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# Factors associated with pain resolution in those with knee pain: the MOST study

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## Abstract

**Objectives:** To determine how many persons with knee pain have subsequent pain resolution and what factors are associated with resolution, focusing especially on types of physical activity.

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- Analysis and interpretation of the data: GR, CEL, MN, NS, DKW.
- Drafting of the article: DTF
- Critical revision of the article for important intellectual content: SRJ, CEL, NS, MN, DKW
- Final approval of the article: All Authors
- Provision of study materials or patients: CEL, MN
- Statistical expertise: SRJ
- Obtaining of funding: DTF, CEL, MN
- Administrative, technical, or logistic support: DTF
- Collection and assembly of data: CEL, MN, GR

Competing interests

No author has competing interests that might bias this work.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joca.2021.03.017.

**Methods:** Using data from MOST, an NIH funded longitudinal cohort study of persons with or at risk of knee osteoarthritis, we studied participants who at baseline reported knee pain on most days at both a telephone interview and clinic visit. We defined pain resolution if at 30 and 60 month exams, they reported no knee pain on most days and compared these participants to those who reported persistent pain later. In logistic regression analyses, we examined the association of baseline risk factors including demographic factors, BMI, depressive symptoms, isokinetic quadriceps strength and both overall physical activity (using the PASE survey) and specific activities including walking, gardening, and different intensities of recreational activities with pain resolution.

**Results:** Of 1,304 participants with knee pain on most days at baseline, 265 (20.3%) reported no knee pain at 30 and 60 months. Lower BMI and stronger quadriceps were associated with higher odds of pain resolution while overall physical activity was not. Of activities, walking decreased the odds of pain resolution (adjOR = 0.86 (95% CI 0.76, 0.98)), but gardening (adjOR = 1.59 (1.16, 2.18)) and moderate intensity recreational activities ((adjOR = 1.24 (1.05, 1.46)) increased it.

**Conclusion:** Pain resolution is common in those with knee pain. Factors increasing the odds of pain resolution include lower BMI, greater quadriceps strength and gardening and moderately intensive recreational activities.

### Keywords

Knee pain; Physical activity; Quadriceps strength; Obesity

## Introduction

Most studies examining prevention of osteoarthritis (OA) have focused on primary prevention, i.e., the prevention of OA in adults with no symptoms or findings. Historically, OA has not been treated as a serious disease receiving little clinical and research resources[1,2.] Consequently, few adults without symptoms of OA have much motivation to adopt strategies that might prevent disease. This changes when a person first gets knee pain, a 'teachable moment'[3] and, when faced with the potential limitations and disability that it might bring, affected persons are motivated to adopt strategies that might prevent a recurrence of the pain. Little is known about preventing recurrence of disease and its primary symptom, pain, when an initial episode has occurred, We shall characterize this pain resolution as an example of secondary prevention.' Using data from a large cohort of adults with or at high risk of knee OA, this analysis compares adults with a report of knee pain who had no subsequent knee pain reports (they did not experience a recurrence) to those who had repeated reports of knee pain. In doing so, we sought to identify behaviors or factors that might act to prevent the recurrence of knee pain.

Among the behaviors likely to affect the odds of recurrence is physical activity defined as any energy expenditure above resting levels[4]. While studies have not addressed the effect of physical activity on pain resolution per se, studies of the effect of physical activity on knee OA risk have shown conflicting results[5,6] Some studies have shown that activity prevents disease while others have shown the disease progresses in those who engage in heavy physical activity[7,8]. Conflicting results are not necessarily related to the OA outcomes

studied, but all studies have summarized the total amount of activity and its effect usually on knee OA[9–11]. While weight-bearing activity may have trophic effects on bone and cartilage and maintain conditioning of transarticular muscles, different types of physical activity may confer different effects on joints and muscles.

In this paper, we examined which factors affect pain persistence or its resolution in those with knee pain. In terms of activity, we looked at both overall activity and specific types of physical activity and their effects on secondary prevention. To do this, we took advantage of a survey on physical activity administered to subjects which asked about specific types of recreational activities such as walking and gardening and intensity of physical activity ranging from light to strenuous.

