Patient Acceptable Symptom State in Knee Osteoarthritis Patients Succeeds Across Different Patient-reported Outcome Measures Assessing Physical Function, But Fails Across Other Dimensions and Rheumatic Diseases

Elien A.M. Mahler, Nadine Boers, Johannes W.J. Bijlsma, Frank H.J. van den Hoogen, Alfons A. den Broeder, and Cornelia H.M. van den Ende

ABSTRACT. ***Objective.*** The aims of this study are (1) to establish the Patient Acceptable Symptom State (PASS) cutoff values of different patient-reported outcome measures (PROM) assessing physical function in patients with knee osteoarthritis (OA), and (2) to assess the influence of sex, age, duration of symptoms, and presence of depressive feelings on being in PASS.

Methods. Patients fulfilling the clinical American College of Rheumatology knee OA criteria received standardized nonsurgical treatment and completed different questionnaires at baseline and 3 months assessing physical function: Knee Injury and Osteoarthritis Outcome Score, Lequesne Algofunctional Index, Lower Extremity Functional Scale, numerical rating scale, and the physical function subscale of the Western Ontario and McMaster Universities Osteoarthritis Index. PASS values were defined as the 75th percentile of the score of questionnaires for those patients who consider their state acceptable.

Results. Of the 161 included patients, 62% were women with a mean age of 59 years (SD 9) and body mass index of 30 kg/m^2 (SD 5). Standardized PASS values (95% CI) for different questionnaires for physical function varied between 48 (44–54) and 54 (50–56). Female patients and patients feeling depressed were found to have a lower probability to be in PASS for physical function, with OR (95% CI) varying from 0.45 (0.23–0.91) to 0.50 (0.26–0.97) and from 0.27 (0.14–0.55) to 0.38 (0.19–0.77), respectively.

Conclusion. PASS cutoff values for physical function are robust across different PROM in patients with knee OA. Our results indicate that PASS values are not consistent across dimensions and rheumatic diseases, and that the use of a generic PASS value for patients with OA or even patients with other rheumatic diseases might not be justifiable. (First Release August 15 2017; J Rheumatol 2018;45:122–7; doi:10.3899/jrheum.170181)

Key Indexing Terms:
PHYSICAL FUNCTION OSTEOARTHRITIS KNEE OUTCOME ASSESSMENT
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From the Department of Rheumatology, Sint Maartenskliniek, Nijmegen; Department of Rheumatology and Clinical Immunology, University Medical Centre Utrecht, Utrecht; Department of Rheumatology, Radboud University Medical Centre, Nijmegen, the Netherlands.

E.A. Mahler, MD, MSc, Department of Rheumatology, Sint Maartenskliniek, and Department of Rheumatology, Radboud University Medical Centre; N. Boers, BSc, Department of Rheumatology, Sint Maartenskliniek; J.W. Bijlsma, MD, PhD, Department of Rheumatology and Clinical Immunology, University Medical Centre Utrecht; F.H. van den Hoogen, MD, PhD, Department of Rheumatology, Sint Maartenskliniek, and Department of Rheumatology, Radboud University Medical Centre; A.A. den Broeder, MD, PhD, Department of Rheumatology, Sint Maartenskliniek, and Department of Rheumatology, Radboud University Medical Centre; C.H. van den Ende, PhD, Department of Rheumatology, Sint Maartenskliniek, and Department of Rheumatology, Radboud University Medical Centre.

Address correspondence to Dr. E.A. Mahler, Rheumatologist-epidemiologist, Department of Rheumatology, Sint Maartenskliniek Nijmegen, PO Box 9011, 6500 GM Nijmegen, the Netherlands.
E-mail: e.mahler@maartenskliniek.nl

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Osteoarthritis (OA) is a joint disease that affects the entire joint and mainly causes pain, disability, and reduced quality of life[1,2]. Because there is no curative treatment available for OA, treatment aims to improve daily functioning and reduce symptoms. In clinical trials with patients, it is considered of great importance to incorporate the patient's interpretation of outcomes in establishing the relevance of findings[3,4]. Both the change in complaints (minimal clinically important improvement) and the absolute level of complaints [Patient Acceptable Symptom State (PASS)] are considered useful concepts for the interpretation of outcomes of clinical trials and the translation of data into daily practice[5].

