

Exercise Therapy for Chronic Pain



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KEYWORDS

- Exercise • Chronic pain • Physical therapy • Endogenous pain modulation
- Fear-avoidance • Neuroscience education

KEY POINTS

- Exercise has been demonstrated in animal and human studies to diminish pain experience by its effect on the endogenous pain modulatory systems.
- Exercise, in general, is therapeutic for a wide variety of chronic pain diagnoses, but it has been difficult to show that one particular approach is superior to another.
- Patients have multiple barriers to successfully participating in exercise including patient-specific factors, environmental factors, and health care delivery factors.
- Evaluation of a patient before exercise prescription should include a comprehensive biopsychosocial assessment and determination of the goals of the exercise program.
- Successful exercise prescription requires coordination of care and good communication between physician, therapist, and patient.
- Successful exercise prescription requires patient education regarding the impact of exercise on the nervous system, education targeting fear-avoidance beliefs, and education about the details of how to do the exercise program.

INTRODUCTION

For people with chronic pain, the prospect of doing exercise may seem like an overwhelming and impossible task. And yet, exercise therapy is frequently prescribed for patients with a wide variety of chronic pain problems. Exercise provides multiple benefits for patients including improvements in strength, flexibility, and endurance; decrease in cardiovascular and metabolic syndrome risk; improved bone health; improved cognition and mood; and often most importantly for the patient, improved pain control (**Box 1**). It therefore might seem that patients should be eager to participate in an exercise program. However, patients with chronic pain frequently present with significant levels of fear-avoidance behaviors and are often resistant to

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Box 1**Exercise benefits**

- Strength
- Flexibility
- Endurance
- Decreased cardiovascular risk
- Better bone health
- Decreased metabolic syndrome
- Improved cognition
- Improved mood
- Improved pain control

participating in an exercise program. Prescribing an appropriate exercise program for a person with chronic pain requires an understanding of the person's biopsychosocial circumstances, an armamentarium of different exercise techniques, and good communication with the therapy team.

PATIENT EVALUATION OVERVIEW

Exercise has been found to be beneficial for patients with a wide variety of chronic pain diagnoses including arthritis, fibromyalgia, complex regional pain syndrome (CRPS), chronic neck pain, and chronic low back pain. No matter what the specific diagnosis, the patient evaluation must include an assessment of the biopsychosocial circumstances of the patient. A physical examination does not provide sufficient information. It is necessary to understand the patient's psychological state and beliefs about pain, health, and wellness. It is important to consider the goals of the exercise program (**Box 2**). Goals might be specific correction of impairments (eg, better range of motion), a reduction of disability (eg, walking without a cane), or improvement in participation (eg, return to work). Acute pain and chronic pain present different challenges. In the case of acute injury, assessment includes analysis of functional biomechanical deficits including muscular weakness, inflexibility, scar tissue, muscle strength imbalance, poor coordination, and decreased endurance. Treatment addresses these specific biomechanical deficits through a specifically tailored exercise program. Pain is often a useful guide for determining the intensity and frequency of exercise activities.

A patient with chronic pain may have all of the functional biomechanical deficits and in addition may be dealing with excessive deconditioning, fear-avoidance, depression, centrally mediated pain, loss of role in family and society, and entrenched

Box 2**Exercise goals**

- Specific correction of impairments (eg, better range of motion)
- Reduction of disability (eg, walking without a cane)
- Improvement in participation (eg, return to work)
- Pain control
- Medical benefits

disability. There has typically been a progressive loss of function and diminishing quality of life. Exercise intervention needs to address the biomechanical issues but must do so in the context of these other complicating conditions. Pain is typically a poor guide for determining the frequency and intensity of exercise. Education of the patient plays an important role in facilitating their participation in an exercise program. This education needs to be about the specific biomechanical issues, about the functioning of the nervous system, and about the psychosocial conditions that contribute to the person's pain and disability.

HOW DOES EXERCISE AFFECT PAIN?

It is not always clear what it is about an exercise program that brings benefit to the patient. Exercise impacts the musculoskeletal system, the cardiovascular system, and the brain. The effects on the brain include impact on sensory processing, and improved motor coordination and cognitive and emotional functioning. For the chronic pain patient the impact on the brain may be the most important for improving the patient's function and sense of well-being. A variety of research studies have demonstrated the impact of exercise on the brain. For example, exercise is an effective treatment of depression, which frequently accompanies chronic pain.¹ Research has also shown that specifically targeted exercise programs can improve chronic pain and function, but changes in pain do not correlate well with improvement in physical measures, suggesting that it may be something other than the change in musculoskeletal function that is mediating the pain relief.²

Pain perception is brought about by a complex interaction between peripheral nociceptive input and modulatory processes at the spinal and supraspinal level. The nervous system has an endogenous pain modulatory system that has inhibitory and facilitatory functions. Pain modulation occurs in cortical, hypothalamic, midbrain, and brainstem structures, and in the spinal cord. The peripheral nervous system also modulates pain perception. Multiple neurotransmitters are involved in pain perception and pain modulation.³⁻⁵ Studies have been done in animals and humans to try to elucidate the impact of exercise on pain perception and on this endogenous pain modulatory system.

Animal studies have addressed the effects of exercise in models of acute pain and chronic neuropathic pain. Stagg and colleagues⁶ evaluated the effect of repeated aerobic exercise on a neuropathic pain model in the rat. They demonstrated that sensory hypersensitivity in a sciatic nerve ligation model of neuropathic pain was reversed by regular moderate aerobic exercise (forced treadmill running). These effects were reversed by naloxone suggesting that endogenous opioids play a role in modulating pain perception in response to exercise. Chen and colleagues⁷ studied a rat model of acute postoperative mechanical hypersensitivity caused by skin/muscle incision and retraction. They looked at the effect of 5 day per week treadmill running for 4 weeks on behavioral markers of pain and on levels of substance P and cytokines in the dorsal root ganglion. They demonstrated that mechanical hypersensitivity was alleviated by the treadmill running and was associated with suppression of excess substance P and inflammatory cytokines in the dorsal root ganglion. Mazzardo-Martins and colleagues⁸ showed an antinociceptive effect of a swimming exercise in a chemical behavioral model of nociception in mice. This antinociceptive effect was blocked by naloxone and by an inhibitor of serotonin synthesis suggesting that this effect was mediated by the opioid and serotonergic systems. Martins and colleagues⁹ studied a mouse model of CRPS-1 and evaluated the effect of high-intensity swimming on mechanical allodynia. There was marked mechanical allodynia

in this model of CRPS-1. High-intensity exercise significantly reduced the allodynia shortly after exercise (30 minutes) and at a delayed evaluation (24 hours). They further demonstrated the role of the opioid systems and the adenosine systems in mediating this response.

