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Cost-effectiveness of interventions based on physical exercise in the treatment of various diseases: A systematic literature review

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Objectives: The aim of this study was to review studies reporting cost-effectiveness of exercise-based interventions in treatment of various diseases.
Methods: Systematic literature search using several databases. Abstracts initially screened independently by two authors, full-text articles again evaluated by two authors, who decided whether an article should be included. Included were scientifically valid articles describing controlled studies that included an exercise-based intervention in the treatment of an established medical condition, and also reported on the cost-effectiveness of the intervention, or its effect on the utilization of health services. Quality was assessed with an established approach.
Results: A total of 914 articles were identified, of them 151 were obtained for closer review. Sixty-five articles describing sixty-one studies were included. Most (82 percent) were randomized trials. Twenty-eight studies dealt with musculoskeletal disorders, fifteen with cardiology, four with rheumatic diseases, four with pulmonary diseases, three with urinary incontinence, and two with vascular disorders. There was one study each in the fields of oncology, chronic fatigue, endocrinology, psychiatry, and neurology. Exercise interventions in musculoskeletal disorders were deemed to be cost-effective in 54 percent, in cardiology in 60 percent, and in rheumatic diseases in 75 percent of the cases. There was some evidence that exercise might be cost-effective in intermittent claudication, breast cancer patients, diabetes, and schizophrenia.
Conclusions: The number of studies assessing cost-effectiveness of exercise interventions in various diseases is still limited. The results show large variation but suggest that some exercise interventions can be cost-effective. Most convincing evidence

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was found for rehabilitation of cardiac and back pain patients; however, even in these cases, the evidence was partly contradictory.

Keywords: Exercise, Cost-effectiveness, Cost-utility, Study quality, systematic review

During the past decades, advances in health care in treatment of various diseases have led to increasing healthcare costs. As the available resources are limited, healthcare interventions should lead to maximal health benefit with the resources available. To achieve fair resource allocation, only methods proven cost-effective should be adopted for routine use.

Ageing populations place increasing demands on health care. To control healthcare costs, we are faced with a situation where some of the preventive and rehabilitative measures of healthcare providers may eventually have to become the patients' responsibility. One such measure to advance patient recovery could be exercise, if proven cost-effective.

Elderly people hospitalized for acute conditions can deteriorate rapidly. Not always because of the condition itself but because of bed rest. Multiprofessional interventions comprising physical training in the acutely hospitalized elderly, according to a recent literature review, reduced hospital stays and need for care in another healthcare facility (16). The effectiveness of mere exercise, however, could not be established, possibly in part because too few studies examined exercise alone (16).

According to a Cochrane review on exercise in the treatment of nonspecific low-back pain, exercise therapy can be slightly effective at decreasing pain and improving function in adults with chronic low back pain (26). Furthermore, there was some evidence that a graded activity program can improve absenteeism outcomes in back pain patients, but evidence for other types of exercise was unclear (26). In coronary heart disease, exercise-based cardiac rehabilitation reduced cardiac deaths (31), and in heart failure patients, it was found to improve exercise capacity and quality of life (51).

In oncology, advances in treatment have prolonged life expectancy. With increasing life expectancy, the side-effects of treatment like osteoporosis and psychosocial impairment have, however, also become more pronounced. In alleviating these side-effects, exercise interventions may help and, according to systematic literature reviews, are effective (33;41;56). McNeely et al. (41) for example, reported that, in breast cancer patients, exercise improves health-related quality of life (HRQoL) and physical capacity and reduces fatigue. Furthermore, physical activity improves cardiorespiratory capacity and well-being in cancer patients (56). Knols et al. (33) reported similar results, but pointed out that the studies concerned with exercise interventions in cancer patients were of moderate quality only, and for confirmation, larger, randomized controlled studies are necessary.

Exercise interventions have also been studied in several other diseases. For instance, in patients with type 2 diabetes, exercise significantly improves glycemic control and reduces visceral adipose tissue and plasma triglycerides (62). In obesity, exercise is associated with weight loss and it improves cardiovascular disease risk factors even if no weight is lost (59). In postmenopausal women, exercise increases the bone mass density of the spine and thus is effective in preventing and treating osteoporosis (5).

Although exercise interventions have been shown to be effective in several studies, information on their cost-effectiveness in disease treatment is sparse. In a review of cost-effectiveness of health care interventions aimed at improving physical activity, Hagberg and Lindholm (21) identified 26 studies published before year 2005. The majority of them investigated exercise in primary prevention. Only ten studies were concerned with exercise in the treatment of people already ill, for example with cardiac diseases, arthrosis, or diabetes. In nine of those ten studies, exercise was judged cost-effective. One study was inconclusive as to cost-effectiveness.

Optimal resource allocation should lead to maximal health benefit in the society, but much uncertainty exists in decision making in health care. The adoption of exercise interventions in health care should be based on verified cost-effectiveness, as is the case with other treatment modalities. As studies reporting on cost-effectiveness have become more common recently, it is reasonable to update, in a systematic manner, what is known about the cost-effectiveness of exercise interventions in the treatment of various medical conditions.

METHODS

In considering the evidence of cost-effectiveness of exercise interventions in the treatment of medical conditions, we focused on controlled studies that reported the effect of exercise on costs or health care utilization. Literature searches were performed using the Medline, Centre for Research and Dissemination, and Cochrane Library electronic databases to June 2008. In addition, some articles were identified by scanning reference lists of the included articles. Finally, we also compared the result of our search with the listing of cost-effectiveness ratios published in the Cost Effectiveness Analysis Registry (https://research.tufts-nemc.org/cear/default.aspx) (14). The detailed search strategy is presented in Table 1.

Table 1. Search Strategies for Identifying Studies Concerned with Cost-Effectiveness of Exercise Interventions in the Treatment of Various Diseases

Medline (until June 2008)	
1.	sports/
2.	exp Exercise/
3.	Physical Fitness/
4.	((prescribe$ or prescript$) adj2 exercise).tw.
5.	2 or 3 or 4
6.	exp Economics/
7.	quality-adjusted life years/
8.	(QALY or QALYs).tw.
9.	6 or 7 or 8
10.	5 and 9
11.	(comment or letter or editorial).pt.
12.	animals/ not (animals/ and humans/)
13.	11 or 12
14.	10 not 13
15.	animal$.sh.
16.	14 not 15
Cochrane Central (until December 2007)	
1.	exercise/ or exercise therapy/
2.	Physical Fitness/
3.	1 or 2
4.	exp economics/
5.	quality-adjusted life years/
6.	(qaly or qalys).ab.
7.	4 or 5 or 6
8.	3 and 7
9.	"Quality of Life"/
10.	"Value of Life"/
11.	9 or 10
12.	3 and 11
13.	12 not 8
CRD (EED, DARE, HTA) (until December 2007)	
#1	MeSH Exercise Therapy EXPLODE 1 2 3 4
#2	MeSH Exercise EXPLODE 1 2 3
#3	MeSH Physical Fitness EXPLODE 1 2
#4	exercise AND (prescription OR prescribed)
#5	#1 OR #2 OR #3 OR #4
#6	qaly OR qalys
#7	#5 AND #6

Screening of the identified articles, based on their abstracts, was undertaken independently by at least two of three authors (ER, RPR, PR) and the selection of relevant articles agreed upon in discussion. Full-text articles obtained for closer inspection were evaluated independently by two authors, who then reached a consensus on which articles should be included in the review. Included were articles that described, in a scientifically valid manner, controlled studies reporting on exercise intervention in the treatment of established medical conditions. As the aim was to assess cost-effectiveness, only studies reporting costs or some measure of health care utilization were included. Studies examining exercise promotion were excluded as were also studies dealing with primary prevention.

