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Prescribing exercise interventions for patients with chronic conditions

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Exercise has been shown to be beneficial in the treatment of many chronic conditions. Mortality benefits from exercise are similar to pharmacologic interventions for secondary prevention of coronary heart disease, stroke rehabilitation, treatment for heart failure and prevention of diabetes.[1] The morbidity benefits of exercise for diseases that are not life-threatening, such as back pain and osteoarthritis, are substantial. However, exercise is underprescribed and frequently overlooked, often in favour of a pharmacologic or surgical intervention.[2–4]

Factors that contribute to underprescription of exercise interventions may include a lack of awareness among many clinicians and patients about the effectiveness of exercise interventions, poor knowledge about what comprises an effective exercise intervention, a lack of relevant training and educational opportunities available to medical practitioners,[4,5] and inadequate descriptions of exercise interventions in published trials and reviews. An analysis of 137 nonpharmacologic interventions from 133 trials found that 61% did not have sufficient information reported (e.g., procedural and intensity details) to enable replication in practice,[6] thus preventing clinicians from being able to prescribe these interventions. An analysis of the reporting of the exercise component used in cardiac rehabilitation trials found that adequate descriptions of the exercise schedule were missing for 58% of the interventions.[7]

We summarize evidence of benefit for using exercise for some key chronic conditions, highlight key outcomes shown to be influenced by exercise and provide a guide to the practical how-to details for an effective disease-specific exercise. We discuss conditions that were selected for their high disability burden[8] and the strength of the evidence for the effectiveness of exercise in managing the condition. The search process we used to locate the evidence presented in this paper is provided in Box 1.

Outcomes for which exercise is effective

We review the evidence for the effectiveness of exercise interventions for osteoarthritis of the hip and knee, chronic nonspecific low-back pain, prevention of falls, heart failure, coronary heart disease, chronic obstructive pulmonary disease (COPD), chronic fatigue syndrome and type 2 diabetes (Appendix 2, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.150684/-/DC1). We present the key clinical and health utilization outcomes that exercise interventions have been shown to affect and not affect in detail.

Simply prescribing exercise, in a generic sense, to a patient is insufficient guidance and is

Box 1: Evidence used in this review

We each contributed to the review by our specialty. We searched PubMed and the Cochrane Library for publications from 2000 to February 2015, using methodological filters (for systematic reviews and randomized controlled trials [RCTs]) and a combination of medical subject headings and free-text terms (Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.150684/-/DC1). The information presented in this article is based on evidence from systematic reviews, if available, or RCTs.

Key points

- Exercise is beneficial for many chronic conditions and can offer benefits that are comparable to pharmacologic interventions, yet exercise is underprescribed.
- Like medication and surgery, exercise is not a single entity and must be tailored to the condition. Exercise must be appropriately implemented to achieve outcomes that are consistent with those reported in intervention trials.
- To prescribe exercise for chronic conditions, clinicians must know sufficient details about the appropriate and effective exercise interventions and their components.
- We describe and discuss the evidence of effectiveness of exercise interventions for the following chronic conditions: osteoarthritis of the hip and knee, chronic nonspecific low back pain, prevention of falls, heart failure, coronary heart disease, chronic obstructive pulmonary disease, chronic fatigue syndrome and type 2 diabetes.

unlikely to achieve the desired outcomes. To help clinicians prescribe evidence-based exercise interventions, we provide practical details for some conditions in Boxes 2–4 (low-back pain, COPD, diabetes) and Appendices 3–6 (osteoarthritis, falls prevention, chronic fatigue syndrome, heart disease; available at www.cmaj.ca/lookup/suppl/doi/10.1503/cmaj.150684/-/DC1).[9–19] Where possible, we chose a single intervention for each condition that had evidence of effectiveness and for which adequate details of the intervention were available. Where this was not possible, a typical intervention or a range of practical details from various studies are presented. The information about each intervention is presented using key headings from the TIDieR (Template for Intervention Description and Replication) guide for intervention reporting.[20] Some of these interventions may be prescribed by family physicians and largely self-actioned by a patient (e.g., for falls prevention), whereas other interventions require a referral to a health care professional with expertise in exercise prescription (e.g., cardiac rehabilitation, exercise for chronic back pain or knee osteoarthritis and pulmonary rehabilitation for COPD).

Box 2: Exercise for chronic nonspecific low-back pain[12]

Rationale for exercise: Each type of exercise has a different rationale. The two main types that can be used are motor control exercises and graded activity.

Motor control exercise: Aims to retrain control of the trunk muscles, posture and movement patterns, using principles of motor learning such as segmentation and simplification. A detailed assessment of recruitment of the trunk muscles, posture, movement pattern and breathing guides the specific treatment for each patient. As control is regained, the exercises progress to more functional activities. Exercises are typically guided by pain and are mostly performed pain-free.

Graded activity: Aims to improve a patient's ability to complete functional activities and incorporates principles from cognitive behavioural therapy and exercise science. The program addresses physical impairments, such as impaired endurance, muscle strength and balance, but also considers psychological barriers to activity resumption, such as pain-related fear, low self-efficacy or misunderstandings about back pain. Principles of cognitive behavioural therapy, such as pacing, goal setting and self-reinforcement, are used. Exercises are progressed in a time-contingent rather than pain-contingent fashion.

