sample completing the study and providing outcome data) is adequate.		
Attempts to collect information on participants who dropped out	Attempts to collect information on participants who dropped out of the study are described.		
Reasons and potential impact of subjects lost to follow-up	Reasons for loss to follow-up are provided.		
Outcome and prognostic factor information on those lost to follow-up	Participants lost to follow-up are adequately described for characteristics of: individual (e.g. age, sex, depression), back pain condition (history of LBP, current functioning), work (type and characteristics of work environment), treatment (type and extent of care received) and social context (compensation status).		

	There are no important differences between participants who completed the study and those who did not.		
Summary study attrition	**Loss to follow-up (from baseline sample to study population analysed) is not associated with key characteristics (i.e. the study data adequately represent the sample) sufficient to limit potential bias to the observed relationship between fear avoidance beliefs and LBP outcome.**		

Bias: prognostic factor measurement

The prognostic factor measurement domain addresses adequacy of prognostic factor measurement.

Studies that measured the fear avoidance beliefs using an unreliable method for all participants or that describe prognostic factor capturing just some variables of fear-avoidance model were considered as being at high risk of bias. Conversely, a study was considered to have low risk of bias if fear avoidance beliefs are measured similarly (same method and setting) for all participants and use a valid, reliable measure, capturing all fear avoidance variables.

Prognostic Factor Measurement			
The PF is measured in a similar way for all participants			
Issues to consider for judging overall rating of risk of bias		**Study methods and comments**	**Rating of reporting**
Definition of the PF	A clear definition or description of Fear Avoidance Beliefs is provided, capturing fear–avoidance variables.		
Valid and reliable measurement of PF	Method of FAB measurement is adequately valid and reliable to limit misclassification bias.		
	Continuous variables are reported or appropriate cut-points (i.e. not data-dependent) are used.		
Method and setting of PF measurement	The method and setting of measurement of FAB is the same for all study participants.		
Proportion of data on PF available for analysis	Adequate proportion of the study sample has complete data for FAB variable.		
Method used for missing data	Appropriate methods of imputation are used for missing FAB data.		
Summary prognostic factor measurement	**FAB are adequately measured in study participants to sufficiently limit potential bias.**		

Bias: outcome measurement

The outcome measurement domain addresses the adequacy of LBP disability outcome measurement toward non-differential measurement related to fear avoidance beliefs.

A study would have high risk of bias if there is likely to be differential measurement of outcome related to the extent of exposure to the prognostic factor. A study would be considered to have low risk of bias if the

outcome is measured similarly for all participants and uses a valid, reliable measure (e.g. pain intensity by a visual analogue scale, VAS, or associated disability using the Roland Morris Disability Questionnaire, RMDQ).

Outcome Measurement			
The outcome of interest is measured in a similar way for all participants			
Issues to consider for judging overall rating of risk of bias		**Study methods and comments**	**Rating of reporting**
Definition of the outcome	A clear definition of the LBP outcome is provided, including duration of follow-up and ICF disability construct.		
Valid and reliable measurement of outcome	The method of outcome measurement used is adequately valid and reliable to limit misclassification bias.		
	Clear and appropriate cut-points for continuous outcome measures (i.e. not data-dependent) are used.		
Method and setting of outcome measurement	The method and setting of outcome measurement is the same for all study participants.		
Summary outcome measurement	**LBP disability outcome is adequately measured in study participants to sufficiently limit potential bias.**		

Bias: study confounding

The Study Confounding domain addresses potential confounding factors and helps the assessor judge whether another factor may explain the study's reported association.

A study will have high risk of bias if it does not control for any variables that have the potential to confound or explain the association between fear avoidance beliefs and outcome; these studies considered some (one or two) of the confounding domains of interest. Conversely, studies with adequate measurement of important potential confounding variables and inclusion of these variables in a prespecified multivariable analysis will have low risk of bias. These studies adequately assessed potential confounders, representing at least three of these domains: individual demographics (for example, age, sex, gender), social support (for example, marital status, socioeconomic status), work factors and environment (for example, occupation, physical demands, workplace culture), psychological factors (for example, depression, anxiety, coping), and LBP complaint factors (for example, baseline pain severity, baseline disability, duration of episode at baseline).

