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Cochrane Database of Systematic Reviews | [Protocol - Overview](#)

Pharmacological treatments for low back pain in adults: an overview of Cochrane Reviews

✉ Aidan G Cashin, Benedict M Wand, Neil E O'Connell, Hopin Lee, Matthew K Bagg, Edel O'Hagan, Christopher G Maher, Andrea D Furlan, Maurits W van Tulder, James H McAuley [Authors' declarations of interest](#)

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Abstract

Objectives

This is a protocol for a Cochrane Review (overview). The objectives are as follows:

To provide accessible, high-quality evidence on the effects of systemic pharmacological interventions for people with non-specific low back pain.

Background

Description of the condition

Low back pain (LBP) is a common health condition that has major impacts on function and disease burden ([Koes 2006](#)). It is estimated that 7.2% (95% confidence interval (CI) 6.4 to 8.0) of people across the globe have LBP at any time ([Abajobir 2017](#)), and an estimated 38.0% (standard deviation (SD) 19.4) might experience LBP during their lifetime ([Hoy 2012](#)). LBP is comparatively more common in people aged 40 to 69 years ([Hoy 2012](#)), and in those experiencing socioeconomic disadvantage ([Buchbinder 2018](#); [Ikeda 2019](#); [Schofield 2012](#)). Amongst other diseases and injuries included in the Global Burden of Disease Study, LBP has been the leading cause of reduced function since 1990; e.g.

57.65 million years lived with disability (95% CI 40.82 to 75.88 million) in 2016 ([Abajobir 2017](#)). LBP is also an increasing cause of overall disease burden. It was the eleventh largest cause of disease burden for women and the seventeenth for men in 1990, but the seventh largest cause for women and tenth for men by 2017 ([Kyu 2018](#)).

The prognosis of acute LBP is typically favourable ([Menezes Costa 2012](#)). However, 30 to 40% of people report symptoms beyond three months ([Henschke 2008](#)), at which time they are considered to have chronic low back pain (CLBP). The cause or causes underlying the development and persistence of LBP are unknown ([Koes 2007](#); [Maher 2017](#)), or cannot be reliably identified ([Hancock 2007](#)), in approximately 85% of cases. The label 'non-specific' LBP means it is not currently possible to attribute the clinical presentation to any specific disease process (e.g. infection, inflammatory condition, cancer) or structural pathology (e.g. fracture, nerve root compression) ([Koes 2007](#); [Maher 2017](#)). Research is ongoing to reliably determine the cause(s) of LBP in those cases currently labelled 'non-specific', though the impact that specific labels would have on management and outcomes is unclear.

There are significant economic consequences associated with non-specific LBP. For example, LBP incurred the third highest costs of any health condition in the USA in 2013 (USD 87.6 billion (95% CI 67.5 billion to 94.1 billion) ([Dieleman 2016](#)). This increased to the highest costs in 2016 (USD 134.5 billion (95% CI, 122.4 billion to 146.9 billion) ([Dieleman 2020](#)). In the UK, the total direct healthcare costs for an individual with CLBP are double that for someone without CLBP, matched by age, sex and geographic region ([Hong 2013](#)). Data from Australia suggest that non-specific CLBP is the most common health-related reason for early retirement ([Schofield 2008](#)), resulting in income poverty for this group ([Schofield 2012](#)).

Description of the interventions

Pharmacological interventions are the most used interventions for LBP ([Carey 2009](#); [Gore 2012](#); [Hart 2015](#); [Ivanova 2011](#)). There are multiple classes of these interventions, including opioid analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), skeletal muscle relaxants, benzodiazepines, antidepressant medicines, anticonvulsant medicines, systemic corticosteroids and anti-nerve growth factor (NGF) medicines. Opioid analgesics or NSAIDs are the most used classes amongst the countries for which data on usage are available (Australia, Italy, Portugal, UK, USA). The relative usage of the less common medicine classes varies across these countries ([Gore 2012](#); [Gouveia 2017](#); [Michaleff 2012](#); [Piccoliori 2013](#)).

