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PATHOPHYSIOLOGICAL CHANGES IN INDIVIDUALS WITH CHRONIC PAIN, ABSENCE OF A MULTIDIMENSIONAL ASSESSMENT, AND CRITERIA FOR PRESCRIBING THERAPEUTIC EXERCISE: SYSTEMATIC REVIEW OF THE CURRENT LITERATURE

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ABSTRACT

Introduction: This systematic review aimed to analyze the current scientific literature on the practice of physical exercises in the treatment of Chronic Pain, the pathophysiological changes present in these individuals, and the criteria for prescribing exercises. ***Methods:*** We used the PRISMA model to prepare this review, which was registered on the PROSPERO platform under registration number CRD42024618037. The review question was "What are the neurofunctional and biomechanical alterations present in individuals with chronic pain? And what are the clinical parameters and criteria for prescribing exercises for pain treatment?". We searched the PubMed Central, EBESCO, Virtual Health Library (VHL), Scielo, Pedro, and Cochrane Library databases for systematic reviews with meta-analyses published in the last 5 years. The selected studies were evaluated qualitatively using the AMSTAR 2 method and quantitatively using descriptive statistics (prevalence, mean, and incidence), presented in narrative format, tables, and graphs. ***Results:*** We selected 40 systematic reviews with meta-analysis, published in 16 countries, that analyzed 111,531 individuals, with a mean of 12,392.33 per study (standard deviation 32,157.86), encompassing both genders and individuals aged between 14 and 80 years. We assessed the methodological quality of the studies using the AMSTAR 2 method, presenting high methodological quality for 72.9% (29 studies) of the Meta-Analysis, 15% (6 studies) of Moderate quality, and 12.5% (5 studies) of Critically Low quality. The pathologies analyzed were Low Back pain, Neck pain, Fibromyalgia, chronic Fatigue syndrome, Musculoskeletal Pain, Upper limb and insertional Achilles tendon tendinopathy, anterior Knee pain, and knee and Hip Osteoarthritis. We analyzed a total of 28 exercise modalities, with therapeutic exercise having the highest prevalence. We observed differences between genders in different pathologies. Therapeutic exercise demonstrated significant improvement in short-term pain and in improving functional capacity, but higher-quality studies and objective evaluation of clinical improvement are still needed. Individuals with chronic pain presented pathophysiological changes used as justification for the studies, but these were not evaluated, given the lack of criteria for exercise prescription. No study presented an evaluation of Kinesiophobia, 29 studies evaluated Functional Capacity, obtaining a Clinical improvement of 55%, Pain was evaluated by 31 studies and obtained a clinical improvement of 50%, Quality of Life was evaluated by only 9 studies, obtaining a clinical improvement of 5%. We observed a total of 55 methods used for evaluation, 76% performed subjective evaluation, and 24% evaluation with objective methods, with functional capacity evaluated objectively in 33% of their evaluations, and Pain in 2%. The Visual Analog Scale (VAS) and the Numerical Rating Scale (NRS) were the most prevalent pain assessments, and 3% of pain assessments were performed by intra-articular blood collection (inflammatory and pro-inflammatory biomarkers). We conclude that this study may help researchers and clinicians gain a more comprehensive understanding of the complexity of evidence-based clinical practice in physical exercise for pain treatment.

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INTRODUCTION

Chronic pain is a pathological condition triggered by the chronicity of an acute pain condition that persists for more than three months, caused by biological and/or psycho-emotional factors. It is currently the leading cause of disability worldwide, generating high costs and excessive demands on the healthcare system.[1,2] Prevention is the best treatment, and is related to improving the management of acute pain, changing lifestyle, social context, and education about pain. The worsening of the clinical condition is directly correlated to an increased risk of developing cardiovascular dysfunctions, neurological dysfunctions, and the risk of mortality.[3] The term

"Healthy Mind, Healthy Body" is described in the times of Ancient Greece where there were already initial reports of the prescription of exercises to promote health, with the development of the study of pain we know that a sedentary lifestyle is inadequate and harmful to these individuals, and public policies are aimed at encouraging the practice of exercises as treatment and prevention.[4,5] According to the World Health Organization, performing movements with the body without a specific purpose and planning, with the objective of moving, is defined as "Physical Activity," which has a lot of consistency in the literature for improving physical and mental health, and should be encouraged as a lifestyle, improving quality of life and life expectancy.[6] Biopsychosocial aspects are extremely relevant in the context of Pain, with a high incidence of psychoemotional disorders, justifying the need for a multidisciplinary and multimodal treatment. "Body and Mind Exercises" is a subcategory of Physical Activities being used in the treatment of Pain, but with a particularity, which is to seek control of breathing as well as thoughts, being associated with Meditation, with the objective of physical and emotional improvement.[1,2,7] When we perform an exercise in a structured and planned manner with the aim of improving Pain, we are referring to "Therapeutic Exercise", which is another subcategory of Physical Activities, strongly recommended by researchers and experts in Pain, who seek to develop a therapeutic exercise program, using a model of evaluation and optimization of motor control in individuals with Chronic Pain, taking into account their individuality and pathophysiological changes, which are still scarce in the literature.[8,9,10]