The quality of the selected controlled studies was scored, on a scale from 0 to 11, as recommended by van Tulder et al. (73). Furthermore, all studies were judged against the criteria for economic analysis given by Drummond et al. (17). The criteria combine 10 main items, scored 1 (criterion met) or 0 (criterion not met), resulting in a maximum score of 10.

The information given in the tables and in the appendix was gathered independently by one of the authors and its accuracy checked by another.

RESULTS

Selected Publications

The literature search identified 874 publications. Another forty studies were identified by scanning reference lists of the included articles and consulting experts in the field of economic analysis. Furthermore, one study was identified when results of the search were compared with the listing of cost-effectiveness ratios published in the Cost Effectiveness Analysis Registry (14). One hundred fifty-one articles were retrieved for closer inspection and of them sixty-five (representing sixty-one separate studies) were deemed to fulfill the inclusion criteria (Figure 1). Excluded were uncontrolled studies, studies with no economic information, or studies in which the exercise intervention was the same in all studied groups preventing the appraisal of the cost-effectiveness of exercise itself. Furthermore, primary prevention studies, reviews, letters and editorials were excluded.

Study Classification

Of the included studies, twenty-eight (represented in 31 references) dealt with musculoskeletal disorders (3;7;13;15;19;20;27–30;34;37–39;43;44;46;47;49;53;55;58;60;61;63;64;66;69;71;75;76), fifteen with cardiology (1;4;6;9;18;22–25;32;42;48;52;77;78), four with rheumatic diseases (2;64;70;72), four with pulmonary diseases (11;12;54;68), three with urinary incontinence (50;57;74), and two with vascular disorders (35;67). In addition, there was one study each in the fields of oncology (20), chronic fatigue (40), endocrinology (45), psychiatry (65), and neurology (36).

The main findings (patients, intervention, control intervention, outcomes, conclusions concerning cost-effectiveness) of the included studies are reported in Tables 2–5 and a more detailed description of the studies can be found in Appendix 1 (which can be viewed online at www.journals.cambridge.org/thc). Some of the studies were the subject of more than one study; in those cases, we combined the results of the separate articles in the tables.

Classified by the country of origin, most studies (n = 16) came from the United Kingdom. There were thirteen studies from the United States, eleven from the Netherlands, five from Canada, three from Australia, and two studies from both Finland and Norway. There was one study each from Denmark, Sweden, Belgium, Italy, Spain, Germany, Hong Kong, China, and Japan.

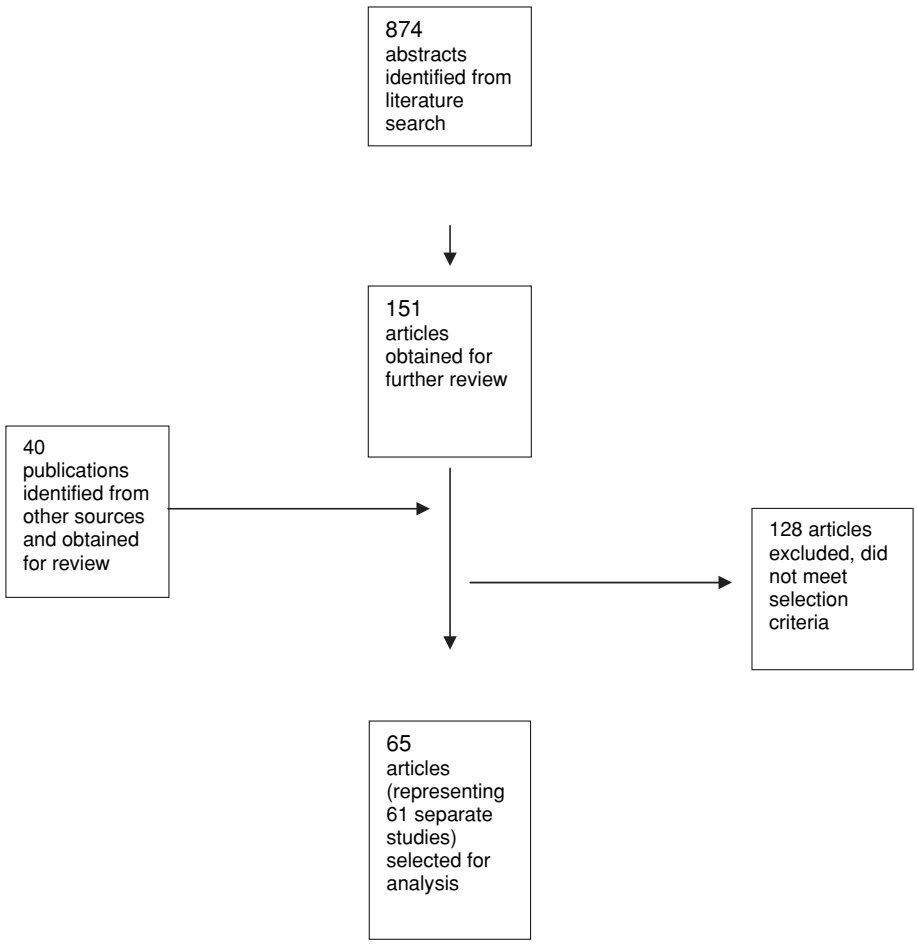

Figure 1. Flow chart showing the various steps of study selection.

Study Quality

The quality scores ranged from 3 to 9 (median, 6) for the studies on musculosceletal disorders, from 2 to 9 (median, 6) for the cardiovascular studies, from 5 to 8 (median, 5.5) for the rheumatology studies, and from 3 to 8 (median, 5) for the studies dealing with miscellaneous disorders.

The scores for the economic analyses ranged from 4 to 10 (median, 8) for the studies on musculosceletal disorders, from 4 to 10 (median, 6) for the cardiovascular studies, from 7 to 9 (median, 9) for the rheumatology studies, and from 3 to 9 (median, 5.5) for the studies dealing with miscellaneous disorders.

Evidence for Cost-Effectiveness of Exercise by Type of Medical Condition

Musculoskeletal Disorders. Twenty-eight studies investigated exercise in the treatment of musculoskeletal disorders (Table 2). Except for one study, all the studies were randomized controlled trials.

BACK PAIN

There were fourteen studies dealing with back pain patients, the majority with chronic back pain. Nine of them reported that exercise saved costs (10;30;37;43;44;64;66;69;76), whereas in three the exercise intervention was found not to be cost-effective.(46;47;60;61;71) In one study on low back pain patients, costs between the three studied modalities (exercise, bed rest, normal activities) did not differ but patients in the normal activity group had better recovery (38). Heymans et al. (27) compared high- and low intensity back schools to usual care. The low-intensity back school was the most effective and cost-effective alternative.

