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Do psychosocial factors predict muscle strength, pain, or physical performance in patients with knee osteoarthritis?

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1        **Do psychosocial factors predict muscle strength, pain or physical performance in patients with knee**  
2    **osteoarthritis?**

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26 **Short title for a running head: Do psychosocial factors predict clinical features in knee osteoarthritis?**

27  
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1 **ABSTRACT**

2 **Objective.** To examine the relationship of psychosocial factors, namely pain catastrophizing, kinesiophobia and  
3 maladaptive coping strategies, with muscle strength, pain and physical performance in patients with knee  
4 osteoarthritis (OA) related symptoms.

5 **Methods.** A total of 109 women (64 with knee OA related symptoms) with a mean age of 65.4 (49 to 81) were  
6 recruited for this study. Psychosocial factors were quantified by the Pain Catastrophizing Scale, Tampa Scale for  
7 Kinesiophobia, and Pain Coping Inventory. Clinical features were assessed using isometric and isokinetic knee  
8 muscle strength measurements, Visual Analogue Scale, Western Ontario and McMaster Universities  
9 Osteoarthritis Index (WOMAC) and functional tests. Associations were examined using correlation and  
10 regression analysis.

11 **Results.** In knee OA patients, pain catastrophizing, kinesiophobia and coping strategy explained a significant  
12 proportion of the variability in isometric knee extension and flexion strength (6.3%-9.2%), accounting for more  
13 overall variability than some demographic and medical status variables combined. Psychosocial factors were not  
14 significant independent predictors of isokinetic strength, knee pain or physical performance.

15 **Conclusions.** In understanding clinical features related to knee OA such as muscle weakness, pain  
16 catastrophizing, kinesiophobia and coping strategy, might offer something additional beyond what might be  
17 explained by traditional factors, underscoring the importance of a biopsychosocial approach in knee OA  
18 management. Further research on individual patient characteristics that mediate the effects of psychosocial  
19 factors is however required in order to create opportunities for more targeted, personalized treatment for knee  
20 OA.

21

22 **Keywords:** Knee osteoarthritis - Psychosocial factors - Muscle strength - Pain - Function

23

## 1 INTRODUCTION

2 Knee osteoarthritis (OA) is the most common chronic joint disease in elderly, with a higher prevalence among  
3 women (1, 2). Given the increase in life expectancy, the number of people living with severe knee OA is  
4 expected to grow and we need to improve our understanding of the disease and related factors to create  
5 opportunities for more targeted treatment options.

6 In primary care, pain is the key symptom for knee OA patients to seek medical treatment. More pain is often  
7 associated with difficulties performing daily activities, such as walking short or long distances, sit-to-stand  
8 activities and stair climbing, all of which can lead to limitations participating in social and outdoor activities and  
9 reduction in quality of life (3, 4). Knee OA patients also often demonstrate muscle weakness in lower extremity  
10 muscles, particularly in the quadriceps (5, 6), and this muscle weakness seems to be related to more pain and  
11 reduced function (7). Causes of muscle weakness in knee OA are likely to be multifactorial and pain is  
12 commonly presumed to be a major source of inhibition in the ability to voluntarily activate muscles around the  
13 knee joint (7). So, bi-directional relationships seem to exist between pain and muscle strength, whereby pain can  
14 influence muscle strength, and in turn be influenced by these factors (8), leading to a downward cascade in  
15 physical performance.

16 Over the past decades our understanding of chronic disease processes has increased substantially and it is now  
17 well established that the biomedical model falls short in explaining and treating chronic musculoskeletal pain  
18 conditions, such as OA (9). Traditionally, OA-related pain has been considered a nociceptive pain, directly  
19 associated to the degree of structural joint damage. However, studies showed inconsistent results investigating  
20 associations between structural joint abnormalities, measured by radiography or Magnetic Resonance Imaging,  
21 and clinical features of the disease (10, 11). OA pain experience and related dysfunctions seem to be  
22 multidimensional in nature, making a broader biopsychosocial approach to knee OA management indispensable.

23 Research suggests that psychosocial variables, including pain catastrophizing, kinesiophobia and maladaptive  
24 pain coping styles, may be important in explaining variations in pain and physical performance in knee OA  
25 patients (12-16). Pain catastrophizing refers to the tendency to focus on and magnify pain sensations and to feel  
26 helpless in the face of pain (17) and kinesiophobia is defined as excessive, irrational, and debilitating fear of  
27 physical movement and activity resulting from a feeling of vulnerability to painful injury or re-injury (18). Pain  
28 coping can be described as the behavioral and cognitive attempts to tolerate or to deal with pain (19). Active pain  
29 coping strategies have been defined as individuals' attempts to manage their pain through their own resources. In

1 contrast, pain responses such as resting, negative thoughts, avoidance behavior, and guarding the painful body  
2 part have been labeled as passive coping (20). OA patients who catastrophize about pain, who have pain-related  
3 fear or who use a maladaptive coping style report more pain and higher levels of physical disability (12-16).  
4 However, it is currently unknown whether psychosocial variables explain variations in objective measures of  
5 muscle strength in people with OA.

6 Understanding the relative importance of psychosocial variables in the clinical expression of the disease is  
7 important as psychosocial factors may act as therapy effect modifiers (characteristics that predict treatment  
8 effects) (21), or outcome predictors (characteristics that predict outcome independent of therapy) (22), both  
9 useful for clinicians to select the best treatment for an individual patient or to provide patient-specific  
10 information on prognosis.

