Physiotherapy for pain: Protocol for a systematic review and meta-analysis of randomised trials

Elisabeth Ginnerup-Nielsen[1], Robin Christensen[2], Kristian Thorborg[3], Simon Tarp[1], Marius Henriksen[1]

1: The Parker Institute, Dept. Rheum., Copenhagen University Hospital, Bispebjerg and Frederiksberg, Copenhagen, Denmark.
2: Institute of Sports Science and Clinical Biomechanics, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark.
3: Artroscopic Center Amager, Italiensvej 1, 2300 København S

Correspondence to:
Dr. Marius Henriksen, PT, MS, PhD
The Parker Institute, Dept. Rheum., Copenhagen University Hospitals, Bispebjerg and Frederiksberg, Copenhagen, Denmark.
Phone: (+45) 38164160, Fax: (+45) 3816 4159
E-mail: Marius.henriksen@regionh.dk

Keywords: Pain, physiotherapy, physical therapy, physical therapist, physical therapy modalities, systematic review, meta-analysis, placebo, sham.

Protocol version
Version 1.2
Issue date: April 3 2014
Amendment: Primary reason for amendment: Correction of search strategy in Medline. Due to different settings concerning truncations and wildcards from PubMed to Ovid interface some search terms and truncations in the "Cochrane Highly Sensitive Search Strategy" (table 2) have been corrected.

Revision chronology:
February 27 2014 Original (version 1)
March 17 2014 Version 1.1
Amendment: Primary reason for amendment: Correction of language and typographical errors.

Word count: 4149

Study registration & Date:
PROSPERO: CRD42014008754.
Registered February 27 2014.

AUTHOR EMAILS

Author	**e-mail**
Elisabeth Ginnerup-Nielsen	eginnerup@yahoo.com
Kristian Thorborg	kristianthorborg@hotmail.com
Robin Christensen	robin.christensen@frh.regionh.dk
Simon Tarp	simon.tarp@regionh.dk
Marius Henriksen	marius.henriksen@regionh.dk

ARTICLE SUMMARY

Article focus:

- Assess the effect of physiotherapy on pain in comparison with sham or no treatment.
- Make stratified analysis of the following conditions from ICD-10: Musculoskeletal diseases, mental disorders, nervous system, neoplasms, genitourinary system, pregnancy/childbirth and external causes.
- Make stratified analysis of the type of intervention: Therapeutic exercise, Passive therapy, Mechanical modalities, Electrotherapeutic or thermal modalities, Patient education, Other.
- Make stratified analysis based on type of comparator: No treatment and Sham (placebo)
- Make stratified analysis based on the type of pain studied: acute pain and chronic pain.

Hypotheses:

- We expect to find a positive effect of physiotherapy on pain
- We expect to find small study bias, with small studies showing larger effect sizes than large studies.

Strengths:

- Prespecified systematic search
- Rigorous analysis plan
- We assess the overall effects of physiotherapy on pain to support, facilitate and develop clinical practice and further research.

Limitations:

- Comprehensive yet potentially inadequate search
- Broad definition of physiotherapeutic modalities
- Restricted search due to the use of search terms related to the outcome
- Systematic searches done in only two bibliographic databases - MEDLINE and PEDro.

ABSTRACT

Background: Every year pain related deficiencies affect about 30 percent of the European population.

The use of physiotherapy is common within treatment of pain disorders, but the effect of physiotherapy on pain has never been evaluated systematically.

The purpose of this study is to systematically assess the clinical effects of physiotherapy on pain in adult patients reported in randomised controlled trials.

Methods: Original full text randomised trials will be located in the databases MEDLINE and PEDro. Studies assessing the effects of physiotherapy on pain are considered eligible. Two researchers will independently screen titles and abstracts for inclusion of potential studies, and extract estimates of the effects of physiotherapy on pain. Random effects meta-analyses will be performed, with subsequent stratified analyses based on condition, physiotherapy modalities and study size.

Discussion: Uncovering the effect on pain of different physiotherapeutic modalities may provide stepping stones for optimization of pain treatment through physiotherapy and lead to considerable economic gain and improved quality of life for patients with pain.

Objectives: The purpose of this study is to systematically assess the clinical effect of physiotherapy on pain in adult patients reported in randomised controlled trials.

Design: Systematic review and meta-analysis of randomised and quasi randomised controlled trials.

