



Master thesis

Effects of High-Intensity Training on pain and physical function in individuals with Osteoarthritis, Rheumatoid Arthritis, and Axial Spondyloarthritis

A Systematic Review

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Abstract

Background:

Individuals with rheumatic diseases such as Osteoarthritis (OA), Rheumatoid Arthritis (RA), and axial Spondyloarthritis (axSpA) usually are less physically active and engage in low-intensity training. Pain and function impairment lead to reduction in their quality of life. Evidence prove High-Intensity Training (HIT) can positively impact pain and function, however, usually neglected. Assessing the previous research and addressing knowledge gaps in this area can lead to more beneficial intervention to improve the overall quality of life among these populations.

Aim:

The aim of this systematic review was to investigate the effects of High-Intensity Training on pain and physical function in individuals with Osteoarthritis, Rheumatoid Arthritis, and axial Spondyloarthritis.

Method:

This review followed the PRISMA guidelines. 18 studies identified from Medline, PubMed, SPORTDiscuss, and CINAHL databases met the inclusion criteria: RCTs including adults with OA, RA, and axSpA, conducting in English, full free text, outcomes related to pain and function, incorporating high-intensity or high-intensity interval training interventions. Quality assessment and overall risk of bias of included studies was evaluated by Cochrane ROB2 tool.

Results:

Nine studies on OA and six on RA, implementing various types of HIT, reported diverse results on its effect on pain and function. While some studies indicated improvement with HIT, others showed no significant change or superiority. Three studies on axSpA, reported positive impacts from HIT, albeit two were pilot RCTs. No serious adverse events were reported. Cochrane ROB2 tool which rates the overall risk of bias as low risk, some concerns and high risk revealed ten, six and two studies at low risk, some concerns and high risk of bias, respectively.

Conclusion:

HIT is a beneficial and promising approach in most situations to managing symptoms including pain and function in individuals with OA, RA, and axSpA. However, contradictory results arise the need for further meticulous and high-quality studies in this area.

Table of Content

Page

1.Background.....	1
1.1 Main characteristics of rheumatic diseases.....	1
1.2 Recommended treatment for rheumatic diseases.....	2
1.3 Consequences of rheumatic diseases.....	3
1.4 High-Intensity training.....	6
1.5 Aim.....	7
2. Method.....	7
2.1 Eligibility criteria.....	8
2.2 Information sources and search strategies.....	8
2.3 Data selection process.....	8
2.4 Quality assessment.....	9
2.5 Data synthesis.....	9
2.6 Ethical consideration.....	9
2.7 Sustainability.....	10
3.Results.....	10
3.1 Study selection.....	10
3.2 Results of quality assessment.....	11
3.3 Study characteristics.....	13
3.3.1 Osteoarthritis.....	13
3.3.1.1 Effects on pain in individuals with Osteoarthritis.....	15
3.3.1.2 Effects on function in individuals with Osteoarthritis.....	15
3.3.2 Rheumatoid Arthritis.....	16
3.3.2.1 Effects on pain in individuals with Rheumatoid Arthritis.....	18
3.3.2.2 Effects on function in individuals with Rheumatoid Arthritis.....	18

3.3.3 Axial Spondyloarthritis.....	19
3.3.3.1 Effects on pain in individuals with axial Spondyloarthritis.....	20
3.3.3.2 Effects on function in individuals with axial Spondyloarthritis.....	20
4 Discussion.....	20
4.1 Osteoarthritis.....	20
4.2 Rheumatoid Arthritis.....	22
4.3 Axial Spandyloarthritis.....	23
4.4 Discussion methods.....	24
5. Conclusion.....	25
6. Reference.....	26

Abbreviation list

% 1RM: % One repetition maximum

ASDAS: Ankylosing spondyloarthritis disease activity score

AxSpA: Axial Spondyloarthritis

BASDAI: Bath ankylosing spondyloarthritis disease activity score

BASFA: Bath ankylosing spondyloarthritis Functional index

BFRT: Blood flow restriction training

DAS28: Disease activity Score for 28 joints

HAQ: Health Assessment Questionnaire

HAQDI: Health Assessment Questionnaire Disability Index

HIIT: High-Intensity Interval Training

HIT: High-intensity training

HR_{max}: Maximum Heart Rate

HRQoL: Health-related quality of life

KOA: Knee Osteoarthritis

MDHAQ: Multidimensional Health Assessment Questionnaire

NMES: Neuromuscular Electrical Stimulation

OA: Osteoarthritis

RA: Rheumatoid arthritis

RPE: Rating of perceived exertion

SF-36: Short-Form 36 Health Survey

SpA: Spondyloarthritis

STS: Sit to stand

TST: Timed stand test

TUG: Timed up to Go test

VAS: Visual Analog scale

WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

1. Background

According to the World Health Organization, musculoskeletal diseases encompass over 150 diverse diseases affecting and impairing the musculoskeletal and different bodily systems (WHO, 2022). Almost 1.71 million individuals suffer from these diseases globally that include persistent pain, activity limitation and impairment in body function (WHO, 2022). Osteoarthritis (OA), Rheumatoid arthritis (RA), and Spondyloarthritis (SpA) are three musculoskeletal diseases also stand as rheumatic diseases. Rheumatic diseases include arthritis and various other conditions impacting the joints, tendons, muscles, ligaments, and bones, leading to pain and function impairment, in which OA and RA are the most common diagnosis (CDC, 2022). OA, RA, and SpA primarily affect the joints and lead to participants restriction (WHO, 2022). The prevalence of these diseases is 15% of population for OA (Johnson & Hunter., 2014), 0.5–1% of adults in developed countries for RA (Almutairi et al., 2021), and 0.5% to 1% in the population for SpA (Reveille et al., 2012; Rudwaleit et al., 2009).

1.1 Main characteristics of rheumatic diseases

OA is defined as a degenerative joint disease impacting mostly middle-aged and elderly individuals (Altman et al., 2016; Filippiadis et al., 2019; Timmins et al., 2017). It can manifest in any joint with synovial fluid but is most common in the hands, knees, and hip (Hunter & Felson., 2006; Kolasinski et al., 2020) in which the knee contributing to over 80% of the overall disease burden (Vos et al., 2012). Symptoms as pain, stiffness, and swelling are common, giving activity limitation and impaired function (Bartels et al., 2016; Roos & Arden., 2016; Kolasinski et al., 2020). Around 10% of males and 13% of females experience OA (Primorac et al., 2020). Risk factors of OA are associated with both individual and joints levels (Palazzo et al., 2016). Individual-level factors consist of older age, gender, genetics, obesity and overweight, while joint-level factors comprise injury, abnormal joint loading, and heavy physical workload in which misalignment of the knee stands out as the most significant predictor of knee OA (KOA) advancement (Johnson & Hunter., 2014).

RA as a chronic autoimmune inflammatory disease, characterized by inflamed and swollen joints which can lead to joints deformity, harm in cartilage and bone beneath it (Lin et al., 2020;

Scott et al., 2010). Joints of the hands, wrists, shoulders, elbows, knees, ankles, and feet are the most affected parts resulting RA (Peter et al., 2021). It shows general symptoms of rheumatic diseases (pain and impairment in function) as well as stiffness, swelling, and fatigue (Boyden et al., 2016; Lee et al., 2020; Metsios & Kitas., 2018; Wasserman et al., 2011). Risk factors for RA include older age, genetics, smoking habits, and female gender in which females to male ratio is 3:1(Alamanos et al., 2006; Almutairi et al., 2021; Carlens et al., 2010; Ruiz-Esquide & Sanmartí., 2012; Wasserman et al., 2011). Additionally, pregnancy, early menarche and irregular menstrual cycles increase risk of RA (Wasserman et al., 2011).

