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Holla, J.F.M.

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PART II

MECHANISMS UNDERLYING THE
DEVELOPMENT OF
ACTIVITY LIMITATIONS

PART II



Chapter 4

Avoidance of activities in early symptomatic knee osteoarthritis: results from the CHECK cohort

Jasmijn F.M. Holla

Marika van der Leeden

Dirk L. Knol

Wilfred F.H. Peter

Leo D. Roorda

Willem F. Lems

Janet Wesseling

Martijn P.M. Steultjens

Joost Dekker

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Abstract

Background. Pain-related avoidance of activities is hypothesized to lead to lower muscle strength and thereby activity limitations. Negative affect (e.g. low vitality, depression) is thought to strengthen the tendency to avoid activities.

Purpose. The aim of this study was to assess the validity of this “avoidance model” in patients with early symptomatic knee osteoarthritis (OA).

Methods. Cross-sectional data ($n = 151$) were used. The associations between pain, negative affect, avoidance, muscle strength and activity limitations were modelled using structural equation modelling.

Results. Pain and negative affect were associated with lower muscle strength via avoidance (mediation by avoidance). Avoidance was associated with activity limitations via lower muscle strength (mediation by muscle strength). There were also direct associations between pain, negative affect, avoidance, muscle strength, and activity limitations.

Conclusions. The results support the validity of the avoidance model, which explains the associations between pain, negative affect, avoidance, muscle strength, and activity limitations in patients with early symptomatic knee OA.

Introduction

Activity limitation (e.g. difficulties in walking, stair-climbing) is one of the primary health complaints in osteoarthritis (OA) patients.¹ One of the factors that may influence the degree of activity limitations is the way in which patients cope with their symptoms.² Avoidance of pain-related activities is a way to cope with pain. Several studies in knee OA patients have demonstrated that the pain coping strategy “avoidance of activities” or “resting” is related to activity limitations.³⁻⁵

During the past decades several theoretical models have been developed to explain activity limitations in chronic pain patients.⁶ Whereas the first models were based on classical and operant conditioning, the latest models are based on a cognitive approach owing to the prevailing assumption that individuals actively process information regarding internal stimuli and external events.⁶ In 1993, based upon previous work in chronic pain (mainly low back pain),⁷⁻¹⁰ Dekker et al.¹¹ proposed a cognitive behavioural model of activity limitations in OA: the avoidance model.

The avoidance model^{11,12} offers an explanation of how avoidance leads to activity limitations. According to this model (**Figure 1**), a patient initially experiences pain during activity. This leads to the expectation that renewed activity results in more pain,¹³ and consequently to the avoidance of activities. In the short term, avoidance may have the desired effect of less pain due to the decreased load on the affected joint. However, in the longer term, inactivity results in physical deconditioning, most notably lower muscle strength. Lower muscle strength leads to an increase in activity limitations.¹²

As shown in **Figure 1**, the model hypothesizes an indirect relationship between pain during activities and lower muscle strength via avoidance.¹¹ Avoidance of activities is hypothesized to mediate the relationship between pain and lower muscle strength: a mediator variable is conceptualized as the mechanism through which one variable influences another variable.^{14,15} Likewise, the relationship between avoidance and activity limitations is hypothesized to be mediated by lower muscle strength.^{11,12}

In addition, it is hypothesized that negative affect plays a moderating role in the avoidance model (**Figure 1**).¹¹ A moderator is a variable that strengthens (or weakens) the relation between a predictor and an outcome.^{14,15} Negative affect, defined as a broad range of aversive mood states including fatigue, low vitality, nervousness and depression, has been shown to be associated with pain and activity limitations in OA patients.^{2,11} Depressive symptoms are a risk factor for physical inactivity,¹⁶ and are associated with decreased pain tolerance.¹⁷ Therefore, negative affect is thought to strengthen (or moderate) the tendency to avoid activities.

In a previous study evidence was obtained for the mediating role of lower muscle strength in the relationship between avoidance of activities and activity limitations in patients with established knee OA.¹² In that study the mediating role of avoidance and the moderating role of negative affect were not examined. Furthermore, although it is expected

that the avoidance model applies to early OA, this has not been empirically tested. In early OA, in which symptoms commence and patients experience pain during activity for the first time, the processes of mental and physical adaptation depicted in the model are thought to be initiated.