Provider: Physiotherapist

Mode: Individual, supervised face-to-face sessions (and exercise practice at home)

Where: Primary care physiotherapy clinic

Materials needed: Simple equipment found in a typical physiotherapy gym

Procedure: A detailed treatment protocol for motor control exercises is available at http://ptjournal.apta.org/content/suppl/2009/11/25/89.12.1275.DC1/Costa_data_supp.pdf.

Number of exercise sessions: 14 sessions

Schedule details: A typical program[12] would comprise 12 sessions over an 8-week period, with 2 booster sessions at 4 and 10 months follow-up plus a concurrent home program.

Duration of each session: Sessions of 1 hour in duration

General considerations

Although there are few absolute contraindications to prescribing exercise for people with chronic conditions, it is important that patients receive a proper assessment by a physician before starting an exercise program. General considerations include an initial supervision period for most conditions, education about what the exercise program involves and how it can help, an understanding of the patient's fears and beliefs (for many conditions, such as low-back pain, cardiac conditions, COPD and chronic fatigue syndrome) and incorporation of strategies that enhance longer-term adherence.[21]

Osteoarthritis of the hip and knee

Exercise is beneficial for improving pain and function in patients with hip or knee osteoarthritis, regardless of their age, disease severity, pain or functional level. It is important to ensure patients understand that osteoarthritis is not a wear-and-tear disease and that discomfort or pain during exercise does not indicate further damage to the joint. A range of exercise types is suitable for patients with osteoarthritis, including muscle strengthening, and aerobic and range-of-motion exercise.[9–11,22] Exercise can be performed on land or in water. Supervised exercise that is supplemented with a home exercise program is preferable where possible.[9] For those who are overweight or obese, combining exercise with weight loss is more effective than either treatment alone.[23] Structured land-based exercises, usually delivered by a physiotherapist, are described in Appendix 3.

Evidence of benefit

For osteoarthritis of the knee, a recent Cochrane review of 54 randomized controlled trials (RCTs) that compared a range of land-based exercises with no-exercise controls showed evidence of benefit.[10] Of these trials, 19 were considered at low risk of bias. Evidence for the immediate benefits on mean pain scores was high quality (44 RCTs involving 3527 participants), and the effect size was considered moderate (standardized mean difference [SMD] –0.49, 95% confidence interval [CI] –0.39 to –0.59] lower in intervention groups; absolute reduction of 12 points [95% CI 10–15] on a 0–100 scale, where 0 represented no pain, compared with control groups). Evidence for the effect on physical function was of moderate quality (44 RCTs involving 3913 participants), was improved in the intervention groups (SMD –0.52, 95% CI –0.39 to –0.64; absolute improvement of 10 points [95% CI 8–13] on a 0–100 scale, where 0 represented no physical disability) and likely of clinical significance.[24] At two to six months after the conclusion of the exercise intervention, the benefits were less extensive but still significant, and after six months, benefits for pain reduction were not maintained, but small benefits (improvement of 4 points, 95% CI 2 to 6) remained for physical function. Exercise effects on quality of life (QoL) (13 RCTs involving 1073 participants) were considered small (SMD 0.28, 95% CI 0.15 to 0.40; absolute change of 4 points [95% CI 2 to 5] on a 0–100 scale [100 was the maximum quality of life]).

For osteoarthritis of the hip, a recent Cochrane review of 10 RCTs of land-based exercise compared with no exercise (of which seven were deemed to have a low risk of bias) showed evidence of benefit.[11] High-quality evidence from nine trials (549 participants) showed that, immediately after treatment, exercise reduced pain (SMD –0.38, 95 CI% –0.55 to –0.20), with an absolute reduction of 8 points (95% CI 4 to 11) on a 0–100 scale (a lower score was better). There was also high-quality evidence (nine RCTs involving 521 participants) that exercise improved physical function immediately after treatment (SMD –0.33, 95% CI –0.54 to –0.05), with an absolute decrease of 7 points (95% CI 1 to 12) on a 0–100 scale (a lower score was better). The benefits for pain and physical function were sustained to at least three to six months after the exercise interventions. Only three small studies (183 participants) evaluated the effect of exercise on QoL, with overall low-quality evidence showing no benefit (SMD 0.07, 95% CI –0.23 to 0.36). The well-documented strong placebo effects for self-reported outcomes in osteoarthritis have not been controlled for in most studies of exercise, because participants have not been blinded to group allocation. Therefore, the exact amounts of beneficial effects directly arising from exercise cannot be determined.

Contraindications

For patients with osteoarthritis of the hip or knee, there are no absolute contraindications to prescribing exercise, although comorbidities need to be taken into account. If the joint is acutely inflamed, the exercise program may need to be modified.

