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Knee Pain and a Prior Injury Are Associated With Increased Risk of a New Knee Injury: Data from the Osteoarthritis Initiative

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Abstract

Objectives—We explored if knee pain or a history of knee injury was associated with a knee injury in the following 12 months.

Methods—We conducted longitudinal knee-based analyses among knees in the Osteoarthritis Initiative. We included both knees of all participants who had at least one follow-up visit with complete data. Our first sets of exposures were knee pain (chronic knee symptoms and severity) at baseline, 12-month, 24-month, and 36-month visits. Another exposure was a history of injury, which we defined as a self-reported injury at any time prior to baseline, 12-month, 24-month, or 36-month visits. The outcome was self-reported knee injury during the past year at 12-month, 24-month, 36-month, and 48-month visits. We evaluated the association between ipsilateral and contralateral knee pain or history of injury and a new knee injury within 12 months of the exposure using generalized linear mixed model for repeated binary outcomes.

Results—A knee with reported chronic knee symptoms or ipsilateral or contralateral history of an injury was more likely to experience a new knee injury in the following 12 months than a knee without chronic knee symptoms (odds ratio [OR]=1.84, 95% confidence interval [CI]=1.57, 2.16)

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or prior injury (prior ipsilateral knee injury OR=1.81, 95% CI=1.56, 2.09; prior contralateral knee injury OR=1.43, 95% CI=1.23, 1.66).

Conclusion—Knee pain and a history of injury are associated with new knee injuries. It may be beneficial for individuals with knee pain or a history of injury to participate in injury prevention programs.

Key Indexing Terms

knee injuries; osteoarthritis; musculoskeletal pain

INTRODUCTION

Individuals with a history of knee injury are 3 to 6 times more likely to develop knee osteoarthritis (KOA) (1, 2) and are on average diagnosed with osteoarthritis approximately 10 years younger than individuals without a history of knee injury (3). Knee injuries are also strongly associated with an accelerated form of knee osteoarthritis (4). Understanding risk factors for knee injury may provide important insight into osteoarthritis prevention. Despite extensive research assessing risk factors for knee injuries among young physically active individuals (under 35 years of age)(5–7) it remains unclear which factors may predispose older adults with, or at risk for, KOA to experience a knee injury.

Individuals with knee pain are at greater risk of falls (8–11) but it is unclear if they are also at risk of knee injuries. Knee pain is associated with altered proprioception (12), which may increase the risk of falls (13, 14). Hence, knee pain may be a risk factor for knee injuries among older adults.

A history of knee injury to the ipsilateral or contralateral knee may also be risk factors for new knee injuries (15–17). Specifically, young physically active individuals with an anterior cruciate ligament (ACL) tear are more than five times as likely to sustain another ACL tear in either knee (16). Despite a history of knee injury being one of the most important risk factors for knee injuries in young physically active individuals (18, 19) there is little evidence to determine if it is also an important risk factor among older and more sedentary adults (20, 21).

The aim of this study was to assess whether knee pain or a history of knee injury increases the risk for a knee injury in the subsequent 12 months among older adults with, or at risk for, KOA. We hypothesized that chronic knee symptoms and greater pain severity predict injuries among individuals with, or at risk for, KOA. Furthermore, we hypothesized that a history of ipsilateral or contralateral knee injury is associated with new injuries.

MATERIALS AND METHODS

To test for an association of knee pain and history of knee injury, with subsequent knee injuries, we conducted longitudinal knee-based analyses using data from the Osteoarthritis Initiative (OAI). We focused on knee-based analyses to test our hypotheses that knee pain or histories of knee injury in the ipsilateral or contralateral knee were important risk factors for new knee injuries. The OAI is a longitudinal observational study of KOA that occurred at

four clinical sites in the United States: Memorial Hospital of Rhode Island, The Ohio State University, University of Maryland and John Hopkins University, and the University of Pittsburgh. The staff at the 4 clinical sites enrolled 4,796 men and women (45 to 79 years of age) between February 2004 and May 2006. The OAI cohort comprised three groups classified at baseline: 1) progression subcohort, including individuals with at least one knee with symptomatic radiographic KOA, 2) incidence subcohort, including individuals at risk for symptomatic radiographic KOA, and 3) non-exposed control subcohort, which included individuals with no KOA and no risk factors for KOA. Detailed descriptions of the eligibility criteria for each subcohort and the OAI protocol are publicly available at the OAI website (22). Institutional review boards at each OAI clinical site and the OAI coordinating center (University of California, San Francisco) approved the OAI study.

