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CLINICAL PROGNOSTIC FACTORS FOR PATIENTS WITH ANTERIOR KNEE PAIN IN PHYSICAL THERAPY; A SYSTEMATIC REVIEW

AM Panken[1,2]
MW Heymans[3,4]
L van Oort[2]
AP Verhagen[2,5]

ABSTRACT

Background: Although many authors have studied the prognostic factors that may contribute to anterior knee pain, synthesis of the existing evidence has not been performed.

Purpose: The purpose of this systematic review is to summarize and examine existing prognostic models in patients with anterior knee pain that first present to physical therapists (primary care setting).

Design: Systematic review

Method: For this review Pubmed, Embase and Cinahl databases were searched and published papers that reported prognostic models for patients with anterior knee pain that first present to physical therapists (primary care setting) were selected. The authors extracted and summarized the univariate and multivariate predictors and evaluated which predictors consistently appeared to be relevant to pain, function, or recovery.

Results: Nine studies were included. The quality scores of these studies ranged from 9 to 17 positive items out of 21 items included in the assessment for quality. None of the prognostic models were validated internally or externally. Four studies were considered to be of sufficient quality. The authors of these four studies found 14 different predictors significantly related to pain intensity of which seven with limited evidence. Fifteen different predictors were found that were related to function of which seven with limited evidence. Furthermore, strong evidence was found that baseline pain intensity, pain coping and kinesiophobia are of no predictive value for pain, and activity related pain, pain coping and kinesiophobia are of no predictive value for function at follow up.

Conclusions: Because of the low quality of a number of studies and the heterogeneity of the examined variables and outcome measures of most of the studies, only limited evidence for seven predictors related to pain and seven predictors related to function in patients with anterior knee pain in a primary care setting was found.

Level of Evidence: 1b

Keywords: anterior knee pain, patellofemoral pain, physical therapy, prediction, prognostic models, primary care setting.

[1] Physical Therapy Practice Panken, Roermond, The Netherlands
[2] Department of Physical Therapy, AVANS University of Applied Sciences, Breda, The Netherlands
[3] Department of Epidemiology and Biostatistics, EMGO+ Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands
[4] Faculty of Earth and Life Sciences, Section Methodology and Applied Biostatistics, Amsterdam, The Netherlands
[5] Department of General Practice, Erasmus MC, Rotterdam, The Netherlands.

CORRESPONDING AUTHOR
Dr. Arianne P. Verhagen
Erasmus MC, P.O. Box 2040, 3000 CA
Rotterdam, NL
Telephone: 0031-(0)107044109
E-mail: a.verhagen@erasmusmc.nl

INTRODUCTION

Anterior knee pain, also known as patella femoral pain syndrome, is a condition that occurs most commonly in active young adults and adolescents, often leading to functional impairments.[1,2] It is characterized by pain in the anterior part of the knee during and after several physical activities (e.g. bodyweight loading of lower extremities) such as walking, stair climbing/descent, squatting, and sitting with the knees flexed.[3] In athletically active men and women the prevalence of anterior knee pain is reported to be 25%.[4,5] The cumulative incidence of anterior knee pain is reported as 9.7/100 athletes and 1.1/1000 athletic exposures.[6] Females are over two times more likely to develop anterior knee pain compared to males.[7] Despite the high prevalence of AKP in young people, there is no consensus in the literature concerning its pathogenesis, prognosis, and treatment.[8,9,10,11] In a random sample of patients with anterior knee pain, 30-50% of the patients still suffered from symptoms after several years.[8,12]

Knowledge of prognostic factors is essential for physical therapists in order to make treatment decisions.[13,14,15] Some authors have shown that several conservative treatment strategies are effective but most of their studies are small and were conducted in a mixed population of patients with anterior knee pain.[16] This makes it difficult to judge which patients will benefit most from a specific treatment option. Clinical prognostic models may provide important input for more specific treatment decisions. These models combine a number of patient characteristics in order to predict prognosis, and they may be used by the physical therapist to advise the patient or tailor treatment to the need of the patient.[17]

In the past decades, many prognostic models have been developed for patients that first present to physical therapy (primary care setting), including several concerning the prognosis of anterior knee pain. The available prediction models are not yet ready for application in clinical practice because of their preliminary stage of development.[18,19,20] These anterior knee pain models vary with regard to patient populations, outcome measures, and relevant prognostic factors, which hampers the generalizability and implementation of these models in clinical practice.

Therefore, the primary aim of this study was to summarize and examine existing prognostic models in patients with anterior knee pain that first present to physical therapists (primary care setting). The secondary aim was to develop a new prognostic model to be used and validated in primary care physical therapy.

METHODS

Data sources and searches

An extensive search of the databases Pubmed, Embase and Cinahl was performed in 2012 and an additional search conducted in January 2015. The search was based on a previously derived and validated search strategy.[19] The specific search strategy is published; see also Appendix A for details.[19] In addition, the reference lists of the identified studies were screened to detect potentially relevant studies.

Study selection

Studies were selected that included prognostic models concerning patients with anterior knee pain or subgroups of patients with anterior knee pain.[19] A prognostic model (or prediction model) is defined as a model that combined at least two characteristics typical based on multivariable analyses.[17] The authors selected studies that were relevant for physical therapists in primary care, published in English, conducting a multivariable analysis and using Patient Related Outcome Measures (PROMS) such as: pain, function or recovery. Randomized controlled trials (RCT's), case studies, retrospective cohort studies and studies that aimed to develop a questionnaire were excluded.[19] RCT's and case studies use strict in- and exclusion criteria, which limits generalizability, retrospective cohort studies have a high risk of bias and therefore limited evidence and questionnaire studies use a different design and purpose.

