Version 7, March 2018

iPCHS/Arthritis Research UK Primary Care Centre
Systematic Review Protocol & Support Template

This template is primarily intended to help you plan your review in a systematic way. A copy of this completed form will be available via the intranet to help others carrying out reviews in the future and to avoid duplicating work already undertaken in the Centre. Keeping a record of all the reviews will also assist in planning the work of the Centre and ensuring adequate methodological support. Not all the information will be relevant to every review and items should be adapted to fit the type of review that is being undertaken.
The template has been updated to include all the items from the PRISMA-P checklist (http://www.prisma-statement.org/Extensions/Protocols.aspx).

Title of the review	Back-UP EU2020 Evidence Synthesis: WP 3
First reviewer	**Gemma Mansell**
Other reviewers (with role/contribution in the review)	**Nadia Corp** (information specialist – search strategy development, identification of databases, data extraction and critical appraisal) **Jonathan Hill** (clinical trials specialist) **Gwenllian Wynne-Jones** (epidemiologist – data extraction and critical appraisal) **Daniëlle van der Windt** (epidemiologist – third reviewer of abstracts/full texts) **Kym Snell** (statistician – data extraction)
Clinical Portfolio Group	Clinical epidemiology
Funding source	Horizon 2020 – Framework Programme for Research and Innovation DLV-777090 (European Commission)
PROSPERO registration number	

Amendments to the protocol	A two-staged approach has been implemented, given the large number of systematic reviews available, and number of prognostic factors considered in these reviews.

1. Background to review

Brief introduction to the subject of the review, including rationale for undertaking the review and overall aim

Neck and low back pain (NLBP) are leading causes for years lived with disability in Europe and worldwide. Management of NLBP is a difficult challenge for healthcare professionals since their decisions have a decisive impact on the patient's future health and welfare, as well as on the economic burden on the public and private healthcare systems. However, health professionals often lack appropriate information to tailor the management and follow-up of individual patients and to predict the outcome of a certain treatment. This review is part of a wider project that aims to develop a cloud computer platform for patients, clinicians and employers which will generate prognostic information on NLBP based on information it receives from patients. The idea is that patients will receive tailored information on their potential for improvement from different treatments.

To help with the development of this platform, an evidence synthesis is needed to identify psychological, social, and clinical factors that predict outcome in NLBP populations, and identify how these factors have been measured. This information will feed into concurrent work on identifying interventions that match particular patient profiles. An umbrella review, which reviews existing systematic reviews and meta-analyses that have been conducted on the topic of interest, will be conducted in the first instance, with newly published relevant primary studies being additionally searched for to ensure the evidence synthesis is up to date.

2. Specific objectives/questions the review will address

To summarize evidence for self-reported prognostic factors predictive of disability, pain, and/or return-to-work/work absence outcomes in patients presenting with low back or neck pain in ambulant or occupational healthcare.

3. a) Eligibility Criteria for including studies in the review

If the PICOS format does not fit the research question of interest, please split up the question into separate concepts and put one under each heading

i. Population, or participants and conditions of interest	Adult populations with neck and/or low back pain of any duration (including whiplash, sciatica and radiculopathies)
ii. Interventions/Exposure/item of interest	Any self-reported variable that is psychological, social or clinical – search strategy to include prognosis and prognostic factors in general rather than focusing on specific factors
iii. Comparisons or control groups, if any	None
iv. Outcomes of interest	Measures of pain, disability (or limitation in function), work absence
v. Setting	Any occupational or ambulant health care setting

vi. Study designs	Systematic reviews or meta-analyses

3. b) Criteria for excluding studies not covered in inclusion criteria

Any specific populations excluded, date range, language, whether abstracts or full text available, etc

Population: we will exclude patients with neck/back pain following severe trauma: e.g. fractures of the spine, spinal cord injury. Whiplash-related injuries will be included, as well as radicular pain

Setting: we will exclude studies focusing on patients admitted to hospital that are not ambulatory care

Publication type: we will exclude non-systematic reviews, editorials, letters

Scientific meeting abstracts for which full data could not be obtained from authors

Articles for which translations could not be obtained

4. Search methods

Electronic databases & websites Please list all databases that are to be searched and include the interface (eg NHS HDAS, EBSCO, OVID etc) and date ranges searched for each. **NB All search strategies should be reviewed by an information specialist BEFORE searching begins**	Phase 1: the following databases from 2008-2018 MEDLINE (OVID) EMBASE (OVID) CINAHL (EBSCO) PsycINFO (EBSCO) Conference abstracts – LBP Forum; Society for Back Pain Research (SBPR); Prevention of Work-related Musculoskeletal Disorders (PREMUS); Society for Occupational Medicine; International Commission for Occupational Health (ICOH) (2015-2017)
Other methods used for identifying relevant research ie contacting experts and reference checking, citation tracking	We will use citation checking of reviews to identify additional potentially eligible reviews
Journals hand searched If any are to be hand searched, please list which journals and date searched from, including a rationale.	N/A