11 The primary aim of this study was to examine the relationship between psychosocial factors, i.e. the degree of  
12 pain catastrophizing, kinesiophobia and maladaptive pain coping style, and muscle strength in patients with knee  
13 OA related symptoms. Secondly, the relationship between psychosocial factors and pain and physical  
14 performance was investigated. Our main hypothesis is that these psychosocial factors are related to clinical OA  
15 features, i.e. that higher degrees of pain catastrophizing and kinesiophobia and maladaptive pain coping styles  
16 are related to less muscle strength, higher pain levels and poorer physical functioning.

17

## 18 **MATERIALS AND METHODS**

### 19 **Participants**

20 One hundred and nine women were selected for this study (Figure 1). All procedures were approved by the local  
21 ethical committee of Biomedical Sciences KU Leuven. A written informed consent was obtained from each  
22 participant. The study was conducted in accordance with the declaration of Helsinki.

23 Women with knee OA related symptoms were recruited by a rheumatologist or orthopedic surgeon during  
24 routine consultations at the University Hospitals Leuven. Asymptomatic women were recruited through several  
25 regional cultural and social organizations. Overall, subjects were excluded if they had musculoskeletal disorders  
26 other than knee OA in one or both limbs in the last six months, previous surgery of lower extremities or low  
27 back, neurological disorders or chronic intake of corticoids or contra-indications for Magnetic Resonance  
28 Imaging (MRI).

1 All participants were referred for a physical exam and standard anterior-posterior weight-bearing radiographs in  
2 fixed knee flexion (Siemens, Siregraph CF, Agfa CR HD5.0 detector 24\*30) were taken bilaterally.  
3 Radiographic readings were done by a single experienced reader (FPL) and each tibiofemoral compartment was  
4 graded using the Kellgren and Lawrence (K&L) scale with recent adjustment (23). For subjects with knee OA  
5 symptoms and a K&L grade of 0,1 or 2, an additional MRI of the knee was performed on a 3.0 T scanner  
6 (Philips Achieva TX, Philips Medical Systems, Best, The Netherlands) using an eight-channel phased array knee  
7 coil in a non-weight-bearing supine position. Semiquantitative scoring of specific structural features in the  
8 tibiofemoral joint was performed separately by two readers (NN and GVDS) using the standardized Boston-  
9 Leeds Osteoarthritis Knee Score (BLOKS) scoring system (24) (data not shown). Full agreement was achieved  
10 for 91% of all scored items. Disagreements were resolved by consensus.

11 In women with knee OA related symptoms and presence of minimum grade 2<sup>+</sup> (osteophytes and joint space  
12 narrowing in the same compartment) on K&L scale on radiography, the American College of Rheumatology  
13 (ACR) classification criteria (25) were verified, including knee pain, stiffness less than 30 minutes and crepitus,  
14 These patients were classified as having **established knee OA**, indicating moderate to severe disease severity.  
15 The tibiofemoral compartment with presence of minimum grade 2<sup>+</sup> on K&L scale on radiography was indicated  
16 as the involved compartment. As strict radiographic criteria do not suffice to capture early joint degeneration,  
17 MRI based classification criteria were used to define patients with **early knee OA** (26). Subjects with early knee  
18 OA showed a combination of knee pain, a K&L grade 0, 1 or 2 (osteophytes only) on radiography and presence  
19 of at least two of four specific MRI criteria described by Luyten et al. (26): (I)  $\geq$  BLOKS grade 2 for size  
20 cartilage loss, (II)  $\geq$  BLOKS grade 2 for percentage full-thickness cartilage loss, (III) signs of meniscal  
21 degeneration and (IV)  $\geq$  BLOKS grade 2 for size of bone marrow lesions (BMLs) in any one compartment. The  
22 tibiofemoral compartment that met these MRI criteria was indicated as the involved compartment.  
23 Patients with signs of OA in the patellofemoral joint on radiography or MRI were excluded.

24 In order to compare the characteristics of the symptomatic knee OA group to a non-diseased group, 45 **control**  
25 **subjects** were also included in the study. They were asymptomatic with no history of knee OA. On radiography  
26 both knees had a K&L grade 0 or 1.

27 The (most) affected side ((most) symptomatic with (highest) structural severity) for the symptomatic knee OA  
28 subjects and an at random side for controls was selected for further analysis.

29 **Independent variables - Assessment of psychosocial factors**

1 ***Pain Catastrophizing***

2 The Dutch Pain Catastrophizing Scale (PCS) is a self-reported questionnaire aiming at assessing the degree to  
3 which the participant engages in pain catastrophizing, consisting of 13 items describing different thoughts and  
4 feelings persons may experience when they have pain. Each item is rated using a 5-point Likert scale, from 0  
5 (not at all) to 4 (all the time). A total score is counted by summing all individual item scores (range 0-52). Higher  
6 scores correspond to more severe catastrophic thoughts about pain. The PCS has acceptable psychometric  
7 properties (27).

8 ***Kinesiophobia***

9 The Tampa Scale for Kinesiophobia (TSK) is a 17-item questionnaire that assesses fear of (re)injury due to  
10 movement. Items are scored on a 4-point Likert scale and total score is calculated (1-4 for each item), after  
11 inversion of the scores of items 4, 8, 12 and 16. Total scores range from 17 to 68, with scores  $\leq 37$  suggesting  
12 low fear of movement and scores  $> 37$  indicating high fear of movement. The Dutch TSK is a reliable and valid  
13 measure (28).

14 ***Pain Coping Style***

15 The Pain Coping Inventory (PCI) consists of 6 scales (33 items) measuring cognitive and behavioral pain-coping  
16 strategies representing two pain coping dimensions: active (subscales distraction, transformation, and reducing  
17 demands) and passive (subscales resting, retreating, and worrying). Patients are asked to indicate how often they  
18 apply a certain strategy when dealing with pain on a 4-point Likert scale ranging from 1 (hardly ever) to 4 (very  
19 often). A total score was calculated for each coping dimension and transformed into a percentage. Psychometric  
20 properties are reported as good in different patient populations (20).

