EFFECTIVENESS OF EXERCISE THERAPY IN OSTEOARTHRITIS OF HIP OR KNEE

ERRATUM

Figure 1, page 3

Osteoarthritis of the hip

a. Hip pain
and
b. One of the following combinations:
b1. - Hip internal rotation < 15°
and
- ESR ≤ 45 mm/1 hour
b2. Hip internal rotation ≥ 15°
and
- Pain on hip internal rotation
and
- Morning stiffness of the hip ≤ 60 minutes
and
- Age > 50 years

Van Baar, Margriet Elisabeth

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EFFECTIVENESS OF EXERCISE THERAPY IN OSTEOARTHRITIS OF HIP OR KNEE

Effectiviteit van oefentherapie bij
artrose van heup of knie

(met een samenvatting in het Nederlands)

Proefschrift ter verkrijging van de graad van doctor
aan de Universiteit Utrecht
op gezag van de Rector Magnificus, Prof.dr. H.O. Voorma
ingevolge het besluit van het College voor Promoties
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Margriet Elisabeth van Baar

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Promotores:	Prof. J.W.J. Bijlsma	Universiteit Utrecht, vakgroep Reumatologie en Klinische Immunologie
	Prof. J. Dekker	NIVEL (Nederlands instituut voor onderzoek van de gezondheidszorg) en Vrije Universiteit Amsterdam, Instituut voor Extramuraal Geneeskundig Onderzoek
	Prof. R.A.B. Oostendorp	Nederlands Paramedisch Instituut en De Vrije Universiteit Brussel, vakgroep Manuele Therapie

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Voor mijn vader

CONTENTS

1

INTRODUCTION

OSTEOARTHRITIS OF HIP OR KNEE

Osteoarthritis (OA) of the hip or knee is a relatively common disorder. Occurrence of symptomatic OA, as opposed to radiological OA, is relatively high. Based on the registration systems in general practice, it was estimated that in the Netherlands in 1994 180.800 patients suffered from OA of the hip and 295.600 persons suffered form OA of the knee[1]. Prevalence in general practice in the Netherlands is between 10 to 13 per 1000 for OA of the hip and 16 to 20 per 1000 for OA of the knee. The variation in prevalences stems from the small differences in diagnostic criteria used in the different registration systems in general practice[2,3]. The total incidence in general practice is 2.1/1000 per year for OA of the hip and 3.6/1000 per year for OA of the knee. The proportion of new complaints, compared to recurring complaints, is in hip patients higher than in knee patients (55% and 42% respectively)[4]. Incidence in general practice increases with age and is maximal in the 65- to 74- year-olds[3,5]. Osteoarthritis of both the hip and knee is more common in female than in male patients. The incidence of hip OA is 2.3/1000 in female and 1.2 in male patients. The incidence of OA of the knee is 3.3/1000 in female and 1.9/1000 in male patients[3].

OA is characterised by a progressive loss of articular cartilage in combination with increased activity of underlying subchondral bone, resulting in stiffening of the subchondral bone (sclerosis) and development of bony outgrowths at the joint margins (osteophytes)[6,7]. When patients become symptomatic, these changes are often combined with a mild degree of secondary inflammation[8]. As OA progresses, the pathological changes in cartilage and bone are followed by pathological changes in synovial membrane, capsule, ligaments and associated musculature. This may lead to capsular restriction, instability of the joint, progressive muscle weakness and muscle atrophy[6,9].

Clinical symptoms and signs include loading-related pain, stiffness of joints after inactivity, restricted range of movement, bone swelling and crepitus. Other possible features are rest or night pain, instability and deformity of joints[6]. The reduced loadability of joints frequently results in disability in mobility and bending.

In most cases the origin of joint destruction is unknown (primary OA). In few cases the cause of joint damage can be identified e.g. a congenital dysplasia or a trauma (secondary OA). Important factors in the etiology of osteoarthritis in general are biomechanical forces on cartilage and subchondral bone, and biochemical changes in cartilage and synovial membrane[10,11]. Specific risk factors for hip OA include developmental abnormality (such as dysplasia), and occupational activities such as farming. Risk factors for knee OA include obesity, previous major knee injury and prior inflammatory joint disease[12].

At present, there is no single accepted classification system for OA. There are two main systems, the radiological criteria of Kellgren and Lawrence and the criteria of the American College of Rheumatology(ACR), based on radiological and or clinical criteria. The Kellgren and Lawrence system was introduced in 1963. Their system is based on radiographic changes in cartilage and underlying subchondral bone[13]. Most studies on OA have applied this classification system. In 1986 the Subcommittee on Criteria for Osteoarthritis of the American College of Rheumatology published classification criteria for the knee[7], followed in 1991 by classification criteria for the hip[14]. These criteria were based on clinical criteria or a combination of clinical and radiological criteria. In this thesis, the clinical criteria of the American College of Rheumatology will be used. The sensitivity and specificity of these criteria are sufficiently high. The sensitivity and specificity of these criteria in hip OA are 86% and 75%, in knee OA 95% and 69%. Furthermore, the use of clinical criteria optimally matches the procedure in general practice.

Figure 1: Clinical criteria for osteoarthritis of the hip or knee of the American College of Rheumatology

Osteoarthritis of the hip	*Osteoarthritis of the knee*
a. Hip pain and	a. Knee pain and
b. One of the following combinations	b. At least 3 of 6:
b1. - Hip internal rotation <15° and - ESR=45 mm/hour	-Age > 50 years -Stiffness < 30 minutes -Crepitus -Bony tenderness -Bony enlargement -No palpable warmth
b2. -Hip internal rotation =15° and -Pain on hip internal rotation and -Morning stiffness of the hip =60 minutes and -Age>50 years.	

MANAGEMENT OF OSTEOARTHRITIS OF THE HIP OR KNEE

Recently, the American College of Rheumatology (ACR) published guidelines for the medical management of osteoarthritis of the hip or knee[15,16]. In figure 2 a summary is given of these guidelines. The ACR guidelines are in line with guidelines on this topic as published earlier[17-19].

Figure 2: Summary of the ACR guidelines[15,16] for medical management of patients with osteoarthritis of the hip and knee

Non-pharmarcological therapy
- Patient education, including self-management programmes
- Health professional social support via telephone contact
- Weight loss (if overweight)
- Physiotherapy including range of motion exercises, strengthening exercises and assistive devices for ambulation
- Occupational therapy, including joint protection and energy conservation and assistive devices for (instrumental) activities of daily living
- Aerobic (aquatic) exercises programmes

Pharmacological therapy
- Intraarticular steroid injections (for knee OA)
- Non-opioid analgesics, e.g. acetaminophen
- Topical analgesics, e.g. capsaicin, and methylsalicylate creams (for knee OA)
- Nonsteroidal antiinflammatory drugs

Since there is no known cure for OA, treatment is aimed at the consequences of disease. Goals of treatment are to control pain and other symptoms, minimise disability and educate the patient and his or her family about the disease and its treatment. In mild OA of the hip, non-pharmacological modalities (including physiotherapy and occupational therapy) and pharmacological modalities should be combined. Acetaminophen is recommended as the first drug of choice. In OA of the knee, non-pharmacological modalities are preferred as a first treatment. Exercise therapy is considered an important part of treatment in both conditions.

Patients with severe symptomatic OA who have pain that has failed to respond to medical therapy and progressive limitations in activities of daily living, should be referred to the orthopaedic surgeon for evaluation, according to the ACR. Surgical treatment includes osteotomy and total joint arthroplasty.

Medical management of osteoarthritis of the hip or knee

In the Netherlands, general practitioners (GPs) have a central position in the health care system. Most of the other care providers, such as physiotherapists and medical specialists are accessible only after referral by a GP[20]. Also for patients with OA of the hip or knee, the GP is a starting point for treatment. In a one-year period, more than half of the patients with osteoarthritis of the hip or knee in the Netherlands consult their general practitioner because of the chronic joint disease (57%)[21].

Important treatment modalities for OA in primary care are patient education, pharmacological therapy and physiotherapy. In a majority of episodes of care by a GP medication is prescribed, namely in 74% of the episodes of care for hip OA, and in 66% of the episodes of care for knee OA. In one out of 5 episodes of care patients are referred to a physiotherapist, in 15% and 23% of the episodes of care respectively[22]. 40% of the patients consulting their GP, are referred to the physiotherapist in the next four years[23]. Patients are referred to a medical specialist less frequently, in 14% and 8% of episodes of care respectively[22].

Physiotherapy and occupational therapy in osteoarthritis of the hip or knee

In the guidelines of the ACR both physiotherapy and occupational therapy are seen as important interventions in OA. In physiotherapy treatment for OA, exercise therapy is the main treatment modality. In a survey on physiotherapy in the Dutch primary health care system, conducted from 1989 to 1992, exercise therapy was the intervention most frequently applied for OA. In 65% of physiotherapy treatments for patients with OA exercise therapy was applied[24]. Other frequently applied interventions were massage and instruction of (home) exercises, in 60 % and 48% of treatments respectively. Treatment modalities such as ultrasound therapy, interferential therapy and short wave therapy were each applied less frequently. They were used in about

one out of four treatments (in 20%, 28% and 28% of treatments respectively). Manual therapy (e.g. traction) was applied to the same extent (in 26% of treatments)[24]. In this survey no data were gathered on outcome of treatment. At the time of this survey, data on the effectiveness of specific treatments in OA were available only to a limited extent to physiotherapists. Reviews on the effectiveness of physiotherapy in OA were hardly available.

Comparison between physiotherapy treatments for hip OA versus knee OA showed no difference in the application of exercise therapy. However, treatments deviated in the application of three interventions: in hip patients ultrasound was less frequently applied and massage and manual therapy were more frequently applied[24]. The less frequent application of ultrasound in hip patients is explicable. Ultrasound is less indicated for hip complaints, since ultrasound will not reach the deeper located hip[25,26]. The more frequent use of massage and manual therapy in hip patients can be explained by more prevalent impairments in joint range of motion and increased muscle tone in hip patients[24]: these interventions are frequently used for recovery of range of motion[27].

Next to physiotherapy, occupational therapy is mentioned by the ACR as an appropriate intervention in OA. In these patients occupational therapy should include the evaluation of the patient's ability to perform activities of daily living and the provision of assistive devices as needed. No quantitative information is available on the use and content of occupational therapy by patients with osteoarthritis of the hip or knee in the Netherlands. In addition, information on effectiveness of occupational therapy in these patients is not available[1].

Psycho-educational interventions in osteoarthritis of the hip or knee

Among the interventions included in the ACR guidelines are the self-management programmes. One of the first programmes was developed in the United States by Lorig et al[28]. This programme, the Arthritis Self-Management Programme, is a community-based intervention that introduces participants to a range of techniques that are useful in managing their arthritis on a daily base. It aims to enhance perceived ability to control various aspects of arthritis, based on the self-efficacy approach. In the Netherlands, a self-management course was developed by Hopman-Rock, applying similar principles[29].

Reviews on the effectiveness conclude that psycho-educational programmes have beneficial effects on pain, depression and probably on disability[1]. Data of the evaluation of the Dutch self-management course revealed similar results. Beneficial effects were found on pain, knowledge, self-efficacy and muscle strength[30].

These psycho-educational interventions are not available on a regular basis in our health care system. Furthermore, introduction of these interventions on a regular

basis is not yet to be expected. Nevertheless, principles of these interventions can be incorporated in the patient education given by regular health care providers, such as GP's and physiotherapists.

THE RATIONALE OF EXERCISE THERAPY IN OSTEOARTHRITIS

Treatment in OA is aimed at control and minimisation of the consequences of disease. These consequences of disease can de described, using the International Classification of Impairments, Disabilities and Handicaps (ICIDH)[31]. This classification was introduced in 1980 by the World Health Organisation and provides a theoretical framework for description of the consequences of disease. The consequences of disease are described in terms of impairments (consequences of disease at the level of the organ/function), disabilities (consequences of disease at the level of the person) and handicaps (consequences at the level of the social roles).

A dominant impairment in OA is pain. In addition, reduced active and passive range of motion[32,33], muscle weakness[34-36], decreased aerobic capacity and exercise tolerance[37-39], joint instability and changed proprioception[40] are characterising kinesiological impairments in OA. Also psychological impairments can play a role in OA, including anxiety, depression and negative affect[36]. These impairments may result in several disabilities. The main disabilities in OA, especially in osteoarthritis of the lower limbs, are disabilities in mobility and bending[41]. Problems arise in walking, climbing stairs, getting in and out a car, riding a bike, putting on shoes etc. Finally, OA may have consequences for the social role of patients, in reducing the ability to work, the performance of housekeeping, shopping, and recreational activities[42].

Three kinds of factors have been hypothesised to contribute to pain and disability in OA. Firstly, pain and disability are hypothesised to be caused by the pathological ***articular processes*** in cartilage and subchondral bone and the pathologic changes in the surrounding tissues. Changes in articular cartilage do not directly cause pain, since cartilage itself is not innervated. However, changes in subchondral bone are assumed to be an important source of pain. Subchondral bone is nociceptive innervated and the development of bony outgrowths may result in increased sensitivity of the nociceptors. Pressure on subchondral bone, sclerosis and cysts may contribute to pain as well[43]. Osteophytes may also irritate surrounding soft tissues[9]. Mechanical limitations of the joint are assumed to be the primary cause of disability. OA causes incongruity of the joint surfaces and this results in limitations of the joint and in disability. Similarly osteophytes and intra-articular loose bodies may limit joint motion, which leads to disability[36,44].

The articular changes lead to characteristic kinesiological features in OA, including reduced range of motion, muscle weakness and decreased aerobic capacity and loading tolerance. These ***kinesiological features*** are seen as the second group of important factors in the process of disablement in patients with OA[36,45,46]. These features are the resultants of mechanisms including a decreased use of the joint due to pain, changed proprioception, effusion or restricted range of motion due to articular processes. Reduced range motion and contractures strongly contribute to disability[41]. In addition, muscle weakness is associated with pain and disability. Muscles are important shock absorbers and help to stabilise the joint. As a consequence muscle weakness leads to unstable joints. Mechanical stress on unstable joints leads to stress and strain in nociceptive innervated tissues. This may cause pain and disability[33,36,47].

Besides articular and kinesiological changes, ***psychological factors*** are seen as the third group of important factors contributing to pain and disability in OA[36,46,48]. In several cross-sectional studies coping style, self-efficacy beliefs and negative affect have been found to be associated with pain and disability. Higher levels of depression and anxiety were associated with higher pain and disability[49-51]. Furthermore a high level of a coping style characterised by the perceived ability to control and decrease pain and a low level of catastrophising was related to low levels of pain, self-reported disability and observed disability[52,53]. In one study, a prospective analysis was conducted studying the relation over time between (un)pleasant events and symptoms. It was found that a decrease in events, either pleasant or unpleasant was followed by an increase in symptoms (pain and disability)[49].

A possible explanation for these relationships is the concept of avoidance of pain-related activities, as stated by Dekker et al[36]. According to this hypothesis, a patient avoids high levels of activity, because activity induces pain. An emotional or catastrophising reaction to pain strengthens a patient's tendency to avoid exercise and related activities. This avoidance enhances muscle weakness and reduced range of motion, which leads to unstable joints, pain and disability[54].

Exercise therapy is defined as a range of activities intended to improve strength, range of motion, endurance, balance, coordination, posture, motor function or motor development. Exercise therapy is always provided in combination with patient-related instruction[55]. Exercise therapy in OA can include a number of specific exercises interventions, such as strengthening exercises, stretching exercises, aerobic endurance activities (walking, cycling, swimming) and aquatic exercises (pool exercises)[33,56-58]. This range of exercises can contribute to reduction of pain and disability in OA.

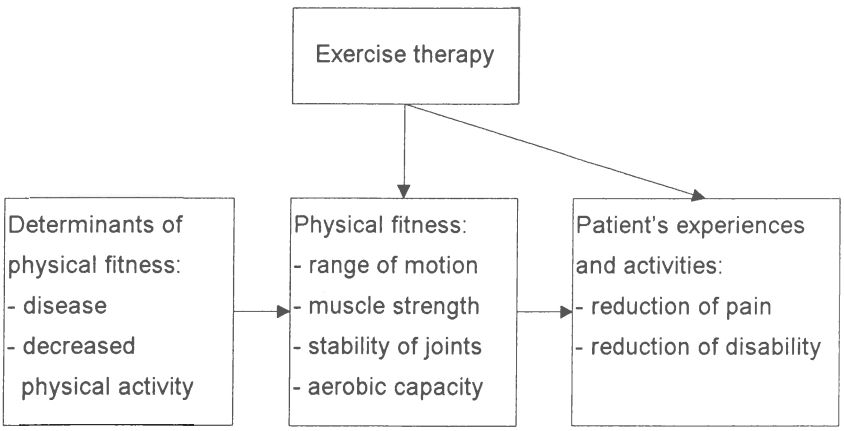
The rationale of exercise therapy is based on the above-described mechanisms contributing to pain and disability in OA. Exercise therapy aims at reduction of the consequences of OA, both at the level of impairments and at the level of disabilities.

Exercise therapy cannot directly influence pain due to articular changes itself, for instance pain caused by osteophytes. However, exercise therapy can result in improvement of muscle strength and range of motion. As a consequence, pain and disability due to muscular and capsular mechanism can be reduced. In addition, exercise therapy and especially aerobic exercises such as walking and swimming, can improve aerobic capacity and exercise tolerance. These improvements are also hypothesised to reduce pain and disability in OA. Thus, exercise therapy is hypothesised to reduce pain and disability in OA through influencing capsular and muscular mechanisms and improving patient's fitness[33,46,57,59].

In addition, certain types of exercise therapy are hypothesised to lead to a direct reduction of disability. These exercises are concerned with improvement of disabilities, for instance in self-care and home management. An example of these exercises is the correction of walking pattern, which directly can contribute to reduction in disability in walking[59].

In figure 3 the rationale of exercise therapy in patients with OA is summarised.

Figure 3: Rationale of exercise therapy in patients with OA (source Dekker et al[59])



Next to these physical mechanisms, exercise therapy is hypothesised to reduce pain and disability through psychological mechanisms as well. Patients receiving exercise therapy are stimulated to take an active approach to pain. Instead of taking rest or withdraw, patients are stimulated to perform the normal daily activities, albeit with

necessary adjustments. Exercise therapy is expected to reduce the tendency for an emotional or catastrophising reaction to pain and thereby remove the reaction of avoidance. As a consequence, no enhancement of muscle weakness and reduced range of motion arises, which would contribute to pain and disability. Thus exercise therapy is hypothesised to reduce pain and disability through removal of the reaction of avoidance.

Based on the rationale of exercise therapy as outlined above, differences in effectiveness of exercise therapy in patients with OA are to be expected. Exercise therapy focuses on specific factors and is therefore expected to benefit specific subgroups. Firstly, beneficial effects of exercise therapy can be expected in patients with relatively high levels of impairments and disabilities at the start of treatment. Exercise therapy aims at reduction of pain and disability through improvement of specific impairments. In patients with small or no impairments, no improvements can be made and therefore no reduction of pain and disability can be expected. It is hypothesised that especially in patients with low muscle strength and restricted ROM at baseline exercise therapy will result in reduction of pain and disability. In addition, it is hypothesised that patients with a high level of disability at baseline will especially benefit from exercise therapy. Secondly, beneficial effects are expected in patients with an emotional or catastrophising reaction to pain. This type of pain coping is hypothesised to strengthen the reaction of avoidance. This avoidance enhances muscle weakness and restricted range of motion, which contributes to pain and disability. Since exercise therapy stimulates an active approach to pain, it can be expected to benefit particularly in patients with an emotional or catastrophising reaction to pain.

Available evidence

At the start of our study there was some evidence for beneficial effects of exercise therapy in patients with OA of the hip or knee. Randomised controlled trials had shown its beneficial effects on pain[60], self-reported disability[61], observed disability (i.e. walking)[60], level of physical activity[60], muscle strength[61] and aerobic capacity[62]. However, the number of randomised clinical trials into the effectiveness of exercise therapy in OA was small. In addition, methodological flaws in most of these studies impeded conclusions about the effectiveness of exercise therapy in OA[59].

Evidence on the effects of exercise therapy in specific subgroups of patients was not available. In a review on exercise therapy in OA (and rheumatoid arthritis)[59] none of the outcome studies had addressed the question whether specific groups of patients with OA particularly benefit from exercise. In addition, no studies were available on the cost-effectiveness of exercise therapy in these patients.

AIM AND RESEARCH QUESTIONS

As has been described above, exercise therapy is a frequently applied intervention in patients with OA of the hip and knee. However, the scientific evidence for the effectiveness of exercise therapy in these patients was limited. At the start of our study only a small number of randomised clinical trials had been conducted. Furthermore, methodological flaws impeded conclusion about effectiveness of exercise therapy.

The aim of this study was to gain insight in the effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee. It was hypothesised that exercise therapy would have beneficial effects on pain and disability in patients with OA of the hip and knee. We designed and conducted a randomised clinical trial into the effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee. We studied the effectiveness of a 12-week exercise programme given by a physiotherapist in primary care. Both short-term (post-treatment, at 12 weeks) and long-term outcome (24 and 36 weeks) were studied. We investigated whether specific groups of patients particularly benefit from exercise therapy. We determined the cost-effectiveness of our intervention. And finally, we determined the evidence available on effectiveness of exercise therapy in OA in a systematic review.
It should be noted that we did study the effectiveness of short-term exercise therapy programme, lasting maximally 12 weeks. Therefore, our data will not provide an insight into the effectiveness of a longer-lasting therapy programme. The question of the effectiveness of such an exercise therapy programme remains to be answered.

The following research questions are being examined in this thesis:

- What is the separate contribution of articular, kinesiological and psychological characteristics to pain and disability in patients with OA of the hip or knee? (Chapter 2)
- What is the short-term effectiveness of exercise therapy in patients with osteoarthritis of hip or knee? (Chapter 3)
- Which groups of patients with osteoarthritis of hip or knee benefit particularly from exercise therapy? (Chapter 4)
- What is the long-term effectiveness of exercise therapy in patients with osteoarthritis of hip or knee? (Chapter 5)
- What is the cost-effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee? (Chapter 6)
- What is the evidence available on the effectiveness of exercise therapy in patients with OA of the hip or knee? (Chapter 7)

REFERENCES

1. Schouten JSAG, Linden SJ van der. *Artrose van heup of knie.* (Osteoarthritis of hip or knee). In: *Volksgezondheid Toekomst Verkenning.* (Public health status and forecasts). Ruwaard D, Kramers PGN, eds. Maarssen the Netherlands: Elsevier/Tijdstroom, 1997:207-23.
2. Thoonen BPA, Knottnerus JA. *Huidige en toekomstige prevalentie van chronische gewrichts-aandoeningen in de huisartspraktijk.* (Actual and future prevalence of chronic articular diseases and osteoporosis in general practice). Huisarts Wet 1991;35:369-73.
3. Schouten JSAG. *Artrose.* (Osteoarthritis). In: *Volksgezondheid Toekomst Verkenning. De gezondheidstoestand van de Nederlandse bevolking in de periode 1950-2010.* (Public health status and Forecasts. The health status of the Dutch population in the period 1950 to 2010). Ruwaard D, Kramers PGN, eds. The Hague the Netherlands: SDU-uitgeverij, 1993; 461-5.
4. Miedema H. *Reuma-onderzoek meerdere echelons (ROME): basisrapport.* (Rheumatism-research on different levels of the health care system: basis report). Leiden the Netherlands: NIPG-TNO, 1994.
5. Felson DT. Epidemiology of hip and knee osteoarthritis. Epid Reviews 1988;10:1-28.
6. Dieppe P. The classification and diagnosis of osteoarthritis. In: Kuettner KE, Goldberg VM, eds. Osteoarthritic disorders. Rosemont IL: American Academy of Orthopaedic Surgeons, 1995: 5-12.
7. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. Arthr Rheum 1986;29:1039-49.
8. Lindblad S, Hedfors E. Arthroscopic and immunohistologic characterization of knee joint synovitis in osteoarthritis. Arthritis Rheum 1987;30;1081-8.
9. Trekheld AJ, Currier DP. Osteoarthritis: effects on synovial tissues. Phys Ther 1988;68:364-70.
10. Mow VC, Setton LA, Guilak F, Rathcliffe A. Mechanical factors in articular cartilage and their role in osteoarthritis. In: Kuettner KE, Goldberg VM, eds. Osteoarthritic disorders. Rosemont IL, American Academy of Orthopaedic Surgeons, 1995:147-72.
11. Poole AR. Imbalances of anabolism and catabolism of cartilage matrix components in osteo-arthritis. In: Kuettner KE, Goldberg VM, eds. Osteoarthritic disorders. Rosemont IL: American Academy of Orthopaedic Surgeons, 1995:247-60.
12. Felson DT. The epidemiology of osteoarthritis: prevalence and risk factors. In: Kuettner KE, Goldberg VM, eds. Osteoarthritic disorders. Rosemont IL: American Academy of Orthopaedic Surgeons, 1995:13-24.
13. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. Ann Rheum Dis 1957;16:494-502.
14. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthr Rheum 1991;34:505-14.
15. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, Moskowitz RW, Schnitzer TJ. Guidelines for the medical management of osteoarthritis. Part I. Osteoarthritis of the hip. Arthr Rheum 1995;38:1535-40.

16. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, Moskowitz RW, Schnitzer TJ. Guidelines for the medical management of osteoarthritis. Part II. Osteoarthritis of the knee. Arthr Rheum 1995;38:1541-6.
17. Dieppe P. Management of hip osteoarthritis. BMJ 1995;311:853-6.
18. Guidelines; Diagnosis and management of osteoarthritis of the hip and knee. J. Roy Coll Physicians, London, 1993;27:391-6
19. Liang MH, Fortin P. Management of osteoarthritis of the hip and knee (editorial). N Eng J Med 1991;325:125-7.
20. Zee J van der, Hutten J. The case of the Netherlands. In: Griffin J, eds. The future of primary care. London: Office for Health Economics, 1996.
21. Waal MWM de, Schellevis FG, Velden J van der. *Consultatie van de huisarts door patiënten met reumatoide artritis of gonartrose/coxartrose.* (General practitioner consultation frequency of patients with rheumatoid arthritis or gonarthrosis/coxarthrosis). Ned Tijdschr Geneeskd 1995;139:1331-5.
22. Groenewegen PP, Bakker DH de, Velden J van der. *Een Nationale Studie naar Ziekten en Verrichtingen in de Huisartspraktijk. Basisrapport: Verrichtingen in de huisartspraktijk.* (Dutch National Survey of General Practice: interventions in general practice). Utrecht the Netherlands: NIVEL, 1992.
23. Miedema HS. *Verwijzingen van patienten met klachten van houdings- en bewegingsapparaat.* (Referrals in patients with musculoskeletal disorders). In: Bruijne J de, Dijkmans BAC, Hazes JWM, Springer MP, eds. *Tien topics in de reumatologie.* (Ten topics in rheumatology). Leiden the Netherlands: Boerhave cursus, 1995:23.
24. Valk RWA van der, Dekker J, Baar ME van. *De fysiotherapeutische behandelingen van patiënten met artrose: een beschrijvend onderzoek.* (Physiotherapy for patients with osteoarthritis: a description). In: Dekker J, Baar ME van. *Beleidsgericht evaluatie- en effectonderzoek extramurale fysiotherapie (BEEF). Eindrapport.* Utrecht the Netherlands: NIVEL, 1995.
25. Kitchen SS, Partridge CJ. A review of therapeutic ultrasound. Physiotherapy 1990;76:593-600.
26. Roebroeck ME, Dekker J, Oostendorp RAB. The use of therapeutic ultrasound by physical therapists in Dutch primary health care. Phys Ther (in press).
27. Dekker J, Baar ME van, Curfs Echr, Kerssens JJ. Diagnosis and treatment in physical therapy: an investigation of their relationship. Phys Ther 1993;73:568-80.
28. Lorig K, Holman H. Arthritis self-management studies: a twelve year review. Healt Educ Q 1993;20:17-28.
29. Hopman-Rock M. Coping with osteoarthritis of the knee and/or hip: the development of a life-style programme. Leiden the Netherlands, TNO Preventie en gezondheid, 1994.
30. Hopman-Rock M, Tak ECPM, Westhoff MH, Huizing A. Living with osteoarthritis of the hip or knee: study results of a health educational programme including group exercise, for elderly people in the community. Abstract, 5th International Conference of the European Group for Research into Elderly and Physical Activity. Oeiras Portugal, 29 sept-5 oct 1997.
31. World Health Organisation. International Classification of Impairments, Disabilities and Handicaps. Geneva Switzerland: World Health Organisation, 1980.

32. Messier SP, Loeser RF, Hoover JL, Semble EL, Wise CM. Osteoarthritis of the knee: effects on gait, strength and flexibility. Arch Phys Med Rehabil 1992;73:29-36.
33. Semble EL, Loeser RF, Wise CM. Therapeutic exercise for rheumatoid arthritis and osteo-arthritis. Seminars Arthritis Rheum 1990;20:32-40.
34. Fisher NM, Gresham G, Pendergast DR. Effects of a quantitative progressive rehabilitation programme applied unilaterally to the osteoarthritic knee. Arch Phys Med Rehabil 1993;74:1319-26.
35. McAlindon TE, Cooper C, Kirwan JA, Dieppe PA. Determinants of disability in osteoarthritis of the knee. Ann Rheum Dis 1993;52:258-62.
36. Dekker J, Boot B, Woude LHV van der, Bijlsma JWJ. Pain and disability in osteoarthritis: a review of biobehavioral mechanisms. J Behav Med 1992;15:189-214.
37. Philbin EF, Groff GD, Ries MD, Miller TE. Cardiovascular fitness and health in patients with end-stage osteoarthritis. Arthritis Rheum 1995;38:799-805.
38. Minor MA, Hewett JE, Webel RTR, Dreisinger TE, Kay Dr. Exercise tolerance and disease related measures in patients with rheumatoid arthritis and osteoarthritis. J Rheumatol 1988;15:905-11.
39. Beals CA, Lampmann RM, Banwell BF, Braunstein EM, Albers JW, Castor CW. measurement of exercise tolerance in patients with rheumatoid arthritis and osteoarthritis. J Rheumatol 1985;12:458-61.
40. Hurley MV, Newham DJ. The influence of arthrogenous muscle inhibition on quadriceps rehabilitation of patients with early, unilateral osteoarthritic knees. Br J Rheum 1993;32:127-31.
41. Badley EM, Wagstaff S, Wood PhH. Measures of functional ability (disability) in arthritis in relation to impairment of range of joint movement. Ann Rheum Dis 1984;43:563-9.
42. Yelin E, Lubeck D, Holman H, Epstein W. The impact of rheumatoid arthritis and osteoarthritis. The activities of patients with rheumatoid arthritis compared to controls. J Rheumatol 1987;14:710-7.
43. Kellgren JH. Pain in osteoarthritis. J Rheumatol 1983;(suppl 9)10:108-9.
44. Brandt KD. Osteoarthritis: clinical patterns and pathology In: Kelley WN, Harris ED, Ruddy S, Sledge CB, eds. Textbook of Rheumatology. Philadelphia: Saunders, 1985:1432-47.
45. Guccione A. Arthritis and the process of disablement. Phys Ther 1994;74:408-14.
46. Ettinger WH Jr, Afable RF. Physical disability from knee osteoarthritis: the role of exercise as an intervention. Med Sci Sports Exerc 1994;26:1435-40.
47. Lankhorst GJ, Stadt RJ van de, Korst JK van der. The relationship of functional capacity, pain and isometric and isokinetic torque in osteoarthritis of the knee. Scandi Rehab Med 1985;17:167-72.
48. Hopman-Rock M, Kraaimaat FW, Odding E, Bijlsma JWJ. Coping with pain in the hip or knee in relation to physical disability in community living elderly people. Arthritis Care Res 1998 (in press).
49. Lunghi ME, Miller PMcC, McQuillan WM. Psychological factors in osteoarthritis of the hip. J Psychosom Res. 1978; 22:57-63.
50. Lichtenberg PA, Skehan MW, Swensen CH: The role of personality, recent life stress and arthritic severity in predicting pain. J Psychosom Res 1984;28:231-6.

51. Summers MN, Haley WE, Reveille JD, Alarcon GA: Radiographic assessment and psychologic variables as predictors of pain and functional impairments in osteoarthritis of the knee or hip. Arthritis Rheum 1988;31:204-9.
52. Keefe FJ, Caldwell DS, Queen KT, Gil KM, Martinez S, Crisson JE, Ogden W, Nunley J. Pain coping strategies in osteoarthritis patients. J Cons Clin Psychol 1987;55:208-12.
53. Keefe FJ, Caldwell DS, Queen KT, Gil KM, Martinez S, Crisson JE, Ogden W, Nunley J. Osteoarthritic knee pain: a behavioral analysis. Pain 1987;28:309-21.
54. Dekker J, Tola P, Aufdemkampe G, Winckers M. Negative affect, pain and disability in osteoarthritis patients: the mediating role of muscle weakness. Behav Res Ther 1993;31:203-6.
55. American Association of Physical Therapists. Guide to physical therapist practice. Phys Ther 1997;77:1217-8.
56. Gerber LH. Exercise and Arthritis. B Rheum Dis 1990;39:1-9.
57. Ike RW, Lampmann RM, Castor CW. Arthritis and aerobic exercise; a review. Physician Sports Med 1989;17:128-38.
58. American Association of Physical Therapists. Guide to physical therapist practice. Phys Ther 1997;77:1271.
59. Dekker J, Mulder PH, Bijlsma JWJ, Oostendorp RAB. Exercise therapy in patients with rheumatoid arthritis and osteoarthritis: a review. Adv Behav Res Ther 1993;15:211-38.
60. Kovar PA, Allegrante JP, MacKenzie R, Peterson MGE, Gutin B, Charlson ME. Supervised fitness walking in patients with osteoarthritis of the knee. Ann Int Med 1992;116:529-34.
61. Jan MH, Lai JS. The effects of physiotherapy on osteoarthritic knees of females. J Formosan Med Assoc 1991;90:1008-13.
62. Minor MA, Hewett JE, Webel RR, Anderson S, Kay DR. Efficacy of physical conditioning exercise in patients with rheumatoid arthritis and osteoarthritis. Arthr Rheum 1989;32:1396-1405.

2

PAIN AND DISABILITY IN PATIENTS WITH OSTEOARTHRITIS OF HIP OR KNEE: THE RELATIONSHIP WITH ARTICULAR, KINESIOLOGICAL AND PSYCHOLOGICAL CHARACTERISTICS

M.E. van Baar, J. Dekker, J.A.M. Lemmens, R.A.B. Oostendorp, J.W.J. Bijlsma

Objective - To determine to what extent articular, kinesiological and psychological factors each contribute to pain and disability in osteoarthritis (OA) patients, after controlling for the other factors.

Methods - Cross-sectional study among 200 patients with OA of the hip or knee. Dependent variables include pain (visual analogue scale), self reported disability (questionnaire) and observed disability (performance of standardised tasks). Independent variables include joint degeneration (radiographs), muscle strength (dynamometer), range of joint motion (goniometer), pain coping (behavioural and cognitive strategies), and psychological well-being (depression, anxiety, cheerfulness). Multiple regression analysis was used.

Results - Pain was found to be associated with muscle weakness and pain coping (p's <0.05). Disability was associated with muscle weakness, range of joint motion, pain, pain coping and psychological well-being (all p's <0.05). Both pain and disability were most strongly associated with kinesiological characteristics and pain coping.

Conclusion - After controlling for the other characteristics, kinesiological and psychological characteristics in OA-patients are each associated with disability. The association with pain is less clear-cut. These results provide a reason for future research on mechanisms underlying these associations.

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chapter 2

INTRODUCTION

Pain and disability are major symptoms in patients with osteoarthritis (OA)[1]. To a certain extent, these symptoms are accounted for by articular degeneration: radiographically assessed degeneration of cartilage and bone is associated with pain and disability, but it appears that the association is rather weak. This conclusion was drawn in a review of 17 studies published before 1990[2]; studies published subsequently have confirmed this conclusion[3-6]. Thus, it appears that the status of the joint is not a sufficient explanation for pain and disability in OA-patients. Additional explanations can be sought in a complex of factors, presumably associated with the development of pain and disability in OA-patients[2,7,8]. These factors can be classified as kinesiological factors (e.g. muscle weakness) and psychological factors (e.g. pain coping).

With regard to kinesiological factors, muscle weakness has been found to be associated with both pain and disability in OA-patients. This association has been observed in four previously reviewed studies [2] and two subsequently published studies[4,5]. The most likely explanation is muscle weakness resulting in unstable joints: mechanical stress on unstable joints leads to strain in innervated tissues, which may cause pain and disability. However, all studies on muscle weakness - except two[4,5] - have failed to control for the extent of articular degeneration. Thus, there is only very limited evidence that muscle weakness contributes to pain and disability, after controlling for articular degeneration. The same criticism applies to the studies on range of joint motion. Disability has been found to be associated with restricted range of joint motion[2], but the studies reporting this association have failed to control for articular degeneration. Therefore, it is not known whether range of joint motion accounts for disability, after controlling for articular degeneration.

With regard to psychological factors, pain and disability in OA-patients have been found to be associated with coping style, self-efficacy beliefs and negative affect[2,9]. Most of these studies did control for the extent of articular degeneration; however, these studies did not control for kinesiological factors. Evidence has been reported that psychological factors affect symptoms in OA-patients by way of muscle weakness[10]. Negative affect is thought to enhance patients' tendency to avoid pain-related activities: avoidance causes muscle weakness and thus pain and disability. Psychological factors may operate in other ways as well, but it is not known whether psychological factors contribute to pain and disability in OA-patients, after controlling for kinesiological factors.

It can be concluded that pain and disability in OA-patients have been shown to be associated with articular, kinesiological and psychological characteristics. However, nowadays it is not clear to what extent each of these factors separately contribute to

pain and disability, after controlling for the other factors. Therefore, the goal of the present study is to determine the most parsimonious set of predictors for pain and disability in OA-patients.

METHODS

Patients

Patients were selected by general practitioners (GPs) to participate in a randomised clinical trial into the effectiveness of exercise therapy in OA patients. These patients were visiting their GP on their own initiative, because of complaints of OA. Inclusion criteria were OA of the knee or hip according to the clinical criteria of the American College of Rheumatology[11,12]. Exclusion criteria were other pathology explaining the complaints, complaints in less than 10 out of the last 30 days, treatment for these complaint with exercise therapy in the preceding six months, under 40 or over 85 years of age, indication for hip or knee replacement, contraindication for exercise therapy, contraindications for analgesics or NSAIDs, and inability to understand the Dutch language. After selection by their GP, patients' eligibility was checked by a specially trained GP-research fellow. The data in the present study were collected at baseline, i.e. when patients entered the trial.

GPs selected 216 patients; 9 patients did not consent to participation and 7 patients were excluded because they did not meet the selection criteria, which resulted in 200 patients remaining. Patients with OA of the hip and OA of the knee were kept separate in the analyses reported below. Patients with OA of both hip and knee were included in both the hip group and the knee group. Patients of whom no radiographs were available were excluded from the present study. This resulted in 73 patients with OA of the hip (including 6 patients with OA of the knee as well) and 112 patients with OA of the knee (including 7 patients with OA of the hip as well; due to missing radiographs, between the hip group and the knee group there is a difference in the number of patients with a double diagnosis).

Radiographs

The radiographs were taken in local hospitals, according to a standard protocol. In hip patients a plain pelvis view was taken with patients in supine position. In knee patients weightbearing anteroposterior radiographs of both knees were taken and lateral radiographs with 60° flexion were taken while patients were recumbent of both knees. All radiographs were evaluated for the presence of features of osteoarthritis by one of the authors (JAML), using grading scales for individual radiographic features[13]. Readings of each hip included 9 scores for superior, medial and axial joint space

narrowing and for osteophytes, subchondral sclerosis and cyst formation in both acetabulum and femur. The scores were assigned on a 0-3 scale. For the knee radiographs, the medial, lateral and patellofemoral compartments of each knee were scored for joint space narrowing, osteophytes, subchondral sclerosis and cyst formation on a 0-3 scale. Scores were added across features and for left and right joint to obtain an overall value of the radiological status of the hip or knee[4,14,15]. In knee patients, also the pattern of knee OA was analysed, according to the system of Ahlback[16,17]. Three patterns of localisation were distinguished 1) isolated patellofemoral OA (PF-OA, sumscore PF compartment ≥ 1 and sumscore medial and lateral compartments =0), 2) isolated tibiofemoral OA (TF-OA, sumscore medial and lateral compartment ≥ 1 and sumscore PF compartment=0) and 3) combined pattern.

Pain and disability

Patients rated their pain on a visual analogue scale (0-100 mm), rating pain in the past week. In addition, present pain and pain in the past month were assessed. Because these pain ratings were highly intercorrelated, analyses were restricted to pain in the past week.

Both observed and self-reported disability were assessed. Self-reported disability is of utmost importance to the patients; but because subjective bias might cause deviations, observed disability was assessed also. Observed disability was determined by studying videos of the patients' performance of a series of standardised tasks using an adaptation of the method described by Keefe[18,19]. Both movement times and quality of performance were assessed. A total score was calculated based on 5 measures: 5m-walking time, stand-to-sit time, reclining time and the levels of guarding and rigidity during the performance of the tasks (see data analysis). Self-reported disability was assessed with the IRGL-questionnaire (Invloed van Reuma op Gezondheid en Leefwijze =Influence of Rheumatic disease on General health and Lifestyle)[20]. This is a Dutch adaptation of the Arthritis Impact Measures Scales. From the IRGL-questionnaire, the subscale 'mobility' was used, which consists of 2 items concerning disability in general and 5 items concerning disability in climbing stairs, cycling and walking.

Muscle strength and range of motion

The isometric muscle strength was measured with the MicroFet (Hoggan Health Industries, Draper, Utah), a hand-held dynamometer[21]. A protocol was used to standardise the measurements. Make tests were used, i.e. the research assistant holds the dynamometer steady while the patient exerts a maximal force against it[22]. Patients were asked to gradually build their force in 2 seconds to a maximal voluntary effort and to maintain this effort during 3 seconds. Starting positions were analogue to

Kendall and Kendall[23]. Muscle strength (in Newtons) was measured bilaterally for 8 muscle actions. For the hip the extension, flexion, abduction, adduction, endorotation and exorotation were measured. For the knee flexion and extension were measured. Reference values for muscle strength were obtained from 10 healthy subjects (5 male and 5 female subjects, mean age 30.8 years ± 8.5). These reference values (mean and standard deviation in Newton) for the hip were: extension: 209 ± 45; flexion: 258 ± 75; abduction: 264 ± 57; adduction: 217 ± 60; endorotation: 184 ± 23; exorotation: 153 ± 39. For the knee, the muscle strength reference values were: flexion: 166 ± 39; extension: 222 ± 49.

Assisted active range of joint motion (in degrees) was measured with a goniometer, according to Norkin and White[24]. These measurements were also standardised in the measurement protocol. Range of motion around the hip was measured by assessing extension, flexion, abduction, adduction, endorotation and exorotation. Range of motion of the knee was measured by assessing flexion and extension.

Muscle strength and range of joint motion were assessed by two research assistants, both of them experienced physical therapists who had been intensively trained to perform these measurements in a standardised way. Follow-up training sessions were held in order to maximise standardisation. Each patient was tested by a single research assistant. Interrater reliability of the physical examination was satisfactory. The mean of intraclass correlation coefficients was 0.78 for muscle strength measurements (range 0.60-0.93) and 0.68 for range of motion measurements (range 0.39-0.90).

Psychological characteristics

Pain coping behaviour was measured with the Pain Coping Inventory[25]. This inventory consists of six subscales, assessing both behavioural and cognitive coping strategies. A high score reflects a high use of the specific strategy when in pain. In addition, an adaptation for OA-patients of the Fear-Avoidance Beliefs Questionnaire was used[26]. This scale measures the extent to which patients believe physical activity to affect their pain. Psychological well-being was assessed on three scales of the IRGL-questionnaire: anxiety, depression and cheerfullness[20] (see above). The higher the score, the more this aspect applies to a patient.

Medication

Patients reported on their use of medication in the last 7 days before inclusion in the study. It was determined whether or not the patient had used paracetamol and/or NSAIDs.

