# Systematic review

Please complete all mandatory fields below (marked with an asterisk *) and as many of the non-mandatory fields as you can then click *Submit* to submit your registration. You don't need to complete everything in one go, this record will appear in your *My PROSPERO* section of the web site and you can continue to edit it until you are ready to submit. Click *Show help* below or click on the icon
to see guidance on completing each section.
This record cannot be edited because it has been rejected

## 1. * Review title.

Give the working title of the review, for example the one used for obtaining funding. Ideally the title should state succinctly the interventions or exposures being reviewed and the associated health or social problems. Where appropriate, the title should use the PI(E)COS structure to contain information on the Participants, Intervention (or Exposure) and Comparison groups, the Outcomes to be measured and Study designs to be included.

The effects of mechanical interventions in the management of knee osteoarthritis: protocol for an OA Trial

Bank systematic review and individual participant data meta-analysis

## 2. Original language title.

For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

Dutch, German, French

## 3. * Anticipated or actual start date.

Give the date when the systematic review commenced, or is expected to commence.

04/11/2019

## 4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

31/12/2020

## 5. * Stage of review at time of this submission.

Indicate the stage of progress of the review by ticking the relevant Started and Completed boxes. Additional information may be added in the free text box provided.
Please note: Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. Should evidence of incorrect status and/or completion date being supplied at the time of submission come to light, the content of the PROSPERO record will be removed leaving only the title and named contact details and a statement that inaccuracies in the stage of the review date had been identified.
This field should be updated when any amendments are made to a published record and on completion and publication of the review. If this field was pre-populated from the initial screening questions then you are not able to edit it until the record is published.

The review has not yet started: No

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

Provide any other relevant information about the stage of the review here (e.g. Funded proposal, protocol not yet finalised).

## 6. * Named contact.

The named contact acts as the guarantor for the accuracy of the information presented in the register record.

Erin Macri

## Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Dr Macri

## 7. * Named contact email.

Give the electronic mail address of the named contact.

e.macri@erasmusmc.nl

## 8. Named contact address

Give the full postal address for the named contact.

Department of General Practice, Erasmus University Medical Center\nDoctor Molewaterplein 40, 3015 GD Rotterdam\nThe Netherlands\n

## 9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

010 703 3459

## 10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

Department of General Practice, Erasmus University Medical Center

## Organisation web address:

## 11. * Review team members and their organisational affiliations.

Give the title, first name, last name and the organisational affiliations of each member of the review team.

Affiliation refers to groups or organisations to which review team members belong.

Dr Erin Macri. Department of General Practice, Erasmus University Medical Center
Assistant/Associate Professor Marienke van Middelkoop. Erasmus University Medical Center, Rotterdam
Professor Sita Bierma-Zeinstra. Erasmus University Medical Center, Rotterdam
Professor Michael Callaghan. Manchester Metropolitan University

## 12. * Funding sources/sponsors.

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Include any unique identification numbers assigned to the review by the individuals or bodies listed.

none

## 13. * Conflicts of interest.

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

Yes

Erin Macri is funded by a Banting Postdoctoral Fellowship (CIHR)

## 14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members.

## 15. * Review question.

State the question(s) to be addressed by the review, clearly and precisely. Review questions may be specific or broad. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS where relevant.

We aim to synthesize RCT evidence to: (i) evaluate relative efficacy of mechanical interventions (i.e., bracing, taping, orthoses, footwear, or canes) in managing knee OA symptoms; (ii) identify subgroups of individuals with knee OA who respond to different mechanical interventions; and (iii) identify mediators of the effect of these mechanical interventions on outcomes, to gain insight into the mechanism of effect of these treatments and to inform future individualized intervention approaches.

## 16. * Searches.

State the sources that will be searched. Give the search dates, and any restrictions (e.g. language or publication period). Do NOT enter the full search strategy (it may be provided as a link or attachment.)

MEDLINE, Embase, CINAHL, CENTRAL, Web of Science. All databases will be searched from inception to the search date.

## 17. URL to search strategy.

Give a link to a published pdf/word document detailing either the search strategy or an example of a search strategy for a specific database if available (including the keywords that will be used in the search strategies), or upload your search strategy.Do NOT provide links to your search results.