21

22 **Dependent variables – Assessment of muscle strength, pain and physical performance**

23 ***Muscle strength***

24 Maximal voluntary knee muscle strength was measured using the Biodex System 3 Pro (Biodex Medical System,  
25 Shirley, NY, USA). Before every test session, the Biodex was calibrated and measurements were performed  
26 according to standard procedures.

27 Muscle strength was measured isometrically (static) for extension and flexion, both in a 60° and 90° flexion  
28 position and isokinetically (dynamic) for extension at low speed (60°/second ) and high speed (240°/second) in  
29 order to examine different aspects of muscle strength. Each isometric test was performed three times with

1 maximal contraction for five seconds and ten seconds rest between trials. For isokinetic testing, three trials were  
2 performed for extension at 60°/second and five trials for extension at 240°/second.

3 All subjects received the same instructions and encouragements to achieve maximal effort. For each test the peak  
4 torque normalized for body weight (Nm/kg) of all trials was used.

5 Intra-rater reliability was assessed by repeated testing on a subset of 12 subjects. High to very high intraclass  
6 correlation coefficients were found for all strength measurements between test and retest (ICC between 0.75 and  
7 0.98).

8

### 9 ***Pain and physical performance***

10 The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (Dutch version) has been  
11 developed for use among knee and/or hip OA patients and is shown to be valid and reliable (29). It consists of 24  
12 items rated on a 5-point Likert scale divided into 3 subscales (i.e. pain, stiffness and physical function). To  
13 assess subjects' pain and subjective physical performance, WOMAC subscales "pain" and "physical function",  
14 respectively, were used. For each subscale, a transformed score from 0 to 100 was calculated, with 100 as best  
15 possible result.

16 In addition, pain intensity was measured with the Visual Analogue Scale (VAS), consisting of a 100-mm line on  
17 which the subject places a mark between the left side (0), representing "no pain", and the right side (100),  
18 representing "worst pain imaginable". The VAS is found to be a reliable measure of pain (30).

19 Objective physical performance was assessed by two functional tests. The Timed "Up & Go" test (TUG)  
20 measured the time taken to stand from a chair, walk three meters, turn around, return to the chair and sit down.  
21 The "Stair Climbing Test (SCT)" measured the time required to ascend five steps, turn around and descend five  
22 steps. These tests were performed three times and a mean value was calculated. Both tests have good reliability  
23 and validity (31, 32).

24

### 25 **Data analysis**

26 Analyses were performed with SPSS for Windows, version 23.0 with an  $\alpha$  level of 0.05.

27 Descriptive statistics were carried out to summarize study population characteristics. Normality of data was  
28 evaluated using the Shapiro-Wilk test. Although small deviations from normality were observed for some  
29 measures, the large number of observations (N=64 and N=45) allowed valid parametric testing.



1 Correlation and regression analyses were performed in the group with knee OA related symptoms (N=64).  
2 First, correlation analyses were performed to examine the associations between psychosocial factors and clinical  
3 features related to knee OA. Results of the correlation analyses were expressed as Pearson correlation  
4 coefficients ( $r$ ) and  $P$ -values.  
5 Multivariable linear regression models were fitted to assess the unique contribution of *psychosocial factors*  
6 (independent variables: pain catastrophizing, kinesiophobia and pain coping style) to the *clinical features related*  
7 *to knee OA* (dependent variables: pain, physical performance and muscle strength). The assumptions of the linear  
8 regression models were checked by analysis of the residuals (normality, homoscedasticity, linear relationship).  
9 Associations between psychosocial factors and muscle strength (normalized for body weight) were determined  
10 accounting for age, pain and structural severity. The association between psychosocial factors and pain (VAS  
11 and WOMAC pain) was determined accounting for structural severity, whereas the association between  
12 psychosocial factors and subjective and objective physical performance (WOMAC function, TUG and SCT) was  
13 determined accounting for age, pain, BMI and structural severity. Results of regression analyses were expressed  
14 as standardized regression coefficients ( $\beta$ ),  $P$ -values and coefficients of partial determination (partial  $R^2$ ).

15

## 16 **RESULTS**

17 Details of subject characteristics are presented in Table 1. Subjects with knee OA related symptoms were  
18 comparable to asymptomatic subjects with respect to age and height, but had significantly higher weight  
19 ( $P=0.004$ ) and higher BMI ( $P=0.003$ ). As expected, knee OA subjects had significantly more pain (all  $P<0.001$ ),  
20 more physical disability (all  $P\leq 0.003$ ) and less muscle strength (all  $P<0.001$ ) compared to asymptomatic  
21 subjects.

22 No significant differences were found between groups for the degree of pain catastrophizing. Compared to the  
23 asymptomatic group, patients with knee OA related symptoms showed significantly more kinesiophobia  
24 ( $P=0.013$ ) and used significantly more active ( $P=0,024$ ) and passive coping ( $P=0.027$ ).

25 Correlation analyses (Table 2) revealed that the degree of pain catastrophizing was significantly and negatively  
26 correlated with isometric knee flexion strength ( $r=-0.259$ ;  $P=0,039$  and  $r=-0,309$ ;  $P=0,013$ ). The degree of  
27 kinesiophobia was significantly and negatively correlated with isometric knee extension strength ( $r=-0.261$ ;  
28  $P=0.037$ ). Although statistically significant, the correlation coefficients found in this study were all rather low,  
29 indicating weak correlations.