Adverse effects

Studies report few adverse events associated with exercise for osteoarthritis, and they are generally minor, usually increased pain or pain at other sites.[10,11]

Chronic nonspecific low-back pain

A typical program would comprise 20 hours of individually supervised sessions over 8–12 weeks and a home program.[25] The type of exercise (e.g., yoga v. graded activity) seems less important than the quality of implementation (e.g., supervision, inclusion of a home program and duration of the program have been shown to improve treatment effect).[25] Exercise programs normally include an education component, incorporation of psychological principles, such as pacing or goal setting, and progress in functional activities.[12,25] Many programs also explicitly address psychological characteristics, such as catastrophizing, pain self-efficacy and fear of injury/movement, that can be barriers to engaging in physical activity.[12] Motor control exercises and graded activity as delivered by a physiotherapist are described in Box 2.

Evidence of benefit

In a Cochrane review of exercise for low-back pain, 43 RCTs involving patients with chronic low-back pain were included.[26] In a meta-analysis of eight RCTs (n = 370), there was mean improvement of pain at earliest follow-up in the exercise group when compared with the control group (10.2 points, 95 CI% 1.3 to 19.1) on a 0–100 pain scale.[26] A companion meta-regression study by the same authors found that the effect of exercise was associated with exercise program characteristics, such as supervision, high dose (> 20 h) and individually designed programs. The authors estimated that an exercise program incorporating the most effective intervention characteristics would provide a larger effect size on pain of 18.1 points (95% CI 11.1 to 25.0) and an effect on function of 5.5 points (95% CI 0.5 to 10.5) on a 0–100 function scale.[25] These effects are modest, although they are similar in size to that provided by other treatments. For example, a Cochrane review of nonsteroidal anti-inflammatory drugs reported an improvement in pain of 12.4 points (95% CI 9.3 to 15.5).[27] For patients with acute low-back pain, there was no significant difference between exercise groups and control groups for pain and function at earliest follow-up (three RCTs, n = 491). The Cochrane review was confined to pain and function outcomes and did not provide information on other outcomes, such as QoL, work status or prevention of future recurrence. This Cochrane review also did not use the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (available at www.gradeworkinggroup.org) to describe the overall quality of the evidence.

Contraindications

Exercise is contraindicated in patients with low-back pain arising from a serious medical condition, such as fracture, infection, cancer or cauda equina syndrome. These conditions should be ruled out before prescribing an exercise program.

Adverse effects

The Cochrane review of exercise for low-back pain did not provide data on adverse effects.[26] In addition to the potential adverse effects of exercise in general, when exercise is used to manage low-back pain the most commonly reported adverse effect is temporary exacerbation of the back pain. In a placebo-controlled trial of motor control exercise (with 77 participants in each group), three participants in the exercise arm reported temporary exacerbation of the pain compared with two in the placebo group.[28]

Prevention of falls

Well-designed exercise programs can prevent falls in community-living older adults[14] when delivered as a single intervention or as part of a multifaceted program.[29] More effective programs include a focus on improving balance[14] (postural control), which has been identified as a key risk factor for falls.[30] Preventive exercise for community-living older adults is discussed in Appendix 4.

Evidence of benefit

In a 2012 Cochrane review, exercise as a single intervention was found to reduce the rate of falls by 30% in intervention groups when compared with control groups.[29] Both group- and home-based exercise that targeted balance, strength and/or fitness was found to be effective (rate ratio for group-based exercise 0.71, 95% CI 0.63 to 0.82, in 16 RCTs involving 3622 participants; rate ratio for home-based exercise 0.68, 95% CI 0.58 to 0.80, in seven RCTs involving 951 participants). Tai Chi was also found to reduce the risk of falling (the proportion of people falling) by 30% (risk ratio [RR] 0.71, 95% CI 0.57 to 0.87, in six RCTs involving 1625 participants).[29] Individual trials of exercise interventions have not been large enough to test exercise as a strategy for prevention of fractures, but some meta-analyses have suggested that exercise can prevent falls causing injuries[13,29,31] (rate ratio 0.63, 95% CI 0.51 to 0.77; 10 RCTs).[31]

Exercise as a single intervention has not been found to be effective in individuals with major risk factors for falls that are not amenable to change with exercise, such as patients with marked visual impairment or those taking psychoactive medications.[29] It appears from the Cochrane review that other evidence-based interventions for the prevention of falls should be prioritized in some patients. For example, the primary intervention for the prevention of falls in patients with marked visual impairment should be a home safety assessment or removal of cataracts. A gradual withdrawal of psychoactive medication should be attempted first in patients who are taking these medications.[29] These populations are likely to receive other benefits from exercise programs. Exercise as a single intervention was not found to be an effective prevention strategy for falls in patients living in high-support care facilities.[32]

Contraindications

There are no absolute contraindications to exercise for the prevention of falls; however, older adults at risk of falling may also have comorbidities (e.g., heart disease); therefore, contraindications outlined elsewhere in this review may be relevant.

Adverse effects

There is a risk that an older adult at risk of falling may fall while exercising. Prescribed exercises and the level of health professional supervision need to be appropriate for each patient's physical and cognitive abilities, and advice needs to be given about the safe conduct of exercise (Appendix 4), such as undertaking balance exercises near a firm support (e.g., a wall or table). Safe storage and application of weights or resistance bands is also important. Individual tailoring of the level of difficulty of the exercise can ensure the exercise is challenging enough to be useful, yet still safe.

COPD

Patients with COPD should be referred to pulmonary rehabilitation[33] when the condition is stable[34] or following a hospital admission for an acute exacerbation.[35] Patients should be taught how to manage symptoms during exercise, especially how to manage breathlessness. Box 3 describes pulmonary rehabilitation.