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Do not make this file publicly available until the review is complete

## 18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

Knee osteoarthritis (including tibiofemoral and patellofemoral)

## 19. * Participants/population.

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

Adults (18 years) with knee OA (tibiofemoral or patellofemoral), diagnosed using any common method (e.g. radiographs, MRI, clinical criteria, diagnosis by a health care professional). We will include post-traumatic OA, and we will exclude patients who have undergone total knee arthroplasty.

## 20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the nature of the interventions or the exposures to be reviewed.

Any intervention involving use, wear or application of mechanical devices (e.g., bracing, taping, orthotics, footwear, cane) that are evaluated after more than one day or application of use. We will include studies that combine these interventions with exercise or education/advice.

## 21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Any non-surgical treatment (e.g. placebo, usual care, any other intervention that does not involve surgery), waiting list, or no treatment.

## 22. * Types of study to be included.

Give details of the types of study (study designs) eligible for inclusion in the review. If there are no restrictions on the types of study design eligible for inclusion, or certain study types are excluded, this should be stated. The preferred format includes details of both inclusion and exclusion criteria.

We will include peer-reviewed RCTs (or quasi-RCTs). We will exclude any other study design (e.g., non-RCTs, pre-post study designs, observational studies). We will also exclude RCTs that only measure the acute effects of a single application of treatment.

## 23. Context.

Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

## 24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion

criteria.

Our primary outcome will be pain.

## Timing and effect measures

Treatment duration will be categorized as short-term ( 4 weeks), medium-term (4 – 12 weeks), and long-term ( 3 months).

## 25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

Secondary outcomes will include function, quality of life, global perceived change, OA feature severity, and biomechanics.

## Timing and effect measures

Treatment duration will be categorized as short-term ( 4 weeks), medium-term (4 – 12 weeks), and long-term ( 3 months).

## 26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Two independent reviewers will screen titles and abstracts of all studied identified through this search strategy. A third reviewer will be consulted with in the event of unresolved disagreements. Following the initial screening, two reviewers will independently review full text manuscripts to identify studies for inclusion in this review. A third reviewer will again be consulted in the event of disagreements.

For all included studies, we will invite original study investigators to share anonymized individualized participant data (IPD) to facilitate IPD analyses. All data-deliverers willing to participate will be asked to sign data delivery licence agreements. Anonymized data will transferred to a secured database at the Erasmus University Medical Center Rotterdam. We will check of the data for completeness and verify participant baseline and follow-up characteristics in comparison to published papers to verify data consistency, and resolve any discrepancies in collaboration with the original study authors. We will convert all data sets to a common format, then combine data sets with a new variable to identify the original trial, and combine all variables that are consistent.

A single co-author will extract data from all included studies, and a second co-author will verify accuracy of all extracted data. From each study, we will extract the following data (study level for systematic review, individual participant level for meta-analyses): study design; sample size; target population; country of study; funding source; inclusion/exclusion criteria; participant characteristics (age, sex, BMI, history of injury or

surgery, comorbidities, psychosocial profile, metabolic profile, physical activity/fitness, lifestyle factors, medication use); type, dose and context of intervention (including compliance, co-interventions); OA characteristics (compartment involvement, prevalence, severity, tissues involved), including pre-post if available; and pain, function, quality of life, biomechanics (e.g. proprioception, knee alignment, strength, kinematics, kinetics) pre-post as available. Global perceived change will also be extracted as available.

## 27. * Risk of bias (quality) assessment.

Describe the method of assessing risk of bias or quality assessment. State which characteristics of the studies will be assessed and any formal risk of bias tools that will be used.

Two co-authors will independently evaluate risk of bias for each included study using the Cochrane Risk of Bias (ROB) tool version 2. Coauthors will consult with original authors in the event of inadequate reporting to clarify methods. We will directly evaluate IPD to confirm balancing of baseline participant characteristics in each arm and to evaluate the extent to which all randomized participants have been included in study analyses.

## 28. * Strategy for data synthesis.

Provide details of the planned synthesis including a rationale for the methods selected. This **must not be generic text** but should be **specific to your review** and describe how the proposed analysis will be applied to your data.

Trial level systematic review: Using all included studies, we will conduct a trial level evaluation of short-term (4 weeks), medium-term (4 – 12 weeks), and long-term (3 months) effects of mechanical treatments in comparison to control treatments. We will evaluate statistical heterogeneity ($I^2$) and will conduct two-stage meta-analyses where possible, by first calculating Hedge's standardized mean differences in each trial and then pooling study results using random effects models. All statistical analyses will be done using Stata (StataCorp, Texas).

