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Three dimensions of pain in osteoarthritis: development and validation of the Osteoarthritis Symptom Inventory Scale

Serge Perrot^{a,b,*}, Anne-Priscille Trouvin^{a,b}, Didier Bouhassira^b

Abstract

We describe here the development and validation of the Osteoarthritis Symptom Inventory Scale (OASIS), a new self-administered questionnaire specifically designed to evaluate the various osteoarthritis (OA) pain symptoms with different dimensions related to OA pain mechanisms. The initial development phase and qualitative study generated a list of 17 descriptors reflecting OA pain and other associated symptoms, leading to the first version of the questionnaire (OASIS17). Each item was quantified on a 0 to 10 Numerical Scale. Validation was performed using 123 consecutive patients with OA pain recruited at 28 centers in France, mainly general practitioner offices. Validation involved (1) determining the questionnaire's factorial structure through exploratory and confirmatory analyses, (2) analyzing convergent and divergent validities (ie, construct validity), (3) assessing each item's test-retest reliability, and (4) evaluating OASIS ability to detect treatment effects (ie, sensitivity to change). The final OASIS version includes 9 items discriminating and quantifying 3 distinct, clinically relevant OA pain dimensions sensitive to treatment. OASIS9 psychometric properties suggest that it could improve the characterization of OA pain profiles for 3 clinically relevant domains: localized, neuropathic-like, and deep pain. The OASIS9 questionnaire could be used to phenotype OA pain patients and identify responders to various therapeutic interventions as a function of OA pain dimensions.

Keywords: Osteoarthritis, Pain, Symptoms, Questionnaire, Qualitative analysis

1. Introduction

Osteoarthritis (OA) pain is a complex and heterogeneous condition.²⁷ However, the description of pain dimensions in OA has rarely been addressed.¹⁴ Pain intensity in OA is commonly assessed with Numerical Rating and Visual Analog Scales.¹⁵ Pain, stiffness, and function can be assessed by the Western Ontario and McMaster Universities OA (WOMAC)⁴ or Lequesne indices, with a good correlation between them. The McGill Pain Questionnaire has been validated in patients with hip and knee OA (KOA)¹³ for investigating sensory and affective pain dimensions. Neuropathic pain characteristics have also been investigated in painful OA using various questionnaires, including PainDETECT and Leeds Assessment of Neuropathic Symptoms and Signs.²¹

Osteoarthritis pain intensity assessments are insufficient for pain analysis since they vary daily and may prove difficult over prolonged periods²⁶ and in patients with different pain trajectories^{3,10} or day and night pain.³² Several studies have highlighted the importance of phenotyping OA pain, particularly for preventing chronicity and detecting pain susceptibility.⁸ However, the utility of OA pain phenotyping for treatment personalization remains to be shown.²⁴ While quantitative sensory testing (QST) has been used for phenotyping OA pain,⁷ this approach is infeasible in everyday practice, and simple questionnaires are required to analyze OA pain quality and to define clinical pain phenotypes.

An OA Research Society International (OARSI) and Outcome Measures in Rheumatology (OMERACT) initiative investigating several OA pain dimensions led to the development of Intermittent and Constant OA Pain (ICOAP), a questionnaire including items on pain intensity, frequency, and impact on mood, sleep, and quality of life.¹⁵ While qualitative pain descriptors were not incorporated into ICOAP, this approach has been used to assess neuropathic pain to improve clinical profile characterization and personalize patient management.⁶ We adopted such an approach to develop a qualitative analysis of OA pain⁸ and a new questionnaire based on pain descriptors, the OA Symptom Inventory Scale (OASIS), to facilitate the identification of different pain phenotypes in patients with OA. In a previous qualitative study based on patient interviews and focus groups, we developed an initial 17-item version (OASIS17).⁹ We describe here the psychometric validation of the OASIS questionnaire and the development of a short and valid OASIS 9-item version.

Our conceptual framework was to detect questionnaire's specific dimensions that may be related to different pain mechanisms, may respond differently to specific approaches, and may help to define

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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responder profiles in OA pain management. We expected factor analyses of the different OASIS versions to define 3 dimensions related to pain pathophysiological mechanisms: nociceptive, neuropathic, and nociplastic. We also aimed to develop a short, easier-to-use questionnaire with less than 15 items.

2. Methods

2.1. Study and ethics statement

Psychometric validation of OASIS was performed using consecutive patients recruited at 28 centers between September 2016 and March 2018. This validation was included in an open-label longitudinal cohort study conducted by general practitioners (GPs), who recommended using a nutritional supplement and a balanced diet to treat OA flare-ups, as recommended by a previous study.¹ This larger study and the substudy described here were approved by the Advisory Committee on Information Processing in Material Research in the Field of Health (ethics committee agreement no: 16-634) and the French National Commission on Computing and Liberties. It was performed according to the ethical standards defined in the Declaration of Helsinki and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. It was registered on the ClinicalTrials.gov site in November 2016 with the identification number NCT02977936.

2.2. Patients

Adult (>18 years) male and female patients with unilateral or bilateral KOA and flare-ups were included if (1) they presented painful KOA with scores ≥ 4 at rest or ≥ 5 during movement (walking) on a 10-point Numerical Rating Scale (NRS) and (2) they were unsatisfied with their symptomatic state (negative PASS [patient acceptable symptom state²⁵]) at the time of recruitment. The KOA diagnosis had to be confirmed by clinical examination, and an X-ray performed within the 2 years preceding inclusion had to show mild-to-moderate joint damage (Kellgren–Lawrence score of 2 or 3).

The following patients were excluded from the study: (1) those with painful knees due to a rheumatological condition other than OA; (2) those with chronic pain likely to interfere with KOA pain; (3) those awaiting knee surgery within the next 3 months; (4) those on chondroitin sulfate treatment, nonsteroidal anti-inflammatory drugs, or any other analgesic for at least one month; (5) those with reduced mobility or bedridden; (6) those with a body mass index >35 kg/m²; (7) those with cognitive disorders preventing study participation; (8) those with known hypersensitivity to at least one component of the supplement; and (9) those who were pregnant or breastfeeding.

Finally, all patients meeting all inclusion criteria and none of the exclusion criteria received written information about the study and gave written informed consent before inclusion.

