*Osteoarthritis and Cartilage* (2002) **10,** 611–616

1063–4584/02/$35.00/0
doi:10.1053/joca.2002.0795, available online at http://www.idealibrary.com on IDEAL®

Osteoarthritis and Cartilage

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# History of acute knee injury and osteoarthritis of the knee: a prospective epidemiological assessment
# The Clearwater Osteoarthritis Study

F. V. Wilder, B. J. Hall, J. P. Barrett, Jr and N. B. Lemrow

*The Arthritis Research Institute of America, Inc., 300 S. Duncan Avenue #240, Clearwater, Florida 34615, U.S.A.*

## Summary

*Objective:* To evaluate the association between acute joint injury to the knee and knee osteoarthritis (OA).

*Design:* Prospective cohort. Sample size=1,436. Men and women aged 40 years and older participating in the population-based Clearwater Osteoarthritis Study (1988–current) with biennial physical exams including serial radiographs. Radiologically confirmed knee OA=27%; self-reported knee injury=11%. Lawrence and Kellgren ordinal scale was used to determine radiological evidence of the study outcome, knee OA. Self-reported history of knee injury was used to determine the study exposure.

*Results:* Individuals with a history of knee injury were 7.4 (95% C.I. 5.9–9.4) times as likely to develop knee OA than were those individuals who did not have a history of knee injury.

*Conclusion:* Acute knee joint injury appears to be a risk factor for the development of knee OA. Prevention strategies for OA should be targeted to those individuals with a history of acute knee injury. © 2002 OsteoArthritis Research Society International. Published by Elsevier Science Ltd. All rights reserved.

*Key words*: Osteoarthritis, Knee injury, Epidemiology, Cohort.

## Introduction

Osteoarthritis (OA), the most common joint disease, is a condition of synovial joints characterized by focal cartilage loss and an accompanying reparative bone response. OA affects more than 21 million Americans, and is a leading cause of disability in the U.S.[1]. It frequently affects the middle-aged and older population, involving various sites such as the neck, lower back, knees, hips and fingers. Individuals with symptomatic knee OA, experiencing pain and loss of function comprise approximately 10% of persons over 65 years of age[2]. While joint injury is widely accepted as a contributory factor in knee OA, past efforts to quantify the risk have produced a broad range of estimates. Davis *et al*. analysed the NHANES I data, finding a strong association between knee injury and unilateral knee OA (OR=16.3 and 10.9 for the right and left knee, respectively). Davis MA, Ettinger WH, Neuhaus JM, Cho SA, Hauck WW. The association of knee injury and obesity with unilateral and bilateral osteoarthritis of the knee[3]. The Framingham Knee Osteoarthritis Study identified major knee injury as a risk factor for knee OA[4]. Among men, the risk of severe radiographic OA with a history of knee injury was 3.46 ($P$<0.01), while women showed a lower risk of 2.18 ($P$<0.01). Findings from the 1998 Lau *et al*. case-control investigation reported a markedly increased risk among both Chinese men and women with a history of joint injury (OR=12.1 and 7.6, respectively)[5]. Gelber *et al*. confirmed these results in a prospective study published in 2000[6]. Joint injury prior to cohort entry or during follow-up substantially increased the risk for subsequent knee OA (RR=5.17). Clearly the strength of the association between joint injury and knee OA has, thus far, reflected great disparity in risk. A portion of the inconsistency may be attributable to the selected study designs (e.g. Framingham used case-control; NHANES used cross-sectional), differing exposure definitions (e.g. 'sustained fractured knee', 'knee injury', 'knee injury requiring crutches', etc.), and the age and geographic location of the populations studied. Further disparity in the point estimates may have been introduced by differing methods of radiological assessment of the knee (weight bearing or non-weight bearing), as well as the consideration of various permutations of potential confounders. The current investigation, studying a population located in the southern United States, seeks to quantify the role of joint injury as a contributory factor in the pathogenesis of knee OA.

