

BMJ Open What is the relationship between physical activity and chronic pain in older adults? A systematic review and meta-analysis protocol

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ABSTRACT

Introduction Chronic pain is highly prevalent in older adults and can cause functional limitations, negatively affecting health and quality of life. Physical activity is a non-pharmacological approach used to prevent chronic pain as it promotes the release of endogenous opioids that block pain sensitivity. Therefore, we developed a systematic review protocol to analyse the relationship between physical activity and the occurrence and intensity of chronic pain in older adults.

Methods and analyses The systematic review will search PubMed, Scopus and Embase databases. The inclusion criteria will be observational studies that had primary chronic pain as an outcome, including persistent and intermittent pain. The population will include older adults from the community, living in a long-stay institution, or in outpatient follow-up. There will be no restriction regarding the year of publication and articles published in Portuguese, English and Spanish will be analysed. Effect or impact measures will be quantified, including OR, HR, prevalence ratio, incidence ratio and relative risk with their 95% CIs. If the data allow, a meta-analysis will be performed. The results may help understand the impact of physical activity as a potential protection factor against the occurrence of pain later in life as well as promote strategic prevention plans and public policies that encourage this practice in older adults.

Ethics and dissemination Ethical approval is not required. The results will be disseminated via submission for publication to a peer-reviewed journal when complete.

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INTRODUCTION

Chronic pain is an emerging global public health problem. Its impact includes significant suffering for patients, their families and society.¹ In addition to the pain itself, other negative consequences may include fatigue, anxiety, depression, social isolation, financial problems, poor quality of life, high costs and burden for healthcare systems.²⁻³ Chronic pain has a prevalence of 20% in adults, which increases to 60% in those aged 60 and older.^{4,5}

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ No previous systematic review on the relationship between physical activity and the occurrence of chronic pain in older adults.
- ⇒ Three important databases (PubMed, Embase and Scopus) will be analysed.
- ⇒ The review process for selection and inclusion of the articles will be performed separately by two researchers and any disagreements will be mediated by a third reviewer to assure a consistent and strict application of the inclusion and exclusion criteria.
- ⇒ There will be no restrictions on the year of publication, and articles published in English, Spanish and Portuguese will be analysed.
- ⇒ The limitation of this review might be the use of a single outcome, chronic pain.

One of the explanations for this increase may be the fact that with extended life expectancy, more chronic conditions and other health problems associated with ageing are often accompanied by chronic pain symptoms.⁶⁻⁸

The relationship between pain and ageing is complex and associated with several negative health outcomes in older adults, since the presence of moderate-to-severe persistent pain results in significantly rapid cognitive decline,⁹ risk of falling and impaired social, civic and political engagement.¹⁰ Moreover, older individuals with chronic pain are more likely to develop frailty,¹¹ feelings of loneliness¹² and worse physical performance.¹³ A recent cohort study⁹ that aimed to verify whether moderate or severe persistent pain was related to cognitive decline in older adults and showed that those practicing vigorous weekly physical activities developed fewer chronic pain symptoms over a decade than those who did not.

Observational studies have reported significantly lower physical activity levels

in older adults with chronic pain than in those without chronic pain in view of the disabling impact of the pain assessed.^{14 15} High-intensity physical activity exhibited a protective action against the development of chronic pain (OR 0.74; (SE) 0.007, 95% (CI) 0.62 to 0.89)¹⁶ as well as lower risk of disability (step counts <4149.5 step/day, HR=1.79, 95% CI 1.02 to 3.14; moderate to vigorous intensity physical activity (MVPA) <15.40 min/day, HR=2.02, 95% CI 1.16 to 3.51), but not light intensity physical activity (LPA) (HR=1.72, 95% CI 0.97 to 3.05).¹⁷ However, moderate-level activity may be useful in preventing disability and frailty in older adults with chronic pain.^{13 16 18} Furthermore, structured exercises and/or general physical activities play an important role in reducing the risk of mortality¹⁹ and in preventing and managing chronic diseases associated with ageing, for example, physical activity can reduce pain in individuals with osteoarthritis.^{20 21}

Physical activity can influence the biopsychic mechanisms underlying chronic pain since muscle contractions during activity afferent A-delta (group III) and C (group IV) nerve fibres, increasing the release of endogenous opioids. These substances, classified as endorphins, enkephalins and dynorphins, are produced by the body itself.²²⁻²⁴ With morphine-like action, the activation of these endogenous opioids in the brainstem nuclei blocks the opioid receptors in the central nervous system, decreasing pain sensitivity and leading to antinociception (pain inhibition). Furthermore, physical activity can activate the non-opioid endocannabinoid system, which has a neuromodulator function and comprises cannabinoid receptors (CB1, CB2), their endogenous ligands (N-arachidonoyl ethanolamine and 2-arachidonoylglycerol endocannabinoids) and the proteins responsible for their metabolism, which when activated in the brain and spinal cord nociceptive processing areas contribute to pain control.^{25 26}