Four review authors were involved in the study selection process (AV, MH, LO and GP). First, two review authors independently screened all references found with the initial search on title and abstract. Next, two review authors independently screened the full texts of the potential eligible articles based on the selection criteria. In case of disagreement consensus was achieved or a third independent review author was contacted.

Data extraction

Data extraction included patient characteristics, country and setting in which the study was executed. Also data on the number of predictors used in the univariable analyses as well as the multivariable analyses were extracted. Data extraction included also the reasons why the chosen predictors were selected for the analyses and whether predictor variables were dichotomized. The authors scored which predictors were univariably significant and/or multivariably significant related to the outcome measures and which predictors were presented in the final prognostic models. Next, data on all outcome measures used and the follow-up period were extracted. In addition, authors examined if predictors and outcome measures were measured in a standardized, valid and reliable way; meaning, had the authors of each study measured what was supposed to be measured (valid) and were the measurements consistent (reliable). Finally, the performance of the prognostic models was assessed and the authors determined whether the models were validated.

Outcome measures

The PROMS pain, function and recovery (as defined in the original studies) were considered as the outcome measures of interest for the current systematic review, as these are common and important complaints in patients with anterior knee pain consulting physical therapists.[21]

Methodological quality assessment

There was no uniform criteria list available for use in assessing the methodological quality of studies on prognostic models. Therefore, a criteria list (previously developed by Oort et al.[19]) was used, which was developed based on several existing criteria lists for assessing the quality of prognostic studies in general [Appendix B]. This list consists of 21 items in six domains. All items were scored as 'positive', 'negative' or 'unclear'.

Two review authors independently assessed each included study (GP, LO or AV). They discussed disagreements until consensus was achieved. If necessary, they utilized a third review author (LO or AV) to resolve the disagreement. Consistent with other systematic reviews, the authors decided to use a summary score to get an overall impression of the study quality.[22,23,24,25] To select studies of sufficient quality, the score of 70% or higher of the maximum score, (15 positive items out of the 21 items of the score list) was chosen for the study to be considered of sufficient quality; all other studies were considered low quality studies. To evaluate the robustness of these conclusions a sensitivity analysis was performed on the choice of cut-off point (a score of 14 or 16 positive items instead of 15 out of 21) to determine whether that changed the conclusion based on the studies with sufficient quality.

Performance assessment

The performance of a prediction model is described by four parameters: explained variation (R^2), discrimination, calibration and clinical usefulness.[17,26] When the included studies reported at least one of these four parameters, we scored the item 'performance' in the criteria list as positive.

The R^2 is an overall measure to quantify how well the data fits a statistical model, in other words if enough relevant predictors are included in the model. The higher the R^2, the better the model fits the data and the most relevant predictors are included in the model.[17] Discrimination refers to the extent in which a model is able to distinguish patients with an outcome from patients without this outcome. The most commonly used performance measure to indicate the discriminative ability of prognostic models is the area under the curve (AUC), or C-statistics.[27,26] Model calibration can be described by use of a calibration plot (e.g. a slope), a classification table or the Hosmer-Lemeshow goodness-of-fit test (H-L).[17,26] Finally, clinical usefulness can be described by measures like accuracy, sensitivity, specificity and positive and negative predictive value.[22]

Data Synthesis and Analysis

Currently, there are no valid methods available to quantitatively pool multivariable prognostic models that contain different predictors (e.g. a meta-analysis). Therefore, a level of evidence synthesis was performed (Table 1) taking the quality of the studies into consideration.[28,29,30] Only the results of the analyses of the studies with sufficient quality, i.e. studies with a score of 15 positive items out of the 21 items of the score list were presented.

Table 1. *Levels of evidence for prognostic factors*	
Level of evidence	
Strong	Consistent findings (≥ 80%) in at least 2 sufficient quality cohorts
Moderate	One sufficient quality cohort and consistent findings (≥ 80%) in one or more low quality cohorts
Limited	Findings of one cohort of sufficient quality or consistent findings in one or more low quality cohorts
Inconclusive	Inconclusive findings irrespective of study quality

RESULTS

Study selection

Nine studies fulfilled the selection criteria (Figure 1).[31,32,33,34,35,36,37,38,39] Appendix C provides the study characteristics of all nine included studies.

Three studies utilized patients recruited from a military population.[33,34,38] Four studies examined patients who were treated in specific clinics[32,35,36,39] and two studies[31,36] have been conducted in primary care. The sample size of the studies varies between 30 and 74 patients, except in one study (n = 310).[31]

OUTCOME MEASURES

Pain. All studies measured pain intensity as an outcome; seven studies used the Numerical Rating Scale