Other variables

Patients reported on the duration of complaints (in weeks). Body mass and height were assessed by the research assistants; body mass index was calculated as body mass/(height)^2.

Data reduction and analysis

For observed disability an overall score was composed. The scores on movement times were transformed into 10 categories, in order to correct for skewed distributions. Subsequently, Z-scores were computed for every measurement, to avoid weighting problems due to differences in score ranges. Then Z-scores were added to obtain an overall score. The resulting overall score was standardised (by division through the standard deviation of the overall score) to render a score with a mean of zero and a standard deviation of one. The internal consistency of the constructed overall score for observed disability was good (α=0.84).

In order to facilitate interpretation, IRGL-ability scores were recoded into disability scores by reversing the sign. Thus, a high score indicates disability, for both observed and self-reported disability.

Muscle strength data were normalised to body mass, by dividing the raw scores by bodymass[27]. Next, Z-scores were computed and added for left and right to obtain one overall score: a patient score, based on 12 tests of the hip (6 muscle actions both left and right) and on four tests of the knee (2 muscle actions, both left and right). This overall score was divided by its standard deviation to enhance comparability. For range of joint motion data a comparable procedure was followed, i.e. calculation of Z-scores and construction of one overall score.

The analyses reported in the present study were repeated using data on OA-joints only. These analyses yielded highly similar results. Because pain and disability concern the functioning of the entire patient, the reported analyses were based on the overall score of radiological status, muscle strength and range of joint motion (instead of data on OA-joints only).

With some patients (maximum 3%) data on the following variables were missing: pain coping, IRGL-scales, duration of complaints and muscle strength. Using the procedure of mean substitution, these patients were included in the analyses.

Bivariate relationships are expressed in Pearson's product moment correlation coefficient. Exceptions are the relationships with the separate radiological scores and the duration of complaints (Spearman's rank order correlation coefficient) and with medication and sex (eta). Multiple regression analyses were performed to determine the most parsimonious set of predictors for pain and disability, after controlling for other characteristics. Stepwise analyses were performed with the characteristics displayed in table 2[28]. Total scores were used for radiological status, muscle strength,

and range of motion. Pain was used as an independent variable in analyses on disability. Beta's of the variables in the final regression equations are reported as outcome of regression analyses. The significance level was set at 0.05. An exception is the significance level for exclusion from the regression equation: the 'exit α' was 0.10. Analyses were performed using SPSS/PC+ version 5.0.

RESULTS

Characteristics of patients

In table 1 clinical characteristics are presented for both hip patients and knee patients. The patients were on average 68 years old and most of them were females. The median duration of complaints was longer than one year. About half of the patients reported to have taken paracetamol in the past week and about 30% had taken NSAIDs. The radiological scores were low, representing mild articular degeneration. In knee patients 7.1% was classified as isolated PF OA, 19.6% as isolated PF OA and 54.5% as combined TF/PF OA (not shown). The average pain scores were just below the mid-point of the scale. Muscle strength of both hip and knee was below the reference values (see Methods). Range of hip motion was below reference values, but range of knee motion was equal to reference values[29]. Patients with OA of both hip OA and knee OA had similar characteristics (not shown).

Table 1: Description of patients with osteoarthritis of the hip or knee

	Hip n=73	Knee n=112
Age (years)	67.7 (8.7)	69.3 (8.1)
% Women	71.2	88.4
Duration of complaints[1] (weeks)	52 (17-158)	65 (18-342)
Body mass index	27.8 (4.1)	28.4 (3.9)
Medication last week		
% paracetamol	49.3	44.6
% NSAID's	28.8	27.7
Radiological status		
1. Joint space narrowing (0-18)[1]	2.5 (3.2)	1.9 (2.2)
2. Osteophytes (0-12 or 0-18)[1,2]	2.6 (2.0	2.3 (2.6)
3. Sclerosis (0-12 or 0-198)[1,2]	0.2 (0.8)	0.1 (0.4)
4. Cyst formation (0-12 or 0-18)[1,2]	0.7 (1.7)	0.0 (0.0)
Total score (0-54 or 0-72)	6.0 (5.9)	4.3 (4.6)
Pain		
Pain last week (0-100)	39.7 (24.5)	48.3 (27.8)
Observed disability[3]		
1. 5-m walking time (secs)[1]		
2. sit time (secs)[1]	4.8 (4.0-5.9)	5.2 (4.5-6.1)
3. recline time (secs)[1]	6.5 (5.0-8.5)	6.5 (5.6-9.0)
4. quarding (0-1)	0.5 (0.5)	0.6 (0.5)
5. rigidity (0-1)	0.4 (0.4)	0.3 (0.4)
Self-reported disability (mobility) (7-28)	-21.0 (5.0)	-19.7 (5.9)
Muscle strength[3] (Newton)		
1. Flexion hip	168.4 (52.8)	153.7 (52.6)
2. Extension hip	115.8 (47.9)	97.6 (48.3)
3. Abduction hip	168.1 (50.8)	164.1 (59.1)
4. Adduction hip	145.0 (54.8)	125.5 (51.4)
5. Endorotation hip	128.3 (43.5)	114.4 (40.8)
6. Exorotation hip	102.6 (29.8)	94.6 (31.7)
7. Flexion knee	92.6 (30.9)	85.0 (29.9)
8. Extension knee	162.3 (47.6)	152.0 (47.5)
Range of motion[3] (degrees)		
1. Flexion hip	114 (12.0)	117.8 (9.6)
2. Extension hip	1.7 (6.7)	2.2 (7.4)
3. Abduction hip	15.6 (5.0)	18.7 (6.4)
4. Adduction hip	11.5 (3.9)	12.1 (3.7)
5. Endorotation hip	24.8 (8.6)	31.3 (7.8)
6. Exorotation hip	32.3 (8.7)	35.5 (8.0)
7. Flexion knee	138.5 (7.4)	134.3 (10.5)
8. Extension knee	1.4 (4.0)	-0.7 (4.8)
Pain coping[4]		
1. Pain transformation (4-16)	9.1 (2.3)	9.0 (2.8)
2. Distraction (5-20)	11.4 (3.4)	10.9 (3.1)
3. Reducing demands (3-12)	6.4 (2.0)	6.6 (2.1)
4. Retreating (7-28)	11.0 (3.4)	11.2 (3.9)
5. Worrying (9-36)	16.5 (3.7)	16.4 (4.7)
6. Resting (5-20)	11.5 (3.3)	11.2 (3.1)
Fear avoidance beliefs about physical activity (0-24)	13.5 (5.8)	14.7 (6.5)
Psychological well-being (IRGL)[5]		
1. Anxiety (10-40)	17.7 (6.0)	18.6 (5.8)
2. Depression (0-24)	4.3 (2.7)	4.9 (3.8)
3. Cheerfulness (0-24)	12.1 (4.3)	11.7 (4.7)

Mean (and standard deviation) are presented, unless otherwise states.
[1] Median and interquartile ranges are presented.
[2] Ranges differ between hip and knee patients due to a different number of diagnosed compartments (see methods).
[3] A high score reflects a high use of this strategy when in pain.
[5] A high score reflects, that this aspect highly applies.

The bivariate correlations between articular, kinesiological, psychological and other variables on the one hand and pain and disability on the other are shown in table 2. Because of the large number, only those correlations significant at the 0.01 level will be mentioned here. Radiological characteristics showed significant correlations with disability in knee patients. Muscle strength was consistently correlated with pain and disability, in both hip patients and knee patients: patients with weaker muscles showed more pain and disability. There were significant correlations between range of joint motion and disability: patients with smaller range of joint motion were more disabled. Pain was correlated with disability. Both pain coping and psychological well-being showed significant correlations with pain and disability; e.g. patients who cope by resting more frequently reported more pain and disability. Older patients were more disabled and, in hip patients, duration of complaints was correlated with pain.

Table 2: Bivariate correlations of radiological, kinesiological, psychological and other variables with pain and disability

	Hip (n=73)			Knee (n=112)		
	Pain	Observed disability	Self-reported disability	Pain	Observed disability	Self-reported disability
Radiological status						
1. Joint space narrowing[1]	-0.15	-0.03	0.21	0.26**	0.28**	0.26**
2. Osteophytes[1]	-0.08	0.04	-0.12	0.07	0.13	0.23*
3. Sclerosis[1]	-0.23*	-0.23*	-0.25*	0.02	0.20*	0.14
4. Cyst formation[1]	0.09	0.08	0.07	-	-	-
Total score	-0.17	-0.01	-0.18	0.14	0.24*	0.28*
Muscle strength[2]						
1. Flexion hip	-0.34**	-0.28*	-0.36**	-0.24**	-0.48**	-0.38**
2. Extension hip	-0.32**	-0.50**	-0.38**	-0.26**	-0.36**	-0.37**
3. Abduction hip	-0.31**	-0.40**	-0.46**	-0.21*	-0.34**	-0.39**
4. Adduction hip	-0.30*	-0.41**	-0.38**	-0.21*	-0.43**	-0.41**
5. Endorotation hip	-0.26*	-0.45**	-0.38**	-0.28**	-0.35**	-0.44**
6. Exorotation hip	-0.31**	-0.48**	-0.44**	-0.08	-0.38**	-0.39**
7. Flexion knee	-0.34**	-0.31**	-0.38**	-0.30**	-0.45**	-0.44**
8. Extension knee	-0.34**	-0.45**	-0.43**	-0.24*	-0.39**	-0.38**
Total score	-0.37**	-0.48**	-0.47**	-0.26**	-0.45**	-0.45**
Range of motion						
1. Flexion hip	-0.09	-0.22	-0.17	-0.15	-0.26**	-0.21*
2. Extension hip	-0.20	-0.38**	-0.37**	-0.19*	-0.31**	-0.29**
3. Abduction hip	-0.14	-0.33**	-0.30**	-0.05	0.39**	-0.23*
4. Adduction hip	-0.08	-0.03	0.07	-0.08	-0.04	-0.14
5. Endorotation hip	0.01	0.14	0.01	-0.19*	-0.23*	-0.23*
6. Exorotation hip	-0.25*	-0.35**	-0.34**	-0.13	-0.34**	-0.31**
7. Flexion knee	-0.26*	-0.35**	-0.31**	-0.16	-0.27**	-0.31**
8. Extension knee	-0.05	-0.16	-0.17	-0.16	-0.06	-0.24*
Total score	-0.25*	-0.46**	-0.37*	-0.27**	-0.45*	-0.47**
Pain	-	0.46**	0.48**	-	0.33*	0.40**
Pain coping[3]						
1. Pain transformation	0.15	-0.06	0.14	0.27**	0.18	0.22*
2. Distraction	0.17	0.06	0.11	0.25**	0.22	0.16
3. Reducing demands	0.07	0.31*	0.15	0.21*	0.15	0.22*
4. Retreating	0.29*	0.5**	0.41**	0.39**	0.33**	0.40**
5. Worrying	0.26*	0.26*	0.33**	0.36**	0.40**	0.35**
6. Resting	0.34**	0.38**	0.48**	0.24**	0.44**	0.41**
Fear Avoidance Beliefs	0.39**	0.34**	0.45**	0.20*	0.22*	0.29**
Psychological well-being[4]						
1. Anxiety	0.25*	0.26*	0.39**	0.30*	0.18	0.24**
2. Depression	0.04	-0.03	0.13	0.28**	0.16	0.13
3. Cheerfulness	-0.14	-0.23	-0.28*	-0.26**	-0.26**	-0.30*
Medication						
1. Paracetamol[5]	0.28*	0.19	0.17	0.51*	0.06	0.12
2. NSAID's[5]	0.03	0.05	0.15	0.29*	0.20	0.54*
Other						
Age	0.14	0.43**	0.31**	0.00	0.40**	0.21*
Sex[5]	0.17	0.11	0.13	0.24	0.41	0.30
Duration of complaints[1]	0.38**	0.12	0.02	0.18	0.13	0.13

* $p \leq 0.05$ ** $p \leq 0.01$
[1] Spierman's rank correlation coefficient.
[2] Muscle strength data are normalised to body weight.
[3] A high score reflects a high use of this strategy when in pain.
[4] A high score reflects that this aspect highly applies.
[5] Eta.

Multivariate analysis

The results of multiple regression analyses with regard to pain are presented in table 3. The amount of finally explained variance (final R^2) was significant in both hip patients and knee patients. However, the number of variables retained in analyses and the final explained variance, especially in knee patients were relatively small. Muscle strength was associated with pain in hip patients, but not in knee patients. Pain coping was associated with pain in both hip and knee patients: hip patients who reported high levels of resting and of fear avoidance beliefs experienced more pain; knee patients who reported a high level of retreating reported more pain. In hip patients, a longer duration of complaints was associated with higher pain levels. In knee patients, psychological well-being was associated with pain: a low score on cheerfulness was reported by patients with higher pain levels. Articular status, range of motion, and medication use were not associated with pain.

Table 3: Multiple regression analysis: pain

	Hip (n=73)	Knee (n=112)
Radiological status	-	-
Muscle strength	-0.22*	-
Range of motion	-	-
Pain coping[1]		
Pain transformation	-	-
Distraction	-	-
Reducing demands	-	-
Retreating	-	0.36**
Worrying	-	-
Resting	0.21*	-
Fear Avoidance Beliefs	0.24*	-
Psychological well-being[2]		
Anxiety	-	-
Depression	-	-
Cheerfulness	-	-0.21*
Medication		
Paracetamol	-	-
NSAID's	-	-
Others		
Age	-	-
Sex	-	-
Duration of complaints[3]	0.31**	-
Final R^2 adjusted	0.32**	0.18**

* $p \leq 0.05$ ** $p \leq 0.01$

[1] A high score reflects a high use of this strategy when in pain.

[2] A high score reflects that this aspect highly applies.

[3] Logarithmic transformation.

The results of multiple regression analyses with regard to disability are presented in table 4. The amount of finally explained variance in disability (final R^2) was significant, in both hip patients and knee patients. This applies to both observed and self-reported disability.

Muscle strength was associated with disability, in both hip patients and knee patients: patients with weaker muscles were more disabled. Range of joint motion was also associated with disability: a smaller range of joint motion was associated with more disability, in both hip patients and knee patients.

Pain was associated with disability, with the exception of observed disability in knee patients. Patients reporting more pain were more disabled. Pain coping was also associated with disability. Hip patients and knee patients who rested frequently were more disabled; hip patients who reduced their demands or had low scores on distraction, and knee patients with high scores on worrying, were more disabled also.

Psychological well-being was associated with self-reported disability in hip patients only; anxious patients reported higher levels of disability. Medication use was associated with disability in knee patients only. Finally, older patients, especially hip patients, were more disabled. Articular status was not associated with disability. The exclusion of pain, as a possible intervening variable between radiological status and disability, did not change the association between radiological status and disability (not shown).

Table 4: Multiple regression analysis: observed and self-reported disability

	Hip (n=73)		Knee (n=112)	
Radiological status	-	-	-	-
Muscle strength	-0.27**	-	-0.24**	-0.22**
Range of motion	-0.23*	-0.19*	-0.27**	-0.28**
Pain	0.28**	0.22*	-	0.21*
Pain coping[1]				
Pain transformation	-	-	-	-
Distraction	-0.18*	-	-	-
Reducing demands	0.23**	-	-	-
Retreating	-	-	-	-
Worrying	-	-	0.20*	-
Resting	-	0.31**	0.21**	0.26**
Fear Avoidance Beliefs	-	-	-	-
Psychological well-being[2]				
Anxiety	-	0.30**	-	-
Depression	-	-	-	-
Cheerfulness	-	-	-	-
Medication				
Paracetamol	-	-	-	-
NSAID's	-	-	-0.16*	-
Others				
Age	0.29**	0.21*	0.19*	-
Sex	-	-	-	-
Duration of complaints[3]	-	-	-	-
Final R^2 adjusted	0.51**	0.48**	0.45**	0.40**

* $p \leq 0.05$ ** $p \leq 0.01$

[1] A high score reflects a high use of this strategy when in pain.

[2] A high score reflects that this aspect highly applies.

[3] Logarithmic transformation.

DISCUSSION

This study demonstrates that - when taking into account articular, kinesiological and psychological characteristics - kinesiological and psychological characteristics are seperately associated with disability in patients with OA of the hip or knee. This applies to both observed and self-reported disability. The association of kinesiological and psychological characteristics with pain is less pronounced.

Bivariate analyses indicated significant correlations between articular, kinesiological and psychological characteristics and pain and disability. Because these bivariate analyses do not control for the effect of other characteristics, multivariate

analyses were performed. In these multivariate analyses, disability was found to be associated with muscle strength, range of joint motion, pain, pain coping and psychological well-being (in hip patients only); the effect of articular status was not significant. Pain was found to be associated with muscle strength (hip patients only) pain coping and psychological well-being (knee patients only).

The present results confirm earlier observations[2,4] that radiographically assessed joint degeneration is not associated with disability, after controlling for other factors such as muscle strength. Pain could be an intervening variable in the causal chain from articular status to disability. Following this, inclusion of both pain and radiological status in the regression analyses would lead to an underestimation of the importance of radiological status for disability. However, exclusion of pain as a predictor for disability did not result in different results; articular status remained absent as predictor of disability.

Compared to radiological status, decreased muscle strength and range of joint motion are more strongly associated with disability: the standardised regression coefficients ranged from 0.19 to 0.28. These findings add to earlier observations[2,5,6] in the sense that - even after controlling for radiological status - kinesiological factors appear to be associated with disability in OA-patients.

Muscle strength and range of motion equally contributed to the understanding of the level of disability: the standardised regression coefficients were similar. Although no causal conclusions can be drawn from the present cross-sectional study, this finding is certainly consistent with muscle strength and range of motion being an important determinants of disability in patients with OA of the hip and/or knee. Decreased muscle strength could be due to disuse and avoidance of pain related activities. Decreased muscle strength causes disability, either directly or through unstable joints. It should be noted, however, that muscle weakness may also be due to factors other than disuse, e.g. reflex inhibition[30]. Decreased joint motion causes disability by mechanisms including capsular contractures, muscle contractures and muscle spasm[2].

The standardised regression coefficients of pain coping were in the same range as the kinesiological factors. Reducing demands, worrying, resting and a low level of distraction frequently were associated with greater disability. These associations occurred after controlling for all other characteristics. This suggests that - in addition to the pathway through muscle strength and range of motion- these psychological characteristics affect disability through other pathways. One possible pathway is aerobic fitness: avoidance of pain related activity may induce reduced aerobic fitness and thus disability[9,31]. Another pathway could be through the patient's self-efficacy beliefs: after sustained avoidance of pain related activity the OA-patient no longer believes in his or her capacity to perform certain activities, which causes disability[9].

Again, it should be noted that the present cross-sectional study does not allow causal conclusions: longitudinal studies and studies on biobehavioural mechanisms of disability in OA patients are required to establish causal relationships. The present results are certainly a reason for such studies to be planned.

The association of disability with pain coping and psychological well-being is less than could be expected from most earlier research[32-34]. In one study[9] comparable results were found. An important difference between the present study and most earlier work is the difference in study population. The present sample consisted of patients applying for treatment in a GP-practice, whereas other studies frequently used patient samples from hospitals or pain clinics. Our sample consisted of patients with relative mild articular disease of relative short duration. The study population of Rejeski et al[9], consisting of community based adults, was comparable to ours. Patient samples from hospitals and pain clinics are more selective, possibly representing patients with a longer chronicity of complaints. It has been argued that with growing chronicity psychological factors gain importance in determining disability[35].

The attempt to explain pain was less successful. In the multivariate analyses, pain was significantly explained but the amount of explained variance was smaller than in the case of disability. Decreased muscle strength was associated with pain only in hip patients. Resting as a coping strategy and fear avoidance beliefs were associated with pain in hip patients and retreating was associated with pain in knee patients. In both hip patients and knee patients radiological status and range of joint motion were not associated with pain. In view of the small amount of explained variance it is clear that processes other than those investigated in the present study also determine pain in OA-patients. Presumably, the processes in the OA-joint (e.g. secondary inflammation) should be scrutinised much more closely. It should be noted that the present results point to a discrepancy between pain and disability: although the kinesiological and psychological characteristics were shown to be of considerable relevance with regard to disability, they seem to be less relevant with regard to pain. This conclusion confirms an earlier - much more tentative - one concerning a discrepancy between determinants of pain and determinants of disability in OA-patients[10].

The results with regard to observed and self-reported disability were only slightly different. Because of the possibility of common subjective factors, it was anticipated that self-reported disability would be associated rather closely with psychological characteristics; while observed disability would be more associated with 'objectively' assessed kinesiological characteristics[9,36]. This expectation was not borne out. Thus, it seems that the determinants of observed and self-reported disability are largely identical. Of course, more and better focused research is required before a definite conclusion can be reached in this area.

The results with regard to hip patients and knee patients were rather similar, although some differences were observed. In hip patients, in contrast to knee patients, muscle strength was significantly associated with pain. Also the duration of complaints was associated with pain in hip patients, in contrast to knee patients. No clear differences were found concerning the associations with disability. The similarity of the results of hip patients and knee patients cannot be attributed to the inclusion in both categories of patients with a double diagnosis. Exclusion of these patients did not change our results. Because of the high degree of similarity, it seems that in OA-hip patients and in OA-knee patients disability is caused and maintained by largely the same set of factors.

Recently, knee OA has also been divided by pattern of localisation into tibiofemoral OA and patellofemoral OA. It has been suggested that causes of these two patterns differ[37]. However, in a recent study this could not be demonstrated[17]. Due to the small numbers of patients with specific pattern, we could not study the relationships with pain and disability in these subgroups.

The clinical implications of the present study are rather straightforward. Firstly, the results suggest that improvement of muscle strength through exercise therapy results in a reduction of both pain and disability. In addition, improvement of range of joint motion may result in a decrease of disability. Some research is available to evaluate these suggestions[31,38]. Secondly, the present results suggest that improvement of coping strategies will contribute to a reduction of disability and possibly pain. Research on cognitive behaviour therapy in OA-patients does support this suggestion[39]. However, additional controlled studies are needed to provide evidence for these suggestions.

In conclusion, the present study on patients with OA of hip or knee has demonstrated that - after controlling for other characteristics - muscle strength, range of joint motion and pain coping are each associated with disability. Pain was associated with muscle strength and pain coping only. These results provide a reason for future research on mechanisms underlying these associations.

REFERENCES

1. Dieppe P. Osteoarthritis. In: Klippel JH, Dieppe PA. Rheumatology. Mosby: St. Louis, 1994:2.1-6.
2. Dekker J, Boot B, Woude L van der, Bijlsma JWJ. Pain and disability in osteoarthritis; a review of biobehavioral mechanisms. J Behav Med 1992;15:189-214.
3. Bagge E, Bjelle A, Edén S, Svanborg A. Osteoarthritis in the elderly: clinical and radiological findings in 79 and 85 year olds. Ann Rheum Dis 1991;50:535-9.

4. McAlindon TE, Cooper C, Kirwan JR, Dieppe PA. Determinants of disability in osteoarthritis of the knee. Ann Rheum Dis 1993;52:258-62.
5. Lethbridge-Çejku M, Scott WS Jr, Reichle R, Ettinger WH, Zonderman A, Costa P, Plato CC, Tobin JD, Hochberg MC. Association of radiographic features of osteoarthritis of the knee with knee pain: data from the Baltimore Longitudinal Study of Aging. Arthritis Care Res 1995;8:182-8.
6. Madsen OR, Bliddal H, Egmose C, Sylvest J. Isometric and isokinetic quadriceps strength in gonarthrosis: interrelations between quadriceps strength, walking ability, radiology, subchondral bone density and pain. Clin Rheum 1995;14:308-14.
7. Guccione AA. Arthritis and the process of disablement. Phys Ther 1994;74:408-14.
8. Ettinger WH, Afable RF. Physical disability from knee osteoarthritis: the role of exercise as an intervention. Med Sci Sports Exerc 1996;26:1435-40.
9. Rejeski WJ, Craven T, Ettinger WH, McFarlane M, Shumaker S. Self-efficacy and pain in disability with osteoarthritis of the knee. J Gerontol Psych Sc 1996;51B:24-9.
10. Dekker J, Tola P, Aufdemkampe G, Winckers M. Negative affect, pain and disability in osteoarthritis patients: the mediating role of muscle weakness. Behav Res Ther 1993; 31:203-6.
11. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. Arthritis Rheum 1986;29:1039-49.
12. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthritis Rheum 1991;34:505-14.
13. Altman RD, Fries JF, Bloch DA, Carstens J, Cook TD, Genant H, et al. Radiographic assessment of progression in osteoarthritis. Arthritis Rheum 1987;30:1214-25.
14. Salaffi F, Cavalieri F, Nolli M, Ferracciolo G. Analysis of disability in knee osteoarhrtitis: relationship with age and psychological variables but not with radiographic score. J Rheumatol 1991;18:1581-6.
15. Pattrick M, Hamilton E, Wilson R, Austin S, Doherty M. Association of radiographic changes of osteoarthritis, symptoms, and synovial fluid particles in 300 knees. Ann Rheum Dis 1993;52:97-103.
16. Ahlbäck S. Osteoarhritis of the knee: a radiographic investigation. Acta Radiologica 1968;(suppl 277):1-61.
17. McAlindon T, Zhang Y, Hannan M, Naimark A, Weissman B, Castelli W, Felson D. Are risk factors for patellofemoral and tibiofemoral knee osteoarthritis different? J Rheumatol 1996;23:332-7.
18. Keefe FJ, Caldwell DS, Queen KT, Gil KM, Martinez S, Crisson JE, Ogden W, Nunley J. Osteoarthritic knee pain: a behavioral analysis. Pain 1987;28:309-21.
19. Dekker J, Tola P, Aufdemkampe G, Winckers M. Categories of pain behaviour in osteoarthritis patients. Physioth Ther Pract 1993;9:157-63.
20. Huiskes CJAE, Kraaimaat FW, Bijlsma JWJ. Development of a self-report questionnaire to assess the impact of rheumatic diseases on health and life-style. J Rehabilitation Sciences 1990;3:65-70.

21. Bohannon RW. Muscle strength testing with hand-held dynamometers. In: Admundsen LR, eds. Muscle strength testing: Instrumented and non-instrumented systems. New York: Churchill Livingstone, 1990:69-88.
22. Bohannon RW. Make tests and break tests of elbow flexor muscle strength. Phys Ther 1988;68:931-3.
23. Kendall H, Kendall F, Wadsworth G. Muscle testing and function. 2nd ed. Baltimore: Williams and Wilkins, 1971.
24. Norkin CC, White DJ. Measurement of joint motion: a guide to goniometry. Philadelphia: FA Davis Company, 1986.
25. Kraaimaat FW, Bakker AH. Pain coping strategies in chronic pain patients: the development of the Pain Coping Inventory (PCI). Nijmegen the Netherlands: Internal report University Hospital Nijmegen, 1995.
26. Waddell G, Newton M, Henderson I, Somerville D, Main CJ. A Fear-Avoidance Beliefs Questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability. Pain 1993;52:157-68.
27. Bassey EJ, Fiatarone MA, O'Neill EF, Kelly M, Evans WJ, Lipsitz LA. Leg extensor power and functional performance in very old men and women. Clin Science 1992;82:321-7.
28. Draper N, Smith H. Applied regression analysis. New York: John Wiley and Sons Inc., 1981.
29. American Academy of Orthopaedic Surgeons. Joint Motion: Method of measuring and recording. Chicago: American Academy of Orthopaedic Surgeons, 1965.
30. Hurley MV, Newham DJ. The influence of arthrogenous muscle inhibition on quadriceps rehabilitation of patients with early, unilateral osteoarthritic knees. Br J Rheum 1993;32:127-31.
31. Dekker J, Mulder PH, Bijlsma JWJ, Oostendorp RAB. Exercise therapy in patients with rheumatoid arthritis and osteoarthritis: a review. Adv Behav Res Ther 1993;15:211-38.
32. Lichtenberg PA, Skehan MW, Swensen CH. The role of personality, recent life stress and arthritic severity in predicting pain. J Psychosom Res 1984;28:231-6.
33. Lunghi ME, Miller PMcC, McQuillan WM. Psycho-social factors in osteoarthritis of the hip. J Psychosom Res 1978;22:57-63.
34. Summers MN, Haley WE, Reveille JD, Alarcon GA. Radiographic assessment and psychologic variables as predictors of pain and functional impairments in osteoarthritis of the knee or hip. Arthritis Rheum 1988;31:204-9.
35. Kröner-Herwig B, Jäkle C, Frettlöh J, Peters K, Seemann H, Franz C, Basler HD. Predicting subjective disability in chronic pain patients. Int J Beh Med 1996;3:30-41.
36. Watson D, Pennebaker JW. Health complaints, stress and distress: Exploring the central role of negative affectivity. Psychol Rev 1989;96:234-54.
37. Cooper C, McAlindon T, Snow S, Vines K, Young Ph, Kirwan J, Dieppe P. Mechanical and constitutional risk factors for symptomatic knee osteoarthritis: differences between medial tibiofemoral and patellofemoral disease. J Rheumatol 1994;21:307-13.
38. Ettinger WH, Burns R, Messier SP, Applegate W, Rejeski WJ, Morgan T, Schumaker S, Berry MJ, O'Toole M, Monu J, Craven T. A randomized trial comparing aerobic exercise

and resistance exercise with a health education program in older adults with knee osteoarthritis. JAMA 1997;277:25-31.

39. Keefe FJ, Caldwell DS, Williams DA, Gil KM, Mitchell D, Robertson C, Martinez S, Nunley J, Beckham JC, Crisson JE, Helms M. Pain coping skills training in the management of osteoarthritic knee pain: a comparative study. Behav Ther 1990;21:49-62.

3

THE EFFECTIVENESS OF EXERCISE THERAPY IN PATIENTS WITH OSTEOARTHRITIS OF HIP OR KNEE: A RANDOMISED CLINICAL TRIAL

M.E. van Baar, J. Dekker, R.A.B. Oostendorp, D. Bijl, Th.B. Voorn, J.A.M. Lemmens, J.W.J. Bijlsma

Objective - To determine the effectiveness of exercise therapy in patients with osteoarthritis of hip or knee.

Methods - A randomised single blind, clinical trial was conducted in primary care. Patients with osteoarthritis of hip or knee (ACR-criteria) were selected. Two intervention groups were compared. Both groups received treatment from the patients' general practitioner, including patient education and medication if necessary. The experimental group also received exercise therapy from a physiotherapist in primary care. The treatment period was 12 weeks. The main outcome measures were pain, medication use (non-steroidal anti-inflammatory drugs, NSAIDs) and observed disability.

Results - 201 patients were randomised. Exercise therapy was associated with a reduction of pain in the past week (difference in change -17.0; 95%CI -23.6, -10.4) and observed disability (-0.19; 95%CI -0.38,-0.01). Effect-sizes were medium (0.58) and small (0.28) respectively. No effect of exercise therapy was found for the use of NSAIDs. Additional beneficial effects ($p \leq 0.05$) were found for the use of paracetamol (effect-size=0.33), global effect as perceived by the patient (effect-size=0.68) and muscle strength of the hip (effect-size=0.34).

Conclusion - After twelve weeks, exercise therapy is effective in reducing pain and disability. The size of the effects is medium and small, respectively.

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INTRODUCTION

Osteoarthritis (OA) is a relatively common musculoskeletal disorder. The incidence in general practice in the Netherlands is 2.1/1000 per year for OA of the hip and 3.6/1000 per year for OA of the knee. Prevalence increases with age[1].

The main symptoms of OA include pain and disability. Especially OA in the lower extremities is a highly disabling condition, resulting in problems with mobility. Important therapeutic approaches include patient education, drug therapy and physiotherapy[2,3]. In the Netherlands, a patient is referred to a physiotherapist in 15.1% and 22.4% of the episodes of care for OA of hip and knee respectively[4]. In the four years after consulting their GP, 40% of the patients is referred to the physiotherapist[5]. Physiotherapists often apply exercise therapy in their treatment of patients with OA[6].

Exercise therapy aims at reduction of pain and disability. This is achieved through improvement of muscle strength, stability of joints, range of joint motion and aerobic capacity. These functions are frequently impaired in patients with OA, presumably contributing to pain and disability[7]. Improving these functions is hypothesised to result in a reduction of pain and disability. In addition, exercise therapy aims directly at reduction of disability, e.g. through corrections of the walking pattern[8].

There is some evidence in favour of exercise therapy for patients with osteoarthritis. Controlled trials have shown its beneficial effects on pain[9,10], level of physical activity[10], walking distance[10], stride length[11], movement times[9,11], self-reported disability[9,12], muscle strength[9,12,13] and aerobic capacity[9,14]. However, clear statements about the effectiveness are premature due to methodological flaws in several previous studies. These include inadequate randomisation, no blinded outcome assessment and insufficient power[8,15]. Two trials with adequate internal validity[9-11] have been published. These trials have studied exercise therapy in a research-setting, using a restricted range of exercises for each patient. In regular health care, exercise therapy is tailored to the patient's individual needs, and therefore a broad range of exercises is applied. Furthermore, these trials studied group treatment, instead of individual treatment which is common in regular health care. Thus, there is a need for a high-quality trial examining the effectiveness of exercise therapy in individual patients.

In the present study we examined the effectiveness of exercise therapy in individual patients with OA of the hip or knee. The effects of exercise therapy given by a physiotherapist are studied when added to a treatment by the general practitioner consisting of patient education and medication if necessary. The hypothesis was that exercise therapy results in less pain, medication use and disability.

METHODS

Study population

Patients were selected by GPs in the period May 1994-February 1996. The GPs were situated in 4 cities and surrounding villages in the eastern part of the Netherlands. Inclusion criteria were OA of hip or knee according to the clinical criteria of the American College of Rheumathology[16,17]. Exclusion criteria were: other pathology explaining the complaints; complaints in less than 10 out of 30 days; treatment for these complaints with exercise therapy in the preceding six months; under 40 or over 85 years of age, indication for hip or knee replacement, contraindication for exercise therapy, contraindications for analgesics or NSAIDs, and inability to understand the Dutch language. After having orally consented, patients were registered and their names forwarded to the research team. Radiographs were obtained and evaluated by one of the authors (JAML) using grading scales (0-3) for individual radiographic features[18]. All patients were visited and their eligibility was checked by a GP research fellow (DB).

We aimed at 200 patients participating in the study (100 in each intervention group). This number of patients leads to a power of 0.80 to detect small to medium-sized effects (effect-size=0.4) with an alpha of 0.05 using a t-test[19], with a magnitude similar to effects found in an earlier study[10].

Design

All eligible patients were asked to give written informed consent. Afterwards, patients were visited and randomly allocated equally to either exercise therapy or the control group, using sequentially numbered, opaque, sealed envelopes of the appropriate stratum containing the treatment assigned (see figure 1). Randomisation was performed by a research fellow. Patients were prestratified on their pain in the past week (VAS 0-30 versus 31-100 mm) and location of OA (hip or knee) in order to achieve comparability in these prognostic factors. Before patient enrolment started, a randomisation list was prepared for each stratum on the principle of random permuted blocks of 4 patients, using a random number table[20]. Then, envelopes were filled, sealed and numbered.

Interventions

Two interventions were compared. The patients in the exercise therapy group were given exercise therapy individually by a physiotherapist in primary care. In addition, their GP provided patient education (including a brochure), and medication if necessary. Treatment of the control group was restricted to treatment by their GP, as

described above (patient education and medication if necessary). The treatment period was 12 weeks plus 24 weeks of follow-up.

Exercise therapy was given according to a written protocol[21](see Appendix). It was established by one of the authors(RABO) in co-operation with some experts in the field. One protocol was developed, for both hip and knee patients. It included exercises for muscle functions (strength and length), mobility and coordination, and exercises for elementary movement abilities and locomotion abilities. Also, instructions for the adaptation of activities of daily living and home exercises were given. Content and intensity of treatment were described in terms of treatment goals and corresponding exercises. For example, one possible treatment goal is improvement of muscle performance, dimension strength. Several starting positions and actions are described, such as stance on knees and steps with affected legs first, with full-weight bearing. Content, intensity and frequency of treatment were tailored to the patient's needs. Depending on the physiotherapist's diagnostic findings, specific treatment goals with corresponding exercises were chosen. Number of sessions per week was prescribed and ranged between one to three times a week, depending on the pain level. As a main complaint in OA, pain was assumed to be an indication for the necessity to receive exercise therapy, and consequently for frequency of sessions. Pain was assessed with a visual analogue scale (VAS, 0 mm no pain, 100 mm very severe pain). A physiotherapy session in primary care lasted approximately 30 minutes. Exercise therapy could be discontinued within the 12-week period if, according to the physiotherapists, treatment goals had been achieved. Physiotherapists were trained to use the protocol in two meetings, by explaining content and discussing and practising exercises.

A protocol was also used for the prescription of medication. The GP prescribed preferably paracetamol; prescription of NSAIDs was restricted to naproxen, diclophenac natrium and ibuprofen (see appendix for medication schedule). The patient was instructed to use as little medication as possible. The GP also provided patient education, using a brochure; the topics covered in the brochure include diagnosis, prognosis, advices concerning rest, daily activities and diet, the use of aids and medical treatment. Patients consulted their GP at least in week 0 and week 12 and further on the patients initiative. Physiotherapists and GPs recorded detailed information about the actual treatments on standardised forms, including any deviation of the protocol.

Outcome assessment

Primary outcome measures were pain past week, use of NSAIDs and observed disability. Patients rated their pain in the past week on a VAS. The use of NSAIDs was based on prescription data and counts of remaining medication during evaluation

sessions. Observed disability was determined by studying videos of the patients' performance of a series of standardised tasks using an adaptation of the method described by Keefe[22,23]. The tasks included walking, sitting down, bending and reclining. Both movement times and quality of performance were assessed. The interobserver reliability of this method is good[23-25]. A total score was calculated based on 5 measures: 5 m-walking time, stand-to-sit time, stand-to-recline time and the levels of guarding and rigidity during the performance of the tasks. Standardised scores (Z-scores) of separate measurements were calculated and were added up to obtain an overall score. In order to enhance comparability, the resulting overall score was standardised to render a score with a mean of zero and a standard deviation of one[26]. The internal consistency of the constructed overall score was good (α=0.84)[27].

Several secondary outcome measures were included, to study the working mechanisms of exercise therapy in OA. These measures include pain at assessment as rated on a VAS; pain in the past month with the IRGL-questionnaire (Influence of Rheumatic disease on General health and Lifestyle)[28]; use of paracetamol assessed in the same way as the use of NSAIDs; global perceived effect as assessed by the patients themselves on a 8-point scale (1=vastly worsened; 8=completely recovered)[29]; self-reported disability with the IRGL-questionnaire[28]; muscle strength of the hip and knee bilaterally measured with a hand-held dynamometer[30]; assisted active range of joint motion of the hip and knee bilaterally measured with a goniometer[31]; level of physical activity (excluding hobbies) measured with a questionnaire[32]; extent to which patients believe physical activity to affect their pain measured with an adaptation of the Fear-Avoidance Beliefs Questionnaire[33] and functional limitations on rising and sitting down measured with the Questionnaire Rising and Sitting down(QR&S)[34]. Overall scores were composed for muscle strength of hip and knee and range of joint motion of the hip and knee[26] (see table 1 for separate measurements). The procedure was comparable to data reduction in observed disability (mean=0, SD=1).(For further details on outcome assessment, see Baar et al[26]).

Patients were evaluated by a blinded research assistant at baseline and at 12 weeks (post-treatment). Patients were also assessed in week 24 and 36 (follow-up): follow-up results will be presented elsewhere. The research assistants had been trained to perform the measurements in a standardised manner. The evaluations took place in local health care centres.

Because of the kind of intervention, patients and physiotherapists could not be blinded for the assigned treatment. The GPs were blinded concerning whether the patient received exercise therapy or not. In addition, the researcher who performed data analyses was blinded until main analyses and decisions concerning cutt-of points for subgroups were made.

Statistical analysis

Analyses were performed according to the intention-to-treat principle[35]. Patient data were analysed in the intervention groups to which they had initially been assigned. This included withdrawals and patients not treated according to the assigned treatment. In addition, a per-protocol analysis was performed excluding patients with deviations from the treatment protocol and late ineligibles.

To analyse the effects, change scores were calculated by subtracting the baseline scores from the post-treatment scores. With regard to medication use and global perceived effect, post-treatment scores were compared because no change scores could be calculated. The scores on global perceived effect were dichotomised in order to study the number of improved patients. In the analysis, the change (or post-treatment) scores were compared between the interventions. Two multivariate analyses (MANCOVA) were performed to test for overall differences between the intervention groups: one on the primary outcome measures (see table 2) and one on the secondary outcome measures (see table 3). Subsequently, univariate tests were performed using analysis of covariance (ANCOVA). Adjusted analyses were performed. The baseline level of each outcome measure was included to improve the precision of the effect estimates. In addition, medication use and fear avoidance beliefs, the measures on which the groups differed at baseline ($p<0.10$), were included as covariates in order to control for baseline differences. Group differences and 95% CIs were calculated for all outcome measures. In addition, effect-sizes were calculated by taking the difference between the change scores of the intervention groups and dividing it by the standard deviation of the change score of the total population. An effect-size of 0.2 was regarded as small, of 0.5 as medium and 0.8 as large[19].

To study whether differences existed in the effects of exercise therapy between osteoarthritis of the hip or knee, the interactions between location of osteoarthritis (hip yes/no and knee yes/no) and treatment was tested with analysis of covariance (ANCOVA). This analysis was restricted to the primary outcome measures.

The analyses were carried out using SPSS/PC+ 5.0.

The study protocol was approved by the ethics committee of the Maastricht University Hospital (Maastricht, the Netherlands).

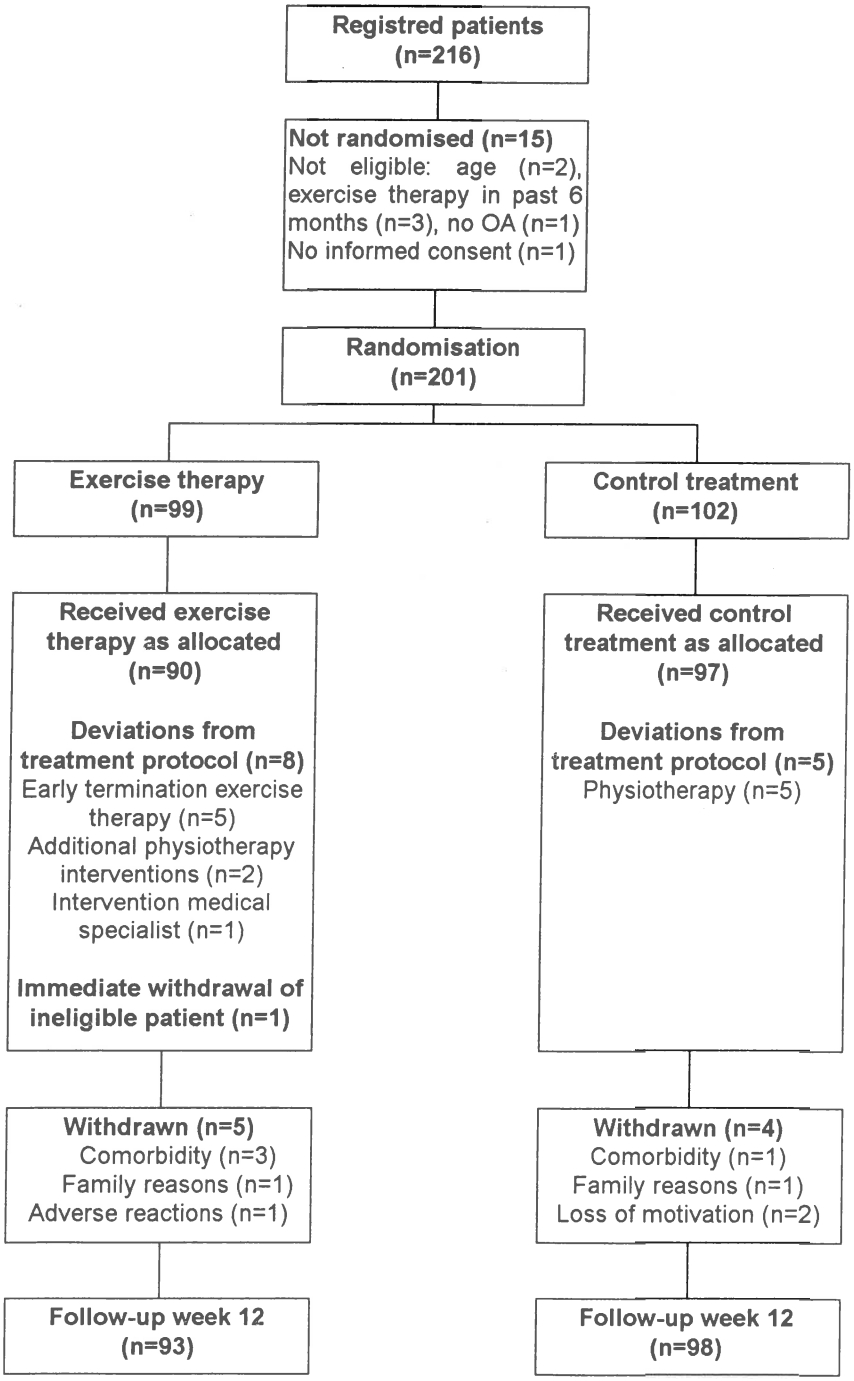
RESULTS

Participant Flow

Figure 1 shows the patient flow and follow-up up to week 12. For 13 patients treatment deviated from the study protocol. For 5 patients exercise therapy was terminated within 6 sessions. Reasons were comorbidity not related to OA (n=4) and the patient's decision to stop after additional medical information (n=1). Two patients receiving exercise therapy were given co-interventions, i.e. physical modalities for pain reduction. To one patient an intervention by a medical specialist was applied (corticosteroid injection). Five patients receiving the control treatment were given physiotherapy, including exercise therapy. This decision was twice based on worsening of complaints. In addition to the treatment deviations, one ineligible patient was withdrawn immediately after randomisation.