Other modifiable factors may also affect the likelihood of pain recurrence and might be targeted in efforts to promote pain resolution. While muscular strength has been linked with the incidence and progression of symptomatic OA[12], its relation to knee pain resolution or persistence is unknown. Also, obesity is strongly associated with incident OA, but its relation to pain persistence or resolution is unstudied. Therefore, in addition to examining specific types of physical activity, we examined known risk factors for OA, knee extensor muscle weakness and obesity and tested whether they affected the likelihood of pain persistence or resolution.

## Methods

We undertook this investigation in the MOST study, a cohort study of 3,026 persons with or at risk of symptomatic knee osteoarthritis. In addition to the baseline examination, subjects were examined at 30 and 60 months. At each examination subjects were asked if they had knee pain on most days of a recent month twice, once in a telephone visit roughly 2 weeks before the clinic exam and then again at the clinic exam.

### Study outcome

**Defining pain resolution—**We limited our focus to persons with consistent frequent knee pain at the baseline exam. In terms of response to the question about frequent knee pain, subjects were often inconsistent in their response to the telephone and clinic interviews. To ensure that we were studying those who had consistent frequent knee pain, we required that they report frequent knee pain at both telephone interview and clinic visit in at least one knee. We then examined the follow-up data on consistent frequent knee pain in the two examinations superceding the initial exam for the period, a follow-up of 5 years. In the follow-up, we characterized persons as having pain resolution if they reported no frequent knee pain at both telephone interview and clinic visit at both of the two follow-up examinations.

### Study exposure variables

**PASE—**We used the Physical Activity Survey in the Elderly (PASE) to measure overall physical activity[13] PASE, a well-validated survey, includes questions about time spent walking and time spent in a variety of recreational activities, divided into questions based on the exertion levels required. To examine the relation of the intensity of daily activities

with our study outcome, we used the following subscales from the PASE: light sport or recreational activity, moderate sport or recreational activity, and strenuous sport or recreational activity. We also included questions related to the frequency of walking, muscle strengthening, lawn work, and gardening (for specific questions in PASE, see Supplement 1). Because of concerns that walking frequency did not represent the duration of walking, we also created a cumulative walking per week measure. Cumulative walking summarized response to frequency of walking (# of days/week) and hours walked each time. For example, a person who reported walking seldom (1–2 days, average 1.5 days) and who walked between 2 and 4 h each time (average 3 h) would have a cumulative walking score of $1.5 \times 3 = 4.5$.

**Strength—**Isokinetic knee extensor strength were measured in both lower limbs at baseline (Cybex 350, HUMAC software version 4.3.2/Cybex 300 for Windows 98, Avocent, Huntsville,AL). Knee extensor strength was recorded as the peak concentric torque at 60°/s. For each limb, we used the maximal strength generated over four trials and then averaged these to calculate a person specific measure of quadriceps strength. The strength measure was not normalized.

**Covariates.:** In addition to strength and physical activity, we examined the association of the following factors with our study outcome given their association with knee OA: baseline age (years)[14], sex (male/female)[9], Body Mass Index (BMI),[15,16] race, depressive symptoms (using Center for Epidemiologic Studies Depression Scale (CES-D) and dichotomized at a value of 16[17]) and level of educational attainment.

All subjects obtained weight bearing fixed flexion PA radiographs of both knees read by a team of experienced readers for Kellgren and Lawrence grade. We defined radiographic OA as present when the KL grade ≥2 in the knee.

**Analysis Plan—**We started by figuring out how many subjects in MOST met the definition of pain resolution. We limited analyses to persons who had consistent frequent knee pain at baseline. We then tested the effect of factors at baseline with the presence of absence of pain resolution at follow-up. Analyses were person specific and baseline factors tested were age, sex, race, clinic site, BMI, strength, depressive symptoms (using CES-D) and overall activity and different measures of physical activity. Since the components of the PASE survey comprised the total physical activity score (and the total score and its components were therefore not independent), we analyzed total PASE score and its components separately. Those who came to follow-up at 30 and 60 months were compared with those who did not using ttests and chisquare tests. Analyses were carried out with SAS 9.4 using multivariable logistic regression with secondary prevention (yes/no) of knee pain as the dependent variable.

## Results

Of 1619 MOST participants with consistent frequent knee pain at baseline, 315 (19.5%) did not participate in 30 and/or 60 month examinations. Those who did not come to these follow-ups were more likely to be men, to be older, to have higher BMI’s and to have lower

PASE scores than the 1,304 who came to both 30 and 60 month examinations. They were less likely to report gardening activities but did not report any differences in walking than those who came to follow-up.