Multiple studies in humans have looked at the relationship between physical activity and pain sensitivity. Improved pain control is associated with exercise for a variety of painful conditions¹⁰ including chronic low back pain,^{11,12} fibromyalgia,¹³ osteoarthritis,¹⁴ neuropathic pain,¹⁵ and CRPS.¹⁶ Various studies of healthy individuals have demonstrated a relationship between a person's participation in general physical activity and aerobic exercise and his or her tolerance to pain.¹⁷ Ellingson and colleagues¹⁸ studied a group of healthy women using self-reported and accelerometer measures to determine their degree of sedentary versus active behavior and evaluated the relationship between levels of physical activity and average intensity and unpleasantness of a heat pain stimulus. They found that those participants who met physical activity recommendations (moderate intensity aerobic activity for minimum of 150 minutes per week or vigorous aerobic activity for minimum of 75 minutes per week) had significantly lower pain unpleasantness ratings and pain intensity ratings to noxious thermal stimuli than the participants who did not meet this activity level. Delfa de la Morena and colleagues¹⁹ studied a more localized hypoalgesic response to exercise. They evaluated the effect of repeated eccentric exercise at high intensity on pressure pain thresholds of the wrist extensors in healthy subjects. They demonstrated that an initial bout of high-intensity eccentric exercise resulted in delayed-onset muscle soreness and lowered pressure pain thresholds 24 hours postexercise consistent with hyperalgesia. Subjects underwent a second bout of eccentric exercise after 7 days. The subjects had delayed-onset muscle soreness after this second bout of exercise, but did not show lowered pain pressure thresholds indicating that there had been adaptations that limited the local hyperalgesia. The authors speculated that a combination of neural, mechanical, and cellular adaptations were responsible for this change. Naugle and colleagues²⁰ sought to determine an intensity threshold for aerobic exercise-induced hypoalgesia. They studied the immediate impact on healthy young men and women of moderate (50% heart rate reserve) and vigorous (70% heart rate reserve) aerobic exercise on pressure and heat pain modulation. Both moderate and vigorous exercise was associated with reduced pain intensity to heat stimulus, and there was a dose response effect with more reduction in pain intensity after vigorous exercise. Vigorous exercise also led to increased pressure pain thresholds.

Researchers have sought to determine how exercise impacts the pain modulatory processes in the central nervous system. Naugle and Riley²¹ studied healthy adults and looked at the relationship between self-reported physical activity and pain facilitatory and inhibitory function. They used tests of temporal summation to evaluate pain facilitation and conditioned pain modulation to evaluate endogenous pain inhibition. They found that levels of total and vigorous physical activity predicted pain facilitation and inhibition.²¹ Meeus and colleagues²² also used temporal summation and conditioned pain modulation to evaluate exercise-induced analgesia in female patients with rheumatoid arthritis, chronic fatigue syndrome, and fibromyalgia and sedentary healthy control subjects. Pain assessment was done before and after submaximal exercise on a bicycle ergometer at 75% age-predicted maximal heart rate for up to 15 minutes. The patients with rheumatoid arthritis demonstrated exercise-induced analgesia expressed by reduced temporal summation of experimental pain. Paracetamol reinforced this response to exercise. The patients with chronic fatigue and fibromyalgia had a less clear response with different responses at different experimental pain locations, suggesting that their endogenous pain modulating system is

dysfunctional. Ellingson and colleagues²³ tried to determine if conditioned pain modulation was responsible for exercise-induced hypoalgesia. They studied healthy subjects and evaluated heat pain intensity and unpleasantness at rest, after nonpainful aerobic cycling exercise, and after painful aerobic cycling exercise. Both exercise conditions resulted in decreased pain responses, although with a larger magnitude response in the painful, more intense exercise condition. These studies suggest that conditioned pain modulation plays a role in exercise-induced analgesia, but that other mechanisms also contribute.

Studies of motor cortex stimulation allow the evaluation of the hypoalgesic effects of activation of the motor cortex without the concomitant action of the musculoskeletal and cardiovascular systems. All exercise involves motor cortex activation and several studies have tried to evaluate the role that the motor cortex plays in exercise-induced analgesia. Yeziarski and coworkers²⁴ studied the effect of electrical stimulation of the motor cortex in primates showing inhibition of the spinal neuronal responses to noxious pressure and pinch stimuli. A study of transcranial magnetic stimulation of the motor cortex in patients with chronic neuropathic pain using PET imaging for evaluation showed that stimulation induced activity during and after stimulation in multiple brain regions including sensory pathways known to be involved in pain processing. Pain relief correlated with regional blood flow changes.²⁵ A recent randomized, sham-controlled trial of repetitive transcranial magnetic stimulation of the motor cortex in chronic myofascial pain showed significant reduction in daily pain scores and enhanced corticospinal inhibition.²⁶ These studies all suggest that activation of the motor cortex contributes to activation of endogenous pain modulatory systems.

There is evidence, however, that endogenous pain modulatory systems may be dysfunctional in at least some chronic pain states. Knauf and Koltyn²⁷ studied the effect of isometric exercise on pain perception in patients with diabetes with and without diabetic neuropathy. They assessed exercise-induced muscle pain and used an experimental thermal pain protocol to assess temporal summation. Patients with diabetes with and without diabetic peripheral neuropathy performed isometric exercise (grip) at 25% maximum voluntary contraction for 3 minutes. Exercise-induced muscle pain was significantly higher in the patients with peripheral neuropathy and they also rated the exercise as more effortful. Temporal summation was assessed in both groups before exercise and was found to be present in both groups with increasing pain ratings with repeated stimulation. After exercise the patients without peripheral neuropathy showed no temporal summation indicative of the presence of exercise-induced hypoalgesia. The patients with peripheral neuropathy continued to have temporal summation and did not seem to gain any pain-relieving benefit from the exercise.²⁷ Naugle and colleagues²⁸ summarized the hypoalgesic effects of exercise in healthy and chronic pain populations in a meta-analytic review. The studies reviewed evaluated the impact of acute exercise on experimentally induced noxious stimulation. Different exercise modalities were studied including aerobic, isometric, and dynamic resistance exercise. Both healthy populations and various chronic pain populations were studied. In the healthy populations the evidence supports that all three types of exercise decrease the perception of experimentally induced pain. In the chronic pain populations the results were more mixed depending on the particular chronic pain condition being studied. For chronic low back pain, findings were similar to healthy participants. For patients with regional chronic pain, exercise of muscles outside the painful region reduced pressure sensitivity of the painful area, but exercise of the painful muscles tended to increase pain sensitivity in those muscles. In fibromyalgia, low-to-moderate intensity activity seems to be effective for eliciting exercise-induced hypoalgesia. However, in some studies of individuals with widespread pain,

moderate-to-vigorous activity led to hyperalgesia. Nijs and colleagues²⁹ also reviewed the literature and came to similar conclusions.

In summary, the literature supports that acute bouts of exercise consistently activate the endogenous pain modulatory systems in healthy adults and have mixed effects on patients with chronic pain depending on the specific diagnosis and type of exercise. The mechanisms involved in exercise-induced hypoalgesia are multifactorial. Likely important contributors to the effect include the release of endogenous opioids and activation of spinal and supraspinal pain inhibitory pathways.

EXERCISE EFFECTS ON SPECIFIC CHRONIC PAIN PROBLEMS

The role of exercise prescribed in a therapeutic manner for the management of a variety of chronic pain conditions has been widely studied. These studies frequently assess function and quality of life, and pain. The effects of exercise for a few of these conditions are summarized next.

