

Patellofemoral Pain Syndrome and Exercise Therapy

Robbart van Linschoten

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Patellofemoral Pain Syndrome and Exercise Therapy

Het patellofemorale pijnsyndroom en oefentherapie

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Chapter 1

General Introduction

BACKGROUND

Knee complaints constitute the second largest reason for consultation in general practice.¹ Of these knee complaints Patellofemoral Pain Syndrome (PFPS) is seen frequently during adolescence and young adult age. Its clinical presentation is characterised by pain around the patella mainly at activities that load the patellofemoral joint like bending knees, walking stairs or kneeling. Also during and after sporting activities (running, jumping and cycling) these symptoms occur and will often lead to functional disability.² The diagnosis is mainly based on clinical symptoms and by excluding other causes of anterior knee pain (tendinopathy, Osgood Schlatter disease, peri-patellar bursitis, intra-articular pathology, osteoarthritis). The pathophysiology of PFPS is unclear which is also reflected in the various names that have been used throughout the years: 'chondromalacia patellae', 'retropatellar chondropathy' and 'anterior knee pain syndrome'.³

Conservative (non-surgical) treatment strategies are considered to be the first choice in the management of complaints. Relative rest, advice on the good outcome of complaints and a so called 'wait and see' strategy are advised.⁴

Opposed to this passive approach an active strategy has been advocated the last decades especially on encouraging the use of exercise therapy. Although exercise therapy is being used in medical practice more frequently, the clinical effects on PFPS are still under scientific debate.⁵

AIMS OF THE THESIS

The main aim of this thesis was to study the clinical effects and cost effectiveness of exercise therapy for patellofemoral syndrome through the execution of a clinical trial and by reviewing the literature. Furthermore the effectiveness of exercise therapy was studied in relation to other conservative strategies. Besides, this thesis studies the present strategies for PFPS and other non-traumatic knee complaints in general practice.

OUTLINE OF THE THESIS

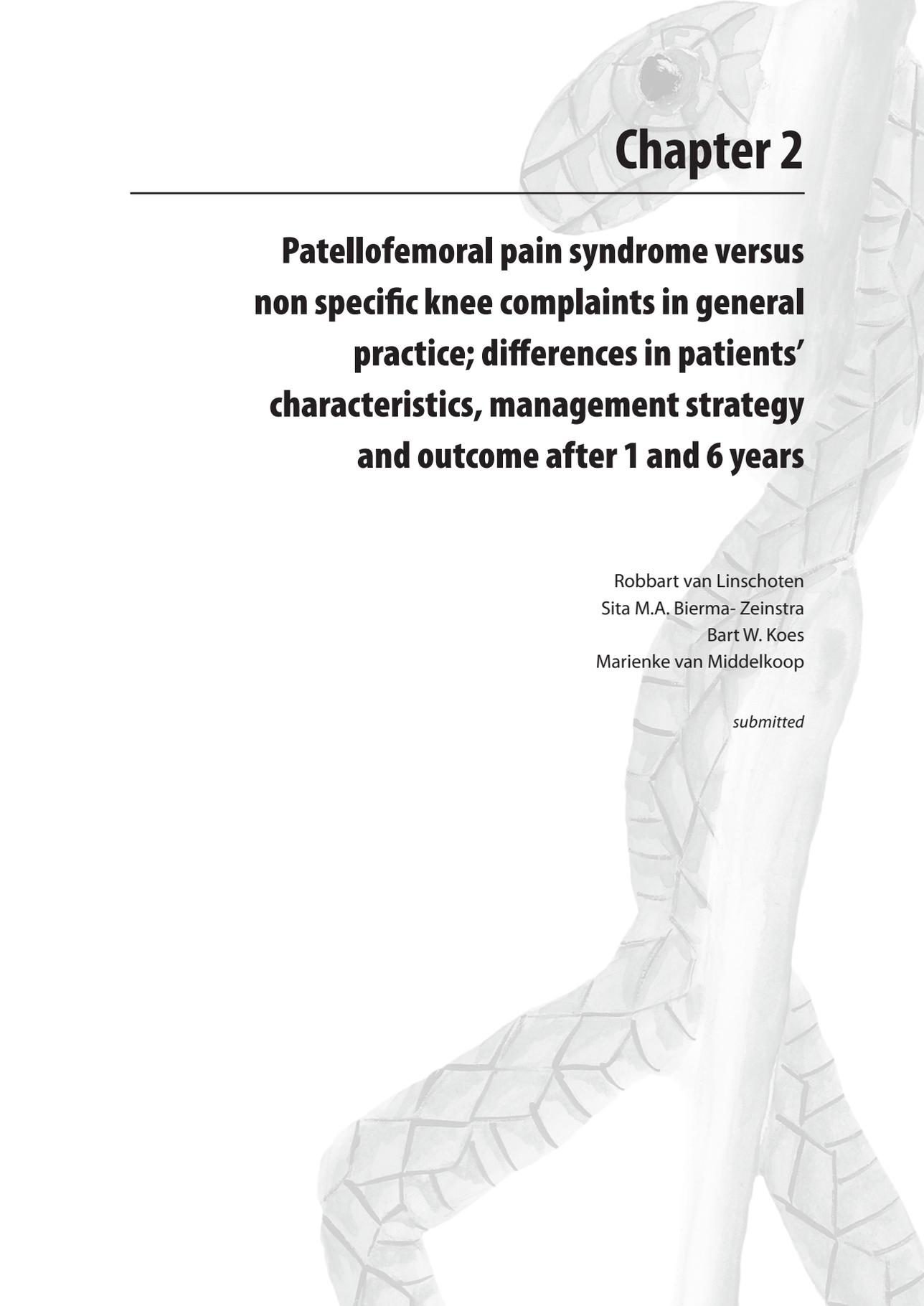
In **Chapter 2** the initial management strategy and long term outcome of PFPS in general practise is described. **Chapter 3** describes the characteristics of sports participants and non-sports participants with knee complaints. In **Chapter 4** the design of a randomised clinical trial (RCT) on exercise therapy for PFPS is described. The results of this RCT are presented in **Chapter 5**. In **Chapter 6** the cost utility of exercise therapy versus usual

care is described. **Chapter 7** offers an overview of the conservative and surgical treatment options for PFPS.

In **Chapter 8** the results of a systematic review comparing the additional value of orthotic devices on exercise therapy for PFPS are presented. The results of a systematic review on exercise therapy for PFPS are presented in **Chapter 9**. The general discussion - **Chapter 10** - reflects on the above mentioned study results and directs to practical and research implications following from this thesis.

REFERENCES

1. van der Waal JM, Bot SD, Terwee CB, van der Windt DA, Schellevis FG, Bouter LM, et al. The incidences of and consultation rate for lower extremity complaints in general practice. *Ann Rheum Dis* 2006;65(6):809-15.
2. Blond L, Hansen L. Patellofemoral pain syndrome in athletes: a 5.7-year retrospective follow-up study of 250 athletes. *Acta Orthop Belg* 1998;64(4):393-400.
3. Witvrouw E, Werner S, Mikkelsen C, Van Tiggelen D, Vanden Berghe L, Cerulli G. Clinical classification of patellofemoral pain syndrome: guidelines for non-operative treatment. *Knee Surg Sports Traumatol Arthrosc* 2005;13(2):122-30.
4. Breedveldt Boer H.P. KWRC, Spinnewijn W.E.M., Heinen N., Burggraaff H.B., Derks C.J.T., Loogman M.C.M. NHG-Standaard Niet-traumatische knieproblemen bij kinderen en adolescenten (eerste herziening). *Huisarts Wet* 2009;52((7)):332-41.
5. Heintjes E, Berger MY, Bierma-Zeinstra SM, Bernsen RM, Verhaar JA, Koes BW. Exercise therapy for patellofemoral pain syndrome. *Cochrane Database Syst Rev* 2003(4):CD003472.



Chapter 2

Patellofemoral pain syndrome versus non specific knee complaints in general practice; differences in patients' characteristics, management strategy and outcome after 1 and 6 years

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ABSTRACT

Background:

Patellofemoral pain syndrome (PFPS) is a common diagnosis in adolescents and young adults in general practice. Characteristics and prognosis in comparison with non-specific knee complaints is unknown.

Method:

The design is an observational prospective cohort study of primary care patients from 12 years old consulting the physician for non-traumatic knee complaints. Patients with PFPS diagnosed by the GP (PFPSgp) are compared to non-specific knee complaints (NSKCgp) and patients fulfilling the clinical criteria for PFPS (PFPScrit) are compared to those not fulfilling these criteria (NSKCrit). The patient's characteristics, the initial management strategy and the outcome of PFPS after 1 and 6 years are compared with non-specific knee complaints (NSKC) in adjusted multivariable analyses.

Results:

At baseline patients in the PFPS group (n=71) show a longer duration of complaints (32.4% versus 9.2%; $p < 0.001$), have a higher proportion of bilateral complaints (46.5% versus 24.1%; $p = 0.01$) show more pain at the patellar edge (57.7% versus 41.4%; $p = 0.046$) and less pain on knee extension (25.4% versus 29.9%; $p = 0.009$) than patients in the NSKC group (n=87). By combining a set of variables suggested to be indicative for PFPS, only 61% overlap of diagnosis was seen. An active advice by the GP was more often applied by patients diagnosed with PFPS (OR 2.90; 95%CI 1.28, 6.55) compared to patients with NSKC. At follow-up diagnosed PFPS patients show significantly less recovery (44 and 60%) compared to NSKC patients (66 and 84%) after 1 and 6 years respectively; OR 0.41; 95%CI 0.20, 0.86 (1 year) and OR 0.24; 95%CI 0.08, 0.68 (6 years).

Conclusions:

In this observational study in general practice 45% of the patients with PFPS show recovery after one year and approximately 60% after six years. By combining a set of variables often suggested to be indicative for PFPS, only 61% overlap in diagnoses of PFPS was seen, indicating the difficulty of diagnosing PFPS.

INTRODUCTION

Non traumatic knee complaints constitute a major reason for consultation in general practice.^{1,2} Specific complaints like patellofemoral pain syndrome, osteoarthritis, patellar tendinopathy, Osgood-Schlatter disease, or peripatellar bursitis are diagnostically distinguished from non-specific knee complaints (NSKC).

Patellofemoral pain syndrome (PFPS) is a condition characterized by diffuse peripatellar and retro-patellar pain, usually elicited by ascending or descending stairs, squatting, cycling and sitting with flexed knees for prolonged periods of time. The condition affects mainly adolescents and young adults.³⁻⁵ The origin of the complaints is not fully understood although weakness and/or tightness of the extensor muscles, changes in medial and lateral quadriceps muscle reflex time, patellar laxity and increased navicular drop are suggested to be associated with PFPS.^{6,7}

Studies indicate 5-6 new cases per 1000 patients per year in Dutch general practice while in young and highly active populations incidence rates may rise to 22 per 1000 patients a year.^{8,9}

In general practice the diagnosis of painful knee disorders is mainly based on the combination of symptoms and clinical findings and in general demands no further radiological assessment.^{10,11} The ICPC system offers diagnostic codes in order to classify for both specific non traumatic knee disorders like PFPS, patellar tendinopathy, Osgood Schatters disease, osteoarthritis as for non-specific knee complaints. Although several diagnostic tests for patellofemoral pain are used, none of them is conclusive.¹² Since clinical findings for PFPS and other non-traumatic knee complaints may vary it is not known which patient characteristics and clinical findings in general practice are associated with the diagnosis of PFPS or with non-specific knee complaints. Additionally, it is unknown to what extent there is an overlap between the diagnosis of the GP and the often suggested characteristics of PFPS, i.e. peripatellar pain, grinding of the patella, pain on bending, stair climbing, cycling and running.¹³⁻¹⁶

Patellofemoral complaints may become chronic and subsequently lead to increased medical care and therapy.^{3,5} The management strategy in general practice is based on clinical guidelines advising on temporarily reduction of provoking activities (running, biking, sports) and may suggest on single leg extension exercise.¹⁰ However, data describing the current initial management strategy for PFPS in general practice and whether this is related to diagnostic considerations and outcome is missing.

Hence, the aims of this study are: 1) To describe the differences in baseline characteristics of patients that are diagnosed with PFPS compared to NSKC. 2) To describe a set of variables often suggested being indicative for PFPS in relation to the diagnoses of the GP. 3) To describe the difference in outcome between patients suffering PFPS compared

to NSKC. 4) To describe the differences in types of interventions applied between the patient groups.

METHODS

Design and data collection

A prospective, observational cohort study with a follow-up of six year was carried out. Patients aged 12 years or above consulting their GP for a new episode of knee complaints were invited to participate in the study during the period October 2001 and October 2003. New complaints were considered as complaints that were presented to the GP for the first time. Recurrent symptoms for which the general practitioner was not consulted within the past 3 months were also considered to be new symptoms. Data were collected using questionnaires and all patients underwent a standardized physical examination by the research examiners at baseline and after one-year follow-up. GPs noted the working diagnosis at baseline of the knee disorders according to the International Classification of Primary Care (ICPC).¹⁷

For the present study only patients with ICPC code L15 (non-specific knee complaints) and L97.1 (patellofemoral pain syndrome) were included. Those with other ICPC codes were excluded. We refer to this diagnosis of the GP as PFPSgp (patellofemoral pain syndrome, L97.1) and NSKCgp (non-specific knee complaints, L15). The researchers did not interfere with the usual care as given by the GP. Detailed information about the study design can be found in a previous publication.¹⁸

Patient's characteristics, initial management strategy and outcome measures

Patient characteristics (age, gender, Body Mass Index, educational status, sports participation), medical history (duration of complaints, affected side, recurrence of complaints, pain intensity, knee function) as well as specific knee examination (Range of Motion, swelling, deformity, painful area, crepitation, contraction tests) were recorded in the baseline questionnaire.

For the definition of PFPS according to suggested clinical criteria patients had to fulfil the following subset of variables: the presence of at least two of the following symptoms (pain while walking stairs, bending, running, cycling, sitting, grinding patella, positive apprehension test, painful patellar edge, axial pressure pain) and peripatellar pain.¹³⁻¹⁶ We refer to this definition as PFPScrit; others were defined as NSKC (NSKCcrit).

The initial management strategy of the GP was also noted. The strategies included "wait and see policy", tailored therapy by the GP, referral to medical specialist or therapist, X-rays and other strategies. The strategies were for analyses divided – not mutually exclusive - into active advice (exercises, weight reduction), non-active advice (rest, wait

and see) and strategies including medication or referral to a physical therapist or orthopedic surgeon.

During one-year follow-up every 3 months questionnaires were sent to the participants and additionally one questionnaire was sent to the participants after 6 year follow-up. Questionnaires within the first year of follow-up reported the medical consumption, pain and functional disability of the knee. Pain was measured on a numeric rating scale which ranges from 0 (no pain) to 10 (unbearable pain). The Lysholm scale and WOMAC osteoarthritis index were used to evaluate functional disability of the knee. After one- and six-year follow-up self-reported recovery was measured on a 7-point Likert scale ranging from "total recovery" (=1) to "worse than ever" (=7). The categories "total recovery" and "major improvement" represent clinically relevant improvement and is defined as "recovery". All other categories represent persistent knee complaints.

Statistical analyses

Descriptive statistics were used to determine patient variables, type of knee complaints, initial policy of the GP and outcome at one and six year follow-up. Differences in baseline characteristics between PFPSgp and NSKCgp, and PFPScrit and NSKCrit were analysed using student t-test for continuous variables and Chi-square for dichotomous variables. The association between initial strategy (active advice, passive advice, medication or referral) and type of knee complaint were tested using univariable logistic regression analyses. The association between outcome at both one and six year follow-up and type of knee complaint were also tested using univariable logistic regression analyses.

The analyses, both for initial strategy and outcome, were adjusted for age, gender, duration of complaints, baseline pain severity and recurrence of complaints. The results are presented as odds ratios (ORs), with 95% confidence intervals (CI). At the p-level of 0.05 results were considered statistically significant. All analyses were performed with the SPSS software package (version 17.0.2, 2009).

RESULTS

In total 1068 patients were enrolled in the study – recruited from 40 GP practices in the Netherlands. From this cohort we extracted all patients who were aged between 12 and 35 years and had non-traumatic knee complaints (n=191). In these 191 patients with non-traumatic knee complaints 74 patients were by the GP diagnosed as PFPS (PFPSgp) whereas 100 were diagnosed as NSKC (NSKCgp) The other 17 patients were diagnosed with Osgood-Schlatters disease, meniscus/ligament pathology and knee distortion and were therefore excluded from the analyses for the current study. Additionally, also all patients with a history of knee surgery were excluded from the analysis (13 NSKCgp

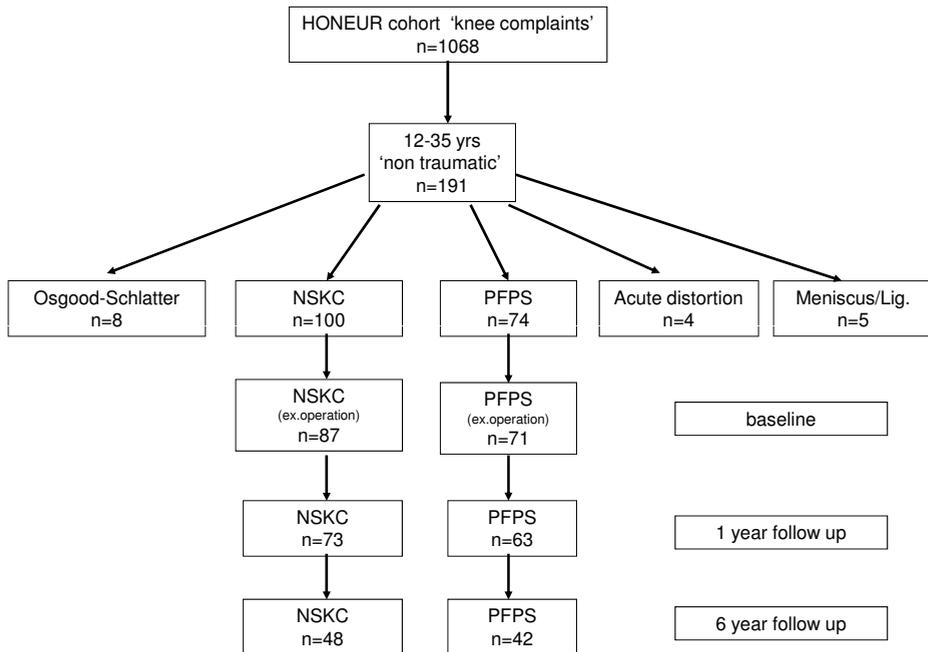


Figure 1. Flowchart of the study

and 3 PFPSgp). (Figure 1) Thus, for the present study, 87 patients with non-specific knee complaints (ICPC L15) and 71 patients with patellofemoral pain syndrome (ICPC L97.1) were included at baseline. Complete follow-up data after 1 year were available for 136 patients with NSKCgp (n=73) and PFPSgp (n=63) and after 6 years for 90 patients (48 NSKCgp, 42 PFPSgp).

Following the clinical criteria for PFPS, 60.6% (n=43) of the patients diagnosed with PFPSgp, suffered PFPScrit, and 48.3% (n=42) of the patients diagnosed with NSKCgp suffered PFPS following the clinical criteria.

Baseline characteristics of the patient groups are presented in Table 1. At baseline patients with PFPSgp suffered significantly longer from knee complaints ($p < 0.001$) had a higher educational level ($p = 0.042$), showed more bilateral complaints ($p = 0.01$), revealed more pain at the patellar edge ($p = 0.046$) and less pain on knee extension ($p = 0.009$) compared to NSKCgp patients.

Patients fulfilling the clinical criteria of PFPS (PFPScrit) included significantly more females, had a lower WOMAC function score and a higher Lysholm score, and showed significantly more peripatellar pain and knee grinding.

Data on initial management strategy by the GP for type of knee complaint are presented in table 2. Active advices were more often opted by the GP in patients with PFPSgp compared to NSKCgp patients (OR 2.90; 95%CI 1.28, 6.55). Though not significant,

Table 1: Baseline characteristics of the study population; values are numbers (percentages) unless otherwise stated

	NSKCgp (n=87)	PFP5gp (n=71)	p-value	NSKCcrit (n=73)	PFP5crit (n=85)	p-value
<i>Demographics</i>						
Age (years), mean (SD)	24.69 (7.30)	23.52 (8.02)	0.344	24.10 (7.57)	24.22 (7.73)	0.916
BMI (kg/l ²), mean (SD)	23.72 (3.79)	23.23 (4.16)	0.442	23.33 (3.94)	23.64 (3.99)	0.637
Gender (female)	43 (49.4%)	34 (47.9%)	0.847	29 (39.7%)	48 (56.5%)	0.036
Education level			0.042			0.422
Low	16 (18.4%)	6 (8.5%)		7 (9.6%)	15 (17.6%)	
Medium	34 (39.1%)	22 (31.0%)		27 (37.0%)	29 (34.1%)	
High	33 (37.7%)	40 (56.3%)		32 (43.8%)	41 (48.2%)	
Sports participants	59 (67.8%)	53 (74.6%)	0.338	50 (68.5%)	62 (72.9%)	0.695
<i>Knee complaints</i>						
Duration of complaints			<0.001			0.720
<3 weeks	40 (46.0%)	15 (22.1%)		24 (32.9%)	31 (36.5%)	
3 – 12 weeks	22 (25.3%)	21 (29.6%)		21 (28.8%)	22 (25.9%)	
12- 52 weeks	8 (9.2%)	23 (32.4%)		11 (15.1%)	20 (23.5%)	
> 52 weeks	13 (14.9%)	9 (12.7%)		10 (13.7%)	12 (14.1%)	
Bilateral	21 (24.1%)	33 (46.5%)	0.010	22 (30.1%)	32 (37.6%)	0.707
Recurrent complaints	40 (46.0%)	40 (56.3%)	0.193	34 (46.6%)	46 (54.1%)	0.751
Pain severity (VAS/10), mean (SD)	4.27 (2.14)	3.63 (2.30)	0.085	3.88 (2.22)	4.06 (2.24)	0.621
WOMAC function (0/100), mean (SD)	78.19 (18.61)	81.87 (15.53)	0.447	83.59 (15.31)	77.00 (18.29)	0.024
Lysholm score on bending, mean (SD)	1.83 (0.78)	1.74 (0.54)	0.372	1.65 (0.71)	1.89 (0.64)	0.032
<i>Physical examination</i>						
Pain knee extension	26 (29.9%)	18 (25.4%)	0.009	19 (26%)	25 (29.4%)	0.496
Pain at patellar edge	36 (41.4%)	41 (57.7%)	0.046	29 (39.7%)	48 (56.5%)	0.053
Peripatellar pain	49 (56.3%)	50 (70.4%)	0.075	14 (19.2%)	85 (100%)	<0.001
Valgus deformity	6 (6.9%)	1 (1.4%)	0.097	2 (2.7%)	5 (5.9%)	0.360
Crepitation	68 (78.2%)	62 (87.3%)	0.102	56 (76.7%)	74 (87.1%)	0.697
Knee grinding	38 (43.7%)	37 (52.1%)	0.318	19 (26%)	56 (65.9%)	<0.001

Table 2. Initial policy by general practitioner; values are numbers (percentages) unless otherwise stated

Initial policy by GP	NSKCgp (n=87)	PPPSgp (n=71) OR (95%-CI)*	p-value*	NSKccrit (n=73)	PPPScrit (n=63) OR (95%-CI)*	p-value*
Passive advice GP	43 (49.4%)	37 (52.1%)	1.28 (0.64;2.55)	33 (45.2%)	47 (55.3%)	1.33 (0.68;2.59)
<i>Wait and see</i>	22	20		16	26	
Rest	22	14		13	23	
<i>Go easy on the knee</i>	29	21		21	29	
Compresses	8	5		2	11	
Active advice GP	16 (18.4%)	24 (33.8%)	2.90 (1.28;6.55)	19 (26.0%)	21 (24.7%)	0.75 (0.35;1.59)
Exercises	14	23		16	21	
<i>Reduce body weight</i>	2	2		3	1	
Medication	16 (18.4%)	5 (7.0%)	0.35 (0.11;1.08)	9 (12.3%)	12 (14.1%)	1.04 (0.40;2.69)
Medication	16	5		9	12	
<i>Injection</i>	0	0		0	0	
Referrals for diagnostics	4 (4.6%)	1 (1.4%)	0.53 (0.05;5.72)	3 (4.1%)	2 (2.4%)	0.39 (0.06;2.69)
Referrals to care givers	29 (33.3%)	28 (39.4%)	0.16 (0.58;2.33)	24 (32.9%)	33 (38.8%)	1.08 (0.55;2.14)
<i>Physical therapist</i>	23	23		18	28	
<i>Orthopedic surgeon</i>	8	7		8	7	

* Analyses adjusted for age, gender, duration of complaints, baseline pain severity and recurrence of complaints;
NSKC = reference category

GPs tended to choose less often medication as an initial strategy for PFPSgp patients compared to NSKCgp patients (OR 0.35; 95%CI 0.11, 1.08; $p=0.07$).

No differences were found for initial policy of the GP between PFPScrit and NSKCcrit patients. However, 14% of the patients fulfilling the clinical criteria for PFPS were prescribed medication.

At one year follow up, 28 out of 63 PFPSgp patients (44.4%) were fully recovered compared to 48 NSKCgp patients out of 73 (65.8%) (OR 0.41; 95%CI 0.20, 0.86). There was a small, but significant difference in the functional outcome score measured by the WOMAC (OR 0.95; 95%CI 0.92, 0.99) in favor of the NSKCgp group (Table 3). This difference was also present between the PFPScrit patients and the NSKCcrit patients (OR 0.96; 0.92, 0.99).

No statistically significant differences were observed regarding pain and functional disability, measured by the Lysholm score, between the patient groups at 12 months follow-up.

At 6-years follow up 59.5% of PFPSgp patients reported complete recovery compared to 83.8% of the NSKCgp patients (OR 0.24; 95%CI 0.08, 0.68). The same percentages were seen between the patients with PFPScrit (61.5%) compared to patients with NSKCcrit (86.8%), (OR 0.27; 0.09, 0.84).

No significant differences between the patient groups were observed for the pain and function scores at six years follow-up.

DISCUSSION

Our study shows that the diagnoses of PFPS in general practice is associated with a longer duration of complaints, higher educational level, higher occurrence of bilateral complaints, pain at the patellar edge and less pain on knee extension compared to NSKCgp patients. A study by Nijs et al. questioned the validity of the patellar grinding test (Clarke's test).¹³ According to our study patellar grinding was not discriminative for the diagnoses of PFPS by the GP. And as Fredericson concluded: the reliability of most clinical tests is low and the diagnosis cannot be determined by any single test and therefore multiple evaluations are recommended.¹² However, we analyzed an extensive set of physical tests and the only statistically significant associations with the diagnoses PFPS were found for pain at the patellar edge and for pain on knee extension. In addition, combining a set of variables previously suggested to be indicative for PFPS (peripatellar pain, grinding of the patella, pain on bending, stair climbing or running) showed that these symptoms were more frequently seen in females and these patients had a significantly lower WOMAC function score and a higher Lysholm score. And, as a part of

Table 3. Outcome at 12 months and 6 years follow-up: values are means (SD) unless otherwise stated

Outcome	NSKCgp (n=73)	PFPSgp (n=63)	OR (95%-CI)*	p-value*	NSKcrit (n=73)	PFPScrit (n=63)	OR (95%-CI)*	p-value*
12 months								
Recovery, n (%)	48 (65.8%)	28 (44.4%)	0.41 (0.20;0.86)	0.018	40 (62.5%)	36 (50.0%)	0.57 (0.27;1.18)	0.128
Pain last 48 hrs	1.70 (2.09)	2.56 (2.47)	1.19 (0.99;1.43)	0.059	1.80 (1.96)	2.36 (2.55)	1.15 (0.96;1.38)	0.134
Functional disability								
WOMAC								
Lysholm	94.16 (8.46)	89.46 (13.85)	0.95 (0.92;0.99)	0.017	94.04 (8.46)	90.22 (13.34)	0.96 (0.92;0.99)	0.034
	85.57 (15.14)	82.57 (16.94)	0.98 (0.95;1.00)	0.10	86.30 (15.02)	83.08 (16.90)	0.98 (0.96;1.01)	0.149
6 years								
Recovery, n (%)	40 (83.3%)	25 (59.5%)	0.24 (0.08;0.68)	<0.01	33 (86.8%)	32 (61.5%)	0.27 (0.09;0.84)	0.024
Pain last 48 hrs	0.89 (1.37)	1.63 (2.12)	0.79 (0.58;1.09)	0.15	0.89 (1.60)	1.49 (1.91)	1.44 (0.99;2.10)	0.057
Functional disability								
WOMAC								
Lysholm	92.74 (11.42)	89.67 (14.55)	1.02 (0.98;1.06)	0.32	94.25 (8.78)	89.29 (14.95)	0.95 (0.90;1.01)	0.085
	89.71 (12.57)	87.56 (13.70)	1.02 (0.98;1.05)	0.43	88.08 (14.22)	88.95 (12.55)	1.01 (0.97;1.05)	0.80

* Analyses adjusted for age, gender, duration of complaints, baseline pain severity and recurrence of complaints;
NSKC = reference category

the criteria for clinical PFPS, peripatellar pain and knee grinding were associated with PFPScrit.

The present study confirms the difficulty in diagnosing PFPS patients in primary care. By excluding anterior knee pain due to intra-articular pathology, plica syndrome, Sinding Larsen's disease, Osgood Schlatter's disease, bursitis or tendinopathy, neuroma's and other rarely occurring pathologies it is suggested that remaining patients with a clinical presentation of anterior knee pain could be diagnosed with PFPS. The present study shows only 60% overlap in patients diagnosed with PFPS by the GP and patients fulfilling the generally accepted clinical criteria for PFPS.⁽¹³⁻¹⁶⁾ This implies that, given the almost identical outcomes between PFPSgp and PFPScrit, the diagnoses of the GP is probably related with the initial policy of the GP. The Dutch clinical guidelines recommend a 'wait and see strategy' and provide a suggestion for home based isometric quadriceps exercises for PFPS.¹⁰ This advice is reflected in our study by comparing PFPSgp and NSKCgp patients; an active advice (including exercise advice) is more frequently advised by general practitioners for PFPSgp compared to NSKCgp. Patients meeting the clinical criteria for PFPS are not more frequently advised to perform exercises in comparison with NSKCcrit patients who did not fulfil these criteria, and no other differences between both groups are seen in the initial policy of the GP.

Exercise therapy for chronic knee pain is one of the options to which GP's may decide based on their personal beliefs and attitude.¹⁹ In our study, 32.4% and 44.4% of the PFPS patients were referred to a physical therapist respectively. Moreover, recent studies have shown the effectiveness of an supervised exercise program for PFPS.^{15,20}

We found a low prescription rate of medication for PFPSgp patients, which is in agreement with both the clinical guideline for general practitioners and with results from literature showing only limited evidence for the effectiveness of NSAIDs for short term pain reduction in PFPS.²¹ It is therefore apparent that a 14% of the patients with PFPScrit were prescribed medication.

At one year follow up data show that only 45% of the patients with PFPSgp experience recovery, which is lower than in the NSKCgp group. At six years the proportion of patients initially diagnosed with PFPS reporting recovery has increased to 59.5%. Comparable results are found for the patients fulfilling the clinical criteria of PFPS; 38.5% of these patients were not fully recovered after 6 years of follow-up compared to 13.2% of the NSKCcrit patients. This implies that both PFPSgp patients and PFPScrit patients have a significantly worse prognosis in comparison with the NSKCgp and NSKCcrit groups, respectively. This raises the question if these persistent complaints in the PFPScrit group and PFPSgp group are caused by the patients included in both groups. However, analysis revealed that percentages recovery between PFPSgp, PFPScrit and the group with overlap of PFPS diagnosis in both groups did not differ (data not shown).

These findings do not reflect the information that is supposed to be given to the patient according to the clinical guideline that prompts to a good prognosis of non-traumatic knee complaints in adolescents and young adults.¹⁰ Two earlier studies reported a tendency to incomplete recovery of PFPS in selected populations.^{22 23} An intervention study by Clark²⁴ reported recovery rates between 13% (education group) and 42% (exercise group) after one year. In a recent randomised controlled trial we found a recovery rate of 50.8% in the control group following a 'wait and see' strategy, and 62.1% in a supervised exercise therapy group at one year follow up.²⁰ More favourable outcomes were reported by Collins¹⁵ in a randomised clinical trial using 4 different treatment strategies with recovery rates ranging from 73% (flat inserts) to 84% (foot orthoses) after one year. The recovery rates in the above mentioned studies vary largely, but most report non-recovery in more than 40% of the patients at long-term.

Elaborating further, it is of interest that although the recovery rates for PFPS patients are low at one and six years, this was not fully reflected in the pain and function scores. At one and six years the pain and function scores between both the PFPSgp group and NSKCgp group, and the PFPScrit and NSKCcrit do not significantly differ. Perceived recovery measured by a Likert scale is a general measure which may comprise several domains including pain and function but from the patient's perspective also the process leading towards full function. Besides, literature suggests that recovery measures may also be determined by the individual appraisal of the impact of symptoms on daily activities and quality of life.²⁵

LIMITATIONS

In general this study has several limitations. The groups studied are small considering the amount of variables which have been tested in relation to the baseline variables, the initial strategy and outcome. Second, the diagnosis for PFPS and NSKC has been made by the GP. In relation to the variety of complaints and the non-specificity of tests for PFPS accurate diagnosis therefore can be questioned. With the available data it was tested if combining a set of variables "specific" for PFPS (peripatellar pain, grinding of the patella, pain on bending, stair climbing or running) would differ between GP diagnosis and "criteria based PFPS diagnosis". Analysis revealed an overlap of only 60% in diagnosis. However, no large differences in outcomes between diagnosed PFPS patients and patients fulfilling the clinical criteria for PFPS could be demonstrated. From a clinical point of view it is suggested that GP's consider PFPS as a specific entity in a way patients can be differentiated with respect to initial strategy and outcome. We had a relatively large percentage lost to follow-up, especially at 6 years follow-up (57%). Likely this is caused because there was no contact between the investigators and patients between

1 and 6 year follow-up. Some people changed address and it was difficult to trace them. However the patients available at 1 and 6 year follow-up seemed not to be a selected group of patients.

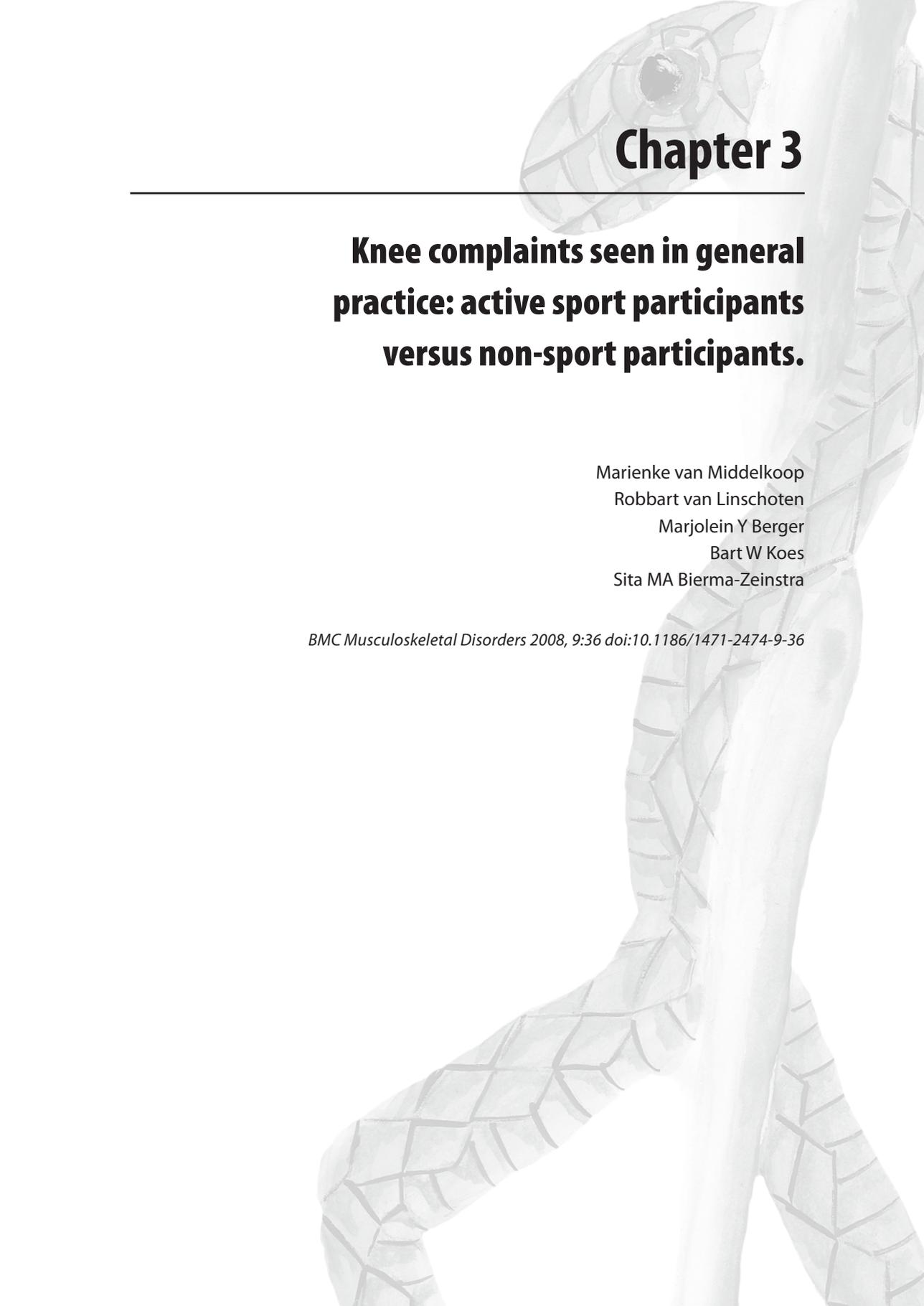
CONCLUSIONS

In this observational study on non-traumatic knee complaints in general practice results indicate that experienced recovery for patellofemoral pain syndrome at one year and six years follow up is low. Long duration of knee complaints, a high educational level, bilateral complaints and pain at the patellar edge are associated with the diagnosis of PFPS by the GP. By combining a set of variables previously suggested to be indicative for PFPS, only 60% of the diagnosed PFPS patients fulfilled these criteria. This implies the difficulty in diagnosing PFPS patients whereas the diagnosis of the GP seems related with the initial policy chosen for these patients.

REFERENCES

1. Belo JN, Berger MY, Koes BW, Bierma-Zeinstra SM. Prognostic factors in adults with knee pain in general practice. *Arthritis Rheum* 2009;61(2):143-51.
2. van der Waal JM, Bot SD, Terwee CB, van der Windt DA, Schellevis FG, Bouter LM, et al. The incidences of and consultation rate for lower extremity complaints in general practice. *Ann Rheum Dis* 2006;65(6):809-15.
3. Thomee R, Augustsson J, Karlsson J. Patellofemoral pain syndrome: a review of current issues. *Sports Med* 1999;28(4):245-62.
4. Heintjes E, Berger MY, Bierma-Zeinstra SM, Bernsen RM, Verhaar JA, Koes BW. Exercise therapy for patellofemoral pain syndrome. *Cochrane Database Syst Rev* 2003(4):CD003472.
5. Witvrouw E, Werner S, Mikkelsen C, Van Tiggelen D, Vanden Berghe L, Cerulli G. Clinical classification of patellofemoral pain syndrome: guidelines for non-operative treatment. *Knee Surg Sports Traumatol Arthrosc* 2005;13(2):122-30.
6. Witvrouw E, Lysens R, Bellemans J, Cambier D, Vanderstraeten G. Intrinsic risk factors for the development of anterior knee pain in an athletic population. A two-year prospective study. *Am J Sports Med* 2000;28(4):480-9.
7. Boling MC, Padua DA, Marshall SW, Guskiewicz K, Pyne S, Beutler A. A prospective investigation of biomechanical risk factors for patellofemoral pain syndrome: the Joint Undertaking to Monitor and Prevent ACL Injury (JUMP-ACL) cohort. *Am J Sports Med* 2009;37(11):2108-16.
8. van der Linden M, Westert G, de Bakker D, Schellevis F. Tweede Nationale Studie naar ziekten en verrichtingen in de huisartspraktijk. Klachten en aandoeningen in de bevolking en in de huisartspraktijk.. Utrecht/Bilthoven: NIVEL/RIVM, 2004.
9. Boling M, Padua D, Marshall S, Guskiewicz K, Pyne S, Beutler A. Gender differences in the incidence and prevalence of patellofemoral pain syndrome. *Scand J Med Sci Sports* 2009.
10. Breedveldt Boer H.P. KWRC, Spinnewijn W.E.M., Heinen N., Burggraaff H.B., Derks C.J.T., Loogman M.C.M. NHG-Standaard Niet-traumatische knieproblemen bij kinderen en adolescenten (eerste herziening). *Huisarts Wet* 2009;52((7)):332-41.
11. Baarveld F, Visser CA, Kollen BJ, Backx FJ. Sports-related injuries in primary health care. *Fam Pract* 2011;28(1):29-33.
12. Fredericson M, Yoon K. Physical examination and patellofemoral pain syndrome. *Am J Phys Med Rehabil* 2006;85(3):234-43.
13. Nijs J, Van Geel C, Van der Auwera C, Van de Velde B. Diagnostic value of five clinical tests in patellofemoral pain syndrome. *Man Ther* 2006;11(1):69-77.
14. Houghton KM. Review for the generalist: evaluation of anterior knee pain. *Pediatr Rheumatol Online J* 2007;5:8.
15. Collins N, Crossley K, Beller E, Darnell R, McPoil T, Vicenzino B. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *Bmj* 2008;337:a1735.
16. Cook C, Hegedus E, Hawkins R, Scovell F, Wyland D. Diagnostic accuracy and association to disability of clinical test findings associated with patellofemoral pain syndrome. *Physiother Can* 2010;62(1):17-24.
17. Lamberts H, Wood M. *ICPC. International Classification of Primary Care*. Oxford: Oxford University Press, 1987.
18. Heintjes EM, Berger MY, Koes BW, Bierma-Zeinstra SM. Knee disorders in primary care: design and patient selection of the HONEUR knee cohort. *BMC Musculoskelet Disord* 2005;6:45.

19. Cottrell E, Roddy E, Foster NE. The attitudes, beliefs and behaviours of GPs regarding exercise for chronic knee pain: a systematic review. *BMC Family Practice* 2010;11(4).
20. van Linschoten R, van Middelkoop M, Berger MY, Heintjes EM, Verhaar JAN, Willemsen S, et al. Supervised exercise therapy versus usual care for patellofemoral pain syndrome: an open label randomised controlled trial. *BMJ* 2009;339:b4074.
21. Heintjes E, Berger MY, Bierma-Zeinstra SM, Bernsen RM, Verhaar JA, Koes BW. Pharmacotherapy for patellofemoral pain syndrome. *Cochrane Database Syst Rev* 2004(3):CD003470.
22. Blond L, Hansen L. Patellofemoral pain syndrome in athletes: a 5.7-year retrospective follow-up study of 250 athletes. *Acta Orthop Belg* 1998;64(4):393-400.
23. Kannus P, Natri A, Paakkala T, Jarvinen M. An outcome study of chronic patellofemoral pain syndrome. Seven-year follow-up of patients in a randomized, controlled trial. *J Bone Joint Surg Am* 1999;81(3):355-63.
24. Clark DI, Downing N, Mitchell J, Coulson L, Syzpryt EP, Doherty M. Physiotherapy for anterior knee pain: a randomised controlled trial. *Ann Rheum Dis* 2000;59(9):700-4.
25. Kamper SJ, Stanton TR, Williams CM, Maher CG, Hush JM. How is recovery from low back pain measured? A systematic review of the literature. *Eur Spine J* 2010.



Chapter 3

Knee complaints seen in general practice: active sport participants versus non-sport participants.

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ABSTRACT

Background:

Since knee complaints are common among athletes and are frequently presented in general practice, it is of interest to investigate the type of knee complaints represented in general practice of athletes in comparison with those of non-athletes. Therefore, the aim of this study is to investigate the differences in type of knee complaints between sport participants, in this study defined as athletes, and non-sport participants, defined as non-athletes, presenting in general practice. Further, differences in the initial policy of the GP, medical consumption, and outcome at one-year follow-up were also investigated.

Methods:

Patients consulting their GP for a new episode of knee complaints were invited to participate in this prospective cohort study. From the total HONEUR knee cohort population (n=1068) we extracted patients who were athletes (n=421) or non-athletes (n=388).

Results:

The results showed that acute distortions of the knee were significantly more diagnosed in athletes than in non-athletes ($p=0.04$). Further, more athletes were advised by their GP to 'go easy on the knee' than the non-athletes ($p<0.01$), but no differences were found in number of referrals and medication prescribed by the GP. The medical consumption was significantly higher among athletes; however, no significant differences were found between the two groups for recovery at one-year follow-up.

Conclusion:

There are no major differences in the diagnosis and prognosis of knee complaints between athletes and non-athletes presented to the GP. This implies that there are no indications for different treatment strategies applied in both groups. However, athletes are more often advised to 'go easy on the knee' and to rest than non-athletes. Further, there is a trend towards increased medical consumption among athletes while functional disability and pain are lower than among the non-athletes.

BACKGROUND

Complaints of the lower extremities are a serious problem because of their high prevalence and high impact on functional and work disability. A study among the Dutch general population showed a one-year prevalence of 21.9% for knee pain; about 33% of subjects reporting knee or hip complaints during the preceding year indicated that they had contacted their general practitioner (GP) for this complaint.¹ Among the Dutch population, knee problems are the most frequently presented complaints of the lower extremities: 21.4 per 1000 person-years for women and 22.8 per 1000 person-years for men.² Since sport activities are strongly promoted, the risk of sport injuries is likely to increase. Knee complaints are very common among sport participants^{3,4} and it is reported that 39.8% of all sports injuries involve the knee.³ Internal knee trauma, such as anterior cruciate ligament rupture, and distortion of the knee are the most common diagnoses of athletic knee injuries.³ In addition, knee disorders such as the runner's knee, the patellofemoral pain syndrome, meniscus lesions and an anterior cruciate ligament rupture are often associated with sport participation.^{5,6} In the Netherlands, almost everyone is registered in a general practice. At the time of conducting this study, all patients had first to visit their GP before being referred to a therapist or specialist in the Dutch health care system. Therefore, most care-seeking sport participants with knee complaints in the Netherlands will visit their GP for primary care. Since knee complaints are common among athletes and are frequently presented in general practice, it is of interest to investigate the type of knee complaints represented in general practice of athletes in comparison with those of non-athletes. These differences could have implications for applied treatment strategies of these knee complaints, i.e. it might be beneficial to treat the athletes different than the non-athletes because of a different diagnosis. Further, it is of interest to explore differences between athletes and non-athletes regarding the GP's initial treatment, medical consumption and prognosis of the two groups. If the medical consumption appears to be the only difference between athletes and non-athletes we will need to reflect on the implications of such difference. Therefore, this study investigated differences in knee complaints between athletes and non-athletes presenting in general practice. The following questions were formulated: (1) Do athletes present with different knee complaints than non-athletes in general practice? (2) Is there a difference in initial policy of the GP between athletes and non-athletes? (3) Is there a difference in medical consumption between athletes and non-athletes during one year follow-up? and (4) Do athletes have a better prognosis than non-athletes at one-year follow-up expressed in recovery, pain intensity and the WOMAC-score?

METHODS

Study design

A prospective, observational cohort study was set up, with a follow-up of one year. A total of 40 GP's from 5 municipalities in the southwest region of the Netherlands (all connected to the Erasmus Medical Centre GP Research Network HONEUR) participated in this study. Recruitment of patients started in October 2001 and finished in October 2003. Patients aged 12 years and older, consulting their GP for a new episode of knee complaints were invited to participate in the study. Complaints that were presented to the GP for the first time, and recurrent complaints for which the GP was not consulted during the preceding 3 months, were considered to be new complaints. During such a consultation, the GP briefly informed the patients of the existence of the study and handed over written information and a baseline questionnaire. Interested patients forwarded their contact details to the researchers. The researchers contacted the patients to give additional information about the study, and to make an appointment to sign informed consent, and to perform a comprehensive standardized physical examination of both knees. GPs noted the working diagnoses of the knee disorders according to the International Classification of Primary Care. The consultations were taken in the same format as they usually take. Patient characteristics, medical history, knee history taking, GP's initial policy and sport activities were recorded in the baseline questionnaire. Follow-up questionnaires were sent to all participants at 3, 6, 9 and 12 months. Patients underwent a standardized physical examination at baseline and at one year follow-up. The researchers did not interfere with usual care with respect to advice, diagnostics or treatment. The Ethics Committee of the Erasmus Medical Centre Rotterdam approved the study. A detailed description of recruitment and data collection are reported elsewhere.⁷

Study population

A total of 1068 patients were recruited from 40 GP's (Fig. 1). From this total cohort population we extracted patients who were active sport participants, defined as athletes ($n = 421$) or non-sport participants, defined as non-athletes ($n = 388$). This selection was based on reported sport activities in the baseline questionnaire. Patients were first asked if they participated in any sport activity. Secondly, each patient could fill in his/her sport participation, to a maximum of three sports. For each sport activity, the type of sport, number of weeks of sport participation per year, and number of mean hours of sport participation per week were registered. Athletes were defined as those who participated in sport for at least 30 weeks per year and minimally 2.5 hours a week for any one type of sport. Athletes who sport for minimally 20 weeks a year and at least 1.5 hours a week within one type of sport, and this for two or more sports, were also defined as athletes.

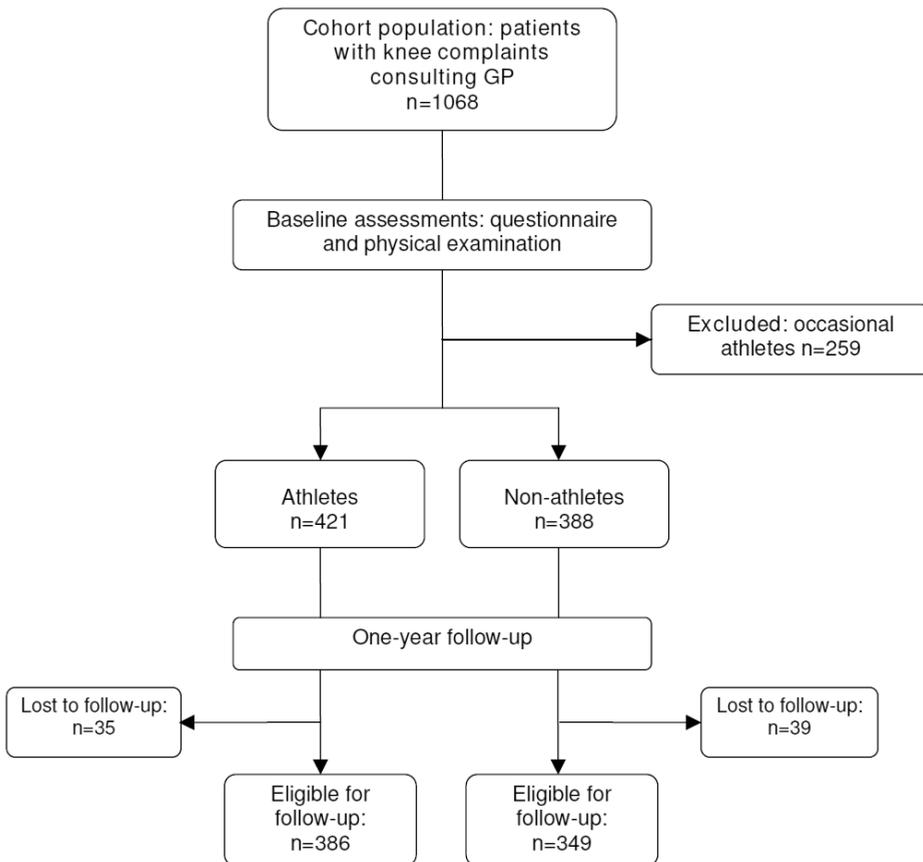


Figure 1. Flowchart of the study

The following activities reported on the questionnaires were not considered as being sport activities: bowls, billiards, darts, diving, golf, jeu de boules, go karting, 'slender you', shooting sports, fishing, and yoga. Non-athletes were defined as patients who reported no participation in sport activities at all. Because of the distinguishing power of this study, occasional athletes ($n = 259$) were excluded from this study (Fig. 1).