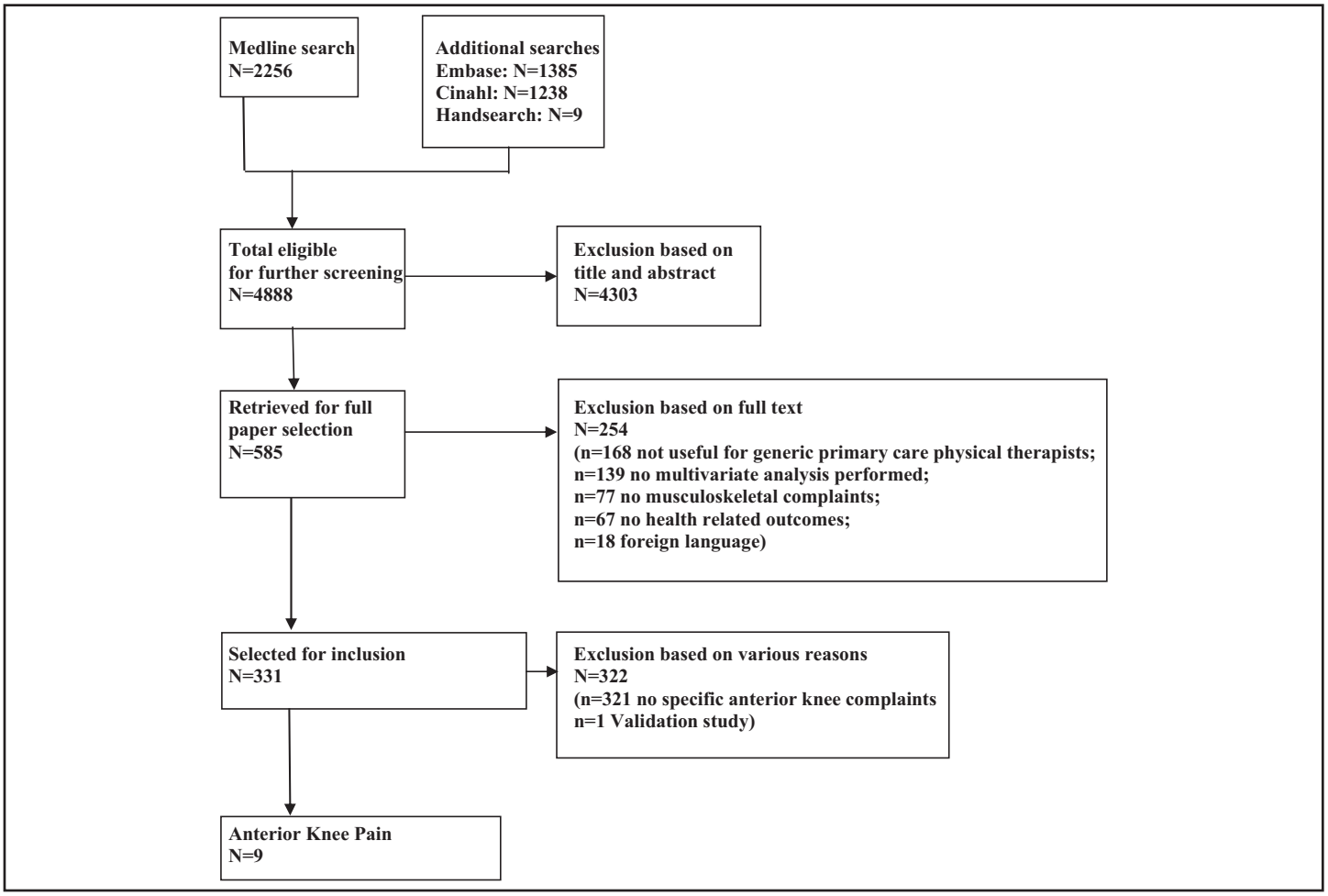

Figure 1. *Flow chart study selection*

(NRS)[33,34,37] or the Visual Analogue Scale (VAS)[31,32,35,38] and two studies[36,39] the Kujala pain score. The validity and reliability of these measurement instruments have been previously reported and are good.[40,41]

Function. Six studies measured function as an outcome[31,32,35,37,39]: using either the Kujala score (also called the Anterior Knee Pain Scale (AKP)), the Activity of Daily Living Scale (ADLS), the Functional Index Questionnaire (FIQ), or the Lysholm and Tegner functional knee scores. The validity and reliability of these instruments are good and the outcomes of the different measurement instruments are comparable.[42,40,43,44,45]

Other. Other outcome measures included the use of a rating scale for subjects' impression of the change (recovery) and physical activity limitations questionnaires.

Methodological quality assessment

The number of positive items ranged from 9[38] to 17[31,37] out of 21 items (Table 2). All studies scored positive on 'inclusion and exclusion criteria', 'prospective design', 'all prognostic factors described used to develop the model', 'standardized or valid measurements' and 'clinical relevant outcome measures'. Two items on which all studies scored negative or unclear were: 'internal validation' and 'external validation'. One study did not describe 'clinical performance measures'.[39] One study scored positive on 'sufficient number of subjects per variable'.[31] Finally, two studies did not provide a clear presentation of the data of all predictors.[38,39] Four studies were considered as of sufficient quality.[31,32,36,37]

For the sensitivity analysis, with 14 positive items the same four studies were found of sufficient quality. However with a cut-off of 16 positive items just three studies remained of sufficient quality.[31,32,37]

Performance assessment

Five studies presented the explained variance by calculating the R^2, which ranged from 0.05 to 0.60 (Appendix C). [31,32,35,36,37] One study presented the discriminative power by calculating the Area Under the Curve (AUC).[31] Three studies presented the clinical usefulness by reporting sensitivity, specificity and likelihood ratios.[34,35,38] One study did not use any of the performance measures.[15]

Data synthesis and Analysis

Univariable analysis

In total, 190 predictors were univariably assessed; 11 predictors were evaluated in more than one study. Only 'pain at baseline' was univariably analyzed in all studies but appeared only univariably significantly related to pain at follow-up in four studies.[31,33,36,37] Duration of symptoms[31,33,34,35,36,39] and age[31,33,34,35,36,37,38] were also frequently assessed univariably, and both were significantly related to pain and function; gender was evaluated in five studies.[31,33,35,37,39]

In the four studies of sufficient quality[31,32,36,37], 29 predictors were found that were univariably significantly related to pain or function, of which 27 were considered unique, meaning they were only evaluated in one study. Four predictors were evaluated in more than one study. Twenty-six predictors were univariably significantly related to pain as well as function. Each included study used their own cut-off points for inclusion of potential predictors in the multivariable analysis and there were hardly any agreements between these chosen cut-off points.