Fibromyalgia

Many researchers have evaluated the effects of exercise on patients with fibromyalgia. A 2007 systematic review of 34 studies showed moderate-quality evidence that moderate-intensity aerobic-only exercise training for 12 weeks has positive effects on global well-being, physical function, and possibly on pain and tender points. Results of strength training were less clear, but may improve symptoms of fibromyalgia including improvement in pain and tender points.³⁰ A 2013 review evaluated the effect of resistance training for managing fibromyalgia. Only five studies met the inclusion criteria. The conclusion was that resistance training was better than a control group for improvement in a multidimensional assessment of function, self-reported physical function, tenderness, and muscle strength. Pain improvement favored aerobic exercise rather than resistance exercise.³¹ Hooten and colleagues³² compared aerobic with strengthening exercise in the context of an interdisciplinary pain management program. Both groups improved in pain severity, strength, pain threshold, and peak oxygen consumption. The only difference between the two groups was a greater increase in oxygen consumption in the aerobic exercise group. McLoughlin and colleagues³³ used functional MRI to evaluate the relationship between physical activity and brain responses to pain in subjects with fibromyalgia. Their results suggested that the fibromyalgia patients who were physically active better preserved their ability to modulate pain compared with their less active peers. In summary, both aerobic and strength training programs are beneficial. However, performing exercise too intensely can precipitate a flare up of symptoms. Therefore, starting at low levels at which the patient can be successful and progressing gradually is more likely to promote benefit from exercise and longer-term adherence to an exercise program.³¹

Osteoarthritis

A wide variety of exercise approaches for osteoarthritis have been studied. A 2012 review of the effectiveness of different exercise approaches for osteoarthritis found strong evidence that aerobic and strengthening exercise programs were beneficial for patients with mild-to-moderate knee and hip osteoarthritis, improving pain and physical function.¹⁴ This comprehensive review did not find differences between types of exercise programs, showing similar improvements in response to aerobic versus strengthening regimens, similar improvements from high- versus low-resistance training, and from dynamic versus isometric training. Bennell and colleagues³⁴ studied the effect of hip-strengthening exercises on people with medial knee osteoarthritis and

varus malalignment, evaluating the impact on pain and function and also the impact on the knee adduction moment. Measures of pain, physical function, and muscle strength improved, but there was no change in knee adduction moment. So, even when exercise does not correct a presumed biomechanical deficit, it can still prove beneficial for improving pain and function. Not surprisingly the benefits of exercise for the patient with osteoarthritis seem to be maintained only as long as the patient continues to participate in an exercise program.^{35,36} As with other chronic pain conditions, evaluating the barriers and facilitators of exercise participation is important in guiding exercise prescription to help the patient commit to and participate in ongoing exercise activity.³⁷

Complex Regional Pain Syndrome

Exercise intervention for CRPS does not always follow traditional exercise models. The focus of recent studies has been on a process of graded motor imagery (GMI), which is an approach that starts with strategies to activate the motor cortex without actually using muscles. This approach is described by Moseley³⁸ in a 2004 randomized controlled trial on patients with upper extremity CRPS. The GMI program consisted of three phases. First, participants were shown pictures of hands, and were asked to identify whether each pictured depicted a right hand or a left hand. Then they imagined performing actions shown in pictures of hands. Finally, they engaged in mirror therapy. Participants in the 6-week GMI program demonstrated improved pain ratings and decreased edema compared with the control group.³⁸ A systematic review in 2009 concluded that GMI should be used to reduce pain in adults with CRPS-1.³⁹ A more recent systematic review by Cossins and colleagues⁴⁰ identified trials showing temporary benefit from repetitive transcranial magnetic stimulation on pain levels and strong evidence for GMI. Sherry and colleagues¹⁶ studied the effect of an intensive exercise program of 14 days mean duration, 5 to 6 hours per day in children with CRPS-1. The treatment philosophy was to re-establish normal use of the affected limb as quickly as possible, primarily through aerobic exercise training. Patients also underwent desensitization. Three-quarters of the families were referred for psychological counseling. A total of 92% of patients had initial complete resolution of pain and return to full function. At long-term follow-up (available for approximately 50% of participants) after a mean of 5 years, 3 months, 88% had no symptoms of CRPS. This type of intense exercise treatment has not been studied in adults with CRPS.

NONSPECIFIC LOW BACK PAIN

The effects of exercise on chronic, nonspecific low back pain have been widely studied. There are many approaches to exercise for back pain including specific exercise protocols targeting specific impairments, general exercise protocols, mind/body techniques of motor control, and multidisciplinary pain management and functional restoration. A 2010 review of 37 randomized controlled trials found that exercise therapy for low back pain, compared with usual care, decreased pain intensity and improved disability and long-term function. There was no evidence that one particular type of exercise was better than another.⁴¹ Mannion and colleagues^{42,43} noted a similar difficulty in demonstrating significant differences in outcomes from different exercise approaches to chronic nonspecific low back pain. Smith and Grimmer-Somers⁴⁴ summarized evidence of the long-term effectiveness of exercise therapy for chronic low back pain. In reviewing 15 trials using various exercise approaches, they found evidence of ongoing pain reduction and decreased recurrence rates up to 6 months

after treatment. Some of the evidence for different exercise approaches for chronic low back pain is summarized next.

Specific Exercise Protocols Targeting Specific Impairments (Spine Stabilization, Direction Specific)

Spine stabilization exercises are commonly prescribed for patients with acute, sub-acute, and chronic low back pain. The goal of this exercise approach is to restore segmental movement and motor control during static and dynamic functional activities. Studies support that these types of exercises have immediate short-term benefit, but limited long-term benefit beyond that of a general exercise program.^{45–47} Research has not shown that it is the specific musculoskeletal outcome of the exercise that is causing the benefit to the patient. Mannion and colleagues² evaluated the effect of spine stabilization treatment on the voluntary and anticipatory activation of the transverse abdominus before and after 9 weeks of spine stabilization treatment. Outcome measures included pain and disability as measured by the Roland Morris disability score. They found that pain and disability improved. Voluntary, but not anticipatory activation of the transverse abdominus improved. However, there was no correlation between the change in abdominal muscle function and change in disability. Only the reduction in catastrophizing and fingertip-to-floor distance contributed to the variance in the Roland Morris scores. Lomond and colleagues⁴⁸ found that general trunk strengthening exercises and specific exercises targeting the trunk stabilizers produced significant improvement in pain and function at 11 weeks and at 6 months after treatment in subjects with chronic low back pain. Muscle activation patterns were similar in the two groups after treatment, but notably were still different from activation patterns in control subjects without low back pain. Wang and colleagues¹¹ in a meta-analysis of core stability exercise versus general exercise for chronic low back pain found that the stability exercise was more effective at improving pain and disability in the short term, but no significant differences for pain were seen at 6 or 12 months. Steiger and colleagues⁴⁹ in a 2012 systematic review asked the question of whether improvements in pain and self-reported disability were contingent on improvement in targeted aspects of performance. Their review included 16 trials, which included a variety of performance measures including mobility, trunk extension strength, trunk flexion strength, and back muscle endurance. They did not find evidence that changes over the course of exercise treatment in these specific parameters were related to changes in pain and self-reported disability.