Three patients (2 patients receiving exercise therapy and 1 receiving the control treatment) were labelled as late ineligibles with the following diagnoses: spinal stenosis, polymyalgia reumatica and hernia nuclei pulposi. The number of withdrawals and reasons for withdrawal were similar in both treatment groups. One patient receiving exercise therapy reported adverse effects (deterioration of complaints) and withdrew after 6 weeks of therapy.

Figure 1: Patient flow and follow-up to week 12



Comparability

The baseline characteristics of patients in the two intervention groups were generally similar, with two exceptions (table 1). Patients allocated to exercise therapy reported a higher use of medication in the 7 days preceding participation in the study and scored higher on fear avoidance beliefs concerning activity.

Treatment

43 GPs from 40 practices and 39 physiotherapists from 29 primary care practices were involved in treatments. The mean number of GP consultations in control patients (1.8, SD 0.9) was higher than in exercise therapy patients (1.6, SD 0.7, p=0.03). The mean number of physiotherapy sessions of was 16.8 (SD 7.0) in exercise therapy patients and 0.6 (SD 2.8) in control patients. (In primary care a session lasts approximately 30 minutes.) Exercise therapy was mainly directed towards improvement of muscle strength, improvement of range of motion and reduction of pain. These treatment goals were chosen by the physiotherapist in 93%, 85% and 80% of all treatments. In 59% of treatments, treatment was focused directly on improvement of walking and other activities. The applied exercises were mainly active exercises and assisted active exercises: these exercise were applied in 98% and 84% of all treatments. Most patients reported to adhere to the home exercise programme: 61 patients reported to exercise 'frequently' or 'very frequently'. In addition, 18 patients reported to exercise 'regularly'(not further defined).

Success of blinding

The success of blinding of the outcome assessors was checked. In 56 patients (36 patients receiving exercise therapy and 20 control patients) the assessors reported disclosure of treatment allocation. No relation between disclosure and outcome assessment was found. The effectiveness of exercise therapy in unmasked patients was comparable to the effects in patients with a successful blinding: the statistical interaction of disclosure (yes/no) and outcome assessment was non-significant (p=0.66 for pain past week, p=0.08 for taking NSAIDs and p=0.58 for observed disability).

Table 1: Comparability of intervention groups concerning prognostic variables and outcome measures[1]

	Exercise therapy n=98		Control n=102	
Gender (female)	76	(78%)	81	(79%)
Age in years[2]	68.3	(8.4)	67.7	(9.2)
Comorbidity	63	(64%)	62	(62%)
Location of OA				
knee	58	(59%)	61	(60%)
hip	36	(37%)	35	(34%)
both	4	(4%)	6	(6%)
Duration of complaints				
≤ 0.5 year	34	(35%)	42	(41%)
0.5 ≤ 1 year	13	(13%)	12	(12%)
1 ≤ 5 years	29	(30%)	25	(25%)
> 5 years	22	(22%)	23	(23%)
Radiological OA (score ≥ 1)				
joint space narrowing	62	(69%)	55	(60%)
osteophytes	65	(72%)	65	(71%)
Previous medical treatment	59	(61%)	64	(64%)
Pain past week[2]	46.9	(27.7)	43.1	(26.8)
at assessment[2]	34.0	(27.2)	28.7	(26.0)
Medication use past week (taking)*				
paracetamol	51	(52%)	39	(38%)
NSAID	34	(35%)	23	(23%)
Observed disability				
5-m walking time in secs[3]	4.9	(4.3, 6.0)	5.0	(4.3, 6.0)
sit time in secs[3]	3.4	(2.9, 4.1)	3.4	(2.9, 4.0)
recline time in secs[3]	6.9	(5.4, 9.0)	6.1	(5.1, 7.9)
guarding (0-1)[2]	0.58	(0.48)	0.53	(0.50)
rigidity (0-1)[2]	0.34	(0.38)	0.33	(0.37)
Self reported disability (IRGL)(-28 - -7)[2]	-20.0	(5.8)	-20.6	(5.4)
Muscle strength in Newton[2]				
flexion hip	162.4	(56.8)	164.8	(58.4)
extension hip	109.3	(52.7)	108.7	(51.1)
abduction hip	172.7	(57.5)	168.4	(60.3)
adduction hip	138.7	(55.2)	137.3	(58.3)
endorotation hip	126.4	(44.0)	117.8	(40.8)
exorotation hip	102.6	(34.4)	97.1	(30.4)
flexion knee	90.4	(32.9)	89.1	(31.7)
extension knee	163.1	(50.2)	156.1	(52.2)
Joint range of motion in degrees[2]				
flexion hip	115.4	(10.5)	115.4	(11.7)
extension hip	1.5	(6.5)	2.9	(7.5)
abduction hip	17.4	(6.0)	18.0	(6.4)
adduction hip	12.1	(4.2)	11.9	(3.5)
endorotation hip	28.9	(9.2)	29.0	(8.6)
exorotation hip	34.7	(8.6)	34.6	(8.7)
flexion knee	136.0	(9.8)	136.6	(9.4)
extension knee	-0.1	(4.6)	-0.0	(4.7)
Physical activity in min/week[2]	1699	(897)	1829	(1119)
Fear avoidance beliefs towards physical activity (0-24)*[2]	14.6	(5.9)	13.1	(6.7)
Questionnaire Rising and Sitting down[2]				
high chair, toilet and bed (0-10)	3.0	(2.6)	2.7	(2.6)
low chair and car (0-10)	5.5	(3.3)	5.0	(3.2)

* Difference between intervention groups, $p \leq 0.10$

[1] Missing values: Comorbidity (1 in exercise therapy, 2 in controls). Duration of complaints (2 in exercise therapy, 6 in controls), Radiological OA (7 in exercise therapy, 12 in controls), Previous medical treatment (1 in exercise therapy, 2 in controls), Self reported disability (1 in exercise therapy), Muscle strength hip (2 in controls), Physical activity (3 in exercise therapy, 1 in controls), Questionnaire Rising and Sitting down (1 in exercise therapy).

[2] Mean (sd).

[3] Median (interquartile range: 25th, 75th percentile).

Outcome

Multivariate analysis (MANCOVA) indicated a significant overall difference ($p<0.001$) between the intervention groups on the primary outcome measures at 12 weeks (post-treatment). The results of the separate primary outcome measures are shown in table 2. Univariate analyses, comparing exercise therapy with the control group showed beneficial effects of exercise therapy on pain in the past week and on observed disability. No effect of exercise therapy was found for the use of NSAIDs. The effect-sizes indicate that exercise therapy was associated with a medium effect on pain and a small effect on observed disability.

Table 2: Primary outcome measures: improvements and differences between intervention groups[1]

Outcome measure	Exercise therapy n=93	Control n=98	Difference (95% CI) exercise therapy-controls	p-value	effect-size
Pain past week	-22.8	-5.7	-17.0 (-23.6, -10.4)	< 0.01	0.58
Medication use: taking NSAID	39 (42%)	35 (36%)	6% (-8%, 20%)	0.38	0.12
Observed disability[2]	-0.21	-0.02	-0.19 (-0.38, 0.01)	0.04	0.28

[1] Analyses are adjusted for baseline differences (fear avoidance beliefs towards physical activity, use of paracetamol, use of NSAIDs) and baseline score on the specific outcome measure.
[2] Missing value: 2 in exercise therapy.

Likewise, multivariate analysis (MANCOVA) on the secondary outcome measures at 12 weeks indicated a significant overall difference ($p<0.001$) between the intervention groups. The results of the univariate analyses regarding the secondary outcome measures are shown in table 3. Beneficial effects of exercise therapy were found on two additional pain measures (pain at assessment and pain past month), use of paracetamol (i.e. a reduction), global perceived effect and muscle strength of the hip. No effects were found for the other outcome measures (8 out of 13). In a per-protocol analysis, similar effects were found, for both primary and secondary outcome measures.

Table 3: Secondary outcome measures: improvements and differences between intervention groups[1]

Outcome measure	Exercise therapy n=93	Control n=98	Difference (95% CI) exercise therapy-controls	p-value	effect-size
Pain at assessment	-10.5	0.7	-11.2 (-17.7, -4.7)	< 0.01	0.40
Pain past month[2]	-4.3	-1.9	-2.5 (-3.4, -1.5)	< 0.01	0.61
Medication use:					
taking paracetamol	33 (35%)	50 (51%)	-16% (-29%, -3%)	0.02	0.33
Global perceived effect					
improved[3]	44 (47%)	18 (18%)	28% (15%, 42%)	< 0.01	0.64
Self reported disability	-1.1	-0.0	-1.1 (-2.3, 0.1)	0.07	0.26
Muscle strength[2]					
hip	0.22	0.04	0.17 (0.02, 0.33)	0.03	0.32
knee	0.19	0.06	0.13 (-0.04, 0.29)	0.14	0.22
Joint range of motion[2]					
hip	0.21	0.06	0.15 (-0.03, 0.32)	0.10	0.23
knee	0.17	0.09	0.08 (-0.09, 0.25)	0.37	0.13
Physical activity[2]					
improved[4]	43 (46%)	47 (48%)	-2% (-17%, 13%)	0.80	0.04
Fear avoidance beliefs towards					
physical activity	-1.2	-0.2	-1.1 (-2.9, -0.8)	0.25	0.15
Questionnaire rising and sitting down[2]					
high chair, toilet and bed	-0.1	-0.0	-0.1 (-0.7, 0.4)	0.61	0.08
low chair and car	-0.2	0.2	-0.4 (-1.1, 0.3)	0.28	0.16

[1] Analyses are adjusted for baseline differences (fear avoidance beliefs towards physical activity, use of paracetamol, use of NSAIDs) and baseline score on the specific outcome measure.

[2] Missing values: Pain last month (2 in exercise therapy), Muscle strength hip (2 in exercise therapy, 4 in control), Knee (1 in exercise therapy), Joint range of motion (1 in exercise therapy), Physical activity (6 in exercise therapy, 1 in control), Questionnaire rising and sitting down (5 in exercise therapy, 1 in controls).

[3] Results on a 8-point scale are dichotomised as improved (completely recovered, very much improved and much improved) and not-improved (slightly improved, not changed, slightly worsened, much worsened and vastly worsed)

[4] Results are dichotomised as improved (increase in physical activity level, change $\geq$ 1 min/week) versus not-improved (stabilisation or decrease in physical activity level, change $\leq$ 0 min/week).

The effectiveness of exercise therapy was similar in patients with OA of the knee and patients with OA of the hip. No significant interactions were found between location of OA (hip: yes/no and knee yes/no) and effectiveness of the interventions: the statistical interactions with the primary outcome measures were non-significant (Hip: p=0.42 for

pain past week, p=0.99 for taking NSAIDs and p=0.12 for observed disability; Knee: p=0.31 for pain past week, p=0.83 for taking NSAIDs and p=0.44 for observed disability).

DISCUSSION

In this trial evidence was found for the effectiveness of exercise therapy in patients with OA of the hip or knee. Patients were treated individually; exercise therapy was tailored to the patient's individual needs. As expected, beneficial effects were found for pain and observed disability. In addition, beneficial effects were found on the use of paracetamol (i.e. a reduction), global effect as perceived by the patient and muscle strength of the hip. The magnitude of the effects was medium for pain and global perceived effect, and small for the other effects. No effects were found for one primary outcome measure (use of NSAIDs) and 8 secondary outcome measures, including self-reported disability and joint range of motion. In conclusion, exercise therapy reduces pain and disability in patients with OA of the hip or knee. The size of the effects is medium to small, respectively.

The clinical relevance of our results can be determined using the calculated effect-sizes. In one study, an effect-size of 0.5 is considered as the threshold for minimal clinical importance[36]. Using this cutt-of point, our beneficial effects on pain and global perceived effect can be considered clinically relevant. The effect on observed disability does not exceed this arbitrary cutt-of point. In another study a difference in success rate of 25% between groups is considered to be clinically relevant[37]. Using this criterion, the effect as perceived by the patient is clinically relevant.

We tried to avoid most methodological flaws, described for several previous studies[8]. Appropriate randomisation was performed using random number tables and concealed assignment of patients. The criteria for the selection of patients and patient characteristics have been clearly described. Treatment was documented in both the experimental (exercise) group and the control group. Patient compliance was checked. Patients were evaluated by blinded outcome assessors and the timing of outcome assessment was similar in the two groups. The statistical power was adequate to detect the expected small to medium effects. Nevertheless, some comments can be made. Firstly, although treatment groups were quite comparable with regard to almost all variables (n=35) assessed, baseline differences existed for medication and fear avoidance beliefs concerning physical activity. In our adjusted analyses we have controlled for these differences. Secondly, no data were available on patients who withdrew from the study. However, the number of study withdrawals post-treatment was small (5%) and number and reasons were comparable across intervention groups.

No indication for selective withdrawal was found and therefore, no additional analyses including study withdrawals were needed. Thirdly, deviations from allocated treatments were registered in 7% of the patients, resulting in a smaller treatment contrast than initially intended. However, this contamination bias does not affect the internal validity of our study, since no indications for selection bias exist. These treatment deviations reflect daily practice and should therefore be investigated in a study into the effectiveness of an intervention. Fourthly, although in a limited number of cases treatment allocation was unmasked, no indication for biased outcome assessment was found. The treatment effects in unmasked patients were similar to the effects in patients with successful blinding. The unmasking of especially exercise therapy can be explained by the more time and energy consuming nature of this treatment condition. Finally, both hip and knee patients were included in our study. Beforehand, no indications existed to expect differences in the effectiveness of exercise therapy between these patient categories. This was confirmed by a subgroup analysis revealing no differences between hip and knee patients.

In analysing the effects of exercise therapy we used change scores between baseline values and post-treatment values. A disadvantage of this method is the relatively high measurement error of the change scores. However, a main advantage of change scores is that they directly reflect the response to treatment in intervention groups. In addition, it enables comparison with most other trials in this field, applying mainly change scores.

Previous clinical trials already had shown beneficial effects of exercise therapy in patients with OA[9-14]. However, the internal validity of previous trials was often inadequate. Methodological flaws include inadequate randomisation, no blinding of outcome assessment and insufficient power[8]. Positive exceptions are the study of Kovar et al[10,11] and the recently published study of Ettinger et al[9]. They both reported beneficial effects on pain and disability. However, these studies were explanatory trials, studying exercise therapy in optimal research-settings. Patients were treated in groups, using more or less standardised treatment for all patients. This restricts the external validity of these studies. The surplus value of our study is in the nature of our intervention. Our trial was a pragmatic trial assessing the impact of exercise therapy in patients treated individually. Within the limits of the protocol, exercise therapy could be tailored to the patient's needs, as is usual in clinical practice. The use of a written protocol resulted in a clearly described intervention. Our study has shown the effectiveness of this modality of exercise therapy, in reducing pain and disability.

The results of this study elucidate the mechanisms underlying exercise therapy only to a small extent. Beforehand, it was expected that exercise therapy would lead to improvement of muscle strength and range of motion, and thereby to a reduction of pain and disability in OA[7]. Muscle strength of the hip was indeed found to be

improved. However, no effects were found for muscle strength of the knee and for range of motion. So, other explanations are needed to clarify the effectiveness of exercise therapy. Exercise therapy possibly has a beneficial effect on aerobic capacity or muscle spasm, which are known to be related to pain and disability [38,39]. This could explain the positive effect of exercise therapy on pain and disability. Because aerobic capacity and muscle spasm were not assessed in our study it is not possible to assess the validity of this explanation. Also, psychological mechanisms such as attention or pain coping could play a role in the effectiveness of exercise therapy. We did not control for attention, so attention could explain our results. However, trials controlling for the effect of attention indicate a beneficial effect of exercise therapy itself[9,11]. Pain coping is related known to be pain and disability in OA and possibly affects the effects of exercise therapy[7,26]. However, no effect was found on a specific pain coping assessment, i.e. the extent patients believe physical activity to affect their pain.

So, the mechanisms underlying the beneficial effect of exercise therapy remain to be elucidated. Our trial was designed as a pragmatic trial, not as an explanatory trial assessing the efficacy of specific components of exercise therapy. Therefore, further research is necessary to explain how the effects of exercise therapy on pain and disability come about.

In conclusion, this randomised clinical trial in primary health care showed beneficial post-treatment effects of exercise therapy on pain and disability in OA in the hip or knee. Effect sizes are medium and small respectively. These results support the current referral pattern to physiotherapy in primary care.

REFERENCES

1. Miedema H. *Reuma-onderzoek meerdere echelons (ROME): basisrapport.* (Rheumatism-research on different levels of the health care system: basis report). Leiden the Netherlands: NIPG-TNO, 1994.
2. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, Moskowitz RW, Schnitzer TJ. Guidelines for the medical management of osteoarthritis. Part I. Osteoarthritis of the hip. Arthritis Rheum 1995;38:1535-1540.
3. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, Moskowitz RW, Schnitzer TJ. Guidelines for the medical management of osteoarthritis. Part II. Osteoarthritis of the knee. Arthritis Rheum 1995;38:1541-1546.
4. Groenewegen PP, Bakker DH de, Velden J van der. *Een Nationale Studie naar Ziekten en Verrichtingen in de Huisartspraktijk. Basisrapport: Verrichtingen in de huisartspraktijk.* (Interventions in General Practice. Dutch National Survey of General Practitioners). Utrecht the Netherlands: NIVEL, 1992.

5. Miedema HS. *Verwijzingen van patienten met klachten van houdings- en bewegingsapparaat.* (Referrals in patients with musculoskeletal disorders) In: Bruijne J de, Dijkmans BAC, Hazes JWM, Springer MP. *Tien topics in de reumatologie.*(Ten topics in rheumatology). Leiden the Netherlands: Boerhave cursus 1995:23.
6. Valk RWA van der, Dekker J, Baar ME van. *De fysiotherapeutische behandelingen van patienten met artrose: een beschrijvend onderzoek.* (Physical therapy for patients with osteoarthritis: a description). In Dekker J, van Baar ME (eds). *Beleidsgericht evaluatie- en effectonderzoek extramurale fysiotherapie (BEEF) Eindrapport.* Utrecht the Netherlands: NIVEL, 1995.
7. Dekker J, Boot B, Van der Woude LHV, Bijlsma JWJ. Pain and disability in osteoarthritis: a review of biobehavioral mechanisms. J Behav Med 1992;15:189-214.
8. Dekker J, Mulder PH, Bijlsma JWJ, Oostendorp RAB. Exercise therapy in patients with rheumatoid arthritis and osteoarthritis: a review. Adv Behav Res Ther 1993;15:211-38.
9. Ettinger WH, Burns R, Messier SP Applegate W, Rejeski WJ, Morgan T, Shumaker S, Berry MJ, O'Toole M, Monu J, Craven T. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. JAMA 1997;277:25-31.
10. Kovar PA, Allegrante JP, MacKenzie CR, Peterson MGE, Gutin B, Charlson ME. Supervised fitness walking in patients with osteoarthritis of the knee. Ann Intern Med 1992;116:529-34.
11. Peterson MGE, Kovar-Toledano PA, Otis JC, Allegrante JP, Mackenzie CR, Gutin B, Kroll MA. Effect of a walking program on gait characteristics in patients with osteoarthritis. Arthritis Care Res 1993;6,11-6.
12. Jan MH, Lai JS. The effects of physiotherapy on osteoarthritic knees of females. J Formosan Med Assoc 1991;90:1008-13.
13. Schilke JM, Johnson GO, Housh TJ, O'Dell JR. Effects of muscle-strength training on the functional status of patients with osteoartritis of the knee. Nursing Research 1996;45:68-72.
14. Minor MA, Hewett JE, Webel RR, Anderson SK, Kay DR. Efficacy of physical conditioning exercise in patients with rheumatoid arthritis and osteoarthritis. Arthritis Rheum 1989;32:1396-1405.
15. Puett DW, Griffin MR. Published trials of nonmedicinal and noninvasive therapies for hip and knee osteoarthritis. Ann Intern Med 1994;121:133-40.
16. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthritis Rheum 1991;34:505-514.
17. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. Arthritis Rheum 1986;29:1039-49.
18. Altman RD, Fries JF, Bloch DA, Carstens J, Cooke TD, Genant H, et al. Radiographic assessment of progression in osteoarthritis. Arthritis Rheum 1987;30:1214-25.
19. Cohen J. Statistical power analysis for the behavioral sciences. London: Academic press Inc., 1977.
20. Pocock SJ. Clinical trials. A practical approach. Chichester: John Wiley and Sons, 1991.

21. Oostendorp RAB, Heuvel JH van den, Dekker J, Baar ME van. Exercise therapy in patients with osteoarthritis of hip or knee: a protocol. Amersfoort/Utrecht the Netherlands: NPI/NIVEL, 1998.
22. Keefe FJ, Caldwell DS, Queen K, Gil KM, Martinez S, Crisson JE, Ogden W, Nunley J. Osteoarthritic knee pain: a behavioral analysis. Pain 1987;28:309-21.
23. Dekker J, Tola P, Aufdemkampe G, Winckers M. Categories of pain behaviour in osteoarthritis patients. Physioth Theory Pract 1993;9:157-63.
24. Keefe FJ. Block AR. Development of an observation method for assessing pain behaviour in chronic low back pain patients. Behav Ther 1982;13:363-75.
25. McDaniel LK, Anderson, KO, Bradley LA, Young LD, Turner RA, Agudelo CA, Keefe FJ. Development of an observation method for assessing pain behavior in rheumatoid arthritis. Pain 1986;24:165-84.
26. Baar ME van, Dekker J, Lemmens JAM, Oostendorp RAB, Bijlsma JWJ. Pain and disability in patients with osteoarthritis of hip or knee: the relationship with articular, kinesiological and psychological characteristics. J Rheumatol 1998;25:125-33.
27. Steultjens MPM, Dekker J, Baar ME van, Oostendorp RAB, Bijlsma JWJ. Consistency and validity of an observational method for assessing disability in mobility in patients with osteoarthritis (submitted).
28. Huiskes CJAE, Kraaimaat FW, Bijlsma JWJ. Development of a self-report questionnaire to assess the impact of rheumatic diseases on health and lifestyle. J Rehab Sciences 1990; 3:65-70.
29. Heijden GJMG van der. Shoulder disorder treatment. Efficacy of ultrasoundtherapy and electrotherapy. Maastricht the Netherlands: University Press Maastricht, 1996.
30. Bohannon RW. Muscle strength testing with hand-held dynamometers. In: Admundsen LR, eds. Muscle strength testing: Instrumented and non-instrumented systems. New York: Churchill Livingstone, 1990:69-88.
31. Norkin CC, White DJ. Measurement of joint motion: a guide to goniometry. Philadelphia: FA Davis Company, 1986.
32. Caspersen CJ, Bloemberg BPM, Saris WHM, Merritt RK, Kromhout D. The prevalence of selected physical activities and their relation with coronary heart disease risk factors in elderly men: the Zutphen study, 1985. Am J Epid 1991;133:1078-92.
33. Waddell G, Newton M, Henderson I, Somerville D, Main CJ. A fear-avoidance beliefs questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability. Pain 1993;52:157-68.
34. Roorda LD, Roebroeck ME, Lankhorst GJ, Van Tilburg T, Bouter LM. Measuring functional limitations in rising and sitting down: development of a questionnaire. Arch Phys Med Rehab 1996;77:663-9. 29.
35. Newell DJ. Intention-to-treat analysis: implications for quantitative and qualitative research. Int J Epid 1992;21:837-41.
36. Bronfort G, Assendelft WJJ, Bouter L. Efficacy of spinal manipulative therapy for headache and conditions other than spinal related pain: a systematic review and best evidence synthesis (submitted).

37. Windt DAMW van der, Heijden GJMG van der, Scholten RJPM, Koes BW, Bouter LM. The efficacy of non-steroidal anti-inflammatory drugs (NSAIDs) for shoulder complaints. A systematic review. J Clin Epidemiol 1995;48:691-704.
38. Philbin EF, Groff GD, Ries MD, Miller TE. Cardiovascular fitness and health in patients with end-stage osteoarthritis. Arthritis Rheum 1995;38:799-805.
39. Hurley MV, Newham DJ. The influence of arthrogenous muscle inhibition on quadriceps rehabilitation of patients with early, unilateral osteoarthritic knees. Br J Rheum 1993;32:127-31.

Appendix 1 Medication schedule

Step		Medication	Dosage
1.		Paracetamol	Max. 6 tablets daily (1 or 2 tab. a time)
2.		Naproxen 250 mg	max. 2 daily
	or	Diclofenac Na. 25 mg	max. 3 daily
	or	Ibuprofen 400 mg	max. 3 daily
3.		Another choice from step 2	idem
4.		Naproxen 500 mg	max. 2 daily
	or	Diclofenac 50 mg	max. 3 daily
	or	Ibuprofen 400 mg	max. 6 daily

4

EXERCISE THERAPY IN PATIENTS WITH OSTEOARTHRITIS OF HIP OR KNEE: OUTCOME IN SPECIFIC SUBGROUPS OF PATIENTS

M.E. van Baar, J. Dekker, D. Bijl, R.A.B. Oostendorp, Th.B. Voorn, J.W.J. Bijlsma

Objective - To investigate whether specific groups of patients with osteoarthritis (OA) of hip or knee particularly benefit from exercise therapy.
Subjects - 200 Patients with osteoarthritis of hip or knee (ACR-criteria) participated. They were randomised and allocated to exercise therapy (n=98) and a control group (n=102).
Methods - All patients received treatment from the patient's general practitioner, including patient education and medication if necessary. Exercise therapy patients also received exercise therapy from a physical therapist in primary care. The treatment period was twelve weeks. Changes in pain, medication use (non-steroidal anti-inflammatory drugs, NSAIDs) and observed disability were compared for specific sub-groups.
Results - Contrary to our expectation, no beneficial effects of exercise therapy were found for patients with low muscle strength, restricted ROM, high levels of disabilities and high levels of passive pain coping strategies. Exploratory analyses indicated beneficial effects in patients without radiological OA, in patients with complaints of recent onset and in patients who complied with exercise therapy.
Conclusion - Only limited evidence was found of the existence of subgroups of patients in whom exercise therapy has beneficial effects. Specification of the indication for exercise therapy in patients with OA of the hip or knee is not yet possible.

Submitted for publication

INTRODUCTION

In recent years the emphasis on exercise therapy as a valuable intervention in patients with osteoarthritis (OA) has increased. In guidelines for medical management, exercise therapy is recommended for treatment of patients with osteoarthritis of the knee or hip[1-3]. The scientific basis for these recommendations has become available only recently. Reviews of earlier literature had led to the conclusion that there is some evidence of a beneficial effect of exercise therapy in patients with OA of the knee or hip[4-7]. In recent controlled trials, additional evidence has been found of the usefulness of exercise therapy in these patients[8-10]. Our own clinical trial into the effectiveness of exercise therapy in patients with OA of knee or hip showed similar results. Patients receiving exercise therapy reported a lower pain level, while also a lower level of disability was observed. In addition, less paracetamol was used, patients reported a more beneficial global treatment effect, and improvement of muscle strength was observed[11].

Until now, hardly any attention has been paid to the effects of exercise therapy in specific subgroups of patients with OA. The one exception being Ettinger et al[8] who studied the influence of sex, age, race, and the degree of obesity. They found beneficial effects of exercise therapy in almost all subgroups studied, i.e. between subgroups no differences seemed to exist. However, they did not explicitly study differences in effectiveness between subgroups by looking at statistical interactions. Therefore it remains unclear whether effectiveness differs between subgroups.

This lack of attention for specific groups of patients who might possibly particularly benefit from exercise therapy is remarkable. Differences in the effects of exercise therapy in patients with OA are to be expected. Outcome in patients with OA can be viewed as the result of a complex of factors involving the severity of disease, impairments, disabilities and psychological, environmental and social factors[4,7]. Exercise therapy focuses on specific factors and is therefore expected to benefit specific subgroups of patients. Provided differences in effectiveness in subgroups can be demonstrated, indications for referral to exercise therapy can be made more explicit and therapy can be focused on these patients.

With regard to subgroups, two specific expectations can be formulated. Firstly, beneficial effects are expected in patients with a relatively high level of impairments and disabilities at the start of treatment. Exercise therapy aims at reduction of pain and disability through improvement of muscle strength, stability of joints, range of motion (ROM) and exercise tolerance. Especially in patients with muscle weakness and reduced range of motion, exercise therapy is expected to result in relatively great reduction in pain and disability. Further, exercise therapy aims directly at reduction of

disabilities, e.g through corrections of the walking pattern[4]. Thus, particularly patients with a high disability level are expected to benefit from exercise therapy[12].

Secondly, beneficial effects are expected in patients with an emotional or catastrophising reaction to pain. In patients with an emotional or catastrophising reaction to pain, relatively high levels of pain and disability have been observed[13,14]. It has been hypothesised that this type of pain coping strengthens a patient's tendency to avoid exercise and related activities. This avoidance enhances muscle weakness which leads to unstable joints, pain and disability[12]. Exercise therapy promotes an active approach of pain by the patients and is therefore expected to be of particular benefit for patients with an emotional or catastrophising reaction to pain.

The goal of this study is to investigate whether specific groups of OA patients particularly benefit from exercise therapy. Beneficial effects are expected in 1) patients with relatively high levels of impairment (muscle weakness and reduced ROM) and disability and in 2) patients with an emotional or catastrophising reaction to pain. In addition, an exploratory analysis was performed to study effect modification by characteristics of patients and characteristics of physical therapy treatments. Characteristics of patients include demographical and clinical features. Characteristics of physical therapy treatment refer to specific treatment goals and the patient's compliance.

METHODS

Patients

Patients were selected by general practitioners (GPs) in the Netherlands in the period May 1994-February 1996. Inclusion criteria were OA of hip or knee according to the clinical criteria of the American College of Rheumathology[15,16]. Exclusion criteria were: other pathology explaining the complaints; complaints in less than 10 out of 30 days; treatment for these complaints with exercise therapy in the preceding six months; under 40 or over 85 years of age; indication for hip or knee replacement; contraindication for exercise therapy; contraindications for analgesics or non-steroidal anti-inflammatory drug's (NSAIDs); and inability to understand the Dutch language. After having orally consented, patients were registered and their names forwarded to the research team. All patients were visited and their eligibility was checked by a GP research fellow. All eligible patients were asked to give written informed consent. Afterwards, patients were randomly allocated to either exercise therapy or the control group, using sequentially numbered, opaque, sealed envelopes containing the treatment assigned. Patients were prestratified on the basis of their pain in the past

week (visual analogue scale (VAS), 0-30 mm versus 31-100 mm) and location of OA (knee or hip) in order to achieve comparability in these prognostic factors.

We aimed at 200 patients participating in the study, as this number of patients leads to a power of 0.80 to detect small to medium-sized effects with an alpha of 0.05, also in subgroup analyses[17].

The study protocol was approved by the ethics committee of the Maastricht University Hospital (Maastricht, the Netherlands).

Interventions

Two interventions were compared. The patients in the exercise therapy group were given exercise therapy individually by a physical therapist in primary care. In addition, their GP provided patient education (including a brochure), and medication if necessary. Treatment of the control group was restricted to treatment by their GP, as described above (patient education and medication if necessary). The treatment period was 12 weeks plus 24 weeks of follow-up.

Exercise therapy was given according to a written protocol[18] (see Appendix) and included exercises for muscle functions (strength and length), mobility and coordination, and exercises for elementary movement abilities and locomotion abilities. Also, instructions for the adaptation of activities of daily living and home exercises were given. Content and intensity of treatment were described in terms of treatment goals and corresponding exercises. Content, intensity and frequency of treatment were tailored to the patient's needs. Depending on the physical therapist's diagnostic findings, specific treatment goals with corresponding exercises were chosen. Number of sessions per week was prescribed and ranged between one to three times a week, depending on the pain level. A physical therapy session in primary care lasted approximately 30 minutes. Exercise therapy could be discontinued within the 12-week period if, according to the physical therapists, treatment goals had been achieved. Physical therapists were trained to use the protocol.

A protocol was also used for the prescription of medication. The GP prescribed preferably paracetamol; prescription of NSAIDs was restricted to naproxen, diclophenac natrium and ibuprofen (see Appendix Chapter 3 for medication schedule). The patient was instructed to use as little medication as possible.

Effect-modifying factors

For each possible effect-modifying factor patients were classified into two groups. If no *a priori* classification was available, subgroups were assigned by the median-split method. In this method, two groups are composed for each variable with the median as cut-off point. The following factors were studied:

Impairments: muscle strength and range of motion (ROM) The isometric muscle strength was measured with the MicroFet (Hoggan Health Industries, Draper, Utah), a hand-held dynamometer[19]. A protocol was used to standardise the measurements. Make tests were used, i.e. the research assistant holds the dynamometer steady while the patient exerts a maximal force against it[20]. Muscle strength (in Newtons) was measured bilaterally for 8 muscle actions. For the hip the extension, flexion, abduction, adduction, endorotation and exorotation were measured. For the knee flexion and extension were measured. Overall scores were composed for hip and knee by calculating standardised scores (Z-scores) of separate measurements and adding them up to obtain an overall score. In order to enhance comparability, the resulting overall score was standardised to render a score with a mean of zero and a standard deviation of one (see Van Baar et al[14]) (median split: median hip=-0,12, knee=-0.04).

Assisted active range of joint motion (in degrees) was measured with a goniometer, according to Norkin and White[21]. ROM of the hip was measured by assessing extension, flexion, abduction, adduction, endorotation and exorotation. ROM of the knee was measured by assessing flexion and extension. Overall scores were computed for hip and knee, following the procedure applied to muscle strength measurements (see Van Baar et al[14])(median split: median hip=0.06, knee=0.17).

Muscle strength and range of joint motion were assessed by two research assistants, both of them experienced physical therapists who had been trained to perform these measurements in a standardised way. Follow-up training sessions were held in order to maximise standardisation. Each patient was tested by a single research assistant. Interrater reliability of the physical examination was satisfactory. The mean of intraclass correlation coefficients was 0.78 for muscle strength measurements (range 0.60-0.93) and 0.68 for range of motion measurements (range 0.39-0.90).

Observed and self-reported disability: Observed disability was determined by studying videos of the patients' performance of a series of standardised tasks using an adaptation of the method described by Keefe[13,22]. The tasks included walking, sitting down, bending and reclining. Both movement times and quality of performance were assessed. The interobserver reliability of this method is good[22-24]. A total score was calculated based on 5 measures: 5m-walking time, stand-to-sit time, stand-to-recline time and the levels of guarding and rigidity during the performance of the tasks. The procedure was comparable to data reduction in muscle strength and ROM measurements (mean=0,SD=1; see Van Baar et al[14])(median split: median=0.00). The internal consistency of the constructed overall score was good (α=0.84)[25]. Self-reported disability was assessed with the IRGL-questionnaire (*Invloed van Reuma op Gezondheid en Leefwijze*=Influence of Rheumatic diseases on General health and

Lifestyle)[26]. This is a Dutch adaptation of the Arthritis Impact Measurements Scales. From the IRGL-questionnaire, the subscale 'mobility' was used, which consists of 2 items concerning disability in general and 5 items concerning disability in climbing stairs, cycling and walking. This ability score was recoded into a disability score by reversing the sign (median split: median=20.5).

Paincoping: Levels of catastrophising and resting were assessed with the Pain Coping Inventory[27]. A high score reflects a high use of the specific strategy when in pain (median split: median=16 and 11). In addition, the extent to which patients believe physical activity to affect their pain was assessed using an adaptation for OA-patients of the Fear-Avoidance Beliefs Questionnaire (median split: median=14)[28].

Characteristics of patients: The influence of the following features was studied:

- demographic characteristics: age (median split: median=69) and sex;
- stratification factors: pain past week assessed with a visual analogue scale (VAS 0-30 mm /31-100 mm), location of OA (hip yes/no and knee yes/no);
- clinical features: OA of the hand according to Altman et al[29](yes/no), radiological OA as measured on grading scales for individual radiographic features (yes/no)(for details see Van Baar et al[14]), obesity (Body Mass Index <30/≥30[30]), duration of complaints (median split:median=52 weeks) and comorbidity (yes/no);
- lifestyle: level of physical activity according to the Zutphen Physical Activity Questionnaire was studied (median split:median=1530 min/week), including walking, bicycling, gardening, doing odd jobs, sports and working (the category hobbies was excluded because of an overrepresentation of sedentary activities)[31];
- psychological well-being: anxiety, depression and cheerfulness (median split: median=17, 3 and 12) as assessed with the IRGL-questionnaire[26].

Characteristics of physical therapy treatment: Physical therapists could tailor treatment to the patient's needs by their choice for specific treatment goals. It was studied whether the specific choice for treatment goals influenced the effectiveness of treatment. Possible treatment goals were alleviation of pain, improvement of muscle strength, improvement of ROM, improvement of coordination, improvement of fitness and improvement of walking. Treatment goals were registered on a standardised form during the period of treatment. In addition, the influence of compliance was studied. Both the patient and the physical therapist reported about the level of exercise compliance. Patients were phoned and asked whether they managed to do their home exercises as often as prescribed. Possible answers were: (almost) never, sometimes, regularly, often and very often. A patient was considered compliant if he/she reported to exercise (very) often. Physical therapists were asked to estimate whether the patient complied with the home exercise instructions in the last 4 weeks of treatment, using the standardised form. Possible answers were: certainly not, probably not,

probably and certainly. A patient was considered compliant when the physical therapist estimated that a patient had certainly exercised.

Outcome measures

Primary outcome measures were pain, use of NSAIDs and observed disability. Patients rated their pain in the past week on a VAS (0 mm no pain - 100 mm very severe pain). The use of NSAIDs was based on prescription data, and on counts of medication during evaluation sessions. Observed disability was determined by studying videos of the patient's performance of 5 standardised tasks (see 'Prognostic factors').

Patients were evaluated by a blinded research assistant at baseline and at 12 weeks (post-treatment). Videos were also scored by these blinded assistants. The research assistants had been trained to perform the measurements in a standardised manner. The evaluations took place in local health care centres.

Statistical analysis

Statistical analyses were performed according to the intention-to-treat principle. All patients and their follow-up results were analysed in the intervention groups as initially assigned. This includes drop-outs and patients not treated according to the assigned treatment[32].

To analyse the effects, change scores were calculated (post-treatment minus baseline). With regard to medication use, post-treatment scores were compared because no change scores could be calculated. To study whether differences existed in the effects of exercise therapy between subgroups, the interaction between subgroup and treatment was tested with analysis of covariance (ANCOVA). The significance level was set at 0.05. Two covariates were included in order to control for baseline differences between the two treatment groups concerning medication use and fear avoidance beliefs (see results). In order to avoid overcorrection, this correction was omitted in analyses of subgroups based on these two characteristics.

The statistical analyses of the subgroups that had been formed on the basis of physical therapy characteristics deviated from the procedure as described above. Exercise therapy patients were divided into two groups based on either the content of treatment (treatment goal chosen or not) or their compliance (complier or not). Analysis of (co)variance was used to test for differences in outcome for these groups, including the covariates as described above.

The analyses were carried out using SPSS/PC+ 5.0.

RESULTS

Patients

In total 201 patients were included in the study, 99 patients were allocated to exercise therapy, 102 patients to the control treatment. One patient allocated to exercise therapy was excluded on the grounds of additional medical information (ESR>45mm/1 hour) immediately after randomisation.

The baseline characteristics in the two intervention groups were generally similar (table 1), with two exceptions. Patients allocated to the exercise therapy group reported a higher use of medication in the 7 days preceding participation in the study and scored higher on fear avoidance beliefs concerning physical activity.

The twelve week evaluation was completed by 191 patients: 93 patients from the exercise therapy group and 98 control patients. Five exercise therapy patients and four control patients withdrew from the study. Reasons for withdrawal were comorbidity (3 patients and 1 control patient respectively), family circumstances (one patient in both groups), adverse effects of exercise therapy (1 patient), and loss of motivation (2 control patients).

Table 1: Comparability of intervention groups at baseline[1]

	Exercise therapy n=98		Control n=102	
Gender (female)	76	(78%)	81	(79%)
Age in years[2]	68.3	(8.4)	67.7	(9.2)
Comorbidity	63	(64%)	62	(62%)
Location of OA				
knee	58	(59%)	61	(60%)
hip	36	(37%)	35	(34%)
both	4	(4%)	6	(6%)
Duration of complaints				
≤ 0.5 year	34	(35%)	42	(41%)
0.5 ≤ 1 year	13	(13%)	12	(12%)
1 ≤ 5 years	29	(30%)	25	(25%)
> 5 years	22	(22%)	23	(23%)
Radiological OA (score ≥ 1)				
joint space narrowing	62	(69%)	55	(60%)
osteophytes	65	(72%)	65	(71%)
Previous medical treatment	59	(61%)	64	(64%)
Pain past week, (visual analogue scale)(0-100)[2]	46.9	(27.7)	43.1	(26.8)
at assessment[2]	34.0	(27.2)	28.7	(26.0)
Medication use past week (taking)				
paracetamol	51	(52%)	39	(38%)
NSAIDs	34	(35%)	23	(23%)
Observed disability				
5-m walking time in secs[3]	4.9	(4.3, 6.0)	5.0	(4.3, 6.0)
sit time in secs[3]	3.4	(2.9, 4.1)	3.4	(2.9, 4.0)
recline time in secs[3]	6.9	(5.4, 9.0)	6.1	(5.1, 7.9)
guarding (0-1)[2]	0.58	(0.48)	0.53	(0.50)
rigidity (0-1)[2]	0.34	(0.38)	0.33	(0.37)

[1] Missing values: Comorbidity (1 in exercise therapy, 2 in controls). Duration of complaints (2 in exercise therapy, 6 in controls), Radiological OA (7 in exercise therapy, 12 in controls), Previous medical treatment (1 in exercise therapy, 2 in controls)

[2] Mean (sd).

[3] Median (interquartile range: 25th, 75th percentile).

Treatment

Exercise therapy patients visited their GP 1.6 (SD=0.7) times in the 12-week treatment period, control patients 1.8 (SD=0.9). The GP prescribed medication for 54% and 66% of the patients respectively, paracetamol and NSAIDs equally. Ibuprofen 400 mg was the preferred NSAID. For 46% of the exercise therapy patients and 34% of the control patients no medication was prescribed.

In the exercise group the mean number of physical therapy sessions was 16.8 (SD 7.0). Exercise therapy was mainly aimed at improving muscle strength in 93% of all patients, range of motion in 85%, and reduction of pain in 80%. Improvement of

coordination, exercise tolerance and walking were chosen less often: for 59%, 28% and 59% of all patients.

Compliance to home exercises was moderate to good: 66% of the patients reported to exercise often or very often. The physical therapist estimated good compliance (i.e. certainly did home exercises) for 53% of the patients, and moderate compliance (i.e. probably did home exercises) for 33%.