Pharmacological interventions may be used to improve pain and physical function, reduce muscular spasm, modulate sensory nerve function or alter the availability of signalling chemicals in the brain. We will focus this Overview of Cochrane Reviews on systemic pharmacological interventions used to improve pain and physical function.

How the intervention might work

Pharmacological interventions for LBP are designed to act on various neurobiological targets within the body, but may also have effects through various psychosocial mechanisms ([Benedetti 2005](#); [Wager 2015](#)). The mechanisms by which different pharmacological interventions might improve pain and function are not fully understood and differ across medicine classes. We present below commonly proposed mechanism(s) for each class of medicine.

Opioid analgesics

Opioid analgesic medicines act on the naturally occurring (endogenous) opioid receptors in the nervous system, to reduce the contribution of nociceptive (danger-signalling) information to the pain experience ([Rivat 2016](#)). Opioid medicines may cause unwanted effects; commonly constipation, nausea and sedation, depending on the location and

type of receptor (Kalso 2004). Longer-term use can contribute to opioid tolerance (requiring progressively higher doses) and possible dependence (Deyo 2015).

NSAID and Paracetamol (Acetaminophen)

NSAIDs and paracetamol act on cyclo-oxygenase (COX) enzymes to interfere with natural inflammatory processes (Brune 2015). Specifically, they reduce the production of prostaglandins — signal chemicals that modulate inflammation, nociception and other autonomic processes (JÄfÄ³wiak-Bebenista 2014). Longer-term use of these medicines is associated with increased risk of cardiovascular diseases or events (e.g. stroke). Certain NSAIDs are associated with gastrointestinal side effects (e.g. stomach ulcers) (van der Linden 2009).

Skeletal Muscle Relaxants

Skeletal muscle relaxants are a range of chemically varied medicines grouped together by their shared pharmacology and function (Trevor 2018). The two main categories discern between antispasmodic medicines and antispastic medicines that are thought to act on the central nervous system, or in some cases, the skeletal muscle cell (Trevor 2018; Witenko 2014). Each muscle relaxant medicine has different clinical uses, mechanism(s) of action and associated side effects, although feelings of dizziness and drowsiness are common to all skeletal muscle relaxants (See 2008).

Benzodiazepines

Benzodiazepines act on the central nervous system, increasing the effects of the neurotransmitter gamma-aminobutyric acid (GABA). Although pharmacologically similar to skeletal muscle relaxants (Trevor 2018), benzodiazepines are not classified by the US Food and Drug Administration as skeletal muscle relaxants and are considered separately by some clinical guidelines (Qaseem 2017). Benzodiazepines produce strong sedative effects and are associated with problems with addiction, overdose and withdrawal (Bachhuber 2016; Hood 2014).

Antidepressants

Antidepressant medicines are another class of medicines of varied chemical structure, subclassified by their function. These medicines act on neurotransmitters (signal chemicals) in the brain. This is thought to produce analgesic effects independent of their effects on depression (Cohen 2001; MicÄ³ 2006), although the precise mechanisms are unclear (Harmer 2017). Categories of antidepressants prescribed to treat pain include tricyclic antidepressants (TCAs, e.g. amitriptyline), selective serotonin reuptake inhibitors (SSRIs, e.g. sertraline) and serotonin-norepinephrine re-uptake inhibitors (SNRIs, e.g. duloxetine). People with LBP may also be prescribed these medicines to improve sleep and reduce depression or anxiety. Side effects differ between the categories, although drowsiness, dry mouth and dizziness are common (Chou 2010).

Anticonvulsants

Anticonvulsant medicines act across several sites in the central nervous system. The analgesic action of anticonvulsant medicines is thought to occur through limiting neuronal excitation and enhancing inhibition, although the precise mechanisms are unclear (Maizels 2005). Anticonvulsant medicines have a long history of off-label use in pain conditions. Common dose-related side effects include drowsiness and dizziness (Derry 2019).