Another common approach is an exercise protocol based on directional preference, such as the McKenzie approach. These exercises are based on the patient's "directional preference," which is determined by identifying a posture or repeated end range movement in a single direction that immediately decreases midline lumbar pain or reduces referred extremity symptoms. Patients are also instructed in body mechanics and posture. Studies have shown benefit in the very early part of treatment, the first few weeks, but again no consistent benefit in the long term over intensive strengthening, or advice to stay active.^{50,51} Hosseinifar and colleagues⁵² compared stabilization exercise with McKenzie exercises looking at pain, disability, and stabilizing muscle thickness. Both exercises improved pain equally, although the stabilization exercises improved disability and muscle thickness more. However, the patients doing the McKenzie exercises were randomized to this group and did not perform the exercises based on their particular directional preference. Long and coworkers⁵³ evaluated the benefit of directional preference-based treatment comparing the effect of treatment matched to patient directional preference with treatment that was not matched. They excluded patients who had been off work for more than a year because

of their back pain, but otherwise did not specify whether the patients had acute, sub-acute, or chronic pain. Patients without a directional preference (26% of the initial sample) were excluded from the study. Patients were randomized to matched directionally based care, opposite directionally based care, or evidence-based care consisting of multidirectional, midrange lumbar exercises and stretches for hip and thigh muscles. Over the 2-week trial period, all three treatment groups improved in measures of pain and function. However, the directionally matched group improved significantly more than either of the other groups and also had significantly greater satisfaction with care.⁵³

General Exercise Protocols (General Flexibility, Strength and Endurance Training)

General exercise protocols addressing general flexibility, strength, and endurance training have all been used for management of chronic low back pain. A 2005 meta-analysis by Hayden and colleagues⁵⁴ found low-to-moderate evidence for the effectiveness of exercise in general for managing chronic low back pain, but the exercise protocols varied over the studies reviewed so it is difficult to point to any one specific treatment as being better than another. Mannion and colleagues^{42,43} compared active physical therapy, muscle reconditioning, and low-impact aerobics in patients with chronic low back pain and found that they were equally effective in reducing pain intensity, pain frequency, and disability. These benefits were maintained at long-term follow-up. A systematic review of the effectiveness of walking for low back pain was limited by the number and the quality of the studies. It showed low-to-moderate evidence that walking is an effective intervention strategy for low back pain.⁵⁵

Mind/Body Techniques of Motor Control (Yoga, Alexander Technique, Tai Chi)

In recent years there has been increasing interest in movement approaches other than traditional physical therapy. Although these various approaches may not always fit the common definition of exercise, they all involve whole body movement with an emphasis on mind-body integration and improvement in subtle aspects of motor control. Yoga, Tai Chi, and the Alexander Technique are examples of this nontraditional approach to movement and exercise but do not represent all of the different techniques available.

Several studies of yoga for chronic pain conditions have demonstrated more effectiveness than minimal intervention, such as a self-care book. Cramer and colleagues⁵⁶ did a randomized controlled trial of a 9-week yoga course versus a self-care manual of home-based exercises for neck pain for patients with nonspecific neck pain. They found that the yoga group demonstrated greater relief of their neck pain, less disability, improved health-related quality of life, and improved pressure pain thresholds. Tekur and colleagues⁵⁷ studied the effects of a 7-day residential program of yoga that included specific poses for back pain and meditation, yogic counseling, and lectures on yoga philosophy. The control group participated in physical therapy exercises for chronic pain and counseling and education sessions. Both groups improved in ratings of pain, depression, and spinal mobility but the improvement was greater in the yoga group. Because of the comprehensiveness of the yoga intervention in this study it is hard to know if it is the specific physical activities that are effective or some combination of the physical, counseling, and educational interventions. Sherman and colleagues⁵⁸ randomized adults with chronic low back pain to 12 weekly yoga classes, conventional stretching exercises, or a self-care book. The yoga classes and the stretching provided benefits including better function and decreased symptoms compared with the self-care book. The benefits lasted several months. A 2013 meta-analysis of yoga including eight randomized controlled trials found a

medium-to-large effect on pain and functional disability. This improvement was seen despite a wide range of styles and duration of treatment. However, the lack of active control groups made it difficult to assess if yoga had benefit over traditional exercise programs.⁵⁹

The Alexander Technique is a movement education technique that teaches skills for observing the subtleties of overall habits of movement and movement coordination and teaches patients to change their habits of movement and movement patterns to facilitate more efficient movement and better coordination. A large 2008 study compared normal care (control), 6 versus 24 Alexander Technique lessons, six sessions of massage, and an exercise prescription from a doctor with behavioral counseling delivered by a nurse. The main outcome measure was function as measured by the Roland Morris disability score and the number of days in pain. Outcomes were measured at 3 months and 12 months. The researchers found benefit in function and number of days in pain at 3 and 12 months from 6 or 24 Alexander Technique lessons, with the 24 lessons having a larger effect. Six lessons combined with aerobic exercise prescription was nearly as effective as 24 lessons. Although massage provided some benefit at 3 months this was not sustained at long-term follow-up. One of the strengths of this study was the number of participants (579) and the setting including multiple different Alexander Technique teachers.⁶⁰

Tai Chi is a gentle exercise technique that incorporates balance, body awareness, strength, and stretching through repeated patterns of movement that are done slowly and continuously, without strain. Hall and colleagues⁶¹ studied a group of 160 volunteers with persistent nonspecific low back pain. The Tai Chi group participated in 18 Tai Chi sessions over 10-weeks in a group setting. The control group was waitlisted and continued their usual health care. The group that participated in Tai Chi had better improvements than the control group in pain intensity, bothersomeness of symptoms, and self-reported disability. The findings were of a similar magnitude to those found in studies of other exercise interventions for chronic low back pain. They were also statistically significant and clinically meaningful even though only 57% of the participants attended 50% or more of the Tai Chi sessions. A total of 75% of participants said they believed the results were worthwhile.

Multidisciplinary Pain Management Programs/Functional Restoration

Multidisciplinary pain programs, also referred to as functional restoration, are programs of intensive daily treatment that includes quota-based exercise targeting improving strength, stamina, flexibility, and functional abilities. Treatment is typically for 6 to 8 hours per day over the course of 3 to 4 weeks. Treatment includes several hours of active therapy and educational sessions and cognitive behavioral therapy. Medication management is often an important component. This approach to the chronic pain patient with entrenched disability was pioneered by Dr Wilbert Fordyce. In a 1973 article, Dr Fordyce and colleagues⁶² described using the approach for selected patients in whom pain was viewed as a learned behavior. The goal of treatment was to diminish pain behaviors and increase well-behaviors and function. Their subjects showed significant improvement in time spent up (not reclining), in distance walked, and exercise tolerance and decreased pain medication use. In the 40 years since this study, there have been multiple studies, meta-analyses, and systematic reviews assessing the benefit of this type of comprehensive treatment with a clear conclusion that this treatment provides benefit for reducing disability, reducing fear-avoidance, decreasing pain, enhancing quality of life, and facilitating return to work.^{63–69} Monticone and colleagues⁷⁰ found persistence of benefits at 1 year posttreatment.

