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Can physical and psychological factors predict pain recurrence or an exacerbation of persistent non-specific low back pain? A protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction Low back pain (LBP) is a global health concern. Approximately two-thirds of those who recover from LBP experience a relapse within a year, with many chronic cases encountering acute flare-ups (exacerbation). This systematic review will synthesise and analyse whether physical and/or psychological features can predict recurrent episodes of LBP or exacerbation of pain.

Methods and analysis This systematic review protocol follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines. Comprehensive literature searches will be conducted in MEDLINE, EMBASE, APA PsycInfo, PubMed, CINAHL Plus, Web of Science, Scopus and ZETOC, spanning from each database's inception through to January 2025. Google Scholar and grey literature sources, including OpenGrey, will also be searched to ensure comprehensive coverage. Two independent reviewers will screen titles, abstracts and full texts, assessing the risk of bias with a modified Quality in Prognosis Studies tool. The overall certainty of evidence will be evaluated using an adapted Grading of Recommendations Assessment, Development and Evaluation approach. If sufficient data homogeneity is present, a meta-analysis will be performed; otherwise, findings will be synthesised narratively. The results will identify the ability of physical and/or psychological factors to predict pain recurrence or acute exacerbation in case of persistent non-specific LBP.

Ethics and dissemination This study protocol does not present any ethical concerns. The findings from the systematic review will be submitted for publication in a peer-reviewed journal and will also be presented at relevant conferences.

PROSPERO registration number CRD42024599514.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This systematic review will be the first to summarise predictive physical and psychological factors for pain recurrence or acute exacerbation in those with recurrent or persistent non-specific low back pain, respectively.
⇒ The protocol is written in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses Protocols guidelines.
⇒ Potential limitations may consist of heterogeneity among studies, which may prevent meta-analysis of the results.

INTRODUCTION

Low back pain (LBP) is a global health concern,[1] affecting individuals of all age groups, with the highest impact among those aged 25–64.[2] This common condition affects both personal health and the broader economy[3–6]. In the UK, visits to general practitioners for LBP alone cost the National Health Service approximately £5 billion per year.[7]

Over two-thirds of individuals who recover from LBP will experience a relapse within a year of their initial episode.[8] Additionally, those who have chronic LBP often develop an acute exacerbation of their persistent LBP.[8–11] Acknowledging the relative contributions of physical and psychosocial factors to LBP within the framework of the biopsychosocial model, helps to provide a more comprehensive understanding of pain development, persistence and recurrence.[12] Physical factors, for instance, may serve as potential biomarkers that help differentiate individuals with LBP from asymptomatic populations[13] and may have relevance for acute exacerbation and repeated episodes of pain. Physical factors include aspects such as muscle strength and endurance,[14 15] changes in the quantity and quality of spinal movement[16–19] and deficits in proprioception and movement precision.[19–22] Furthermore, people with LBP often present with altered muscle activity,[23–25] including increased trunk

muscle coactivation[26 27] as well as delayed and reduced variability of anticipatory postural adjustments,[28 29] and may present with morphological changes of the lumbar muscles.[30] A recent systematic review indicates that people with recurrent LBP (rLBP) show muscle activity changes even during pain remission, particularly in the form of increased co-contraction, altered distribution of muscle activity and delayed activation of deeper trunk muscles for postural control.[31] Changes in sensory perception and altered pain sensitivity[32] are also common features of people with persistent LBP and may have relevance for the recurrent and persistent nature of LBP. Besides physical changes in the presence of LBP, psychological factors, such as fear of movement, pain catastrophising and poor self-efficacy, are common and have been shown to be relevant for the transition from acute to chronic pain.[33–35] Such factors not only contribute to physical changes but may also serve as predictors of future disability, as they often hinder recovery and limit rehabilitation efforts.[36]

Despite the high prevalence of non-specific rLBP and acute exacerbation of non-specific persistent LBP, the literature has not been systematically reviewed to determine whether physical and/or psychological features can predict LBP recurrence or exacerbation. Therefore, the objective of this systematic review will be to identify predictors of non-specific LBP recurrence and exacerbation.