For 13 patients (8 exercise therapy patients and 5 control patients) treatment deviated from the study protocol. For 5 patients exercise therapy was terminated within 6 sessions. Reasons were comorbidity not related to OA (n=4) and the patient's decision to stop after additional medical information (n=1). Two patients receiving exercise therapy were given co-interventions, i.e. physical modalities for pain reduction. To one patient an intervention by a medical specialist was applied (corticosteroid injection). Five patients receiving the control treatment were given physical therapy, including exercise therapy. This decision was twice based on worsening of complaints.

Muscle strength, range of motion and disabilities

In table 2 the effects of treatment are presented for subgroups of patients, on the basis of their muscle strength, ROM and level of disability. The expected beneficial effects of exercise therapy in patients with relatively low muscle strength and restricted ROM at baseline is not confirmed. In general, in these subgroups the effectiveness of exercise therapy is similar. One significant interaction was found between a patient's ROM at baseline and the effectiveness of exercise therapy. However, this finding was contrary to our expectations: beneficial effects of exercise therapy were found in patients with a high ROM at baseline.

In only one out of six tests does the level of disability influence the effectiveness signifcantly. As expected, in patients with a high level of observed disability at baseline a greater benefit of exercise therapy on observed disability was found.

Table 2: Effect of exercise therapy in subgroups: muscle strength, range of motion and disabilities

A. Muscle strength

Muscle strength hip	Low		High		p-value interaction
	ex.th.	control	ex.th.	control	
Pain past week[1]	-24	-9	-21	-4	0.87
Medication use: % taking NSAID's	50	44	32	29	0.89
Observed disability[2]	-0.29	-0.02	-0.11	-0.03	0.32
Muscle strength knee	**Low**		**High**		**p-value interaction**
	ex.th.	control	ex.th.	control	
Pain past week[1]	-26	-6	-20	-6	0.40
Medication use: % taking NSAID's	44	39	41	32	0.80
Observed disability[2]	-0.32	0.02	-0.09	-0.05	0.13

B. Range of motion

ROM hip	Low		High		p-value interaction
	ex.th.	control	ex.th.	control	
Pain past week[1]	-24	-2	-21	-10	0.17
Medication use: % taking NSAID's	50	33	42	30	0.71
Observed disability[2]	-0.31	-0.11	-0.11	0.09	0.99
ROM knee	**Low**		**High**		**p-value interaction**
	ex.th.	control	ex.th.	control	
Pain past week[1]	-21	-14	-24	2	0.02
Medication use: % taking NSAID's	50	43	33	30	0.76
Observed disability[2]	-0.21	0.00	-0.20	-0.04	0.81

[1] Mean change, visual analogue scale (0-100).
[2] Mean change, Z-score (mean=0, SD=1).

Table 2 (continued)

C. Disabilities

Observed disability	High		Low		p-value interaction
	ex.th.	control	ex.th.	control	
Pain past week[1]	-17	-6	-29	-6	0.11
Medication use: % taking NSAID's	41	33	41	40	0.61
Observed disability[2]	0.16	0.18	-0.60	-0.19	0.03
Self-reported disability	**High**		**Low**		**p-value interaction**
	ex.th.	control	ex.th.	control	
Pain past week[1]	-21	-21	-24	-2	0.14
Medication use: % taking NSAID's	31	31	52	44	0.70
Observed disability[2]	-0.10	-0.04	-0.32	-0.06	0.57

[1] Mean change, visual analogue scale (0-100).
[2] Mean change, Z-score (mean=0, SD=1).

Pain coping

In table 3 the effects of exercise therapy are shown for patients with different levels of paincoping. There was no evidence supporting the hypothesis of greater benefit of exercise therapy in patients with high levels of worrying, resting and fear avoidance beliefs concerning physical activity. No significant interactions were found. Furthermore, trends were only partially in accordance with the expectations.

Table 3: Effect of exercise therapy in subgroups: pain coping

Worrying	Low		High		p-value interaction
	ex.th.	control	ex.th.	control	
Pain past week[1]	-19	-10	-26	-2	0.07
Medication use: % taking NSAIDs	44	32	39	42	0.30
Observed disability[2]	-0.36	0.04	-0.11	-0.10	0.06
Resting	**Low**		**High**		**p-value interaction**
	ex.th.	control	ex.th.	control	
Pain past week[1]	-20	-9	-25	-3	0.15
Medication use: % taking NSAIDs	37	29	47	45	0.69
Observed disability[2]	-0.13	0.03	-0.31	-0.08	0.70
Fear avoidance beliefs towards physical activity	**weak**		**strong**		**p-value interaction**
	ex.th.	control	ex.th.	control	
Pain past week[1]	-22	-1	-24	-11	0.31
Medication use: % taking NSAIDs	41	31	42	42	0.49
Observed disability[2]	-0.08	-0.02	-0.29	0.03	0.31

[1] Mean change, visual analogue scale (0-100).
[2] Mean change, Z-score (mean=0, SD=1).

Characteristics of patients

Exploratory analyses were performed to study effect modification by fourteen features for the effectiveness of exercise therapy, including demographic characteristics, clinical features, lifestyle and psychological well-being. A total number of 42 interactions were tested (14 features and 3 outcome measures); three significant interaction terms were found. In patients without radiological evidence of OA, relatively great beneficial effects of exercise therapy were found on pain (p=0.01) and observed disability (p=0.02), compared to patients with radiological OA. In addition, in patients with complaints of recent onset relatively beneficial effect on observed disability was found (p=0.02).

Characteristics of physical therapy treatment

The next step in our analyses was to study post hoc the prognostic value of several characteristics of physical therapy treatment. These analyses concerned treatment goals and patient compliance.

Firstly, the effectiveness of exercise therapy was compared for 1) patients whose treatment was aimed at a specific treatment goal (i.e. alleviation of pain) versus 2) patients whose treatment was not aimed at this specific treatment goal. The prognostic value of six treatment goals was tested; between the two exercise groups no significant differences in effectiveness were found ($p>0.05$).

Secondly, the effectiveness of exercise therapy was compared for patients with different levels of compliance. Both patients and therapists reported about exercise compliance. Using the patient's information, no differences in effectiveness were found between compliers and non-compliers. Using the physical therapist's estimation of compliance, a relatively beneficial effect of exercise therapy is found in compliant patients. The use of NSAIDs was lower in compliers (23% versus 54%, $p=0.00$) and also a stronger reduction in disability level was observed (-0.38 vs -0.06, $p=0.04$). No difference was found for pain.

Next, we also studied possible determinants of compliance: we analysed whether compliers and non-compliers (according to the physical therapist) differed in baseline characteristics and baseline scores on outcome measures. Only two significant differences were found: compliers had a higher paracetamol consumption and a higher muscle strength of the hip.

DISCUSSION

Several randomised clinical trials have shown the effectiveness of exercise therapy for OA patients[8-11,32-36]. However, until now the question whether subgroups of patients could be identified in whom exercise therapy would have relatively beneficial effects, had hardly been addressed. One of the objectives of our trial was to study the prognostic value of baseline characteristics for the effectiveness of exercise therapy in OA patients. We tested two specific hypotheses. Beneficial effects of exercise therapy were expected in patients with a relatively low muscle strength, restricted ROM and high levels of disabilities. In addition, beneficial effects were expected in patients with a relatively high level of an emotional reaction to pain. None of these hypotheses were confirmed. In general, the effectiveness of exercise therapy was similar, regardless of the patient's baseline level of muscle strength, ROM, disabilities and paincoping strategies.

In patients with OA, several impairments and disabilities can be distinguished. Only a subset of these impairments and disabilities are used as a basis for treatment goals. Treatment is primarily aimed at alleviation of these impairments and disabilities[37]. Therefore, the occurrence of low muscle strength, restricted ROM and a high disability level will not necessarily lead to treatment directed at these impairments

and disabilities. Probably, the physical therapist sees possibilities for improvement in selected patients only and therefore directs treatment to these treatment goals in selected patients. Following this argumentation we have performed additional analyses to study whether it makes a difference if the reduction of a specific impairment, for instance muscle strength, is used as a treatment goal or not. We did not find any significant differences in effects of exercise therapy between treatments directed towards a specific treatment goal and treatment not directed towards this specific goal.

One possible explanation for our results is the unequal distribution of treatments over the conditions (treatment goal used or not). Some treatment goals were selected in a large majority of treatments. This applies particularly to the goals 'improvement of muscle strength', 'improvement of ROM' and 'pain reduction'. Therefore, the number of treatments not directed to these goals was small. Because of this small number of treatments in one condition, statistical differences were hardly demonstrable.

Another possible explanation is in the nature of our exercise therapy. Several specific exercise therapy interventions could be applied, such as strengthening, stretching and locomotion training. In this way, treatment could be tailored to the patient's needs. However, this range of interventions possibly hampered our study into the existence of subgroups of patients. Probably, one single, more specific exercise therapy intervention would result in more specific effects of exercise therapy. Especially patients with problems in this specific area could then be expected to particularly benefit from this intervention. For example, the intervention 'strengthening' would result in improvement of muscle strength and might be particularly beneficial to patients with reduced muscle strength.

We also studied the relation between exercise compliance and outcome. Using the patient's information we found no relation between compliance and outcome of exercise therapy. Compliance as estimated by the physical therapist was related to a more beneficial outcome of exercise therapy. These findings must be interpreted with caution since physical therapists' estimations are probably biased by the results of treatment. However, in the study of Ettinger et al[8] also a dose response relationship was reported between compliance and outcome in patients with knee OA. In the Ettinger study, compliance was assessed as presence or absence during prescribed exercise sessions: bias in the assessment of compliance is not likely. Thus, compliance seems to be associated with a beneficial outcome of exercise therapy. A more detailed analysis of these data revealed a relationship between compliance and outcome in aerobic exercises but not in resistance exercises[38].

Next, we examined possible determinants of compliance. We tested for baseline differences between the compliers and non-compliers. Only two minor differences were found (compliers had a higher paracetamol consumption and a higher muscle strength of the hip). Using regression analysis, Rejeski et al[38] also concluded that

compliance could not be predicted with any consistency by demographic, fitness, psychosocial and disability-related characteristics. Prior exercise behaviour seems to be an important determinant of compliance. After completing a first treatment period, prior exercise behavior was found to be the strongest predictor for compliance in following periods[38].

We found no evidence for our second hypothesis, concerning the beneficial effects of exercise therapy in patients with high levels of passive pain coping strategies. This finding can possibly be explained in a way similar to the explanation of the results of our first hypothesis: not the mere existence of these passive pain coping strategies influences the effectiveness of treatment, but whether or not a treatment is directed to adapting these strategies. We did not obtain information on this aspect from the physical therapists. Therefore, further research is necessary to study this suggestion.

Exploratory analyses were performed concerning effect modification by characteristics of the patients. Evidence was found of beneficial effects of exercise therapy in patients without radiological evidence and in patients with complaints of recent onset. Taking the number of tests into account (n=42), these results should be interpreted with caution. However, information on both features is commonly available in clinical practice and therefore of great potential value in making the indication for referral in OA more explicit. Thus, further research into effect modification by radiological evidence of OA and duration of disease is recommended.

In conclusion, only limited evidence was found for the existence of subgroups of OA patients in whom exercise therapy has beneficial effects. Our hypotheses on beneficial outcomes of exercise therapy in patients with low muscle strength, restricted ROM, high levels of disabilities and high levels of passive pain coping strategies could not be confirmed. Given the results of exploratory analyses, further research should focus on radiological evidence of OA and duration of disease, on specific exercise therapy interventions, and on compliance as a determinant of outcome.

REFERENCES

1. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, Moskowitz RW, Schnitzer TJ. Guidelines for the medical management of osteoarthritis. Part I. Osteoarthritis of the hip. Arthritis Rheum 1995;38:1535-1540.
2. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, Moskowitz RW, Schnitzer TJ. Guidelines for the medical management of osteoarthritis. Part II. Osteoarthritis of the knee. Arthritis Rheum 1995;38:1541-1546.
3. Anonymous. Diagnosis and management of osteoarthritis of the hip and knee. J Roy Coll Physicians, London, 1993;27:391-6.

4. Dekker J, Mulder PH, Bijlsma JWJ, Oostendorp RAB. Exercise therapy in patients with rheumatoid arthritis and osteoarthritis: a review. Adv Behav Res Ther 1993;15:211-38.
5. Puett DW, Griffin MR. Published trials of non-medical and non-invasive therapies for hip and knee osteoarthritis. Ann Intern Med 1994;121:133-40.
6. Minor MA. Exercise in the management of osteoarthritis of the knee and hip. Arthr Care Res 1994;7:198-204.
7. Ettinger WH, Afable RF. Physical disability from knee osteoarthritis: the role of exercise as an intervention. Med Sci Sports Exerc 1996;26:1435-40.
8. Ettinger WH, Burns R, Messier SP, Applegate W, Rejeski WJ, Morgan T, Schumaker S, Berry MJ, O'Toole M, Monu J, Craven T. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. JAMA 1997;277:25-31.
9. Börjesson M, Robertson E, Weidenhielm L, Mattson E, Olsson E. Physiotherapy in knee osteoarthrosis: effect on pain and walking. Physiother Res Int 1996;1:89-97.
10. Schilke JM, Johnson GO, Housh TJ, O'Dell JR. Effects of muscle-strength training on the functional status of patients with osteoartritis of the knee. Nursing Research 1996;45:68-72.
11. Baar ME van, Dekker J, Oostendorp RAB, Bijl D, Voorn ThB, Lemmens JAM, Bijlsma JWJ. The effectiveness of exercise therapy in patients with osteoarthritis of knee or hip: a randomised clinical trial (accepted for publication).
12. Dekker J, Boot B, Woude L van der, Bijlsma JWJ. Pain and disability in osteoarthritis; a review of biobehavioral mechanisms. J Behav Med 1992;15:189-214.
13. Keefe FJ, Caldwell DS, Queen K, Gil KM, Martinez S, Crisson JE, Ogden W, Nunley J. Osteoarthritic knee pain: a behavioral analysis. Pain 1987:28;309-321.
14. Baar ME van, Dekker J, Lemmens JAM, Oostendorp RAB, Bijlsma JWJ. Pain and disability in patients with osteoarthritis of hip or knee: the relationship with articular, kinesiological and psychological characteristics. J Rheumatol 1998:25;125-33.
15. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthritis Rheum 1991;34:505-514.
16. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. Arthritis Rheum 1986;29:1039-49.
17. Cohen J. Statistical power analysis for the behavioral sciences. London: Academic press Inc., 1977.
18. Oostendorp RAB, Heuvel JH van den, Dekker J, Baar ME van. Exercise therapy in patients with osteoarthritis of knee or hip: a protocol. Amersfoort/Utrecht the Netherlands: NPi/NIVEL, 1996.
19. Bohannon RW. Muscle strength testing with hand-held dynamometers. In: Admundsen LR, eds. Muscle strength testing: Instrumented and non-instrumented systems. New York: Churchill Livingstone, 1990:69-88.
20. Bohannon RW. Make tests and break tests of elbow flexor muscle strength. Phys Ther 1988;68:931-3.

21. Norkin CC, White DJ. Measurement of joint motion: a guide to goniometry. Philadelphia: FA Davis Company, 1986.
22. Dekker J, Tola P, Aufdemkampe G, Winckers M. Categories of pain behaviour in osteoarthritis patients. Physioth Theory Pract 1993;9:157-63.
23. Keefe FJ. Block AR. Development of an observation method for assessing pain behaviour in chronic low back pain patients. Behav Ther 1982;13:363-75.
24. McDaniel LK, Anderson, KO, Bradley LA, Young AD, Turner RA, Agudelo CA, Keefe FJ. Development of an observation method for assessing pain behavior in rheumatoid arthritis. Pain 1986;24:165-84.
25. Steultjens MPM, Dekker J, van Baar ME Oostendorp RAB, Bijlsma JWJ. Consistency and validity of an observational method for assessing disability in mobility in patients with osteoarthritis (submitted).
26. Huiskes CJAE, Kraaimaat FW, Bijlsma JWJ. Development of a self-report questionnaire to assess the impact of rheumatic diseases on health and lifestyle. J Rehab Sciences 1990; 3:65-70.
27. Kraaimaat FW, Bakker A, Evers AWM. *Pijncoping-strategieën bij chronische pijnpatiënten: De ontwikkeling van de Pijn-Coping-Inventarisatielijst (PCI)*. (Pain coping strategies in chronic pain patients: the development of the Pain Coping Inventory). Gedragstherapie 1997;30:185-201.
28. Waddell G, Newton M, Henderson I, Somerville D, Main CJ. A fear-avoidance beliefs questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability. Pain 1993;52:157-68.
29. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. Arthritis Rheum 1990;33:1601-10.
30. Passmore R, Eastwood MA. Human nutricion and dietetics. Edinburgh: Churchill Livingstone, 1986:270.
31. Caspersen CJ, Bloemberg BPM, Saris WHM, Merrit RK, Kromhout D. The prevalence of selected physical activities and their relation with coronary heart disease risk factors in elderly men: the Zutphen study, 1985. Am J Epid 1991;133:1078-92.
32. Newell DJ. Intention-to-treat-analysis: implications for quantitative and qualitative research. Int J Epid 1992;21:837-41.
33. Kovar PA, Allegrante JP, MacKenzie CR, Peterson MGE, Gutin B, Charlson ME. Supervised fitness walking in patients with osteoarthritis of the knee. Ann Int Med 1992;116:529-34.
34. Jan MH, Lai JS. The effects of physiotherapy on osteoarthritic knees of females. J Formosan Med Assoc 1991;90:1008-13.
35. Minor MA, Hewett JE, Webel RR, Anderson SK, Kay DR. Efficacy of physical conditioning exercise in patients with rheumatoid arthritis and osteoarthritis. Arthr Rheum 1989;32:1396-1405.
36. Chamberlain MA, Care G, Harfield B. Physiotherapy in osteoarthritis of the knees. Int J Rehab Med 1982;4:101-106.

37. Dekker J, Baar ME van, Curfs EChr, Kerssens JJ. Diagnosis and treatment in physical therapy: an investigation of their relationship. Phys Ther 1993;73:568-80.
38. Rejeski WJ, Brawley LR, Ettinger W, Morgan T, Thompson C. Compliance to exercise therapy in older participants with knee osteoarthritis; implications for treating disability. Med Sci Sports Exerc 1997;29:977-85.

5

LONG-TERM EFFECTIVENESS OF EXERCISE THERAPY IN PATIENTS WITH OSTEOARTHRITIS OF HIP OR KNEE

M.E. van Baar, J. Dekker, R.A.B. Oostendorp, D. Bijl, Th.B. Voorn, J.W.J. Bijlsma

Objective - To determine the long-term effectiveness of exercise therapy in patients with osteoarthritis of hip or knee.

Methods - A randomised single blind, clinical trial was conducted in a primary care setting. Patients with osteoarthritis of hip or knee (ACR-criteria) were selected. Two intervention groups were compared. Both groups received treatment from the patients' general practitioner, including patient education and medication if necessary. The experimental group also received exercise therapy from a physiotherapist in primary care. The treatment period was 12 weeks with a 24-week follow-up. The main outcome measures were pain, medication use (non-steroidal anti-inflammatory drugs, NSAIDs) and observed disability.

Results - 201 patients were randomised and 183 patients completed the trial. At 24 weeks exercise therapy was associated with a small to moderate effect on pain past week (difference in change -11.5; 95%CI -19.7, -3.3). At 36 weeks no differences were found between intervention groups.

Conclusion - Beneficial post-treatment effects of exercise therapy decline over time and finally disappear.

Submitted for publication

INTRODUCTION

In recent treatment guidelines for osteoarthritis (OA) of the hip or knee the use of exercise therapy has been advocated[1,2]. These guidelines are in line with ideas about treatment of osteoarthritis of the hip or knee as published earlier[3,4].

Exercise therapy in OA aims at reduction of pain and disability[5]. This is achieved through improvement of muscle strength, stability of joints, range of motion and aerobic fitness. These functions are frequently impaired in patients with OA, presumably contributing to pain and disability[6]. Improving these functions is assumed to result in reduction of pain and disability. In addition, exercise therapy aims directly at reduction of disability, e.g. through correction of the walking pattern[7,8].

The scientific evidence supporting the effectiveness of exercise therapy in patients with OA is still expanding. Several randomised clinical trials have shown beneficial effects of exercise therapy on pain, disability and patient's global assessment[9-15]. In our own clinical trial on OA of the hip or knee we found similar post-treatment effects. Exercise therapy was associated with a reduction on pain and observed disability. No effect of exercise therapy was found on the use of NSAIDs[16].

However, most randomised clinical trials were confined to post-treatment results, ignoring long-term follow-up. Studies into the long-term effects of exercise therapy in patients with OA of the hip or knee are few. In two randomised controlled trials long-term effects were investigated[17,9]. In the first trial, long-term effects were studied of both aerobic and non-aerobic 12-week exercise programmes. Comparison with baseline data showed beneficial effects at nine months after completion of treatment on pain, and on observed and self-reported disability. However, data were presented for a mixed sample of both OA and rheumatoid arthritis patients and no intention-to-treat analysis was performed; therefore, no insight was given into long-term effects in OA patients[17]. The second trial studied the effectiveness of two programmes consisting of a three-month center-based phase followed by a 15-month home based phase[9,10]. Combining data from follow-ups at 3, 9 and 18 months, beneficial effects were reported concerning pain, self-reported disability, observed disability, muscle strength and aerobic capacity. Separate long-term follow-up data were presented for pain, self-reported disability and gait characteristics including walking speed. These data indicate a maximal beneficial effect at 3 months (after completion of the supervised programme) for self-reported disability and pain, and at 9 months for walking speed. Most effects showed a slight decline afterwards, even when the home-based exercise programme was continued. However, the effects of exercise therapy after completion of the exercise programmes were not studied.

In uncontrolled studies too hardly any attention has been paid to the long-term effects of exercise therapy in OA. Fisher et al[18] reported beneficial long-term effects (8

and 12 months) of a 4-month muscle rehabilitation program. Beneficial effects on pain and observed disability (including walking) remained at post-treatment levels, at both 8 and 12 months. Beneficial effects on muscle strength and endurance had declined at 12 months, but remained significantly higher than baseline levels. In a case study, Marks[19] presented effects of quadriceps exercises on muscle strength. After a six-week supervised training period quadriceps torque had improved by 40%, with a 10% reduction after a six week non-training period.

In conclusion, the long-term effects of exercise therapy in OA of the hip or knee have hardly been investigated. Ongoing exercise programmes, as studied by Ettinger et al[9,10] seem associated with prolonged beneficial effects of exercise therapy. However, it remains unclear how long beneficial effects remain after completion of the exercise therapy. Also, it is not clear which factors are associated with a beneficial long-term outcome of exercise therapy.

We here report on the long-term effects of exercise therapy in patients with OA of the hip or knee. The effects of exercise therapy at 12 and 24 weeks after completion of the exercise therapy programme are presented. In addition, the prognostic value of patient characteristics for long-term outcome is analysed in an exploratory analysis. The short-term effects of exercise therapy in our trial have been reported in detail[16] elsewhere.

METHODS

Study population

Patients were selected by GPs in the period May 1994-February 1996. The GPs were situated in 4 cities and surrounding villages in the eastern part of the Netherlands. Inclusion criteria were OA of hip or knee according to the clinical criteria of the American College of Rheumathology[20,21]. Exclusion criteria were: other pathology explaining the complaints; complaints in less than 10 out of 30 days; treatment for these complaints with exercise therapy in the preceding six months; under 40 or over 85 years of age, indication for hip or knee replacement, contraindication for exercise therapy, contraindications for analgesics or NSAIDs, and inability to understand the Dutch language. After having given oral consent, patients were registered and their names forwarded to the research team. Radiographs were obtained and evaluated by one radiologist using grading scales (0-3) for individual radiographic features[22]. All patients were visited and their eligibility was checked by a GP research fellow (DB). All eligible patients were asked to give written informed consent. Afterwards, patients were randomly allocated equally to either exercise therapy or the control group, using sequentially numbered, opaque, sealed envelopes of the appropriate stratum

containing the treatment assigned. Patients were prestratified on their pain in the past week (VAS 0-30 versus 31-100 mm) and location of OA (hip or knee) in order to achieve comparability in these prognostic factors.

We aimed at 200 patients participating in the study, as this number of patients leads to a power of 0.80 to detect small to medium-sized effects with an alpha of 0.05[23].

The study protocol was approved by the ethics committee of the Maastricht University Hospital (Maastricht, the Netherlands).

Interventions

Two interventions were compared. The patients in the exercise therapy group were given exercise therapy individually by a physiotherapist in primary care. In addition, their GP provided patient education (including a brochure), and medication if necessary. Treatment of the control group was restricted to treatment by their GP, as described above (patient education and medication if necessary). The treatment period was 12 weeks plus 24 weeks of follow-up.

Exercise therapy was given according to a written protocol[24] (see Appendix) and included exercises for muscle functions (strength and length), mobility and coordination, and exercises for elementary movement abilities and locomotion abilities. Also, instructions for the adaptation of activities of daily living and home exercises were given. Content and intensity of treatment were described in terms of treatment goals and corresponding exercises. Content, intensity and frequency of treatment were tailored to the patient's needs. Depending on the physiotherapist's diagnostic findings, specific treatment goals with corresponding exercises were chosen. Number of sessions per week was prescribed and ranged between one to three times a week, depending on the pain level. A physiotherapy session in primary care lasted approximately 30 minutes. Exercise therapy could be discontinued within the 12-week period if, according to the physiotherapists, treatment goals had been achieved. Physiotherapists were trained to use the protocol.

A protocol was also used for the prescription of medication. The GP prescribed preferably paracetamol; prescription of NSAIDs was restricted to naproxen, diclophenac natrium and ibuprofen (see appendix chapter 3 for medication schedule). The patient was instructed to use as little medication as possible. The GP also provided patient education, using a brochure; the topics covered in the brochure include diagnosis, prognosis, advices concerning rest, daily activities and diet, the use of aids and medical treatment. GPs were instructed to minimise treatment in the follow-up period. Physiotherapists and GPs recorded detailed information about the actual treatments on standardised forms, including any deviation of the protocol.

Outcome assessment

Primary outcome measures were pain, use of NSAIDs and observed disability. Patients rated their pain in the past week on a visual analogue scale (VAS, 0 mm no pain -100 mm very severe pain). The use of NSAIDs was based on prescription data and counts of remaining medication during evaluation sessions. Observed disability was determined by studying videos of the patients' performance of a series of standardised tasks using an adaptation of the method described by Keefe[25,26]. The tasks included walking, sitting down, bending and reclining. Both movement times and quality of performance were assessed. The interobserver reliability of this method is good[26-28]. A total score was calculated based on 5 measures: 5 m-walking time, stand-to-sit time, stand-to-recline time and the levels of guarding and rigidity during the performance of the tasks. Standardised scores (Z-scores) of separate measurements were first calculated and then added up to obtain an overall score. In order to enhance comparability, the resulting overall score was standardised to render a score with a mean of zero and a standard deviation of one[29]. The internal consistency of the constructed overall score was good (a=0.84)[30].

A set of 13 *secondary outcome measures* were included in the trial. In this article, a subset of these secondary outcome measures is included. This applies to the following outcome measures: use of paracetamol assessed in the same way as the use of NSAIDs; global perceived effect as assessed by the patients themselves on a 8-point scale (1=vastly worsened; 8=completely recovered)[31]; self-reported disability with the IRGL-questionnaire (Influence of Rheumatic disease on General health and Lifestyle)[32]; muscle strength measured with a hand-held dynamometer[33] and joint motion measured with a goniometer[34]. Overall scores were composed for muscle strength of hip and knee and joint range of motion of hip and knee. The procedure was similar to data reduction in observed disability (mean=0, SD=1, see Baar et al[29]).

The following *prognostic* factors were studied:

- demographic characteristics: age and sex;
- clinical features: location of OA (hip yes/no and knee yes/no); OA of the hand according to Altman et al[35](yes/no), radiological OA as measured on grading scales for individual radiographic features (yes/no)(for details see Van Baar et al[29]), obesity (Body Mass Index <30/³30[36]), duration of complaints and comorbidity (yes/no);
- baseline levels of outcome measures: pain past week, medication use (NSAIDs, paracetamol), observed and self-reported disability, muscle strength and range of joint motion, both for hip and knee;
- paincoping strategies (six dimensions) as assessed with the Pain Coping Inventory[37]. In addition, the extent to which patients believe physical activity to affect their pain was assessed using an adaptation for OA-patients of the Fear-Avoidance Beliefs Questionnaire[38];

- lifestyle: level of physical activity according to the Zutphen Physical Activity Questionnaire was studied, excluding sedentary hobbies[39];
- psychological well-being: anxiety, depression and cheerfulness as assessed with the IRGL-questionnaire[32];
- compliance to exercise therapy as reported by both the patient and the physiotherapist. Patients were phoned at week 6 and week 12 and asked whether they managed to do their home exercises as often as prescribed. Possible answers were: (almost) never, sometimes, regularly, often and very often. Physiotherapists were asked to estimate whether the patient complied with the home exercise instructions in the last four weeks of treatment, using a standardised form. Possible answers were: certainly not, probably not, probably and certainly. A patient was considered compliant 1) when the patient reported to exercise (very) often or 2) when the physiotherapist estimated that the patient had certainly exercised at home.

Patients were evaluated by a blinded research assistant at baseline and at 12 weeks (post-treatment), 24 weeks and 36 weeks. The research assistants had been trained to perform the measurements in a standardised manner. The evaluations took place in local health care centres.

Statistical analysis

Analyses were performed according to the intention-to-treat principle[40]. Patient data were analysed in the intervention groups to which they had initially been assigned. This included withdrawals and patients not treated according to the assigned treatment. In addition, a per-protocol analysis was performed excluding patients with deviations from the treatment protocol and late ineligibles.

To analyse the effects, change scores were calculated (follow-up minus baseline). With regard to medication use and global perceived effect, follow-up scores were compared because no change scores could be calculated. The scores on global perceived effect were dichotomised in order to study the number of improved patients. In the analysis, the change (or follow-up) scores were compared between the interventions, by using analysis of covariance (ANCOVA). Adjusted analyses were performed. The baseline level of each outcome measure was included to enhance the precision of the effect estimates. In addition, medication use and fear avoidance beliefs, the measures on which the groups differed at baseline (see Results section), were included as covariates in order to control for baseline differences. Group differences and 95% confidence intervals were calculated for all outcome measures. In addition, effect-sizes were calculated by taking the difference between the change scores of the intervention groups and dividing it by the standard deviation of the change score of the total population. An effect-size of 0.2 is considered a small

beneficial effect of exercise therapy, 0.5 as a medium effect and 0.8 as a large effect[23].

The analysis for studying the prognostic value of patient characteristics for long-term outcome of exercise therapy was restricted to exercise therapy patients. These patients were classified as 1) stable or improved versus 2) deteriorated, based on their results on the primary outcome measures during follow-up (week12-week36). Patients were classified as stable or improved on pain past week or observed disability if their scores in week 36 were equal or lower compared to week 12. Patients were classified as stable or improved on NSAIDs if they did not change medication use (or non-use) or if they had stopped using NSAIDs in the period week12-week36. Chi-square tests and t-test for independent samples were used to test for baseline differences between these two groups.

The analyses were carried out using SPSS/PC+ 5.0.

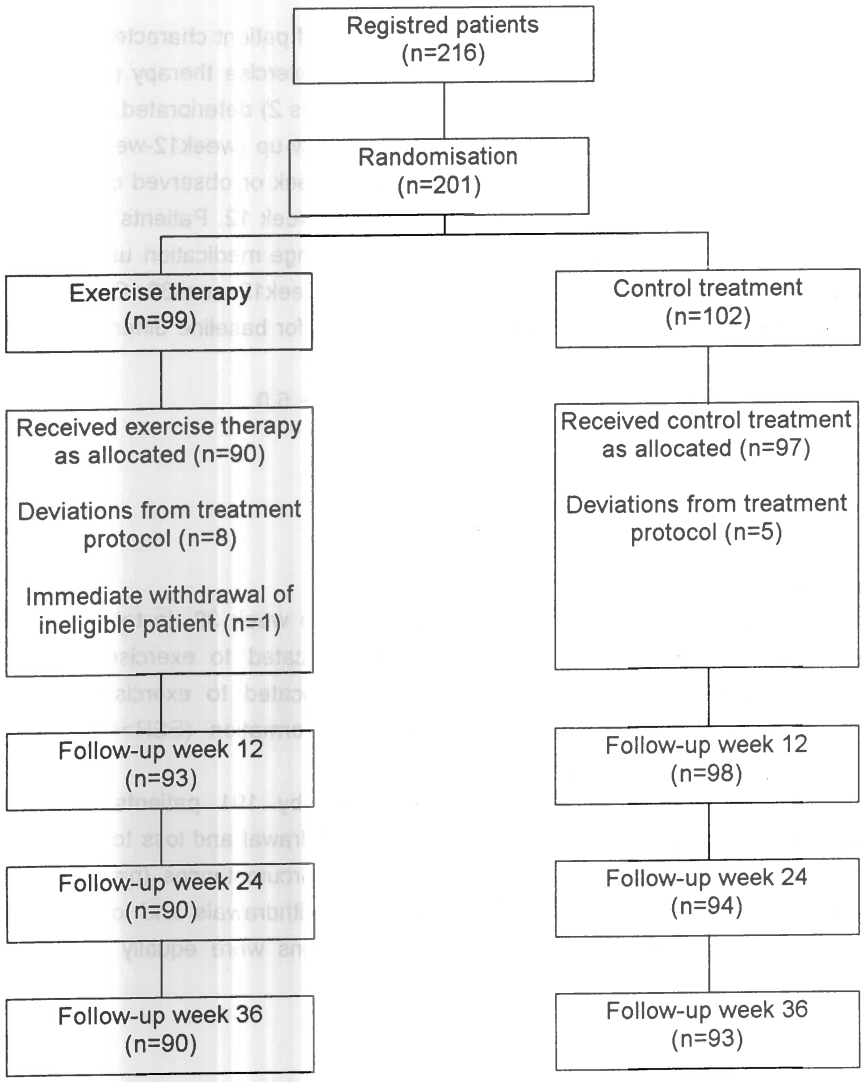
RESULTS

Participant flow

Figure 1 shows the patient flow and follow-up up to week 36. In total 201 patients were included in the study, 99 patients were allocated to exercise therapy, 102 patients to the control treatment. One patient allocated to exercise therapy was excluded on the grounds of additional medical information (ESR>45 mm/1 hour) immediately after randomisation.

The week 12 assessment was completed by 191 patients; 183 patients completed the trial up to 36 weeks. Reasons for withdrawal and loss to follow-up were comorbidity (n=8), loss of motivation (n=6), family circumstances (n=2) and adverse effects of exercise therapy (n=1). The number of withdrawals and loss to follow-up was relatively low. In addition, numbers and reasons were equally divided across intervention groups.

Figure 1: Participant flow and follow-up



The baseline characteristics in the two intervention groups are presented in table 1. Patients were generally similar, with two exceptions. Patients allocated to the exercise therapy group reported a higher use of medication in the 7 days preceding participation in the study and scored higher on fear avoidance beliefs concerning physical activity.

Table 1: Comparability of intervention groups at baseline[1]

	Exercise therapy n=98		Control n=102	
Gender (female)	76	(78%)	81	(79%)
Age in years[2]	68.3	(8.4)	67.7	(9.2)
Comorbidity	63	(64%)	62	(62%)
Location of OA				
knee	58	(59%)	61	(60%)
hip	36	(37%)	35	(34%)
both	4	(4%)	6	(6%)
Duration of complaints				
≤ 0.5 year	34	(35%)	42	(41%)
0.5 ≤ 1 year	13	(13%)	12	(12%)
1 ≤ 5 years	29	(30%)	25	(25%)
> 5 years	22	(22%)	23	(23%)
Radiological OA (score ≥ 1)				
joint space narrowing	62	(69%)	55	(60%)
osteophytes	65	(72%)	65	(71%)
Previous medical treatment	59	(61%)	64	(64%)
Pain past week, (visual analogue scale)(0-100)[2]	46.9	(27.7)	43.1	(26.8)
at assessment[2]	34.0	(27.2)	28.7	(26.0)
Medication use past week (taking)				
paracetamol	51	(52%)	39	(38%)
NSAIDs	34	(35%)	23	(23%)
Observed disability				
5-m walking time in secs[3]	4.9	(4.3, 6.0)	5.0	(4.3, 6.0)
sit time in secs[3]	3.4	(2.9, 4.1)	3.4	(2.9, 4.0)
recline time in secs[3]	6.9	(5.4, 9.0)	6.1	(5.1, 7.9)
guarding (0-1)[2]	0.58	(0.48)	0.53	(0.50)
rigidity (0-1)[2]	0.34	(0.38)	0.33	(0.37)

[1] Missing values: Comorbidity (1 in exercise therapy, 2 in controls). Duration of complaints (2 in exercise therapy, 6 in controls), Radiological OA (7 in exercise therapy, 12 in controls), Previous medical treatment (1 in exercise therapy, 2 in controls)

[2] Mean (sd).

[3] Median (interquartile range: 25th, 75th percentile).

Treatment

Exercise therapy patients visited their GP 1.6 (SD=0.7) times in the 12-week treatment period, control patients 1.8 (SD=0.9). The GP prescribed medication for 54% and 66% of the patients respectively.

In the exercise group the mean number of physical therapy sessions was 16.8 (SD 7.0)(for details, Baar et al.[16]).

Compliance to home exercises was moderate to good: 66% of the patients reported to exercise often or very often. The physical therapist estimated good compliance (i.e. certainly did home exercises) for 53% of the patients, and moderate compliance (i.e. probably did home exercises) for 33%.

Primary outcome measures

Long-term results on the primary outcome measures are presented in table 2. At 24 weeks (12 weeks after completion of treatment), a beneficial effect was found for pain past week. Compared to the post-treatment level (week 12) the effect size had declined to 0.36, indicating a small to moderate effect. No effects were found for NSAIDs and observed disability. At 36 weeks (24 weeks after completing treatment), no differences were found between intervention groups.

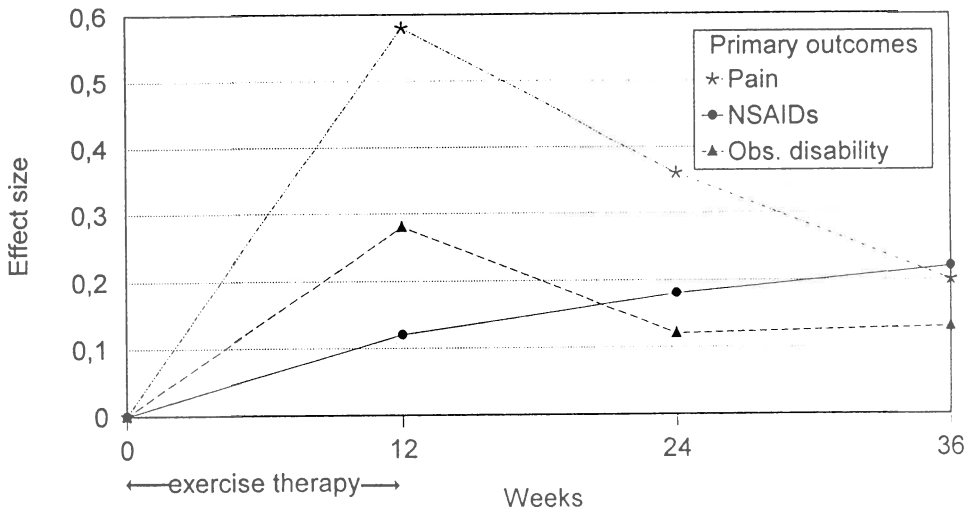
Table 2: Primary outcome measures: improvements and differences between intervention groups[1]

Outcome measure	Exercise therapy		Control		Difference (95%CI)		Effect size
	n	mean change	n	mean change			
Pain past week							
week 12	93	-22.8	98	-5.7	-17.0	(-23.6,-10.4)	0.58
week 24	88	-17.2	91	-5.6	-11.5	(-19.7, -3.3)	0.36
week 36	90	-15.5	92	-8.9	-6.6	(-14.7,1.6)	0.20
Medication use : NSAIDs							
week 12	93	42%	98	36%	6%	(-8%,20%)	0.12
week 24	90	39%	94	48%	-9%	(-22%,4%)	0.18
week 36	90	40%	93	51%	-10%	(-23%,3%)	0.22
Observed disability							
week 12	91	-0.21	98	-0.02	-0.19	(-0.38,-0.01)	0.28
week 24	88	-0.13	91	-0.04	-0.09	(-0.30,0.12)	0.12
week 36	88	-0.16	91	-0.06	-0.10	(-0.31,0.11)	0.13

[1] Analyses are adjusted for baseline differences (fear avoidance beliefs towards physical activity, use of paracetamol, use of NSAIDs) and baseline score on specific outcome parameter.

For the primary outcome measures, an overview of effect sizes over the course of the trial is given in figure 2. Beneficial effects for pain and disability were maximal at week 12, just after completion of treatment. In the follow-up period the size of the effects declined to non-significant levels in week 36, except for the results on the use of NSAIDs, which remained stable during follow-up.

Figure 2: Effect sizes of primary outcome measures in the course of the trial



Secondary outcome measures

Long-term results on the secondary outcome measures are presented in table 3. At 24 weeks, beneficial effects of exercise therapy were found for use of paracetamol and patient's global perceived effect. No effects were found for self-reported disability, muscle strength and ROM. Similar effects were found at week 36. Corresponding to the primary outcome measures, the size of the effects declined in the follow-up period (week 12-36). Again, an exception is found in the use of medication: the effects on the use of paracetamol remained stable during follow-up.

Table 3: Secondary outcome measures: improvements and differences between intervention groups[1]

Outcome measure	Exercise therapy		Control		Difference (95%CI)		Effect size
	n	mean change	n	mean change			
Medication use : paracetamol							
week 12	93	35%	98	51%	-16%	(-29%,-3%)	0.33
week 24	90	39%	94	55%	-17%	(-30%,-3%)	0.32
week 36	90	41%	93	57%	-17%	(-30%,-3%)	0.32
Global perceived effect: improved[2]							
week 12	91	47%	98	18%	28%	(15%,42%)	0.64
week 24	88	49%	91	25%	24%	(10%,38%)	0.50
week 36	90	46%	93	29%	17%	(3%,31%)	0.35
Self-reported disability[3]							
week 12	93	-1.1	98	-0.0	-1.1	(-2.3,0.1)	0.26
week 36	90	-1,2	92	-0,3	-0.8	(-2.2,0.5)	0.18
Muscle strength hip							
week 12	91	0.22	94	0.04	0.17	(0.02,0.33)	0.32
week 24	85	0.16	87	0.13	0.04	(-0.14,0.21)	0.06
week 36	85	0.26	87	0.22	0.04	(-0.12,0.21)	0.08
Muscle strength knee							
week 12	92	0.19	98	0.06	0.13	(-0.04,0.29)	0.22
week 24	88	0.14	91	0.14	0.00	(-0.17,0.17)	0.00
week 36	86	0.19	90	0.19	0.00	(-0.18,0.17)	0.01
Joint range of motion hip							
week 12	92	0.21	98	0.06	0.15	(-0.03,0.32)	0.23
week 24	87	0.36	90	0.27	0.09	(-0.13,0.31)	0.11
week 36	87	0.19	89	0.19	0.00	(-0.21,0.22)	0.01
Joint range of motion knee							
week 12	92	0.17	98	0.09	0.08	(-0.09,0.25)	0.13
week 24	90	0.11	94	0.15	-0.04	(-0.24,0.17)	0.05
week 36	87	0.11	90	0.05	0.05	(-0.15,0.25)	0.10

[1] Analyses are adjusted for baseline differences (fear avoidance beliefs towards physical activity, use of paracetamol, use of NSAIDs) and baseline score on specific outcome parameter.
[2] Results on a 8-point scale are dichotomised as improved (completely recovered, very much improved and much improved) and not-improved (slightly improved, not changed, slightly worsened, much worsened and vastly worsened).
[3] Not assessed at 24 week follow-up.