2.3. Study design

Two visits were scheduled for each patient: an initial visit and a follow-up visit at 3 months. The patients were also asked to complete and return the questionnaires described below at 10, 20, 30, 60, and 90 days.

During the initial visit after patient selection, patients (**Table 1**) were asked to (1) rate the mean intensity of their pain during the last 24 hours on an 11-point (0–10) NRS, (2) complete the OASIS17, and (3) complete the Douleur Neuropathique 4 (DN4) and the Lequesne index. At the end of their initial visit, the GP

Table 1

Demographic characteristics of the patients.

	N = 118
Age	62.9 ± 9.5
Sex	82 women (69.5%)
Weight	72.9 ± 13.6 kg
BMI	26.4 ± 4.0
NRS for pain	6.1 ± 1.9
DN4	Negative test in 90.7%
Lequesne index	7.7 ± 3.9
Treatment for pain	16.9%

BMI, body mass index; DN4, Douleur Neuropathique 4; NRS, Numerical Rating Scale.

recommended a dietary supplement, a fixed combination of *Boswellia*, turmeric, and red algal extracts, as would be the case in routine clinical practice.

After the initial visit, patients were asked to complete several questionnaires and to provide information about their compliance and use of concomitant analgesics or anti-inflammatory drugs to evaluate supplement efficacy and tolerance over the 90 days of dietary supplementation. Patients completed the Patient Global Impression of Change (PGIC), the NRS for pain, OASIS17, and the Lequesne index on days 0, 30, 60, and 90. The Numerical Rating Scale for pain and PGIC were also tested on 10 and 20 days of treatment.

The PGIC was designed to assess the patient's perception of change in their global health state (symptoms and quality of life) after treatment within the past 10 days.¹¹ It is a 7-point scale, with options 1 (very much worsened), 2 (much worsened), 3 (minimally worsened), 4 (no change), 5 (minimally improved), 6 (much improved), and 7 (very much improved).

The Lequesne index was designed to assess function and pain.¹⁸ This index includes 11 items grouped into 3 dimensions: pain (5 items), maximum distance walked (2 items), and activities of daily living (4 items). A score is given for each item, and per-dimension scores are calculated by summing the scores for all associated items. Each dimension's score ranges from 0 to 8. The Lequesne index is calculated by summing the scores of the 3 dimensions, ranging from 0 to 24. Based on their Lequesne index, patients were classified into 6 classes: 0, no handicap; 1 to 4, mild handicap; 5 to 7, moderate handicap; 8 to 10, severe handicap; 11 to 13, very severe handicap; and ≥ 14 , extremely severe handicap.

The DN4 questionnaire was designed to screen for neuropathic pain components. Patients are considered likely to have neuropathic pain if their DN4 score is ≥ 4 .⁵

All these data were collected again during an end-of-study visit performed 3 months after its start. Data were then captured in an electronic case report form.

2.4. Construction of the initial Osteoarthritis Symptom Inventory Scale questionnaire

The initial version of the OASIS questionnaire was created in a previous qualitative study based on focus groups and patient interviews.⁹ Based on the results of this qualitative study, we obtained a pool of 26 distinct items to describe OA pain and associated physical and psychological symptoms. Discussions with a panel of 8 French, Swiss, and Belgian experts grouped

these 26 items into 7 domains. We did not retain questions on mood, image, and general symptoms to focus on OA pain descriptors and characteristics. Retaining only 4 domains directly related to OA pain (pain sensations, pain variations, pain-triggering factors, and pain and physical activity) reduced the questionnaire to 17 items. We tested the initial 17-item questionnaire (OASIS17) in 20 patients with KOA to assess its face validity and to adapt the items' wording to improve their comprehension. Patients were asked to complete the initial OASIS17 version and to rate each item for clarity, understanding, and relevance to their pain symptoms.

2.5. Assessment of the Osteoarthritis Symptom Inventory Scale questionnaire's psychometric properties

2.5.1. Factor analysis

Exploratory factor analyses were used to determine whether the scale's 17 items describing painful OA symptoms could be combined into independent factors representing different OA pain dimensions. Principal component analysis (PCA) was the extraction method used for factor analysis. Independent factors were identified by the Varimax rotation method. The factor analysis was performed twice (at baseline and after 60 days) to determine whether the dimensions obtained were stable over time. Confirmatory factor analyses were performed on different OASIS questionnaire versions to identify and retain items and dimensions that fit our theoretical model¹⁶ with a standardized root mean residual (SRMR) <0.08, a root mean square error of approximation (RMSEA) ≤0.06, and an adjusted goodness of fit index (AGFI) >0.9.

2.5.2. Reliability and internal consistency

Reliability was assessed using the intraclass correlation coefficient (ICC) determined between days 0 and 30 for a subset of 67 patients with no significant changes in their NRS or PGIC during this 30-day period (additional data, Supplementary Table 1, available at <http://links.lww.com/PAIN/B771>). For internal consistency, Cronbach alpha (α) coefficients were calculated for all items and each dimension.

2.5.3. Convergent and divergent validity

The relationships between global pain intensity measured on the NRS, Lequesne score, DN4 score, and the total OASIS score and its subscores were assessed using Spearman rank correlation coefficient (r_s).

2.5.4. Sensitivity to change

Spearman rank correlation coefficients were calculated to assess relationships between the changes (ie, differences) in the total OASIS score and subjective evaluations made by the patients (PGIC) over the study period (3 months).

3. Results

This study enrolled 123 patients between September 2016 and March 2018. Of these 123 patients, 118 took at least one capsule of the dietary supplement and were assigned to the intention-to-treat (ITT) group. Their clinical and demographic characteristics are provided in **Table 1**. Among the 5 patients not included in the ITT group, 3 were excluded because they did not meet all

inclusion criteria or met some exclusion criteria, one had not taken any supplement doses, and one was a self-included GP.

3.1. Acceptability

OASIS17 was completed accurately and appeared to have been fully understood, notably by elderly subjects. The mean time to complete the questionnaire was less than 5 minutes for most patients (ie, approximately 85%).