Other implications such as physical changes may occur that can improve a person's ability to support bone and cartilage by providing muscle support movement around a joint, with the potential to relieve stiffness²⁷ and, ultimately, bringing some pain relief. Moderate-intensity physical activities also stimulate cellular immunity, while prolonged or high-intensity practices without adequate rest can promote a decrease in cellular immunity, increasing the susceptibility to other diseases.²⁸ Therefore, physical activity has multifactorial benefits with important local and systemic effects on skeletal muscle, the cardiovascular system and the autonomic nervous system²⁹ and has consequently been targeted as a strategy to reduce chronic pain symptoms.¹⁵

Despite the importance of the topic in public health and geriatrics/gerontology, we identified only one systematic review of observational studies published in 2013 that analysed the association between physical activity and pain.³⁰ This systematic review included eight articles and aimed to investigate whether older people with musculoskeletal chronic pain were less physically active than were

those without chronic pain. The same study included a meta-analysis of five studies.³⁰ The main finding of this systematic review was that older adults with chronic musculoskeletal pain had lower levels of physical activity than those without pain, with a significant standardised mean difference (-0.20, CI -0.34 to -0.706, $p < 0.004$) and low and non-significant heterogeneity of the included studies (32%).³⁰ However, this study was restricted only to older adults with musculoskeletal pain.

Although previous studies have reported a high prevalence of chronic pain in older adults as well as its association with several negative outcomes,^{9 18 30} to the best of our knowledge, no previous systematic review and meta-analysis has explored the relationship between physical activity and the occurrence of chronic pain and whether this impact changes with advancing age. Furthermore, this review will investigate the types and intensity levels of physical activity that could be protective against chronic pain and, ultimately, address the gap in the scientific knowledge on this topic. There is a clear need for a systematic review on this topic to increase our understanding of this problem affecting many older adults and to develop better strategies to prevent chronic pain later in life. Therefore, this systematic review and meta-analysis will aim to analyse the relationship between physical activity and the occurrence and intensity of chronic pain in older individuals. Moreover, we aim to evaluate whether this impact varies with advanced age as well as with the type and intensity of physical activity. The key findings from this study may help health professionals to understand the role of physical activity as a potential protective factor against the occurrence of pain in older adults. This in turn may help to promote strategic preventive actions and public policies to encourage this practice in this age group.

METHODS

This systematic review will follow the guidelines of the Preferred Report for Systematic Reviews and Meta-analyses (PRISMA).^{31 32} It will use the PECO structure: P (older adults), E (physical activity), C (sedentary behaviour), O (chronic pain). This systematic review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO), and any changes during the study will be reported.

DEFINITIONS

Primary and secondary chronic pain and pain intensity

Pain is characterised as an unpleasant, sensitive and emotional experience associated with an actual or potential injury.³³ It can manifest in several forms and is classified as acute or chronic, varying in duration (time of occurrence), location (local, general) and severity (mild, moderate, severe),^{33 34} in subjective measure, since the sensation is different, and its threshold may be associated with ageing.³⁵

Chronic pain, that is, long-term pain, is described as pain of a continuous or recurrent nature lasting at least 3 months³⁵ that does not present a single state in terms of presence or intensity.⁴⁵³⁴ The severity of chronic pain is determined by its intensity, even if subjective, by the suffering experienced in association with it, and its interference in daily activities and other social contexts. This intensity can be assessed verbally or on a numerical or visual rating scale, encoding severity on a scale ranging from 0 (no pain) to 10 (worst imaginable pain).³⁶ Conversely, acute pain is described as a local and short-lasting sensation³⁷ that can be classified as primary or secondary.³⁷

Primary chronic pain is characterised by the absence of a clear underlying condition or an impact that is disproportionate to any observable injury or disease.³⁸ Additionally, to be classified as primary, the prerequisite is that the pain cannot be explained by another chronic condition, with pain being the main disease.³⁸ Primary chronic pain is subdivided into chronic generalised pain (fibromyalgia), complex regional pain syndrome (chronic pain after peripheral nerve injury), chronic primary headache or orofacial pain (chronic migraine, temporomandibular disorders, trigeminal autonomic headaches), chronic visceral pain primary (chest, abdominal, epigastric, pelvic, chronic bladder pain syndrome), and primary chronic musculoskeletal pain (chronic neck, thoracic, lumbar, limb pain).³⁹