Evidence of benefit

The evidence for pulmonary rehabilitation comes from two Cochrane reviews — one for patients with stable COPD[34] and one following hospital admission for an acute exacerbation of COPD.[35] The review of pulmonary rehabilitation compared with usual care or no exercise training in patients with stable COPD (65 RCTs involving 3822 participants) found improvement in those who received pulmonary rehabilitation for a number of outcomes. There was moderate-quality evidence for the effect of pulmonary rehabilitation on QoL (MD –6.9 points, 95% CI –9.3 to –4.5, on the total score for the St. George's Respiratory Questionnaire),[34] in favour of the intervention group (a lower score is better). This effect size exceeded a minimal important difference (MID) of –4 points.[36] There were similar findings for other measures of

QoL (see Appendix 2). Maximal exercise capacity improved in the intervention groups (MD 6.8 watt [W], 95% CI 1.9 to 11.7), which exceeded the MID of 4 W,[37] although evidence quality was rated as low (16 RCTs involving 779 participants). Functional exercise capacity (measured by the six-minute walk test) also improved in the pulmonary rehabilitation groups (MD 43.9 m, 95% CI 32.6 to 55.2). This value was greater than the MID of 30 m (95% CI 25 to 33),[36] but the evidence quality was rated as very low.

In the second review (nine RCTs involving 432 participants) of patients with COPD who were randomly assigned to pulmonary rehabilitation or usual care after hospital admission for an acute exacerbation of COPD, the intervention group experienced a reduction in mortality (odds ratio [OR] 0.29, 95% CI 0.10 to 0.84) and hospital readmissions (OR 0.2, 95% CI 0.08 to 0.6; number needed to treat 4, 95% CI 3 to 8).[35] Overall, the trials were rated as moderate quality.

Contraindications

There are few absolute contraindications to exercise training within a pulmonary rehabilitation program. Most physical and medical comorbidities can be managed by expert clinicians; however, unstable cardiac disease may put patients at risk, and participation may not be possible for those with severe arthritis or severe neurologic or cognitive disorders.

Adverse effects

No adverse effects from pulmonary rehabilitation were reported in trials included in either of the Cochrane reviews.[34,35]

Type 2 diabetes

Evidence supports aerobic exercise, progressive resistance training or a combination of the two if it is structured (defined as planned, individualized and supervised) for the improvement of glycemic control.[17] Given the relative equivalency of metabolic benefits across aerobic and resistance exercise modalities, choice of exercise modality should be driven by patient choice or preference, and presence and type of comorbidities. For example, the presence of sarcopenia, mobility impairment, osteoporosis, frailty and osteoarthritis would suggest using resistance training rather than aerobic exercises, especially if the risk of falling is also present. Severe peripheral neuropathy or peripheral vascular disease with foot ulcers may also preclude weight-bearing aerobic exercise but still allows for resistance training to occur. There is a dose–response relation, with better outcomes associated with an exercise duration greater than 150 minutes per week[17] and higher intensity resistance training.[16] Exercise does not have to be performed in one session for benefits to accrue. Exercise for patients with diabetes is discussed in Box 4.

Evidence of benefit

A comprehensive meta-analysis of exercise efficacy for glycemic control in participants with type 2 diabetes that included 47 RCTs (8538 patients)[17] found that structured, supervised exercise training of at least 12 weeks duration (23 RCTs involving aerobic and/or resistance training) was associated with a decline in glycosylated hemoglobin (HbA_{1c}) level (–0.67%, 95% CI –0.84% to –0.49%) compared with participants in the control group.[17] Similar benefits, when compared with the control groups, were also found for aerobic exercise (–0.73%, 95% CI

Box 3: Exercise for patients with chronic obstructive pulmonary disease[15]

Rationale for exercise: To improve exercise capacity and quality of life, and to reduce breathlessness, hospital admissions and length of hospital stay.

Provider: Physiotherapist or exercise physiologist trained in pulmonary rehabilitation and holding current cardiopulmonary resusitation (CPR) certification

Mode: Exercise prescription should be individually tailored based on initial assessment; however, a number of patients can be supervised at the same time. It should be delivered face-to-face, although some sessions can be performed unsupervised at home.

Where: Hospital outpatient departments; appropriate community facilities

Materials needed: Flat walking track (preferably indoor and air-conditioned), resistance bands, hand weights and pulse oximeter. Optional: stationary cycle ergometer, treadmill, fixed-weight machines and supplemental oxygen. Assessment tools: Six-minute walk test (6MWT) procedures and instructions, dyspnea scale, pulse oximeter, device to measure blood pressure, spirometer, disease-specific quality of life questionnaire (e.g., St. George's Respiratory Questionnaire or Chronic Respiratory Disease Questionnaire). Assessment: Spirometry; resting blood pressure, heart rate and oxygen saturation; 6MWT performed twice to account for the known learning effect and the better walk distance recorded and used for exercise prescription; oxygen saturation and pulse rate monitored continuously throughout the 6MWT, with values recorded every minute; dyspnea during the 6MWT.