In this study, we included all knees among OAI participants who attended the baseline visit and at least one follow-up visit, irrespective of whether or not they had KOA. Our first sets of exposures were knee pain (chronic knee symptoms and severity) at baseline, 12-month, 24-month, and 36-month visits. Another exposure was a history of injury, which we defined as a self-reported injury at any time prior to baseline, 12-month, 24-month, or 36-month visits. The outcome was self-reported knee injuries that occurred during the subsequent year – assessed at 12-month, 24-month, 36-month, and 48-month OAI visits.

Knee Pain

To determine if knee pain was associated with subsequent knee injuries we defined pain based on the presence of chronic knee symptoms or pain severity. At each OAI visit participants answered “During the past 12 months, have you had any pain, aching, or stiffness in or around your right knee?” If the participant answered “yes” then they were asked “During the past 12 months, have you had pain, aching, or stiffness in or around your right knee on most days for at least one month? By most days, we mean more than half the days of a month.” The same questions were asked for the left knee. We defined chronic knee symptoms as pain on most days of a month in past 12 months (23, 24).

Knee pain severity was based on the WOMAC pain subscale, a validated outcome measure for KOA(25). The WOMAC pain subscale has five questions that inquire about pain in the last 7 days with walking, stairs, lying in bed, sitting or lying down, and standing. The WOMAC pain subscale was knee specific and we used data from both knees. Each item is scored 0 (none) to 4 (extreme pain) and the subscale ranges from 0 to 20. However, across the annual OAI visits, 95% of knees had WOMAC pain scores between 0 and 9 and > 50% had a WOMAC pain score=0 or 1. Furthermore, we detected a nonlinear association between WOMAC pain and injury. Because of the skewed pain scores and nonlinear association we dichotomized knee severity for our primary analyses as no-to-little pain (0 to 2) or knee pain (3). The knee pain data are publicly available (Files: allclinical00 (version 0.2.2), allclinical01 (version 1.2.1), allclinical03 (3.2.1), allclinical05 (5.2.1)) (22).

History of Knee Injuries

To determine if a history of joint-specific knee injury was associated with subsequent knee injuries we defined a history of knee injury based on self-reported data from the baseline,

12-, 24-, and 36-month OAI visits. At the OAI baseline visit participants answered “Have you ever injured your right knee badly enough to limit your ability to walk for at least two days?” At each follow-up visit, participants were asked “Since your last annual visit to the OAI clinic about 12 months ago, have you injured your right knee badly enough to limit your ability to walk for at least two days?” Similar questions were asked for the left knee. The injury data are publicly available (Files: allclinical00 (version 0.2.2) allclinical01 (version 1.2.1), allclinical03 (3.2.1), allclinical05 (5.2.1)) (22).

New Knee Injuries

Our main outcome was self-reported knee injury at an OAI follow-up visit. This was defined based on the follow-up visit self-reported questions listed in the previous section. These data are publicly available (Files: allclinical01 (version 1.2.1), allclinical03 (3.2.1), allclinical05 (5.2.1), allclinical06 (version 6.2.1))(22).

Radiographic Assessments

We conducted secondary analyses based on the absence or presence of radiographic KOA at the OAI baseline visit. Weight-bearing, bilateral, fixed-flexion, posterior-anterior knee radiographs were obtained at the OAI baseline. Central readers scored the images for Kellgren-Lawrence Grades (0 to 4). We defined the subset with radiographic KOA as individuals with both knees having Kellgren-Lawrence Grade ≥ 2 . We defined the subset without radiographic KOA as individuals with both knees having Kellgren-Lawrence Grade=0 or 1 throughout the study period (baseline to 48 months). We also defined a subset with unilateral KOA as individuals with no osteoarthritis in the ipsilateral knee but with contralateral radiographic KOA. The agreement for these readings (read-reread) was good (weighted kappa (intra-rater reliability)=0.70 to 0.78). These Kellgren-Lawrence grades are publicly available (File: kXR_SQ_BU##_SAS (version 0.6, 1.6, 3.5, 5.5, 6.3))(22).