SpA is a diverse inflammatory disease encompasses conditions like ankylosing spondyloarthritis, psoriatic arthritis, reactive arthritis, and arthritis linked to inflammatory bowel disease (Ma et al., 2023). It can be axial (axSpA), including individuals with both radiographic axSpA (individuals with visible structural damage in the sacroiliac joints or spine seen on radiographs) and non-radiographic axSpA (individuals without such structural damage) or peripheral. (Sieper & Poddubnyy., 2017). AxSpA primarily impacting the spine and its symptoms are inflammatory back pain, stiffness, involvement of spine and sacroiliac joint (Ward et al., 2019). Peripheral SpA characterized by enthesitis (the point where a tendon or ligament attaches to the bone) and dactylitis (swelling of an entire digit) (Rudwaleit et al., 2011; Sieper & Poddubnyy., 2017). These symptoms typically emerge between ages 20 and 30 (Feldtkeller et al., 2003; Redeker et al., 2019). In individuals with non-radiographic axSpA, both genders are equally affected (van Tubergen., 2015). However, in radiographic axSpA the ratio of male-to-female is approximately 2–3:1(Sieper & Poddubnyy., 2017). Radiographic axSpA displays a strong genetic predisposition, with limited exploration into environmental influences (Wang & Ward., 2018). Some studies have highlighted potential connections between childhood microbial exposures as a risk factor for axSpA and the onset of radiographic axSpA later in life, also individuals with positive HLA-B27 gene can show the disease around 5 years earlier compared to those who test negative for it (Dougados et al., 2015; Jaakkola et al., 2006; Rudwaleit e al., 2009; Wang & Ward., 2018).

1.2 Recommended treatment for rheumatic diseases

Physical activity and exercise play a crucial role in alleviating pain, managing symptoms on body function and body structure, activity limitation, and participation restriction of

individuals with rheumatic diseases (ACR, 2023; Rausch Osthoff et al., 2018). However, individuals with rheumatic diseases such as some with OA, individuals with RA and axSpA need pharmacological treatment in combination with non-pharmacological intervention (Kolasinski et al., 2020; Combe et al., 2017; Coulter et al., 2020). Physical activity includes all movements performed by the skeletal muscles that consume energy, including tasks related to work, recreational, or home responsibilities, and organized activities like exercise classes in which classified based on intensity levels, including light, moderate, and vigorous (Caspersen et al., 1985; Wallis et al., 2013).

For individuals with OA, exercise is considered a fundamental and recommended treatment (Bannuru et al., 2019; UK, NCGC, 2014). This non-pharmacological approach effectively reduce pain and improve function (Fransen et al., 2015; Gay et al., 2016; Golightly et al., 2012). Similarly, in individuals with RA, exercise has the potential of positively influence on overall symptoms of disease, improvement in function, strength, and cardiovascular fitness (Baillet et al., 2012; Hurkmans et al., 2009; Metsios & kitas., 2018). Also, physical activity and exercise is advised to do regularly to control and managing disease for those with axSpA (Rausch Osthoff et al., 2018), as exercise interventions have shown positive outcomes in improving pain, function, cardiovascular fitness, and quality of life among these individuals (O'Dwyer et al., 2014; Pécourneau et al., 2018; Martins et al., 2014).

1.3 Consequences of rheumatic diseases

Individuals with OA, RA and SpA exhibit lower level of physical activity than their healthy counterparts meaning the low adherence rate of exercises and encounter the risk of cardiovascular diseases (Agca et al., 2017; Hernández-Hernández et al., 2014; Koivuniemi et al., 2013; Swinnen et al., 2014). This discrepancy may be attributed to potential reluctance from some healthcare providers and individuals to participate in physical activity due to concerns about exacerbating symptoms or causing joint damage (Henchoz et al., 2013; Iversen et al., 2015; Neuberger et al., 2007). In addition, pain and impairment in function among these individuals gradually can lead to decrease level of

physical activity and health-related quality of life (Salaffi et al., 2018; Palazzo et al., 2016).

Physical function refers to the ability to perform activities of daily living (ADLs) and other tasks that need motion (Liu et al., 2014; Wang et al., 2020) and is typically assessed by physical performance tests (Salarian et al., 2010; Van Lummel et al., 2013). Physical performance defined as the ability of an individual to perform physical tasks or daily activities effectively which is assessed by objective measurement of whole-body function associated to mobility such as gait speed (Beudart et al., 2019). Those with lower level of physical performance encounter with limitation in body function and activities (Wang et al., 2020).

Pain and Physical function in individuals with rheumatic diseases can be evaluated with using specific questionnaires and performance tests. Western Ontario and McMaster Universities Osteoarthritis Index questionnaire (WOMAC) (Bellamy et al., 1988) for individuals with OA. Health Assessment questionnaire (HAQ) for individuals with RA (Bruce & Fries., 2003). Ankylosing Spondyloarthritis disease activity score (ASDAS) (Machado et al., 2018), Bath Ankylosing spondyloarthritis disease activity index (BASDAI) (Garrett et al., 1994), and Bath Ankylosing Spondyloarthritis questionnaire, Functional Index (BASFI) (Calin et al., 1994) for individuals with axSpA. (Table 1). Although WOMAC questionnaire can be used for patient groups other than OA, but it has been originally developed for people with OA of the hip and knee (McConnell et al., 2001). Similarly, while the Health Assessment questionnaire (HAQ) is widely used for assessing different diseases, it has been become one of the most frequent and required dependent variable for trials including individuals with RA (Bruce & Fries., 2003).

Table 1: Questionnaires for assessing pain and function in individuals with OA, RA, and axSpA.

Disease	Questionnaire	Measures
OA	WOMAC	Pain, physical function scales
RA	HAQ	Pain, function, and general health status
axSpA	ASDAS	Disease activity and pain
axSpA	BASDAI	Disease activity and pain
axSpA	BASFI	Physical function

Definition: OA: Osteoarthritis; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index questionnaire; RA: Rheumatoid Arthritis; HAQ: Health assessment questionnaire; axSpA: axial Spondyloarthritis; ASDAS: Ankylosing Spondyloarthritis disease activity score; BASDAI: Bath Ankylosing spondyloarthritis disease activity index; BASFI: Bath Ankylosing Spondyloarthritis questionnaire, Functional Index.

Questionnaires include some questions asking how much or how many hours pain is felt by individuals and how much is difficult to do daily activities such as raising from a chair, dressing, stair climbing and other tasks. The total score is evaluated by instructions provided in each questionnaire. Physical performance and function in the lower extremities in individuals with OA, RA, and axSpA can be examined with different tests such as Timed Up and Go (TUG) where individual is asked to stand up from an armless chair, walking three meters, turned around and sitting back on the chair and the time is recorded (Podsiadlo & Richardson., 1991), Sit to Stand (STS) in which the number of completed rises from a chair performed in 60 seconds is recorded (Bohannon., 1995), Timed Stand Test (TST) where the number of stand-ups that an individual can perform from an armless chair in 30 seconds is counted (Newcomer et al., 1993), Stair Climbing test, where the time for climbing up 11 stairs is taken (Almeida et al., 2010) and Timed Chair rise test, where the time is taken for 10 repetitions of stand and sit from a chair (Csuka & McCarty., 1985). Additionally, walking tests are also used to assess physical function among these individuals. For example, 6-Minutes walking (6MW) and Gait speed tests are used for individuals with OA. 6MW test is the maximum distance an individual can walk in six minutes (Ettinger et al., 1997; Kovar et al., 1992). In the Gait speed test individual walks on a GaitMat II platform (3.66 m long) at a comfortable pace as per provided instructions and the average gait speed from three attempts is recorded (Kressig & Beauchet., 2006; Fien et al., 2016). 50-foot walking test is used for individuals with RA, in which the time needed to walk 50-foot is taken (Rikli & Jones., 2013). These different physical performance and functional tests can be used for assessing function in individuals with OA, RA, and axSpA.