Multivariable analysis

Table 3 presents the overview of the predictors related to pain and function in the studies of sufficient quality and additional low quality studies as a result of the multivariable analyses. Predictors only assessed in low quality studies (quality score of 14 positive items or less) are not presented in this table. Because only one study assessed recovery as outcome (N = 1)[31], analysis of recovery as an outcome is not presented in this table.

Pain. Of the 29 univariably significant predictors 14 were multivariably significantly related to pain in at least one study of sufficient quality (Table 3). Seven out of these 14 predictors were found in only one high quality study. 'Duration of symptoms' was the only significant predictor found in a study of sufficient quality[31] as well as a low quality study[39] however 'duration of symptoms' was not significantly related to pain in another low quality study.[33]

'Pain at baseline' was univariably significant related to pain at follow-up in four studies, but in none of the studies after multivariate analysis.

Function. Of the 27 univariably significant predictors 15 were significantly related to function in at

Table 2. *Criteria list of methodological quality developed by Oort et al*[19]

	Collins[31]	Domenech[32]	Iverson[33]	Lesher[34]	Natri[35]	Pattyn[36]	Piva[37]	Sutlive[38]	Witvrouw[39]
Study design									
a) Cohort	+	+	?	-	?	+	+	?	+
b) Population	+	+	+	+	+	-	+	+	+
c) Exclusion/Inclusion criteria	+	+	+	+	+	+	+	+	+
d) Prospective design	+	+	+	+	+	+	+	+	+
Study attrition									
e) Drop outs	+	+	+	+	+	+	+	-	?
f) Deal with missings	+	+	+	-	+	+	+	-	-
Prognostic factors									
g) Prognostic factors	+	+	+	+	+	+	+	+	+
h) Valid measurements	+	+	+	+	+	+	+	+	+
i) Linearity assumption studied	?	?	?	?	?	?	+	?	?
j) No dichotomization of prognostic variables	+	+	-	-	+	+	+	-	?
k) Data prognostic factors	+	+	+	+	+	+	+	-	-
Outcome measures									
l) Outcome measures	+	+	+	+	+	+	+	+	+
m) Standard, valid measurements	+	+	+	+	+	+	+	+	+
n) Data presentation outcome measures	+	+	+	+	-	+	+	+	+
Analysis									
o) Univariate estimates	-	-	-	-	-	-	-	-	+
p) Sufficient numbers of subjects per variable	+	-	-	-	-	-	-	-	-
q) Explained method	+	+	-	-	-	+	+	-	+
r) Multivariate estimates	+	+	-	-	+	+	+	-	+
Clinical performance									
s) Clinical performance	+	+	+	+	+	+	+	+	-
t) Internal validation	-	-	-	-	-	-	-	-	-
u) External validation	-	-	-	-	-	-	-	-	-
Total score#	17	16	12	11	13	15	17	9	11

For definitions criteria and operationalization of the criteria see Appendix B

\+ positive score on a item

\- negative score on a item

\# Total score: sum of all positive scores

Table 3. *Predicting variables and their level of evidence after multivariable analysis*

Predictors	Pain		Level of Evidence to be of predictive value related to pain	Function		Level of Evidence to be of predictive value related to function
	Low quality studies (N=5)[33,34,35,38,39]	Studies of sufficient quality (N=4)[31,32,36,37]		Low quality studies (N=2)[35,39]	Studies of sufficient quality (N=4)[31,32,36,37]	
MRI (CSA Quadriceps)		+	Limited		+	Limited
AKP		+	Limited		+	Limited
FABQ-PA		+	Limited		+	Limited
Catastrophizing		+	Limited		+	Limited
Frequency of pain		+	Limited	0	+	Inconclusive
FABQ-W		+	Limited		0	Limited for no association
Recruitment		+	Limited		0	Limited for no association
Muscle length Gastrocnemius		0	Limited for no association		+	Limited
FIQ		0	Limited for no association		+	Limited
Anxiety (HAD)		0	Limited for no association		+	Limited
Gender (female)	0, 0, 0	+, 0, 0	Inconclusive	0, 0	+, +, 0	Inconclusive
Height	0	+	Inconclusive	0	+	Inconclusive
Quadriceps strength	0, 0	+, 0	Inconclusive	0	+, 0	Inconclusive
Age	0	+, 0, 0	Inconclusive	0	+, 0, 0	Inconclusive
Duration symptoms	+, 0	+	Inconclusive	+, 0	+	Inconclusive
Weight	0, 0	+	Inconclusive	0, 0	+	Inconclusive
Pain coping (CSQ)		0,0	Strong for no association		0,0	Strong for no association
Kinesiophobia (TSK)		0,0	Strong for no association		0,0	Strong for no association
Pain baseline	0	0, 0, 0, 0	Strong for no association	0	+, 0, 0	Inconclusive
Activity related pain	0	+	Inconclusive	0	0, 0	Strong for no association
Triple Jumptest	0	0	Moderate for no association	0	0	Moderate for no association
Muscle length Quadriceps,	0	0	Moderate for no association	0	0	Moderate for no association
Hamstrings and Soleus						
ADLS	0	0	Moderate for no association	0	0	Moderate for no association
Bilateral symptoms	0	0	Moderate for no association			
Steptest	0	0	Moderate for no association			
BMI		0	Limited for no association		0	Limited for no association

Table 3. *Predicting variables and their level of evidence after multivariable analysis (continued)*