Clinical Data

Demographic, anthropometric, and other participant characteristics were acquired based on a standard protocol. We extracted age, body mass index (BMI), sex, self-reported strong prescription medication use, Physical Activity Scale for the Elderly scale, and responses regarding frequent knee bending activities. For *post hoc* analyses we adjusted for frequent knee bending, which we defined as a person who did any of the following tasks for ≥ 4 days per week in the 30 days prior to a study visit: 1) climbed up “10 or more flights of stairs during a single day”, 2) kneeled “30 minutes or more during a single day”, 3) squatted “30 minutes or more during a single day”, or 4) got “in and out of a squatting position 10 or more times during a single day”. The protocol and data are publicly available (Files: enrollees (version 20), allclinical## (version 0.2.2, 1.2.1, 3.2.1, 5.2.1, 6.2.1) (22).

Statistical Analyses

We evaluated the association between knee pain (chronic symptoms and severity) and a history of knee injury prior to the baseline, 12-month, 24-month, 36-month OAI visits and a knee injury within 12 months by performing knee-based longitudinal analyses using a logistic regression with repeated measures (generalized linear mixed model) to adjust for

and 12 (0.1%) knees had three or four reported injuries during the observation period. Of the 875 new knee injuries, 335 new injuries occurred among those with radiographic KOA at baseline, 153 new injuries occurred among those without radiographic KOA, and 46 new injuries occurred among those with unilateral KOA.

In our primary analyses, we found that knees with reported chronic knee symptoms were 1.84 times as likely to experience an ipsilateral knee injury in the following 12 months (Table 2) compared with knees without chronic knee symptoms. Similarly, knees with greater knee pain severity (WOMAC pain score ≥ 3) were almost twice as likely to have an ipsilateral knee injury in the following 12 months (Table 3). Contralateral knee pain (chronic knee symptoms or pain severity) was not associated with a knee injury in the following 12 months. Knees with a history of knee injury in the ipsilateral or contralateral knee were more likely to have a new knee injury (history of ipsilateral knee injury OR=1.81; history of contralateral knee injury OR=1.43, Table 2). Similar findings were observed when adjusting for knee pain severity instead of chronic knee symptoms (Table 3).

These findings were supported in our secondary and *post hoc* analyses. One exception was that a history of a contralateral knee injury was not related with a new knee injury among those without radiographic osteoarthritis at baseline. Analyses among 653 participants with unilateral KOA were limited because only 46 injuries occurred. In unadjusted analyses, we found that knees without radiographic osteoarthritis – but with contralateral radiographic osteoarthritis – were more likely to have a new knee injury if they had chronic knee symptoms in either knee, severe knee pain in the ipsilateral knee, and a history of knee injury in either knee (see Supplemental File, Tables 1 and 2).

We conducted several *post hoc* analyses by adjusting for potential confounders among the full cohort and they supported the primary results (see Supplemental File, Tables 3 and 4). The person-based analyses supported the primary results that an individual with knee pain (frequent [OR=1.69] or severe [OR=1.62]) or a history of injury (OR=1.88) was more likely to have a new knee injury in either knee (see Supplemental File, Tables 5 and 6). Finally, WOMAC knee pain as a continuous predictor (scale 0 to 20) was associated with a new knee injury (OR=1.11, per one point increase in WOMAC pain score; see Supplemental File, Table 7).

DISCUSSION

Despite knee injuries being associated with a greater risk for early-onset osteoarthritis (3) and accelerated KOA (4) very little is known about possible risk factors for injuries among adults over 45 years of age. We found that among knees with or without KOA that a history of knee injury and ipsilateral knee pain are associated with new knee injuries. These findings were consistent when we defined pain based on severity or the presence of chronic knee symptoms.

Since knee pain, irrespective of the presence of radiographic osteoarthritis, is associated with a greater risk of injuries it may be beneficial to determine if aggressive treatment of knee pain is an important intervention to prevent future knee injuries. If so, then it may be

advisable for clinicians to manage knee pain, even in the absence of radiographic osteoarthritis, based on KOA treatment guidelines. Most osteoarthritis treatment guidelines (35) advocate managing knee symptoms with a pharmacological intervention as well as exercise programs, which could include goals for pain modification and injury/fall prevention.