This suggested motor control model seeks to evaluate and optimize different dysfunctional changes, such as cardiovascular and neurological dysfunction, fear and avoidance of movement, muscle inhibition or hyperactivation, joint hypo and hypermobility, changes in the reflex arc between agonists and antagonists, changes in the sensorimotor system, body and gait perception, requiring a multimodal treatment model that we do not observe in the literature, with many studies addressing exercise methods focusing on a single dysfunctional change.[10] In recent years, the number of studies analyzing the practice of exercise in pain treatment has been substantial and is continuing to grow in development. To the best of our knowledge, no specific exercise method has been identified that yields a significant improvement in outcomes. There is considerable inconsistency in the literature, and the certainty of the evidence is low. We observed in previous studies that individuals with chronic pain are unable to adhere to exercise, and we already know that the exercise program, as well as reducing the incidence of adverse events, can contribute to better adherence.[11,12,13] Chronic Musculoskeletal Pain can be diagnosed according to its pathophysiology and phenotyping, and can be classified as primary or secondary. The different types of Pain present dysfunctional changes that impact the practice of exercises. However, such changes and criteria for prescribing exercises are scarce in the literature. In clinical practice, we observe that the same individual can present more than one type of Pain. We did not find studies in the literature that addressed the practice of exercises as a treatment for Pain, analyzing different types of Pain.[5,13,14,15,16] The objective of our study was to search the literature for dysfunctional changes, prescription criteria, and the best evidence for exercise practice in individuals with chronic pain.

METHODOLOGY

This systematic review was conducted in accordance with the PRISMA 2020 guidelines and was initially registered on the PROSPERO platform under the registration number CRD42024618037.[17]

The guiding question for the study was developed using the PICO method.[18:] PICO Method (Public, Intervention, Comparison, Outcomes):

P: Individuals with primary chronic pain and secondary chronic musculoskeletal pain.

I: Physical exercises for the treatment of primary chronic pain and secondary chronic musculoskeletal pain, evaluation of neurofunctional and biomechanical changes in individuals with primary chronic pain and secondary chronic musculoskeletal pain.

C: Healthy individuals, individuals with chronic pain who received placebo treatment, no treatment, or other treatment modalities that did not include physical exercise.

O: Identify the neurofunctional and biomechanical changes presented by individuals with primary and secondary chronic pain, and what are the clinical parameters and criteria for prescribing exercise in the treatment of this population.

Question that guided the research: *What neurofunctional and biomechanical alterations are present in individuals with chronic pain? And what are the clinical parameters and criteria for prescribing exercises for pain management?*

Keywords: We utilized the authors' expertise to conduct a thorough search for a comprehensive sample of all physical exercise methods employed in pain treatment by professionals in clinical practice.

Physical exercise: Physical exercise, Exercise, Resistance exercise, Aerobic exercise, Functional exercise, Pilates, Motor control, Yoga, Weight training, Strength training, Cross training, Motor control, Dynamic stretching, Stretching, Joint mobility, Mobility, Cognitive training, Myofascial release roller, Stabilization, Plyometrics, Core training, Agility.

Primary chronic Musculoskeletal pain: Chronic pain, chronic low back pain, neck pain, neck pain, fibromyalgia.

Chronic secondary Musculoskeletal pain: Musculoskeletal pain, shoulder pain, rotator cuff syndrome, adhesive capsulitis, impingement syndrome, tendinopathy, osteoarthritis, arthritis, knee pain, anterior knee pain, patellar tendinopathy, Achilles tendinopathy, gluteal tendinopathy, femoroacetabular impingement, labral tear, hip osteoarthritis, epicondylitis, carpal tunnel syndrome, plantar fasciitis, metatarsalgia, shoulder instability, ankle instability, myofascial pain syndrome, bursitis.

Additional terms listed below were included in the search after being observed:

*Thai chi, transcutaneous electrical stimulation, vibration training.
*Chronic fatigue syndrome, irritable bowel syndrome. We utilized the Boolean operators "AND" and "OR" to create the search strategy, connecting all physical exercise methods with all pathologies

Inclusion Criteria:

- Studies that observed clinical improvement in pain, measured by improved functional capacity, reduced pain threshold, or improved quality of life.
- Studies that used exercise as a clinical outcome for treatment, either alone or in combination with other treatment methods.
- Studies that observed neurofunctional and biomechanical changes.
- Systematic Reviews with Meta-Analysis;

Exclusion criteria

- Studies that were not available for open access.
- Studies published more than 1 year ago in the PubMed database and more than 5 years ago in other databases.

Database: The databases chosen for research were PubMed Central, EBESCO, Virtual Health Library (BVS), Scielo, Pedro, and the Cochrane Library.

PUBMED: Search carried out on July 9, 2023, the following search strategy: ((Physical exercise) or (Exercise) or (Resistance exercise) or (Aerobic exercise) or (Functional exercise) or (Pilates) or (Motor

control) or (yoga) or (Weight training) or (Strength training) or (cross training) or (motor control) or (dynamic stretching) or (stretching) or (joint mobility) or (mobility) or (cognitive training) or (myofacial release roller) or (stabilization) or (plyometrics) or (core training) or (Agility)) and ((Chronic pain) or (Chronic low back pain) or (neck pain) or (neck pain) or (fibromyalgia) or (Musculoskeletal pain) or (shoulder pain) or (rotator cuff syndrome) or (adhesive capsulitis) or (impingement syndrome) or (tendinopathy) or (arthrosis) or (arthritis) or (knee pain) or (anterior knee pain) or (patellar tendinopathy) or (Achilles tendinopathy) or (gluteal tendinopathy) or (femoral acetabular impingement) or (labral tear) or (hip arthrosis) or (epicondylitis) or (carpal tunnel syndrome) or (plantar fasciitis) or (metatarsalga) or (shoulder instability) or (ankle instability) or (myofascial pain syndrome) or (bursitis)). Using the systematic review and meta-analysis filters published in the last year.

Ebesco: Search carried out on March 2, 2024, the following search strategy: (chronic pain AND physical exercise benefits AND (evaluation or assessment)) AND TI meta-analysis Utilizando os filtros publicados nos últimos cinco anos, revisões sistemáticas e Metanálise.

BVS: Search carried out on March 2, 2024, the following search strategy: (Chronic pain) AND (physical exercise benefits) AND (evaluation or assessment) Utilizando os filtros publicados nos últimos cinco anos, revisões sistemáticas e Metanálise.