Individuals with OA often have insufficient physical activity due to pain and functional limitations, hindering them from meeting the recommended 150 minutes of weekly exercise (Aglamiş et al., 2009; Farr et al., 2008; Tucker et al., 2011; Wallis et al., 2013), such as those with RA (Paul et al., 2014; Hernández-Hernández et al., 2014) and axSpA (Fabre et al., 2016; Haglund et al., 2012). Engaging in low level of physical activity exposes these individuals to comorbidities where those with OA and RA exhibit multiple risk factors related to cardiovascular disease, including obesity and comorbidities related to metabolic syndrome (Hoeven et al., 2013; Williams et al., 2016; Azeez et al., 2020; Metsios & kitas., 2018; Peter et al., 2021). In addition, RA as a systemic disease can manifest to pulmonary, psychological, and skeletal systems (McInnes & Schett., 2011),

and most individuals with axSpA face an elevated risk of cardiovascular diseases (Agca et al., 2017; Mathieu & Soubrier., 2019; Zhao et al., 2019).

Evidence show high-intensity training (HIT) can lead to greater effects than low or moderate intensity training on health outcomes in both healthy and those with medical condition (Helgerud et al., 2007) as there is a dose-response correlation (Sandstad et al., 2015), but individuals with rheumatic diseases such as those with OA, RA, and axSpA usually engage at low intensity activities and are less active than their peer healthy populations (ACR, 2023; Rausch Osthoff et al., 2018).

1.4 High-Intensity Training

Exercise intensity classified as "high" can be delineated using various metrics and forms, for example, 76-96% of maximum Heart Rate (HRmax) in endurance training, 70-85% of 1 repetition maximum (1RM) in resistance and strength training, rate of perceived exertion ranging from 14 to 17 on the Borg scale indicating "somewhat hard" to "very hard", and high-intensity interval training (HIIT) (Riebe., 2013, pp. 165-167). Among these, HIIT as a popular fitness trend involving intense activity followed by rest or low-intensity exercises is increasingly recommended for management of chronic pain that is common in rheumatic diseases (Botta et al., 2022; MacInnis & Gibala., 2017). It also serves as a credible substitute for moderate-intensity continuous training which is advised as the gold standard in numerous guidelines (Garber et al., 2011; Santos et al., 2020; Thum et al., 2017). Various types of HIT can improve immune system response and anti-inflammatory function (Andonian et al., 2018). Particularly, HIIT can elicit comparable or potentially enhanced adaptations in various physiological, performance, and health-related parameters among both healthy individuals and those with medical conditions (Gibala et al., 2012; Wen et al., 2019). These findings suggest possibility of HIT intervention for improving inflammatory and rheumatic diseases such as OA, RA, and axSpA.

It has been proved that exercise effectively relieves certain distressing symptoms associated with neuropathy (Dobson et al., 2014; Wonders et al., 2013) and physical activity at all intensities positively impacts disease symptoms among individuals with OA, RA, and axSpA, but these individuals do not meet the recommended amount of physical activity or often engage in lower intensity interventions (ACR, 2023; Rausch Osthoff et al., 2018). Especially, HIT is usually neglected by some health care givers and individuals, for example in individuals with axSpA; as there is a concern about worsening the situation (Beavers et al., 2010; Lundberg & Nader., 2008; Thomas., 2013). The impact of physical activity on high intensity remains relatively underexplored and there is a need for further research to investigate the specific effects of HIT interventions on symptoms as pain and function. Addressing this knowledge gap will not only contribute to our understanding of optimal exercise strategies for these populations but also inform the development of more targeted and effective interventions to improve outcomes and enhance the quality of life among these individuals.

1.5 Aim

The aim of this systematic review was to investigate the effect of high-intensity training on pain and physical function in individuals with Osteoarthritis (OA), Rheumatoid Arthritis (RA) and Axial Spondyloarthritis (axSpA).

The underlying research questions were:

- Does high-intensity training positively impact pain among individuals with Osteoarthritis, Rheumatoid Arthritis and axial Spondyloarthritis?
- Does high-intensity training positively impact function among individuals with Osteoarthritis, Rheumatoid Arthritis and axial Spondyloarthritis?

2.Method

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis – the PRISMA 2020 statement- guidelines (Prisma statement., 2021).

2.1 Eligibility criteria

Included studies met the following criteria: i: Randomized controlled trials (RCTs), ii: Adult individuals with OA, RA, and axSpA, iii: Studies in the English language, iv: Studies available in full free text, v: Studies incorporating HIT or HIIT interventions, vi: Studies with outcomes related to pain, function, or physical performance. Studies encompassing animals, protocols, opinion, editorials, reviews and follow up were excluded.

2.2 Information sources and search strategies

The search process started in January 2024 and included literature without limitations on publication date. The Medline, PubMed, SPORTDiscuss, and CINAHL databases were systematically searched for relevant literature. Key search terms included "Rheumatic diseases", "Rheumatoid arthritis", "Osteoarthritis", and "Spondyloarthritis". The search focused on terms related to high-intensity and high-intensity interval training, pain, and physical function. Search terms were "Rheumatic diseases" AND "Osteoarthritis" OR "OA" , Knee, Hand, Hip, Shoulder, Spine OR "KOA" OR "Degenerative joint disease" OR "Cartilage degradation" AND "Rheumatoid arthritis" OR "RA" AND "Spondyloarthritis" OR "Spondylarthritis" OR "Spondylitis" OR "Axial Spondyloarthritis" OR "AxSpA" AND "High intensity training" OR "High intensity exercise" OR "High intensity interval training" OR "HIIT", OR "High resistance training" OR "High intensity strength and endurance training" AND "Pain" AND "Function". Only articles in English and studies on human were included during the search process.

2.3 Data selection process

Upon the conclusion of the comprehensive literature search across databases, the titles, and abstracts of identified studies underwent screening by the author to ascertain eligibility criteria. Irrelevant and repeated articles were excluded and those alignment with the inclusion criteria were extracted for detailed examination of study design, participant characteristics, intervention specifics, and the outcomes of interest. The selection process prioritized the extraction of the most pertinent studies, ensuring a rigorous and methodical approach to data inclusion.

2.4 Quality assessment

The methodological internal validity of the included RCTs was assessed using the Cochrane Risk of Bias 2 (ROB2) tool. This tool, developed by the Cochrane Collaboration, systematically evaluates the risk of bias across key domains to ensure the robustness of study findings. This tool includes five main domains which are: 1- randomization process (addresses the participants assigned to the groups to minimize the risk of selection bias to treatment group), 2- assignment of interventions (examines if there were any deviations from the intended intervention and whether these have been reported), 3- missing outcome data (addresses the missing data of measurements and whether the reasons for this missing data have been correctly reported), 4- measurement of the outcome (determines the reliability and validity of measurements, blinded method, and any differences in measuring outcomes between groups), 5-selection of the reported result (evaluates whether the results have been reported properly based on the statistical significance of the findings and presence of any selective outcome reporting biases). Each domain is rated as "low risk", "some concerns", or "high risk" based on the specific criteria outlined in the ROB2 tool and overall risk of bias will be assessed by using the provided specific guidelines. The evaluation across these domains informs the overall risk of bias for each included study, contributing to an understanding of the study's internal validity (Higgins JPT., 2023).