Study Confounding		
Important potential confounding factors are appropriately accounted for		
Issues to consider for judging overall rating of risk of bias	**Study methods and comments**	**Rating of reporting**

Important confounders measured	All important potential confounders are measured, including a reasonably comprehensive set of factors representing our domains of interest: individual demographics (e.g. age, sex, gender), social support (e.g., marital status, socioeconomic status), work factors and environment (e.g. occupation, physical demands, workplace culture), psychological factors (e.g. depression, anxiety, coping), and LBP complaint factors (e.g. baseline pain severity, baseline disability, duration of episode at baseline).		
Definition of the confounding factor	Clear definitions of the important confounders measured are provided (e.g. including dose, level, and duration of exposures).		
Valid and reliable measurement of confounders	Measurement of all important confounders is adequately valid and reliable (e.g. may include relevant outside sources of information on measurement properties, also characteristics, such as blind measurement and limited reliance on recall).		
Method and setting of confounding measurement	The method and setting of confounding measurement are the same for all study participants.		
Method used for missing data	Appropriate methods are used if imputation is used for missing confounder data.		
Appropriate accounting for confounding	Important potential confounders are accounted for in the study design (e.g. matching for key variables, stratification, or initial assembly of comparable groups; see variables below).		
	Important potential confounders are accounted for in the analysis (i.e. appropriate adjustment). Minimal control for potential confounding in included studies will consider 1 - 2 of the domains of interest. Adequate control for confounding will consider at least three of the five domains of interest. The domains of interest are: individual demographics (e.g. age, sex, gender), social support (e.g. marital status, socioeconomic status), work factors and environment (e.g. occupation, physical demands, workplace culture), psychological factors (e.g. depression, anxiety, coping), and LBP complaint factors (e.g. baseline pain severity, baseline disability, duration of episode at baseline).		
Summary study confounding	**Important potential confounders are appropriately accounted for, limiting potential bias with respect to the relationship between FAB and LBP outcome.**		

Bias: statistical analysis and reporting

The statistical analysis and reporting domain addresses the appropriateness of the study's statistical analysis and completeness of reporting. A study was considered to have low risk of bias if the statistical analysis is appropriate for the data, statistical assumptions are satisfied, and all primary outcomes are reported.

Statistical Analysis and Reporting			
The statistical analysis is appropriate, and all primary outcomes are reported			
Issues to consider for judging overall rating of risk of bias		**Study methods and comments**	**Rating of reporting**
Presentation of analytical strategy	There is sufficient presentation of data to assess the adequacy of the analysis.		
Model development strategy	The strategy for model building (i.e. inclusion of variables in the statistical model) is appropriate and is based on a conceptual framework or model.		
	The selected statistical model is adequate for the design of the study.		
Reporting of results	There is no selective reporting of results (studies report only factors positively associated with outcomes).		
Summary statistical analysis and reporting	**The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid or spurious results, and selective reporting is unlikely.**		

Appendix 3. Records excluded at title/ abstract screen. Characteristics of excluded studies [ordered by study ID]

ID	Author	Reason for exclusion
1	Indahl A., 1999	Inappropriate publication type: review
2	Pfingsten M., 2001	Inappropriate publication type
3	Heinrich M., 2011	Inappropriate population: chronic low back pain
4	Scholich S.L., 2011	Inappropriate population: chronic low back pain
5	Hasenbring M., 2001	Inappropriate publication type
6	Coudeyre E., 2006	Inappropriate publication type: RCT without secondary prognosis analysis
7	Buchbinder R., 2001	Inappropriate study's aim
8	Flynn T., 2002	Inappropriate study's aim
9	TCTR20150626001, 2015	Inappropriate publication type
12	Lamb S.E., 2010	Inappropriate publication type: RCT without secondary prognosis analysis
14	Reis S., 1999	Inappropriate study's aim: no FAB exposure
15	Guetin S., 2016	Inappropriate design and aim of study
16	Gillette R.D., 1996	Inappropriate publication type: review
18	Schultz I.Z., 2008	Inappropriate study's aim
19	Hoiriis K.T., 2004	Inappropriate publication type: RCT without secondary prognosis analysis
20	Mannion A.F., 1999	Inappropriate population: chronic low back pain
21	Apeldoorn, A.T., 2012	Inappropriate population: subacute and also chronic low back pain
23	Indahl A, 1999	Inappropriate publication type: review
24	Roland M., 1983	Inappropriate study's aim: no FAB exposure
26	Pincus T., 2002	Inappropriate publication type: review
27	Soderlund A., 2009	Inappropriate population: whiplash associated disorders (WAD)
28	Hurley D.A., 2009	Inappropriate population: chronic low back pain
30	Modic M.T., 2005	Inappropriate study's aim: no FAB exposure
31	Swinkels-Meewisse, 2006	Inappropriate study's aim
32	Berube M., 2017	Inappropriate publication type: review
33	Goertz C.M., 2013	Inappropriate study's aim
34	Hilde G., 2006	Inappropriate publication type: review
35	Newcomer K.L., 2010	Inappropriate population: acute and also chronic low back pain
36	Riley S.P., 2020	Retrospective study: acute and also chronic low back pain
38	Leonhardt C., 2009	Inappropriate population: acute and also chronic low back pain
39	Linton S.J., 2000	Inappropriate study's aim
40	Grotle M., 2010	Inappropriate population: acute, subacute and also chronic low back pain
41	Pool JJM, 2010	Inappropriate population: neck pain
42	Klyne D.M., 2019	Inappropriate study's aim
43	Edmond S.L., 2014	Retrospective study and inappropriate population (neck pain)
44	Koppenhaver S.L., 2012	Inappropriate study's aim
45	Oleske D.M., 2000	Inappropriate study's aim: no FAB exposure
46	Nordin M., 2002	Inappropriate study's aim: no FAB exposure
47	Sharpe L., 2014	Inappropriate study's aim: no FAB exposure