In four studies, exercise was compared to usual care and in one study to physician consultation. In three of them, exercise was reported to be more cost-effective than usual care (43;44;76). In the study by Johnson et al. (30), the reduction in pain and disability produced by the intervention was small and nonsignificant. Wright et al. (76) found a back program with exercise (consisting of exercise, manipulation, joint and tissue mobilization, and so on) to lead to earlier return to

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Table 2. Patients, Interventions, and Outcomes in the Identified Studies Dealing with Musculoskeletal Disorders

	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Randomized controlled studies					
Brox et al. 1993, Norway (7)	125 18- to 66-year-old patients with treatment resistant rotator cuff disease for at least 3 months	Supervised exercise regimen consisting of relaxed repetitive movements (rotation, flexion - extension, abduction - adduction) for approximately an hour in a daily training session. Supervised x2/week, otherwise at home. Training for 3–6 months, with supervision gradually being reduced	Arthroscopic surgery or placebo soft laser treatment	Mean change in Neer score -0.3 for placebo, 10.8 for exercise, 20.2 for surgery. Overall improvement in Neer score did not differ significantly between exercise and surgery	Average costs £720/patient for operated and £390/patient for supervised exercise patients. Average length of sick leave did not differ between the 3 groups during 6-month observation. Differences between 2 active treatments not significant or clinically important but costs of exercise regimen lower
Timm 1994, USA (64)	250 subjects with chronic low back pain following laminectomy randomized into 5 groups	Low-tech exercise comprised 8-week supervised and unsupervised McKenzie-type and spinal stabilization exercises. High-tech exercise group received an 8-week clinical program of cardiovascular, isotonic and isokinetic exercise	Physical agents, joint manipulation, usual care	Low- and high-tech exercise were the only effective treatments for chronic low back pain. Low-tech exercise produced the longest period of relief	Low-tech exercise was the most cost-effective treatment with a weekly cost of $15,23 for a one week interval of relief. For the other groups the cost per interval of relief ranged from $32,50 to $921.
Malmivaara et al. 1995, Finland (38)	186 acute low back pain patients	Exercise intervention consisting of one session individual physiotherapist instruction and written recommendations on back-extension and lateral bending movements to be performed every other hour	Bed rest or normal activity as tolerated	Patients in normal activity group had better recovery than bed rest or exercise patients. Continuing ordinary activities within the limits permitted by the pain leads to more rapid recovery than bed rest or back-mobilizing exercises	Overall costs of care did not differ significantly among the groups

Table 2. Continued

	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Torstensen et al. 1998, Norway (66)	208 chronic low back pain patients patients	Medical exercise therapy consisting of 1-hr group sessions with 7–9 exercises. 2–3 sets, 20- 30 repetitions aiming to influence endurance, circulation, and coordination	Conventional physiotherapy or self-exercise	No difference between medical exercise therapy and conventional physiotherapy, but both significantly better than self-exercise	Return to work equal for all 3 interventions at 15-month assessment. Regarding costs for days on sick leave, medical exercise therapy group saved $122,531, and conventional physiotherapy $254,200 compared with self-exercise group
Moffett et al. 1999, UK (44)	187 patients aged 18–60 years with mechanical low back pain	Exercise program consisting of 8 1-hr group sessions including stretching, low impact aerobic exercises, strengthening exercises	Usual care	At 6 months and 1-year intervention group showed significantly greater improvement in disability questionnaire score	Mean total costs/patient at 1 year £360 in the exercise group and £508 in the control group. At 6 months and 1 year intervention group reported less days off work. Exercise class was more clinically effective than usual care and was cost-effective
Hopman-Rock & Westhoff, 2000, The Netherlands (28)	120 osteoarthritis patients	Intervention program consisting of 6 weekly 2-hr sessions (health education, physical exercises comprising of warming up, exercises for the knee and hip, cooling down and relaxation). Dynamic exercises altered with static exercises. Participants encouraged to do the exercises at home at least 3 times a week	Usual care	Intervention had moderate effect on pain. Pain level decreased just after intervention, however this effect had disappeared at follow-up. Pain intolerance was still slightly decreased at follow-up	No differences in use of medication, or in the number of GP or PT consultations. At follow-up fewer PT consultations in the experimental group although GP consultations did not change
Roush et al. 2000, USA (55)	64 patients with anterior knee pain	Home therapy consisting of modified straight leg raise (Muncie method)	Traditional home therapy consisting of traditional "T" straight leg raise exercise and pillow squeeze exercise or physical therapy 3 times a week for 6 weeks	Percent improvement significantly better in participants using the Muncie method compared with those using traditional home therapy or formal physical therapy	Cost/ participant in home therapy and Muncie method groups the same ($291.00). Cost for physical therapy group ranged from $1,261.00 to $1,711.00. Findings suggest that Muncie method results in improved clinical outcome at a lower cost

Sevick et al. 2000, USA (58)	439 knee osteoarthritis patients	Resistance exercises for strengthening of major muscles	Health education or 3-month facility-based and 15-month home-based aerobic (walking) exercise	Resistance and aerobic exercise groups both had better scores than the education control group on outcome variables including self-reported physical disability, knee pain, 6-min walking distance, and lifting and carrying task	Total cost of educational intervention $344, of aerobic exercise $324, of resistance training $325/participant. Compared with educational control, resistance training was more economically efficient than aerobic exercise in improving physical function. On all but two of the outcome variables, the incremental savings per incremental effect for the resistance exercise group was greater than for the aerobic exercise group
Patrick et al. 2001, USA (49)	249 adults with osteoarthritis aged 55 to 75	Aquatic exercise classes	Usual care	QWB improved slightly in the treatment group at 20 weeks but remained the same in control group (N.S.). Mean CHDR increased in the treatment group and the disability measure of HAQ and the physical domain score of PQOL were improved	Mean direct and non-direct annualized health care costs for treatment group participant $3,634 and for control group participant $3,182. Incremental cost per QALY gained based on QWB $69,400 (no discounting) and $205,186 discounting 3%, based on CHDR $10,958 (no discounting) and $32,643 discounting at 3%. The aquatics-based exercise program did not demonstrate reduced costs and improved health outcomes compared with usual care
Korthals-de Bos et al. 2003, The Netherlands (34)	183 patients with neck pain for at least 2 weeks	Physiotherapy composed of individualized exercise therapy in a maximum of 6 30-min sessions including active and postural or relaxation exercises, stretching, and functional exercises	Manual therapy (spinal mobilization) or GP care (counseling, education, drugs)	Manual therapy group showed a faster improvement than physiotherapy or GP groups up to 26 weeks, but at 52 weeks differences were negligible.	Total costs €447 for manual therapy, €1,297 for physiotherapy, €1,379 for GP care, respectively. Cost-effectiveness and cost-utility ratios showed that manual therapy was more effective and less costly than physiotherapy or GP care

Table 2. Continued

	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Niemistö et al. 2003 & 2005, Finland (46;47)	204 chronic low back pain patients aged 24–46	Manipulative-treatment: 4 sessions during 4 weeks consisting of manipulation using a muscle-energytechnique and stabilizing exercises aiming to correct the lumbopelvic rhythm	Physician consultation alone (educational information)	Significant improvement in both groups on every self-rated outcome measure. Only slightly more significant reduction in VAS in the combination group. HRQOL improved equally in both groups	A 1-point improvement in the combination group compared to the consultation group in VAS scale cost $512. Total annual cost savings were higher in the consultation group. Consultation alone appeared to be more cost-effective for both healthcare use and work absenteeism than the combination therapy
Beaupre et al. 2004, Canada (3)	131 total knee arthroplasty waiting list patients	Exercise designed to improve knee mobility and strength. Simple strengthening exercises with progressive resistance added 3 times per week for 4 weeks	Usual care	No differences between the groups following intervention at any postoperative measurement points	Health service costs following discharge from acute care hospital $CDN 1,369 for treatment group, $CDN 1,366 for control group (N.S.). Total LOS following discharge 10.2 for treatment group, 11.7 for control group (N.S.). Functional recovery and health service utilization similar in both groups
McCarthy et al. 2004 & Richardson et al. 2006, UK (39;53)	214 patients meeting the American College of Rheumatology's classification of knee osteoarthritis	Class-based exercise program supplementing a home-based program by 8 weeks of twice-weekly knee-classes consisting of stretching, balance training, weight bearing exercises, quadriceps exercises	Home exercise program to increase lower limb strength, and endurance	Both groups reported an increase in EQ-5D scores. Class-based group showed a 0.023 QALY gain compared with the home-based group (N.S.)	Total mean cost per patient in class-based group £440.04, in home-based group £445.52. The addition of a class-based exercise program is likely to be cost-effective and, on current evidence, should be implemented