2.5 Data synthesis

The synthesis process focused on the systematic extraction and organization of pertinent information, emphasizing intervention specifics, including type and duration, discerning any discernible impacts on pain and physical function outcomes, demographics characteristics (age and sex) and adherence rate.

2.6 Ethical considerations

In adherence to ethical standards, an evaluation was conducted for each included article by the author to ascertain compliance with the Declaration of Helsinki (WMA, 2013). Each study was reviewed for participant's informed consent and approval by an eligible center. This meticulous ethical review underscores the commitment to safeguarding the rights, well-being, and privacy of the participants involved in the respective studies, aligning with established ethical principles in research.

2.7 Sustainability

Physical activity and exercise have recognized as a non-pharmacological intervention that can enhance the effectiveness of pharmacological treatments in various diseases like OA, RA, and axSpA. Individuals with OA, RA, and axSpA should adopt optimal management strategies to prevent exacerbation of their conditions. Nevertheless, in alignment with the Agenda 2030 by the United Nations Development Program (UNDP, 2022), this systematic review contributes to the global goals, particularly goal 3 (good health and well-being) as the results of this review can provide helpful information about the influence of HIT on pain and function among individuals with OA, RA, and axSpA. Furthermore, in the pursuit of equality, the review employed a diverse range of databases, encompassing various populations and demographics accordance with goal 5 (gender equality) and goal 10 (reduced inequalities), ensures a comprehensive representation of perspectives in the synthesized literature. this systematic review holds broader implications for societal quality of life. Potential benefits of increase in physical activity level among individuals with diseases like OA, RA, and axSpA including improved function and pain underscore the significance of promoting active lifestyles. So, this could bring positive outcomes for society such as improved overall health and quality of life, reduced healthcare costs associated with managing chronic conditions, and a more productive and engaged population.

3.Results

3.1 Study selection

During the systematic literature search, 968 studies were initially identified from prominent databases: 270 from PubMed, 364 from Medline, 215 from CINAHL, and 119 from SPORTDiscuss. After the initial screening of the titles, 717 studies were excluded, leaving 251 for further evaluation and 185 studies were omitted based on the abstract. From the remaining 66 studies, 48 were excluded based on predefined criteria. Finally, 18 studies met the eligibility criteria for inclusion in the review. Among the 18 included studies, the distribution across specific disease were as follows: OA: nine studies, RA: six studies, axSpA: three studies. The PRISMA flow chart of the search methodology is shown in Figure 1.

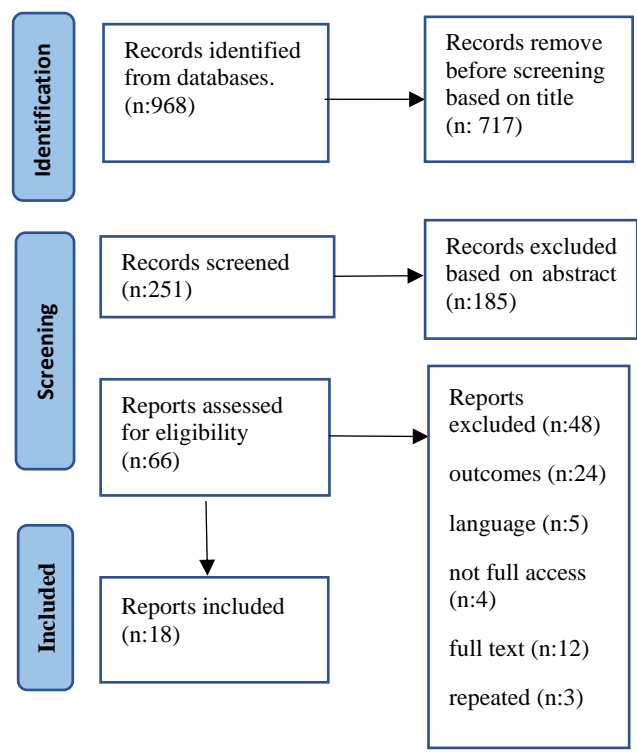


Figure1: PRISMA Flow chart of literature selection

3.2 Results of quality assessment

After assessing the validity of included RCTs by the ROB2 tool, it was revealed that among studies for OA, six were assessed at low risk, two at some concerns and one at high risk. Quality assessment of RA studies included three at low risk, two at some concerns and one at high risk, also among studies dedicated for axSpA, one was assessed at low risk and two at some concerns (table 2).

Table 2: Indicates the risk of bias in the main domains, presented for OA, RA, and axSpA separately.

<i>Quality assessment results of OA</i>						
Author, Year	Randomization (selection bias)	Assignment to intervention	Missing outcome data	Measurement of outcome	Reported Results	Overall risk of bias
Baker et al, 2001	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Calatayud et al, 2017	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
De Zwart et al, 2022	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Ferraz et al, 2017	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Foroughi et al, 2011	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Keogh et al, 2018	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Mangione et al, 1999	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Thorstensson et al, 2005	Low risk	Some concerns	Low risk	Some concerns	Low risk	High risk
Waller et al, 2017	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

<i>Quality assessment results of RA</i>						
Author, Year	Randomization (selection bias)	Assignment to intervention	Missing outcome data	Measurement of outcome	Reported Results	Overall risk of bias
De jang et al, 2003	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Lange et al, 2019	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Lemmy et al, 2009	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Piva et al, 2019	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Seneca et al, 2015	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Van de Ende et al, 1996	Some concerns	Some concerns	Low risk	Low risk	Low risk	High risk

<i>Quality assessment results of axSpA</i>						
Author, Year	Randomization (selection bias)	Assignment to intervention	Missing outcome data	Measurement of outcome	Reported Results	Overall risk of bias
Sveaas et al, 2014	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Sveaas et al, 2018	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Sveaas et al, 2020	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Table 2. Validity assessed by Cochrane Risk of Bias 2 (ROB2) tool in five main domains: 1- Randomization process. 2- Assignment to intervention. 3- Missing outcome data. 4- Measurements of outcomes (reliability and validity of measurements blinded method, and any differences in measuring outcomes). 5- Reported results. Rated as "Low Risk", "Some Concerns", or "High Risk" and the overall risk of bias assessed by the provided algorithms in the ROB2 tool (Higgins JPT., 2023).

3.3 Study characteristics

3.3.1 Osteoarthritis

Across the nine studies focused on OA, the main disease was KOA, displaying varying degrees across the different studies. Participants had a mean age between 54.8 ± 7.1 and 71.1 ± 7.7 among different studies, both genders were included, albeit with a higher representation of females. Different types of high-intensity training (HIT), with supervision or without were implemented among studies, and only in one study that was a RCT pilot study, the main intervention was HIIT. Additionally, some had a control group without exercise or normal activity or sham and in some there were low-intensity training groups and all reported high adherence rate following the intervention. The primary tool for pain assessment was the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), supplemented by other measures such as Visual analog scale (VAS), Intermittent and Constant OA pain, Short-Form 36 Health Survey (SF-36), Lequesne Index, Arthritis Impact Measurement Scale 2, and Knee injury and osteoarthritis outcome score. The function was evaluated through the WOMAC functional subscale, SF-36, and various physical functioning tests, including Timed up to go (TUG), Stair Test, 6-Minute Walk, 30 Seconds Sit-to-Stand (STS), Gait Speed, and Chair Stand (table 3).