49	Schultz I.Z., 2002	Inappropriate population: subacute and also chronic low back pain
50	Demmelmaier I, 2010	Inappropriate population: general population
51	Brunner E., 2013	Inappropriate publication type: review
53	Buitenhuis J., 2006	Inappropriate population: whiplash associated disorders (WAD)
54	Vlaeyen J.W.S., 2002	Inappropriate population: chronic low back pain
55	Hancock MJ, 2009	Inappropriate study's aim
57	Agnello A., 2010	Inappropriate publication type: review
58	Linton, S. J., 1998	Article not avaible
59	Wertli M.M., 2014	Inappropriate publication type: review
61	May S., 2012	Inappropriate publication type: review
63	Werneke M.W., 2005	Inappropriate study's aim
64	Werneke M.W., 2008	Retrospective study: acute and also chronic low back pain and neck pain
65	Moore J.E., 2010	Inappropriate publication type: review
66	Vela LI, 2011	Inappropriate study's aim
67	Grotle M., 2006	Inappropriate population: acute and also chronic low back pain
68	Coste J, 1994	Inappropriate study's aim: no FAB exposure
69	Grotle M., 2005	Inappropriate follow-up period
70	Mahmud M.A., 2000	Inappropriate study's aim: no FAB exposure
71	Stockton and Lanier, 1988	Inappropriate study's aim: no FAB exposure
72	Scott W, 2014	Inappropriate population: whiplash associated disorders (WAD)
73	Mariano TY, 2018	Inappropriate publication type: review
75	Olaya-Contreras P, 2011	Inappropriate follow-up period
77	Zufferey P., 1998	Retrospective study: acute and also chronic low back pain
78	Verhagen A.P., 2007	Inappropriate publication type: review
80	McIntosh G., 2006	Inappropriate study's aim: no FAB exposure
81	Pruneti C., 2014	Inappropriate population: acute and also chronic low back pain
83	Cai C., 2007	Retrospective study: acute and also chronic low back pain
84	Fernandes L, 2012	Inappropriate population: acute and also chronic low back pain
86	Leonhardt C, 2007	Inappropriate study's aim
89	Rahmat A., 2017	Retrospective study: acute and also chronic low back
90	Céline M., 2011	Inappropriate population: chronic low back pain
94	Wideman T.H., 2011	Inappropriate population: musculoskeletal pain
95	Werneke M., 2003	Inappropriate population: low back pain and neck pain
98	Bannon B.L., 2019	Article not avaible
99	Mishra B.K., 2007	Inappropriate study's aim and inappropriate population
101	van der Windt, 2007	Inappropriate population: both low-back pain and shoulder pain
102	Westman A., 2008	Inappropriate population: Chronic musculoskeletal pain
103	Hendrick P., 2013	Inappropriate study's aim: no FAB exposure and inappropriate follow-up period
104	Verwoerd A.J.H., 2015	Inappropriate population: patients with sciatica
105	Hendrick P., 2009	Inappropriate study's aim: no FAB exposure
106	Ferrari S., 2019	Inappropriate population: spondylolisthesis and retrospective study: sub-acute and also chronic pain
107	Nordeman L., 2006	Inappropriate study's aim: no FAB exposure
108	Nicholas M.K., 2011	Inappropriate publication type
109	Hazard R.G., 1997	Inappropriate follow-up period
110	ISRCTN32765488, 2003	Inappropriate study's aim