The PASS is considered a state and is defined as the highest level of symptoms that the majority of patients consider acceptable[6,7]. Although the PASS has shown to be a relevant concept in rheumatology, only a few studies have

estimated and validated the PASS in knee OA[8,9,10,11]. However, different values were obtained, which might be explained by the selection of patients in a specific setting or country, or by the use of different followup periods across studies. In addition, different approaches have been used in the involvement of domains [i.e., pain, patient's global assessment (PtGA), function] and rheumatic diseases for estimating PASS values. This has led to the estimation of generic PASS values incorporating different domains, as well as more specific PASS values for only 1 domain [i.e., pain, PtGA), function] or for 1 rheumatic disease. As a result, the generalizability of PASS values to other patient settings, countries, languages, and cultures is speculative[7,11]. Hence, more insight into the variability of PASS values in different patient groups and/or settings is needed.

In addition, the extent to which PASS values reflecting a specific outcome domain, i.e., physical function, are robust across different questionnaires is unknown. Earlier studies examining the PASS value for physical function in OA have mostly used the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[12], while other reliable and valid patient-reported outcome measures (PROM) for physical functioning are available. Frequently used validated questionnaires to assess physical functioning in OA are the short version of the Knee Injury and Osteoarthritis Outcome Score (KOOS-PS)[13], Lequesne Algofunctional Index (LAI)[14], the Lower Extremity Functional Scale (LEFS)[15], and the physical function subscale of the WOMAC (WOMAC-PF)[12]. For the comparison of research findings using PASS cutoff values across studies, insight is needed in the variability of the PASS value across different questionnaires measuring the same construct; e.g., the PASS for self-reported physical function in OA.

Also, earlier research showed inconsistency in the influence of factors such as sex, age, and duration of symptoms on the PASS cutoff value[6,7,11]. Further, because the PASS is based on patients' opinion, it could be hypothesized that the presence of depressive symptoms influences patients' evaluation of their clinical status. So, it may be possible that depressive symptoms affect the acceptability of functioning; it has long been established that there is a strong relationship between the level of depression and the severity of pain[16,17].

Therefore, we conducted this prospective study with the following aims: (1) to establish the PASS values across different PROM assessing physical function in patients with knee OA, and (2) to assess the influence of sex, age, duration of symptoms, and comorbid depressive state on this estimated PASS value.

MATERIALS AND METHODS

Design, setting, and participants. Consecutive patients (≥ 18 yrs) with knee OA referred by orthopedic surgeons to our specialty knee and hip rheumatology OA outpatient clinic between July 2012 and January 2014 were eligible for participation in this prospective observational cohort study, as described elsewhere[18]. All patients fulfilled the American College of Rheumatology clinical OA criteria: knee pain (over 15 days last month) and at least 3 of the following: age over 50 years, morning stiffness for at least 30 min, crepitus, bony tenderness, bony enlargement, or no palpable warmth[19]. The exclusion criterion was indication within 3 months for knee replacement surgery. The local Medical Research Ethics Committee, region Arnhem-Nijmegen (the Netherlands) approved the study design (study number 2012/375). All patients signed informed consent.

Stepped care approach. Nonsurgical treatment modalities for the management of knee OA are recommended by several (inter)national consensus-based guidelines[20,21,22,23]. Therefore, all patients received multimodal conservative treatment based on a Dutch multidisciplinary stepped care approach for treatment of knee OA[24]. This includes education, referral for physical therapy (prescription for both aerobic and strengthening exercises according to the graded activity principle), step-up analgesics guided by a patient's pain level, lifestyle advice, and advice on weight reduction for patients with a body mass index (BMI) ≥ 28 kg/m^2. This approach recommends that more advanced options are considered only if the options listed previously failed to yield satisfactory results[24]. Patients attended a 90-min group visit (4–6 patients) to the rheumatology outpatient department, led by a physician assistant and a specialized nurse and supervised by a rheumatologist. When analgesics were found to be necessary, patients started with a fixed dose of 1000 mg paracetamol (acetaminophen) 3 times a day. In case of lack of efficacy of paracetamol, a nonsteroidal antiinflammatory drug (NSAID) was added. The patients were contacted after 4 weeks by telephone and if necessary, the analgesics were switched.