Predictors	Pain		Level of Evidence to be of predictive value related to pain	Function		Level of Evidence to be of predictive value related to function
	Low quality studies (N=5)[33,34,35,38,39]	Studies of sufficient quality (N=4)[31,32,36,37]		Low quality studies (N=2)[35,39]	Studies of sufficient quality (N=4)[31,32,36,37]	
Depression (HAD)		0	Limited for no association		0	Limited for no association
Sporter		0	Limited for no association		0	Limited for no association
Quality of movement		0	Limited for no association		0	Limited for no association
Single legged jump test		0	Limited for no association			
Working state		0	Limited for no association			
Work type					0	Limited for no association
Allocated preferred treatment					0	Limited for no association

MRI= Magnetic resonance imaging; CSA= Cross sectional area; AKP= Anterior Knee Pain Scale; FABQ-PA= Fear Avoidance Belief questionnaire-Physical Activity; FABQ-W= Fear Avoidance Belief questionnaire-Work; FIQ=Functional Index Questionnnaire; HAD=Hospital Anxiety and Depression score; CSQ=Coping Strategies Questionnaire; TSK=Tampa Scale Kinesiophobia; ADLS=Activities of Daily Living Scale; BMI=Body Mass Index

0: a study with no association between the predictor and the outcome measure

+: a study with a significant association between the predictor and the outcome measure

When there is notified 0,0,0,+, it is meant that there are 3 studies without a significant relationship with the outcome measure and one study with a significant relationship

least one study of sufficient quality (Table 3). Pain at baseline was examined in all studies of sufficient quality but was only significantly related to function in one of these studies.

Levels of evidence

Association

Limited evidence was found for seven predictors to be related to pain (frequency of pain[36], Catastrophizing (PCS)[32], anterior knee pain score (AKPS)[31], Fear avoidance (FABQ-PA, FABQ-W)[37], magnetic resonance imaging (MRI)[36] and recruitment[31]).

Furthermore *limited evidence* was found for seven predictors to be related to function (Catastrophizing (PCS)[32], Anxiety (HAD)[32], AKPS[31], FABQ-PA[37], MRI[36], gastrocnemius length[37] and the Functional Index Questionnaire knee score (FIQ)[31]).

No association

Strong evidence for no predictive value for pain at follow up was found for three variables (baseline pain intensity, pain coping, and kinesiophobia). Also strong evidence for no predictive value was found for three variables related to function at follow-up (i.e. 'activity related pain', 'pain coping' and 'kinesiophobia').

Moderate evidence was found for five predictors for not being related to pain (triple jump test, muscle length [Quadriceps, Hamstrings and Soleus], ADLS, bilateral symptoms and step test) and for three predictors for function (triple jump test, muscle length [Quadriceps, Hamstrings and Soleus] and ADLS).

*Limited evidence was found_f*or nine predictors for not being a predictor for pain (BMI, muscle length gastrocnemius, anxiety (HAD), depression (HAD), FIQ, being an athlete, quality of movement, working state and single legged jump test) and for eight predictors for not being a predictor for function (BMI, anxiety (HAD), FABQ-W, being an athlete, quality of movement, recruitment, work type and allocated preferred treatment).

DISCUSSION

Main findings

A wide variety of potential predictors were found (n = 193) that were related to pain or function in nine studies of patients with AKP or PFP.[31-39] Out of 193 predictors, just 34 unique predictors were significantly related to pain or function, of which 19 predictors in four studies were found in studies of sufficient quality.[31,32,36,37] Too few studies assessed recovery, so the authors were unable to generate evidence on this outcome measure. Only limited evidence was found for several predictors because most of the predictors were assessed in just one study of sufficient quality. This limits the strength of the current conclusions. Furthermore the authors were unable to derive a single, multiple factor prediction model for pain or function in patients with anterior knee pain because of the variety in predictors.

Comparison with the literature

This is the first review on prognostic models in patients with anterior knee pain. All studies[31-39] used pain intensity and/or function as outcome measures. Remarkably, the predictor 'baseline pain intensity' was evaluated in all studies[31-39] but was not related to pain intensity or function at follow-up. This might indicate that focusing on decreasing the baseline pain intensity as a treatment goal might not be relevant in patients with anterior knee pain. This can be explained when viewed in relationship to cognitive-behavioral theory.[46,47] This theory indicates that patients should view pain in general as a common condition that can be self-managed, rather than as a serious condition that needs careful protection. The patients should not be guided by pain, but rather, should focus on the activities they are able to perform.[46,47]

Methodological considerations

A summary score was used to report overall study quality. However, this is not recommended by Hayden et al[48] who indicate that to judge overall quality (or risk of bias), one could describe studies with a low risk of bias as those in which all, or the most important (as determined a priori), of the six important bias domains (study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding and statistical analysis and reporting) are rated as having low risk of bias. No difference in the conclusions was found following the recommendations of Hayden et al compared to using the established summary score. The same four studies remained of sufficient quality.[31,32,36,37]

Classifying prognostic models with regard to levels of evidence (e.g. strong, moderate, limited evidence or inconclusive) is under discussion.[25] However, the authors believe that the quality of the study likely influences the selection of most relevant predictors. For prognostic models it is unclear at the moment, which methodological quality items are of greatest relevance. As it is important to avoid compensation for less important items and because studies with high quality scores were expected to select the most important predictors, authors decided to use a level of evidence approach despite the earlier discussion.