113	Darlow B., 2015	Inappropriate population: acute and also chronic low back pain
114	Coudeyre E., 2007	Inappropriate study's aim
115	NCT01918228	Inappropriate study's aim
116	Thomas J.S., 2020	Inappropriate study's aim
117	Chenot J-F, 2019	Inappropriate study's aim
118	PACTR201910691645076, 2019	Inappropriate study's aim
119	Rantonen J, 2018	Inappropriate study's aim
120	Gaines W.G., 1999	Inappropriate study's aim
121	Ash L.M., 2008	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
123	Skovron M.L., 1992	Inappropriate publication type
124	French S.D., 2013	Inappropriate study's aim
125	Stanton T.R., 2011	Inappropriate study's aim: no FAB exposure
126	Olsson L.E., 2016	Inappropriate population: total hip arthroplasty (THA)
127	Rebbeck T.J., 2007	Inappropriate population: whiplash associated disorders (WAD)
128	Corbiere M., 2011	Inappropriate population: musculoskeletal pain
129	Boersma K., 2006	Inappropriate population: neck pain
130	Heymans MW, 2007	Retrospective study: chronic low back pain
131	Oleinick A., 1996	Inappropriate study's aim: no FAB exposure
132	Graves J.M., 2012	Inappropriate study's aim
133	Diaz-Ledezma C, 2009	Inappropriate study's aim and retrospective study
134	Anguita-Palacios M.C., 2016	Inappropriate population: knee arthroscopy ambulatory surgery
135	Pincus T., 2006	Inappropriate publication type: review
136	Meier M.L., 2015	Inappropriate study's aim
138	Rosenbloom B.N., 2020	Inappropriate population: children and adolescents
140	Markfelder T., 2020	Inappropriate publication type
141	Turk D.C., 2010	Inappropriate publication type: review
142	McNeil D.W., 2018	Inappropriate population: chronic pain
143	George SZ, 2006	Inappropriate population: pain-free individuals
144	Hirsh A.T., 2008	Inappropriate population: healty individuals
145	den Hollander M., 2010	Inappropriate population: chronic pain
146	Coudeyre E., 2007	Inappropriate study's aim
147	George S.Z., 2006	Inappropriate study's aim
148	Nava-Bringas, 2017	Inappropriate population: chronic pain
149	Swinkels-Meewisse, 2006	Inappropriate study's aim
150	Indahl A., 1998	Inappropriate study's aim
151	Dixon A.N., 1999	Inappropriate study's aim: no FAB exposure
152	Corley A.M., 2016	Inappropriate study's aim
153	Indahl A., 1995	Inappropriate study's aim: no FAB exposure
154	RBR-7ffw9k	Inappropriate publication type
155	Durand M.J., 2002	Inappropriate publication type
156	Cedraschi C., 2005	Inappropriate publication type
157	Apkarian A.V., 2010	Inappropriate publication type
158	Melloh M, 2009	Inappropriate publication type: review
161	Brennan G.P., 2006	Inappropriate study's aim
162	Louw A., 2019	Inappropriate study's aim
163	Nagarajan M., 2010	Inappropriate study's aim

164	Buchbinder R., 2007	Inappropriate study's aim
165	Stewart A.M., 2012	Inappropriate outcome: expectations of RTW
166	Storheim K., 2003	Inappropriate study's aim
167	Goldman E.F., 2010	Inappropriate population: hamstring injuries
169	Newcomer K.L., 2008	Inappropriate study's aim
170	Luque-Suarez A., 2008	Inappropriate publication type: review and inappropriate population: whiplash associated disorders (WAD)
171	Huijnen I.P.J., 2010	Inappropriate study's aim
174	Trost Z, 2007	Article not avaible
178	Gerwin R.D., 2010	Inappropriate publication type: book
179	McIntosh G., 2000	Inappropriate publication type: review
180	Goubert L., 2004	Inappropriate study's aim
181	Valat J., 1997	Article not avaible
182	Truchon M., 2008	Inappropriate study's aim: no FAB exposure
183	Selhorst M., 2015	Inappropriate population: adolescents
184	ACTRN12616000017426, 2016	Inappropriate study's design
185	Davenport T.E., 2016	Inappropriate study's aim
186	Heneweer H., 2010	Inappropriate study's aim
187	Saner J., 2011	Inappropriate study's aim
188	Saner J., 2015	Inappropriate study's aim
189	Louw A., 2015	Inappropriate population: neurological deficit
190	Suni J.H., 2016	Inappropriate study's aim
191	Reid S., 1997	Inappropriate follow-up period
193	Jensen O.K., 2010	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
194	Franklin G.M., 2009	Inappropriate study's aim: no FAB exposure
195	Fagundes F.R.C., 2015	Inappropriate study's aim and inappropriate follow-up period
197	Poiraudeau S., 2006	Inappropriate follow-up
198	Magel J., 2017	Inappropriate study's aim
199	Prkachin K.M., 2007	Inappropriate follow-up
200	Öhlund C., 1994	Inappropriate study's aim: no FAB exposure
202	Karsdorp P.A., 2012	Inappropriate population: healty individuals
203	Ciccone D.S., 2001	Inappropriate population: also chronic LBP
205	Trost Z., 2011	Inappropriate study's aim
207	Thomas J.S., 2007	Inappropriate study's aim
208	Trost Z., 2012	Inappropriate study's aim and inappropriate population: healty individuals
211	Ohlman T., 2018	Inappropriate population: healty individuals
212	Sterling M., 2008	Inappropriate population: whiplash associated disorders (WAD)
213	George S.Z., 2004	Inappropriate study's aim
214	Luijsterburg P.A.J., 2008	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
215	Dasinger L.K., 2000	Inappropriate study's aim
216	Smucker D.R., 1998	Inappropriate study's aim: no FAB exposure
217	Lehmann T.R., 1993	Inappropriate study's aim: no FAB exposure
221	Keogh E., 2010	Inappropriate population: hand fractures
225	Kovacs F.M., 2012	Inappropriate popolation and inappropriate follow-up period
226	Margison D.A., 2007	Inappropriate study's aim