Table 1 Potential physical predictors of pain recurrence and exacerbation in non-specific low back pain

Potential physical predictors	Outcome of measurement
Lumbar kinematic features	Active range of motion Speed of movement Smoothness of movement
Muscle activity	Amplitude of muscle activity Timing of activation Muscle coactivation
Proprioception	Reposition error
Muscle properties	Total cross-sectional area Index of fatty tissue Connective tissue changes
Motor output	Muscle strength Endurance or fatigue
Pain sensitivity	Pain pressure threshold Conditioned pain modulation Temporal summation of pain Hot and cold detection threshold Hot and cold pain threshold

METHODS AND ANALYSIS

This protocol is reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P)[37] and updated guidance of the Cochrane Handbook for Systematic Reviews of Interventions.[38] The protocol has been prospectively registered on PROSPERO (CRD42024599514). Findings from this systematic review and meta-analysis will be reported following the PRISMA 2020 guidelines.[39]

Eligibility criteria

To outline the key elements of eligibility for this systematic review, the PICOS framework has been applied: P for Population, I for Index prognostic factor, C for Comparator prognostic factors (alternate prognostic variables that, in a sense, can be compared), O for Outcome(s) and S for Study design.[40]

Population

The population of interest includes people aged 18 years or older with a history of non-specific LBP who are in a period of remission at the start of the study, as well as people aged 18 or older with a history of non-specific, persistent LBP. Due to the heterogeneity identified during the scoping search for rLBP, we will consider studies that include people with a history of LBP who have recovered and were pain-free for at least 1 month at the time of assessment[41] but without imposing a timeframe for how long they have been pain-free. For persistent LBP, we will consider studies where people have experienced LBP for more than 3 months.[42] Regarding recurrence or exacerbation, we will include studies that report the number of days with LBP, days on sick leave or pain intensity.[41]

Index prognostic factors (potential physical and psychological predictors of LBP recurrence and exacerbation)

Physical predictors will include physical factors such as lumbar kinematics (eg, range, speed and smoothness of lumbar movement), muscle activity, proprioception, muscle morphological properties and measures of pain sensitivity assessed using validated and objective methods (table 1). Additionally, psychological predictors will be considered, such as fear of movement, coping strategies, self-efficacy, pain catastrophising and levels of anxiety and depression (table 2).

Outcomes

The primary outcome of interest is the number of episodes or days with LBP, measured through reports of LBP recurrence or exacerbation at any time point over a period of follow-up. We will include studies that report either the number of days within one episode or the number of episodes within a given time frame. Secondary outcomes include pain intensity and disability levels.

Studies

We will include cohort and longitudinal studies that have included people with a history of LBP (who either recovered and were pain- free at the time of assessment) or people with persistent LBP to document recurrence or exacerbation of symptoms over time. To be included, studies must have a follow-up duration of at least 3 months and report whether participants experienced a new

Table 2 Potential psychological predictors of pain recurrence and exacerbation in non-specific low back pain

Potential psychological predictors	Description	Example questionnaire(s)
Fear of movement	The fear of pain or re-injury associated with movement	Tampa Scale for Kinesiophobia[62] Fear-avoidance beliefs questionnaire[63]
Coping strategies	Methods individuals used to manage stress and pain	Coping strategy questionnaire[64] Pain coping inventory[65]
Self-efficacy	Confidence in one's ability to manage pain effectively	Pain self-efficacy questionnaire[66]
Pain catastrophising	Tendency to magnify or focus on pain-related thoughts	Pain catastrophising scale[67]
Anxiety and depression	Emotional states that may affect pain and recovery	Hospital anxiety and depression scale[68]

episode or exacerbation of their LBP as well as studies that report the duration or number of episodes.

Exclusion criteria

Studies involving people with radicular pain, serious spinal pathologies (eg, tumours, infections, cauda equina syndrome) or pregnancy will be excluded. Additionally, case reports, case-control studies and articles with only an abstract will be excluded.