UK BEAM Trial Team 2004, UK (69)	1,287 back pain patients	Best care (BC) + +exercise consisting of up to 8 60-min group sessions over 4–8 weeks and "refresher" class 12 weeks after randomization	BC in general practice, BC + manipulation, or BC + manipulation + exercise	All three active treatments increased participants' average QALYs	Total costs: BC £346, BC + exercise £486, BC + manipulation £541, BC + manipulation + exercise £471. ICER for manipulation and exercise £3,800/QALY, for manipulation alone relative to manipulation and exercise £8,700. If manipulation was not available, ICER for exercise alone relative to BC £8,300. Spinal manipulation is a cost-effective addition to "best care". Manipulation alone probably gives better value for money than manipulation followed by exercise
Carr et al. 2005, UK (10)	237 patients with back pain lasting more than 6 weeks	"Back to Fitness" group exercise program consisting of 8 1-hr physiotherapist-led classes including low impact aerobics, strengthening, stretching and relaxation	Individual physiotherapy	No statistically significant differences in change scores between groups on any outcome measure	Health care costs were lower in the exercise group (£193/patient) than in the physiotherapy group (£338). Group exercise therapy less costly and, therefore, more cost-effective
Cochrane et al. 2005, UK (13)	312 osteoarthritis patients >60 years	Water exercise comprising of twice weekly 1 hr sessions in community swimming pool with warm-up, joint range of motion movements, muscle strengthening, coordination and balance, cardiovascular conditioning	Usual care	Short-term efficacy of water exercise in management of lower limb OA confirmed	Mean cost per participant for the delivery of the exercise intervention £142.47 per annum. A saving in water exercise group of £123–175 per patient per annum. Incremental cost-effectiveness ratios ranged from £3838 to £5951 per QALY. The water-exercise program produced a favorable cost-benefit outcome

Table 2. Continued

	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Lewis et al. 2005, UK (37)	80 patients with mechanical low back pain for more than 3 months	Group manual therapy and stabilization comprising of 8 1-hr exercise classes involving aerobic and spinal stabilization exercises	Exercise classes comprising of 8 30-min sessions of individual treatment involving manual therapy and spinal stabilization exercises	Significant reduction in questionnaire scores in both groups. Significant increases in range for all physical movements tested in both groups	Cost of running exercise group £360, of treating patients individually £600. Exercise group 40% more cost-effective than individual treatments
Wright et al. 2005, UK (76)	111 patients aged 18–65 with a new episode of simple back pain causing them to be off work or on modified work for less than 1 year	Exercise group received one treatment (manipulation, joint and soft tissue mobilization, steroid injection, or specific exercises) and subsequently 1-hr group exercise sessions 3 times a week for 2 weeks. Exercise comprised of aerobic exercise, spinal stability, muscle strengthening	Usual care	SF-12 Health Survey scores improved in both groups	The cost of service provision per patient was £ 134,79 for the usual care group and £857,92 for the exercise group. Median number of days to return to work 20 for the usual care group, 13 for the exercise group. Costs of the program more than reimbursed as a consequence of earlier return to work The estimated cost saving of providing the simple back program ranged from £250 to £578 for each patient.
Thomas et al. 2005, UK (63)	759 adults aged ≥45 years with knee pain	2-year home-exercise program comprising of quadriceps strengthening and aerobic exercises taught in a graded program and resisted exercises taught using rubber exercise bands	Monthly telephone contact, exercise and monthly telephone contact, or usual care	Significantly greater improvements in WOMAC pain scores in exercise groups compared with no-exercise groups (mean change –0.74 compared with no exercise)	Costs to healthcare provider for 2-year period £112 per person for exercise program and £61 for telephone intervention. Point estimate given by ICER equates to £ 2,570 per patient with a clinically significant improvement. Exercise therapy can provide significant benefits for people with knee pain, but the cost of delivering the program unlikely to be offset by reduction in medical resource use

Geraets et al. 2006, The Netherlands (19)	176 primary care patients with chronic shoulder complaints	Graded exercise therapy (GET), a behavioral treatment program with graded activity and time-contingency and operant conditioning administered by physiotherapists. Maximally 18 60 min group sessions over 12 weeks	Usual care	GET was more effective than UC in restoring daily activities. No significant differences in shoulder disability questionnaire or HRQoL	Intervention cost of GET €268, of UC €61. GET significantly reduced direct health care costs, but total cost during 1-year follow-up were higher due to higher costs of the intervention. Incremental cost-effectiveness €5278 per unit of improvement in EQ-5D
Heymans et al. 2006, The Netherlands (27)	299 non-specific low back pain patients aged 18–65 years	High-intensity back school (16 1-hr sessions of work-simulating and strength training exercises), low-intensity back school (4 90-min sessions consisting of strength exercises and home training)	Usual care	Beneficial effects on functional status and kinesiophobia at 3 months in favor of the low-intensity back school	Median number of sick-leave days 68, 75, and 85 in the low-intensity back school, usual care, and high-intensity back school, respectively. This difference was not statistically significant.
Coupe et al. 2007, The Netherlands (15)	200 osteoarthritis patients	Graded activity directed at increasing level of activity in a time-contingent manner. 12-week period with a maximum of 18 sessions, followed by 5 preset booster moments with a maximum of 7 sessions	Usual care	At 65 weeks no difference between the groups in improvement with respect to baseline in any of the outcome measures	Mean difference in total costs between the groups -€773 in favor of graded activity (N.S.). Incremental cost-effectiveness ratio of €51,385 per QALY for graded activity versus usual care. No evidence that behavioral graded activity is more effective or less costly than usual care.
Hurley et al. 2007, UK (29)	418 individuals aged 50–91 years with chronic knee pain	Individual or group rehabilitation (twice weekly sessions for 6 weeks performing simple exercises to improve functioning)	Usual care	WOMAC-func improved in rehabilitation groups. Proportion of participants with clinically meaningful improvement in functioning greater following rehabilitation than usual care	Rehabilitation cost £224 more per person than usual care. Probability of rehabilitation being more cost-effective than usual primary care 90% if decision makers willing to pay £1900 for improvements in functioning. Group rehabilitation increases probability of cost-effectiveness over individual rehabilitation

Table 2. Continued

	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Johnson et al. 2007, UK (30)	234 patients with persistent low back pain	Intervention arm received 8 2-hr group exercise sessions over 6 weeks comprising of active exercise and education (PT using CBT approach)	Usual care	The intervention showed a small, non-significant effect at reducing pain and disability.	Mean difference in costs £27 higher in the intervention arm. The cost of the intervention was low with an incremental cost-effectiveness ratio of £5,000 per QALY. 90% probability that treatment produced a cost per QALY of £30,000 or less
Williamson et al. 2007, UK (75)	181 patients with severe osteoarthritic knee pain waiting knee arthroplasty	Group physiotherapy once a week for 6 weeks consisting of an exercise circuit with muscle contractions, balance training, stair climbing etc.	Acupuncture or advice	Short-term reduction in Oxford Knee Score in the acupuncture group, otherwise no clinically or statistically significant differences between the groups	Cost for group physiotherapy £9/patient. A trend toward a shorter in-patient stay of 1 day for the physiotherapy group compared with the acupuncture group
Søgaard et al. 2006 & 2008, Denmark (60;61)	90 20- to 60-year-old patients with severe chronic low back pain caused by localized lumbar or lumbosacral segmental instability	Individual physiotherapist guided exercise therapy twice weekly for 8 weeks	Group meetings over 8-weeks to facilitate inter-patient exchange of experiences, or usual care (oral instruction and video-tape for exercises for home- training)	N.S. difference in improvement among the groups	Probability of behavioral approach being cost-effective close to 1 given pain as the prioritized effect measure, and 0.8 - 0.6 (dependent on willingness to pay) given disability as the prioritized effect measure. Probability of training approach being cost-effective modest due to inferior effectiveness