227	Thomas E, 1999	Inappropriate study's aim: no FAB exposure
232	Truchon M., 2005	Inappropriate study's aim: no FAB exposure
235	Macfarlane G.J.,	Inappropriate study's aim: no FAB exposure
236	Jellema P., 2006	Inappropriate follow-up
238	Hiebert R., 2012	Inappropriate follow-up
239	Tate R.B., 1999	Inappropriate study's aim: no FAB exposure
240	ISRCTN94152969	Inappropriate study's design
241	Louw A., 2015	Inappropriate population: LBP with distal radiation below the knee (radiculopathy)
242	Coste J., 2004	Inappropriate follow-up and no FAB exposure
243	Ursin H., 1999	Inappropriate publication type: review
245	van der Weide W.E., 1999	Inappropriate follow-up period
246	Valentin G.H., 2016	Inappropriate publication type: review
248	Kovacs F., 2007	Inappropriate population: chronic back pain
250	Verwoerd M., 2019	Inappropriate publication type: review
254	Perron M., 2018	Inappropriate population: also chronic LBP
255	Goertz M.N., 1990	Inappropriate publication type: review
257	Vangronsveld K.L., 2011	Inappropriate population: neck pain
258	Kall L.B., 2009	Inappropriate population: whiplash associated disorders (WAD)
259	Vernon H., 2010	Inappropriate population: whiplash associated disorders (WAD)
260	Lee J.E., 2013	Inappropriate population: healty individuals
261	Kovacs F.M., 2006	Inappropriate study's design and aim
262	Gomez-Perez L., 2011	Inappropriate population: chronic LBP and acute muscoloskeletal pain
264	Knezevic A., 2018	Inappropriate population: chronic muscoloskeletal pain
265	Koleck M., 2006	Inappropriate follow-up and no FAB exposure
266	Schultz I.Z., 2004	Inappropriate population: also chronic LBP
267	Adams H., 2007	Inappropriate population: whiplash associated disorders (WAD)
268	Deyo R.A., 1988	Article not avaible
270	Ramond A., 2011	Inappropriate publication type: review
271	Heneweer H, 2007	Inappropriate follow-up period
272	Niemisto L., 2003	Inappropriate publication type: review
273	Damush T.M., 2003	Inappropriate study's aim
274	Benjaminsson A., 2007	Inappropriate study's aim
275	Shaw W.S., 2006	Inappropriate publication type: review
276	de Jong J.R., 2008	Inappropriate population: neck pain
277	Bergbom S., 2011	Inappropriate population: muscoloskeletal pain and inappropriate study's aim
278	Verbunt J.A.	Inappropriate population: chronic LBP
280	Grotle M., 2006	Inappropriate population: chronic LBP
282	Rolli S., 2012	Inappropriate follow-up and no FAB exposure
284	Lakke S., 2009	Inappropriate publication type: review
287	Grotle M., 2006	Inappropriate population: also chronic LBP
289	Pauli J., 2019	Inappropriate publication type: review
290	Vingård E., 2002	Inappropriate study's aim: no FAB exposure
291	Costa Lda C., 2011	Inappropriate population: chronic LBP
292	Denison E., 2004	Inappropriate population: chronic muscoloskeletal pain
293	Wand B.M., 2010	Inappropriate study's design (RCT without follow-up) and aim