Systemic Corticosteroids

Corticosteroids are a class of medicines that are structurally similar to the naturally occurring human adrenal hormone cortisol, considered an important regulator of homeostasis ([Chou 2016](#); [van der Laan 2008](#)). These medicines mimic the physiological actions of cortisol to produce a wide range of effects, including both anti-inflammatory and immunosuppressive ones. Corticosteroid medicines differ by their relative potency, duration and mechanism(s) of action. Short-term use of corticosteroids is associated with increased rates of sepsis, venous thromboembolism, and fracture ([Waljee 2017](#)).

Anti-NGF

Anti-NGFs are a class of biologic medicines that consist of humanised monoclonal antibodies directed against NGF. These medicines are intended to disrupt the pro-nociceptive function of NGF in the pain experience ([Schmelz 2019](#)). There is no consensus on a specific mechanism-oriented therapeutic approach for anti-NGF in low back pain ([Schmelz 2019](#)). Common side effects include peripheral oedema, arthralgia, extremity pain, and abnormal peripheral sensations ([Bannwarth 2017](#)).

Why it is important to do this overview

Pharmacological interventions are the interventions most used by people with LBP to manage their pain. People with LBP, clinicians, researchers and health policymakers need accessible, high-quality information on the strength of the evidence for efficacy, effectiveness and safety of pharmacological interventions, and the confidence they can have in the evidence ([Chou 2018a](#); [Chou 2018b](#); [Lim 2019](#)). Cochrane Reviews have investigated the effects of pharmacological interventions and are available to decision-makers through the Cochrane Library. There are multiple reviews, of varying currency, scope and methodology. This may inhibit decision-makers' access to this evidence.

There is a need to systematically synthesise this evidence into a single accessible Overview. An Overview should improve access to high-quality information and describe the currency and scope of the information. This may support people with LBP, clinicians and policymakers to use this evidence in their health decision-making ([Hunt 2018](#)). Information on currency, scope and methodology across the reviews may also support researchers conducting updates of reviews or planning prospective reviews.

Objectives

To provide accessible, high-quality evidence on the effects of systemic pharmacological interventions for people with non-specific low back pain.

Methods

This Overview will be conducted with respect to the Cochrane Back and Neck Group's updated method guideline for systematic reviews ([Furlan 2015](#)), and Chapter V (Overview) of the *Cochrane Handbook for Systematic Reviews of Interventions* (second edition) ([Higgins 2019](#)).

Criteria for considering reviews for inclusion

Types of studies

We will include systematic reviews of randomised controlled trials published in the Cochrane Library. We will exclude reviews that include randomised and non-randomised designs, unless the data for the randomised designs are available separately. We will note and otherwise exclude Cochrane protocols and Cochrane Reviews withdrawn from the Cochrane Library. We will verify the inclusion criteria of the included systematic reviews, if necessary, by contacting the authors of these reviews.

Types of participants

We will include systematic reviews that include trials of adults, 18 years or older, with non-specific LBP (e.g. non-radicular LBP, with or without non-specific degenerative changes), of any duration. LBP is defined as a primary area of pain between the twelfth rib and gluteal fold, with or without associated leg pain ([Koes 2006](#)). We will exclude systematic reviews that include trials of participants with spinal stenosis (back and leg pain associated with narrowing of the spinal canal), low back pain caused by known structural or pathological processes (e.g. nerve root compression, osteoporosis, fractures, infection, neoplasm, metastasis) or specific medical conditions (e.g. pregnancy, inflammatory disease) ([Koes 2007](#); [Maher 2017](#)), unless the review reports results for non-specific LBP separately. We will exclude reviews that include studies of participants younger than 18 years unless they report separate results for the studies of participants 18 years or older.