Search strategy

Comprehensive searches will be conducted across several databases, including MEDLINE, EMBASE, APA PsycInfo, PubMed, CINAHL Plus, Web of Science, Scopus and ZETOC. Additional searches will cover Google Scholar and grey literature sources such as OpenGrey. The initial search strategy will be developed in MEDLINE and subsequently tailored for the other databases. Only English language publications will be included. The search strategy has been developed in collaboration with a specialist librarian at the University of Birmingham, UK. The search strategy for each database is provided in online supplemental file 1.

Selection process

Before the eligibility screening starts, the search results identified by the specified databases will be collected into a digital library and organised by search database using EndNote V.20 (Clarivate Analytics) reference management software. At this stage, any duplicate articles will be identified and removed.

Then, in the initial step of the screening process, two reviewers (KW and CWGY) will independently screen titles and abstracts using an online screening form, created and piloted based on eligibility criteria, within the web-based application Rayyan (http://rayyan.qcri.org). Studies will be categorised as 'include', 'exclude' or 'maybe'. In the second step, full texts of studies deemed potentially relevant will be retrieved and independently assessed by each reviewer (KW and CWGY) against the eligibility criteria. Studies will be included if both reviewers agree on eligibility. Any disagreements will be resolved through discussion, or, if necessary, by consulting a third author (DF).

Data collection process

Both reviewers (KW and CWGY) will independently extract data using a standardised extraction form developed for this review. Each reviewer will assess and extract relevant data individually. In cases of disagreement, the two reviewers (KW and CWGY) will discuss to reach a consensus. If necessary, a third reviewer (DF) will be consulted to resolve any remaining disagreements, ensuring accurate and comprehensive data extraction before proceeding with eligible studies. To facilitate accurate classification and interpretation of studies, a PRISMA flow diagram will be presented, detailing both included and excluded studies, along with the reasons for exclusion.

Data items

For the process of data extraction, the CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS) will be used.[43 44] Data will be extracted across 11 CHARMS domains, which include (1) source of data, (2) participants, (3) outcome to be predicted, (4) candidate predictors, (5) sample size, (6) missing data, (7) model development, (8) model performance, (9) model evaluation, (10) results and (11) interpretation and discussion. If missing data or ambiguously presented results are identified, the corresponding author will be contacted for clarification and additional details. If the author does not respond within 6 weeks, or if the clarification provided does not meet the criteria for inclusion, the data will not be presented.

Risk of bias

The methodological quality of the included studies will be evaluated using the modified Quality in Prognosis Studies tool,[45 46] as recommended by the Cochrane Prognosis Methods Group.[47] This tool assesses the risk of bias (RoB) across six domains: (1) study participation, (2) study attrition, (3) measurement of prognostic factors, (4) control of confounding variables, (5) outcome measurement and (6) analysis and reporting methods. Rather than scoring individual items, all items are collectively considered to provide an overall risk assessment for each domain. Each

domain for the included studies will be independently evaluated by two reviewers (KW and CWGY) as having a low, moderate or high risk of bias. An overall bias rating will then be assigned as follows: low if five or six domains have a low risk of bias, moderate if four domains have a low risk and high if only one to three domains have a low risk of bias. Any disagreements will be resolved through discussion or, if necessary, by involving a third reviewer (DF). For the sensitivity analysis, we will assess the impact of study quality by including only studies with a low RoB in the meta-analysis. This will allow us to examine how study quality may affect the overall results.

Certainty of evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach will be used to assess the overall certainty of evidence in this review.[48 49] The GRADE system is particularly effective in evaluating individual prognostic factors, as it provides a structured framework to determine the strength and certainty of the evidence.[50] When applying the GRADE approach, several factors that may reduce the quality of evidence will be taken into account. These include the phase of investigation, study limitations, inconsistency of results across studies, indirectness of evidence, imprecision in estimates and potential publication bias. Conversely, two factors that may increase the quality of evidence are a moderate or large effect size, as well as the presence of an exposure-response gradient. These considerations will help ensure that the quality of evidence is accurately assessed, ultimately guiding the interpretation and recommendations derived from the findings.