294	Bishop M.D., 2011	Inappropriate population: healty individuals
295	George S.Z., 2006	Inappropriate follow-up period and inappropriate study's aim
297	ACTRN12615000448549, 2015	Inappropriate study's design
298	Stanhope J., 2021	Inappropriate publication type: review
299	Xia T., 2016	Inappropriate study's design: RCT without follow-up
301	Ben Ami N., 2020	Inappropriate follow-up period
302	Hallegraeff J.M., 2020	Inappropriate follow-up period and inappropriate study's aim (no FAB exposure)
303	Matsudaira K., 2017	Inappropriate publication type: review
304	Henrotin Y., 2011	Inappropriate population: general practitioners and rheumatologists
305	Berenguera A., 2011	Inappropriate study's aim
306	Rodriguez-Blanco T., 2010	Inappropriate study's aim
307	Liedl A., 2010	Inappropriate population: post-traumatic stress disorder
308	Hall A.M., 2011	Inappropriate study's aim: no FAB exposure
309	Steenstra I.A., 2017	Inappropriate publication type: review
310	Pind R., 2014	Inappropriate study's aim: no FAB exposure
311	Casserley-Feeney S.N., 2012	Inappropriate population: also chronic LBP
312	NCT04155970, 2019	Inappropriate study's design
313	George S.Z., 2005	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
314	Werneke M., 2005	Inappropriate publication type: letters
315	Asenlof P., 2013	Inappropriate population: whiplash associated disorders (WAD)
316	Long A., 2008	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
317	Williams R.A., 1998	Inappropriate study's aim: no FAB exposure
318	Kovacs F.M., 2011	Inappropriate study's aim: no FAB exposure and inappropriate population: also chronic LBP
319	Darlow B., 2014	Inappropriate study's design and inappropriate population: also chronic LBP
320	Gatchel R.J., 1995	Inappropriate study's aim: no FAB exposure
321	George S.Z., 2002	Inappropriate follow-up period
323	Olaya-Contreras P., 2015	Inappropriate follow-up period
324	Gagne De, 1999	Inappropriate publication type: thesis
325	Stisen D.B., 2016	Inappropriate study's aim
326	Nieto R., 2009	Inappropriate population: whiplash associated disorders (WAD)
327	Kreddig N, 2015	Inappropriate study's design and inappropriate population: also chronic LBP
328	Hannibal K., 2015	Inappropriate follow-up period
329	Kovacs F.M., 2005	Inappropriate study's aim: no FAB exposure
330	Vangronsveld K.L.H., 2008	Inappropriate population: whiplash associated disorders (WAD)
331	Hadler N.M., 1995	Inappropriate study's aim: no FAB exposure
332	Reis S., 2007	Inappropriate study's aim: no FAB exposure
333	Shaw W., 2013	Inappropriate follow-up period
334	Bunketorp L., 2006	Inappropriate population: whiplash associated disorders (WAD)
339	Kovacs F.M., 2012	Inappropriate follow-up period and inappropriate study's aim (no FAB exposure)
340	Carey T.S., 2003	Inappropriate study's aim: no FAB exposure
341	Scholich S.L., 2012	Inappropriate population: chronic LBP

342	Al-Obaidi S.M., 2000	Inappropriate population: chronic LBP
343	Linton S.J., 2011	Inappropriate population: musculoskeletal pain and inappropriate study's aim (no FAB exposure)
344	Soderlund A., 2011	Inappropriate population: whiplash associated disorders (WAD)
345	Wertli M.M., 2014	Inappropriate publication type: review
346	Robinson J.P., 2013	Inappropriate population: whiplash associated disorders (WAD)
347	Fritz J.M., 2001	Inappropriate follow-up period
348	Besen E., 2017	Inappropriate follow-up period and inappropriate study's aim (no FAB exposure)
349	Kovacs F.M., 2005	Inappropriate study's aim: no FAB exposure
350	Landers M.R., 2008	Inappropriate population: neck pain
351	Casey C.Y., 2008	Inappropriate population: neck and back pain with radiculopathy and inappropriate follow-up period
352	Epping-Jordan J.E., 1998	Inappropriate study's aim: no FAB exposure
353	Laufer Y., 2012	Inappropriate study's design
354	Groeneweg R., 2017	Inappropriate population: neck pain
355	Sullivan M., 2017	Inappropriate population: post-traumatic stress disorder
356	Zimney K., 2014	Inappropriate follow-up period
357	Korkmaz N., 2009	Inappropriate study's design
359	Lindström I., 1994	Inappropriate study's aim: no FAB exposure
360	Davis D.S., 2013	Inappropriate population: chronic LBP
361	NCT04812158, 2021	Inappropriate study's design
362	NCT04086667, 2019	Inappropriate study's design
363	Cooper R.G., 2003	Inappropriate publication type: editorial
364	Bring A., 2016	Inappropriate population: whiplash associated disorders (WAD)
365	Traeger A.C., 2017	Inappropriate study's design
366	Carstens J.K.P., 2014	Inappropriate follow-up period
368	Soucy I., 2006	Inappropriate population: also chronic LBP
369	Grimmer-Somers K., 2008	Inappropriate study's design and aim
370	Glattacker M., 2018	Inappropriate population: chronic LBP

Appendix 4. Records excluded at full text review. Characteristics of excluded studies [ordered by study ID]