EXERCISE PRESCRIPTION AND GUIDELINES

From the previous review, it is clear that patient outcomes are better for those patients who exercise than for those who do not. However, based on the data, it can be hard to know exactly which exercise intervention one should choose. The specifics of the exercise regimen likely matter less than the way in which exercise is prescribed and taught and the supportiveness of the environment. If you can get your patients moving, they will typically feel better eventually. The key to effective exercise prescription for chronic pain is identifying and promoting strategies that facilitate actual participation in exercise.

There are multiple barriers to exercise participation for patients with chronic pain (Box 3). These can be divided into patient factors, environmental factors, and health care–delivery factors. Patient barriers include pain, fear-avoidance, excessive deconditioning, lack of education and understanding about the benefit of exercise, lack of education and understanding about the neurophysiology of pain and central sensitization, strong beliefs that exercise can be harmful, depression, potential dysfunctional endogenous pain modulation, and lack of self-efficacy. Environmental factors include

Box 3

Barriers to exercise participation

Patient factors

- Pain, particularly centrally mediated pain
- Dysfunctional endogenous pain modulation
- Fear-avoidance
- Excessive deconditioning
- Lack of education and understanding about the neurophysiology of pain and central sensitization
- Strong beliefs that exercise can be harmful
- Depression
- Lack of self-efficacy

Environmental factors

- Lack of access to a place to exercise
- Perceived or real lack of time to exercise
- Lack of support for exercise from family and work place
- Variable accessibility of appropriate health care providers

Health care delivery factors

- Overly strong focus on the biomedical model of pain
- Lack of attention to the psychological and central nervous system contributions to pain
- Lack of coordination of care between the physician and therapist
- Poor communication between health care providers and patients regarding the value and importance of exercise
- Poor education of the patient about the meaning of pain
- Lack of sufficient supervision so that the patient feels safe exercising and understands appropriate strategies for progressing exercise

lack of access to a place to exercise, perceived or real lack of time to exercise, lack of support for exercise from family and work place, and variable accessibility of appropriate health care providers. Health care–delivery factors include overly strong focus on the biomedical model of pain with lack of attention to psychological and central nervous system contributions to pain, lack of coordination of care between the physicians prescribing the exercise and the therapist carrying out the prescription, poor communication between health care providers and patients regarding the value and importance of exercise, poor education of the patient about the meaning of pain, and lack of sufficient supervision so that the patient feels safe exercising and understands appropriate strategies for progressing exercise activities. When prescribing exercise, these barriers need to be recognized and addressed.

Exercise prescription for the chronic pain patient needs to attend to the functional biomechanical issues, the cognitive-behavioral issues, and the functioning of the endogenous pain modulatory system to be successful. The patient evaluation should identify if there are specific biomechanical deficits to be addressed, such as lack of flexibility, strength deficits, endurance deficits, or problems with balance and motor control. This evaluation allows the provider to identify the types of specific exercise (eg, aerobic, strength training, stretching, balance, motor control) that will be helpful for correcting these deficits. Patients need specific, detailed advice about the intensity, frequency, and duration of exercise. For example, they need advice about how long to hold a stretch, how many repetitions to do, and how many repetitions to increase. They need to know which qualities of movement to focus on (eg, speed, accuracy, power, or range of motion). They need to understand what system should be used to determine progression of exercise. Should progression be guided by symptoms; by physiologic parameters, such as heart rate; or by quota-based guidelines? Guidelines for progression may be different for different aspects of an exercise program. For example, a patient with upper extremity CRPS may be able to progress aerobic activity on a stationary bike according to physiologic parameters, but need to progress the GMI program for the upper extremity based on symptoms. Giving patients a variety of exercises that address their needs, from which they can choose, adds flexibility to the program and a better sense of control for the patient.

Evaluation should also identify the patient's beliefs and understanding about their pain problem. Most patients with chronic pain still believe that there is a specific problem in their body producing nociceptive input that is driving their pain. They typically believe that if something causes pain, then it is dangerous. Unless these beliefs can be changed, it is unlikely that a patient will persevere enough with an exercise program to succeed. Neuroscience education is a strategy that has shown efficacy for changing patient beliefs and facilitating exercise participation. Louw and colleagues⁷¹ in a 2011 systemic review of eight studies of the effect of neuroscience education for patients with chronic musculoskeletal pain found "there is compelling evidence that an educational strategy addressing neurophysiology and neurobiology of pain can have a positive effect on pain, disability, catastrophization, and physical performance." A practical description of this approach is available from several authors.^{72–74}

Education about fear-avoidance has also shown benefit for increasing activity participation. Fear-avoidance promotes persistent pain experience and disability. In the fear-avoidance model, injury leads to a pain experience that in the presence of negative affect and frightening illness information causes pain catastrophizing. This leads to pain-related fear, avoidance (of activity) and hypervigilance (regarding symptoms), disuse, depression, and disability, all of which contribute to an ongoing pain experience.⁷⁵ A quota-based approach to exercise with fear-avoidance education studied by Kernan and Rainville⁷⁶ led to functional gains and decreased kinesiophobia

and improved measures of disability in patients with chronic low back pain. In a primary care setting, education targeting fear-avoidance beliefs and encouraging activation for patients with chronic back pain led to sustained reductions in fear-avoidance beliefs, activity limitations caused by back pain, and days missed from usual activities caused by back pain.⁷⁷

Strategies to facilitate exercise adherence are also important. Cecchi and colleagues⁷⁸ found that exercise adherence almost doubled the probability of a favorable response to an exercise program at 1-year follow-up in chronic low back pain patients. Medina-Mirapeix and colleagues⁷⁹ assessed factors that predicted adherence to the frequency and duration components of a home exercise program in patients with nonspecific neck and low back pain. They found that self-efficacy (the belief in one's own ability to succeed in a particular situation, in this case exercise) was predictive of adherence to the frequency and duration aspects of a home exercise program. Similarly, Courneya and McAuley⁸⁰ found that self-efficacy was an important predictor of physical activity in a sample of young healthy adults. Medina-Mirapeix and colleagues also looked at how the interaction and communication between the physical therapist and the patient impacted home exercise adherence. They found that clarifying doubts and questions from the patient was associated with a higher likelihood of adherence to the recommended frequency of home exercise. Slade and colleagues⁸¹ did a review of patients' beliefs and perceptions about exercise for nonspecific low back pain. They concluded that people prefer and are more likely to participate in exercise activities designed with a consideration of their preferences and consistent with their circumstances, fitness level, and prior exercise experiences. They noted that people did not continue if the exercise program interfered with everyday life, seemed ineffective, or was too difficult to do. Good communication with the therapist was important to patients to allow for questions to be answered and to facilitate making the intervention relevant to the patient. Creating a consultative rather than prescriptive process was important to patients.