## Methods

The objective of the current study is to evaluate the association between acute joint injury to the knee and the subsequent development of knee OA among men and women aged 40 years and older. In 1988, The Arthritis Research Institute of America (ARIA) located in Clearwater, Florida, initiated The Clearwater Osteoarthritis Study (COS). The COS is an on-going population-based prospective cohort study designed to identify the major risk factors for the development of OA, differentiate risk factors for localized and generalized primary OA, as well as to identify

Received 8 March 2002; revision requested 9 December 2001; revision received 24 January 2002; accepted 1 October 2001.

risk factors for the progression of OA. Currently in its 14th year, the 25-year longitudinal study follows individuals 40 years of age and older, collecting demographic, historical, clinical, and radiological data. To date, more than 3500 enrollees have been recruited and examined. ARIA is located appropriately in Pinellas County, Florida drawing upon a population with a large percentage of residents 65 years and older (22.5%)[7]. In 1990, Pinellas county ranked first of all U.S. counties in total population 65 years of age and older. Furthermore, Pinellas County ranked first in those 85 years of age and older[8]. The study sample of this older community comprises volunteer participants who are recruited by various methods. These include: invitational letters, television and radio announcements, newspaper articles publicizing the COS study, articles posted in community organizations' bulletins, as well as seminars held at community clubs and organizations. In efforts to include younger subjects who are more likely to be free of OA, concerted recruitment efforts are used to encourage participation by employees of the Pinellas County School System, the City of Clearwater, and Pinellas County, Inc.

At initial contact with participants a description of study procedures is given, followed by a screening questionnaire, detailing inclusion and exclusion criteria. After eligibility is determined and the informed consent is obtained, participants are asked to complete a self-administered, mostly pre-coded *COS History Questionnaire*[9]. This collects detailed information pertaining to demographics, family history, childhood history, adult habits and behavior, adult diet and work history, leisure/sports activities, ailments, injury history, medicines taken during adult life, self-functional assessment, and joint symptoms. The 139-item questionnaire is completed at the subject's home and is collected at the time of the scheduled appointment. Those study participants who completed four or more history questionnaires and physical exams were included in the current analyses.

At the initial and all subsequent ARIA appointments, a physical exam is conducted, including X-rays. The *COS Physical Exam*[10] is completed by the clinicians at that time. The physical exam has an emphasis on clinical and functional joint evaluation. The following study subjects were excluded from enrollment: individuals with self-reported rheumatoid arthritis or variants (lupus erythematosus, ankylosing spondylitis, etc.); gout; disabling neuralgic disease; those confined to a wheelchair; and lastly, those mentally incompetent. Study participants are re-evaluated biennially, updating both the history questionnaire and the clinical exam information.

A licensed X-ray technician using standard exposure techniques takes anterior weight-bearing knee radiographs. X-rays are interpreted by a board-certified radiologist. The study outcome was OA of the knee. A case was defined when radiographic structural evidence of disease was found. We felt this measure of outcome was objective, quantifiable, and reproducible. Each knee radiograph was graded 0 to 4 for OA by the ordinal criteria of Kellgren and Lawrence[11]: 0, absent; 1, questionable osteophytes and no joint space narrowing; 2, definite osteophytes with possible joint space narrowing; 3, definite joint space narrowing with moderate multiple osteophytes and some sclerosis; 4, severe joint space narrowing with cysts, osteophytes and sclerosis present. Subjects whose X-rays are interpreted as grades 0 or 1 are considered disease-free for knee OA; subjects whose knee radiographs are interpreted as grades 2, 3, or 4 are classified as cases. Every 10th subject's assembled films are independently interpreted by a non-affiliated radiologist blinded to the results of the first reading. In case of discrepancy in classification, the radiologist's reading is selected for OA. The study radiologist is blinded to information about the individual study participants. The study exposure was defined as having a history of knee injury. The *COS History Questionnaire* contains a component inquiring about study participants' previous joint injuries. Two germane questions utilized for the current study were '*Have you ever had a fractured knee?*' or, '*Have you ever had a severe twisting of either knee with resultant sprain or swelling lasting more than two weeks?*' A positive response to either of these questions resulted in the study subject being categorized for either knee as exposed to previous knee injury. In 1994, six years after commencing the Clearwater Osteoarthritis Study, we modified the original *COS History Questionnaire*, creating additions and changes to many of the questionnaire's components. Given to each subject at their fourth biennial examination, the revised *COS History Questionnaire* collected relevant information pertaining to participants' knee injury history. Thus, only those Clearwater Osteoarthritis Study participants examined four or more times were selected for the current investigation.