1 **Multivariable linear regression: association between psychosocial factors and clinical features related to**  
2 **knee OA**

3 *Association with muscle weakness (Table 3 and 4)*

4 In this study population, the degree of **pain catastrophizing** was significantly associated with isometric  
5 extension strength (in 60°:  $\beta=-0.262$ ;  $P=0.041$ ; Partial  $R^2=0,067$ ) and isometric flexion strength (in 60°:  $\beta=-$   
6  $0.259$ ;  $P=0.040$ ; Partial  $R^2=0,065$  – in 90°:  $\beta=-0.308$ ;  $P=0.013$ ; Partial  $R^2=0,092$ ). More pain catastrophizing was  
7 associated with less isometric knee extension and flexion strength. Age, pain and structural severity accounted  
8 for 3,2%-7,5% of the variability in isometric knee strength and pain catastrophizing accounted for an additional  
9 6,5%-9,2% of the variability.

10 The degree of **kinesiophobia** and the use of an **active coping style** were significantly associated with isometric  
11 extension strength ( $\beta=-0.255$ ;  $P=0.045$ ; Partial  $R^2=0,063$  and  $\beta=0.255$ ;  $P=0.047$ ; Partial  $R^2=0,063$ , respectively).  
12 More kinesiophobia and less use of an active coping style were associated with less isometric knee extension  
13 strength. Age, pain and structural severity accounted for 3,2%-5,4% of the variability in isometric knee  
14 extension strength and kinesiophobia and the use of an active coping style each accounted for an additional 6,3%  
15 of this variability.

16 Passive coping was not significantly associated with isometric knee muscle strength.

17 None of the psychosocial factors were significantly associated with isokinetic muscle strength. Pain was  
18 significantly associated with isokinetic knee extension strength at high speed (240°/sec) ( $\beta=0.255$ ;  $P=0.034$ ;  
19 Partial  $R^2=0,073$ ) and accounted for 7,3% of the variability in isokinetic knee extension strength. In general, age,  
20 pain and structural severity accounted for 7.3%-8.1% of the variability in isokinetic knee strength and  
21 **psychosocial factors were not significant independent predictors of isokinetic extension strength.**

22 *Association with knee pain and physical performance (Table 5)*

23 In knee OA patients, none of the psychosocial factors showed a significant association with knee pain (measured  
24 by VAS and WOMAC pain) and physical performance (measured by WOMAC function, TUG and SCT). In this  
25 study, psychosocial factors accounted for less than 3.8% of the variability in knee pain and physical  
26 performance.

27

28 **DISCUSSION**

29 This study examined the relationship between psychosocial factors, i.e. pain catastrophizing, kinesiophobia and  
30 maladaptive pain coping style, and muscle strength, knee pain and physical performance in patients with knee

1 OA related symptoms. Results indicate that none of the studied psychosocial factors are independently  
2 associated with knee pain or physical performance. Pain catastrophizing, kinesiophobia and coping strategy did  
3 explain a small, but statistically significant proportion of the variance in isometric knee extension and flexion  
4 strength (6.5%-9.2%, 6.3% and 6.3%, respectively). These results were obtained after verifying some general  
5 variables (age, pain, BMI and structural severity) as they are believed to be important in explaining muscle  
6 strength in OA patients. Psychosocial variables accounted for more overall variance in isometric muscle strength  
7 than demographic and medical status variables combined.

8

### 9 **Association with knee pain and physical performance**

10 In previous studies, pain catastrophizing, kinesiophobia and maladaptive coping style have been associated with  
11 knee pain and physical performance in knee OA patients (12-15). In addition, in patients undergoing total knee  
12 replacement, high pre-surgical levels of pain catastrophizing and maladaptive pain coping strategies predicted  
13 post-surgical pain, but fear of movement did not contribute to knee function (33). Evidence for the role of  
14 catastrophizing, kinesiophobia, and inadequate coping strategies in maintaining chronic pain and related  
15 disability has also been provided in patients with fibromyalgia, chronic low back pain, and other chronic pain  
16 disorders (34-36). In chronic low back pain for instance, it has been shown that a decrease in catastrophizing  
17 mediated improvements in physical performance, even when there was no opportunity to be physical active (34).  
18 In patients with chronic pain and chronic fatigue syndrome, a clear association between pain catastrophizing and  
19 physiological exercise capacity performance was shown (37). In contrast to these findings, our study could not  
20 reveal an independent association between these psychosocial factors on one hand and knee pain or subjective  
21 and objective physical performance on the other hand.

22 When trying to determine reasons for the differences between our and previous findings, it is important to realize  
23 that in knee OA, the pain experience is likely to be influenced by a multitude of structural, physical, and  
24 psychosocial factors (38), which are different for every individual patient. Over the past decades, there is  
25 growing body of research suggesting that altered central nociceptive processing mechanisms play a significant  
26 role in a subgroup of knee OA patients (around 30%), particularly those with moderate to severe symptomatic  
27 OA (39, 40). In this subgroup, the clinical picture is dominated by sensitization of the central nervous system  
28 and enhanced nociceptive facilitation due to psychosocial factors, rather than by biomechanical or structural  
29 factors causing nociceptive pain (39, 41, 42). In contrast, in patients with predominantly nociceptive pain the  
30 clinical picture is dominated by biomechanical or structural factors. This implies that in knee OA different

1 people experience pain for different reasons. In our study and in previous studies, no specific methods to  
2 diagnose potential involvement of central sensitization (i.e. quantitative sensory testing, brain imaging  
3 techniques, efficacy of centrally acting drugs) were used, therefore it is unknown which pain phenotypes are  
4 present in the different study populations. Dominance of central sensitization is more likely to be present in  
5 patients with moderate to severe symptomatic OA (40). Although our knee OA patients were all symptomatic  
6 (mean WOMAC pain=72.7, mean VAS=35), only 25% had a K&L grade  $\geq 3$ .