Types of intervention and comparison

We will include systematic reviews that include trials of systemic pharmacological interventions, used with the intent to improve pain and function, for people with LBP. In this Overview we will consider systemic pharmacological interventions broadly as any medicine that affects the body as a whole, rather than individual parts or organs, that may be used with the intent to improve pain and function. We make no restriction on route of administration or dose. We will include systematic reviews that include trials evaluating comparisons between pharmacological interventions and placebo/sham interventions (efficacy comparisons), no intervention (including waiting-list control and continuation of usual care), or other pharmacological or non-pharmacological interventions (effectiveness comparisons). We will also include systematic reviews that include trials evaluating combinations of pharmacological interventions.

Types of outcomes measure

The outcomes for this Overview reflect the core outcome set for non-specific LBP ([Chiarotto 2015](#)), and recommendations of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) ([Dworkin 2005](#)). We make no restriction on time of measurement. We will group outcomes into a short-term period (≤ 3 months postintervention), an intermediate-term period (> 3 months and ≤ 12 months postintervention), and a long-term period (> 12 months postintervention). We will include the outcome measure closest to the midpoint of the period in cases where a review reports outcome data for multiple time points within a period, or measured the outcome at different time periods.

Primary outcomes

1. Pain, defined as pain intensity, measured on a continuous self-report scale (e.g. a visual analogue scale (VAS), numerical rating scale (NRS), the brief pain inventory (BPI) ([Cleeland 1989](#)) or other validated measure), or in dichotomous format (e.g. as the proportion of participants in each group who attained a predetermined threshold of improvement).
2. Physical function, defined as back-pain related function, measured through continuous self-report scales (e.g. Roland-Morris Disability Questionnaire (RMDQ) ([Roland 1983](#)), Oswestry Disability Index (ODI) ([Fairbank 1980](#))), functional testing protocols or other validated quantitative measures.
3. Safety, defined as adverse effects including amongst others: incidence and severity of adverse effects, trial withdrawal due to adverse effects and incidence of serious adverse effects, as described by the systematic review.

Secondary outcomes

1. Participant ratings of improvement, defined as global perceived effect, measured with a validated tool.
2. Health-related quality of life, measured with a validated tool (e.g. the 36-Item Short Form Health Survey (SF-36) ([Ware 2000](#))).
3. Workplace participation, measured with days to return-to-work, days of absenteeism or days of reduced work activities.

Search methods for identification of reviews

Electronic searches

We will search the Cochrane Database of Systematic Reviews (The Cochrane Library, current issue) using a combination of Medical Subject Headings (MeSH) and keywords ([Appendix 1](#)), without restriction. We will manage citations using [EndNote 2017](#) and [Covidence](#).

Data collection and analysis

Selection of reviews

Two authors (AGC and HL or BMW) will independently screen the title and abstract of each citation against the inclusion criteria. We will obtain the full texts of reviews meeting these criteria and screen them again to confirm inclusion. We will resolve any disagreements through discussion or recourse to a third author (MKB). Overview authors who are authors of any included reviews will not be involved in decisions involving those reviews. We will document instances where multiple reviews are identified for the same intervention, and instances where primary studies are included in multiple reviews ([Pieper 2014](#)). We will describe the selection process in an adapted PRISMA flow chart ([Moher 2009](#)).

Data extraction and management

Two overview authors (AGC and HL or BMW) will independently extract data using a standardised electronic data extraction form. We will resolve discrepancies through discussion or recourse to a third overview author (MKB). Overview authors who are authors of any included reviews will not be involved in this process. We will request additional information from the included review authors, where necessary, up to three times over six weeks. We will extract the description of the results in cases where statistical results are not available.

We will extract the following data from each review.