Scielo: Search carried out on March 2, 2024, the following search strategy: (chronic pain) AND (physical exercise) AND (evaluation or assessment)

Pedro: Search carried out on March 2, 2024, the following search strategy: chronic pain, physical exercise, evaluation, or assessment.

Cochrane Library: Search carried out on March 2, 2024, the following search strategy: ((Physical exercise) or (Exercise) or (Resistance exercise) or (Aerobic exercise) or (Functional exercise) or (Pilates) or (Motor control) or (yoga) or (Weight training) or (Strength training) or (cross training) or (motor control) or (dynamic stretching) or (stretching) or (joint mobility) or (mobility) or (cognitive training) or (myofacial release roller) or (stabilization) or (plyometrics) or (core training) or (Agility)) and ((Chronic pain) or (Chronic low back pain) or (neck pain) or (neck pain) or (fibromyalgia) or (Musculoskeletal pain) or (shoulder pain) or (rotator cuff syndrome) or (adhesive capsulitis) or (impingement syndrome) or (tendinopathy) or (arthrosis) or (arthritis) or (knee pain) or (anterior knee pain) or (patellar tendinopathy) or (Achilles tendinopathy) or (gluteal tendinopathy) or (femoral acetabular impingement) or (labral tear) or (hip arthrosis) or (epicondylitis) or (carpal tunnel syndrome) or (plantar fasciitis) or (metatarsalga) or (shoulder instability) or (ankle instability) or (myofascial pain syndrome) or (bursitis))

Study Selection: Studies were eligible after analyzing the inclusion and exclusion criteria, following the methodological rigor of identification, screening, and inclusion, with each stage clearly demonstrated and its respective databases specified. From the full reading stage onwards, studies that were not available in open access or that were excluded by the exclusion criteria will be presented.

Data Collection: After formulating the question for this review, a text document and a spreadsheet were created containing the information to be collected, organized by group of pathologies and tests. Data collection was performed manually after the study had been read in full.

Data has been collected and analyzed

General study information: Year of publication, country and author, participant characteristics, methodology describing the exercise method used and how it was analyzed and compared, study results, and their statistical significance. In all data collections, we present an analysis of the methodological quality and certainty of the evidence presented by the study, using the AMSTAR 2 method.

Analysis of exercises, dysfunctional changes and perspective of clinical improvement in pain observed in the literature in the treatment of chronic pain

Exercise analysis: We extracted information about the exercise method descriptions used in the studies and the results analyzed by each study.

Dysfunctional changes: We extracted information regarding dysfunctional changes cited in the studies, which were used to justify the intervention or were analyzed methodologically.

Pain Improvement: We extract information related to the temporal analysis of Pain, considering improvement over 3 to 6 months as Short Term, 6 to 12 months as Medium Term, and more than 12 months as Long Term.

Analyzes of dysfunctional improvement in neuromuscular changes and motor control after exercise therapy: We considered the dysfunctional changes presented in the literature, considering whether the study evaluated methodologically and presenting whether there was improvement, worsening, or if it was not evaluated.

Joint Dysfunctions: We consider all analyses of the range of motion, mobility, and joint stability.

Muscle Dysfunction: We consider all aspects of muscle analysis, including flexibility, strength, endurance, power, fatigue, and neuromuscular activation.

Gait Changes: We consider any change that could optimize and improve the gait movement cycle or pathophysiological adaptations.

Postural Control: We consider the analysis of body perception, static, and dynamic posture.

Balance and sensorimotor system: We consider improvement at the cortical or motor level, which presents an improvement or worsening in maintaining the center of gravity over the support base.

Analysis of clinical improvement after exercise therapy in individuals with chronic pain: We consider the improvement of Kinesiophobia, Functional Capacity, Pain, and Quality of Life, assessed subjectively through questionnaires and scales or even objectively with exams and clinical tests, considering the statistical improvement or worsening, and reporting if it was not assessed.

Analysis of exercise prescription in individuals with chronic pain: We consider exercise type, frequency, intensity, and progression criteria as essential outcomes for exercise prescription in individuals with chronic pain.

Type of exercise: was extracted according to the definition of the study, and its characteristics when presented.

Frequency: We consider the time of each exercise session, and its frequency, whether weekly or monthly, is also defined by the number of sessions per week or month.

Intensity: Intensity parameters varied between the percentage of one maximum repetition, percentage of heart rate, VO2, Volume, and the perception of effort to classify exercises as low or high intensity.

Criteria for Progression: We consider individuality, tolerance, and pain threshold, as well as the quality of movement execution and frequency, as criteria for exercise progression.

Presentation of results: The results will be presented through descriptive text, tables, and graphs.

***Analysis of risk of bias and methodological quality*:** We used the AMSTAR 2 tool to analyze the risk of bias and methodological quality of the meta-analyses.[19]

Certainty of Evidence: We used Level I evidence studies as inclusion criteria, according to evidence-based practice, selecting only systematic reviews with meta-analysis. The certainty of evidence was

assessed by the GRADE method analysis performed by the authors of the selected studies.[20]

Data Synthesis: The results were initially summarized in a narrative and descriptive manner, extracting information corresponding to the study's outcome. They were then tabulated and converted into numerical spreadsheets so that the data could be statistically summarized, enabling a more accurate analysis of the results.

Sensitivity and Heterogeneity of the Studies: We employed subgroup analysis, which initially revealed clinical heterogeneity among the groups in terms of individual characteristics, exercise-based clinical interventions, and pain assessment**.**

***Statistical analysis of results*:** We used descriptive statistics to analyze the results, including sum, mean, percentage, and prevalence, using Microsoft Excel software.

Missing data: To minimize the risk of bias and better interpret the results, the number and percentage of missing data were shown in all statistical analyses.