7 Within this context, it is not surprising that significant associations between psychological factors on one hand  
8 and pain or physical performance on the other hand were not discovered in our patient population, emphasizing  
9 possible dependence on specific study population characteristics. Differences in the characteristics of the study  
10 populations in terms of pain phenotypes between studies might explain the discrepancies in the results.  
11 Psychosocial factors might predict pain and physical performance in some patients rather than in the whole knee  
12 OA population.

13

#### 14 **Association with muscle strength**

15 The muscles around the knee have an important function as they produce movement but also absorb limb loading  
16 and provide dynamic joint stability. Quadriceps muscle weakness is well documented among knee OA patients  
17 (5, 6) and evidence supports the use of strengthening exercises to improve pain and physical function in this  
18 population (43).

19 Our study findings indicate that knee pain is a significant predictor of isokinetic knee extension strength at high  
20 speed (240°/sec), explaining 7.3% of the variability in muscle strength. This finding suits our current  
21 understanding of nociception-motor interaction in patients with (chronic) pain (44). The interaction between  
22 nociception and motor output is very complex, especially in cases of chronic nociception such as in OA. Current  
23 knowledge of nociception-motor interactions (44) has informed us that nociceptive stimuli result in cortical  
24 delay of motor output in humans and reduced activity of the painful muscle. People show adapted movement  
25 patterns when they are in pain. Nociception impairs motor output through central mechanisms: activated neurons  
26 in the somatosensory-cortex produce a pain-dependent inhibitory input to the primary motor cortex (both  
27 ipsilateral and contralateral), and tonic human muscle nociception results in long-lasting inhibition of the  
28 primary motor cortex (45). This way, nociception may indeed prevent maximal voluntary knee muscle strength,  
29 explaining our observations. In our study, knee pain was not significantly associated with isometric muscle

1 strength or isokinetic muscle strength at low speed. These muscle strength measures are less challenging than  
2 isokinetic muscle strength at high speed, which might explain the lack of significant associations.

3 The degree of pain catastrophizing, kinesiophobia and the use of active coping independently predict isometric  
4 knee extension and flexion strength. The psychosocial variables accounted for more overall variability in  
5 isometric muscle strength than demographic and medical status variables (age, pain, BMI and structural severity)  
6 combined. These findings fit in the cognitive behavioural model of fear of movement (36), which is based on the  
7 assumption that, for some patients, pain experience will lead to fear of movement or to a maladaptive coping  
8 style (avoidance behaviour). In the long term, avoidance of movement and physical activity might result in  
9 physical changes (e.g. muscle weakness) and psychological changes (e.g. depression, more fear of movement)  
10 that contribute to the symptom complex of chronic pain patients (36).

11 Our results suggest that, in understanding clinical features related to knee OA such as decrease in muscle  
12 strength, pain catastrophizing, kinesiophobia and coping strategy, offer something additional beyond what might  
13 be explained by traditional factors. In accordance with the biopsychosocial approach in chronic pain  
14 management, physical as well as psychosocial impairments could be addressed in knee OA management, with  
15 individual treatment considerations for each patient. In most knee OA patients, local application of different  
16 modalities with attention to biological features is appropriate. Indeed, exercise therapy and manual therapy for  
17 example are strongly recommended in most of the current evidence-based guidelines for OA management (43).  
18 However, interventions focused on decreasing pain catastrophizing and kinesiophobia and improve self-  
19 management might also be useful and are currently only sparsely used. Such interventions include, but are not  
20 limited to, therapeutic pain neuroscience education, graded exposure, graded activity, and pain coping skills  
21 training. Studies have shown positive results for integrated exercise and psychological treatments in a variety of  
22 chronic conditions including cancer (46), low back pain (47) and fibromyalgia (48). In knee OA, a combined  
23 treatment comprising of pain coping skills training and exercise therapy improved patient outcome (49).

24 The present study has some limitations. First, investigating associations between psychosocial factors and  
25 clinical features, we accounted for age, pain, BMI and structural severity. However, other factors, such as work,  
26 habitual physical activity, symptom duration or current treatment, that were not taken into account, could also  
27 have influenced clinical features. It is also important to note that no correction for multiple testing was used in  
28 this study. Furthermore, the study population included only women as knee OA is more common among women  
29 and gender-specific characteristics are avoided, with consequently a more homogeneous study population which

1 improved statistics. However, therefore, we need to be careful in generalizing the study results to the male OA  
2 population. Additionally, it has to be mentioned that in our knee OA subjects, the level of pain catastrophizing  
3 was not significantly different from asymptomatic subjects and was rather low (mean 16.0 (SD 9.7)), as it is  
4 indicated that a total PCS score of 30 or more represents a clinically relevant level of catastrophizing (50), which  
5 could have influenced the results. Lastly, the group size was rather small in this study which precludes definitive  
6 conclusions at this stage.

7 To improve our understanding of OA-related factors and to create opportunities for more targeted treatment,  
8 further research is necessary to integrate our current understanding of (OA) pain, including the involvement of  
9 central sensitization and nociception-motor interactions. Future studies with a larger sample size, using analyses  
10 that account for all variables that might be important in explaining clinical features related to knee OA, should  
11 re-explore the associations studied here within each of the different pain phenotypes-based subgroups in the OA  
12 population.