Outcome measures and data collection. Patients were asked to complete questionnaires at baseline and at 3 months, including sociodemographic information such as sex, age, and duration of symptoms. The postal questionnaires included the following 4 PROM to measure physical function.

KOOS-PS. The KOOS-PS is a 7-item short questionnaire with 4 items on daily activities and 3 items on sport and recreation (5-point Likert scale version from 0 to 4)[13]. Scores range from 0 to 28, and in our study the scores were converted to normalized scores ranging from 0 to 100, with higher scores defining higher levels of disability. The KOOS-PS has been shown to be valid and reliable in knee OA[13,25,26,27].

LAI. The LAI is an 11-item questionnaire that measures pain, walking distance, and daily activities. The total score ranges from 0 to 24 points[14]. The degree of functional disability corresponds with the following scores: a score ≥ 14 points indicates extremely severe disability, a score of 11–13 very severe disability, a score of 8–10 severe disability, a score of 5–7 moderate disability, and a score of 1–4 minimal disability. The LAI has been shown to be reliable, although its validity has been questioned[28].

LEFS. The LEFS is a 20-item condition-specific questionnaire on daily and recreational activities created for the use in patients with musculoskeletal conditions of the lower extremity, including knee OA (5-point Likert scale version from 0 to 4)[15]. The total score ranges from 0 to 80 points, with higher scores defining higher levels of functioning. The LEFS has been validated (also in Dutch) and shown to be reliable in patients with knee OA[29,30].

WOMAC-PF. The KOOS includes the WOMAC OA index in its complete and original format (with permission). We used the 17-item subscale with questions about activities of daily living from the KOOS to calculate WOMAC-PF score, originally developed for people with OA (5-point Likert scale version from 0 to 4). The score ranges from 0 to 68 points and in our study was converted to normalized scores ranging from 0 to 100, with higher scores defining higher levels of disability. The WOMAC is the most widespread studied and used instrument in individuals with knee OA and is shown to be valid and reliable[12].

Other patient-related outcome measures. Next to the PROM mentioned above, the questionnaire also included the depression subscale of the Hospital Anxiety and Depression Scale (HADS), which assesses depression and is validated and reliable and has been validated in patients with OA[16,17,31]. The depression subscale consists of 7 items with possible scores ranging from 0 to 21. A HADS score > 8 was considered as indicating

depressive symptoms. Further, patients were asked to rate their functioning and pain in the preceding week on a 0-10–point numerical rating scale (NRS) in which 0 equals no symptoms[24]. The PtGA of knee OA effect was measured identically as well.

The PASS has been defined as the value below which the majority of patients consider themselves in an acceptable state of symptoms. At baseline and after 3 months, the PASS for physical function was defined using an external anchor question considering their condition of knee OA. This single question was asked of the patients: "Think about all consequences of the knee osteoarthritis in the last week. If you were to remain for the rest of your life as you were during the last week, would the current state be acceptable or unacceptable for you?"[32].

Patients were included in the analysis of our current study if they completed both the baseline and followup measurements.

Statistical analysis. Descriptive statistics were used to describe the study population. All continuous outcomes are shown as means with SD when appropriate and dichotomous outcomes are shown in numbers with percentages. All scores of the PROM were normalized (and inverted when necessary) to a range of 0 to 100, with 100 being maximal complaints. Scale scores of KOOS-PS, LAI, LEFS, and WOMAC-PF were assessed for normality and missing data. Floor and ceiling effects for each questionnaire at baseline were considered present if > 15% of the patients scored the best or worst possible score, respectively. The 75th percentile of the cumulative distribution score of the PROM scores at 3 months in patients who considered themselves at an acceptable state was used to determine the cutoff value of the PASS. This approach has been validated as a comparable alternative to the receiver-operation characteristic curve[6,10,11,32]. Thereafter, these cutoff values with their 95% CI of the 4 different PROM assessing physical function were compared.