Several possible confounders were considered when testing this hypothesis. Most of the definitions of such are self-evident. Age used was age at study entry, body mass index was (weight/height$^2$), and occupational history was a dichotomous variable noting those individuals with a possible history of physical stress to the knee. Smoking status (ever/never), diabetes (yes/no), and physical activity were also examined. It has been suggested that those who participate in more strenuous activities are in one view more likely to sustain injuries, while at the same time more likely to retain their muscle strength and balance abilities. For the current analyses, those individuals who reported that they exercised continuously for at least 20 minutes three or more times per week were categorized as physically active.

## Data analyses

The interobserver variability of X-ray interpretations was calculated using the kappa coefficient[12], measuring the amount of agreement that is above random chance. During a preliminary examination of the data, the significance of association between knee injury and the dichotomous outcome of knee OA was assessed using the Mantel–Haenszel chi-square test statistic[13]. Putative confounders for this association were identified and included in the adjusted analyses. As the study participants had been observed for unequal lengths of time and some observations were censored, proportional hazards (Cox's) regression was employed[14,15] to quantify the relationship between acute joint injury and knee OA while simultaneously controlling for the influence of extraneous factors. The period of observation was the interval between study entry time and either: (1) the development of knee OA; (2) study withdrawal; or (3) censoring. The exponentiated beta coefficients were used to calculate the hazard ratio (risk ratio). Statistical Analyses Software (SAS), Version 8.12[16] was employed, specifically PROC PHREG, for the computer analysis of these data. It should be noted that the results reported for the unadjusted analyses also used Cox's regression, with knee injury as the only independent variable in the model. All risk ratios reported within are hazard ratios. Power calculations were conducted

Table I
*Descriptive findings: knee OA by characteristics of interest*

| | Total (*N*=1436) | | Knee OA (*N*=392) | | No knee OA (*N*=1044) | |
|---|---|---|---|---|---|---|
| | *N* | %* | *N* | %* | *N* | %* |
| Knee injury | 152 | 10.6 | 127 | 32.4 | 25 | 2.4 |
| Female | 1016 | 70.8 | 259 | 66.1 | 757 | 72.5 |
| 40–54 years | 489 | 34.1 | 72 | 18.4 | 417 | 39.9 |
| 55–64 years | 375 | 26.1 | 107 | 27.3 | 268 | 25.7 |
| 65–74 years | 447 | 31.1 | 172 | 43.9 | 275 | 26.3 |
| 75+ years | 89 | 6.2 | 37 | 9.4 | 52 | 5.0 |
| Smoker (ever) | 689 | 48.0 | 169 | 43.1 | 520 | 49.8 |
| Physically active | 405 | 28.2 | 109 | 27.8 | 296 | 28.4 |
| | *N* | Mean | *N* | Mean | *N* | Mean |
| BMI mean study entry | 1436 | 25.9 | 392 | 27.5 | 1044 | 25.3 |
| BMI mean–Age 45 | 1436 | 23.8 | 379 | 24.7 | 1044 | 23.5 |

*Percentage reflects the number of subjects in each category divided by the total number of study subjects (*N*=1436; *N*=392 and *N*=1044).