Of 1304 MOST participants with consistent frequent knee pain at baseline who participated in both 30 and 60 month examinations, 265 (20.3%) reported no such knee pain at 30 and 60 months. Of these participants, 106/806 (13.2%) with pain and OA in the same knee(s) had pain resolution vs 141/444 (31.8%) without OA in the same knee(s). The remainder of the 1,304 had pain in one knee and OA in the other. Of those with bilateral consistent frequent knee pain, 9.2% achieved pain resolution whereas of those with unilateral consistent frequent knee pain, 22.4% achieved it. Compared with persons who had persistent knee pain, those with pain that resolved were more likely to have a lower BMI, were less likely to be depressed, less likely to be African American and had greater quadriceps strength (see Table I).

In multivariable analyses, we found that persons whose consistent frequent knee pain resolved were more likely to have a lower BMI and to have greater quadriceps strength (Table II) and were also more likely to engage in outdoor gardening activities than those with persistent pain. Overall PASE score was not associated with pain resolution (adjOR = 0.94 (95% CI 0.80, 1.09)). However, specific levels and types of activities affected the odds of pain resolution. While regular walking was associated with a lower likelihood of pain resolution, gardening and moderate sport or recreational activities were both associated with an increased likelihood that pain would resolve. Greater quadriceps strength was also associated with pain resolution. Analyses of those with knee radiographic OA and those without it at baseline showed no difference in results.

To understand better the association of baseline walking with later pain, we explored cumulative walking to see if there was an association with dose. We found a slightly weaker association of cumulative walking with failure of pain to resolve (adj OR = 0.87 (95% CI 0.75, 1.00)). We found no thresholds for walking above which it increased the likelihood of pain resolution. We also found that persons who walked more often had lower BMIs than those who did not do so ($r = -.13$, $p < .0001$ for correlation between walking frequency and BMI). We also carried out analyses in which we excluded persons who at least ‘sometimes’ engaged in light, moderate or strenuous activity and who did not engage in gardening or lawn activities or in strengthening exercises. This left us with 987 sedentary individuals whose only major activities would have been walking. In these analyses, results were not much different from the larger sample in that cumulative walking at baseline was associated with a reduced risk of pain resolution (adjOR = 0.84, 95% CI 0.70, 1.01) and other factors affecting pain reduction were similar to the larger sample.

When we examined persons by baseline BMI, we found that the factors we identified as associated with pain resolution were much more strongly related to this outcome in persons with BMI <30. Among those with BMI ≥ 30, in whom pain resolution was less frequent (15.2% vs 25.8% in those with BMI <30), few factors were associated with pain resolution (Table III).

## Discussion

In what is to our knowledge, the first study to examine later pain resolution in those with consistent frequent knee pain, we found that this experience was not rare, occurring in roughly 20% of those with consistent frequent knee pain. The experience was more common in persons with no radiographic OA in their painful knee(s) than in persons who had X-ray OA. Persons with lower BMIs and those with stronger quadriceps muscles were more likely than others to experience pain resolution. While we did not find an association of overall levels of physical activity with pain resolution, we found alluring evidence that those who reported gardening activities and who reported moderate recreational activities were more likely to experience pain resolution than those who did not.

While we found a substantial subset of MOST subjects actually had no recurrence of pain after reporting consistent frequent knee pain at baseline, this finding has not been reported by studies examining trajectories of pain in those with OA. For example, using data taken every 18 months over 6 years from the Knee Clinical Assessment Study (CAS-K) in the United Kingdom, Nicholls and coauthors identified five trajectories, and were able to reproduce three trajectories (mild and non-progressive, moderate, and severe and non-improving) using data from the Osteoarthritis Initiative (OAI)[18]. Similar trajectories of knee pain have been reported in the French Knee and Hip Osteoarthritis Long-term Assessment (KHOALA) cohort[19], the Tasmanian Older Adult Cohort Study (TASOAC)[20], and in the United Kingdom[21]. The findings from our study add a notion that recovery from pain may occur, though it may be not be common enough, especially in those with OA, to be included as a distinct trajectory.

