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ORIGINAL ARTICLE

Prognostic Factors in Adults With Knee Pain in General Practice

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Objective. **To predict the 1-year outcome of incident nontraumatic knee symptoms in adults presenting in general practice.**

Methods. **Adults age >35 years with nontraumatic knee symptoms (n = 480) were followed for 1 year. At baseline, data on knee symptoms and demographics were collected and a physical examination performed. Knee symptoms were assessed by self-report questionnaires at 3-month intervals. After 1 year the physical examination was repeated. Multivariate prognostic regression models of patient characteristics, symptom characteristics, and physical examination were used to predict persisting knee symptoms after 1 year. Areas under receiving operating characteristic curves (AUCs) were used to determine the predictive value of the model. To assess the added predictive value of symptom characteristics and physical examination, these models were added to the model of patient characteristics. The improvement was expressed as the difference between the 2 AUCs.**

Results. **In the multivariate prognostic model of patient characteristics, age >60 years, educational level, kinesophobia, and comorbidity of the skeletal system were associated with persistent knee symptoms after 1 year (AUC 0.67). Of the symptom characteristics, history of nontraumatic knee symptoms, bilateral symptoms, and duration of symptoms >3 months were associated (AUC 0.73). For determinants of physical examination, crepitus of passive extension was associated (AUC 0.55). The added value of the symptom characteristics model to the patient characteristics model was 0.09 (AUC 0.76). Physical examination added no further value.**

Conclusion. **Symptom characteristics are the strongest predictors of persisting knee symptoms at 1-year followup. Physical examination has no added value in predicting persistent knee symptoms in general practice.**

INTRODUCTION

Musculoskeletal conditions are a major burden on individuals, health systems, and social care systems, with indirect costs due to disability being predominant (1). Although musculoskeletal pain, injury, and dysfunction affect all ages, the elderly are particularly susceptible (2). The clinical syndrome of joint pain and stiffness in older people is the most common cause of disability and health care consultation in this age group (3).

In general practice, knee symptoms (traumatic and nontraumatic) take second place after back pain in the prevalence of musculoskeletal disorders (48/1,000 patients per year), mostly presenting as knee pain or functional loss of the knee joint (4,5). Of these symptoms, ~20% are traumatic (5).

Approximately 60% of patients with nontraumatic knee symptoms are >25 years old. Disorders most diagnosed within this group are bursitis, tendinitis, and osteoarthritis (OA) (4). In the elderly, the most common cause of knee symptoms is the presence of OA. In general practice, knee OA is common, and diagnosed patients often have a long history of knee symptoms prior to the diagnosis (6).

In spite of the high prevalence of knee symptoms in general practice, few studies to our knowledge have assessed the signs, symptoms, and prognosis of nontraumatic knee symptoms in general practice (7–9). Until now, only a few studies on prognostic factors of knee OA used a clinical outcome to assess progression of knee OA (10,11).

To improve the management of nontraumatic knee symptoms, more knowledge is needed on the predictors of persisting or worsening knee symptoms, and on the predictors of good or bad prognosis. Moreover, establishing which patients are at higher risk for progression or persisting knee symptoms would be useful in studying the effect of disease-modifying therapies and in elucidating the disease process. Therefore, we performed a prospective cohort study in general practice to assess which signs and

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symptoms, based on clinical history and physical examination taken at baseline, are predictive for persisting symptoms at 1-year followup in patients with nontraumatic knee symptoms.

PATIENTS AND METHODS

Study design and population. For this study, a subgroup of the prospective Huisartsen Onderzoek Netwerk Erasmus Universiteit Rotterdam (HONEUR) knee cohort was used; details on this cohort have been reported earlier (12). In brief, consecutive patients visiting their general practitioner with a new episode of knee symptoms were enrolled in the study and followed for 1 year. In this prospective cohort study, 40 general practitioners from 5 municipalities in the southwest region of The Netherlands participated, connected to the Erasmus Medical Center General Practitioner Research Network HONEUR and representing a total patient population of ~84,000. Recruitment began in October 2001 in 1 municipality and a new municipality was added approximately every 3 months. All general practitioners continued to recruit until October 2003 (12).

New symptoms were defined as symptoms presented to the general practitioner 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. Exclusion criteria were knee symptoms that required urgent medical attention (fractures, infection), patients with malignancies, neurologic disorders, or systemic musculoskeletal diseases (e.g., Parkinson's disease, rheumatoid arthritis, amyotrophic lateral sclerosis), as well as patients being incapable of understanding the ramifications of participation.

At baseline and at 1-year followup, patients underwent a standardized physical examination of their knee by trained physiotherapists. The physical examination at baseline was planned as close to the date of consultation of the general practitioner as possible. Disability and pain were assessed every 3 months by means of self-reported questionnaires.