Strengths and limitations

The decision to base the conclusions of this review on studies with sufficient quality may have influenced the selection of the most relevant predictors. On the other hand we chose this cut-off because including studies of low quality might have led to the erroneously selection of predictors based on studies with major methodological problems. For example, it is advised that the number of candidate variables to develop a prognostic model should not exceed a tenth of the study population in the smallest outcome group as this easily leads to an incorrect estimation of the predictors in the model.[49,50] However, most of the studies included (7 out of 8)[32-39] did not comply with this rule. Furthermore, researchers dichotomize the predictors with the aim of making the final model more feasible in daily practice, but this may lead to loss of information (with regard to the measurement scale range and precision of outcome predictions) and a loss of statistical power.[37] In

four out of eight studies the predictors were dichotomized before entering the regression analysis.[33,34,38,39]

This systematic review was limited to English-language articles and did not consider grey literature (the kind of material that is not published in easily accessible journals or databases, including things like abstracts of research presented at conferences, unpublished theses, and so on); therefore, some studies have been missed. However, an extensive search has been performed in accordance with the directives for systematic reviews, so authors assume that the articles that were potentially missed would not have majorly altered any of the findings.

The most important limitation is the heterogeneity of the included studies. A wide variety of potential predictors were found; there was hardly any overlap between studies in the choice of predictors for the analysis and therefore in the final set of predictors. This heterogeneity resulted in inconclusive evidence for most predictors. Furthermore only two of the studies of sufficient quality evaluated psychological factors, however these factors were not the same in both studies.[32,36] This means that authors were unable to draw conclusions on the possible predictive value of psychological predictors.

Recommendations for future studies

Based on the current results, the authors would recommend the development and validation of a new prognostic model for patients with anterior knee pain (i.e. including variables such as: frequency of pain, catastrophizing, anterior knee pain score, fear avoidance (FABQ-PA and FABQ-W), MRI, recruitment, anxiety, gastrocnemius length and the FIQ-score). Regardless of how the model is developed, it is essential for its potential applicability that the performance and validity of a model is evaluated. Ideally more than one performance measure should be used. Only one study used more than one performance measure.[31] Moreover, none of the studies validated their final prognostic models. Therefore the presented prognostic models, in their current form, are not yet suitable for use in daily clinical care.

Furthermore, in authors' opinion, the methodological quality of future studies can easily be improved. Methodological flaws frequently occurring in these studies can in future be resolved by making small changes in the study methodology. Many reports are available with guidelines how to develop a high quality prognostic model.[18,17]

CONCLUSION

Clinicians have to base their treatment strategy on determinants relevant for the prognosis. Based on the current results clinicians do not need to consider pain or activity related pain for treatment decisions, as they appear to be unrelated to decrease in pain or increase in function in patients with anterior knee pain. However clinicians should consider catastrophizing, a high score on the FABQ, HAD, AKP, FIQ, gastrocnemius length and a high frequency of pain for their treatment decisions because these variables are significantly related to the outcome measures pain and/or function in patients with anterior knee pain that first present to a physical therapist.

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APPENDIX A: THE COMBINATION OF KEYWORDS THAT WERE USED FOR MEDLINE DATABASE SEARCH

"Decision Support Techniques"[Mesh] OR "Predictive Value of Tests"[Mesh] OR "clinical prediction"[tiab] OR prognos*[tiab] OR predict*[tiab]) AND ("Primary Health Care"[Mesh] OR "Physicians, Family"[Mesh] OR "general practice"[tiab] OR "general practitioner"[tiab] OR "primary care"[tiab] OR "Physical Therapy (Specialty"[Mesh] OR "physical therapy modalities"[Mesh] OR "Rehabilitation"[Mesh" OR physiotherapy*[tiab] OR "physical therapy"[tiab] OR "physical therapist"[tiab] OR "physical therapists"[tiab] OR "physical therapeutic"[tiab]) AND ("Musculoskeletal Diseases"[Mesh] OR "Muscle, Skeletal"[Mesh] OR "Back Pain"[Mesh] OR "Back Injuries"[Mesh] OR "Neck Pain"[Mesh] OR "Neck Injuries"[Mesh] OR "Fractures, Bone"[Mesh]).

Afterwards the inclusion procedure, selection of studies with regard to patellar complaints were based on the keywords: patellofemoral, patellar femoral, patellar femoral pain syndrome, patellar, anterior knee pain, patella femoral, patellafemoral, knee pain, patellar arthritis, patella arthritis, patello arthritis, patellar injury, patella injury, patello injury.

APPENDIX B

METHODOLOGICAL ASSESSMENT OF STUDIES ABOUT PROGNOSTIC MODELS, DEVELOPED BY OORT ET AL19

Criteria list	
Criteria	**Score**
Study design	
a) Inception cohort	+ / - / ?
b) Source population	+ / - / ?
c) Inclusion and exclusion criteria	+ / - / ?
d) Prospective design	+ / - / ?
Study attrition	
e) Number of drop-outs	+ / - / ?
f) Information given on method how they deal with missing data	+ / - / ?
Prognostic factors	
g) All prognostic factors described used to develop the model	+ / - / ?
h) Standardized or valid measurements	+ / - / ?
i) Linearity assumption studied	+ / - / ?
j) No dichotomization of prognostic variables	+ / - / ?
k) Data presentation all prognostic factors	+ / - / ?
Outcome measures	
l) Description of outcome measures described	+ / - / ?
m) Standardized or valid measurements	+ / - / ?
n) Data presentation of most important outcome measures	+ / - / ?
Analysis	
o) Presentation of univariate crude estimates	+ / - / ?
p) Sufficient numbers of subjects per variable	+ / - / ?
q) Selection method of variables explained	+ / - / ?
r) Presentation of multivariate estimates	+ / - / ?
Clinical performance / validity	
s) Clinical performance	+ / - / ?
t) Internal validation	+ / - / ?
u) External validation	+ / - / ?