One of the barriers to self-efficacy with respect to exercise in the chronic pain patient is prior experience of aggravation of pain symptoms after engaging in exercise or other activity. The quota-based approach to exercise is very valuable for building patients' confidence that they can succeed with exercise (**Box 4**). This approach starts with identifying a baseline level of function that is achievable for the patient. The goal is to start at a level at which the patient can be successful. A rate of progression is determined that is safe and achievable. Each day's activity is based on the specific quota for that day and is not pain-contingent. It is emphasized to the patient that it is important to not do more when feeling good, or less when feeling bad. This approach to

Box 4**Quota-based reactivation**

- Identify a baseline level of function at which the patient can be successful
- Determine a rate of progression that is safe and achievable
- Do ONLY what is on the schedule for the day, not more if feeling good, or less if feeling bad
- Activity levels are NOT pain-contingent, but based on the predetermined quota for the day
- If patient falls off the progression, go back to an achievable level and resume the process
- Goal is to remove pain as the guiding control of activity and replace control with a rational process that determines a reasonable activity level

exercise has demonstrated effectiveness for patients with chronic low back pain. It allows patients to be successful and therefore build confidence and have reduced fear of reinjury with exercise. This process helps to break patients out of the fear-avoidance cycle.⁷⁶ As patients are successful with exercise, their self-efficacy with regard to exercise increases.

Box 5 summarizes decisions to be made when prescribing exercise. An effective exercise prescription starts with education of the patient focusing on neuroscience education so that they better understand the meaning of their pain and also understand the benefits of exercise for improving their pain modulating system. Education must also include specific, detailed exercise recommendations so that the patient understands exactly what they are supposed to do and so that they understand that the exercise activities are safe and are not going to put them at risk of injury or reinjury. Patients typically need frequent reassurance from the physician and the therapist. To prevent confusion, the physician and therapist need to communicate regularly so that the patient is getting the same message from all members of their treatment team. Specific exercise choice needs to make biomechanical sense, but also needs to meet the needs and preferences of the patient. Exercise intensity needs to start at a level and progress at a rate at which the patient can be successful. Through this process the patient learns to differentiate important pain (pain that should be attended to) from unimportant pain (pain that is not providing information about injury or potential for injury). This knowledge allows them to persevere in their exercise activity even when it does not immediately relieve their pain and especially when it flares up their symptoms. Over time, the improvements in strength, flexibility, conditioning, and body mechanics gained through exercise diminish the risk of reinjury and diminish fear-avoidance by helping patients feel in control of their bodies and safe in their daily activities.

SUMMARY

Although there is a lot of research evidence that exercise is helpful for a multitude of chronic pain conditions, it has been difficult to clearly demonstrate the superiority of one approach over another. The benefit of exercise for pain control likely comes

Box 5

Decisions to make when prescribing exercise

- Does the program need to address specific biomechanical deficits?
- What types of exercise will be helpful and accepted by the patient?
- What dose of exercise is recommended including intensity, frequency, and duration?
- What quality of movement should be emphasized? Speed, accuracy, power, range of motion?
- What system for progressing exercise? Guide by symptoms? Physiologic changes? Quota-based?
- Are there a range of exercises that can be useful to give the patient as much choice as possible?
- What education does the patient need and who will provide it?
- If multidisciplinary care is needed, but not available, how can the physician and the therapist facilitate a behavioral approach?

from the impact of exercise on the endogenous opioid system and on central pain modulatory systems. Patients with some chronic pain conditions seem to have a dysfunctional endogenous pain modulatory system, which should be considered when prescribing exercise. The prescription of exercise for chronic pain must address the biomechanical issues and the psychosocial factors that contribute to the patient's pain and disability. Patient education, coordination of care within the health care team, and selecting an exercise regimen that is meaningful to and achievable by the patient are all important components to promote a successful rehabilitation program.

REFERENCES

1. Blumenthal JA, Babyak MA, Doraiswamy PM, et al. Exercise and pharmacotherapy in the treatment of major depressive disorder. *Psychosom Med* 2007; 69(7):587–96.
2. Mannon AF, Caporaso F, Pulkovski N, et al. Spine stabilisation exercises in the treatment of chronic low back pain: a good clinical outcome is not associated with improved abdominal muscle function. *Eur Spine J* 2012;21(7):1301–10.
3. Ness T, Randich A. Substrates of spinal cord nociceptive processing. In: Fishman SM, Ballantyne JC, Rathmell JP, editors. *Bonica's management of pain*. 4th edition. Baltimore (MD): Lippincott, Williams & Wilkins; 2010. p. 35–48.
4. Randich A, Ness T. Modulation of spinal nociceptive processing. In: Fishman SM, Ballantyne JC, Rathmell JP, editors. *Bonica's management of pain*. 4th edition. Baltimore (MD): Lippincott, Williams & Wilkins; 2010. p. 48–60.
5. Lorenz J, Hauck M. Supraspinal mechanisms of pain and nociception. In: Fishman SM, Ballantyne JC, Rathmell JP, editors. *Bonica's management of pain*. 4th edition. Baltimore (MD): Lippincott, Williams & Wilkins; 2010. p. 61–73.
6. Stagg NJ, Mata HP, Ibrahim MM, et al. Regular exercise reverses sensory hypersensitivity in a rat neuropathic pain model: role of endogenous opioids. *Anesthesiology* 2011;114(4):940–8.
7. Chen YW, Tzeng JI, Lin MF, et al. Forced treadmill running suppresses postincisional pain and inhibits upregulation of substance P and cytokines in rat dorsal root ganglion. *J Pain* 2014;15(8):827–34.
8. Mazzardo-Martins L, Martins DF, Marcon R, et al. High-intensity extended swimming exercise reduces pain-related behavior in mice: involvement of endogenous opioids and the serotonergic system. *J Pain* 2010;11(12):1384–93.
9. Martins DF, Mazzardo-Martins L, Soldi F, et al. High-intensity swimming exercise reduces neuropathic pain in an animal model of complex regional pain syndrome type I: evidence for a role of the adenosinergic system. *Neuroscience* 2013;234: 69–76.
10. Sullivan AB, Scheman J, Venesy D, et al. The role of exercise and types of exercise in the rehabilitation of chronic pain: specific or nonspecific benefits. *Curr Pain Headache Rep* 2012;16(2):153–61.
11. Wang XQ, Zheng JJ, Yu ZW, et al. A meta-analysis of core stability exercise versus general exercise for chronic low back pain. *PLoS One* 2012;7(12): e52082. <http://dx.doi.org/10.1371/journal.pone.0052082>.
12. Murtezani A, Hundozi H, Orovcanec N, et al. A comparison of high intensity aerobic exercise and passive modalities for the treatment of workers with chronic low back pain: a randomized, controlled trial. *Eur J Phys Rehabil Med* 2011;47(3): 359–66.
13. Busch AJ, Webber SC, Brachaniec M, et al. Exercise therapy for fibromyalgia. *Curr Pain Headache Rep* 2011;15:358–67.