Outcome in per-protocol analysis

A per-protocol analysis was conducted, excluding all patients who were classified as late ineligibles due to changed medical diagnosis (n=4) or treatment not according to the protocol (n=21). For 13 patients (eight of whom had been allocated to exercise therapy) treatment in the intervention period deviated from the protocol. Treatment in

the follow-up period had to be restricted to a minimum. However, in 8 patients (5 exercise therapy patients and 3 control patients) a medical specialist intervened, by performing a total hip replacement (n=4), a total knee replacement (n=1), an arthroscopy (n=1), a meniscus operation (n=1) or a corticosteroid injection (n=1).

The results of the per-protocol analysis were similar to the results of the intention-to-treat analysis. The effect sizes were somewhat higher, as can be explained by the nature of the analysis. This applies to both primary and secondary outcome measures (data not presented).

Prognostic value of patient characteristics for long-term outcome

Exploratory analyses were performed to study the prognostic value of demographic characteristics, clinical features, kinesiological characteristics, lifestyle, psychological well-being and compliance for the long-term outcome of exercise therapy. It was studied whether differences existed between stable or improved patients versus deteriorated patients during long-term follow-up (week12-36). Patients were classified as stable versus deteriorated, based on their results on two primary outcome measures (pain past week and observed disability). A classification based on NSAIDs did not result in a useful division of patients (see table 4).

Table 4: Long-term effects: results of exercise therapy at 36 weeks, compared to results in week 12 (n=90)

Outcome measure	Stable or improved[1] n	Deteriorated n
Pain past week	46	44
Medication use: NSAIDs	86	4
Observed disability[2]	39	48

[1] Results are dichotomised as stable or improved (reduction or stabilisation of pain, medication use or disability) versus deteriorated (increase of pain or disability, start taking NSAIDs).
[2] Missing values: 3

A number of 62 tests (31 characteristics and 2 outcome measures) were performed to study differences between stable or improved patients versus deteriorated patients. Two significant differences were found: stable or improved patients as regards their observed disability, were relatively often overweight at baseline (BMI $\geq$30) (46% versus 19%, p=0.01), and stable or improved patients as regards their pain, reported lower levels on the paincoping strategy 'transforming of pain' at baseline (8.3 versus 10.4, p=.001).

DISCUSSION

Several randomised clinical trials have shown beneficial effects of exercise therapy in patients with OA immediately after completion of treatment[9-15]. Long-term effects have hardly been investigated. To compensate for this remarkable omission, we have studied the effectiveness of exercise therapy in patients with OA at 12 and 24 weeks after completion of treatment. Our results indicate a slow decline of the beneficial effects of exercise therapy, ending in similarity of clinical status between exercise therapy and control patients.

Our results are in line with the few earlier studies on this topic, in the sense that all studies reported some decline in the post-treatment effects[9,10,17-19]. However, in earlier work the decline seems less pronounced both in controlled trials[9,10,17] and in one uncontrolled study[18].

Several explanations apply. The trial of Minor[17] lacked an intention-to-treat analysis. This probably resulted in an overestimation of treatment effects[40]. In the FAST-trial[9,10] treatment continued, albeit in a home based setting, until the last assessment. Therefore, no 'non-training' effect could be studied. In the uncontrolled study[18], 4 out of 15 patients dropped out during the intervention. There the remaining patients were probably a select and highly motivated group of patients, resulting in beneficial and sustaining effects.

Our results are in line with a study into the effects of stopping exercise programs in healthy older adults[41]. The beneficial effects on cardiovascular capacity and muscle strength after a 16-week cardiovascular or resistance exercise programme decreased after a 10-week non-training period.

Exploratory analyses were performed concerning the prognostic value of patient characteristics for long-term outcome. A beneficial long-term outcome was found in patients with overweight at baseline and in patients with a relatively low level of the specific pain coping strategy (transformation of pain). However, given the high number of performed tests (n=62), it is entirely possible that these results are due to chance.

We did not find a relation between treatment compliance and beneficial long-term outcome. However, we did not have data on long-term compliance, i.e. on compliance after completion of the exercise therapy treatment. Therefore, we have no insight into the highly relevant relation between long-term compliance and long-term outcome. In future trials long-term compliance should be studied.

The clinical implications of our results for the application of exercise therapy in OA patients are clear. The evidence available clearly indicates the usefulness of exercise therapy in patients with OA of the hip or knee[9-16]. Small to moderate beneficial effects can be generated on pain and disability, the main symptoms of OA. However, the effects slowly declining indicates that measures must be taken to

maintain beneficial effects of exercise therapy. One measure is to introduce some form of retraining or prolonged training. Both intermittent exercise therapy treatment and follow-up booster sessions can be applied. There are some indications for optimal content and adequate timing of exercise therapy. In the FAST-trial the relation between compliance and outcome was studied[42]. The most beneficial outcome was found in OA patients doing aerobic exercises three days a week for approximately 35 minutes each session. Patients spending more time exercising during a session had outcomes similar to non-exercising patients. These results are based on a secondary analysis of the dose-response relation between compliance and outcome. However, to our knowledge no clinical studies on this topic are available as yet.

Another measure is to maximise the patient's compliance to exercise therapy, even after having completed a supervised programme. An important component of an exercise therapy programme should be to facilitate acceptance and practice of exercises. Sluijs et al[43] distinguished short-term and long-term compliance and, subsequently, different approaches to be applied by health care providers. To improve long-term compliance, a self-regulation approach seems useful. In future trials, explicit attention should be paid to improvement of both short-term and long-term compliance.

In conclusion, exercise therapy is effective in patients with OA of the knee or hip. However, these effects decline over time and finally disappear. Future research should focus on finding ways of optimally maintaining beneficial effects over time. Important issues are optimal content and timing of therapy and compliance of the patient with exercise therapy.

REFERENCES

1. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, Moskowitz RW, Schnitzer TJ. Guidelines for the medical management of osteoarthritis. Part I. Osteoarthritis of the hip. Arthritis Rheum 1995;38:1535-1540.
2. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, Moskowitz RW, Schnitzer TJ. Guidelines for the medical management of osteoarthritis. Part II. Osteoarthritis of the knee. Arthritis Rheum 1995;38:1541-1546.
3. Dieppe P. Management of hip osteoarthritis. BMJ 1995;311:853-6.
4. Liang MH, Fortin P. Management of osteoarthritis of the hip and knee (editorial). N Eng J Med 1991;325:125-7.
5. Dieppe P. The classification and diagnosis of osteoarthritis. In: Kuettner KE, Goldberg VM. Osteoarthritic disorders. Rosemont IL: American Academy of Orthopaedic Surgeons, 1995: 5-12.
6. Dekker J, Boot B, Woude LHV van der, Bijlsma JWJ. Pain and disability in osteoarthritis: a review of biobehavioral mechanisms. J Behav Med 1992;15:189-214.

7. Minor MA. Exercise in the management of osteoarthritis of the knee or hip. Arthritis Care Res 1994;7:198-204.
8. Dekker J, Mulder PH, Bijlsma JWJ, Oostendorp RAB. Exercise therapy in patients with rheumatoid arthritis and osteoarthritis: a review. Adv Behav Res Ther 1993;15:211-38.
9. Ettinger WH, Burns R, Messier SP, Applegate W, Rejeski WJ, Morgan T, Shumaker S, Berry MJ, O'Toole M, Monu J, Craven T. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. JAMA 1997;277:25-31.
10. Messier SP, Thompson CD, Ettinger WH. Effects of long-term aerobic or weight training regimens on gait in an older, osteoarthritic population. J Appl Biomech 1997;13:205-25.
11. Börjesson M, Robertson E, Weidenhielm L, Mattson E, Olsson E. Physiotherapy in knee osteoarthrosis: effect on pain and walking. Physiother Res Int 1996;1:89-97.
12. Kovar PA, Allegrante JP, MacKenzie CR, Peterson MGE, Gutin B, Charlson ME. Supervised fitness walking in patients with osteoarthritis of the knee. Ann Intern Med 1992;116:529-34.
13. Peterson MGE, Kovar-Toledano PA, Otis JC, Allegrante JP, Mackenzie CR, Gutin B, Kroll MA. Effect of a walking program on gait characteristics in patients with osteoarthritis. Arthritis Care Res 1993;6:11-6.
14. Schilke JM, Johnson GO, Housh TJ, O'Dell JR. Effects of muscle-strength training on the functional status of patients with osteoarthritis of the knee. Nurs Res 1996;45:68-72.
15. Jan MH, Lai JS. The effects of physiotherapy on osteoarthritic knees of females. J Formosan Med Assoc 1991;90:1008-13.
16. Baar ME van, Dekker J, Oostendorp RAB, Bijl D, Voorn ThB, Lemmens JAM, Bijlsma JWJ. The effectiveness of exercise therapy in patients with osteoarthritis of hip or knee: a randomised clinical trial. J Rheumatol (accepted for publication).
17. Minor MA, Hewett JE, Webel RR, Anderson SK, Kay DR. Efficacy of physical conditioning exercise in patients with rheumatoid arthritis and osteoarthritis. Arthritis Rheum 1989;32: 1396-1405.
18. Fisher NM, Pendergast DR, Gresham GE, Calkins E. Muscle rehabilitation: its effects on muscular and functional performance of patients with knee osteoarthritis. Arch Phys Med Rehab 1991;72:367-74.
19. Marks R. Quadriceps exercises for osteoarthritis of the knee. A single case study comparing short-term versus long-term training effects. Physiother 1994;80:195-9.
20. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. Arthritis Rheum 1986;29:1039-49.
21. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthritis Rheum 1991;34:505-514.
22. Altman RD, Fries JF, Bloch DA, Carstens J, Cooke TD, Genant H et al. Radiographic assessment of progression in osteoarthritis. Arthritis Rheum 1987;30:1214-25.
23. Cohen J. Statistical power analysis for the behavioral sciences. London: Academic press Inc., 1977.

24. Oostendorp RAB, Heuvel JH van den, Dekker J, Baar ME van. Exercise therapy in patients with osteoarthritis of knee or hip: a protocol. Amersfoort/Utrecht the Netherlands: NPI/NIVEL, 1998.
25. Keefe FJ, Caldwell DS, Queen K, Gil KM, Martinez S, Crisson JE, Ogden W, Nunley J. Osteoarthritic knee pain: a behavioral analysis. Pain 1987;28:309-21.
26. Dekker J, Tola P, Aufdemkampe G, Winckers M. Categories of pain behaviour in osteoarthritis patients. Physioth Theory Pract 1993;9:157-63.
27. Keefe FJ. Block AR. Development of an observation method for assessing pain behaviour in chronic low back pain patients. Behav Ther 1982;13:363-75.
28. McDaniel LK, Anderson, KO, Bradley LA, Young AD, Turner RA, Agudelo CA, Keefe FJ. Development of an observation method for assessing pain behavior in rheumatoid arthritis. Pain 1986;24:165-84.
29. Baar ME van, Dekker J, Lemmens JAM, Oostendorp RAB, Bijlsma JWJ. Pain and disability in patients with osteoarthritis of hip or knee: the relationship with articular, kinesiological and psychological characteristics. J Rheumatol 1998;25:125-33.
30. Steultjens MPM, Dekker J, Baar ME van, Oostendorp RAB, Bijlsma JWJ. Consistency and validity of an observational method for assessing disability in mobility in patients with osteoarthritis (submitted).
31. Heijden GJMG van der. Shoulder disorder treatment. Efficacy of ultrasoundtherapy and electrotherapy. Maastricht the Netherlands: University Press Maastricht, 1996.
32. Huiskes CJAE, Kraaimaat FW, Bijlsma JWJ. Development of a self-report questionnaire to assess the impact of rheumatic diseases on health and lifestyle. J Rehab Sciences 1990; 3:65-70.
33. Bohannon RW. Muscle strength testing with hand-held dynamometers. In: Admundsen LR, eds. Muscle strength testing: Instrumented and non-instrumented systems. New York: Churchill Livingstone, 1990:69-88.
34. Norkin CC, White DJ. Measurement of joint motion: a guide to goniometry. Philadelphia: FA Davis Company, 1986.
35. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. Arthritis Rheum 1990;33:1601-10.
36. Passmore R, Eastwood MA. Human nutrition and dietetics. Edinburgh: Churchill Livingstone, 1986:270.
37. Kraaimaat FW, Bakker A, Evers AWM. *Pijncoping-strategieën bij chronische pijnpatiënten: De ontwikkeling van de Pijn-Coping-Inventarisatielijst (PCI)*. (Pain coping strategies in chronic pain patients: the development of the Pain Coping Inventory). Gedragstherapie 1997;30:185-201.
38. Waddell G, Newton M, Henderson I, Somerville D, Main CJ. A fear-avoidance beliefs questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability. Pain 1993;52:157-68.
39. Caspersen CJ, Bloemberg BPM, Saris WHM, Merritt RK, Kromhout D. The prevalence of selected physical activities and their relation with coronary heart disease risk factors in elderly men: the Zutphen study, 1985. Am J Epid 1991;133:1078-92.

40. Newell DJ. Intention-to-treat analysis: implications for quantitative and qualitative research. Int J Epid 1992;21:837-41.
41. Sforzo GA, McManis BG, Black D, Luniewski D, Scriber KC. Resilience to exercise detraining in healthy older aldults. JAGS 1995;43:209-15.
42. Rejeski WJ, Brawley LR, Ettinger W, Morgan T, Thompson C. Compliance to exercise therapy in older participants with knee osteoarthritis: implications for treating disability. Med Sci Sports Exerc 1997;29:977-85.
43. Sluijs EM, Knibbe JJ. Patient compliance with exercises: different theoretical approaches to short-term and long-term compliance. Patient Educ Couns 1991;17:191-204.

6

COST-EFFECTIVENESS OF EXERCISE THERAPY IN PATIENTS WITH OSTEOARTHRITIS OF HIP OR KNEE

Th.J.G. Weijnen, M.E. van Baar, J. Dekker, J.W.J. Bijlsma, R.A.B. Oostendorp, Th.B. Voorn, F.Th. de Charro

Objective - To determine the costs associated with exercise therapy in patients with osteoarthritis (OA) of hip or knee, to determine the outcome of exercise therapy using generic measures and to study the consequences for the costs at societal level of increased referral for exercise therapy.

Methods - A randomised single blind, pragmatic clinical trial, comparing exercise therapy with GP treatment. The treatment period was 12 weeks with a 24-week follow-up.

Results - Total costs per patient in the exercise therapy group were Dfl.1823 and in the control group Dfl. 1442. Exercise therapy had an effect on the pain and energy dimensions of the Nottingham Health Profile at the end of the treatment period. A 10 % increase in referrals to a physiotherapist would result in a 0.5% increase in societal costs of treatment in patients with OA.

Conclusion - The costs per patient of treatment with exercise therapy are modest. Exercise therapy is effective in reducing pain and increasing energy. An increased number of referrals for exercise therapy would result in a modest increase in societal costs.

Submitted for publication.

INTRODUCTION

Osteoarthritis (OA) of the hip or knee is a relatively common musculoskeletal disorder. The incidence in general practice in the Netherlands is 2.1/1000 per year for OA of the hip and 3.6/1000 per year for OA of the knee. Prevalence increases with age[1]. OA is characterised by degeneration of cartilage and formation of new bone at the margins of the joints. The main symptoms of OA are pain and disability, for example disability in walking and in sitting down. Treatment of OA is aimed at pain relief and minimising disability.

Several randomised clinical trials[2-4], including our own study[5], have shown that exercise therapy indeed reduces pain and disability in patients with OA. As far as we are aware, the costs and cost-effectiveness of exercise therapy have not been studied. Treatment with exercise therapy in itself costs a certain amount of money, but these costs, however, are not known. Furthermore, because exercise therapy is effective in reducing pain and disability, it could contribute to a reduction in costs in other health care sectors (e.g. costs of medicine consumption, costs of medical-specialist aid). This potential cost reduction has also not been studied. Thus our first goal was to determine comprehensively the costs associated with exercise therapy in patients with OA of the hip or knee.

In order to enable a comparison of the cost-effectiveness of different health care provisions, effectiveness should be measured with generic (non-disease specific) measures. By using generic measures, the cost-effectiveness of exercise therapy in OA-patients can be compared not only with other treatments of OA, but also with different health care interventions. Thus our second goal was to determine the outcome of exercise therapy in patients with OA of the hip or knee, using generic measures.

Finally, if the positive effect of exercise therapy becomes widely known, this could lead to an increased referral rate. At societal level, this could be associated with either an increase or a decrease in the costs of treatment of OA-patients. Thus, our third goal was to study the consequences of an increase in the number of patients referred for exercise therapy for the costs at societal level.

METHODS

Design

In this study two interventions were compared. The exercise therapy group received exercise therapy given by a physiotherapist in primary care. In addition, the patient's GP gave information about OA (including a brochure) and medication (if necessary).

Treatment of the control group was restricted to information about OA and medication (if necessary). The patients were treated during a period of 12 weeks and were subsequently followed up during a period of 24 weeks.

Supervised individual exercise therapy was given according to a written protocol[6]. This exercise therapy included exercises for muscle functions (strength and length), mobility and coordination, and exercises for elementary movement abilities and locomotion abilities. Also, instructions for the adaptation of activities of daily living and home exercises were given. Content, intensity and frequency of treatment were tailored to the patient's needs. Number of sessions per week was prescribed and ranged between one to three times a week, depending on the pain level. The design of the trial has been described in detail elsewhere[6].

Patients

Patients were selected by GP's over the period May 1994 - February 1996. Inclusion criteria were OA of hip or knee, according to the clinical criteria of the American College of Rheumatology[7,8]. Exclusion criteria were: other pathology explaining the complaints; complaints in less than 10 out of 30 days; treatment with exercise therapy in the last six months; age younger than 40 years or older than 85 years; indication for hip or knee replacement; contraindication for exercise therapy; contraindication for analgesics or NSAID's; difficulties in understanding the Dutch language and no informed consent.

Costs

In the cost calculation, all cost to society were included. Not only were treatment costs within the health care sector included, but also costs related to the treatment of OA outside the health care sector. The latter consisted of costs borne by patients and costs related to absence at work due to OA[9].

The two most important categories of costs within the health care sector are the cost of treatment by the GP and the physiotherapist. Other costs within the health care sector are: costs of other exercise therapies (i.e. exercise therapy according to Cesar and exercise therapy according to Mensendieck); cost of medicine consumption; the OA-related costs of medical-specialist aid; the OA-related cost of hospitalisation; cost of home care and cost of district nursing.

Costs outside the health care sector are costs covered by the patients themselves and costs of production losses caused by OA-related absenteeism or disablement. In order to calculate the costs of production losses, the friction costs method was applied[9]. The principle of this method is that production losses are limited to a period needed to fulfil the vacancy in the production process. This period is assumed to be 2.5 months. Cost of production losses is the value of the hours the

patient could not work in a professional way due to OA. In this study the average age was 68.0 (68.3 in the exercise therapy group and 67.7 in the control group). Patients older than 65 years do not normally participate in the production process. We therefore found only a few patients who were active in the production process and consequently costs of production losses related to OA were not high.

The valuation of the volume of resources used was based on 1995 prices. In theory, costs to society should be valued according to market prices which reflect full competition. In practice these prices were not available. So reimbursement was used as a proxy for costs to society. There may be differences between the theoretical market prices and the reimbursement rates, but these differences would have an equal impact in the experimental and control group.

In the Netherlands, patients can be insured via Sick Funds or the private health insurance system. Where there were differences between reimbursement rates from the Sick Funds and private health insurance, a weighted average was calculated. The weight was the ratio between Sick Fund patients and patients insured by private health insurance.

Drug prices were derived from a list produced by the medical insurance board[10]. Calculations have been made to account for the margins for the pharmacist and VAT, which were not included in the list. Patients themselves reported their costs. Costs of production losses were valued by applying an hourly rate representing the average contribution of an employee to net domestic product[9].

Effectiveness

To measure health outcome the Nottingham Health Profile[11,12], the EuroQol-5D[13,14] and the Karnofsky Performance Index[15,16] were applied.

Only the first part of the Nottingham Health Profile (NHP) was used, consisting of 38 dichotomous items, grouped in 6 scales: energy, pain, emotion, sleep, social isolation and mobility. Each scale ranges from 0 to 100, where 0 represents the state "no complaints". A rise on the scale implies an increase in the level of complaints and so a deterioration of the patient's health-state.

The Karnofsky Performance Index questionnaire consists of 10 descriptions of present health-state. If a patient is able to live a normal life and has no complaints or illnesses, the Karnofsky Index is 1.0; the worst health-state receives a valuation of 0.1. The Karnofsky Performance Index is averaged using the arithmetic mean of the individual scores.

The EQ-5D instrument consists of a health state descriptive system and a visual analogue scale; the thermometer. The descriptive system classifies health states according to 5 dimensions of health: mobility, self-care, usual activities, pain/dis-

comfort and anxiety/depression. Within each dimension three levels are distinguished: (1) no problems, (2) some problems and (3) extreme problems.
The thermometer of the EQ-5D instrument is a vertical line, anchored at 0 as the worst imaginable health-state and at 100 as the best imaginable state. Patients are asked to value their quality of life on this thermometer. The EQ-5D health states have been assessed by valuation research in different countries[14].

A health index was determined by valuing the health states from the EQ-5D descriptive system. The valuation of a health state can be derived from the scores of the patients themselves or from values of a reference population. In our study a value set was applied from a reference population consisting of Dutch students[17]. These students were asked to assess on the thermometer all possible 243 health-states of the EQ-5D instrument. A model was constructed to estimate a value set on the basis of the assessment of the 243 health states. The EQ-5D index, which results from applying this value set, reaches a maximum value of 69.70 for full health. This occurs when respondents classify themselves as having no problems on all the five dimensions of the EQ-5D. Conversely for a health state with extreme problems on all the five dimensions the resulting index is 6.30.

A cost-effectiveness ratio was calculated, which indicates the cost per percentage point improvement on the health index. This implies the rescaling of the EQ-5D-index. Full health is set at 100 % and the health state with extreme problems on all the 5 dimensions at 0 %.

Statistical analysis

The analysis was performed according tot the intention to treat principle. All patients and their follow-up results were analysed according to the intervention groups initially assigned. This included patients not treated according to the assigned treatment.

To analyse the effects on the generic effect measures, change scores were calculated (follow-up scores minus baseline scores). An ANCOVA-procedure was conducted with a correction for baseline differences in the composition of the treatment groups. These baseline differences concern medication use (use of NSAID's and use of paracetamol) and 'fear avoidance beliefs towards physical activity'. Also, the baseline value of each generic effect measure was included to improve the precision of the effect estimates (see Baar et al[5] for further details).

Tests for significant differences between the exercise therapy group and the control group ($p \leq 0.05$) were conducted using SPSS for Windows, version 6.1.3. The 'independent samples T test' and the 'Mann-Whitney test' for the EQ-5D scores were applied to test for significant differences. Effect sizes were calculated[18]. An effect-size of 0.2 was regarded as small, an effect-size of 0.5 as medium and 0.8 as large.

Societal costs

We studied the consequences that a 10 % increased number of referrals by the GP to the physiotherapist would have on the costs to society. Information was available on three months prevalence of OA in a GP's practice[19] and the associated percentages of GP referrals to the physiotherapist[20]. Prevalence per year is maximally 4 times the quarterly prevalence. If a disease has a chronic nature with a low incidence and a high prevalence, the quarterly prevalence equals the yearly prevalence[19]. We assumed that for OA of hip and knee, the ratio between the yearly and quarterly prevalence was a factor between 2 and 3. Therefore two alternatives were explored: In the first alternative the quarterly prevalence was converted to yearly prevalence by applying a factor of two. This was the lowest estimate of the yearly prevalence. In the second alternative a conversion factor of three was applied. This resulted in the highest estimate of the yearly prevalence. From this estimated yearly prevalence in a GP's practice were derived yearly referrals to the physiotherapist.

Annual societal costs were calculated as follows. Costs of treatment by the GP were calculated by multiplying the yearly number of patients not referred to the physiotherapist by the average costs per patient of treatment in the control group. Costs of treatment by the physiotherapists were calculated by multiplying the yearly number of referrals to the physiotherapist by the average costs per patient in the exercise therapy group.

RESULTS

Participant flow

201 patients gave informed consent. They were randomly assigned either to the exercise therapy group (n=99) or to the control group (n=102). Immediately after randomisation one patient was withdrawn because of ineligibility due to additional medical information and was excluded from analysis. 3 Patients in the exercise therapy group and 5 patients in the control group were not treated according to the protocol.

During the treatment period of 12 weeks, 5 patients in the exercise therapy group and 4 in the control group dropped out. Information on these patients was not used in the analysis of the costs and effects. As a result the calculation about the treatment period was conducted using 93 patients in the exercise therapy group and 98 patients in the control group. In the follow-up period 3 patients dropped out from the exercise therapy group and 5 patients from the control group. This means that the analysis in regard to the follow-up period was conducted using 90 patients in the exercise therapy group and 93 patients in the control group.

Costs

In table 1 costs of treatment are presented for the exercise therapy group and the control group. After 12 weeks the costs of the exercise therapy group were Dfl. 367 higher than the costs of the control group. This difference reflects the cost of physiotherapy. However the higher costs of physiotherapy were partly compensated for by the lower costs of home care, district service and loss of production in the exercise therapy group.

Table 1: Average costs per patient in de period week 1 -12, week 13 - 36 en total

Average costs (Dfl.)*	Week 1 – 12		Week 13 - 36		Total week 1 - 36	
	Exercise therapy	Control	Exercise therapy	Control	Exercise therapy	Control
GP	50	59	32	31	82	90
Physiotherapist (exercise therapy)	502	19	138	135	640	154
Medical specialist aid and hospitalisation	11	13	648	384	659	397
Other exercise therapy	0	0	0	8	0	8
Medication	34	36	46	48	80	84
Community nursing	4	0	9	0	13	0
Home care	74	109	164	278	238	387
Patient costs	24	31	87	88	111	119
Production losses	0	65	0	138	0	203
Total average costs per patient	**699**	**332**	**1124**	**1110**	**1823**	**1442**
Difference exercise therapy – control	**367**		**14**		**381**	

* US $ 1 = Dfl. 1.72: January 1995.

Total average costs in the follow-up period (week 13-36) were approximately the same for the two groups. After 36 weeks costs in the exercise therapy group were still higher (Dfl. 381) than in the control group due to the higher costs for physiotherapy, medical specialist aid and hospitalisation. These higher costs are partly mitigated by lower costs for home care and production losses. A few patients, equally distributed over the intervention groups, cause the costs for hospitalisation in the follow-up period. 5 Patients in the exercise therapy group and 4 patients in the control group were hospitalised in this period.

Effectiveness

Table 2 presents the adjusted improvements in week 12 compared to week 0. This table also presents the differences in improvement between the exercise therapy group and the control group.

The differences on the energy and pain dimensions of the NHP were significant at 5%. The effect size of the energy dimension was 0.27 and can be considered small. The effect size on the dimension pain was 0.40, which is a medium size effect.

Table 2: Adjusted improvements and differences between treatment groups in week 12[1]

Outcome measure	Exercise therapy n = 93	Control n = 98	Difference (95% CI) exercise therapy-control	p-value	effect-size[3]
Nottingham Health Profile[2]					
Emotional reactions	0.0	-1.3	1.3 (-2.4, 5.0)	0.48	0.11
Energy	-9.2	-1.5	-7.7 (-14.9, -0.6)	0.03	0.27
Mobility	-3.7	-1.0	-2.7 (-6.6, 1.2)	0.17	0.19
Pain	-13.9	-3.4	-10.5 (-17.4, -3.6)	0.00	0.40
Sleep	-3.8	-1.6	-2.2 (-8.1, 3.7)	0.46	0.10
Social isolation	0.6	-0.1	0.7 (-2.9, 4.3)	0.70	0.06
EQ-5D					
EQ-5D thermometer[4]	1.6	-1.1	2.7 (-0.7, 6.1)	0.12	0.21
EQ-5D index[5]	2.5	1.4	1.1 (-0.7, 3.0)	0.24	0.16
Karnofsky Performance Index	0.03	0.01	0.02 (-0.01, 0.05)	0.12	0.20

[1] Adjusted for baseline differences (fear avoidance beliefs towards physical activity, use of paracetamol, use of NSAID's) and baseline scores on the specific outcome measure. Missing: EQ-5D thermometer (1 in control group); EQ-5D index (1 in exercise therapy group).
[2] On a scale of 1 to 100; 0: optimal level; 100: worst level.
[3] 0.2: small effect; 0.5: medium size effect; 0.8: large effect.
[4] On a scale of 0 to 100; 0: worst imaginable state; 100: best imaginable state.
[5] On a scale of 6.3 to 69.7; 6.3: most negative possibility; 69.7: most positive possibility.

Table 3 presents the adjusted improvements in the scores at week 36 in comparison to week 0. The differences in improvement are also included in table 3. For the NHP-scores, only the difference on the energy dimension was significant, with a small effect of 0.29. The effect on the pain dimension, found in week 12, disappeared in week 36. In week 36 the difference for the adjusted EQ-5D thermometer was significant with a small effect of 0.31.

Table 3: Adjusted improvements and differences between treatment groups in week 36[1]

Outcome measure	Exercise therapy n = 90	Control n = 93	Difference (95% CI) exercise therapy-control		p-value	effect-size[3]
Nottingham Health Profile[2]						
Emotional reactions	-0.2	-1.4	1.2	(-2.7, 5.0)	0.55	0.09
Energy	-8.3	1.1	-9.4	(-17.5, -1.3)	0.02	0.29
Mobility	-2.4	-4.0	1.6	(-3.2, 6.5)	0.51	0.10
Pain	-14.9	-10.8	-4.1	(-11.8, 3.5)	0.29	0.15
Sleep	-2.4	-1.7	-0.7	(-8.0, 6.6)	0.85	0.03
Social isolation	-2.08	-1.8	-0.2	(-3.3, 2.8)	0.89	0.02
EQ-5D						
EQ-5D thermometer[4]	-0.4	-4.9	4.5	(0.6, 8.4)	0.02	0.31
EQ-5D index[5]	2.8	1.9	0.9	(-1.4, 3.1)	0.46	0.11
Karnofsky Performance Index	0.02	-0.01	0.03	(-0.00, 0.06)	0.06	0.26

[1] Adjusted for baseline differences (fear avoidance beliefs towards physical activity, use of paracetamol, use of NSAID's) and baseline scores on the specific outcome measure. Missing: NHP (2 in control group); EQ-5D thermometer (1 in exercise therapy group, 2 in control group); EQ-5D index (2 in control group).
[2] On a scale of 1 to 100; 0: optimal level; 100: worst level.
[3] 0.2: small effect; 0.5: medium size effect; 0.8: large effect.
[4] On a scale of 0 to 100; 0: worst imaginable state; 100: best imaginable state.
[5] On a scale of 6.3 to 69.7; 6.3: most negative possibility; 69.7: most positive possibility.

Cost-effectiveness ratio

In table 4 the cost-effectiveness ratios are presented for the exercise therapy group and the control group after week 36. This cost-effectiveness ratio is the cost per percentage point improvement on the EQ-5D-Index. The cost-effectiveness ratio for exercise therapy was Dfl. 414 and the cost-effectiveness ratio in the control group was Dfl. 481. Although the average cost per patient for exercise therapy was higher, these cost-effectiveness ratios indicate that exercise therapy was more cost-effective than the treatment in the control group.

Table 4: Cost-effectiveness ratio after 36 weeks

	Improvement on EQ-5D index	Percentage improvement on EQ-5D-index	Total costs per patient after 36 weeks (Dfl.*)	Cost-effectiveness ratio
Exercise therapy	2.8	4.4	1823	414
Control	1.9	3.0	1442	481

* US $ 1 = Dfl. 1,72: January 1995.

Increased number of referrals

The prevalence per annum at national level of OA of the hip and OA of the knee in a GP's practice was estimated at a minimum of 136 347 patients and a maximum of 204 521patients. The distance between the lower and the higher level is due to the two ratio's used to transform the quarterly prevalence into annual prevalence (see method section). In order to estimate the number of patients referred for exercise therapy, the percentages of referrals to the physiotherapist in a GP's practice were used. This number of patients was estimated as between 26 280 and 39 420 patients a year. With a 10 % rise of referrals the number of referrals for exercise therapy would rise by 2 628 at the lower level and 3 942 at the higher level. Table 5 shows the consequences of this increase of the number of referrals for national costs. These consequences are expressed in terms of changes compared to the base-scenario. The base-scenario describes the national costs of treatment in patients with OA by GP's and by physiotherapists with exercise therapy for the estimated total number of patients with OA in GP's practice in the Netherlands.

At the lower level the total national costs would rise by Dfl. 1 001 000. Compared to the base scenario, the increase of the national costs will be 0,5 %. At the higher level the total national costs rise by Dfl. 1 502 000. Compared to the national expenditure on physiotherapy, the total national costs increase by 0.1% at the lower level and increase by 0.2% at the higher level.

Table 5: Consequences of a 10 % increase of the referrals to physiotherapy for the number of patients and the costs

	Lower bound	Higher bound
Rise of number of referrals to physiotherapy	2.628	3.942
Changes in societal costs	Changes compared to base scenario x Dfl. 1000*	
Costs within the health care sector		
GP	-21	-32
Physiotherapy (exercise therapy)	1 277	1 916
Medical specialist aid and hospitalisation	688	1 033
Other exercise therapy	-21	-32
Medication	-11	-16
Community nursing	34	51
Home care	-391	-587
Total costs within the health care sector	1 555	2 333
Costs outside the health care sector		
Patient costs	-21	-31
Production losses	-533	-800
Total national costs	**1 001**	**1 502**
% change compared to base scenario	*0.5%*	*0.5%*
Total national costs of physiotherapy in OA of hip and knee compared to the national expenditure on physiotherapy % change	*0.1%*	*0.2%*

* US $ 1 = Dfl. 1.72: January 1995.

DISCUSSION

Average costs to society per patient in the exercise therapy group are Dfl. 1823 ($ 1060) and in the control group Dfl. 1442 ($ 838) after 36 weeks. Exercise therapy is on balance Dfl. 381 ($ 222) more expensive. This difference mainly reflects the higher costs of physiotherapy treatment (exercise therapy). However, the costs in the exercise therapy group are relatively small when compared to the costs per patient of total hip replacement of $ 10 258 to $ 11 912[21].

The NHP shows that patients in the exercise therapy group have less pain and more energy. The effect on pain is medium sized and the effect on energy is small. However the reduction in pain is temporary. This effect disappeared after week 36.

These results from the generic Nottingham Health Profile measure correspond to the results from the disease specific measures. Here an effect was also found on pain and disability after 12 weeks, which disappeared after 36 weeks[5].

Recently data on the cost-effectiveness of hip (THA) and knee (TKA) replacements in patients with primary osteoarthritis have been published[21]. In this study the NHP has been applied together with a 15-dimensional measure from which a health related quality of life index (HRQoL-index) was derived (the 15-D). Here, the postoperative improvements after 24 months according to the NHP and the HRQol-index were very marked compared to the improvements after 36 weeks due to exercise therapy. On the pain dimension of the NHP the researchers found improvements between the preoperative and 24 month follow up scores of 44 to 48 points for THA. In our study we found an improvement of 15 points after 36 weeks in the exercise therapy group. On the HRQoL-index for THA an improvement of 6 to 9 points was found on a scale of 0 to 100. We found in the exercise therapy group an improvement of 3 points on a scale of 6.3 to 69.7. In the control group we found an improvement of 2 points. If we transform our HRQoL-index to a scale between 0 and 100, this means an improvement of 4 points for exercise therapy and 3 points for the control group. For the THA and TKA cost-effectiveness ratios were published. These ratios reflect the costs per point improvement on the health index after 24 months. For THA a c/e-ratio of $ 1 330 to $ 1 693 was calculated, and for TKA the c/e-ratio was $ 1 400 to $ 3 777. For the exercise therapy group a c/e-ratio could be calculated after 36 weeks. This c/e-ratio was $ 241 (Dfl. 414). The c/e-ratio after 36 weeks for the control group was $ 279 (Dfl. 481). The c/e-ratios of THA and TKA cannot be compared directly with the c/e-ratio of exercise therapy because exercise therapy is not a long term solution. Due the chronic nature of OA, it can be assumed that exercise therapy will have to be repeated. This will affect the costs, but not the effectiveness. This means that exercise therapy can be repeated 5 to 7 times before the c/e-ratio of exercise therapy reaches the level of the c/e-ratio of THA.

Societal costs were estimated on the basis of the cost per patient. At the lower level of the estimates, a 10 % higher referral rate from the GP to the physiotherapist causes a rise in societal costs per year of Dfl 1 001 000. At the higher level, 10 % higher referrals will result in a rise in societal costs of Dfl. 1 502 000 per year. Compared to the base scenario the increase in societal costs will be 0.5 %. The increased referral of 10 % increases the national expenditure on physiotherapy by 0.1% to 0.2 %.

We may conclude that extra costs per patient of exercise therapy are small. Although exercise therapy is effective in reducing pain and increasing energy, the size of these effects is medium to small. The effect on pain disappears after 36 weeks.

Societal costs rise as a result of increased referrals. However the rise in total societal costs can be viewed as modest.

REFERENCES

1. Miedema H. *Reuma-onderzoek meerdere echelons (Rome): basisrapport.* (Rheumatism-research on different levels of the health care system: basis report). Leiden the Netherlands: NIPG-TNO, 1994.
2. Ettinger WH, Burns R, Messier SP, Applegate W, Rejeski WJ, Morgan T, Shumaker S, Berry MJ, O'Toole M, Monu J, Craven T. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. JAMA 1997;277:25-31.
3. Kovar PA, Allegrante JP, MacKenzie R, Peterson MGE, Gutin B, Charlson ME. Supervised fitness walking in patients with osteoarthritis of the knee. Ann Intern Med 1992;116:529-34.
4. Jan MH, Lai JS. The effects of physiotherapy on osteoarthritic knees of females. J Formosan Med Assoc 1991;90:1008-13.
5. Baar ME van, Dekker J, Oostendorp RAB, Bijl D, Voorn ThB, Lemmens JAM, Bijlsma JWJ. The effectiveness of exercise therapy in patients with osteoarthritis of hip or knee: a randomised clinical trial. J. Rheumatol. (accepted for publication).
6. Oostendorp RAB, Heuvel JH van den, Dekker J, Baar ME van. Exercise therapy in osteoarthritis of the hip or knee: a protocol. Amersfoort/Utrecht the Netherlands: NPI/NIVEL, 1998.
7. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. Arthr Rheum 1986;29:1039-49.
8. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthr Rheum 1991;34:505-14.
9. Rutten FFH, Ineveld BM van, Ommen R van, Hout BA. van, Huijsman R. *Kostenberekening bij gezondheidszorgonderzoek, richtlijnen voor de praktijk. Rapport opgesteld in opdracht van de Stuurgroep Toekomstscenario's Gezondheidszorg.* (Cost calculations in health care research, guidelines for practice). Utrecht the Netherlands: Jan van Arkel, 1993.
10. Ziekenfondsraad. *Farmaco-therapeutisch Kompas* (Farmaco-therapeutic Compass). Amstelveen the Netherlands: Centrale Medisch Pharmaceutische Commissie van de Ziekenfondsraad, 1995.
11. Hunt SM, McEwen J, McKenna SP. Measuring health status. London: Croom Helm, 1986.
12. Erdman RAM, Passchier J, Kooijman M, Stronks DL. The Dutch version of the Nottingham Health Profile: investigation of psychometric aspects. Psychological Reports 1993;72:1027-35.
13. The EuroQol Group. A new facility for the measurement of health-related quality of live. Health Policy 1990;16:199-208

14. Brooks R with the EuroQol Group. EuroQol: The current state of play. Health Policy 1996;37:53-72
15. Hutchinson TA, Boyd NF, Feinstein AR, et al. Scientific problems in clinical scales, as demonstrated in the Karnofsky index of performance status. J Chron Dis 1979;32:661-6.
16. Grieco A, Long CJ. Investigation of the Karnofsky performance status as a measure of quality of life. Health Psychol 1984;3:129-42.
17. Busschbach JJ van, McDonnel J, Hout BA van. Testing different parametric relations between the Euroqol health description and health valuation in students. Proceedings of the EuroQol meeting. October 17-19 1996 in Oslo. Oslo Norway: National Institute of Public health, 1997.
18. Cohen J. Statistical power analysis for the behavioral sciences. London: Academic press Inc., 1977.
19. Velden J van der, Bakker DH de, Claessens AAMC, Schellevis FG. *Een Nationale Studie naar Ziekten en Verrichtingen in de Huisartspraktijk. Basisrapport: Morbiditeit in de huisartspraktijk.* (Dutch National Survey of General Practice: Morbidity in general practice). Utrecht the Netherlands: NIVEL, 1991.
20. Groenewegen PP, Bakker DH de, Velden J van der. *Een Nationale Studie naar Ziekten en Verrichtingen in de Huisartspraktijk. Basisrapport: Verrichtingen in de huisartspraktijk.* (Dutch National Survey of General Practice: interventions in general practice). Utrecht the Netherlands: NIVEL, 1992.
21. Rissanen P, Aro S, Sintonen H, Asikainen K, Slätis P, Paavolainen P. Costs and cost-effectiveness in hip and knee replacements. A prospective study. Int J Technol Assess Health Care 1997;13:575-88.

7

EXERCISE THERAPY IS EFFECTIVE IN PATIENTS WITH OSTEOARTHRITIS OF HIP OR KNEE: A SYSTEMATIC REVIEW OF RANDOMISED CLINICAL TRIALS

M.E. van Baar, W.J.J. Assendelft, J. Dekker, R.A.B. Oostendorp, J.W.J. Bijlsma

Objective - To review the effectiveness of exercise therapy in patients with osteoarthritis (OA) of the hip or knee

Methods - A computerised literature search of MEDLINE, Embase and Cinahl was carried out. Randomised clinical trials on exercise therapy in OA of the hip or knee were selected if (i) treatment had been randomly allocated and (ii) if pain, self-reported disability, observed disability or patient's global assessment of effect had been used as outcome measures. The validity of trials was systematically assessed by independent reviewers. Effect sizes and power estimates were calculated. A best evidence synthesis was conducted, weighting the studies with respect to their validity and power.

Results - Six of the 11 assessed trials satisfied at least 50% of the validity criteria. Two trials had sufficient power to detect medium sized effects. Effect sizes indicated small to moderate beneficial effects of exercise therapy on pain, small beneficial effects on both disability outcome measures and moderate to great beneficial effects according to the patients global assessment of effect.

Conclusions - There is evidence of beneficial effects of exercise therapy in patients with OA of the hip or knee.

INTRODUCTION

Osteoarthritis(OA) is a relatively common musculoskeletal disorder. The incidence in general practice in the Netherlands is 2.1/1000 per year for OA of the hip and 3.6/1000 per year for OA of the knee. Prevalence increases with age[1]. In recent treatment guidelines for OA of the hip and knee both non-pharmacological and pharmacological approaches are advocated[2,3]. Exercise therapy is considered to be an important non-pharmacological modality.

The goal of exercise therapy in OA patients is to reduce pain and disability. In order to achieve this, exercise therapy aims at the improvement of muscle strength, stability of joints, range of motion and aerobic fitness. These functions are frequently impaired in patients with OA, presumably contributing to pain and disability[4]. Improving these functions is assumed to result in a reduction of pain and disability. In addition, exercise therapy aims directly at reduction of disability, e.g. through corrections of the walking pattern[5].

Since the publication of the treatment guidelines mentioned above, several new randomised clinical trials (RCTs) on exercise therapy in OA patients have been published[6-10]. These newly published RCTs have not been included in previous reviews either[5,11-17]. Furthermore, the methodology for reviews of the literature has evolved considerably[18-20]. Current methodology requires several explicit and systematic steps to be made in reviews of the literature: a systematic search of the literature[21], selection of studies based on explicit inclusion and exclusion criteria[22], assessment of methodological quality[23], and a systematic approach towards data extraction and data analysis[24]. Neither the treatment guidelines nor the previously published reviews satisfy the current methodological requirements for literature reviews. So, considerable improvement can be made by summarising the evidence available on exercise therapy in OA of the hip or knee by (i) including newly published RCTs and (ii) applying presently required review methodology.

Our objective is to determine the effectiveness of exercise therapy in patients with OA of the knee or hip, based on a systematic review of the evidence from RCTs. We will focus on the effects on pain, self-reported disability, observed disability and patient's global assessment of effect. These outcome measures are recommended for RCTs in patients with OA of the hip and knee[25].