ID	Author	Reason for exclusion
10	Dionne C.E., 2005	Inappropriate population: also cervicothoracic, thoracic BP and with distal radiation below the knee
13	Verbunt J.A., 2008	Inappropriate population: LBP with distal radiation below the knee
17	Hill J.C., 2008	Inappropriate population: also LBP with distal radiation below the knee
22	George S. Z., 2008	Inappropriate population: also acute or sub-acute LBP with distal radiation below the knee
25	Ganesh, 2019	Inappropriate population: also LBP with distal radiation below the knee
29	Truchon M., 2012	Inappropriate population: also LBP with distal radiation below the knee
37	Hunt, D.G., 2002	Inappropriate study's aim: no FAB exposure
52	Roland M.O., 1983	Inappropriate study's aim: no FAB exposure
56	Hancock M.J., 2009	Inappropriate population: also LBP with distal radiation below the knee
60	Werneke M.W., 2004	Inappropriate population: also LBP with distal radiation below the knee
62	Werneke M.W., 2001	Inappropriate population: also LBP with distal radiation below the knee
76	Shaw WS, 2005:	Inappropriate follow-up period
79	Schmidt C.O., 2016	Inappropriate population: < 6 month (>12 weeks)
82	Dunn K.M., 2011	Inappropriate population: upper body pain and LBP with distal radiation below the knee
85	Öncü, J., 2016	Unclear pain site: Örebro Musculoskeletal Pain Questionnaire (ÖMPQ) evaluates number of regions of the body where pain is experienced
87	Faber E., 2006:	Inappropriate population: also LBP with distal radiation below the knee
88	Dionne C.E., 2007	Inappropriate population: back and neck pain
91	Fulton-Kehoe D., 2008	Inappropriate population: also LBP with distal radiation below the knee
92	Wideman T.H., 2012	Inappropriate population: back and neck pain
93	Gheldof, Els L M 2007	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
96	Foster N.E., 2010	Inappropriate population: also LBP with distal radiation below the knee and chronic LBP
97	Bousema E.J., 2007	Inappropriate outcome: disuse in CLBP
100	Smeets 2009	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
111	Hazard R.G., 1996	Inappropriate study's aim: no FAB exposure
112	Nordin M., 2010	Inappropriate study's aim: no FAB exposure
122	Fischer C.A., 2014	Inappropriate study's aim: no FAB exposure
137	Kovacs2007	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy) and chronic LBP
159	Cats-Baril W.L., 1991	Unclare population
160	Fritz J.M., 2002	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
168	George S.Z., 2008	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
172	Turner J.A., 2008	Inappropriate population: also LBP with distal radiation below the knee, different pain site
173	Felício D.C., 2016	Unclare population: also LBP with distal radiation below the knee (radiculopathy)

175	Chibnall, 2009	Inappropriate population: also LBP with distal radiation below the knee
176	Burton A.K., 2004	Inappropriate population: acute and chronic LBP
177	Schiøttz-Christensen B., 1999	Inappropriate population: also LBP with distal radiation below the knee
192	Wahlgren D.R., 1997	Inappropriate study's aim: no FAB exposure
196	Karjalainen K., 2003	Inappropriate study's aim: no FAB exposure
201	Picavet H.S., 2002	Inappropriate population: also chronic LBP
204	Hasenbring M.I., 2012	Inappropriate population: thoracic and lumbar pain
209	Du Bois M., 2009	Inappropriate population: also LBP with distal radiation below the knee
210	Haldorsen E.M., 1998	Inappropriate population: different LBP diagnosis
218	Wand B.M., 2009	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
219	Singer J., 1987	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
220	Gatchel R.J., 1995	Inappropriate study's aim: no FAB exposure
222	Gareth T.J.,2006	Inappropriate study's aim: no FAB exposure and inappropriate follow-up period
223	Cherkin D.C., 1996	Inappropriate population: also LBP with distal radiation below the knee
224	Schultz I.Z., 2005	Inappropriate follow-up period, inappropriate population: also chronic LBP, no FAB exposure
228	Jellema P.H., 2007	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
229	Seferlis T., 2000	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy) and inappropriate study's aim: no FAB exposure
230	Burton AK, 1991	Inappropriate study's aim: no FAB exposure
231	Dozois D.J., 1996	Inappropriate study's aim: no FAB exposure
233	Hagen E.M., 2005	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy), muscoloskeletal pain
234	Haldorsen E.M.H., 1998	Inappropriate study's aim: no FAB exposure
237	Storheim K., 2005	Unclare population: LBP with pain radiating to the leg but radiculopathy was excluded (?)
244	Henschke N., 2008	Inappropriate study's aim: no FAB exposure
247	Steenstra I.A., 2005	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
249	Helmhout, 2010	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy) and chronic LBP
251	Infante-Rivard C., 1996	Inappropriate population: specific back pain
252	McIntosh G, 2000	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy) and inappropriate study's aim: no FAB exposure
253	Grotle M., 2007	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
256	Pedersen P.A., 1981	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy), chronic LBP and no FAB exposure
263	Cheung P.W.H., 2018	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy), chronic LBP
269	Burton A.K., 1995	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy), chronic LBP
279	Tsang C.C., 2017	Inappropriate population: back and neck pain
281	Esteve R., 2017	Inappropriate population: back and neck pain
283	Heymans M.W., 2009	Inappropriate population: also LBP with distal radiation below the knee

		(radiculopathy)
285	Fransen M., 2002	Inappropriate study's aim: no FAB exposure and inappropriate follow-up period
286	Main C.J., 1995	Inappropriate publication type
288	Boersma K., 2005	Inappropriate population: back and neck pain
296	Shaw W.S., 2007	Inappropriate study's aim: no FAB exposure
300	Valencia C., 2011	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
322	George S.Z., 2003	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
336	Law R.K.Y., 2013	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
337	Heymans M.W., 2010	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
338	van den Hoogen H.J., 1997	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy) and inappropriate study's aim (no FAB exposure)
358	Truchon M., 2010	Inappropriate population: also LBP with distal radiation below the knee (radiculopathy)
367	Turner, J.A., 2006	Unclare population: back pain or low back pain?