For this study, all patients age ≥35 years with nontraumatic knee symptoms were included. At baseline and at followup, data on knee symptoms (duration, intensity), daily activities, and social circumstances were collected and a physical examination of the knee was performed.

Functional disability and pain were assessed both at baseline and at followup by self-report questionnaires containing the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (13,14), the Medical Outcomes Study Short Form 36 Health Survey (SF-36) (15,16), the Knee Society Score (KSS) function questions (17,18), the Lysholm Knee Scoring Scale (19–21), the Tampa Scale for Kinesophobia (assessed at baseline) (22,23), and questions about experience of recovery or worsening (assessed at 1-year followup).

The physical examination assessed signs (e.g., swelling, temperature) and symptoms (e.g., function, pain) of the knee and hip. Further details about the physical signs and how they were elicited and scored are available from the corresponding author. For the outcome of persisting knee symptoms at 1-year followup, an additional question addressing experienced recovery or worsening, scored on a 7-point Likert scale, was added to the last questionnaire.

Statistical analysis. For the missing data, a multiple imputation strategy (multiple imputation by chained equations) was used (24). First, to assess which factors of the medical history and physical examination reported at baseline were associated with persisting knee symptoms (i.e., persisting or worsening knee symptoms) at 1-year followup, a univariate analysis was performed. The baseline factors that were analyzed were based on the literature (5,10) and on experienced clinical relevance. The determinants were divided in 3 subgroups: patient characteristics, symptom characteristics, and physical examination findings.

Patients with persisting knee symptoms were defined as patients who, after 1 year of followup, experienced knee symptoms (somewhat better, no recovery, worse, much worse, or worse than ever) versus recovered patients who experienced knee symptoms (much better or no symptoms).

In the multivariate backward logistic regression analysis, factors with $P < 0.2$ in the univariate analysis were included (P entry 0.05, P removal 0.10). To assess the prognostic value of determinants with persisting knee symptoms, a prognostic model was built by backward logistic regression and the area under the receiver operating characteristic curve (AUC) was estimated. Three models were built: the patient characteristics model, the self-reported symptom characteristics model, and the physical examination findings model.

To assess the added predictive value of self-reported symptom characteristics, these factors were added to the model of patient characteristics; improvement was expressed as the difference between the AUCs. Adding the physical findings model to the model of patient and symptom characteristics assessed the added predictive value of determinants of physical examination. For this model, the AUC was also estimated. In addition, based on the age groups used in the American College of Rheumatology (ACR) clinical classification criteria of knee OA (25), we also performed these analyses separately for the patient age subgroups 35–49 years and ≥50 years.

We chose to dichotomize most variables because this allows estimation of odds ratio parameters through a logistic regression analysis (26), which are easier to interpret in clinical practice. However, the consequences of dichotomizing are an overall reduced statistical power, loss of information, and an increased probability of a Type II error (27,28). SPSS software, version 11 (SPSS, Chicago, IL) was used to analyze the data.

RESULTS

Study population. A total of 549 patients were included. Their mean ± SD age was 53.8 ± 11.4 years, their mean ± SD body mass index (BMI) was 27.1 ± 4.3 kg/m^2, and 269 (49%) were women. Details on the baseline characteristics of the study group are presented in Table 1.

Table 1. Baseline characteristics and univariate analysis of the association between factors and persisting knee symptoms for the total group and for the age subgroups*