Outcome measures

The four follow-up questionnaires reported on the medical consumption, pain, and functional disability of the knee of all participants. The medical consumption of the patients, expressed in frequency of visits, was calculated over the 12 months follow-up period. Pain was measured on a numerical rating scale (VAS) ranging from 0 (no pain) to 10 (unbearable pain). The WOMAC osteoarthritis index evaluates the functional disability of the knee with a score ranging from 0 (poor) to 100 points (excellent).^{8,9} After one-year follow-up, satisfaction with the GP's given policy, discomfort during employment

and daily activities, and experienced recovery were registered. Patients' satisfaction was measured on an 11-point numerical rating scale from 0 (completely unsatisfied) to 10 (completely satisfied). Discomfort during employment and daily activities was measured dichotomously ("yes" or "no"). Experienced recovery was measured on a 7-point Likert scale ranging from total recovery (= 1) to worse than ever (= 7). The categories 'total recovery' and 'major improvement' represent a clinically relevant improvement and are in this study defined as being recovered. All other categories represent persistent knee complaints

Statistical analyses

Descriptive statistics were used to characterize demographic information, and chi-square and t-tests were applied to test the baseline differences for age, gender, BMI, WOMAC score and pain. Logistic regression analyses were used to test the association between athletic status and i) the type of knee complaint, ii) initial policy of the GP, iii) medical consumption, iv) patient satisfaction with GPs policy, v) recovery at one-year follow-up, and, vi) discomfort during employment and daily activities. All of these analyses were adjusted for age, gender and BMI. In addition, models ii, iii, iv, v and vi were adjusted for trauma and baseline severity (measured by the WOMAC). Model vi was also adjusted for the appropriate baseline discomfort score. Linear regression was used to test the association between athletic status and pain and function, as measured by the WOMAC. These analyses were adjusted for the potential confounders age, gender, BMI, trauma and baseline severity (WOMAC). The analyses for pain and function (WOMAC) were also adjusted for appropriate baseline pain and function scores, respectively. The results of the logistic regression analyses are presented as odds ratios (ORs), with 95% confidence intervals (CI). A p-value less than 0.05 was considered significant. All analyses were performed with the SPSS software package (version 11.0, 2001).

RESULTS

Study population

Comparison of baseline characteristics between dropouts (lost to follow-up at one year) and non-dropouts showed no significant differences with respect to gender, age) and the WOMAC score. The pain score at baseline of the dropouts was significantly lower compared to the pain score of the non-dropouts (mean difference 0.69). Table 1 presents baseline characteristics of the athletes and non-athletes. The mean age(SD) of the total study population (n = 809) was 45.3(16.9) years. The mean age of the athletes was significantly lower than the non-athletes. The total study population consisted of 440 men (54.4%) and the mean BMI was 26.3(4.7); the BMI of the athletes was significantly lower

Table 1. Baseline characteristics of the study population

		Athletes (n=421)	Non-athletes (n=388)	p-value
Age (years)	Mean (SD)	41.0 (16.7)	50.0 (15.9)	0.000
Gender (male)	N (%)	244 (58%)	196 (50.5%)	0.034
BMI (m ² /kg)	Mean (SD)	25.2 (4.1)	27.6 (4.9)	0.000
Functional disability				
WOMAC score	Mean (SD)	74.5 (19.5)	66.6 (21.1)	0.000
Pain (VAS)	Mean (SD)	4.20 (2.15)	4.46 (2.19)	0.000
<i>Type of knee complaints*</i>				
Trauma	N (%)	147 (34.9%)	111 (28.6%)	0.26
Bilateral	N (%)	19 (4.5%)	13 (3.4%)	0.76
Recurrent	N (%)	159 (37.8%)	165 (42.5%)	0.24
General knee complaints	N (%)	138 (32.8%)	138 (35.6%)	0.62
Jumper's knee	N (%)	37 (8.8%)	38 (9.8%)	0.27
Acute distortion	N (%)	37 (8.8%)	20 (5.2%)	0.04
Osteoarthritis	N (%)	21 (5.0%)	49 (12.6%)	0.32
Osgood-Schlatter	N (%)	7 (1.7%)	1 (0.3%)	0.57
Acute meniscus / ligament rupture	N (%)	21 (5.0%)	17 (4.4%)	0.73
Chronic internal trauma	N (%)	45 (10.7%)	24 (6.2%)	0.07
Patellofemoral pain syndrome	N (%)	52 (12.4%)	37 (9.5%)	0.56
Chronic meniscus fracture	N (%)	5 (1.2%)	10 (2.6%)	0.29

* Analyses adjusted for gender, age and BMI. Significant differences are printed **bold**.

(25.2(4.1)) than the non-athletes (27.6(4.9)). The functional disability score at baseline (WOMAC score) showed a significantly higher outcome, indicating better functioning, among the athletes. Among the athletes, cycling was the most commonly practiced sport (54.2%), followed by walking (24.2%), fitness (17.1%), soccer (15.4%) and tennis (13.1%). At baseline, 177 (21.9%) athletes practiced two types of sports, and 101 (12.5%) athletes practiced three types of sports.

Type of knee complaints

The different types of knee complaints among the study population are listed in Table 1. About 32% of all knee complaints in both groups were traumatic injuries. Almost 30% of the athletes sustained this injury during a sport activity. In total, 50% of the athletes reported an association between their knee complaint and their sport activity. The most frequently presented knee complaints in general practice are designated as general knee complaints: 32.8% among athletes versus 35.6% among non-athletes. The patellofemoral pain syndrome (11%) is also a relatively often-diagnosed knee complaint. The proportion of acute distortions showed a significant difference: 5.2% of the non-athletes

was labelled as ‘acute distortion’ compared with 8.8% of the athletes ($p = 0.04$); however this difference is small. Osteoarthritis is also often diagnosed in general practice (8.7%). Osteoarthritis is more frequently seen among the non-athletes (12.6%) than among the athletes group (5.0%); however, there was no significant difference in frequency ratio in the adjusted analysis.

GP’s initial policy and medical consumption The initial policy of the GP at baseline is shown in Table 2. Most patients were advised to ‘go easy on the knee’, to ‘rest’ and to ‘wait and see’. More athletes were advised to ‘go easy on the knee’ ($p = 0.002$). More than 25% of the patients were referred to a therapist and almost 25% of all patients were prescribed medication. No statistical differences were found between the two groups regarding medication ($p = 0.33$), and referrals for additional diagnostic testing (x-rays) ($p = 0.91$) and to specialists/therapists ($p = 0.61$).

Table 3 shows the medical consumption, expressed in numbers of patients visiting a specialist or paramedic. More than one third of the patients revisited the GP for their knee complaints; significantly ($p = 0.03$) more athletes revisited the GP than non-athletes, but the difference is small. A therapist or specialist was visited by 40.6% of the athletes versus 38.7% of the non-athletes ($p = 0.045$). However, when the analysis was adjusted for ‘revisiting the GP’, there was no longer a relationship between being an athlete and medical consumption ($p = 0.20$). Most patients visited a physiotherapist (30%) or an orthopaedic surgeon (19%). The mean number of visits to the physiotherapist

Table 2. Initial policy of the general practitioner at the first visit for knee complaints

Treatment by GP	Athletes	Non-athletes	OR (95% CI)	p-value
<i>‘Save the knee’</i>			1.64 (1.20 – 2.23)	0.002
Wait and see	24.5%	19.8%		
Rest	26.4%	21.1%		
Go easy on the knee	42.5%	30.9%		
Compresses	10.9%	9.3%		
<i>Active strategy</i>			1.20 (0.83 – 1.73)	0.33
Exercises	19.5%	13.9%		
Reduce body weight	3.1%	7.5%		
<i>Medication</i>			0.84 (0.59 – 1.20)	0.33
Medication	19.5%	28.1%		
Injection	-	1.0%		
<i>Referrals for diagnostics</i>	13.5%	19.8%	0.98 (0.64 – 1.48)	0.91
<i>Referrals to care givers</i>			1.09 (0.79 – 1.49)	0.61
Therapist	29.5%	23.5%		
Medical specialist	10.2%	12.4%		

Analyses adjusted for gender, age, BMI, trauma and baseline Womac-score.

Significant differences are printed **bold**.

Table 3. Medical consumption at one-year follow-up

Medical consumption	Athletes	Non-athletes	OR (95%CI)	p-value
Revisiting visit general practitioner	36.8%	35.8%	1.43 (1.04-1.96)	0.029
Visit to therapist or specialist:	40.6%	38.7%	1.38 (1.01 – 1.88)	0.045
<i>Physiotherapist</i>	30.4%	29.6%		
<i>Specialist</i>	6.2%	4.4%		
<i>Rheumatologist</i>	0.0%	0.8%		
<i>Orthopaedic surgeon</i>	20.0%	18.0%		
<i>Revalidation specialist</i>	0.2%	0.0%		
<i>Therapist Cesar/ Mensendieck</i>	0.7%	1.0%		

Analyses adjusted for gender, age, BMI, trauma and baseline Womac-score.

Significant differences are printed bold.

was 10.3(7.5) among the athletes versus 11.1(8.7) among the non-athletes. In general, patients were very satisfied with the GP's policy of their knee complaints. Almost 43% of the patients scored an eight or higher on the numerical rating scale. The mean score on the 11-point numerical rating scale, among the athletes was 7.2(2.6) versus 7.6(2.5) among the non-athletes ($p = 0.90$; OR 0.99, 95%CI 0.93–1.06). Patients who were referred to a therapist (physiotherapist, manual therapist or occupational therapist) were generally very satisfied with their treatment: 62.1% of the athletes scored an eight or higher on the 11-point numerical scale versus 66.0% of the non-athletes ($p = 0.86$; OR 1.01, 95%CI 0.90–1.13).

Course and prognosis

Total recovery at one-year follow-up was reported by 59.8% of the athletes versus 50.7% of the non-athletes. However, self-reported recovery at one-year follow-up was not associated with being an athlete or not ($p = 0.40$; OR 1.15, 95%CI 0.83–1.58). Figure 2 shows the unadjusted mean pain and WOMAC scores at three-month intervals throughout one-year follow-up. The mean pain intensity scores of both groups decreased during follow-up. The mean pain score at one-year follow-up of the athletes was slightly lower than that of the non-athletes; however the difference was not significant ($p = 0.20$). The WOMAC functional disability score was higher during the entire follow-up among the athletes compared with the non-athletes; however, there was no significant difference at one-year follow-up between the two groups ($p = 0.21$). About 10% of the athletes experienced discomfort during employment due to their knee complaints at one-year follow-up versus almost 15% of the non-athletes ($p = 0.054$; OR 0.62, 95%CI 0.38–1.01). The athletes also experienced less discomfort during any daily duties (17.6%) (employment, volunteer work, studies and housekeeping) compared to the non-athletes (29.6%) ($p = 0.003$; OR 0.56, 95%CI 0.38–0.83).

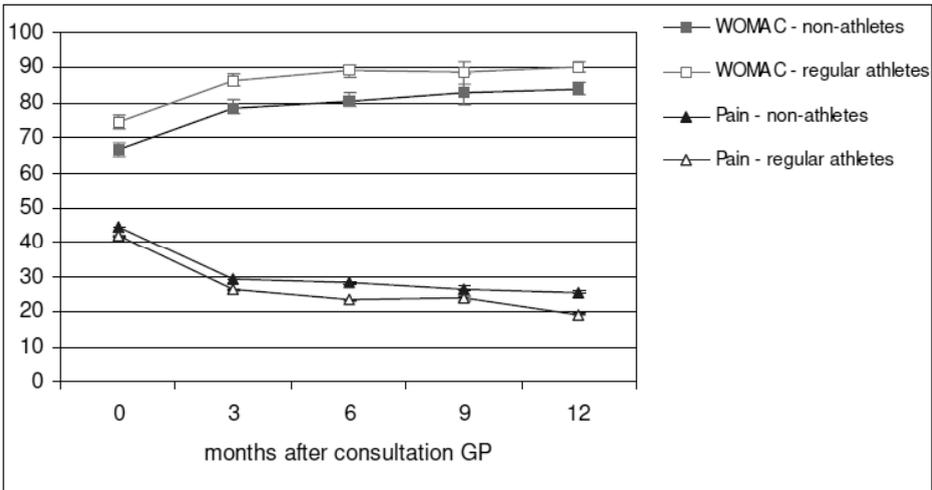


Figure 2. Course of knee complaints (mean scores and 95% CI). Pain scores were multiplied with a factor 10 for graphical display

DISCUSSION

In this observational cohort study in general practice, most knee complaints were labelled as general knee complaints. Acute distortions were diagnosed significantly more often among athletes than non-athletes, but the difference was small. The GP advised more athletes to 'go easy on the knee' compared to non-athletes. Revisits to the GP occurred more frequently among athletes, and the athletes more frequently visited a therapist or specialist. At one-year follow-up the athletes experienced less discomfort during daily activities and employment due to their knee complaints than the non-athletes. Because this is, to our knowledge, the first study comparing athletes and non-athletes with knee complaints, we cannot make any comparisons on this subject with current literature. However, in the present study, traumatic injuries were seen in almost 35% of the athletes and almost 30% of the traumatic injuries of this group were sustained during a sport activity. In total, 50% of the athletes associated their knee complaint with their sport participation. In subgroup analyses, there were no differences in the type of knee complaints between the athletes who associated their complaint with their sport participation and those who did not. This implies that there is no specific knee complaint that can be associated with sport participation. Most studies on knees and athletes focus on knee injuries, which are mostly traumatic, whereas in our study only 35% of the knee complaints in athletes, presented in primary care, were traumatic. Therefore, future research should not only focus on traumatic knee injuries in athletes, but also on non-traumatic injuries. Osteoarthritis was more often presented among the non-athletes: 12.6% among the non-athletes versus 5.0% among the athletes; however,

the adjusted OR shows no significant difference. The difference between the two groups can probably be attributed to the differences in age, gender and BMI rather than to sport participation itself. The non-athletes were significantly older, had a higher BMI and included more females than the group of athletes. These latter findings are supported by other showing that higher age, BMI and female gender are associated with knee osteoarthritis.¹⁰⁻¹²

Acute distortions were seen significantly more often in athletes (8.8%) than in non-athletes (5.2%), but the difference is small. Most of the distortions of the athletes occurred during soccer, cycling, fitness, tennis and walking. There were few differences in the initial policy of the GP between the two groups. In this context it must be mentioned that there can be an overlap between the different treatment strategies, i.e. one patient could receive more than one advice and/or treatment at their first consultation at the GP. However, athletes were more often advised to 'go easy on the knee' than the non-athletes; this is probable related to the physical activity level of the athletes or to the type of knee complaints. Patients with acute distortions were significantly more often advised to 'go easy on the knee', whereas patients with osteoarthritis and chronic meniscus fractures were significantly less often advised to do this. These findings might also be related to the fact that it is difficult for non-athletes to reduce their level of physical activities.

In the Dutch healthcare system patients generally have to visit their GP before being referred to a therapist or specialist. Consequently, we found a strong relationship between revisiting the GP and medical consumption ($p < 0.001$). Therefore, we repeated the analysis for medical consumption (therapist or specialist) with adjustment for revisiting the GP. The adjusted analysis no longer showed a significant difference in medical consumption between the two groups ($p = 0.20$). Thus, referral to therapists or specialists in this study is more dependent on the number of GP visits than on being an athlete or not. In the adjusted analysis we also found a significant difference in revisiting the GP between the two groups. However, the difference between both groups is very small: 36.8% versus 35.8%. Analyses showed that revisiting GP is more dependent on age and functional disability at baseline than on being an athlete or not. It is however noteworthy that there is a trend towards increased medical consumption among the athletes while the functional disability scores are higher and the pain scores lower than among the non-athletes. Besides, the athletes experienced less discomfort during their daily and work duties than the non-athletes, which might indicate that the athletes make greater demands on their body than the non-athletes. The role of the GP in this relationship remains unknown, i.e. it is unknown if the GP is aware of the physical activity level of the individual patient at consultation. At one-year follow-up, almost 55% of the athletes indicated that they had recovered from their knee complaint versus 45% of the non-athletes. This difference is, however, not significant ($p = 0.40$); the multivariate

analysis showed that the recovery ratio is more dependent on age, gender and trauma than on physical activity level. Therefore, this study does not give any indications for the GP to inform athletes different than non-athletes regarding the prognosis of their knee complaints. Finally, we did not find any substantial differences in the diagnosis and prognosis of the knee complaints between athletes and non-athletes but we did find a difference in medical consumption between the athletes and non-athletes. Apparently athletes do prefer a more active strategy compared to non-athletes. However, the exact reason for this higher medical consumption remains unknown.

LIMITATIONS

More than one third of the knee complaints are labeled by the GP as 'general knee complaints', indicating some difficulty in arriving a precise diagnosis of the knee complaints of their patients.

Although the group of athletes consisted of more males and younger people, because all analyses were adjusted for age, gender and BMI this difference should have no impact on our final conclusions. Further, the physical workload of the patients might have influenced the results of this study. The baseline questionnaire included some questions about work tasks; unfortunately, this information was not sufficient to analyze this potential confounder.

CONCLUSION

To our knowledge, this is the first study comparing athletes and non-athletes regarding knee pain in general practice. The results of this study indicate that there are no major differences in diagnosis and prognosis of knee complaints between athletes and non-athletes presented to the GP. This implies that there are no indications for different treatment strategies applied in both groups. Though, athletes are more often advised to 'go easy on the knee' and to rest than the non-athletes. However, this advice might be related to the physical activity level of the patients. Further, there is a trend towards increased medical consumption among athletes while the functional disability scores are higher and the pain scores are lower than among the non-athletes.

Acknowledgements

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REFERENCES

1. Picavet HS, Schouten JS. Musculoskeletal pain in the Netherlands: prevalences, consequences and risk groups, the DMC(3)-study. *Pain*. 2003;**102**(1-2):167-78.
2. van der Waal JM, Bot SD, Terwee CB, et al. The incidences of and consultation rate for lower extremity complaints in general practice. *Ann Rheum Dis*. 2006;**65**(6):809-15.
3. Majewski M, Susanne H, Klaus S. Epidemiology of athletic knee injuries: A 10-year study. *Knee*. 2006;**13**(3):184-8.
4. Giza E, Micheli LJ. Soccer injuries. *Med Sport Sci*. 2005;**49**:140-69.
5. Fredberg U, Bolvig L. Jumper's knee. Review of the literature. *Scand J Med Sci Sports*. 1999;**9**(2):66-73.
6. Witvrouw E, Lysens R, Bellemans J, et al. Intrinsic risk factors for the development of anterior knee pain in an athletic population. A two-year prospective study. *Am J Sports Med*. 2000;**28**(4):480-9.
7. Heintjes EM, Berger MY, Koes BW, et al. Knee disorders in primary care: design and patient selection of the HONEUR knee cohort. *BMC Musculoskelet Disord*. 2005;**6**:45.
8. Roorda LD, Jones CA, Waltz M, et al. Satisfactory cross cultural equivalence of the Dutch WOMAC in patients with hip osteoarthritis waiting for arthroplasty. *Ann Rheum Dis*. 2004;**63**(1):36-42.
9. Bellamy N, Buchanan WW, Goldsmith CH, et al. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol*. 1988;**15**(12):1833-40.
10. D'Ambrosia RD. Epidemiology of osteoarthritis. *Orthopedics*. 2005;**28**(2 Suppl):s201-5.
11. Du H, Chen SL, Bao CD, et al. Prevalence and risk factors of knee osteoarthritis in Huang-Pu District, Shanghai, China. *Rheumatol Int*. 2005;**25**(8):585-90.
12. Sandmark H, Hogstedt C, Lewold S, et al. Osteoarthrosis of the knee in men and women in association with overweight, smoking, and hormone therapy. *Ann Rheum Dis*. 1999;**58**(3):151-5.



Chapter 4

The PEX study - Exercise therapy for patellofemoral pain syndrome: design of a randomized clinical trial in general practice and sports medicine [ISRCTN83938749]

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ABSTRACT

Background

Patellofemoral complaints are frequently seen in younger and active patients. Clinical strategy is usually based on decreasing provoking activities as sports and demanding knee activities during work and leisure and reassuring the patient on the presumed good outcome. Exercise therapy is also often prescribed although evidence on effectiveness is lacking. The objective of this article is to present the design of a randomized clinical trial that examines the outcome of exercise therapy supervised by a physical therapist versus a clinically accepted “wait and see” approach (information and advice about the complaints only). The research will address to both effectiveness and cost effectiveness of supervised exercise therapy in patients with patellofemoral pain syndrome (PFPS).

Methods/design

136 patients (adolescents and young adults) with patellofemoral pain syndrome are recruited in general practices and sport medicine centers. They will be randomly allocated receiving either 3 months of exercise therapy or usual care. The primary outcome measures are pain, knee function and perception of recovery after 3 months and 12 months of follow up and will be measured by self-reporting. Measurements will take place at baseline, 6 weeks, and 3 monthly until 1 year after inclusion in the study.

Secondary outcome measurements include an economic evaluation. A cost-utility analysis will be performed that expresses health improvements in Quality Adjusted Life Years (QALYs) and incorporates direct medical costs and productivity costs.

Discussion

This study has been designed after reviewing the literature on exercise therapy for patellofemoral pain syndrome. It was concluded that to merit the effect of exercise therapy a trial based on correct methodological concept needed to be executed.

The PEX study is a randomized clinical trial where exercise therapy is compared to usual care. This trial started in April 2005 and will finish in June 2007. The first results will be available around December 2007.

BACKGROUND

Patellofemoral pain syndrome (PFPS) is a common complaint in adolescents and younger adults. Though exact epidemiological data do not exist, 5-6 six new cases per year in Dutch GP-practices may be expected.^{1,2} The symptom most frequently reported is a diffuse peripatellar and retropatellar localized pain, typically provoked by ascending or descending stairs, squatting, cycling and sitting with flexed knees for prolonged periods of time.^{2,3} Weakness of the knee extensors and abnormal firing patterns of the nerves innervating these knee extensors have been found in patients with PFPS. These phenomena are thought to cause maltracking of the patella through the femoral groove, resulting in increased intrapatellar pressure. Tight anatomical structures and heavy physical loading may add to the pressure. This pressure probably causes patellofemoral pain.

PFPS frequently becomes a chronic problem, forcing the patient to stop sports and other similar activities.⁴ The long-term prognosis is generally more favorable for young patients, but seems to be independent of the presence of cartilage damage or gender.⁵

Clinical guidelines of the Dutch College of General Practitioners advise GPs to inform the patient about the background of the condition and its favorable prognosis.⁶ Patients are advised to refrain from all (sports-) activities that provoke pain, and to find alternative exercises to keep in shape. Non-weight bearing quadriceps strengthening exercises may be considered, but the guidelines explicitly mention that evidence for its effectiveness is lacking. Patellar taping is not advised. In case of prolonged unresponsive, severe complaints, referral to an orthopedic surgeon may be considered. General practitioners do not always adhere to these guidelines and prescriptions for analgesics such as paracetamol and NSAIDs to reduce pain and referrals to physical therapists (exercise therapy) are among the treatments regularly encountered (unpublished data authors). People involved in sports and athletic activities may consult sports clinics with their symptoms. In sports clinics it is more common to refer to physical therapy for exercises (unpublished data authors).

Evidence for the effectiveness of conservative therapies for PFPS is scarcely available.² Exercise therapy is based on the theoretical assumption that muscle weakness or imbalance is a major contributor in the development of PFPS. The recent Cochrane review performed by our group identified only 3 trials comparing exercise therapy with a control group not receiving exercise therapy.⁷

We found limited evidence that exercise was beneficial, though the quality of the trials was such that further research was recommended to confirm this conclusion.⁷ Recently a small placebo controlled trial was published investigating the short-term effectiveness of exercise therapy combined with taping and passive manual mobilization of the patella. The control group received sham ultrasound and placebo-taping. The authors

reported beneficial effects in the intervention group (n=33) compared the control group (n=34) after 6 weeks follow-up.⁸ Cost effectiveness data are not available at all.

Because physicians, especially the GP and sports physician, frequently are confronted with patients with PFPS, but by lack of evidence are unable to apply the most (cost)effective treatment, a randomized intervention study is highly indicated. The 'wait and see' policy advocated in the guidelines should be compared to the more active approach of exercise therapy under supervision of a physical therapist, in order to assess (cost) effectiveness of both approaches.

The trial will target patients (adolescents and young adults) presenting in general practice and sports clinics with the symptoms of PFPS and no history of previous active treatment with exercises. In this article we will present the detailed protocol of the trial. This trial started April 2005 and patients will be included until June 2006.

METHODS/DESIGN

Study design

This study is a randomized clinical trial to study short-term and long-term (cost) effectiveness of exercise therapy in combination with advice and information on the background of PFPS compared to advice and information on the background of PFPS only ("wait and see")

The study design (Figure 1) was approved by the Medical Ethics Committee at the Erasmus MC – university medical centre Rotterdam. All patients gave written informed consent.

Patient selection

Patients eligible for this trial are adolescents and young adults in the age of 14 to 40 years consulting the GP or sports physician for PFPS lasting longer than two months but not longer than 2 years. Recruitment will take place in "HONEUR" practices (a research network of 38 general practices allied with the Department of General Practice of Erasmus MC) and in 4 sports medical centers in Rotterdam, Leidschendam, Breda and Gorinchem.

The recruitment period is planned from April 2005 until June 2006.

In- and exclusion criteria

Inclusion criteria are the following diagnostic criteria; Presence of at least 3 symptoms of the following: pain when walking stairs, pain when squatting, pain when running, pain when cycling, pain when sitting with knees flexed for a prolonged period of time, grinding of the patella, positive physical tests (Clarke's test, Rabot sign, patella release test).

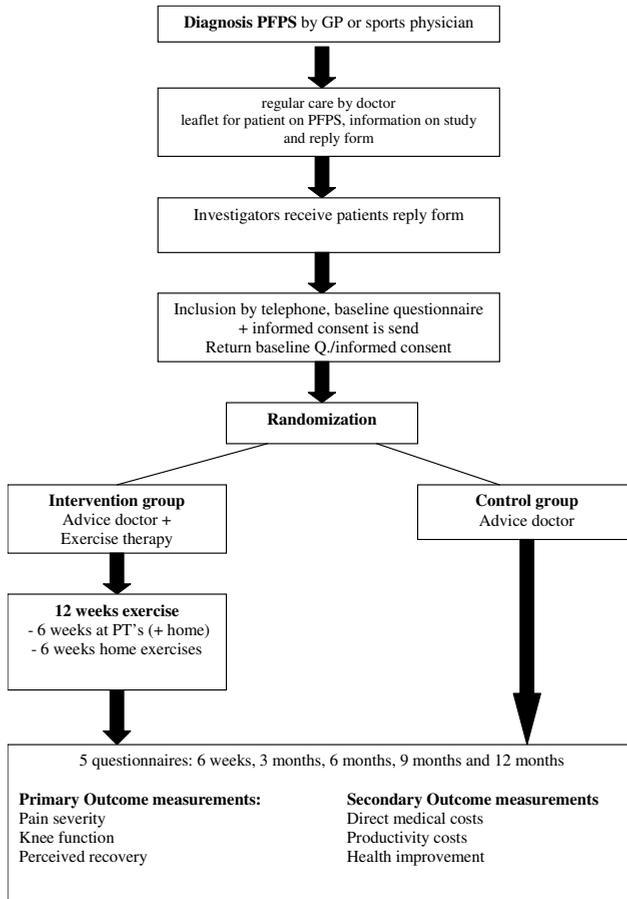


Figure 1 Flow chart of the study design

The exclusion criteria are: knee osteoarthritis / arthritis, previous knee injury or knee operations, patellar tendinopathy, M.Osgood Schlatter, or other defined pathological conditions of the knee.

Sample size

Sample size is based on studies included in our systematic review.⁷ In a single study investigating a similar contrast of interventions there was an absolute increase in recovery of 22% (19% recovery in the usual care group to 41% recovery in the exercise therapy group) after one year, OR 2.21 (95%CI 0.87 - 5.64).⁹ This represents a clinically relevant increase and is expected to be even more pronounced after 3 months follow-up. Such a difference can be detected statistically (power 0.80, alpha 0.05 one-sided test) with 61 patients per group. With a potential dropout rate of 10% a total of 136 patients should be included.

Intervention

The interventions that will be compared in this trial are: A) Exercise therapy for a period of 6 weeks, provided by a physical therapist according to a standardized protocol drawn up according to present international expert opinion and modified by local participating physical therapists into a practical protocol which is feasible in daily practice. The program consists of static and dynamic muscular exercises for quadriceps muscles, balance exercises and flexibility exercises. Patients are directed to practice 7 times a week during 20 minutes.

Instructions concerning the exercises will be noted on the “workout book” (Figure 2) which has been designed for the study. The notes regarding frequency and duration of exercises are sent to the investigators after the three month period of exercise.

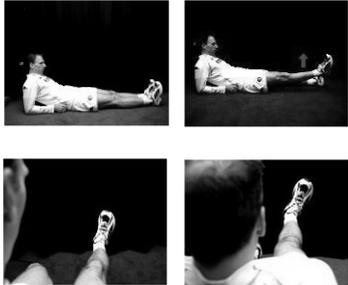
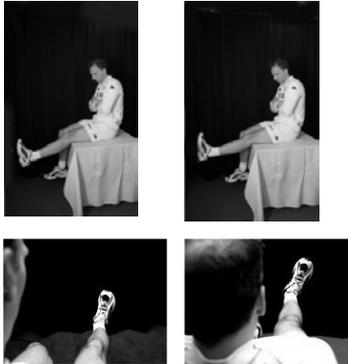
<p>Straight leg raising Straight leg raising (supine) (leg in external rotation)</p> <p>3 series, 30 reps</p>	
<p>Leg extensions: 10° flexion to full extension</p> <p>3 series, 30 reps</p>	
<p>Isometric VMO/ Adductor Magnus contraction in full extension Contraction of quadriceps muscles, external rotation of the foot.</p> <p>3 series, 8 reps, 10-15 seconds</p>	

Figure 2: Sheet from the workout book with example exercises

Patients will receive standardized information about the background and prognosis of PFPS on a specially designed leaflet. After the period of 6 weeks patients will be advised to keep up the exercises at home for the following 6 weeks.

B) The control group will receive the standardized information and advice. This advice consists of the information usually given by GPs, according to the guidelines: information about the background of the condition and its good prognosis, advice to refrain from all (sports-) activities that provoke pain, and to find alternatives to keep in shape.

An information leaflet for the patients has been compiled to contribute to the standardization for both groups.

Co-interventions:

During the one year follow-up other interventions like the use of ice applications, bandages or braces, or consumption of oral analgesics (NSAIDs or paracetamol) indicated by pain severity are allowed for both groups. Information about these co-interventions will be collected after 6 weeks and every 3 months and during one year follow-up and will be used in the cost-effectiveness analysis.

Randomization

After recruitment through the participating GP's and sport physicians the patient is finally accepted in the study after written informed consent and reassessment of the inclusion and exclusion criteria. Following this informed consent and baseline assessments, patients are allocated to the intervention or control group using a blinded and computer based randomization list. The randomization table will be stratified for the setting (general practice versus sports clinic) and for age (14-18 versus 19-40). Patients are informed about the treatment allocation and subsequently the patients in the exercise group receive their treatment from a physical therapist in a predetermined center, whereas patients in the control group will not receive this intervention.

Measurements

Outcome parameters:

Primary outcome measures are: perceived recovery (measured with a 7 point Likert scale), functional disability using a disease-specific disability scale (Kujala Patellofemoral Scale) and a pain severity using a numerical rating scale after 3 and 12 months of follow-up.¹⁰⁻¹² (Table 1)

Secondary outcome measures are cost-effectiveness after one year, the primary outcome parameters at 6 weeks follow-up, quality of life (Euroqol) and a numerical rating scale (NRS 0-10) for difficulties encountered during work, school or sports activities.¹³ Medical consumption (visits to health care providers and consumptions of prescription

Table 1: Questionnaires for primary and secondary outcome measurements

Primary outcome measurements	
Perceived recovery	Likert scale
Functional disability	Kujala Patellofemoral Scale
Pain Severity	Numerical Rating Scale (NRS)
Secondary outcome Measurements	
Direct medical costs	Healthcare Consumption
Productivity costs	PRODISQ
Health (improvement)	EuroQoI

or over the counter medication), absence from work or decreased productivity at work, and other indirect and direct costs are all included in the economic evaluation.

Baseline and follow-up questionnaires at 6 weeks and 3 and 12 months will be filled out by the patients themselves. Quality of life, direct costs and productivity costs and compliance to the interventions will be measured after 6 weeks and every 3 months during one year also by self-reporting..

Analyses

All analyses will take place after the trial has finished, no intermediate analyses will be performed.

To evaluate the effectiveness of supervised exercise therapy in patients with PFPS differences in clinical outcome measures between intervention and control group will be analyzed on the basis of intention to treat. Additionally, analysis per protocol will be conducted. Dichotomous outcomes at three and 12 months follow-up will be analyzed using logistic regression techniques and continuous outcomes with linear regression techniques. Of the primary outcomes perceived recovery will be dichotomized to recovered (fully, strongly) or not recovered (slightly-strongly worsened). Other primary outcome measurements will be analyzed as continuous variables. Analyses will be adjusted for baseline values and for co-interventions and possible prognostic factors in case the effect estimate changes with more than 10% when including these variables in the model.

Additionally the overall one year dichotomous outcomes will be analyzed using GEE (generalized estimating equations), continuous outcomes will be analyzed using linear regression for repeated measurements.¹⁴ Both techniques take the correlation of multiple measurements within one patient into account.

Research question 2 "What is the cost-effectiveness of supervised exercise therapy in patients with PFPS" is the basis for the economic evaluation.

In the economic evaluation (a cost utility analysis) both the costs and the consequences of both treatment options are compared and incremental costs and incremental health effects the latter (in terms of quality of life) is estimated.

The economic evaluation is performed alongside the randomized clinical trial. Patients will complete questionnaires for costs and quality of life after 6 weeks and every 3 months. Only if the difference in health between the treatment arms appears not to be stable over time, an additional modeling study using a Markov model will be performed. Statistical methods are used to describe uncertainty in costs and effects estimates based on patient data. A 95% confidence interval for the cost-utility ratio will be calculated and an acceptability curve will be presented.

Cost-analysis

For the economic evaluation a societal perspective is employed. The relevant costs are divided into direct medical costs and productivity costs.

- Direct costs

The costs of health care utilization during the twelve months follow-up consist of visits to a general practitioner, medical specialist, physiotherapist, manual therapist, prescribed and over the counter (OTC) medicines, alternative practitioners and hospitalization and appliances. In the patient questionnaire we ask for the health care consumption in the past six weeks. The costs for the period between two measurements (mostly 3 months) are established through linear interpolation. The medical consumption is valued based on resource costs and guideline costs.¹⁵

- Productivity costs

The productivity costs are defined as the costs of absence from work due to PFPS, including the impact of compensation mechanisms the costs of efficiency loss due to PFPS and the costs of hindrance at unpaid work. In the questionnaire the patients are asked to report the reason for absence from work and the number of absent days.^{16 17} To this end we will use the PRODISQ questionnaire.¹⁸ The valuation of an hour work the average productivity costs per hour worked will be based on the Net National Income per working hour.¹⁵ The friction cost method is used to value the productivity costs related to paid work.¹⁹ Productivity costs can also occur when people with health complaints are still working, but at a lower productivity level. This is called efficiency loss. The efficiency losses without absence are established by means of the Quality and Quantity-method.¹³ Productivity losses at unpaid work are assessed by hindrance at unpaid work and the number of hours that housekeeping tasks were taken over by other people, and for how many hours paid help was needed. The costs of one hour of housekeeping tasks is set at the current price of one hour of simple professional home care.

- Patient outcome analysis in the economic evaluation

The patellar pain may affect Health Related Quality of Life. This is measured with a generic instrument, the EuroQol instrument EQ-5D^{20 21} The EQ-5D descriptive system consists of five dimensions (Mobility, Self Care, Usual Activities, Pain/Discomfort and Anxiety/Depression) with three levels each (no problems, some problems and extreme problems), thus defining 243 (35) distinct health states. Respondents of the EuroQol EQ-5D describe their own health using this descriptive system. Preference weights based on the Time Trade-Off method for the 243 EQ-5D health states are available from a large-scale study in the UK and a recent Dutch study to calculate EQ-5D index scores that can be used as utilities to calculate QALYs.^{20 21 22}

DISCUSSION

The PEX-study has been designed after reviewing the literature on exercise therapy for patellofemoral pain syndrome.⁷ It was concluded that though exercise therapy may have a beneficial effect on PFPS the scientific evidence is limited due to small sample size and a small amount of studies including a control group.

Based on available literature our research group expects to discover (beneficial) changes from exercise therapy in perceived recovery, pain severity and functional disability in the PEX study.

The PEX study is a randomized clinical trial where exercise therapy is compared to usual care. The trial started in April 2005 and is expected to finish in June 2007. The first results will be available around December 2007.

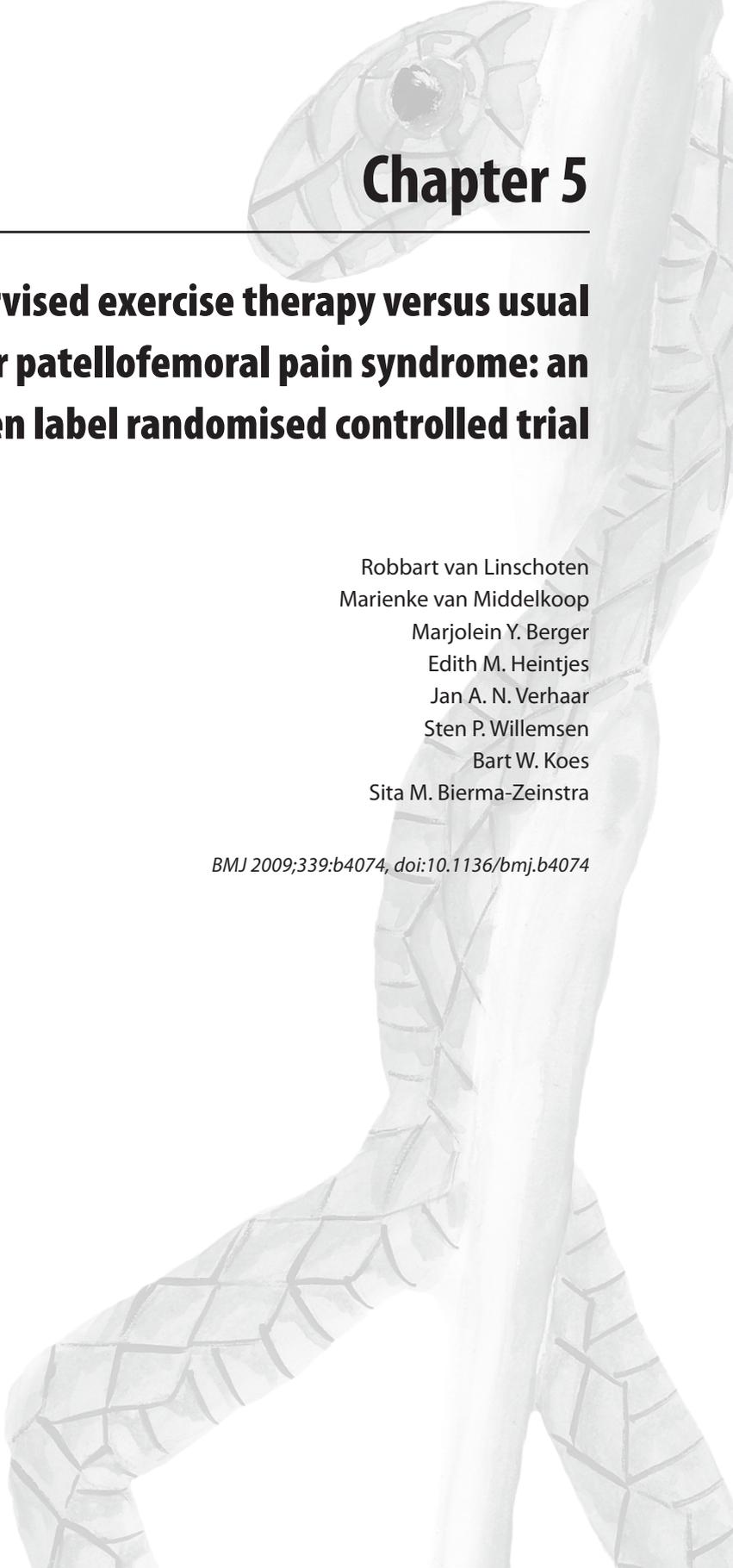
Acknowledgements

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REFERENCES

1. Van der Velden J. Een nationale studie naar ziekten en verrichtingen in de huisartspraktijk. Basisrapport: morbiditeit in de huisartspraktijk. Utrecht: NIVEL, 1991.
2. Arroll B, Ellis-Pegler E, Edwards A, Sutcliffe G. Patellofemoral pain syndrome. A critical review of the clinical trials on nonoperative therapy. *Am J Sports Med* 1997;25(2):207-12.
3. Cutbill JW, Ladly KO, Bray RC, Thorne P, Verhoef M. Anterior knee pain: a review. *Clin J Sport Med* 1997;7(1):40-5.
4. Witvrouw E, Lysens R, Bellemans J, Cambier D, Vanderstraeten G. Intrinsic risk factors for the development of anterior knee pain in an athletic population. A two-year prospective study. *Am J Sports Med* 2000;28(4):480-9.
5. Natri A, Kannus P, Jarvinen M. Which factors predict the long-term outcome in chronic patellofemoral pain syndrome? A 7-yr prospective follow-up study. *Med Sci Sports Exerc* 1998;30(11):1572-7.
6. Cirkel JW, Klaassen WRC, Kunst JA, Aarns TEM, Plag EC, Goudswaard AN, et al. Niet-Traumatische knieproblemen bij kinderen en adolescenten; NHG-Standaard. *Huisarts Wet* 1998;41(5):246-251.
7. Heintjes E, Berger MY, Bierma-Zeinstra SM, Bernsen RM, Verhaar JA, Koes BW. Exercise therapy for patellofemoral pain syndrome. *Cochrane Database Syst Rev* 2003(4):CD003472.
8. Crossley K, Bennell K, Green S, Cowan S, McConnell J. Physical therapy for patellofemoral pain: a randomized, double-blinded, placebo-controlled trial. *Am J Sports Med* 2002;30(6):857-65.
9. Clark DI, Downing N, Mitchell J, Coulson L, Syzpyt EP, Doherty M. Physiotherapy for anterior knee pain: a randomised controlled trial. *Ann Rheum Dis* 2000;59(9):700-4.
10. Van Der Heijden GJ, Leffers P, Wolters PJ, Verheijden JJ, van Mameren H, Houben JP, et al. No effect of bipolar interferential electrotherapy and pulsed ultrasound for soft tissue shoulder disorders: a randomised controlled trial. *Ann Rheum Dis* 1999;58(9):530-40.
11. Kujala UM, Jaakkola LH, Koskinen SK, Taimela S, Hurme M, Nelimarkka O. Scoring of patellofemoral disorders. *Arthroscopy* 1993;9(2):159-63.
12. Crossley KM, Bennell KL, Cowan SM, Green S. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil* 2004;85(5):815-22.
13. Brouwer WB, Koopmanschap MA, Rutten FF. Productivity losses without absence: measurement validation and empirical evidence. *Health Policy* 1999;48(1):13-27.
14. Diggle PJ, Liang KY, Zeger SL. Analysis of Longitudinal Data. Oxford: Clarendon Press, 1994.
15. Oostenbrink JB, Koopmanschap MA, Rutten FFH. Handleiding voor kostenonderzoek; methoden en richtlijnrijzen voor economische evaluaties in de gezondheidszorg. Amstelveen: College voor zorgverzekeringen, 2000.
16. Jacob-Tacken KH, Koopmanschap MA, Meerding WJ, Severens JL. Correcting for compensating mechanisms related to productivity costs in economic evaluations of health care programmes. *Health Econ* 2005;14(5):435-43.
17. van Roijen L, Essink-Bot ML, Koopmanschap MA, Bonsel G, Rutten FF. Labor and health status in economic evaluation of health care. The Health and Labor Questionnaire. *Int J Technol Assess Health Care* 1996;12(3):405-15.
18. Koopmanschap M. PRODISQ: a modular questionnaire on productivity and disease for economic evaluation studies. *Expert Rev Pharmacoeconomics Outcomes Res* 2005;5(1):23-28.
19. Koopmanschap MA, Rutten FF, van Ineveld BM, van Roijen L. The friction cost method for measuring indirect costs of disease. *J Health Econ* 1995;14(2):171-89.
20. Brooks R. EuroQol: the current state of play. *Health Policy* 1996;37(1):53-72.

- 21 Dolan P, Gudex C, Kind P, Williams A. The time trade-off method: results from a general population study. *Health Econ* 1996;5(2):141-54.
- 22 Lamers LM, Stalmeier PF, McDonnell J, Krabbe PF, van Busschbach JJ. [Measuring the quality of life in economic evaluations: the Dutch EQ-5D tariff]. *Ned Tijdschr Geneesk* 2005;149(28):1574-8.



Chapter 5

Supervised exercise therapy versus usual care for patellofemoral pain syndrome: an open label randomised controlled trial

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ABSTRACT

Objective

To assess the effectiveness of supervised exercise therapy compared with usual care with respect to recovery, pain, and function in patients with patellofemoral pain syndrome.

Design

Open label randomised controlled trial.

Setting

General practice and sport physician practice.

Participants

Patients with a new episode of patellofemoral pain syndrome recruited by their general practitioner or sport physician.

Interventions

The intervention group received a standardised exercise programme for 6 weeks tailored to individual performance and supervised by a physical therapist, and were instructed to practise the tailored exercises at home for 3 months. The control group were assigned usual care, which comprised a “wait and see” approach of rest during periods of pain and refraining from pain provoking activities. Both the intervention group and the control group received written information about patellofemoral pain syndrome and general instructions for home exercises.

Main outcome measures

The primary outcomes were self reported recovery (7 point Likert scale), pain at rest and pain on activity (0-10 point numerical rating scale), and function (0-100 point Kujala patellofemoral score) at 3 months and 12 months follow-up.

Results

A total of 131 participants were included in the study: 65 in the intervention group and 66 in the control group. After 3 months, the intervention group showed better outcomes than the control group with regard to pain at rest (adjusted difference -1.07 , 95% confidence interval -1.92 to -0.22 ; effect size 0.47), pain on activity (-1.00 , -1.91 to -0.08 ; 0.45), and function (4.92, 0.14 to 9.72; 0.34). At 12 months, the intervention group continued to show better outcomes than the control group with regard to pain (adjusted difference in pain at rest -1.29 , -2.16 to -0.42 ; effect size 0.56; pain on activity -1.19 , -2.22 to -0.16 ; effect size 0.54), but not function (4.52, -0.73 to 9.76). A higher

proportion of patients in the exercise group than in the control group reported recovery (41.9% v 35.0% at 3 months and 62.1% v 50.8% at 12 months), although the differences in self-reported recovery between the two groups were not statistically significant. Pre-defined subgroup analyses revealed that patients recruited by sport physicians (n=30) did not benefit from the intervention, whereas those recruited by general practitioners (n=101) showed significant and clinically relevant differences in pain and function in favour of the intervention group.

Conclusion

Supervised exercise therapy resulted in less pain and better function at short term and long term follow-up compared with usual care in patients with patellofemoral pain syndrome in general practice. Exercise therapy did not produce a significant difference in the rate of self-reported recovery.

Trial registration ISRCTN83938749.

INTRODUCTION

Patellofemoral pain syndrome can be defined as pain around the patella that occurs during or after high loaded flexion and extension of the knee.¹⁻³ The main symptom is pain, and the condition generally progresses to impaired function. Physicians, especially general practitioners (GPs) and sport physicians are frequently confronted with patients who have patellofemoral pain syndrome. Although there are no precise epidemiological data, an average GP practice in the Netherlands reports about five or six new cases a year.⁴ In sport medicine practices, patellofemoral pain syndrome comprises up to 25% of all new running injuries.^{5,6} Women are more likely to be affected than men.⁷ Pain usually starts during adolescence when participation in sporting activities is high,⁷ although symptoms can occur over a prolonged period of time.⁸ Extensive diagnostic investigations do not yield specific pathology. There is no agreement concerning the etiology of patellofemoral pain syndrome or the most appropriate treatment. There is, however, general consensus that the preferred treatment approach is non-surgical. Rest during periods of pain and refraining from pain provoking activities are advised; this “wait and see” approach is advocated in the Dutch national GP guidelines and is considered usual care.⁹

An active approach to treating patellofemoral pain syndrome has been advocated since the 1990s. Strategies range from simple quadriceps strengthening to more complex exercise therapy including taping or bracing.^{1,3,6,8,10,11} According to a systematic review on the benefits of exercise therapy for patellofemoral pain syndrome,¹² there is only limited evidence that exercise is more effective than no exercise with respect to pain reduction. Furthermore, the evidence as to whether exercise provides functional improvement is conflicting.

The objective of the present study was to investigate in the short term as well as in the long term the effects of exercise therapy compared with usual care in patients with patellofemoral pain syndrome.

METHODS

The study protocol has been published previously.¹³ Briefly, patients aged between 14 and 40 years consulting their GP or sport physician for patellofemoral pain syndrome were eligible for this trial. Inclusion criteria comprised the presence of at least three of the following symptoms: pain when walking up or down stairs; pain when squatting; pain when running; pain when cycling; pain when sitting with knees flexed for a prolonged period of time; grinding of the patella; and a positive clinical patellar test (such as Clarke’s test or patellar femoral grinding test).^{14,15} Symptoms had to have persisted for

longer than 2 months but not longer than 2 years. Patients were excluded if they had knee osteoarthritis, patellar tendinopathy, Osgood-Schlatter disease, or other defined pathological conditions of the knee, or had previous knee injuries or surgery. Patients were also excluded if they had already been treated with supervised exercise therapy. Recruitment took place in 38 "HONOUR" practices—general practices allied with the Department of General Practice at Erasmus University Medical Center—and in four sports medical centers in Rotterdam, Leidschendam, Breda, and Gorinchem. Eligible patients were informed about the study and introduced to the research team, who provided patients with more extensive information, checked that patients met the inclusion and exclusion criteria, and obtained informed consent. After inclusion, patients were randomly allocated to the intervention (exercise therapy) or the control (usual care). The randomisation was done by an independent researcher who used a computer generated list in which patients were stratified by age (14-17 years or 18 years and older) and by recruiting physician (GP or sport physician). A block size of eight was used within the four strata.

Interventions

Patients in the intervention group followed a standardized exercise protocol tailored to individual achievement and were supervised by a physical therapist. The program consisted of a general warm up on a bicycle ergometer followed by static and dynamic muscular exercises for the quadriceps, adductor, and gluteal muscles. The program also included balance exercises and flexibility exercises for major thigh muscles. Patients exercised for 25 minutes supervised by the physical therapist. The load of the exercise program was increased every 2 weeks during the first 6 weeks by increasing the number of repetitions or the intensity of the exercises. The increment of the exercise protocol was monitored by the physical therapist who was guided by pain reaction on exertion. Patients visited the therapist nine times in 6 weeks. In addition, they were instructed to practice the exercises daily for 25 minutes over a period of 3 months. To enhance compliance, patients received a tutorial with photographs, a text explaining the exercises, and a diary to register the amount of exercising. Both the intervention group and the control group received standardised information and advice from their GP or sport physician about the background of patellofemoral pain syndrome and its good prognosis, as well as advice to refrain from all sports activities that provoke pain. Patients were recommended to use a simple analgesic such as paracetamol when pain was severe and to find alternative ways to keep in shape.

Instructions for daily isometric quadriceps contractions were given to both groups according to the guidelines for Dutch GPs.⁹ All this information was compiled to a leaflet that was handed to the patients in both groups to promote standardisation (see web extra).

Other interventions—like the use of bandages or braces, insoles, or ice applications, or consumption of medication other than simple analgesics—were allowed in both groups. Information about these additional interventions was collected after 6 weeks and at 3, 6, 9, and 12 months using self-report questionnaires. Physicians were instructed not to refer patients in the control group to a physical therapist during the first 3 months of follow-up (that is, when participants in the intervention group were receiving the exercise therapy), and patients in the control group were instructed not to visit a physical therapist during this period.