Procedure: See the Pulmonary Rehabilitation Toolkit[15] (www.pulmonaryrehab.com.au) for details on how to provide pulmonary rehabilitation.

Number of exercise sessions: 16–24 sessions face-to-face

Schedule details: 2–3 sessions per week for 8–12 weeks, with at least an extra 1–2 sessions a week unsupervised at home

Duration and intensity of each session: Each session should be about 60 minutes. The session must include aerobic training at a starting intensity for ground walking of 80% of the 6MWT speed; starting duration 10–15 minutes building to 30 minutes by the 3rd–5th session; resistance exercises for upper and lower limb muscle groups of 8–10 repetitions x 2–3 sets of each exercise. For cycle and treadmill training intensity, refer to the Pulmonary Rehabilitation Toolkit.

Other: The Lung Foundation Australia provides an online course on pulmonary rehabilitation (available at http://lungfoundation.com.au/health-professionals/training-and-education/pulmonary-rehabilitation-training-online/).

Box 4: Exercise for patients with type 2 diabetes[16,17]

Rationale for exercise: Traditionally, improving glycemic control has been the main focus of exercise interventions in patients with type 2 diabetes. However, many of the associated comorbidities are also relevant to prescribing exercise (e.g., obesity, osteoarthritis, peripheral neuropathy, falls risk, peripheral vascular disease and depression).

Provider: Physician referral to allied health provider or community fitness facility with competence in managing older adults with chronic disease. Prior to referral, physician screening for proliferative retinopathy, unstable angina, uncontrolled blood pressure, hyperglycemia or hypoglycemia, extent of peripheral vascular and neuropathic disease, and the presence of autonomic neuropathy (e.g., orthostatic hypotension, bradycardia or lack of sweating) may be indicated in patients with these comorbidities.[16]

Mode: Aerobic exercise, resistance training and a combination of both are the most effective for glucose control.[17] The combination offers the best treatment for both diabetes and common comorbidities and is recommended in current position statements.[16] The exercise needs to be structured, which is defined as planned, individualized and supervised.[17] Both group and individual training are effective. Patients with extensive comorbidities and frailty require more individualized training and supervision.

Where: Outpatient clinics of hospitals and health centres, allied health practices, community fitness facilities or at home with supervision

Materials needed: Aerobic exercise: good walking shoes, aerobic equipment if desired (treadmill, stepper, bike, etc.). Resistance training: free weights or machine-based training. Low-intensity training with bands or no equipment is not effective. A glucose-monitoring device, blood pressure cuff and easy access to high glucose drinks and snacks is recommended.

Procedure: Aerobic exercise should consist of large-muscle activities (e.g., walking, running, cycling and swimming) tailored to preferences and comorbidities, in particular to osteoarthritis. Resistance training (include multijoint exercises and large muscle groups) may include free weights or machine-based training (preferred for progression and safety in novices), with attention to rotator cuff disease and lower extremity arthritis that may require modification of exercises selected.[16]

Number of exercise sessions: 2–3 sessions per week for resistance training; 3–5 sessions per week for aerobic exercise; continue indefinitely

Schedule details: Exercise may need to be timed to coincide with peaks of glycemia postprandially and should not be undertaken after insulin or oral hypoglycemic administration without eating a meal beforehand. Shorter sessions may be accumulated across the day to achieve the full duration. No more than two consecutive days without exercising. Aerobic and resistance training may be done on separate days, which may improve efficacy and feasibility.

Duration and intensity of each session:

Aerobic exercise: Accumulate 150 minutes of moderate intensity (40%–59% VO_2 reserve [the difference between the rate of oxygen consumption at rest and at maximal exercise] or heart rate reserve, or 55%–69% of maximum heart rate or rated perceived exertion of 12–13 on a 6–20 point Borg Rating of Perceived Exertion Scale) in 3–5 sessions per week; OR 75 minutes of vigorous intensity (60%–84% VO_2 reserve or heart rate reserve, or 70%–89% maximum heart rate or rated perceived exertion of 14–16 on the 6–20 point Borg Scale) in 3–5 sessions per week.

Resistance training: Moderate to vigorous intensity (rated perceived exertion of 15–18 on a 6–20 point Borg Scale), 8–10 exercises; 2–4 sets of 8–10 repetitions per set) in 2–3 sessions per week

Other: Progression is necessary for improvement. As soon as the intensity of the workload drops below the required levels, the workload (e.g., pace, incline and amount of weight lifted) should be increased to reach the intensity targets. Intercurrent illness or laser surgery may require temporary cessation of exercise and resumption at a slightly lower intensity until former levels are regained. Communication between the physician, diabetes educator and fitness professional is necessary for optimal management of all aspects of diabetes.