Data synthesis and meta-analysis

The primary objective of this systematic review is to summarise physical and psychological factors that may predict the recurrence or exacerbation of LBP. A quantitative synthesis will be performed if sufficient homogeneity is observed in the measurement methodologies used for the predictors and the statistical methods employed across studies. Furthermore, if at least five primary studies are available, meta-regression will be performed to explore the sources of heterogeneity and examine the impact of various factors on outcomes. In cases where a meta-analysis is not feasible due to data limitations or significant heterogeneity, a qualitative synthesis of the findings will be conducted.

Accuracy of study selection

To assess inter-rater reliability for each phase of study selection, RoB assessment and quality appraisal, the Kappa statistic with 95% CI will be used. Statistical analyses will be performed using SPSS Statistics V.29 (IBM).

Summary statistics

Non-dichotomous outcome measures, such as pain, disability and the frequency of LBP occurrences/exacerbation, will be summarised using the mean difference or adjusted mean difference. For the occurrence of rLBP episodes, which is a dichotomous outcome, the pooled risk ratio (RR) will be calculated using data from cohort studies. If the RR is not directly provided in the original studies, it will be estimated based on the number of events observed in groups with and without exposure to the specific predictor of interest. In cases where it is not possible to compute the RR with the available data, the corresponding author of the study will be contacted to request the raw data. If there is no response after reasonable efforts, the study will be excluded from the meta-analysis. All statistical conversions, including those for estimating RR or other relevant metrics, will be thoroughly detailed and reported in the main article.

Data synthesis

Data synthesis will involve pooling the results if there is sufficient homogeneity in the measurement methodologies used for the predictors and the statistical methods employed across two or more predictors. If the studies show significant variability or if the data cannot be combined due to differences in methodologies or statistical approaches, a meta-analysis will not be feasible. In such cases, a qualitative synthesis will be conducted to summarise the findings and provide insights into the trends and patterns across the studies included in the systematic review.

Meta-analysis

If a meta-analysis is possible, fixed-effect or random-effect models will be applied depending on the level of heterogeneity observed. Fixed-effect models will be used when heterogeneity is low. In contrast, random-effects models will be chosen for moderate to high heterogeneity.[51] The data will be examined through a predefined subgroup analysis, considering the predictors' domains and measurement methods of the predictors. When a predictive factor or outcome is measured in multiple ways within a study, we will address this by grouping the measures into the same domain, such as fear of movement, pain catastrophising or poor self-efficacy, based on their conceptual relevance. If harmonisation of the measures is feasible, we will apply standardisation techniques (eg, z-scores or effect sizes) to combine them into a single metric for analysis. However, if harmonisation is not possible due to differences in measurement scales or constructs, we will stratify the results by the type of measure used and evaluate potential heterogeneity. Regarding outcomes, recurrence or exacerbation will be classified into two categories: studies reporting recurrence based on pain intensity (eg, pain>2/10) and studies reporting recurrence based on the duration of LBP or associated sick leave (eg, number of days with LBP or sick leave). For studies reporting correlation coefficients, we will extract and analyse these results separately. For studies presenting regression models, we will use beta coefficients and their corresponding confidence intervals or SE. If necessary, we will adjust these beta coefficients by approximating their relationship to correlation coefficients, as suggested by Peterson and Brown (2005),[52] to

facilitate integration with other effect size metrics. We will apply these adjustments where appropriate and clearly describe the process and its impact on the analysis. When combining results is not feasible due to significant methodological differences, we will stratify the analysis by the type of statistic reported (eg, correlations vs regression coefficients) and evaluate any heterogeneity between these subgroups. A forest plot will be used as a graphical tool to present the vote-counting synthesis, illustrating the direction of the effect for each predictor. It will also display study-specific estimates alongside the meta-analysis summary result of the adjusted prognostic effect (RR).