IPD analyses: We will conduct an IPD-level meta-analysis of short-term (4 weeks), medium-term (4 – 12 weeks), and long-term (3 months) effects of mechanical treatments in comparison to other treatments. With our combined IPD dataset, our primary aim is to conduct a one-stage IPD meta-analysis. We will conduct responder analyses to identify subgroups of individuals who respond to various mechanical interventions. Subgroups of interest include: mild vs. severe OA, tibiofemoral vs. patellofemoral OA, varus vs. valgus alignment, obese vs. non-obese, and post-traumatic vs. non-traumatic OA. We will also conduct mediation analyses, with a hypothesis that biomechanical factors may mediate the effect of mechanical interventions (e.g. kinematics, kinetics, proprioception, hypermobility). Due to likely collinearity of these biomechanical measures, we will employ a single mediator model for these analyses.

## 29. * Analysis of subgroups or subsets.

State any planned investigation of ‘subgroups’. Be clear and specific about which type of study or

participant will be included in each group or covariate investigated. State the planned analytic approach.

We will conduct responder analyses (tests of interaction) to identify subgroups of individuals who respond to various mechanical interventions. Subgroups of interest include: mild vs. severe OA, tibiofemoral vs. patellofemoral OA, varus vs. valgus alignment, obese vs. non-obese, and post-traumatic vs. non-traumatic OA.

## 30. * Type and method of review.

Select the type of review and the review method from the lists below. Select the health area(s) of interest for your review.

### Type of review

Cost effectiveness
No

Diagnostic
No

Epidemiologic
No

Individual patient data (IPD) meta-analysis
Yes

Intervention
No

Meta-analysis
No

Methodology
No

Narrative synthesis
No

Network meta-analysis
No

Pre-clinical
No

Prevention
No

Prognostic
No

Prospective meta-analysis (PMA)
No

Review of reviews
No

Service delivery
No

Synthesis of qualitative studies
No

Systematic review
Yes

Other
No

## Health area of the review

Alcohol/substance misuse/abuse
No

Blood and immune system
No

Cancer
No

Cardiovascular
No

Care of the elderly
No

Child health
No

Complementary therapies
No

Crime and justice
No

Dental
No

Digestive system
No

Ear, nose and throat
No

Education
No

Endocrine and metabolic disorders
No

Eye disorders
No

General interest
No

Genetics
No

Health inequalities/health equity
No

Infections and infestations
No

International development
No

Mental health and behavioural conditions
No

Musculoskeletal
Yes

Neurological
No

Nursing
No

Obstetrics and gynaecology
No

Oral health
No

Palliative care
No

Perioperative care
No

Physiotherapy
No

Pregnancy and childbirth
No

Public health (including social determinants of health)
No

Rehabilitation
No

Respiratory disorders
No

Service delivery
No

Skin disorders
No

Social care
No

Surgery
No

Tropical Medicine
No

Urological
No

Wounds, injuries and accidents
No

Violence and abuse
No

## 31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.
English

There is not an English language summary

## 32. * Country.

Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved.

Netherlands

## 33. Other registration details.

Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. (N.B. Registration details for Cochrane protocols will be automatically entered). If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

## 34. Reference and/or URL for published protocol.

Give the citation and link for the published protocol, if there is one

Give the link to the published protocol.

Alternatively, upload your published protocol to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

No I do not make this file publicly available until the review is complete

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

## 35. Dissemination plans.

Give brief details of plans for communicating essential messages from the review to the appropriate audiences.

We plan to publish a detailed protocol, and to publish results of this systematic review and IPD meta-analysis.

## Do you intend to publish the review on completion?

Yes

## 36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords will help users find the review in the Register (the words do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

knee osteoarthritis; individual participant data; bracing; taping; cane; insoles; footwear

## 37. Details of any existing review of the same topic by the same authors.

Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

## 38. * Current review status.

Review status should be updated when the review is completed and when it is published. For newregistrations the review must be Ongoing.
Please provide anticipated publication date

Review_Ongoing

## 39. Any additional information.

Provide any other information the review team feel is relevant to the registration of the review.

## 40. Details of final report/publication(s).

This field should be left empty until details of the completed review are available.

Give the link to the published review.