–1.06% to –0.40%), resistance training (–0.57%, 95% CI –1.14% to –0.01%), and combined aerobic and resistance exercise (–0.51%, 95% CI –0.79% to –0.23%). Exercise duration of greater than 150 minutes per week was associated with a greater reduction in HbA_{1c} level (weighted mean difference [WMD] –0.89%, 95% CI –1.26% to –0.51%) compared with durations of 150 minutes or less per week (WMD –0.36%, 95% CI –0.50% to –0.23%). Physical activity advice alone was not effective (–0.16%, 95% CI –0.50% to 0.18%). This review did not use the GRADE approach to describe the overall quality of the evidence. The overall effect of structured exercise on HbA_{1c} level (–0.67%, 95% CI –0.84 to –0.49) was similar to the effect of adding metformin to insulin treatment (–0.60%, 95% CI –0.30% to –0.91%) that was reported in a meta-analysis of 35 RCTs involving patients with diabetes.[38]

Structured exercise or exercise combined with dietary advice has not been shown to reduce cardiovascular mortality in type 2 diabetes.[39] However, mortality risk associated with reductions in HbA_{1c} level was evaluated in a prospective cohort study involving 11 205 patients with type 2 diabetes in Denmark.[40] A linear relation was found in patients with an index HbA_{1c} level greater than 8%, with the lowest mortality associated with the greatest decline in HbA_{1c} level.

Contraindications

There are few contraindications to moderate or vigorous exercise for patients with type 2 diabetes and include progressive proliferative retinopathy (not the more common nonproliferative retinopathy), end-stage heart failure, malignant arrhythmias or inoperable known aneurysms. Temporary contraindications include acute retinal surgery, recovery from which precludes any activities that cause large elevations in blood pressure/intraocular pressure for one to two weeks. Temporary contraindications also include periods of hypoglycemia or poor glucose control until stabilized, acute systemic infections, severe exacerbations of inflammatory joint disease or musculoskeletal injury, or during temporary instability of ischemic heart disease, hypertension or heart failure until controlled.[16]

Adverse effects

Potential adverse effects of exercise for type 2 diabetes are linked to poor metabolic control, with further dysregulation of glucose homeostasis, as well as common comorbidities of this condition that include coronary artery disease, osteoarthritis, mobility impairment, neuropathy, peripheral vascular disease, visual impairment or proliferative retinopathy, and orthostatic hypotension.[16] In the systematic review that included 47 RCTs, 30 did not report adverse events.[17] Of those that did, no major adverse events were reported and, in a few studies, minor events included musculoskeletal injury or discomfort, hypoglycemic episodes (in two studies) and cardiovascular disease events that were unrelated to the intervention.

Chronic fatigue syndrome

The most effective type, duration and intensity of exercise for chronic fatigue syndrome are unclear. Appendix 5 describes an example of one exercise intervention (graded exercise therapy).

Evidence of benefit

The evidence comes from a recent Cochrane review (eight RCTs involving 1518 participants) of exercise therapy compared with usual care, wait list, or relaxation and flexibility training.[41] There was moderate-quality evidence for the effect of exercise on fatigue, with a mean reduction of 2.8 points (95% CI 1.57 to 4.07) on a 0–33 point scale (a lower score indicates less fatigue). Studies that used other scoring for the fatigue scale had similar results (see Appendix 2). In four RCTs (involving 489 participants, with moderate-quality evidence) that measured self-perceived changes in overall health, more participants in the exercise groups reported improvement than in the control groups (RR 1.83, 95% CI 1.39 to 2.40). Two RCTs (low-quality evidence) measured sleep, with a mean sleep score of 1.5 points (95% CI 0.02 to 2.95) lower in the exercise groups, with a lower score suggesting improved sleep quality. There was also low-quality evidence (five RCTs) for the effect on physical functioning, with mean scores 13.10 points (95% CI 1.98 to 24.22) higher in the exercise therapy groups. The review authors were unable to draw conclusions about the effect of exercise therapy on QoL, pain, anxiety, depression, use of health service resources and drop-out rate.

Contraindications

There are no absolute contraindications to exercise for patients with chronic fatigue syndrome.

Adverse events

There is limited evidence about adverse events. In the Cochrane review,[41] serious adverse reactions (worsening symptoms and deterioration in function) were only reported by one study (n = 319) but were uncommon (two participants) in both groups (RR 0.99, 95% CI 0.14 to 6.97).

Coronary heart disease and heart failure

Patients should always work within their exercise tolerance and progress gradually. Initially, direct supervision of resistance training is advocated. Beneficial gains are possible in those at highest risk (e.g., a history of acute myocardial infarction with comorbidities or advanced heart failure) and in those who adhere to the prescription.[19] For optimal care, exercise is only one component of a comprehensive program. Appendix 6 describes the possible components of this type of program.

Evidence of benefit

A Cochrane review of 47 RCTs (10 794 participants with coronary heart disease who were predominantly male and middle-aged) found that exercise-based cardiac rehabilitation compared with usual care reduced overall mortality (RR 0.87, 95% CI 0.75 to 0.99) and cardiovascular mortality (RR 0.74, 95% CI 0.63 to 0.87) at 12 months or more, and all hospital admissions (RR 0.69, 95% CI 0.51 to 0.93) in the shorter term (< 12 months follow-up), with no evidence of heterogeneity of effect across trials.[42] There was no reduction in the risk of total myocardial infarction or revascularization. The impact on QoL was unclear, with 7 out of the 10 trials that measured it reporting a significantly higher QoL in the exercise group, but a meta-analysis was not performed because of heterogeneity.