- Review Characteristics
 - Objectives of the review
 - Dates of publication, most recent search and planned update
 - Resources searched
 - Number of included trials
 - Characteristics of included participants (e.g. duration of pain, pain severity, sex, age, race, comorbidities, prior treatment history (to the extent possible))
 - Description of interventions and comparisons
 - Outcomes and time points assessed
 - Details of meta-analyses, if applicable
- Statistical summaries
 - Point estimates, 95% CIs and accompanying measures of heterogeneity for the pooled estimates of intervention effects; for all relevant comparisons at all available time points (e.g. risk ratios (RRs), risk difference (RD), odds ratios (ORs), number needed to treat for an additional beneficial effect (NNTB) or additional harmful effect (NNTH), mean differences (MDs), standardised mean difference (SMDs))
 - Results of responder analyses, including prespecified criteria for response and power calculation
 - Results from exploration of heterogeneity, including subgroup analyses/meta-regression and whether these were prespecified
 - Results from sensitivity analyses, including details of the approach taken and whether these were prespecified
 - The judgements of risk of bias in the evidence, including details of the approach used (e.g. Cochrane ROB tool)
 - The judgements of confidence in the evidence, including details of the approach used (e.g. GRADE)

Assessment of methodological quality of included reviews

Quality of included reviews

We will use the AMSTAR 2 (A MeaSurement Tool to Assess systematic Reviews) instrument to assess methodological quality of the included reviews ([Shea 2017](#)). The 16 items in the AMSTAR 2 instrument provide a broad assessment of systematic review quality that, taken together, inform a judgement of confidence in the review findings. We will develop this judgement using the proposed AMSTAR 2 scheme, with particular consideration of the seven items (protocol registered before commencement of the review (item 2), adequacy of the literature search (item 4), justification for excluding individual studies (item 7), risk of bias from individual studies being included in the review (item 9), appropriateness of meta-analytical methods (item 11), consideration of risk of bias when interpreting the results of the review (item 13), assessment of presence and likely impact of publication bias (item 15)) that may critically affect the validity of a review ([Shea 2017](#)). We (AGC and HL or BMW) will assess items and form judgements of confidence independently and in duplicate for each sampled review. We will resolve discrepancies through consensus or recourse to a third author (MKB). Overview authors will not be involved in this process for any of the sampled reviews in which they have been involved. We will contact review authors a maximum of three times over six weeks if clarification is required or information is missing.

Risk of bias of primary studies included in reviews

We will report the 'Risk of bias' assessments for the primary studies in each included systematic review. We will not repeat or update these assessments. In instances where the Cochrane 'Risk of bias' tool is not used, we will summarise the alternative tool and methods used, including details regarding dimensions assessed (e.g. allocation concealment, participant blinding), and results of the assessments ([Bialy 2011](#); [Foisys 2011](#)).

Certainty of evidence in included reviews

We will report, where available, the GRADE judgement of certainty for each core comparison for our primary outcomes ([Balslem 2011](#)). The GRADE approach uses five considerations (risk of bias, consistency of effect, imprecision, indirectness and publication bias) to assess the certainty of the body of evidence for each outcome. Two overview authors (AGC and HL or BMW) will use a checklist to independently conduct GRADE assessments of certainty in the evidence where this has not occurred in the included reviews and the required information is available ([Meador 2014](#)). We will resolve discrepancies through consensus, or recourse to a third author (MKB). GRADE judgements indicate the following degree of confidence in the conclusions of the systematic review.

- High: very confident that the true effect lies close to that of the estimate of the effect.
- Moderate: moderately confident in the effect estimate – the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- Low: confidence in the effect estimate is limited – the true effect may be substantially different from the estimate of the effect.
- Very Low: very little confidence in the effect estimate and the true effect is likely to be substantially different from the estimate of the effect.

We will report the approach used and the assessments of the certainty of the evidence, where included reviews have used alternative tools to GRADE.

Data synthesis

We will present data from each review for each primary and secondary outcome in order of certainty (i.e. high-certainty evidence first, followed by moderate-certainty evidence, etc.); for efficacy (intervention vs placebo) comparisons, followed by effectiveness comparisons; at each level of follow-up (i.e. short-term, followed by intermediate-term, etc.). We expect the judgement of certainty in the intervention effect to be a GRADE rating in the majority of cases. We will only present narrative descriptions of results where statistical outcome data are not available. We will stratify data by the duration of LBP observed in the included studies; acute (0 to 6 weeks); sub-acute (6 to 12 weeks); chronic (> 12 weeks); mixed (multiple symptom durations grouped together, e.g. acute and subacute or subacute and chronic); and unclear (symptom duration not reported).