Heterogeneity

To assess statistical heterogeneity, the I^2 statistic and the Q statistic will be used, with a significance threshold set at<0.1.[53] In addition to the Q statistic, the I^2 test will be used to assess the extent of heterogeneity. The I^2 test produces a score ranging from 0% to 100%, where scores of 0–30%, 30–50%, 50–70% and 70–100% correspond to low, moderate, considerable and substantial heterogeneity, respectively.[54] If the heterogeneity is found to be low (I^2<50%), a fixed-effects model will be applied. Conversely, if substantial heterogeneity (I^2>50%) is detected, a random-effects model will be used to account for this variability.[55]

Subgroup analysis

Subgroup analyses will then be conducted based on the type of physical factors (eg, range of motion, proprioception, muscle coactivation, cross-sectional area of muscle, muscle strength, muscle endurance, pain pressure threshold), psychological factors (eg, Tampa Scale for Kinesiophobia, Pain Coping Inventory, Pain Self-Efficacy Questionnaire, European Quality of life - 5 Dimensions), follow-up duration (short (≤6 months) vs long (>6 months))[56] and participant population.

Reporting bias

Publication bias across the studies will be examined using a funnel plot, which displays the study estimates (on the x-axis) in relation to their precision (on the y-axis). A funnel plot is generally advised when there are 10 or more studies included.[57] Ideally, the plot should exhibit a symmetrical, funnel-shaped pattern, with results from larger studies concentrated in the centre and smaller studies distributed evenly on either side. If the funnel plot is symmetrical, it suggests the absence of reporting bias; however, asymmetry may indicate the presence of publication bias. Egger's test will be conducted to quantitatively assess publication bias, with a threshold of p<0.1 indicating potential bias.[58] This significance level is chosen due to the test's relatively low statistical power. If publication bias is identified, the trim and fill method will be employed to address it.[59]

Confirmation of predictive factors

To confirm whether a factor is predictive or not, two key criteria, based on established methodology, will be applied.[60 61] First, the factor must show a statistically significant effect for a sufficient proportion of the included studies. Rather than adhering to a rigid threshold, we will emphasise a more detailed evaluation, considering study size, quality and context. Second, the factor should consistently demonstrate the same effect direction (positive or negative) across studies. When multivariate analyses are available, they should further validate the predictive value of the factor by adjusting for potential confounding variables.

Patients and public involvement

The research question for this study was developed through collaborative discussions with patients and the research team at the Centre of Precision Rehabilitation for Spinal Pain (CPR Spine) at the University of Birmingham. Given the high rate of recurrence and the increasing prevalence of LBP in this population, we identified a pressing need to develop this systematic review protocol. While patients are not involved in the data collection or analysis phases of this review, the findings will be shared with relevant patient groups and presented at public engagement events to support improved care for individuals affected by LBP.

Ethics and dissemination

Since no patient data are being gathered, ethical approval is not needed for this systematic review. The outcome of this review will be presented at conferences and published in peer-reviewed journals.

Implication of results

The findings from this study will provide a valuable synthesis of existing evidence on potential physical and psychological factors that can predict pain recurrence or an exacerbation of persistent non-specific LBP. The findings may guide the development of preventive programmes tailored to address these identified factors, ultimately reducing LBP recurrence and exacerbation, and helping to improve quality of life and function. Despite anticipated challenges due to variability in study methodologies that may prevent meta-analysis, a thorough narrative analysis will enable this review to meet its goals by providing an in-depth qualitative interpretation of the current evidence.

X Janet Deane @DrJanetDeane and Deborah Falla @Deb_Falla

Contributors The systematic review protocol was developed collaboratively, with input from all authors. The primary reviewers for the study will be KW, CWGY and DF. KW is a PhD candidate, with DF as the lead supervisor and JD and MM as co-supervisors. KW drafted the protocol under DF's guidance, incorporating detailed feedback from CWGY, JD and MM on manuscript drafts. All authors reviewed and approved the final version for publication. DF acts as the guarantor for the study.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, conduct, reporting or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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