3.2. Questionnaire development using factor analyses

3.2.1. Principal component analysis

Principal component analysis analyses of OASIS17 (**Table 2**) showed that the first 3 principal components (PCs) explain 52.1% of the total variance (34.3% for PC1, 9.6% for PC2, and 8.1% for PC3). The first 4 PCs explained 59.0% of the total variance (6.8% for PC4), and the first 5 explained 64.7% of the total variance (5.7% for PC5). Since our goal was to develop a shorter questionnaire, we removed the last 4 items, keeping only those explaining 90% of the total variance, creating the OASIS13 version.

3.2.2. Reliability

The initial OASIS17 was administered to all 123 patients. The ICC was calculated between days 0 and 30 using a subset of 67 patients with no significant changes in their NRS or PGIC during this 30-day period (Supplementary Table 1; see additional data, available at <http://links.lww.com/PAIN/B771>). The ICC for each OASIS17 item was between 0.36 and 0.82. Reliability was considered poor (<0.50) for 4 items: "Do you experience permanent background pain?" (0.36), "Do you have pain attacks during the day?" (0.38), "Does your pain vary from day to day?" (0.45), and "Is your pain more intense at night than during the day?" (0.41), the same 4 items that were deleted after the PCA analysis to obtain the OASIS13 version.

3.2.3. Factor identification

Factor analysis of OASIS13 identified a 3-factor solution explaining 55.5% of the total variance (**Table 3**). Each of the 3 independent factors corresponds to a relevant OA pain pathophysiology mechanism. Based on the items of each of the 3 dimensions, we labeled them as localized, neuropathic-like, and deep pain. These names were proposed based on their included descriptors.

Factor 1 included 5 items potentially related to localized joint-related OA pain mechanisms to define a "localized pain" dimension: crushing pain, painful stiffness, pain around the joint, joint swelling, and painful activity limitation.

Factor 2 included 4 items potentially related to a neuropathic pain component to define a "neuropathic-like pain" dimension: burning pain sensation, tingling pain, electric shock pain, and foreign body sensation. The first 3 items are classically used to detect neuropathic pain in neuropathic pain questionnaires such as DN4⁵ and Neuropathic Pain Symptom Inventory (NPSI).⁶

Factor 3 included 4 items potentially related to more constant pain mechanisms to define a "deep pain" dimension: constant deep pain, stabbing pain, weather-sensitive pain, and pain without activity.

Table 2
Principal component analyses OASIS17.

	Value	Difference	Proportion	Cumulated
Deep pain	5.83677424	4.19794508	0.3433	0.3433
Stabbing pain	1.63882917	0.25287360	0.0964	0.4397
Electric shocks	1.38595556	0.22322515	0.0815	0.5213
Crushing pain	1.16273041	0.19382626	0.0684	0.5897
Burning pain	0.96890415	0.14071668	0.0570	0.6467
Tingling in the joints	0.82818747	0.09330437	0.0487	0.6954
Pain outside of the joint	0.73488310	0.03593178	0.0432	0.7386
Foreign body sensation	0.69895132	0.04134572	0.0411	0.7797
Joint stiffness	0.65760560	0.08113282	0.0387	0.8184
Joint swelling	0.57647278	0.07225941	0.0339	0.8523
Pain influenced by weather conditions	0.50421337	0.03856788	0.0297	0.8820
Pain without physical activity	0.46564549	0.05727831	0.0274	0.9094
Pain-related activity limitation	0.40836719	0.05773481	0.0240	0.9334
Nocturnal peak of pain	0.35063238	0.01661740	0.0206	0.9540
Permanent pain	0.33401498	0.10176213	0.0196	0.9737
Diurnal peak of pain	0.23225285	0.01667292	0.0137	0.9873
Variable pain	0.21557992		0.0127	1.0000

The factor analysis remained stable when repeated at 2 months (60 days), with the same 3 dimensions identified (Table 3).

3.2.4. Confirmatory factor analyses of the 3 OASIS13 dimensions and OASIS9 development

We performed additional analyses to assess OASIS13 3-dimensional model and its alignment with the theoretical model. These analyses showed that the 3 dimensions defined in OASIS 13 did not reach significance, with an SRMR = 0.0837 (a value < 0.05 is recommended), an RMSEA = 0.0875 (a value ≤ 0.06

indicates good adjustment), and an AGFI = 0.81 (a value >0.9 is recommended).¹⁶

Therefore, we decided to remove the weakest items in each factor, performing confirmatory analyses for the 3 dimensions using 9 items. We removed 4 items, 1 from factor 3 (“deep pain”), 2 from factor 2 (“electric shock” and “foreign body sensation”), and 1 from factor 1 (“diffuse pain”).

Finally, confirmatory analyses for the OASIS9 items and their 3 dimensions showed that the theoretical model fitted well with this version of the OASIS questionnaire (SRMR = 0.0617, RMSEA = 0.0645, and AGFI = 0.87; Fig. 1).

Table 3
OASIS13 factor analyses at baseline and 60 days.

	Factor 1 Baseline	Factor 1 60 days	Factor 2 Baseline	Factor 2 60 days	Factor 3 Baseline	Factor 3 60 days
Deep pain	0.47356	0.54669	-0.00400	0.33099	0.57400	0.54904
Stabbing pain	0.10718	0.33016	0.26231	0.74731	0.64746	0.05659
Electric shocks	-0.03058	0.38412	0.50054	0.77767	0.46936	0.09223
Crushing pain	0.69719	0.75040	0.26727	0.10984	0.12409	0.33206
Burning pain	-0.05992	0.25252	0.80063	0.73983	0.07245	0.25069
Tingling in the joint	0.27316	0.04051	0.68678	0.72860	0.26502	0.44906
Pain outside of the joint	0.51829	0.59552	0.45663	0.30945	0.17407	0.43294
Foreign body sensation	0.51403	0.51335	0.52857	0.56016	0.12509	0.02360
Joint stiffness	0.66780	0.67396	-0.07822	0.44439	0.37545	0.13888
Joint swelling	0.70399	0.76303	0.21354	0.28902	-0.12633	0.11995
Pain influenced by weather conditions	0.03995	0.24430	0.07036	0.09660	0.69167	0.87431
Pain without physical activity	0.30131	0.47595	0.27474	0.47708	0.61895	0.47944
Pain-related activity limitation	0.70755	0.71935	-0.16311	0.32097	0.27229	0.31772

Bold entries: items retained in each factor.