METHODS

Literature search

A comprehensive computer aided search of Medline (1/1966-9/1997), Embase (1/1988-9/1997) and Cinahl (1/1982-9/1997) databases was carried out. A highly sensitive search strategy for RCTs was used[26], in combination with specific keywords and free textwords for OA and exercise therapy. Keywords and free textwords used for OA were osteoarthr*, coxarthr*, gonarthr*, hip and knee. Keywords and free textwords used for exercise therapy were: exercise, exercise therapy, hydrotherapy, walking, kinesiotherapy, physical therapy and physiotherapy. The Cochrane Controlled Trial Register[27] was searched also. In Medline, an additional search for systematic reviews was carried out[28]. Finally, a computer aided search was carried out in a local library specialised in literature on allied health professions. References of relevant review articles and trials were screened. The search was conducted by one reviewer (WJJA).

Criteria for studies considered for inclusion

Trial reports that met the following criteria were eligible:

1) The trial concerned patients with OA of knee or hip. Either clinical or radiological criteria (or a combination) for OA were considered up to standard.
2) Treatment had been allocated using a random procedure[29].
3) At least one of the treatments had included exercise therapy. Exercise therapy was defined as a range of activities intended to improve strength, range of motion, endurance, balance, co-ordination, posture, motor function or motor development. Exercise therapy can be performed actively, passively or against resistance[30]. No restrictions were made as to type of supervision and group size. Additional interventions were allowed.
4) At least one of the following outcome measures had been included: pain, self-reported disability, observed disability and patient's global assessment of effect.
5) Results had been published as a full report.

Trials reports were excluded if 1) they concerned peri-operative exercise therapy or 2) intervention groups received identical exercise therapy and therefore no contrast existed between the intervention groups. No restrictions were made concerning the language of publication[31].

Assessment of methodological quality

A list of specific criteria for the methodological quality assessment was used, consisting of internal validity criteria, descriptive criteria and statistical criteria (see table 1). The internal validity criteria refer to requirements for design and conduct of intervention research. The descriptive and statistical criteria refer to the external

validity of a study. This list of criteria is a modified version of a list that has already been used in a number of systematic reviews, also in the field of physical therapy[20,23] and includes all criteria of Schultz et al[29], Jadad et al[32] and Verhagen et al[33]. For this review, the operationalisation was adjusted for application to OA and exercise therapy.

Table 1: Criteria for the methodological assessment of randomised clinical trials (for details see Appendix I)

A Validity criteria	
V1	Randomisation: adequate procedure for generation of a random number list
V2	Randomisation: concealed random allocation of treatments, by an independent person not responsible for determining eligibility of patients.
V3	Co-interventions: control for co-interventions in design
V4	Co-interventions: reported for each group
V5	Adherence to interventions: >70% in index group, and in placebo-controlled trials also in reference groups
V6	Care provider blinded
V7	Patient blinded
V8	Outcome assessment blinded
V9	Relevant outcome measures: at least two of the following outcome measures: pain, disability and patient global assessment
V10	Withdrawals and drop-outs: ≤20% for short term follow-up and ≤ 30% for long-term follow-up and no substantial bias (inequality between groups; reason for withdrawal/drop-out)
V11	Identical timing of outcome assessment for all intervention groups
V12	Intention-to-treat analysis
B Descriptive criteria	
D1	Specification of eligibility criteria, including explicit classification criteria for OA. Both an established set of criteria (i.e. of American College of Rheumatology) and clinical criteria including symptoms are up to standard.
D2	Baseline similarity regarding age, radiological OA, duration of disease, location of OA and baseline main outcome measure(s)
D3	Description of interventions: adequate description of type, modality, application technique, intensity, duration and number or frequency of sessions for both the index intervention and reference groups.
D4	Adverse effects described and attributed to allocated treatment, or explicit report of 'no adverse effects'
D5	Short term follow-up: outcome assessment at the end of the intervention period
D6	Long-term follow-up: outcome assessment ≥ 6 months after randomisation
C Statistical criteria	
S1	Sample size: to be presented at randomisation and for most important outcome assessments
S2	Presentation of point estimates and distribution measures, for each important outcome measure separately

* Operationalisation of criteria: see Appendix I.

The information from the study reports about each criterion was analysed. If sufficient information was given, the design and conduct of the study were assessed. If bias was unlikely, the criterion was rated positive. If bias was likely, the criterion was rated negative. In case information was lacking or insufficient, the criterion was rated inconclusive (don't know). A total score for internal validity was calculated by summing up the number of positive criteria. Equal weights were applied, resulting in an internal validity score with a range of 0 to 12.

The methodological quality of the study reports was assessed by two reviewers independently (MvB) and (WJJA). One trial, written by one of the reviewers (MvB), was assessed by the other initial reviewer (WJJA) and a third reviewer (DAWM van der Windt). In case of disagreement a consensus method was used to discuss and solve the disagreement between the reviewers. When disagreement persisted a fourth reviewer (JD) was available to arbitrate.

Data extraction and presentation

Quantitative data were extracted by one reviewer (MvB). Effect sizes and their variances were computed[34]. For differences in continuous outcome measurements Hedges *g* was computed, for differences in proportions Cohen's *h* was computed. Computation of Hedges *g* required group means and standard deviations. In the absence of these data, effect sizes were calculated from z-scores and sample sizes[34]. If possible, effect-sizes were based on change scores (post-treatment minus pre-treatment). In the absence of change scores, post-treatment scores were used. Effect sizes were interpreted as described by Cohen[35]: an effect size of 0.2 is considered a small beneficial effect of exercise therapy, 0.5 as a medium effect and 0.8 as a large effect.

Power estimates were made, to study whether trials could detect an existing difference between interventions[35]. The power was based on the mean group size of a study in combination with two hypothetical levels of effect-sizes for exercise therapy in OA which we considered clinically relevant, namely effect-sizes of 0.2 and 0.5. Power was calculated for a t-test for the difference between the means of two independent samples of equal size and equal variance. A two-tailed t-test was assumed with a significance level of 0.05[35].

Best evidence synthesis

Studies were weighted as to 1) their validity and 2) power level. Studies which satisfied at least 50% (=6 criteria) of the validity criteria were classified as studies with "acceptable validity", versus studies with "low validity". In addition, studies with a "sufficient power" of at least 0.80 (based on an effect size of 0.5) were distinguished from studies with a lower power. A power of 0.80 is generally considered sufficient to

detect medium significant differences between interventions[35]. Conclusions will be based on studies with both acceptable validity and sufficient power. Other studies were considered to be of minor importance.

RESULTS

Selection of the studies

We initially identified 19 publications concerning 17 trials that met our inclusion criteria. Seven studies were excluded from the review: four studies concerned peri-operative exercise therapy[36-39] and three studies did not have a contrast for exercise therapy between the intervention groups[40-42].

Consequently, twelve publications concerning 10 trials were included in our systematic review[6-10,43-49]. The information was combined for two trials which were reported twice[9/47,45,46]. In addition, one paper accepted for publication was included[50].

Assessment of methodological quality

There was initial disagreement between the two independent reviewers on 42 (21%) of the 10x20= 200 items scored. Disagreement mainly concerned the following criteria: (V3) control for co-interventions in trial design, (D2) baseline similarity, (D3) adequate description of interventions and (V12) intention-to-treat analysis. Nearly all disagreements were due to reading errors or a difference in interpretation of the methodological criteria. After the consensus meeting no disagreement persisted.

Table 2 presents for each trial the validity criteria for which bias was considered likely. Also the validity criteria are presented for which incomplete information hampered the methodological assessment. The criteria concerning the informativeness of the study (e.g. description and statistics) for which information is lacking or incomplete are presented as well.

The trials are listed in hierarchical order, according to their validity scores. Equally ranked trials are ordered alphabetically.

Table 2: Methodological assessment of trials of exercise therapy for osteoarthritis of knee or hip, ranked in order of validity score (for explanation of items see table 1)

First author (reference)	Validity score*	Bias considered likely	Incomplete information for validity assessment	Incomplete information for description and data extraction	
Van Baar[50]	9	V6,7	V2	D6	
Ettinger[9,47]	8	V3,4,6,7		D2,4	
Callaghan[8]	7	V4,6,7	V2,5	D1,4,6	S2
Borjesson[7]	6	V6,7	V2,4,5,8	D4,6	
Minor[48]	6	V3,6,7,12	V2,8	D2,4,6	S1
Sylvester[49]	6	V4,5,6,7	V2,3	D1,3,4,6	
Kovar[45,46]	5	V4,6,7,8	V2,3,12	D3,6	
Schilke[10]	5	V3,4,6,7	V2,5,8	D1,2,3,4,6	
Bautch[6]	4	V4,6,7	V2,3,5,8,12	D2,4,6	
Chamberlain[43]	4	V4,6,7,10,12	V2,3,5	D2,6	S2
Jan[44]	0	V1,2,4,6,7,9,11	V3,5,8,10,12	D1,3,4,6	S1

* Validity score: sum of all items with bias unlikely; each item given equal weight (range 0-12).

Validity criteria

None of the trials satisfied all validity criteria. Six trials satisfied at least 6 out of 12 validity criteria (50% of the criteria)[7-9,48-50]. One trial did not satisfy any of the validity criteria[44].

As a consequence of the nature of exercise therapy, neither care providers nor patients can be blinded for exercise therapy. Thus, the criteria (V6) blinding of care providers and (V7) blinding of patients were not met in any of the trials studied. Most prevalent shortcomings concerned co-interventions: the design of 3 trials did not control for co-interventions (V3) and in 8 trials there was no report of co-interventions for each group (V4). In two trials bias was likely due to the absence of an intention-to-treat analysis (V12).

Many trials lacked sufficient information on several validity criteria. Methodological assessment was hampered most often by incomplete information about concealment of treatment allocation (V2), the level of compliance (V5), control for co-interventions in the design (V3) and blinding of outcome assessment (V8).

Informativeness of the study

Information on adverse effects of exercise therapy (D4) and long-term outcome assessment (D6, ≥ 6 months) was often missing in trial reports. In two trial reports long-term follow-up was mentioned but no results were presented[48,50]. Other frequent deficiencies were in reporting on specification of eligibility criteria (D1) and description of the interventions (D3).

Sample size and power

The sample size of the trials varied widely (table 3). Five trials compared groups of less than 25 patients, two trials compared 100 or more patients. The median group size was 34. In table 3 power calculations are presented for each study. Two studies[9,50] were designed with sufficient power (≥0.80) to detect medium sized effects (effect-size=0.5). These studies were both of acceptable validity (≥50% criteria positive). Two studies[44,45] were designed with a nearly sufficient power to detect medium sized effects (0.67 and 0.71 respectively); these latter studies had a low validity score.

Table 3: Power calculations* for all included trials

First author (reference)	Validity score	Mean number of patients per group	Power with effect size =0.2	Power with effect size=0.5
Baar[50]	9	100	0.29	0.94
Ettinger[9,47]	8	146	0.40	0.99
Callaghan[8]	7	9	0.07	0.16
Borjesson[7]	6	34	0.13	0.53
Minor[48]	6	38	0.14	0.57
Sylvester[49]	6	7	0.07	0.14
Kovar[45,46]	5	51	0.17	0.71
Schilke[10]	5	10	0.07	0.18
Bautch[6]	4	17	0.09	0.29
Chamberlain[43]	4	21	0.10	0.35
Jan[44]	0	47	0.16	0.67

* Based on a *t* test for differences between the means of two independent samples of equal size and equal variances (Cohen[35]); a power ≥0.80 is generally considered sufficient.

Effectiveness of exercise therapy: comparison with placebo treatment or no treatment

The majority of the trials included in this review were designed to study the differences between exercise therapy and placebo treatment or no treatment. The design and results of 8 trials[6-10,45,50] are presented in table 4. One of these trials also aimed to study differences between different exercise therapy interventions[8] (also see table 6).

Table 4: Characteristics of included studies: comparison of exercise therapy with placebo treatment or no treatment

First author(s) (reference)	Participants; setting of recruitment	Interventions (number of randomised patients)
van Baar[50] Validity score: 9 Power‡: 0.94	OA hip and knee, clinical criteria ACR; Primary care: general practitioner	Standardised co-intervention: patient education and medication if necessary by general practitioner (mean number visits 1.7) I: Supervised individual therapy: strengthening and ROM exercises, functional training and instructions for activities of daily living, 1-3 times a week, 12 weeks (mean number of sessions 16.8) (99) R: None (102)
Ettinger[7] Messier[47] Validity score: 8 Power‡: 0.99	OA knee: pain, radiographic evidence (osteophytes), functional limitations; Community: advertisements, mailing, recruitment through physicians	I1: Supervised group therapy: aerobic exercise (walking) at 50-70% max. heart rate; 1 hour, 3 times a week, 12 weeks; followed by home-based walking program, 3 times a week, 15 months including supervision: 4 home visits and ± 28 telephone calls (144) I2: Supervised group therapy: resistance exercises, gradually increasing weights (upper and lower extremities) 1 hour, 3 times a week, 12 weeks; followed by home based program, 3 times a week, 15 months; supervision, see above (146) R: Supervised group therapy: patient education (OA including exercise, social interaction), 90 min, once a month, 12 weeks; followed by ± 18 structured telephone interviews, (arthritis, general health status and medication) in 15 months (149)
Callaghan[8] Validity score: 7 Power‡: 0.16	OA knee: radiographic evidence + symptoms, both not specified, on waiting list physiotherapy; Hospital: orthopaedic clinics	I1: Supervised individual therapy: non-weight-bearing strengthening exercises, 20 min, twice a week, 4 weeks (8) I2: Individual therapy: 1 session patient education, 1 tuition home exercises followed by weightbearing strengthening exercises at home, twice daily, 4 wks (10) R: Supervised sham electrical stimulation, 20 min, twice a week, 4 weeks; group vs individual unclear (9)
Börjesson[7] Validity score: 6 Power‡: 0.53	OA knee: medial OA, grade I-III according to Ahlback + symptoms (not specified), scheduled for surgery; Outpatient department	I: Supervised group therapy: dynamic and isometric strengthening knee/leg and ROM exercises knee, 40 minutes, 3 times a week, 5 weeks; home exercises, 40 min, twice a week, 5 weeks (34) R: None (34)

Reported results: intention-to-treat*	Our conclusions†
Pain (0-100 scale, mean change) at 12 weeks I: -22.8 R: -5.7 Self-reported disability: IRGL (range -28, -7: mean change) at 12 weeks I: -1.1 R: 0.0 Observed disability: Keefe (including 5-m walking time, mean change) at 12 weeks I: -0.21 R: -0.02 Patient's global assessment of effect (number of patients much improved or completely recovered) at 12 weeks I: 44 R: 18	Significant differences in pain (ES=0.6), observed disability (ES=0.3), global improvement (ES=0.6) in favour of exercise therapy; no difference in self-reported disability (ES=0.3)
Pain (6 items, 1-6 scale, mean±SD) average score at 3, 9 and 18 months I1: 2.14±0.60 I2: 2.21±0.72 R: 2.40±0.61, Self-reported disability: physical disability score: (23 items, 5 point scale, mean ±SD) average score at 3, 9 and 18 months I1: 1.72±0.48 I2: 1.74±0.48 R: 1.9±0.48 Observed disability: 6-min walking distance (feet, mean±SD) average score at 3, 9 and 18 months I1: 1507±192 I2: 1406±205 R: 1349 ±195; time to climb and descend stairs (sec, mean±SD) I1: 12.7±4.8 I2: 13.2±4.8 R: 13.9±4.8; time to lift and carry 10 pounds (sec, mean±SD) I1: 9.1±2.4 I2: 9.3±2.4 R: 10.0±1.2; time to get in and out of a car (sec, mean±SD) I1: 8.7±3.6 I2: 9.0±3.6 R: 10.6±3.6	Significant differences in pain (ES_{I1-R}=0.5, ES_{I2-R}=0.3), self-reported disability (ES_{I1-R}=0.4, ES_{I2-R}=0.4), observed disability (walking, ES_{I1-R} =0.9, ES_{I2-R} =0.3) in favour of exercise therapy groups
Pain (0-10 scale, median % change (negative score = reduction)) at 4 weeks I1:,18% I2:-21%, R:0% Observed disability: 50-m walking test (sec, median % change) at 4 weeks I1:-4% I2: -6% R: 2%	No significant differences in pain and observed disability. Insufficient data presentation for calculation of effect sizes
Pain (11 point scale, mean ±SD) at baseline I: 3.4±2.0 R: 3.3±1.4 at 12 weeks I: 3.0±1.5 R: 3.3±1.5 Observed disability: walking speed (m/sec, mean±SD) at baseline I: 1.01±0.17 R: 1.09±0.20; at 12 weeks I: 1.09±0.17 R: 1.11±0.18; ability to step down (number of patients improved) I: 12 R: 4 Patient's global assessment of effect (number of patients improved) at 12 weeks I: 20 R: 1	Significant differences in global improvement (ES=1.4) in favour of exercise therapy; no differences in pain (ES=0.2), walking speed (ES=-0.1)

First author(s) (reference)	Participants; setting of recruitment	Interventions (number of randomised patients)
Kovar[45] Peterson[46] Validity score: 5 Power‡: 0.71	OA knee, 'documented diagnosis' (not specified), ≥4 months pain during weightbearing activities, radiographic evidence of specific features (joint space narrowing, marginal spurs, subchondral cysts), use NSAID's ≥ 2 days a week; Patients referred to hospital, outpatients clinics, known arthritis patients in community based sites	I: Supervised group therapy: fitness walking (≤30min), light stretching and strengthening exercises; co-intervention: patient education (OA, walking, barriers, benefits); 90 min, 3 times a week, 8 weeks (52) R: Weekly telephone call discussing activities of daily living, once a week, 8 weeks (50)
Schilke[10] Validity score: 5 Power‡: 0.18	OA knee, not specified; Hospital: rheumatology clinic	I: Supervised individual therapy: isokinetic strength training on isokinetic dynamometer, gradually increasing; 3 times a week, 8 weeks (10) R: No treatment (10)
Bautch[6] Validity score: 4 Power‡: 0.29	OA knee, clinical and radiological criteria ACR; Primary care, hospital: rheumatology and orthopaedic clinics and advertisement	Standardised co-intervention: patient education (health, exercise and arthritis), 1 hour, once a week, 12 weeks I: Supervised group(?) therapy: individualised, low intensity walking program (50% maximal oxygen consumption), including principles of joint protection + ROM exercises and strengthening quadriceps, 3 times a week, 12 weeks (17) R: No treatment (besides standardised co-intervention) (17)
Jan[44] Validity score: 0 Power‡: 0.67	OA knee, not specified; Hospital physiotherapy department	Standardised co-intervention: Supervised individual ultrasound therapy with continuous wave, 10 min or short wave therapy 20 min, dosage?, randomly assigned, ≥4 times a week I: Individual, home based dynamic strengthening exercise (straight leg raising), ≥200 times daily (45 knees) R: No treatment (besides standardised co-interventions)(49 knees)

Abbreviations: OA = osteoarthritis, ACR = American College of Rheumatology, I = exercise intervention group, R = reference group, ROM = range of motion, ES = effect size

* Reported data for pain, self-reported disability, observed disability and patient's global assessment of effect
† Our conclusions, based on change scores (if presented) or post-treatment scores
‡ Based on effect size of 0.5 and a *t* test for differences between the means of two independent samples of equal size and variance (Cohen[35])

Reported results: intention-to-treat*	Our conclusions†
Pain: subscale AIMS (0-10 scale, mean ±SD) at baseline I: 5.15±1.99 R: 4.87±2.31 at 8 weeks I: 3.77±1.73 R: 4.77±2.12 Self-reported disability: AIMS subscale physical activity (standardised score 0-10, mean±SD) at baseline I: 6.15±2.27 R: 5.72±2.49 at 8 weeks I: 3.74±2.69 R: 5.96±2.32 Observed disability: 6-min walking distance (m, mean±SD) at baseline I: 381±114 R: 356±130 at 8 weeks I: 451±118 R: 339±125	Significant differences in pain (ES=0.5), self-reported disability (ES=0.9), observed disability (ES=0.9) in favour of exercise therapy
Pain: subscale Osteoarthritis Screening Index (? Items, 0-10cm scale, mean±SD) at baseline I: 15.80±4.88 R: 9.70±6.73 at 8 weeks I: 9.70 ±4.72 R: 10.10±6.44); subscale AIMS (no data presentation) Self-reported disability: subscales AIMS (no data presentation) Observed disability: 50-foot walking time (sec, mean) at baseline I: 12.09 R: 16.74 at 8 weeks I: 11.74 R: 15.73	No significant differences in pain (ES_{OASI}=0.1), self-reported disability, observed disability. Insufficient data presentation for calculation of effect sizes self-reported and observed disability
Pain (10 cm scale, mean ±SD) at baseline I: 4.20±2.25 R: 2.07±1.12 at 12 weeks I: 2.71±2.52 R: 3.51±3.87 Self-reported disability: AIMS (mean±SD) at baseline I: 26.19±7.78 R: 21.37±8.17 at 12 weeks I: 23.37±9.60 R: 17.88±7.17	No significant differences for pain (ES=0.3), self-reported disability (ES=-0.7)
Self-reported disability: functional incapacity score (10 items, 3 point scale, mean change±SD) post-treatment (timing follow-up is unclear, mean number of sessions=41.2) I + ultrasound: -6.30±0.55 I + short wave: -5.88±0.44 R + ultrasound: -4.00±0.42 R + short wave: -3.96±0.34	Significant difference in self-reported disability (ES=1.0) in favour of exercise therapy groups

In table 5 effect sizes and the 95% CIs are presented for all studied outcome parameters.

Table 5: Best evidence synthesis. Effect sizes and 95% confidence intervals for pain, self-reported disability, observed disability and patient's global assessment of effect

First author (reference)	Pain	Self-reported disability	Observed disability in walking	Patient's global assessment of effect
Acceptable validity, sufficient power				
Baar[50]	0.58 (0.54,0.62)	0.26 (0.22,0.30)	0.28 (0.24,0.32)	0.64 (0.60,0.68)
Ettinger[9] (aerob.ex.)	0.47 (0.44,0.50)	0.41 (0.38,0.44)	0.89 (0.85,0.93)	NM
Ettinger[9] (resist.ex.)	0.31 (0.28,0.34)	0.36 (0.33,0.39)	0.31 (0.28,0.34)	NM
Acceptable validity, low power				
Callaghan[8]	NA	NM	NA	NM
Borjesson[7]	0.20 (0.08,0.32)	NM	-0.11(-0.17,-0.05)	1.40 (1.28,1.52)
Low validity, low power				
Kovar[45]	0.52 (0.43,0.61)	0.88 (0.78,0.98)	0.92 (0.82,1.02)	NM
Schilke[10]	0.07 (-0.32,0.46)	NA	NA	NM
Bautch[6]	0.25 (-0.01,0.51)	-0.65 (-0.93,-0.37)	NM	NM
Jan[44]	NM	1.01 (0.91,1.10)	NM	NM

Abbreviations: NM = not measured, NA = not able to calculate effect sizes due to insufficient data presentation.

Pain was used as an outcome measure in seven trials. In one trial data presentation was insufficient to calculate effect sizes[8]. One trial[9] included two comparisons between exercise therapy interventions and a placebo treatment. Therefore, two effect sizes are presented, one of the effect of aerobic exercises and one of the effect of resistance exercises.

In the two trials with acceptable validity and sufficient power[9,50] the lower limit of the 95% CI exceeded 0.2 (small effect), in one of them the lower limit exceeded 0.5 (medium effect)[50]. These beneficial effects were found for different contents of the exercise therapy intervention. One trial concerned supervised individual therapy, including strengthening exercises, ROM exercises and functional training[50]. The other trial concerned supervised group therapy followed by a home based program. Exercises included aerobic or resistance exercises[9]. In both trials, the supervised parts of the interventions took 12 weeks to complete. The participants were suffering from hip or knee OA[50] or knee OA[9].

The lower limit of the 95% CI of the effect size of the trial with acceptable validity but low power[7] was relatively close to 0. In one of the three trials[6,10,45] with low validity and low power, the lower limit of the 95% CI exceeded 0.2. This study concerned supervised group therapy mainly consisting of 'fitness walking'[45].

So, the evidence indicates a small to moderate beneficial effect of exercise therapy on pain.

Self-reported disability was used as an outcome measure in six trials. In one trial data presentation was insufficient to calculate effect sizes[10].

In two trials with acceptable validity and sufficient power, the lower limits of the 95% CI exceeded an effect size of 0.2[9,50]. The 95%CIs of the three trials with low validity and low power[6,44,45] include one extreme value of -0.9[6]. This is probably a biased estimate, due to the forced use of post-treatment scores in combination with a significant baseline difference for this outcome parameter.

It can be concluded that there is evidence for a small beneficial effect of exercise therapy on self-reported disability.

Walking, the most frequently used outcome parameter for *observed disability*, was assessed in six trials. In two trials data presentation was insufficient to calculate effect sizes[8,10].

In the two trials with acceptable validity and sufficient power[9,50] the lower limit of the 95% CI exceeded 0.2, indicating a small beneficial effect of exercise therapy on walking performance. The 95% CI of the trial with acceptable validity but low power[7] ranged from -0.17 to -0.05. Again, this is probably a biased estimate, due to the forced use of post-treatment scores in combination with a significant baseline difference for walking. The trial with a low validity score and low power[45] resulted in an 95% CI exceeding 0.8.

In conclusion, the evidence indicates a small beneficial effect of exercise therapy on walking performance.

In only two trials a *global assessment of effect by the patient* was used as outcome parameter. In the trial with acceptable validity and sufficient power[50], the lower limit of the 95% CI exceeded 0.6. In the trial with acceptable validity and low power[7] the 95% CI exceeded 1.2. These data indicate a medium to great beneficial effect of exercise therapy, according to the patients global assessment.

Comparison between different exercise therapy programmes

Four trials[8,43,48,49] explicitly studied the differences between different exercise therapy interventions. The design and results of these trials are presented in table 6. One of these trials[8] been included in table 4 too since it also included a comparison between exercise therapy and placebo treatment.

Table 6: Characteristics of included studies: comparison between different exercise therapy programmes

First author(s) (reference)	Participants; setting of recruitment	Interventions (number of randomised patients)
Callaghan[8] Validity score: 7 Power‡: 0.16	OA knee: radiographic evidence + symptoms, both not specified, on waiting list physiotherapy; Hospital: orthopaedic clinics	I1: Supervised individual therapy: non-weightbearing strengthening exercises, 20 min, twice a week, 4 weeks (8) I2: Individual therapy: 1 session patient education, 1 tuition home exercises followed by weightbearing strengthening exercises at home, twice daily, 4 weeks (10) R: Supervised sham electrical stimulation, 20 min, twice a week, 4 weeks; group vs individual unclear (9)
Minor[48] Validity score: 6 Power‡: 0.57	OA or RA hip, knee, tarsal joints: pain, stiffness, crepitus and radiographic evidence of specific features (joint space narrowing, no criteria specified), duration ≥6 months; Community, outpatient clinics	I1: Supervised group therapy: aerobic walking program (60-80% max. heart rate), gradually increasing + active ROM and isometric strengthening exercises; 1 hour, 3 times a week, 12 weeks (36) I2: Supervised group therapy: aerobic hydrotherapy: jogging and calisthenics (60-80% max. heart rate), gradually increasing + active ROM and isometric strengthening exercises; 1 hour, 3 times a week, 12 weeks (47) I3: Supervised group therapy: nonaerobic ROM program: active ROM exercises, isometric strengthening exercises, relaxation exercises; 1 hour, 3 times a week, 12 weeks (32)
Sylvester[49] Validity score: 6 Power‡: 0.14	OA hip, not specified; Hospital: orthopaedic and rheumatology clinics	I1: Supervised group therapy: hydrotherapy, 10 strengthening exercises; twice a week, 6 weeks (7) I2: Supervised group therapy: 10 strengthening exercises; co-intervention: short wave diathermy, not specified; twice a week, 6 weeks (7)
Chamberlain[43] Validity score: 4 Power‡: 0.35	OA knee: radiographic evidence grade (2+ Kellgren and Lawrence) and specified clinical and laboratory criteria; Hospital physiotherapy department	Standardised co-intervention: paracetamol when necessary I1: Supervised exercise therapy: 2 exercises aimed at improvement strength and endurance quadriceps; co-intervention: short wave diathermy; group vs individual unclear; 3 times a week, 4 weeks; identical home exercises, twice a day, 4 weeks (24) I2: Home exercises twice a day: see above; instruction sessions: 3 times in 4 weeks (18)

Abbreviations: OA = osteoarthritis, I = exercise intervention group, R = reference group, RA = rheumatoid arthritis, ROM = range of motion

* Reported data for pain, self-reported disability, observed disability and patient's global assessment of effect
† Our conclusions, based on change scores (if presented) or post-treatment sores
‡ Based on effect-size of 0.5 and a *t* test for differences between the means of two independent samples of equal size and variance (Cohen[35])

Reported results: intention-to-treat*	Our conclusions†
Pain (0-10 scale, median % change (negative score = reduction)) at 4 weeks I1: 18% I2: -21% R: 0% Observed disability: 50-m walking test (sec, median % change) at 4 weeks I1: -4% I2: -6% R: 2%	No significant differences in pain and observed disability Insufficient data presentation for calculation of effect sizes
No intention-to-treat analysis Pain: AIMS subscale (0-10 scale, mean change±SD) at 12 weeks I1+I2: -0.76±1.7 I3: -0.31±1.9 Self-reported disability: AIMS-scale physical activity (0-10 scale, mean change ±SD) at 12 weeks: I1+I2: -0.89±1.9 I3: -0.33±3.0 Observed disability: 50-foot walking time (sec, mean change±SD) at 12 weeks I1+I2: -1.0±1.6 I3: -0.52±1.9 No data presentation of results for OA patients at 6 and 9 months	Biased results No significant difference in pain (ES=0.3), self-reported disability (ES=0.3), observed disability (ES=0.3) in favour of aerobic exercise
Pain (0-100 scale, median and range) at baseline I1: 78(65-95) I2: 83(58-95) at 6 weeks I1: 41(19-71) I2: 51(9-83) Self-reported disability: Oswestry low back pain (% maximal attainable score, median and range) at baseline I1: 49(27-60) I2: 67(42-73) at 6 weeks I1: 27(20-40) I2: 58(13-60)	Significant difference in self-reported disability, not in pain Insufficient data presentation for calculation of effect sizes
No intention-to-treat analysis Data presentation restricted to z-values Pain (VAS, scale unclear) at baseline z=0.39, at 4 weeks z=1.68 Self-reported disability (4 items, ? scale) at baseline z=0.26, at 4 weeks z=0.58	Biased results Significant difference in pain (ES=0.6) in favour of home exercises; no difference in self-reported disability (ES=0.2)

Three trials[8,48,49] had an acceptable validity score (≥50% of criteria); however, power was insufficient (<0.80) in all trials. Effect sizes could be calculated for two studies, one with acceptable validity (3 outcome measures)[48] and one with low validity (two outcome measures)[43]. All but one of the calculated 95% CI included 0. The exception was the 95% CI for pain in the low validity study[43], exceeding 0.2 with its lower limit, indicating a small beneficial effect on pain in favour of home exercises.

In conclusion, no evidence is available in favour of one particular type of exercise therapy program.

DISCUSSION

In this systematic review we have summarised the evidence available on the effectiveness of exercise therapy in osteoarthritis of the hip or knee. We assessed the methodological quality and the power of 11 randomised clinical trials.

It can be concluded that exercise therapy is effective in patients with OA of the hip or knee. Available evidence indicates beneficial effects on all studied outcome parameters: pain, self-reported disability, observed disability in walking, and patient's global assessment of effect. Effect sizes indicated small effects on both disability outcome measures, a small to moderate effect on pain, and a moderate to great effect according to the patient's global assessment of effect. Since pain and disability are main symptoms in patients with OA, exercise therapy seems indicated. However, the size of the effects is modest and needs to be enlarged.

Some critical remarks have to be made. These conclusions are based on a small number of good studies. Only two randomised clinical trials had an acceptable validity score as well as sufficient power[9,50]. Another two studies had an acceptable validity score, but low power[7,8]. Next, trials frequently did not include all relevant outcome measures. Therefore, for some outcome measures evidence is based on a limited number of studies, especially as regards observed disability (i.e. walking) and patient's global assessment of effect. Then, hardly any information is available on long-term effects of exercise therapy. In only two publications of one trial long-term effects were reported. Beneficial effects were reported for pain and disability[9,47] However, in this trial exercise therapy was continued to some extent during the entire follow-up period. Therefore no insight was gained into duration of effects after completing exercise therapy. This lack of information concerning long-term effects is a remarkable omission, since the clinical impression is that effects disappear over time. Finally, the effectiveness of exercise therapy in patients with hip OA has hardly been studied. In only one trial[50] had patients with hip OA been included. In that trial both hip

and knee patients were studied. Therefore, there is only limited insight into the effectiveness of exercise therapy in OA of the hip.

There is insufficient evidence to draw conclusions on the optimal content of an exercise therapy intervention. The two trials with acceptable validity and sufficient power showed beneficial effects of different types of exercise therapy: aerobic exercises, resistance exercises, or a mixture of several types of exercise therapy[9,50]. The effect sizes of different exercise therapy interventions were comparable. Trials comparing effects of different exercise therapy programmes remained inconclusive[8,43,48,49].

The methodological assessment revealed some major threats to the validity of clinical trials concerning exercise therapy. Blinding of providers and patients was absent in all studies. As a consequence of the nature of exercise therapy, blinding of both providers and patients is not possible. Therefore, blinding of outcome measurement is vital. However, in only half of the trial reports blinded outcome assessment was explicitly reported. Another potential source of bias was the frequently occurring absence of information on adherence to the intervention. This hampers the interpretation of a negative study. It remains unclear whether the exercise therapy intervention was ineffective due to the intervention itself or due to the participants hardly or not adhering.

We tried to satisfy the current requirements for systematic reviews[18-20]. We included a methodological quality assessment to elucidate sources of bias in included trials. In addition, we studied the power of trials included, i.e. whether a trial could detect an existing difference between interventions. Methodological quality and power were used to weight the level of evidence of a study[51].

Because of the high number of underpowered trials, statistical pooling would be indicated. However, we preferred a best evidence synthesis, based on methodological quality and power analysis. The evidence of trials comparing exercise therapy with a placebo treatment or no treatment was well elucidated in two valid and high powered studies. In addition, the heterogeneity of exercise therapy, the reference treatment and follow-up (timing of outcome assessment) did not merit statistical pooling. The evidence from trials comparing different exercise therapy programmes were not pooled, mainly because of the heterogeneity of the programmes at issue.

To enable direct comparison between trials, we calculated effect sizes for the same outcome measures in different trials. However, in our calculations we were hampered by insufficient data presentation in trial reports. Firstly, in several trials we had to use post-treatment data as a basis for effect size calculations, instead of the preferred change scores and their standard deviations. Effect sizes based on post-treatment scores proved to be less adequate, especially in trials with small sample sizes. In these trials, treatment groups sometimes differed at baseline for an outcome

measure. As a consequence, post-treatment outcomes were only partly informative, as were effect sizes based on these data. Secondly, in three trials no effect-sizes could be calculated.

In conclusion, evidence available indicates beneficial short term effects of exercise therapy in patients with OA of hip or knee. However, further clinical trials are needed to study long-term effectiveness of exercise therapy and effectiveness of exercise therapy in hip patients. In the design and conduct of these trials specific attention should be paid to a sufficient sample size, adhere to exercise therapy, control for co-interventions, blinded outcome assessment and an adequate data analysis including an intention-to-treat analysis. The incorporation of a standard set of outcome measures[25] in combination with the adoptation of a standard for reporting results[52] will greatly enhance evidence synthesis in this area.

REFERENCES

1. Miedema H. *Reuma-onderzoek meerdere echelons (ROME): basisrapport.* (Rheumatism-research on different levels of the health care system: basis report). Leiden the Netherlands: NIPG-TNO, 1994.
2. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, Moskowitz RW, Schnitzer TJ. Guidelines for the medical management of osteoarthritis. Part I. Osteoarthritis of the hip. Arthritis Rheum 1995;38:1535-40.
3. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, Moskowitz RW, Schnitzer TJ. Guidelines for the medical management of osteoarthritis. Part II. Osteoarthritis of the knee. Arthritis Rheum 1995;38:1541-6.
4. Dekker J, Boot B, Woude L van der, Bijlsma JWJ. Pain and disability in osteoarthritis: a review of biobehavioral mechanisms. J Behav Med 1992;15:189-214.
5. Dekker J, Mulder PH, Bijlsma JWJ, Oostendorp RAB. Exercise therapy in patients with rheumatoid arthritis and osteoarthritis: a review. Adv Behav Res Ther 1993;15:211-38.
6. Bautch JC, Malone DG, Vailas AC. Effects of exercise on knee joints with osteoarthritis: a pilot study of biologic markers. Arthritis Care Res 1997;10:48-55.
7. Börjesson M, Robertson E, Weidenhielm L, Mattson E, Olsson E. Physiotherapy in knee osteoarthrosis: effect on pain and walking. Physiother Res Int 1996;1:89-97.
8. Callaghan MJ, Oldham JA, Hunt J. An evaluation of exercise regimes for patients with osteoarthritis. Clin Rehabil 1995;9:213-8.
9. Ettinger WH, Burns R, Messier SP, Applegate W, Rejeski WJ, Morgan T, Schumaker S, Berry MJ, O'Toole M, Monu J, Craven T. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. JAMA 1997;277:25-31.
10. Schilke JM, Johnson GO, Housh TJ, O'Dell JR. Effects of muscle-strength training on the functional status of patients with osteoarthritis of the knee. Nurs Res 1996;45:68-72.

11. Semble EL, Loeser RF, Wise CM. Therapeutic exercise for rheumatoid arthritis and osteoarthritis. Semin Arthritis Rheum 1990;20:32-40.
12. Minor MA. Physical activity and management of arthritis. Ann Behav Med 1991;13:117-24.
13. Marks R. Quadriceps strength training for osteoarthritis of the knee: a literature review and analysis. Physiother 1993;79:13-8.
14. Puett DW, Griffin MR. Published trials of non-medical and non-invasive therapies for hip and knee osteoarthritis. Ann Intern Med 1994;121:133-40.
15. Ytterberg SR, Mahowald ML, Krug HE. Exercise for arthritis. Bailliere Clin Rheum 1994;8:161-89.
16. La Mantia K, Marks R. The efficacy of aerobic exercises for treating osteoarthritis of the knee. NZ J Physiother 1995:23-30.
17. Hoving JL, Heijden GJMG van der. *Fysiotherapie bij heupklachten. Systematische review van klinisch effectonderzoek.* (Physiotherapy and manual therapy for hip complaints. A systematic review of controlled trials). Ned Tijdschr Fysiother 1997;107:2-9.
18. Mulrow CD, Oxman AD. Cochrane Collaboration Handbook [updated September 1997]. The Cochrane Collaboration. The Cochrane Library [database on disk and CDROM]. Oxford: Update Software, [updated quarterly].
19. Oxman AD, Cook DJ, Guyatt GH. Users' guide to the medical literature VI. How to use an overview. Evidence-based medicine working group. JAMA 1994;272:1367-71.
20. Tulder MW van, Assendelft WJJ, Koes BW, Bouter LM. Method guidelines for systematic reviews in the cochrane collaboration back review group for spinal disorders. Spine 1997; 22:2323-30.
21. Counsell C. Formulating questions and locating primary studies for inclusion in systematic reviews. Ann Intern Med 1997;127:380-7.
22. Meade MO, Richardson WS. Selecting and appraising studies for a systematic review. Ann Intern Med 1997;127:531-7.
23. Vet HCW de, de Bie RA, van der Heijden GJMG, Verhagen AP, Sijpkes P, Knipschild PG. Systematic reviews on the basis of methodological criteria. Physiother 1997;83:284-9.
24. Lau J, Ioannidis JPA, Schmid CH. Quantitative synthesis in systematic reviews. Ann Intern Med 1997;127:820-6.
25. Bellamy N, Kirwan J, Boers M, Brooks P, Strand V, Tugwell P, Altman R, Brandt K, Dougados M, Lequesne M. Recommendations for a core set of outcome measures in future phase III clinical trials in knee, hip, and hand osteoarthritis. Consensus development at OMERACT III. J. Rheumatol 1997;24:799-802.
26. Greenhalgh T. How to read a paper - medline database. BMJ 1997;315:180-3.
27. Cochrane controlled trial register. Cochrane Collaboration. The Cochrane Library. Oxford: Update Software, [updated quarterly].
28. Hunt DL, McKibbon KA. Locating and appraising systematic reviews. Ann Intern Med 1997;126:532-8.
29. Schultz KF, Chalmers I, Grimes DA, Altman DG. Assessing the quality of randomization from reports of controlled trials published in obstetrics and gynecology journals. JAMA 1994;272:125-8.

30. American Physical Therapy Association. Guide to physical therapist practice. Phys Ther 1997;77:1163-650
31. Gregoire G, Derderian F, Lorier JLe. Selecting the language of the publications included in a meta-analysis: is there a tower of babel bias? J Clin Epidemiol 1995;48:158-63.
32. Jadad AR, Moore A, Carroll D, Jenkinson C, Reynolds DJM, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996;17:1-12.
33. Verhagen AP, Vet HCW de, Bie RA de, Kessels AGH, Boers M, Bouter LM, Knipschild PG. The Delphi List: a criteria list for quality assessment of randomized clinical trials developed by Delphi consensus. Submitted.
34. Rosenthal R. Parametric measures of effect size. In: Cooper H, Hedges HV, eds. The handbook of research synthesis. New York: Sage Foundation, 1994:231-244.
35. Cohen J. Statistical power analysis for the behavioral sciences. Hillsdale: Lawrence Erlbaum Associates,1988.
36. Kumar PJ, McPherson EJ, Dorr LD, Wan Z, Baldwin K. Rehabilitation after total knee arthroplasty: a comparison of 2 rehabilitation techniques. Clin Orthop 1996;331:93-101.
37. D'Lima DD, Colwell CW Jr, Morris BA, Hardwick ME, Kozin F. The effect of preoperative exercise on total knee replacement outcomes. Clin Orthop 1996;326:174-82.
38. Patterson AJ, Murphy NM, Nugent AM, Finlay OE, Nicholls DP, Boreham CA, Steele I, Henderson SA, Beringer TR. The effect of minimal exercise on fitness in elderly women after hip surgery. Ulster Med J 1995;64:118-25.
39. Wijgman AJ, Dekkers GH, Waltje E, Krekels T, Arens HJ. *Geen positief effect van preoperatieve oefentherapie en instructie bij patienten die heupartroplastiek zullen ondergaan.* (No positive effect of preoperative exercise therapy and teaching in patients to be subjected to hip arthroplasty.) Ned Tijdschr Geneeskd 1994;138:949-52.
40. Green J, McKenna F, Redfern EJ, Chamberlain MA. Home exercises are as effective as outpatient hydrotherapy for osteoarthritis of the hip. Br J Rheumatol 1993;32:812-5.
41. Grigor'eva VD, Suzdal'nitskii DV, Strel'tsova EN, Nikolaeva TG. *Vliianie krio- i krioelektroterapii na regional'nuiu gemodinamiku u bol'nykh koksartrozom.* (The effect of cryo- and cryoelectrotherapy on regional hemodynamics in coxarthrosis patients). Vopr Kurortol Fizioter Lech Fiz Kult 1992:49-54.
42. Singer F, Schieler K. *Vergleich der Kurzwellendiathermie, pulsierender hoch -und niederfrequenter elektro-magnetischer Energie und Heilgymnastik bei der Behandlung der Coxarthrose.* (A comparison of short wave diathermy, pulsed electromagnetic energy (high and low frequency) and orthopaedic gymnastics in treatment of osteoarthritis of the hip). Zf Phys Med 1977:172-7.
43. Chamberlain MA, Care G, Harfield B. Physiotherapy in osteoarthritis of the knees. Int J Rehab Med 1982;4:101-106.
44. Jan MH, Lai JS. The effects of physiotherapy on osteoarthritic knees of females. J Formosan Med Assoc 1991;90:1008-13.
45. Kovar PA, Allegrante JP, MacKenzie R, Peterson MGE, Gutin B, Charlson ME. Supervised fitness walking in patients with osteoarthritis of the knee. Ann Intern Med 1992;116:529-34.

