Exercise therapy for bone and muscle health -an overview of systematic reviews

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Abstract

Background: Musculoskeletal conditions (MSCs) are widely prevalent in present-day society, inflicting high costs and substantially influencing health and quality of life. The main aim of this overview was to synthesize evidence from systematic reviews on the effects of exercise therapy on pain and physical function for MSCs. In addition, the evidence for the effect of exercise therapy on disease pathogenesis, and whether particular components of exercise programs are associated with the size of the treatment effects were also explored.
Methods: We included four common musculoskeletal conditions: fibromyalgia, low back, neck and shoulder pain, and four specific musculoskeletal diseases: osteoarthritis (OA), rheumatoid arthritis (RA), ankylosing spondylitis (AS) and osteoporosis. We first included Cochrane reviews with last up-date January 2007 or later, and then searched for non-Cochrane reviews published after this date. Pain and physical functioning were selected as primary outcomes.
Results: Nine reviews with a total of 224 trials and 24,059 patients were included. In addition, one review addressing the effect of exercises on pathogenesis was included. Overall, we found solid evidence supporting exercise therapy in the management of musculoskeletal conditions, but there are substantial differences in the amount of research evidence between the included diagnostic groups. The standardised mean differences for knee OA, low back pain, fibromyalgia and shoulder pain varied between 0.30 and 0.65 and were statistically significant in favour of exercises for both pain and function. For neck pain, hip OA, RA and AS, the effect estimates were generally smaller and not always statistically significant. There is little or no evidence that exercise therapy can influence disease pathogenesis. The only exception is with osteoporosis, where there is evidence that exercise therapy increases bone mineral density in postmenopausal women, while no significant effects were found in clinically relevant outcomes (fractures). For low back pain and knee osteoarthritis, there is evidence suggesting that the treatment effect increases with the number of exercise sessions.
Conclusion: There is empirical evidence that exercise therapy has beneficial clinical effects for most MSCs. Except for osteoporosis, there seems to be a gap in the understanding of the ways in which exercise therapy influences disease mechanisms.

Keywords

fibromyalgia, low back pain, neck pain, shoulder pain, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, osteoporosis, pain, physical function

Background

Musculoskeletal conditions (MSCs) are common and have important consequences for the individual and the society. MSCs are the most common cause of severe long-term pain and physical disability, and in Europe, 20 - 30% of adults are affected at any one time [1-3]. It is estimated that MSCs represents nearly 25% of the total cost of illness in Sweden [4], and they are one of the most common causes of health problems limiting work ability [5]. About one in five consultations in primary care are for MSCs, and some of these patients are referred to other health professionals such as physiotherapists, occupational therapists or chiropractors; or to medical specialists such as rheumatologists, or orthopaedic surgeons. The burdens that MSCs create have been recognized by the United Nations and WHO, with their endorsement of the Bone and Joint Decade 2000–2010 [6]. The prevalence of many of these conditions increases markedly with age and many are affected by some common lifestyle factors (obesity, smoking and physical inactivity). With the increasing number of older people and the changes in lifestyle, the burden of MSCs and other non-communicable diseases is predicted to increase [7].

Musculoskeletal conditions form a heterogeneous group of over 200 different health problems that are linked anatomically and by their association with pain and impaired physical function [8]. They include conditions from those of acute onset and short duration to lifelong disorders. For many common musculoskeletal conditions such as regional pain syndromes, the underlying pathogenesis is poorly understood and it is often not possible to produce a clear-cut diagnosis. Others, such as osteoarthritis, are biologically well defined, but clinically less well understood, while for example rheumatoid arthritis is both biologically and clinically well defined [9].

While for decades inactivity and bed rest were mainstays in the management of many diseases, there is now an increasing amount of evidence supporting the opposite, i.e. that physical activity and exercises are beneficial to health promotion and treatment. Even if exercise and physical activity are closely related constructs, they have distinct meanings. The term *physical activity* includes everyday activities that can contribute to wellbeing, whereas *exercises* are physical activities that are planned, structured and repetitive [10]. The focus of this overview is *exercise therapy,* which involves the prescription of a physical activity program that involves the client undertaking voluntary muscle contraction and/or body movement with the aim of relieving symptoms or improving function, or improving, retaining or slowing deterioration of health [11].