These exercise programs could also be beneficial if applied to individuals with a history of knee injury. We found that a history of knee injury, in either knee, was associated with a new knee injury. This was consistent among knees with and without KOA; however, a history of contralateral knee injury was not associated with new injuries among knees without radiographic KOA. A history of knee injury could be related to bilaterally altered biomechanics (36–39) or neuromuscular control (40–42), that predisposes the ipsilateral or contralateral knee to a new injury. For example, individuals with a history of an ACL injury have altered biomechanics and neuromuscular control in the injured and uninjured knees, both of which could predispose the knees to a future ACL injury (38, 40). This may explain why an injury in either knee could increase the risk of a new injury. Furthermore, knee pain in either knee was associated with a new injury in the unadjusted analyses. However, when we combine all the variables into the model contralateral knee pain is no longer associated with new knee injuries. This could be because ipsilateral knee pain or a history of injury in either knee is more relevant when assessing risk of a new knee injury. Hence, knees with a history of knee injury, with or without osteoarthritis, may benefit from exercise programs that incorporate neuromuscular training with a goal of preventing injuries or falls.

Injury prevention programs are commonly advocated for young physically active individuals because these programs improve performance, reduce the risk of injuries, and may subsequently reduce the risk of osteoarthritis. This last point is based on consistent evidence that knee injuries increase the risk of KOA (1–3). We previously demonstrated that among adults over 45 years of age that knee injuries are associated with incident KOA, particularly accelerated KOA (4). Based on the current analyses, we found that knee pain and a history of knee injury increases the risk of a knee injury among adults with and without radiographic osteoarthritis. This supports a hypothesis that some knees may experience a dangerous cycle of injuries, pain, and structural progression (see Figure 1). Prior to the onset of KOA (accelerated or common osteoarthritis) ipsilateral knee pain and a history of injury may be risk factors for a new injury that could trigger the onset of accelerated or common KOA, which are associated with knee symptoms. Once a patient has osteoarthritis we found that a history of knee injury or ipsilateral knee pain, which could be attributable to osteoarthritis, are still risk factors for a new knee injury. This new injury could exacerbate osteoarthritis progression and increase knee symptoms. We should strive to avoid this vicious cycle. Therefore, among older adults who report knee pain or a history of knee injury we should explore injury/fall prevention strategies.

Despite evidence that knee pain and a history of knee injury are associated with a greater risk for knee injuries there are a few key limitations. Firstly, the current study could not identify the underlying cause of knee pain (e.g., referred hip pain, patellofemoral lesions, tendinopathy, pre-radiographic degenerative changes). Furthermore, it is unclear if the knee had pain immediately prior to the new injury. Despite these limitations, we observed an

association between knee pain and knee injuries. Interestingly, we found similar associations between pain and injuries among those with and without radiographic osteoarthritis. Prior research has indicated that knee pain was associated with falls (8–10, 13), even when most (>80%) of the individuals with knee pain had no clinician-diagnosed KOA (14). This highlights the importance of knee pain as a risk factor for knee injuries irrespective of whether or not KOA was present. Some sources of knee pain (e.g., patellofemoral pathology, ligamentous instability, effusion) may be more likely alter proprioception (12) or increase the risk of subsequent injuries than other sources of pain. Future research that clarifies the source of the knee pain may help us understand the possible link between knee pain and subsequent injuries and ultimately lead to better injury prevention strategies.

It would also be beneficial to understand which injuries increase the risk of subsequent injuries and which new injuries are occurring. We could not address these important questions with existing data within the OAI. Despite not knowing the source of the knee pain or the type of injury this study represents an important first step in understanding the association between knee pain, history of knee injury, and new knee injuries. Future studies could also pursue this research in population-based cohorts but these findings will likely be confirmed since they complement the existing literature about the association between knee pain and falls (8–10, 13) and findings among younger physically active individuals (15–17).

In conclusion, we found that self-reported knee pain and a history of knee injury are associated with a greater risk for a new knee injury among knees with or without KOA. Hence, some knees may experience a dangerous cycle of injuries, pain, and structural progression. Since knee injuries are a key risk factor for KOA it may be ideal to test the benefit of implementing injury prevention strategies among adults with knee pain or a history of knee injuries. This may entail treatment strategies to reduce knee pain as well as exercise programs that aim to promote neuromuscular control and reduce the risk of injury/falls (8–10).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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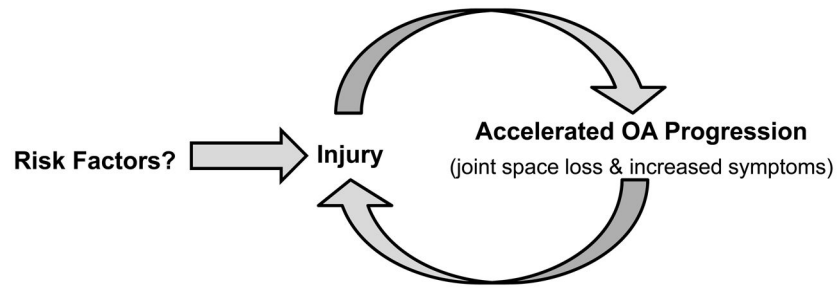


