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Determinants of responsiveness to multidisciplinary chronic pain management interventions: protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction The current manuscript presents a protocol for a systematic review and meta-analysis of the evidence regarding the determinants of responsiveness to multidisciplinary management of chronic pain, with pain intensity, pain-related interference, physical functioning and health-related quality of life as the main outcomes, with consideration to multiple secondary outcomes.

Methods and analysis To identify relevant studies, the Ovid MEDLINE, PubMed, Ovid PsycINFO, EBSCO CINAHL and Scopus databases will be searched for all studies exploring factors associated with responsiveness to multidisciplinary pain management from study inception to the present. Cohorts, case–control studies and randomised controlled trials will be included. Independent screening for eligible studies will be completed by a total of four researchers using defined criteria. Data extraction will be executed by two researchers. Study heterogeneity will be estimated using the I^2 index. A meta-analysis will be performed using random effects models. Publication bias will be evaluated by means of funnel plots and Egger's test.

Ethics and dissemination The proposed study does not involve collection of primary data. Therefore, no ethical approval is required. The results of the systematic review and meta-analysis will be presented in a peer-reviewed journal and at conferences.

PROSPERO registration number CRD42021236424.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The current manuscript presents a detailed protocol for a systematic review, which aims to provide an outline of studies examining factors predicting responsiveness to multidisciplinary chronic pain management.

⇒ The review is comprehensive as it will include search of multiple databases, and several possible prognostic factors, chronic pain conditions and outcome variables.

⇒ During the systematic review, both data screening and collection, assessment of the risk of bias and judgement of the quality of evidence will be performed independently by at least two researchers of the five-member team, all with clinical and/or scientific expertise in chronic pain.

⇒ The Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines and good practice will be followed in data extraction and review development and reporting.

⇒ Limiting the inclusion criteria to English papers may result in language bias.

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INTRODUCTION

Disability related to chronic pain arises from somatic pathology and is always contributed by psychological and social aspects.[1] Due to this biopsychosocial nature of chronic pain, a multidisciplinary approach has long been regarded as superior to narrower, unimodal chronic pain treatment modalities in terms of improvements in pain, physical functioning, psychological factors (eg, self-management of pain, coping resources, emotional burden), working ability and well-being.[2–6] The International Association for the Study of Pain (IASP) defines multimodal treatment as treatment provided by professionals from different disciplines.[7] According to a meta-analysis, patients treated by multidisciplinary approach functioned 75% better than patients either untreated or treated by conventional, unimodal treatment approaches at long-term follow-up.[3] Although multidisciplinary pain management is difficult to measure due to the diverse economic effects of pain on individuals and society,[8] the cost-effectiveness of the approach has been supported.[9]

The importance of patient selection has been highlighted, as not all patients benefit from multidisciplinary pain management.[1] However, indefinitely, systematic reviews examining the current topic do not exist. To execute a comprehensive systematic review of the effectiveness of multidisciplinary management of chronic pain is far from easy due to the heterogeneity of studies.[10] The studies

available in the literature vary in terms of, for instance, patient selection, outcome variables, pain sites and type of pain examined and the definition of interdisciplinary management.

Identifying factors that may predict whether patients benefit from a multimodal approach would provide remarkable assistance in clinical decision-making. Identifying these factors would help clinicians to customise the treatment more efficiently to meet individual needs, and thus offer best possible pain treatment for each individual.

It is, thus, essential to systematically consider all previously studied factors that may predict the responsiveness to multidisciplinary management of chronic pain. The aim of the study presented herein is to identify and systematically analyse previously published data regarding this topic. Thus, the main research question of the presented systematic review is 'Which baseline factors may predict who will benefit from multidisciplinary management of chronic non-cancer pain?'.

METHODS AND ANALYSIS

The current study protocol describes a systematic review and meta-analysis exploring the determinants of responsiveness to multidisciplinary chronic pain management interventions in adults. The review has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) on 3 March 2021 (registration number: CRD42021236424).

The planned start date of the study will be 1 September 2022. The planned end date of the study will be 15 February 2023. Current study status: review protocol has been developed.

Eligibility criteria

The included articles are required to be (1) original research articles, (2) published in full text, (3) published in a peer-reviewed journal, (4) published in English, (5) have a longitudinal (baseline–outcome) setting, and (6) report empirical data (cohort, case–control or randomised controlled trial (RCT); observational studies are also included). There will be no limitations on year of publication. Eligibility criteria, defined according to population, intervention, comparison and outcomes (PICO), are listed below in separate sections.