Table 3: Study characteristics of Osteoarthritis (OA)

Author, Year	Disease	Intervention Type	N: IG / CG	Sex IG(F/M)/ CG(F/M)	Age(mean)	Intensity	Time/week, Minutes, Total week	Adherence (%)	Outcome Assessment Tools (Pain / Function)	Results (Pain / Function)
Baker et al, 2001	Radiographic KOA	IG: home based PST CG: placebo and nutrition intervention	IG:23 CG:23	IG:17 / 6 CG: 19/4	IG:69 ± 6 CG:68 ± 6	Based on patients' perception of difficulty (RPE 8: Hard)	3, N, 16	Mean: IG:84 ±27% CG:65±32%	WPMAC Pain / WOAMC Function + Timed Chair Stand + Stair climbs test	Substantial ↑ in pain and function
Calatayud et al, 2017	End- stage KOA	IG: Supervised HIST CG: NI	IG:22 CG:22	NI (Total: F:37/ M: 7)	IG:66.8 CG:66.7	Based on 10RM for each participant	3, N, 8	NI	VAS+ WOMAC pain dimension / SF-36+ Womac Functional+ TUG + Stair climbs test	↑ in pain and function

Table 3 (Continued)

Author, Year	Disease	Intervention Type	N: IG / CG	Sex IG(F/M)/CG(F/M)	Age(mean)	Intensity	Time/week, Minutes, Total week	Adherence (%)	Outcome Assessment Tools (Pain / Function)	Results (Pain / Function)
De Zwart et al, 2022	KOA	Supervised and individualized HIRT/ Supervised and individualized LIRT	HIRT :89 LIRT :88	HI:57/32 LI:50 / 38	HIRT: 67.3±5.7 LIRT: 67.9±6.	HIRT:70-80% 1RM LIRT:40-50% 1RM	3(2supervised+1 at home), N, 12	HIRT:88% LIRT:82%	VAS+ The Intermittent and Constant OA Pain/ Womac Functional+ TUG, 6MW, Stair climbs test	Both intensity ↑ pain and function (No greater improvement for HIRT)
Ferraz et al, 2017	KOA	Supervised HIRT/ LIRT/ LIRT with BFRT	All:16	All: F	HIRT:59.9±4 LIRT: 60.7±4 BFRT:60.3±3	HIRT:80% 1RM LIRT:30% 1RM BFRT:30% RM	2, NI, 12	HIRT:90%/ LIRT:85%/ BFRT:91%	WOMAC Pain and physical Function + SF-36 / TST + TUG	No differences in SF-36 between groups/ WOMAC pain ↑ in LIRT and BFRT, WOMAC function ↑ in BFRT and HIRT. ↑ in TST for HIRT and BFRT
Foroughi et al, 2011	Primary KOA	IG: HIPRT CG: Sham exercise	IG:26 CG:28	All: F	IG:66 (8) CG:65 (7)	80% Of 1RM	3, NI, 24(6 month)	IG:97% CG:99%	WOMAC Pain/ Gait Speed test	HIPRT did not lead to greater ↑ in pain or Max gait speed
Keogh et al, 2018	KOA	Unsupervised HIIT Cycling / Unsupervised MICT Cycling	HIIT:9 MICT:8	HIIT:6/3 MICT:7/1	HIIT:59.1 (6.7) MICT:66.1 (8.8)	HIIT: cadence up to 110 rpm MICT: cadence: 60-80 rpm	4,25 min, 8	HIIT:94% MICT: 88%	WOMAC+ Lequesne Index/ TUG+30s STS+ Habitual gait speed	HIIT group significant ↑ in TUG compared to MICT, No differences in other outcomes between groups
Mangione et al, 1999	Radiographic KOA	HI stationary cycling / LI stationary cycling	HI:19 LI:20	HI:14/5 LI:12/8	HI:71.1 ± 7.7 LI:71.0 ± 6.2	HI:70% HRR LI:40% HRR	3,25 min, 10	92.2% (Nearly Identical between groups)	AIMS2 pain subscale, WOMAC, VAS/ Timed chair rise, 6MW, Gait test	AIMS2 Pain subscale ↑ greater in HI/ Both groups showed ↑ in Timed chair rise, 6MW
Thorstensson et al, 2005	Grade III radiographic KOA	IG: Supervised HI WBE / CG: no exercise	IG:30 CG:31	IG:15/15 CG16/15	IG:54.8± 7.1 CG:57.3 ± 4.7	≥ 60% of HRmax	2,60 min, 6	IG:89.9% CG:NI	KOOS / SF-36, Ergometer test, 5 Functional performance tests	→ on pain and function
Waller et al, 2017	Mild KOA	IG: Supervised HIR aquatic training CG: normal PA	IG:43 CG:44	All F	IG:63.8 CG:63.9	As hard and Fast as Possible (measuring HRmax and RPE)	3,60 min, 16(4 month)	IG:88% CG:68%	KOOS, VAS/ Walking Speed (UKK2 KM Walking test)/ LTPA	No significant differences in ↑ pain for HI / Significant ↑ in Walking speed test and Average LTPA for HI

Definitions: KOA: Knee OA; IG: Intervention group; CG: Control group; PST: Progressive strength training; HIST: High intensity strength training; HIRT: High intensity resistance training; LIRT: Low intensity resistance training; BFRT: Blood flow restriction training; HIPRT: High intensity progressive resistance training; HIIT: High intensity interval training; MICT: Moderate intensity continuous training; HI: High intensity; LI: Low intensity; WBE: Weight bearing exercise; NI: No information; RPE: Rating of perceived exertion; 1RM: 1 Repetition maximum; rpm: Revolutions per minutes; HRR: Heart rate reserve, HRmax: Heart rate maximum; WPMAC: Western Ontario and McMaster Universities Osteoarthritis Index; AIMS2: Arthritis Impact Measurement Scale 2; VAS: Visual analog scale; SF-36: Short-Form 36 Health Survey; KOOS: Knee injury and osteoarthritis outcome score; TUG: Time up to go test; TST: Timed stand test; STS: Sit to stand test; 6MW: 6 Minutes walking test; LTPA: Leisure time physical activity; ↑: Improvement in pain or function; ↓: Worsening in pain or function; →: Not change in pain or function

3.3.1.1 Effects on pain in individuals with Osteoarthritis

The outcomes revealed that three studies (Baker et al., 2001; Calatayud et al., 2017; Mangione et al., 1999) reported a reduction in pain following HIT ($p = 0.013$, $p = <.0001$, $p = <.000$, respectively) and in the study by Mangione et al. (1999), pain improvement was observed only in the AIMS2 pain subscale, not in VAS and WOMAC. Study of Thorstensson et al. (2005) reported no significant effect on pain resulting from HIT ($p = 0.49$). Moreover, other investigations stated that HIT and HIIT did not exhibit superiority effects on pain over other types or intensities.

3.3.1.2 Effects on function in individuals Osteoarthritis

In terms of changes in function, the study by Keogh et al. (2018) demonstrated improvement only in the TUG as superior for the HIIT group ($p = 0.004$). Four studies including (Baker et al., 2001; Calatayud et al., 2017; Ferraz et al., 2017; and Waller et al., 2017) reported enhancements in function favoring HIT groups (all $p < 0.05$), although in the study by Ferraz et al. (2017), BFRT group showed improvement in function as well. In this study, in the HIRT and BFRT groups, WOMAC physical function ($p = 0.02$, $p = 0.019$, respectively) and TST ($p < 0.0001$, $p = 0.01$, respectively) improved, but there was no improvement in the TUG test. Study by Thorstensson et al. (2005) indicated no significant effect on function following HIT ($p = 0.08-0.9$). Additionally, three studies (De Zwart et al., 2022; Foroughi et al., 2011; and Mangione et al., 1999) explored the notion that HIT did not yield greater improvements in function compared to low-intensity or sham interventions.