The aim of the present study was to assess the validity of the avoidance model in patients with early symptomatic knee OA. It was hypothesized that (1) higher pain is associated with lower muscle strength via avoidance of activities (mediation of avoidance), (2) avoidance is associated with a higher degree of activity limitations via lower muscle strength (mediation of muscle strength), and (3) negative affect (i.e. feelings of fatigue, low vitality, depression and nervousness) strengthens the relationship between higher pain and avoidance of activities (moderation of negative affect).

Methods

Participants

A cross-sectional study was conducted in a sample of 151 participants with early symptomatic knee OA from the Cohort Hip and Cohort Knee (CHECK) study.¹⁸ Two-year follow-up data were used.

CHECK is a prospective cohort study of 1,002 individuals with early symptomatic OA of the knee or hip. On entry, all participants had pain or stiffness of the knee or hip, and were aged 45-65 years. They had not yet consulted their physician for these symptoms, or the first consultation was within 6 months before entry. Participants with any

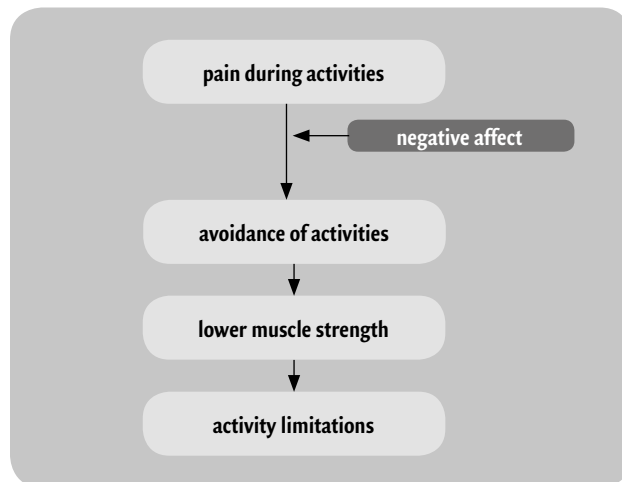


Figure 1. Hypothesized model of the associations between pain, negative affect, avoidance of activities, lower muscle strength, and activity limitations in knee osteoarthritis patients.

other pathological condition that could explain the symptoms were excluded (e.g. other rheumatic disease, previous hip or knee joint replacement, congenital dysplasia, osteochondritis dissecans, intra-articular fractures, septic arthritis, Perthes' disease, ligament or meniscus damage, plica syndrome, Baker's cyst). Additional exclusion criteria were: comorbidity that did not allow physical evaluation and/or follow-up of at least 10 years, malignancy in the last 5 years, and inability to understand the Dutch language.

The CHECK cohort was formed from October 2002 till September 2005. Nationwide, 10 general and academic hospitals in the Netherlands are participating, located in urbanized and semi-urbanized regions. General practitioners in the surroundings of the participating centres were invited to refer eligible persons. All patients that visited the general practitioner on their own initiative, potentially fulfilling the inclusion criteria, were referred to one of the 10 participating centres. In addition, participants were recruited through advertisements and articles in local newspapers and on the Dutch Arthritis Association website. The physicians in the participating centres checked whether referred patients as well as patients from their outpatient clinics fulfilled the inclusion criteria.

After 2 years of follow-up all participants with knee symptoms recruited through Reade, Centre for Rehabilitation and Rheumatology, in Amsterdam ($n = 151$), were invited to additionally participate in the present study. The additional measurements needed (muscle strength and a performance-based measure of activity limitations) were integrated in the existing measurement schedule for CHECK.

The CHECK study was approved by the medical ethics committees of all participating centres. The additional measurements necessary for the present study were approved by the medical ethical committee of the Slotervaart Hospital and Reade. All participants gave their written informed consent before entering the study.