Figure 1.
A Vicious Cycle of Injury and Accelerated Knee Osteoarthritis

Table 1
 Descriptive Baseline Characteristics of the Study Knees in Primary and Secondary Analyses

	Full OAI Cohort (n = 8,870 knees)	Bilateral ROA (n = 2,694 knees)	No ROA (n = 2,408 knees)	Unilateral ROA (n = 653 knees)
Females (n (%))	5182 (58.4%)	1676 (62.2%)	1346 (55.9%)	320 (49.0%)
Chronic knee symptoms (n (%)) [†]	3221 (36.3%)	1264 (46.9%)	639 (26.6%)	146 (22.4%)
WOMAC knee pain score	2916 (32.9%) [‡]	1221 (45.3%) [‡]	512 (21.3%)	120 (18.4%)

Note. ROA = radiographic osteoarthritis (Kellgren-Lawrence Grade 2).

[†]Frequent and WOMAC knee pain are reported for both knees within a participant for the Full OAI cohort and among those with bilateral ROA or No ROA because both knees could contribute an outcome. Frequent and WOMAC knee pain are reported for the knee without ROA.

Table 2

Chronic knee symptoms and history of injury predict a new knee injury within 12 months

	Frequency of Injuries/Total Observations	Unadjusted Odds Ratio for Injury	Adjusted* Odds Ratio for Injury
Full Osteoarthritis Initiative (4,435 participants, 875 injuries)			
No Chronic Ipsilateral Knee Symptoms	422/21312 (2.0%)	Reference	Reference
Chronic Ipsilateral Knee Symptoms	453/10118 (4.5%)	2.09 (1.82, 2.40)	1.84 (1.57, 2.16)
No Chronic Contralateral Knee Symptoms	502/21311 (2.4%)	Reference	Reference
Chronic Contralateral Knee Symptoms	373/10119 (3.7%)	1.52 (1.32, 1.75)	1.02 (0.87, 1.20)
No History of Ipsilateral Knee Injury	443/22275 (2.0%)	Reference	Reference
History of Ipsilateral Knee Injury	432/9155 (4.7%)	2.09 (1.81, 2.41)	1.80 (1.56, 2.09)
No History of Contralateral Knee Injury	518/22275 (2.3%)	Reference	Reference
History of Contralateral Knee Injury	357/9155 (3.9%)	1.63 (1.41, 1.89)	1.43 (1.23, 1.66)
Bilateral ROA (1,347 participants, 335 injuries)			
No Chronic Ipsilateral Knee Symptoms	123/5324 (2.3%)	Reference	Reference
Chronic Ipsilateral Knee Symptoms	212/4177 (5.1%)	2.00 (1.59, 2.52)	1.78 (1.37, 2.30)
No Chronic Contralateral Knee Symptoms	147/5323 (2.8%)	Reference	Reference
Chronic Contralateral Knee Symptoms	188/4178 (4.5%)	1.56 (1.24, 1.96)	1.09 (0.85, 1.41)
No History of Ipsilateral Knee Injury	153/6198 (2.5%)	Reference	Reference
History of Ipsilateral Knee Injury	182/3303 (5.5%)	1.89 (1.49, 2.39)	1.65 (1.29, 2.10)
No History of Contralateral Knee Injury	168/6198 (2.7%)	Reference	Reference
History of Contralateral Knee Injury	167/3303 (5.1%)	1.82 (1.44, 2.32)	1.63 (1.28, 2.09)
No ROA at All Visits (1,204 participants, 153 injuries)			
No Chronic Ipsilateral Knee Symptoms	100/7460 (1.3%)	Reference	Reference
Chronic Ipsilateral Knee Symptoms	53/2091 (2.5%)	1.77 (1.25, 2.50)	1.62 (1.07, 2.45)
No Chronic Contralateral Knee Symptoms	110/7461 (1.5%)	Reference	Reference
Chronic Contralateral Knee Symptoms	43/2090 (2.1%)	1.37 (0.95, 1.97)	1.01 (0.66, 1.56)
No History of Ipsilateral Knee Injury	90/7333 (1.2%)	Reference	Reference
History of Ipsilateral Knee Injury	63/2218 (2.8%)	2.11 (1.50, 2.97)	2.00 (1.39, 2.86)
No History of Contralateral Knee Injury	107/7333 (1.5%)	Reference	Reference
History of Contralateral Knee Injury	46/2218 (2.1%)	1.39 (0.95, 2.02)	1.19 (0.81, 1.75)