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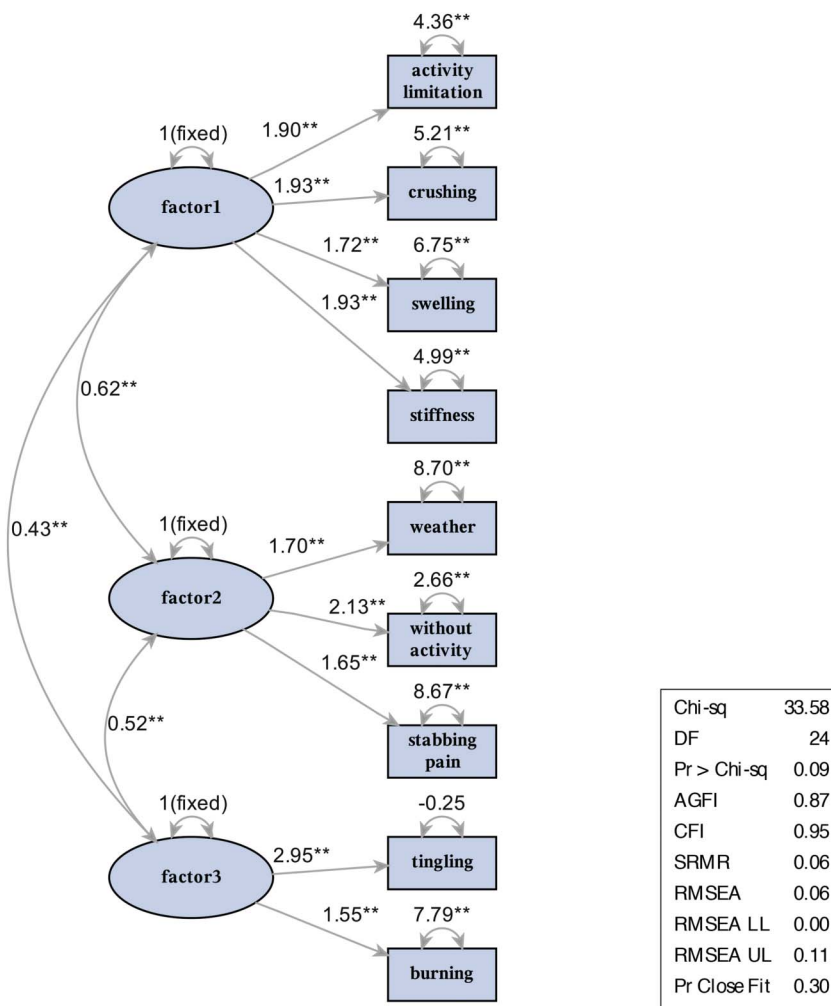


Figure 1. OASIS9 confirmatory analyses. AGFI, adjusted goodness of fit index; OASIS, Osteoarthritis Symptom Inventory Scale; RMSEA, root mean square error of approximation; SRMR, standardized root mean residual.

3.3. Prevalence of OASIS9 items in the intention-to-treat group

The scores for the 9 items in the final OASIS9 questionnaire ranged from 2.0 to 6.4, with positive scores obtained for more than 42 (35.6%) patients (Table 4). Distribution of scores for each item is described in Figure 2, and follow-up of domain scores and total scores along the study is presented in Figure 3.

3.4. Internal validity of the OASIS9 questionnaire

The OASIS9 questionnaire’s internal consistency, taken as a whole, is satisfactory, with a Cronbach α of 0.77. It remained satisfactory after the deletion of each component variable, with partial alpha coefficients >0.72 and differences with the overall alpha coefficient <10% (Table 5). The internal consistency of all 3 dimensions varied. It was satisfactory for “localized pain” (Cronbach α = 0.73) and moderately satisfactory for “neuropathic-like pain” (Cronbach α = 0.66) and “deep pain” (Cronbach α = 0.60; Supplementary Table 2, see additional data, available at <http://links.lww.com/PAIN/B771>). OASIS9 items were not all correlated with each other (Table 6), but all items within the 3 dimensions were strongly correlated (Supplementary

Table 2, see additional data, available at <http://links.lww.com/PAIN/B771>).

Table 4
OASIS9 items prevalence and scores in the global population.

Dimension	Item	Mean	SEM	No. of patients with score >0
Localized pain	Joint stiffness	5.0	2.9	85
	Joint swelling	4.3	3.1	74
Neuropathic-like	Pain-related activity limitation	6.4	2.8	90
	Crushing pain	2.7	3.0	57
Deep pain	Burning pain	2.4	3.2	45
	Tingling in the joints	2.0	2.9	42
	Stabbing pain	3.4	3.4	59
	Pain influenced by weather conditions	3.9	3.4	67
	Pain without physical activity	4.8	2.7	90

3.5. Validity of Osteoarthritis Symptom Inventory Scale and its 3 dimensions

Validity was assessed by the correlation of OASIS total scores and its 3 subscores with other variables, such as pain intensity (NRS), pain quality (DN4), and loss of function (Lequesne index) at baseline (Table 7).

3.5.1. Convergent validity of Osteoarthritis Symptom Inventory Scale and its subscores with pain intensity

Spearman correlation coefficients between OASIS9 total scores or its subscores with NRS were significant (Table 7), confirming the relevance of the questionnaire and its dimensions for assessing pain intensity. Interestingly, NRS was less strongly

correlated with each subscore than the total score, suggesting that each dimension only partly assesses pain intensity.

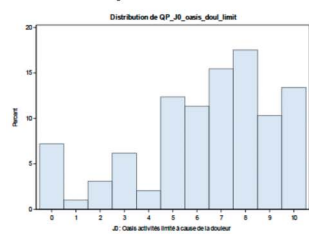
3.5.2. Convergent and divergent validity of Osteoarthritis Symptom Inventory Scale and its subscores with neuropathic pain

Pearson correlation coefficient between OASIS9 total scores and DN4 scores was weakly significant ($r = 0.21, P = 0.03$) (Table 7). Correlations between dimensions 1 or 3 and DN4 scores were not significant ($P = 0.4$ and $P = 0.09$, respectively). However, dimension 2 and DN4 scores were significantly correlated ($r = 0.35$ and $P = 0.0004$). The significant correlation between DN4 scores and dimension 2 but not dimensions 1 and 3 confirms that dimension 2 is linked explicitly to the neuropathic pain component.