Measures

Pain

Pain during activities was assessed with the pain subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).¹⁹ This subscale consists of five items, which assess the amount of knee pain experienced during activities the past 48 h. Items are answered on a five-point scale. The subscale scores range from 0 to 20, with higher scores indicating more pain. The WOMAC is widely used in clinical research, and has been shown to be reliable, valid and responsive for use in OA patients [WOMAC pain subscale – Cronbach's $\alpha = 0.88$, intra-class correlation coefficient (ICC) = 0.77].¹⁹⁻²¹

Negative affect

Negative affect was assessed using the vitality and mental health subscale of the Short Form 36 Health Survey (SF-36).²² The vitality subscale consists of four items, which assess feelings of energy and fatigue. Items are answered on a six-point scale. The subscale scores are linearly converted to a 0 to 100 scale, with higher scores indicating more feelings of energy and less feelings of fatigue. Background information on the SF-36 as well as standard scoring algorithms are available elsewhere.²³ The mental health subscale consists of five items, which assess feelings of depression and nervousness. Items are answered on a six-point scale. The subscale scores are linearly converted to a 0 to 100 scale, with higher scores indicating less

feelings of depression and nervousness. The SF-36 has been shown to be a reliable and valid measure of health-related quality of life in different patient groups including OA (mean Cronbach's α across subscales and samples with different chronic conditions = 0.84).^{22,24}

Avoidance of activities

Avoidance of activities was assessed with the resting subscale of the Pain Coping Inventory (PCI).²⁵ This subscale consists of five items, which assess the level to which patients avoid activities when experiencing pain. Items are answered on a four-point scale, ranging from 1 (hardly ever) to 4 (very often) in terms of frequency with which the strategy (e.g. stopping activities or confining oneself to simple activities) is applied when dealing with pain. The subscale scores range from 5 to 20, with higher scores indicating a more frequent use of avoidance of activities as a coping style. The PCI has been shown to be a reliable and valid measure of pain coping in OA patients (Cronbach's $\alpha > 0.68$).^{4,25,26}

Muscle strength

Muscle strength in Newton meter (Nm) of the quadriceps and hamstrings was assessed using an isokinetic dynamometer (EnKnee; Enraf-Nonius, Rotterdam, the Netherlands). Measurements were made in sitting position at an angular velocity of 60° per second, which reflects a speed of movement usually applied during daily tasks, e.g. walking. These measurements have been shown to be reproducible and valid.^{27,28} A single physical therapist assessed all patients according to a standardized protocol. Following instruction, patients performed one test measurement. After a 30-s rest, patients performed three maximal quadriceps strength measurements during knee extension, and three maximal hamstrings strength measurements during knee flexion.

For analysis the maximum voluntary contraction obtained from three measurements of the quadriceps and three measurements of the hamstring muscles of the index knee (most affected knee) were summed and divided by two to obtain a measure of total muscle strength around the index knee. The measure was corrected for weight by dividing it by the patient's weight.²⁹

Most participants identified their most affected (index) knee in the clinical interview. For participants with bilateral symptoms we defined an index knee based on the following decision tree: (1) highest Kellgren and Lawrence score,³⁰ (2) lowest degree of active knee flexion, (3) highest pain during active knee flexion, and (4) crepitus during knee flexion. In participants for whom we could not define an index knee based on these signs, we randomly assigned an index knee.

Activity limitations

Activity limitations were assessed both with a self-report and a performance-based measure. Self-reported activity limitations were assessed with the physical functioning subscale of the WOMAC: the WOMAC-PF (Cronbach's $\alpha = 0.96$, ICC = 0.92).^{19,20} This subscale consists of 17 items that are answered on a five-point scale, ranging from 0 (none) to 4 (extreme) in terms of the degree of difficulties one has in executing activities (e.g. walking or stair-climbing). The subscale scores ranges from 0 to 68, with higher scores indicating more activity limitations.