Van der Roer et al. 2008, The Netherlands (71)	114 chronic non-specific low back pain patients	Intensive exercise therapy consisting of 10 individual and 20 group sessions	Guideline	N.S. differences in functional status, pain intensity and QALYs. At 52-week follow-up, 45% of the exercise group had improved versus 32% in the guideline group	Costs per QALY amounted to € 5,141. The cost-effectiveness planes for all outcomes showed no significant differences in cost-effectiveness between the groups. No convincing evidence supporting nationwide implementation of intensive group training protocol in primary care
Non-randomized with matched controls					
Mitchell and Carmen 1990, Canada (43)	709 soft tissue injury or back pain patients	Intensive, time-limited exercises emphasizing mobility, muscle strengthening, work conditioning, sequence training, and appropriate education (average number of treatment days 12–17)	Usual care	At follow-up higher percentage of those working in the experimental group than in the control group	Total compensation costs (including costs of the intervention) lower in the experimental group

BC, best care; CBT, cognitive behavioral therapy; CHDR, current health desirability rating; EQ-5D, = EuroQol health-related quality of life instrument; GET, graded exercise therapy; GP, general practitioner; HAQ = Health Assessment Questionnaire, HRQoL = Health-related quality of life, ICER = Incremental cost-effectiveness ratio; LOS, length of stay; N.S., statistically non-significant; PQOL, perceived quality of life scale; PT, physiotherapist; QALY, quality-adjusted life-year; QWB, quality of well-being scale; SF-12 Health Survey, SF-12 health-related quality of life instrument; UC, usual care; VAS, Visual Analogue Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; $CDN, Canadian dollar.

work and thus to be cost-saving compared to usual care. By contrast, manipulative treatment together with stabilizing exercises was less cost-effective than physician consultation alone regarding both healthcare use and work absenteeism (46;47).

Compared to self-exercise, medical exercise therapy and conventional physiotherapy were both reported to be clinically superior and cost-saving in chronic low back pain patients (66).

In a large UK trial, best care in general practice was compared with best care combined with exercise, manipulation, or both (69). Spinal manipulation was found to be a cost-effective addition to best care and appeared to give better value for money than manipulation followed by exercise.

A group exercise program was more cost-effective than individual physiotherapy (10). Likewise, manual therapy together with spinal stabilization exercises was more cost-effective when given in groups as compared to individual treatment (37).

OSTEOARTHRITIS

In osteoarthritis patients exercise interventions were found to be cost-effective in only three (13;39;53;58) of the eight included studies. (References 39 and 53 represent the same study.) In the other five (3;15;28;49;75), the effect of exercise was modest compared to its costs.

KNEE PAIN

In all three studies dealing with chronic knee pain, exercise appeared to be an effective intervention (29;55;63). However, only the studies by Roush et al. (55) and Hurley et al. (29) found that exercise is likely to be cost-effective compared to the control intervention.

SHOULDER COMPLAINTS

Graded exercise therapy was more effective than usual care in patients with chronic shoulder complaints. It also reduced direct healthcare costs, but total costs during the 1-year follow-up were higher due to higher costs of the intervention (19).

In treatment-resistant rotator cuff disease, both a supervised exercise regimen and arthroscopic surgery were more effective than placebo soft laser treatment. The improvement in the surgery group was greater, but the differences between the two groups were not significant or clinically important, and the costs of the exercise regimen were lower (7).

NECK PAIN

In patients with neck pain, manual therapy was more cost-effective than physiotherapy comprising of individualized exercise therapy or usual care (34).

Cardiovascular Diseases. The second largest group of studies covered the use of exercise interventions in the treatment of patients with cardiovascular diseases (Table 3). The majority (eleven of fifteen) of them (1;4;6;9;23;24;32;48;52;77;78) dealt with coronary artery disease (CAD), two with chronic heart failure (18,22), one with essential hypertension (25), and one with hypertension in dialysis patients (42). Most of the studies (eleven of fifteen) were randomized controlled trials.

CORONARY ARTERY DISEASE

In CAD patients, three studies comparing an exercise intervention with usual care considered the exercise intervention to be cost-effective (1;6;77). Furthermore, one study reported exercise to be more cost-effective than stent angioplasty (24). One study comparing formal rehabilitation after myocardial infarction to early return to normal activities without rehabilitation, however, found the latter more cost-effective in low-risk patients (23). In patients exhibiting mental stress-induced ischemia, stress management was shown to be beneficial over exercise and was associated with lower medical costs (4). A high-frequency exercise program, when compared to a low-frequency program led to slightly better quality of life (QoL) at approximately double cost but no conclusion or results on cost-effectiveness were reported (48).

One study reported that a modified, reduced cost cardiac rehabilitation program is more cost-effective than traditional rehabilitation (9). The distribution of the exercise intervention over 12 months, as opposed to 3 months, did not affect cost-effectiveness (52) and home-based rehabilitation did not differ in a significant manner from center-based rehabilitation regarding effectiveness or costs (32).

One study reported that a gradual increase in moving around and walking led to shorter hospital stay and lower hospital costs compared to absolute bed rest in myocardial infarction patients (78). Absolute bed rest in myocardial infarction, however, is currently an obsolete treatment modality in western countries.

HEART FAILURE

In heart failure patients, exercise interventions appeared to be cost-effective compared to usual care (18;22).

HYPERTENSION

In hypertensive patients, drug therapy was clearly less costly per mmHg reduction in systolic blood pressure than exercise therapy (25). In hemodialysis patients with hypertension, a greater reduction in antihypertensive medication was seen in the exercise group (42).

Rheumatic Diseases. In three of the four studies on rheumatology, exercise was considered cost-effective (Table 4). Both of the studies on ankylosing spondylitis showed positive cost-effectiveness results (2;72), but in rheumatoid arthritis, patient costs and quality-adjusted life-years (QALYs) were in favor of usual care (70). Intensive exercise training was more effective than usual care in

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Table 3. Patients, Interventions, and Outcomes in the Identified Studies Dealing with Cardiologic Disorders

	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Randomized controlled studies					
Arthur et al. 2000, Canada (1)	249 low-risk patients awaiting elective CABG	Preoperative individualized exercise training (warm-up, stretching, aerobic interval training, cool down) twice a week in a supervised environment	Usual care	Intervention related to a significant reduction in length of total, postoperative, and ICU hospital stay	Costs of the intervention more than offset by the cost savings realized by the reduced length of stay
Carlson et al. 2000, USA (9)	80 35- to 75-year-old, low–moderate-risk patients referred to outpatient cardiac rehabilitation after cardiovascular surgery or event	Modified, reduced cost cardiac rehabilitation (MP = after 4 weeks patients weaned from ECG-monitor and gradually from supervised exercise sessions to an off-site exercise regimen)	Traditional cardiac rehabilitation	Both protocols provided comparable improvements in clinical parameters	MP cost $738 less/ patient and required 30% less staff. MP or a similar protocol can provide cost-effective cardiovascular risk reduction to patients
Nieuwland et al. 2000, The Netherlands (48)	130 CAD patients	6-week high-frequency (2 sessions 5 days a week) exercise program	6-week low-frequency (1 session twice a week) exercise program	Mean exercise capacity increased in both programs. During high-frequency program QoL increased slightly more, and more individuals improved in subjective physical functioning	Mean costs €4,455 and €2,273 for the high- and low-frequency programs, respectively. No conclusions about cost-effectiveness
Georgiou et al. 2001, USA (18)	99 heart failure patients	14-month-long moderate exercise training (stretching followed by 40 min cycling thrice weekly for 8 weeks and twice weekly thereafter for 1 year)	Usual care	Estimated increment in life expectancy in the training group 1.82 years/ person in a time period of 15,5 years	Incremental cost for the training group $3,227/ patient. The cost-effectiveness ratio for long-term exercise training $1,773/ life-year saved. Long-term exercise training is cost-effective
Blumenthal et al. 2002, USA (4)	94 CAD patients exhibiting mental stress-induced ischemia	Exercise program consisting of aerobic exercises 3 times per week for 16 weeks (10 min warm-up, 35 min of walking and jogging)	Stress management program and usual care	Stress management patients tended to have fewer cardiac events after 1 and 2 years than exercise patients	Stress management associated with lower medical costs than exercise in the first 2 years and was considered beneficial