A recent Cochrane review of 33 RCTs (4740 participants with heart failure, mostly with heart failure due to reduced ejection fraction and categorized as New York Heart Association classes II and III) found that exercise-based rehabilitation compared with no exercise controls had no effect on all-cause mortality up to 12 months follow-up (RR 0.93, 95% CI 0.69 to 1.27).[43] Compared with the control group, exercise-based rehabilitation reduced the rate, over one year, of all hospital admissions (15 trials involving 1328 participants; RR 0.75, 95% CI 0.62 to 0.92) and hospital admission specific to heart failure (12 trials involving 1036 participants; RR 0.61, 95% CI 0.46 to 0.80). There was also a statistically significant and clinically important improvement in disease-specific QoL (up to 12 months) in the exercise groups (13 trials involving 1270 participants; MD –5.8, 95% CI –9.2 to –2.4, on a 0–105 scale, where a lower score is better). The overall risk of bias across the trials was moderate.

Contraindications

Absolute contraindications to exercise for patients with coronary heart disease and/or heart failure include unstable ischemia, uncontrolled heart failure or arrhythmias, uncontrolled hypertension or diabetes, acute systemic illness or fever, severe and symptomatic valvular heart disease or any other cardiac condition that the family physician believes is life threatening.[19]

Adverse events

Vigorous exercise can trigger a cardiovascular event, particularly in people who are habitually sedentary. Potential harms of exercise among patients with established coronary heart disease or heart failure are a nonfatal cardiac arrest (about 1 per 115 000 patient-hours of supervised exercise in patients with heart disease; about half the rate in patients with heart failure) or death (about 1 per 750 000 patient-hours of participation).[19]

Conclusion

Exercise is an effective but neglected treatment for many chronic conditions. However, similar to surgery, exercise is not a single entity but must be tailored to the condition. If exercise interventions are not implemented in a manner that is consistent with how they were used in trials (e.g., at a lower intensity, shorter duration or with different components), the fidelity of the intervention is compromised, and clinicians and patients cannot expect to realize outcomes similar to those achieved in the trials.

Unless clinicians can access sufficient details about exercise interventions to prescribe them, they either guess at how to use them or do not use them at all. General practitioners have identified the need for exercise details and resources to assist them with exercise prescription.[4,44] Even when a family physician may not be involved in delivering the exercise intervention, they should know the main elements of an evidence-based exercise intervention so they can discuss with patients and refer appropriately. We have summarized the available evidence to assist clinicians in using and prescribing exercise interventions in practice.

Exercise prescription also requires clinicians to be able to manage patients' misconceptions, fears and motivation, particularly for those who are unwell. Although these are also challenges for pharmacologic interventions, the challenges are of a higher degree for exercise. However, the potential rewards for clinicians and patients make overcoming the challenges worthwhile.

References

1. Naci H, Ioannidis JPA. Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study. *BMJ* 2013;347:f5577.
2. Glauser TA, Salinas GD, Roepke NL, et al. Management of mild-to-moderate osteoarthritis: a study of the primary care perspective. *Postgrad Med* 2011;123:126-34.
3. Mafi JN, McCarthy EP, Davis RB, et al. Worsening trends in the management and treatment of back pain. *JAMA Intern Med* 2013;173:1573-81.
4. Persson G, Brorsson A, Ekvall Hansson E, et al. Physical activity on prescription (PAP) from the general practitioner's perspective — a qualitative study. *BMC Fam Pract* 2013;14:128.
5. Weiler R, Chew S, Coombs N, et al. Physical activity education in the undergraduate curricula of all UK medical schools: Are tomorrow's doctors equipped to follow clinical guidelines? *Br J Sports Med* 2012;46:1024-6.
6. Hoffmann TC, Erueti C, Glasziou PP. Poor description of nonpharmacological interventions: analysis of consecutive sample of randomised trials. *BMJ* 2013;347:f3755.
7. Abell B, Glasziou P, Hoffmann T. Reporting and replicating trials of exercise-based cardiac rehabilitation: Do we know what the researchers actually did? *Circ Cardiovasc Qual Outcomes* 2015;8:187-94.
8. Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010 [Published erratum in Lancet 2013; 381:628]. *Lancet* 2012;380:2163-96.
9. Juhl C, Christensen R, Roos EM, et al. Impact of exercise type and dose on pain and disability in knee osteoarthritis: a systematic review and meta-regression analysis of randomized controlled trials. *Arthritis Rheumatol* 2014;66:622-36.
10. Fransen M, McConnell S, Harmer AR, et al. Exercise for osteoarthritis of the knee. *Cochrane Database Syst Rev* 2015;(1):CD004376.
11. Fransen M, McConnell S, Hernandez-Molina G, et al. Exercise for osteoarthritis of the hip. *Cochrane Database Syst Rev* 2014;(4):CD007912.
12. Macedo LG, Latimer J, Maher CG, et al. Effect of motor control exercises versus graded activity in patients with chronic nonspecific low back pain: a randomized controlled trial. *Phys Ther* 2012;92:363-77.
13. Robertson MC, Campbell AJ, Gardner MM, et al. Preventing injuries in older people by preventing falls: a meta-analysis of individual-level data. *J Am Geriatr Soc* 2002;50:905-11.
14. Sherrington C, Tiedemann A, Fairhall N, et al. Exercise to prevent falls in older adults: an updated meta-analysis and best practice recommendations. *N S W Public Health Bull* 2011;22:78-83.
15. Alison J, Barrack C, Cafarella P , et al. The Pulmonary Rehabilitation Toolkit on behalf of The Australian Lung Foundation. Brisbane: The Australian Lung Foundation; 2009. Available: www.pulmonaryrehab.com.au (accessed 2015 Dec. 3).
16. Hordern MD, Dunstan DW, Prins JB, et al. Exercise prescription for patients with type 2 diabetes and pre-diabetes: a position statement from Exercise and Sport Science Australia. *J Sci Med Sport* 2012;15:25-31.
17. Umpierre D, Kramer CK, Leita CB, et al. Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes. *JAMA* 2011;305:1790-9.
18. White PD, Goldsmith KA, Johnson AL, et al. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. *Lancet* 2011;377:823-36.
19. Fletcher GF, Ades PA, Kligfield P, et al. Exercise standards for testing and training: a scientific statement from the American Heart Association. *Circulation* 2013;128:873-934.
20. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;348:g1687.
21. Jordan JL, Holden M, Eej E, et al. Interventions to improve adherence to exercise for chronic musculoskeletal pain in adults. *Cochrane Database Syst Rev* 2010;(1):CD005956.
22. Uthman OA, van der Windt DA, Jordan JL, et al. Exercise for lower limb osteoarthritis: systematic review incorporating trial sequential analysis and network meta-analysis. *BMJ* 2013; 347:f5555.
23. Messier SP, Mihalko SL, Legault C, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. *JAMA* 2013;310:1263-73.
24. Tubach F, Ravaud P, Baron G, et al. Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: the minimal clinically important improvement. *Ann Rheum Dis* 2005;64:29-33.
25. Hayden JA, van Tulder MW, Tomlinson G. Systematic review: strategies for using exercise therapy to improve outcomes in chronic low back pain. *Ann Intern Med* 2005;142:776-85.