	Baseline characteristics		Univariate analysis, OR (95% CI)		
	Total population (n = 549)	Available at followup (n = 480)	Total population (n = 480)	Age 36–49 years (n = 185)	Age ≥50 years (n = 295)
Patient characteristics					
Age, mean ± SD years	53.8 ± 11.4	53.6 ± 11.2			
Age >60 years	147 (26.8)	129 (26.9)	2.16 (1.42–3.28)†		2.06 (1.28–3.31)†
Women	269 (49.0)	239 (49.8)	1.56 (1.08–2.24)†	1.29 (0.71–2.34)	1.66 (1.04–2.64)†
BMI, mean ± SD kg/m^2	27.1 ± 4.3	27.1 ± 4.2			
BMI >25 kg/m^2	362 (65.9)	328 (68.3)	1.12 (0.76–1.66)	0.94 (0.50–1.74)	1.24 (0.76–2.05)
Low/moderate educational level	363 (66.1)	322 (67.1)	2.02 (1.36–2.99)†	2.29 (1.23–4.28)†	1.74 (1.04–2.91)†
Private insurance	253 (46.1)	228 (47.5)	0.83 (0.58–1.19)	0.96 (0.53–1.75)	0.76 (0.48–1.20)
Presence comorbidity skeletal system	299 (54.5)	264 (55.0)	1.80 (1.25–2.60)†	1.82 (1.00–3.31)†	1.67 (1.04–2.68)†
Presence other comorbidity	117 (21.3)	97 (20.2)	1.20 (0.77–1.89)	1.03 (0.49–2.15)	1.33 (0.74–2.37)
Kinesophobia, mean ± SD Tampa total score‡	25.7 ± 6.2	25.5 ± 6.0			
Kinesophobia, Tampa score >25	253 (46.1)	219 (45.6)	1.99 (1.37–2.89)†	1.07 (0.58–1.95)	2.85 (1.76–4.62)†
Paid employment >8 hours/week	325 (59.2)	288 (60.0)	0.49 (0.33–0.71)†	0.54 (0.21–1.35)†	0.51 (0.32–0.81)†
Sport	326 (59.4)	300 (62.5)	0.78 (0.54–1.13)†	1.18 (0.63–2.19)	0.62 (0.39–1.00)†
Symptom characteristics					
Duration of symptoms >3 months	155 (28.2)	134 (27.9)	3.04 (1.98–4.65)†	2.76 (1.36–5.60)†	3.11 (0.82–5.32)†
Signs/symptoms of the knee					
Warm	205 (37.4)	191 (39.8)	1.67 (1.15–2.42)†	2.09 (1.13–3.85)†	1.44 (0.90–2.30)†
Swollen	217 (39.5)	197 (41.0)	1.28 (0.88–1.86)†	1.04 (0.55–1.94)	1.35 (0.85–2.16)
Crepitus	338 (61.6)	300 (62.5)	1.85 (1.26–2.70)†	1.50 (0.79–2.86)	2.23 (1.38–3.59)†
History of nontraumatic knee symptoms	81 (14.8)	66 (13.8)	5.12 (2.97–8.81)†	1.87 (0.57–6.12)†	6.27 (3.31–11.86)†
History of traumatic knee symptoms	307 (55.9)	265 (55.2)	2.26 (1.47–3.46)†	1.72 (0.88–3.36)	2.64 (1.51–4.61)†
Presence of locked knee	64 (11.7)	57 (11.9)	1.10 (0.63–1.91)	0.74 (0.85–2.20)	1.24 (0.61–2.52)
Bilateral symptoms	172 (31.3)	142 (29.6)	3.74 (2.33–6.00)†	2.47 (1.19–5.13)†	4.99 (2.62–9.50)†
Recurrent symptoms	231 (42.1)	205 (42.7)	1.75 (1.21–2.53)†	1.11 (0.61–2.01)	2.34 (1.45–3.78)†
Feeling of giving way	202 (36.8)	178 (37.1)	1.46 (1.00–2.13)†	1.10 (0.57–2.11)	1.58 (0.99–2.54)†
Limited when walking stairs	439 (80.0)	383 (79.8)	1.45 (0.91–2.30)†	1.16 (0.60–2.27)	1.56 (0.81–2.99)
Cause of symptoms overburden	168 (30.6)	139 (29.0)	0.93 (0.62–1.38)	1.04 (0.56–2.27)	0.92 (0.54–1.57)
Pain (11-point scale), mean ± SD§	4.3 ± 2.1	4.3 ± 2.1	1.02 (0.93–1.11)	1.03 (0.90–1.20)	1.00 (0.89–1.12)†
SF-36 total score (0–100), mean ± SD	67.8 ± 11.2	68.2 ± 11.0	0.98 (0.97–1.00)†	1.00 (0.97–1.02)	0.98 (0.96–1.00)†
SF-36 PCS score, mean ± SD	65.1 ± 23.4	65.2 ± 23.1	1.00 (0.99–1.00)†	1.01 (0.99–1.02)	0.99 (0.98–1.00)
SF-36 MCS score, mean ± SD	80.5 ± 16.5	81.0 ± 15.9	1.00 (0.99–1.00)	1.00 (0.98–1.02)	0.99 (0.98–1.01)
WOMAC scores (0–100), mean ± SD					
Total	29.3 ± 19.7	28.9 ± 19.7	1.00 (0.99–1.00)	1.01 (0.99–1.03)	0.99 (0.98–1.01)
Physical functioning	27.8 ± 21.1	27.4 ± 21.1	1.00 (0.99–1.00)	1.01 (0.99–1.02)	0.99 (0.98–1.01)
Pain	29.7 ± 18.7	29.3 ± 18.7	1.00 (0.99–1.01)	1.00 (0.99–1.02)	1.00 (0.99–1.01)
Stiffness	31.8 ± 24.6	31.5 ± 24.4	1.00 (0.99–1.01)	1.01 (0.99–1.02)	1.00 (0.99–1.01)
Lysholm total score (0–100), mean ± SD	67.5 ± 18.7	69.1 ± 16.3	1.00 (0.98–1.01)	1.01 (0.99–1.03)	0.99 (0.98–1.01)
Physical examination					
Varus	108 (19.6)	89 (18.5)	2.04 (0.60–6.85)	NA	1.30 (0.36–4.71)
Valgus	159 (28.9)	145 (30.1)	1.49 (0.68–3.28)	1.64 (0.43–6.32)	1.38 (0.52–3.66)
Swollen knee joint	169 (30.8)	151 (31.5)	1.29 (0.88–1.91)†	1.33 (0.69–2.56)	1.22 (0.75–1.98)
Warm knee joint	127 (23.1)	112 (23.3)	0.84 (0.25–2.81)	0.42 (0.04–4.07)	1.19 (0.26–5.41)
Pain passive flexion	273 (49.7)	237 (49.4)	1.25 (0.87–1.80)	1.08 (0.59–1.99)	1.25 (0.78–2.00)
Pain passive extension	163 (29.7)	138 (28.8)	1.11 (0.75–1.66)	0.63 (0.31–1.30)	1.40 (0.85–2.30)†
Pain active flexion	209 (38.1)	180 (37.5)	1.18 (0.77–1.83)	1.82 (0.84–3.92)†	0.98 (0.57–1.68)
Pain active extension	91 (16.6)	77 (16.0)	1.31 (0.77–2.23)	1.82 (0.74–4.43)†	1.22 (0.62–2.40)
Crepitus passive flexion	193 (35.2)	165 (34.4)	1.24 (0.85–1.81)	1.36 (0.70–2.65)	1.10 (0.69–1.77)
Crepitus passive extension	119 (21.7)	102 (21.3)	1.84 (1.18–2.89)†	1.23 (0.57–2.67)	1.40 (0.85–2.30)
Crepitus active flexion	223 (40.6)	194 (40.4)	1.12 (0.73–1.74)	1.33 (0.63–2.82)	0.89 (0.51–1.57)†
Crepitus active extension	242 (44.1)	204 (42.5)	1.53 (0.93–2.52)†	1.32 (0.56–3.13)	1.53 (0.82–2.85)
Positive anterior drawer test	100 (22.3)	90 (18.8)	0.92 (0.24–3.49)	0.59 (0.04–6.08)	1.25 (0.25–6.14)
Floating patella	146 (27.1)	125 (26.0)	0.97 (0.64–1.47)	0.74 (0.35–1.59)	1.01 (0.61–1.68)
Bony swelling of the joint	55 (10.1)	52 (10.8)	1.92 (1.03–3.59)†	0.84 (0.23–3.08)	2.32 (1.10–4.91)†
Pain internal rotation hip	91 (16.6)	72 (15.0)	1.88 (1.11–3.17)†	1.97 (0.76–5.09)†	1.76 (0.94–3.32)†
Restriction internal rotation hip	134 (24.5)	111 (23.1)	1.47 (0.95–2.27)†	0.83 (0.35–1.97)	1.66 (0.99–2.80)†
Presence Heberden's nodes	107 (19.5)	94 (19.5)	1.41 (0.86–2.31)†	1.64 (0.62–4.35)	1.20 (0.66–2.17)
Baker's cyst	14 (2.6)	14 (2.9)	0.98 (0.92–1.04)	0.64 (0.11–3.59)	1.25 (0.78–1.98)
Bursitis prepatellaris	77 (14.0)	66 (13.8)	1.00 (0.59–1.68)	0.95 (0.38–2.39)	0.98 (0.52–1.85)
Pain iliotibial tract	85 (15.5)	70 (14.6)	1.20 (0.72–2.01)	0.85 (0.37–1.95)	1.52 (0.78–2.98)