***Protocol Change*:** Initially, we expected to summarize the exercise groups into strength training, Pilates, stabilization, body and mind, and physical activities. When analyzing the data, we chose to use the WHO classification, specifically the physical activity subcategory of body and mind exercises and therapeutic exercises, due to the similarity and characteristics of the exercise methods.

RESULTS

Our systematic review found a total of 32,700 studies, 40 systematic reviews with meta-analysis were selected by the inclusion and exclusion criteria[21-60], 35 studies were excluded because they were not available in open access for reading and 17 studies because they did not present methodological criteria, which included evaluation of neurofunctional and musculoskeletal dysfunctions, or physical exercises as an outcome for pain treatment, the excluded studies are presented in Appendix 1, and the detailed study selection process is presented in Figure 1 below:

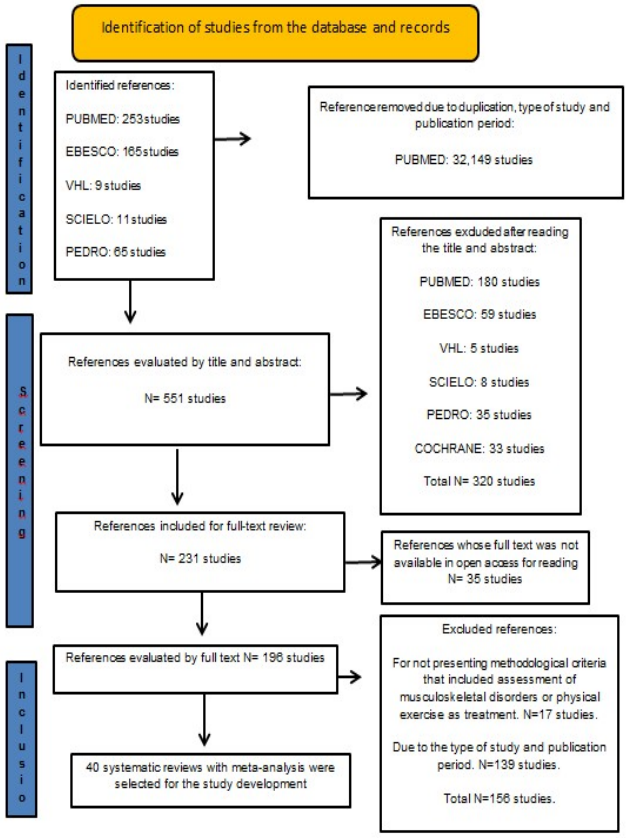
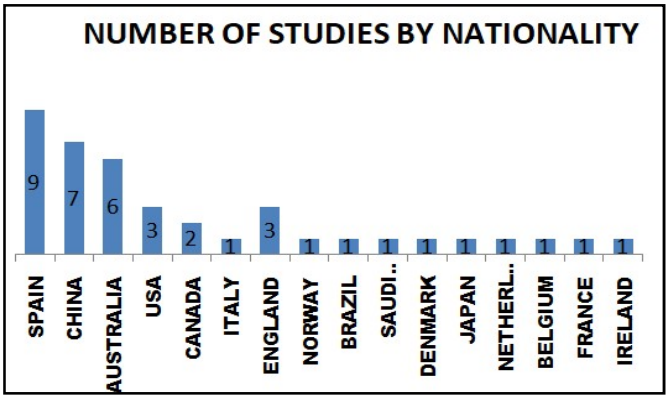


Figure 1. selection of studies

The characteristics of the studies were analyzed by collecting information regarding the author, year of publication, and country, where we carried out an updated search of studies published between 2019 and 2024, characteristics of the individuals, such as the number of participants, gender and age, methods used, and the results presented by the studies are shown in Appendix 2, Table 1

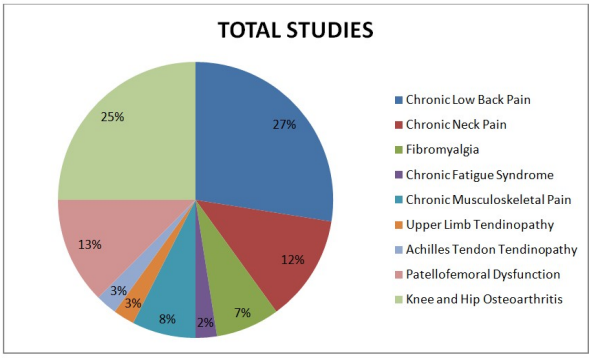
Graphical representation of the number of studies by nationality:



The studies were carried out in 16 countries, the European continent represented 47% of the studies, followed by Asia 23%, Oceania and America 15% of the studies. Graphical representation of the number of studies by nationality:

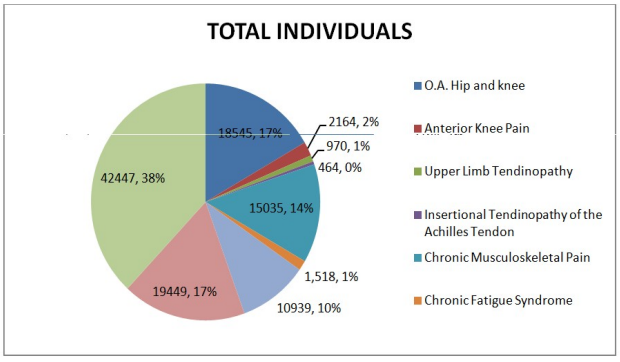
Exercise therapy was applied to the treatment of Chronic Low Back Pain 11 studies, Knee and Hip Osteoarthritis 10 studies, Chronic Neck Pain 5 studies, Patellofemoral Dysfunction 5 studies, Chronic Musculoskeletal Pain 3 studies, Fibromyalgia 3 studies, Upper Limb Tendinopathy 1 study, Achilles Insertional Tendinopathy 1 study and Chronic Fatigue Syndrome 1 study.