Data sources: We will search the bibliographic databases: MEDLINE and PEDro from their inception to the present.

Selection criteria: We will include studies if they are randomised or quasi-randomised controlled trials that compare "physiotherapy" with a sham or no intervention in adult patients presumably having pain.

Data collection and analysis: We will use a piloted collection form for study characteristics. These will be extracted by the first author (EGN) and spot checked by (MH). We will analyse the results with random effects meta-analyses, and use fixed effects models to evaluate the potential for small-study bias. For crossover trials, we will extract data from the first period only because of possible carry-over effects. Whenever possible, we use results from the intention-to-treat population.

We will present stratified analyses according to the following research questions: Are the effects of physiotherapy on pain equivalent to that seen with the control, or are the effects more likely to result from bias in the study designs?

Do different physiotherapeutic modalities, different conditions, and different types of control groups generate distinct pain outcomes?

Timeline and perspectives: After the protocol has been approved and registered in PROSPERO, the systematic review and subsequent meta-analysis will be undertaken; the quantitative analyses and the preliminary report will be completed by 1 August 2014.

Funding: The study is not directly funded, but The Oak Foundation supports The Parker Institute with grants.

Registration: The study is registered in PROSPERO (CRD42014008754).

Keywords: Pain, physiotherapy, physical therapy, physical therapist, physical therapy modalities, systematic review, meta-analysis, placebo, sham

INTRODUCTION

Background

Pain is defined as: "*An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage*"(1) Acute pain typically occurs due to acute tissue damage and the pain has the appropriate purpose of limiting the harmful conduct. If the pain persists without any obvious purpose it may become chronic, frequently defined as "pain persisting more than 12 weeks" or "pain persisting after the time that healing would have been thought to have occurred" (1) Every year pain related deficiencies affect about 25-35 percent of the European population (2) and a recent telephone survey in 15 European countries found 19 percent reporting pain within the last week and 19 percent having lost their job due to pain problems. Yet about 30 percent of these people were currently not receiving any treatment (3)

The experience of frequent chronic or acute pain has a severe influence on peoples' lives with 55 percent of patients with acute pain and 75 percent of patients with chronic pain reporting that pain has affected their social relations and quality of life (4;5) and healthcare and socioeconomic costs of conditions associated with chronic pain run into billions of euros annually and represent 3–10 percent of gross domestic product in most European countries (2)

Our knowledge about the pathogenesis of pain is based on the gate-control theory - A theory that has yet to be proven and has difficulties explaining the nature of especially chronic pain (6) Currently WHO does not have any updated guidelines on treatment of neither chronic nor acute pain, though a preliminary delphi study does recommend physiotherapy as part of the pain treatment (7).

Physiotherapy and pain management

Physiotherapy is common in pain management in Western Europe with some studies reporting that about 20 % of people with chronic pain have received physiotherapy for their pain(3) Positive effects of physiotherapy have been found in areas such as low

back pain, cancer and knee osteoarthritis (8-10) Many of the studies, however, are of a low methodological quality, with treatment modalities and pain intensity often poorly defined or not assessed. Hence there still are some uncertainties about the actual effects of physiotherapy on pain. The uncertainty is reflected in the International guidelines for treatment of common chronic pain disorders. As an example, referral to a physiotherapist regarding exercise is recommended for both knee osteoarthritis and low back pain yet the recommendations are unspecific with regards to which exercise regime to apply (11;12)

According to the World Confederation of Physical Therapists (WCPT) "*Physical therapy provides services to individuals and populations to develop, maintain and restore maximum movement and functional ability throughout the lifespan. This includes providing services in circumstances where movement and function are threatened by ageing, injury and pain*" (13)

In other words, physiotherapy aims to optimize the physical potential with the individual and pursue the highest degree of societal participation. These definitions obviously imply that optimisation or restoration of physical impairments, such as range of motion, muscle strength/endurance, coordination, etc., is pivotal in physiotherapy. Pain is frequently associated with physical impairments but can in itself significantly limit physical potential – also in the absence of objective physical impairments - and may in turn also affect societal participation. In many conditions, pain is considered a cardinal symptom, and a potential outcome besides improvements in physical performance, and improvements in performance are often thought to mediate improvements in pain. Compared to other treatments of pain (such as surgery and pharmacotherapy), physiotherapy is cost-effective and often with no or little side effects (14)

Why this review is important

Considering the 55 – 75 percent claiming, that pain affects their social relations negatively and the fact that about 30 percent of patients with pain, are currently not receiving any treatment, it seems appropriate to let physiotherapy become a more integrated part of pain treatment. However, it is not clear if physiotherapy in general has a beneficial role in management of pain.