While systematic reviews of randomised trials usually summarize the evidence of one kind of intervention for a single condition, overviews of systematic reviews can summarize evidence from more than one systematic review of the same intervention for different conditions. There is, to our knowledge, only one published overview of systematic reviews that has focused on the effects of exercises for musculoskeletal conditions [12]. This overview was based on reviews published up to July 2007, and did not include specific diseases such as osteoporosis and inflammatory joint diseases. Thus, the most updated evidence may not be included in this overview. The main aim of the present overview was to synthesize evidence from systematic reviews on the effects of exercise therapy on pain and physical function for eight selected musculoskeletal conditions and diseases. In addition, we explored the evidence for the effect of exercise therapy on disease pathogenesis, and whether particular components of exercise programs are associated with the size of the treatment effects.

Methods

Criteria for considering reviews for inclusion

For this overview, we included systematic reviews on the effects of exercise therapy for four common conditions (fibromyalgia, low back pain, neck pain and shoulder pain) and four specific musculoskeletal diseases (osteoarthritis, rheumatoid arthritis, ankylosing spondylitis and osteoporosis). Other related conditions and musculoskeletal malformations and traumas were not included in this overview. All types of land-based exercise therapy interventions were considered.

Search methods for the identification of reviews

We first searched in the Cochrane database of systematic reviews. All Cochrane reviews on exercises for the above-mentioned musculoskeletal conditions were considered for inclusion. The search was performed in March 2012. Two authors (GS and KBH) assessed the eligibility of reviews based on the inclusion criteria presented above. Cochrane reviews with last literature search January 2007 or before were not included, and we replaced these reviews by searching for non-Cochrane systematic reviews in Medline, Embase, Cinahl, Amed, and PEDro, published after this date. The electronic search strategy for Medline is provided in Additional file 1. Two authors (GS and KBH) then screened these records for new reviews. If several reviews fulfilled our inclusion criteria we included only one review per combination of disease, intervention and outcome using the following rules: we chose the newest review of high quality. If two or more reviews were equal regarding these criteria, we chose the review with the highest number of primary studies. We also searched in the same databases for reviews with an explicit aim to investigate the effect of exercises on pathogenesis in MSC with no restrictions regarding publication date.

Types of outcome measures

Exercise therapy can have clinical effects by improving dominant symptoms, and we therefore chose to primarily focus on the core symptoms of MSCs:

- any measure of pain,
- physical disability or physical function.

In addition, we collected data on the effect of exercise therapy on disease pathogenesis, and whether particular components of exercise programs are associated with the magnitude of treatment effects.

We did not focus on the general health benefits or complications of exercises because small-to-medium randomized controlled trials (RTCs) with short-term to intermediate follow-up may be inadequate to assess other health benefits such as the cardiovascular risk profile and the incidence of complications. Other potentially relevant outcomes, such as work participation and health-related quality of life, compliance or costs, were not evaluated.

Data collection and analysis

One reviewer (GS) extracted data regarding population, intervention, comparison and outcomes (inclusion criteria) and methodological quality of included trials. The methodological quality was assessed according to the Measurement Tool to Assess Systematic Reviews (AMSTAR) checklist [13]. The eleven criteria shown in Table 1 were rated as “met,” “unclear/partly met,” or “not. A second reviewer (KBH) independently verified the accuracy of the numeric results. Most reviews included several comparisons, and we included analyses that compared any exercise intervention with no or minimal exercise intervention. As pain and function most often are continuous outcomes, data were summarized using the standardised mean differences (SMD) or mean differences (MD) with 95% Confidence Intervals (95%CI) as reported in the included reviews. For dichotomous outcomes, Odds Ratios and 95% CI were presented. Pooled effect estimates were presented according to the model used in the reviews. For reviews that explored whether particular components of exercise programs were associated with the magnitude of treatment effects, we extracted the coefficients from meta-regression- or sub-group analyses. Results from the review investigating the evidence for the effect of exercise therapy on disease pathogenesis were reported as in the original review.

Results

We identified 18 potentially relevant Cochrane systematic reviews. After reading the full text reviews, two were excluded because they did not focus on land-based exercise therapy, two because of not relevant outcomes, four because of other diagnoses, and finally four because they had not been updated after January 2007. The excluded Cochrane reviews and reason for exclusion are listed in Additional file 2. The search for non-Cochrane reviews after 2007 resulted in 963 hits (low back pain - 474 refs, shoulder pain - 186 refs, neck pain - 303 refs). 951 were excluded after screening of title and abstract and 12 were retrieved in full text. Based on methodological quality and publication date three of these were included.