13 In addition, as the effect of psychosocial factors on physical performance might be mediated through pain and  
14 muscle strength, these mediating factors merit investigation in future studies. A randomized controlled trial  
15 could be performed in which these mediating factors are manipulated in order to investigate the association  
16 between psychosocial factors (cause) and physical performance (consequence).

17 In conclusion, results of this study suggest that psychosocial factors, namely pain catastrophizing, kinesiophobia  
18 and coping style, might play a significant role in dysfunctions such as muscle weakness in knee OA patients,  
19 underscoring the role of a biopsychosocial approach in knee OA management. However, further research on  
20 individual patient characteristics that mediate the effects of psychosocial factors is required in order to create  
21 opportunities for more targeted, personalized treatment for knee OA.

22

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6

7 **CONFLICT OF INTEREST**

8 The authors declare that they have no conflicts of interest.

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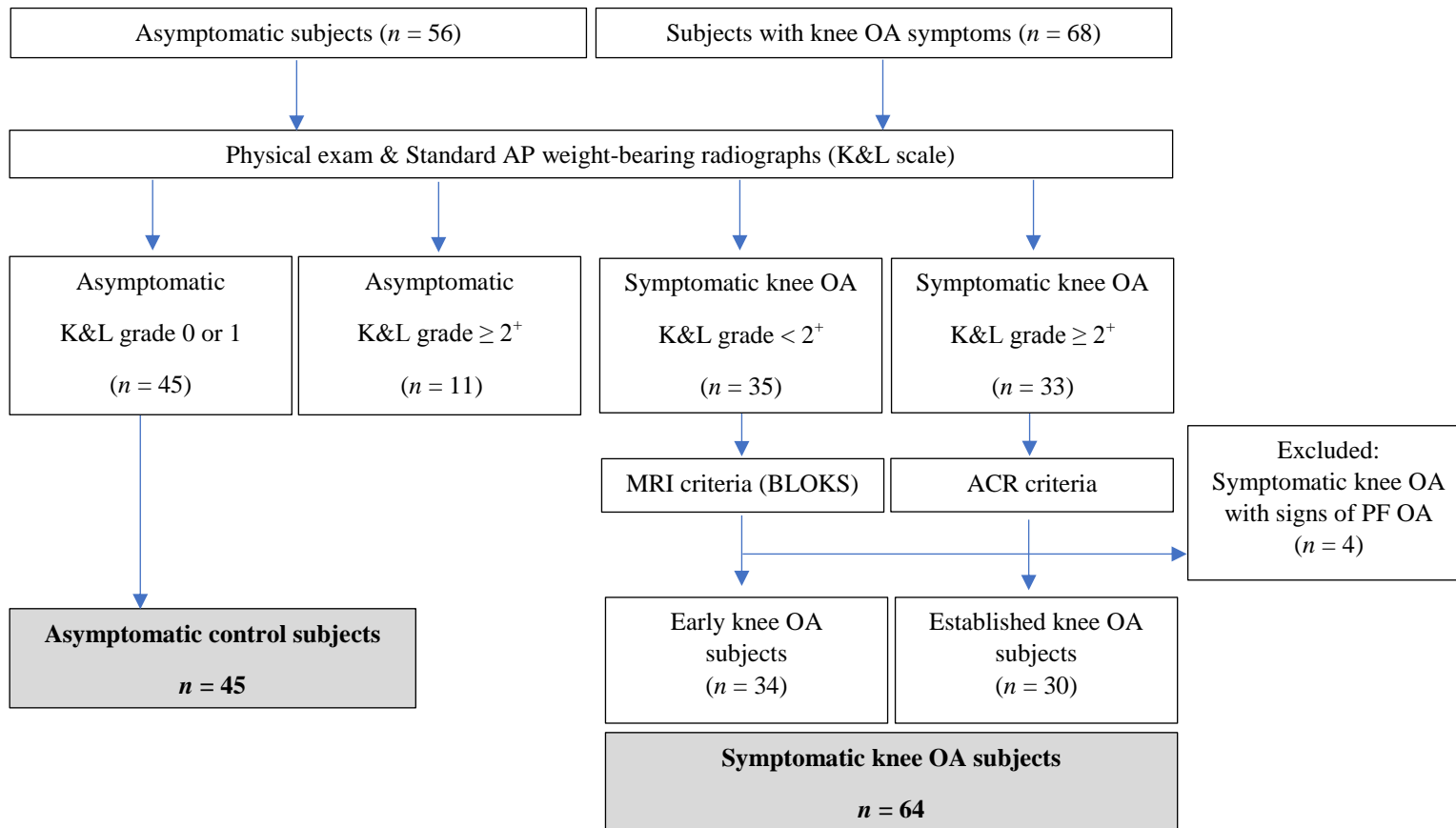


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**Figure 1. Flowchart showing the selection of the study participants.**

OA = osteoarthritis; PF = Patellofemoral; AP = anterior-posterior; K&L = Kellgren and Lawrence; MRI = Magnetic Resonance Imaging; BLOKS = Boston-Leeds Osteoarthritis Knee Score; ACR = American College of Rheumatology