* Values are the number (percentage) unless otherwise indicated. For all scores except the Lysholm and SF-36, lower scores represent better function/outcome. OR = odds ratio; 95% CI = 95% confidence interval; BMI = body mass index; SF-36 = Short Form 36 Health Survey; PCS = physical component summary; MCS = mental component summary; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; NA = not available.

† $P < 0.2$.

‡ Range 17–68. Lower score represents less fear of movement.

§ Range 0–10, where 0 = no pain and 10 = worst pain.

Table 2. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores during 1 year of followup*

	N†	Total score	Pain	Stiffness	Physical functioning
Baseline	549	29.3 ± 19.7	29.7 ± 18.7	31.8 ± 24.6	29.0 ± 21.0
3 months	431	18.9 ± 18.0	17.8 ± 17.3	22.6 ± 22.1	18.7 ± 18.9
6 months	411	16.5 ± 18.1	15.9 ± 17.6	19.1 ± 21.9	16.3 ± 18.9
9 months‡	75	14.4 ± 17.3	14.1 ± 15.9	15.7 ± 20.2	14.3 ± 17.9
1 year	480	14.3 ± 18.0	13.7 ± 17.7	16.6 ± 21.5	14.2 ± 18.5

* Values are the mean ± SD unless otherwise indicated. WOMAC scores range from 0–100, with lower scores representing better function.
† Patients with available data.
‡ Only available in a select part of the study population.