Description of included reviews

We included six Cochrane systematic reviews comprising patients with fibromyalgia [14], osteoporosis [15], knee osteoarthritis [16], hip osteoarthritis [17], rheumatoid arthritis [18] and ankylosing spondylitis [19]. In addition, three non-Cochrane reviews comprising patients with shoulder pain [20], neck pain [21] and low back pain [22] were included. The nine included reviews comprised at total of 224 trials with 24,059 patients. Characteristics of the included reviews are shown in Table 2.

Four reviews [14, 15, 18, 19] were assessed to be of high methodological quality (all 11 criteria met), while in three reviews [16, 17, 22] eight to nine criteria were met. Finally, in two reviews [20, 21] only three to four criteria were met. In addition, we included one review which investigated the evidence for the effect of exercise therapy on disease pathogenesis [23].

Effects of exercises

The effects on clinical outcomes are summarized in Table 3 (pain) and Table 4 (physical functioning).

Fibromyalgia

Fibromyalgia (FM) is characterized by persistent widespread musculoskeletal pain and tenderness. In clinical practice, chronic generalized musculoskeletal pain in all four quadrants of the body that cannot be traced to a specific structural or inflammatory cause are often diagnosed as FM. FM is also associated with other symptoms such as fatigue, stiffness, mood disturbance, abdominal pain and headache. The 1990 American College of Rheumatology (ACR) diagnosis of FM was based on a history of widespread pain for a duration of longer than three months, and the presence of excessive tenderness on applying pressure to 11 of 18 specific muscle-tendon sites, while the preliminary 2010 ACR criteria is based on a combination of widespread pain and multi-symptom severity and does not require a physical or tender point examination [24].

The Cochrane review of Busch et al. [14] compared first aerobic-only exercise interventions (only protocols of American College of Sports Medicine recommended intensity) to untreated control groups. Statistical pooling based on three trials with 183 patients indicate a positive non-significant effect in favour of exercises in pain: SMD = 0.65 (95%CI: -0.09 to 1.39) and a statistically significant effect in physical function (three trials/253 patients): SMD 0.66 (95%CI: 0.41 to 0.92). Thereafter, meta-analyses from two low quality trials compared strength-only exercise interventions to untreated control groups, and found a large and significant effect on pain (based on one trial with 21 patients): SMD 3.00 (95%CI: 1.68 to 4.32) and a non-significant effect in physical function: SMD 0.52 (95%CI: -0.07 to 1.10). Based on the number and quality of included trials, Bush et al. concluded that there is evidence of a moderate quality demonstrating that short-term aerobic training at the intensity recommended for increases in cardio respiratory fitness have beneficial effects in physical function and possibly in pain. We were not able to identify any analyses exploring the effects of particular components of exercise. Pedersen and Saltin [23] found limited evidence for the effect of exercise on pathogenesis, i.e. at least one relevant study of moderate quality is available.

Low back pain

Low back pain (LBP) is generally defined as pain located between the lowest ribs and the inferior gluteal folds, with or without pain radiation to the lower limbs [25]. Clinical guidelines classify LBP into 1) "non-specific" LBP, 2) LBP with nerve root affection, and 3) possible serious spinal pathology ("red flags") [26]. After 1 month with LBP symptoms, a specific cause can be identified for approximately 15% of patients [25]. Clinically, patients with LBP form a heterogeneous group presenting with pain of varying duration, as well as disability in terms of impaired body functions and structures, activity limitations, and participation restrictions in work and leisure.

The review by Ferreira et al. [22] sought to establish the effect of exercise on pain and disability in patients with chronic non-specific low back pain, with a major aim of explaining between-trial heterogeneity. For exercise versus minimal care (11 trials), they found a significant weighted mean difference (WMD) of -4.83 (on a 0-100 scale) favouring exercise for pain, (95%CI -9.36 to - 0.30). For exercise versus no treatment (5 trials) the WMD was also significantly in favour of exercise (-9.27, 95%CI -17.00 to -1.55). Further, they found positive and significant effects for disability. For exercise versus minimal care (14 trials), the WMD was -6.41 (95%CI -9.76 to -3.05) and for exercise versus no treatment (9 trials), the WMD was -3.31 (95%CI -4.83 to -1.79).