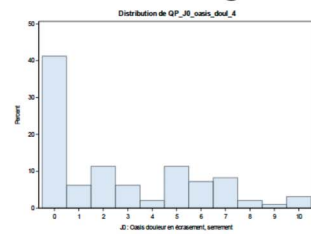
OASIS9: scores obtained for each item

Dimension 1 : localized pain

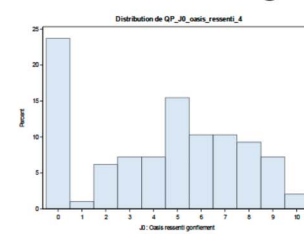
Activity limitation



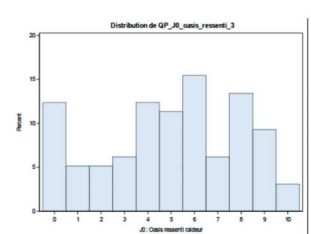
Crushing



Swelling

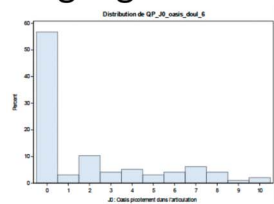


Stiffness

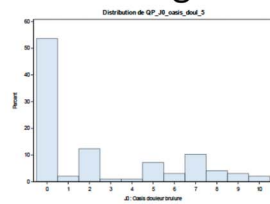


Dimension 2 : neuropathic-like pain

Tingling

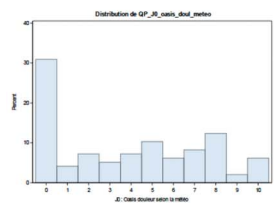


Burning

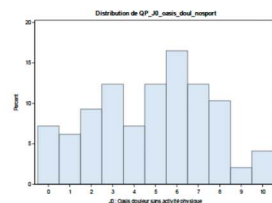


Dimension 3 : deep pain

Weather sensitive pain



Pain without activity



Stabbing pain

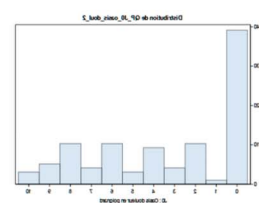


Figure 2. OASIS9 items scores. OASIS, Osteoarthritis Symptom Inventory Scale.

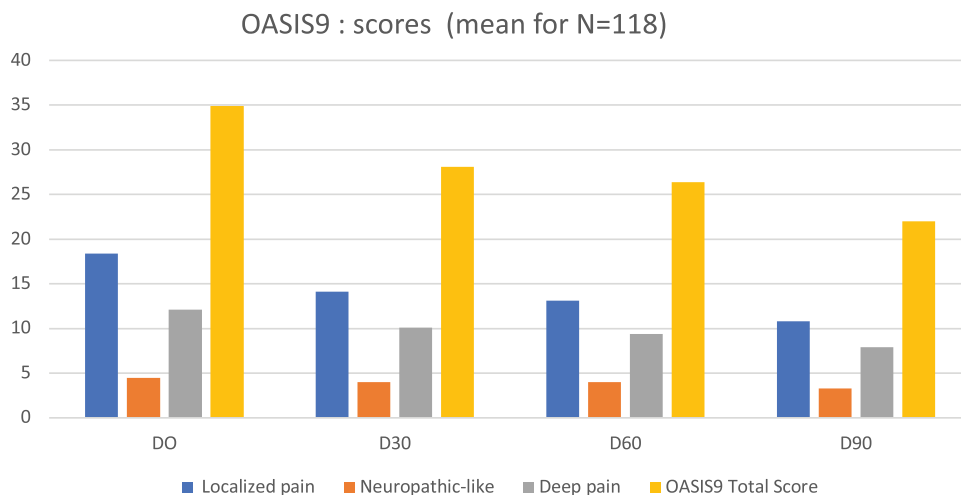


Figure 3. OASIS9 scores study follow-up. OASIS, Osteoarthritis Symptom Inventory Scale.

3.5.3. Convergent validity with functional impairment: Lequesne index

All Pearson correlation coefficients between OASIS9 total scores or its subscores and Lequesne indices were significant (Table 7), confirming the global relevance of the questionnaire and its 3 dimensions for functional assessment. The correlation was stronger for the “localized pain subscore” dimension than for the “neuropathic-like” or “deep pain” dimensions.

3.6. Sensitivity to change: correlations between Osteoarthritis Symptom Inventory Scale and patient global impression of change scores at 1, 2, and 3 months

Changes in the PGIC and OASIS total scores between visits were weakly inversely correlated (1 month: $r_s = -0.30$; 2 months: $r_s = -0.23$; and 3 months: $r_s = -0.31$), indicating that global improvements in PGIC scores were associated with decreased OASIS total scores.

3.7. Clinical use of the OASIS9 questionnaire

The original French version of the OASIS9 questionnaire and its English translation are provided in Figures 4A and B, respectively. The questionnaire was translated by an iterative forward–backward translation sequence but has not yet been formally validated in English-speaking patients.

OASIS9 should be used as separate subscores, the sum of all domain items, and as a total score. Each patient’s clinical profile characterization should be followed during treatment using each subscore and the total score.

4. Discussion

This study described the development and validation of a novel instrument, the OASIS questionnaire, to evaluate various OA pain symptoms based on qualitative pain descriptors. The psychometric properties of the version of the questionnaire, a 9-item version, OASIS9, indicate that this self-administered

Table 5
OASIS9— internal validity.