Graphical representation of the percentage of studies by pathology



We analyzed 111,531 individuals, with an average of 12,392.33 per study (standard deviation 32,157.86), representing both genders aged between 14 and 80 years.

Graphical representation of the percentage of individuals by pathology



Only 50% of the studies reported the gender of the individuals (55,536 individuals), with 66% being female (36,871 individuals) and 34% being male (18,665 individuals). Male individuals had a higher prevalence of Upper Limb Tendinopathies and Anterior Knee Pain, with the other pathologies being more prevalent in female individuals.

Chronic Low Back Pain: Three studies (27%) reported the gender of the Participants, totaling 33,502 individuals, with 35% Men and 65% Women.

Chronic Neck Pain: Two studies (40%) reported the Gender of the participants, totaling 4,105 individuals, 23% Men and 77% Women.

Fibromyalgia: Two studies (67%) reported the Gender of Participants, a total of 529 individuals 2% Men and 98% Women.

Chronic Fatigue Syndrome: One study (100%) reported the Gender of the Participants, a total of 1,511 individuals, 29% Men and 71% Women.

Chronic Musculoskeletal Pain: Two studies (67%) reported the genders of the participants, a total of 2,640 individuals: 31% Men, 69% Women.

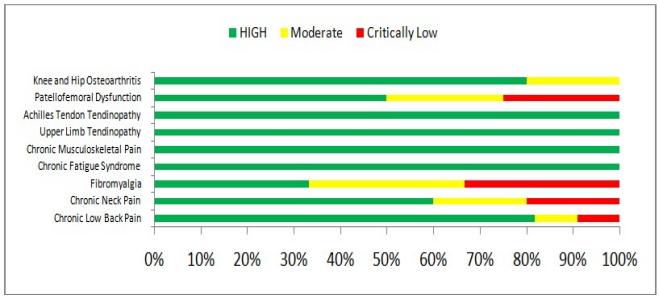
***Upper Limb Tendinopathy*:** One study (100%) reported the Gender of the participants, totaling 970 individuals, with 53% Men and 47% Women.

Achilles insertional tendinopathy: No studies reported the gender of participants.

Anterior Knee Pain: Three studies (60%) reported the Gender of the participants, totaling 695 individuals, with 57% Men and 43% Women.

Knee and Hip Osteoarthritis: six studies (54%) reported the gender of the participants, totaling 11,584 individuals, 33% men and 67% women. We assessed the methodological quality of the studies using the AMSTAR 2 method, presenting high methodological quality for 72.9% (29 studies) of the Meta-Analysis, 15% (6 studies) of Moderate quality, and 12.5% (5 studies) of Critically Low quality.
The analysis of the studies will be presented in Appendix 3, Table 2.

Graphical representation of methodological quality results:

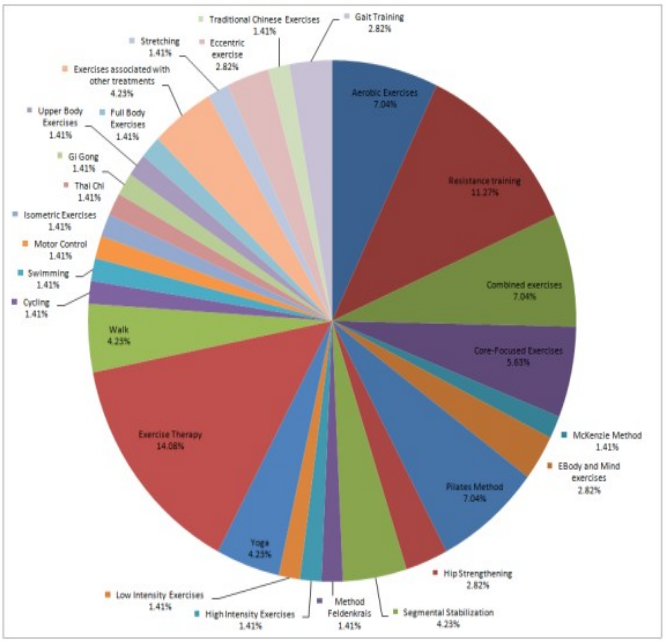


The Meta-Analysis related to Chronic Musculoskeletal Pain, Chronic Fatigue Syndrome, Upper Limb Tendinopathy, and Achilles Tendon Insertional Tendinopathy presented High Methodological Quality.
In the Meta-Analysis regarding Knee and Hip Osteoarthritis, the Methodological quality was High in more than 80% of the studies, and only two studies presented Moderate methodological quality. The Meta-Analysis regarding Chronic Neck Pain presented 60% of High Methodological Quality, one study of Moderate Quality, and one study of Critically Low Quality. The Meta-Analyses regarding Anterior Knee Pain were varied, being classified as High Methodological Quality in two studies, Critically Low in one study, and one study of Moderate quality. The Meta-Analyses related to Fibromyalgia were also varied, with one study being classified as High Methodological Quality, one study as Moderate, and one study as Critically Low.

The characteristics of the exercises, dysfunctional changes, and temporal improvement of pain were extracted by reading the text, being synthesized in groups, and will be presented in Appendix 4, Table 3.