To examine the influence of covariates on the estimated absolute PASS value, a univariate and multivariate logistic regression was performed. As dependent variable, the absolute PASS value on group level of a particular PROM assessing physical function was used, separately for each PROM. The independent variables were sex, age, duration of symptoms, and having depressive feelings at baseline. To improve interpretation and clinical applicability, we dichotomized all independent variables: age ≥ 65 years (yes/no), duration of symptoms > 5 years (yes/no), and HADS > 8 (yes/no) as validated by Axford, *et al*[17]. Statistical analyses were performed using STATA version 13.1.

RESULTS

Patient characteristics. In total, 272 eligible consenting patients were invited to participate, of whom 185 (68%) completed the baseline measurements. A total of 161 (87%) who completed the measurements at 3 months' followup were included in the analyses. Around two-thirds (62%) of the patients were female, the mean age was 59 years (SD 9), and the mean BMI was 29.7 kg/m^2 (SD 5.0; Table 1). No differences were found between the participants and nonparticipants with regard to sex, although the participants were significantly older than the nonparticipants (59 yrs vs 56 yrs; p value = 0.02). The sociodemographic and disease-related characteristics of the patients are presented in Table 1. For each instrument, there were ≤ 5% missing values at both timepoints.

PASS cutoff values. Table 2 displays that the PASS cutoff values for function determined by 4 questionnaires range from 48 for the standardized LAI (95% CI 44–54) to 54 for the standardized LEFS (95% CI 50–56). This table shows that the cutoff values with their 95% CI for the PASS for physical function are comparable across the 4 different standardized

Table 1. Sociodemographic and disease-related characteristics of study sample (n = 161). Values are given as mean (SD) unless indicated otherwise. The mean scores of the KOOS-PS, LEFS, LAI, and WOMAC-PF are presented using the usual score range and using a normalized score (0–100).

Characteristics	Baseline	3 Months
Female, n (%)	99 (62)	
Age, yrs	59 (9)	
BMI, kg/m^2	29.7 (5)	
Duration of symptoms, n (%)		
> 5 yrs	59 (37)	
Localization of symptoms, n (%)		
Left knee	39 (24)	
Right knee	56 (35)	
Both sides	66 (41)	
Patients considering their state to be acceptable, n (%)	77 (49)	87 (56)
PROM regarding physical function		
KOOS-PS		
Range 0–28	18.3 (5.2)	17.8 (5.3)
Range 0–100	53.6 (16.8)	51.7 (15.8)
LAI		
Range 0–24	11.0 (4.0)	10.9 (4.3)
Range 0–100	45.8 (16.7)	45.4 (18.1)
LEFS*		
Range 0–80	40.6 (14.1)	41.0 (15.3)
Range 0–100	49.2 (17.6)	48.8 (19.1)
WOMAC-PF		
Range 0–68	32.8 (13.2)	32.0 (13.2)
Range 0–100	48.2 (19.4)	47.0 (20.5)
Other PROM		
NRS function (range 0–10)	5.5 (2.4)	5.4 (2.5)
NRS pain (range 0–10)	5.6 (2.1)	5.5 (2.2)
NRS PtGA (range 0–10)	5.6 (2.6)	5.5 (2.2)
Depression (HADS; range 0–21)		
No depressive feelings	4.6 (3.0)	3.6 (1.9)
Depressive feelings	8.5 (3.9)	10.3 (2.9)

*For all PROM except LEFS, higher scores reflect a higher level of disability. BMI: body mass index; WOMAC-PF: Western Ontario and McMaster Universities Osteoarthritis Index physical function subscale; LAI: Lequesne Algofunctional Index; LEFS: Lower Extremity Functional Scale; KOOS-PS: Knee Injury and Osteoarthritis Outcome Score, short version; PROM: patient-reported outcome measure; NRS: numerical rating scale; PtGA: patient's global assessment; HADS: Hospital Anxiety and Depression Scale.