At 1-year followup, 480 (87.4%) persons were still available for the study; of these, 236 (49.2%) reported persisting knee symptoms. The 69 (12.6%) patients lost to followup showed no significant differences compared with those not lost to followup regarding baseline age, sex, BMI, KSS knee and function score, SF-36 score, comorbidity, and WOMAC scores. Of the persons lost to followup, reasons for no longer participating were lack of time/lack of interest (n = 36, 52.2%), severe comorbidity (n = 15, 21.7%), or treatment by an orthopedic surgeon (n = 4, 5.8%), and 14 (20.3%) patients provided no reason.

Multiple imputation was used to replace the missing values. There were 8 missing values for the dependent variable persistent knee symptoms. Of the patient characteristics, symptom characteristics, and characteristics of physical examination, the range of missing values was 3–20. An exception was the Heberden's nodes characteristic, for which there were 178 missing values. Further information about the proportion of missing data for each covariate is available from the corresponding author.

During 1-year followup, 43 (9.0%) patients underwent an operation for their knee. Of these, 18 (41.9%) reported persisting knee symptoms and 25 (58.1%) reported recovery ($P = 0.26$). Also during the 1-year followup, the WOMAC scores increased, with the largest increase at the 3-month followup measurement (Table 2).

Univariate analysis of the total group (n = 480). The factors analyzed in the univariate analysis and their association with persisting knee symptoms are shown in Table 1. Of the patient characteristics, 7 variables were significant at $P < 0.20$: age >60 years, female sex, a low/moderate educational level, comorbidity of the skeletal system, kinesophobia (Tampa score >25), paid employment >8 hours per week, and sport participation.

Of the self-reported symptom characteristics, 12 variables were significant at $P < 0.20$: a warm knee, a swollen knee, crepitus of the knee, the presence of bilateral symptoms, duration of symptoms >3 months, feeling of giving way, limitation when walking stairs, recurrent symptoms, a history of nontraumatic knee symptoms, a history of traumatic knee symptoms, SF-36 physical component summary (PCS) score (continuous variable), and the SF-36 total score (continuous variable). The baseline WOMAC total score, WOMAC physical functioning score, WOMAC pain score, and WOMAC stiffness score were not associated with persisting knee symptoms.

Of the variables on physical examination, 7 variables were significant at $P < 0.20$: a swollen knee joint, crepitus with passive extension, crepitus with active extension, a bony swelling of the joint, pain of internal rotation of the hip, a restriction of internal rotation of the hip, and the presence of Heberden's nodes.

Multivariate analysis of the total group (n = 480). Of the patient characteristics, 4 variables remained in the multivariate prognostic model: age >60 years, a low/moderate educational level, presence of comorbidity of the skeletal system, and kinesophobia (AUC = 0.67, median predicted values 0.49, range 0.54, interquartile range [IQR] 0.28) (Table 3). Of the self-reported symptom characteristics, 4 variables remained in the model: the presence of bilateral symptoms, a history of knee symptoms (traumatic and nontraumatic), and duration of symptoms >3 months (AUC = 0.73, median predicted values 0.36, range 0.68, IQR 0.34). Of the variables on physical examination, only the crepitus of passive extension of the knee remained in the model (AUC 0.55, median predicted values 0.47, range 0.16, IQR 0.0).

To assess the added value of self-reported symptom characteristics on the model of patient characteristics, we added the model of self-reported symptom characteristics to the model of patient characteristics and calculated the AUC (Table 3). The strongest predictors in this new model were the symptom characteristics variables. The AUC improved, with an increase of 0.09 to 0.76 (median predicted values 0.42, range 0.83, IQR 0.37). We then added the variable of crepitus of passive extension of the knee to assess the added value of this variable, but the model did not improve any further (AUC 0.76, median predicted values 0.45, range 0.83, IQR 0.36).

Univariate analysis of the age 35–49 years subgroup (n = 185). For the age group 35–49 years, the factors analyzed in the univariate analysis and their association with persisting knee symptoms are shown in Table 1.