Meanwhile, chronic pain is considered secondary when it is caused by an underlying condition, that is, associated with other diseases.³⁸ Secondary pain can be subdivided into chronic cancer-related pain (caused by the cancer itself or its metastases or treatment),⁴⁰ chronic post-surgical or post-traumatic pain (after a surgical procedure or tissue injury), chronic secondary headache or orofacial pain (all types of headache and orofacial pain with an underlying cause), chronic secondary visceral pain (originating from the internal organs, with an underlying cause),⁴¹ and chronic secondary musculoskeletal pain (local or systemic pain with an underlying cause).⁴²

Physical activity

Physical activity can be described as any body movement produced by skeletal muscles that significantly increases energy expenditure and whose intensity can be considered according to the energy expenditure in a given activity.⁴³ Daily living activities such as working, playing, performing household chores, travelling and leisure activities are classified as physical activity.²¹⁴⁴ Other forms include structured exercise activities, such as aerobic conditioning, strength, facilitation and movement stabilisation exercises or walking, performed on land or in water and guided/not guided by a professional.²⁷⁴³⁴⁵

Older adults

An older adult is defined as an individual aged 65 or older in developed countries,⁴⁶ while developing countries define older adults as those aged 60 or older.⁴⁷ Both

definitions will be considered in this systematic review, and studies that present data related to primary chronic pain and to physical activity will be included.

Search strategy and eligibility criteria

PubMed, Scopus and Embase databases will be searched. This step has started in January 2022. There will be no restrictions for the year of publication, and articles published in English, Spanish and Portuguese will be analysed. The following inclusion criteria will be used: (a) observational studies (cross-sectional, cohort and case-control), (b) participants aged 60 or 65 years or older, depending on the country where the study was conducted, (c) older adults living in the community or living in a long-stay institution, (d) older adults in outpatient follow-up and (e) primary chronic pain as an outcome, including persistent (for at least 3 months) and intermittent pain.

The following exclusion criteria will be adopted: (a) hospitalised older patients, (b) patients suffering from cancer-related chronic pain or chronic pain secondary to other morbidities as an outcome, (c) older adults diagnosed with mental illness, (d) randomised clinical trials, case series and case reports, (e) opinion articles, comments, editorials, letters to the editor, systematic and integrative reviews and qualitative research, (f) studies published more than once (the one with the largest sample will be considered) and (g) studies in which the main data are not accessible even after contacting the authors.

MeSH (Medical Subject Headings) terms and keywords relevant to physical activity, chronic pain and older adults will be used in the search strategy to cover all studies on the topic (box 1).

Reviewer training

The authors responsible for the search and inclusion/exclusion stage will be trained. The eligibility criteria will be tested on 100 titles and abstracts of articles identified in the search strategy. The reviewers will be trained to assess the risk of bias and quality of evidence of the included studies.⁴⁸

Box 1 Search strategy for studies on physical activity and chronic pain in older people

1=exercise OR exercises OR "physical activity" OR "physical activities" OR "exercise training" OR "exercise trainings" OR "endurance training" OR "fitness training" OR "fitness workout" OR "physical conditioning" OR "physical exertion" OR "physical workout"
 2 = "chronic pain" OR "chronic pains" OR "chronic intractable pain"
 3=aged OR elderly OR elder OR aging OR ageing OR "old adult" OR "old adults" OR "older adult" OR "older adults" OR geriatric OR "senior citizen" OR senior
 4 = #1 AND #2 AND #3

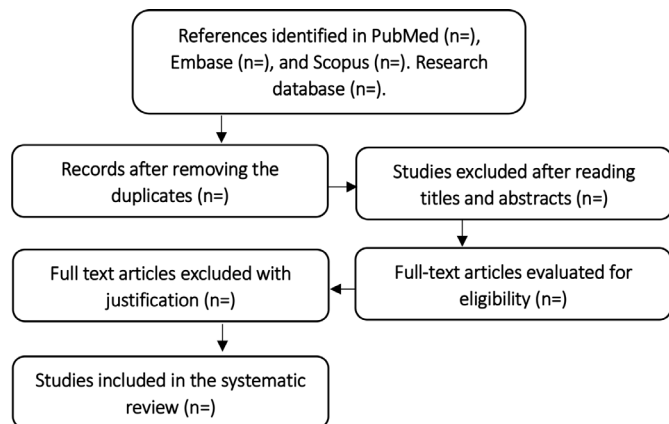


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart: search strategy and the inclusion of in a systematic review of the impact of physical activity on chronic pain in older people.

Review process

The articles will be searched by two independent researchers (RM and ALJ). Subsequently, the articles will be grouped, and duplicate studies will be removed using the Mendeley software. The selected articles will be screened by two independent researchers (RM and ALJ) using the Rayyan software,⁴⁹ and potential disagreements will be assessed and resolved by a third senior researcher (EAS). The studies will be included after reading the titles and then the abstracts. Subsequently, the selected articles will be evaluated to determine their eligibility. If any important data are missing in the article, one of the researchers will contact the respective authors directly for clarification. Disagreements regarding inclusion will be discussed and resolved by a third reviewer (EAS). Inter-reviewer reliability will be measured using Cohen's Kappa statistic.⁵⁰ A flowchart of the review process will be prepared according to PRISMA-P recommendations (figure 1).