PROM assessing physical function. The PASS values of NRS function, pain, and PtGA turned out to be consistent as well with a cutoff value of 60 (50–60). The 75th percentile of the NRS for function gives a PASS value of 60 (data not shown).

At 3 months' followup, 56% (95% CI 48–64) of the patients considered their state to be acceptable. The proportion of patients with depressive symptoms remained stable at 3 months' followup (30% vs 31%). The univariate logistic regression analysis showed that age and duration of symptoms are not associated with reaching the estimated PASS value for physical function, whereas a significant association was found between sex and being in PASS in 3 out of 5 PROM regarding function. Female patients have a smaller probability of reaching the estimated absolute PASS value for physical

Table 2. The estimated PASS cutoff values at 3 months' followup for different PROM assessing physical function.

PROM	PASS Value at 3 Months (95% CI)
KOOS-PS	
Range 0–28	19.5 (18.0–20.7)
Range 0–100	52.8 (48.5–56.8)
LEFS	
Range 0–80	37.0 (35.2–40.0)
Range 0–100	53.8 (50.0–56.1)
LAI	
Range 0–24	11.5 (10.5–13.0)
Range 0–100	47.9 (43.8–54.2)
WOMAC-PF	
Range 0–68	34.0 (31.0–38.0)
Range 0–100	50.0 (45.6–55.9)
NRS function	
Range 0–10	6.0 (5.0–6.0)
Range 0–100	60.0 (50.0–60.0)

All PROM present scores with higher scores defining a higher level of disability with the exception of the nonstandardized LEFS score range, where higher scores define higher level of functioning. PASS: Patient Acceptable Symptom State; PROM: patient-reported outcome measure; WOMAC-PF: Western Ontario and McMaster Universities Osteoarthritis Index physical function subscale; LAI: Lequesne Algofunctional Index; LEFS: Lower Extremity Functional Scale; KOOS-PS: Knee Injury and Osteoarthritis Outcome Score, short version; NRS: numerical rating scale.

function than male patients with a significant OR varying from 0.27 (95% CI 0.14–0.55) to 0.38 (95% CI 0.19–0.77) for the different PROM. Also, having depressive symptoms turned out to be associated with reaching the estimated absolute PASS value; patients having depressive symptoms have a smaller probability of reaching an acceptable state for physical function than patients without depressive symptoms, with a significant OR around 0.50 for all PROM except the KOOS-PS (Table 3). The multivariate logistic regression analyses yielded similar results (data not shown).

DISCUSSION

We documented the PASS cutoff values for physical function and its determinants across different PROM in a cohort of patients with knee OA in the Netherlands. Our results show that these PASS cutoff values are relatively robust across different questionnaires measuring physical function. Also, in our knee OA cohort, and in line with previous results for OA, patients consider a higher level of symptoms acceptable than previously reported for other rheumatic diseases[6,10]. In addition, we observed that women and depressive patients have a lower chance of reaching the estimated PASS value. The consistency of the cutoff values of the PASS for physical function across different PROM assessing the same construct physical function in a specific cohort represents the robustness of the PASS values for physical function across these 4 different PROM measuring physical function. To our knowledge, the robustness of the PASS regarding 1 outcome domain, i.e., physical functioning, measured with 4 different PROM, has never been studied before. Therefore, our findings suggest that different questionnaires may be used to determine PASS cutoff values for physical function of a certain population and setting. Future research is warranted to investigate this finding in other populations and settings, and to examine whether this robustness is also valid for other outcome domains.