Deleted variable	Raw variables		Standardized variables	
	Correlation with total	Alpha	Correlation with total	Alpha
Stabbing pain	0.385340	0.745751	0.390022	0.752366
Crushing pain	0.505471	0.725784	0.510143	0.734024
Burning pain	0.281026	0.761296	0.278660	0.768662
Tingling	0.554572	0.718636	0.550664	0.727653
Stiffness	0.496172	0.727387	0.500240	0.735567
Swelling	0.387102	0.744313	0.398762	0.751059
Weather sensitive	0.361387	0.749991	0.365571	0.756002
Pain without activity	0.582169	0.716682	0.577447	0.723391
Pain-related activity limitation	0.444985	0.735481	0.451128	0.743136

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Table 6

OASIS9 correlation between items.

Spearman correlation coefficients

	Stabbing	Crushing	Burning	Tingling	Stiffness	Swelling	Weather-sensitive pain	Pain without activity	Activity limitation pain-related
Stabbing pain	1.00000	0.30263 0.0026	0.14303 0.1622	0.37362 0.0002	0.26013 0.0101	0.08205 0.4243	0.16008 0.1173	0.37265 0.0002	0.22333 0.0279
Crushing		1.00000	0.19209 0.0594	0.38478 <0.0001	0.36207 0.0003	0.40444 <0.0001	0.12500 0.2225	0.20283 0.0463	0.40918 <0.0001
Burning			1.00000	0.52127 <0.0001	-0.00888 0.9312	0.19158 0.0601	0.20857 0.0403	0.21352 0.0357	-0.03946 0.7012
Tingling				1.00000	0.33600 0.0008	0.24616 0.0151	0.27472 0.0065	0.36560 0.0002	0.13468 0.1884
Stiffness					1.00000	0.34231 0.0006	0.35402 0.0004	0.34429 0.0006	0.49104 <0.0001
Swelling						1.00000	0.10257 0.3174	0.30487 0.0024	0.41004 <0.0001
Weather							1.00000	0.40614 <0.0001	0.19349 0.0576
Pain without activity								1.00000	0.34239 0.0006
Activity limitation									1.00000

questionnaire: (1) can discriminate between and quantify 3 distinct clinically relevant OA pain dimensions, (2) is valid and reliable, and (3) is sensitive to treatment effects.

In clinical practice, OASIS9 can be used as a total score, calculated as the sum of all items, and as 3 subscores, determining each domain's importance for the patient. This approach is similar to the WOMAC questionnaire, which has 3 domains and provides scores for each domain and a global score.

Several questionnaires for OA pain assessment have already been developed. WOMAC is the most widely used

OA-specific scale.¹⁴ It evaluates the intensity of hip and knee OA pain while performing 5 activities: standing, walking, climbing stairs, resting, and sleeping. The Lequesne algofunctional index is also a questionnaire exploring pain and function.¹⁸ The Hip Disability and OA Outcome Score and Knee Injury and OA Outcome Score were developed²³ to analyze functional limitations related to OA pain²² but not specifically to analyze pain symptoms.

This study aimed to develop a questionnaire on qualitative pain aspects based on qualitative analyses⁹ and according to pain pathophysiological mechanisms. OA Research Society

Table 7

OASIS9 convergent and divergent validity.

Pearson coefficient correlation

	OASIS9	Localized	Neuropathic	Deep pain	DN4	Lequesne index	NRS
OASIS9	1.00000	0.80794 <0.0001	0.64922 <0.0001	0.79293 <0.0001	0.21432 0.0350	0.54425 <0.0001	0.54745 <0.0001
Localized		1.00000	0.25842 <0.0001	0.40528 <0.0001	0.04661 0.4171	0.52337 <0.0001	0.46635 <0.0001
Neuropathic-like			1.00000	0.41355 <0.0001	0.34957 0.0004	0.25371 0.0126	0.27287 0.0081
Deep pain				1.00000	0.17042 0.0951	0.40252 <0.0001	0.45632 <0.0001
DN4					1.00000	0.09717 0.3463	0.09659 0.3570
Lequesne						1.00000	0.45554 <0.0001
NRS							1.00000 <0.0001

Correlations between OASIS9 total scores, subscores, and other questionnaires at baseline. DN4, Douleur Neuropathique 4; NRS, Numerical Rating Scale.

A OASIS9 QUESTIONNAIRE		Sélectionnez 0= aucune sensation 10= sensation extrême	Sous-score total	Score total
Domaine 1 Douleurs localisées (L)	<p>Ressentez-vous des douleurs comme un écrasement ?</p> <p>Avez-vous un enraidissement ou une raideur ?</p> <p>Avez-vous des sensations de gonflement de l'articulation ?</p> <p>Devez-vous limiter vos activités physiques à cause de la douleur ?</p>	<p>0 1 2 3 4 5 6 7 8 9 10</p> <p>0 1 2 3 4 5 6 7 8 9 10</p> <p>0 1 2 3 4 5 6 7 8 9 10</p> <p>0 1 2 3 4 5 6 7 8 9 10</p>	L1+L2+L3+L4	L+N+P
Domaine 2 Douleurs d'allure neuropathique (N)	<p>Ressentez-vous des douleurs comme des brûlures ?</p> <p>Ressentez-vous des picotements dans l'articulation et autour</p>	<p>0 1 2 3 4 5 6 7 8 9 10</p> <p>0 1 2 3 4 5 6 7 8 9 10</p>	N1+N2	
Domaine 3 Douleurs profondes (P)	<p>Vos douleurs sont-elles influencées par les conditions météorologiques ?</p> <p>Ressentez-vous vos douleurs même sans activité physique ?</p> <p>Ressentez-vous des douleurs comme un coup de poignard ?</p>	<p>0 1 2 3 4 5 6 7 8 9 10</p> <p>0 1 2 3 4 5 6 7 8 9 10</p> <p>0 1 2 3 4 5 6 7 8 9 10</p>	P1+P2+P3	

(Continued on next page)