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Table 3. Continued

	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Hall et al. 2002, Australia (23)	142 low-risk AMI patients	Return to normal activities after 6 weeks of standard rehabilitation (low level training and counseling)	Early return to normal activities 2 weeks after AMI with no formal rehabilitation	No statistically significant differences between the groups in any of the outcomes measured or in the use of other health services	Direct cost for 14 sessions of rehabilitation AUD $301.91 per patient. Early return to normal activities without formal rehabilitation is cost-effective for low-risk patients
Hambrecht et al. 2004, Germany (24)	101 male patients with stable CAD	Exercise training: first 2 weeks in-hospital exercise 6 times per day for 10 min on a bicycle ergometer. After discharge exercise on bicycle ergometer for 20 min per day, one 60-min group training session of aerobic exercise per week	Stent angioplasty	Exercise training resulted in significantly higher event-free survival (88% vs. 70%). PCI and exercise equally effective in improving symptom-free exercise tolerance.	Training intervention significantly more cost-effective: to improve Canadian Cardiovascular Society class by 1 class cost $6,956 for PCI compared with $3,429 for exercise
Yu et al. 2004, Hong Kong (77)	193 recent AMI and 76 elective PCI patients	Cardiac rehabilitation and prevention program (CRPP), a 2-year, 4 phase exercise program of mostly aerobic exercise supplemented with education	Conventional care	In CRPP group, 6 of 8 SF-36 dimensions improved significantly. In control group 4 dimensions improved. Improvement in QOL after CRPP maintained for at least 2 years. Mean QALY gain in CRPP group at 2 years 0.6.	Total healthcare cost $15,292 per patient for study, and $15,707 for control group, respectively. Cost-utility of rehabilitation $640 saved per QALY gained
Briffa et al. 2005, Australia (6)	113 patients after acute coronary syndrome	Rehabilitation (18 60–90 min outpatient sessions of aerobic circuit training interspaced with resistance training. In addition 12 educational and 6 psychosocial counseling sessions)	Conventional care	At 12 months significant improvement in utility (0.026) in rehabilitation group. However difference in improvement between the groups not statistically significant	Mean total cost/patient: conventional treatment AUD 4,541, rehabilitation AUD 4,937. Incremental cost per QALY saved AUD 4, 2535 for rehabilitation

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Table 3. Continued

	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Reid et al. 2005, Canada (52)	392 CAD patients	Distributed (over 12 months) cardiac rehabilitation (27 supervised exercise classes over 1 year)	Standard cardiac rehabilitation (exercise classes twice weekly for 13.5 weeks)	No clinically meaningful or statistically significant between group differences for outcomes at 12 or 24 months	Costs of programs similar; at 2 years total direct costs of standard rehabilitation $5,132, of distributed rehabilitation $5,267
Jolly et al. 2007, UK (32)	525 patients who had experienced myocardial infarction or coronary revascularization within previous 12 weeks	Home-based rehabilitation (exercise, relaxation, education, lifestyle counseling, manual, home visits, telephone contacts)	Centre-based rehabilitation programs (from 9 sessions at weekly intervals to 24 individualized sessions over 12 weeks of mainly walking, fixed cycling and rowing with group-based education)	No clinically or statistically significant differences in any of the primary or secondary outcomes between the groups	Direct rehabilitation costs for home-based program £198, for centre-based program £157. Including patient costs increased mean center-based cost to £182
Non-randomized controlled studies					
Harada et al. 2001, Japan (based on abstract only, full-text in Japanese)(25)	114 patients with essential hypertension	Exercise therapy	Drug therapy		Cost-effectiveness per 1 mmHg systolic blood pressure reduction yen 11,286 for exercise therapy, yen 2,441 for drug therapy
Miller et al. 2002, USA (42)	40 hemodialysis patients with hypertension	Exercise consisting of stationary cycling during each hemodialysis treatment	Usual care	Pre- and postdialysis blood pressures not significantly different between the groups but 54% in exercise group had reduction of antihypertensive medication compared to 13% in the control group	Average annual cost saving $885/patient-year in the exercise group
Zhang and Sun 2006, China (78)	80 myocardial infarction patients	Gradual increase of moving around and exercise (walking) over 14 days	Absolute bed rest	Barthel index (an index of independence) significantly higher in the intervention group (81.4 vs. 70.7). Recurrence rate of myocardial infarction over 2 years lower in the rehabilitation group (5% vs. 22%)	Shorter hospital stay and hospital costs (yuan 9,021 vs. 12,383) in the intervention group

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Table 3. Continued

	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Retrospective studies					
Hagerman et al. 2005, Sweden (22)	48 chronic heart failure patients	Physical training program for 8 weeks consisting of dynamic endurance training with unilateral or bilateral quadriceps muscles	Conventional treatment	Exercise training did not affect mortality	Exercise training resulted in significantly less hospitalization events and hospitalization days due to cardiac problems at 5 years after follow-up

AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CRPP, cardiac rehabilitation and prevention program; ICU, intensive care unit; MP, modified protocol; QALY, quality-adjusted life-year; QOL, quality of life; PCI, percutaneous coronary intervention; SF-36, SF-36 health-related quality of life instrument.

patients with arthritis admitted to hospital because of disease activity flare or for elective joint replacement (8). The cost-effectiveness results, however, were contradictory depending on how QALYs were determined.

Miscellaneous Disorders. Results concerning the cost-effectiveness of exercise interventions in chronic obstructive pulmonary disease (COPD) patients were equivocal with two studies showing some positive effects (11;68), whereas a third one (54) found a significant advantage from exercise (Table 5).

In the treatment of urinary incontinence, results of the three included studies were either negative or inconclusive regarding cost-effectiveness (50;57;74).

Positive cost-effectiveness results were also reported in two studies dealing with peripheral arterial disease (35;67), one study with breast cancer patients (20), one study in diabetes (45), and one study with schizophrenic patients (65).

Overview of Outcomes

The studied exercise interventions in musculoskeletal disorders were deemed to be cost-effective in 54 percent (fifteen of twenty-eight) of the cases, in cardiology in 60 percent (nine of fifteen) of the cases, and in rheumatic diseases in 75 percent (three of four) of the cases. Furthermore, there was some evidence that exercise interventions might be cost-effective in the treatment of intermittent claudication (two of two studies), breast cancer patients (one of one), diabetes (one of one), and schizophrenia (one of one).

DISCUSSION

We conducted a systematic review on the evidence of cost-effectiveness of exercise interventions in various diseases and critically examined the study quality. Our findings provide a basis for decision makers when considering which exercise interventions should be adopted for routine use. Several studies have shown the efficacy of various types of exercise interventions; their cost-effectiveness, however, remains poorly documented. As healthcare resources are limited, it is important that only cost-effective interventions are used.