Methodological assessment of studies about prognostic models.

Operationalization of items.

Study participation

a) Inception cohort: **positive** when patients were identified at an early uniform point (inception cohort) in the course of their complaints (e.g. first point at which symptoms were first noticed or first consultation at physiotherapy practice). **Also positive** in case of a heterogeneous population (survival cohort) for which subgroups of patients were identified and analysed (first episode of complaints or first consultation at physiotherapy practice). **Negative** when no inception cohort was used.

b) Source population: **positive** when population was described in terms of sampling frame (primary care, general population, physiotherapy practice) and recruitment procedure (place and time-period of recruitment and type of methods used to identify the sample). **Negative** when not both of these features are given. **Also negative** when it is likely that the recruitment procedure led to selection of participants that are systematically different from eligible non-participants.

c) Inclusion and exclusion criteria: **positive** when criteria were formulated for at least 4 out of 5 of the (for the study) most relevant characteristics, mostly:

1. Age
2. Sex
3. Relevant co-morbidity
4. Duration of complaints
5. Type of complaints

Negative when ≤3 criteria were formulated. **Also negative** when it is likely that the criteria used for inclusion/exclusion led to selection of participants that are systematically different from eligible non-participants.

d) Prospective design: **positive** when a prospective design was used. **Also positive** in case of a historical cohort of which the determinants (prognostic factors) are measured before the outcome was determined. Negative if a historical cohort is used, considering prognostic factors at time zero which are not related to the primary research question for which the cohort is created or in case of an ambispective design.

Study attrition

e) Drop-outs: **positive** when total number of drop-outs (loss to follow-up) was ≤20%. **Also positive** when appropriate procedures were used to deal with missing values (e.g. use of multiple imputation). **Negative** when the total number of drop-outs exceeds the 20% cut-off point and no appropriate procedures were used to deal with missing values.

f) **Positive** if method is described. **Negative** if not.

Prognostic factor measurement

g) Clinical relevant potential prognostic factors: **positive** when the article describes at least one of the following factors at baseline:

6. Physical/disease factors (e.g. severity of pain, range of motion, duration of complaints, localization of complaints)
7. Psychosocial factors (e.g. live events, anxiety, depression)
8. Sociodemographic factors, other than gender and age (e.g. employment status, occupation, co-morbidity)

Negative when the article does not describe at least one of the factors mentioned above at baseline.

h) Standardized or valid measurements: **positive** if at least one of the factors of g), excluding age and gender, are measured in a standardized, valid and reliable way.

i) **Positive** if studied (and accounted for if necessary) or not relevant (in case of no continuous predictors used), **negative** if not.
j) **Positive** if prognostic variable isn't dichotomized or dichotomization is sensible to do. **Negative** if prognostic variable is dichotomized.
k) Data presentation of most important prognostic factors: **positive** when frequencies, percentages or mean (and standard deviation or CI), or median (and Inter Quartile Range) are reported for all prognostic factors in the final model. In all other cases: **negative**.

Outcome

l) Clinical relevant outcome measure(s): **positive** if at least one clinical relevant outcome criteria for recovery is reported. In all other cases: **negative**.
m) Standardized or valid measurements: **positive** if one or more of the main outcome measures are measured in a standardized, valid and reliable way. In all other cases: **negative**.
n) Data presentation of most important outcome measures: **positive** if frequencies, percentages or mean (and standard deviation/CI), or median (and Inter Quartile Range) are reported for one or more of the main outcome measures for the most important follow-up measurements. In all other cases: **negative**.

Analysis

o) Univariate crude estimates presented: **positive** if univariate crude estimates (RR, OR, HRR) between prognostic factors separately and outcome are provided. **Negative** if only p-values or wrong association values (Spearman, Pearson, sensitivity) are given, or if no tests are performed at all.
p) Sufficient numbers of subjects per variable: **positive** if it is mentioned (or easy derivable) that the number of cases (and non-cases) in the multivariate analysis was at least 10 times the number of independent variables that were put in the multivariate analysis. In all other cases: **negative**.
q) **Positive** if references are used to explain the selection method of variables. **Also positive** if an appropriate rationale is given. **Negative** if not.
r) Multivariate estimates presented: **positive** if multivariate estimates (with CI or p-values) are presented of all prognostic factors that are part of the final clinical prediction rule. **Negative** if not.

Clinical performance/validity

s) Performance measurement: **positive** if the study provides information about performance measurement (e.g. discrimination, calibration, explained variance). In all other cases: **negative**.
t) Internal validation: **positive** if appropriate techniques are used to assess internal validity of the prognostic model (e.g. cross-validation or bootstrapping). In all other cases: **negative**.

External validation: **positive** if the prognostic model is tested in a different population. **Negative** if not.