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B OASIS9 QUESTIONNAIRE		SELECT 0 IF YOU DO NOT FEEL SUCH A SENSATION, OR 10 IF YOU DO FEEL IT INTENSELY	Total subscore	Total score
Dimension 1: localized pain (L)	Does your pain feel like crushing?	0 1 2 3 4 5 6 7 8 9 10	L1+L2+L3+L4	L+N+D
	Do you have stiffness in the joint?	0 1 2 3 4 5 6 7 8 9 10		
	Do you feel that the joint is swollen?	0 1 2 3 4 5 6 7 8 9 10		
	Do you need to limit your physical activities because of the pain?	0 1 2 3 4 5 6 7 8 9 10		
Dimension 2 : Neuropathic-like pain (N)	Does your pain feel like burning?	0 1 2 3 4 5 6 7 8 9 10	N1+N2	
	Do you feel tingling in and around the joint?	0 1 2 3 4 5 6 7 8 9 10		
Dimension 3: Deep pain (D)	Is your pain influenced by weather conditions?	0 1 2 3 4 5 6 7 8 9 10	D1+D2+D3	
	Do you feel pain even without physical activity?	0 1 2 3 4 5 6 7 8 9 10		
	Does your pain feel like being stabbed?	0 1 2 3 4 5 6 7 8 9 10		

Figure 4. OASIS9 Questionnaire. (A) French version. (B) English version. OASIS, Osteoarthritis Symptom Inventory Scale. OASIS9 © Serge Perrot, 2022.

International and OMERACT developed a qualitative methodology to create ICOAP, a questionnaire including items exploring pain intensity, frequency, and impact on mood, sleep, and quality of life.¹⁵ This qualitative approach explored changes in pain characteristics over time relative to the priorities and concerns of patients with hip or knee pain. Finally, this study defined 2 different OA pain conditions related to the context of OA progression, with intermittent and intense pain having the greatest impact on quality of life. The 2 OA pain conditions they described are related to pain fluctuations rather than directly to qualitative pain aspects. The OASIS9 questionnaire includes a more detailed pain analysis than these previous questionnaires exploring pain intensity and function through a qualitative pain

analysis, as already proposed for neuropathic pain in the NPSI and NPS.^{6,17}

Our main objective was to provide a simple, easy-to-use instrument for daily practice and clinical studies on OA pain. Therefore, we deliberately reduced the number of items to the minimum required to reliably evaluate the various OA pain components. Descriptors not robustly loaded with a particular factor in the factor analysis or unreliable in confirmatory analyses were removed from the questionnaire's final 9-item version.

Our first working hypothesis was that OA pain has 4 distinct dimensions related to the pain mechanisms involved (mechanical, inflammatory, neuropathic, and nociplastic), as suggested by OA pain mechanism studies.^{19,23,29} However, our results

suggest that there are only 3 dimensions to OA pain characteristics, consistent with the 3 main pain mechanisms (nociceptive, neuropathic, and nociplastic), with no differentiation between mechanical and inflammatory pain. Complex pain mechanisms operate in OA, involving all joint structures, the nerves, and the central nervous system. Peripheral pain mechanisms²³ are very important, particularly during the acute phase. Items corresponding to the first dimension identified here may be related to peripheral nociceptive mechanisms.³¹

The neuropathic pain component has already been discussed in OA,¹² and the second dimension identified here was associated with symptoms usually related to neuropathic pain, as assessed by the NPSI questionnaire,⁶ which shows a good correlation with the DN4 screening questionnaire for neuropathic pain.

Central modifications have also been shown by QST and conditioned pain modulation in patients with OA,² suggesting that it is important to consider central sensitization in OA pain. Symptoms associated with the third dimension (“Is your pain influenced by weather conditions?”, “Do you feel pain even without physical activity?”, and “Do you feel a stabbing pain?”) may reflect central mechanisms and sensitization since some have been described in the Central Sensitization Inventory questionnaire.²⁰ One important feature of the OASIS9 questionnaire is its treatment sensitivity. Decreased OASIS9 total scores were associated with subjective improvement, as assessed by the PGIC, after 3 months of treatment, although PGIC assessment at 3 months could be subject to recall bias. Indeed, in this study, we did not expect to show any preferential therapeutic effect on the individual dimensions. Using the OASIS9 in future trials should facilitate the analysis of the effects of different pharmacological and nonpharmacological approaches on the various OA pain symptoms and dimensions. This property should be tested in controlled studies to identify responders’ phenotypes according to the treatment type. Our study’s sample size was relatively small and may represent a limitation. Larger studies should be developed to confirm OASIS9’s ability to identify different pain phenotypes and mechanisms.

In conclusion, OASIS9’s psychometric properties suggest that it is suitable for evaluating different OA pain dimensions. The various descriptors appear to be sufficiently reliable. The OASIS9 questionnaire’s sensitivity to change suggests that it could be used in future pharmacological studies to identify patient subgroups that may differ in their response to treatment and to improve personalized OA pain management.

Conflict of interest statement

S. Perrot declares no conflict of interest related to the submitted work. He has received fees for advisory board for Menarini, Pfizer, MSD, UPSA, Grunenthal, Sanofi, and as a speaker for Pfizer, UPSA, Grunenthal, Sanofi, not related to the submitted work. A.-P. Trouvin declares no conflict of interest. D. Bouhassira declares no conflict of interest related to the submitted work. Consulting activities for Bayer, Novartis, Grunenthal, Vertex, Air Liquide over the last 3 years, not related to the submitted work.

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Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at <http://links.lww.com/PAIN/B771>.