In addition, in most studies reporting increase in 1RM muscle strength in the HIT group such as studies by (Baker et al., 2001; Ferraz et al., 2017; and Foroughi et al., 2011), improvement in function was reported also, exception of the study by De Zwart et al. (2022). In the study by Ferraz et al. (2017) HIRT and BFRT groups showed more within-group significant improvement in 1RM (+33% and +26% for leg press, +22% and +23% for knee extension respectively, $p < 0.0001$), and TST test (+14%, $p < 0.0001$ and +7%, $p = 0.01$, respectively) compared to LIRT group, but there were no significant differences between HIRT and BFRT groups in 1RM and functional capacity (all $p > 0.05$). In the study by Waller et al. (2017), the HIT group showed increase in walking speed after intervention and at 12 months follow up ($p = 0.002$ and $p = 0.032$, respectively) and higher level of leisure-time physical activity (LTPA) ($p = < 0.001$) during and immediately after the HIT.

3.3.2 Rheumatoid Arthritis

Among six studies included individuals with RA, there were higher number of females and participants were in the early to moderate stage, except one study that the severity of disease had not been mentioned. Variety of HIT, including HIIT, resistance, and aerobic with or without supervision were utilized across different studies. In addition, in one study the intervention dedicated for control group was not usual care or sham exercise but was neuromuscular electrical stimulation (NMES). Additionally, adherence rate following HIT was high across the studies. Tools for assessing pain, were Dutch Arthritis impact measurement scale, VAS, and Numeric Rating Scale. Tests including 30s arm curl, 30s chair stand, 50-foot walking, Gait speed, 5repetition chair stand, single leg stand, stair climbing, STS tests and TUG were used to evaluating function and performance additional to using of McMaster Toronto Arthritis, SF-36, Health assessment questionnaire (HAQ), and Fear Avoidance Belief Questionnaire- Subscale of Physical activity questionnaires. (Table 4)

Table 4: Study characteristics of Rheumatoid Arthritis (RA)

Author, Year	Disease	Intervention type	N (IG/CG)	Sex(F/M)	Age (mean OR median)	Intensity	Time/week, Minutes, Total Week	Adherence (%)	Outcome assessment tool (Pain/ Function)	Results (pain, Function)
De Jong et al, 2003	RA	IG: HI (bicycle +circuit exercise of muscle strength, endurance, and mobility training + sport or game CG: UC	IG:150 CG:150	IG:119/31 CG:118/32	median age: IG: 54.0(16) CG: 53.5(18)	Bicycle training: 70-90% HRmax,4-5 RPE	2, 85 Min, 24 month(2 years)	median; IG:74% CG: NI	-/ MACTAR, HAQ,	HIWB training was more effective for ↑ function than UC
Lange et al, 2019	Low- moderate RA	IG: Supervised gym-based moderate-HI aerobic(interval) and RT/ CG: home based LI training	IG:36 CG:38	IG:27/9 CG:29/9	mean age: IG:69.14 ± 2.61 CG:70.11 ± 2.30	70-80 % HRmax / 70-80 % 1RM	3, NI, 20	IG: mean;78% CG: NI	-/ HAQDI, TUG, STS	moderate to HIT effective on ↑ function but not superior to LI
Lemmy et al, 2009	RA (Functional class I or II)	IG: Supervised HIPRT / CG: home based, LI (ROM) training	IG:13 CG:15	IG:11/2 CG:12/3	mean age: IG:55.6±8.3 CG:60.6±11.2	80% 1 RM	2, N, 24	IG:73% CG:54%	-/MDHAQ, 30s arm curl, 30s chair stand, 50-foot walking test	HIPRT safe and effective for ↑ function
Piva et al, 2019	Moderate RA	IG: HI volitional training quadriceps ST CG: NMES	IG:28 CG:31	IG:23/5 CG:25/6	mean age: IG:61.0 ±11.0. CG:57.2 ± 8.6	80 % 1RM	2-3,45Min,16	median; IG: 36 (18,37) CG: 36 (35,37)	NRS / HAQDI, LEFS, Gait speed, 5rep chair stand, single leg stand, stair climbing	HI can ↑ pain and function but not superior to NMES
Seneca et al, 2015	Early RA in remission or, Low-moderate disease activity	IG: Partly supervised HIT (bike exercise+ ST) CG: Self-administered HI exercises	IG:25 CG:26	IG:17/8 CG:18/8	median age: IG:61(27-79) CG:54(23-71)	Bike exercise: 15-16 RPE + ST: 12RM	2, 60 Min, 6	IG:92.2% CG:NI	NRS/ HAQ-DI, SF-36, FABQ-PA	Supervised HIT can ↑ pain and function but not superior to Self-administered HIT
Van de Ende et al, 1996	Moderate RA	Group HIIT / Group LI NWB / Individually LI NWB / HE:(ROM and Isometric exercise for home)	All group: N:25	HIIT: 13/12 Group LI: 16/9/ Individually LI: 16/9 HE: 18/7	mean age: Group HIIT:51.1/ Group LI:47.7/ Individually LI:53.1/ HE:56.1	HIIT:70-85% HRmax and high pace/ LI: Low pace without resistance	HIIT:3, 60Min, 12 LI:2, 60Min, 12 HE: 2, 15Min, 12	For all supervised exercise group: 75%	Dutch-AIMS, VAS / HAQ,50-foot walking test, stair test	→ in pain / → in HAQ, Dutch-AIMS/ ↑ in Function in HIIT but not superior effect than LI

Definitions: HI: High intensity; LI: Low intensity; RT: Resistance training; HIPRT: High intensity progressive training ; ST: Strength training ; UC: Usual care; NI: No information; HRmax : Heart rate maximum; 1RM: 1 Repetition maximum; RPE: Rating of perceived exertion; MACTAR: McMaster Toronto Arthritis, patient preference disability questionnaire; HAQ: Health Assessment Questionnaire; LI NWB: Low intensity not weight bearing; HE: Home exercise; HAQDI: Health Assessment Questionnaire Disability Index; MDHAQ: Multidimensional Health Assessment Questionnaire; DAS28: Disease activity Score for 28 joints; NRS: Numeric Rating Scale; SF-36 : Short-Form 36 Health Survey; FABQ-PA: Fear Avoidance Belief Questionnaire- Subscale of Physical activity; Dutch-AIMS : Dutch Arthritis impact measurement scale; VAS: Visual Analog scale; NMES: Neuromuscular Electrical Stimulation; ROM: Range of motion; TUG: Timed up to Go test; STS: Sit to stand test; LEFS: Lowr Extremity Functional Scale ↑: Improvement in pain or function; ↓ : Worsening in pain or function; → : Not change in pain or function

3.3.2.1 Effects on pain in individuals with Rheumatoid Arthritis

Across the studies only Piva et al., 2019; Seneca et al., 2015; and Van de Ende et al., 1996 reported results for pain, in which in the studies by Piva et al. (2019) and Seneca et al. (2015) there were no significant differences between groups in pain improvement ($p = 0.620$ and $p = 0.263$, respectively) after HIT and Van de Ende et al. (1996) reported no significant differences in change in pain among intervention groups although HIT group showed more within group improvement.