The number of included articles was higher in the present review than in a previous literature review on cost-effectiveness of exercise interventions by Hagberg and Lindholm (21). This may in part be because of our relatively loose inclusion criteria. In addition to studies reporting pure cost-effectiveness data, we also included studies reporting on healthcare service utilization. Furthermore, studies with varying kinds of exercise interventions and control interventions were included. Another explanation is the fact that the number of studies investigating exercise and reporting on cost-effectiveness or healthcare utilization data have increased since the review by Hagberg and Lindholm (21), which covered studies published before year 2005. Twenty-eight of the studies included in this review were published in year 2005 or later.

There was great heterogeneity in the study settings of the included studies, and in many of them, exercise was combined with other interventions, most often with education or advice. There was also great variance in what exercise was compared to, ranging from usual care to surgical procedures and educative measures. Also, several studies compared different exercise or physiotherapy interventions of varying intensity. As the populations and interventions studied varied greatly, it was not possible to combine the results to draw conclusions about the effectiveness of exercise interventions in specific patient populations. Furthermore, the fact that, in many cases exercise was combined with advice or education prevents solid conclusions about the effectiveness of exercise per se. Consequently, in the future randomized

Table 4. Patients, Interventions, and Outcomes in the Identified Studies Dealing with Rheumatologic Disorders

	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Randomized controlled studies					
Bakker et al. 1994, The Netherlands (2)	144 patients with ankylosing spondylitis	Supervised group physical therapy comprising of weekly 3-hr group sessions consisting of physical training, sporting activities and hydrotherapy	Unsupervised exercises	Significant differences in favor of the intervention group in mobility, fitness and global health	Total medical costs decreased during the 9-month follow-up by 44% in the intervention and by 35% in the control group, respectively. Beneficial effects of group therapy cost $409/patient with ankylosing spondylitis/year
Van Tubergen et al. 2002, The Netherlands (72)	120 patients with ankylosing spondylitis	Combined spa and exercise therapy (two different spas) consisting of physical exercises, walking, postural correction therapy provided 5 days a week for 3 weeks	Usual care	Mean AUC of EQ-5D change during study period 0.11 for spa group 1, 0.02 for spa group 2, -0.06 for usual care	Mean total costs per patient €3,023 for spa group 1, €3,240 for spa group 2, €1,754 for usual care. Costs per QALY €7,465 for spa group 1, €1,8575 for spa group 2. Combined spa-exercise therapy besides standard treatment and weekly physical therapy is more effective and shows favorable cost-effectiveness and cost-utility ratios compared with standard treatment alone
Van den Hout et al. 2005, The Netherlands (70)	309 rheumatoid arthritis patients	Long-term intensive exercise program (RAPIT) comprising of high-intensity weight-bearing exercise classes, 75-min sessions twice a week for 2 years	Usual care	Estimated annual difference of 0.037 QALYs in favor of usual care	Total annual societal costs per patient €4,749 for RAPIT and €4,147 euros for usual care. Costs and QALYs in favor of usual care

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Table 4. Continued

	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Bulthuis et al. 2008, The Netherlands (8)	85 patients with arthritis admitted to hospital because of disease activity flare or for elective joint replacement.	3-week intensive exercise training (IET) program: twice a day 75-min individual and group physical therapist sessions aiming to improve range of motion, muscle strength, aerobic capacity, physical function and daily activities	Usual care	Using SF-6D no differences in QALYs. Using VAS QALYs gained in favor of IET	Total cost of IET estimated at €2,991 per patient. Mean total costs €718 lower for IET group per patient per year compared with UC. Incremental cost-utility ratio based on VAS after 6 months of follow-up €20,100/ QALY gained. In 49% of cases the intervention was cost-saving. After 1 year of follow-up, the intervention was cost-saving and IET was the dominant strategy

AUC, area under the curve; EQ-5D, EuroQol health-related quality of life instrument; IET, intensive exercise training; QALY, quality-adjusted life-year; RAPIT, long-term intensive exercise program; SF-6D, SF-6D health-related quality of life instrument; VAS, Visual Analogue Scale.

controlled trials studying pure exercise interventions are needed to define the effect and cost-effectiveness of mere physical training.

Due to the small number of studies dealing with specific conditions, and the fact that reporting was in some cases incomplete, it is difficult to draw conclusions about the effect of patient characteristics (e.g., age, gender, previous physical activity, severity of illness), or the characteristics of the exercise interventions (intensity and workload, adherence to physical training) to the outcomes regarding health and costs. In future studies, it would be important to identify those patients that are expected to benefit the most from exercise interventions.

The overall quality of the included studies varied widely and was, on average, only mediocre. There was no systematic difference regarding quality between the different disease groups. The economic quality of the studies judged against the criteria by Drummond et al. (17) tended to reach somewhat higher scores than the overall quality and, was judged, on average, to be fair to good in studies dealing with musculoskeletal disorders and rheumatology. There was also much variance in how the outcomes were reported, which precludes the use of meta-analysis for combining the results of different studies. Only a few studies reported outcomes as cost/QALY, which enables the comparison of different kinds of interventions in health care. In prospective studies, it would be useful to use the same instruments to measure the outcomes, which would allow pooling of the results of different studies together.

CONCLUSION

The number of studies assessing cost-effectiveness of exercise interventions in various diseases is still rather limited, and the results show large variation. The results suggest that some exercise interventions, however, can be cost-effective. In rheumatology, the percentage of studies reporting positive cost-effectiveness outcomes was the highest, but the number of studies was low. Most convincing evidence for cost-effectiveness was found for rehabilitation of cardiac patients and back-pain patients; however, even in these cases, the evidence was partly contradictory.

SUPPLEMENTARY MATERIAL

Appendix 1: www.journals.cambridge.org/thc

Table 5. Patients, Interventions, and Outcomes in the Identified Studies Dealing with Miscellaneous Disorders

	Type of study	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Pulmonary diseases						
Ries et al. 1995, USA (54)	RCT	119 COPD patients stable on standard medical regimen	8-week comprehensive pulmonary rehabilitation program consisting of 12 4-hr sessions including education, physical and respiratory care instruction, psychosocial support and supervised exercise (walking, upper-extremity exercises)	8-week education program of 4 2-hr sessions that included videotapes	Comprehensive rehabilitation program significantly improved exercise performance and symptoms for patients with moderate to severe COPD	Slight but non-significant differences in favor of comprehensive rehabilitation in survival (67% vs 56%) and duration of hospital stay (-2.4 days/patient per year compared with +1.3 days/patient per year). General quality of life did not differ between the groups
Troosters et al. 2000, Belgium (68)	RCT	100 patients with severe COPD	6-month outpatient rehabilitation program comprising of 1,5 h sessions 3 times a week the first 3 months, then 2 times a week for 3 months. Exercise included cycling, treadmill walking, stair climbing and peripheral muscle training	Usual care	Exercise program did not alter pulmonary function but improved functional and maximal exercise performance, peripheral and respiratory muscle strength, and quality of life	Program cost $57 per patient per session. Mean cost of the program per patient $2,615+/− 625. Mean improvement of 52 meters in 6-min walking test at 6 months cost $2,615
Clini et al. 2001, Italy (12)	Retrospective case-control study	43 chronic airway obstruction patients compared with 43 matched controls	Inpatient pulmonary rehabilitation program (PRP) comprising of 10–12 daily sessions (5 sessions/ week) incorporating supervised incremental exercise and abdominal muscle activities	Outpatient PRP comprising of 20–24 sessions (3 sessions/ week)	Both PRPs resulted in similar significant improvements in cyclometer peak workload, isoload D and isoload F	Inpatient PRP cost € 2,720/patient, outpatient PRP €3,677/patient. Although the single daily session was less expensive, outpatient PRP total costs were greater because of higher number of sessions and the cost of daily transportation. A shorter inpatient PRP may result in improvement in exercise tolerance similar to a longer outpatient PRP but with lower costs