5. Methods of review

How will search results be managed & documented? ie which reference management software, how duplicates dealt with	COVIDENCE will be used to manage the flow of articles within the review. All references from the electronic searches will be downloaded into Endnote reference management software, where duplicates will be identified and removed. Titles will be screened and those that are clearly irrelevant will be removed (the first ~100 titles will be screened by both GM and NC. If agreement is high, GM will then screen all remaining titles).
Selection process Number of reviewers, how agreements to be reached and disagreements dealt with, etc.	Two reviewers (GM, NC) will be responsible for identifying relevant papers. Title screening will be followed by a review of abstracts, where those that do not meet the inclusion criteria will be excluded (independently by GM and NC). Review of full texts will be undertaken independently by GM and NC to determine eligibility. Reasons for rejecting papers at the full text stage will be recorded. A checklist with the inclusion criteria will be used to assess each reference for relevance, and the reason for exclusion at the full text stage will be recorded. Any discrepancies between the two will be discussed between GM and NC initially, with DvdW asked to help resolve any disagreements.
Quality assessment Tools or checklists used with references or URLs, was this piloted? Is it to be carried out at same time as data extraction?	Systematic reviews and meta-analysis studies will be assessed using the ROBIS tool Risk of bias assessment will be piloted on ~3 papers initially and the results compared between reviewers to assess consistency between reviewers. Critical appraisal will be conducted at the same time as data extraction.
How is data to be extracted? What information is to be collected on each included study? If databases or forms on Word or Excel are used, were these piloted and how is this recorded and by how many reviewers?	A two-staged approach to data extraction will be used (given the large number of reviews and included candidate prognostic factors): *Stage 1:* The following data will first be extracted from the reviews: - healthcare setting of studies; - search dates; number of studies included; - study design (cohort, RCT); - characteristics of study populations (pain location, diagnosis, age); - prognostic factors identified by the review; - strength of evidence for the factor. If the magnitude of an association is not reported the author conclusions will be recorded Extracted data will be summarised for each prognostic factor, describing the proportion of reviews which found that prognostic factor to have an important and/or statistically significant association with outcome. *Stage 2:* An a-priori threshold will be used to take prognostic factors forward to stage 2: prognostic factors will be considered to have consistent evidence for their association with an outcome of interest, if more than one systematic review and 50% or more of these reviews report a significant/important association In stage 2, more detailed information will be extracted on: - measures used to collect the prognostic factors and outcomes - whether or not a meta-analysis has been conducted. If yes, , details will be extracted regarding the number of studies included, total sample size used for the meta-analysis, follow-up time points, fixed or random effects model,

	univariable or multivariable analysis, and the strength of the association (summary estimate and 95% confidence interval). - If no meta-analysis has been performed, information will be extracted regarding the methods used for a narrative evidence synthesis (e.g. whether the synthesis takes account of statistical significance only, or also strength of the association, consistency of findings, risk of bias, etc.). An Excel spreadsheet will be used to extract information for each included review / prognostic factor. Bespoke data extraction forms for stage 1 and stage 2 will be pilot-tested and discussed within the study team to ensure all items of interest are collected within the forms, and to optimise consistency of data extraction. Three reviewers will each extract data and assess risk of bias from the full texts (GM to perform data extraction on all included references, with NC and GW-J/KS performing data extraction on 50% of the references each), with any disagreements being initially discussed and resolved within the review team. DvdW will be asked to help with any unresolved disagreements.
Outcomes to be extracted & hierarchy/priority of measures ie which measure is preferred and if that is not available which is next in order of preference?	Validated measures of - Pain - Disability - Work absence, return to work or work productivity
Narrative synthesis Details of what methods, how synthesis will be done and by whom. Is the Narrative Synthesis Framework to be used?	A descriptive summary of the included studies will be provided, accompanied by a table of the data extraction and critical appraisal findings. Data on the prognostic factors identified will be focused on, along with any specific detail as to the consistency of a prognostic factor's strength across particular patient characteristics (e.g. age, back or neck pain, pain duration), if recorded. A narrative synthesis will describe the magnitude and quality of evidence for each prognostic factor. We will use the approach from Walton et al (2013) which takes into account the age of the included review and risk of bias assessment when synthesising the results. Greater weight will be given to more recent reviews (published since 2013), and to those are rated as having a low overall risk of bias.
Meta-analysis Details of what and how analysis and testing will be done. If no meta-analysis is to be conducted, please give reason.	NA

Will the overall strength of evidence be assessed? If so, how? ie using GRADE?	All studies meeting the inclusion criteria will be kept in the review regardless of assessed study quality. However the findings will be presented taking risk of bias into account. An adapted GRADE approach will be used to grade confidence in the evidence. For prognostic factors, this means that GRADE will assess factors as having high, moderate, low, or very low confidence in terms of strength and direction of association with outcome. We will use the methods proposed by Walton et al [2013]: - High confidence: factors for which consistent high-quality evidence from at least one high quality SR (low RoB) and no conflicting SRs - Moderate confidence: consistent findings from at least one recent medium-quality SR (moderate RoB), with the majority of findings from other concurrent SRs (where applicable) in the same direction of effect - Low confidence: summary findings are of low or unclear RoB from the majority of SRs and with conflicting results, or when only a single SR reports significant but only moderate-level findings for that factor. - Very low confidence: none of the above conditions are met. For each of these assessments, the age and quality of the reviews was taken into account, with moderate or high confidence only for factors where more high quality and more recent reviews are available for a given prognostic factor. Using more recent reviews will also help to limit the impact of double counting evidence from prognostic factor studies included in multiple reviews [Walton et al. 2013]

6. Presentation of results	
Outputs from review Papers and target journals, conference presentations, reports, etc	It is anticipated that this work will be presented within the wider Back-UP team meetings, as well as at international conferences (e.g. Forum – Quebec 2019) and in one peer-reviewed journal (J Pain/Spine/Physiotherapy). The findings will also be reported as per Horizon 2020 funding requirements. The PRISMA guidelines will be followed when writing up the results.

7. Timeline for review – when do you aim to complete each stage of the review	
Protocol	March 2018
Literature searching	April – July 2018
Data extraction	August 2018 – December 2018
Quality Appraisal	January – March 2019
Synthesis	April – July 2019
Writing up	August 2019 – December 2019