Performance-based activity limitations were assessed with a timed stair-climbing test. The stairs had 12 steps with a rise of 16 cm and a run of 30 cm. Participants began the task

by standing on a line that was 58 cm from the first step. Participants were instructed to climb the stairs step by step as quickly as they felt safe and comfortable. They were encouraged not to use the handrail, but were not prohibited from doing so for safety. The task ended when participants stood with both feet upstairs. The task was scored as the total time needed to climb the stairs. A longer time to complete the task indicates more activity limitations. Excellent test-retest reliability was reported for a comparable stair-climbing task in patients with knee OA (Pearson's correlation coefficient (r) of 3-month test-retest reliability data = 0.87).³¹

Statistical analysis

The data were explored using SPSS version 15.0 (SPSS Inc., 2006). Prior to the analyses, we checked if the assumptions for linear regression (e.g. no strong multicollinearity, homoscedasticity, linearity) were met.³²

The relationships as proposed by the avoidance model (**Figure 1**) were modelled using structural equation modelling (SEM), in Mplus version 6.12.³³ SEM allows the simultaneous modelling of several related regression relationships. Because all variables in the model were continuous, linear regression models were used. Regression coefficients were estimated using robust maximum likelihood estimation (MLR).

In a structural equation model, a variable can be a dependent variable in one relationship and an independent variable in another. These variables are referred to as mediating variables.³³ In assessing mediation it is important to make a distinction between various associations and their corresponding weights. The total association between an independent variable and a dependent variable is composed of an indirect association between the independent variable and the dependent variable via the mediator and a direct association between the independent variable and the dependent variable. For example, in **Figure 2** path *a* represents the association between the independent variable pain and the mediator variable avoidance, and path *b* represents the association between the mediator variable avoidance and the dependent variable muscle strength (indirect association). Path *d* represents the direct association between pain and muscle strength. Avoidance is statistically shown to be a mediator of the association between pain and muscle strength if the indirect association between pain and muscle strength (path *a* × path *b*) differs significantly from zero.³⁴ The rationale behind this method is that mediation depends on the extent to which the independent variable is associated with the mediator (path *a*) and the extent to which the mediator is associated with the outcome variable (path *b*).³⁵ If one of these associations (path *a* or path *b*) does not exist, the regression coefficient of the mediator (path *a* × path *b*) is not significantly different from zero: there is no mediation.

To obtain one outcome measure for activity limitations the variables WOMAC-PF and timed stair-climbing test were combined into one latent variable for activity limitations. Because of the high correlation between the subscales for vitality and mental health of the SF-36 ($r = 0.74$), these variables were combined into one observed variable for negative affect by averaging the scores. To facilitate the interpretation of the results, prior to analysis the negative affect score was multiplied by -1 so that a higher score indicated more feelings of fatigue, low vitality, depression and nervousness. In this way, for all variables in the model a higher score indicated a higher degree of the variable of interest (i.e. a higher degree of pain, negative affect, avoidance, muscle strength and activity limitations).

Moderation was tested using an interaction term between pain and negative affect.^{15,32} Bootstrap methods were used to estimate standard errors (SE) and 95% confidence intervals (95% CI) for both indirect (mediation) and direct associations.³⁴⁻³⁶ The bootstrap was used because this method does not assume normality of the sampling distribution of the indirect (mediation) effect.^{34,36} Bootstrapped standard errors were computed using 1,000 draws.

Goodness of fit of the structural equation models was assessed by the chi-square test of model fit (χ^2 , criterion $p > 0.05$), the root mean square error of approximation (RMSEA, criterion < 0.06), the comparative fit index (CFI, criterion > 0.95), and the standardized root mean square residual (SRMR, criterion < 0.08).³⁷ When the hypothesized model did not fit the data adequately, the model was revised. The goodness of fit of the revised model was tested and compared with the previous model using the Satorra-Bentler scaled chi-square difference test (TRd).^{38,39} Modification indices³³ were used to guide the revisions which were primarily based on knowledge of direct associations and plausibility. The correlation coefficient squared (R^2) was calculated to express the amount of variability in avoidance, muscle strength and activity limitations that was explained by the other variables in the model.³²

Table 1. Characteristics of the study population (n = 151)