Table 5. Continued

	Type of study	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Carrieri-Kohlman et al. 2005, USA (11)	RCT	103 patients with stable COPD	Dyspnea self-management program (DM) + 24 exercise sessions aiming at steady state exercise consisting of continuous walking for as long as 30 min at a level 1 workload lower than maximum	DM only or DM +l4 exercise sessions	All 3 versions of the dyspnea self-management program resulted in similar improvement in dyspnea with activities of daily living. The greater number of supervised exercise sessions improved laboratory dyspnea and performance more than the other two doses of exercise-training	No significant difference between the groups in number of exacerbations or hospitalizations
Urinary incontinence						
Ramsay et al. 1996, UK (50)	RCT	74 patients with mixed pattern of urinary symptoms	Pelvic floor exercises consisting of both fast and slow twitch contractions during a 5-day hospital stay	The same pelvic floor exercises in 2 2-hr outpatient sessions	Significant decrease in frequency, nocturia, number of incontinent episodes and visual analogue scores for both groups	Outpatient treatment costs £66/ patient; inpatient costs £126/patient. Outpatient conservative treatment is as successful and possibly better than inpatient treatment, and is significantly cheaper
Schnelle et al. 2003, USA (57)	RCT	190 incontinent, long-stay nursing home residents	Patients prompted to toilet and encouraged to walk and do repeat sit-to-stands several times a day. Once a day upper body resistance training.	Usual care	Intervention group had significantly better functional outcomes (strength, mobility endurance, urinary and fecal incontinence) and a 10 % reduction in the incidence of acute conditions (N.S.)	No significant differences between groups in the cost of assessing and treating acute conditions

Williams et al. 2006, UK (74)	RCT	238 women with urodynamic stress incontinence in whom previous primary behavioral intervention had failed	Intensive pelvic floor muscle therapy (PFMT)	Vaginal cone therapy or primary behavioral intervention	Improvements from baseline for all three groups for all incontinence and storage symptom variables, but no differences in effectiveness between the groups	Costs of intervention £287, £338 and £305 per patient, for the behavioral intervention, PFMT and vaginal cone groups, respectively. Costs for alleviating symptoms by PFMT high, much higher than for a simple nurse-led continence service
Vascular diseases						
Treesak et al. 2004, USA (67)	Modeling using clinical data from 2 RCTs	Hypothetical cohorts of peripheral arterial disease patients with claudication and ilio-femoral arterial disease	2 30-min supervised exercise sessions/week for 3 or 6 months with graded treadmill walking being the main exercise modality	Percutaneous transluminal angioplasty (PTA)	At 3 months, PTA was more effective, at 6 months, exercise was more effective	Total cost of the 3-month exercise rehabilitation program $2,939, of the 6-month program $4,963. At 3 months, PTA resulted in an additional 38 meters at an additional cost of $6,719, for an ICER of $177/meter. At 6 months, exercise resulted in an additional 137 meters walked and with less costs ($61/meter gained). Exercise rehabilitation at 6 months is more effective and costs less than PTA, and is therefore cost-saving
Lee et al. 2007, UK (35)	Non-randomized controlled study	70 patients with intermittent claudication	Supervised exercise program (SEP) comprising of graduated physical exercise for 60 min, 3 times each week	Usual care	SEP was associated with a positive effect size in the SF-36 index and in 2 SF-36 QoL domains but a negative effect size in a further 2 domains. SEP resulted in a 0.027 QALY gain over usual care in the first year post-treatment	Cost/QALY gained by SEP £1,780 at 1 year

Table 5. Continued

	Type of study	Patients	Intervention	Control intervention	Outcomes	Conclusions (cost-effectiveness)
Oncology						
Gordon et al. 2005, Australia (20)	Non-randomized controlled study	67 breast cancer patients	Home-based physiotherapy intervention	No intervention or group-based exercise and psychosocial intervention	Proportion of rehabilitated cases (based on changes in HRQoL between 6 and 12 months post-diagnosis) similar across the three groups	Total program cost (average/person) AUD 342 for home-based intervention, AUD 1038 for group-based intervention. Home-based intervention most efficient option with an incremental cost of AUD 1,344/QALY gained. Incremental cost/QALY gained from group-based program AUD14,478. Both interventions considered to be low-cost low-technological health promoting programs representing excellent public health investments
Chronic fatigue						
McCrone et al. 2004, UK (40)	Partly RCT, partly comparative study	142 patients with chronic fatigue	Graded exercise therapy (GET) comprising of 6 45-min sessions (delivered by physiotherapists and tailored to physical capacity) aiming for a gradual increase in aerobic activities	Usual care + self-help booklet, or cognitive behavioural therapy (CBT)	No significant outcome differences between the two therapy groups. The combined therapy group (both GET and CBT groups) had significantly better outcomes than the standard care group	Cost of 1 hr of CBT £40, of GET £41. The cost-effectiveness of CBT and GET similar unless higher value placed on outcomes, in which case CBT showed improved cost-effectiveness. Therapy would have a 81.9% chance of being cost-effective if society was willing to attach a value of £500 to each four-point improvement in fatigue

Endocrinology						
Nguyen et al. 2007, USA (45)	Retrospective cohort study	527 patients with diabetes	Enhanced fitness program (EFP), a group-based exercise program comprising of 5 min warm up, 20–25 min moderate-intensity aerobics, 20 min resistance strength training, 10 min flexibility and balance training 3 times/week	Usual care	After exposure to the program a trend toward lower hospital admissions in EFP participants	Total healthcare costs were not different. EFP participants who attended $\geq$1 exercise session/week on average had 41% less total healthcare costs compared with those attending $<$1 session/week and control subjects
Psychiatry						
Torres-Carbajo et al. 2005, Spain (65)	Non-randomized controlled study	40 schizophrenic patients	Exercise program (for a mean of 4.1 years one day a week for 1 hr) consisting of 30-min coordination, cooperation, speed, agility, balance, and group participation exercises and 30-min soccer game)	Usual care	Both groups showed significantly fewer relapses than in their earlier history, but the reduction was significantly greater in the exercise group	Hospitalization costs in the exercise group €7,200, in the control group €115,200. Enrolment in an exercise program considered a more effective and efficient treatment than standard care for schizophrenic patients and may reduce overall healthcare costs
Neurology						
Lemstra et al. 2002, Canada (36)	RCT	80 migraine patients	Intervention composed of 18 group-supervised exercise therapy sessions (submaximal aerobic exercise, stretching, light weight training) 2 stress management and relaxation lectures, 1 dietary lecture, 2 massage therapy sessions	Usual care	Intervention group experienced statistically significant changes in self-perceived pain frequency, pain intensity, pain duration, functional status, quality of life, health status, pain related disability, and depression. These differences retained their significance at 3-month follow-up	No statistically significant changes in medication use or work status

AUD, Australian dollar; CBT, cognitive behavioral therapy; COPD, chronic obstructive pulmonary disease; DM, dyspnea self-management program; EFP, enhanced fitness program; GET, graded exercise therapy; HRQoL, health-related quality of life; PFMT, pelvic floor muscle therapy; PRP, pulmonary rehabilitation program; PTA, percutaneous transluminal angioplasty; QALY, quality-adjusted life-year; RCT, randomized controlled trial; SEP, supervised exercise program.

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