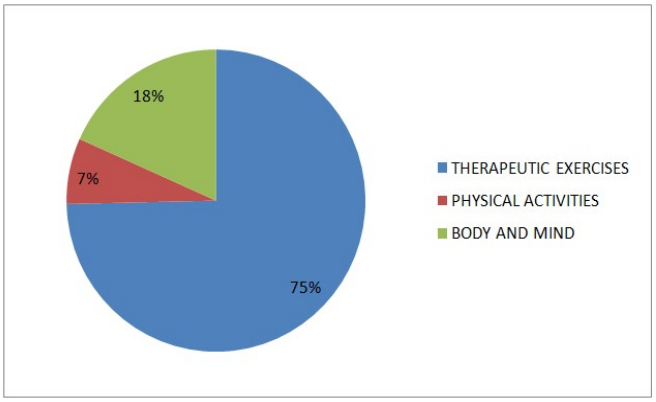
Analysis of Exercise Methods for Pain Treatment: We observed a total of 28 exercise modalities, 20 modalities were classified as Therapeutic Exercise, 3 modalities as Physical Activities, and 5 modalities as Body and Mind Exercises.

Graphical representation of the prevalence of exercise methods presented in the studies:



Analysis of the Prevalence of Exercise Classification by Subgroups in Pain Treatment: Studies that used a structured and planned exercise method for pain treatment were classified as therapeutic exercise. Yoga, Gi Gong, Thai Chi, and traditional Chinese exercises were considered body and mind exercises. In our study, we considered the Pilates method a therapeutic exercise because it does not include meditation in its structure. We understand that breathing and concentration are fundamental in any exercise practice. Walking, swimming, and cycling were considered physical activities.

Graphical representation of the percentage prevalence of exercise modalities, summarized by therapeutic exercise, body and mind and physical activities groups:



Analysis of dysfunctional changes in individuals with pain: The results extracted from the studies were synthesized into subgroups with heterogeneity among pathologies and will be presented in a descriptive narrative format below:

Dysfunctional changes observed in the literature in chronic low back pain: It was possible to observe a dysfunctional pattern among individuals with chronic low back pain, with loss of body awareness, postural changes and motor control, observed due to lumbar instability, joint changes such as deficit in hip mobility for rotation and extension, deficit in rotation of the thoracic spine, pelvic tilt and lumbar and thoracic scoliosis with an increase in the Cobb angle. The mobility deficits mentioned above were associated with changes in motor control, with dysfunction of lumbar spine movements to perform daily tasks and maintain posture. Body mass index was also associated with increased pain, with pain being a determining factor in performing exercises. It was observed that when performing movements that increase sensitivity to pain, central sensitization will also increase, worsening the clinical condition and making adherence to exercise difficult. The stabilizing muscles showed a deficit in muscular strength and a decreased threshold for fatigue, a deficit in motor control presented by compensatory changes in the movements performed by individuals with pain. The sensorimotor system also presented dysfunctions such as balance deficits and body perception. Functional and cardiorespiratory capacity also appear to be affected.

Dysfunctional changes observed in the literature in chronic neck pain: The dysfunctional changes presented by individuals with chronic neck pain were instability of cervical injuries associated with mobility deficit, muscle strength deficit, whether of the deep stabilizers or the superficial muscle layer, changes in motor control, loss of body perception associated with postural changes, changes in the sensorimotor system, and changes in the standard pattern.

Analysis of dysfunctional changes presented by individuals with Fibromyalgia: It was possible to observe the presence of pain, tissue stiffness, whether joint or muscular, loss of functional capacity, decreased cardiorespiratory capacity, changes in the control of voluntary muscle contraction, and reduced muscle activation when compared to healthy individuals, greater fatigability, and increased perception of effort after exercise, associated with increased anxiety symptoms.

Analysis of dysfunctional changes presented by individuals with chronic Fatigue Syndrome: The most evident dysfunctional changes in these individuals are muscle fatigue, pain, and loss of functional capacity, which is associated with physical deconditioning.

Analysis of Dysfunctional Changes presented by individuals with musculoskeletal pain: Among the dysfunctional changes observed in the studies, we can mention Pain and difficulty in self-managing Pain, loss of functional capacity, and deficit in multi-joint muscle strength.

Analysis of dysfunctional changes in Upper Limb Tendinopathy: It was possible to observe a deficit in muscular strength, loss of joint mobility in the upper limbs, pain, postural changes, and impaired neuromuscular control, all of which were associated with a loss of functional capacity.

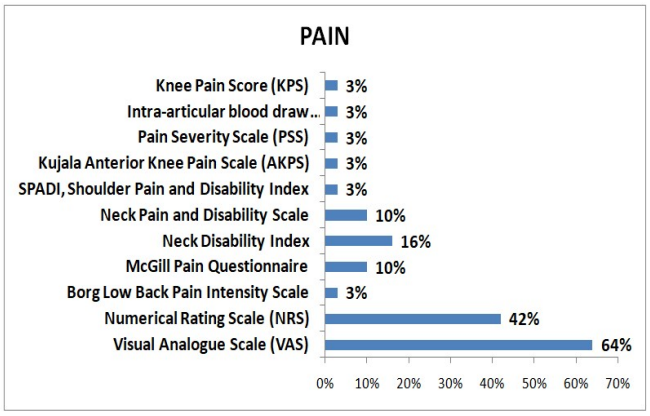
Analysis of dysfunctional changes presented by individuals with insertional tendinopathy of the Achilles tendon: It was possible to observe in the literature dysfunctional changes, such as pain, myotendinous stiffness, limitation of ankle dorsiflexion, and loss of functional capacity, as characteristics of Achilles Tendinopathy.

Analysis of dysfunctional changes presented by individuals with Anterior Knee Pain (patellofemoral dysfunction): Individuals with Anterior Knee Pain presented Pain, loss of functional capacity, patellofemoral joint stiffness, edema, loss of hip and lower limb mobility, difference in limb length, biomechanical gait alterations, deficits in hip and knee extensor muscle strength, overload of the extensor mechanism, loss of hamstring flexibility, kinesiophobia, and weakness of the CORE muscles.