With regards to pain, evidence does not support that more physical activity increases pain. In fact, more physical activity likely reduces pain. Like many observational studies examining physical activity and its relation to later outcomes, we did not find an association of the summed amount of self reported activity with later pain. One previous study comparing objectively measured physical activity in adults with symptomatic knee OA from the Osteoarthritis Initiative (OAI) and age-matched adults without OA in the National Health and Nutrition Examination Survey (NHANES), found simlar low levels of physical activity in terms of time spent in Moderate to Vigorous Intensity Physical Activity (MVPA)[22]. In a similar fashion, the same proportion of adults within MOST who had either no, mild, or moderate to severe knee pain met the 2008 Physical Activity Guidelines for Americans[23]. In terms of the effects of activity, data from a secondary analysis of a large clinical trial (n = 2,889) in adults with diabetes without knee pain, showed those who were randomized to an intensive diet and exercise program were 15% less likely to develop knee pain 1 year later compared with those in a diabetes education (control) group, (RR 0.85, 95% confidence 0.74–0.98)[24]

While we are not aware of other studies focusing on muscle strength and recurrent pain resolution or persistence, longitudinal studies looking at muscle strength and OA have shown that quadriceps strength lowers the risk of subsequent symptomatic knee OA[25,26], consistent with our findings.

In this work, we attempted to go beyond overall activity and focus on whether specific types of activities might reduce risk of pain recurrence. Among the activities that emerged as enhancing the odds of pain resolution was gardening. Gardening entails a variety of activities including kneeling and squatting, and rising repeatedly from these positions, balancing, and lifting and carrying. All of these activities have been included in exercises for OA[27] and their combination carried out repeatedly could be beneficial. These findings are suggestive and need confirmation.

In addition, participants who reported participating in moderate recreational activities (see Supplement 1 for wording of question) were more likely to have pain resolution. The findings regarding gardening and moderate activities may suggest that complex activities that require balance and strength, and are not stereotyped, may offer a pathway to pain resolution for those with knee pain.

On the other hand, our finding that walking reduces the likelihood of pain resolution runs counter to activity recommendations and contradicts findings from randomized trials of aerobic walking as exercise in knee OA[28]. These studies did not examine pain resolution. In exploring this finding, we were unable to identify thresholds of walking that may be beneficial. Our findings need to be examined in other studies testing pain resolution, but if corroborated, may suggest that stereotyped activities may be less effective in preventing recurrent knee pain than complex ones.

Among limitations are the possibility that pain was sampled infrequently and those we identified as having resolution of pain may have, at follow-up, been between flares of pain one of which may have been caught at baseline. Certainly, there was regression to the mean of pain severity in many MOST participants after baseline, but while that may influence the high rate of pain resolution seen, it should not affect analyses of factors associated with this resolution. As well, we employed a patient-reported measure of physical activity, the PASE, which like other self-reported measures is subject to imperfect recall. While an accelerometer-enabled monitor is better able to measure the intensity of physical activity and the frequency of walking, specific activities, such as gardening are best recorded with patient-reported measures. Also, we did not include data on treatments which are available for some of the interval of follow-up. Lastly, we studied pain on most days in the last month and that does not necessarily equate to all knee pain nor to pain with specific activities.

## Conclusion

In this first study, to our knowledge, of pain resolution in older adults with knee pain, we found that those with lower BMI and those with stronger quadriceps muscles were more likely to have resolution of pain and perhaps that gardening and moderate recreational activities were also associated with resolution of pain.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table I**

Frequency of those who meet criteria for secondary prevention in MOST (pain resolution) vs those who do not