46. Peterson MGE, Kovar-Toledano PA, Otis JC, Allegrante JP, Mackenzie CR, Gutin B, Kroll MA. Effect of a walking program on gait characteristics in patients with osteoarthritis. Arthritis Care Res 1993;6:11-6.
47. Messier SP, Thompson CD, Ettinger WH. Effects of long-term aerobic or weight training regimens on gait in an older, osteoarthritic population. J Appl Biomech 1997;13:205-25.
48. Minor MA, Hewett JE, Webel RR, Anderson S, Kay DR. Efficacy of physical conditioning exercise in patients with rheumatoid arthritis and osteoarthritis. Arthritis Rheum 1989;32: 1396-1405.
49. Sylvester KL. Pilot study. Investigation of the effect of hydrotherapy in the treatment of osteoarthritic hips. Clin Rehab 1989;4:223-8.
50. Baar ME van, Dekker J, Oostendorp RAB, Bijl D, Voorn ThB, Lemmens JAM, Bijlsma JWJ. The effectiveness of exercise therapy in patients with osteoarthritis of hip or knee: a randomised clinical trial. J Rheumatol (accepted for publication).
51. Cook, DJ, Guyatt GH, Laupacis A, Sackett DL. Rules of evidence and clinical recommendations on the use of antithrombotic agents. Chest 1992;102:305S-11.
52. Begg C, Cho M, Eastwood S, Horton R, Moher D, Olkin I, Pitkin R, Rennie D, Schulz K, Simel D, Stroup DF. Improving the quality of reporting of randomized clinical trials: the CONSORT statement. JAMA 1996;276:637-9.

APPENDIX I

Specification of the criteria from table 1. Each criterion must be applied independently of the other criteria.

V1. A random (unpredictable) assignment sequence. Methods of allocation using date of birth, date of admission, hospital numbers, or alternation should not be regarded as appropriate.

V2. Assignment generated by an independent person not responsible for determining eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or the decision about eligibility of the patient.

V3. Co-interventions concerning other physical therapy modalities and medication are either standardised or avoided in trial design.

V4. A report on the above mentioned co-interventions for each group separately

V5. The reviewer determines when the adherence to the interventions is acceptable when based on the reported intensity, duration, number and frequency of sessions for both the index intervention and control intervention(s). Criterion adherence >70% in indexgroup(s) and, in placebo-controlled trials also in control group(s)

V6. The reviewer determines when enough information about the blinding is given in order to score a 'yes'. For exercise therapy this item always scores a 'no'.

V7. The reviewer determines when enough information about the blinding is given in order to score a 'yes'. For exercise therapy this item always scores a 'no'.

V8. The reviewer determines (per outcome parameter) when enough information about blinding is given to score a 'yes.

V9. At least two of the important outcome parameters for trials in OA: pain, functional status (including performance based parameters) and patient global assessment (Bellamy et al[25]).

V10. Participants who were included in the study but did not complete the observation period or were not included in the analysis must be described. If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up and does not lead to substantial bias a 'yes' is scored. No drop-outs reported scores as 'don't know'.

V11. Timing of outcome assessment identical for all intervention groups; for all important outcome assessments.

V12. All randomised patients are reported/analysed for the most important moments of effect measurement (minus missing values) irrespective of non-compliance and co-interventions.

D1. In order to score a 'yes' explicit classification criteria for OA should be described (an established set of criteria (i.e. of American College of Rheumatology) or clinical criteria, including presence of symptoms.

D2. In order to receive a 'yes' groups have to be similar regarding four of the most important prognostic factors: age, radiological OA, duration of disease, and baseline main outcome measure(s). If a baseline difference exists in one of these factors, a 'no' applies.

D3. Adequate description of type, modality, application technique, intensity, duration, number of frequency of sessions for both the index intervention and control intervention(s) in order to replicate the study.

D4. Each event described and correctly attributed to allocated treatment; if explicit report of 'no adverse effects' a 'yes' applies. Scores either a 'yes' or a 'no', a 'don't know' doesn't exists.

D5. Outcome assessment at the end of the intervention period

D6. Outcome assessment $\geq$ 6 months after randomisation

S1. To be presented per group at randomisation and for most important outcome assessments.

S2. Both point estimates and measures of variability should be presented (to be scored for each important outcome parameter separately). Point estimates are: means, medians, modes, etc.; Measures of variability are: standard deviations, 95% confidence intervals, etc. For dichotomous or categorical data proportions have to be presented.

8

GENERAL DISCUSSION

In this final chapter of this thesis we discuss the main results of our study into the effectiveness of exercise therapy in OA of the hip and knee. First, some general issues concerning the design and conduct of our randomised clinical trial are highlighted. We subsequently critically review the answers to our research questions as presented in the foregoing chapters of this thesis. Finally, implications for clinical practice and future research are considered.

GENERAL ISSUES

Both hip and knee patients

In our randomised clinical trial patients with hip OA as well as patients with knee OA were included. At the time this trial was designed there were no reasons to expect differences in effectiveness of exercise therapy between these groups. In addition, exercise therapy is generally similar in both patient groups.

In this thesis we have examined differences between hip patients and knee patients. Firstly, it was studied whether differences exist in the relationship between articular, kinesiological and psychological characteristics and pain and disability. As presented in Chapter 2, the results were generally similar. In both hip and knee patients, pain and disability were most strongly associated with kinesiological characteristics and pain coping. However, some differences were found concerning the associations with pain, but not with disability. In hip patients, in contrast to knee patients, muscle strength and duration of complaints were associated with pain.

Secondly, we studied differences in effectiveness of exercise therapy between hip patients and knee patients. The effectiveness of exercise therapy in these patients was similar. We found no significant interactions between the location of OA and pain, the use of NSAIDs and observed disability (see Chapter 3 and Chapter 4).

Our results support the current ideas about similarities (and differences) between hip and knee OA. These disorders have common risk factors, a similar pathogenesis, a common pathology and similarities in outcome. However, for different locations a different balance of risk factors exists. The same applies to disease process and outcome[1]. As a consequence, the decision whether or not to combine hip patients and knee patients is dependent on the goal of the study .In studies addressing risk factors and pathogenesis a distinction seems necessary. In studies examining the effectiveness of interventions, hip patients and knee patients can probably be combined.

At present, there is still no clear indication for a different rationale of exercise therapy in hip and knee OA. Therefore, in future trials studying the effectiveness of exercise therapy programmes in OA patients, both hip patients and knee patients can be included. However, as long as working mechanisms of exercise therapy in OA patients need further exploration, any differences between the two groups should be examined. In such a trial patients should be stratified on location of OA (hip versus knee.). Intervention groups will then be of a similar composition as regards location of OA, and examination of differences will be possible.

Classification criteria for OA of the hip or knee

Patients in our study were patients applying for treatment in general practice. The clinical criteria of the American College of Rheumatology were used[2,3]. As a consequence, a patient's participation did not depend on radiological changes showing on an X-ray. To restrict the study to patients with at least mild OA, patients with complaints in less than 10 out of 30 days preceding randomisation were excluded.

Baseline data revealed that the included patients were patients with relatively mild OA. In about 30% of the patients no radiological changes were diagnosed. About 40% of the patients had had complaints for less than a half year and again about 40% had not been treated before by his or her general practitioner (see Chapter 2). So, the use in general practice of the clinical criteria of the ACR has clearly resulted in a study population of patients with mild OA.

At the start of our study we chose to use the clinical criteria of the ACR because the use of an established set of criteria for classification of patients has advantages, when communicating about a study. We preferred the ACR criteria to the Kellgren and Lawrence criteria. The latter are based on radiographic changes, ignoring symptoms[4]. Applying the Kellgren and Lawrence criteria to our study population would have resulted in ignoring 30% of the patients applying for treatment, because of their symptoms. The relationship between radiographic changes and symptoms is known to be weak. In an elderly population as many as 60% of the persons with severe radiographic changes (3+) in the knee showed no symptoms[5]. These findings support

our opinion that a classification which includes clinical features is more relevant in a clinical setting, especially in general practice.

Recruitment of general practitioners, physiotherapists and patients

We aimed at 200 patients participating in the study, as this number of patients would lead to sufficient power. We had planned patients to be recruited by 50 general practitioners over a period of 15 months. This was based on data on prevalence of OA of hip and knee in general practice, the assumption that only one out of three patients would meet into our criteria, and the estimation that one out of two patients would refuse to give informed consent. We ended up with 77 GPs from 64 practices willing to recruit patients over a period of 21 months (May 1994-February 1996). Only 57% percent of the GPs (44 GPs) actually registered one or more patients for our trial. This percentage is relatively low, compared to the percentage in another trial. In that trial, (comparing physiotherapy and injection in shoulder disorders,) 80% of the GPs actually recruited patients[6]. A possible explanation is in the nature of our research question. This was primarily concerned with the surplus value of a physiotherapy intervention and not with an intervention performed by a GP. Therefore, GPs were probably less involved in our study.

Recruitment of physiotherapists was guided by the principle that each participating patient should be able to visit a physiotherapist in his or her own neighbourhood. Therefore, we recruited physiotherapist equally distributed over the participating cities and villages. This resulted in a relatively high number of participating physiotherapists: 82 physiotherapists from 47 practices were informed about the trial and were trained to use the protocol. About half of these physiotherapists (39 physiotherapists in 29 practices) actually treated patients after referral from a GP. The remaining physiotherapists did not receive any patient from the local GPs within the scope of the trial.

The participating GPs succeeded in including 200 patients. Several measures had been taken to reach this number of patients. The number of participating practices was increased by increasing the number of participating cities and villages. The inclusion period was extended. Also, we tried to maximise the GPs' motivation and the motivation of their assistants to participate in the study by informing them through our newsletter and phoning them regularly. In addition, GPs were visited to clarify recruitment procedures, and small presents were given them.

In conclusion, patient inclusion in the trial was successful, in that the target number was reached in a reasonable period of time, even though only slightly more than half of the participating GPs actually registered patients for our trial.

RESEARCH QUESTIONS

Contribution of articular, kinesiological and psychological characteristics to pain and disability

We examined the separate contribution of articular, kinesiological and psychological characteristics to pain and disability in hip and knee OA, using a cross-sectional analysis. After controlling for other characteristics, kinesiological and psychological characteristics were each separately found to be associated with disability. These characteristics were also found to be associated with pain, but less pronounced (see Chapter 2).

The examination of kinesiological features was restricted to two characteristics, namely muscle strength and range of motion. Our results indicate that these features are indeed important determinants of disability and, to a lesser extent, pain. However, there are several other related characteristic features in OA, including decreased aerobic capacity, decreased exercise endurance, joint instability and arthrogenous muscle inhibition[7]. These features too may play a role in the process of pain and disability in OA and they should be included in future research.

The psychological characteristics examined were pain coping behaviour, including fear avoidance beliefs towards physical activity and psychological well being. Future research should address pain coping behaviour as a probably important determinant of pain and disability in OA.

Several mechanisms explaining the association of muscle strength, range of motion and pain coping with pain and disability were discussed. Due to the cross-sectional character of our analyses we could not prospectively study the actual mechanisms underlying the associations between articular, kinesiological and psychological characteristics and pain and disability. A longitudinal analysis is necessary to study these characteristics in relation to pain and disability in OA. At this moment such an analysis on our data is being conducted.

Short-term effectiveness of exercise therapy in OA of hip or knee

Beneficial effects of exercise therapy were found for pain and observed disability at week 12 and for pain at week 24 (see Chapters 3 and 5) . At week 12, after completion of exercise therapy, the size of the beneficial effects was maximal. In the follow-up period the size of the effects declined and finally disappeared. So, exercise therapy in a primary care setting is effective in patients with OA of the hip and knee, and effects on pain remain up to 3 months after completion of therapy.

Our randomised clinical trial into the effectiveness of exercise therapy in OA of the hip or knee is a so-called pragmatic trial, studying the effectiveness of treatment in an

everyday setting, i.e. a physiotherapy practice. Previous RCTs were mainly explanatory trials, studying exercise therapy in research-settings. As a consequence of the pragmatic design of our trial, content, intensity and frequency of treatment were tailored to the patients' needs. In most previous trials content, intensity and frequency of exercise therapy was strictly prescribed and circumstances were optimised to generate a maximum effect of exercise therapy.

A disadvantage of a pragmatic trial is the possible lack of clarity concerning content of treatment. We have overcome this drawback by taking two measures. Firstly, exercise therapy treatment was described in a written protocol (see Appendix). This protocol included a set of treatment goals with corresponding exercises. In addition, instructions were given for patient education, advice and home exercises. Depending on the physiotherapist's diagnostic findings individual treatment goals with corresponding exercises were chosen. Frequency of sessions was prescribed and ranged between once and three times a week, depending on the pain level. Physiotherapists were trained to use the protocol. Secondly, detailed information about treatments given was registered by the physiotherapists. For every period of two weeks information was registered about the number of sessions, treatment goals chosen, interventions applied and, if there were, deviations from the protocol. So, while giving room for tailoring treatment to a patient's needs, the intervention studied is well-defined.

Another consequence of our pragmatic design was the impossibility to study the effectiveness of a specific part of our intervention, for instance the effect of attention. We did not study or control for the effect of attention. In daily practice, attention is an inseparable part of exercise therapy as given by a physiotherapist in primary health care. In a pragmatic trial, comparing existing interventions, it is, therefore, not useful to study the separate effect of attention. In contrast with our trial, Ettinger et al[8] studied the effect of exercise therapy while controlling for the effect of attention. Exercise therapy was compared with a group therapy which consisted mainly of patient education. A similar design was studied by Kovar et al[9], comparing exercise therapy with a placebo-intervention consisting of telephone calls discussing activities of daily living. In both trials a beneficial effect was found for exercise therapy itself[8,9].

We used three primary outcome measures in our trial, namely pain past week, the use of NSAIDs, and observed disability. Assessment of pain by using a visual analogue scale has proved to be a valid, reliable, and responsive assessment which takes only a short time to complete[10,11]. The assessment of both the use of NSAIDs and observed disability deserves some discussion.

In our study population, OA patients applying for treatment in a GP practice, the use of NSAIDs as outcome measure was not particularly informative. The number of

patients using NSAIDs at baseline was low (57/200, 28.5%). This number of patients using NSAIDs showed a slight increase in both interventions groups, apparently not influenced by exercise therapy. If patients used NSAIDs we assessed quantity of medication use by prescription data from GPs and counts of remaining medication at outcome assessments. These data again showed a small and stable use of NSAIDs. Therefore, we conclude that in general it is not advisable to use medication counts of NSAIDs as a primary outcome measure in future OA trials in general practice. Only in trials aimed at the prevention of the use of NSAIDs in OA, medication counts of NSAIDs seem appropriate. Such trials can probably be expected in knee OA. According to the guidelines for treatment of OA of the knee from the ACR, for these patients the non-pharmacological treatment modalities are the first choice of treatment. It is interesting to know whether the use of NSAIDs can be postponed or even totally prevented by these treatment modalities.

The outcome measure observed disability was based on a combination of movement times and quality of performance. Videos were studied of the patients performance of a series of standardised tasks, using an adaptation of the method as described by Keefe[12-14]. These tasks include walking, sitting down, bending and reclining. The surplus value of our assessment of observed disability over a simple assessment of observed disability, for instance 50-foot walking time, is not clear. Comparison with the simple measures of observed disability in other studies is difficult. In addition, assessment of observed disability was relatively time-consuming and required quite a lot of facilities, like a video camera, a test-room etc. The use of observed disability as an outcome measure in future trials should be reconsidered. The surplus value of our assessment of observed disability over self-reported disability is subject of further study[15].

Recommendations were recently published concerning design and conduct of clinical trials in patients with osteoarthritis[16,17]. The recommended core set included validated measures of pain, physical function (i.e. self-reported disability), patient global assessment and, in studies with a duration longer than one year, and imaging of joints. A performance-based measure of function (i.e. observed disability) is seen as an optional measurement. No specific recommendation for an instrument assessing observed disability was made. It is stated that 'the usefulness of this measure in clinical trials remains unclear'. The most frequently used outcome measure for observed disability in trials involving exercise therapy in hip or knee OA is concerned with walking, for instance the 50-foot walking time (see Chapter 7). If one decides to include observed disability in future trials, the assessment of a 50-foot walking time seems advisable, for reasons of comparison.

In addition to the primary outcome measures, several secondary outcome measures were used to study working mechanisms of exercise therapy in OA. Some

assessments demand quite an effort of patients, especially the assessment of muscle strength and range of motion. To my opinion, in the design of a trial the burden to the patient and the relevance of the data should carefully be weighed against each other, taking into account the condition of the study population. In any case, assessment should cause the least possible discomfort to the patient. This may also help to reduce withdrawals to a minimum. However, as long as the working mechanisms of exercise therapy in OA are still unclear, it remains necessary to include measurements assessing the process of exercise therapy in OA, including measurements of muscle strength and range of motion.

As a consequence of the nature of exercise therapy; neither physiotherapists nor patients could be blinded for the allocated intervention. In the 12-week treatment period, the general practitioner was not informed about whether the patient received exercise therapy or not.

With such a study design, blinded outcome assessment is of great importance. Our outcome assessors were not informed about the allocated treatments. In addition, patients were instructed not to inform the outcome assessors. The success of blinding was checked by questioning the assessors whether or not the patient had informed them about the allocated treatment. There was no association between disclosure of allocation and outcome assessment (see Chapter 4).

Some improvement can be made in studying potential bias due to absent blinding or unmasking of outcome assessors. Firstly, we did not study the patients' preference for one of the interventions in our trial. Patients possibly have a preference for one intervention, and this can influence results of both therapy and outcome assessment. Studying the patients' preference before randomisation enables one to study influences of any preferences on the results of the trial[7].

Secondly, a more adequate way to study success of blinding would have been to ask the assessor to guess the allocated treatment, including reasons for their assumption. The association between this guess and outcome assessment can be studied. This relationship is more meaningful because it is not only the actual knowledge about the allocated treatment, as gained by disclosure of treatment, but also the assessors beliefs (as reflected in a guess) that can bias outcome assessment.

Outcome in specific subgroups of patients with OA of the hip or knee

Our third research question was concerned with the effectiveness of exercise therapy in specific subgroups of patients. In Chapter 4 it is reported that only limited evidence was found for the existence of subgroups of patients in which exercise therapy has beneficial effects. Beneficial effects may probably be expected in patients without

radiological OA, and with a recent onset of complaints. Also compliance with exercise therapy seems related to a beneficial outcome. Comparison with earlier research was hardly possible because only few studies on this subject are available. We had to conclude that specification of the indication for exercise therapy in patients with OA of the hip or knee is not yet possible.

The rationale of effectiveness of exercise therapy in patients with OA of the hip and knee is based on several factors, including articular, kinesiological and psychological factors. The effectiveness of exercise therapy is a consequence of the changes in these associated factors. Therefore, analysing the mere occurrence of a factor (for instance muscle weakness) and the effectiveness of exercise therapy may be too simplistic. It is probably not the simple occurrence of a factor which influences the effectiveness of exercise therapy, but the fact whether a factor is a causative factor in the chain from disease (OA) to consequences of disease. We have performed post-hoc analyses to study this hypothesis. We examined the relation between treatment goals as indicated by the physiotherapists and effectiveness of treatment. However, even in this analysis we did not find any significant association. One problem with this analysis is the operationalisation of the principle 'causative factor' by means of the treatment goals registered by physiotherapists. These goals can be expected to reflect important impairments and disabilities but do not have to be the key factors in the pathway from pathology to disability or handicap. In addition, these treatment goals are restricted to kinesiological features, ignoring the psychological factors. Other factors contributing to the consequences of OA are also not accounted for.

Future research examining this hypothesis is necessary. This should include a broad analysis of causative factors and use of sound theoretical insights as regards cause and effect relationships. There are several models, each presenting a comprehensive overview of causative factors of disability and their interactions[18-20]. In these models the central part is the pathway from pathology to disability. In addition, the influence of both extra-individual factors (health care, external supports, physical and social environment) and intra-individual factors (coping, lifestyle changes) on consequences of disease is recognised. These models can possibly help us unravel the process of disablement in OA and thereby contribute to our knowledge of the rationale of exercise therapy in OA.

Long-term effectiveness of exercise therapy in OA of hip or knee

Our fourth research question addressed the long-term effects of exercise therapy. How long do beneficial effects remain after completion of the exercise therapy programme? Our results indicate that beneficial post-treatment effects decline over time in the follow-up period and finally disappear. At 24 weeks, 12 weeks after completion of the

programme, a beneficial effect on pain was found. At 36 weeks, no effects were found. Long-term outcome could not be predicted by patient characteristics at baseline or compliance to exercise therapy (see Chapter 5).

Compliance to therapy is a prerequisite for the success of therapy. As mentioned earlier, compliance has to be studied in a randomised clinical trial concerning exercise therapy. Otherwise the interpretation of a negative trial is hampered: it remains unclear whether a therapy was ineffective due to the intervention itself or due to the participant hardly or not adhering.

Assessment of compliance is rather problematic. There is a great variety of instruments measuring compliance, including diaries, keeping appointments, questionnaires, observations, effect of therapy, apparatus that measures movements, interviews and information from the social environment. In an inventory of instruments measuring compliance it was concluded that none of the instruments available satisfied the requirements of a valid and reliable assessment of compliance[21]. Main measurement problems are 1) inadequacy of patient's self-report due to reliance on patient's memory 2) evocation of socially desirable responses 3) assessment of compliance as a dichotomy instead of measuring the degree of compliance[22].

We have assessed compliance to exercise therapy by means of questionnaires. Both the patient and the physiotherapist reported about the level of exercise compliance. Patients were phoned at week 6 and week 12 and asked whether they managed to do their home exercises as often as prescribed. Possible answers were: (almost) never, sometimes, regularly, often and very often. Physiotherapists were asked to estimate whether the patient complied with the home exercise instructions in the last 4 weeks of treatment, using a standardised form. Possible answers were: certainly not, probably not, probably and certainly. Compliance as reported by the patient and the estimation of the physiotherapist was moderately associated (Kendall's tau=0.24). Only 15% showed a marked difference between the patient's report and the physiotherapist's estimation of compliance. In these cases, patients reported to have exercised at least regularly and the physiotherapist estimated that the patient did not comply (probably or certainly), or vice versa[23]. Both measures seem to contribute to our perception of the patient's compliance. The physiotherapists' estimation is a valuable addition in that this method to a large extent overcomes the problem of socially desirable responses.

A new way of assessing compliance was recently developed by Kerssens et al[24]. It was applied to patients with back pain. Physiotherapists recorded the kind of instructions given to their patients in each sessions on a registration form. The form included precoded topics, in four areas, including doing exercises. By means of a questionnaire, patients were asked which activities they employed in their daily life. This questionnaire was answered on three occasions (first visit, post-treatment and six

months after completion of therapy). The questions were related to self-care activities, including pain management, lifting techniques, daily activities and general fitness. Comparing the instructions patients received from their physiotherapist (registration form) with the activities they reported to have undertaken (patient questionnaire) resulted in a measurement of adherence. Reliability of this method proved to be good. In addition, several aspects of validity were studied and found to be sufficient[24]. A main constraint in the application of this method is its time-consuming character. The physiotherapist has to record each session the kind of instructions given and the patient is asked to fill in the questionnaire several times. This restricts the practical value of this method for future trials. So, this assessment of compliance is a promising method, avoiding the main measurement problems in compliance. The development of a short form version would facilitate its use in future research.

We did not study long-term compliance, i.e. compliance to exercises in the period after the completion of exercise therapy. As a consequence we could not study a possible relationship between long-term compliance and long-term outcome. In the design of future trials concerning exercise therapy attention should be paid to assessment of compliance, both short-term and long-term.

Cost-effectiveness of exercise therapy in OA of the hip or knee

The cost-effectiveness of exercise therapy was examined. Direct costs, related to OA patients seeking therapy as well as indirect costs, related to production losses to society because of absence to work due to OA, were surveyed. The effectiveness of exercise therapy was assessed using general health questionnaires, including the Nottingham health profile, the Karnofski Performance Index and the EuroQol-5D. The use of these questionnaires enables comparison with cost-effectiveness analyses of other interventions and diseases.

It was planned beforehand to calculate a cost-effectiveness ratio, i.e. the costs per quality-adjusted-life-year gained. The quality adjustment would be performed on the basis of the EQ-5D index. For the calculation of this index, the description of general health status on the EQ-5D dimensions has to be combined with a system rating this description. Several rating systems exist, based on different study populations such as samples of healthy citizens, students, health care workers etc. Due to the small changes on the EQ-5D-dimensions and the assumption that there is no difference in life years gained between the intervention groups, the choice of the rating system would strongly influence the magnitude of the cost per quality-adjusted-life-years gained. Therefore, we refrained from calculating this ratio. As an alternative, the costs per point improvement on the EQ-5D-index were calculated for each intervention group. In addition, the costs of two referral scenarios were calculated: a base-scenario with the actual level of referral to physiotherapy, and a growth-scenario

in which the level of referral to physiotherapy in OA would increase with 10 % (see Chapter 6).

An alternative solution applicable in the field of physiotherapy and related research is to use a more disease-specific outcome measure for calculation of a cost effectiveness ratio. Possible outcome measures are pain past week (as measured with a VAS) or a global measure of improvement by the patient. Both measures are frequently used in outcome research on physiotherapy and related fields. This enables comparison within the field.

Notwithstanding the problems mentioned above, we succeeded in determining the cost-effectiveness of exercise therapy in OA of the hip or knee in the Netherlands. To our knowledge, data on cost-effectiveness of exercise therapy programmes in OA were not available before. Ettinger et al gave some indication of the costs of their exercise intervention as studied in the FAST-trial. In this trial patients received a rather comprehensive supervision throughout the 18-months follow-up period, including home visits and structured telephone calls. This resulted in 'relatively high direct costs[8]. In the Netherlands one cost-effectiveness analysis has been performed on group exercise therapy in ankylosing spondilitis[25]. Results similar to our data were found. The beneficial effects of group exercise therapy were combined with higher medical costs (Dfl 771 per patient per year). These costs mainly consisted of the additional costs of group exercise therapy.

Comparison or utilisation of our data in other countries is hampered by the differences in health care systems. Therefore, introduction of a similar intervention in other countries should be preceded by a cost-effectiveness analysis. In addition, future randomised clinical trials on exercise therapy programmes should be combined with a cost-effectiveness analysis. This will stimulate the development of a optimal exercise programme, in terms of both clinical effectiveness and cost-effectiveness.

Systematic review on the effectiveness of exercise therapy in patients with OA of the hip or knee

A systematic review was conducted to determine the evidence available on exercise therapy in OA of the hip or knee. This review was completed only recently and includes all randomised clinical trials published recently, including our own paper on short-term effectiveness of exercise therapy in OA of the hip or knee. In addition, the presently required review methodology was applied (Chapter 7). The evidence available indicates favourable short-term effects of exercise therapy in patients with OA of the hip or knee. Only a few trials have focused on the long-term effectiveness and effectiveness in hip patients, so conclusions regarding these topics are tentative. Conclusions on the optimal content of an exercise therapy intervention are not

possible, since trials focusing on comparison of different exercise therapy programmes remained inconclusive.

The review methodology applied was up to standard. Some minor improvements can be made though. As regards our search strategy, we did not check for other trial reports of exercise therapy in OA of the hip or knee, either unpublished or not yet published. As a result we probably missed small or negative studies which are less likely to be published[26]. Moreover, one reviewer conducted the quantitative data extraction. A more sophisticated method would have been to perform this procedure with two reviewers, which would led to a verification of the end result[27].

The methodological quality of the included trials was comparable to the methodological quality of trials in another systematic review in the field of physiotherapy recently published. In our review more than half of the trials assessed (6/11) satisfied at least 50% of the validity criteria. Similar results were found in a review on physiotherapy for shoulder disorders, where comparable criteria had been applied (11/20)[28].

We conducted a best evidence synthesis, based on methodological quality and power analysis. Effect sizes were calculated to enable direct comparison between different trials. Calculation of effect-sizes was hampered by insufficient data presentation in trial reports. Adoption of the CONSORT statement, the standard for reporting results of randomised clinical trials[29] by all researchers in this area will enhance future evidence synthesis.

In conclusion, our systematic review can be improved by conducting a more comprehensive search strategy and by two reviewers carrying out the data extraction procedure by two reviewers. The evidence available indicates beneficial short-term effects of exercise therapy. Future trials should focus on long-term effects, effects in hip patients and on optimal content of exercise therapy. The methodological criteria can be used to optimise design and conduct of these trials. Adoption of a standard for reporting results will greatly enhance evidence synthesis in an update of this review.

IMPLICATIONS FOR CLINICAL PRACTICE

Exercise therapy in OA

The evidence presented in this thesis clearly indicates the usefulness of exercise therapy in patients with OA of the hip or knee. Therefore, a referral from a general practitioner to a physiotherapists for exercise therapy seems indicated. Furthermore, exercise therapy should be the main component of a physiotherapy treatment in patients with OA of the hip or knee. In a survey on physiotherapy in Dutch primary care, conducted from 1989 to 1992, it was found that exercise therapy was already

included in the majority of physiotherapy treatments for OA (65%)[30]. In our opinion, exercise therapy should in principle be part of every treatment of patients with OA of the hip or knee. This requires some change in the physiotherapists' clinical practice.

After completion of exercise therapy, effects decline and finally disappear. This development is often seen in health care interventions, and is therefore not remarkable. Nevertheless, physiotherapists should try to prevent this decline as much as possible, within the constraints of a limited number of sessions. This can be done by optimising both content and timing of treatment. The content of therapy can probably be optimised by including the principles of the successful psycho-educational interventions in patient education given by a physiotherapist. Recently, some specific recommendations were given to improve patient education as regards the stimulation of self-efficacy. It was recommended to give more instructions concerning daily activities (taking care of the complaints in daily activities) and general fitness, especially towards the end of treatment. These instructions probably contribute to the prevention of recurrence of complaints, the main objective in a last phase of treatment[31].

Also an adaptation of the timing of sessions seems appropriate. Research has shown that supervision is highly beneficial to compliance and treatment outcome[32]. In addition, follow-up sessions have been found to be the most effective way to increase compliance to therapy[33,34]. So, the incorporation of follow-up sessions as a part of a physiotherapy treatment in OA seems highly indicated.

Specification of indication for exercise therapy

Specification of the indication for exercise therapy appeared to be rather problematic. Our results indicate that beneficial effects of exercise therapy are possibly greater in patients with mild OA (no radiological changes or short duration of complaints) and in patients who complied with exercise therapy. However, no definite specification of the indication for referral can be given at this moment. So, the decision to refer for exercise therapy remains the result of the GP's opinion in combination with the patient's view. Important factors contributing to this decision are the patient's possibilities to improve (taking into account comorbidity) and the motivation of the patient to comply with exercise therapy.

Remuneration system

In the Netherlands the remuneration system for physiotherapy, exercise therapy-Cesar and exercise therapy-Mensendieck was changed in 1996. For publicly insured patients, the maximum number of sessions per indication per year was restricted to 9. For patients with a complementary insurance an additional number of 9 sessions is

reimbursed, resulting in a maximum number of 18 sessions per indication per year. This also applies to the indication OA of the hip or knee.

Our results indicate that only a small proportion of treatments for OA was finished within 9 sessions (14.0%). The mean number of sessions per treatment was 16.8, considerably higher than the maximum of 9 reimbursed sessions. It is doubtful whether effects of a treatment consisting of 9 sessions are identical to effects as found in our trial. These effects will probably be less marked and comparable with the effects of treatment at 6 weeks. (The mean number of sessions at 6 weeks was 9.3). At that stage, no beneficial effects were found for the primary outcome measures: pain, the use of NSAIDs and observed disability. As regards the secondary outcome measures, beneficial effects were found for the use of paracetamol, global perceived effect, muscle strength of the hip, and range of motion of the hip (data not presented in this thesis, see Baar et al[23]). In patients with a complementary insurance effects similar to our trial can be expected.

Recent data indicate that the majority of publicly insured patients have a complementary insurance (92%, personal communication, A. Pijnenborg, NIVEL). As a consequence, most publicly insured patients can apply for reimbursement of one exercise therapy treatment of a sufficient number of sessions a year. Nevertheless, for patients without a complementary insurance the restriction in number of sessions will result in a short and probably less than optimal treatment. Therefore, it seems necessary to reconsider the restriction in the number of sessions for patients with OA of the hip or knee.

IMPLICATIONS FOR FUTURE RESEARCH

Mechanisms underlying pain and disability in OA

In this thesis we have studied to a limited extent the mechanisms underlying pain and disability. A cross-sectional analysis was conducted, studying the relation of articular, kinesiological and psychological characteristics with pain and disability in OA. Therefore, no causal conclusions could be drawn as regards the underlying mechanisms. A longitudinal analysis, including articular, kinesiological and psychological features is now being conducted. This study will contribute to our understanding of these mechanisms. One interesting topic is the cause of muscle weakness in OA. The question is whether muscle weakness is a result of disuse atrophy due to pain in OA or that is a consequence of reflex inhibition caused by the disease itself[7]. In a recent study some support was found for the latter. Muscle weakness was found to exist in patients with radiographic OA but without detectable joint pain or muscle atrophy. It is suggested that knee extensor weakness may be a

risk factor in the development of pathological changes in OA. As a consequence, exercises to strengthen quadriceps possibly prevent development of the pathological changes and consequently decrease the risk of pain and disability in knee OA[35]. This and other hypotheses deserve further study.

Content and timing of exercise therapy in OA of the hip and knee

We studied the effectiveness of short-term exercise therapy in OA and found beneficial effects after completion of therapy. Future research needs to focus on methods to optimise long-term effectiveness of exercise therapy. Attention should be focused on both content and timing of exercise therapy.

Optimisation of the content can probably most easily be achieved by including the principles of the successful psycho-educational interventions in an exercise therapy protocol (see also Chapter 1). In the psycho-educational interventions, patients are taught how to adjust their daily activities as dictated daily by disease symptoms. In addition to teaching patients what to do, patients should be instructed on how to approach situations and make adjustments depending on each individual's own needs[36].

In general, patient education is guided by the principle to increase the patient's self-efficacy by setting realistic, attainable goals, and providing feedback. In addition, information should be tailored to the patient's needs and tuned to his/her individual situation[37]. Applying the principles of self-management fits into this general idea of patient education, but requires a more comprehensive approach of patient education. The content of this approach can be derived from arthritis patient education programmes, for instance the self-management course developed in the Netherlands[38].

Further refinement of exercise therapy in terms of specific exercises, is not yet available. Therefore, the exercise therapy protocol as used in this trial may serve as a basis for future trials on exercise therapy in OA. Expanding the number of examples of possible exercises would be useful, as this would result in more clarity about the actual content of the exercise therapy intervention.

Next to the optimal content, the optimal timing of exercise therapy sessions should be assessed. One possibility is to reduce the frequency of sessions in the last phase of a regular treatment. In this way the period of time in which exercise therapy is supervised by the physiotherapist is prolonged. This probably boosts clinical effectiveness of exercise therapy, at no extra costs. Another possibility is to extend regular treatment with follow-up sessions. These sessions are found to be highly effective as regards increasing compliance. It can be hypothesised that this will result in prolonged beneficial effects of exercise therapy.

Subgroup analyses

Until now, there is no evidence whether there are subgroups that especially benefit from exercise therapy in OA. Future trials should focus on this issue. The value of prognostic characteristics of 1) early stage OA and 2) compliance to therapy should be studied. In addition, the hypotheses analysed in Chapter 5 deserve further study. Confirmation of our hypotheses can possibly be found if a more specific exercise intervention is studied. For example, it might be that strengthening exercises result in improvement of muscle strength and, therefore, particularly benefit patients with muscle weakness.

As stated before, future research should focus on assessment of causative factors in the chain from OA to the consequences of OA. Such research might greatly contribute to our understanding of the existence of subgroups that especially benefit from exercise therapy in OA. In any study the complexity of the process of disablement in patients with OA should be taken into account.

In the future research into the existence of subgroups deserves priority. Because of the high prevalence of OA, societal costs of exercise therapy in OA are high, although individual costs are modest. Therefore, specification of the indication for referral for exercise therapy is highly relevant from both the clinical and the societal perspective.

Randomised clinical trial on exercise therapy in OA

In my opinion, a new randomised clinical trial studying the effectiveness of prolonged exercise therapy, including principles of psycho-educational programmes is desirable. Combining the effectiveness of exercise therapy with the effectiveness of psycho-educational principles might result in a highly promising intervention as regards clinical effectiveness. Moreover, implementation of such an intervention in physiotherapy practice would be rather simple, because of the great similarity between it and present-day practice. In the design and conduct of such a trial the requirements for sufficient validity and power should be met.

REFERENCES

1. Dieppe P. The classification and diagnosis of osteoarthritis. In: Kuettner KE, Goldberg VM, eds. Osteoarthritic disorders. Rosemont IL: American Academy of Orthopaedic Surgeons, 1995: 5-12.
2. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthr Rheum 1991;34:505-14.
3. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. Arthr Rheum 1986;29:1039-49.
4. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. Ann Rheum Dis 1957;16:494-502.
5. Felson DT, Naimark A, Anderson J, Kazis L, Castelli W, Meenan RF. The prevalence of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. Arthr Rheum 1987;30:914-8.
6. Windt DAMW van der, Koes BW, Aarts M van, Heemskerk MAMB, Bouter LM. Practical aspects of conducting a randomised trial in primary care: patient recruitment and outcome assessment (submitted for publication).
7. Hurley MV, Newham DJ. The influence of arthrogenous muscle inhibition on quadriceps rehabilitation of patients with early, unilateral osteoarthritic knees. Br J Rheum 1993;32:127-31.
8. Ettinger WH, Burns R, Messier SP Applegate W, Rejeski WJ, Morgan T, Shumaker S, Berry MJ, O'Toole M, Monu J, Craven T. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. JAMA 1997;277:25-31.
9. Kovar PA, Allegrante JP, MacKenzie CR, Peterson MGE, Gutin B, Charlson ME. Supervised fitness walking in patients with osteoarthritis of the knee. Ann Intern Med 1992;116:529-34.
10. Huskisson EC. Measurement of pain. Lancet 1974,1127-31.
11. Carlsson AM. Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. Pain 1983;16:87-101.
12. Keefe FJ. Block AR. Development of an observation method for assessing pain behaviour in chronic low back pain patients. Behav Ther 1982;13:363-75.
13. Keefe FJ, Caldwell DS, Queen K, Gil KM, Martinez S, Crisson JE, Ogden W, Nunley J. Osteoarthritic knee pain: a behavioral analysis. Pain 1987;28:309-21.
14. Dekker J, Tola P, Aufdemkampe G, Winckers M. Categories of pain behaviour in osteoarthritis patients. Physioth Theory Pract 1993;9:157-63.
15. Steultjens MPM, Dekker J, Baar ME van, Oostendorp RAB, Bijlsma JWJ. Consistency and validity of an observational method for assessing disability in mobility in patients with osteoarthritis. Submitted for publication.
16. Altman RD, Brandt KD, Hochberg MC, Moskowitz RM, for the Task Force. Design and conduct of clinical trials in patients with osteoarthritis; recommendations from a task force of the Osteoarthritis Research Society. Osteoarthritis Cartilage 1996;4:217-43.

17. Hochberg MC, Altman RD, Brandt KD, Moskowitz RM, for the Task Force. Design and conduct of clinical trials in patients with osteoarthritis; preliminary recommendations from a task force of the Osteoarthritis Research Society. J Rheumatol 1997; 24:792-4.
18. Guccione AA. Arthritis and the process of disablement Phys Ther 1994:74;408-14.
19. Ettinger WH, Afable RF. Physical disability from knee osteoarthritis: the role of exercise as an intervention. Med Sci Sports Exer 1994;26:1435-40.
20. Verbrugge LM, Jette AM. The disablement process. Sco Sci Med 1994;38:1-14.
21. Beurskens AJHM, Bouter LM, Heijden GJMG van der. *Compliance-bepaling bij oefentherapie. Een beoordeling van de beschikbare instrumenten.* (Assessment of compliance in exercise therapy. An evaluation of instruments available). Ned Tijdschr Fysiother 1992;102:2-7.
22. Turk DC, Salovey P. Litt MD. Compliance; a cognitive-behavioural perspective. In: Gerber KE, Nehemkis AM, eds. Compliance: the dilemma of the chronically ill. New York: Springer Publishing Company, 1986:44-72.
23. Baar ME van, Dekker J, Bijl D, Weijnen T, Bijlsma JWJ, Oostendorp RAB, Charro F de, Lemmens JAM, Voorn ThB. *Het effect van oefentherapie bij artrose van heup of knie. Eindrapportage.* (Effectiveness of exercise therapy in osteoarthritis of hip or knee. Final report). (Internal report) Utrecht, the Netherlands: NIVEL, 1997.
24. Kerssens JJ, Sluijs EM, Knibbe JJ, Verhaak PFM, Hermans IMJ. Adherence and self-care activities of patients with back pain (submitted for publication).
25. Bakker C, Hidding A, Linden SJ van der, Doorslaer E van. Cost effectiveness of group physical therapy compared to individualized therapy in ankylosing spondilytis. A randomized clinical trial. J Rheumatol 1994; 21: 264-8.
26. Dickersin K. The existence of publication bias and risk factors for its occurrence. JAMA 1990;263:1385-9.
27. Tulder MW van, Assendelft WJJ, Koes BW, Bouter LM. Method guidelines for systematic reviews in the cochrane collaboration back review group for spinal disorders. Spine 1997; 22:2323-30.
28. Heiden GJMG van der, Windt DAMW van der, Winter AF de. Physiotherapy for patients with soft tissue shoulder disorders: a systematic review of randomised clinical trials. BMJ 1997;315:25-30.
29. Begg C, Cho M, Eastwood S, Horton R, Moher D, Olkin I et al. Improving the quality of reporting of randomized clinical trials: the CONSORT statement. JAMA 1996;276:637-9.
30. Valk RWA van der, Dekker J, Baar ME van. *De fysiotherapeutische behandelingen van patienten met artrose: een beschrijvend onderzoek.* (Physiotherapy for patients with osteoarthritis: a description). In: Dekker J, Baar ME van. *Beleidsgericht evaluatie- en effectonderzoek extramurale fysiotherapie (BEEF) Eindrapport.* Utrecht the Netherlands: NIVEL, 1995.
31. Kerssens JJ, Sluijs EM, Knibbe JJ, Verhaak PFM, Hermans IMJ. Back care instructions in physical therapy; a trend analysis of individual back care problems (submitted for publication).

32. Friedrich M, Cermak T, Maderbacher P. The effect of brochure versus therapist teaching on patients performing therapeutic exercise and on changes in impairment status. Phys Ther 1996:76:1082-8.
33. Dishman RK. Compliance/Adherence in health related exercise. Health Psychol 1982:1237-67.
34. Haynes RB. Determinants of compliance: the disease and the mechanics of treatment. In Haynes RB, Taylor DW, Sackett DL, eds. Compliance in health care. Baltimore: The Johns Hopkins University Press 1979: 49-62.
35. Slemenda C, Brandt KD, Heilman DK, Mazzuca S, Braunstein EM, Katz BP, Wolinski FD. Quadriceps weakness and osteoarthritis of the knee. Ann Intern Med 1997;127:97-104.
36. Hirano PC, Laurent DD, Lorig K. Arthritis patient education studies, 1987-1991: a review of the literature. Pat Educ Couns 1994;24:9-54.
37. Sluijs EM, Knibbe JJ. Patient compliance with exercises: different theoretical approaches to short-term and long-term compliance. Pat Educ Couns 1991;17:191-204.
38. Hopman-Rock M. Coping with osteoarthritis of the knee and/or hip: the development of a lifestyle programme. Leiden the Netherlands, TNO Preventie en gezondheid, 1994.

SUMMARY

In **Chapter 1** an introduction to this thesis is given. The present study aimed at investigating the effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee. Osteoarthritis of the hip or knee is highly prevalent. OA is characterised by a progressive loss of articular cartilage in combination with increased activity of underlying subchondral bone. The main symptoms of OA are pain and disability. Especially OA in the hip or knee is a strongly disabling condition, leading to disability in ambulation and transfer.

Since there is no known cure for OA, treatment is aimed at the consequences of disease. Goals of treatment are to control pain and other symptoms, minimise disability and educate the patient and his or her family about the disease and its treatment.