Characteristic	Value
Age (years), mean \pm SD	58.5 \pm 5.0
Female, n (%)	120 (79.5)
Body-mass index (kg/m ²), mean \pm SD	25.6 \pm 3.8
Knee symptoms, n (%)	
Unilateral	47 (31.1)
Bilateral with index knee	93 (61.0)
Bilateral with equal symptoms	11 (7.3)
Duration of knee symptoms (years), median (IQR)	3.7 (2.8-5.0)
Clinical knee OA (ACR criteria), n (%)	118 (78.1)
KL-grade \geq 2, n (%)	29 (19.2)
WOMAC pain score (range: 0-20), mean \pm SD	5.0 \pm 3.8
SF-36 vitality score (range: 0-100), mean \pm SD	63.9 \pm 19.7
SF-36 mental health score (range: 0-100), mean \pm SD	75.6 \pm 16.4
PCI resting score (range: 5-20), mean \pm SD	9.3 \pm 2.6
Muscle strength (Nm/kg), mean \pm SD	1.0 \pm 0.3
WOMAC physical function score (range: 0-68), mean \pm SD	15.5 \pm 12.1
Timed stair climbing test (s), mean \pm SD	5.2 \pm 2.0

IQR = Interquartile range, SD = standard deviation, OA = osteoarthritis. ACR = American College of Rheumatology, KL-grade = Kellgren and Lawrence grade, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index, SF-36 = Short Form 36 Health Survey, PCI = Pain Coping Inventory.

Results

Study population

Characteristics of the study population and mean scores on pain, negative affect (i.e. vitality and mental health), avoidance of activities, muscle strength and activity limitations are presented in **Table 1**.

Goodness of fit of the structural equation models used to assess the validity of the avoidance model

The model fit indices of the structural equation models used to test the hypotheses described in “the introduction” are given in **Table 2**. The hypothesized model (**Figure 1**) did not adequately fit the data. Therefore paths were added or removed stepwise to improve the model fit. The steps made to revise the model are presented in **Table 2**. From model 1a (**Figure 1**) the interaction between pain and negative affect was removed (model 1b), and paths were added between pain and activity limitations (model 1c), avoidance and activity limitations (model 1d), pain and muscle strength (model 1e), and negative affect and activity limitations (model 1f) (**Table 2**). The final revised model in which both indirect and direct associations between the variables were included fit the data well according to the criteria $CFI > 0.95$ and $SRMR < 0.08$ but not RMSEA. This final model is shown in **Figure 2**.

The mediating role of avoidance of activities: hypothesis 1

The final structural equation model used to test the validity of the avoidance model (model 1f) is shown in **Figure 2**. The indirect association between pain and muscle strength via avoidance (**Figure 2** – path a × path b) was marginally statistically significant [standardized regression coefficient $[\beta] = -0.05$, $p = 0.09$]. Besides this trend towards an indirect associa-

Table 2. Model fit indices for the structural equation models used to validate the avoidance model

Model	χ^2	df	p value	TRd	RMSEA	CFI	SRMR
Criteria			>0.05		<0.06	>0.95	<0.08
1a (Figure 1)	158.02	11	<0.001		0.298	0.460	0.224
1b: 1a – interaction pain × negative affect	202.79	8	<0.001	2.02	0.402	0.382	0.215
1c: 1b + pain → activity limitations	55.15	7	<0.001	182.33**	0.213	0.847	0.101
1d: 1c + avoidance → activity limitations	29.67	6	<0.001	24.61**	0.162	0.925	0.079
1e: 1d + pain → muscle strength	19.15	5	0.002	14.01**	0.137	0.955	0.043
1f: 1e + negative affect → activity limitations (final model; Figure 2)	12.24	4	0.02	5.82*	0.117	0.974	0.040

Model 1a-1f refer to the steps taken to improve the model fit as described in the “Results” section. χ^2 chi-square test of model fit, df = degrees of freedom, TRd = Satorra-Bentler scaled chi-square difference test, RMSEA = root mean square error of approximation, CFI = comparative fit index, SRMR = standardized root mean square residual. * $p < 0.05$ ** $p < 0.01$.

tion, pain was directly associated with muscle strength ($\beta = -0.25, p < 0.001$). Of the total association between pain and muscle strength, 15.3% was mediated by avoidance. When negative affect was excluded from model 1f the indirect association between pain and muscle strength via avoidance was statistically significant ($\beta = -0.08, p = 0.01$). In the model without negative affect 25.2% of the total association between pain and muscle strength was mediated by avoidance. The hypothesis that avoidance mediates the relationship between higher pain and lower muscle strength was confirmed in the analysis without negative affect.