Outcome measurement

Follow-up self-report questionnaires were filled in by patients at baseline, at 6 weeks, and at 3 months, 6 months, 9 months, and 12 months after inclusion in the study. Primary outcomes measured at 3 and 12 months follow-up were: perceived recovery compared with at the start of the study, measured on a 7 point Likert scale ranging from “completely recovered” to “worse than ever”; functional disability, measured using the Kujala Patellofemoral Scale, a disease specific validated disability scale ranging from 0 (complete disability) to 100 (fully functional)¹⁶; and pain severity at rest and on activity, measured using a numerical rating scale ranging from 0 (no pain) to 10 (unbearable pain).^{17 18} Patients were deemed to have recovered if they rated themselves as “fully recovered” or “strongly recovered” on the Likert scale, whereas those who rated themselves as “slightly recovered” to “worse than ever” were deemed to have not recovered. This threshold was used to dichotomise perceived recovery into two clear categories: “recovered” and “not recovered.”

Sample size

Our sample size calculation was based on a previous study by Clark et al that undertook a similar comparison of interventions.¹⁹ They reported an absolute increase in recovery after one year of 22% in the exercise therapy group (19% recovery in the usual care group compared with 41% recovery in the exercise therapy group). Such a difference can be detected statistically with 61 patients in each group (power 0.80, alpha 0.05, one sided test for the additional value of supervised exercise therapy). We anticipated that we would need a study population of 136 patients, allowing for a potential dropout rate of 10%.

Statistical analysis

Differences between the intervention and control group were analysed on an intention to treat basis. Subgroup analysis was performed for predefined subgroups based on age and type of recruiting physician. Differences in dichotomous outcomes (between “recovered” patients and “not recovered” patients) were analysed using logistic regres-

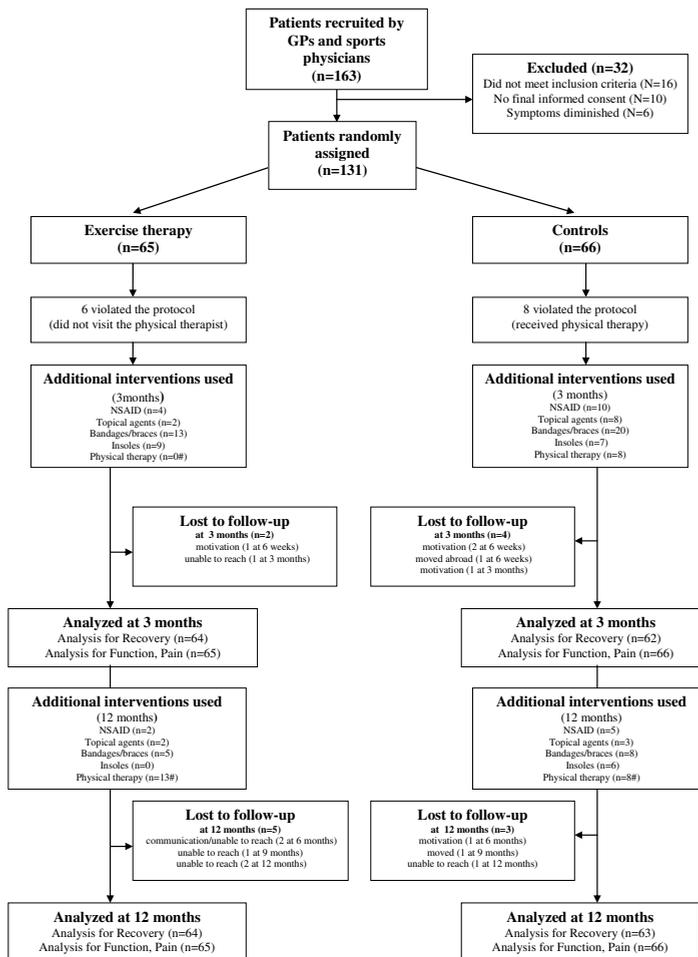


Figure 1 Flow chart of the recruitment, inclusion, assignment, and subsequent follow-up of the study patients. #=physical therapy additional to intervention

sion techniques for repeated measurements (including measurements at 6 weeks and at 3, 6, 9, and 12 months) and expressed in odds ratios. Differences in continuous outcomes (pain scores and functional scores) were analysed with linear regression techniques for repeated measurements, which take the correlation of multiple measurements within one patient into account.

Possible prognostic variables (age, gender, BMI, duration of knee symptoms, presence of bilateral symptoms, educational level, work participation, sports participation, and recruiting physician) were tested for their prognostic value in univariate regression analyses. All analyses were adjusted for baseline values and for possible prognostic factors. The influence of exercise therapy on each outcome was tested using a model that

included prognostic variables with a P value of 0.1 or less and baseline values for pain at rest, pain on activity, and function score. Although the sample size calculation was based on a one sided testing approach, for the convenience of the reader we chose to show the results for the more conservative two sided tests, which were statistically significant at a P value of 0.05. For statistically significant dichotomous outcomes, the number needed to treat is given (defined as 1/risk difference for the defined outcome). For continuous data, we report effect sizes (Cohen's d), which are defined as the difference in outcome between the groups divided by the standard deviation of the baseline scores for this outcome.²⁰ Differences in the number of additional interventions used in both groups were tested with Chi square statistics at a significance level of P=0.05. Analyses were conducted with SPSS 12.0 (SPSS; Chicago, IL, USA) and SAS 8.2 (SAS Institute; Cary, NC, USA).

RESULTS

Between April 2005 and April 2007, 163 patients with patellofemoral pain syndrome were recruited by the participating GPs and sport physicians. Of these individuals, 16 patients did not meet the inclusion criteria, 10 withdrew consent after being informed more extensively, and six were excluded because their symptoms had diminished. Therefore, a total of 131 patients were enrolled in the study and randomly assigned to the intervention group or the control group. Figure 1 shows the recruitment, inclusion, assignment, and subsequent follow-up of the study patients.

The exercise therapy group (n=65) and control group (n=66) had similar baseline characteristics (table 1). Almost twice as many women as men were included in the whole sample. Bilateral knee symptoms were more common than unilateral symptoms, and the study population had a high level of sports participation.

PRIMARY OUTCOME PARAMETERS

Tables 2 and 3 show the primary outcome measurements (recovery, function scores, and pain) at baseline and at 3 and 12 months follow-up. Outcomes at 3 and 12 months were missing for some patients, but available data from other time points were included in the analyses. This approach meant that the number of patients was not always equal for the different outcome measures. Both the intervention and control group had a lower pain score at 3 months follow-up than at baseline. The adjusted analysis at 3 months showed a significant difference in pain at rest (-1.07, 95% CI -1.92 to -0.22; P=0.01) and pain on activity (-1.00, -1.91 to -0.08; P=0.03) in favour of the exercise group. The func-

tion score was considerably higher in the exercise than in the control group (adjusted difference 4.92, 0.14 to 9.72; $P=0.04$). Effect sizes for exercise therapy ranged from 0.47 (pain at rest) and 0.45 (pain on activity) to 0.34 (function). There was no significant difference in self-reported recovery, as defined by the outcome measurement “recovered,” between the groups at 3 months. When we used the outcome measurement “improved” (that is, “fully recovered,” “strongly recovered,” or “slightly recovered”), however, we found that recovery at 3 months was significantly more likely in the exercise group than in the control group (81% improved v 53% improved; adjusted odds ratio 4.07, 95% CI 1.86 to 8.90; number needed to treat 3.6).

Between 3 and 12 months, another eight patients were lost to follow-up (five in the intervention group and three in the control group; see fig 1). One person who was lost

Table 1. Baseline characteristics of the study population

	Exercise therapy (n=65)	Control (n=66)	Total (n=131)
Age in years (mean (SD))	24.7 (8.6)	23.3 (7.8)	24.0 (8.2)
Age ≥ 18 years (%)	69.3	69.7	69.5
Male gender (%)	35.4	36.4	35.9
BMI (mean (SD))	23.2 (3.9)	23.0 (3.4)	23.1 (3.6)
Duration of symptoms			
2-6 months (%)	69.2	66.6	67.9
6-24 months (%)	31.8	33.4	32.1
Bilateral knee symptoms (%)	55.4	65.2	60.3
Educational			
Low (elementary school, lower level high school) (%)	23.4	22.7	23.6
Medium or high (upper level high school, vocational college, university) (%)	76.6	77.3	76.4
Hours of work a week			
None (%)	26.2	28.8	27.4
<25 hrs (%)	35.4	36.4	35.9
≥ 25 hrs (%)	38.5	34.8	36.6
Sports participation	75.4	75.8	75.6
Recruiting physician			
General practitioner (%)	76.9	77.3	77.1
Sport physician (%)	23.1	22.7	22.9
Function score out of 100 (mean (SD))	64.4 (13.9)	65.9 (15.2)	65.1 (14.5)
Pain at rest out of 10 (mean (SD))	4.14 (2.3)	4.03 (2.3)	4.08 (2.3)
Pain on activity out of 10 (mean (SD))	6.32 (2.2)	5.97 (2.3)	6.15 (2.2)

BMI, body mass index; SD, standard deviation.

Table 2 Recovery at 3 and 12 months follow-up

	Exercise therapy (n=65)			Control (n=66)			Adjusted odds ratio† (95% CI) at 3 months	Adjusted odds ratio† (95% CI) at 12 months
	Baseline	3 months (n/N (%))	12 months (n/N (%))	Baseline	3 months (n/N (%))	12 months (n/N (%))		
Recovered*	—	26/62 (41.9)	36/58 (62.1)	—	21/60 (35.0)	30/59 (50.8)	1.34 (0.65 to 2.79)	1.60 (0.77 to 3.34)

Frequencies are reported for those patients available at that time point. Adjusted odds ratios are reported for the total available in analysis.

*Recovered=fully or strongly recovered.

†Recovery was adjusted for duration of symptoms.

Table 3 Function and pain scores at 3 and 12 months follow-up

	Exercise therapy (n=65)			Control (n=66)			Adjusted difference* (95% CI) at 3 months	Adjusted difference* (95% CI) at 12 months
	Baseline (mean (SD))	3 months (mean (SD))	12 months (mean (SD))	Baseline (mean (SD))	3 months (mean (SD))	12 months (mean (SD))		
Function score (0-100)	64.4 (13.9)	78.8 (15.5)	83.2 (14.8)	65.9 (15.2)	74.9 (17.6)	79.8 (17.5)	4.92 (0.14 to 9.72)	4.52 (−0.73 to 9.76)
Pain at rest (0-10)	4.14 (2.3)	2.30 (2.5)	1.43 (2.2)	4.03 (2.3)	3.22 (2.8)	2.61 (2.9)	−1.07 (−1.92 to −0.22)	−1.29 (−2.16 to −0.42)
Pain on activity (0-10)	6.32 (2.2)	3.81 (2.9)	2.57 (2.9)	5.97 (2.3)	4.60 (3.0)	3.54 (3.38)	−1.00 (−1.91 to −0.08)	−1.19 (−2.22 to −0.16)

Mean scores are reported for those patients available at that time point. Adjusted differences are reported for the total available in analysis.

*Function score was adjusted for baseline score, age, and duration of symptoms. Pain at rest was adjusted for baseline score and age. Pain on activity was adjusted for baseline score, age, and gender. Positive adjusted differences for the function score, and negative difference for pain scores, are in favour of the exercise group.

before the 3 month follow-up was located and available for follow-up in the 3-12 month period.

At the 12 month follow-up, further improvement on pain and function scores from baseline was noted for both groups. The adjusted differences in pain scores between the groups still showed a significant difference in favour of the exercise group (pain at rest −1.29, 95% CI −2.16 to −0.42; $P < 0.01$ and pain on activity −1.19, −2.22 to −0.16; $P = 0.02$). The effect sizes for exercise therapy on pain were 0.56 and 0.54, respectively. The difference in function scores at 12 months, however, did not reach statistical significance (4.52, 95% CI −0.73 to 9.76; $P = 0.09$). The different between the two groups in the

proportion of patients reporting “recovery” at 12 months was not significant. Additional analysis of the data excluding the participants who violated the protocol during the first 3 months of follow-up showed greater differences in the outcome parameters of pain and function at 3 and 12 months. The odds ratio for the outcome parameter “recovery” at 12 months increased from 1.60 to 2.10 (95% CI 0.94 to 4.66; $P=0.07$).

SUBGROUP ANALYSIS

Tables 4 and 5 present data for the subgroup analysis by recruiting physician. Among patients recruited by a GP, those in the exercise group had significantly higher and clinically relevant differences on the pain and functional outcome parameters compared with the control group at both 3 and 12 months follow-up (effect size pain at rest 0.67 ($P<0.01$) at 3 months and 0.79 ($P<0.01$) at 12 months; effect size pain on activity 0.62 ($P<0.01$) and 0.65 ($P=0.02$); and effect size function 0.57 ($P<0.01$) and 0.55 ($P<0.01$)). Among patients recruited by a sport physician, however, those in the exercise group did not show better outcomes than those in the control group at either follow-up point. Still no significant differences were found between the treatment and intervention groups for recovery at 3 and 12 months. A further subgroup analysis was done on the basis of age. The effect estimates for recovery, pain, and function at 3 and 12 months for patients aged 14-17 years and for those aged 18 years or older were similar to those in the whole cohort. Because of lower power, there were no significant differences between the exercise therapy and control groups according to age, except for pain on activity at 3 months and pain at rest at 12 months in patients aged 18 years or older.

ADDITIONAL INTERVENTIONS

There was no significant difference between the intervention group and the control group in the self-reported total amount of additional interventions used (non-steroidal anti-inflammatory drugs (NSAIDs), bandages/braces, insoles, oral medication, and topical agents) during the first 3 months (that is, when participants in the intervention group were receiving the tailored exercise therapy). The use of oral NSAIDs and topical agents in the control group, however, was two to four times higher than in the intervention group ($P=0.096$ and $P=0.051$, respectively; fig 1). Analysis of interventions used during the following 9 months (up to 12 months follow-up) showed similar disparities between the two groups in additional intervention use. The self-reported use of NSAIDs and topical agents was about three times higher in the control group than in the intervention

Table 4 Recovery at 3 and 12 months follow-up for patients recruited by a general practitioner compared with those recruited by a sport physician

	Exercise therapy (n=50)		Control (n=51)		Adjusted odds ratio† (95% CI) at 3 months	Adjusted odds ratio† (95% CI) at 12 months		
	Baseline	3 months (n/N (%))	Baseline	3 months (n/N (%))				
	12 months (n/N (%))	12 months (n/N (%))	12 months (n/N (%))	12 months (n/N (%))				
Patients recruited by general practitioners								
Recovered*	—	22/48 (45.8)	28/44 (63.4)	—	14/46 (30.4)	22/45 (48.8)	2.10 (0.89 to 4.93)	1.95 (0.82 to 4.65)
Patients recruited by sport physicians								
Recovered*	—	4/14 (28.6)	8/14 (57.1)	—	7/14 (50.0)	8/14 (57.1)	0.39 (0.08 to 1.83)	0.97 (0.22 to 4.25)

Frequencies are reported for those patients available at that time point. Adjusted odds ratios are reported for the total available in analysis.

*Recovered=fully or strongly recovered.

†Recovery was adjusted for duration of symptoms.

Table 5 Function and pain scores at 3 and 12 months follow-up for patients recruited by a general practitioner compared with those recruited by a sport physician

	Exercise therapy (n=50)			Control (n=51)			Adjusted difference* (95% CI) at 3 months	Adjusted difference* (95% CI) at 12 months
	Baseline (mean (SD))	3 months (mean (SD))	12 months (mean (SD))	Baseline (mean (SD))	3 months (mean (SD))	12 months (mean (SD))		
Patients recruited by general practitioners								
Function score (0-100)	63.9 (14.0)	79.2 (15.5)	84.7 (13.2)	66.6 (14.8)	73.4 (17.8)	78.6 (18.3)	8.23 (3.18 to 13.28)	7.90 (2.20 to 13.60)
Pain at rest (0-10)	4.50 (2.3)	2.22 (2.3)	1.23 (2.0)	4.18 (2.4)	3.50 (2.8)	2.82 (3.1)	-1.56 (-2.52 to -0.61)	-1.82 (-2.82 to -0.82)
Pain on activity (0-10)	6.44 (2.2)	3.78 (2.8)	2.45 (2.6)	5.98 (2.4)	4.91 (2.9)	3.64 (3.5)	-1.42 (-0.39 to -2.45)	-1.49 (-0.29 to -2.69)
Patients recruited by sports physicians								
Function score (0-100)	65.8 (14.0)	77.5 (16.4)	78.4 (18.6)	63.6 (16.6)	79.6 (16.7)	83.9 (14.7)	-4.11 (-15.54 to 7.33)	-5.31 (-17.24 to 6.62)
Pain at rest (0-10)	2.93 (2.1)	2.57 (3.3)	2.07 (2.7)	3.53 (1.9)	2.29 (2.5)	1.93 (2.2)	0.77 (-1.15 to 2.69)	0.56 (-1.15 to 2.28)
Pain on activity (0-10)	5.93 (1.9)	3.93 (3.4)	2.93 (3.5)	5.93 (2.0)	3.57 (3.0)	3.21 (3.0)	0.41 (-1.83 to 2.64)	-0.21 (-2.49 to 2.06)

Mean scores are reported for those patients available at that time point. Adjusted differences are reported for the total available in analysis.

*Function score was adjusted for baseline score, age, and duration of symptoms. Pain at rest was adjusted for baseline score and age. Pain on activity was adjusted for baseline score, age, and gender. Positive adjusted differences for the function score, and negative difference for pain scores, are in favour of the exercise group.

group ($P=0.059$ and $P=0.09$, respectively) whereas the use of supportive aids (bandages/braces) was about two times higher in the control group ($P=0.09$).

DISCUSSION

In patients with patellofemoral pain syndrome, exercise therapy produces better results regarding pain and function at 3 months and at 12 months than usual care. We did not find a significant difference between the exercise therapy group and the control group in self-reported “recovery” (that is, patients who designated themselves as “fully recovered” or “strongly recovered”) at either 3 months or 12 months. Recovery at 3 months was significantly more likely in the exercise group than in the control group when we used the outcome measurement “improved” (that is, “fully recovered,” “strongly recovered,” or “slightly recovered”). After 12 months, nearly all patients had improved, and the difference between the groups was no longer significant. We therefore conclude that, although exercise therapy is effective for improving pain and function, these benefits are not clearly reflected in patients’ self-reported recovery. Although perceived recovery is relevant as a clinical outcome, understanding what exactly comprises recovery from the patient’s point of view is difficult. We suspected that external factors might influence prognosis and possibly also effectiveness, so we stratified our analysis for age and type of recruiting physician.

Clinically relevant and statistically significant effects of exercise on pain and function were found in patients recruited by the GP. This subgroup was relatively large ($n=101$) and contributed considerably to the overall results. The group recruited by the sport physician was small ($n=30$), however, and did not show any effect of exercise therapy compared with usual care. The confidence intervals for this analysis were wide, so coincidental findings owing to the small numbers of patients recruited by sport physicians cannot be excluded. There were no possible explanatory differences in baseline characteristics (including frequency and duration of symptoms, sports participation, and BMI) between patients recruited by a GP and those recruited by a sport physician. There was no difference between the exercise therapy group and the control group in the number of additional interventions used during the first 3 months of the study, although there was a two-fold to three-fold higher use of NSAIDs and a four times higher use of topical agents in the control group. These figures remained stable during the course of one year. These additional interventions might have influenced the outcome measurements. The use of additional interventions was higher in the control group, however, implying that differences in outcome measurements between the groups are more likely to be underestimated than overestimated. Although not significant, the higher use of additional interventions in the control group may indicate a trend towards greater use of

self-supportive means by patients with patellofemoral pain syndrome not referred to an exercise program. When considered alongside the better outcome on pain scores in the exercise group, the data indicate that the control group had an objective need to use pain medication.

COMPARISON WITH OTHER STUDIES

Various studies have evaluated the efficacy of exercise therapy for patellofemoral pain syndrome. Early studies without a control group indicated that rehabilitation including exercise therapy could be beneficial for patients with patellofemoral pain syndrome.^{21 22}

Witvrouw et al studied the effect of open compared with closed chain exercises in patients with patellofemoral pain syndrome.^{23 24} Both types of exercise led to an improvement in pain scores and an increase in strength of the quadriceps and hamstrings. The authors stated that, as a result of their study, they would use both open and closed kinetic chain exercises in the non-operative treatment protocol for patients with patellofemoral pain.^{23 24} Given these findings, both isometric/concentric and eccentric exercises were used in the present study. Patients were also allowed to practice in an open and closed kinetic chain position. Various other studies have evaluated the efficacy of exercise therapy for patellofemoral pain syndrome. Systematic reviews, however, have reported that most of these studies are of poor methodological quality in that they lack randomisation, a control group, or clearly defined outcome parameters.^{12 25} To our knowledge, six randomised studies, including our own study, have compared exercise therapy with non-exercise therapy. One low quality study found that a special brace designed to provide progressive resistance exercise during activities of daily living improved function and pain,²⁶ whereas another study found no significant differences in outcomes between patients on a home exercise program and those with a patellar brace.²⁷ Additionally, three trials studied the effects of physiotherapy (including exercise therapy) compared with other treatment or placebo treatment.^{19 28 29} The small study by Crossley et al compared the effect of a 6 week program of exercise therapy plus taping, mobilization techniques, and biofeedback with a placebo therapy (sham ultrasound, placebo taping, and application of non-therapeutic gel).²⁸ After 6 weeks, the multimodal physiotherapy group showed a significant decrease in worst pain, usual pain, and anterior knee pain compared with the placebo group. The recent study by Collins et al compared the use of insoles (flat or prefabricated) with 6 weeks of multimodal physiotherapy (including exercises).²⁹ At 6, 12, and 52 weeks, no differences were found between groups regarding pain, function, and recovery. These studies, however, do not answer the question of whether the effect of supervised exercises is additive to usual care, as was tested in our study. In the small study by Clark et al,¹⁹ exercise, taping,

and education were compared with exercise and education, taping and education, and education alone. Exercise was not significantly better than non-exercise for pain and function after 3 months. At 12 months, however, pain scores were significantly better for the exercise group. A high proportion of patients (approximately 40%) was lost to follow-up at 12 months in this study though, which could have influenced these results.

STRENGTHS AND LIMITATIONS OF STUDY

A methodological problem that cannot be solved in randomised controlled trials of exercise therapy is that patients in the intervention group cannot be blinded for the exercise therapy and, therefore, may be biased for positive outcome (placebo effect). To overcome this problem in part, a blinded external observer could be used to provide objective and observational measures of functional outcomes. Some intervention studies on exercise therapy in patellofemoral pain syndrome have used quantifiable measures for muscle strength as an outcome. However, several studies have shown that the relationship between increase in muscle strength and clinical outcome is inconsistent.³⁰⁻³² In addition; these studies clearly illustrate the difficulty of interpreting the effect of therapy using muscle strength as an outcome measure for knee function. Therefore, as no validated objective outcome measures for patellofemoral pain syndrome are currently available, the use of validated subjective outcome measures seems appropriate. Along with the observed effect of exercise therapy, the role of supervision and attention of a physical therapist as well as the use of an exercise diary may have influenced the outcome in the intervention group. The attention from the physical therapist is an integral part of the supervised exercise therapy intervention.

On the other hand, the use of an exercise diary in the intervention group to assess compliance may have caused a bias owing to awareness of being involved in a study (Hawthorne effect).³³ In addition, our control group was allowed to do single isometric quadriceps contractions and is, therefore, not a real non-exercise group. This resembles the usual care ("wait and see" approach) prescribed by GPs in the Netherlands according to national guidelines.⁹ We thus studied the additional value of supervised exercise therapy but not the effect of doing exercises, which might have diminished the contrast between the groups. Although we noted that eight patients in the control group received physical therapy (that is, they violated the protocol), we do not know to what extent this physical therapy resembled the standardized supervised exercise therapy in the intervention group. Therefore, an analysis by protocol by comparing physical therapy with no physical therapy does not seem appropriate. The differences between the intervention group and the control group were further diminished by violation of the protocol by 14 people: 6 people in the intervention group did not visit the physical

therapist and subsequently did not receive the supervised exercise therapy, and eight people in the control group visited a therapist and received physical therapy although they were instructed not to. Additional analysis of the data excluding the participants who violated the protocol during the first 3 months of follow-up showed greater differences in the outcome parameters on pain and function at 3 and 12 months. This change indicates that the effects of exercise therapy may indeed be even higher than those reported in our primary analysis. A final remark can be made about the diagnosis of patellofemoral pain syndrome. Patients were recruited by GPs and sport physicians who were offered a set of inclusion and exclusion criteria, some of which were related to physical examination. The researchers did not supervise the physicians in their judgment of diagnosis. Nevertheless, we think that this approach reflects common practice and therefore increased the clinical applicability of our results.

CONCLUSIONS

This study provides evidence that supervised exercise therapy for patellofemoral pain syndrome in general practice is more effective than “usual care” for the outcome parameters pain at rest, pain on activity, and function at 3 and 12 months. However, supervised exercise therapy had no effect on perceived recovery. Further research should aim to elucidate the mechanisms whereby exercise therapy results in better outcome.

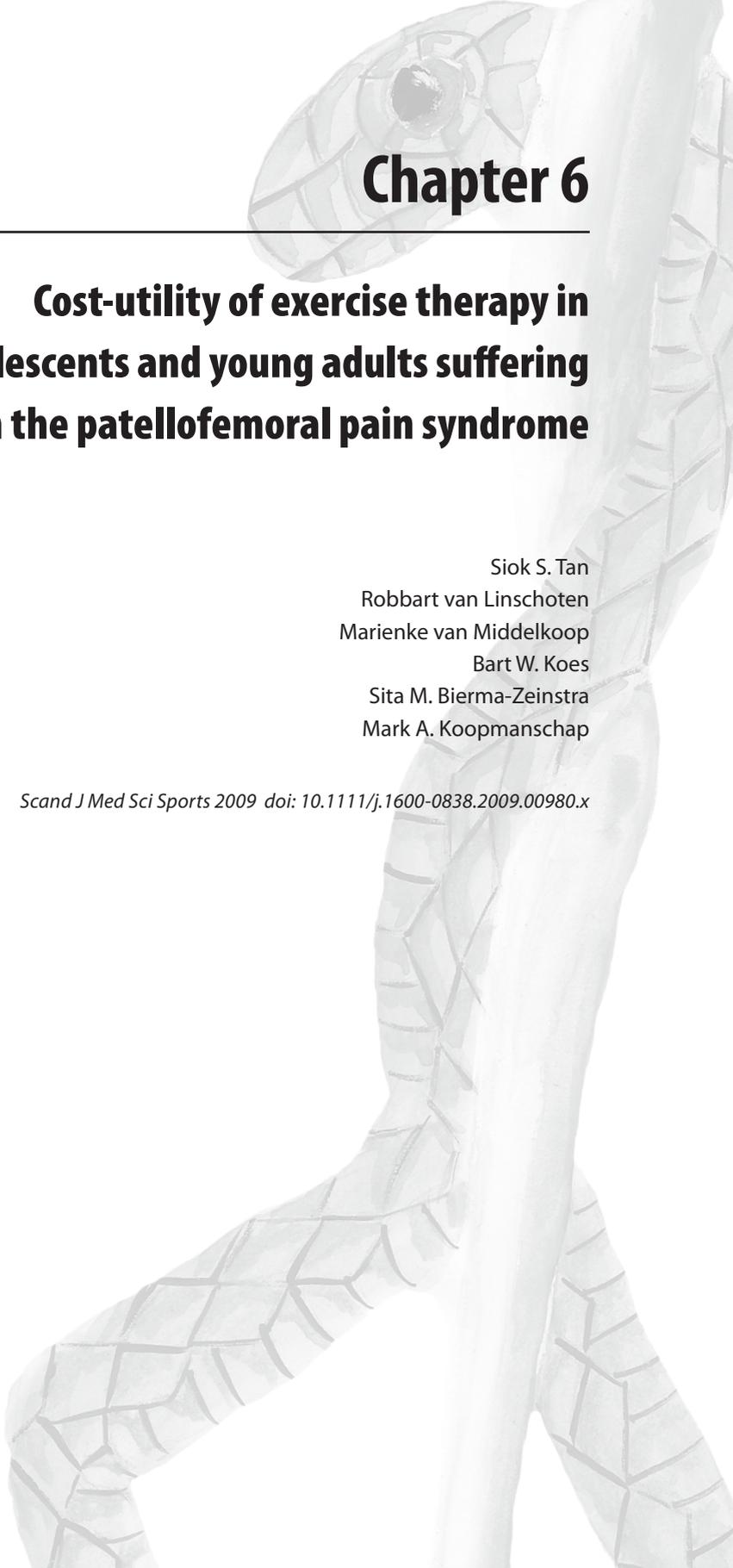
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REFERENCES

1. Thomee R, Augustsson J, Karlsson J. Patellofemoral pain syndrome: a review of current issues. *Sports Med* 1999;28:245-62.
2. Sanchis-Alfonso V. *Anterior knee pain and patellar instability*. Springer Verlag, 2006.
3. Witvrouw E, Werner S, Mikkelsen C, Van Tiggelen D, Vanden Berghe L, Cerulli G. Clinical classification of patellofemoral pain syndrome: guidelines for non-operative treatment. *Knee Surg Sports Traumatol Arthrosc* 2005;13:122-30.
4. Van der Velden J. Een nationale studie naar ziekten en verrichtingen in de huisartspraktijk. *Basisrapport: morbiditeit in de huisartspraktijk*. Utrecht: NIVEL, 1991.
5. Taunton JE, Ryan MB, Clement DB, McKenzie DC, Lloyd-Smith DR, Zumbo BD. A retrospective case-control analysis of 2002 running injuries. *Br J Sports Med* 2002;36:95-101.
6. Dixit S, DiFiori JP, Burton M, Mines B. Management of patellofemoral pain syndrome. *Am Fam Physician* 2007;75:194-202.
7. Den Hertog PC, van Kampen LTB, Ooijendijk WTM, Schmikli SL, Schoots W, Vriend I. Ongevallen en Beweging in Nederland: Kerncijfers 2000-2001 voor beleid en onderzoek. *Stichting Consument en Veiligheid*, 2003.
8. Nimon G, Murray D, Sandow M, Goodfellow J. Natural history of anterior knee pain: a 14- to 20-year follow-up of nonoperative management. *J Pediatr Orthop* 1998;18:118-22.
9. Cirkel JW, Klaassen WRC, Kunst JA, Aarns TEM, Plag EC, Goudswaard AN, et al. Niet-Traumatische knieproblemen bij kinderen en adolescenten; NHG-Standaard. *Huisarts Wet* 1998;41:246-51.
10. Cutbill JW, Ladly KO, Bray RC, Thorne P, Verhoef M. Anterior knee pain: a review. *Clin J Sport Med* 1997;7:40-5.
11. McConnell J. The physical therapist's approach to patellofemoral disorders. *Clin Sports Med* 2002;21:363-87.
12. Heintjes E, Berger MY, Bierma-Zeinstra SM, Bernsen RM, Verhaar JA, Koes BW. Exercise therapy for patellofemoral pain syndrome. *Cochrane Database Syst Rev* 2003(4):CD003472.
13. Van Linschoten R, van Middelkoop M, Berger MY, Heintjes EM, Koopmanschap MA, Verhaar JA, et al. The PEX study—exercise therapy for patellofemoral pain syndrome: design of a randomized clinical trial in general practice and sports medicine [ISRCTN83938749]. *BMC Musculoskelet Disord* 2006;7:31.
14. Malanga GA, Andrus S, Nadler SF, McLean J. Physical examination of the knee: a review of the original test description and scientific validity of common orthopedic tests. *Arch Phys Med Rehabil* 2003;84:592-603.
15. Nijs J, Van Geel C, Van der auwera C, Van de Velde B. Diagnostic value of five clinical tests in patellofemoral pain syndrome. *Man Ther* 2006;11:69-77.
16. Kujala UM, Jaakkola LH, Koskinen SK, Taimela S, Hurme M, Nelimarkka O. Scoring of patellofemoral disorders. *Arthroscopy* 1993;9:159-63.
17. Downie WW, Leatham PA, Rhind VM, Wright V, Branco JA, Anderson JA. Studies with pain rating scales. *Ann Rheum Dis* 1978;37:378-81.
18. Crossley KM, Bennell KL, Cowan SM, Green S. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil* 2004;85:815-22.
19. Clark DI, Downing N, Mitchell J, Coulson L, Syzpryt EP, Doherty M. Physiotherapy for anterior knee pain: a randomised controlled trial. *Ann Rheum Dis* 2000;59:700-4.
20. Hartung J, Knapp G, Sinha BK. *Statistical meta-analysis with application*. Wiley, 2008.

21. Dehaven KE, Dolan WA, Mayer PJ. Chondromalacia patellae in athletes. Clinical presentation and conservative management. *Am J Sports Med* 1979;7:5-11.
22. Whitelaw GP Jr, Rullo DJ, Markowitz HD, Marandola MS, DeWaele MJ. A conservative approach to anterior knee pain. *Clin Orthop Relat Res* 1989;234-7.
23. Bizzini M, Childs JD, Piva SR, Delitto A. Systematic review of the quality of randomized controlled trials for patellofemoral pain syndrome. *J Orthop Sports Phys Ther* 2003;33:4-20.
24. Timm KE. Randomized controlled trial of Protonics on patellar pain, position, and function. *Med Sci Sports Exerc* 1998;30:665-70.
25. Lun VM, Wiley JP, Meeuwisse WH, Yanagawa TL. Effectiveness of patellar bracing for treatment of patellofemoral pain syndrome. *Clin J Sport Med* 2005;15:235-40.
26. Crossley K, Bennell K, Green S, Cowan S, McConnell J. Physical therapy for patellofemoral pain: a randomized, double-blinded, placebo-controlled trial. *Am J Sports Med* 2002;30:857-65.
27. Collins N, Crossley K, Beller E, Darnell R, McPoil T, Vicenzino B. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *BMJ* 2008;337:a1735.
28. Witvrouw E, Lysens R, Bellemans J, Peers K, Vanderstraeten G. Open versus closed kinetic chain exercises for patellofemoral pain. A prospective, randomized study. *Am J Sports Med* 2000;28:687-94.
29. Witvrouw E, Danneels L, Van Tiggelen D, Willems TM, Cambier D. Open versus closed kinetic chain exercises in patellofemoral pain: a 5-year prospective randomized study. *Am J Sports Med* 2004;32:1122-30.
30. Gobelet C, Frey M, Bonard A. Muscle training techniques and retropatellar chondropathy. *Rev Rhum Mal Osteoartic* 1992;59:23-7.
31. Stiene HA, Brosky T, Reinking MF, Nyland J, Mason MB. A comparison of closed kinetic chain and isokinetic joint isolation exercise in patients with patellofemoral dysfunction. *J Orthop Sports Phys Ther* 1996;24:136-41.
32. Dursun N, Dursun E, Kilic Z. Electromyographic biofeedback-controlled exercise versus conservative care for patellofemoral pain syndrome. *Arch Phys Med Rehabil* 2001;82:1692-5.
33. Mayo E. Hawthorne and the Western Electric Company: the social problems of an industrial civilisation. Routledge, 1949.



Chapter 6

Cost-utility of exercise therapy in adolescents and young adults suffering from the patellofemoral pain syndrome

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ABSTRACT

OBJECTIVE:

The objective of this paper was to determine the cost effectiveness of exercise therapy (intervention group) compared with “usual care” (control group) in adolescents and young adults with patellofemoral pain syndrome in primary care.

Methods:

This multicenter prospective randomized clinical trial with cost-utility analysis was conducted at 38 general practices and three sport medical advice centers in the Netherlands for 2007. A total of 131 patients were included.

Results:

The annual direct medical costs per patient were significantly higher for the intervention group (€434) compared with the control group (€299) mainly caused by additional physiotherapy visits. The average annual societal costs per patient were significantly lower in the intervention group (€1011 vs. €1.166). Productivity costs were the largest cost component, in particular costs due to reduced efficiency at paid work which were responsible for 47% and 56% of the total costs in the intervention and control group respectively. Patients in the intervention group experienced a slightly, but not significantly, higher quality of life (0.8722 vs. 0.8617).

Conclusion:

With a cost effectiveness ratio of €14.738 per quality adjusted life year, exercise therapy appears to be cost effective as compared with “usual care.”

INTRODUCTION

Patellofemoral pain syndrome (PFPS) is a common complaint in adolescents and younger adults. The incidence of PFPS increases from age 14 with a peak incidence around age 25 and is higher for women than for men.^{1,2} The most typical symptom of PFPS is a diffuse peripatellar and retropatellar localized pain, typically provoked by ascending or descending stairs, squatting, cycling and sitting with flexed knees for prolonged periods of time.^{3,4} Clinical guidelines of the Dutch College of General Practice recommend a conservative treatment for PFPS by informing the patient about the background of the condition and its favorable prognosis (usual care).⁵ General practitioners do not always adhere to these guidelines. From a pilot study on patients with PFPS visiting the general practitioner, it was shown that 35% of patients were referred to exercise therapy by a physiotherapist at the first visit. After 12 months of follow-up, 64% of the patients were referred to exercise therapy.¹ Economic evaluations are a prerequisite for the reimbursement and implementation of treatments in many countries, because they can provide healthcare decision makers with valuable information on the relative efficiency of alternative treatments. Costs are preferably determined from a societal perspective in which all relevant costs are included.⁶ However, many economic evaluations only include direct medical costs. As productivity costs may account for more than 50% of the total costs, disregarding these costs may significantly effect the cost effectiveness (CE) ratio.⁷ As PFPS frequently occurs in young (working) patients, a productivity cost reduction due to absence from paid work and reduced efficiency at paid and unpaid work may be expected. These productivity cost reductions might partially compensate for the additional cost of exercise therapy. A few studies have previously evaluated the effectiveness of exercise therapy. A Cochrane review by Heintjes et al. (2003) summarized the evidence for treatment efficacy in reducing anterior knee pain and improving knee function in patients with PFPS. They found one high- and two low-quality studies which used a control group not receiving exercise therapy. One high- and one low-quality study observed exercise therapy to be more effective in treating PFPS with respect to pain reduction. Additionally, one low quality study reported significantly greater functional improvement with exercise. However, the quality of the trials was such that further research was necessary to confirm this conclusion.⁸ No earlier studies have yet assessed the cost (-effectiveness) of exercise therapy in patients with PFPS. Because of the lack of information on the costs as well as on the effectiveness of exercise therapy, general practitioners lack the knowledge to apply the most cost effective treatment to patients with PFPS. Therefore, the aim of the present study was to determine the cost effectiveness of exercise therapy (intervention group) compared with "usual care" (control group) in adolescents and young adults dealing with PFPS in primary care.

MATERIALS AND METHODS

This cost-utility study was performed in conjunction with a randomized clinical trial. More details of the study design can be read in the protocol published in 2006.¹ In short, adolescents and young adults between 14 and 40 years of age presenting with symptoms of PFPS and no history of previous active treatment with exercises within the last 6 months were eligible for enrolment by the general practitioner or sport physician. The complaints should have persisted for longer than 2 months but no longer than 2 years.

Furthermore, at least three of the following symptoms should have been present: pain when walking stairs, pain when squatting, pain when running, pain when cycling, pain when sitting with knees flexed for a prolonged period of time, grinding of the patella and a positive clinical patellar test (such as Clarke's test or "signe du rabot").^{9,10} Patients were excluded when suffering from radiologically confirmed knee osteoarthritis/arthritis, patellar tendinopathy, Osgood-Schlatter disease or other defined pathological conditions of the knee or had previous knee injuries and/or surgery. The patients were randomized to exercise therapy (intervention group) or "usual care" (control group), stratified for clinical setting (general practitioner/sport physician) and age (<18 years/≥18 years). The randomization was done by an independent researcher using a computer generated list. Patients in the intervention group received advice and information on the background of PFPS by a physician and were appointed to a standardized exercise program, supervised by physiotherapists (nine sessions during 6 weeks), with continuation of home exercises. Patients in the control group only received advice and information on the background of PFPS by a physician, similar to the advice given by general practitioners and sport physicians in a normal care situation. As this is a pragmatic trial using the intention-to-treat principle, a minority of patients in the control group might have received a small amount of exercise therapy. Recruitment took place in the 38 HONEUR practices (a research network of general practices allied with the Department of General Practice of Erasmus MC, University Medical Center) and at the sport medical advice centers in Rotterdam, Leidschendam and Gorinchem. Enrolment commenced in August 2005 and finished in May 2007. The follow-up period was 1 year.

The primary outcome measures of the randomized clinical trial included pain, knee function and perception of recovery. These clinical results will be reported in a forthcoming publication.

The present paper will focus on the cost-utility study and is based on an intention-to-treat analysis. The cost-utility study was primarily conducted from a societal perspective, but the healthcare perspective was also appraised. Data on direct medical costs, productivity costs and quality of life were collected using standardized questionnaires which were sent to the home addresses of the patients at baseline and 6, 13, 26, 39 and 52 weeks after randomization. The recall period was 6 weeks. Annual costs were deter-

mined by adding up the costs per period. The costs for the time between the measurement periods (week 6–7, week 14–20, week 27–33 and week 40–46) were established through linear interpolation. The last observation carried forward (LOCF) method was applied in case of missing values. All costs were based on Euro 2007 cost data. Where necessary, costs were adjusted to 2007 using the general price index from the Dutch Central Bureau of Statistics.

Direct medical costs

Total direct medical costs for individual patients were determined by multiplying resource use by the corresponding unit prices. Data on resource use of visits to healthcare providers (including the general practitioner, physiotherapist and medical specialist), medical imaging services (magnetic resonance imaging, computed tomography and x-rays), medications and disposables (including cold and hot compresses, orthopedic insoles, elastic bandages, braces and tape) were acquired from the questionnaires. Resource use of visits to the physiotherapist was additionally obtained from the physiotherapist. Resource use of medical imaging services which were used to exclude patients with other diagnoses than PFPS were not incorporated in the direct medical costs because they took place before enrolment. Such resource use is normally excluded in an economic evaluation (Drummond, 2005). Unit costs of visits to the general practitioner and physiotherapist were based on a detailed microcosting study. Using standardized reporting templates, seven general practitioners and eight physiotherapists were each individually asked to estimate the time spent by the general practitioner/physiotherapist and the assistant on an average patient. Unit costs were based on the normative income for free labor practitioners, the collective labor agreement of general practitioner care and the number of workable hours per year.¹¹⁻¹³ Annual overhead costs were allocated to patients using a marginal mark-up percentage. The resource use of visits to other healthcare providers was valued using reference unit prices.¹³

The resource use of medical imaging services was valued using the fees as issued by the Dutch Healthcare Authority. Wholesale prices were used to value the resource use of medications and disposables. Because patients were asked whether they made use of disposables at every measurement moment, we assumed that cold and hot compresses were used once monthly. Orthopedic insoles, elastic bandages and braces were assigned a life expectancy of 4 years, whereas tape was assumed to be purchased each year.

Productivity costs

The productivity costs involved productivity losses resulting from absence from paid work and reduced efficiency at paid and unpaid work.

Absence from paid work

The number of absent days from paid work due to PFPS problems was valued using the overall average net value added per employee to avoid differences in productivity losses between the intervention and control group to be caused by (income) differences which are related to age and gender but not to PFPS problems.

Reduced efficiency at paid work

Reduced efficiency at paid work was also valued using the overall average net value added per employee. The efficiency loss was established by means of the quality and quantity method as developed by Brouwer et al. and incorporated in the PRODISQ instrument.^{14 15} The patients gave their mark for the quality of their work on the last working day of each 6 weeks on a visual analog scale from 0 (worst quality) to 10 (best quality). The same question was posed for the quantity of their work on their last working day. These marks were assumed to be representative for the overall recall period. The efficiency loss during paid work in terms of hours lost was then determined to be $(1 - (\text{quality}/10) \times (\text{quantity}/10)) \times \text{working hours per day}$.

Reduced efficiency at unpaid work

Patients were asked to indicate how many hours of housekeeping tasks were taken over by their family, other people and paid aid due to PFPS problems. The number of hours housekeeping tasks that were taken over was valued using the current price of simple professional home care.¹³

Quality of life

The quality of life was measured by means of the EQ-5D instrument. The EQ-5D has five dimensions: mobility, self-care, activity, pain and anxiety. Each dimension has three levels: no problems (level 1), some problems (level 2) and serious problems (level 3). Hence, EQ-5D has 243 possible health states. Utility values for these health states were measured with the time trade-off technique on a random sample of the general adult population of the Netherlands.¹⁶ The scores range from 0.329 (worst situation) to 1.0 (perfect health).

Patients were also asked to indicate how they experienced their current health state on a visual analog scale, 0 being worst imaginable health and 100 being best imaginable health. Furthermore, patients were asked to indicate how they experienced the severity of their PFPS problems at rest during the last week on a scale from 0 (no pain) to 10 (worst imaginable pain).

STATISTICAL ANALYSES

Statistical analyses were conducted with the statistical software program SPSS for Windows version 15.0. In addition to descriptive statistics, tests for normal distribution of the total cost estimates were performed using the Kolmogorov–Smirnov test. Differences between the intervention and control group and between baseline and follow up scores were assessed by means of the independent sample t-test (for variables showing a normal distribution), the Mann–Whitney U-test (for variables not normally distributed) or Pearson’s chi-square test (for variable fractions). To adjust for multiple testing, one-way analyses of variance with post hoc testing (type Bonferroni) were additionally performed for direct medical cost values. Using non-parametric bootstrapping (drawing 2500 observations at random from the available patient sample), the degree of uncertainty for costs and health effects and the cost-utility ratio was examined on the so-called CE-plane. In addition, an acceptability curve was generated to indicate the probability that the intervention has lower incremental costs per quality adjusted life year (QALY) gained than various thresholds for the maximum willingness to pay for an extra QALY.

RESULTS

A patient flowchart is provided in Fig.1. A total of 163 patients consulted our HONEUR practices or sport medical advice centers during the year 2005, of which 16 did not meet our inclusion criteria, 10 did not receive informed consent and six experienced dimin-

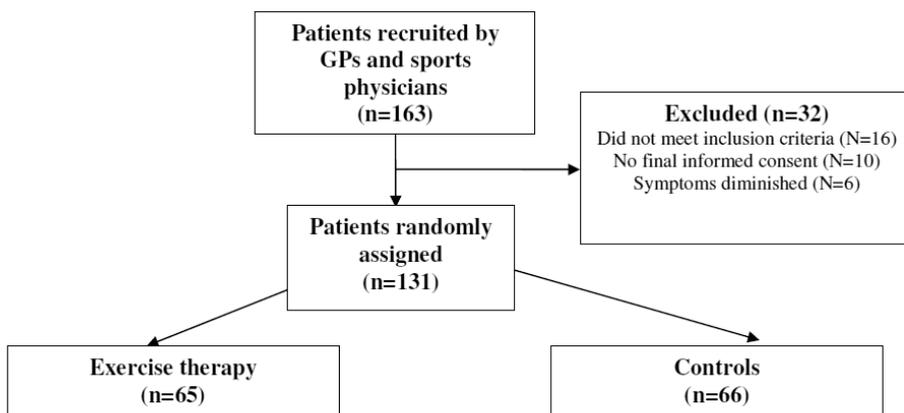


Figure 1: Patients Flowchart

ished complaints. Thus, 131 patients were recruited, of which 65 in the intervention and 66 in the control group.

For the intervention group, 100% of the questionnaires were returned at baseline, 86% after 6 weeks, 79% after 13 weeks, 83% after 26 weeks, 74% after 39 weeks and 83% after 52 weeks. For the control group, 100% of the questionnaires were returned at baseline, 91% after 6 weeks, 89% after 13 weeks, 78% after 26 weeks, 66% after 39 weeks and 88% after 52 weeks.

Table 1 presents the general characteristics at baseline of the patients in the two groups. Two thirds of the patients were females. Even though there were no significant differences between the groups, the mean age of the patients, the proportion of patients with paid work as their primary occupation, the number of working hours per week and the income per hour were slightly higher in the intervention group than in the control group.

Direct medical costs

Appendix 1 provides a detailed summary of the medical consumption of both groups. Around 83% of all patients visited the general practitioner at baseline. For the intervention group, the shares of patients visiting the general practitioner went down to 25%

Table 1. General characteristics of the respondents at baseline

		Intervention group (n=65)	Control group (n=66)
Average age		24.7 (med 24.0; sd 8.6)	23.4 (med 22.0; sd 7.8)
Sex	Men	35.4%	36.4%
	Women	64.6%	63.6%
Body Mass Index		23.2 (med 22.5; sd 3.9)	23.0 (med 22.8; sd 3.4)
Primary occupation			
	School	40.6%	45.5%
	Paid work	50.0%	42.4%
	Other	9.4%	12.1%
Education	Low	9.2%	6.1%
	Medium	60.0%	69.7%
	High	30.8%	24.2%
Paid work		70.8%	69.7%
Average hours of work per week		29.1 (med 34.0; sd 21.3)	24.8 (med 25.5; sd 17.5)
Average income per hour		€ 15.35 (med 13.5; sd 10.8)	€ 12.39 (med 12.8; sd 6.5)
Sports		76.6%	78.1%
Average hours of sports per week		4.9 (med 4.0; sd 3.5)	5.1 (med 4.0; sd 3.6)

med = median sd = standard deviation

BMI=weight/(length²)

Table 2. Mean direct medical costs per respondent for the past 6 weeks per measurement moment (Euro 2007) (median)

	Baseline	6 weeks	13 weeks	26 weeks	39 weeks	52 weeks
Intervention group						
General practitioner	15 (15)	5 (0)	1 (0)	1 (0)	1 (0)	1 (0)
Sport physician	16 (0)	3 (0)	7 (0)	1 (0)	0 (0)	1 (0)
Physiotherapist	9 (0)	100 (91)	47 (23)	21 (0)	18 (0)	26 (0)
Medical specialist	1 (0)	0 (0)	1 (0)	3 (0)	5 (0)	2 (0)
Company physician	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
MRI / CT	12 (0)	0 (0)	0 (0)	12 (0)	12 (0)	0 (0)
X-ray	5 (0)	0 (0)	2 (0)	2 (0)	1 (0)	0 (0)
Medication	2 (0)	2 (0)	1 (0)	0 (0)	1 (0)	1 (0)
Disposables	2 (0)	2 (0)	2 (0)	2 (0)	2 (0)	2 (0)
Total	63 (24)	112 (114)	61 (46)	43 (4)	41 (3)	32 (3)
SD	96	68	87	119	142	104
25 percentile	15	49	3	0	0	0
75 percentile	74	162	76	46	16	11
Control group						
General practitioner	15 (15)	3 (0)	2 (0)	2 (0)	2 (0)	2 (0)
Sport physician	11 (0)	6 (0)	5 (0)	2 (0)	0 (0)	1 (0)
Physiotherapist	1 (0)	12 (0)	14 (0)	21 (0)	12 (0)	12 (0)
Medical specialist	3 (0)	0 (0)	1 (0)	4 (0)	4 (0)	3 (0)
Company physician	0 (0)	2 (0)	3 (0)	3 (0)	0 (0)	1 (0)
MRI / CT	0 (0)	0 (0)	0 (0)	4 (0)	4 (0)	8 (0)
X-ray	3 (0)	3 (0)	3 (0)	4 (0)	1 (0)	2 (0)
Medication	2 (0)	1 (0)	1 (0)	3 (0)	3 (0)	3 (0)
Disposables	2 (1)	2 (1)	2 (1)	2 (1)	2 (1)	2 (1)
Total	37 (17)	30 (4)	32 (4)	45 (3)	28 (3)	34 (1)
SD	38	62	76	108	92	158
25 percentile	15	0	0	0	0	0
75 percentile	55	25	20	15	13	8

MRI = magnetic resonance imaging

CT = computer tomography

SD = standard deviation

at 6 weeks and to 6% at 13 weeks. For the control group, the percentages amounted to 20% and 14%, respectively.