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References

- [1] Ait Abdellah S, Gal C, Leblanc A, Trouvin AP, Perrot S. Clusters of responders and predictive factors for response to supplementation with *Boswellia*, turmeric, and red algae extracts in painful knee osteoarthritis: a prospective observational study using an arsenal of patient-centered measures. *Open Access Rheumatol* 2021;13:1–13.
- [2] Arant KR, Katz JN, Neogi T. Quantitative sensory testing: identifying pain characteristics in patients with osteoarthritis. *Osteoarthritis Cartilage* 2022;30:17–31.
- [3] Bastick AN, Wesseling J, Damen J, Verkleij SP, Emans PJ, Bindels PJ, Bierma-Zeinstra SM. Defining knee pain trajectories in early symptomatic knee osteoarthritis in primary care: 5-year results from a nationwide prospective cohort study (CHECK). *Br J Gen Pract* 2016;66:e32–9.
- [4] Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol* 1988;15:1833–40.
- [5] Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, Cunin G, Fermanian J, Ginies P, Grun-Overdyking A, Jafari-Schluep H, Lanteri-Minet M, Laurent B, Mick G, Serrie A, Valade D, Vicaud E. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). *PAIN* 2005;114:29–36.
- [6] Bouhassira D, Attal N, Fermanian J, Alchaar H, Gautron M, Masquelier E, Rostaing S, Lanteri-Minet M, Collin E, Grisart J, Boureau F. Development and validation of the neuropathic pain symptom inventory. *PAIN* 2004;108:248–57.
- [7] Cardoso JS, Riley JL III, Glover T, Sibille KT, Bartley EJ, Goodin BR, Bulls HW, Herbert M, Addison AS, Staud R, Redden DT, Bradley LA, Fillingim RB, Cruz-Almeida Y. Experimental pain phenotyping in community-dwelling individuals with knee osteoarthritis. *PAIN* 2016;157:2104–14.
- [8] Carlesso LC, Neogi T. Identifying pain susceptibility phenotypes in knee osteoarthritis. *Clin Exp Rheumatol* 2019;37(suppl 120):96–9.
- [9] Cedraschi C, Delézy S, Marty M, Berenbaum F, Bouhassira D, Henrotin Y, Laroche F, Perrot S. “Let’s talk about OA pain”: a qualitative analysis of the perceptions of people suffering from OA. Towards the development of a specific pain OA-related questionnaire, the Osteoarthritis Symptom Inventory Scale (OASIS). *PLoS One* 2013;8:e79988.
- [10] Collins JE, Katz JN, Dervan EE, Losina E. Trajectories and risk profiles of pain in persons with radiographic, symptomatic knee osteoarthritis: data from the osteoarthritis initiative. *Osteoarthritis Cartilage* 2014;22:622–30.
- [11] Farrar JT, Young JP, LaMoreaux L, Werth JL, Poole MR. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *PAIN* 2001;94:149–58.
- [12] French HP, Smart KM, Doyle F. Prevalence of neuropathic pain in knee or hip osteoarthritis: a systematic review and meta-analysis. *Semin Arthritis Rheum* 2017;47:1–8.
- [13] Grafton KV, Foster NE, Wright CC. Test-retest reliability of the Short-Form McGill Pain Questionnaire: assessment of intraclass correlation coefficients and limits of agreement in patients with osteoarthritis. *Clin J Pain* 2005;21:73–82.
- [14] Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain. *Arthritis Care Res* 2011;63:S240–52.
- [15] Hawker GA, Davis AM, French MR, Cibere J, Jordan JM, March L, Suarez-Almazor M, Katz JN, Dieppe P. Development and preliminary psychometric testing of a new OA pain measure—an OARS/OMERACT initiative. *Osteoarthritis Cartilage* 2008;16:409–14.
- [16] Hu LT, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. *Struct Equ Mod A Multidiscip J* 1999;6:1–55.

- [17] Jensen MP. Introduction: chronic pain studies of the lidocaine patch 5% using the Neuropathic Pain Scale. *Curr Med Res Opin* 2004;20:S1–4.
- [18] Lequesne MG. The algofunctional indices for hip and knee osteoarthritis. *J Rheumatol* 1997;24:779–81.
- [19] Malfait AM, Miller RE, Miller RJ. Basic mechanisms of pain in osteoarthritis: experimental observations and new perspectives. *Rheum Dis Clin North Am* 2021;47:165–80.
- [20] Mayer TG, Neblett R, Cohen H, Howard KJ, Choi YH, Williams MJ, Perez Y, Gatchel RJ. The development and psychometric validation of the central sensitization inventory. *Pain Pract* 2012;12:276–85.
- [21] Moreton BJ, Tew V, das Nair R, Wheeler M, Walsh DA, Lincoln NB. Pain phenotype in patients with knee osteoarthritis: classification and measurement properties of painDETECT and self-report Leeds assessment of neuropathic symptoms and signs scale in a cross-sectional study. *Arthritis Care Res* 2015;67:519–28.
- [22] Nilsson A, Bremander A. Measures of hip function and symptoms: Harris Hip Score (HHS), Hip Disability and Osteoarthritis Outcome Score (HOOS), Oxford Hip Score (OHS), Lequesne Index of Severity for Osteoarthritis of the Hip (LISOH), and American Academy of Orthopedic Surgeons (AAOS) Hip and Knee Questionnaire. *Arthritis Care Res (Hoboken)* 2011;63(suppl 11):S200–7.
- [23] O'Neill TW, Felson DT. Mechanisms of osteoarthritis (OA) pain. *Curr Osteoporos Rep* 2018;16:611–6.
- [24] Pan F, Jones G. Clinical perspective on pain and pain phenotypes in osteoarthritis. *Curr Rheumatol Rep* 2018;20:79.
- [25] Perrot S, Bertin P. "Feeling better" or "feeling well" in usual care of hip and knee osteoarthritis pain: determination of cutoff points for patient acceptable symptom state (PASS) and minimal clinically important improvement (MCII) at rest and on movement in a national multicenter cohort study of 2414 patients with painful osteoarthritis. *PAIN* 2013;154:248–56.
- [26] Perrot S, Marty M, Legout V, Moysse D, Henrotin Y, Rozenberg S. Ecological or recalled assessments in chronic musculoskeletal pain? A comparative study of prospective and recalled pain assessments in low back pain and lower limb painful osteoarthritis. *Pain Med* 2011;12:427–36.
- [27] Perrot S. Osteoarthritis pain. *Best Pract Res Clin Rheumatol* 2015;29:90–7.
- [28] Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes* 2003;31:64.
- [29] Trouvin AP, Perrot S. Pain in osteoarthritis. Implications for optimal management. *Joint Bone Spine* 2018;85:429–34.
- [30] Tubach F, Ravaud P, Baron G, Falissard B, Logeart I, Bellamy N, Bombardier C, Felson D, Hochberg M, van der Heijde D, Dougados M. Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: the minimal clinically important improvement. *Ann Rheum Dis* 2005;64:29–33.
- [31] Vincent TL. Peripheral pain mechanisms in osteoarthritis. *PAIN* 2020;161(suppl 11):S138–46.
- [32] Woolhead G, Gooberman-Hill R, Dieppe P, Hawker G. Night pain in hip and knee osteoarthritis: a focus group study. *Arthritis Care Res (Hoboken)* 2010;62:944–9.