The mediating role of lower muscle strength: hypothesis 2

The hypothesis that avoidance of activities is associated with a higher degree of activity limitations via lower muscle strength (Figure 2 – path b \times path c) was confirmed. The indirect association between avoidance and activity limitations via muscle strength was significant ($\beta = 0.04, p = 0.01$). Besides this indirect association avoidance was directly associated with activity limitations ($\beta = 0.20, p < 0.001$). Of the total association between avoidance and activity limitations, 18.1% was mediated by muscle strength.

The moderating role of negative affect: hypothesis 3

Negative affect did not strengthen the association between pain and avoidance of activities. The interaction term between pain and negative affect was not significantly ($p = 0.24$) associated with avoidance of activities.

Therefore, the interaction between pain and negative affect was removed from the model

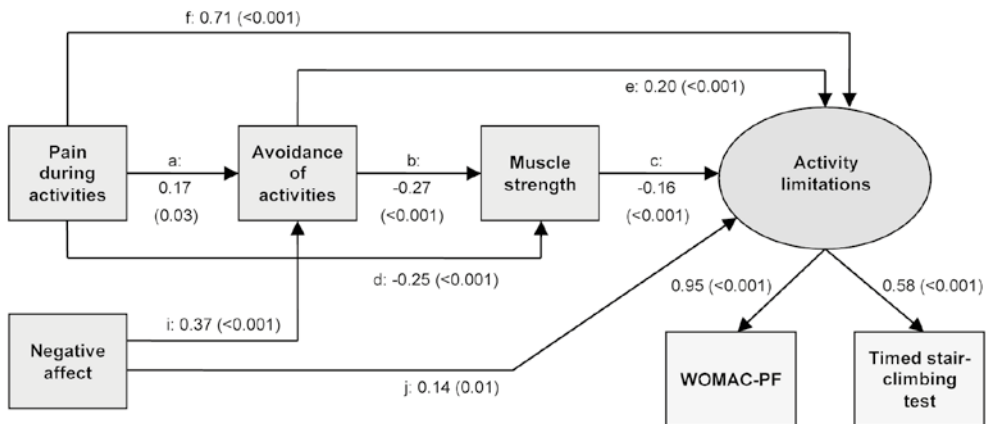


Figure 2. Final structural equation model describing the associations between pain during activities, negative affect, avoidance of activities, muscle strength and activity limitations (model 1f). WOMAC-PF = physical function subscale of the Western Ontario and McMaster Universities Osteoarthritis Index. Pain during activities was assessed with the pain subscale of the WOMAC. Negative affect was computed by averaging the subscale scores for vitality and mental health of the Short Form 36 Health Survey (SF-36). The negative affect score was multiplied by -1 so that higher scores indicated a higher degree of negative affect. Avoidance of activities was assessed with the resting subscale of the Pain Coping Inventory (PCI). Muscle strength was assessed using an isokinetic dynamometer. The associations are presented as standardized regression coefficients (p-value).

(Table 2). In the revised model negative affect was hypothesized to lead to lower muscle strength via the mediator avoidance of activities (i.e. avoidance as a mediator between negative affect and lower muscle strength). The results showed that negative affect was significantly associated with muscle strength via avoidance (Figure 2 – path i \times path b, $\beta = -0.10$, $p = 0.004$). Negative affect was not directly associated with muscle strength: the direct path between negative affect and muscle strength was not added to the final model. Thus, the association between negative affect and muscle strength was fully mediated by avoidance. The results confirm the hypothesis that avoidance mediates the relationship between negative affect and lower muscle strength.

Pain and negative affect explained 21.8% of variance in avoidance of activities. Pain, negative affect and avoidance explained 17.8% of variance in muscle strength. Pain, negative affect, avoidance and muscle strength explained 87.4% of variance in activity limitations (Figure 2). The hypothesized indirect association between pain and activity limitations via avoidance and muscle strength accounted for 9.9% of the total association between pain and activity limitations. The indirect association between negative affect and activity limitations via avoidance and muscle strength accounted for 38.2% of the total association between negative affect and activity limitations.