**Table 1. Characteristics of patients with knee OA related symptoms and control subjects \***

Characteristics	Symptomatic Knee OA subjects <i>n</i> = 64	Asymptomatic subjects <i>n</i> = 45	<i>P</i>
Age, years	65.6 (7.3)	65.0 (5.2)	0.628
Weight, kg	72.3 (10.8)	66.5 (9.6)	0.004 <sup>†</sup>
Height, m	1.62 (0.06)	1.62 (0.05)	0.946
BMI, kg/m <sup>2</sup>	27.8 (4.4)	25.4 (3.4)	0.003 <sup>†</sup>
K&L grade			
K&L 0	<i>n</i> = 11 (17%)	<i>n</i> = 18 (40%)	
K&L 1	<i>n</i> = 18 (28%)	<i>n</i> = 27 (60%)	
K&L 2 <sup>-</sup>	<i>n</i> = 5 (8%)		
K&L 2 <sup>+</sup>	<i>n</i> = 14 (22%)		
K&L 3	<i>n</i> = 8 (12.5%)		
K&L 4	<i>n</i> = 8 (12.5%)		
Involved compartment			
Medial compartment knee OA	<i>n</i> = 30 (47%)		
Lateral compartment knee OA	<i>n</i> = 6 (9%)		
Bicompartmental knee OA	<i>n</i> = 17 (27%)		
<b><i>Muscle strength</i></b>			
Isometric knee extension in 60°, Nm/kg	1.27 (0.34)	1.69 (0.40)	<0.001 <sup>†</sup>
Isometric knee extension in 90°, Nm/kg	1.35 (0.41)	1.76 (0.40)	<0.001 <sup>†</sup>
Isometric knee flexion in 60°, Nm/kg	0.62 (0.19)	0.84 (0.23)	<0.001 <sup>†</sup>
Isometric knee flexion in 90°, Nm/kg	0.53 (0.14)	0.67 (0.16)	<0.001 <sup>†</sup>
Isokinetic knee extension 60°/s, Nm/kg	0.96 (0.34)	1.33 (0.26)	<0.001 <sup>†</sup>
Isokinetic knee extension 240°/s, Nm/kg	0.54 (0.21)	0.72 (0.15)	<0.001 <sup>†</sup>
<b><i>Pain</i></b>			
VAS score, 0-100	35 (27)	2 (2)	<0.001 <sup>†</sup>
WOMAC pain score, 0-100	72.7 (18.9)	97.9 (2.7)	<0.001 <sup>†</sup>
<b><i>Physical performance</i></b>			
WOMAC function score, 0-100	70.5 (20.0)	98.2 (3.3)	<0.001 <sup>†</sup>
TUG, sec	5.74 (1.24)	5.00 (0.92)	0.001 <sup>†</sup>
SCT, sec	6.24 (1.49)	5.49 (1.07)	0.003 <sup>†</sup>
<b><i>Pain catastrophizing</i></b>			

Total Score on PCS, 0-52	16.0 (9.7)	15,2 (9.7)	0.677
<b>Kinesiophobia</b>			
Score on TSK, 17-68	37.1 (5.2)	34.5 (6.1)	0.013 <sup>†</sup>
<b>Pain coping style</b>			
Active coping on PCI, %	57.16 (11.77)	51,99 (11.40)	0.024 <sup>†</sup>
Passive coping on PCI, %	49.00 (10.74)	44.50 (9.65)	0.027 <sup>†</sup>

OA = osteoarthritis; BMI = Body Mass Index; K&L = Kellgren and Lawrence; VAS = Visual Analogue Scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; TUG = Timed Up and Go Test; SCT = Stair Climbing Test; PCS = Pain Catastrophizing Scale; TSK = Tampa Scale for Kinesiophobia; PCI = Pain Coping Inventory

\* Data are presented as Mean (SD) or Frequencies (%). The *P* value corresponds to an Independent Samples t-test comparing the two groups.

<sup>†</sup>Significant difference between groups (*P* < 0.05)



**Table 2. Correlation between psychosocial factors and muscle strength, pain and physical performance in 64 subjects with knee OA related symptoms**

	Pain catastrophizing (Total score on PCS)		Kinesiophobia (Score on TSK)		Active coping style (Active coping on PCI)		Passive coping style (Passive coping on PCI)	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
<b>Muscle strength</b>								
Isometric knee extension in 60°, Nm/kg	-0.235	0.062	-0.172	0.174	0,221	0,079	0.091	0.474
Isometric knee extension in 90°, Nm/kg	-0.199	0.116	<b>-0.261</b>	<b>0.037*</b>	0.167	0.188	0.058	0.648
Isometric knee flexion in 60°, Nm/kg	<b>-0.259</b>	<b>0.039*</b>	-0.096	0.449	0.057	0.654	0.051	0.688
Isometric knee flexion in 90°, Nm/kg	<b>-0.309</b>	<b>0.013*</b>	-0.114	0.368	0.080	0.532	0.007	0.957
Isokinetic knee extension 60°/s, Nm/kg	-0.073	0.568	-0.122	0.336	0.174	0.170	0.068	0.594
Isokinetic knee extension 240°/s, Nm/kg	-0.026	0.841	-0.051	0.692	0.234	0.065	0.183	0,152
<b>Pain</b>								
VAS score	-0.197	0.118	-0.043	0,734	-0.065	0.610	-0.162	0.200
WOMAC pain score	0.091	0.474	-0.043	0,734	-0.153	0.228	0.048	0.707
<b>Physical performance</b>								
WOMAC function score	-0.011	0.932	-0.106	0.406	-0.061	0.629	0.074	0.559
TUG	0,002	0.986	0.102	0.432	-0.020	0.874	0.033	0.800
SCT	0.035	0.787	0.143	0.267	-0.049	0.706	-0.160	0.215

VAS = Visual Analogue Scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; TUG = Timed Up and Go Test; SCT = Stair Climbing Test;

PCS = Pain Catastrophizing Scale; TSK = Tampa Scale for Kinesiophobia; PCI = Pain Coping Inventory

\* significant associations based on correlation analysis (Pearson correlation) ( $P < 0.05$ )

**Table 3. Multivariable linear regression analysis: associations between psychosocial factors and isometric muscle strength in 64 knee OA subjects**