26. Hayden JA, van Tulder MW, Malmivaara A, et al. Exercise therapy for treatment of non-specific low back pain. *Cochrane Database Syst Rev* 2005;(3):CD000335.
27. Roelofs PDDM, Deyo RA, Koes BW, et al. Non-steroidal anti-inflammatory drugs for low back pain. *Cochrane Database Syst Rev* 2008;(1):CD000396.
28. Costa LOP, Maher CG, Latimer J, et al. Motor control exercise for chronic low back pain: a randomized placebo-controlled trial. *Phys Ther* 2009;89:1275-86.
29. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2012;(9):CD007146.
30. Lord SR, Ward JA, Williams P, et al. Physiological factors associated with falls in older community-dwelling women. *J Am Geriatr Soc* 1994;42:1110-7.
31. El-Khoury F, Cassou B, Charles M-A, et al. The effect of fall prevention exercise programmes on fall induced injuries in community dwelling older adults: systematic review and meta-analysis of randomised controlled trials. *BMJ* 2013;347:f6234.
32. Cameron ID, Gillespie LD, Robertson MC, et al. Interventions for preventing falls in older people in care facilities and hospitals. *Cochrane Database Syst Rev* 2012;(12):CD005465.
33. Bolton CE, Bevan-Smith EF, Blakey JD, et al. British Thoracic Society guideline on pulmonary rehabilitation in adults. *Thorax* 2013;68(Suppl 2):ii1-30.
34. McCarthy B, Casey D, Devane D, et al. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2015;(2):CD003793.
35. Puhan MA, Gimeno-Santos E, Scharplatz M, et al. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2011;(10):CD005305.
36. Holland AE, Spruit MA, Troosters T, et al. An official European Respiratory Society/American Thoracic Society Technical Standard: field walking tests in chronic respiratory disease. *Eur Respir J* 2014;44:1428-46.
37. Puhan MA, Chandra D, Mosenifar Z, et al. The minimal important difference of exercise tests in severe COPD. *Eur Respir J* 2011;37:784-90.
38. Hirst JA, Farmer AJ, Ali R, et al. Quantifying the effect of metformin treatment and dose on glycemic control. *Diabetes Care* 2012;35:446-54.
39. Look Ahead Research Group; Wing RR, Bolin P, Brancati FL, et al. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med* 2013;369:145-54.
40. Skriver MV, Sandbæk A, Kristensen JK, et al. Relationship of HbA1c variability, absolute changes in HbA1c, and all-cause mortality in type 2 diabetes: a Danish population-based prospective observational study. *BMJ Open Diabetes Res Care* 2015;3:e000060.
41. Larun L, Brurberg K, Odgaard-Jensen J, et al. Exercise therapy for chronic fatigue syndrome. *Cochrane Database Syst Rev* 2015;(2):CD003200.
42. Heran BS, Chen J. Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database Syst Rev* 2011;(7):CD001800.
43. Taylor RS, Sagar V, Davies E, et al. Exercise based rehabilitation for heart failure. *Cochrane Database Syst Rev* 2014;(4):CD003331.
44. Swinburn BA, Walter LG, Arroll B, et al. Green prescriptions: attitudes and perceptions of general practitioners towards prescribing exercise. *Br J Gen Pract* 1997;47:567-9.

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