Considering the burden and costs to society associated with prescribing physiotherapy for various types of pain, it is important to assess whether the effect seen with physiotherapy is equivalent to that seen with appropriate sham controls. If the controversial hypothesis that "*all clinical effects of physiotherapy are due to placebo effects and contextual factors*" is correct, it would mean that in all properly conducted sham-controlled trials on physiotherapy, one "placebo intervention" had been compared with another.

Objectives

The aim of this study is to assess if the effects of physiotherapy on pain is equivalent to that seen with control/sham/placebo, and whether the observed effect (if any) is likely to results from bias in the study designs. Secondarily we want to determine whether different physiotherapeutic modalities, different conditions, and different types of control groups generate distinct pain outcomes.

METHODS

Protocol and registration

This protocol is registered with International prospective register of systematic reviews (PROSPERO; identifier: CRD42014008754). We will conduct the review according to this protocol and report any deviations from it in a "Differences between protocol and review" appendix of the systematic review. Study selection, assessment of eligibility criteria, data extraction, and statistical analysis will be performed according to the "*Cochrane Collaboration Methodological Expectations for Cochrane Intervention Reviews*" (MECIR) guidelines' (15).

The manuscript will be prepared following the "*Preferred Reporting Items for Systematic reviews and Meta-Analyses*" (PRISMA) statement (16).

Eligibility criteria

We will include randomised or quasi-randomised, controlled trials that compare physiotherapy with sham/placebo or non-intervention control in adults (19+ years) presumably having pain. Any type of intervention referred to as physiotherapy or physical therapy or explicitly described as being delivered by a physiotherapist, physiotherapists, physical therapist or physical therapists within the title or abstract is considered eligible if pain is assessed as a treatment outcome. We will include trials if pain has been estimated at baseline and follow-up by the patients on a visual analogue scale (VAS) or another generally accepted and/or validated ranking scale.

Only full text trial reports in English will be considered. If several articles reports from the same trial, we will prioritise the "primary publication"; i.e. typically defined as the first full-text publication reporting on the primary outcome. Remaining reports will be checked for complementary data on pain outcomes, descriptions of study participants, or design characteristics. If outcome data differ between reports, we will extract the data that most closely adhere to the intention-to-treat principle. Two reviewers (EGN and MH) will evaluate the reports independently for eligibility. Disagreements will be resolved by consensus or discussion with a third reviewer (KT).

Information sources

We will search the databases MEDLINE and PEDro. MEDLINE will be searched via Ovid; Ovid MEDLINE is published by the U.S. National Library of Medicine and it is the world's premier, comprehensive biomedical database covering biomedical publications from 1948 – present. Ovid MEDLINE is updated daily.

PEDro is the Physiotherapy Evidence Database. PEDro is a free database of over 26,000 randomised trials, systematic reviews and clinical practice guidelines in physiotherapy. In PEDro the oldest record on the database (a clinical trial) was published in 1929; PEDro is updated once per month.

We will search both databases from their inception to the present.

Further, we will search for errata or retractions from included studies published in full-text in MEDLINE and PEDro and report the date this was done within the review.

Search strategy

We will create a search strategy based on the proposed search with Boolean operators (**Table 1**). As all of the three main issues in this search strategy have to be included in the total search, the results of the three searches, one for each column, have to be combined with 'AND', while each "intervention" and "outcome" term have to be combined with "OR" as every article containing at least one of these words is considered eligible (17) In an attempt to make our search the most sensitive possible we will, in the Ovid database, use a modified version of the "Cochrane highly sensitive search strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision); based on the PubMed form",(18) (**table 2**) in combination with the items in table 1.