Independent variables	Dependent variables											
	Isometric muscle strength, Nm/kg											
	Knee extension 60°			Knee extension 90°			Knee flexion 60°			Knee flexion 90°		
	$\beta$	<i>P</i>	Partial $R^2$	$\beta$	<i>P</i>	Partial $R^2$	$\beta$	<i>P</i>	Partial $R^2$	$\beta$	<i>P</i>	Partial $R^2$
<i>Step 1</i>												
Age	-0.004	0.977	0.000	0.048	0.705	0.002	0.128	0.314	0.016	0.124	0.328	0.015
Pain (WOMAC pain)	0.182	0.163	0.032	0.227	0.081	0.049	0.163	0.208	0.025	0.163	0.211	0.025
Structural severity (K&L grade)	-0.010	0.941	0.000	-0.052	0.684	0.003	-0.159	0.210	0.025	-0.188	0.138	0.035
<i>Step 2: Pain Catastrophizing</i>												
Total Score on PCS	<b>-0.262</b>	<b>0.041*</b>	<b>0.067</b>	-0.221	0.082	0.048	<b>-0.259</b>	<b>0.040*</b>	<b>0.065</b>	<b>-0.308</b>	<b>0.013*</b>	<b>0.092</b>
<i>Step 2: Kinesiophobia</i>												
Score on TSK	-0.176	0.176	0.030	<b>-0.255</b>	<b>0.045*</b>	<b>0.063</b>	-0.058	0.655	0.003	-0.073	0.568	0.005
<i>Step 2: Pain coping style</i>												
Active Coping on PCI	<b>0.255</b>	<b>0.047*</b>	<b>0.063</b>	0.204	0.111	0.040	0.075	0.557	0.005	0.096	0.450	0.009
Passive Coping on PCI	0.096	0.470	0.009	0.043	0.742	0.002	0.003	0.981	0.000	-0.047	0.715	0.002

PCS = Pain Catastrophizing Scale; TSK = Tampa Scale for Kinesiophobia; PCI = Pain Coping Inventory

\* significant associations based on regression analysis ( $P < 0.05$ )

**Table 4. Multivariable linear regression analysis: associations between psychosocial factors and isokinetic muscle strength in 64 knee OA subjects**

Independent variables	Dependent variables					
	Isokinetic muscle strength, Nm/kg					
	Knee extension 60°/sec			Knee extension 240°/sec		
	$\beta$	<i>P</i>	<i>Partial R</i> <sup>2</sup>	$\beta$	<i>P</i>	<i>Partial R</i> <sup>2</sup>
<b>Step 1</b>						
Age	0.035	0.783	0.001	-0.010	0.937	0.000
Pain (WOMAC pain)	0.221	0.090	0.046	<b>0.275</b>	<b>0.034*</b>	<b>0.073</b>
Structural severity (K&L grade)	-0.167	0.187	0.027	-0.098	0.438	0.009
<b>Step 2: Pain Catastrophizing</b>						
Total Score on PCS	-0.082	0.522	0.006	-0.051	0.692	0.002
<b>Step 2: Kinesiophobia</b>						
Score on TSK	-0.097	0.447	0.009	-0.038	0.767	0.001
<b>Step 2: Pain coping style</b>						
Active Coping on PCI	0.202	0.109	0.040	0.279	0.027	0.075
Passive Coping on PCI	0.040	0.759	0.001	0.179	0.165	0.030

PCS = Pain Catastrophizing Scale; TSK = Tampa Scale for Kinesiophobia; PCI = Pain Coping Inventory

\* significant associations based on regression analysis ( $P < 0.05$ )

**Table 5. Multivariable linear regression analysis: associations between psychosocial factors and knee pain and physical performance in 64 knee OA subjects**

Independent variables	Dependent variables														
	Pain						Physical performance (subjective)			Physical performance (objective)					
	VAS <sup>a</sup>			WOMAC Pain <sup>a</sup>			WOMAC Function <sup>b</sup>			SCT <sup>b</sup>			TUG <sup>b</sup>		
	$\beta$	<i>P</i>	Partial $R^2$	$\beta$	<i>P</i>	Partial $R^2$	$\beta$	<i>P</i>	Partial $R^2$	$\beta$	<i>P</i>	Partial $R^2$	$\beta$	<i>P</i>	Partial $R^2$
<b><i>Pain Catastrophizing</i></b>															
Total Score on PCS	-0.196	0.125	0.038	0.098	0.444	0.010	-0.037	0.539	0.001	0.027	0.830	0.001	0.002	0.989	0.000
<b><i>Kinesiophobia</i></b>															
Score on TSK	-0.040	0.758	0.002	-0.033	0.798	0.001	-0.038	0.519	0.001	0.153	0.206	0.023	0.123	0.318	0.015
<b><i>Pain coping style</i></b>															
Active Coping on PCI	-0.067	0.603	0.004	-0.158	0.215	0.025	0.043	0.459	0.002	-0.077	0.531	0.006	-0.054	0.667	0.003
Passive Coping on PCI	-0.169	0.188	0.028	0.037	0.774	0.001	0.017	0.770	0.000	-0.143	0.243	0.019	0.047	0.707	0.002

VAS = Visual Analogue Scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; SCT = Stair Climbing Test; TUG = Timed Up and Go Test;

PCS = Pain Catastrophizing Scale; TSK = Tampa Scale for Kinesiophobia; PCI = Pain Coping Inventory

\* significant associations based on regression analysis ( $P < 0.05$ )

<sup>a</sup> accounting for structural severity (K&L grade) <sup>b</sup> accounting for age, pain (WOMAC pain), BMI and structural severity (K&L grade)