Ferreira et al. [22] also explored between trials variability by meta-regression analyses, and found that only dosage was significantly associated with effect size in pain. Dosage means number of exercise hours and sessions, and results suggest that for each additional exercise session, the effect size would increase by 0.13 (95% CI: 0.02 to 0.24) on a 100-point scale. There is no evidence for the effect of exercises on pathogenesis.

Neck pain

Although there is no general agreement on the classification of neck pain, the Task Force on Neck Pain and Its Associated Disorders [27] suggested a classification of neck pain severity from Grade 1 (No signs or symptoms suggestive of major structural pathology and no or minor interference with activities of daily living; will likely respond to minimal intervention such as reassurance and pain control; does not require intensive investigations or ongoing treatment) to Grade IV (Signs or symptoms of major structural pathology, such as fracture, myelopathy, neoplasm, or systemic disease; requires prompt investigation and treatment). Most people with neck pain do not recover completely, and between 50% and 85% of those who experience neck pain at some initial point will report neck pain again 1 to 5 years later [28].

Leaver et al. [21] reported pooled outcomes from three trials showing significant reductions in pain (on a 0-100 scale) at the conclusion of a course of specific exercises (WMD -12.00, 95% CI -22.00 to -2.00). Pooled results from two trials that reported disability outcomes from general strength and conditioning exercise showed no significant difference compared with minimal intervention at the conclusion of treatment (WMD 1.00, 95%CI -3.00 to 5.00). We were not able to identify any reviews exploring between trial heterogeneity or investigating the effect of exercises on pathogenesis.

Shoulder pain

Shoulder pain and shoulder disorders cover a broad spectrum of pain, symptoms, and diagnoses, e.g. tendonitis, rotator cuff disease, subacromial pain, impingement syndrome, or repetitive strain. As with neck pain, there is no general agreement on the classification of painful shoulder conditions [29]. Clinically, patients often present shoulder pain together with stiffness, reduced range of motion, and/or with pain or other symptoms radiating to the more proximal part of the arm.

Marinko et al. [20] included three studies with pain as an outcome and compared the effects of exercise versus other treatments on pain levels. Data were pooled by use of a random-effects model with an overall standard mean difference in favour of the exercise intervention of -0.30 (95%CI -0.48 to -0.12). Four studies included function as an outcome and compared the effect of exercise versus no intervention or an alternative intervention. Data were pooled by use of a random-effects model, with an overall effect of 0.15 (95%CI 0.01 to 0.29), indicating a minimal positive effect over no care or alternative interventions. We were not able to identify any reviews exploring between trial heterogeneity or investigating the effect of exercises on pathogenesis.

Osteoporosis

Osteoporosis is characterized by a decrease in bone mineral density (BMD), resulting in an increased risk of fractures. The diagnostic criterion for osteoporosis is defined as bone mineral density more than 2.5 standard deviations below the mean bone density of young adult women, while the term "established osteoporosis" includes the presence of a fragility fracture [30]. Clinically, osteoporosis is recognized by characteristic fractures after minimal traumas, most often in the hip, vertebrae, or distal forearm. Clinical consequences of osteoporotic fractures include pain and physical disability with loss of independence and need for long-term care as a consequence. Increased mortality is also seen as a direct result of fracture.

In the Cochrane review “Exercise for preventing and treating osteoporosis in postmenopausal women”, Howe et al. [15] identified 43 RCTs with more than 4000 participants. None of the studies included pain or physical function as an outcome. Concerning disease pathogenesis in terms of BMD, meta-analyses from 24 RCTs with 1,441 participants revealed significant differences in favour of exercise for percentage change in BMD at the spine (Mean Difference (MD) 0.85; 95%CI 0.62 to 1.07), and trochanter (10 RCTs with 815 participants) [MD 1.03; 95% CI 0.56 to 1.49)] when comparing any exercises to any non-exercise control. Thus, there is strong evidence for the effect of exercises on osteoporosis pathogenesis, which is also confirmed by Pedersen and Saltin [23]. When exploring the most effective intervention for BMD at the spine, Howe et al. [15] found a combination of exercise programmes (MD 3.22; 95%CI 1.80 to 4.64) to be most effective, while non-weight bearing high force exercise such as progressive resistance strength training for the lower limbs was most effective for the neck of the femur (MD 1.03; 95%CI 0.24 to 1.82). Prevention of fractures is a main aim in management strategies for osteoporosis, and Howe et al. [15] reported that the risk of fracture in exercise groups was not significantly different from that in controls [(Odds Ratio, 0.61; 95% CI 0.23 to 1.64) four RCTs and 539 participants].