Appendix 5. Detailed QUIPS risk of bias assessments [ordered by study ID]

Study: Sieben, 2005		
Domain	**Risk of bias level**	**Support for judgement**
Study Participation	Low	Participation rate 47,8%; Selection criteria, baseline sample and recruitment were adequately described
Study Attrition	Moderate	78.4% follow-up; non-responders were younger; no reasons provided for loss to follow-up
Prognostic Factor Measurement	Low	Valid and reliable measure of PF
Outcome Measurement	Moderate	Valid and reliable measure of outcome but adapted version instead of the original instrument for the secondary measurements
Study Confounding	Low	Adequate adjustment (demographic, biological, psychological and social measures)
Statistical Analysis and Reporting	Moderate	Insufficient presentation of data (dropout rate of 21.6%); appropriate analysis for research question and study design; no apparent selective reporting of results

Study: Wolff, 2020		
Domain	**Risk of bias level**	**Support for judgement**
Study Participation	High	Participation rate unclear; Baseline characteristics not adequately described
Study Attrition	High	Response rates end of study = 86%; no information provided on differences in characteristics, on reasons for loss on differences found between dropouts and those with follow-up data
Prognostic Factor Measurement	Low	Valid and reliable measure of PF
Outcome Measurement	Low	Valid and reliable measure of outcome
Study Confounding	High	Univariate only
Statistical Analysis and Reporting	Moderate	Analysis not sufficient; no apparent selective reporting of results

Study: Klyne, 2020		
Domain	**Risk of bias level**	**Support for judgement**
Study Participation	Moderate	Participation rate 8,3%; Selection criteria, baseline sample and recruitment were adequately described
Study Attrition	Moderate	Response rates end of study = 69%; no reasons provided for loss to follow-up; baseline characteristics between who did and did not follow-up no described
Prognostic Factor Measurement	Low	Valid and reliable measure of PF
Outcome Measurement	Low	Valid and reliable measure of outcome
Study Confounding	Low	Adequate adjustment (demographic, biological, psychological and social measures)
Statistical Analysis	Moderate	No reported statistical analysis; no apparent selective reporting of

and Reporting		results

Study: Swinkels-Meewisse, 2006		
Domain	**Risk of bias level**	**Support for judgement**
Study Participation	Low	Participation rate 90%; Selection criteria, baseline sample and recruitment were adequately described
Study Attrition	Moderate	Response rates end of study = 78%; no reasons provided for loss to follow-up; provided differences between participants who completed the study and those who did not
Prognostic Factor Measurement	Moderate	Only TSK to evaluate Fear of Movement/(Re)Injury; Valid and reliable measure of PF
Outcome Measurement	Low	Valid and reliable measure of outcome
Study Confounding	Low	Adequate adjustment (demographic, biological, psychological and social measures)
Statistical Analysis and Reporting	Low	Appropriate analysis for research question and study design; no apparent selective reporting of results

Study: Sieben, 2002		
Domain	**Risk of bias level**	**Support for judgement**
Study Participation	Moderate	Participation rate unclear; baseline characteristics quite well described
Study Attrition	Moderate	Response rates end of study = 68%; no information provided on reasons for loss; no differences found between dropouts and those with follow-up data
Prognostic Factor Measurement	Moderate	Evaluating only pain-related fear and pain catastrophizing; valid and reliable measure of PF
Outcome Measurement	Moderate	Only disability evalutated; valid and reliable measure of outcome
Study Confounding	Moderate	Minimal adjustment (pain-related fear, pain catastrophizing, pain)
Statistical Analysis and Reporting	Moderate	No analyses with appropriate, large sample sizes

Study: Klenerman, 1995		
Domain	**Risk of bias level**	**Support for judgement**
Study Participation	Moderate	Participation rate unclear; baseline characteristics quite well described
Study Attrition	High	41% follow-up at 12 months; no information provided on reasons for loss
Prognostic Factor Measurement	Moderate	FAB evaluated quite well; valid and reliable measure of PF
Outcome Measurement	Low	Valid and reliable measure of outcome
Study Confounding	Moderate	Minimal adjustment (demographic, FAB, historical)
Statistical Analysis and Reporting	Moderate	No suffcient presentation of data; appropriate analysis for research question and study design; no apparent selective reporting of results

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