Table 1: Search strategy

		Terms combined with AND		
		Intervention	Outcome	Design (Search filter)
Terms combined with	OR	"Physical Therapy Modalities" "Physical Therapy Modalities"[Mesh] "Physical therapy modality" "physiotherapy modality" "physiotherapy modalities" "Physical Therapy" Physiotherapy Physiotherapies "physical therapies" "Physical Therapists"[Mesh] "Physical Therapists" "Physical Therapist" Physiotherapist Physiotherapists	Pain "Pain"[Mesh] "acute pain" ”acute pain” [Mesh] ”chronic pain” ”chronic pain” [Mesh]	English; Adult: 19+ years, RCT

Table 2: Search strategy inspired by Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximizing version

#1	Randomized controlled trials as Topic/
#2	Randomized controlled trial/
#3	Random allocation/
#4	Double blind method/
#5	Single blind method/
#6	Clinical trial/
#7	exp Clinical Trials as Topic/
#8	(clinic$ adj trial$1).tw.
#9	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.
#10	Placebos/
#11	Placebo$.tw.
#12	Randomly allocated.tw.
#13	(allocated adj2 random).tw.
#14	sham.m_titl.
#15	limit 14 to abstracts
#16	quasi.m_titl.
#17	limit 16 to abstracts

The MeSH thesaurus is used for indexing articles from some of the world's leading biomedical journals for the MEDLINE/Pubmed database. Each bibliographic reference is associated with a set of MeSH terms that describe the content of the item.

The search strategy will include MeSH-terms related to physical therapy and pain: “Physical therapy modalities"[Mesh], "Physical therapists"[Mesh], "Pain"[Mesh], "Chronic pain"[Mesh]) and "Acute pain"[Mesh]). In addition, following simple search terms will be used "Physiotherapists" "Physiotherapist", "Physical therapist", "Physical therapists", "Physical therapies", Physiotherapies, Physiotherapy, "Physical therapy", "Physical therapy modality", "Physical therapy modalities", Physiotherapy modality”, “physiotherapy modalities”, “Chronic pain”, “Acute pain” and “Pain”.

We will use the same search strategy in PEDro. As PEDro does not have MeSH terms and you cannot combine ANDs and ORs in a single search we will enclose the words in inverted commas (eg, “*physical therapy*“) which combines the two terms with an AND operator and then combine these with the above mentioned pain related search terms. We have restricted our search by including only studies with physiotherapy related search terms in the title or abstract. We have also chosen to include outcome related “pain terms” in our search strategy to restrict the number of hits as the first three elements of our PICO search (patient, intervention and comparison) lead to a very comprehensive and widespread search result. We are aware of the fact that we might miss relevant studies having pain as a minor outcome or physiotherapy related terms not mentioned in title or abstract.

Study selection

Two review authors [EGN and MH] will independently screen titles and abstracts for inclusion of all the potential studies we identify as a result of the search and code them as 'retrieve' (eligible or potentially eligible/unclear) or 'do not retrieve'. We will retrieve the full-text study reports/publication and two review authors [EGN and MH] will independently scrutinize the full-text and identify studies for eligibility, and record

reasons for exclusion of the ineligible studies. We will resolve any disagreement through discussion or, if required, we will consult a third person [KT].

We will identify and exclude duplicates and collate multiple reports of the same study so that each trial, rather than each report, is the unit of interest in the review. We will record the selection process in sufficient detail to complete a PRISMA flow diagram (16).

Data extraction and management

We will use a data collection form for study characteristics and outcome data that has been piloted. When several pain scales have been used, we will choose the one that is assessed as the primary pain outcome. If pain has been assessed at several time points we will choose the time point closest to the end of treatment with the anticipation of maximal efficacy achieved. One review author [EGN] will extract study characteristics from included studies. A second review author [MH] will spot-check study characteristics for accuracy against the trial report.

We will extract the following study characteristics:

General study information: Article title, main author, year of publication, journal, country of origin, number of participants, type and source of financial support.

Characteristics of the participants: Mean age, gender, condition and mean duration of condition.

Characteristics of the intervention: Type of intervention, type of sham/control, study duration from baseline to assessment of primary pain outcome at follow-up.

Outcome measures: Type of pain (chronic or acute).

Statistical estimates: We will extract the mean and standard deviation (SD) for the change from baseline for each group. When necessary we will extract from figures in the articles. If some of the estimates cannot be retrieved, we will contact the authors for additional data. For crossover trials, we will extract data from the first period only,

because of possible carry-over effects (19). Whenever possible, we use results from the intention-to-treat population.

Outcome measures

The primary outcome will be pain intensity recorded as change in pain intensity from baseline to follow-up. When several pain scales have been used, we will choose the one that is presented from the authors as the (most) primary pain outcome. If pain outcomes are reported at several time points, we will extract the time point closest to the end of treatment.