In the intervention group, the fraction of patients visiting a physiotherapist showed a fast increase to 88% at 6 weeks and a decrease from 13 weeks onwards to 26% at 39 weeks. The average number of visits was four per patient at 6 weeks and two at 13 weeks. At the other measurement moments, the number of visits per patient was around one. In the control group, the fraction of patients visiting a physiotherapist showed a more or

Table 3. Annual direct medical costs with descriptive statistics (Euro 2007)

	Average number of units per patient year	Average costs per patient	Median costs per patient	SD	Mann-Whitney U Asymp. Sig. (2-tailed)
Intervention group					
General practitioner	0.94	13.94	0.00	38.23	-
Sport physician	0.26	15.18	0.00	69.38	-
Physiotherapist	12.94	295.74	205.74	334.83	-
Medical specialist	0.38	22.77	0.00	121.79	-
Company physician	0.00	0.00	0.00	0.00	-
MRI / CT	0.20	52.60	0.00	314.10	-
X-ray	0.22	10.41	0.00	60.49	-
Medication	-	7.52	0.00	25.63	-
Disposables	-	15.77	0.00	22.79	-
Total	-	433.92	228.60	786.01	-
Control group					
General practitioner	0.60	18.13	0.00	40.56	0.442
Sport physician	0.31	18.39	0.00	81.07	0.737
Physiotherapist	5.52	126.19	0.00	385.58	0.000
Medical specialist	0.38	22.42	0.00	107.23	0.728
Company physician	0.21	12.71	0.00	68.83	0.083
MRI / CT	0.13	34.54	0.00	169.59	0.688
X-ray	0.49	23.24	0.00	66.31	0.007
Medication	-	22.89	0.00	81.43	0.106
Disposables	-	20.90	7.50	27.83	0.256
Total	-	299.41	58.59	732.46	0.000

MRI = magnetic resonance imaging

CT = computer tomography

SD = standard deviation

less continuous pattern of around 13% during the entire follow-up. The average number of visits was always lower than one per patient, caused by a few patients with a relatively high number of visits. Medication was used by about 6% of the patients in the intervention group and 10% in the control group during follow up. In both groups, one-third of the medications was prescribed by a physician. The medications most frequently used were paracetamol, naproxen, nurofen, diclofenac, glucosamine and tramadol. A summary of the direct medical costs per 6 weeks is given in Table 2.

The unit costs of medical consumption are shown in Appendix 2. At 6 and 13 weeks the medical costs per patient were higher for the intervention group than for the control group (Mann–Whitney U-test: $P_6 < 0.001$; $P_{13} = .023$), which coincided with higher costs for physiotherapy ($P_6 < 0.001$; $P_{13} < 0.001$). At 6 weeks, the costs for x-rays were significantly lower for the intervention group than for the control group ($P_6 < 0.045$). No significant

Table 4: Productivity costs due to absence from paid work in the past 6 weeks per measurement moment (Euro 2007).

	Baseline	6 weeks	13 weeks	26 weeks	39 weeks	52 weeks
Intervention group						
Number of respondents with a paid job	45	40	42	44	44	46
Share of respondents absent	11%	15%	7%	5%	5%	9%
Number of days absent, mean (SD)	3.8 (1.3)	6.5 (1.2)	1.0 (*)	1.0 (*)	1.0 (*)	1.6 (0.3)
Costs due to absence from work, mean (SD)						
<i>Per respondent with a paid job</i>	37.61 (113.12)	86.84 (212.60)	6.36 (23.22)	4.05 (18.77)	4.05 (18.77)	12.59 (41.63)
<i>Per respondent</i>	26.03 (95.41)	53.44 (171.34)	4.11 (18.83)	2.74 (15.50)	2.74 (15.50)	8.91 (35.38)
Control group						
Number of respondents with a paid job	45	46	44	43	42	49
Share of respondents absent	11%	17%	14%	12%	12%	4%
Number of days absent, mean (SD)	1.5 (1.0)	7.8 (4.7)	1.0 (*)	1.0 (*)	1.9 (2.3)	1.3 (0.4)
Costs due to absence from work, mean (SD)						
<i>Per respondent with a paid job</i>	23.75 (89.87)	121.01 (312.91)	12.15 (30.92)	10.36 (28.89)	23.33 (98.47)	4.54 (22.72)
<i>Per respondent</i>	6.19 (74.78)	84.34 (266.32)	8.10 (25.80)	6.75 (23.70)	14.84 (79.00)	3.37 (19.62)

SD = standard deviation

* = not available

cost differences for any of the other cost components (visits to healthcare providers, medical imaging services, medications and disposables) were found 26, 39 and 52 weeks after randomization. Annual direct medical costs for both the intervention and the control group are presented in Table 3. The direct medical cost estimates for the intervention and control group were €434 (SD 786) and €299 (SD 732), respectively (Mann–Whitney U-test: $P < 0.001$). When multiple testing is not taken into account, the annual costs of visits to the physiotherapist ($P < 0.001$) and x-rays ($P = 0.007$) were significantly different. Using one-way analyses of variance with post hoc testing, the P-value is no longer significant ($P = 0.003$). No significant differences were found for any of the other cost components.

Productivity costs

Absence from paid work

Table 4 presents the productivity costs per 6 weeks due to absence from paid work. Patients in the intervention group were slightly, but not significantly, more absent from paid work in comparison to the control group. In both groups, the highest absence from work was observed at 6 weeks (15% and 17%), with a decrease up until 39 weeks (5% and 12%). At 52 weeks, 9% of the patients in the intervention and 4% of the patients in the control groups were absent from work. The annual costs due to absence from paid work per patient were €72 (SD 269) and €113 (SD 349) for the intervention and control group, respectively (Mann–Whitney U-test: $P = 0.729$).

Reduced efficiency at paid work Appendix 3 shows the scores on reduced efficiency at paid work for the intervention and the control group over time. The efficiency loss during paid work in terms of hours lost was lower in the intervention in comparison to the control group at baseline and during follow-up. Seventy-nine percent of the patients in the intervention group and 71% in the control group indicated that the reduced efficiency was caused by PFPS problems. The efficiency loss for both groups was highest at baseline (21% and 20%) and lowest at 52 weeks (5% and 2%), with a continuous decrease from 6 weeks onwards. The intervention group had a peak (14%), whereas the control group had a small dip (1%) in efficiency loss at 39 weeks. However, the differences between both groups were never significantly different (Pearson's chi-square test: $P > 0.206$). The annual costs due to reduced efficiency at paid work were €473 (SD 2371) and €648 (SD 2066) for the intervention and control group respectively (Mann–Whitney U-test: $P = 0.223$).

Reduced efficiency at unpaid work

At baseline about 3% of the patients in the intervention group and 10% of the patients in the control group had housekeeping tasks taken over (Pearson's chi-square test:

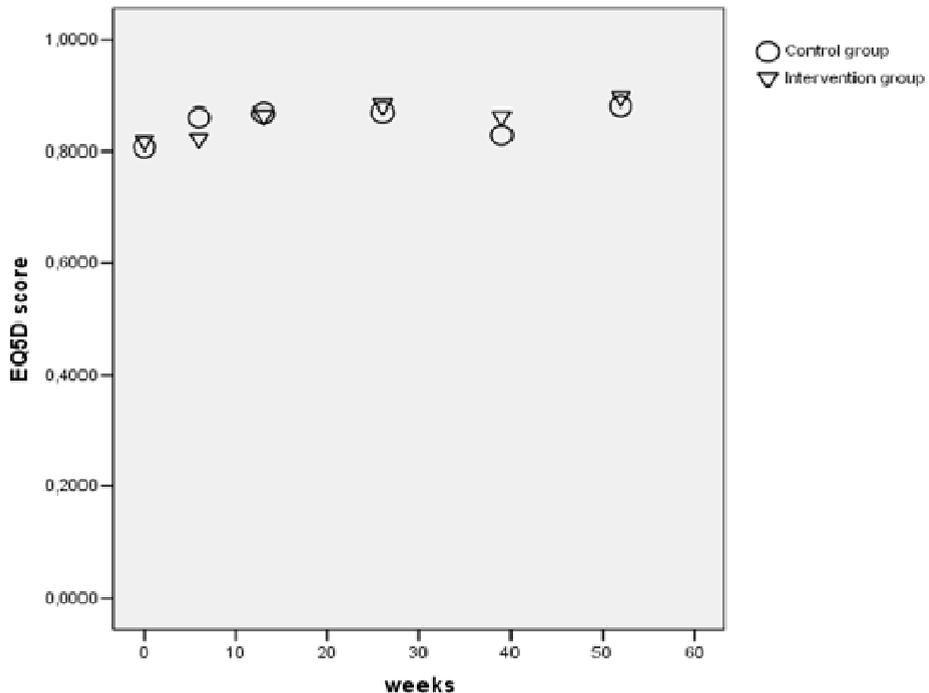


Figure 2: Quality of life (utility values) for the intervention and the control group as measured by the EQ-5D.

$P=0.090$). These fractions remained stable during follow-up and were significantly different only at 6 weeks ($P=0.025$). Virtually all hours were taken over by family members. None of the patients made use of paid aid. The annual costs of taking over housekeeping tasks were €32 (SD 251) and €105 (SD 529) for the intervention and control group, respectively (Mann–Whitney U-test: $P=0.228$).

Quality of life

Figure 2 shows the scores on the EQ-5D over time for the intervention and the control group. The quality of life scores on the EQ-5D were never significantly different between the intervention and the control group. However, the quality of life for both groups was lowest at baseline and highest at 52 weeks, with a slight increase in quality of life from 13 weeks onwards. The scores on the EQ-5D at baseline were 0.8191 (SD=0.1422) in the intervention group and 0.8073 (SD=0.1706) in the control group. At 52 weeks the scores were, respectively, 0.8973 (SD=0.1719) and 0.8812 (SD=0.2046). The intervention group had a small dip in quality of life score at 6 weeks, 0.8223 (SD=0.1571), compared with the control group, 0.8609 (SD=0.1249; $P=0.121$). The intervention group had a peak quality of life score at 39 weeks, 0.8632 (SD=0.1967), compared with the control group, 0.8287

Table 5: Productivity costs due to reduced efficiency at unpaid work in the past 6 weeks per measurement point (Euro 2007)

	Baseline		6 weeks		13 weeks		26 weeks		39 weeks		52 weeks	
	Intervention group	Control group										
% respondents of whom housekeeping tasks were taken over	3.1%	10.6%	3.2%	6.1%	4.8%	7.6%	0.0%	7.6%	1.6%	7.6%	1.6%	7.6%
number of hours housekeeping tasks which were taken over	0.28	0.34	0.10	0.21	0.08	0.48	0.00	1.71	1.55	3.18	0.08	0.35
cost due to reduced efficiency at unpaid work (€ 2007)	2.40	2.94	0.83	1.84	0.69	4.20	0.00	14.84	13.41	27.59	0.67	3.02
SD	15.59	10.46	5.55	9.31	359	22.21	0.00	105.83	107.29	148.26	5.38	12.59

($S=0.2194$; $P=0.346$). Inspecting each EQ-5D dimension, the intervention group only had significantly less problems on activity at 26 weeks (Pearson's chi-square test: $P=0.019$) and only significantly more problems on mobility at 39 weeks ($P<0.022$). Appendix 4 and 5 show the EQ-5D VAS scores on the current health state (Appendix 4) and the severity of PFPS problems at rest (Appendix 5) for the intervention and the control group over time.

During follow-up, the intervention group experienced slightly higher current health, albeit not significant ($P>0.099$). For both groups, the current health state was virtually lowest at baseline (78.62 vs 79.95) and highest at 52 weeks (84.03 vs 83.62), with a slight increase from 6 weeks onwards. The intervention group experienced a lower severity of their PFPS problems during treatment follow-up ($P<0.042$). The severity was highest at baseline (4.14 vs 4.03) and lowest at 52 weeks (0.302 vs 0.358), with a continuous decrease from baseline onwards.

Cost-effectiveness

Table 5 provides the total annual costs and quality of life per patient in the intervention and control group. The total annual costs per patient were €155 lower for the intervention group compared with the control group (€1011 vs €1.166; Mann-Whitney U-test: $P=0.030$). Furthermore, an average patient gained 0.0105 QALY due to the intervention (independent sample t-test: $P=0.666$), which resulted in a societal average CE-ratio of €14.738 per QALY.

However, the variance around this CE-ratio was substantial. Using non-parametric bootstrapping (2500 draws), the simulated 95% confidence interval for the CEratio ranged from - €210.206 to +€178 822. The CEplane (Fig. 3) showed that the intervention was dominant in 52% of the cases (positive health effects and cost savings) and for 14% it was inferior. The probability that the intervention had positive health effects was about 70%, the probability for cost savings was about 68%. The acceptability curve showed a probability of 73% that the cost per QALY were lower than €20 000. When only direct medical costs were included, average incremental costs per patient were €135 and the average cost per QALY €12 754. The bootstrapped confidence interval for the CE-ratio was again wide, ranging from -€114 042 to +€122 151.

The probability for cost savings was about 17%. The acceptability curve showed a probability of 57% that the cost per QALY was lower than €20 000 and 66% that it was lower than €80 000.

DISCUSSION

This is the first economic evaluation on exercise therapy in adolescents and young adults with PFPS. The annual direct medical costs per patient were significantly higher

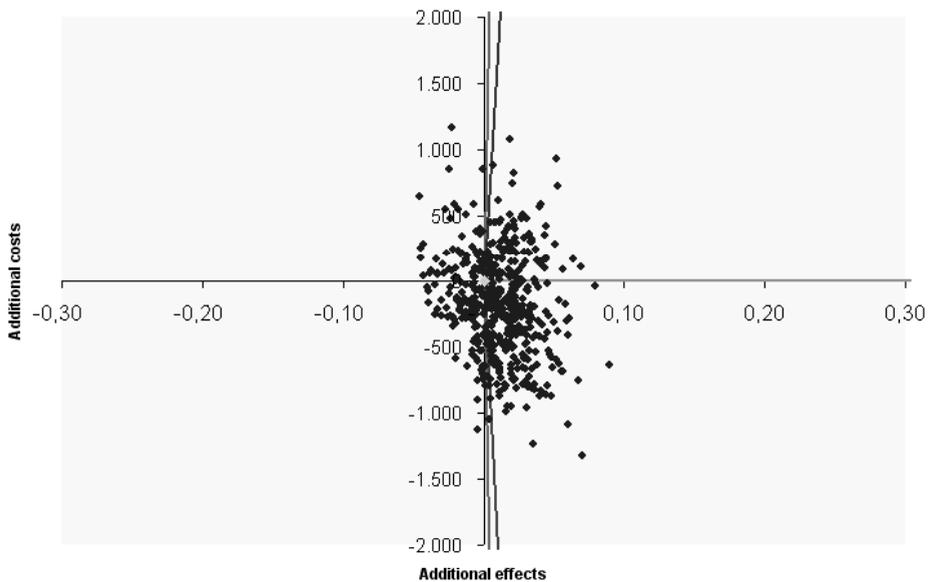


Figure 3: CE-plane which examined the degree of uncertainty for costs and health effects and the cost-utility ratio CE: Cost Effectiveness

for the intervention group (€434; SD 786) compared with the control group (€299; SD 732) mainly caused by additional physiotherapy visits. Productivity costs amounted to €577 (SD 2384) and €867 (SD 2192) for the two groups, respectively, even though the difference in productivity cost between the two groups was not significant. From the societal perspective, the annual total costs per patient were significantly lower for the intervention group (€1011) compared with the control group (€1166) (borderline significance when taking into account multiple testing). This finding confirms that the inclusion of productivity costs considerably affects the total costs and the CE-ratio. Economic evaluations are preferably determined from a societal perspective in which all relevant costs are included.⁶ Our results suggest that productivity costs are the most important cost component, even more so than direct medical costs. Particularly costs which occurred due to reduced efficiency at paid work were substantial. The latter result reinforces the conclusions of earlier studies in, e.g. low back pain, that productivity losses are significant despite the relatively young (working) patient sample.¹⁷ Quality of life appears to correlate well with the health state and experienced severity of PFPS problems.

Exercise therapy resulted in a significant lower experienced severity, especially at 6, 13 and 26 weeks (Appendix 4 and 5). This finding is in agreement with that of Timm(1998), who concluded that exercise therapy almost halves the pain scores and drastically improves functional ability after 4 weeks.¹⁸ In contrast, the randomized controlled trial

carried out by Clark et al. (2000) concluded that exercise therapy resulted in significantly greater pain reduction only after 52 weeks.¹⁹ Other randomized studies that compared exercise therapy with non-exercise therapy in PFPS studied outcomes after exercise therapy vs. brace treatment, or studied the effect of multimodal physiotherapy including exercises and are therefore not directly compared with the present study.²⁰⁻²² Regarding the expected time period, it is very speculative whether continued exercise therapy would raise health effects and improve cost-effectiveness. This should be subject of another study. However, it can be concluded that when the positive health effects of the current exercise therapy would sustain in the longer run, with low or zero medical costs, the cost-effectiveness will improve. Although our study excluded patients with clearly defined other anterior knee pain syndromes than PFPS, all different entities within PFPS were included (e.g. maltracking problem, strength problem, bone abnormality). Possibly the results would be different in certain sub-entities of PFPS, but subgroup analysis could not be performed for such sub-entities as they were not defined in our study. However, given the fact that diagnoses of such sub-entities is hardly feasible in primary care settings, the results presented here apply to the whole group of PFPS and are relevant for the primary care setting. Resource use of medical imaging services which were used to exclude patients with other diagnoses than PFPS were not incorporated in the direct medical costs because they took place before enrolment. Even though the physician's preference in using imaging studies or braces may be important to explain differences between patients in general, it does not explain the difference between the patients of our intervention and control group because the indications for the imaging studies of PFPS patients in the intervention group did not differ from those in the control group. Remarkably, eight patients in the intervention group reported zero visits to the physiotherapist. In these cases, the number of visits as provided by the physiotherapist was used in the cost calculations.

Additionally, only 14% of the patients reported exactly the same number of physiotherapy visits as the physiotherapist. Of the remaining patients, 47% reported less and 39% more visits per year than the physiotherapist. The average numbers of visits per year were 7.9 and 7.4 according to the patients and physiotherapists, respectively, which was slightly lower than the projected 9.0 visits. Even though the use of two independent sources for the cost calculation generally provokes inconsistency, it takes advantage of more accurate and complete data. Furthermore, only 88% of the patients in the intervention group visited a physiotherapist at 6 weeks. This implies that at least some of the intervention patients did not meet the terms of the standardized exercise program they were appointed to. However, these patients were not excluded from the analyses because our study was set up on an intention-to-treat basis which more accurately reflects reality. This study has several limitations. Direct medical unit costs are ideally based on the microcosting methodology. Because all relevant cost components are identified at

the most detailed level, the microcosting methodology provides cost estimations that most accurately reflect actual costs. As this methodology is time consuming, especially when administrative information systems are absent or inadequate, it has not been widely used in economic evaluations. Therefore, we restricted the use of microcosting estimates to visits to the general practitioner and physiotherapist. Compared with Dutch reference unit prices, the use of microcosting estimates did likely not result in different conclusions regarding the relative costs of exercise therapy and 'usual care'.¹³ The resource use of visits to the general practitioner was virtual equal between the exercise therapy and "usual care" groups. The difference between the microcosting estimate and reference unit price was negligible for visits to the physiotherapist, particularly when productivity costs were considered. Dutch reference unit prices were used as a proxy to the other medical unit costs. Another limitation of our study concerned the inclusion of only a small number of patients, although special attention was paid to selecting representative practices and sport medical advice centers. The variance in quality of life between patients was limited, but the variance for all cost categories was substantial (Table 5). This resulted in wide confidence intervals for the CE-ratio's, implying considerable uncertainty for decision makers whether to adopt exercise therapy. Our uncertainty analysis indicated that there is a probability of 70% that exercise therapy produces positive health effects, 73% that the cost per QALY gained is lower than €20 000 and 68% that exercise therapy saves societal costs. Whether these results are sufficiently acceptable to use exercise therapy instead of the conservative strategy is up to the decision maker (e.g. policy maker, general practitioner or patient). During the course of our study we faced some other methodological challenges. We applied a naïve method to deal with missing observations (LOCF) compared with, for instance, multiple imputation.²³ However, the influence of the imputation method was limited as the number of missings was small. The variable "income" had the lowest response rate (71%). As a result, the average net value added per employee (€89.06) was based on a limited number of responses. With respect to absence from paid work, we had many missing data on the duration of absence. Therefore, we imputed values for the missing data based on the overall average duration of absence per measurement moment.

PERSPECTIVES

This study was conducted in the Netherlands. However, we believe that our resource use findings could be representative of other countries, especially those in which the general practitioner operates as the gatekeeper of health care. Clinical guidelines of the Dutch College of General Practice recommend a conservative treatment for PFPS.⁵ However, with a CE-ratio of €14.738 per QALY, our study revealed a considerable

probability that exercise therapy is cost saving or cost effective as compared with the conservative strategy. Although there seems to be a rationale to question the current guidelines, an efficient policy concerning physiotherapy requires treatment consensus and an optimal interaction with other health providers such as general practitioners and medical specialists. Therefore, future studies should investigate the possibilities to further implement this exercise therapy.

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REFERENCES

1. van Linschoten R, van Middelkoop M, Berger MY, Heintjes EM, Koopmanschap MA, Verhaar JA, et al. The PEX study - Exercise therapy for patellofemoral pain syndrome: design of a randomized clinical trial in general practice and sports medicine [ISRCTN83938749]. *BMC Musculoskelet Disord* 2006;7:31.
2. Arendt EA. Musculoskeletal injuries of the knee: are females at greater risk? *Minn Med* 2007;90(6):38-40.
3. Arroll B, Ellis-Pegler E, Edwards A, Sutcliffe G. Patellofemoral pain syndrome. A critical review of the clinical trials on nonoperative therapy. *Am J Sports Med* 1997;25(2):207-12.
4. Cutbill JW, Ladly KO, Bray RC, Thorne P, Verhoef M. Anterior knee pain: a review. *Clin J Sport Med* 1997;7(1):40-5.
5. Cirkel JW, Klaassen WRC, Kunst JA, Aarns TEM, Plag EC, Goudswaard AN, et al. Niet-Traumatische knieproblemen bij kinderen en adolescenten; NHG-Standaard. *Huisarts Wet* 1998;41:246-251.
6. Drummond M. *Methods for the economic evaluation of health care programmes*. New York: Oxford University Press, 2005.
7. Tranmer JE, Guerriere DN, Ungar WJ, Coyte PC. Valuing patient and caregiver time: a review of the literature. *Pharmacoeconomics* 2005;23(5):449-59.
8. Heintjes E, Berger MY, Bierma-Zeinstra SM, Bernsen RM, Verhaar JA, Koes BW. Exercise therapy for patellofemoral pain syndrome. *Cochrane Database Syst Rev* 2003(4):CD003472.
9. Malanga GA, Andrus S, Nadler SF, McLean J. Physical examination of the knee: a review of the original test description and scientific validity of common orthopedic tests. *Arch Phys Med Rehabil* 2003;84(4):592-603.
10. Nijs J, Van Geel C, Van der auwera C, Van de Velde B. Diagnostic value of five clinical tests in patellofemoral pain syndrome. *Man Ther* 2006;11(1):69-77.
11. College Tarieven Gezondheidszorg Zio. Brief aan de Minister van VWS inzake de herijking normatieve inkomens voor beroepsbeoefenaren. Utrecht: College Tarieven Gezondheidszorg/Zorgautoriteit in oprichting, 2002.
12. College Tarieven Gezondheidszorg Zio. Invoering aanwijzing nieuw bekostigingssysteem huisartsen - Rekennorm: A 05-34-a6 Deelnotitie B. Utrecht: CTG/ZAio, 2005.
13. Oostenbrink JB, Bouwmans CAM, Koopmanschap MA, Rutten FFH. Dutch manual for costing: methods and standard costs for economic evaluations in health care. Rotterdam: College voor zorgverzekeringen, Institute for Medical Technology Assessment, Erasmus MC, 2004.
14. Brouwer WB, Koopmanschap MA, Rutten FF. Productivity losses without absence: measurement validation and empirical evidence. *Health Policy* 1999;48(1):13-27.
15. Koopmanschap MA. PRODISQ: a modular questionnaire on productivity and disease for economic evaluation studies. *Expert Rev Pharmacoecon Outcomes Res* 2005;5(1):23-8.
16. Lamers LM, McDonnell J, Stalmeier PF, Krabbe PF, Busschbach JJ. The Dutch tariff: results and arguments for an effective design for national EQ-5D valuation studies. *Health Econ* 2006;15(10):1121-32.
17. Hoeijenbos M, Bekkering T, Lamers L, Hendriks E, van Tulder M, Koopmanschap M. Cost-effectiveness of an active implementation strategy for the Dutch physiotherapy guideline for low back pain. *Health Policy* 2005;75(1):85-98.
18. Timm KE. Randomized controlled trial of Protonics on patellar pain, position, and function. *Med Sci Sports Exerc* 1998;30(5):665-70.

19. Clark DI, Downing N, Mitchell J, Coulson L, Syzpryt EP, Doherty M. Physiotherapy for anterior knee pain: a randomised controlled trial. *Ann Rheum Dis* 2000;59(9):700-4.
20. Lun VM, Wiley JP, Meeuwisse WH, Yanagawa TL. Effectiveness of patellar bracing for treatment of patellofemoral pain syndrome. *Clin J Sport Med* 2005;15(4):235-40.
21. Collins N, Crossley K, Beller E, Darnell R, McPoil T, Vicenzino B. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *Bmj* 2008;337:a1735.
22. Crossley K, Bennell K, Green S, Cowan S, McConnell J. Physical therapy for patellofemoral pain: a randomized, double-blinded, placebo-controlled trial. *Am J Sports Med* 2002;30(6):857-65.
23. Oostenbrink JB, Al MJ, Rutten-van Molken MP. Methods to analyse cost data of patients who withdraw in a clinical trial setting. *Pharmacoeconomics* 2003;21(15):1103-12.

APPENDICES

Appendix 1 (Table A1 and A2)

Appendix 2 (Table B1 and B2)

Table A1. Healthcare utilisation in 6 weeks for the intervention group, n = 65 (median)

		Baseline	6 weeks	13 weeks	26 weeks	39 weeks	52 weeks
General practitioner	Contact	83.3%	24.6%	6.2%	6.6%	3.1%	7.7%
	Mean	1.05 (1.0)	0.35 (0.0)	0.08 (0.0)	0.09 (0.0)	0.05 (0.0)	0.09 (0.0)
Sport physician	Contact	16.9%	4.7%	3.1%	1.5%	0.0%	1.5%
	Mean	0.28 (0.0)	0.05 (0.0)	0.12 (0.0)	0.02 (0.0)	0.00 (0.0)	0.02 (0.0)
Physiotherapist	Contact	3.1%	87.7%	58.5%	36.9%	26.2%	20.0%
	Mean	0.38 (0.0)	4.38 (4.0)	2.04 (0.0)	0.92 (0.0)	0.79 (0.0)	1.12 (0.0)
Medical specialist	Contact	3.1%	1.5%	1.5%	1.5%	3.1%	3.1%
	Mean	0.02 (0.0)	0.00 (0.0)	0.02 (0.0)	0.05 (0.0)	0.09 (0.0)	0.03 (0.0)
Company physician	Contact	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	Mean	0.02 (0.0)	0.00 (0.0)	0.00 (0.0)	0.00 (0.0)	0.00 (0.0)	0.00 (0.0)
MRI / CT	Contact	0.0%	0.0%	0.0%	3.1%	3.1%	0.0%
	Mean	0.05 (0.0)	0.00 (0.0)	0.00 (0.0)	0.05 (0.0)	0.05 (0.0)	0.00 (0.0)
X-ray	Contact	6.2%	0.0%	3.1%	1.5%	1.5%	0.0%
	Mean	0.11 (0.0)	0.00 (0.0)	0.05 (0.0)	0.05 (0.0)	0.03 (0.0)	0.00 (0.0)
Medication		13.8%	6.2%	6.2%	7.7%	6.2%	4.6%
	Prescription	7.7%	3.1%	1.5%	1.5%	3.1%	1.5%
	Over the counter	6.2%	3.1%	4.6%	6.2%	3.1%	3.1%
Disposables		52.4%	56.6%	73.4%	67.2%	73.4%	71.9%

Table A2. Healthcare utilisation in 6 weeks for the control group, n = 66 (median)

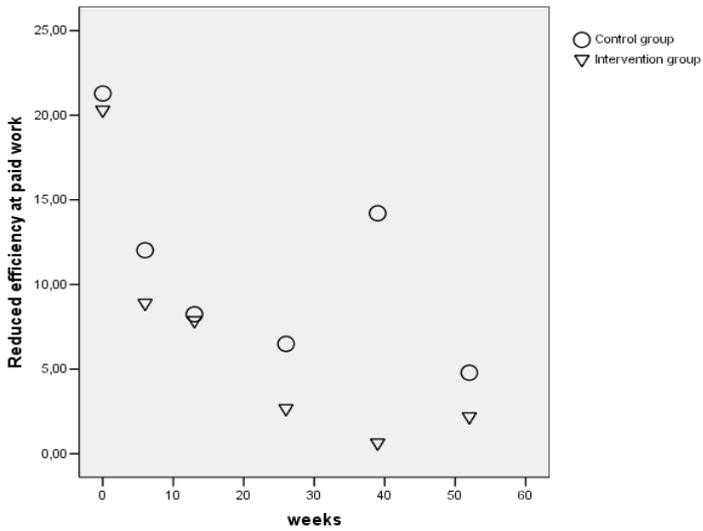
		Baseline	6 weeks	13 weeks	26 weeks	39 weeks	52 weeks
General practitioner	Contact	84.4%	19.7%	13.6%	13.8%	9.1%	7.6%
	Mean	1.05 (1.0)	0.21 (0.0)	0.17 (0.0)	0.15 (0.0)	0.11 (0.0)	0.12 (0.0)
Sport physician	Contact	25.0%	3.0%	1.5%	1.5%	0.0%	1.5%
	Mean	0.18 (0.0)%	0.11 (0.0)	0.09 (0.0)	0.03 (0.0)	0.00 (0.0)	0.02 (0.0)
Physiotherapist	Contact	12.5%	16.7%	13.6%	13.6%	10.6%	3.0%
	Mean	0.03 (0.0)	0.55 (0.0)	0.61 (0.0)	0.92 (0.0)	0.52 (0.0)	0.55 (0.0)
Medical specialist	Contact	1.6%	0.0%	1.5%	4.5%	4.5%	1.5%
	Mean	0.05 (0.0)	0.00 (0.0)	0.02 (0.0)	0.06 (0.0)	0.06 (0.0)	0.05 (0.0)
Company physician	Contact	1.6%	1.5%	3.0%	3.1%	0.0%	1.5%
	Mean	0.00 (0.0)	0.03 (0.0)	0.05 (0.0)	0.05 (0.0)	0.00 (0.0)	0.02 (0.0)
MRI / CT	Contact	4.7%	0.0%	0.0%	1.5%	1.5%	3.0%
	Mean	0.00 (0.0)	0.00 (0.0)	0.00 (0.0)	0.02 (0.0)	0.02 (0.0)	0.03 (0.0)
X-ray	Contact	10.9%	6.1%	6.1%	7.7%	3.0%	3.0%
	Mean	0.06 (0.0)	0.06 (0.0)	0.06 (0.0)	0.09 (0.0)	0.03 (0.0)	0.05 (0.0)
Medication		10.6%	10.6%	9.1%	7.6%	10.6%	13.6%
	Prescription	1.5%	1.5%	3.0%	4.5%	3.0%	6.1%
	Over the counter	9.1%	9.1%	6.1%	3.0%	7.6%	7.6%
Disposables		50.0%	62.1%	59.1%	60.6%	60.6%	60.6%

Table B1. Unit costs of health care utilization (€ 2007)

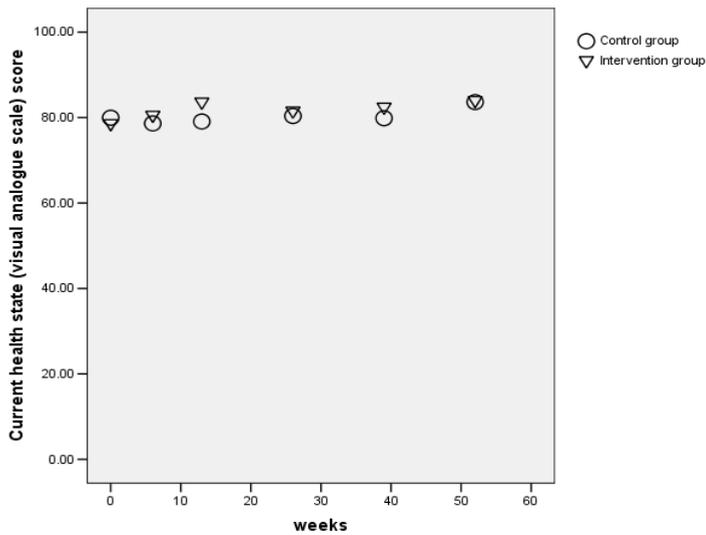
Unit costs of health care utilization (€ 2007)	
General practitioner (one visit)	14.77
Sport physician (one visit)	59.20
Physiotherapist costs (one visit)	22.86
Medical specialist (one visit)	59.20
Company physician (one visit)	59.20
MRI / CT	263.00
X-ray	47.20
Paracetamol (500 mg)	0.04
Naproxen (250 mg)	0.16
Nurofen (200 mg)	0.10
Diclofenac (25 mg)	0.13
Glucosamine (400 mg)	0.22
Tramadol (100 mg)	0.32
Cold compress	2.00
Hot compress	2.00
Orthopedic insoles	150.00
Elastic bandage	30.00
Brace	60.00
Tape	5.00

Table B2 Resource use and unit costs of the general practitioner and physiotherapist

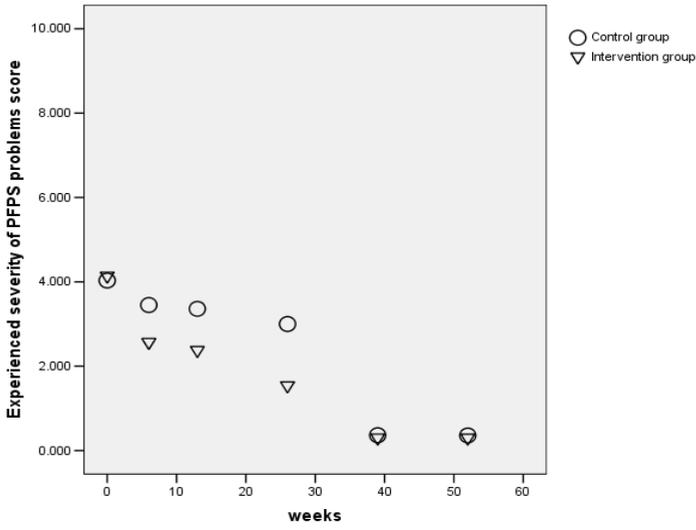
	General Practitioner		Physiotherapist	
	Mean	SD	Mean	SD
LABOUR				
General practitioner / physiotherapist	9.67	0.81	20.08	13.39
Resource use (minutes)	10.33	0.87	45.00	30.00
Unit costs (€ 2007 per minute)	0.94	0.00	0.45	0.45
Assistant	1.24	1.97		
Resource use (minutes)	3.44	5.47		
Unit costs (€ 2007 per minute)	0.36	0.00		
OVERHEADS	3.86	0.71	2.78	2.28
Resource use (minutes)	36%	5%	14%	40%
TOTAL	14.77	2.87	22.86	16.70



Appendix 3 Reduced efficiency at paid work for the intervention and the control group as measured by the visual analogue scale (in %)



Appendix 4 Current health state for the intervention and the control group as measured by the EUROQOL visual analogue scale



Appendix 5 Severity of PFPS problems in rest in the past week for the intervention and the control group measured on a scale from 0 (no pain) to 10 (worst imaginable pain)



Chapter 7

Patellofemoral pain: an overview of exercise therapy and surgery

*(Stand van zaken, Patellofemorale
pijn: oefentherapie en chirurgie)*

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ABSTRACT

Patellofemoral pain syndrome is a common condition during adolescence and young adulthood.

Many factors have been proposed on its etiology ranging from local mechanical abnormalities at the patellofemoral joint to decreased neuro-muscular control or failure of the biological envelope of function.

The diagnosis is mainly based on anamnestic elements and by the exclusion of other pathological conditions around the knee joint. The value of physical examination and additional examinations remains poor.

There is consensus that non-operative treatment is therapy of first choice. A wait-and-see policy is advised. Research however shows that for patients with PFPS an active approach with an extensive supervised exercise program is more effective than a wait-and-see policy.

In patients with recurrent patellar dislocation and long-term patellofemoral pain, a diagnostic work-up for maltracking may take place. The development of new radiological techniques may help to visualize anatomical abnormalities that can cause patellofemoral maltracking. In positive cases surgery may be indicated.

It is concluded that patellofemoral pain syndrome is common and its complaints are difficult to treat. The natural evolution of the syndrome might be less favorable than previously suggested.

INTRODUCTION

Patellofemoral pain is frequently encountered in young and physically active persons. For example, during their training, about 25% of military recruits experience restrictions due to patellofemoral complaints.¹ In a two-year prospective study, the incidence of patellofemoral pain in students training to teach physical education was 10%.² In the population at risk, general practitioners (GPs) will encounter 10-12 new patients per year, while in sports medicine clinics up to 25% of the consultations are related to these complaints.^{3,4}

This article describes the background of patellofemoral pain syndrome, the changing views on its causes, and the consequences for different treatment options.

PATELLOFEMORAL PAIN SYNDROME

Patellofemoral symptoms can range from mild and activity-related pain to serious debilitating pain resulting from repeated patellar dislocations. There is growing consensus to use the term 'patellofemoral pain syndrome' (PFPS) for this disorder when there is pain at or around the patella which worsens on prolonged sitting with bended knees, crouching, kneeling, climbing stairs and/or riding a bicycle. Other specific causes of pain should be excluded, e.g. patellar tendinopathy, Osgood-Schlatter disease, intra-articular injury and/or osteoarthritis.⁵

The Dutch guideline 'Non traumatic knee problems in children and adolescents' for GPs describes the diagnosis and treatment of PFPS. The guideline recommends to provide patients with information on the background of the condition, its favorable evolution, and the advice to reduce sports-related activities that provoke pain for one month. If necessary isometric exercises for the quadriceps muscle can be advised.⁶

Recently, two systematic reviews reported on the conservative treatment of PFPS.^{7,8} In a review on pharmacotherapy it was concluded that there is limited evidence for the beneficial effect of NSAIDs on short-term pain relief.⁸ The anabolic steroid nandrolone could be effective but is considered too controversial for use in PFPS. The effect of glycosaminoglycans remains unclear.

The review on the effects of exercise therapy for PFPS in 2003 however concluded that there was limited evidence for the positive effect of exercise therapy on pain.⁷ The effects on functional improvement were contradictory.

There are no systematic reviews which summarize the effects of surgical treatment for PFPS. Studies on the outcome measures of pain and function after surgical intervention are generally only moderate in their methodological design, i.e. they are mainly non-

randomized controlled trials, have a retrospective design, or lack a comparison group, thereby limiting the scientific evidence for surgical interventions.

BACKGROUND ON ETIOLOGY, PATHOPHYSIOLOGY AND PROGNOSIS

Three main theories on the etiology of PFPS have been proposed. Patellofemoral complaints are thought to be related to a mechanical/structural origin, a neuromuscular origin (dynamic 'maltracking'), or to a biological origin (tissue homeostasis, also referred to as the 'envelope of function').⁹

Mechanical Model

The mechanical theory is based on findings of structural and biomechanical abnormalities to the extensor mechanism of the knee.¹⁰ In this model the complaints are assessed in a spectrum ranging from isolated patellofemoral pain to recurrent patellar dislocations. Radiological studies have shown that in patients with patellofemoral pain, anatomical abnormalities can be found that may lead to pain and instability.¹¹ Based on radiological criteria, four groups of patients with patellofemoral pain can be distinguished: 1) patients with objective patellar instability; these patients have a history of at least one patellar dislocation and objective radiological abnormalities; 2) patients with potential patellar instability; these patients do not have a patellar dislocation but have objective radiological abnormalities; 3) patients with patellofemoral pain without dislocation and without objective radiological abnormality; and 4) patients with patellofemoral arthrosis.

Neuromuscular Model

The neuromuscular model is an extension of the mechanical model. It is based on the theory of maltracking of the patella. Due to neuromuscular insufficiency, mainly due to altered contraction patterns of the quadriceps muscles and especially the vastus medialis obliquus, the gliding of the patella on the trochlea leads to excessive compression forces on the one hand and traction forces on the other. Moderating or improving the patellofemoral gliding mechanism by the application of a tape construction around the patella, combined with specific training for the thigh muscles, appears to lead to a reduction of peri-patellar pain.^{12,13}

Biological Model

Of more recent date is the theory that patellofemoral pain originates from the disruption of tissue homeostasis. This model is based on the concept of pathophysiological disrup-

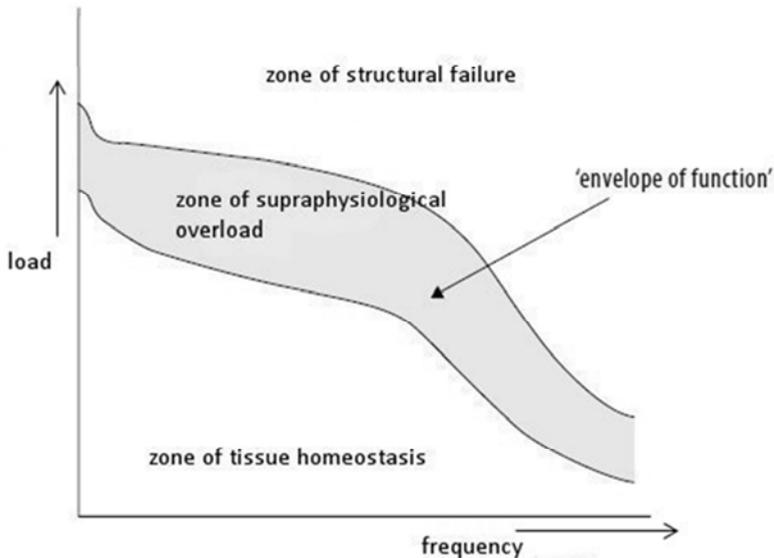


Figure 1. Graphic representation of 'the envelope of function' that expresses the organic capacity of the tissues: with increasing activity, in terms of frequency and/or load, the capacity/homeostasis of the tissues is diminished.¹⁴

tion of the organic capacity of the tissues which constitute the extensor mechanism of the knee.^{9,14}

In this concept of the 'envelope of function' it is presumed that overload of the patellofemoral joint can lead to different pathophysiological processes which may result in loss of tissue homeostasis and subsequent peripatellar pain (Figure 1).

The three theories outlined above are not exclusive and may be considered complementary to each other. The maltracking of the patella due to patellar instability can lead to overloading of the patellofemoral joint which may result in disruption of tissue homeostasis. However, such a disruption can also arise as a result of overload through a continued functional usage beyond the 'envelope of function'.

The assumption that the prognosis of PFPS is generally good can be disputed. In a select sample, 30-50% of patients with patellofemoral pain complaints did not recover after several years.^{15,16}

DIAGNOSTICS AND VALUE OF ADDITIONAL EXAMINATION

In general the data from medical history and physical examination are sufficient to lead to the diagnosis 'PFPS' or 'patellar dislocation'. From history, key elements for PFPS are: peripatellar pain (mostly related to loading and with a non-traumatic origin), pain during squatting, pain when sitting with prolonged knee flexion ('movie-sign') and crepitation of the patella. Some patients may report giving way or pseudo giving way of the knee or actual dislocation of the patella. On physical examination effusion of the knee is generally absent (unless following a patellar dislocation). Pain is indicated at the patellar margins (facets) and various provocation tests are available, e.g. the 'patellar apprehension test', 'signe du robot' and Clarke's test (Figure 2). However, the probability that a positive test result is distinctive in relation to non-specific knee pain is limited. The likelihood ratio is approximately 2.3, i.e. the chance of having PFPS at a positive test outcome is 2.3 times the chance of having non-specific knee complaints.¹⁷

Although severe and debilitating pain may be a reason for additional examination, radiological examination will generally be performed after the clinical assumption of more specific causes of peripatellar pain (e.g. patellar instability, maltracking, patellofemoral arthritis, osteochondritis dissecans).

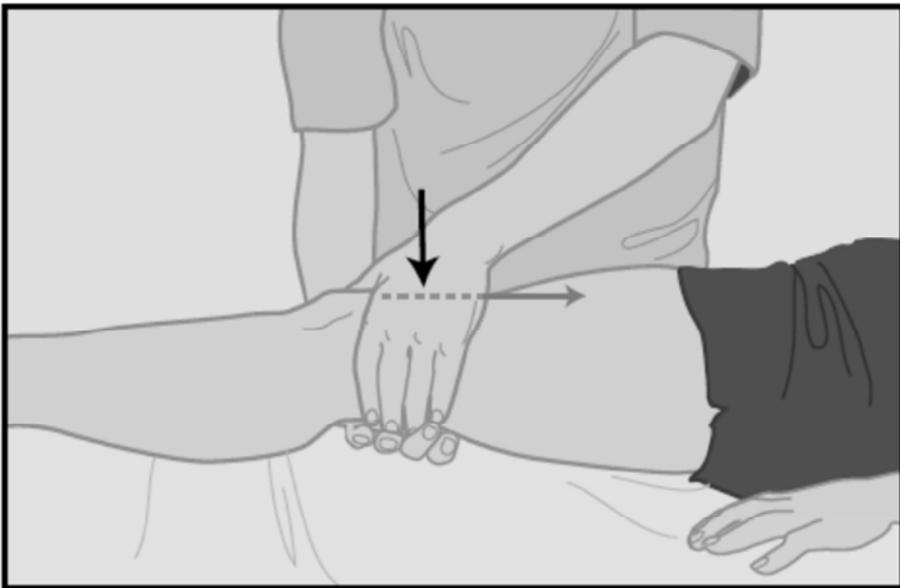


Figure 2. Clarke's test can be applied in a patient with patellofemoral pain. If contraction of the M. quadriceps with compression of the patella causes the patient's pain to be reproduced, then the test result is positive.

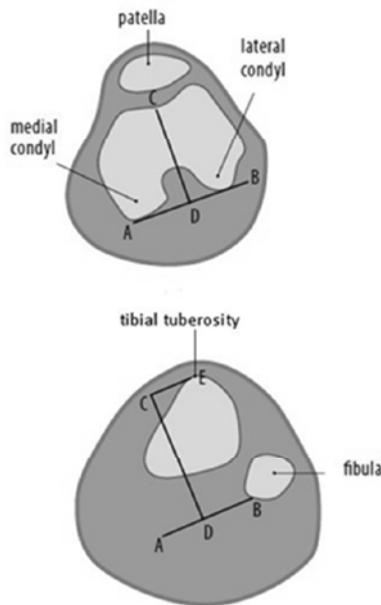


Figure 3. With a CT scan, the lateral distance between the deepest point of the trochlea and the midpoint of the tuberositas tibiae is determined to establish whether there is maltracking of the patella: (a) on a CT slice at the height of the trochlea, the posterior intercondylar line is drawn (A-B). Then a vertical line (D-C) is drawn to the deepest point of the trochlea. (b) These lines are copied on a scan at the height of the tuberositas tibiae, then the distance to the tuberosity is determined (C-E), i.e. the extent of lateralization.

Radiological research has shown that four factors are significantly correlated with maltracking and patellar instability.¹⁸ These factors are: trochlea dysplasia, the patellar angle in relation to the femur in the coronal plane (the so-called patellar tilt), patella alta (vertical malposition of the patella) and an enlarged lateral distance between the trochlea and the tibial tuberositas. The latter refers to the situation in which the tuberositas is positioned relatively more lateral to the trochlea and leads to pulling of the patella by the patellar tendon to the lateral part of the trochlea.

The bony anatomy of the patellofemoral joint can be depicted with conventional X-ray and CT scan.¹⁹ A conventional X-ray is suitable for determining patella alta or trochlea dysplasia. A patella alta can be visualized on a lateral X-ray view, although controversy still exists as to the best method to measure its height.²⁰ To depict the lateral distance between the trochlea and the tuberositas tibiae, a CT scan is necessary. Recently, a new method has been developed to measure this distance more reliably (Figure 3).²¹

The tracking of the patellofemoral joint is affected by the anatomy of the cartilage. MRI examination is the most suitable for determining this anatomy. Because of the lack of reference values, current research is addressing the depth of the trochlea (the sulcus angle) and the distance between the trochlea and tuberositas tibiae.

EFFECTIVENESS OF TREATMENT OPTIONS FOR PATELLOFEMORAL PAIN

Conservative treatment including exercise therapy

Much research has been done on the effects of conservative treatment for PFPS. Treatment may consist of simple interventions but more often consists of combinations of physiotherapy, exercise therapy or treatment with tape, braces/bandages or insoles.²²⁻²⁵ Some studies have compared the various interventions with each other, and a few studies have compared the intervention group with a control group.

One of the systematic reviews reported that there is only limited evidence for the effectiveness of exercise therapy on pain complaints.⁷ However, it is known that 30% of the patients with PFPS is referred to a physiotherapist after visiting the GP.²⁶ The additional value of exercise therapy compared to a wait-and-see policy as advised in the Dutch GP guidelines was, however, not previously investigated.

Our group has reported on the effects of supervised and protocolized exercise therapy in patients with PFPS; the PEX study.²⁷ In that study, 65 patients followed an intensive and differentiated exercise program for 3 months with home exercises under the supervision of a physiotherapist. The effects on pain, function and recovery were compared to a control group (n=66) which followed the usual advice according to the GP guideline (Figure 4). The patients were followed for 1 year. After 3 months the intervention group showed significantly better pain and function scores than the control group. Even after 12 months, the difference in pain reduction was significantly in favor of the exercise group. However, no difference was found in the rate of recovery between both groups: after 1 year 62% of the patients in the exercise group reported recovery versus 50% in the control group.²⁷

That study shows that a protocolized and supervised extensive physical exercise program is more effective than a passive strategy regarding pain reduction and functional improvement (Table 1).

Effectiveness of operative treatment

Although the treatment of patellofemoral pain focuses on conservative measures, surgery may be considered. In the past, many patients with patellofemoral pain underwent a transposition of the tibial tuberositas (the Hauser procedure), which is nowadays regarded as obsolete. In this procedure the tuberositas is transposed to posterior which markedly increases patellofemoral pressure, resulting in patellofemoral osteoarthritis.²⁸

In addition, the so-called 'lateral release' of the articular capsule at the lateral side of the patella was often performed. However, biomechanical research has shown that this treatment is counterproductive because the stability of the patella after a lateral release is further reduced.²⁹

Surgery is indicated only in patients with anatomical abnormalities. Nowadays, due to new radiological techniques, anatomical abnormalities that can cause patellofemoral



Figure 4. The so-called 'lunge' as part of the exercise program in the PEX study after treatment for patellofemoral pain syndrome.²⁷ In this position the patella of the anterior knee is pressed against the femur

Table 1. Effect of intensive, protocolized and supervised exercise therapy for patients with PFPS²⁷

Difference between intervention (n=65) and control group (n=66)				
Outcome	After 3 months	Effect Size[*]	After 12 months	Effect Size[*]
Pain#	-1.07	ES 0.47	-1.29	ES 0.57
<i>-at rest</i>				
<i>-at activities</i>	-1.00	ES 0.45	-1.19	ES 0.54
Function[‡]	4.92	ES 0.34	4.52	ES 0.31
Recovered in %	7 %	-	11 %	-

significant values are printed bold/italic

^{*} effect size is defined as the difference between both groups, divided by the standard deviation for the outcome measure at baseline

[#] scored at a scale from 0-10 (with increasing pain intensity). Negative differences (pain scores) in favor of exercise therapy

[‡] positive differences (function scores and recovery) in favor of exercise therapy

maltracking are better visualized. However, the relationship between the maltracking and patellar pain is not always unambiguous which implies that the decision for surgery needs to be made with caution. The GP guideline recommends that patients with protracted patellofemoral pain should be referred to an orthopedic surgeon. When maltracking is suspected, the surgeon may confirm the diagnosis by additional radiological examination. A relatively common abnormality in patients with persistent patellofemoral pain is an enlarged lateral distance between tibial tuberositas and trochlea (Figure 3).