Direct associations between pain, negative affect, avoidance, muscle strength and activity limitations

To improve the fit of the hypothesized model (Figure 1), direct paths between the variables were added (Figure 2). The results showed that besides the hypothesized indirect associations most variables in the model were directly associated with each other: (1) pain was positively associated with avoidance (path a), negatively associated with muscle strength (path d), and positively associated with activity limitations (path f); (2) negative affect was positively associated with avoidance (path i) and activity limitations (path j); (3) avoidance was negatively associated with muscle strength (path b), and positively associated with activity limitations (path e); and (4) muscle strength was negatively associated with activity limitations (path c). The Pearson correlation between pain and negative affect was 0.39 ($p < 0.001$).

Discussion

In the present study the validity of the avoidance model was assessed in patients with early symptomatic knee OA. We investigated the associations between pain, negative affect, avoidance of activities, muscle strength and activity limitations using SEM. We hypothesized that (1) avoidance of activities plays a mediating role in the relationship between higher pain and lower muscle strength: this hypothesis was confirmed. The indirect relationship between pain and muscle strength via avoidance was marginally significant; when negative affect was excluded from the model the indirect association was significant. We hypothesized that (2) lower muscle strength plays a mediating role in the relationship between avoidance and activity limitations: this hypothesis was confirmed, as the indirect relationship between avoidance and activity limitations via muscle strength was significant.

We hypothesized that (3) negative affect would play a moderating role in the avoidance model, by strengthening the tendency to avoid activities. This hypothesis was not confirmed. Instead, our results suggest that negative affect leads to lower muscle strength, via avoidance of activities. In other words, avoidance is a mediator between negative affect and lower muscle strength. This –slightly revised– avoidance model (**Figure 3**) seems to offer a valid explanation of the associations between pain, negative affect, avoidance of activities, lower muscle strength and activity limitations.

When we excluded negative affect from model 1f, the indirect association between pain and muscle strength via avoidance changed from marginally statistically significant ($p = 0.09$) to statistically significant ($p = 0.01$). Apparently the association between pain and avoidance is partially explained by negative affect. Several studies have shown that pain and negative affect are associated,^{40,42} and also in the present study these variables were moderately to highly correlated.³² These findings indicate that although it is important to separate pain and negative affect conceptually, empirically these concepts are not completely separable.

In the final structural equation model direct associations between pain, negative affect, avoidance, muscle strength and activity limitations were added to improve the model fit (**Figure 2**). Prior research has shown that pain, negative affect and avoidance of activities are also directly associated with activity limitations in knee OA patients.^{2,4,12,16,43,44} Originally, we did not include these direct associations in our analyses, as the present study was aimed at assessing the mechanisms described in the avoidance model. These direct associations indicate the existence of other pathways between pain and activity limitations than those hypothesized in the avoidance model. Alternative pathways may involve poor voluntary effort⁴⁵ or low self-efficacy beliefs.¹²

In the final model (**Figure 2**), the indirect association between pain and activity limitations via avoidance and muscle strength accounted for 9.9% of the total association between pain and activity limitations. The indirect association between negative affect and activity limitations accounted for 38.2% of the total association between negative affect and activity limitations. Again, these percentages indicate that avoidance is not the only mechanism explaining activity limitations in knee OA: the present study shows that avoidance is one mechanism, among other mechanisms.

All individual parameter estimates of the paths in the models were statistically significant (**Figure 2**), and the model had an adequate model fit according to the criteria CFI > 0.95 and SRMR < 0.08 (**Table 2**). The final model did not meet the fit criteria for the χ^2 test, and RMSEA. However, these fit indices are very sensitive to sample size: the χ^2 tends to over-reject true population models in large sample sizes and the RMSEA tend to over-reject true population models in sample sizes ≤ 250 .³⁷ To minimize the Type I and Type II error rate, in studies with a sample size ≤ 250 Hu and Bentler³⁷ recommended to use concurrent values of CFI > 0.95 and SRMR < 0.08 as criteria for adequate fit. The final model met these criteria.