Appendix C. *Characteristics of the included studies*

Author, Publication Year	N, Quality (Q), Setting, Country	Number of Univar. Variab.	Number of Multivar. Variab.	(Number of) Prediction variables	Outcome Follow-up	Performance	Notes
Collins[31] 2012	N=310 Q=17/21[€] Primary care Australia and the Netherlands	-	17	Pain: (Four variables) -Symptom duration -Recruitment -Activity related pain -AKPS Function AKPS: (Three variables) -Symptom duration -Pain intensity -AKPS Function FIQ: (Five variables) -Symptom duration -AKPS -pain intensity -female gender -FIQ	Pain: -VAS/NRS Function: -AKPS -FIQ Follow-up: 3 and 12 months	Explained Variation (R^2): Pain: 0.260[#]/ 0.237[$] AKP: 0.330[#] /0.317[$] FIQ: 0.273[#] /0.235[$] Area Under the Curve (AUC): Pain: 0.790/0.736# AKP: 0.675/0.304# FIQ: 0.611/0.563#	[#]3 month follow-up [$]12 month follow-up Cut off measurement instruments for respectively: Pain is 60, AKP is 80 and FIQ is 14;
Doménech[32] 2014	N=47 Q=16/21[€] Orthopaedic Clinic Spain	-	7	Pain: -Catastrophizing (PCS) Function: (Two variables) -Catastrophizing -Anxiety	Pain: -VAS Function: -Lysholm Follow-up: 6 months	Explained Variation (R^2) : Pain : 0.49 Function : 0.58	
Iverson[33] 2008	N=49 Q=11/21[¥] Military Population Texas	41	40	Pain: (Five variables) -Difference in hip internal rotation > 14[o] -Ankle dorsiflexion > 16[o] -Navicular drop > 3 mm -No stiffness with sitting -Squatting most painful	Pain: -NRS Recovery: -GRCQ Follow-up: Same day after treatment	Pain: Sn: 0.36- 0.73 Sp: 0.63- 0.93 LR+: 1.9- 4.9 LR-: 0.4- 0.7	No performance measures of the model, only of the predictors separate
Lesher[34] 2006	N=50 Q=11/21[¥] Military Population Texas	28	6	Pain: (Two variables) -Tibial angulation -Patellar tilt test	Pain: -NRS Recovery: -GRCQ Follow-up: Same day after treatment	Pain: Sn predictors: 0.53- 0.88 Sn model 0.53 Sp predictors: 0.51- 0.75 Sp model 0.88 LR+ predictors: 1.8- 2.1 LR+ model 4.4 LR- predictors: 0.24- 0.63 LR- model 0.53	Performance measures of the model and of the predictors separate
Natri[35] 1998	N=49 Q=13/21[¥] Clinic Finland	19	19	Pain: -Patellar crepitation Function:Lysholm: (Three variables) -Bilateral symptoms -Patella apprehension	Pain: -VAS[1] Function: -Lysholm -Tegner Follow-up:	Pain: -VAS: R^2 : 0.16 Function: -Lysholm: R^2 : 0.60 -Tegner: R^2: 0.52	Determinants at follow-up are measured at 6 months and are predicting the outcome at 7 years

Appendix C. *Characteristics of the included studies (continued)*

Author, Publication Year	N, Quality (Q), Setting, Country	Number of Univar. Variab.	Number of Multivar. Variab.	(Number of) Prediction variables	Outcome Follow-up	Performance	Notes
				-Patella crepitation Function-Tegner: (Five variables) -Bilateral symptoms -Patella appreh. -Patella grinding -Patella crepitation	6 months and 7 years		
Pattyn[36] 2012	N=40 Q=15/21[€] Orthopaedic surgeon Belgium	21	4	Pain: (Three variables) -CSA total quadriceps -Avg PT Ecc 60 -Frequency of pain Function: (Three variables) -CSA total quadriceps -Avg Peak Torque, Ecc 60°/sec -Frequency of pain	Pain: -Kujala Function: -Kujala Follow-up: 7 weeks	Pain: R^2: 0.54/0.46 Function: R^2: 0.54/0.46	R^2 / adjusted R^2
Piva[37] 2008	N=74 Q=17/21[€] Primary Care Physical therapist Pittsburgh USA	18	8	Pain: (Six variables) -Age -Sex -Height -Weight -Change in FABs-PA -Change in FABs-W	Pain: -NRS Physical function: -ADLS Follow-up: 8 weeks	Pain: R^2: Model 1: 0.05 Model 2: 0.33 Model 3: 0.43 Function: R^2: Model 1: 0.12 Model 2: 0.37	Model 1 for pain and function: age, sex, height, weight Model 2 for pain and function: age, sex, height, weight, FABs-PA
				Function: (Six variables) -Age -Sex, -Height -Weight -Change in FABs-PA -gastrocnemius length		Model 3: 0.45	Model 3 for pain: age, sex, height, weight, FABs-PA, FABs-W Model 3 for function: age, sex, height, weight, FABs-PA, gastrocnemius length
Sutlive[38] 2004	N=45 Q=11/2[¥] Military Population Texas	24	8	Pain: (Six variables) -Forefoot alignement -Great toe extension -Navicular drop test -calcaneal stance - 90/90 SLR-test -Difficulty walking	Pain: -VAS Recovery: GRCQ Follow-up: 3 weeks	Pain: Sn: 0.13 – 0.71 Sp: 0.48 – 0.97 LR+: 1.4 – 4.0	No performance measures of the model, only of the predictors separate
Witvrouw[39] 2001	N=30 Q=9/21[¥] University Hospital Belgium	39	39	Pain: (Two variables) -Reflex response time Vastus Medialis Oblique -Duration of symptoms	Pain: -Kujala Function: Kujala Follow-up: 5 weeks and 3 months	No performance measures	

VAS= Visual Analogue Scale; NRS=Numerical Rating Scale; AKPS= Anterior Knee Pain Scale; FIQ=Functional Index Questionnaire knee; GRCQ=Global rating of Changes Questionnaire; CSA=Cross sectional area;FABs-PA=Fear Avoidance Beliefs-Physical Activities; FABs-W=Fear Avoidance Beliefs-Work; ADLS=Activity of Daily Living Scale; Sn=Sensitivity; Sp (Specificity); LR+ (positive Likelihood Ratio); LR- (negative Likelihood Ratio); R^2 (Explained Variation)

[€] Study with sufficient quality

[¥] Study with low quality