Data extraction and study quality assessment

The data will be extracted using a standardised form prepared by the authors containing author/year/place (city/country), type of study, target population (number of participants, age group, sex and institutionalised or community-based), physical activity (occurrence, type, frequency, and Physical Activity Measure), chronic pain (occurrence and frequency), relation of physical activity and the occurrence of chronic pain. If necessary, additional columns will be added to the data extraction table (table 1).

The Downs and Black⁵¹ instrument with 27 items will be used to assess the risk of bias, but as not all items are applicable to observational studies, a subset of 16 items (questions 1–3, 5–7, 9–12, 17, 18, 20, 21, 25, 26)⁵¹ will be used. Each manuscript will be scored according to the number of items considering the percentage of the total (0 to 16 points). Low risk of bias will be defined by a score of >70%.⁵¹ In addition, the Grading of Recommendations, Assessment, Development and Evaluation

Table 1 Form for extracting data on the relationship between physical activity and chronic pain in older adults

Author/ year/ location	Type of study (if cohort, indicate follow-up time)	Target population*	Prevalence of chronic pain†	Chronic pain diagnosis	Chronic pain intensity	Type of physical activity	Frequency of physical activity‡	Physical activity level	Measure of relationship between physical activity and the occurrence of chronic pain
*Institutionalised or community-based, age group and sex.									
†Yes or no, location/duration.									
‡Yes or no, minutes per week.									
§According to sex and age group and measures of effect (relative risk (RR), OR, incidence ratios, HR (HR), prevalence ratios (PR) with the respective CIs)									

(GRADE) evidence system will be used to assess the quality of evidence. Quality of evidence will ultimately be graded as high quality, moderate quality, low quality or very low quality.^{52 53} The GRADEpro GDT software will be used to assess the overall quality of evidence.⁵⁴

Statistical analysis

The relationship between physical activity and the occurrence and intensity of chronic pain in older adults will be displayed through descriptive tables summarising the data from all eligible articles. Effect measures will be quantified, including prevalence ratios (PR), incidence ratios, OR, HR, relative risk (RR) and their respective 95% CIs and p values. A Forest plot of the random-effects model will be constructed using ORs and their respective 95% CIs. If the data allow, a meta-analysis will be performed, and RR, PR and HR and their respective 95% CIs will be converted into ORs and included in the analyses. The combined results will be stratified by age groups. Moreover, if articles from these two groups are identified, they will be compared and analysed separately in ‘institutionalised’ and ‘non-institutionalised older adults’. Heterogeneity will be quantified using I^2 ⁵⁵ and a Forest plot will be used to display effect sizes between studies.⁵⁶ For studies with I^2 values greater than or equal to 50%, meta-regression can be performed according to the exposure variables described above. Publication bias will be assessed using a funnel plot.⁵⁷ whose asymmetry will be assessed using Egger’s test.⁵⁸

Patient and public involvement

No patients involved

DISCUSSION

Studies on chronic pain in older adults are extremely relevant, as this symptom affects a large part of this population, causing several negative impacts including mental health problems.^{9–12 27} Our findings will potentially contribute to the understanding of the effect of physical activity on the occurrence of chronic pain of different types and intensities. Our results may also support public health policies to implement preventive actions in different scenarios and, ultimately, improvements in health and quality of life later in life.

The present systematic review protocol is the first study to investigate the protective effect of physical activity on the occurrence and intensity of chronic pain in older adults and to identify the most appropriate type, frequency and intensity of physical activity. We also aim to establish which factor is the most beneficial. Regarding the age group, we will evaluate differences between chronic pain in people aged 60–80 and those aged 80 and over.

We will include an in-depth study to address the knowledge gaps in the literature and support future research on the subject. Furthermore, this research will not restrict the year of publication when selecting the articles and Downs and Black will be used to assess the risk of bias and

the GRADEpro GDT software will be used to assess the overall quality of evidence from the studies. We anticipate certain limitations, such as difficulties in performing a meta-analysis since different types of physical activity and chronic pain will be reported in the articles.

Ethical aspects

Ethical approval was not deemed necessary for this study as data were obtained from peer-reviewed publications, and information that could identify the participants of the original studies was not included.

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Contributors EAS, ATOR and RM formulated to the conception and design of the study; RM, EAS, ATOR, ALJ and MN contributed to the methodologic aspects; RLSM, EAS, ATOR, ALJ and MN contributed to the data analysis plan; all authors contributed to the writing and editing of the manuscript and approved the final manuscript.

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Competing interests None declared.

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