* In addition to the variables indicated above each model was adjusted for sex, age, and body mass index at each visit. Bold = significant odds ratios.

Table 3

Knee pain severity and history of injury predict a new knee injury within 12 months

	Frequency of Injuries/Total Observations	Unadjusted Odds Ratio for Injury	Adjusted* Odds Ratio for Injury
Full Osteoarthritis Initiative (4,435 participants, 877 injuries)			
No Ipsilateral Knee Pain (WOMAC 2)	441/22188 (2.0%)	Reference	Reference
Ipsilateral Knee Pain (WOMAC 3)	436/9292 (4.7%)	2.25 (1.96, 2.59)	1.94 (1.66, 2.26)
No Contralateral Knee Pain (WOMAC 2)	536/22187 (2.4%)	Reference	Reference
Contralateral Knee Pain (WOMAC 3)	341/9293 (3.7%)	1.47 (1.27, 1.70)	0.98 (0.84, 1.15)
No History of Ipsilateral Knee Injury	444/22321 (2.0%)	Reference	Reference
History of Ipsilateral Knee Injury	433/9159 (4.7%)	2.09 (1.81, 2.41)	1.76 (1.52, 2.05)
No History of Contralateral Knee Injury	518/22321 (2.3%)	Reference	Reference
History of Contralateral Knee Injury	359/9159 (3.9%)	1.64 (1.42, 1.91)	1.44 (1.23, 1.67)
Bilateral ROA (1,347 participants, 335 injuries)			
No Ipsilateral Knee Pain (WOMAC 2)	124/5533 (2.3%)	Reference	Reference
Ipsilateral Knee Pain (WOMAC 3)	211/4072 (5.2%)	2.15 (1.70, 2.71)	1.90 (1.47, 2.45)
No Contralateral Knee Pain (WOMAC 2)	156/5433 (2.9%)	Reference	Reference
Contralateral Knee Pain (WOMAC 3)	179/4072 (4.4%)	1.46 (1.16, 1.83)	1.01 (0.78, 1.30)
No History of Ipsilateral Knee Injury	153/6201 (2.5%)	Reference	Reference
History of Ipsilateral Knee Injury	182/3304 (5.5%)	1.89 (1.49, 2.39)	1.64 (1.28, 2.09)
No History of Contralateral Knee Injury	168/6201 (2.7%)	Reference	Reference
History of Contralateral Knee Injury	167/3304 (5.1%)	1.83 (1.44, 2.32)	1.66 (1.29, 2.12)
No ROA at All Visits (1,204 participants, 154 injuries)			
No Ipsilateral Knee Pain (WOMAC 2)	111/7866 (1.4%)	Reference	Reference
Ipsilateral Knee Pain (WOMAC 3)	43/1723 (2.5%)	1.69 (1.16, 2.45)	1.40 (0.93, 2.10)
No Contralateral Knee Pain (WOMAC 2)	116/7866 (1.5%)		Reference
Contralateral Knee Pain (WOMAC 3)	38/1723 (2.2%)	1.47 (1.00, 2.15)	1.19 (0.78, 1.82)
No History of Ipsilateral Knee Injury	90/7366 (1.2%)		Reference
History of Ipsilateral Knee Injury	64/2223 (2.9%)	2.13 (1.51, 3.00)	2.00 (1.39, 2.87)
No History of Contralateral Knee Injury	107/7366 (1.5%)		Reference
History of Contralateral Knee Injury	47/2223 (2.1%)	1.41 (0.97, 2.05)	1.18 (0.81, 1.74)

* In addition to the variables indicated above each model was adjusted for sex, age, and body mass index at each visit. Bold = significant odds ratios.