3.3.2.2 Effects on function in individuals with Rheumatoid Arthritis

Studies by De Jong et al. (2003) and Lemmy et al. (2009) stated HIT is more effective for improving function than usual care and low-intensity training. ($p = 0.034$ and $p < 0.05$ in all functional tests, respectively). Other investigations including Lange et al., 2019; Piva et al., 2019; Seneca et al., 2015; and Van de Ende et al., 1996 reported HIT or HIIT can improve function (all $p < 0.05$), but it is not more effective than other intensities or exercise types. Piva et al. (2019) investigated within-group changes in function were significant in stair climbing and chair stand tests in the exercise group ($p = 0.034$ and $p = 0.024$ respectively), and there was a significant change in lower extremity functional scale in the NMES group ($p = 0.001$), but there were no statistically significant differences in function between groups. Similarly, study by Seneca et al. (2015), reported effectiveness of supervised HIT is comparable to self-administered HIT, in which there were no significant differences between groups. In this study function was assessed by HAQ-DI, SF-36 (physical component score), and FABQ-PA reporting ($p = 0.972$, $p = 0.802$, and $p = 0.922$ respectively).

3.3.3 Axial Spondyloarthritis

Among the three studies included for axSpA, both genders were included although in two studies there were more females in the intervention group. Mean age was under 50 across studies and the preliminary intervention was HIIT. Two had small sample sizes in which were RCT pilot studies. All investigations reported adherence rates equal to or more that 80% following HIIT. Ankylosing spondyloarthritis disease activity score (ASDAS), Bath ankylosing spondyloarthritis disease activity index (BASDAI), and Bath ankylosing spondyloarthritis Functional index (BASFI) tools were used for assessing pain and function (Table 5).

Table 5: Study characteristics of axial Spondyloarthritis (axSpA)

Author, Year	Disease	Intervention type	N(IG/CG)	Sex (F/M)	Age (mean)	Intensity	Time/week, Minutes, Total week	Adherence %	Outcome assessment tools (Pain/ Function)	Result (Pain/ Function)
Sveaas et al, 2014	Active ax Spa	IG: HIIT (endurance)and ST (2sessions supervised+1session individually / CG: UC	IG:10 CG:14	IG: 8/2 CG:4 /10	IG:46.6(13.6) CG:49.9(11.1)	70-95%HRmax/ 8-10 M Rep	3,40-60Min, 12	≥80%	ASDAS, BASDAI / BASFI	Pain↑ Function ↑
Sveaas et al, 2018	Active ax Spa	IG: HIIT (endurance)and ST (2sessions supervised+1session individually / CG: UC	IG:10 CG:14	IG: 8/2 CG:4 /10	IG:46.6(13.6) CG:49.9(11.1)	70-95%HRmax/ 8-10 M Rep	3,40-60Min, 12	≥80%	– / Last question of BASFI for assessing the ability to do a full day’s activities	– / ↑ (ability to do a full day’s activities (Function)
Sveaas et al, 2020	Moderate to High ax SpA	IG: HIIT endurance and ST (2sessions supervised+1session individually / CG: UC	IG:50 CG:50	IG: 25/25 CG:28/22	IG:45.1(23-68) CG:47.2(24-69)	70-95%HRmax/ 8-10 MRep	3,40-60Min, 12	≥80%	ASDAS, BASDAI / BASFI	Pain↑ / Function ↑

Definition: IG: Intervention group, CG: Control group, HIIT: High intensity interval training; UC: Usual care; HRmax: Heart rate maximum; MRep: Maximum repetition; ASDAS: ankylosing spondyloarthritis disease activity score; BASDAI: Bath ankylosing spondyloarthritis disease activity index; BASFI: Bath ankylosing spondyloarthritis Functional index; ↑: Improvement in pain or function; ↓ : Worsening in pain or function, → : Not change in pain or function

3.3.3.1 Effects on pain in individuals axial Spondyloarthritis

Sveaas et al., 2014; and Sveaas et al., 2020 reported improvement in pain following HIIT. In the study by Sveaas et al. (2020) both indexes of BASDAI for (neck, back, and hip pain) and for peripheral pain showed significant treatment effects ($p = <0.001$ and $p = 0.016$, respectively) and Sveaas et al. (2014) reported $p = 0.02$ as statistically significant difference in pain favoring HIIT group.

3.3.3.2 Effects on function in individuals with axial Spondyloarthritis

All three studies including Sveaas et al., 2014; Sveaas et al., 2018; and Sveaas et al., 2020 showed improvement in function for the HIIT group ($p = 0.02$, $p = 0.02$, $p = <0.001$, respectively). In the study by Sveaas et al. (2018) function assessment by BASFI was mentioned as the ability to do a full day's activity.

4. Discussion

This systematic review examined the effects of HIT on pain and function in individuals with OA, RA, and axSpA and explored valuable evidence from RCTs. The effects of HIT have been discussed according to the results of this study, however there is antithesis data.

4.1 Osteoarthritis

Among the studies including individuals with OA in this review, there were contradictory results regarding the effects of HIT on pain and function. For example, similarly, studies by Baker et al., 2001; Calatayud et al., 2017; Waller et al., 2017; and Keogh et al., 2018; showed improvements in function, however others reported no change (Thorstensson et al., 2005) or no superiority favoring HIT (De Zwart et al., 2022; Ferraz et al., 2017; Foroughi et al., 2011; Mangione et al., 1999). Interestingly in the study by Keogh et al. (2018), only TUG test improved in HIIT group, while there were no significant differences in other outcomes. Studies by De Zwart et al., 2022; and Foroughi et al., 2011 showed pain and function improvement by HIT but its effect was not greater than other studied intensities. This might be attributed to factors such as variations in study populations, implementing different types of HIT, differences in intervention protocols, and methodological limitations. In a pilot study by Golightly et al. (2021), assessing the effects of a 12-week HIIT on individuals with OA, all outcomes related to pain and function were significantly improved. The results of study by Golightly et al. (2021) were in line with findings from a single-group double pretest-posttest

study conducted by Bressel et al. (2014), examining the effects of 6-week HIIT on an aquatic treadmill in individuals with OA which reporting significant improvements in pain and function. Interestingly, HIT in the study by Golightly et al. (2021), was alike to the study by Mangione et al. (1999) included in this review. Both studies implemented a similar type of HIT, however, their interpretation from its effects on pain and function was different. Golightly et al. (2021) reported improvement in pain and function, while Mangione et al. (1999) stated no superiority for HIT compared to low-intensity training. This discrepancy could be attributed to differences in the specific nature of the interventions employed or participants demographics. For instance, in the study by Golightly et al. (2021) HIT was performed interval, whereas in the study by Mangione et al. (1999), the training protocol was not interval and participants performed HIT unceasing. However, it needs to be considered that the study by Golightly et al. (2021) was a pilot study and study conducted by Mangione et al. (1999) was a RCT with a control group performing low-intensity training. Additionally, the mean age of participants in the study by Mangione et al. (1999) was higher, potentially influencing pain perception and function. Moreover, these inconsistent results observed in the study by Waller et al. (2017) included in this review, and study conducted by Bressel et al. (2014). Both studies performed an aquatic intervention but the results on pain were opposite. Bressel et al. (2014) realized improvement in pain, whereas the study by Waller et al. (2017) in this review, reported no significant differences in pain perception. It should be considered that Bressel et al. (2014) used a water jet for exposing intensity during training that was walking barefoot on an aquatic treadmill and training protocol was interval. In contrast, in the study by Waller et al. (2017) participants engaged in high-intensity resistance aquatic training, potentially resulting in greater load on the knee joint and pain.