Osteoarthritis

Osteoarthritis (OA) is most frequently observed in hands, hips and knees, and is characterized by joint pain, stiffness and functional limitations. From being thought of as a simple degenerative disease, there is now increasing evidence for the involvement of inflammation [31]. The term symptomatic OA is used when both joint-related symptoms and radiographic signs are present [32].

Although evidence-based recommendations for the treatment of OA consider exercise as a cornerstone of modern OA management, the research evidence from clinical trials in hand OA is very limited and conflicting [33]. For hip OA, Fransen et al. [17] included five RCTs with 204 patients and reported a small, non-significant effect of exercise on pain in patients with hip OA (SMD -0.33, 95%CI -0.84 to 0.17). For physical function, the effect was also small and non-significant (SMD -0.10, 95%CI -0.51 to 0.32). The amount of research evidence for knee OA is substantially larger. Fransen et al. [16] pooled the results from 32 RCTs with more than 3,600 patients, and reported a beneficial effect of exercises with a SMD of -0.40 (95%CI -0.30 to -0.50) for pain; and SMD -0.37 (95%CI -0.25 to -0.49) for physical function. Interestingly, sub-group analyses revealed that studies evaluating programs providing at least 12 direct supervision occasions produced significantly greater effects than programs providing less than 12 supervised sessions for both pain [SMD -0.46 (95%CI -0.60 to -0.32) vs. SMD -0.28 (95%CI -0.40, -0.16)] and function [SMD -0.45 (95%CI -0.62 to -0.29) vs. SMD -0.23 (95%CI -0.37 to -0.09)].

According to Pedersen and Saltin [23], there is no evidence for the effect of exercise on the OA pathogenesis.

Rheumatoid arthritis

Rheumatoid arthritis (RA) is the most common inflammatory rheumatic joint disease. The systemic inflammation leads to synovitis and bone erosion, primarily affecting the small joints of hands and feet, but the larger joints can also be involved. Further, RA is associated with extra-articular manifestations and substantial comorbidity, and a considerably increased risk of cardiovascular diseases is reported [34]. The most typical clinical features of RA are joint pain, stiffness and reduced physical functioning.

In their Cochrane review of dynamic exercises for RA, Hurkmans et al. [18] identified eight RCTs in total. For short-term aerobic capacity and muscle strength training, statistical pooling of two trials (74 patients) revealed a non-significant trend for a positive effect of exercises on functional ability (SMD -0.40, 95%CI -0.86 to 0.06), while data from one trial (50 patients) indicate a similar effect on pain (SMD -0.53, 95% CI -1.09 to 0.04). For short-term aerobic exercises only the meta-analysis showed a SMD of -0.27 (95%CI -0.79 to 0.26) for the effects of exercise on pain (one trial/56 patients), and a SMD of -0.03 (95%CI -0.46 to 0.51) for functional ability (two trials/66 patients). We were not able to identify any analyses exploring the effects of particular components of exercise on the effect on clinical outcomes, and there is no evidence for the effect of exercise on RA pathogenesis [23].

Ankylosing spondylitis

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease predominantly affecting the axial skeleton and sacroiliac joints. The main clinical characteristics are pain, stiffness and loss of spinal mobility, caused by inflammation and damage of spinal structures [35]. Other common features of AS are peripheral arthritis, enthesitis and anterior uveitis, and recent research has also revealed that AS is associated with an increased risk of cardiovascular diseases [36]. Radiographic sacroiliitis has traditionally been the diagnostic hallmark of AS, but the absence of definite radiographic sacroiliitis in the early disease stage has resulted in a delay of diagnosis. Efforts have therefore been made to facilitate an early, pre-radiological diagnosis of axial spondyloarthritis [37].

When comparing home exercises with no intervention (1 trial/155 patients), Dagfinrud et al. [19] found a significant positive effect of exercise on pain for patients with AS (SMD 0.49, 95%CI 0.17 to 0.81), and a non-significant effect on function (SMD 0.12, 95%CI -0.20 to 0.43). There is to our knowledge no evidence for the effect of exercise on AS pathogenesis, or whether particular components of exercise can improve clinical outcomes.