We will not perform any novel statistical synthesis of data or make any indirect comparisons. We will convert effect sizes, where possible, to common scales to facilitate interpretation (e.g. we will convert measures of pain intensity on continuous scales to a common 0 to 100 scale). If available, we will present dichotomous outcomes as RR and RD, (and can use the RD to calculate the NNTB and NNTH). We will limit the comparisons presented to the data available in the included reviews.

In interpreting reductions in pain intensity, we will consider a 10-point or more reduction in pain intensity as a minimally important difference, as suggested by the Outcome Measures in Rheumatology (OMERACT) guidelines (Busse 2015). In interpreting reductions in disability, we will convert the scales of the extracted pooled effects to a common 0 to 100 scale and consider a 10-point or more reduction in disability as a minimally important difference (Chou 2017).

For dichotomised data (responder analyses), we will consider analyses based upon a 30% or greater reduction in pain to represent a moderately important benefit, and a 50% or greater reduction in pain intensity to represent a substantially important benefit, as suggested by the IMMPACT guidelines (Dworkin 2008). Where possible, we will present RR and RD with 95% CIs for dichotomised outcome measures. We will report the NNTB and NNTH as an absolute measure of treatment effect.

We plan to present the short-term efficacy of the intervention compared to placebo on pain intensity in a 'Summary of findings' table (Table 1), as described in Chapter V of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019). We will present the results of the remaining primary and secondary outcomes at each time point in an 'Overview of reviews' table (Table 2). We will also include a 'Summary of results' table (Table 3), as proposed by McClurg 2016, highlighting the certainty and clinical relevance of the evidence, by considering both the GRADE score and minimally important difference for the primary outcomes at each time point.

Table 1. Template for a 'Summary of findings' table

Open in table viewer

Pharmacological interventions for low back pain in adults ≤3 months postintervention (short-term)						
Outcome	Intervention and placebo	Illustrative comparative risks		Relative effect	Number of participants	Certainty of the evidence
		(95% CI)		(95% CI)	(studies)	(GRADE)
		Assumed risk	Corresponding risk			
		With placebo	With intervention			
Pain						
	Intervention/placebo #1					
	Intervention/placebo #2					
	Etc...					

Draft 'Summary of findings' table. The table will present the short-term efficacy of each pharmacological intervention compared to placebo on pain intensity.

Table 2. Template for an 'Overview of reviews' table

Open in table viewer

[Intervention] for low back pain in adults [time point]

Outcome	Intervention and Comparison intervention	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
		Assumed risk	Corresponding risk				
		With comparator	With intervention				

Pain

Intervention/Comparison
#1

Intervention/Comparison
#2

Etc...

Physical function

Intervention/Comparison
#1

Intervention/Comparison
#2

Etc...

Participant ratings of improvement

Intervention/Comparison
#1

Intervention/Comparison
#2

Etc...

Health-related quality of life

Intervention/Comparison
#1

Intervention/Comparison
#2

Etc...

Workplace participation

Intervention/Comparison #1
Intervention/Comparison #2
Etc...
Safety
Intervention/Comparison #1
Intervention/Comparison #2
Etc...

Draft 'overview of reviews' table (Fortin 2018; Higgins 2019). Separate tables are planned for each follow-up time point.

Table 3. Template for a 'Summary of results' table

[Open in table viewer](#)