Assessment of risk of bias in included studies

Two review authors (EGN and MH) will independently assess risk of bias for each study according to the mandatory bias items (**Table 3**), using the 'Cochrane Collaboration's tool for assessing risk of bias in randomised trials' (20). We will resolve any disagreements by discussion and by consensus involving an experienced Cochrane methodologist (RC).

Table 3: Cochrane Collaboration's tool for assessing risk of bias in randomised trials

Bias domain	Source of bias	Support for judgement	Risk of bias		
			Low	Unclear	High
Selection Bias	Random Sequence Generation	Methods used to allocate sequence. Are the groups comparable			
	Allocation Concealment	Method used to conceal the the allocation sequence. Could intervention allocations have been forseen before or during enrolment			
Performance bias	Blinding of participants and personel	Meassures used to blind trial participants and researchers from knowledge of which intervention a participant received.			
Detection bias	Blinding of otcome Assessment	Meassures used to blind outcome assessment from knowledge of which intervention a participant received.			
Attrition bias	Incomplete outcome Data	Describe the completeness of outcome data for each main outcome, including attritions and exclusions from the analysis. State whether attrition and exclusions were reported the numbers in each intervention group. (compared with total randomised participants), reasons for attrition or exclusions in analysis for the review.			
Reporting bias	Selective reporting	State how selective outcome reporting was examined and what was found			

We will judge each bias domain as high, low or unclear and provide a quote from the study report together with a justification for our judgment in the 'Risk of bias' table. We will summarise the risk of bias judgements across all studies included in the meta-analysis for each of the domains listed. Any discrepancies in quality ratings will be resolved by discussion. Where information on risk of bias relates to unpublished data or correspondence with a trialist, we will note this in the 'Risk of bias' table.

Statistical methods

Summary measure: Pain data extracted and collected as means and standard deviations in two groups, will be analysed applying the Hedges bias-corrected standardised mean difference (SMD) as the effect size. The advantage of this effect size is the fact that it provides a common metric; it is an intuitive index where values of 0.20, 0.50, and 0.80 correspond to small, medium and large effects in the social sciences.

The effect sizes will be signed so that negative values (SMD < 0) indicate a benefit of physiotherapy treatment (i.e., pain reduction).

Evidence synthesis: If the treatment effect sizes are consistent, then we will focus on the combined effect, reporting this as being robust across the range of studies included in the analysis.

In order to identify potential inconsistency we will quantify the amount of heterogeneity (i.e., study-to-study dispersion) to test whether the true effect is the same in all studies (by definition) we will compute Cochran's Q-test for homogeneity.(21) We will apply the I^2 metric, as a measure of the amount of inconsistency (I^2) across studies in the meta-analysis (22): The I^2 takes values from 0 to 100% and often cut-offs are used to claim that important inconsistency exists or not (21). Independent of the heterogeneity and inconsistency observed, we will use standard random effects meta-analysis as default option (23) whereas the fixed effect analysis will be applied for the purpose of sensitivity analysis. The random effects meta-analysis assumes the true treatment effect differs from study to study and provides an estimate of the average treatment effect. As we move from fixed effect to random effects, extreme studies will lose influence if they are large, and will gain influence if they are small (24).

Assessment of heterogeneity and stratified analyses

Random-effects models do not explain why heterogeneity exists (24).

Combining all physiotherapy trials in a single meta-analysis will inevitably bring together material with an element of diversity. We will refer to that as clinical heterogeneity, which may or may not be responsible for observed discrepancies in the results of the

studies (24). We will explore possible reasons for heterogeneity and inconsistency between studies using stratified meta-regression analysis (25).

We will use two different methods to identify the factor(s) that best account for heterogeneity between the studies. First, univariate random-effects meta-regression will be used to study the changes in effect size when groups of trials are stratified by various trial characteristics (25). We anticipate that a successful stratification of trial outcome will produce a large difference in the effect sizes of trials with the characteristic compared with those without (26). Second, these will be supported by meta-regression analysis to look at changes to the statistical heterogeneity measure (i.e., standard deviation for the combined estimate, Tau-squared) when study results are modelled against a specific trial covariate (27). **Table 4** illustrates the stratified analyses that will be performed using ICD-10 and WCPT as a reference (13)(28). We have chosen to stratify for the following types of conditions and interventions.

Table 4: Stratified analysis.