| | **Achieved Pain Resolution (*N* = 265)** | **Did not achieve Pain Resolution (*N* = 1,039)** |
|---|---|---|
| Mean age in years (s.d.) | 61.9 (7.78) | 61.3 (7.89) |
| Sex (%F) | 64.5 | 66.1 |
| Mean BM1 (s.d.) | 29.7 (6.00) | 31.8 (6.55) |
| % Depressive Symptoms | 7.1 | 17.4 |
| % African American | 13.6 | 18.9 |
| Mean PASE score (s.d.) | 174(59.6) | 183 (84.2) |
| Quadriceps strength (s.d.) | 82.4 (42.5) | 78.0 (37.8) |
| % Walk (Never) | 13.6 | 13.7 |
| % Walk (Seldom) | 19.9 | 17.7 |
| % Walk (Sometimes) | 23.0 | 20.8 |
| % Walk (Often) | 43.6 | 47.8 |
| % Light recreational activity (Never) | 77.0 | 80.3 |
| % Light recreational activity (Seldom) | 12.5 | 12.9 |
| % Light Recreational activity (Sometimes) | 7.0 | 4.6 |
| % Light Recreational Activity (Often) | 3.5 | 2.3 |
| % Moderate Recreational Activity (Never) | 79.1 | 84.1 |
| % Moderate Recreational Activity (Seldom) | 8.7 | 8.6 |
| % Moderate Recreational Activity (Sometimes) | 4.9 | 3.0 |
| % Moderate Recreational Activity (Often) | 7.3 | 4.3 |
| % Strenuous sport (Never) | 75.6 | 75.5 |
| % Strenuous sport (Seldom) | 6.6 | 7.0 |
| % Strenuous sport (Sometimes) | 9.8 | 10.5 |
| % Strenuous sport (Often) | 8.0 | 7.0 |
| % Lawn | 51.6 | 48.1 |
| % Garden | 42.5 | 32.5 |

**Table II**

Association of Factors in MOST at baseline with Resolution of Knee Pain 30 and 60 months after baseline

| Risk Factor at Baseline | Adjusted Odds Ratio for Pain Resolution (95% CI)* | *P* value |
|---|---|---|
| BMI (per s.d.) | 0.71 (0.60, 0.84) | <.0.001 |
| Isokinetic Quadriceps Strength (per s.d.) | 1.24 (1.02, 1.52) | 0.03 |
| Light Sport or Recreational Activity)† | 1.14 (0.94, 1.39) | 0.19 |
| Moderate Sport or Recreational Activity)† | 1.24 (1.05, 1.47) | 0.01 |
| Strenuous Sport or Recreational Activity)† | 0.91 (0.78, 1.06) | 0.19 |
| Frequency of Walking)† | 0.85 (0.74, 0.96) | 0.01 |
| Muscle strengthening)† | 1.08 (0.96, 1.23) | 0.21 |
| Lawn work (yes/no) | 0.85 (0.62, 1.16) | 0.30 |
| Gardening (yes/no) | 1.58 (1.15, 2.16) | 0.004 |

*Odds Ratio above 1 signifies that it increases odds of pain resolution. If odds ratio is <1, it increases odds of pain persistence. Odds ratios are adjusted for age, sex, race, clinic site, educational attainment and depressive symptoms.

†These were treated as ordinal variables based on the response categories to the questions shown in Table I.

For each variable, we tested whether there was an increase in odds with an increase in the response category (e.g., from never to seldom).

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**Table III**

Association of Factors in MOST at baseline with Resolution of Knee Pain 30 and 60 months after baseline in those with BMI <30 vs those with BMI ≥30

| Risk Factor at Baseline | BM1 <30 | | BMI ≥30 | |
|---|---|---|---|---|
| | Adjusted Odds Ratio for Pain Resolution (95% CI)* | *P* value | Adjusted Odds Ratio for Pain Resolution (95% CI)* | *P* Value |
| BM1 (per s.d.) | 0.59 (0.36, 0.97) | .04 | 0.95 (0.70, 1.30) | .76 |
| Isokinetic Quadriceps Strength (per s.d.) | 1.36(1.03, 1.80) | .03 | 1.13 (0.83, 1.53) | .45 |
| Light Sport or Recreational Activity | 1.17(0.89, 1.54) | .26 | 1.19(0,88,1.60) | .26 |
| Moderate Sport or Recreational Activity | 1.27(1.02, 1.57) | .03 | 1.30 (0.98, 1.71) | .07 |
| Strenuous Sport or Recreational Activity | 0.89 (0.72, 1.08) | .24 | 0.86 (0.66, 1.13) | .29 |
| Frequency of Walking | 0.80 (0.65, 0.98) | .03 | 0.96 (0.77, 1.20) | .73 |
| Muscle strengthening | 1.10 (0.93, 1.30) | .27 | 1.04 (0.86, 1.27) | .66 |
| Lawn work (yes/no) | 0.82 (0.53, 1.27) | .38 | 0.93 (0.57, 1.51) | .75 |
| Gardening (yes/no) | 1.67(1.09, 2.57) | .02 | 1.46 (0.90, 2.37) | .12 |

*See Table II.