In 2007 we presented the results of a prospective study on the effects of a medially directed tuberositas osteotomy for the treatment of patellofemoral pain³⁰ (Figure 5). Both the pain and function scores improved significantly after surgery, with a follow-up of 24 months (Table 2). The pain score on a visual analog scale of 100 mm (0 = no pain; 100 = greatest possible pain) decreased from an average of 52 points preoperatively to an average of 12 points postoperatively.

CONCLUSION

Over the last 40 years there has been a shift in the diagnostic and treatment approach for PFPS. The earlier dominance of the strictly mechanical theory has been replaced by a more functional approach. It is now clear that there is no one-to-one relationship between existing anatomical or radiological abnormalities and instability or pain. For treatment options this means that a decision regarding surgery needs considerable caution.

Recent research shows that for patients with PFPS in general practice an active approach with an extensive supervised exercise program is more effective than a wait-and-see policy. Also, for prolonged and sometimes seriously debilitating pain it is important to inform patients about the natural evolution of patellofemoral complaints, even though it may be less favorable than previously suggested.

In patients with recurrent patellar dislocations, patellar instability or prolonged patellofemoral pain imaging for maltracking may reveal the cause of the complaints. The use of modern CT techniques is a prerequisite for this. With a proven anatomical abnormality surgery may well be indicated.

LEARNING POINTS

- Patellofemoral pain syndrome is common and its complaints are difficult to treat. The natural evolution of the syndrome might be less favorable than previously suggested.

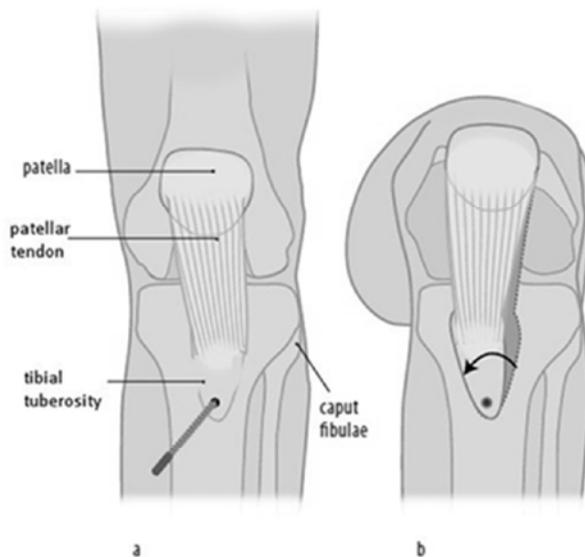


Figure 5. (a) The tibial tuberosity is detached and the distal part is fixed. (b) When bending the knee the proximal part is tilted in the medial direction until a 'neutral' position is reached with respect to the position of the patella in the trochlea. The tibial tuberosity is then fixed in that position.³⁰

Table 2. Results of operative intervention for recurrent patellar dislocation or severe patellar pain in a study in a study by Koeter et al.³⁰

Outcome	Mean (range) Pre-operative	2 years Post-operative
Function score#	62 (31-86)	92 (55-100)
Pain score [¥]	55 (20-91)	14 (0-80)

#function score measured with Lyshom knee score (1-100); a higher score means better function

[¥] pain score at a visual analogue scale of 0-100mm; a higher score means more pain

- There is consensus that non-operative treatment is therapy of first choice. A wait-and-see policy is advised. Research shows that for patients with PFPS an active approach with an extensive supervised exercise program is more effective than a wait-and-see policy.
- In patients with recurrent patellar dislocation and long-term patellofemoral pain, a diagnostic work-up for maltracking may take place. In positive cases surgery may be indicated.

REFERENCES

1. Milgrom C, Finestone A, Eldad A, Shlamkovitch N. Patellofemoral pain caused by overactivity. A prospective study of risk factors in infantry recruits. *J Bone Joint Surg Am* 1991;73(7):1041-3.
2. Witvrouw E, Lysens R, Bellemans J, Cambier D, Vanderstraeten G. Intrinsic risk factors for the development of anterior knee pain in an athletic population. A two-year prospective study. *Am J Sports Med* 2000;28(4):480-9.
3. van der Linden M, Westert G, de Bakker D, Schellevis F. Tweede Nationale Studie naar ziekten en verrichtingen in de huisartspraktijk. Klachten en aandoeningen in de bevolking en in de huisartspraktijk.. Utrecht/Bilthoven: NIVEL/RIVM, 2004.
4. Baquie P, Brukner P. Injuries presenting to an Australian sports medicine centre: a 12-month study. *Clin J Sport Med* 1997;7(1):28-31.
5. Witvrouw E, Werner S, Mikkelsen C, Van Tiggelen D, Vanden Berghe L, Cerulli G. Clinical classification of patellofemoral pain syndrome: guidelines for non-operative treatment. *Knee Surg Sports Traumatol Arthrosc* 2005;13(2):122-30.
6. Breedveldt Boer HP, Klaassen WRC, Spinnewijn WEM, Heinen N, Burggraaff HB, Derks CJT, et al. NHG-Standaard Niet-traumatische knieproblemen bij kinderen en adolescenten; revisie 2009. *Huisarts Wet* 2009;52(7):332-41.
7. Heintjes E, Berger MY, Bierma-Zeinstra SM, Bernsen RM, Verhaar JA, Koes BW. Exercise therapy for patellofemoral pain syndrome. *Cochrane Database Syst Rev* 2003(4):CD003472.
8. Heintjes E, Berger MY, Bierma-Zeinstra SM, Bernsen RM, Verhaar JA, Koes BW. Pharmacotherapy for patellofemoral pain syndrome. *Cochrane Database Syst Rev* 2004(3):CD003470.
9. Dye SF. The pathophysiology of patellofemoral pain: a tissue homeostasis perspective. *Clin Orthop Relat Res* 2005(436):100-10.
10. Insall J, Falvo KA, Wise DW. Chondromalacia Patellae. A prospective study. *J Bone Joint Surg Am* 1976;58(1):1-8.
11. Keser S, Savranlar A, Bayar A, Ege A, Turhan E. Is there a relationship between anterior knee pain and femoral trochlear dysplasia? Assessment of lateral trochlear inclination by magnetic resonance imaging. *Knee Surg Sports Traumatol Arthrosc* 2008;16(10):911-5.
12. McConnell J. The physical therapist's approach to patellofemoral disorders. *Clin Sports Med* 2002;21(3):363-87.
13. Crossley K, Cowan SM, Bennell KL, McConnell J. Patellar taping: is clinical success supported by scientific evidence? *Man Ther* 2000;5(3):142-50.
14. Dye SF. The knee as a biologic transmission with an envelope of function. *Clin Orthop* 1996;325:10-18.
15. Kannus P, Natri A, Paakkala T, Jarvinen M. An outcome study of chronic patellofemoral pain syndrome. Seven-year follow-up of patients in a randomized, controlled trial. *J Bone Joint Surg Am* 1999;81(3):355-63.
16. Blond L, Hansen L. Patellofemoral pain syndrome in athletes: a 5.7-year retrospective follow-up study of 250 athletes. *Acta Orthop Belg* 1998;64(4):393-400.
17. Nijs J, Van Geel C, Van der Auwera C, Van de Velde B. Diagnostic value of five clinical tests in patellofemoral pain syndrome. *Man Ther* 2006;11(1):69-77.
18. Dejour H, Walch G, Nove-Josserand L, Guier C. Factors of patellar instability: an anatomic radiographic study. *Knee Surg Sports Traumatol Arthrosc* 1994;2(1):19-26.
19. Davies AP, Costa ML, Shepstone L, Glasgow MM, Donell S. The sulcus angle and malalignment of the extensor mechanism of the knee. *J Bone Joint Surg Br* 2000;82(8):1162-6.

20. Seil R, Muller B, Georg T, Kohn D, Rupp S. Reliability and interobserver variability in radiological patellar height ratios. *Knee Surg Sports Traumatol Arthrosc* 2000;8(4):231-6.
21. Koeter S, Horstmann WG, Wagenaar FC, Huysse W, Wymenga AB, Anderson PG. A new CT scan method for measuring the tibial tubercle trochlear groove distance in patellar instability. *Knee* 2007;14(2):128-32.
22. Crossley K, Bennell K, Green S, Cowan S, McConnell J. Physical therapy for patellofemoral pain: a randomized, double-blinded, placebo-controlled trial. *Am J Sports Med* 2002;30(6):857-65.
23. Lun VM, Wiley JP, Meeuwisse WH, Yanagawa TL. Effectiveness of patellar bracing for treatment of patellofemoral pain syndrome. *Clin J Sport Med* 2005;15(4):235-40.
24. Clark DI, Downing N, Mitchell J, Coulson L, Syzpryt EP, Doherty M. Physiotherapy for anterior knee pain: a randomised controlled trial. *Ann Rheum Dis* 2000;59(9):700-4.
25. Collins N, Crossley K, Beller E, Darnell R, McPoil T, Vicenzino B. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *Bmj* 2008;337:a1735.
26. Heintjes EM. Non-traumatic knee complaints in adolescents and young adults in general practice. Erasmus Universiteit Rotterdam, 2006.
27. van Linschoten R, van Middelkoop M, Berger MY, Heintjes EM, Verhaar JAN, Willemsen S, et al. Supervised exercise therapy versus usual care for patellofemoral pain syndrome: an open label randomised controlled trial. *BMJ* 2009;339:b4074.
28. Grelsamer RP. Patellar malalignment. *J Bone Joint Surg Am* 2000;82-A(11):1639-50.
29. Christoforakis J, Bull AM, Strachan RK, Shymkiw R, Senavongse W, Amis AA. Effects of lateral retinacular release on the lateral stability of the patella. *Knee Surg Sports Traumatol Arthrosc* 2006;14(3):273-7.
30. Koeter S, Diks MJ, Anderson PG, Wymenga AB. A modified tibial tubercle osteotomy for patellar maltracking: results at two years. *J Bone Joint Surg Br* 2007;89(2):180-5



Chapter 8

The additional effect of orthotic devices on exercise therapy for patients with patellofemoral pain syndrome: a systematic review

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ABSTRACT

Objective:

The aim of the study is to determine “The additional effect of orthotic devices over exercise therapy on pain and function” for patellofemoral pain syndrome (PFPS).

Methods:

A systematic literature search was conducted in MEDLINE, CINAHL, EMBASE, Cochrane and PEDro. Randomised controlled trials and controlled clinical trials of patients diagnosed with PFPS evaluating a clinically relevant outcome were included. Treatment had to include exercise therapy combined with orthotics, compared with an identical exercise programme with or without sham orthotics. Data were summarised using a best evidence synthesis.

Results:

Eight trials fulfilled the inclusion criteria, of which three had a low risk of bias.

There is moderate evidence for no additive effectiveness of knee braces to exercise therapy on pain (effect sizes (ES) varied from -0.14 to 0.04) and conflicting evidence on function (ES -0.33).

There is moderate evidence for no difference between knee braces and exercise therapy versus placebo knee braces and exercise therapy on pain and function (ES -0.1 – 0.10).

Conclusion:

More studies of high methodological quality are needed to draw definitive conclusions on the additional effects of orthotic devices over exercise therapy for PFPS.

INTRODUCTION

Patellofemoral pain syndrome (PFPS) is a common diagnosis in young adults and adolescents. The exact incidence of PFPS in the general population has not been properly evaluated.¹ In a military population, the overall risk of PFPS is 3%, with an incidence rate of 22 injuries/1000 person-years.² In an athlete population, the cumulative incidence risk and rate for the development of new unilateral PFPS is 9.66 per 100 athletes and 1.09 per 1000 athletic exposures, respectively.³ PFPS is defined by a complex of symptoms in which pain around the patella is the most dominant, and the complaint is associated with activities that load the patellofemoral joint, such as squatting, stair ascending and descending, walking, running and jumping.⁴ Patients with PFPS are often highly limited in physical activities due to pain. It is suggested that the cause of PFPS is a combination of proximal, distal and local factors that influence the movement of the patella within the trochlea of the femur.⁵ Patients with PFPS are often referred to a physical therapist. There is evidence that some interventions applied by physical therapists have significant beneficial effects on pain and function compared with no treatment.^{4,6} Treatment strategies that are applied in clinical practice include exercise therapy to increase muscle strength, improve neuromuscular coordination and enhance flexibility. Occasionally, orthotic devices are added to the treatment to relieve pain, and it is suggested that orthotics correct for possible malalignment. Up to now, no systematic review has been published on the additional value of orthotics on exercise therapy. Therefore, the aim of this study was to determine the effectiveness, in measures of pain and function, of a physiotherapeutical intervention consisting of exercise therapy and orthotic devices or exercise therapy and placebo orthotics compared with exercise therapy only for patients with PFPS.

Orthotic devices in this review include patellar bracing, patellar taping and foot orthotics.

METHODS

A literature search was conducted in MEDLINE, CINAHL, EMBASE, Cochrane and PEDro by two independent researchers (MvM and NMS). Wherever possible, the Cochrane Library search filter for randomised controlled trials (RCT) and controlled clinical trials (CCT) was applied to make a restriction for the design. If it was impossible to use the filter in the database, the specific limits options were used for RCT and CCT. Studies were collected from 1990 up to January 2010 with a language restriction for English, German and Dutch studies (online appendix 1). Finally, the reference lists of the included articles were searched for more relevant articles.

Criteria for considering studies for this review

Studies were included if they met the following criteria: (1) RCT or CCT. (2) The study population had to include patients diagnosed with PFPS or anterior knee pain. (3) The intervention had to consist of exercise therapy aiming at muscle strengthening and stretching exercises, combined with foot or knee orthotics (including tape, braces and insoles). The control group had to receive an identical exercise program with or without sham orthotics. (4) The outcome measures assessed were pain and function either reported by the patient using a questionnaire or by the assessor using an objective performance measure of the knee. Studies were excluded when they did not fulfil the above-mentioned inclusion criteria on design, intervention and outcome. Two review authors (NMS, MvM) working independently from one another examined all citations (including titles and abstracts) from the electronic search. Full articles were obtained for those citations thought to fulfil the inclusion criteria. A third reviewer (SMAB-Z) was consulted if consensus was not reached.

Assessment of risk of bias in included studies

The risk of bias assessment was conducted using the 12 criteria recommended by the Cochrane Back Review Group and evaluated independently by two researchers (RvL and NMS) (online appendix 2). The 12 questions were answered with 'yes', 'no' or 'unclear'. If there was a difference in the scores between the assessors, agreement was reached after discussion. Studies with six or more positive items were considered to have a low risk of bias. This cut-off point is supported by empirical evidence.⁷ Agreement between the two authors was calculated by Cohen's κ .⁸ Values of κ between 0.40 and 0.59 have been considered to reflect fair agreement, between 0.60 and 0.74 to reflect good agreement and 0.75 or more to reflect excellent agreement.⁹

Data extraction

Data extraction was performed independently by two researchers (SMAB-Z and NMS). The following data were extracted: study design, baseline characteristics, duration of the complaints, duration and specific details of the intervention, outcome measures and results. Data were extracted for short (0–12 weeks) and long-term (>12 weeks) outcomes. The change scores over time were extracted from the studies or in the absence calculated for the orthotic (O) and the control (C) groups. Subsequently, the differences in change scores between O and C were extracted or calculated, together with a 95% CI. If the raw data were not presented in the study, data were extracted from the figures. The authors were not contacted for data that were not provided. If studies do not provide enough information to calculate the 95% CI, information about significant differences between the groups is abstracted from the studies. Effect sizes (ES) were calculated by dividing the mean difference between O and C by the pooled SD of the baseline scores,

Table 1. Best evidence synthesis

Strong evidence	consistent findings among multiple low risk of bias RCT (consistency: $\geq 75\%$ of the trials report the same findings).
Moderate evidence	consistent findings among multiple high risk of bias RCT and/or CCT and/or one low risk of bias RCT.
Limited evidence	one high risk of bias RCT and/or CCT or consistent findings among multiple CCT
Conflicting evidence	inconsistent findings among multiple RCT and/or CCT
No evidence from trials	no RCT or CCT could be found.

when available.¹⁰ Cohen labelled an ES small if $d=0.20$, medium if $d=0.50$ and large if $d=0.80$.¹¹

Data synthesis

A qualitative data analysis was applied using a best evidence synthesis, consisting of five levels to assess the power of the results. A modified version recommended by the Cochrane Back Review Group was used¹². (table 1)

RESULTS

Information about the number of studies identified from the databases, included and excluded for analysis is shown in figure 1. The search retrieved 269 articles leading to 153 unique articles. Five studies were identified from a hand search of the reference lists. From the 158 publications, 142 studies were excluded based on the title and abstract. Eight studies were excluded based on the full text. The reason for exclusion was a design other than a RCT or CCT, the absence of an intervention consisting of exercise therapy combined with foot or knee orthotics and the absence of outcome measures for pain and function. Finally, seven RCT and one CCT were included and used for analysis.^{13–20} Of the eight studies included two compared an exercise and orthotics group with both an exercise-only and an exercise and placebo orthotics group. The results of the placebo orthotics group were analysed separately.

Risk of bias in included studies

The interrater reliability of the risk of bias assessment was good (κ 0.73). The risk of bias of the eight included studies was 'low' in three studies^{13 14 18} and 'high' in five studies^{15–17 19 20} (table 2). Six studies used an adequate method of randomisation; in one study the method of randomisation was unclear. In four studies the treatment allocation was concealed. In none of the studies was the care provider, the patient or the outcome assessor blinded to the intervention. In three studies the drop-out rate was described

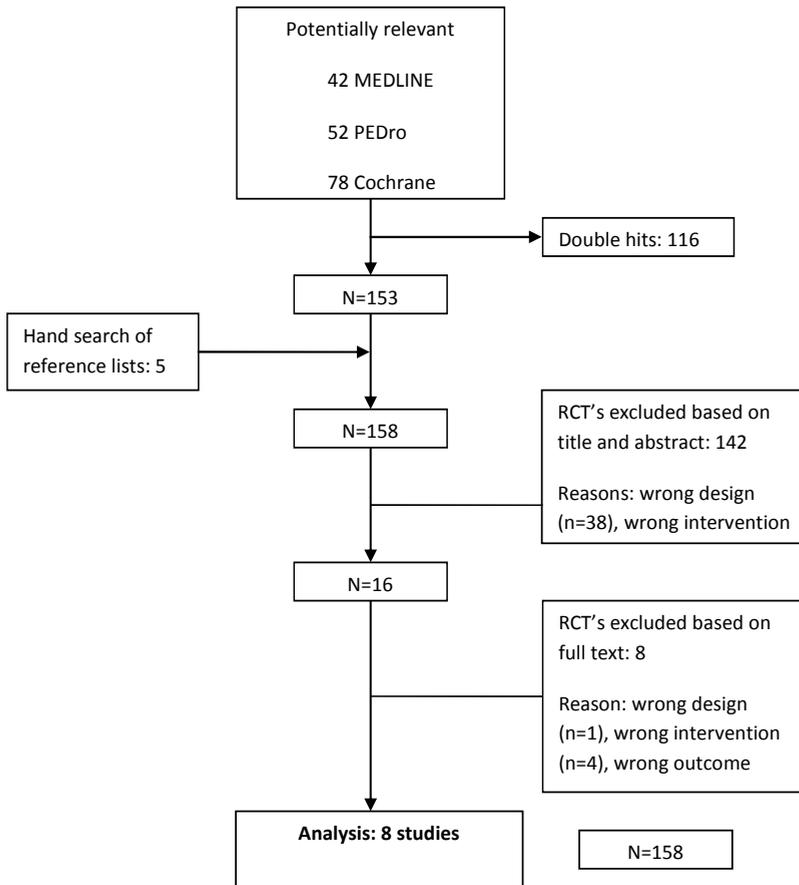


Figure 1. Flow diagram of systematic review inclusion and exclusion of articles

and acceptable, and seven studies analysed the patients in the group to which they were allocated.

Characteristics of included studies

The characteristics of the included studies are described in table 3. The studies included 325 participants, of which 50.3% were women and the mean age of the population was 25.8 years. The duration of complaints varied between the studies from 2 weeks to 15 years. Outcome measures used for pain were: the verbal pain score 15 and the visual analogue scale (VAS) for pain at rest or at different activities.²¹ Questionnaires used to assess function were the Kujala patellofemoral score (KPS)²², the knee function¹⁸, the functional index questionnaire (FIQ)²³ and the Western Ontario and McMaster Universities osteoarthritis questionnaire.²⁴ One study also used an additional step test to measure the performance of the knee. Measurements were performed at different time points ranging from 2 weeks to 1 year. The exercise therapy programmes that were applied are

Table 2. Risk of Bias (RoB) in included studies

RoB items	Denton15	Miller19	Lun18	Whittingham20	Clark13	Kowall17	Collins14	Eng16
Adequate method of randomization	Y	N	Y	Y	Y	Y	Y	U
Treatment allocation concealed	N	U	Y	Y	Y	U	Y	U
Patient blinded to the intervention	N	N	N	N	U	N	N	N
Care provider blinded to the intervention	N	N	N	N	U	N	N	N
Outcome assessor blinded to intervention	N	N	N	N	Y	N	N	N
Dropout rate described and acceptable	N	Y	Y	N	N	N	Y	N
Participants analysed in the group to which they were allocated	Y	Y	N	Y	Y	Y	Y	Y
Reports free of suggestion of selective outcome reporting	U	U	U	U	U	U	Y	U
Groups similar at baseline regarding prognostic indicators	Y	N	Y	Y	Y	N	Y	Y
Co-interventions avoided or similar	N	U	U	U	Y	U	Y	U
Compliance acceptable in all groups	U	U	Y	U	U	U	Y	U
Timing of outcome assessments similar in all groups	N	N	Y	Y	Y	Y	Y	Y
Total score	3	2	6	5	7	3	9	3

described in table 3. A variety of interventions was used for muscle strengthening and balance or proprioception training. All studies used quadriceps stretching techniques, several used hamstring and iliotibial band, gastrocnemius and hip flexors stretching techniques. In one study the exercise intervention consisted of home exercises only. Four studies appended a home exercise programme to the supervised exercise therapy. One study used a multimodal approach of exercise therapy, patellar mobilisation and patellar taping.¹⁴ In addition to the exercise therapy foot or knee orthotics were added to the treatment.

Effectiveness of interventions

Due to the clinical heterogeneity of interventions, outcome measures and time to follow-up, pooling of data from the included studies was impossible.

Table 3. Exercise programs used in the included articles

	Exercises	Stretching
Denton, 2005	three phases of quadriceps strengthening exercises	quadriceps, hamstring, iliotibial band and hip flexors
Miller, 1997	closed kinetic chain exercises, VMO strengthening	VMO
Lun, 2005	a progressive 6-stage drop squat program	quadriceps, hamstring, spinal rotation, supine hip external rotation
Whittingham, 2004	non-weight bearing and weight-bearing exercises	quadriceps, hamstring, iliotibial band and gastrocnemius
Clark, 2000	wall squads, sit to stand, gluteus muscles, progressive step down, proprioceptive balance exercises	quadriceps, hamstring, iliotibial band and gastrocnemius
Kowall, 1996	progressive isometric, isotonic and isokinetic exercises	quadriceps, hamstrings
Collins, 2008	muscle strengthening of vasti muscle and hip external rotator	stretches of hamstring and anterior hip
Eng, 1993	isometric quadriceps femoris muscle contractions and straight leg raising	quadriceps and hamstring

Knee braces and exercise therapy versus exercise therapy only

One low risk of bias study¹⁸ and two high risk of bias studies^{15,19} described the additional effect of knee braces on exercise therapy at short term (table 2). Two studies did not provide enough information to calculate effect sizes or 95% CI.^{15,19}

Information about significant differences between the groups is abstracted from the studies.

The study of Miller et al¹⁹ described three groups, of which two groups used different knee braces. Group 1 used a Palumbo dynamic patellar brace (DynOrthotics, Vienna, Virginia, USA) in addition to exercise therapy. The aim of the dynamic patellar brace is to give an active, medially displacing force on the lateral border of the patella, maintaining constant pressure during flexion, extension and rotation of the knee.²⁵ Group 2 used the Cho-Pat knee strap (Cho-Pat, Hainesport, New Jersey, USA) in addition to exercise therapy. The strap functions dynamically as the knee bends and straightens and improves tracking and assists in spreading pressure uniformly over the surface area.¹⁹ For the study of Denton et al¹⁵ the Protonics system (Inverse Technology, Lincoln, Nebraska, USA) was used. The Protonics system includes a brace set to resist knee flexion to increase hamstring activity and inhibit the activity of the tensor fasciae lata. The study of Lun et al¹⁸ used a Y-shaped patellar brace to help control patellar movement (Special FX knee brace; Generation II Orthotics, Richmond, British Columbia, Canada). In none of the studies was a significant difference between the knee brace group and the control group found on pain (ES varied from -0.14 to 0.04). On the outcome function, one low risk of bias study revealed a significant difference between the knee brace group and the control group (ES -0.33).¹⁸ In contrast to these results, one high risk of bias study revealed no significant difference between the knee brace group and the control group

on function (ES not available).¹⁵ Therefore, there is moderate evidence that there is no difference in effectiveness between knee braces plus exercise therapy versus exercise therapy only on pain at short term. There is conflicting evidence on the additional effect of knee braces on exercise therapy regarding function. In addition, according to the results of one high risk of bias study, there is limited evidence that knee braces have no additional effect on exercise therapy on the performance of the knee.¹⁵ Knee braces and exercise therapy versus placebo braces and exercise therapy. One low risk of bias study used a knee sleeve to measure the additional effect of a placebo knee brace in addition to exercise therapy at short term (table 2).¹⁸ The knee sleeve was constructed with the same material as the patella brace. No hole was made in the sleeve over the patella. No significant difference was found between the knee brace and exercise group and the placebo brace and exercise group on pain and function (ES varied from -0.1 to 0.10). Therefore, there is moderate evidence that there is no difference between knee braces and exercise therapy versus placebo knee braces and exercise therapy on pain and function.

Tape and exercise therapy versus exercise therapy only

One low risk of bias¹³ and two high risk of bias studies^{17, 20} described the additional effect of tape on exercise therapy (table 2). One study did not provide enough information to calculate ES or 95% CI.¹⁷ Information about significant differences between the groups is abstracted from the study. Patellar taping was used to pull the patella medially. A significant reduction in pain and improvement in function was found in one high risk of bias study at short term after a treatment of exercise therapy and patellar taping compared with exercise therapy alone (ES varied from 1.89 to 2.89).²⁰ In contrast to these results, one low¹³ and one high risk of bias study¹⁷ found no significant reduction in pain and improvement in function (ES varied from -0.19 to 0) at short term. At long term, one low risk of bias study found no significant difference on pain and function outcomes between the tape and exercise group and the exercise-only group.¹³ Therefore, there is conflicting evidence on the additional effect of tape on the outcomes pain and function at short term, while there is moderate evidence that there is no difference in effectiveness on pain and function outcomes between exercise and tape versus exercise only at long term.

Tape and exercise therapy versus placebo tape and exercise therapy

One high risk of bias study²⁰ compared an exercise and placebo taping group with an exercise and tape group (table 2). For the placebo taping the tape was placed across the surface of the patella without patella alignment correction. A significant difference between the exercise and tape group compared with the exercise and placebo tape group was found on pain and function at short term (ES varied from 1.0 to 3.0). Therefore,

there is limited evidence that taping and exercise therapy improves pain and function significantly better than placebo taping and exercise therapy at short term.

Foot orthotics and exercise therapy versus exercise therapy only

In one low 14 and one high risk of bias study 16 foot orthotics were applied additionally to an exercise programme (table 2). Collins et al¹⁴ used prefabricated orthotics (Vasily International, Broadbeach, Queensland, Australia), which were fitted into the shoes. Comfort was the primary goal of the orthotics, by heat moulding and adding wedge or heel raises. Eng and Pierrynowski¹⁶ used soft foot orthotics with medial wedges to position the subtalar joint towards a neutral position (Spenco Sports Medicine Products, Toronto, Ontario, Canada). Collins et al¹⁴ found no significant difference between the exercise and foot orthotics group and the exercise-only group on pain at short and long term (ES varied from -0.22 to 0.20). In contrast, Eng and Pierrynowski¹⁶ found a significant difference in favour of exercise combined with foot orthotics for pain during running, but no significant difference between the groups was found for pain during walking at short term. Therefore, there is conflicting evidence for the additional effect of foot orthotics on exercise therapy for pain at short term, and there is moderate evidence that there is no significant difference between exercise and foot orthotics versus exercise only on pain at long term. Collins et al 14 is the only study available measuring function. There is conflicting evidence within that study on both short and long-term follow-up on the additional effect of foot orthotics over exercise therapy on function.

DISCUSSION

Knee braces and exercise therapy

According to the results of this review, knee braces or placebo knee braces have no additional effect over exercise therapy on pain and function for patients with PFPS. None of the braces evaluated in this study resulted in a significant improvement when compared with exercise only. These results are supported by a recent systematic review for anterior knee pain and osteoarthritis, which concluded that there was disputable evidence from low-quality studies for patellar bracing benefits.²⁶ The studies included in this review all used different knee braces, i.e., the Protonics system,¹⁵ the Palumbo dynamic patellar brace and the Cho-Pat knee strap¹⁹ and a Y-shaped knee brace.¹⁸ Denton et al¹⁵ applied Protonics knee braces as an additional intervention superiorly to exercise therapy. A study not included in this review examined the effect of the Protonics knee brace compared with a proprioceptive neuromuscular facilitation programme or no treatment.²⁷ The Protonics system was more effective for the patients with PFPS. However, it is unclear what mechanism is responsible for the effect of the Protonics system. McCrory

et al²⁸ concluded that a single application of the Protonics brace did not alter anterior pelvic tilt, hip internal rotation or adduction, or tibial external rotation during a lateral step up and gait. Earl et al²⁹ stated that the Protonics brace may unload the quadriceps and therefore decrease the load of the patellofemoral joint. It appears that the Protonics system decreases pain when compared with proprioceptive neuromuscular facilitation or no treatment, but has no additional effect to exercise therapy on pain and function. Furthermore, the effect of the Protonics system may be attributed to the specific set of exercises performed daily to strengthen the hamstrings that are accompanied by the brace. Further research in this field should focus on the heterogeneity of exercise and knee brace protocols, to make the studies comparable and to create a body of evidence on the possible additional effect of knee braces on exercise therapy for patients with PFPS.

Tape and exercise therapy

According to the results of this review, there is conflicting evidence for the additional effect of tape superiorly to exercise therapy on pain and function. Furthermore, there is limited evidence that taping and exercise therapy improve pain and function significantly better than placebo taping and exercise therapy in the short term. These results are supported by a review of Overington et al,³⁰ who stated that some studies found pain reduction by the addition of taping, whereas other studies found no additional effect on a general exercise programme by taping. Crossley et al⁴ concluded in 2001 in their review that RCT had failed to find a beneficial effect of patellar taping in addition to physiotherapy. This review was published before the results of the study of Whittingham et al were published.²⁰ Although the results of two recent reviews revealed that medially directed tape decreased pain significantly more than no tape, it is still unclear if tape has an additional value in the treatment of PFPS patients.²⁶⁻³¹ The rationale behind the use of medial-directed tape, first used by McConnell is to pull the patella medially to realign the patella within the femoral trochlea.³² In the literature there is no agreement about the effect of tape on patella position. One study found no significant difference in patellar position in taped and non-taped conditions,³³ whereas other studies did find a significant difference in patellar position.³⁴⁻³⁵ Although patellar taping seems to reduce pain, the mechanism behind the pain reduction is still unclear.

Foot orthotics and exercise therapy

There is conflicting evidence for the additional effect of foot orthotics on pain and function compared with exercise therapy alone. A recent review³⁶ concluded that combining foot orthotics with physiotherapy showed significantly greater improvements than foot orthotics alone. The results of a prospective study demonstrate that a disturbance of the normal dynamic foot alignment is a risk factor for the development of PFPS.³⁷ Another

prospective study has identified a pronated foot type (measured as navicular drop) as being a risk factor for the development of PFPS.² A possible rationale behind the use of foot orthotics is to reduce excessive pronation. In the included studies no diagnostic criteria were formulated for the use of foot orthotics. It is hypothesised that patients who have excessive foot pronation will benefit more from foot orthotics than patients with normal foot posture.³⁶ Collins et al¹⁴ found significant differences between the foot orthotics and exercise and the exercise-only groups for function, measured with the FIQ, at the short-term follow-up and on the KPS at long-term follow-up. In contrast to the results that are established in this review, Collins et al¹⁴ concluded that there was no difference in effectiveness between foot orthotics and exercise therapy nor was there any benefit of adding foot orthotics to exercise therapy. This contradiction is caused by Collins et al¹⁴ using a 99% CI and a significance cut-off value of $p \leq 0.01$, whereas we applied a 95% CI and a significance cut-off value of $p \leq 0.05$.

LIMITATIONS

This review has some limitations. There is a small number of studies available describing the additional effect of orthotics or placebo orthotics to exercise therapy on the outcomes pain and function. For that reason one CCT¹⁹ is included in this review, although this study has a risk of selection bias and confounding. Furthermore, only three of the eight included studies in this review are classified as 'low risk of bias' according to the guidelines of van Tulder et al.⁷ Because of the lack of low risk of bias studies on this topic it was impossible to draw the conclusion of 'strong evidence'. Besides, three of the eight studies included did not provide the raw data and therefore the data from figures had to be extracted. This may have caused inaccuracies. Because these three studies did not supply data, it was impossible to calculate the ES. There are inconsistencies in the pain and function measures used. The VAS is used to evaluate the pain, but there is no agreement in which situation the pain should be evaluated.

The most frequently used questionnaires in the included RCT to measure self-reported function are the KPS 22 and the modified FIQ. In the literature, the KPS and the VAS for worst pain are described as being the most reliable measures for detecting a treatment effect.²¹ The modified FIQ also seems to be a valid measure.³⁸

FURTHER RESEARCH

Although PFPS results in a variety of limitations in physical activities in young active adults, there are still many uncertainties about the most optimal treatment of the syndrome.

To identify subgroups of patients that are most likely to benefit from orthotic devices could be a way forward in clinical research and very useful in clinical practice. For example, knee bracing and taping may be used by patients with malalignment of the patellofemoral joint, and foot orthotics may be applied by patients with an excessive pronation of the foot. However, when subgroups of PFPS patients are analysed, sample sizes have to increase, which affects the feasibility of the studies. To detect subgroups responsive to specific treatment, dedicated trials designed to assess subgroup effects are needed. More low risk of bias studies on this topic are needed, using adequate randomisation and providing enough information to calculate ES and 95% CI. Blinding of the patients and the care providers is difficult when exercise is concerned; however, other potential sources of bias must be considered in future studies. In future research, agreement should be reached about the outcome measures used in order to facilitate comparisons between the studies and pooling of the results. In addition to pain and functional outcome measures, a global effect scale rated by the patient should be used to explain patients' perceptions of their improvement following an intervention.²¹

CONCLUSIONS

There is no additional effect of knee braces over exercise therapy regarding pain and function outcomes for patients with PFPS. The evidence for the additional effect of tape and foot orthotics on exercise therapy is conflicting when compared with exercise only. The combination of tape and exercise seems to be preferable when compared with placebo tape and exercise. This conclusion is based on a small number of high risk of bias studies. More studies with high methodological quality are needed to draw definitive conclusions. Future research should address subgroups to reflect the current strategies as they are used in physiotherapeutic practice. As there are uncertainties in the current literature according to the treatment strategies applied to patients with PFPS, practitioners should rely on their clinical reasoning skills (including vigilant follow-up and re-assessment) and patient presentation to arrive at a management plan.

REFERENCES

1. Callaghan MJ, Selfe J. Has the incidence or prevalence of patellofemoral pain in the general population in the United Kingdom been properly evaluated? *Phys Ther Sport* 2006 ; 8 : 37 – 43 .
2. Boling MC, Padua DA, Marshall SW, et al. A prospective investigation of biomechanical risk factors for patellofemoral pain syndrome: the Joint Undertaking to Monitor and Prevent ACL Injury (JUMP-ACL) cohort. *Am J Sports Med* 2009 ; 37 : 2108 – 16 .
3. Myer GD, Ford KR, Barber Foss KD, et al. The incidence and potential pathomechanics of patellofemoral pain in female athletes. *Clin Biomech* (Bristol, Avon) 2010 ; 25 : 700 – 7 .
4. Crossley K, Bennell K, Green S, et al. A systematic review of physical interventions for patellofemoral pain syndrome. *Clin J Sport Med* 2001 ; 11 : 103 – 10 .
5. Davis IS, Powers CM. Patellofemoral pain syndrome: proximal, distal, and local factors, an international retreat, April 30–May 2, 2009, Fells Point, Baltimore, MD. *J Orthop Sports Phys Ther* 2010 ; 40 : A1 – 16 .
6. van Linschoten R, van Middelkoop M, Berger MY, et al. Supervised exercise therapy versus usual care for patellofemoral pain syndrome: an open label randomised controlled trial. *BMJ* 2009 ; 339 : b4074 .
7. van Tulder MW, Suttorp M, Morton S, et al. Empirical evidence of an association between internal validity and effect size in randomized controlled trials of lowback pain. *Spine* 2009 ; 34 : 1685 – 9 .
8. Higgins J, Green S. Selecting studies and collecting data. In: *Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.2* . The Cochrane Collaboration, 2009 .
9. Orwin R. Evaluating coding decisions. New York, NY : Russell Sage Foundation, 1994 .
10. Cohen J . Statistical power for the behavioral sciences, 2nd edn. Hillsdale, NJ: Lawrence Erlbaum Associates, 1988 .
11. Cohen J. A power primer. *Psychol Bull* 1992 ; 112 : 155 – 9 .
12. van Tulder M , Furlan A, Bombardier C, et al. Updated method guidelines for systematic reviews in the Cochrane collaboration back review group. *Spine* 2003; 28 : 1290 – 9 .
13. Clark DI, Downing N, Mitchell J, et al. Physiotherapy for anterior knee pain: a randomised controlled trial. *Ann Rheum Dis* 2000 ; 59 : 700 – 4 .
14. Collins N, Crossley K, Beller E, et al. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *BMJ* 2008 ; 337 : a1735 .
15. Denton J, Willson JD, Ballantyne BT, et al. The addition of the Protonics brace system to a rehabilitation protocol to address patellofemoral joint syndrome. *J Orthop Sports Phys Ther* 2005 ; 35 : 210 – 19 .
16. Eng J J, Pierrynowski M R. Evaluation of soft foot orthotics in the treatment of patellofemoral pain syndrome. *Phys Ther* 1993 ; 73 : 62 – 8 ; discussion 68–70 .
17. Kowall MG, Kolk G, Nuber GW, et al. Patellar taping in the treatment of patellofemoral pain. A prospective randomized study. *Am J Sports Med* 1996 ; 24:61 – 6
18. Lun VM, Wiley JP, Meeuwisse WH, et al. Effectiveness of patellar bracing for treatment of patellofemoral pain syndrome. *Clin J Sport Med* 2005 ; 15:235 – 40 .
19. Miller MD, Hinkin DT, Wisnowski JW. The efficacy of orthotics for anterior knee pain in military trainees. A preliminary report. *Am J Knee Surg* 1997;10:10–13 .
20. Whittingham M, Palmer S, Macmillan F. Effects of taping on pain and function in patellofemoral pain syndrome: a randomized controlled trial. *J Orthop Sports Phys Ther* 2004 ; 34 : 504 – 10 .
21. Crossley K M, Bennell KL, Cowan SM, et al. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil* 2004 ; 85 : 815 – 22 .

22. Kujala U M, Jaakkola LH, Koskinen SK, et al. Scoring of patellofemoral disorders. *Arthroscopy* 1993 ; 9 : 159 – 63 .
23. Chesworth B M, Culham E, Tata GE, et al. Validation of outcome measures in patients with patellofemoral syndrome. *J Orthop Sports Phys Ther* 1989;10:302 – 8 .
24. Bellamy N, Buchanan WW, Goldsmith CH, et al. Validation study of WOMAC a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol* 1988 ; 15 : 1833 – 40 .
25. Palumbo PM Jr . Dynamic patellar brace: a new orthosis in the management of patellofemoral disorders. A preliminary report. *Am J Sports Med* 1981; 9 : 45 – 9 .
26. Warden S J, Hinman RS, Watson MA Jr, et al. Patellar taping and bracing for the treatment of chronic knee pain: a systematic review and meta-analysis. *Arthritis Rheum* 2008 ; 59 : 73 – 83 .
27. Schneider F , Labs K, Wagner S. Chronic patellofemoral pain syndrome: alternatives for cases of therapy resistance. *Knee Surg Sports Traumatol Arthrosc* 2001; 9 : 290 – 5 .
28. McCrory J L, Quick NE, Shapiro R, et al. The effect of a single treatment of the Protonics system on lower extremity kinematics during gait and the lateral step up exercise. *Gait Posture* 2007 ; 25 : 544 – 8 .
29. Earl JE, Piazza SJ, Hertel J. The Protonics knee brace unloads the quadriceps muscles in healthy subjects. *J Athl Train* 2004 ; 39 : 44 – 9 .
30. Overington M , Goddard D, Hing W. A critical appraisal and literature critique on the effect of patellar taping – is patellar taping effective in treatment of patellofemoral pain syndrome? *N Z J Physiother* 2006;3 4 :66–80.
31. Aminaka N , Gribble P A. A systematic review of the effects of therapeutic taping on patellofemoral pain syndrome. *J Athl Train* 2005 ; 40 : 341 – 51 .
32. McConnell J . The management of chondromalacia patellae: a long term solution. *Aust J Physiother* 1986; 32 :215–23.
33. Gigante A, Pasquinelli FM, Paladini P, et al. The effects of patellar taping on patellofemoral incongruence. A computed tomography study. *Am J Sports Med* 2001; 2 9 : 88 – 92.
34. Derasari A, Brindle TJ, Alter KE, et al. McConnell taping shifts the patella inferiorly in patients with patellofemoral pain: a dynamic magnetic resonance imaging study. *Phys Ther* 2010 ; 90 : 411 – 19 .
35. Worrell T, Ingersoll CD, Bockrath-Pugliese K, et al. Effect of patellar taping and bracing on patellar position as determined by MRI in patients with patellofemoral pain. *J Athl Train* 1998 ; 33 : 16 – 20.
36. Barton CJ, Munteanu SE, Menz HB, et al. The efficacy of foot orthoses in the treatment of individuals with patellofemoral pain syndrome: a systematic review. *Sports Med* 2010 ; 40 : 377 – 95 .
37. Thijs Y, Van Tiggelen D, Roosen P, et al. A prospective study on gait-related intrinsic risk factors for patellofemoral pain. *Clin J Sport Med* 2007 ; 17 : 437 – 45 .
38. Selfe J, Harper L, Pedersen I, et al. Four outcome measures for patellofemoral joint problems – part 1: development and validity. *Physiotherapy* 2001;87:507–15 .

1. RCT's of knee braces and exercise therapy versus exercise therapy only

Diagnostic criteria	Duration of complaints (wk)	Orthotic Group (O)		Control Group (C)		Follow-up time (wk)	Outcome measure	Change scores ^a	Mean difference (95% CI) ^b	Effect Size
		treatment	number of subjects	treatment	number of subjects					
Denton et al. 2005										
PFPS	>4	Protonics system and exercise therapy	17	Exercise therapy	17	6	Pain: VPS during lateral step-up test Function: KSQ	O: 4.6† C: 3.3†	1.3 (c)	c
34% female Age: 13-55 Mean (SD): 28 (?)							Performance: Step-up test	O: 28.9† C: 24†	4.9 (c)	c
								O: 4† C: 5†	-1 (c)	c
Miller et al. 1997										
AKP	3	Palumbo Dynamic Patellar Brace and exercise therapy	20	Exercise therapy	13	2-3	Pain: VAS during activity	O: 2.04 C: 0.69	1.35 (c)	c
19% female Age: ?							Pain: VAS during activity	O: 1.78 C: 0.69	1.09 (c)	c

Diagnostic criteria	Duration of complaints (wk)	Orthotic Group (O)		Control Group (C)		Follow-up time (wk)	Outcome measure	Change scores ^a	Mean difference (95% CI) ^b	Effect Size
		treatment	number of subjects	treatment	number of subjects					
Lun et al. 2005										
PFPS	2	Home exercise and therapy	32	Home exercise therapy	34	12	Pain: VAS during sport activity	O: 1.5 C: 1.5	0 (-0.61 – 0.61)	0
79% female		an Y-shaped patellar brace					1 hour after sport activity	O: 1.5 C: 1.9	-0.4 (-0.95 – 0.15)	-0.14
Age: 18-60							following 30 min. of sitting with flexed knees	O: 1.5 C: 1.4	0.1 (-0.53 – 0.83)	0.04
Mean (SD): 35 (?)							Function: KF	O: 2 C: 5	-3 (-5.06 – -0.95)*	-0.33

a: Change scores in the O and C group. Positive scores indicate improvement, i.e. less pain or better function.

b: Difference in change scores between O and C

c: Not enough information was provided to make this assessment

Notes: **VPS**=Verbal Pain Score (0-10). **KSQ**=Kujala Score Questionnaire (0-100). **VAS**=Visual Analogue Score (0-100). **KF**=Knee function scale (0-53). **CI**=Confidence Interval. **?** indicates unknown/not reported. * Significant difference between orthotic group and control group. † Data abstracted from figures.

2. RCT's of knee braces and exercise therapy versus placebo braces and exercise therapy

Diagnostic criteria	Duration of complaints (wk)	Orthotic Group (O)		Control Group (C)		Follow-up time (wk)	Outcome measure	Change scores ^a	Mean difference (95% CI) ^b	Effect Size
		treatment	number of subjects	treatment	number of subjects					
Lun et al. 2005										
PFPS	2	Home exercise therapy and an Y-shaped patellar brace	32	Home exercise therapy and knee sleeve	31	12	Pain: VAS during sport activity	O: 1.6 C: 1.5	0.1 (-0.57 – 0.77)	0.03
79% female										
Age: 18-60										
Mean (SD): 35 (?)							1 hour after sport activity following 30 min. of sitting with flexed knees	O: 2.2 C: 1.9	0.3 (-0.28 – 0.88)	0.10
							Function: KF	O: 4 C: 5	-1 (-2.98 – 0.98)	-0.12

a: Change scores in the O and C group. Positive scores indicate improvement, i.e. less pain or better function.

b: Difference in change scores between O and C

c: Not enough information was provided to make this assessment

Notes: **VAS**=Visual Analogue Score (0-100); **KF**=Knee function scale (0-53); **CI**=Confidence Interval. **?** indicates unknown/not reported. * Significant difference between orthotic group and control group.

3. RCT's of tape and exercise therapy versus exercise therapy only

Diagnostic criteria	Duration of complaints (wk)	Orthotic Group (O)		Control Group (C)		Follow-up time (wk)	Outcome measure	Change scores ^a	Mean difference (95% CI) ^b	Effect Size
		treatment	number of subjects	treatment	number of subjects					

Whittingham et al. 2004

PFPS	?	10	4	Pain:VAS during: previous 24 hours	1.8 (1.60-2.00)*	2.00
20% female	Medially-directed tape and exercise therapy	Exercise therapy		O: 7.5 C: 5.7		
Age: 17-25				O: 7.4 C: 5.7	1.7 (1.50-1.99)*	1.89
Mean (SD): 18.7 (1.2)				Function: FIQ	2.6 (2.38-2.82)*	2.89

Clark et al. 2000

AKP/PFPS	>12	20	12	Pain: Mean VAS during climbing stairs and walking	-7.4 (-18.03-3.23)	-0.19
44% female	Education, exercise therapy and tape	Education and exercise therapy		O: 39.7 C: 47.1		
Age: 15-40				Function: WOMAC	0 (-3.45-3.45)	0
Mean (SD): ?				O: 13.7 C: 13.7		

			52	Pain: Mean VAS during climbing stairs and walking	0.7 (-6.30-7.70)	0.02
				O: 40.0 C: 39.3		
				Function: WOMAC	2.3 (-3.00-7.60)	0.18
				O: 10.4 C: 8.1		

Kowall et al. 1996

?	>4	12	4	Pain:VAS	0 (c)	0
68% female	Exercise therapy and tape	Exercise therapy		O: 14 † C: 14 †		

Age: 14-40
Mean (SD): 29 (?)

a: Change scores in the O and C group. Positive scores indicate improvement, i.e. less pain or better function.

b: Difference in change scores between O and C

c: Not enough information was provided to make this assessment

Notes: **VAS**=Visual Analogue Score (0-100). **FIQ**=Functional Index Questionnaire (0-16). **WOMAC**=Western Ontario and McMaster Universities Osteoarthritis Questionnaire (0-100). **CL**=Confidence Interval. **?** indicates unknown/not reported. * Significant difference between orthotic group and control group. † Data abstracted from figures.

4. RCT's of tape and exercise therapy versus placebo tape and exercise therapy

Diagnostic criteria	Duration of complaints (wk)	Orthotic Group (O) treatment	number of subjects	Control Group (C) treatment	number of subjects	Follow-up time (wk)	Outcome measure	Change scores ^a	Mean difference (95% CI) ^b	Effect Size
PFPS	?	Medially-directed tape and exercise therapy	10	Placebo tape and exercise therapy	10	4	Pain: VAS during previous 24 hours	O: 7.5 C: 6.6	0.9 (0.75-1.05)*	1.00
20% female							a step test without tape	O: 7.4 C: 6.3	1.1 (0.99-1.21)*	1.38
Age: 17-25							Function: FIQ	O: 8.4 C: 5.7	2.7 (2.46-2.94)*	3

Whittingham et al. 2004

a: Change scores in the O and C group. Positive scores indicate improvement, i.e. less pain or better function.

b: Difference in change scores between O and C

c: Not enough information was provided to make this assessment

Notes: **VAS**=Visual Analogue Score (0-100). **FIQ**=Functional Index Questionnaire (0-16). **CI**=Confidence Interval. **?** indicates unknown/not reported. * Significant difference between orthotic group and control group.

5. RCT's of foot orthotics and exercise therapy versus exercise therapy only

Diagnostic criteria	Duration of complaints (wk)	Orthotic Group (O) treatment	number of subjects	Control Group (C) treatment	number of subjects	Follow-up time (wk)	Outcome measure	Change scores ^a	Mean difference (95% CI) ^b	Effect Size
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Collins et al. 2008

PFPS	>6	44	Exercise therapy and foot orthotics	45	6	Pain: VAS for: usual pain	O: 19.4 C: 21.2	-1.8 (-5.40-1.80)	-0.10
55.9% female						worst pain	O: 28.5 C: 32.2	-3.6 (-5.90-1.29)	-0.22
Age: 18-40						Function: KSQ	O: 83.6 C: 83.4	0.2 (-1.69-2.09)	0.02
Mean (SD): 29.3 (5.8)						Function: FIQ	O: 13.3 C: 12.9	0.5 (0.26-0.74)*	0.22

52

Pain: VAS for: usual pain	O: 14.4 C: 13.9	0.4 (-3.45-4.25)	0.02
worst pain	O: 18.8 C: 22.2	-3.3 (-8.24-1.64)	0.20
Function: KSQ	O: 91.5 C: 87.9	3.6 (1.58-5.61)*	0.34
Function: FIQ	O: 13.8 C: 14.2	-0.5 (-1.04-0.04)	-0.22

Eng et al. 1993

PFPS	>6	10	Exercise therapy and foot orthotics	10	6	Pain: VAS during: walking	O: 2† C: 0.5†	1.5 (c)	c
100% female						running	O: 3† C: 0.5†	2.5 (c)*	c
Age: 13-17									
Mean (SD): 14.8 (1.2)									

a: Change scores in the O and C group. Positive scores indicate improvement, i.e. less pain or better function.

b: Difference in change scores between O and C

c: Not enough information was provided to make this assessment.

Notes: **KSQ**=Kujala Score Questionnaire (0-100). **VAS**=Visual Analogue Score (0-100). **FIQ**=Functional Index Questionnaire (0-16). **CI**=Confidence Interval. † indicates unknown/not reported. * Significant difference between orthotic group and control group. † Data abstracted from figures.