Of the patient characteristics, 3 variables were significant at $P < 0.20$: low/moderate educational level, comorbidity of the musculoskeletal system, and paid employment >8 hours per week. Of the self-reported symptom

Table 3. Multivariate prognostic logistic regression models of patient characteristics, symptom characteristics, and variables of physical examination (n = 480)*

Model	OR (95% CI)	AUC	Nagelkerke R^2
Patient characteristics		0.67	0.12
Age >60 years	2.02 (1.30–3.13)		
Low/moderate educational level	1.74 (1.16–2.63)		
Comorbidity of musculoskeletal system	1.70 (1.15–2.50)		
Kinesophobia	1.85 (1.26–2.72)		
Symptom characteristics		0.73	0.23
Bilateral symptoms	2.96 (1.77–4.97)		
History of nontraumatic knee symptoms	4.30 (2.38–7.79)		
History of traumatic knee symptoms	1.56 (0.97–2.49)		
Duration >3 months	2.18 (1.36–3.48)		
Physical examination		0.55	0.03
Crepitus passive extension	1.91 (1.01–3.63)		
Patient and symptom characteristics		0.76	0.27
Age >60 years	1.40 (0.86–2.29)		
Low/moderate educational level	1.84 (1.17–2.87)		
Comorbidity of musculoskeletal system	1.50 (0.99–2.28)		
Kinesophobia	1.49 (0.98–2.26)		
Bilateral symptoms	2.74 (1.62–4.64)		
History of nontraumatic knee symptoms	3.45 (1.85–6.44)		
History of traumatic knee symptoms	1.50 (0.93–2.43)		
Duration >3 months	2.15 (1.32–3.48)		
Patient and symptom characteristics plus physical examination		0.76	0.27
Age >60 years	1.35 (0.83–2.22)		
Low/moderate educational level	1.82 (1.16–2.85)		
Comorbidity of musculoskeletal system	1.47 (0.97–2.24)		
Kinesophobia	1.48 (0.97–2.25)		
Bilateral symptoms	2.74 (1.62–4.63)		
History of nontraumatic knee symptoms	3.28 (1.75–6.15)		
History of traumatic knee symptoms	1.49 (0.92–2.42)		
Duration >3 months	2.13 (1.31–3.45)		
Crepitus passive extension	1.39 (0.83–2.33)		

* OR = odds ratio; 95% CI = 95% confidence interval; AUC = area under the receiving operating characteristic curve.

characteristics, 4 variables were significant at $P < 0.20$: duration of symptoms >3 months, a warm knee, a history of nontraumatic knee symptoms, and the presence of bilateral symptoms. Of the characteristics on physical examination, 3 variables were significant at $P < 0.20$: pain with active flexion of the knee, pain with active extension of the knee, and pain of internal rotation of the hip.

Multivariate analysis of the age 35–49 years subgroup (n = 185). Of the patient characteristics, 2 variables remained in the multivariate model: low/moderate educational level and presence of comorbidity of the musculoskeletal system (AUC = 0.63, median predicted values 0.42, range 0.30, IQR 0.30) (Table 4). Of the self-reported symptom characteristics, 2 variables remained in the multivariate model: duration of symptoms >3 months and a warm knee (AUC = 0.64, median predicted values 0.31, range 0.99, IQR 0.67). Of the characteristics on physical examination, no variables remained in the multivariate model.

To assess the added value of self-reported symptom characteristics on the model of patient characteristics, we added the model of self-reported symptom characteristics to the model of patient characteristics and calculated the AUC (Table 4). The strongest predictors in this new model were a low/moderate educational level, duration of symptoms >3 months, and a warm knee. The AUC improved, with an increase of 0.08 to 0.71 (median predicted values 0.31, range 0.99, IQR 0.68).

Univariate analysis of the age ≥50 years subgroup (n = 295). In the age group ≥50 years, 7 patient characteristics variables were significant at $P < 0.20$: age >60 years, female sex, low/moderate educational level, comorbidity of the musculoskeletal system, kinesophobia, paid employment, and sport participation.

Of the self-reported symptom characteristics, 10 variables were significant at $P < 0.20$: duration of symptoms >3 months, a warm knee, crepitus of the knee, a history of nontraumatic knee symptoms, a history of traumatic knee symptoms, feeling of giving way, bilateral symptoms, SF-36 total score, SF-36 PCS score, and recurrent symptoms.

Of the characteristics of physical examination, 5 variables were significant at $P < 0.20$: crepitus of active flexion, pain when passive extension, a bony swelling of the

Table 4. Multivariate prognostic logistic regression models of patient characteristics, symptom characteristics, and variables of physical examination of patients age 36–49 years (n = 185)*

Model	OR (95% CI)	AUC	Nagelkerke R^2
Patient characteristics		0.63	0.07
Low/moderate educational level	2.09 (1.11–3.96)		
Comorbidity of the musculoskeletal system	1.73 (0.93–3.19)		
Symptom characteristics		0.64	0.18
Duration >3 months	3.05 (1.47–6.33)		
Warm knee	1.94 (1.02–3.67)		
Patient and symptom characteristics		0.71	0.25
Low/moderate educational level	2.35 (1.21–4.57)		
Comorbidity of the musculoskeletal system	1.76 (0.93–3.33)		
Duration >3 months	2.85 (1.35–6.01)		
Warm knee	2.48 (1.28–4.80)		

* OR = odds ratio; 95% CI = 95% confidence interval; AUC = area under the receiving operating characteristic curve.

joint, pain of internal rotation of the hip, and restriction of internal rotation of the hip.