Analysis of dysfunctional changes presented by individuals with Knee and Hip Osteoarthritis: Loss of functional capacity, pain, weakness and muscular inhibition of the lower limbs and CORE, decreased joint mobility associated with joint instability of the pelvis and lower limbs, balance deficit, changes in motor control, dynamic postural changes and body perception, physical deconditioning and increased BMI, deficit in agility of the lower limbs and changes in gait were the main dysfunctional changes cited by the authors.

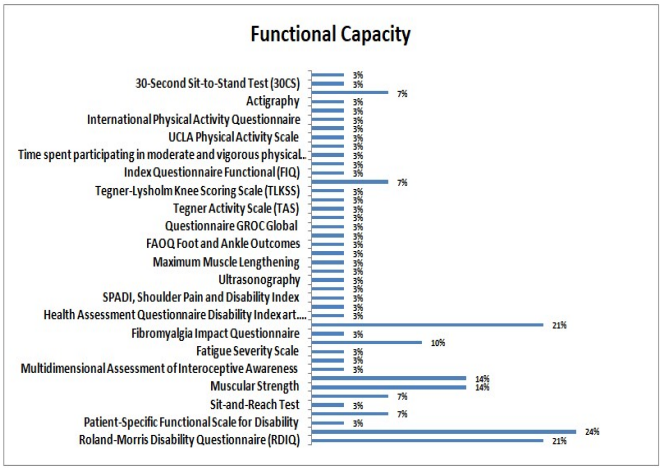
Analysis of the Assessment of Kinesiophobia, Pain, Functional Capacity, and Quality of Life: No study presented an evaluation of Kinesiophobia, 29 studies evaluated Functional Capacity, obtaining a Clinical improvement of 55%, Pain was evaluated by 31 studies and obtained a clinical improvement of 50%, Quality of Life was evaluated by only 9 studies, obtaining a clinical improvement of 5%. We observed a total of 55 methods used for evaluation, 76% performed subjective evaluation, and 24% evaluation with objective methods, with functional capacity evaluated objectively in 33% of their evaluations and Pain in 2%. The Visual Analog Scale (VAS) and the Numerical Rating Scale (NRS) were the most prevalent pain assessments, and 3% of pain assessments were performed by intra-articular blood collection (inflammatory and pro-inflammatory biomarkers).

Graphical representation of the prevalence percentage of pain assessment methods:



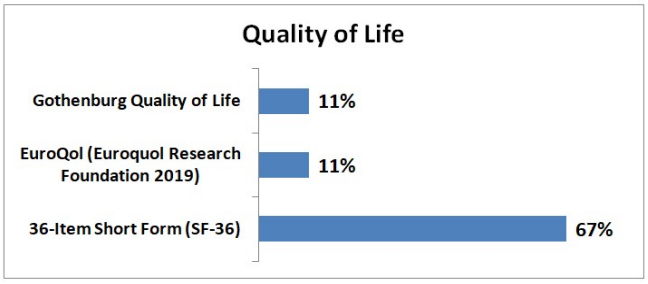
The Roland-Morris Disability Questionnaire (RDQ), Oswestry Disability Index (ODI), and the Western Ontario and McMaster Universities Osteoarthritis Index were the most prevalent methods of assessing functional capacity. Range of Motion, Muscle Strength, and Physical Activity Levels by accelerometer or pedometer device were the most prevalent assessments in the objective evaluation of functional capacity.

Graphical representation of the prevalence percentage of Functional Capacity assessment methods:



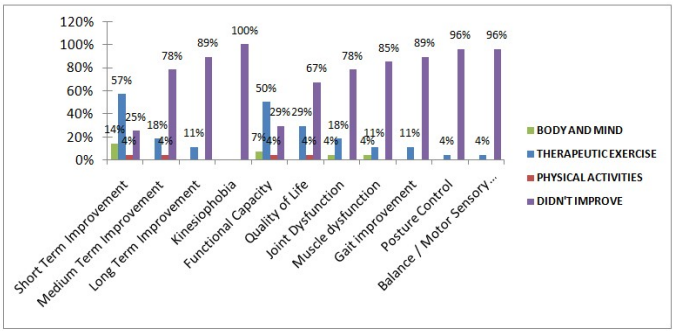
The 36-item Short Form (SF-36) was the most prevalent assessment of Quality of Life.

Graphical representation of the prevalence percentage of Quality of Life assessment methods



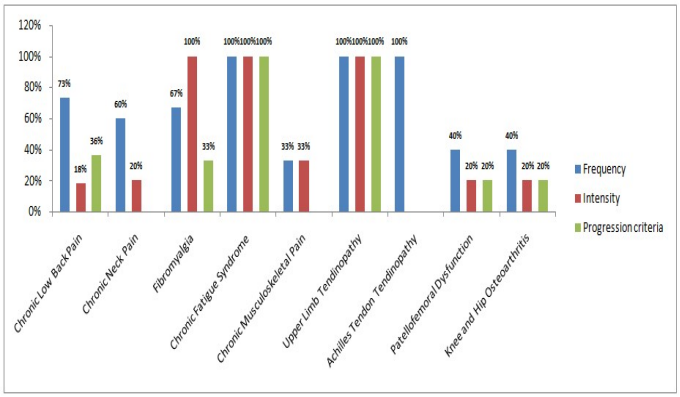
Clinical improvement of pain: Therapeutic exercise represented 57% of the clinical improvement in Short-Term Pain, 50% of the improvement in Functional Capacity, and 29% of Quality of Life. It improved 18% of joint dysfunctions, 11% of Muscle and Gait dysfunctions, and 4% of the improvement in Postural Control and Optimization of the Sensorimotor System. Body and Mind Exercises represented 14% of the clinical improvement in Short-Term Pain, 7% of the improvement in Functional Capacity, and 4% of Muscle and Joint Dysfunctions. Physical Activity represented 4% of the clinical improvement in Pain in the Short and Medium Term, 4% of the improvement in Functional Capacity, and Quality of Life. We observed positive results only for Short-Term Pain and Functional Capacity; in all other outcomes, most studies did not observe any improvement or were not evaluated.