Population

The participants included need to be adult patients (over 16 years of age, no maximum age limit) with chronic pain who have been treated by a multidisciplinary pain management team. Pain will be defined as chronic when the duration of pain exceeds 3 months. Articles with a patient population comprising palliative care patients or postoperative pain patients with an average of an expected trend of healing will be excluded. In the case of incoherence, the whole study group will discuss each of these individually.

Intervention or prognostic factor

To ensure adherence to IASP definition of multidisciplinary treatment,[7] multidisciplinary teams included herein needed to comprise a minimum of three separate professional groups (eg, physician, physical therapist, psychologist and psychiatric nurse; consultation may be performed routinely or on demand).

All independent baseline variables that were examined as potential determinants of responsiveness to multidisciplinary pain management are included. These may include, for example, sociodemographic, symptom-related, physical well-being-related and psychological factors (eg, resilience, catastrophising, coping, perceived stress, psychological flexibility).

Comparison or comparator

All alternative exposures within the prognostic factors will be taken into account.

Outcome

Responsiveness will be defined as a positive effect of an intervention on the examined outcome variables.

All articles with (1) pain (pain intensity or pain interference) or (2) physical functioning or (3) health-related quality of life (HRQoL) as one primary outcome will be considered eligible. A rationale for determining HRQoL and physical functioning as primary outcomes in addition to pain is that they reflect pain-related disability well.[11–14] In addition to these, other relevant outcomes will be considered (eg, psychological factors, depression, working ability, analgesic consumption); however, articles comprising these as a primary outcome with no evaluation of any of the three determined main outcomes as a primary outcome will be excluded. The primary focus will be on the situation immediately after a multidisciplinary treatment intervention, but studies with long-term follow-up data (eg, outcome consideration after several years of follow-up) will also be considered. Any outcome measurements will be included (eg, patient-reported outcome measures, evaluation by professional, objective measures).

Search methods, information sources, study selection and data management

A comprehensive electronic search of the medical and rehabilitation literature using medical subject headings and text related to responsiveness to multidisciplinary chronic pain management will be performed.

The search strategy has been developed to adhere to the PICO descriptors. Based on this, four domains will be set: chronic pain, responsiveness or predictor, multidisciplinary intervention (divided into two domains for searches) and outcome. These domains will be joined with operator 'AND'. Regarding each domain, encompassing terms determined based on a comprehensive consideration of literature will be used in the searches. A content expert (MM) has developed the search strategy in consultation with a senior information specialist. The

comprehensiveness of the search strategy has been peer reviewed by an informatician at the Terkko faculty library of the Helsinki University Faculty of Medicine.

Ovid MEDLINE, PubMed, Ovid PsycINFO, EBSCO CINAHL and Scopus will be used to execute electronic searches from inception to the present. The online supplemental appendix A presents search strategies for all searched databases.

A four-member team, all with clinical and/or scientific expertise in chronic pain, contribute to the study selection process. The selection decisions will be based on inclusion criteria. First, articles that meet the search terms will be screened by title by one researcher (MM). Second, the remaining articles will be screened by abstract by two researchers separately (MM, MH). Third, the remaining articles will be screened by full text in terms of PICO eligibility and study objective relevance by three researchers separately (MM, MP, MH). Fourth, one researcher (PV) will finally review all of the articles in order to ensure the relevance regarding the study objective and eligibility criteria. All conflicts will be discussed with the full review team. Original study authors will be contacted if eligibility criteria remain elusive following a review by the full review team.

The final study inclusion, accompanied with reasons for exclusion, will be presented in a Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols flow diagram.[15] EndNote reference software will be used to record and deduplicate search results.

Data collection process and data items
The following study information will be included: article data (author, publication year); study population (number of patients treated and analysed, age, pain-related information (duration, localisation, diagnosis), eligibility criteria); study design and intervention (eg, duration, setting, professions included); predictive variables; outcomes (type of measurement, all follow-up time points, outcome variables (eg, pain intensity, pain interference, HRQoL, physical functioning, psychological factors, depression))); and research and statistical information (blinding method in RCTs, imputation method, withdrawals of data).