14. Golightly YM, Allen KD, Caine DJ. A comprehensive review of the effectiveness of different exercise programs for patients with osteoarthritis. *Phys Sportsmed* 2012; 40(4):52–65.
15. Dobson JL, McMillan J, Li L. Benefits of exercise intervention in reducing neuropathic pain. *Front Cell Neurosci* 2014;8:102.
16. Sherry DD, Wallace CA, Kelley C, et al. Short- and long-term outcomes of children with complex regional pain syndrome type I treated with exercise therapy. *Clin J Pain* 1999;15(3):218–23.
17. Anshell MH, Russell KG. Effect of aerobic and strength training on pain tolerance, pain appraisal and mood of unfit males as a function of pain location. *J Sports Sci* 1994;12(6):535–47.
18. Ellingson LD, Colbert LH, Cook DB. Physical activity is related to pain sensitivity in healthy women. *Med Sci Sports Exerc* 2012;44(7):1401–6.
19. Delfa de la Morena JM, Samani A, Fernandez-Carnero J, et al. Pressure pain mapping of the wrist extensors after repeated eccentric exercise at high intensity. *J Strength Cond Res* 2013;27(11):3045–52.
20. Naugle KM, Naugle KE, Fillingim RB, et al. Intensity thresholds for aerobic exercise-induced hypoalgesia. *Med Sci Sports Exerc* 2014;46(4): 817–25.
21. Naugle KM, Riley JL 3rd. Self-reported physical activity predicts pain inhibitory and facilitatory function. *Med Sci Sports Exerc* 2014;46(3):622–9.
22. Meeus M, Hermans L, Ickmans K, et al. Endogenous pain modulation in response to exercise in patients with rheumatoid arthritis, patients with chronic fatigue syndrome and comorbid fibromyalgia, and healthy controls: a double-blind randomized controlled trial. *Pain Pract* 2014. <http://dx.doi.org/10.1111/papr.12181>.
23. Ellingson LD, Koltyn KF, Kim JS, et al. Does exercise induce hypoalgesia through conditioned pain modulation? *Psychophysiology* 2014;51:267–76.
24. Yezierski RP, Gerhart KD, Schrock BJ, et al. A further examination of effects of cortical stimulation on primate spinothalamic tract cells. *J Neurophysiol* 1983; 49(2):424–41.
25. Peyron R, Faillenot I, Mertens P, et al. Motor cortex stimulation in neuropathic pain. Correlations between analgesic effects and hemodynamic changes in the brain. A PET study. *Neuroimage* 2007;34(1):310–21.
26. Dall'Agnol L, Medeiros LF, Torres IL, et al. Repetitive transcranial magnetic stimulation increases the corticospinal inhibition and the brain-derived neurotrophic factor in chronic myofascial pain syndrome: an explanatory double-blinded, randomized, sham-controlled trial. *J Pain* 2014;15(8):845–55.
27. Knauf MT, Koltyn KF. Exercise-induced modulation of pain in adults with and without painful diabetic neuropathy. *J Pain* 2014;15(6):656–63.
28. Naugle KM, Fillingim RB, Riley JL 3rd. A meta-analytic review of the hypoalgesic effects of exercise. *J Pain* 2012;13(12):1139–50.
29. Nijs J, Kosek E, Van Oosterwijck JV, et al. Dysfunctional endogenous analgesia during exercise in patients with chronic pain: to exercise or not to exercise. *Pain Physician* 2012;15:ES205–13.
30. Busch AJ, Barber KA, Overend TJ, et al. Exercise for treating fibromyalgia syndrome. *Cochrane Database Syst Rev* 2007;(4):CD003786. <http://dx.doi.org/10.1002/14651858.CD003786.pub2>.
31. Busch AJ, Webber SC, Richards RS, et al. Resistance exercise training for fibromyalgia. *Cochrane Database Syst Rev* 2013;(12):CD010884. <http://dx.doi.org/10.1002/14651858.CD010884>.

32. Hooten WM, Qu W, Townsend CO, et al. Effects of strength vs aerobic exercise on pain severity in adults with fibromyalgia: a randomized equivalence trial. *Pain* 2012;153(4):915–23.
33. McLoughlin MJ, Stegner AJ, Cook DB. The relationship between physical activity and brain responses to pain in fibromyalgia. *J Pain* 2011;12(6):640–51.
34. Bennell KL, Hunt MA, Wrigley TV, et al. Hip strengthening reduces symptoms but not knee load in people with medial knee osteoarthritis and varus malalignment: a randomized controlled trial. *Osteoarthritis Cartilage* 2010;18(5):621–8.
35. Ettinger WH, Burns R, Messier SP, et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). *JAMA* 1997;277:25–31.
36. van Barr M, Dekker J, Oostendorp R, et al. Effectiveness of exercise in patients with osteoarthritis of the hip or knee: nine months follow up. *Ann Rheum Dis* 2001;60:1123–30.
37. Bennell KL, Dobson F, Hinman RS. Exercise in osteoarthritis: moving from prescription to adherence. *Best Pract Res Clin Rheumatol* 2014;28(1):93–117.
38. Moseley GL. Graded motor imagery is effective for long-standing complex regional pain syndrome: a randomized controlled trial. *Pain* 2004;108:192–8.
39. Daly AE, Bialocerkowski AE. Does evidence support physiotherapy management of adult complex regional pain syndrome type one? A systematic review. *Eur J Pain* 2009;13:339–53.
40. Cossins L, Okell RW, Cameron H, et al. Treatment of complex regional pain syndrome in adults: a systematic review of randomized controlled trials published from June 2000 to February 2012. *Eur J Pain* 2013;17:158–73.
41. van Middelkoop M, Rubinstein SM, Verhagen AP, et al. Exercise therapy for chronic nonspecific low-back pain. *Best Pract Res Clin Rheumatol* 2010;24:193–204.
42. Mannion AF, Muntener M, Taimela S, et al. A randomized clinical trial of three active therapies for chronic low back pain. *Spine (Phila Pa 1976)* 1999;24(23):2435–48.
43. Mannion AF, Muntener M, Taimela S, et al. Comparison of three active therapies for chronic low back pain: results of a randomized clinical trial with one-year follow-up. *Rheumatology* 2001;40:772–8.
44. Smith C, Grimmer-Somers K. The treatment effect of exercise programmes for chronic low back pain. *J Eval Clin Pract* 2010;16:484–91.
45. Liddle SD, Baxter GD, Gracey JH. Exercise and chronic low back pain: what works? *Pain* 2004;107:176–90.
46. Brennan GP, Fritz JM, Hunter SJ, et al. Identifying subgroups of patients with acute/subacute “nonspecific” low back pain: results of a randomized clinical trial. *Spine (Phila Pa 1976)* 2006;31:623–31.
47. Koumantakis GA, Watson PJ, Oldham JA. Trunk muscle stabilization training plus general exercise versus general exercise only: randomized controlled trial of patients with recurrent low back pain. *Phys Ther* 2005;85:209–25.
48. Lomond KV, Henry SM, Hitt JR, et al. Altered postural responses persist following physical therapy of general versus specific trunk exercises in people with low back pain. *Man Ther* 2014;19(5):425–32.
49. Steiger F, Wirth B, de Bruin ED, et al. Is a positive clinical outcome after exercise therapy for chronic non-specific low back pain contingent upon a corresponding improvement in the targeted aspect(s) of performance? A systematic review. *Eur Spine J* 2012;21:575–98.