Discussion

In this overview of systematic reviews on exercise therapy for muscle and bone health, we included nine systematic reviews with a total of 224 trials and 24,059 patients. Overall, there is a substantial amount of empirical evidence supporting exercise therapy as a mainstay in the management of musculoskeletal conditions. However, there are differences in the number of included trials between the diagnostic groups included in the present overview. For common conditions such as chronic non-specific low back pain and knee osteoarthritis, there are a substantial number of trials with relatively consistent results demonstrating that exercises have small to moderate beneficial effects on pain and function. For others, such as the inflammatory joint diseases (RA and AS), there are only one or two trials comparing exercises with non-exercise or minimal exercise interventions. When comparing the effect sizes on pain and physical functioning, there seems to be a trend towards larger effects of exercises on pain. The effect sizes were generally larger in favour of pain compared to physical function, with significant positive effects for six conditions on pain and five conditions on physical function. This may indicate that there is no linear relationship between symptoms and functioning, and it may suggest that a relatively large reduction in symptoms is needed to improve physical function. Also, there are several other important components influencing function, such as environmental and personal factors.

We also intended to explore the evidence for the effect of exercise therapy on disease pathogenesis. Except for osteoporosis, we were not able to identify evidence on the influence of pathogenesis. Although the disease mechanisms for the common MSCs are largely unknown, there seems to be a gap in the understanding of why exercise therapy improves clinical outcomes. From a clinical point of view, the most interesting question is "which exercises for which patients". We therefore also explored whether particular components of exercise programs are associated with the size of the treatment effects. Since we did not include single trials comparing different exercise interventions, we only identified indirect comparisons from the reviews. For LBP and knee OA, where the substantial number of trials allows explorative subgroup- or meta-regression analyses, the results suggests that "more is better", i.e. that the treatment effect increases with the number of exercise sessions. However, it is unclear whether the estimated increase is of clinical relevance.

One previous overview has addressed the effect of exercise therapies for MSCs [12]. Dziedzic et al. also concluded that exercise therapy is a beneficial component of the management of musculoskeletal conditions for reducing pain and disability, and that there is limited evidence for the benefit of one particular approach to exercise over another. However, they also emphasis one important clinical caveat, namely that there is evidence that exercises should not be recommended in acute low back pain [12], which is also supported by an updated systematic review [38].

There are several methodological challenges in summarizing evidence from systematic reviews only. There are a substantial number of new trials published in this field every year, and systematic reviews published some years ago may therefore not be based on the most updated evidence. We therefore intended to include Cochrane reviews, since these should be regularly updated. However, this overview clearly shows that this is not the case. We excluded three out of nine eligible Cochrane reviews because they had not been updated after 2007. The decision to exclude Cochrane reviews that have not been updated the last five years is arbitrarily chosen and can be discussed. However, considering the substantial number of new trials that have been published on this topic in the last few years, we would argue that including reviews more than five years old would not reflect the most updated evidence.

Although we performed extensive literature searches, the selection of the three non-Cochrane reviews can be also questioned. However, other systematic reviews on the effects of exercises for LBP, neck pain and shoulder pain also came to more or less similar results. For LBP, Macedo et al. [39] systematically reviewed 14 RCTs on the effects of motor control exercises for persistent LBP. Their pooled estimates for the comparison between motor control exercise and minimal intervention in reducing pain and disability at both the short- and long-term were higher than in the review of Ferreira et al. [21]. van Middelkoop et al. [40] provided an overview on the effects of exercise therapy in patients with chronic LBP. They included 37 RCTs that compared exercises to usual care. Exercise therapy improved post-treatment pain intensity and disability. They found no evidence that one particular type of exercise therapy was clearly more effective than others. Regarding neck pain, Sihawong et al. [41] reviewed nine trials on the effects of various types of exercise for prevention and cure of nonspecific neck pain in office workers. They found strong evidence for the effects of muscle strengthening and endurance exercises in treating neck pain. Moderate evidence supported the use of muscle endurance exercise in reducing disability attributed to neck pain. Teasell et al. [42] reviewed the strength of evidence supporting various therapies for whiplash-associated disorder (WAD). They included 40 trials, and found that exercise and mobilization programs for acute and chronic WAD had the strongest supporting evidence, although many questions remain regarding the relative effects of various protocols. For shoulder pain, a recent systematic review of four RCTs examining the effects of exercise for rotator cuff tendinopathy, the authors concluded that the available literature was supportive that exercise reduced pain and functional disability [43]. In a systematic review from 2011, Brudvig et al. [44] summarized the published research evidence on the effects of therapeutic exercise and joint mobilization towards therapeutic exercise alone in patients with shoulder dysfunction. They found no evidence for the beneficial effects of the combination of therapeutic exercise and joint mobilization versus therapeutic exercise alone for reducing pain and increasing function.