We found a higher PASS value for physical function than the generic, multinational PASS value reported previously, applicable for 5 different rheumatic conditions (including hip and knee OA) and for different outcome domains (pain, PtGA, physical function)[10]. Our values are comparable with other studies reporting on the PASS value of physical function in the context of nonsurgical treatment of OA[10,11]. However, our findings support earlier findings that PASS values might be variable across different rheumatic diseases, countries, types of intervention, and outcome domains. In previous studies, higher PASS values for patients with OA than for other rheumatic diseases were found, which may be caused by not having high expectations from optimized nonsurgical treatment modalities in knee OA compared to, for example, expectations from rheumatoid arthritis treatment[10]. Bellamy, *et al* questioned the generalizability of PASS values to other countries, languages, and cultures, because they found considerable variation in PASS values

Table 3. Significant OR of the univariate logistic regression for each PROM for reaching the absolute PASS value.

	PASS				
	NRS Function	KOOS-PS	LAI	LEFS	WOMAC-PF
Dependent variables					
Female	0.45 (0.23–0.91)	0.47 (0.24–0.93)	0.50 (0.26–0.97)		
Age ≥ 65 yrs					
Duration of symptoms > 5 yrs					
Depressive feelings	0.38 (0.19–0.77)		0.27 (0.14–0.55)	0.32 (0.16–0.64)	0.36 (0.18–0.72)

The OR is given for every independent variable in the logistic regression with 95% CI for each PROM for function. All OR significant at the 0.05 level are shown. PASS: Patient Acceptable Symptom State; PROM: patient-reported outcome measure; NRS: numerical rating scale; WOMAC-PF: Western Ontario and McMaster Universities Osteoarthritis Index physical function subscale; LAI: Lequesne Algofunctional Index; LEFS: Lower Extremity Functional Scale; KOOS-PS: Knee Injury and Osteoarthritis Outcome Score, short version.

across countries[11]. In addition, the variability in PASS values across countries was confirmed in recent studies from France reporting on relatively low PASS values for physical function in patients with knee and hip OA[6]. The observation that lower PASS values after total joint replacement were estimated than after NSAID treatment in Spanish patients with OA suggests that the type of intervention could affect PASS values as well[11,33]. This is in line with previous suggestions that patients expect greater effects from surgery than from nonsurgical therapy[34]. Finally, several studies documented that PASS values for physical function are higher than those for other domains[10,11]. Taking the above considerations into account, it is conceivable that PASS values are generalizable only to 1 outcome domain in a specific disease for a certain type of intervention, and thus that the use of a generic PASS value is not justifiable. An alternative could be to determine PASS values for each study separately, by including the standardized question in the data collection, rather than applying a generic (multinational) estimated value.

An intriguing finding of our study was that patients having depressive feelings are associated with a lower chance of reaching the estimated PASS value. In fact, this could be in line with the previous notion that acceptability of a certain disease state is not only dependent on the absolute level of complaints, but is also dependent on other factors, and in this particular case on the patient's mood. If future research does confirm this finding, this may create a new point of view when treating a patient with OA who does not reach an acceptable symptom state.

Potential limitations of our study include the quite small cohort used in our study compared to the cohorts used in earlier studies to determine the PASS. However, because we used a homogeneous cohort, our findings seem generalizable to Dutch patients who are not yet deemed eligible for surgery. Another limitation for studies examining PASS values in general could be that a response shift took place, in which perception of the disease state changes during the assessments[35]. In addition, a general limitation for studies using PASS values is that there is no uniform approach to establishing a PASS value; the question asked to the patient varied across earlier studies and the time extent was different[6]. If the PASS is to become a universal concept for defining interventional success, a standard anchor question for meaningful comparison of results across groups should be established, in particular with regard to the duration of an acceptable state. We would suggest that PASS implies a state without change, that is, the time spent in the state as "rest of your life" as recommended by the Outcome Measures in Rheumatology 8[34,36].

PASS cutoff values are robust for physical function across different PROM in patients with knee OA. However, our results indicate that PASS values are not consistent across dimensions and rheumatic diseases, and that the use of a generic PASS value for patients with OA or even patients with other rheumatic disorders might not be justifiable.

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