A coding sheet will be developed in order to be able to transform the described data into categorical data. The data extraction sheet will be pilot tested in the first five studies. Two reviewers (MM, MP) will independently extract data from all included studies and cross-compare them at review completion. In the case of discrepancies, a third experienced researcher will be consulted (PO).

Risk of bias in individual studies
The search for eligible studies, the critical appraisal of the risk of bias and quality evaluation will be completed by several experienced independent researchers. The risk of bias will be evaluated at the individual study level by means of Cochrane Collaboration's tool for assessing risk of bias in randomised trials and Newcastle-Ottawa Scale

in observational studies.[16 17] Information regarding the risk of bias will be summarised in the narrative synthesis.

The quality of the evidence will be summarised using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[18] Based on the GRADE evaluation, the quality of evidence will be regarded as high, moderate, low or very low.[18] Several GRADE domains (eg, risk of bias, imprecision, inconsistency, publication bias, effect size) will be considered, and based on these, evidence may be downgraded or upgraded. The whole review group will contribute to the quality of evidence consideration. A summary of table findings will be presented.

Bias across studies
Publication bias will be evaluated by means of funnel plots and Egger's test.

Data synthesis and meta-analysis estimation
All included articles will be considered in a narrative synthesis. Outcome data will be comprehensively collected from the individual studies. All outcomes presented will be considered in the data synthesis. Predictive variables will be evaluated in association with outcomes as follows: positive association, negative association and no association.

A minimum of two studies need to provide data on the same predictor group in order for these variables to be included in a quantitative analysis. Outcome data will be processed in an outcome-specific and statistic-specific manner as effect sizes (eg, risk ratios (RR), ORs, mean differences, beta coefficients (B), correlation coefficients) with 95% CIs. ORs will be converted to RRs where possible.

The Review Manager (RevMan) software V.5.4 (The Cochrane Collaboration, Copenhagen, Denmark) and Stata MP V.16 (StataCorp, Texas, USA) will be used to pool the results of the individual studies. The threshold for statistical significance will be set at $p=0.05$. Heterogeneity between studies will be estimated using the I^2 index. In the case of substantial heterogeneity ($I^2>50\%$), the subsequent meta-analysis will be omitted, and data will be synthesised only qualitatively.[19] Meta-analysis will be performed using random effects models, weighting individual studies by sample size. Synthesised effect sizes will be reported as pooled ORs with 95% CIs. Sensitivity analyses to explore sources of heterogeneity will be considered; they will be primarily performed by restricting the analysis to subsets of studies.

Patient and public involvement
No patient was involved.

DISCUSSION
A multidisciplinary approach is essential in effective chronic pain management.[1] It is known, however, that not all patients benefit from multidisciplinary chronic pain

management.[10] The importance lies in identifying who may benefit and who may not. The current systematic review project will centre on providing updated evidence regarding factors that may associate with responsiveness to multidisciplinary chronic pain management interventions. The review will use robust methodology and examine a wide range of prognostic variables, also taking into account several secondary outcomes—in addition to improvement in the pain situation, physical functioning and HRQoL as primary outcomes.

The major strengths of the present systematic review are that it (1) aims for a meta-analysis, (2) includes prospective cohorts, case–control studies and RCTs, (3) searches through a vast diversity of journals and databases, and (4) aims to investigate diverse predictive variables and several chronic pain situations. Also, the current review will investigate a wide array of primary (pain intensity and pain interference, physical functioning, heath-related quality of life) and secondary outcomes. In chronic pain management, a multidisciplinary management approach may lead to improvements in other outcomes besides pain (eg, improvements in psychological well-being), which may markedly improve individuals' HRQoL.[10] Therefore, it is essential to consider multiple outcome domains when evaluating treatment responsiveness. Limiting the inclusion criteria to English papers may result in language bias, which therefore needs to be considered a limitation.

A multidisciplinary approach is a gold standard in chronic pain management[4]; however, several factors may pose challenges in regard of responsiveness. Treatment needs to be provided in a timely fashion, and potential comorbidities (eg, psychiatric diseases and symptoms) need to be recognised and treated. The current review aims to identify potential challenges—and, on the other hand, protective factors—regarding responsiveness, which may be beneficial in planning timely treatment with adequate content for chronic pain.

ETHICS AND DISSEMINATION
The proposed study does not involve collection of primary data. Therefore, no ethical approval is required. The results of the systematic review and meta-analysis will be presented in a peer-reviewed journal and at conferences.

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