An interesting finding in the present review is that Cochrane reviews seem to be of higher methodological quality than non-Cochrane reviews, which is also consistent with reviews specifically addressing this issue [45, 46]. Because the reviews provide limited information about included trials, the conclusions from tertiary research (overview of systematic reviews) may become too general to be considered as clinically relevant. We will argue that findings from overviews can be valuable as a ‘compass’ for the clinician, and that the decision on the type, dose and timing of intervention should be shared between the clinician and patient at each clinical encounter. Another limitation related to clinical relevance is the magnitude of the estimated effect sizes. Using a traditional and very rough definition, SMDs between 0.30 and 0.65 can be considered as small to moderate. However, whether the effects are clinically worthwhile is a complex question that should also include the patient's perceptions of risks and costs with the actual treatment. The definition of relatively broad diagnostic groups employed in the present overview might also be considered as a limitation from a clinician's point of view. For the regional pain syndromes (low back pain, shoulder pain and neck pain) it is obvious that 'one size does not fit all', i.e. the effect of exercise therapy might not be equal across diagnostic sub-groups. For example, for back pain a recent randomised trial compared stratification of the management according to the patient's prognosis with non-stratified current best practice, and found that stratified care produced disease-specific and general health benefits [47].

Although few reviews addressed potential adverse effects, exercises for people with MSCs is in general safe and well tolerated, but patients may report minor adverse effects of exercise such as pain and discomfort [48]. For osteoporosis, Howe et al. [15] found that fractures and falls were reported as adverse events in some studies, but there was no significant effect on the numbers of fractures. On the other hand, results from a systematic review showed that exercise can reduce falls, fall-related fractures, and several risk factors for falls in individuals with low BMD [49]. In general, there are few contraindications to prescription of exercise, but co-morbidities should be considered. When prescribing exercise therapy as part of the disease management, the exercise program must be individually adopted and targeted, according to the individual patient's disease severity, physical fitness and co-morbid condition. A number of co-morbidities may have an influence on the burden and prognosis of musculoskeletal conditions, and of particular importance, inflammatory rheumatic diseases are associated with a considerably increased risk for cardiovascular diseases [36].

Conclusion

In conclusion, the present overview shows that exercise therapy can decrease pain and improve physical functioning, but there are substantial differences in the amount of research evidence between the included diagnostic groups. While, for example, the relevant comparison for knee OA included 32 trials with more than 3,600 patients, the results for RA and AS are based on one or two trials with between 50 and 150 patients. Consequently, the pooled estimates for knee OA, low back pain, fibromyalgia and shoulder pain showed consistently statistically significant effects in favour of exercises for both outcomes, while for neck pain, hip OA, RA and AS, the effect estimates were generally smaller and not always statistically significant. However, for the management of all MSCs included in the present overview, exercise therapy is unanimously recommended. There are, however, important limitations when it comes to implications for clinical practice and research. Firstly, for prescription of exercise programs with optimal health benefits for the individual patient, more knowledge is needed on which particular elements and modes of exercise therapy, as well as the doses and frequency of delivery, that can improve outcomes of interest. Secondly, the knowledge of the potential influence of exercise therapy on disease parthenogenesis and the long-term effects on disease progression is currently very limited. Thirdly, there is still an open question whether the magnitude of the positive effects is clinically worthwhile and whether exercise therapy is a cost-effective intervention.

Competing interests

All authors declare they have no competing interests.

Authors' contributions

All authors contributed to the planning of this review, and all participated in the different phases of the trial-selection process. GS and KBH extracted data and KBH wrote the first draft of the article. All authors read and provided feed-back on the draft-versions of the article, and approved the final version. KBH is the guarantor.

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