Our confirmation of hypothesis 2 (i.e. mediation by muscle strength) is in line with the results of a previous study in patients with established knee OA.¹² The added value of the present study is that we also examined the mediating role of avoidance of activities (hypothesis 1) and the role of negative affect in the avoidance model (hypothesis 3). In addition, the present study was directed at patients with early symptomatic knee OA: it is assumed that the relationships described in the avoidance model are initiated in early stage OA because

in this stage patients experience activity-related pain for the first time, leading to the described process of adaptation.

The relationships proposed by the avoidance model were analysed using structural equation models in which the two measures of activity limitations were combined into a latent variable, while pain, negative affect, avoidance and muscle strength were analysed as observed variables. These models were used instead of full latent variable models because this was more appropriate for the present study's sample size. A strength of the present study is that we analysed the association between avoidance and activity limitations using a latent variable constructed of both a self-report and a performance-based measure of activity limitations. Therefore, the associations found between avoidance and activity limitations cannot be explained by a correlation between self-report measures.

Model 1f (Figures 2 and 3), in which negative affect was hypothesized to lead to lower muscle strength via the mediator avoidance of activities, was formulated based on the results of the analyses instead of a stated hypothesis. The results of the final structural equation model are interesting: they seem to imply that negative affect strengthens pain-related avoidance and thereby leads to lower muscle strength. However, because the final model was not formulated based on a stated hypothesis the findings are in need of replication. In addition, we used a cross-sectional design to study a model describing longitudinal relationships. This is a limitation of the present study. The next step is to validate the avoidance model in a longitudinal study, which will provide stronger evidence for causality.

Avoidance of activities was assessed with the resting subscale of the Pain Coping Inventory, which is a reliable and valid,^{4,25,26} but self-report measure of the level to which patients avoid activities when experiencing pain. Because self-report measures are susceptible to response and recall bias, in further research it is recommended to additionally use an accelerometer to measure avoidance of activities. Negative affect was assessed using the

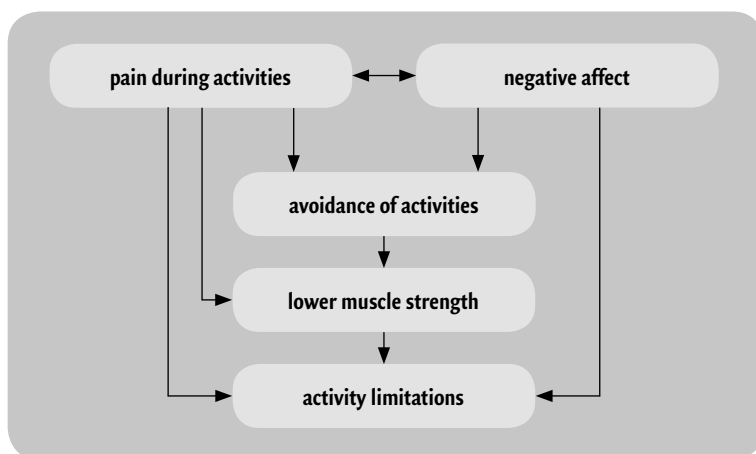


Figure 3. Results-based model of the associations between pain, negative affect, avoidance of activities, lower muscle strength and activity limitations.


vitality and mental health subscales of the SF-36, which is a generic questionnaire designed to measure health related quality of life. Negative affect might be better assessed with a more specific questionnaire designed to measure aversive mood states, unfortunately such a questionnaire is not included in the CHECK study.

In summary, the avoidance model seems to offer a valid explanation of the associations between pain, negative affect, avoidance of activities, muscle strength and activity limitations in patients with early symptomatic knee OA. Pain and negative affect were positively associated with avoidance, and avoidance was negatively associated with muscle strength (mediation by avoidance). Avoidance of activities was negatively associated with muscle strength, and muscle strength was negatively associated with activity limitations (mediation by lower muscle strength). There were also direct associations between pain, negative affect, avoidance, muscle strength and activity limitations. These results are summarized in **Figure 3**. Further confirmation in a longitudinal study is required.

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