APPENDIX 1

Sources of risk of bias

Item	Judgment
A) Sequence generation	
1. Was the method of randomization adequate?	Yes / No / Unsure
B) Allocation concealment	
2. Was the treatment allocation concealed?	Yes / No / Unsure
C) Blinding of participants, personnel and outcome	
Was knowledge of the allocated interventions adequately prevented during the study?	
3. Was the patient blinded to the intervention?	Yes / No / Unsure
4. Was the care provider blinded to the intervention?	Yes / No / Unsure
5. Was the outcome assessor blinded to the intervention?	Yes / No / Unsure
D) Incomplete outcome data	
Were incomplete outcome data adequately addressed?	
6. Was the drop-out rate described and acceptable?	Yes / No / Unsure
7. Were all randomized participants analysed in the group to which they were allocated?	Yes / No / Unsure
E) Other sources of potential bias	
8. Were the groups similar at baseline regarding the most important prognostic indicators?	Yes / No / Unsure
9. Were co-interventions avoided or similar?	Yes / No / Unsure
10. Was the compliance acceptable in all groups?	Yes / No / Unsure
11. Was the timing of the outcome assessment similar in all groups?	Yes / No / Unsure

APPENDIX 2.

Criteria for a judgment of 'yes' for the sources of risk of bias

1. Was the method of randomization adequate?

A random (unpredictable) assignment sequence. Examples of adequate methods are coin toss (for studies with two groups), rolling a dice (for studies with two or more groups), drawing of balls of different colours, drawing of ballots with the study group labels from a dark bag, computer-generated random sequence, pre-ordered sealed envelopes, sequentially-ordered vials, telephone call to a central office, and pre-ordered list of treatment assignments

Examples of inadequate methods are: alternation, birth date, social insurance/security number, date in which they are invited to participate in the study, and hospital registration number

2. Was the treatment allocation concealed?

Assignment generated by an independent person not responsible for determining the 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 on the decision about eligibility of the patient.

Was knowledge of the allocated interventions adequately prevented during the study?

3. Was the patient blinded to the intervention?

This item should be scored “yes” if the index and control groups are indistinguishable for the patients or if the success of blinding was tested among the patients and it was successful.

4. Was the care provider blinded to the intervention?

This item should be scored “yes” if the index and control groups are indistinguishable for the care providers or if the success of blinding was tested among the care providers and it was successful

5. Was the outcome assessor blinded to the intervention?

Adequacy of blinding should be assessed for the primary outcomes. This item should be scored “yes” if the success of blinding was tested among the outcome assessors and it was successful or:

for patient-reported outcomes in which the patient is the outcome assessor (e.g., pain, disability): the blinding procedure is adequate for outcome assessors if participant blinding is scored “yes”

for outcome criteria assessed during scheduled visit and that supposes a contact between participants and outcome assessors (e.g., clinical examination): the blinding procedure is adequate if patients are blinded, and the treatment or adverse effects of the treatment cannot be noticed during clinical examination

for outcome criteria that do not suppose a contact with participants (e.g., radiography, magnetic resonance imaging): the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed when assessing the main outcome

for outcome criteria that are clinical or therapeutic events that will be determined by the interaction between patients and care providers (e.g., co-interventions, hospitalization length, treatment failure), in which the care provider is the outcome assessor: the blinding procedure is adequate for outcome assessors if item “E” is scored “yes”

for outcome criteria that are assessed from data of the medical forms: the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed on the extracted data

Were incomplete outcome data adequately addressed?

6. Was the drop-out rate described and acceptable?

The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and drop-outs does not exceed 20% for during follow-up and does not lead to substantial bias a 'yes' is scored. (N.B. these percentages are arbitrary, not supported by literature).

7. Were all randomized participants analysed in the group to which they were allocated?

All randomized patients are reported/analyzed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values) irrespective of non-compliance and co-interventions.

Other sources of potential bias:

8. Were the groups similar at baseline regarding the most important prognostic indicators?

In order to receive a "yes", groups have to be similar at baseline regarding demographic factors, severity of complaints, and value of main outcome measure(s).

9. Were co-interventions avoided or similar?

This item should be scored "yes" if there were no co-interventions or they were similar between the index and control groups.

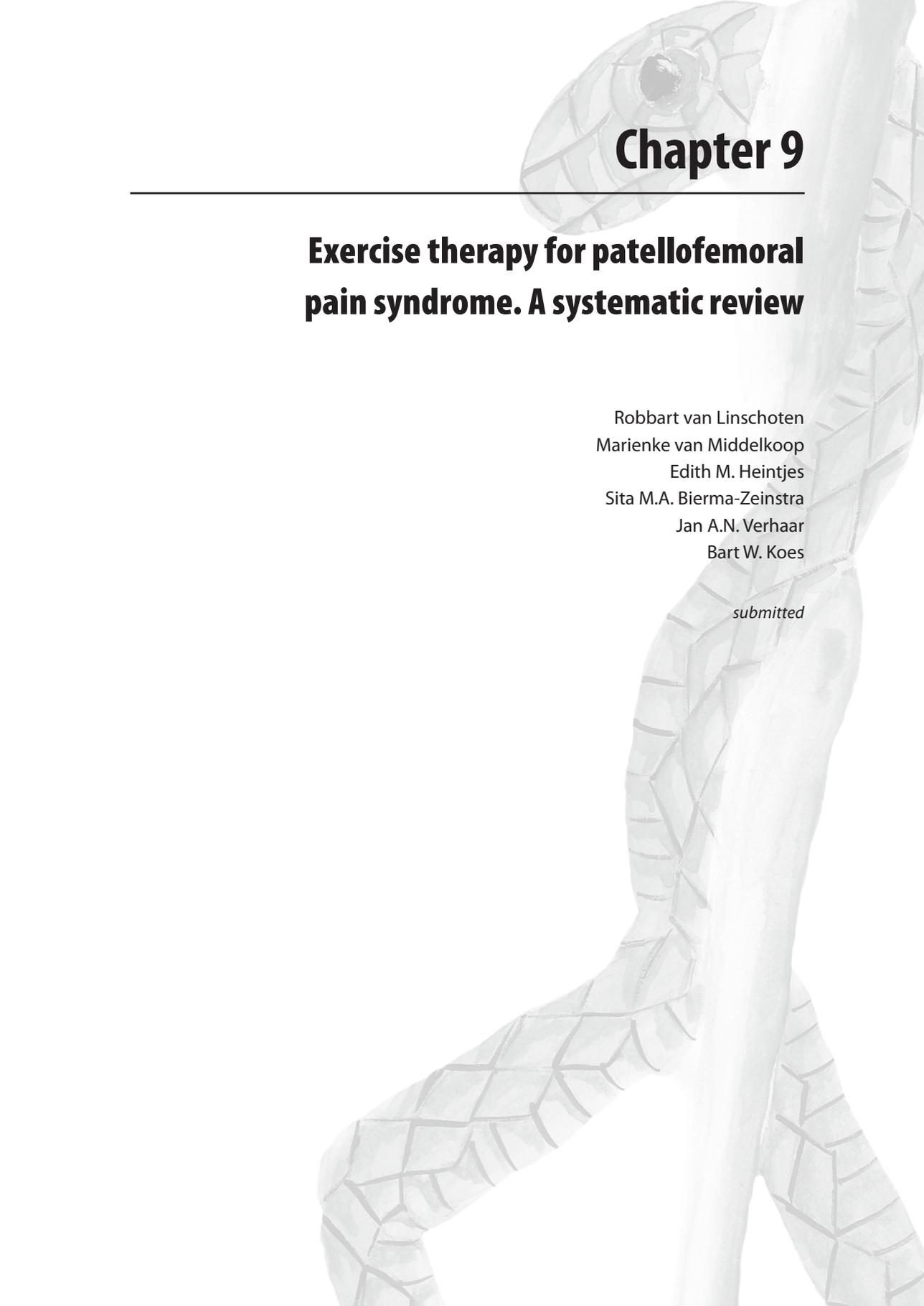
10. Was the compliance acceptable in all groups?

The reviewer determines if the compliance with the interventions is acceptable, based on the reported intensity, duration, number and frequency of sessions for both the index intervention and control intervention(s). For example, physiotherapy treatment is usually administered over several sessions; therefore it is necessary to assess how many sessions each patient attended. For single-session interventions (for ex: surgery), this item is irrelevant.

11. Was the timing of the outcome assessment similar in all groups?

Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments.

Note: These instructions are adapted from van Tulder 2003, Boutron et al, 2005 (CLEAR NPT) and the Cochrane Handbook of Systematic Reviews of Interventions.



Chapter 9

Exercise therapy for patellofemoral pain syndrome. A systematic review

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ABSTRACT

Background:

Exercise therapy is frequently used for patellofemoral pain syndrome (PFPS) though evidence for its effectiveness is still unclear.

Objectives:

To evaluate the effects of exercise therapy aimed at reducing knee pain and improving knee function for patients with PFPS.

Search methods: We searched the Cochrane Bone, Joint and Muscle Trauma Group Specialized Register (December 2009), the Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2009, Issue 4), MEDLINE, EMBASE, and other databases to December 2009.

Selection criteria:

Randomized trials of exercise therapy aiming at quadriceps strengthening for patients with patellofemoral pain syndrome. Primary outcomes were pain, knee function and recovery.

Data collection and analysis:

Two pairs of two authors independently selected trials based on pre-defined inclusion criteria, extracted data and assessed risk of bias. Disagreements were settled by consensus.

Results:

At short term and long term exercise therapy is effective on pain reduction compared to no intervention ('wait and see strategy'). At short term exercise therapy is also effective on improving knee function but at long term these effects are not significant. The effect of exercise therapy is however not clearly reflected on the outcome measures for recovery.

At short term exercise therapy is more effective on pain reduction than other conservative, non-pharmacological strategies (brace, tape, insoles).

No differences in effect were found when exercise strategies for quadriceps muscle strengthening were compared with other exercise strategies (VMO feedback retraining, closed kinetic chain, open kinetic chain, hip abductor exercise, abdominal muscle exercise).

Authors' conclusions:

This review shows that exercise therapy is effective on reducing pain and improving function for patients with patellofemoral pain syndrome.

BACKGROUND

Description of the condition

Patellofemoral pain syndrome (PFPS) is a common problem among adolescents and young adults. Incidence rates vary from 22 new cases per 1000 persons/year in highly active populations to 5 to 6 new cases per 1000 in general practice.^{1,2} PFPS is characterized by retropatellar pain (behind the kneecap) or peripatellar pain (around the kneecap) mostly occurring when load is put on the knee extensor mechanism as in stair climbing, squatting, running or cycling or sitting with flexed knees. The etiology of the condition is not known as well as the origin of the pain. Also most favourable treatment options are still under debate. There is however consensus that a conservative, non-surgical approach is the cornerstone in treatment. In these strategies exercise therapy is often prescribed especially to strengthen the quadriceps muscles.

Description of the intervention

According to various authors quadriceps strengthening exercises are the most promising and frequently used conservative treatment method for patellofemoral pain.³⁻⁹

Exercise therapy comprises a broad range of possible variations and accompanying terms.

Contraction of the quadriceps muscles - and other muscles involved in knee function - can either be concentric, eccentric or isotonic. During concentric contractions the muscles shorten whereas during eccentric contractions they lengthen in an actively controlled manner. During isotonic contraction the muscle tension remains the same. Exercises in which the position of the knee does not change are referred to as static or isometric.

In isokinetic exercises the lower leg moves at a predetermined, constant speed which requires an isokinetic dynamometer to control the velocity.

Exercises that involve contact of the foot with a surface are referred to as "closed kinetic chain exercises", as opposed to "open kinetic chain" exercises.

Hence, exercises can be described in three dimensions: the presence of reaction forces caused by contact of the foot with a surface (open versus closed kinetic chain), the type of muscle activity (concentric, eccentric, isotonic), and joint movement (dynamic versus no movement: isometric or static).

Combinations of above denominations apply to every type of exercise, and the terminology used for exercise programs reflects the emphasis intended by the therapist or researcher. Besides strengthening of the quadriceps muscle, many exercises will also result in coordination of muscle contraction. Emphasis during exercise therapy may be put on the coordinate contraction of medial versus lateral part of the quadriceps muscle but also on coordinate contraction of hip adductor and hip abductor and gluteal

muscles. Electromyographic biofeedback visualizes specific muscle contractions and may help the patient target the Vastus Medialis Obliquus muscle (VMO) during exercise.

Why it is important to do this review

Exercise therapy is frequently used in the treatment of patellofemoral pain syndrome and is believed to be an effective means in reducing pain and restoring function of patients. Although PFPS is under scope of research the past 25 years the mechanism of exercise therapy on the condition and its effectiveness remains unclear. Its effectiveness has been systematically reviewed in 2003 showing limited evidence with respect to pain reduction and conflicting evidence on improving function.⁸ The review called for larger and methodological more sound studies to draw conclusions upon the effectiveness of exercise therapy.

Our review complements the above review in order to re-assess the effectiveness of exercise therapy and also includes over 10 clinical trials that have been undertaken after the first review.

Objectives

To evaluate the short (three months or less) and longer term effects of exercise therapy, for reducing pain intensity and improving function in people suffering from patellofemoral pain syndrome (anterior knee pain).

The comparisons of interest are

1. Exercise therapy versus 'placebo' treatment or no treatment/waiting list control
2. Exercise therapy versus other types of intervention (non-surgical or surgical)
3. Different types of exercise therapy

METHODS

Criteria for considering studies for this review

Types of studies

Randomized clinical trials that evaluated the effects of exercise therapy designed to reduce pain intensity and/or improve function and/or recovery compared with usual or conventional care for patients with patellofemoral pain syndrome.

Types of participants

Adolescent and adult patients suffering from patellofemoral pain syndrome (designated by the author as such or as "anterior knee pain syndrome", "patellar dysfunction" "chondromalacia patellae" or "chondropathy"). Studies which specifically focused on

other named knee pathologies such as Hoffa's syndrome, Osgood Schlatter syndrome, Sinding-Larsen-Johansson syndrome, iliotibial band friction syndrome, tendinitis, neuromas, intra-articular pathology including osteoarthritis, rheumatoid arthritis, traumatic injuries (such as injured ligaments, meniscal tears, patellar fractures and patellar dislocation), plica syndromes, and more rarely occurring pathologies were excluded.^{6,10}

Types of interventions

We included studies evaluating exercise therapy for patellofemoral pain syndrome. Exercises could be applied on their own or in combination with other non-surgical interventions as long as the main discriminating intervention was exercise therapy. Exercises could be performed at home or under supervision of a therapist. We separated studies into three areas considering to what control group exercise therapy was compared. We therefore included trials comparing exercise therapy versus no treatment or 'placebo' treatment or waiting list control. We compared exercise therapy to other interventions, including surgery, and we compared different exercise therapies with each other (e.g. closed versus open kinetic exercises or quadriceps muscle exercises versus abdominal or hip muscle exercises).

Types of outcome measures

Primary outcomes

The primary outcome was knee pain measured by validated self-reporting methods (Visual Analogue Scale [VAS], numerical rating scale [NRS] of McGill Pain questionnaire). Pain scores are reported for pain in daily life (usual pain), for worst pain and for pain at activities (like in sports) if available.¹¹

Secondary outcomes

Secondary outcomes focus on functional disability level (i.e. decreased knee function in activities of daily living) and subjective perception of recovery. Questionnaires focusing on knee function (such as Functional Index Questionnaire, WOMAC Osteoarthritis Index, and Kujala Patellofemoral Function Scale, Lysholm scale etc.) and the ability to perform tests (squatting, hopping on one leg etc.) were considered measures for functional disability.^{12,13}

Recovery of patellofemoral pain syndrome is an outcome measure inconsistently reported in studies and also using different methods. In this review 'number of patients no longer troubled by symptoms' or 'perceived recovery' measured on a Likert scale were included as a secondary outcome measure.¹⁴ Adverse effects like knee swelling or substantially increasing pain levels as a direct effect of treatment were taken into consideration as well. As changes in knee function measured on impairment level only

(i.e. range of motion, muscle strength etc.) do not directly represent changes in the symptoms of patellofemoral pain or the resulting disability, they were not considered clinically relevant outcome measures in this review.^{15 16}

Outcome measured within three months after the baseline measurement are considered short term outcome of exercise therapy whereas measurements from three months and longer are considered long term outcome.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register (December 2009), and Cochrane Rehabilitation and Related Therapies Field Specialized Register (December 2009), the Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2009, Issue 4), MEDLINE (1950 to November 2009), EMBASE (1980 to December 2009), CINAHL - Cumulative Index to Nursing and Allied Health Literature (1982 to December 2008), AMED - Allied and Complementary Medicine (1985 to December 2009), PEDro - the Physiotherapy Evidence Database (www.pedro.org.au) (December 2009), and reference lists of articles. No language restriction was applied.

In MEDLINE the subject-specific search strategy was combined with all phases of the optimal trial search strategy¹⁷, and was modified for use in other databases. (See Appendix 1)

We also searched the WHO International Clinical Trials Registry Platform for ongoing and recently completed trials (December 2009).

Data collection and analysis

Data from the electronic searches were collected and analyzed by two reviewers who reviewed titles and abstracts for the identification of unique studies.

Selection of studies

Two pairs of reviewers (MB, SBZ, RL, MM) independently selected the trials, initially based on title and abstract. From the title, keywords and abstract they assessed whether the study met the inclusion criteria regarding diagnosis, design and intervention. Of the selected references, the full article was retrieved for final assessment. Next, they independently performed a final selection of the trials to be included in the review, using a standardized form. Disagreements were solved in a consensus meeting.

Data extraction and management

Data was extracted by pairs of two reviewers (EH, RB, RL, MM) independently regarding the interventions, type of outcome measures, follow-up, loss to follow-up, and outcomes, using a standardized form.

Assessment of risk of bias in included studies

A modification of The Cochrane Collaboration's tool for assessing risk of bias was used by two independent pairs of reviewers to assess the studies included in the review.¹⁷⁻¹⁹ This tool incorporates assessment of randomization (sequence generation and allocation concealment), blinding (based on primary outcomes), completeness of outcome data (again for primary outcomes), selection of outcomes reported and other sources of bias. The scoring scheme is based on 12 aspects of trial methodology.

Studies from the review in 2003 were reassessed for risk of bias using the new tool. In the case of including studies from our own research group the assessment of risk of bias was done by two independent researchers of the department of General Practice at ErasmusMC not involved in above mentioned trials.⁸

Trials on exercise therapy cannot be blinded for the intervention, in most cases neither for the care provider and nor for the outcome assessor. In case of PFPS there is no blinding for outcome because of the lack of an objective outcome measurement.

Measures of treatment effect

Outcome measures were classified in terms of the domain assessed, e.g. pain, function or recovery. Results were analyzed at both short term (three months or less) and long term (one year or longer) intervals. Risk ratios with 95% confidence intervals were calculated for dichotomous outcomes. Mean differences with 95% confidence intervals were calculated for continuous outcomes as appropriate. Pain scores (VAS, NRS) were measured or transferred to a 0-10 scale. Function scores were presented on a 0-100 scale.

Dealing with missing data

Where possible we performed intention-to-treat analyses to include all people randomized. However, where drop-outs were identified, the actual denominator of participants contributing data at the relevant outcome assessment was used. We were alert to the potential mislabelling or non-identification of standard errors and standard deviations (SDs). Unless missing standard deviations could be derived from confidence intervals or standard errors, we did estimate values based on comparable data included in this review in order to present these in the analyses.

Where data were presented as median (inter-quartile range), we did not attempt to transform data to achieve normality or estimate mean and SD.

Assessment of heterogeneity

Heterogeneity was assessed by visual inspection of the forest plot (analysis) along with consideration of the χ^2 test for heterogeneity and the I^2 statistic).¹⁷ Heterogeneity was considered statistically significant at $P < 0.1$.

Assessment of reporting biases

Our search of clinical trial registers assisted in decreasing publication bias. We also investigated selective outcome reporting by comparing the study outcomes with those routinely presented for similar studies, and also by comparing the methods section of papers with the results reported.

Data synthesis

When considered appropriate, results of comparable groups of trials were pooled.

In order to correct for bias introduced by 'double counting' of subjects in trials which had two control groups in the same meta-analysis the number of subjects in the intervention group was divided by two. As planned, we used the random-effect model and 95% confidence intervals. Also, outcomes identified as being measured using different instruments and/or with different scales across studies would be pooled using the mean difference.²⁰ In cases of clear or significant heterogeneity, we viewed the results of the random-effects model but opted not to pool data.

Subgroup analysis and investigation of heterogeneity

We planned subgroup analysis to determine the effects of gender, duration of complaints, body mass index, frequency of sports participation on the outcomes of interest.

Sensitivity analysis

Where appropriate, we planned sensitivity analyses investigating the effects of risks of bias by excluding studies with high risk of bias.

RESULTS**Description of studies**

All studies contained at least one group of participants with PFPS in which the effects of exercises was compared with a control group. Randomized controlled trials, quasi randomized trials and concurrent controlled trials were identified. Only RCT's were included in this review.

Results of the search

From the 1014 abstracts retrieved from the search strategies described above, 23 trials were included in this review, including four quasi-randomized trials while seven trials were excluded from the previous review. Two ongoing trials were also identified.

Included studies

Design

19 trials were considered randomized and four trials were considered quasi randomized.²¹⁻²⁴ 14 trials used two groups for studying intervention vs. control; seven trials used a comparison between three groups and two trials compared between four groups.

Sample sizes

The overall sample in the 23 trials consisted of 1503 participants. For three studies data were not available (97 patients). From one study the data from a control group were not used since this did not match the type of comparison (31 participants). In total 1472 participants were included. The number of patients in the intervention groups in the individual studies ranged from six patients to 65.^{25 26}

Setting

Patients were recruited from various settings like orthopaedic clinics²⁷, general practices²⁶, physiotherapy practices⁷ and open populations²⁸. About half of the patients were referred by an orthopaedic surgeon/hospital specialist while the other half was recruited from family medicine and the community. Studies were undertaken in 14 different countries.

Participants

The majority of studies included male and female patients with a predominance of females and ages ranging from 12 to 60 years and a mean age under 30 years. One study involved female patients only²⁹ and two studies male patients only.^{23 27} The duration of complaints ranged from four weeks minimum to nine years.^{22 30} The diagnosis was set by orthopedic surgeons, general practitioners or sports physicians based on clinical symptoms and occasionally after radiological examination.¹⁵

Interventions

A range of exercise interventions were evaluated in the included trials. We have distinguished the following comparisons within the different trials: 1. Exercise interventions compared with no treatment, 'placebo' or waiting list control, 2. Exercise therapy versus another type of intervention- like taping or insoles and 3. Exercise therapy versus another

type of exercise. Group one and two is further divided into two different categories. The third comparison has been subdivided in 'exercise versus different type of exercise' and 'closed versus open kinetic chain exercise'. See Appendix 3, Table 1, Table 2 and Table 3. The intervention period ranged from three weeks²⁹ to three months.²⁶ Exercise therapy was in all studies implemented and mostly supervised by physical therapists on an out-patient basis. Most patients were instructed to practice at home additionally. Two studies investigated home exercises alone and compared with no or other interventions.²⁴
³¹ The included studies are arranged according to the comparisons that are studied and based on study date.

Exercise therapy versus no treatment, 'placebo' or waiting list control

There are eight studies in this comparison.^{23 24 26 27 32-35} Timm compared an exercise program with a Protonic brace to no treatment.²³ The study by Clark compares exercise therapy and education versus education alone.³² Crossley studied physical treatment (including exercise therapy) and compared this intervention with placebo treatment.³³ Loudon compared supervised exercise therapy with an instructional leaflet.²⁴ The study by Herrington compared a supervised exercise-group and home exercise-group with no intervention but did not supply data for assessment of outcome.²⁷ Leg press exercise and leg press/hip adduction exercise were both compared to no intervention by Song.³⁴ From the study by Syme data from a selective-VMO training group and a general Quadriceps training group respectively were compared with a non-treatment control group.³⁵ Finally, van Linschoten compared a supervised exercise program with usual care ('wait and see policy').²⁶

Exercise therapy versus other intervention

A total of six studies compared exercise therapy with another type of intervention (non-surgical or surgical).^{15 25 28 31 32 36} Gobelet compared both an isokinetic exercise group and a group performing static exercises with a muscle electrostimulation group at home.¹⁵ From the study by Clark the data comparing exercise therapy versus tape-intervention are used.³² In the study by Taylor exercise therapy including patella mobilization/manipulation was compared with patella manipulation.²⁵ Wiener-Ogilvie compared an exercise group with a group receiving foot orthoses.³⁶ From the study by Lun data from a structured home rehabilitation program was compared with a patellar brace group only.³¹ In the study by Collins data from the physiotherapy group (including exercise) was compared with a flat insert group and an orthoses group.²⁸

Exercise therapy versus other type of exercise

15 studies compared different types of exercise with each other.^{7 15 21 22 24 27 29 30 34 35 37-41} Colón compared conservative isometric exercised versus Pogo stick bouncing.²¹ Gobelet

studied the outcome of isokinetic exercises versus static proprioceptive exercises.¹⁵ Gaffney compared isometric exercises versus eccentric and isometric exercises.³⁷ Wijnen compared an individual exercise program (McConnell) versus a standard home exercise schedule (with Coumans bandage).³⁸ Thomee compared a group of patients who followed a program of isometric exercises with a group who followed eccentric exercises.²² Harrison compared a supervised exercise program with and without a McConnell approach versus a conservative home exercise program.³⁹ Witvrouw studied open kinetic chain exercises versus closed kinetic chain exercises.⁷ Schneider compared physiotherapeutic exercises on a neurophysiological basis with exercises combined with a special knee splint.⁴⁰ Loudon compared a supervised exercise program with a home exercises.²⁴ Herrington compared single joint non-weight bearing exercises versus multi joint weight bearing exercises.²⁷ Avraham compared straight leg raising (SLR) versus hip rotator strengthening and versus SLR and hip rotator strengthening.⁴¹ Nakagawa made a comparison between a general knee muscle exercise program including abdominal and hip strengthening versus a general knee muscle exercise program.³⁰ Bakhtiary compared open kinetic chain exercises versus closed kinetic chain exercises.²⁹ Song compared leg press only exercises versus leg press combined with hip abductor exercises.³⁴

Outcomes

Trials on outcomes pain and function scores used different measurements. Pain intensity is mainly scored by Visual Analogue Scale (VAS) or Numerical Rating Scale (NRS). Function scores use different methods like Kujala Patellofemoral Score (KPS or AKPS), Functional Index Questionnaire (FIQ) and Lysholm score.³²⁻³⁴ Two studies used recovery - measured on a Likert scale - as outcome measurement.²⁶⁻³³ Outcomes were measured at different time intervals. Most studies measured outcome directly after finishing the intervention and sometimes during the intervention period. Some studies measured outcome both during and after the intervention period as well after a follow-up period ranging from 1 year²⁶⁻²⁸ to maximum five years.⁹

Excluded studies

Seven trials were excluded from the review for various reasons: two studies were Concurrent Controlled Trials.⁴²⁻⁴³ Two trials studied a contrast which was not the scope of this review.¹⁶⁻⁴⁴ Two studies had insufficient reporting of results⁴⁵⁻⁴⁶ and one study was available as abstract only without data reporting.⁴⁷ The studies of Stiene⁴³ (CCT) and Dursun¹⁶ (scope of intervention) were excluded from this review compared to the protocol.

Ongoing studies

There are two ongoing studies awaiting for review.⁴⁸⁻⁴⁹ The study of Mei-Hwa Jan compares a muscle strengthening group versus a tape group and versus a stretching group

and has not been published yet.⁴⁸ The study by Dolak compares early hip strengthening exercises versus progressive quadriceps exercises in females and is not included in the review since it has been published after December 2009.⁴⁹

New studies found in this update

This update found 13 newly published RCT's on exercise therapy for PFPS. Six studies used an exercise group versus no intervention^{24 26 27 33-35}, while four trials studied exercise versus another intervention^{25 28 31 36} and in six trials different types of exercise were studied.^{27 29 30 35 41}

Risk of bias in included studies

The risk of bias of the 23 trials was challenging to assess due to the insufficient reporting according to CONSORT recommendations.⁵⁰ Full details of the risk of bias for the 23 trials are provided in Appendix 1, Figure 1 and Figure 2.

Allocation (selection bias)

Allocation of the participants was concealed in eight out of 23 studies mainly by using sealed and opaque envelopes or in some cases a computer generated list. In 15 studies the process of allocation was not specified or unclear.

Blinding (performance bias and detection bias)

Due to the type of intervention (exercise therapy) blinding of the patients was not possible. Also the care giver - in most studies the physical therapist supervising the exercise program - could not be blinded. Finally the assessor for the outcome measure (pain and function scales) was mainly the subject itself who can therefore also not be blinded.

Incomplete outcome data (attrition bias)

Thomee²² did not supply the VAS pain data but reported changes only. The study of Avraham⁴¹ did not report data, the study of Wiener-Ogilvie³⁶ supplied the change of VAS scores only.

Selective reporting (reporting bias)

Selective reporting was difficult to assess across the included studies due to the absence of reporting of prior study designs. For the majority of the included studies we therefore rated this criterion as unknown.

Other potential sources of bias

Furthermore other risks of bias were acknowledged such as high dropout rates in small studies, insufficient compliance to the intervention and inadequate reporting of intention-to-treat analysis.

EFFECTS OF INTERVENTIONS**1. Exercise therapy versus no treatment / 'placebo' or waiting list control.***Short term effects on pain*

Pooled data from Timm and Crossley show significant pain reduction at one month in favor of the intervention group.^{23 33} The overall effect on pain reduction is -2.39 (95%CI -4.06, -0.73). Pooled data at three months from four studies show significant pain reduction in the exercise group compared to the control (non-exercise group).^{24 26 32 35} The overall effect on pain at three months is -1.42 (95%CI -2.09; -0.76).

Song³⁴ and Syme³⁵ report pain reduction after eight weeks of different exercise regimens versus control: -2.38 (95%CI -3.47;-1.29) (VAS pain score) and -8.9 (95%CI -15.37; -2.44) on McGill pain questionnaire. Pain at activity was not significantly different between groups at three months in the study by van Linschoten (-0.79, 95%CI -1.90; 0.32).²⁶

Herrington reported no differences in effect after a 6 weeks program of non-weight bearing or weight bearing versus control though raw data were not reported.²⁷

Long term effects on pain

Two studies reported a significant effect on pain reduction in favor of the intervention group after 1 year follow up.^{26 32} The pooled effect for pain reduction at 12 months is -1.30 (95%CI -2.15; -0.46). van Linschoten reported no significant difference for pain at activity after one year: -0.97 (95%CI -2.05; 0.11).²⁶

Short term effects on function

At three months the pooled data of function measured by the Kujala Patellofemoral score in 3 studies show significant positive effects in favor of the exercise group.^{24 26 32} Overall effect: 4.16 [CI 0.08; 8.24]. The individual studies by Timm²³ and Crossley³³ report improvement of function on the Kujala PF score at one month in favor of the exercise group: 26.85 (CI -9.95, 63.66).

At eight weeks there was a significant increase in function score measured by the Lysholm score in the study by Song (10.37 (CI 6.71; 14.03)).³⁴ Syme reported a non-significant increase on function (modified FIQ) at eight weeks (12.77 CI -2.03; 27.56).³⁵

Long term effects on function

At 12 months pooled data from the studies by Clark and van Linschoten result in a non-significant increase in function score: 2.38 [CI -2.72; 7.48].^{26 32}

Short term effect on recovery

One study found no effect on recovery at three months, measured by a Likert scale for perceived recovery: (RR 1.20, 95%CI 0.76, 1.88).²⁶

Long term effect on recovery

Two studies report no significant difference in recovery rates between exercise and non-exercise groups at 12 months.^{26 32} Clark³² reports 'patients no longer troubled by complaints' (RR 2.21, 95%CI 0.87; 5.64) and van Linschoten²⁶ reported perceived recovery: RR 1.22 (95%CI 0.89; 1.68).

2. Exercise therapy versus other type of intervention (non-surgical or surgical)*Short term effects on pain*

Pooled data from two studies show significant pain reduction at six weeks in the exercise group compared with other interventions: -12.34 (CI -18.01; -6.67).^{25 28}

At three months the pooled data from two trials show a significant difference on pain reduction in favor of exercise therapy versus other interventions: -8.44 (CI -14.32; -2.56).^{28 32}

Lun reported at three months a non-significant difference in pain reduction (1.07 CI -7.68; 9.83) when a structured rehabilitation program (including brace) was compared with a patellar brace group.³¹ In the trial by Wiener-Ogilvie³⁶ data extraction was not possible due to insufficient reporting for intervention and control groups. At eight weeks however no significant differences for pain reduction were reported.

Long term effects on pain

Pooled data on pain outcome at 12 months follow up show no significant difference between the exercise group and the other intervention group (-1.55, 95%CI -3.61, 0.52).^{28 32}

Short term effects on function

The pooled data from two studies on function at three months show no significant difference between exercise therapy and other interventions: 3.22 (95%CI -0.02, 6.45).^{28 32}

At four weeks Gobelet found no significant difference for function scores (Arpège score): 1.10 (95%CI -0.18; 2.38) in this trial.¹⁵

Pooled data from Collins²⁸ show a significant difference for function scores (Kujala PF score) between exercise and insoles and flat inserts. Difference: 6.18 (95%CI 1.28,

11.08) in favor of the exercise group. At three months Lun reported a non-significant difference in functional outcome (Werner adjusted scale) in favour of the exercise group: 2.00 (95%CI -1.88, 5.88).³¹

Wiener-Ogilvie reported no significant differences on function outcome (SF/36) between groups at eight weeks.³⁶

Long term effects on function

At 12 months pooled data from two studies show no significant difference in function outcome -9.05 (CI-18.41, 0.30).^{28 32}

3. Exercise therapy versus another type of exercise therapy

3A. Various exercise strategies

Short term effects on pain

Pooled data at four to six weeks show no difference in pain scores between different regimes of exercise therapy.^{30 39 40} Overall effect: 0.50 (95%CI -0.85, 1.84). At three months pooled data of five studies show no significant difference on pain intensity when various exercise modalities are compared: -0.07 [-0.65, 0.51].^{24 34 35 39 40} Wijnen³⁸ found at six weeks no difference in pain scores between a 'McConnell regimen' group compared with a group using a knee bandage with standard home exercise schedule (0.30, 95%CI -1.73; 2.33). Thomee²² studied the effect of isometric exercise versus eccentric exercise during 12 weeks. Data extraction was not possible because of non-validated pain scores. The authors reported no difference in pain scores between both groups.

Long term effects on pain

Harrison found no difference between groups for pain scores after one year (0.41, 95%CI -0.92; 1.74).³⁹

Short term effects on function

At eight weeks pooled data of the studies by Wijnen, Song and Syme show no significant difference on function scores when various exercise programs are compared: -2.11 (95%CI -12.29, 8.06).^{34 35 38} Gobelet found no difference on the Arpège function score at four weeks between different groups (0.40 (95%CI -0.80, 1.60)).¹⁵ At three months Loudon reported no difference in function scores for both exercise groups. -2.30 (95%CI -11.54, 6.94).²⁴ Also Harrison found no difference in effect on function between exercise therapy versus 'McConnell exercise regime' measured with a Reid-scale at 3 months: -3.00 (95%CI -10.66, 4.66).³⁹

Long term effects on function

At one year Harrison found no difference between function scores in the exercise vs. 'McConnell exercise group' (1.00 (CI -8.03; 10.03)).³⁹ The study by Colón examined the effect of isometric exercises (straight leg raising) versus Pogo stick bouncing.²¹ Data extraction was not possible because of insufficient data reporting. The authors reported that both groups showed decrease of complaints and improvement of function. Avraham^{26 34} studied three types of exercise interventions including TENS.⁴¹ Data extraction was not possible because of insufficient reporting. The authors state that no significant differences were found between groups in the outcome measures pain and function separately.

Short term effect on recovery

No statistical significant difference was found between both intervention groups in the study done by Colón after six to eight weeks follow-up (RR 0.85, 95%CI 0.55;1.31).²¹

3B. Closed kinetic chain exercise versus open kinetic chain exercise*Short term effects on pain*

At six weeks pooled data of three studies show no difference for pain reduction between closed versus open kinetic exercise: -0.44 (-1.32, 0.45).^{7 27 37} Bakhtiary reported no significant difference between closed kinetic versus open kinetic exercise for pain scores at three weeks (-0.30, 95%CI -1.65; 1.05).²⁹ At three months Witvrouw found no significant difference in pain scores in daily life (-0.90, 95%CI -4.43; 2.63) nor during sports (-0.20, 95%CI -1.61; 1.21).⁷ Colón reported no significant difference in pain improvement between both intervention groups (1.13, 95%CI 0.83, 1.55).²¹

Long term effects on pain

Witvrouw reported effects on pain scores after five years.⁹ There was a significant effect on 'worst pain' reduction in favor of the open kinetic training group (1.90, 95%CI 0.61; 3.19). Pain scores during sports at five years were also in favor of the open kinetic exercise group (2.20, 95%CI 0.99; 3.41). Pain scores in daily life however showed a significant improvement for the closed kinetic group -0.90 (95%CI -1.62; -0.18).

Short term effects on function

The pooled data of Witvrouw and Herrington show no difference for function scores at 6 weeks between open versus closed kinetic exercise (0.59, 95%CI -5.42, 6.59)).^{7 27} At three months Witvrouw reported a non-significant difference between both groups -3.00 (95%CI -22.99; 16.99).⁷

Long term effects on function

Witvrouw reported function scores at five years but statistical differences could not be calculated due to insufficient data reporting.⁹ The authors stated that the overall outcomes of the patients are usually good and equal for both groups.

Short term effects on recovery

Gaffney found no statistical significant differences between both intervention groups on recovery after 6 weeks follow-up (1.37, 95%CI 0.87, 2.17).³⁷

Subgroup analysis

Subgroup analysis to determine the effects of gender, duration of complaints, body mass index, and quantity of sports participation on the outcomes of interest was not possible due to the small number of participants in the studies and the inconsistent reporting of baseline characteristics. For future studies it is of interest to stratify for these presumed prognostic factors.

Sensitivity analysis

Sensitivity analysis was performed replicating the pooled data after excluding one high risk of bias study in which exercise therapy was compared with no intervention for pain scores. This resulted in a slightly higher effect of the intervention.²⁴

DISCUSSION

In this review we examined the effects of exercise therapy on outcomes pain, function and recovery for patients suffering from patellofemoral pain syndrome. Our goal was to review the effectiveness of exercise therapy. In the systematic review by Heintjes the authors concluded that more trials were needed to substantiate the efficacy of exercise treatment compared to a non-exercising control group.⁸ They also pointed to the need for higher quality in methodology, study design and reporting.

In the update of the literature we found 13 newly published RCT's meeting the inclusion criteria and they were added to this review. Seven studies published beyond the date of the first review were regarded low risk of bias and six studies however still suffered from methodological drawbacks, mainly because of improper allocation methods, non-reporting of the study design or dealing with 'intention to treat analysis'. In general the risk of bias is decreasing in the studies published after the review in 2003.

Heintjes found only limited evidence for the effectiveness of exercise therapy regarding pain and conflicting evidence regarding function.⁸

Based on pooled data from all available trials in this review it is concluded that exercise therapy is significantly more effective on pain reduction than a non-exercise strategy ('wait and see') or other strategies. At short term exercise therapy is also more effective on function improvement than a 'wait and see' policy. For pain scores sensitivity analysis showed that the effects remain when data are based on high quality trials only.

Patellofemoral pain syndrome is a clinical entity which is characterized by knee pain and loss of function. In most trials pain scores depict pain in daily life as 'usual pain' (VAS, NRS). For data synthesis pain scores in daily life ('usual pain') were pooled at comparable time points. Some authors make a distinction between 'usual pain' and 'worst pain' or 'pain at activity' in order to describe the course of pain in PFPS in daily life and during activities. When available we only pooled data from the same pain measurement. We did not consider it appropriate to pool all these data since most studies report a significant difference in magnitude of pain at different circumstances.

In order to describe the course of knee function for PFPS various function scores are used. Kujala reported a high reliability for the Anterior Knee Pain Score when measuring the effect of therapy for PFPS.¹³ In most recent studies there is a tendency for authors to report these scores. However some studies report function scores with (modified) FIQ scores or less appropriate the Lysholm score. Effect of exercise therapy on knee function was determined with the pooled data of the Kujala PF score only in this review.

The effect of exercise therapy on recovery for PFPS is difficult to address since no more than two studies reported on recovery. Clinically recovery implicates relieve of pain and fully restored function. However in the study by van Linschoten the effect on pain and function scores were not reflected in the effect on recovery between groups.²⁶ Clark used several items to depict recovery.³² We considered 'patients no longer troubled by their knee complaints' to be the most applicable to serve as a recovery score. However exercise therapy did not prove to be more effective than a placebo strategy after one year in this study. It therefore can be questioned if recovery is a valid outcome measurement to determine the effectiveness for PFPS. On the other hand incomplete recovery might reflect the true nature of PFPS and gives an additional comprehension of the natural course of PFPS or the effects of therapeutic interventions.⁵¹⁻⁵³

Besides exercise many other combinations of interventions are used for PFPS. Results from this review indicate that exercise therapy is more effective on pain reduction than other strategies. Taping, bracing and insoles are frequently used for the treatment of PFPS alone or in a combination of modalities including exercise therapy. When exercise therapy is compared with a single other intervention strategy exercise therapy is more effective on pain reduction. This review however gives no information on the additional value of other strategies when they are combined with exercise therapy. Recent reviews suggest that there is limited evidence for the effectiveness of additional use of

prefabricated insoles combined with exercise therapy versus foot orthoses alone⁵⁴ and moderate evidence of no additional effect of knee braces to exercise therapy.⁵⁵

Exercise therapy focuses mainly on knee muscles exercise (quadriceps muscles). The studies on exercise therapy reflect the changing opinions through the years concerning preferred treatment strategy. In the late seventies and mid-eighties questions arose about the effect and possible side effects of open and close kinetic chain exercises for PFPS. The studies of Gaffney, Witvrouw, Herrington and Bakhtiary provide evidence that closed kinetic exercise is equally effective as open kinetic exercise for PFPS.^{7 27 29 37} The last decade attention focuses on complex knee and hip stabilizing therapy versus simple knee strengthening exercises. Recent studies by Song and Nakagawa examined the additional effect of hip stabilizing exercise therapy.^{30 34} Only Nakagawa found in a small pilot study (n=14) a positive effect of 'hip/abdominal exercise' on pain versus knee muscle strengthening alone.³⁰

Quality of the evidence

The review indicates that exercise therapy is more effective than a 'wait and see' approach for patellofemoral pain syndrome regarding outcomes 'pain and function'. To date there are several high quality studies supporting the effect of this strategy.^{26 32-35} It will be however impossible to blind the patient for the intervention and therefore the placebo effect cannot be ruled out even in what are considered high quality studies.

On the outcome measure pain there are sufficient high quality studies showing a difference in effect when exercise therapy is compared to taping, bracing or the use of flat inserts in the treatment strategy of patellofemoral pain syndrome.^{28 31 32}

Potential biases in the review process

We executed a comprehensive literature search through up-to-date electronical medical databases which resulted in 1014 abstracts. Patellofemoral pain syndrome is a common complaint in the general population. Exercise therapy is frequently used in general medicine and physical therapy practices. As a result we included 23 studies from 14 different countries. It is however possible that small studies executed by single researchers stay unpublished in the international literature. Furthermore visual judgment of the studies included in the review show skewness in the funnel plot which may also suggest underreporting of non-effective or contra-effective studies on exercise therapy.

Agreements and disagreements with other studies or reviews

To our knowledge there is one systematic review published considering the effects of exercise therapy for patellofemoral pain syndrome⁸ and three which describe the methodological aspects of studies concerning exercise therapy.⁵⁶⁻⁵⁸ Furthermore there are several non-systematic reviews.⁵⁹⁻⁶¹ In these reviews it was concluded that due to

inadequate study design there was only limited evidence for the effectiveness of exercise therapy and conflicting evidence for other non-surgical interventions. The present review includes new studies and provides evidence that an exercise regimen does appear to be effective when compared to 'wait and see' group. When exercise therapy is compared to other non-surgical interventions exercise therapy proves to be more effective than the latter.

Authors' conclusions

Implications for practice

This review provides evidence that exercise therapy is beneficial for patients with patellofemoral pain syndrome when compared to no treatment ('wait and see approach'). Exercise therapy is effective in reducing knee pain at short and long term and improving knee function at short term following an exercise protocol which at least contains strengthening exercises of the knee muscles. The significant improvement of pain and function scores are clinically relevant resulting in approximately 30-40% more pain reduction than for usual care, with a mean effect size of 0.55 for pain and 0.45 for function for short term. The clinical effectiveness is supported by a recent study which suggests that supervised exercise therapy is also cost effective.⁶²

The authors of the review suggest that the duration of the exercise protocol is at least six weeks but might be continued up to 12 weeks. The addition of other types of muscle exercises (hip, abdominal) does not prove to be more effective than knee exercises alone. The use of insoles, tape, brace, manipulation of the knee joint and TENS do not prove to be more effective and in several cases less effective than exercise therapy alone. Although exercise therapy effectively reduces pain and improves function these outcome measures are not reflected in perceived recovery. To the authors opinion both therapist and patients must be aware of these observations in order to provide rational and objective goals when commencing exercise therapy.

Implications for research

This review includes a reasonable number of trials that study different kind of exercise protocols - all including knee muscle strengthening - for patellofemoral pain syndrome with well-defined outcome parameters. Further research should aim at the mechanisms why exercise therapy is more effective than no exercise ('wait and see' approach). Research is needed why not all patients benefit from exercise therapy and which patients are most likely to benefit from exercise therapy. Besides subgroups might be identified which will benefit from additional treatment strategies such as insoles or other regimens which focus on biomechanical factors.

Although there is a common opinion that the natural course of patellofemoral pain syndrome is mild more research is needed to identify the risk factors for prolonged pain and potential association with degenerative joint disease.⁶³ Since not all patients show full recovery it is imperative that this outcome measurement must be taken into account in new studies.

Recently in clinical practice there is a tendency towards protocols that exist of combined knee, hip and abdominal muscle exercise for patellofemoral pain syndrome. More research is needed to study the additional effects of these protocols on clinical outcome parameters.

Differences between protocol and review

1. This review covers different kinds of exercise therapy for patellofemoral pain syndrome. Exercise therapy is compared to placebo or no therapy, is compared to other non-surgical or surgical therapies or compares different types of exercise therapy. Studies were included when the main intervention consisted of exercise therapy - of any kind - and may also contained additional interventions. In the protocol exercise therapy was aimed at strengthening knee extensor musculature, either at home or under supervision of a therapist
2. In the review outcome measures timing within three months after starting the intervention are considered short term outcome of exercise therapy whereas measurements from three months and longer are considered long term outcome. In the protocol measurements up to one year follow-up were considered short term outcomes, thereafter long term.
3. In the review the methodological quality of the studies was assessed using a modification of of The Cochrane Collaboration's tool for assessing risk of bias.¹⁷ In the protocol the criteria list recommended by the Cochrane Bone, Joint and Muscle Trauma Group, combined with the Delphi list and one additional question adapted from the criteria list for Methodological Quality Assessment was used.
4. In the review, when possible, data from the studies were separated and allocated to the type of interventions and comparisons that were appropriate. In the protocol the main comparisons were exercise therapy - aiming at strengthening knee extensor musculature - versus no exercise and closed kinetic versus open kinetic chain exercise.

APPENDICES

APPENDIX 1. DATA AND ANALYSES

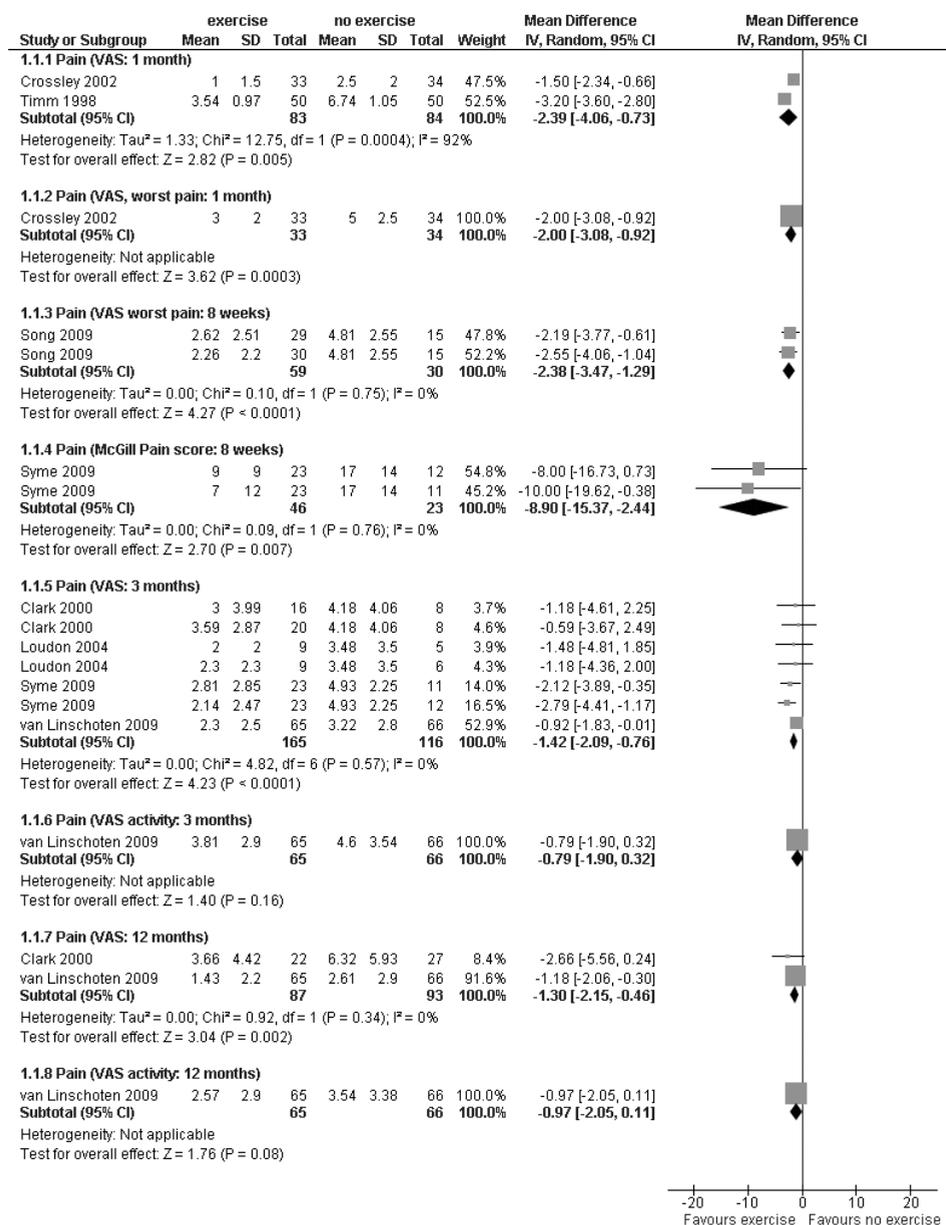


Figure 1. Forest plot of comparison: Exercise therapy versus no treatment, placebo or waiting list. Outcome: Pain, continuous data.