Multivariate analysis of the age ≥50 years subgroup (n = 295). Of the patient characteristics, 4 variables remained in the multivariate model: age >60 years, female sex, kinesophobia, and sport participation (AUC = 0.69, median predicted values 0.52, range 0.57, IQR 0.25) (Table 5). Of the self-reported symptom characteristics, 4 variables remained in the multivariate model: duration >3 months, a history of nontraumatic knee symptoms, recurrent symptoms, and bilateral symptoms (AUC = 0.76, median predicted values 0.42, range 0.85, IQR 0.64). Of the characteristics of physical examination, no variables remained in the multivariate model.

To assess the added value of symptom characteristics on the model of patient characteristics, we added the model of symptom characteristics to the model of patient characteristics and calculated the AUC (Table 5). In this new model, the strongest predictors were the variables of self-reported symptom characteristics. The AUC improved, with an increase of 0.11 to 0.80 (median predicted values 0.48, range 0.91, IQR 0.72).

DISCUSSION

The present study investigated the prognostic factors of patient characteristics, symptom characteristics, and findings from physical examination to predict persisting knee

Table 5. Multivariate prognostic logistic regression models of patient characteristics, symptom characteristics, and variables of physical examination of patients age ≥50 years (n = 295)*

Model	OR (95% CI)	AUC	Nagelkerke R^2
Patient characteristics		0.69	0.15
Age >60 years	2.00 (1.21–3.31)		
Female sex	1.64 (1.00–2.69)		
Kinesophobia	2.77 (1.69–4.56)		
Sport	0.64 (0.39–1.07)		
Symptom characteristics		0.76	0.30
Duration >3 months	2.10 (1.14–3.85)		
History of nontraumatic knee symptoms	5.03 (2.52–10.07)		
Recurrent symptoms	1.79 (1.04–3.10)		
Bilateral symptoms	3.54 (1.77–7.09)		
Patient and symptom characteristics		0.80	0.35
Age >60 years	1.69 (0.96–2.98)		
Female sex	1.45 (0.83–2.52)		
Kinesophobia	2.21 (1.26–3.85)		
Sport	0.67 (0.38–1.20)		
Duration >3 months	2.15 (1.14–4.04)		
History of nontraumatic knee symptoms	3.57 (1.73–7.36)		
Recurrent symptoms	1.78 (1.00–3.14)		
Bilateral symptoms	3.43 (1.68–7.00)		

* OR = odds ratio; 95% CI = 95% confidence interval; AUC = area under the receiving operating characteristic curve.

symptoms at 1-year followup in patients visiting their general practitioner with incident knee symptoms.

The following were associated with persisting knee symptoms: age >60 years, low/moderate education level, comorbidity of the skeletal system, kinesophobia, presence of bilateral symptoms, history of traumatic or nontraumatic knee symptoms, duration of symptoms >3 months, and crepitus of passive extension of the knee. The self-reported symptom characteristics variables were the strongest predictors of persisting knee symptoms, whereas the findings from physical examination showed no added prognostic value.

Similarly, in the subgroups based on age, self-reported symptom characteristics were the strongest predictors for persisting knee symptoms, and the determinants from the physical examination had no prognostic value. In the younger age group (36–49 years), duration of symptoms >3 months was a strong predictor for persisting knee symptoms. In the older age group (≥50 years), a history of nontraumatic knee symptoms was the strongest predictor.

Despite the high prevalence of knee symptoms in general practice (5), few studies have investigated prognostic factors of knee symptoms in a primary care setting (8,29).

Compared with a secondary care population, our population had less severe symptoms and better knee function (30); this might lead to different prognostic factors for persisting knee symptoms compared with a secondary care population. The findings on prognostic factors emerging from this study could be used to better inform patients, and as a basis for management of clinical treatment.

Our study population was relatively heterogeneous. All patients with nontraumatic knee symptoms were included in the study, and the predictors were applied to all patients in the study. However, compared with a nationwide registration study (31), our population differed not substantially from patients with knee symptoms in other Dutch general practices (12). Therefore, we assume our population to be representative of a primary care population and we do not expect bias due to selective recruitment.