Type of condition	Type of intervention	Type of comparator	Type of pain
▪ Musculoskeletal diseases ▪ Mental disorders ▪ Nervous system ▪ Neoplasms ▪ Genitourinary system ▪ Pregnancy/childbirth ▪ External causes ▪ Other	▪ Therapeutic exercise (eg functional exercise, aquatic therapy, active stretching) ▪ Passive therapy* (eg. Manual therapy, acupuncture, Mobilizations. ▪ Mechanical modalities (eg. supportive devices, orthoses etc.) ▪ Electrotherapeutic or thermal modalities ▪ Patient education ▪ Other	▪ No treatment ▪ Sham (Placebo)	▪ Chronic pain ▪ Acute pain
Chronic pain is defined as pain duration for more than 3 months at study inclusion. Pain duration for less than 3 months at study inclusion is defined as acute pain. * If delivered by a physiotherapist			

Summary of findings table

We will create a 'Summary of findings' table using the following major outcome: pain intensity. Two people [EGN and MH] will independently assess the quality of the evidence. We will use the five GRADE considerations (study limitations, consistency of results, imprecision, indirectness and publication bias) to assess the quality of a body of evidence as it relates to the studies, which contribute data to the meta-analyses for the pre-specified major outcomes. We will justify all decisions to down- or upgrade the quality of studies using footnotes and we will make comments to aid reader's understanding of the review where necessary. For dichotomous outcomes, the absolute risk difference will be calculated using the Risk Difference statistic in RevMan and the result expressed as a percentage. For continuous outcomes, the absolute benefit will be calculated as the improvement in the intervention group minus the improvement in the control group, in the original units.

Discussion

This study questions the effect of physiotherapy on pain.

Uncovering the effect on pain of different physiotherapeutic modalities may optimize pain treatment in the long term. Considering the huge costs associated with especially chronic pain, offering an optimized treatment might lead to considerable economic gain, as well as an improved quality of life for patients with pain. It will also help physiotherapists in choosing between many different treatment modalities, currently found within pain management.

In 2009 Aschwort et al. (29) did a systematic review of the effect of home versus center based physical activity programs on different lifestyle diseases. They found better adherence with the home based programs, but were not able to make any conclusions about specific exercise modalities. As in this study we wish to have an overview of the effect of different physiotherapeutic treatment modalities on different conditions.

The strengths of our study are the prespecified systematic search and rigorous analysis that are suitable for our objectives. Unfortunately, the use of outcome terms in a very

broad and comprehensive search and the broad definition of physiotherapy make it difficult to conclude anything about the effects of specific physiotherapeutic treatment modalities for specific painful conditions, which clearly is a limitation. Hence, regardless of the conclusion, researchers in physiotherapy should be encouraged to do further systematic studies as neither suspension of physiotherapeutic pain treatment practice until the necessary evidence is available nor continuation of the current practice without further systematic research would be tenable or ethical.
Furthermore, scoping the effects of physiotherapy within a certain area should optimize the treatment guidelines and hereby increase the influence of physiotherapy within this area.

Abbreviations

VAS: Visual analogue scale

SD: Standard deviation

ITT: Intention to treat

SMD: Standardized mean difference

Competing interests

EGN: None declared.

RC: RC is involved in many health-care initiatives and research that could benefit from wide uptake of this publication (including Cochrane, OMERACT, and the GRADE Working Group).

KT: KT is associated with the Danish Association of Physiotherapists as board member of the Research Foundation and research Advisory Board. KT is senior researcher at the Arthroscopic Centre Amager, Copenhagen University Hospital that attracts external funding from governmental, non-profit sources and commercial sources.

ST: None declared

MH: MH is associated with the Danish Association of Physiotherapists as board member of the Research Foundation and research Advisory Board. MH is head of the physiotherapy research unit at The Parker Institute that attracts external funding from governmental, non-profit and commercial sources.

The Parker Institute is grateful for the financial support received from public and private foundations, companies and private individuals over the years. The Parker Institute is supported by a core grant from the Oak Foundation; The Oak Foundation is a group of philanthropic organizations that, since its establishment in 1983, has given grants to not-for-profit organizations around the world.

Acknowledgements

The authors wish to acknowledge both the scientific and personal support provided by Professor Bente Danneskiold-Samsøe, DM and Professor Henning Bliddahl, DM, during this project.

Reference List

(1) Merskey H. The definition of pain. European psychiatry 1991.