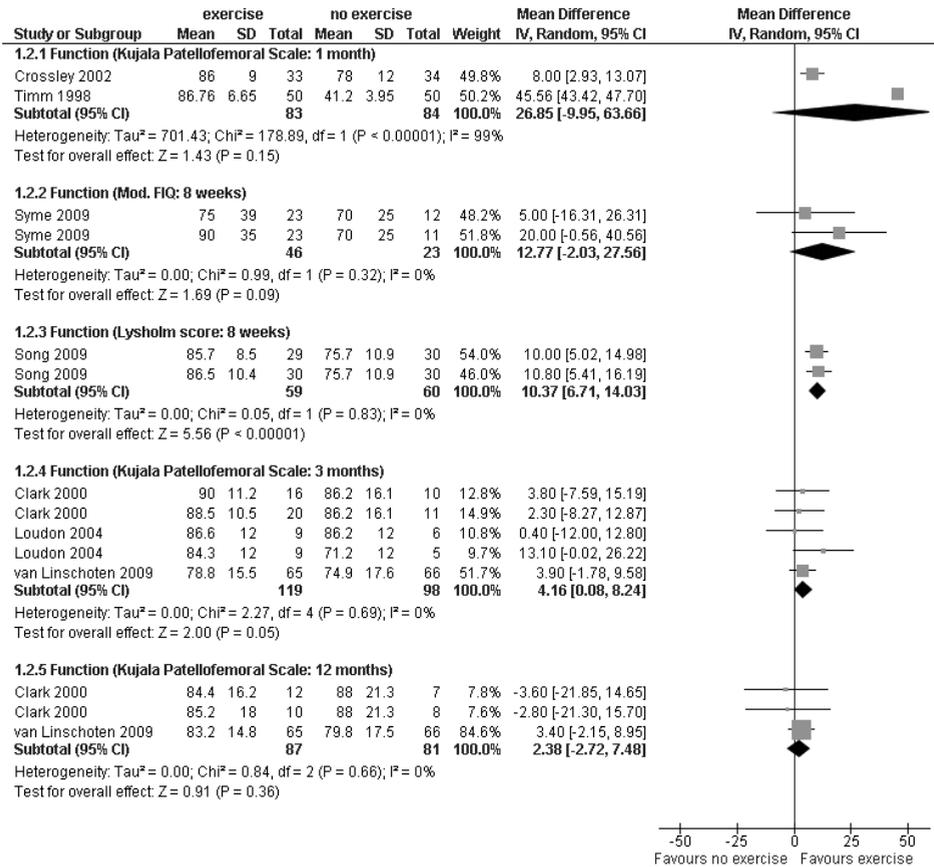


Figure 2. Forest plot of comparison: Exercise therapy versus no treatment, placebo, waiting list. Outcome: Function, continuous data

	1. Randomization adequate?	2. Allocation concealed?	3. Patient blinded?	4. Care provider blinded	5. Outcome assessor blinded?	6. Drop-out rate	7. Intention-to-treat?	8. Free of selective reporting?	9. Similar baseline characteristics	10. Co-interventions?	11. Compliance?	12. Timing outcome
Avraham 2007	?	?	+	+	+	+	+	?	?	?	?	+
Bakhtiary 2008	+	+	+	+	+	?	+	?	+	?	?	+
Clark 2000	+	+	+	+	+	+	+	?	+	+	?	+
Collins 2008	+	+	+	+	+	+	+	+	+	+	+	+
Colón 1988	+	+	+	+	+	+	?	+	?	?	?	+
Crossley 2002	+	+	+	+	+	+	+	?	+	?	+	+
Gaffney 1992	?	+	+	+	+	+	?	+	+	?	+	+
Gobelet 1992	?	+	+	+	+	+	?	+	?	?	+	+
Harrison 1999	+	+	+	+	+	+	?	?	+	?	?	+
Herrington 2007	?	?	+	+	+	?	+	?	+	?	?	+
Loudon 2004	+	+	+	+	+	?	+	+	?	?	+	+
Lun 2005	+	+	+	+	+	+	+	?	+	?	+	+
Nakagawa 2008	+	?	?	+	+	+	+	?	+	?	+	+
Schneider 2001	?	?	+	+	+	+	?	?	+	?	?	+
Song 2009	+	+	+	+	+	+	+	?	+	?	+	+
Syme 2009	+	+	+	+	+	+	+	?	+	?	+	+
Taylor 2003	+	?	+	+	+	+	?	?	?	?	?	?
Thomee 1997	?	+	+	+	+	+	+	+	?	?	+	+
Timm 1998	+	?	+	+	+	+	?	?	+	?	?	+
van Linschoten 2009	+	+	+	+	+	+	+	+	+	+	+	+
Wiener-Ogilvie 2004	+	?	+	+	+	+	?	?	+	?	+	+
Wijnen 1996	+	+	+	+	+	+	+	?	+	?	+	+
Witvrouw 2000	+	?	+	+	+	+	+	?	+	+	+	+

Figure 3 Methodological quality summary: review authors' judgments about each methodological quality item for each included study.

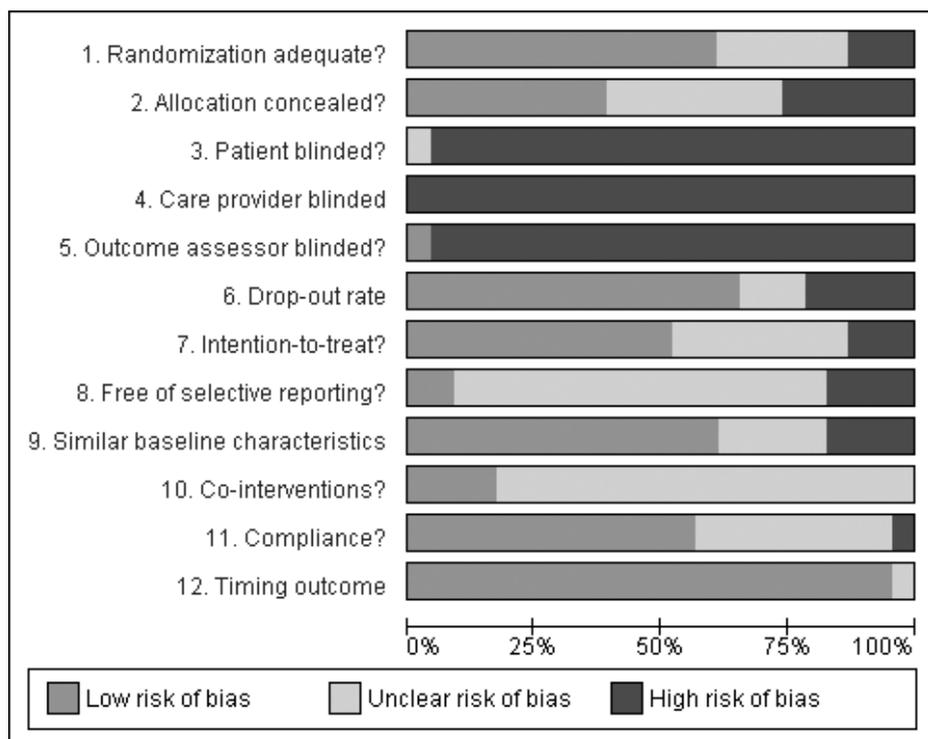


Figure 4 Methodological quality graph: review authors' judgments about each methodological quality item presented as percentages across all included studies

APPENDIX 2.

Search strategy for MEDLINE (OVID WEB)

1. Arthralgia/
2. Knee Joint/ or Knee/ or Patella/
3. and/1-2
4. anterior knee pain.tw.
5. ((patell\$ or femoropatell\$ or femoro-patell\$ or retropatell\$) adj2 (pain or syndrome or dysfunction)).tw.
6. ((lateral compression or lateral facet or lateral pressure or odd facet) adj syndrome).tw.
7. ((chondromalac\$ or chondropath\$) adj2 (knee\$1 or patell\$ or femoropatell\$ or femoro-patell\$ or retropatell\$)).tw.
8. or/4-7
9. or/3,8
10. exp Exercise Therapy/
11. (exercis\$ or strengthen\$ or stretch\$).tw.
12. (stabil\$ adj3 train\$).tw.
13. or/10-12
14. and/9,13
15. randomized controlled trial.pt.
16. controlled clinical trial.pt.
17. Randomized Controlled Trials/
18. Random Allocation/
19. Double Blind Method/
20. Single Blind Method/
21. or/15-20
22. exp Animals/ not Humans/
23. 21 not 22
24. clinical trial.pt.
25. exp Clinical Trials as topic/
26. (clinic\$ adj25 trial\$).tw.
27. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj25 (blind\$ or mask\$)).tw.
28. Placebos/
29. placebo\$.tw.
30. random\$.tw.
31. Research Design/
32. or/24-31
33. 32 not 22
34. 33 not 23

35. Comparative Study.pt.
 36. Evaluation Studies.pt.
 37. Follow Up Studies/
 38. Prospective Studies/
 39. (control\$ or prospectiv\$ or volunteer\$).tw.
 40. or/35-39
 41. 40 not 22
 42. 41 not (23 or 34)
 43. 23 or 34 or 42
 44. 43 and 14 (160 records)
 Search strategy for Cochrane Central Register of Controlled Trials (Clinical Trials) (Wiley InterScience interface), EMBASE, CINAHL (Ovid interface), AMED (Ovid interface) and PEDro (www.pedro.org.auinterface) contained similar search settings.

Table 1 Exercise therapy versus no treatment, 'placebo' or waiting list control

Study ID (arranged by date)	Exercise Protocol	Control Group	Notes
Subcategory 1a. Exercise alone versus control			
Clark 2000	Exercise	No treatment	Additional intervention in both groups: education
Loudon 2004	Supervised exercise therapy + home exercise	Informational leaflet	
Loudon 2004	Home exercise with education component	Informational leaflet	
Herrington 2007	Weight-bearing exercises	No treatment	
Herrington 2007	Non-weight-bearing exercises	No treatment	
Song 2009	Leg press exercise	No intervention	
Van Linschoten 2009	Supervised exercise program + home exercises	Wait and see policy	
Syme 2009	General quadriceps training group	No intervention	Additional interventions included: knee strapping in the intervention group to avoid taping
Song 2009	Leg press and hip adduction exercises	No intervention	
Subcategory 1b. Exercise + other intervention versus control			
Timm 1988	Exercise program with a Protonic brace	No treatment	
Clark 2000	Exercise+tape	no treatment	
Crossley 2002	Physical therapy (including exercise therapy) + EMG biofeedback	Placebo	
Syme 2009	Selective-VMO training group + EMG feedback+ patellar taping	No intervention	

APPENDIX 3. COMPARISONS OF EXERCISE TREATMENT VERSUS CONTROLS

Table 2 Exercise therapy versus other type of intervention

Study ID (arranged by date)	Exercise Protocol	Control Group	Notes
Subcategory 2a. Exercise alone versus other type of intervention			
Gobelet 1992	Pain free isokinetic exercises	Home electrostimulation	
Gobelet 1992	Proprioceptive static exercise	Home electrostimulation	
Clark 2000	Exercise	Tape	Additional intervention in both groups: education
Wiener Ogilvy 2004	Exercise therapy	Foot orthoses	
Lun 2005	Structured home exercise	Patellar brace	
Collins 2008	Physiotherapy (including exercise)	Orthoses	
Collins 2008	Physiotherapy (including exercise)	Flat inserts	
Subcategory 2b. Exercise + another intervention versus another intervention alone			
Clark 2000	Exercise + tape	Tape	Additional intervention in both groups: education
Taylor 2003	Exercise + patellar mobilization	Patellar mobilization	
Wiener Ogilvy 2004	Exercise therapy + foot orthoses	Foot orthoses	
Lun 2005	Structured home exercise + patellar brace	Patellar brace	
Collins 2008	Physiotherapy (including exercise) + orthoses	Orthoses	

Table 3 Exercise therapy versus other type of exercise**3A. Comparison of different types of exercise therapy**

Study ID (arranged by date)	Exercise Protocol	Control Group	Notes
Colon 1988	Pogo stick bounces	Conservative isometric exercises	
Gobelet 1992	Pain free isokinetic exercises	Proprioceptive static exercise	
Thomee 1997	Isometric exercises	Eccentric exercises	
Wijnen 1996	Exercise program + home exercises (McConnell approach)	Standardized home exercise program (including Coumans bandage)	Additional intervention in the exercise group: patellar taping. Control group: knee bandage
Harrison 1999	Supervised exercise program	Conservative home exercise program	
Harrison 1999	Supervised exercise program (McConnell approach)	Conservative home exercise program	Additional intervention in the exercise group: patellar taping, EMG feedback
Schneider 2001	Physiotherapeutical exercises (neurophysiological basis)	Exercises (with splint)	Additional intervention in the control group: splint
Loudon 2004	Supervised exercise therapy + home exercise	Home exercise with education component	
Avraham 2007	Straight leg raising	Hip rotator strengthening	Additional intervention both groups: TENS
Nakagawa 2008	Quadriceps exercises + abdominal + hip-abductor/rotator exercises	Quadriceps exercises	Additional intervention both groups: patellar mobilization& stretching
Syme 2009	Selective-VMO training group (McConnell approach)	General group (quadriceps concentric/eccentric)	Additional intervention in intervention group: patellar taping& EMG feedback. Controls: patellar strapping
Song 2009	Leg press+ hip adduction exercises	Leg press exercises only	

3B. Comparison of different types of exercise - Closed versus open kinetic chain exercise

Gaffney 1992	Eccentric + concentric exercise	Concentric isometric exercise	Additional intervention in the exercise group: patellar taping
Witvrouw 2000	Closed kinetic chain exercise	Open kinetic chain exercise	
Herrington 2007	Multi joint weight bearing	Single joint no weight bearing	
Bakhtiary 2008	Closed kinetic exercises	Open kinetic exercises	

REFERENCES

1. Boling M, Padua D, Marshall S, Guskiewicz K, Pyne S, Beutler A. Gender differences in the incidence and prevalence of patellofemoral pain syndrome. *Scand J Med Sci Sports* 2009;Sep 17:Epub Ahead of Print.
2. Linden vd, FG, Westert M, Bakker dG, Schellevis D. *Tweede Nationale Studie naar ziekten en verrichtingen in de huisartspraktijk. Klachten en aandoeningen in de bevolking en in de huisartspraktijk*. Utrecht/Bilthoven: NIVEL/RIVM, 2004.
3. McConnell J. The management of chondromalacia patellae: A long term solution. *Australian Journal of Physiotherapy* 1986;32:215-23.
4. Natri A, Kannus P, Jarvinen M. Which factors predict the long-term outcome in chronic patellofemoral pain syndrome? A 7-yr prospective follow-up study. *Medicine & Science in Sports & Exercise* 1998;30(11):1572-77.
5. Powers CM. Rehabilitation of patellofemoral joint disorders: a critical review. *Journal of Orthopaedic and Sports Physical Therapy* 1998;28(5):345-53.
6. Thomee R, Augustsson J, Karlsson J. Patellofemoral pain syndrome: a review of current issues. *Sports Medicine* 1999;28(4):245-62.
7. Witvrouw E, Lysens R, Bellemans J, Peers K, Vanderstraeten G. Open versus closed kinetic chain exercises for patellofemoral pain. A prospective, randomized study. *American Journal of Sports Medicine* 2000;28(5):687-94.
8. Heintjes E, Berger MY, Bierma-Zeinstra SM, Bernsen RM, Verhaar JA, Koes BW. Exercise therapy for patellofemoral pain syndrome. Review. *Cochrane Database Syst Rev* 2003;4:CD003472.
9. Witvrouw E, Danneels L, Van Tiggelen D, Willems TW, Cambier D, . Open Versus Closed Kinetic Chain Exercises in Patellofemoral Pain A 5-Year Prospective Randomized Study. *The American Journal of Sports Medicine*, 2004;Vol. 32:1122-30.
10. Nissen CW, Cullen MC, Hewett TE, Noyes FR. Physical and arthroscopic examination techniques of the patellofemoral joint. *Journal of Orthopaedic and Sports Physical Therapy* 1998;28(5):277-85.
11. Crossley KM, Bennel KL, Cowan SM, Green S. Analysis of Outcome Measures for Persons With Patellofemoral Pain: Which Are Reliable and Valid? *Arch Phys Med Rehabil* 2004;85:815-22.
12. Chesworth BM, Culham E, Tata GE, Peat M. Validation of outcome measures in patients with patellofemoral syndrome. *J Orthop Sports Phys Ther*. 1989;10(8):302-08.
13. Kujala UM, Jaakkola LH, Koskinen SK, Taimela S, Hurme M, Nelimarkka O. Scoring of patellofemoral disorders. *Arthroscopy* 1993;9(2):159-63.
14. van Linschoten R, van Middelkoop M, Berger MY, Heintjes EM, Koopmanschap MA, Verhaar JA, et al. The PEX study - Exercise therapy for patellofemoral pain syndrome: design of a randomized clinical trial in general practice and sports medicine [ISRCTN83938749]. *BMC Musculoskelet Disord*. 2006(Mar 17):7-31.
15. Gobelet C, Frey M, Bonard A. Muscle training techniques and retropatellar chondropathy. *Revue du Rhumatisme et des Maladies Osteo-Articulaires* 1992;59(1):23-27.
16. Dursun N, Dursun E, Kilic Z. Electromyographic biofeedback-controlled exercise versus conservative care for patellofemoral pain syndrome. *Archives of Physical Medicine and Rehabilitation* 2001;82(12):1692-95.
17. Higgins S, Green JPT. Appendix 5b: Highly sensitive search strategies for identifying reports of randomized controlled trials in MEDLINE;Cochrane Handbook for Systematic Reviews of Interventions: The Cochrane Collaboration, 2009.

18. van Tulder M, Furlan A, Bombardier C, Bouter L; Editorial Board of the Cochrane Collaboration Back Review Group. Updated method guidelines for systematic reviews in the cochrane collaboration back review group. *Spine (Phila Pa 1976)* 2003;28(12):1290-99.
19. Boutron I, Moher D, Tugwell P, Giraudeau B, Poiraudeau S, Nizard R, et al. A checklist to evaluate a report of a nonpharmacological trial (CLEAR NPT) was developed using consensus. *J Clin Epidemiol* 2005;58(12):1233-40.
20. Furlan AD, Pennick V, Bombardier C, van Tulder M; Editorial Board, Cochrane Back Review Group. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. *Spine (Phila Pa 1976)* 2009;34(18):1929-24.
21. Colon VF, Mangine R, McKnight C, Kues J. The pogo stick in rehabilitating patients with patellofemoral chondrosis. *Journal of Rehabilitation* 1988;54(1):73-77.
22. Thomee R. A comprehensive treatment approach for patellofemoral pain syndrome in young women. *Physical Therapy* 1997;77(12):1690-703.
23. Timm KE. Randomized controlled trial of Protonics on patellar pain, position, and function. *Medicine and Science in Sports and Exercise* 1998;30(5):665-70.
24. Loudon JD, Gajewski B, Goist-Foley HL, Loudon KL. The effectiveness of exercise in treating patellofemoral-pain syndrome. *J Sport Rehabil* 2004;13:323-42.
25. Taylor KE, Brantingham JW. An investigation into the effect of exercise combined with patella mobilization/manipulation in the treatment of patellofemoral pain syndrome: a randomized, assessor-blinded, controlled clinical pilot trial. *European Journal of Chiropractic* 2003;51:5-17.
26. van Linschoten R, van Middelkoop M, Berger MY, Heintjes EM, Verhaar JA, Willemsen SP, et al. Supervised exercise therapy versus usual care for patellofemoral pain syndrome: an open label randomised controlled trial. *BMJ* 2009;Oct 20;339:b4074.
27. Herrington L, Al-Sherhi A. A controlled trial of weight-bearing versus non-weight-bearing exercises for patellofemoral pain. *Journal of orthopaedic & sports physical therapy* 2007;37(4):155-60.
28. Collins N, Crossley K, Beller E, Darnell R, McPoil T, Vicenzino B. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *BMJ* 2008;24(337):a1735.
29. Bakhtiary AH, Fatemi E. Open versus closed kinetic chain exercises for patellar chondromalacia. *Br J sports Med* 2008;42:99-102.
30. Nakagawa TH, Muniz TB, Baldon Rde M, Dias Maciel C, de Menezes Reiff RB, Serrão FV. The effect of additional strengthening of hip abductor and lateral rotator muscles in patellofemoral pain syndrome: a randomized controlled pilot study. *Clinical Rehabilitation* 2008;22(12):1051-60.
31. Lun VMY, Wiley JP, Meeuwisse WH, Yanagawa TL. Effectiveness of patellar bracing for treatment of patellofemoral pain syndrome. *Clin J Sport Med* 2005;15(4):235-40.
32. Clark DI, Downing N, Mitchell J, Coulson L, Syzpryt EP, Doherty M. Physiotherapy for anterior knee pain: a randomised controlled trial. *Annals of the Rheumatic Diseases* 2000;59(9):700-04.
33. Crossley K, Bennell K, Green S, Cowan S, McConnell J. Physical therapy for patellofemoral pain: a randomized, double-blinded, placebo-controlled trial. *American Journal of Sports Medicine* 2002;30(6):857-65.
34. Song CY, Lin YF, Wei TC, Lin DH, Yen TY, Jan MH. Surplus value of hip adduction in leg-press exercise in patients with patellofemoral pain syndrome: a randomized controlled trial. *Phys Ther* 2009;89(5):409-18.
35. Syme G, Rowe P, Martin D, Daly G. Disability in patients with chronic patellofemoral pain syndrome: a randomised controlled trial of VMO selective training versus general quadriceps strengthening. *Man Ther* 2009;14(3):252-63.

36. Wiener-Ogilvie S, Jones RB. A randomised trial of exercise therapy and foot orthoses as treatment for knee pain in primary care. *British Journal of Podiatry*, 2004;43-49.
37. Gaffney K, Fricker P, Dwyer T, Barrett E, Skibinski K, Coutts R. Patellofemoral joint pain: a comparison of two treatment programmes. *Excel* 1992;8:179-89.
38. Wijnen LCAM, Lensens AF, Kuys-Wouters YMS, De Bie RA, Borghouts JAJ, Bulstra SK. McConnell therapy versus Coumans bandage for patellofemoral pain - a randomised pilot study. *Nederlands Tijdschrift voor fysiotherapie* 1996;Sept(Special):12-17.
39. Harrison EL, Sheppard MS, McQuarrie AM. A randomized controlled trial of physical therapy treatment programs in patellofemoral pain syndrome. *Physiotherapy Canada* 1999;51(2):93-100, 06.
40. Schneider F, Labs K, Wagner S. Chronic patellofemoral pain syndrome: alternatives for cases of therapy resistance. *Knee Surg Sports Traumatol, Arthrosc* 2001;9:290-95.
41. Avraham F, Aviv S, Ya'akobi P, Faran H, Fisher Z, Goldman Y, et al. The efficacy of treatment of different intervention programs for patellofemoral pain syndrome - a single blinded randomized clinical trial. Pilot study. *The Scientific World Journal* 2007;7:1256-62.
42. McMullen W, Roncarati A, Koval P. Static and isokinetic treatments of chondromalacia patella: A comparative investigation. *Journal of Orthopaedic & Sports Physical Therapy* 1990;12(6):256-66.
43. Stiene HA, Brosky T, Reinking MF, Nyland J, Mason MB. A comparison of closed kinetic chain and isokinetic joint isolation exercise in patients with patellofemoral dysfunction. *Journal of Orthopaedic & Sports Physical Therapy* 1996;24(3):136-41.
44. Kowall MG, Kolk G, Nuber GW, Cassisi JE, Stern SH. Patellar taping in the treatment of patellofemoral pain. A prospective randomized study. *American Journal of Sports Medicine* 1996;24(1):60-66.
45. Eburne J, Bannister G. The McConnell regimen versus isometric quadriceps exercises in the management of anterior knee pain. A randomised prospective controlled trial. *The Knee* 1996;3:151-53.
46. Roush MB, Sevier TL, Wilson JK, Jenkinson DM, Helfst RH, Gehlsen GM, et al. Anterior knee pain: a clinical comparison of rehabilitation methods. *Clinical Journal of Sport Medicine* 2000;10(1):22-28.
47. Beetsma AJ, Zomerdijsk TE, van Horn JR, Van Wijck R. Functional treatment of the patellofemoral pain syndrome in adolescent girls - is the McConnell program efficacious? - a pilot study. *Acta Orthopædica Scandinavia. Supplementum* 1996;68(274):25.
48. Mei HJ-. Comparison of The Clinical Effects Between Different Physical Therapy Tools in Patellofemoral Pain Patients.
49. Dolak K, Silkman C, Medina McKeon J, Hosey R, Lattermann C, Uhl T. Hip strengthening prior to functional exercises reduces pain sooner than quadriceps strengthening in females with patellofemoral pain syndrome: a randomized clinical trial. *J Orthop Sports Phys Ther.* 2011;41(8):560-70.
50. Moher D, Hopewell S, Schulz KF, Montori V, GÅ, tzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;23(340):doi: 10.1136/bmj.c869.
51. Kannus P, Niittymäki S. Which factors predict outcome in the nonoperative treatment of patellofemoral pain syndrome? A prospective follow-up study. *Medicine & Science in Sports & Exercise* 1994;26(3):289-96.
52. Nimon, G.Murray, D.Sandow, M.Goodfellow, J. Natural history of anterior knee pain: a 14- to 20-year follow-up of nonoperative management. *J Pediatr Orthop* 1998;18(1):118-22.
53. Blond, L.Hansen, L. Patellofemoral pain syndrome in athletes: a 5.7-year retrospective follow-up study of 250 athletes. *Acta Orthop Belg* 1998;64(4):393-400.

54. Barton CJ, Munteanu SE, Menz HB, Crossley KM. The efficacy of foot orthoses in the treatment of individuals with patellofemoral pain syndrome: a systematic review. *Sports Med* 2010;40(5):377-95.
55. Swart NM, van Linschoten R, Bierma-Zeinstra SM, van Middelkoop M. The additional effect of orthotic devices on exercise therapy for patients with patellofemoral pain syndrome: a systematic review. *Br J Sports Med* 2011.
56. Crossley K, Bennell K, Green S, McConnell J. A systematic review of physical interventions for patellofemoral pain syndrome. *Clin J Sport Med* 2001;11(2):103-10.
57. Bizzini M, Childs JD, Piva SR, Delitto AJ. Systematic review of the quality of randomized controlled trials for patellofemoral pain syndrome. *Orthop Sports Phys Ther* 2003;33(1):4-20.
58. Barton CJ, Webster KE, Menz HB. Evaluation of the scope and quality of systematic reviews on nonpharmacological conservative treatment for patellofemoral pain syndrome. *J Orthop Sports Phys Ther* 2008;38(9):529-41.
59. Callaghan MJ, Oldham JA. The role of quadriceps exercise in the treatment of patellofemoral pain syndrome. Review. *Sports Med* 1996;21(5):384-91.
60. Arroll B, Ellis-Pegler E, Edwards A, Sutcliffe G. Patellofemoral pain syndrome. A critical review of the clinical trials on nonoperative therapy. *American Journal of Sports Medicine* 1997;25(2):207-12.
61. Zomerdijk TE, Beetsma AJ, Dekker R, Van Wijck R, Van Horn JR. Conservative treatment of the Patellofemoral Pain syndrome -a systematic review of literature. *Nederlands tijdschrift voor fysiotherapie* 1998;108(4):95-102.
62. Tan SS, van Linschoten RL, van Middelkoop M, Koes BW, Bierma-Zeinstra SM, Koopmanschap MA. Cost-utility of exercise therapy in adolescents and young adults suffering from the patellofemoral pain syndrome. *Scand J Med Sci Sports*. 2009;Aug 23:568-79.
63. Davis IS, Powers CM. Patellofemoral pain syndrome: proximal, distal, and local factors, an international retreat, april 30-may 2, 2009, fells point, Baltimore, MD. *J Orthop Sports Phys Ther* 2010;40(3):A1-A48.



Chapter 10

General Discussion

INTRODUCTION

The main aim of this thesis was to assess the evidence for the effectiveness of exercise therapy for patellofemoral pain syndrome (PFPS) in relation to other conservative strategies and to describe present strategies for PFPS in general practice.

In this general discussion we describe the most important results, discuss the findings in a broader perspective, present implications for medical practice, and make recommendations for further research.

Patellofemoral pain syndrome is frequently encountered in general practice, in sports medicine, and in orthopaedic clinics. Complaints start during adolescence or young adult age and, although the complaints are considered to be self-limiting, recovery rates are as low as 44% after 1 year to 60% at 6 years (Chapter 2).

In the absence of pathological findings there is increasing consensus that the syndrome may well be diagnosed by excluding specific pathology around the knee and by anamnestic criteria. These include a non-traumatic onset of pain around the patella, grinding of the patella, and pain on activities like stair climbing, running, biking or sitting with bended knees. The treatment options are mainly conservative and general practitioners (GPs) show a preference for an active strategy which includes physical therapy and exercise therapy (Chapter 2). In medical practice exercise therapy is an accepted strategy but its sustainable clinical effect is still debated. The results of a randomized trial (the PEX study), which compared exercise therapy to a wait-and-see strategy in a GP and sports medicine setting, showed a better outcome on pain and function scores in favour of exercise therapy (Chapters 4 and 5). Also, a systematic review on the effects of exercise therapy showed that exercise therapy is effective in reducing pain on the short and long term, and in improving function on the short term, compared to no treatment/usual care for patients with PFPS (Chapter 7). Other conservative strategies for PFPS include the use of braces, tape and insoles. A systematic review comparing the additional effects of orthotic devices on exercise therapy for PFPS, found conflicting evidence for the effectiveness of tape and foot orthotics on pain and function compared to exercise therapy alone (Chapter 8).

INCIDENCE, ETIOLOGY AND RISK FACTORS FOR PFPS IN GENERAL PRACTICE

Patellofemoral pain syndrome usually expresses at adolescent/young adult age, affecting women twice as often as men, and is thought to have a multifactorial genesis. It is frequently encountered in active populations and may constitute 25% of consultations in sports medicine clinics.¹⁻⁴ To date, however, it is unclear whether physical (over)load is causative in PFPS or if the complaints are merely expressed under specific circumstances.

The data on PFPS and its relation to physical activities are not conclusive, probably due to incomplete methodology and incomplete or lack of registration.

In Dutch general practice, the ICPC-2 coding system is used for the registration and classification of diseases/complaints, the reasons for encounter, and for the process of care referral.⁵ This system can give insight into the frequency of general knee complaints in the primary care population and, depending on the national translation of the ICPC, may also determine specific knee conditions such as PFPS. Patellofemoral pain syndrome is classified under diagnosis code L99.7. Although precise data in primary care are lacking, in GP practices in the age group 15-24 years, up to 9 cases of PFPS per 1000 registered persons per year are likely to be classified under this code.⁶ However, it remains unclear exactly when GPs allocate such a code to a specific patient. Registration data in physical therapy practices in the Netherlands show that approximately 26,000 cases of PFPS are treated annually. Of these, 30% attend the physical therapist without consulting a physician.⁷

Nevertheless, these data and the ICPC coding system provide no information on sports participation or activity level. Some small studies in general practice on sports injuries are available but are also based on the ICPC registration system and therefore lack information on typical sports-related injury patterns and specific musculoskeletal diagnosis.^{8,9}

In the Netherlands, extensive epidemiological data on sports injuries are available and provide information on general diagnosis (sprain, strain, contusion, fracture), injury location, causes of injury (acute versus overload) and type of sports, but do not provide specific data for PFPS or other chronic knee problems.¹⁰

In our studies (Chapters 2 and 3) we used data from the Honeur knee cohort which were collected by history taking, questionnaires and standardised physical examination in patients consulting the GP for non-traumatic knee pain.¹¹ In Chapter 3 we found that PFPS comprises the second working diagnosis after 'general knee complaints' in a sporting population in Dutch general practice. However, no difference in prevalence was found between active participants and non-athletes regarding the diagnosis PFPS. In subgroup analyses we found no difference in the type of knee complaints between athletes who associated their complaint with their sport participation and those who did not. There are, however, some limitations regarding these data. The major limitation is that data collecting in this study was designed for the primary diagnosis and course of incident knee complaints and not for injury incidence in matched groups prospectively. Secondly the attribution of physical complaints to the respective sports activity was based on subjective information from the participants, and the mean age of the study group (41.0 years) was higher than normal regarding the PFPS age groups.^{12,13} Taking into account these limitations, our study shows that active sport participants do not consult the GP more frequently for PFPS than non-athletes.

In order to prevent and/or treat PFPS, more information is needed on its etiology. Therefore, it is suggested that for sports injury registration more diagnostic data should be collected on chronic injuries such as PFPS. Also, in general practice or physical therapy practice, details on sports participation (or the reason for encounter) should be added to the registration of the medical diagnosis.

DIAGNOSTICS FOR PFPS IN GENERAL PRACTICE

Knee complaints (non-traumatic and traumatic) are the second largest reason for consultation for musculoskeletal complaints in general practice.^{14 15}

For non-traumatic knee complaints in adults and the elderly, the (working) diagnosis is largely symptom based and will usually not require extensive diagnostic work-up.^{9 16 17} For PFPS the diagnostic criteria are also mainly based on symptoms (pain) and physical findings (pain around the patella and on patellar compression), although these findings have low specificity for PFPS.^{18 19} Also radiological examination is not sensitive for PFPS and is generally used for the documentation of patellar instability or patellofemoral osteoarthritis.^{20 21} Clinically, other painful conditions at the anterior side of the knee (patellar tendinopathy, juvenile osteochondrosis and referred pain from the medial knee compartment) may be difficult to distinguish from PFPS. Without a reference or gold standard, the diagnosis of PFPS may therefore be questionable, or be considered as a 'waste basket' diagnosis.¹²

Notwithstanding these remarks, there is growing consensus that PFPS is a clinical entity in which long duration of peripatellar pain, functional disability and the absence of specific pathology are key elements.¹²

For this thesis, in general practice we studied the characteristics of patients who were diagnosed with PFPS versus those who were registered as having non-specific knee complaints (Chapter 2). Analyses revealed that the diagnosis PFPS (made by GPs) was associated with the duration of complaints, the appearance of bilateral complaints, and apparent pain at the patellar edge and on knee extension. These findings are in accordance with the criteria that match PFPS but are, however, not specific.^{16 18} The use of a set of criteria which are considered to be associated with PFPS showed only 61% overlap in the diagnosis set by the GP. Therefore, we conclude that for diagnosing PFPS, GPs probably rely on simple criteria and that the diagnosis seems to be related to the initial policy chosen for these patients. Our results also indicate the difficulty of diagnosing PFPS due to the absence of a gold standard.

Therefore, more studies are needed to differentiate the diagnostic criteria for PFPS in relation to other non-traumatic knee complaints, and to establish whether these criteria are both reproducible and reliable.

TREATMENT OF KNEE COMPLAINTS IN GENERAL PRACTICE

In our observational studies (Chapters 2 and 3) we compared the initial strategy regarding non-traumatic knee complaints by the GP for athletes and non-athletes and for non-specific knee complaints and PFPS. It was found that GPs more frequently recommend a passive strategy for athletes with knee complaints than for non-athletes. However, no difference in referral to physical therapy concerning athletes and non-athletes was found. Referral to a physical therapist was strongly related to a second consultation with the GP. In 2006, in Dutch healthcare the mandatory referral to a physical therapist by the GP was abandoned. Our study data were obtained between 2001 and 2003. Recent data from physical therapy practice show that about 30% of patients with knee complaints visit a physical therapist by self-referral; these figures have increased since the introduction of direct access to physical therapy.⁷ Whether this means there is an absolute increase of physiotherapy treatment for knee complaints is not clear, since no combined data before this policy change are available. For reasons of efficiency it is recommended to study the patterns of referral and self-referral to physical therapy, especially regarding their relation with the diagnosis and current guidelines for knee complaints in primary care and physical therapy.

When comparing strategies for non-specific knee complaints and PFPS in general practice we found that in about 50% of both cases, GPs apply a passive strategy such as rest and a 'wait and see policy' (Chapter 2). In the cases labelled as 'PFPS' the GP more often promotes an active approach, including muscle exercises (33.8% versus 18.4%) and 30% of the PFPS cases were referred to a physical therapist. However, neither the past nor the present Dutch Guidelines for primary care include physical therapy as a treatment option for PFPS, but only mention isometric quadriceps exercises for home practice.^{16 22} Therefore our study reveals a discrepancy between the Guidelines and actual medical practice.

Guidelines are based on scientific evidence and/or expert opinions, and medical practice is also directed by facilities, medical experience and the personal attitude of physicians and patients. Cottrel et al. described the wide variety in beliefs and attitudes of GPs regarding exercise therapy for knee osteoarthritis and chronic knee pain.²³ The authors concluded that exercise may well be underused in the management of chronic knee pain and knee osteoarthritis, even though guidelines for knee osteoarthritis recommend the use of exercise therapy and physiotherapy. In contrast, our study revealed the opposite: GPs favour an active approach for PFPS whereas the current guideline does not support this strategy. However, because there is now sufficient evidence for the effectiveness of exercise therapy for PFPS (Chapters 5 and 7), we recommended that this advice should be incorporated in the medical guideline.

CHRONIC KNEE COMPLAINTS OR THE NATURAL COURSE OF PFPS

In our observational study in general practice we found that following initial strategies, 44% of the patients diagnosed with PFPS by the GP had recovered after 1 year and 60% after 6 years (Chapter 2). In these patients different initial strategies were applied, including a 'wait and see' strategy. Our randomized trial on exercise therapy for PFPS showed almost 50% recovery after 1 year in the 'wait and see' (control) group that was recruited by the GPs (Chapter 5). In one of the first observational studies, Sandow et al. reported that 2-8 years after the initial visit about 50% of the adolescent girls rarely had pain and 50% of them were not restricted in sports activities.²⁴ Kannus et al. reported that after 7 years follow-up, 67% had made a complete recovery.²⁵ Blond et al. reported that after a mean follow-up of 5.7 years in a sports medicine setting, 50% of the patients showed good prognosis following an initial home exercise program.²⁶ Collins et al. reported that in 73% there was clinical improvement after 1 year in a control group which used flat inserts at the start of the study.²⁷ However, it is disputed whether the use of inserts is a true placebo control. In the study by Clarke et al., 87% of the controls (who were educated on the complaints only) were still troubled by pain after 1 year compared to 60% of the patients who underwent an exercise program.²⁸ Although the latter study is prospective, the drop-out rate after 1 year ranged from 30-50%, which may have affected the recovery rates. Since patients in these latter studies were recruited from different populations (e.g. orthopaedic centres, general practices, an open population, etc.) the recovery rates may differ due to the severity and duration of complaints. Also, recovery may not have been measured in the same way in each study.

However, in general the data from these studies suggest that recovery occurs in 50-70% of patients on the long term, which probably reflects the natural course of PFPS.

EXERCISE THERAPY FOR PFPS

Study design and limitations

Chapters 4 and 5 present the design and results of a randomised clinical trial on exercise therapy and patellofemoral pain syndrome. In 2003, Heintjes et al. concluded that although exercise therapy is an accepted therapeutic strategy in clinical practice, the effect on outcome measures, such as pain and function scores, are limited or conflicting.²⁹ The authors concluded that the majority of studies lack proper methodological elements. Therefore, we carefully planned a study on the effectiveness of exercise therapy which was supervised by a physical therapist and compared this intervention to a group of patients which followed a 'wait and see' strategy, since this reflects usual care in Dutch general practice.²² We recruited patients from GP practices and from sports

medicine practices, since PFPS shows a high prevalence in the latter. We aimed to establish whether the effects in both subgroups would be similar.^{3,26}

Based on an expected clinically relevant outcome, we calculated that the study population should comprise 136 participants in order to show a statistically significant effect on outcome measures.²⁸ We expected to recruit these patients within 14 months and anticipated that similar numbers would be derived from GP practices and from sport physician practices.

Since we stratified the patients by the recruiting physician (GP/sports medicine) before randomization, we optimised equal distribution of co-variables over the two treatment groups within the strata. Such stratification makes subgroup analysis (including drop-outs from the study) more reliable.³⁰ However, during the study we noticed that recruitment of participants, especially by sports physicians, was impeded. First, patients with PFPS recruited from sports medicine practices were (in some cases) not 'new episode' cases and had already been treated by a physical therapist or had received exercise therapy. This was one reason for exclusion from the study. Second, eligible patients who visited the sports physician insisted on an exercise regimen and therefore declined to participate in a study where they might be assigned to the 'wait and see' strategy. This resulted in a misbalance between the two subgroups: of the 131 study patients, 101 patients were recruited by GPs and only 30 by sports physicians. Therefore, it is debatable whether the participants recruited by sports physicians actually differed from the 'usual' patients in sports medicine and, therefore, that selection bias was introduced.

Moreover, there is a major issue that cannot be resolved in our study (and other studies) on exercise therapy.³¹ Although we studied the course of pain, function and recovery in the intervention and control group, our study group was not blinded for the intervention since 'placebo exercise' does not exist. Also, the physical therapists who supervised the participants were not blinded. Therefore encouragement, attention and the personal beliefs of the physical therapists are potential effects, in addition to the 'true' effect of exercise. Although we used validated and accepted outcome measures, pain and function scores are provided by the participants themselves which may also introduce a potential bias. However, since there is no objective outcome measure for PFPS (e.g. muscular strength or radiographic measures), we think that the use of validated pain scores and specific function scores offer comparable data to other studies, and are the best we can get.³² In addition, they more realistically reflect the effect as experienced in actual clinical practice than placebo-controlled trials.

Clinical outcomes

Chapter 7 presents our updated review on exercise therapy and PFPS: 13 studies were added to the systematic review dating from 2004, which also include an increasing number of high-quality studies. The pooled data from these studies show that exercise

therapy for PFPS leads to significant pain reduction on the short and long term, and to functional improvement on the short term. The effects of exercise therapy are not clearly reflected in the measurement of recovery.

Analysis of the data in our randomized trial (Chapter 5) also showed that patients who followed a supervised exercise protocol benefit significantly more from their treatment than those who were offered usual care. The exercise program resulted in a significant and clinically relevant reduction of pain intensity and improvement of function scores. However, in our study this improvement was not reflected in a significant difference in the rate of recovery between the groups (measured on a 7-point Likert scale).

Crossley et al. also used a dichotomized 5-point Likert scale to measure response to treatment and noted a marked improvement for participants in the physical therapy group (OR 3.39; 95% CI, 1.69-6.80) compared to those in the placebo group.³³ In their study, the intervention consisted of multimodal physical therapy which included exercise therapy, patellar taping, ultrasound treatment and electrostimulation. Therefore, from their study it is difficult to conclude what the contribution of exercise was on recovery rate compared to our study which focused on exercise therapy alone.

We also chose to dichotomize for recovery and included the items 'full recovery' and 'strong recovery' for the outcome recovery, but failed to show a difference between the intervention group and controls. However, when 'slight recovery' was included in 'recovery', analysis showed that participants in the intervention group reported a significantly higher recovery rate than the control group at 3 months (OR 4.1; 95%CI, 1.87-8.90).

Although 'perceived recovery' is accepted as a valid instrument to measure clinical outcome for musculoskeletal conditions, it may not only comprise the domains of pain and function but also the patient's perspective on the process which leads to full function.³⁴ Moreover, literature suggests that recovery may also be determined by the individual appraisal of the impact of symptoms on daily activities and quality of life. Since our group and others suggest that recovery from PFPS may be incomplete on the long term, it is recommended to include 'recovery' (in addition to pain and function scores) as an outcome measure in future studies. The use of a Likert scale of global perceived recovery is an appropriate instrument for comparison between studies.³⁵

We found that the effects of intervention were more pronounced in the GP subgroup and were absent in the sports physician subgroup. Baseline characteristics showed no differences between the patients recruited by the GP and the sports physician on major contributors such as duration of complaints, pain severity, age, gender, body mass index, or volume of sport participation. Misleading results (either false positive or false negative) are often present in subgroup analyses especially in small subgroups. Given the small numbers and wide confidence intervals for measurements in the sports physician subgroup, it is likely that the difference is coincidental. However, one can speculate on the possible difference between these groups of patients. Exercise therapy can be

considered a training regimen which delivers its effect by physiological, functional, and biological means on the musculoskeletal system. It is possible that patients visiting the sports physician already show higher levels of 'neuromuscular fitness' and therefore training effects are less pronounced compared with patients who visit their GP. Although we found no difference in sports participation between the subgroups, the participants recruited by sports physicians might have continued their sports activities at a higher level during the intervention period, thereby adding more load on the patellofemoral joint and (possibly) contributing to prolonged continuation of complaints. Larger studies in clinics including more sports participants are needed to establish whether a true additional effect of exercise is present or absent in this subgroup.

In spite of the above-mentioned limitations regarding the methodology in studying the effects of exercise therapy, our study supports the clinical observations which favour exercise therapy over a 'wait and see' strategy. The effects of exercise therapy are significant and clinically relevant, producing effect sizes of 0.50 for pain and 0.40 for function scores when compared with usual care. These effect sizes are considered moderate and are comparable with the effect sizes found for exercise therapy for knee osteoarthritis

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Cost-effectiveness of exercise therapy for PFPS

Chapter 6 describes the cost-effectiveness of supervised exercise therapy versus usual care. Exercise therapy leads to significantly higher annual direct medical costs per patient, mainly caused by visiting a physical therapist (+ 135 euro). However, the average annual societal costs per patient were significantly lower in the intervention group (- 155 euro). This indicates that there is a small surplus in net economic effect of exercise therapy compared to a 'wait and see' strategy. It was estimated that there is a societal average cost-effectiveness ratio of -14,738 euro per quality-adjusted life-year in favour of exercise therapy.

However, it should be noted that the cost-effectiveness ratio had a wide variance in the confidence interval. Furthermore the average age of our patients (24.0 years) was reflected in 70% of paid work and since this type of knee complaint results in low costs for sick leave or reduced productivity, the majority of costs will be caused by direct medical costs, i.e. visits to the physical therapist. However, since this study was an open-label study reflecting normal practice and the clinical results (including placebo effect) were clinically relevant, it is (economically) justified to refer patients with PFPS to a physical therapist for exercise therapy.

Supervised exercise, home exercises or a combination?

Our treatment protocol consisted of initially supervised and an individually-tailored multi-exercise muscle strengthening program which was combined with home exercises.

However, it is worth establishing whether an exercise program for PFPS without supervision of a physical therapist will result in the same clinical improvement and an additional reduction of medical costs. Very few studies have investigated the value of home exercise for PFPS. Lun et al. found no difference in clinical effect between a home exercise program and other types of interventions (brace, sleeve), but did not compare the interventions with a control group.³⁸ Loudon et al. compared supervised exercise therapy with a home-based program and found no clear distinction in outcome between groups.³⁹

One study on exercise therapy for osteoarthritis showed that supervision by a physical therapist of a lower limb strengthening program was more effective on pain reduction and improvement of locomotor function than an individual home exercise program.⁴⁰ Furthermore a systematic review on knee osteoarthritis suggests that class-based exercise therapy may also be economically more efficient than home-based exercise.⁴¹

To our knowledge no studies have investigated the cost-effectiveness of home-based exercises versus supervised exercise therapy for PFPS.

Based on these sparse data it remains unclear whether a home-based exercise program for PFPS is clinically and economically as effective as a supervised program.

EXERCISE THERAPY IN OTHER MUSCULOSKELETAL CONDITIONS

Several systematic reviews have examined exercise therapy for various musculoskeletal conditions. Meta-analysis revealed a significant beneficial treatment effect for knee pain and for physical function for patients with knee osteoarthritis.^{41 42}

For hip osteoarthritis a small treatment effect for pain and function was measured following strengthening exercises and water-based exercises.^{41 43}

A meta-analysis on non-specific low-back pain showed that exercise therapy seems slightly effective in decreasing pain and improving function in adults with chronic low-back pain.^{44 45 46} A review on the non-operative treatment of mid-portion Achilles tendinopathy on pain scores showed that eccentric exercises are superior to a wait-and-see treatment.⁴⁷

Holmich et al. reported a significant clinical effect of an active training program on long-standing adductor-related groin pain versus a passive physiotherapy program in soccer players.⁴⁸

From literature it is clear that patients with specific and non-specific musculoskeletal conditions can benefit clinically from exercise therapy, whereas a variety of exercise modalities may contribute to this effect. However, the mechanism of action is not well understood and different components may contribute to the physiological and biological changes induced by exercise. The effects of exercise can be found (peripherally) on muscle and tendon tissue, cartilage and bone, but also at the central level by regulation of neurotransmitters (serotonin, $\hat{\alpha}$ -endorphins).^{49,50}

It is well known that all parts of the musculoskeletal system (including bone, cartilage and tendon) respond to mechanical stimuli and that the lack of these stimuli leads to loss of tissue properties. In this reversible training model the effects can be represented in an inverted parabolic way: increase of mechanical stress leads to augmented effects but may lead to negative effects when the locomotor system is overloaded.⁵¹ Human studies and animal models have shown that repetitive mechanical overloading may damage the individual components of the system (loss and breakdown of muscle cells, apoptosis of tendons cells, loss of bone mineralization and breakdown of cartilage).^{52,53} On the contrary, underloading of the musculoskeletal systems leads to negative effects resulting in muscle wasting with corresponding loss of strength, thinning of cartilage, and bone demineralization.

For cartilage tissue, current knowledge suggests that healthy cartilage is protected by moderate loading and that even osteoarthritis can be modulated by physiological joint loading.⁵² Although the underlying mechanism still needs to be elucidated, basic science suggests that mechanical stimulation of the cells of the locomotor system leads to genetic regulation within the cells and to a subsequent biological response.⁵⁴ This pathway (by some called 'mechanotransduction') might be the underlying mechanism in maintaining healthy musculoskeletal tissue, promoting tissue repair, and subsequent clinical improvement or recovery.⁵⁵

To date, the majority of explanatory research on PFPS focuses on treatment variables within this 'biomedical model' and searches for biomechanical, radiological or pathophysiological changes at the level of the patellofemoral joint which may be associated with PFPS.⁵⁶⁻⁵⁸

As stated above, exercise therapy may also have a central effect at the level of neurotransmitters which can be reflected in psychological outcome measures; also, many studies associate pain reduction and functional improvement with an increase of well-being in various chronic conditions.⁵⁹⁻⁶¹

However, only a few studies have explored the psychological factors that may play a role in the course of PFPS or its relation with the effects of exercise therapy. Clark et al. noted a significant decrease in anxiety and depression scores in both exercise intervention and control patients after 3 months without a significant difference between groups.²⁸ It is noteworthy that all groups in the latter study improved on pain

and function scores without significant differences between these groups; therefore, it is suggested that improvement of pain and function is reflected in a decrease of anxiety and depression. Carlsson et al. found only a few differences between their group of PFPS patients and matched controls (both non patients and psychiatric outpatients), on anxiety and passive attitude.⁶² In a series of 50 patients with long-standing PFPS, Thomee et al. concluded that the way patients with PFPS experience their pain, the coping strategies used for pain and their degree of well-being, were in agreement with other patient groups who have chronic pain.⁶³ Jensen et al. concluded that levels of mental distress were higher in the group with PFPS than in the control group of healthy subjects, while levels of self-perceived health were lower. According to the authors these data indicate that the levels of knee pain and knee function correlate closely to the degree of mental distress and self-perceived health in individuals with PFPS.⁶⁴

In conclusion, results from these studies associate some psychological outcome measures with the course of PFPS. However, it can be hypothesized that these outcome measures are actually modified by the level of pain and function rather than being independent prognostic factors.

ADDITIONAL STRATEGIES FOR PFPS

In countries such as Australia and the UK, tape, braces and orthoses are frequently used in physiotherapeutic practice as a combined strategy for PFPS together with exercise therapy, electrical therapy, massage techniques or manual therapy.

Chapter 8 explores the additional value of orthoses, braces and tape on exercise therapy by means of a systematic review. It is concluded that there is no evidence for the additional effect of knee braces on exercise therapy regarding pain and function outcomes, while the evidence for the additional effect of tape and foot orthotics on exercise therapy is conflicting when compared to exercise alone. These conclusions are based on data from eight randomised trials of which three had a low risk of bias. These findings are supported by a recent review by Barton et al. who also concluded that there is only limited evidence for the effect of prefabricated insoles on short-term improvement for PFPS compared to flat inserts.⁶⁵

The rationale behind tape, braces and orthoses is that they are supposed to act mechanically on the position of the knee joint, patella, distal tibia or foot. Although biomechanical research tries to relate foot position, tibia rotation and patella position with PFPS the effects of interventions for biomechanical factors and the clinical outcome of PFPS are difficult to address.⁶⁶ There are several reasons for this.

First, the etiology of PFPS is not clearly understood and may be associated with risk factors other than static mechanical (structural) factors alone. Whereas altering the

static biomechanics of the lower limb may result in altered loading of the patella femoral joint, it is during movement that the dynamic components (e.g. muscular strength and endurance, as well as neuromuscular coordination) may perform their action on the patellar joint. It is more likely that these factors will be influenced by (neuro-muscular) training than by biomechanical measures. In addition, biological factors like age and gender (e.g. PFPS has a high prevalence during adolescence and among females) may also play a role in etiology.

Second, the factors contributing to the prognosis of PFPS are not yet well established. A recent study revealed that the two most consistent predictors of poor outcome in individuals with PFPS over a 1-year period were a long duration of knee pain and a low baseline knee function score⁶⁷. This is interesting since in that study besides biological factors (age, gender, and bodyweight) also biomechanical factors (foot arch height) were not associated with outcome.