Although one may assume that most patients >35 years of age will have knee symptoms indicative of OA, the results cannot be directly interpreted as predictors of OA. The diagnosis of OA can be supported by radiologic criteria; however, in the present study we chose not to include radiographs of the knee because only a small proportion of patients in primary care are referred for radiographs (4). Moreover, radiologic severity does not seem to be related to progression of knee OA (10). Based on the age groups in the ACR classification criteria for knee OA (25), we performed subgroup analyses for the older and younger persons in our study group, which led to slight differences in the prognostic variables. However, the present results cannot be directly interpreted as predictors for OA in patients >50 years of age.

For the outcome, we used patients' self-reported recovery or persisting knee symptoms at 1 year of followup compared with those at baseline (thentest), and such self-reports may be susceptible to recall bias (32). However, it is reported that recall bias does not invalidate the thentest results (33).

With regard to the self-reported symptom characteristics, it is debatable whether generic health measures such as the SF-36 should be included. However, in our univariate and multivariate analyses, these variables were not statistically significant and had no predictive value. Even if these variables were included in patient characteristics, they still had no prognostic value. Therefore, we do not expect bias due to the choice to include generic health measures in the self-reported symptom characteristics.

At baseline, data about knee symptoms (duration, intensity), daily activities, and social setting were collected by self-report questionnaires so that self-reported symptom characteristics would not only be disease specific, but would also depend on the experience of the patient. However, in clinical practice, both symptom characteristics and the patient's experience play a role in the decision to visit a general practitioner. For example, pain could be experienced in different ways. In addition to the level of pain and the extent of limitations caused by pain, the patient's interpretation of their symptoms will influence their decision to visit a general practitioner.

Crepitus of passive extension of the knee was associated with persisting knee symptoms in the physical examination model, but this determinant had no added value in the prediction of persisting knee symptoms. In our study, the physical examination was performed by trained physiotherapists according to a standardized test protocol (12). In clinical practice, due to lack of standardization of the examination of the knee joint, the physical examination may be even less predictive than it was found to be in the present study. However, with respect to the diagnostic value, the general practitioner may still elect to perform the physical examination of the knee.

Although treatment could have an effect on the prognosis, we decided to only assess baseline factors in this study. With regard to treatment, only a total knee replacement would provide total recovery from knee symptoms. In our cohort, 43 (9.0%) patients underwent an operation for their knee. Of these, 18 (41.9%) reported persisting knee symptoms and 25 (58.1%) reported a recovery. Therefore, we do not suspect bias due to treatment.

The models in this study could be overfitted and therefore over-optimized because we did not validate them by bootstrapping or external validation. However, our findings correspond with those of van der Waal et al (29). In our study, we also investigated the determinants of physical examination on persisting knee symptoms, which, to our knowledge, no previous studies have investigated in a general practice population.

In contrast to our finding that self-reported symptom characteristics are the strongest predictors of persisting knee symptoms, Thomas et al found clinical history, physical examination, and severity of radiographic knee OA on plain radiograph to be of limited value over generic factors in predicting a poor outcome after 18 months of followup (34). However, in their study patients were recruited by postal surveys addressing knee pain. This is a major difference from our study, in which patients visiting their general practitioner with incident nontraumatic knee pain were included.

Additionally, our findings correspond with the findings

from other studies of prognostic indicators for patients with musculoskeletal pain in primary care, in which a longer history of pain, previous episodes of pain, and multiple-site pain were the strongest predictors of future pain status (7).

In conclusion, the present study shows that variables of symptom characteristics are the strongest predictors of persistent knee symptoms. Of the predictors found, most are not amenable to modification; this causes limitations with respect to the treatment of nontraumatic knee symptoms. However, in the case of kinesophobia, specific interventions (e.g., sport activities) can be considered. Perhaps intensive treatment (e.g., through education, medication, or physiotherapy) of patients with a higher risk of persisting knee symptoms might provide a better outcome. Therefore, further research on the treatment of knee symptoms is needed. Furthermore, for the individual prognosis of a patient, a prediction rule is needed to provide risk estimations of persisting knee symptoms. To develop a prediction rule, the prognostic models have to be internally and externally validated. Should a prediction rule be developed, we advise that it be based on data from more primary care knee cohorts with longer periods of followup. With regard to the major burden of knee symptoms, further research on prevention is also recommended.

AUTHOR CONTRIBUTIONS

Dr. Belo had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study design. Belo, Berger, Koes, Bierma-Zeinstra.
Acquisition of data. Belo, Bierma-Zeinstra.
Analysis and interpretation of data. Belo, Koes, Bierma-Zeinstra.
Manuscript preparation. Belo, Berger, Koes, Bierma-Zeinstra.
Statistical analysis. Belo, Bierma-Zeinstra.

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