Graphical representation of the percentage of clinical improvement in pain:



Analysis of Parameters for Exercise Prescription in Individuals with Chronic Pain: We can observe parameters for performing exercises such as frequency, intensity, and criteria for progression in individuals with Chronic Fatigue Syndrome and Upper Limb Tendinopathy. For the other pathologies, not all criteria for prescribing exercises were presented, with frequency being the most prevalent criterion, and intensity and criteria for progression of exercises cited in a few studies.

Graphical representation of the percentage analysis of the criteria for exercise prescription, presented by the studies:



DISCUSSION

The high prevalence of studies published in recent years on the subject demonstrates that the recommendations of the International Association for the Study of Pain and the World Health Organization to encourage physical exercise as a treatment for pain are being implemented by international researchers and research centers.[11] Our results corroborate the current literature on the importance of physical exercise for the treatment of various pathologies, demonstrating the importance of diversified and multimodal knowledge, in all age groups and genders, and differences can be observed between the pathologies that should be researched.[61] We chose to include in our study the largest possible number of pathologies associated with Chronic Pain, due to the prevalence of individuals who present more than one type of primary and secondary Chronic Musculoskeletal Pain in clinical practice, noting that there are few studies in the literature that used an exercise protocol for the treatment of chronic Pain in its real dimension and complexity.[62,63] The lack of data on the profile of individuals, such as age, gender, and the number of participants observed in the studies, makes it difficult to understand and clarify the results, which is of great importance for the applicability of the exercises in clinical practice.[64]

New studies should consider the gender of individuals for the development of the exercise protocol and for a better methodological analysis of the results. The current literature is quite consistent in demonstrating physiological differences between genders, such as menopause and the menstrual cycle of female individuals, as well as the different hormonal productions that directly impact the performance and progression of exercises, being associated with clinical worsening or improvement of pain.[64,65] Despite the high methodological quality presented by most studies, the low certainty of evidence leads us to improve the quality of clinical trials, where we present several topics that should be analyzed and implemented in future studies.[66,67] The different exercise methods analyzed were classified into subgroups as recommended by the World Health Organization classification for exercise practice. Thus, we can observe a greater prevalence of therapeutic exercises in the treatment of pain, as well as in the clinical improvement of individuals. This can be an important resource for a better clinical approach, maintaining and encouraging the practice of physical activities and body and mind exercises for improved health and longevity.[3,5,6] The excessive number of studies that seek to research a single exercise method for pain treatment is inefficient and does not meet the recommendations of experts in addressing individuality, assessment, and prescription focused on dysfunctional and multidimensional pain improvement. Saying that any exercise can be beneficial for clinical pain improvement can leave the individual susceptible to adverse events, hindering adherence, which is essential to achieve beneficial results from exercise practice.[12,68]

By using exercise with a specific purpose to treat Pain in a Multidimensional context, for which the most appropriate term is therapeutic exercise, we will increase the hypothesis of a more comprehensive and significant clinical improvement, as we observed in our preliminary results, significantly improving Short-Term Pain and Functional Capacity.[9,10,68] We observed that Pain, loss of Functional Capacity, Quality of Life and dysfunctional changes were observed in all studies, justifying the outcome of Physical Exercise in the treatment of Pain, findings that should be used for the development of treatment programs, but were not used and when analyzing the methods of evaluating the results, it was possible to observe that the majority of studies did not evaluate these clinical outcomes, leaving a gap in scientific knowledge.[5,9,10,11,63,68] We can mention muscular dysfunction caused by inhibition, deficit in strength and resistance to fatigue, joint dysfunction due to deficit in stability or loss of range of motion, changes in the sensorimotor system, which are linked to deficit in motor control and functional capacity, prevalent in individuals with chronic pain, as we have previously observed in other studies, these dysfunctional changes have already been objectively evaluated by biomechanical, physiological, clinical

and neuroimaging exams, reinforcing a pathophysiological profile of these individuals.[69] Increased BMI and physical deconditioning were evident among these individuals and should not be neglected during treatment, especially since they are associated with an increase in the systemic inflammatory process and poor physiological functioning necessary for maintaining health and tissue repair, fundamental factors to aid in the treatment of pain.[70,71] Among the evaluation methods, the lack of objective evaluations and the evaluation of Kinesiophobia demonstrates the lack of critical analytical knowledge of the current scenario that we observe in the practice based on evidence of physical exercise in the treatment of Pain.[72,73,74] When analyzing the parameters for prescribing exercises, the lack of prescription criteria is evident, which does not match the justification of the studies when analyzing exercise practice as an outcome for pain treatment.[75,76] Some studies have cited pain tolerance as a criterion for performing and progressing exercises. Current literature shows that, regardless of pain, exercising does not worsen the clinical condition. Pain levels are also influenced by cognitive, affective, and behavioral factors, which makes clinical practice difficult when only pain is considered a factor for improvement or even a criterion for progression. Guiding and educating these individuals can prevent somatization and worsening central pain sensitization.[77,78] In conclusion, our study can help clinicians and researchers to better understand the complexity of exercise practice for pain treatment. Therapeutic exercise is the most prevalent method for clinical improvement of dysfunctional changes. Objective assessments are necessary to demonstrate clinical results, and rehabilitation programs and study protocols should consider the importance of criteria for exercise prescription and progression. The tables and appendices cited in the text are displayed in the Prospero registration number CRD42024618037. We would like to thank our families, patients and teachers, and especially the Pain group at Hospital das Clínicas. The authors declare no conflicts of interest and did not receive funding for this study.

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