	Important difference	Small difference (may not be important)	Little or no difference	Unclear evidence of harm	Clear evidence of harm
High certainty evidence	INTERVENTIONS (insert list) which improve/decrease/prevent OUTCOME	INTERVENTIONS (insert list) which improve slightly/decrease slightly OUTCOME	INTERVENTIONS (insert list) which result in little or no difference in OUTCOME	INTERVENTIONS (insert list) which result in unclear evidence of harm in OUTCOME	INTERVENTIONS (insert list) which result in clear evidence of harm in OUTCOME
Moderate certainty evidence	INTERVENTIONS (insert list) which probably improve/decrease/prevent OUTCOME	INTERVENTIONS (insert list) which probably improve slightly/decrease slightly OUTCOME	INTERVENTIONS (insert list) which probably result in little or no difference in OUTCOME	INTERVENTIONS (insert list) which probably result in unclear evidence of harm in OUTCOME	INTERVENTIONS (insert list) which probably result in clear evidence of harm in OUTCOME
Low certainty evidence	INTERVENTIONS (insert list) which may improve/decrease/prevent OUTCOME	INTERVENTIONS (insert list) which may improve slightly/decrease slightly OUTCOME	INTERVENTIONS (insert list) which may result in little or no difference in OUTCOME	INTERVENTIONS (insert list) which may result in unclear evidence of harm in OUTCOME	INTERVENTIONS (insert list) which may result in clear evidence of harm in OUTCOME

Very low certainty evidence	It is uncertain whether INTERVENTIONS (insert list) improve/decrease/prevent OUTCOME because the certainty of the evidence is low
------------------------------------	---

No data or no studies	OUTCOME was not measured, not reported, or no studies were found that evaluated the impact of INTERVENTION on OUTCOME
------------------------------	---

Draft 'Summary of results' table, adapted from [McClurg 2016](#). Separate tables are planned for each stated primary outcome at each follow-up time point. The table will only contain comparisons of efficacy and effectiveness of the intervention. Differences will be scaled according to interpretation in the boundaries of the confidence interval (CI) around the minimal important difference (MID) threshold; important difference where the boundaries of the CI fall completely within the MID; small difference where the boundaries of the CI span both sides of the MID; little or no difference where the boundaries of the CI are completely outside the MID but do not cross the midline; unclear evidence of harm where the boundaries of the CI span both sides of the midline; clear evidence of harm where the boundaries of the CI fall completely within harm ([Herbert 2011](#)).

We will ensure that the Overview's messages are clearly articulated and summarised in the text, and highlight any caution required in interpreting results ([Crick 2015](#); [Ioannidis 2008](#)).

We will report and discuss methodological strengths and important limitations across the included reviews.

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AGC conceived the overview, provided methodological expertise and wrote the protocol.

BMW conceived the overview and provided methodological and statistical expertise.

NEO conceived the overview and provided methodological and statistical expertise.

HL provided systematic review, methodological and clinical area expertise.

MKB provided systematic review and methodological expertise.

EO provided methodological expertise.

CGM provided systematic review, methodological and clinical area expertise.

ADF provided systematic review, methodological and clinical area expertise.

MWvT provided systematic review, methodological and clinical area expertise.

JHM is the guarantor, conceived the overview, and provided systematic review and clinical area expertise.

All authors read, contributed to and approved the final version of the manuscript.

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Declarations of interest

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CGM has received competitive grants from government agencies and industry to support his research. As an invited speaker at conferences, he has had his expenses covered and also received small gifts such as a box of chocolates or a bottle of wine. He has received honoraria for marking theses, reviewing grants and preparing talks. CGM has published

multiple papers on low back pain, some of which may be referenced in the review, and is on the Editorial Board of Cochrane Back and Neck review group. Mitigation of conflict of interest: CGM will not be involved in editorial decisions on this review.

ADF is co-ordinating Editor of the Cochrane Back and Neck review group. Mitigation of conflict of interest: ADF will not be involved in decisions to approve or reject this review. She has published multiple papers on low back pain, some of which may be referenced in the review. The institutions where ADF works have received various grants from external organisations, including government and public institutions in Ontario, Canada, and the UK.

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Appendices

Appendix 1. Search strategy: The Cochrane Library

#1 MeSH descriptor back pain explode all trees

#2 MeSH descriptor pain explode all trees

#3 (back or spine or spinal) adj2 pain

#4 lumbar* or lumbo*

#5 backache* or back ache*

#6 (#1 OR #2 OR #3 OR #4 OR #5)

(Limited to Cochrane Reviews and Cochrane protocols)