It was revealed that although HIT might not provide a superior effect compared to other intensities or usual care, it is noteworthy that it also does not lead to symptom worsening especially where most studies in this review reported the effectiveness of high-intensity resistance training on increasing 1RM with impact on the function. This was aligned with a study conducted by King et al. (2008), reporting HIT not leading to flare up pain or negative impact on function but also makes a substantial increase in muscle strength. Findings of current review about the effects of HIT on pain and function in individuals with OA follows the results of a narrative review by Tarantino et al. (2023). Tarantino et al. (2023) reported HIT improve pain and function among individuals with OA, but somewhere it is not superior to other training

types. Differences in reporting results across studies in this review, need for more precise and high-quality studies regarding the effects of HIT on pain and function in all types of OA.

4.2 Rheumatoid Arthritis

Across RA studies in this review, only three reported results related to pain, however the results were not aligned, where Van de Ende et al. (1996) reported no change, while Piva et al., 2019 and Seneca et al., 2015 showed improvement but no greater effect on pain favoring HIT. On the other hand, although two studies reported a positive effect on function following HIT, but the results of most studies were comparable in that HIT does not lead to a greater impact on function. Regarding these results, it is notable to be considered studies by De Jong et al., 2033; Lange et al., 2019; and Lemmey et al., 2009 acknowledged that HAQ questionnaire is not a sensitive instrument for assessing changes in exercise trials as it cannot consider complex, repetitive, and endurance tasks. However, this tool is constantly used for assessing the daily level of activities or functional abilities in studies of individuals with RA. These findings in this review, can be compared with the results of a study conducted by Andonian et al. (2021). Andonian et al. (2021) reported HIIT lead to a greater impact on disease activity or pain and fitness only in older RA individuals with lower fitness level. In the study by Andonian et al. (2021) disease activity and pain were assessed by DAS-28 (determined from patient-completed pain and overall health visual analog scales). In addition, a pilot study by Bartlett et al. (2018), reported no change in pain and self-reported physical activity following HIIT, but significant improvement in function including walking and chair stand in older adults with RA. Results of the study by Bartlett et al. (2018) in pain was in line with the results of Van de Ende et al. (1996) included in this review, however their interpretation of the effects on function was different. Van de Ende et al. (1996) reported no greater effects on function for HIIT than low-intensity training. Regarding this discrepancy, it good to be considered that in the study by Bartlett et al. (2018) there was no control group with training intervention, potentially impacting the results. Another pilot study by Sandstad et al. (2015) examining the effects of HIIT on rheumatic diseases including seven RA individuals showed that such exercises can be a promising non-pharmacological treatment for these individuals with no increase in pain. This result is not generalizable for RA population as the number of RA individuals included in this study is low.

According to the results of this review, it needs to be considered that both groups in the Seneca et al. (2015) underwent HIT where one was partly supervised, and other was self-

administered. Additionally, in the study by Piva et al. (2018) the control group received an external intervention by NMES, so it cannot assess the exact effect of HIT. Noteworthy, all included studies with individuals with RA in this review, used individuals with low-moderate RA or in remission except the study by De Jong et al. (2003) in which did not mention the intensity of disease; and high number with female genders. Thus, these contradictories underline the necessity for more solid and precise study protocols with more sensitive tools to assessing the changes among this population and considering both gender for generalization.

4.3 Axial Spondyloarthritis

Although three studies included individuals with axSpA reported improvement in pain and function following HIIT there is a necessity for more studies. The studies by Sveaas et al., 2014 and Sveaas et al., 2018; were pilot studies with small sample sizes and a greater number of females, so the results of these studies might not be suitable for generalization for a larger population and both genders. In the study by Sveaas et al. (2020), the sample size is large and gender distribution good but still, there are some limitations. In this study, 40% of the participants are under pharmacological treatment during the study period which can impact the exercise-induced outcomes on pain, and function. It is also noteworthy, in none of studies observational or physical function tests were utilized to assess function and all results were self-reported. Unlike the reported results for pain in these studies, a qualitative study by Bilberg et al. (2020) reported that HIIT is a physical challenge for individuals with axSpA and can increase their pain, but participants were satisfied and proud of managing HIIT. Interestingly, results of a cross-sectional comparative study by Fongen et al. (2013) revealed individuals with axSpA with high diseases activity reporting low activity levels and engaging less in high intensity activities. The number of studies examining the effects of HIT on pain and function in individuals with axSpA is limited so the influence remains unexplored and need for more high-quality studies. Two RCT studies, conducted by Haglo et al. (2021) and Norden et al. (2023), investigating the effects of HIIT on individuals with rheumatic diseases, reported effectiveness of HIIT among these individuals. In these studies individuals with RA, and axSpA were included as well in the study population. However, in the study by Haglo et al. (2021) both groups underwent HIIT, and effect of supervision was examined and Norden et al. (2023) revealed no change in pain but enhance in the self-reported physical activity. Overall, regarding these variations in results, further meticulous investigations are needed to understand the best non-pharmacological treatment for individuals with axSpA.

All in all, these contradictory findings from this systematic review, underscore the need for further well-designed and RCT studies to clarify and robustly examine the effects of HIT interventions on pain and function in individuals with OA, RA, and axSpA. Future research should consider addressing methodological limitations, such as small sample sizes, lack of power, and gender biases, to provide more meticulous evidence for clinical practice. Especially the effects of HIIT as a training trend needs to be explored more precisely as it has been reported that regular HIIT positively can influence muscle metabolism and cardiovascular health (Gibala et al., 2012; Gallo-Villegas et al., 2018), as well as pain and function (Botta et al., 2022). It has been stated that HIIT can facilitate the initiation of training sessions, particularly for individuals facing barriers to commencing an exercise session such as individuals with OA, RA, and axSpA (Smith-Ryan et al., 2020; Smith-Ryan et al., 2015).

4.4 Discussion methods

The study systematically reviewed RCTs to examine the effects of HIT on pain and function in individuals with OA, RA, and axSpA. Adhering to rigorous standards, the PRISMA guidelines were followed to ensure methodological robustness. It was done with meticulous exploration and retrieval of pertinent studies by searching across PubMed, Medline, SPORTdiscus, and CINAHL databases. Despite substantial number of studies after the first screening, Medline provided the highest number of relevant studies, and duplications were seen constantly across databases. Only RCT studies were chosen for review due to their ability to offer more precise and robust results in exercise interventions. This decision strengthens the study's focus on investigating the effects of HIT on pain and function in individuals with OA, RA, and axSpA as pain and function impairment significantly impact the quality of life in these populations. However, the review was not without limitations. The exclusive focus on RCT may have overlooked insights from other study designs. Additionally, the absence of criteria for factors like disease duration, medication use, and comorbidities in the inclusion criteria could have affected the final results. Other possible underlying causes might be that most of studies did not have a control group without any exercises intervention or limitations including small sample size, lack of power or only female gender. Following that, any systematic review needs to assess the internal quality of included studies. Therefore, the Cochrane ROB 2 tool was employed to assess the quality of RCTs. It revealed varying risk levels among the included studies. This arises the need for

consideration due to the inherent limitations within each study. Moreover, potential errors in outcome reporting make the quality assessment a challenging process.

5. Conclusion

The results of this review indicate inconsistent findings about the effects of HIT on pain and function among individuals with OA, RA, and axSpA. While different findings were observed across the studies about the effects of HIT on pain and function in individuals with OA, HIT showed potential to improve pain and function. Similarly, individuals with RA exhibited mixed results, highlighting the need for more valid tools, and further investigation. Conversely, HIT appeared to improve both pain and function in studies included individuals with axSpA in this review, but still there were some antithesis results compared to another studies. It was proved HIT is not harmful for these populations. In conclusion, the effects of specific implementation of HIT in these populations remain relatively unknown, underscoring the necessity for more robust research in the future.

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