Third, the application of supportive means like braces or insoles may act as a placebo therapy itself rather than a true biomechanical therapy since patients are not blinded for this kind of therapy. Two studies tried to overcome this aspect by using 'placebo taping' versus 'therapeutic taping' and by using 'flat inserts' versus custom made insoles.²⁷
³³ Although therapeutic taping appeared to be more effective, its result could not be extracted from the study since taping was a part of a multi-modal approach.³³ Concerning the effect of insoles versus flat inserts only a minor effect was seen at 6 weeks in favour of insoles, which was lost after 12 and 52 weeks follow-up.²⁷

Therefore, the currently available data do not indicate the surplus value of supportive means on exercise therapy for PFPS, although they are frequently used.

IMPLICATIONS FOR PRACTICE AND RESEARCH

PFPS is no longer considered a defined pathological condition of the cartilage caused by biomechanical aberrations, but rather a clinical condition in which pain is mediated by different known and unknown factors. Exercise therapy may (overall) be beneficial to patients with a new episode of patellofemoral pain. Therefore in medical practice, in addition to a 'wait and strategy', exercise should be considered as an initial therapeutic approach. However, the expectations of physicians and patients on outcome should be realistic, since many studies report that a substantial number of patients are not recovered after 1 year. The general belief that PFPS is a prognostically mild and self-limiting condition should be dispelled.

Other practical strategies include refraining from pain-provoking activities; however, although the natural course of PFPS is slow, younger patients may not like reducing their

physical activities for a long period. There appears to be no necessity for a general use of taping or bracing of the patellofemoral joint or the general use of foot orthoses.

From a research point of view many questions remain to be answered. Based on the fact that exercise therapy is effective in pain reduction and improving function, future research should aim at identifying patients who are likely to show a positive response to exercise therapy and those who do not. It is suggested to establish subgroups of patients with known risk factors for PFPS (e.g. high training load, decreased quadriceps and hamstring strength, increased hip external rotator strength, increased navicular drop and altered dynamic kinematics on jumping and landing) to explore the effect of specific measures like insoles, tape and training modalities on outcome.^{2 66 68 69}

Bearing in mind the high incidence of PFPS in an active population it is proposed to intensify the liaison with sports medicine clinics to recruit these patients on a larger scale in order to study the proposed effect modifiers.

REFERENCES

1. Milgrom C, Finestone A, Eldad A, Shlamkovitch N. Patellofemoral pain caused by overactivity. A prospective study of risk factors in infantry recruits. *J Bone Joint Surg Am* 1991;73(7):1041-3.
2. Witvrouw E, Lysens R, Bellemans J, Cambier D, Vanderstraeten G. Intrinsic risk factors for the development of anterior knee pain in an athletic population. A two-year prospective study. *Am J Sports Med* 2000;28(4):480-9.
3. Baquie P, Brukner P. Injuries presenting to an Australian sports medicine centre: a 12-month study. *Clin J Sport Med* 1997;7(1):28-31.
4. Boling M, Padua D, Marshall S, Guskiewicz K, Pyne S, Beutler A. Gender differences in the incidence and prevalence of patellofemoral pain syndrome. *Scand J Med Sci Sports* 2010;5:725-30.
5. Lamberts H, Wood M. *ICPC. International Classification of Primary Care*. Oxford: Oxford University Press, 1987.
6. van der Linden M, Westert G, de Bakker D, Schellevis F. Tweede Nationale Studie naar ziekten en verrichtingen in de huisartspraktijk. Klachten en aandoeningen in de bevolking en in de huisartspraktijk.. Utrecht/Bilthoven: NIVEL/RIVM, 2004.
7. Kooijman MK, Swinkels ICS, Leemrijse C, de Bakker D, Veenhof C. Landelijke Informatievoorziening Paramedische Zorg (LiPZ). Utrecht: NIVEL, 2010.
8. Valkenberg HD, G.A. Schoots, W. Vriend, I. Sportblessures bij de huisarts: registratie, behandeling en verwijsbeleid. *Sport en Geneeskunde (Dutch)* 2010;43(2):6-14.
9. Baarveld F, Visser CA, Kollen BJ, Backx FJ. Sports-related injuries in primary health care. *Fam Pract* 2011;28(1):29-33.
10. Anonymous. Factsheet Sportblessures: Consument en Veiligheid, 2009.
11. Heintjes EM, Berger MY, Koes BW, Bierma-Zeinstra SM. Knee disorders in primary care: design and patient selection of the HONEUR knee cohort. *BMC Musculoskelet Disord* 2005;6:45.
12. Witvrouw E, Werner S, Mikkelsen C, Van Tiggelen D, Vanden Berghe L, Cerulli G. Clinical classification of patellofemoral pain syndrome: guidelines for non-operative treatment. *Knee Surg Sports Traumatol Arthrosc* 2005;13(2):122-30.
13. van Linschoten R, van Middelkoop M, Heintjes EM, Verhaar JAN, Koes BW, Bierma-Zeinstra SMA. Exercise therapy for patellofemoral pain syndrome; a systematic review. submitted.
14. van der Waal JM, Bot SD, Terwee CB, van der Windt DA, Schellevis FG, Bouter LM, et al. The incidences of and consultation rate for lower extremity complaints in general practice. *Ann Rheum Dis* 2006;65(6):809-15.
15. Jordan KP, Kadam UT, Hayward R, Porcheret M, Young C, Croft P. Annual consultation prevalence of regional musculoskeletal problems in primary care: an observational study. *BMC Musculoskelet Disord* 2010;11:144.
16. Breedveldt Boer H.P. KWRC, Spinnewijn W.E.M., Heinen N., Burggraaff H.B., Derks C.J.T., Loogman M.C.M. NHG-Standaard Niet-traumatische knieproblemen bij kinderen en adolescenten (eerste herziening). *Huisarts Wet* 2009;52((7)):332-41.
17. van Middelkoop M, van Linschoten R, Berger MY, Koes BW, Bierma-Zeinstra SM. Knee complaints seen in general practice: active sport participants versus non-sport participants. *BMC Musculoskelet Disord* 2008;9:36.
18. Fredericson M, Yoon K. Physical examination and patellofemoral pain syndrome. *Am J Phys Med Rehabil* 2006;85(3):234-43.
19. Nijs J, Van Geel C, Van der Auwera C, Van de Velde B. Diagnostic value of five clinical tests in patellofemoral pain syndrome. *Man Ther* 2006;11(1):69-77.

20. Laprade J, Culham E. Radiographic measures in subjects who are asymptomatic and subjects with patellofemoral pain syndrome. *Clin Orthop Relat Res* 2003(414):172-82.
21. Keser S, Savranlar A, Bayar A, Ege A, Turhan E. Is there a relationship between anterior knee pain and femoral trochlear dysplasia? Assessment of lateral trochlear inclination by magnetic resonance imaging. *Knee Surg Sports Traumatol Arthrosc* 2008;16(10):911-5.
22. Cirkel JW, Klaassen WRC, Kunst JA, Aarns TEM, Plag EC, Goudswaard AN, et al. Niet-Traumatische knieproblemen bij kinderen en adolescenten; NHG-Standaard. *Huisarts Wet* 1998;41:246-251.
23. Cottrell E, Roddy E, Foster NE. The attitudes, beliefs and behaviours of GPs regarding exercise for chronic knee pain: a systematic review. *BMC Family Practice* 2010;11(4).
24. Sandow MJ, Goodfellow JW. The natural history of anterior knee pain in adolescents. *J Bone Joint Surg Br* 1985;67(1):36-8.
25. Kannus P, Natri A, Paakkala T, Jarvinen M. An outcome study of chronic patellofemoral pain syndrome. Seven-year follow-up of patients in a randomized, controlled trial. *J Bone Joint Surg Am* 1999;81(3):355-63.
26. Blond L, Hansen L. Patellofemoral pain syndrome in athletes: a 5.7-year retrospective follow-up study of 250 athletes. *Acta Orthop Belg* 1998;64(4):393-400.
27. Collins N, Crossley K, Beller E, Darnell R, McPoil T, Vicenzino B. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *Bmj* 2008;337:a1735.
28. Clark DI, Downing N, Mitchell J, Coulson L, Syzpryt EP, Doherty M. Physiotherapy for anterior knee pain: a randomised controlled trial. *Ann Rheum Dis* 2000;59(9):700-4.
29. Heintjes E, Berger MY, Bierma-Zeinstra SM, Bernsen RM, Verhaar JA, Koes BW. Exercise therapy for patellofemoral pain syndrome. *Cochrane Database Syst Rev* 2003(4):CD003472.
30. Bierma-Zeinstra SM, Verhagen AP. Osteoarthritis subpopulations and implications for clinical trial design. *Arthritis Res Ther* 2011;13(2):213.
31. van Linschoten R, van Middelkoop M, Berger MY, Heintjes EM, Verhaar JAN, Willemsen S, et al. Supervised exercise therapy versus usual care for patellofemoral pain syndrome: an open label randomised controlled trial. *BMJ* 2009;339:b4074.
32. Crossley KM, Bennell KL, Cowan SM, Green S. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil* 2004;85(5):815-22.
33. Crossley K, Bennell K, Green S, Cowan S, McConnell J. Physical therapy for patellofemoral pain: a randomized, double-blinded, placebo-controlled trial. *Am J Sports Med* 2002;30(6):857-65.
34. Kamper SJ, Stanton TR, Williams CM, Maher CG, Hush JM. How is recovery from low back pain measured? A systematic review of the literature. *Eur Spine J* 2011;20(1):9-18.
35. Bombardier C. Outcome assessments in the evaluation of treatment of spinal disorders: summary and general recommendations. *Spine (Phila Pa 1976)* 2000;25(24):3100-3.
36. Cohen J. *Statistical power analysis for behavioural sciences*. New York: Academic Press, 1977.
37. Bjordal JM, Ljunggren AE, Klovning A, Slordal L. Non-steroidal anti-inflammatory drugs, including cyclo-oxygenase-2 inhibitors, in osteoarthritic knee pain: meta-analysis of randomised placebo controlled trials. *Bmj* 2004;329(7478):1317.
38. Lun VM, Wiley JP, Meeuwisse WH, Yanagawa TL. Effectiveness of patellar bracing for treatment of patellofemoral pain syndrome. *Clin J Sport Med* 2005;15(4):235-40.
39. Loudon JD, Gajewski B, Goist-Foley HL, Loudon KL. The effectiveness of exercise in treating patellofemoral-pain syndrome. *J Sport Rehabil*. 2004;13:323-342.
40. McCarthy CJ, Mills PM, Pullen R, Richardson G, Hawkins N, Roberts CR, et al. Supplementation of a home-based exercise programme with a class-based programme for people with osteoarthritis

- of the knees: a randomised controlled trial and health economic analysis. *Health Technol Assess* 2004;8(46):iii-iv, 1-61.
41. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, et al. OARSIS recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. *Osteoarthritis Cartilage* 2010;18(4):476-99.
 42. Fransen M, McConnell S. Exercise for osteoarthritis of the knee. *Cochrane Database Syst Rev* 2008(4):CD004376.
 43. Fransen M, McConnell S, Hernandez-Molina G, Reichenbach S. Exercise for osteoarthritis of the hip. *Cochrane Database Syst Rev* 2009(3):CD007912.
 44. Hayden JA, van Tulder MW, Malmivaara AV, Koes BW. Meta-analysis: exercise therapy for nonspecific low back pain. *Ann Intern Med* 2005;142(9):765-75.
 45. van Middelkoop M, Rubinstein SM, Verhagen AP, Ostelo RW, Koes BW, van Tulder MW. Exercise therapy for chronic nonspecific low-back pain. *Best Pract Res Clin Rheumatol* 2010;24(2):193-204.
 46. van Middelkoop M, Rubinstein SM, Kuijpers T, Verhagen AP, Ostelo R, Koes BW, et al. A systematic review on the effectiveness of physical and rehabilitation interventions for chronic non-specific low back pain. *Eur Spine J* 2011;20(1):19-39.
 47. Magnussen RA, Dunn WR, Thomson AB. Nonoperative treatment of midportion Achilles tendinopathy: a systematic review. *Clin J Sport Med* 2009;19(1):54-64.
 48. Holmich P, Uhrskou P, Ulnits L, Kanstrup IL, Nielsen MB, Bjerg AM, et al. Effectiveness of active physical training as treatment for long-standing adductor-related groin pain in athletes: randomised trial. *Lancet* 1999;353(9151):439-43.
 49. Bender T, Nagy G, Barna I, Tefner I, Kadas E, Geher P. The effect of physical therapy on beta-endorphin levels. *Eur J Appl Physiol* 2007;100(4):371-82.
 50. Rethorst CD, Landers DM, Nagoshi CT, Ross JT. Efficacy of exercise in reducing depressive symptoms across 5-HTTLPR genotypes. *Med Sci Sports Exerc* 2010;42(11):2141-7.
 51. Astrand P-O, Rodahl K. *Textbook of Work Physiology*. 3rd Edition. ed. New York: Mc-Graw – Hill, 1986.
 52. Sun HB. Mechanical loading, cartilage degradation, and arthritis. *Ann N Y Acad Sci* 2011;1211:37-50.
 53. Fredericson M, Jennings F, Beaulieu C, Matheson GO. Stress fractures in athletes. *Top Magn Reson Imaging* 2006;17(5):309-25.
 54. Zhang J, Wang JH. Mechanobiological response of tendon stem cells: implications of tendon homeostasis and pathogenesis of tendinopathy. *J Orthop Res* 2009;28(5):639-43.
 55. Khan KM, Scott A. Mechanotherapy: how physical therapists' prescription of exercise promotes tissue repair. *Br J Sports Med* 2009;43(4):247-52.
 56. Powers CM, Doubleday KL, Escudero C. Influence of patellofemoral bracing on pain, knee extensor torque, and gait function in females with patellofemoral pain. *Physiother Theory Pract* 2008;24(3):143-50.
 57. Koeter S, Horstmann WG, Wagenaar FC, Huysse W, Wymenga AB, Anderson PG. A new CT scan method for measuring the tibial tubercle trochlear groove distance in patellar instability. *Knee* 2007;14(2):128-32.
 58. Sanchis-Alfonso V. *Anterior Knee Pain and Patellar Instability*. London: Springer Verlag, 2006.
 59. Clark AM, Haykowsky M, Kryworuchko J, MacClure T, Scott J, DesMeules M, et al. A meta-analysis of randomized control trials of home-based secondary prevention programs for coronary artery disease. *Eur J Cardiovasc Prev Rehabil* 2010;17(3):261-70.

60. Guidon M, McGee H. Exercise-based interventions and health-related quality of life in intermittent claudication: a 20-year (1989-2008) review. *Eur J Cardiovasc Prev Rehabil* 2010;17(2):140-54.
61. Pedersen BK, Saltin B. Evidence for prescribing exercise as therapy in chronic disease. *Scand J Med Sci Sports* 2006;16 Suppl 1:3-63.
62. Carlsson AM, Werner S, Mattlar CE, Edman G, Puukka P, Eriksson E. Personality in patients with long-term patellofemoral pain syndrome. *Knee Surg Sports Traumatol Arthrosc* 1993;1(3-4):178-83.
63. Thomee P, Thomee R, Karlsson J. Patellofemoral pain syndrome: pain, coping strategies and degree of well-being. *Scand J Med Sci Sports* 2002;12(5):276-81.
64. Jensen R, Hystad T, Baerheim A. Knee function and pain related to psychological variables in patients with long-term patellofemoral pain syndrome. *J Orthop Sports Phys Ther* 2005;35(9):594-600.
65. Barton CJ, Munteanu SE, Menz HB, Crossley KM. The efficacy of foot orthoses in the treatment of individuals with patellofemoral pain syndrome: a systematic review. *Sports Med* 2010;40(5):377-95.
66. Davis IS, Powers CM. Patellofemoral pain syndrome: proximal, distal, and local factors, an international retreat, April 30-May 2, 2009, Fells Point, Baltimore, MD. *J Orthop Sports Phys Ther* 2010;40(3):A1-16.
67. Collins NJ, Crossley KM, Darnell R, Vicenzino B. Predictors of short and long term outcome in patellofemoral pain syndrome: a prospective longitudinal study. *BMC Musculoskelet Disord* 2010;11:11.
68. Barton CJ, Levinger P, Menz HB, Webster KE. Kinematic gait characteristics associated with patellofemoral pain syndrome: a systematic review. *Gait Posture* 2009;30(4):405-16.
69. Boling MC, Padua DA, Marshall SW, Guskiewicz K, Pyne S, Beutler A. A prospective investigation of biomechanical risk factors for patellofemoral pain syndrome: the Joint Undertaking to Monitor and Prevent ACL Injury (JUMP-ACL) cohort. *Am J Sports Med* 2009;37(11):2108-16.

SUMMARY

The aim of thesis was to study the effects of exercise therapy on patellofemoral pain syndrome (PFPS) in relation to other conservative strategies. Besides, this thesis describes the present strategies for PFPS in general practice.

In **Chapter 2** observational, prospective data on PFPS in general practice are presented. In this study the baseline characteristics, initial treatment and outcome for patients with PFPS are compared with patients who suffer from non-specific knee complaints (NSKC). Patients were followed for one year and re-questioned at six years. At baseline PFPS patients have a longer duration of knee complaints, present more bilateral complaints and show more pain at the patellar edge than patients with NSKC. The general practitioners choose more often an active approach for the PFPS patients compared to the NSKC patients. After one year and six year follow up the PFPS group showed significantly less recovery than the NSKC group (44.4% vs. 65.8% at one year and 60% vs. 83.3% at six years). The diagnosis of PFPS in this study was set by the GP. When using a set of defined clinical variables which are thought to be specific for PFPS it showed that in 60% of cases there was an overlap between the GP-diagnosis and the diagnosis by criteria.

It is concluded that recovery rates for PFPS are low after one and six years compared with NSKC and since there is just 60% overlap in diagnosis of PFPS it indicates the difficulty of diagnosing PFPS in general practice. Furthermore the diagnosis of the GP seems related with the initial policy chosen for these patients.

Chapter 3 describes the study on knee complaints in general practice in which active sport participants are compared with non-sport participants. The study followed 421 athletes and 388 non-athletes for one year. At initial consultation acute distortions of the knee were significantly more diagnosed in athletes than in non-athletes ($p=0.04$). Further, the initial treatment policy to 'go easy on the knee' was significantly more advised for athletes than for non-athletes ($p<0.01$). However no differences were found in the number of referrals and medication prescribed by the GP. Although small, the medical consumption was significantly higher among athletes. Referral to the physiotherapist was more frequent for athletes than for non-athletes. However, no differences for medical consumption between groups were found when the analysis was adjusted for 'revisiting the GP'.

In conclusion in this study no major differences in the diagnosis and prognosis of knee complaints between athletes and non-athletes presented to the GP were found. There was however a trend towards an increased medical consumption among athletes while functional disability and pain were lower than among the non-athletes.

In **Chapter 4** the design of a randomized clinical trial on exercise therapy for PFPS is described. Based on a systematic review of the literature it was concluded that to merit

the effect of exercise therapy a trial based on correct methodological concept needed to be executed.

The study was designed as an open label randomized controlled trial with an intervention group undergoing 3 months of protocolized exercise therapy including six weeks of initial supervision by a physical therapist. The control group received 'usual care' as per the Dutch guidelines for PFPS in general practice. Patients were recruited from general practices and sport medicine centers. The primary outcome measures were pain, knee function and perception of recovery after 3 months and 12 months of follow up to be measured by self-reporting. The secondary outcome measurements included an economic evaluation. A cost-utility analysis was performed that expresses health improvements in Quality Adjusted Life Years (QALYs) and incorporated direct medical costs and productivity costs.

Based on previous studies it was calculated that 136 patients should be enrolled in the study for the detection of clinical significant differences between groups and that the recruitment period expected to last 15 months.

In **chapter 5** the results of a randomized controlled trial on exercise therapy for PFPS are presented. A total of 131 participants were included in the study: 65 in the intervention group and 66 in the control group. After 3 months, the intervention group showed better outcomes than the control group with regard to pain at rest, pain on activity and function. At 12 months, the intervention group continued to show better outcomes than the control group with regard to pain but not to function. The effect size for pain ranged from 0.47 to 0.56 at 3 and 12 months while the effect size for function was 0.34 at 3 months.

A higher proportion of patients in the exercise group than in the control group reported recovery (41.9% v 35.0% at 3 months and 62.1% v 50.8% at 12 months), although the differences in self-reported recovery between the two groups were not statistically significant. Predefined subgroup analyses revealed that patients recruited by sport physicians ($n=30$) did not benefit from the intervention, whereas those recruited by general practitioners ($n=101$) showed significant and clinically relevant differences in pain and function in favour of the intervention group.

From the results in this study it is concluded that supervised exercise therapy results in less pain and better function at short term and long term follow-up compared with usual care in patients with patellofemoral pain syndrome in general practice. Exercise therapy does not produce a significant difference in the rate of self-reported recovery.

Chapter 6 presents the results of the cost-utility analysis concerning supervised exercise therapy versus 'usual care' in primary care and sports medicine. The data of 131 patients enrolled in the study show that the annual direct medical costs per patient were significantly higher for the intervention group (€434) compared with the control group

(€299). This was mainly caused by additional physiotherapy visits. The average annual societal costs per patient were significantly lower in the intervention group (€1011 vs. €1.166). Productivity costs were the largest cost component, in particular costs due to reduced efficiency at paid work which were responsible for 47% and 56% of the total costs in the intervention and control group respectively. Patients in the intervention group experienced a slightly, but not significantly, higher quality of life (0.8722 vs. 0.8617).

Taking into account the wide confidence intervals for the CE-ratio's in this study it appears that exercise therapy is cost effective as compared with "usual care."

Chapter 7 describes the current concept of patellofemoral pain syndrome.

The chapter describes the different patho-physiological theories which relate to the etiology of PFPS. The differences and similarities between the mechanical, the neuro-muscular and the biological model are described. The diagnosis of PFPS - which is mainly based on anamnestic elements and by excluding other pathological issues- and the value of additional examination are explained. Treatment of PFPS is predominantly conservative though for some specific cases surgery may be chosen. The development of new radiological techniques may help to visualize anatomical abnormalities that can cause patellofemoral maltracking.

It is concluded that patellofemoral pain syndrome is common and its complaints are difficult to treat. The natural evolution of the syndrome might be less favorable than previously suggested.

Chapter 8 presents the results of a systematic review on the additional effect of orthotic devices over exercise therapy on pain and function for PFPS.

A systematic literature search was conducted in MEDLINE, CINAHL, EMBASE, Cochrane and PEDro up to January 2010. Eight randomized controlled trials and controlled clinical trials of patients diagnosed with PFPS evaluating a clinically relevant outcome were included. Treatment had to include exercise therapy combined with orthotics, compared with an identical exercise program with or without sham orthotics. The data were summarized using a best evidence synthesis.

From the review it is concluded that there is no additional effect of knee braces over exercise therapy regarding pain and function outcomes for patients with PFPS. The evidence for the additional effect of tape and foot orthotics on exercise therapy is conflicting when compared with exercise only. The combination of tape and exercise seems to be preferable when compared with placebo tape and exercise. These conclusions are based on a small number of high risk of bias studies. More studies of high methodological quality are needed to draw definitive conclusions.

In **Chapter 9** the results of a systematic review on exercise therapy for PFPS are described.

The objective of the study was to assess the effects of exercise therapy which target at reducing knee pain and improving knee function for patients with PFPS. For this evaluation the Cochrane Bone, Joint and Muscle Trauma Group Specialized Register (December 2009), the Cochrane Central Register of Controlled Trials (The Cochrane Library 2009, Issue 4), MEDLINE, EMBASE, and other databases were searched up to December 2009.

In the review 23 randomized controlled trials of exercise therapy with 1472 participants suffering from patellofemoral pain syndrome were included. The primary outcomes were pain, knee function and recovery.

The results of the review show that at short term and long term exercise therapy is effective on pain reduction compared to no intervention ('wait and see strategy'). At short term exercise therapy is also effective on improving knee function but at long term these effects are not significant. The effect of exercise therapy is however not clearly reflected on the outcome measures for recovery.

At short term exercise therapy is more effective on pain reduction than other conservative, non-pharmacological strategies (brace, tape, insoles).

No differences in effect were found when exercise strategies for quadriceps muscle strengthening were compared with other exercise strategies (VMO feedback retraining, closed kinetic chain, open kinetic chain, hip abductor exercise or abdominal muscle exercise).

The conclusion of this review is that that exercise therapy is effective on reducing pain and improving function for patients with patellofemoral pain syndrome.

Chapter 10 is a general discussion and reflects on the above executed studies and chapters. The chapter gives a direction for future studies and indicates to the various factors which may contribute to the etiology and/or prognosis of PFPS. Identifying prognostic factors and to study the effect of exercise therapy for subgroups is recommended.

It is concluded from above mentioned studies that exercise therapy can be used as an initial therapeutic approach for PFPS in primary care instead of a 'wait and see' strategy. However, since the recovery rates are still moderate after one year the expectations of physicians and patients on outcome should be realistic.

SAMENVATTING

Het doel van dit proefschrift was om de effecten van oefentherapie bij het patellofemorale pijnsyndroom (PFPS) in relatie tot andere conservatieve strategieën te bestuderen. Daarnaast beschrijft dit proefschrift de huidige strategieën in de eerste lijn voor het PFPS.

In **Hoofdstuk 2** worden observationele, prospectieve gegevens over het PFPS in de huisartsenpraktijk gepresenteerd. In deze studie worden de kenmerken bij aanvang van de klachten, de initiële behandelstrategie en de uitkomst voor patiënten met het PFPS vergeleken met de gegevens van patiënten die niet-specifieke knieklachten (NSKC) hebben. Patiënten zijn gedurende een jaar gevolgd en zijn na 6 jaar opnieuw ondervraagd. Tijdens de start van de studie blijken PFPS patiënten langer knieklachten te hebben, vaker bi-laterale knieklachten te hebben en vaker pijn aan te geven aan de randen van de knieschijf. Huisartsen kiezen bij PFPS patiënten vaker voor een actieve behandelstrategie dan bij NSKC. Na één jaar en zes jaar follow-up vertoont de groep PFPS patiënten een significant lager herstel dan de NSKC groep (44.4% vs. 65.8% na één jaar en 60% vs. 83.3% na zes jaar). De diagnose PFPS in de studie werd gesteld door de huisartsen. Indien gebruik werd gemaakt van een set van kenmerken die geacht wordt specifiek te zijn voor het PFPS dan bleek er 60% overlap te bestaan in de diagnose volgens de criteria en die volgens de huisarts.

De conclusie van de studie is dat het herstelpercentage voor PFPS na één en zes jaar laag is ten opzichte van NSKC en dat met slechts 60% overlap in de diagnose van de huisarts en volgens de criteria, de moeilijkheid van het stellen van de diagnose in de huisartsenpraktijk wordt aangetoond.

Hoofdstuk 3 beschrijft de verschillen in type knieklachten tussen sporters en niet-sporters in de huisartsenpraktijk. Daarnaast worden ook de verschillen in beleid van de huisarts, de medische consumptie en de uitkomst na één jaar geanalyseerd. Patiënten die de huisarts voor de eerste keer bezochten in verband met knieklachten werden uitgenodigd deel te nemen aan de studie. Uit de totale studie populatie ($n=1068$) van het HONEUR knie cohort werden sporters ($n=421$) en niet-sporters ($n=388$) geselecteerd. Acute distorsies werden door de huisarts significant meer gediagnosticeerd bij sporters dan bij niet-sporters ($p=0.04$). Verder werden sporters vaker geadviseerd om 'het rustig aan te doen' met de knie dan niet-sporters ($p<0.01$). De medische consumptie onder sporters was hoger dan onder niet-sporters. Er werden echter geen verschillen gevonden tussen sporters en niet-sporters betreffende het herstel van de knieklachten na één jaar follow-up. Er kan dus geconcludeerd worden dat er nauwelijks verschillen zijn in type knieklachten, gepresenteerd in de huisartsenpraktijk, tussen sporters en niet-sporters. Sporters werden echter vaker geadviseerd om de knie 'te sparen' en 'het rustig aan te doen' in vergelijking met niet-sporters. Verder was er een positieve trend in medische consumptie van de sporters terwijl de functionele beperkingen en de pijn

minder waren in vergelijking met de niet-sporters. Ondanks de adviezen van de huisarts en de hogere medische consumptie van de sporters was er geen verschil in herstel na één jaar follow-up.

In **Hoofdstuk 4** wordt het ontwerp van een gerandomiseerde klinische studie voor oefentherapie bij het PFPS beschreven. Gebaseerd op een systematisch onderzoek van de literatuur werd geconcludeerd dat om de effecten van oefentherapie op hun waarde te schatten een studie – gebaseerd op de juiste methodologische grondslagen – diende te worden uitgevoerd.

De studie werd opgezet als een niet-geblindeerde, gerandomiseerde interventiestudie met controlegroep. De interventiegroep werd gedurende drie maanden onderworpen aan geprotocolleerde oefentherapie, waarbij de eerste zes weken een fysiotherapeut instructie gaf. De controle groep kreeg de ‘gebruikelijke zorg’ zoals die beschreven staat in de standaard ‘niet acute knieklachten bij adolescenten’ van de het Nederlands Huisartsen Genootschap (NHG). Patiënten werden geworven in huisartspraktijken en sportmedische centra. De primaire uitkomstmaten waren pijn, kniefunctie en subjectief herstel na drie en twaalf maanden follow-up en werden vastgelegd door middel van zelfrapportage. De secundaire uitkomstmaten bevatten economische evaluaties. Een kosten-baten analyse werd uitgevoerd die verbeteringen van gezondheid vastlegt in ‘Kwaliteit van Levensjaren’ (QALYs) en bevatte directe medische kosten en productiviteitskosten.

Gebaseerd op eerdere studies werd er vanuit gegaan dat er 136 patiënten dienden te worden gerekruteerd om klinisch significante verschillen tussen de groepen te kunnen aantonen. De totale rekruteringsperiode werd geschat op 15 maanden.

In **Hoofdstuk 5** worden de resultaten van een gerandomiseerde studie naar de effecten van oefentherapie bij het PFPS gepresenteerd. In totaal werden 131 deelnemers in de studie geïnccludeerd: 65 in de interventiegroep en 66 in de controlegroep. Na drie maanden had de interventie groep een significant betere uitkomst met betrekking tot pijnreductie in rust, pijnreductie bij inspanning en kniefunctie. Na twaalf maanden liet de de interventiegroep nog steeds betere resultaten zien dan de controlegroep met betrekking tot pijnscores maar niet meer voor de functiescores. De effectmaten voor pijnreductie varieerden van 0.47 tot 0.56 tijdens 3 en 12 maanden follow-up. De effectmaat voor functie bedroeg 0.34 na 3 maanden.

Een groter deel van de patiënten in de oefengroep dan in de controlegroep rapporteerde herstel (41.9% vs 35.0% na 3 maanden en 62.1% vs 50.8% na 12 maanden), hoewel de verschillen tussen de groepen niet significant was. Analyse van vooraf bepaalde subgroepen liet zien dat patiënten die werden gerekruteerd door de sportarts (n=30) niet sterker verbeterden door het oefenprogramma, terwijl patiënten die door de huisarts (n=101) werden aangemeld significante en klinisch relevante verbeteringen in pijn- en functiescores lieten zien ten opzichte van de controle groep..

Op basis van de resultaten van deze studie wordt geconcludeerd dat gesuperviseerde oefentherapie resulteert in grotere pijnvermindering en sterkere functieverbetering op korte en lange termijn vergeleken met 'gebruikelijke zorg' voor het patellofemoraal pijnsyndroom in de huisartsenpraktijk. Oefentherapie leidt niet tot significante verschillen in subjectief herstel tussen beide patiëntengroepen.

Hoofdstuk 6 toont de resultaten van de kosten-effectiviteits analyse die werd uitgevoerd met betrekking tot gesuperviseerde oefentherapie versus 'gebruikelijke zorg' in de huisartsen – en sportartsenpraktijk. De gegevens van 131 patiënten die in de studie werden geïnccludeerd laten zien dat de jaarlijkse medische kosten per patiënt hoger zijn in de interventiegroep (€434) dan in de controlegroep (€299). Dit werd voornamelijk veroorzaakt door het bezoek aan de fysiotherapeut. De gemiddelde jaarlijkse maatschappelijke kosten waren significant lager in de interventiegroep (€1011 vs. €1166). Productiviteitskosten waren de hoogste kostencomponent, vooral kosten die werden veroorzaakt door verminderde effectiviteit bij betaald werk waren verantwoordelijk voor 47% en 56% van de totale kosten in de interventie en respectievelijk de controle groep. Patiënten in de interventiegroep rapporteerden een klein, maar niet significant verbeterde kwaliteit van leven (0.8722 vs. 0.8617).

Wanneer er rekening wordt gehouden met de grote betrouwbaarheidsintervallen in deze studie lijkt de conclusie gerechtvaardigd dat oefentherapie kosteneffectief is ten opzichte van 'gebruikelijke zorg' bij patiënten met PFPS.

Hoofdstuk 7 beschrijft de huidige inzichten met betrekking tot het patellofemoraal pijnsyndroom.

Het hoofdstuk gaat in op de verschillende pathofysiologische theorieën en de etiologische achtergrond van het PFPS. De verschillen en overeenkomsten tussen het mechanische, het neuro-musculaire en het biologische model worden beschreven. De diagnose patellofemoraal pijnsyndroom, welke hoofdzakelijk is gebaseerd op anamnesticke kenmerken en het uitsluiten van andere kniepathologie alsmede de waarde van aanvullend onderzoek wordt besproken. De behandeling van PFPS is voornamelijk conservatief van aard hoewel voor sommige specifieke gevallen een chirurgische benadering kan zijn aangewezen. De ontwikkeling van nieuwe radiologische technieken kan helpen om anatomische afwijkingen zichtbaar te maken die samenhangen met het foutief sporen ('maltracking') van de knieschijf.

De conclusie van het hoofdstuk is dat patellofemorale pijnklachten veel voorkomen en de klachten vaak moeilijk zijn te behandelen. Het natuurlijk beloop van patellofemoraal pijnsyndroom kan bovendien minder voorspoedig zijn dan eerder werd gedacht.

Hoofdstuk 8 geeft de resultaten van een systematisch literatuuroverzicht naar de aanvullende effecten van orthoses toegevoegd aan oefentherapie op pijn en functie voor het PFPS.

De literatuur werd systematisch doorzocht gebruik makend van MEDLINE, CINAHL, EMBASE, Cochrane en PEDro tot januari 2010. Acht gerandomiseerde en klinische studies met een controlegroep die patiënten met het PFPS bestudeerden en een klinisch relevante uitkomst bevatten, werden in het overzicht geïncludeerd. Behandeling diende te bestaan uit oefentherapie gecombineerd met orthoses en werd vergeleken met identieke oefentherapie met of zonder placebo orthoses. De gegevens werden samengevat gebruik makend van 'best evidence synthesis'.

Uit de literatuurstudie kan worden geconcludeerd dat er geen toegevoegd effect is van knie-braces bovenop oefentherapie met betrekking tot pijn en functie bij patiënten met het PFPS. Het bewijs voor aanvullend effect van tape en zooltjes op oefentherapie is conflicterend wanneer vergeleken wordt met oefenen alleen. De combinatie van tape en oefenen lijkt aan te raden wanneer vergeleken wordt met placebo tape en oefenen. Deze conclusies zijn gebaseerd op een klein aantal methodologisch zwakke studies. Er zijn meer studies nodig van hoge methodologische kwaliteit om definitieve conclusies te kunnen trekken.

In **Hoofdstuk 9** worden de resultaten van een systematisch literatuuronderzoek naar oefentherapie voor het PFPS beschreven.

Het doel van de studie was na te gaan wat de effecten van oefentherapie zijn op het verminderen van pijn en het verbeteren van kniefunctie voor patiënten met PFPS. Voor deze evaluatie werd gebruik gemaakt van bronnen uit de Cochrane Bone, Joint and Muscle Trauma Group Specialized Register (December 2009), de Cochrane Central Register of Controlled Trials (Cochrane Library 2009, Issue 4), MEDLINE, EMBASE, alsmede andere bronnen welke werden doorzocht tot december 2009. In het literatuuroverzicht werden 23 studies geïncludeerd met in totaal 1472 patiënten die klachten hadden passend bij het PFPS. De primaire uitkomstmaten waren pijn, kniefunctie en herstel.

De resultaten van de literatuurstudie laten zien dat op korte termijn en lange termijn oefentherapie effectief is op het verminderen van pijn ten opzichte van geen interventie ('afwachtend beleid'). Op korte termijn is oefentherapie ook effectief op het verbeteren van de kniefunctie hoewel op lange termijn deze effecten niet significant meer zijn. De effecten van oefentherapie worden echter niet duidelijk weerspiegeld in de uitkomstmaat 'herstel'.

Op de korte termijn is oefentherapie effectiever op pijnvermindering dan andere conservatieve, niet-farmacologische maatregelen (bandages, tape, zooltjes).

Er worden geen verschillen in effect gevonden als oefenstrategieën, gericht op het versterken van de grote bovenbeenspieren (Mm quadriceps), worden vergeleken met andere oefenvormen (selectieve VMO training, gesloten keten-oefenen, open keten-oefenen, heup-abductieoefeningen of buikspieroefeningen).

De conclusie van deze literatuurstudie is dat oefentherapie effectief is op het verminderen van pijn en het verbeteren van functie bij patiënten met het patellofemorale pijnsyndroom.

Hoofdstuk 10 is de algemene discussie en geeft een beschouwing op bovenstaande studies en hoofdstukken. Het hoofdstuk geeft richting aan studies welke in de toekomst kunnen worden uitgevoerd en benadrukt de verschillende factoren die kunnen bijdragen aan de etiologie en/of prognose van het PFPS. Het wordt aanbevolen om prognostische factoren te identificeren en om het effect van oefentherapie in specifieke subgroepen te bestuderen.

Uit de bovenstaande studies in dit proefschrift wordt geconcludeerd dat oefentherapie kan worden aangewend als initiële therapeutische strategie voor het PFPS in de eerste lijn in plaats van een afwachtend beleid. Echter, omdat het subjectief herstel van PFPS na een jaar als redelijk wordt ervaren, dienen zowel de arts/therapeut als de patiënt een realistische verwachting van de effecten van oefentherapie hebben.

CURRICULUM VITAE

Robbart van Linschoten is geboren op 10 november 1961 in Son en Breugel. Na het behalen van het VWO diploma aan het Comenius College in Capelle aan den IJssel ging hij in 1980 Geneeskunde studeren aan de Erasmus Universiteit te Rotterdam. Reeds vroeg in zijn medische opleiding raakte hij geïnteresseerd in de sportgeneeskunde wat resulteerde in een onderzoeksstage en assistenschap bij de sportmedische afdeling van de Nederlandse Sport Federatie (hoofd: Drs. Leo Heere). In 1989 startte hij zijn opleiding tot sportarts onder auspiciën van het NIOS met deelstages Fysiologie aan het Janus Jongbloed Research Centrum in Utrecht (opleider Dr. Wytse Erich), Cardiologie op het Thoraxcentrum van het ErasmusMC (opleider Prof. Dr. Maarten Simoons) en Orthopedie aan het ErasmusMC (opleider Prof. Dr. Bert van Linge). In 1993 volgde inschrijving in het register Sportgeneeskunde van de SGRC en werd hij aangesteld als bondsarts bij de Koninklijke Nederlandse Zwembond en als medisch coördinator van het Sportmedisch Adviescentrum te Rotterdam. In de periode 1989 tot 2009 was hij clubarts in het betaald voetbal bij achtereenvolgens Dordrecht'90 en Feyenoord Rotterdam. De start van zijn promotie-onderzoek vond plaats in 2004 onder begeleiding van Prof. Dr. Sita Bierma-Zeinstra en Prof. Dr. Jan Verhaar. Sinds 2010 is hij werkzaam als Sports Medicine Consultant bij Aspetar, Qatar Orthopedic and Sports Medicine Hospital in Doha (CMO: Prof. Dr. Gerard Saillant).

Hij is getrouwd met Mirjam Peters en hebben drie kinderen: Reinier, Juriaan en Karlijn

DANKWOORD

Hoogeleerde vrouw Bierma-Zeinstra, beste Sita; ergens in 2004 werden we aan elkaar voorgesteld. Jouw 'HONNEUR knieklachten cohort' was juist van start gegaan en mijn interesse in het patellofemorale pijn syndroom in een jonge en sportieve populatie werd al jaren gevoed door mijn werk als sportarts. Ik ben je zeer erkentelijk voor de kans die je mij hebt geboden om mijn latente wetenschappelijke interesse in dit onderwerp uit te diepen. Met mijn achtergrond als praktisch werkzame dokter viel het niet mee om weer aansluiting te krijgen met de laatste ontwikkelingen voor het opzetten van een goede klinische trial en vooral het opschrijven van de resultaten. Heel hartelijk dank voor je geduld en positieve bijdragen in dit traject.

Hoogeleerde heer Verhaar; beste Jan; onze professionele relatie dateert alweer uit 1996 toen jij als nieuwe hoogleraar orthopedie aan het ErasmusMC werd aangesteld. Vanaf het begin heb je namens de afdeling orthopedie de sportgeneeskunde actief ondersteund. Dit deed je door je in te zetten voor de sportrefereeravonden en ook door de poli orthopedie toegankelijk te houden voor de sporters - van amateur tot topnivo - in de regio. Ik weet dat je zeer kritisch bent op het consumentengedrag van de sporter en zijn begeleiders, maar waardeer je constructieve bijdragen voor de sportgeneeskunde in het algemeen. Ik wil je dan ook hartelijk danken voor je bereidheid om als promotor van mijn proefschrift op te treden.

Geachte vrouw van Middelkoop, beste Marienke; 'Wat goed is, komt snel' is een gezegde in de sportwereld en zo heb ik dat met jou ook ervaren. Werd je in 2004 nog aangetrokken als 'mijn' onderzoeksassistent voor de PEX-studie, zo passeerde je in 2008 al de finishlijn door je eigen promotie af te ronden. Met jouw achtergrond als bewegingswetenschapper en zeer bedreven in de data-analyses kon ik mij eindelijk na 20 jaar over de drempel van de biostatistiek heenzetten! Ook je heldere formulering van de begrippen risikofactoren en prognostische factoren hebben mijn 'luiheid' over dit onderwerp weten af te schudden. Heel hartelijk dank voor de geweldige ondersteuning van mijn proefschrift - ik durf de stelling aan dat het zonder jouw hulp niet tot stand was gekomen (stelling 12?) en natuurlijk voor de niet wetenschappelijke uitweidingen over het voetbal en schaatsen op de Westzeedijk.

Hoogeleerde heer Koes, beste Bart; oorspronkelijk was je mijn eerste promotor, maar met 3 hoogleraren op de bok werd het een beetje druk op de wagen. Jouw bijdragen aan mijn manscripten weet ik zeer op waarde te schatten en vooral de positieve aansporingen hebben iedere keer weer een zetje gegeven in de goede richting.

Naast mijn directe begeleiders wil ik hierbij ook anderen bedanken die een rol hebben gespeeld in de reis door de wereld van wetenschap en publiceren gedurende de laatste jaren.

Dank aan Edith Heintjes die het raamwerk leverde van de PEX-studie en door wie ik ook kon voortbouwen op de review naar de effecten van oefentherapie en het patellofemorale pijnsyndroom.

Dank aan alle huisartsen en fysiotherapeuten die participeerden in de PEX-studie en die met elkaar ervoor zorgden dat er voldoende patiënten werden geïncludeerd en dat zij onder deskundige leiding konden oefenen.

Dank aan mijn voormalige collega's van de medische staf bij Feyenoord die mij voorzichtig kwamen storen met de alledaagse voetbalproblemen van het elftal terwijl ik moeizaam de analyses probeerde te doorgronden. Speciale dank aan Marcel die graag wilde figureren als model voor het oefenboek.

Dank aan mijn kamergenoten – hoewel mijn bureau eerder virtueel was - op de Westzeedijk – de gesprekken waren geanimeerd en reikten verder dan alleen de wetenschap .

Dank aan Rene, de vliegende keep op huisartsgeneeskunde, die, ook al woon ik op 6000 km afstand, mijn connectie met de buitenwereld intact houdt.

Dank ook aan alle anderen die bewust of onbewust een rol hebben gespeeld in de totstandkoming van dit boekje.

Tenslotte, dank aan de belangrijkste personen in mijn leven. Lieve Mirjam, al heel veel jaar ben je mijn vaste en overtuigde volger op het kronkelige pad van de sportgeneeskunde. Ook mijn promotietraject heb je onvoorwaardelijk gesteund en daar wellicht nog meer vertrouwen in gehad dan ik zelf op bepaalde momenten. Zoals je weleens zegt 'we zijn een business-unit' en ik hoop dat we nog mooie zaken gaan beleven!

Lieve Reinier, Juriaan en Karlijn, er waren vele zondagen dat ik zelfs het vlees niet kwam snijden, maar jullie interesse in mijn vorderingen en het uiteindelijke resultaat hebben meegeholpen om het af te krijgen. Wat hierna komt.....?

SUMMARY OF PHD TRAINING AND TEACHING ACTIVITIES 2005-2011

General Courses

- 2007 Biostatistics, SPSS training; PAOG, UMC St. Radboud, Nijmegen

Presentations

(Inter) national conferences

- 2005 Exercise therapy and patellofemoral pain syndrome; design of a Randomized Clinical Trial; Dutch Association of Sports medicine, Annual congress
- 2006 Groin complaints in soccer, the role of the sports physician; Annual Sports Medicine Symposium, Groningen
- 2006 Achilles tendinopathy and sports; scientific meeting of the Dutch Association of Football Doctors and Medical Consultants, Amsterdam
- 2007 Clinical examination of the sports hernia; Society of Medicine and Science in Tennis, Annual congress, Antwerp
- 2007 Patellofemoral pain syndrome, the state of science, Annual Sports Medicine Symposium Groningen
- 2007 Patellofemoral pain syndrome, practice, theory and science; Dutch Association of Sports medicine, Annual congress
- 2008 Exercise therapy for Patellofemoral pain syndrome – results after 3 months of follow-up; Dutch Society of Primary Care Physicians, Annual scientific congress, Rotterdam
- 2008 Exercise therapy for Patellofemoral pain syndrome, 3 and 12 months results; Dutch Association of Sports medicine, Annual congress
- 2009 Exercise therapy for Patellofemoral pain syndrome, results of clinical trial; American College of Sports medicine, Annual congress, Seattle
- 2009 Exercise therapy for Patellofemoral pain syndrome, results of clinical trial, Royal Dutch Society of Physical therapist, Annual congress, Amsterdam

Posters

- 2008 Exercise therapy for Patellofemoral pain syndrome – The PEX study: recovery, pain and function after 3 months of follow-up; EULAR, Annual congress, Paris
- 2010 Exercise therapy for Patellofemoral pain syndrome, a systematic review; Dutch Society of Primary Care Physicians, Annual scientific congress, Amsterdam
- 2011 Exercise therapy for Patellofemoral pain syndrome, a systematic review; American College of Sports medicine, Annual congress, Denver

Publications

van Linschoten R, van Middelkoop M, Berger MY, Heintjes EM, Koopmanschap MA, Verhaar JAN, Koes BW, Bierma-Zeinstra SM. The PEX study - Exercise therapy for patellofemoral painsyndrome: design of a randomized clinical trial in general practice and sports medicine [ISRCTN83938749]. *BMC Musculoskelet Disord* 2006 Mar 17;7:31.

van Linschoten R., den Hoed P.T., de JonghA.C. [Guideline 'Chronic Achilles tendinopathy, in particular tendinosis, in sportsmen/sportswomen'] *Ned Tijdschr Geneeskd* 2007;151:2319-24 Dutch

van Middelkoop M, van Linschoten R, Berger MY, Koes BW, Bierma-Zeinstra SMA. Knee complaints seen in general practice: active sport participants versus non-sport participants. *BMC Musculoskeletal Disorders* 2008, 9:36 (19 March 2008)

van Linschoten R., van Middelkoop M., Berger M.Y., Heintjes E.M., Verhaar J.A.N., Willemsen S.P., Koes B.W., Bierma-Zeinstra S.M. Supervised exercise therapy versus usual care for patellofemoral pain syndrome: an open label randomised controlled trial. *BMJ* 2009 Oct 20;339:b407

Tan S.S., van Linschoten R., van Middelkoop M., Koes B.W., Bierma-Zeinstra S.M., Koopmanschap M.A. Cost-utility of exercise therapy in adolescents and young adults suffering from the patellofemoral pain syndrome. *Scand J Med Sci Sports* 2009 Aug 23.

van Linschoten R, van Middelkoop M, Berger MY, Heintjes EM, Verhaar JA, Willemsen SP, Koes BW, Bierma-Zeinstra SM. [Supervised exercise therapy versus usual care for patellofemoral pain syndrome] *Ned TijdschFysiotherapie* 2010;3,100-111 Dutch

van Linschoten R. [Athletes' screening; useful or mandatory?] *Huisarts Wet* 2010;11:627-630. Dutch

van Linschoten R., Koeter S. [Patellofemoral pain: physiotherapy and surgery] *Ned Tijdschr Geneeskd* 2010;154:31;A822. Dutch

van Linschoten R, van Middelkoop M, Berger MY, Heintjes EM, Verhaar JA, Willemsen SP, Koes BW, Bierma-Zeinstra SM. [Supervised exercise therapy versus usual care for patellofemoral pain syndrome]. *Huisarts Wet* 2010; 53(5): 248-256 Dutch

Swart NM, van Linschoten R, Bierma-Zeinstra SM, van Middelkoop M. The additional effect of orthotic devices on exercise therapy for patients with patellofemoral pain syndrome: a systematic review. *Br J Sports Med* 2011 Mar 14. [Epub ahead of print]

van Linschoten R. [Acute pain at the Achilles tendon – an isolated rupture of the distal M. plantaris]. *Sport en Geneeskunde* 2011; 44(5): 34-27 Dutch

Guideline development

2002- 2007 Chairman CBO/VSG multi-disciplinary guideline committee 'Achilles tendinopathy in sports'

Reviewer

The Flemish/Dutch Journal of Sports Medicine (Sport en Geneeskunde)

Board Membership

Chairman, Dutch Institute for Sports Physicians Training (NIOS)

Teaching activities

2001- 2010 Supervisor, sports medicine training, electives, ErasmusMC, Rotterdam

2001- 2010 Guest lecturer, National Training Institute for Plaster Technicians (LOG), ErasmusMC, Rotterdam

2011- present Assistant professor at Weill Cornell Medical College-Qatar

Professional activities

1992 - 1996 Chief Medical Officer, Royal Dutch Swimming Federation

1993 - 2010 Sports medicine physician / co-owner: Sportmedisch Adviescentrum Rotterdam

2000 - 2010 Sports medicine consultant, Ikazia Hospital (Rotterdam), t Lange land Hospital (Zoetermeer), Albert Schweitzer Hospital (Dordrecht)

2001 - 2009 Chief Medical Officer, Feyenoord Rotterdam, professional football

2010 - present Sports Medicine Consultant, Aspetar, Qatar Orthopedic and Sports medicine Hospital, Doha

Society member

Dutch Society of Sports Medicine (VSG), Member of merit

American College of Sports Medicine (ACSM)

Other Publications

Jones C.J., Dworacek B., Ruprecht J., Kesecioglu J., van Linschoten R.. No effect of doxapram during enflurane-nitrous oxide anesthesia. *Acta Anaesthesiol Belg* 1990;41(4):307-11.

van Linschoten R, Backx FJ, Mulder OG, Meinardi H. Epilepsy and sports. *Sports Med* 1990 Jul;10(1):9-19. Review.

van Linschoten R. [A hundred years of orthopedics in the Netherlands. X. Sports injuries] *Ned Tijdschr Geneesk* 1998 Jul 11;142(28):1627-8. Dutch.

Zwart R.C., Bac D.J., van Linschoten R., den Hoed P.T. [Acute ischemic colitis and long distance running] *Geneeskunde en Sport* 2001, 34, 4; 147-149. Dutch

Jolanda Kluin, Pieter T. den Hoed, Robbart van Linschoten, John C. IJzerman, Cornelis J. van Steensel. Endoscopic Evaluation and treatment of Groin pain in the athlete. *Am J Sports Med* 2004; 32; 4, 944-949

van Linschoten R., den Hoed P.T. [Diagnostic image (172). A man with blisters after the use of a cold pack. Cryotrauma caused by frozen cold pack] *Ned Tijdschr Geneesk* 2004, 148(3), 134. Dutch