Exercise therapy is a frequently applied intervention in patients with OA of the hip and knee. However, at the start of the present study the scientific evidence for the effectiveness of exercise therapy in these patients was limited. We designed and conducted a randomised clinical trial into the effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee. We studied the effectiveness of a 12-week exercise programme given by a physiotherapist in primary care. It was hypothesised that exercise therapy would have beneficial effects in patients with OA of the hip and knee. The data were used also to study to what extent various clinical characteristics of the patients were associated with pain and disability. The following research questions were formulated:

1. What is the separate contribution of articular, kinesiological and psychological characteristics to pain and disability in patients with OA of the hip or knee?
2. What is the short-term effectiveness of exercise therapy in patients with osteoarthritis of hip or knee?
3. Which groups of patients with osteoarthritis of hip or knee benefit particularly from exercise therapy?
4. What is the long-term effectiveness of exercise therapy in patients with osteoarthritis of hip or knee?
5. What is the cost-effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee?

6. What is the evidence available on the effectiveness of exercise therapy in patients with OA of the hip or knee?

The objective of **Chapter 2** was to determine to what extent articular, kinesiological and psychological factors each contribute to pain and disability in patients with OA of the hip or knee, after controlling for other factors. Earlier studies have shown that pain and disability in OA were associated with these factors, but failed to control for the other factors.

Baseline data were used from 200 patients included in our randomised clinical trial. Dependent variables included pain (assessed with a visual analogue scale), observed disability (performance of standardised tasks) and self-reported disability (questionnaire). The independent factors include joint degeneration (radiographs), muscle strength (hand-held dynamometer) range of motion (goniometer), pain coping (behavioural and cognitive strategies) and psychological well-being (anxiety, depression, cheerfulness).

Pain was found to be associated with muscle weakness and pain coping. Disability was found to be associated with muscle weakness, range of motion, pain, pain coping and psychological well-being. Both pain and disability were most strongly related with kinesiological characteristics and pain coping.

In **Chapter 3** we examined the **s**hort-term effectiveness of exercise therapy in patients with OA of the hip and knee. A randomised single blind, clinical trial was conducted in primary care. Patients with osteoarthritis of hip or knee, according to the criteria of the American College of Rheumatology were included. Two interventions were compared. The patients in the exercise therapy group were given exercise therapy individually by a physiotherapist in primary care. Exercise therapy was given according to a written protocol. Content and intensity and frequency could be tailored to the patient's needs. In addition, their GP provided patient education (including a brochure), and medication if necessary. Treatment of the control group was restricted to treatment by their GP, as described above (patient education and medication if necessary). The treatment period was 12 weeks plus 24 weeks of follow-up.
The primary outcome measures were pain, medication use (non-steroidal anti-inflammatory drugs, NSAIDs) and observed disability.

We randomised 201 patients, 99 patients were allocated to exercise therapy and 102 patients to the control treatment. 191 patients were assessed at 12 weeks, after completion of exercise therapy. Exercise therapy was associated with a reduction of pain in the past week (difference in change -17.0; 95%CI -23.6, -10.4) and observed disability (-0.19; 95%CI -0.38,-0.01). Effect-sizes were medium (0.58) and small (0.28) respectively. No effect of exercise therapy was found for the use of

NSAIDs. Additional beneficial effects ($p \leq 0.05$) were found on three secondary outcome measures: for the use of paracetamol (effect-size=0.33), global effect as perceived by the patient (effect-size=0.68) and muscle strength of the hip (effect-size=0.34). The effectiveness of exercise therapy was similar in patients with OA of the hip and in OA of the knee.

Thus, after twelve weeks exercise therapy is effective in reducing pain and disability. The size of the effects is medium and small, respectively.

In **Chapter 4** we investigated whether specific groups of OA patients particularly benefit from exercise therapy. This analysis was based on the short-term effectiveness (at 12 weeks). Beneficial effects were expected in 1) patients with relatively high levels of impairments (muscle weakness and reduced range of motion) and disability and in 2) patients with an emotional or catastrophising reaction to pain.

Analysis of covariance was used to examine the interaction between subgroups of OA patient and exercise therapy. None of our hypotheses were confirmed. In general, the effectiveness of exercise therapy was similar, regardless of the patient's baseline level; of muscle strength, ROM, disabilities and paincoping strategies.

In addition, effect modification by characteristics of patients and characteristics of physiotherapy treatments were studied in an exploratory analysis. Characteristics of patients include demographic and clinical features. Characteristics of physiotherapy treatment refer to specific treatment goals and the patient's compliance. These analyses indicated beneficial effects of exercise therapy in patients without radiological OA, in patients with complaints of recent onset and in patients who complied to exercise therapy.

In conclusion, only limited evidence was found for the existence of subgroups of patients in whom exercise therapy has beneficial effects. Specification of the indication for referral for exercise therapy in patients with OA of the hip or knee is not yet possible.

In **Chapter 5** the long-term effectiveness of exercise therapy in OA of the hip or knee was examined. The effects of exercise therapy at 12 and 24 weeks after completion of the exercise therapy program were reported.

At 24 weeks 184 patients were evaluated and 183 patients completed the trial at 36 weeks. At 24 weeks, 12 weeks after completion of exercise therapy a beneficial effects was found for pain past week (difference in change -11.5; 95% CI -19.7,-3.3) Compared to week 12 the size of the effect had declined. No effects were found for the use of NSAIDs and observed disability. At 36 weeks no effects were found on the primary outcome measures. With regard to the secondary outcome measures, beneficial effects were found at 24 weeks and 36 weeks for the use of paracetamol

(effect size 0.32 at both assessments) and patient's global perceived effect (effect size 0.50 and 0.35 respectively).

In addition, exploratory analyses were performed to study the prognostic value of patients' characteristics for long-term outcome of exercise therapy. These characteristics included demographic characteristics, clinical features, kinesiological characteristics, pain coping strategies, level of physical activity, psychological well-being and compliance with exercise therapy. A beneficial long-term outcome was found in patients with overweight at baseline and in patients with a relatively low level of the specific pain coping strategy (transformation of pain). However, given the high number of performed tests (n=62), it is entirely possible that these results are due to chance. We did not find a relationship between compliance to exercise therapy and beneficial long-term outcome.

In conclusion, beneficial post-treatment effects of exercise therapy decline over time and finally disappear. As yet, is it unclear which patient characteristics are related to beneficial long-term outcome.

In **Chapter 6** we examined the cost-effectiveness of exercise therapy in patients with OA of the hip or knee. Both direct costs, related to health care costs of patients seeking therapy, and indirect costs, related to production losses, were assessed. The effectiveness of exercise therapy was assessed using general health questionnaires, including the Nottingham Health profile, the Karnofski Performance Index and the EuroQol-5D.

After 12 weeks total mean costs per patient in the exercise therapy group is Dfl 699, compared to Dfl 332 in the control group (difference Dfl 367) After 36 weeks the total mean costs per patient amounted to Dfl 1823 in the exercise therapy group and Dfl 1442 in the control group (difference Dfl. 381). The higher costs in the exercise therapy group mainly reflect the costs of exercise therapy itself. In addition, higher costs of specialist care and hospitalisation were found. These costs were partly compensated by the lower costs of home care and loss of production.

Beneficial effects of exercise therapy were found, if assessed by general health questionnaires. After 12 weeks, beneficial effects were found on the dimensions pain and energy of the NHP (effect sizes 0.40 and 0.27 respectively). After 36 weeks beneficial effects were found on the dimension energy of the NHP and the thermometer of the EQ-5D (effect sizes 0.29 and 0.31 respectively).

A cost-effectiveness ratio was calculated, being the costs per percent point improvement on the EQ-5D-index. The cost-effectiveness ratio was Dfl. 414 in the exercise therapy group and Dfl. 481 in the control group.

The consequences for the costs at the societal level of an increased referral for exercise therapy were calculated. A 10 % increase in referrals to a physiotherapist

would result in a 0.5% increase of societal costs of treatment in patients with OA (Dfl. 1 001 000 - Dfl. 1 502 000 per year). National expenditure on physiotherapy would increase with 0.1% to 0.2%.

We concluded that extra costs per patient of exercise therapy are small. Exercise therapy is effective in reducing pain and increasing energy, although the size of effects is medium to small. Societal costs of treatment of OA by general practitioner and physiotherapist rise as a result of increased referrals. However, the rise of the total societal costs can be characterised as modest.

In **Chapter 7** we reviewed the evidence available on the effectiveness of exercise therapy in patients with OA of the hip or knee. We focused on the effects on pain, self-reported disability, observed disability and patient's global assessment of effect.

A comprehensive computerised literature search of Medline, Embase and Cinahl was carried out. Randomised clinical trials on exercise therapy of the hip or knee were selected if treatment had been randomly allocated and if pain, self-reported disability, observed disability or patient's global assessment of effect had been used as outcome measures.

We assessed the methodological quality and power of 11 randomised clinical trials. Six of the 11 assessed trials satisfied at least 50% of the validity criteria. Most prevalent shortcomings concerned report or control for co-interventions. Methodological assessment was hampered most often by incomplete information on randomisation, compliance to therapy control for co-interventions in the design and blinding of outcome assessment.

A best evidence synthesis was performed, in which studies were weighted as to 1) the validity and 2) power. Effect sizes were calculated to enable direct comparison between trials. Conclusions were primarily based on two studies with both acceptable validity ($\geq$50%of criteria) and sufficient power ($\geq$0.80). These studies indicated small to moderate favourable effects of exercise therapy on pain, small favourable effects on both disability outcome measures and moderate to great favourable effects according to the patient's global assessment of effect.

In conclusion, the evidence available indicates beneficial effects of exercise therapy in patients with OA of the hip or knee.

In **Chapter 8** we discussed the main results of our study into the effectiveness of exercise therapy in OA of the hip and knee. Firstly, some general issues were put forward concerning the design and conduct of our randomised clinical trial. We discussed the inclusion of both hip and knee patients, the relevance of the clinical criteria of the American College of Rheumatology in general practice and problems and solutions concerning patient inclusion.

Furthermore, we critically reviewed the answers to our research questions. We discussed the limitations of our analyses of the association between articular, kinesiological and psychological characteristics on the one hand and pain and disability on the other hand. With respect to our randomised clinical trial, the consequences of our pragmatic design were discussed. The relevance of our primary outcome measures for future trials in OA were discussed. In addition, the relevance of the high number of secondary outcome measures was critically reviewed. Other topics were the importance of blinded outcome assessment in exercise trials and the possible improvements of assessment of compliance. The necessity of a broad analysis of causative factors, based on theoretical insights, is emphasised in the study of effectiveness of exercise therapy in specific subgroups of patients. Concerning the cost-effectiveness analysis the problems and solutions of the calculation of cost-effectiveness ratios are discussed. Based on our systematic review, possible improvements are described for future trials and for an update of our systematic review on the effectiveness of exercise therapy in OA.

Finally, implications for clinical practice and future research were given. The referral to a physiotherapist for exercise therapy is advocated, as well as the application of exercise therapy in all physiotherapy treatments for OA. Recommendations are given for optimal content and timing of exercise therapy in patients with OA. Implications for future research are given concerning the mechanisms contributing to pain and disability in OA, adaptation of the exercise therapy protocol, content of future subgroupanalyses and design and conduct of a randomised clinical trial studying the effectiveness of exercise therapy including principles of psycho-educational programmes.

SAMENVATTING

Dit proefschrift beschrijft het onderzoek naar de effectiviteit van oefentherapie bij artrose van heup of knie. In **hoofdstuk 1** wordt een inleiding gegeven op dit proefschrift. Artrose van de heup of knie is een veel voorkomende aandoening. Artrose wordt gekenmerkt door een progressief verlies van gewrichtskraakbeen in combinatie met een toegenomen activiteit van het onderliggende subchondrale bot. De belangrijkste klachten bij artrose zijn pijn en functionele beperkingen. Vooral artrose van de heup of knie leidt tot veel functionele beperkingen, met name in mobiliteit.

Vanwege het ontbreken van een curatieve behandeling, is de behandeling gericht op de bestrijding van de symptomen van de aandoening. Behandeldoelen zijn het verminderen van pijn en andere symptomen, minimaliseren van beperkingen en het voorlichten van de patiënt en de familie over de aandoening en mogelijke behandeling.

Oefentherapie is een veel toegepaste behandeling bij patiënten met artrose van de heup of knie. Bij aanvang van ons onderzoek was er echter slechts beperkt wetenschappelijk bewijs voor de effectiviteit van oefentherapie bij deze patiënten.

Wij hebben een gerandomiseerd klinisch experiment uitgevoerd om na te gaan wat het effect was van oefentherapie bij artrose van heup of knie. De oefentherapie bestond uit een behandeling van maximaal 12 weken, gegeven door de fysiotherapeut in de eerste lijn. De verwachting was dat het toepassen van oefentherapie zou leiden tot minder pijn, minder gebruik van medicatie en een betere functionele toestand patiënten met artrose van de heup of knie. De gegevens uit het onderzoek zijn tevens gebruikt voor onderzoek naar de mate waarin klinische kenmerken van patiënten samenhangen met pijn en beperkingen. De volgende onderzoeksvragen zijn aan de orde gekomen:

1. Wat is de afzonderlijke bijdrage van articulaire, kinesiologische en psychologische factoren aan pijn en beperkingen bij patiënten met artrose van de heup of knie?
2. Wat is de effectiviteit van oefentherapie bij patiënten met artrose van heup of knie na 12 weken?
3. Welke patiënten met artrose van heup of knie hebben vooral baat bij oefentherapie?
4. Wat is de effectiviteit van oefentherapie bij patiënten met artrose van de heup of knie op lange termijn (24 en 36 weken)?

5. Wat is de kosten-effectiviteit van oefentherapie bij patiënten met artrose van heup of knie?
6. Welk bewijs is er in de literatuur voor de effectiviteit van oefentherapie bij artrose van heup of knie?

Het doel van **hoofdstuk 2** was na te gaan in welke mate articulaire, kinesiologische en psychologische factoren ieder afzonderlijk bijdragen aan pijn en beperkingen bij patiënten met artrose van de heup of knie. Eerder onderzoek heeft aangetoond dat pijn en beperkingen bij artrose met deze factoren samenhangen. Echter in dat onderzoek werd niet gecontroleerd voor de andere factoren.

Er zijn gegevens gebruikt van de eerste meting bij 200 patiënten die deelnamen aan ons gerandomiseerd klinisch experiment. Afhankelijke variabelen waren pijn (gemeten met een visueel analoge schaal), geobserveerde beperkingen (uitvoering van gestandaardiseerde taken) en gerapporteerde beperkingen (vragenlijst). De onafhankelijke variabelen waren gewrichtsdegeneratie (röntgenfoto's) spierkracht (handheld dynamometer), bewegingsuitslag van gewrichten (goniometer), pijncoping (omgaan met pijn middels gedragsmatige en cognitieve strategieën) en psychologisch welbevinden (somberheid, opgewektheid en angst),

Pijn was geassocieerd met relatief lage spierkracht en pijncoping. Functionele beperkingen gingen samen met relatief geringe spierkracht, een beperkte bewegingsuitslag, pijn, pijncoping en een relatief laag psychologisch welbevinden. Zowel pijn als beperkingen waren vooral sterk geassocieerd met kinesiologische kenmerken en pijncoping.

In **hoofdstuk 3** is nagegaan wat de effectiviteit van oefentherapie na 12 weken is bij patiënten met artrose van heup of knie. Wij hebben een gerandomiseerd enkelblind klinisch experiment uitgevoerd in de eerstelijns gezondheidszorg. Patiënten met artrose van heup of knie, volgens de criteria van het American College of Rheumatology, werden ingesloten in het onderzoek. Twee behandelingen werden vergeleken. De patiënten in de oefentherapie groep ontvingen individuele oefentherapie, gegeven door fysiotherapeuten werkzaam in de eerste lijn. De oefentherapie werd gegeven volgens een schriftelijk protocol. Inhoud, intensiteit en frequentie van de behandeling konden worden aangepast aan de gezondheidstoestand van de patiënt. Daarbij ontvingen de patiënten van hun huisarts schriftelijke voorlichting over artrose, en medicatie indien noodzakelijk. De behandeling van de controlegroep is beperkt tot de behandeling door de huisarts, namelijk voorlichting over de aandoening en medicatie indien noodzakelijk. De behandelperiode duurde maximaal 12 weken, met een follow-up van 24 weken. De primaire uitkomstmaten waren pijn, het gebruik van niet-steroide anti-

inflammatoire geneesmiddelen (NSAID's) en geobserveerde beperkingen bij gestandaardiseerde taken

Wij randomiseerden 201 patiënten; 99 patiënten werden toegewezen aan de oefentherapiegroep, 102 patiënten aan de controlegroep. Na 12 weken, na afsluiting van de behandeling, zijn bij 191 patiënten metingen afgenomen. Oefentherapie bleek een aantoonbaar positief effect te hebben op pijn en geobserveerde beperkingen. Er was sprake van een vermindering van pijn in de afgelopen week en van de geobserveerde beperkingen. De verschillen tussen de oefentherapiegroep en de controlegroep waren gemiddeld -17.0 voor pijn (95% betrouwbaarheidsinterval -23.6, -10.4) en -0.19 voor geobserveerde beperkingen (95% betrouwbaarheidsinterval -0.38, -0.01). De grootte van het effect was respectievelijk middelgroot (0.58) en klein (0.28). Geen effect van oefentherapie werd gevonden op het gebruik van niet-steroide anti-inflammatoire geneesmidddelen (NSAID's). Ook voor drie secundaire uitkomstmaten waren positieve effecten ($p<0.05$) van oefentherapie aantoonbaar. De positieve effecten zijn een lager gebruik van paracetamol (effect-grootte = 0.33), een groter door de patiënt ervaren herstel (effect-grootte=0.68) en een toename van de spierkracht rond de heup (effect-grootte=0.34). De effectiviteit van oefentherapie bij patiënten met artrose van de heup was gelijk aan die bij patiënten met artrose van de knie.

Geconcludeerd kan worden dat oefentherapie na 12 weken aantoonbaar effectief is in het verminderen van pijn en beperkingen, de belangrijkste klachten bij deze patiënten. De grootte van de effecten kan worden gekarakteriseerd als klein tot middelgroot.

In **hoofdstuk 4** is de vraag onderzocht bij welke subgroepen van patiënten de effecten van oefentherapie nu vooral optreden. Deze analyse was gebaseerd op de effectiviteit van oefentherapie na 12 weken. Verwacht werd dat het effect van oefentherapie vooral zou optreden bij 1) patiënten die voor de behandeling een relatief slechte spieren/of gewrichtsfunctie hadden of een hoog niveau van beperkingen en bij 2) patiënten die angstig op pijn reageren.

Het effect van de interactie tussen subgroepen van artrosepatiënten en behandeling is getoetst met covariantie-analyse. Geen van onze verwachtingen is bevestigd. De effectiviteit van oefentherapie was in het algemeen even groot, ongeacht de uitgangssituatie van de patiënt ten aanzien van spierkracht, bewegingsuitslag, functionele beperkingen en pijncoping.

Aanvullend is voor een aantal andere kenmerken uit de medische anamnese en de fysiotherapeutische behandeling nagegaan of deze van invloed waren op het effect van oefentherapie. De kenmerken uit de medische anamnese betroffen demografische en klinische kenmerken. Kenmerken van de fysiotherapeutische behandeling betroffen behandeldoelen en therapietrouw van de patiënt. Uit deze analyses kwamen slechts

enkele aanwijzingen. Mogelijk zijn het al dan niet hebben van radiologische aangetoonde afwijkingen aan het gewricht, de duur van de klachten en de therapietrouw van de patiënt van belang voor de uitkomst van oefentherapie.

Geconcludeerd moet worden dat de informatie die beschikbaar is op het moment van verwijzen naar de fysiotherapeut nauwelijks aanwijzingen geeft over welke patiënten nu vooral baat hebben bij oefentherapie. Op dit moment kan dus geen duidelijke toespitsing van de indicatiestelling voor oefentherapie bij artrose worden gegeven.

In **hoofdstuk 5** is nagegaan wat de effectiviteit van oefentherapie op lange termijn is bij artrose van heup of knie. De effecten van oefentherapie na 24 en 36 weken, 12 en 24 weken na afloop van de behandeling, worden gepresenteerd.

Na 24 weken zijn bij 184 patiënten metingen afgenomen; 183 patiënten namen ook deel aan de laatste metingen 36 weken na de start van het onderzoek. Na 24 weken, 12 weken na de afsluiting van de behandelperiode, was een positief effect aantoonbaar voor pijn. Het verschil tussen de oefentherapiegroep en de controlegroep was -11.5 (95% betrouwbaarheidsinterval -19.7;-3.3). Ten opzichte van week 12, onmiddellijk na afloop van de behandeling, is het effect kleiner geworden. Geen effecten zijn aanwijsbaar ten aanzien van het gebruik van NSAID's en geobserveerde beperkingen. Na 36 weken kon geen positief effect meer worden aangetoond op primaire uitkomstmaten.
Wat betreft de secundaire uitkomstmaten zijn positieve effecten aantoonbaar - zowel na 24 weken als na 36 weken - voor het gebruik van paracetamol (effect-grootte 0.32 op beide meetmomenten) en het ervaren herstel (effect-grootte 0.50 resp. 0.35).

Aanvullend is een exploratieve analyse gedaan naar de voorspellende waarde van patiëntkenmerken voor de uitkomst van oefentherapie op langere termijn. De kenmerken betroffen demografische factoren, ziektekenmerken, kinesiologische kenmerken, pijncoping-strategieën, het niveau van lichamelijke activiteit, psychologisch welbevinden en therapietrouw. Een positief effect op lange termijn werd gevonden bij patiënten met overgewicht bij aanvang van het onderzoek en patiënten met een relatief laag niveau van een specifieke pijncoping strategie (pijn transformatie). Gezien het grote aantal uitgevoerde toetsen (n=62) kunnen deze resultaten echter volledig berusten op toeval. We hebben geen samenhang kunnen aantonen tussen therapietrouw en een positief effect op de lange termijn.

Geconcludeerd kan worden dat positieve effecten van oefentherapie na afloop van de behandeling geleidelijk kleiner worden en uiteindelijk verdwijnen. Op dit moment is het onduidelijk welke kenmerken van patiënten samenhangen met een positief van oefentherapie op de lange termijn.

In **hoofdstuk 6** is de vraag naar de kosten-effectiviteit van oefentherapie bij artrose van heup of knie onderzocht. Wat is de verhouding tussen de kosten en baten van een behandeling met oefentherapie bij patiënten met artrose van heup of knie? Zowel directe kosten, samenhangend met kosten in de gezondheidszorg door het hulp zoeken van patiënten, als de indirecte kosten, samenhangend met productieverlies zijn vastgesteld. De effectiviteit van oefentherapie is bepaald met behulp van generieke meetinstrumenten voor vaststelling van de algemene gezondheidstoestand, namelijk de Nottingham Health Profile (NHP), de Karnofski Performance Index (KPI) en de EuroQol-5D (EQ-5D).

Na 12 weken zijn de gemiddelde kosten per patiënt in de oefentherapiegroep Fl. 699,-, vergeleken met Fl. 332,- in de controle groep. Het verschil tussen beide groepen is Fl. 367,-. Na 36 weken bedragen de totale kosten per patiënt gemiddeld Fl. 1823,- in de oefentherapiegroep en Fl. 1442,- in de controlegroep. Het verschil tussen beide groepen bedraagt nu Fl. 381,-. De hogere kosten in de oefentherapiegroep worden vooral veroorzaakt door de kosten van de oefentherapiebehandeling. Ook zijn de kosten van medisch specialistische hulp en ziekenhuisopname in deze groep iets hoger. Deze hogere kosten worden gedeeltelijk gecompenseerd door de lagere kosten van thuiszorg en productieverlies.

Ook met de generieke meetinstrumenten kon een positief effect van oefentherapie worden vastgesteld. Na 12 weken was een positief effect aantoonbaar voor de dimensies pijn en energie van de NHP (effect-grootte respectievelijk 0.40 en 0.27). Na 36 weken werden positieve effecten gevonden voor de dimensie energie van de NHP en de thermometer van de EQ-5D (effect-grootte respectievelijk 0.29 en 0.31).

Er is een kosten-effectiviteitsratio berekend, namelijk de kosten per procent verbetering op de EQ-5D-index. Deze kosten-effectiviteitsratio was Fl. 414,- in oefentherapiegroep en Fl. 481,- in de controlegroep.

De gevolgen voor de kosten op maatschappelijk niveau van een toename van verwijzingen voor oefentherapie zijn bescheiden. Een toename van 10% in de verwijzingen naar een fysiotherapeut zou leiden tot een toename van 0.5% in de maatschappelijke kosten van de behandeling van patiënten met (Fl. 1.001.000 - Fl. 1.502.000 per jaar). De nationale uitgaven voor fysiotherapie zouden toenemen met 0.1% tot 0.2%.

Wij concludeerden dat de extra kosten per patiënt voor oefentherapie beperkt zijn. Oefentherapie is effectief in de vermindering van pijn en vergroting van energie, hoewel de grootte van de effecten niet moet worden overschat. De maatschappelijke kosten van de behandeling van artrose door de huisarts en fysiotherapeut nemen toe bij een toename van het aantal verwijzingen voor oefentherapie. Echter, de toename van de totale maatschappelijke kosten kan worden gekenschetst als beperkt.

In **hoofdstuk 7** wordt een overzicht gegeven van de onderzoeken naar de effectiviteit van oefentherapie bij artrose van heup of knie. In dit overzicht worden de beschikbare publicaties kritisch beoordeeld en systematisch besproken. Wij richtten ons vooral op de effecten ten aanzien van pijn, gerapporteerde beperkingen, geobserveerde beperkingen en de inschatting van effect door de patiënt.

Een uitgebreide zoekactie, met behulp van de computer is uitgevoerd in de gegevensbestanden Medline, Embase en Cinahl. Gerandomiseerde klinische experimenten over oefentherapie bij artrose van heup of knie werden geselecteerd voor nader onderzoek indien de behandeling was toegewezen door randomisatie (loting) en indien een relevante uitkomstmaat was gebruikt (pijn, gerapporteerde beperkingen, geobserveerde beperkingen, de inschatting van de patiënt).

We hebben de methodologische kwaliteit en power beoordeeld van in totaal 11 gerandomiseerde klinische experimenten. Zes van de 11 experimenten voldeden aan 50% van de criteria voor validiteit. De meest voorkomende tekortkomingen betroffen de rapportage en/of controle over co-interventies. De methodologische beoordeling werd vooral bemoeilijkt door onvolledige informatie over randomisatie, therapietrouw, controle voor co-interventies in de onderzoeksopzet en blindering van de metingen.

Een zogenaamde "best-evidence" synthese is uitgevoerd, waarin de studies zijn gewogen naar 1) de validiteit en 2) de power. Voor vergelijking van de verschillende studies zijn effect-groottes berekend. De conclusies van dit hoofdstuk zijn voornamelijk gebaseerd op de twee onderzoeken met zowel acceptabele validiteit ($\geq$50% van de criteria positief) als voldoende power ($\geq$0.80). Deze onderzoeken wijzen op een klein tot middelgroot positief effect van oefentherapie ten aanzien van pijn, kleine positieve effecten op beide uitkomstmaten betreffende beperkingen en een middelgroot tot groot positief effect zoals dat wordt ervaren door de patiënt.

Het beschikbare onderzoek wijst dus in de richting van positieve effecten van oefentherapie bij patiënten met artrose van heup of knie.

In **hoofdstuk 8** worden de belangrijkste resultaten van ons onderzoek naar de effectiviteit van oefentherapie bij artrose van heup of knie besproken. Ten eerste worden een aantal algemene punten besproken over de opzet en uitvoering van ons gerandomiseerd klinisch experiment. Dit betreft de inclusie van zowel heuppatiënten als kniepatiënten, de relevantie van de klinische criteria van het American College of Rheumatology voor de huisartspraktijk en de problemen en oplossingen betreffende de inclusie van patiënten.

Vervolgens worden onze antwoorden op onderzoeksvragen kritisch besproken. De beperkingen van onze analyses naar de samenhang tussen articulaire, kinesiologische en psychologische kenmerken enerzijds en pijn en beperkingen anderzijds worden besproken. Ten aanzien van ons gerandomiseerd klinisch experiment worden

de gevolgen van een pragmatische onderzoeksopzet aangegeven. Ook wordt de relevantie van onze primaire en secundaire uitkomstmaten besproken. Andere onderwerpen die aan de orde komen zijn het belang van geblindeerde metingen in oefentherapie-experimenten en mogelijke verbeteringen in het meten van therapietrouw. De noodzaak van een brede, door theorie gestuurde analyse van causale factoren, wordt benadrukt bij onderzoek naar de effectiviteit van oefentherapie bij specifieke subgroepen van patenten. Betreffende de kosten-effectiviteitsanalyse, worden de problemen en oplossingen bij de berekening van kosten-effectiviteitsratio's besproken. Op basis van de resultaten van het systematische literatuuroverzicht worden mogelijke verbeteringen beschreven voor toekomstige experimenten en voor een bijstelling van onze systematische review over de effectiviteit van oefentherapie bij artrose.

Tenslotte, worden implicaties voor de klinische praktijk en toekomstig onderzoek gegeven. De verwijzing van artrosepatiënten naar de fysiotherapeut(e) wordt bepleit, evenals het gebruik van oefentherapie in alle fysiotherapeutische behandelingen van artrose. Aanbevelingen worden gegeven voor de optimale inhoud en 'timing' van oefentherapie bij patiënten met artrose. Aanbevelingen voor toekomstig onderzoek betreffen de mechanismen die bijdragen aan pijn en beperkingen bij artrose, de aanpassing van het protocol voor oefentherapie, de inhoud van toekomstige subgroepanalyses en de opzet en uitvoering van een gerandomiseerd klinisch experiment naar de effectiviteit van oefentherapie, waarbij gebruik gemaakt wordt van de principes van de psycho-educatieve programma's.

APPENDIX

EXERCISE THERAPY
IN
OSTEOARTHRITIS OF THE HIP OR KNEE:
A PROTOCOL

R.A.B. Oostendorp, J.H. van den Heuvel,
J. Dekker, M.E. van Baar

- Dutch National Institute for Allied Health Professions
  PO Box 1161 - 3800 BD Amersfoort, The Netherlands
  Telephone: ..-3133 4622980 - Fax: ..-3133 4651546

- Netherlands Institute of Primary Health Care
  PO Box 1568 - 3500 BN Utrecht, The Netherlands
  Telephone: ..-3130 2729700 - Fax: ..-3130 2729729

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[1] Original Dutch version, titled 'Oefentherapie bij artrose van heup of knie: een protocol' was made in 1993.

appendix

CONTENTS

INTRODUCTION

Principle

Patients are treated with exercise therapy according to the protocol. In the event that this treatment is harmfull to the patient's health, deviation from the protocol is allowed. Deviations have to be motivated and registered on the registration form.

Frequency of visits and duration of episode

- The duration of a visit is 30 minutes.
- The duration of an episode of care is 12 weeks at most, or shorter if anticipated treatment goals and desired outcomes are achieved.
- Frequency of visits is dependent on the intensity of pain. The pain intensity is measured with a visual analogue scale (VAS).

First visit

- Assess the patient's pain, using the VAS. Patients are categorized into three groups based on their pain. Assess the pain category which applies to the patient.
- Assess the patient's impairments and disabilities. Identify specific goals of treatment. Choose a specific intervention. The presented specific interventions are examples. Personal interpretation -within the boundaries of the protocol- are permitted.
- Give home exercises, patient education and advices for activities of daily living and work. The promotion of safe and regular exercise is of great importance for an optimal outcome of treatment.
- In the event of inflammation, the degree of inflammation has to be assessed. Besides pain medication, rest and exercise within the pain-free zone can be applied.

Follow-up visits

- Reexamine the patients pain every two weeks, using the VAS. Reexamine the patients impairments and disabilities. If necessary, modify or redirect treatment goals and interventions.
- Use the protocol.
- Give home exercises, patient education and advices for activities of daily living and work. The promotion of safe and regular exercise is of great importance for an optimal outcome of treatment.

appendix

TREATMENT PROTOCOL FOR PATIENTS WITH VAS-SCORE 0-30

Frequency
Frequency of visits is one visit a week.

1. Impairment : Muscle performance
Intervention : Active exercises

Impairment	Starting position	Action	Goal
Impaired muscle performance Dimension: Active stability and coordination	Stance on knees One leg bend in hip (90°) and knee (90°), with foot flat on the ground, while the other leg is in kneeling position One foot in front of the other foot Stance	Provoke weighttransfer by exercises with ball, round balancing platform etc. Full weight-bearing	Improvement muscle performance
Impaired muscle performance Dimension: Strength	See above	See above, as well as steps with affected leg first etc. Full weigth-bearing	Improvement muscle performance

2. Impairment : Range of motion
Intervention : Active exercises
Passive exercises

Impairment	Starting position	Action	Goal
Restricted range of motion Dimension: Arthrogenic	Supine/Prone/Lying on the side/Crawling position As described in Mink et al. (340-348; 383-388)	Tractions Second and third degree	Improvement range of motion
Restricted range of motion Myogenic	Supine/Prone/Lying on the side/Crawling position As described in Evjenth and Hamberg (78-115)	Three-dimensional lengthening	Improvement range of motion

3. Disability : Coordination / Elementary sensorimotor skills
Intervention : Active exercises of abilities

Disability	Starting position	Action	Goal
Disability in coordination / elementary sensorimotor skills	Stance/Sit	Walking exercises with increased degrees of complexity Climbing stairs Adjustment gait pattern Adjustment sitting, rising form a chair Bending, squatting	Improvement coordination / elementary sensorimotor skills

4. Disability : Locomotion skills
Intervention : Active exercises of abilities

Disability	Starting position	Action	Goal
Disability in locomotion: walking, cycling	Stance/Sit	Walking, cycling, if desired home trainer/ treadmill	Improvement locomotion skills

5. Patient education, advice and home exercises

A. The promotion of exercise in general is of great importance. This concern activities such as regular walking, cycling and swimming.

B. Advices for adjustment of activities.
Concerning sports:
- reduction of sports training with instants of jumping;
- tailoring sports training with prolonged dynamic load.

Concerning home management, work and leisure activities:
- avoid prolonged static load.

C. Home exercises, derived form the exercises as specified in 1 up to 4, are of great importance for an optimal outcome of treatment.

D. Instruction about loadability and load of the hip and knee region.

appendix

TREATMENT PROTOCOL FOR PATIENTS WITH VAS-SCORE 31-60

Frequency of visits
Frequency of visits is twice a week.

1. Impairment : Pain
Intervention : Active exercises
Passive exercises

Impairment	Starting position	Action	Goal
Pain	As described in Mink et al. (340-348; 383-388) Supine/Lying on the side/Prone	Traction from rest position of joint First and second degree Hold-relax (post-isometric relaxation)	Pain reduction

2. Impairment : Muscle performance
Intervention : Active exercises

Impairment	Starting position	Action	Goal
Impaired muscle performance Dimension: Active stability and coordination	Supine	'Bridging' with resistance on pelvis, one or two feet on supporting surface	Improvement muscle performance
	Lying on the side	Foot on supporting surface or on wall, resistance on pelvis	Idem
	Crawling position	Non-affected leg stretched, resistance to pelvis/leg	Idem
		On the corner of the surface, affected leg on 'rola', resistance to leg	Idem
	Sit	Resistance on pelvis, lateral, forwards, backwards	Idem
	Stance/Stance on 1 leg	Maintenance of position pelvis (horizontal)	Idem
Dimension: Strength	Supine/Lying on the side	Roll over with initiation from the leg	Improvement muscle performance
	Supine	Three-dimensional movement patterns of leg	Idem
	Crawling position	Three-dimensional movement patterns of leg	Idem

3. Impairment : Range of motion
Intervention : Passive exercises
Active exercises

Impairment	Starting position	Action	Goal
Restricted range of motion Dimension: Arthrogenic	As described in Mink cs (340-348; 383-388)	Tractions Second and third degree	Improvement range of motion
Restricted range of motion Dimension: Myogenic	As described in Evjenth and Hamberg (78-115)	Three-dimensional Hold-Relax	Improvement range of motion

4. Disability : Coordination / Elementary sensorimotor skills
Intervention : Active exercises of abilities

Disability	Starting position	Action	Goal
Disability in coordination / elementary sensorimotor skills	Stance/Sit/Supine	Adjustment gait pattern Adjustment sitting, reclining, rising from a chair, from a bed Bending, squatting, kneeling	Improvement coordination / elementary sensorimotor skills

5. Disability : Locomotion
Intervention : Interventions to reduce load

Disability	Starting position	Action	Goal
Disability in walking	Stance	Prescription and application of a cane (contralateral), according to the patient's needs and the therapist's view	Load reduction

6. Disability : Personal care
Intervention : Active exercises of abilities

Disability	Starting position	Action	Goal
Disability in dressing	Stance/Sit	Training of dressing, especially using skirts, trousers, socks and stockings and shoes including shoelaces	Improvement skills personal care

7. Disability : Domestic skills
Intervention : Active exercises of abilities

Disability	**Starting position**	**Action**	**Goal**
Disabilities in domestic activities	Stance/Sit	Training of shopping, cooking etc.	Improvement domestic activities

8. Patient education, advice and home exercises

A. The promotion of exercise in general is of great importance. This concerns activities such as regular walking, cycling and swimming. All activities ahould be performed within patient's loadability.

B. Advices for adjustment of activities.
Concerning sports:
- cessation of sports training with instants of jumping;
- cessation of sports training with instants of running;
- reduction of sports training with prolonged load during walking.

Concerning home management, work and leisure activities:
- reduction of climbing stairs;
- reduction of instants of lifting and carrying, both with regard to magnitude and duration;
- avoid prolonged static load;
- avoid prolonged dynamic load.

C. Home exercises, derived form the exercises as specified in point 1 up to 7, are of great importance for an optimal outcome of treatment.

D. Instruction about loadability and load of the hip and knee region.

TREATMENT PROTOCOL FOR PATIENTS WITH VAS-SCORE 61+

Frequency of visits
Frequency of visits is three times a week.

1. Impairment : Pain
Intervention : Passive exercises
Active exercises

Impairment	Starting position	Action	Goal
Pain	As described in Mink et al (340-348; 383-388)	Traction from rest position of the joint First degree	Pain reduction
	Supine Lying on the side	Exercise within the pain-free zone	Idem

2. Impairment : Range of motion
Intervention : Active assistive exercises

Impairment	Starting position	Action	Goal
Restricted range of motion Myogenic and arthrogenic	Lying on the side	In direction of flexion and extension, with manual support of the leg Up to limits of ROM	Maintenance of range of motion
	Supine	Abduction as described above Up to limits of ROM	Idem

3. Impairment : Muscle performance
Intervention : Active exercises

Impairment	Starting position	Action	Goal
Impaired muscle performance Dimension: Strength	Supine	Isometric, especially towards extension and abduction Light manual resistance	Maintenance muscle performance
Impaired muscle performance Dimension: Active stability	Supine, knee flexed to 90 degrees, foot on supporting surface	Resistance close to the joint Light manual resistance	Maintenance of muscle performance

4. Disability : Coordination / Elementary sensorimotor skills
Intervention : Active exercises of abilities

Disability	Starting position	Action	Goal
Disability in coordination / elementary sensorimotor skills	Stance/Sit/Supine	Adjustment walking pattern Adjustment sitting, reclining, rising from a chair, from a bed Bending, squatting, kneeling	Improvement coordination / elementary sensorimotor skills

5. Disability : Locomotion
Intervention : Interventions to reduce load

Disability	Starting position	Action	Goal
Disability in walking	Stance	Prescription and application of a cane (contralateral)	Load reduction

6. Disability : Personal care
Intervention : Active exercises of abilities (including assistive and adaptive devices and assistance of other persons)

Disability	Starting position	Action	Goal
Disability in dressing	Stance/Sit	Training of dressing, especially using skirts, trousers, socks and stockings and shoes including shoelaces	Improvement skills personal care

7. Disability : Domestic activities
Intervention : Active exercises of abilities (including assistive and adaptive devices and assistance of other persons)

Disability	Starting position	Action	Goal
Disabilities in domestic activities	Stance/Sit	Training cooking, shopping etc	Improvement domestic skills

8. Patient education, advice and home exercises

A. The promotion of exercise in general is of importance; however without exacerbation of pain. Cycling and swimming is promoted if these activities do not cause pain.

B. Advices for adjustment of activities.
Concerning sports:
- cessation of sports training with prolonged load during walking.

Concerning home management, work and leisure activities:
- climbing stairs one step at a time with preferred leg first and avoid climbing stairs if possible;
- avoid static load;
- avoid dynamic load;
- avoid instants of lifting and carrying.

C. Home exercises, derived form the exercises as specified in point 1 up to 7, are of great importance for an optimal outcome of treatment.

D. Instruction about loadability and load of the hip and knee region.

REFERENCES

American Physical Therapy Association. Guide to Physical Therapy Practice. Physical Therapy 1997; 77, 1163-1650.

Beckers D, Buck M. Het PNF-concept in de praktijk Hoensbroek, the Netherlands: Revalidatie Informatie Centrum, 1988.

Boschma JC. Oefentherapie bij aandoeningen. Utrecht, the Netherlands: Bohn, Scheltema & Holkema, 1985.

Evjenth O, Hamberg J. Muskeldehnung, warum und wie? Eine effektive Behandlungsmethode bei Schmerzen und Bewegungseinschränkung. Zug, Switzerland: Remed Verlag, 1981.

Geers A. Kinesiologie: onderzoek en behandeling van de tonische en fasische spieren. Lochem, the Netherlands: De Tijdstroom, 1988.

Hendriks EJM, Brandsma JW, Heerkens YF, Oostendorp RAB, Nelson RM. Intraobserver and interobserver reliability of assessments of impairments and disabilities. Physical Therapy 1997; 77: 1097-1106.

International Classification of Impairments, Disabilities and Handicaps 1980. Geneva, Switzerland; World Health Organization, 1980.

Mink AJF, ter Veer HJ, Vorselaars JACTh. Functie-onderzoek en manuele therapie. Extremiteiten; deel 2. Eindhoven, the Netherlands, 1983.

Sullivan PE, Markos PD, Minor MAD. PNF: ein Weg zum therapeutischen Uben. Proprioceptive neuromuskulaire Fazilitation: Therapie und klinische Anwendung. Stuttgart, Germany: Fischer, 1985.

APPENDIX

VAS-FORM

To be filled in by the physiotherapist

Name patient : .....

Physical therapist: .....

Date : .....

With this form we would like to get an impression of your pain.

Can you please rate your pain with a clear mark at a right angle on the line at a point which represents the level of your pain.

Please indicate with a clear mark how you have experienced your pain past week

no pain _____ very severe pain

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Dit boekje is de neerslag van het werk van velen. Aan het eigenlijke onderzoek, het gerandomiseerde klinisch experiment, werkten 201 patiënten, en vele huisartsen en fysiotherapeuten actief mee.
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CURRICULUM VITAE

Margriet Elisabeth van Baar werd geboren op 2 oktober 1965 te Zaandam. In 1983 behaalde zij het eindexamen Atheneum-B aan het St. Michael College te Zaandam. Daarna studeerde zij Bewegingswetenschappen aan de Vrije Universiteit te Amsterdam, waar zij in 1989 afstudeerde met als afstudeerrichting Gezondheidkunde met betrekking tot bewegen.

Van mei 1990 tot mei 1991 volgde zij de post-doctorale opleiding Epidemiologisch onderzoek van het Instituut voor Extramuraal Geneeskundig Onderzoek (EMGO-Instituut) aan de Vrije Universiteit te Amsterdam. In 1993 is zij geregistreerd als epidemioloog A.

In 1991 was zij werkzaam bij het Onderzoekscentrum 1e-2e lijn van het Academisch Ziekenhuis van de Vrije Universiteit te Amsterdam. Vanaf 1991 was zij tevens werkzaam bij het NIVEL (Nederlands instituut voor onderzoek van de gezondheidszorg) te Utrecht. Bij het NIVEL heeft zij onderzoek gedaan op het gebied van de fysiotherapie. In 1993 is zij gestart met het onderzoek naar de effecten van oefentherapie bij artrose van heup of knie.

Sinds juni 1998 werkt zij bij het Instituut Maatschappelijke Gezondheidszorg (iMGZ) van de Erasmus Universiteit te Rotterdam.