(2) Breivik H, Eisenberg E, O'Brien T. The individual and societal burden of chronic pain in Europe: the case for strategic prioritisation and action to improve knowledge and availability of appropriate care. BMC Public Health 2013;13:1229.

(3) Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. Eur J Pain 2006 May;10(4):287-333.

(4) Langley PC. The societal burden of pain in Germany: health-related quality-of-life, health status and direct medical costs. J Med Econ 2012;15(6):1201-15.

(5) McCarberg BH, Nicholson BD, Todd KH, Palmer T, Penles L. The impact of pain on quality of life and the unmet needs of pain management: results from pain sufferers and physicians participating in an Internet survey. Am J Ther 2008 Jul;15(4):312-20.

(6) Moayedi M, Davis KD. Theories of pain: from specificity to gate control. J Neurophysiol 2013 Jan;109(1):5-12.

(7) Kumar N. WHO Normative Guidelines on Pain Management. Geneva: World Health Organization 2007.

(8) Bystrom MG, Rasmussen-Barr E, Grooten WJ. Motor control exercises reduces pain and disability in chronic and recurrent low back pain: a meta-analysis. Spine (Phila Pa 1976) 2013 Mar 15;38(6):E350-E358.

(9) Fransen M, McConnell S, Bell M. Exercise for osteoarthritis of the hip or knee. Cochrane Database Syst Rev 2003;(3):CD004286.

(10) Rueda JR, Sola I, Pascual A, Subirana CM. Non-invasive interventions for improving well-being and quality of life in patients with lung cancer. Cochrane Database Syst Rev 2011;(9):CD004282.

(11) Savigny P, Kuntze S, Watson P, Underwood M, Ritchie G, Cotterell M, et al. Low Back Pain: early management of persistent non-specific low back pain. London: National Collaborating Centre for Primary Care and Royal College of General Practitioners 2009;14.

(12) McAlindon TE, Bannuru RR, Sullivan MC, Arden NK, Berenbaum F, Bierma-Zeinstra SM, et al. OARSI Guidelines for the Non-Surgical Management of Knee Osteoarthritis. Osteoarthritis and Cartilage 2014.

(13) World Confederation for Physical therapy. Policy Statement - Description of physical therapy. 2011.

(14) Turk DC. Clinical effectiveness and cost-effectiveness of treatments for patients with chronic pain. Clin J Pain 2002 Nov;18(6):355-65.

(15) Chandler J, Churchill R, Higgins J, Lasserson T, Tovey D. Methodological standards for the conduct of new Cochrane Intervention Reviews.

(16) Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 2009;151(4):264-9.

(17) Bartels EM. How to perform a systematic search. Best Pract Res Clin Rheumatol 2013 Apr;27(2):295-306.

(18) Higgins JPT, Green S. Highly sensitive search strategies for identifying reports of randomized controlled trials in MEDLINE. Cochrane Handbook for Systematic Reviews of Interventions 4.2. 5 [updated May 2005]; Appendix 5b. The Cochrane Library 2005;(3).

(19) Curtin F, Altman DG, Elbourne D. Meta-analysis combining parallel and cross-over clinical trials. I: Continuous outcomes. Stat Med 2002 Aug 15;21(15):2131-44.

(20) Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.

(21) Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003 Sep 6;327(7414):557-60.

(22) Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002 Jun 15;21(11):1539-58.

(23) DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986 Sep;7(3):177-88.

(24) Lau J, Ioannidis JP, Schmid CH. Summing up evidence: one answer is not always enough. Lancet 1998 Jan 10;351(9096):123-7.

(25) Thompson SG, Sharp SJ. Explaining heterogeneity in meta-analysis: a comparison of methods. Stat Med 1999 Oct 30;18(20):2693-708.

(26) Thompson SG, Higgins JP. Treating individuals 4: can meta-analysis help target interventions at individuals most likely to benefit? Lancet 2005 Jan 22;365(9456):341-6.

(27) Thompson SG, Higgins JP. How should meta-regression analyses be undertaken and interpreted? Stat Med 2002 Jun 15;21(11):1559-73.

(28) WHO. International Statistical Classification of Diseases and Related Health Problems 10th Revision. 2010.

(29) Ashworth NL, Chad KE, Harrison EL, Reeder BA, Marshall SC. Home versus center based physical activity programs in older adults. Cochrane Database Syst Rev 2005;(1):CD004017.