50. Machado LA, de Souza MS, Ferrieira PH, et al. The McKenzie method for low back pain: a systematic review of the literature with a meta-analysis approach. *Spine (Phila Pa 1976)* 2006;31:E254–62.
51. Peterson T, Kryger P, Ekdahl C, et al. The effect of McKenzie therapy as compared with that of intensive strengthening training for treatment of patients with subacute or chronic low back pain: a randomized controlled trial. *Spine (Phila Pa 1976)* 2002;27:1702–9.
52. Hosseinifar M, Akbari M, Behtash H, et al. The effects of stabilization and McKenzie exercises on transverse abdominus and multifidus muscle thickness, pain and disability: a randomized controlled trial in nonspecific chronic low back pain. *J Phys Ther Sci* 2013;25(12):1541–5.
53. Long A, Donelson R, Fung T. Does it matter which exercise? A randomized control trial of exercise for low back pain. *Spine (Phila Pa 1976)* 2004;29(23):2593–602.
54. Hayden JA, van Tulder MW, Malmivaara AV, et al. Meta-analysis: exercise therapy for nonspecific low back pain. *Ann Intern Med* 2005;142(9):765–75.
55. Hendrick P, Te Wake AM, TikkiSETTY AS, et al. The effectiveness of walking as an intervention for low back pain: a systematic review. *Eur Spine J* 2010;19:1613–20.
56. Cramer H, Lauche R, Hohmann C, et al. Randomized-controlled trial comparing yoga and home-based exercise for chronic neck pain. *Clin J Pain* 2013;29:216–23.
57. Tekur P, Nagarathna R, Chametcha S, et al. A comprehensive yoga program improves pain, anxiety and depression in chronic low back pain patients more than exercise: an RCT. *Complement Ther Med* 2012;20(3):107–18.
58. Sherman KJ, Cherkin DC, Wellman RD, et al. A randomized trial comparing yoga, stretching, and a self-care book for chronic low back pain. *Arch Intern Med* 2011;171(22):2019–26.
59. Holtzman S, Beggs RT. Yoga for chronic low back pain: a meta-analysis of randomized controlled trials. *Pain Res Manag* 2013;18(5):267–72.
60. Little P, Lewith G, Webley F, et al. Randomised controlled trial of Alexander technique lessons, exercise, and massage (ATEAM) for chronic and recurrent back pain. *Br J Sports Med* 2008;42(12):965–8.
61. Hall AM, Maher CG, Lam P, et al. Tai Chi exercise for treatment of pain and disability in people with persistent low back pain: a randomized controlled trial. *Arthritis Care Res* 2011;63(11):1576–83.
62. Fordyce WE, Fowler RS Jr, Lehmann JF, et al. Operant conditioning in the treatment of chronic pain. *Arch Phys Med Rehabil* 1973;54:399–408.
63. Flor H, Fydrich T, Turk DC. Efficacy of multidisciplinary pain treatment centers: a meta-analytic review. *Pain* 1992;49(2):221–30.
64. Guzman J, Esmail R, Karjalainen K, et al. Multidisciplinary rehabilitation for chronic low back pain: systematic review. *BMJ* 2001;322:1511–6.
65. Proctor TJ, Mayer TG, Theodore B, et al. Failure to complete a functional restoration program for chronic musculoskeletal disorders: a prospective 1-year outcome study. *Arch Phys Med Rehabil* 2005;86(8):1509–15.
66. Kool JP, Oesch PR, Bachmann S, et al. Increasing days at work using function-centered rehabilitation in nonacute nonspecific low back pain: a randomized controlled trial. *Arch Phys Med Rehabil* 2005;86(5):857–64.
67. van Geen JW, Edelaar MJ, Janssen M, et al. The long-term effect of multidisciplinary back training: a systematic review. *Spine (Phila Pa 1976)* 2007;32(2):249–55.

68. Norlund A, Ropponen A, Alexanderson K. Multidisciplinary interventions: review of studies of return to work after rehabilitation for low back pain. *J Rehabil Med* 2009;41:115–21.
69. Mayer TG, Gatchel RJ, Brede E, et al. Lumbar surgery in work-related chronic low back pain: can a continuum of care enhance outcomes? *Spine J* 2014;14:263–73.
70. Monticone M, Ferrante S, Rocca B, et al. Effect of a long-lasting multidisciplinary program on disability and fear-avoidance behaviors in patients with chronic low back pain. Results of a randomized controlled trial. *Clin J Pain* 2013;29(11):929–38.
71. Louw A, Diener I, Butler D, et al. The effect of neuroscience education on pain, disability, anxiety, and stress in chronic musculoskeletal pain. *Arch Phys Med Rehabil* 2011;92:2041–56.
72. Nijs J, van Wilgen CP, Oosterwijck JV, et al. How to explain central sensitization to patients with “unexplained” chronic musculoskeletal pain: practice guidelines. *Man Ther* 2011;16:413–8.
73. Nijs J, Meeus M, Cagnie B, et al. A modern neuroscience approach to chronic spinal pain: combining neuroscience education with cognition-targeted motor control training. *Phys Ther* 2014;94:730–8.
74. Butler D, Moseley GL. *Explain pain*. Adelaide (Australia): NOI Group Publishing; 2003.
75. Vlaeyen JW, Linton SJ. Fear-avoidance model of chronic musculoskeletal pain: 12 years on. *Pain* 2012;153:1144–7.
76. Kernan T, Rainville J. Observed outcomes associated with a quota-based exercise approach on measures of kinesiophobia in patients with chronic low back pain. *J Orthop Sports Phys Ther* 2007;37(11):679–87.
77. Von Korff M, Balderson BH, Soudners K, et al. A trial of an activating intervention for chronic back pain in primary care and physical therapy settings. *Pain* 2005;113:323–30.
78. Cecchi F, Pasquini G, Paperini A, et al. Predictors of response to exercise therapy for chronic low back pain: result of a prospective study with one year follow-up. *Eur J Phys Rehabil Med* 2014;50:143–51.
79. Medina-Mirapeix F, Escolar-Reina P, Gascon-Canovas JJ, et al. Predictive factors of adherence to frequency and duration components in home exercise programs for neck and low back pain: and observational study. *BMC Musculoskelet Disord* 2009;10:155–63.
80. Courneya KS, McAuley E. Are there different determinants of the frequency, intensity, and duration of physical activity? *Behav Med* 1994;20(2):84–90.
81. Slade SC, Patel S, Underwood M, et al. What are patient beliefs and perceptions about exercise for non-specific chronic low back pain? A systematic review of qualitative studies. *Clin J Pain* 2014;30(11):995–1005. <http://dx.doi.org/10.1097/AJP.000000000000044>.