Table II
*Descriptive findings: acute knee injury by characteristics of interest*

| | Total (*N*=1436) | | Knee injury (*N*=152) | | No knee injury (*N*=1284) | |
|---|---|---|---|---|---|---|
| | *N* | %* | *N* | %* | *N* | %* |
| Female | 1016 | 70.8 | 88 | 57.9 | 928 | 72.3 |
| 40–54 years | 489 | 34.1 | 33 | 21.7 | 456 | 35.5 |
| 55–64 years | 375 | 26.1 | 38 | 25.0 | 337 | 26.3 |
| 65–74 years | 447 | 31.1 | 69 | 45.4 | 378 | 29.4 |
| 75+ years | 89 | 6.2 | 9 | 5.9 | 80 | 6.2 |
| Smoker (ever) | 689 | 48.0 | 67 | 44.1 | 622 | 48.4 |
| Physically active | 405 | 28.2 | 48 | 31.6 | 357 | 27.8 |
| | *N* | Mean | *N* | Mean | *N* | Mean |
| BMI mean study entry | 1436 | 25.9 | 152 | 28.1 | 1284 | 25.7 |
| BMI mean–age 45 | 1436 | 23.8 | 144 | 25.1 | 1284 | 23.7 |

*Percentage reflects the number of subjects in each category divided by the total number of study subjects (*N*=1436; *N*=152; and *N*=1284).

to determine sufficiency of sample size for detecting an association of 3.0 or greater between injury and knee OA. This study had over 90% power to detect such an association if indeed one existed (two-tailed; alpha=0.05).

## Results

Interreader reliability by a second radiologist reflected 93% agreement (kappa=0.85). The mean period of observation among those with and without a history of knee injury was 4.22 and 7.69 years, respectively. Among the 1,436 study participants, 27.3% were incident cases of radiologically confirmed knee OA (*N*=392). A history of acute knee injury was reported by 10.6% of all study subjects (*N*=152). Several factors associated with knee OA and with knee injury were investigated to summarize their relationship with the outcome and to identify potential confounders (Table I & II). A factor was considered a confounder if it was associated with knee OA (outcome) and was differentially distributed between those reporting knee injuries (exposed) and those not reporting knee injuries (non-exposed). The following factors were considered: gender, age at study entry, body mass index (weight/height$^2$), occupational history, smoking status, diabetes, and physical activity. The mean age of those developing and not developing knee OA was 63.8 and 58.5 years, respectively. The mean age at study entry among subjects with and without a history of knee injury was 63.1 and 59.6 years, respectively. The mean body mass index (BMI) at study entry among those who subsequently developed OA was 27.5, while the corresponding BMI among those reporting a history of knee injury was 28.1. Additionally, the self-reported subjects' BMI at age 45 years was also evaluated for those who developed knee OA (24.7) and for those noting a history of knee injury (25.1).

The unadjusted risk ratio, generated using Cox's regression with knee injury as the only independent variable, quantified the association between acute knee injury and knee OA. These data indicated that those individuals who sustained an acute knee injury are over nine times more likely to develop knee OA than are those individuals who did not sustain an acute knee injury (risk ratio=9.7; CI 7.8–12.1) (Table III). Stratification by gender revealed little difference in risk for knee OA when examining the role of

Table III
*Gender-specific risk ratios*: knee OA and acute knee injury*

| | Unadjusted | Adjusted* | Risk ratio 95% CI | Risk ratio 95% CI |
|---|---|---|---|---|
| Total | 9.7† | 7.8–12.1 | 7.4† | 5.9–9.4 |
| Females | 9.5† | 7.2–12.6 | 7.2† | 5.2–9.8 |
| Males | 9.2† | 6.4–13.4 | 8.7† | 5.9–12.9 |

*Adjusted risk estimates include the following confounders: age at study entry, gender, BMI at study entry, BMI at age 45 years, and smoking (ever/never).
CI=Confidence interval.
†=*P*-value<0.0001.

Table IV
*Evaluation of potential influence due to losses to follow-up*

| | Lost to follow-up % | Not lost to follow-up % |
|---|---|---|
| Knee injury | 2.2 | 11.5 |
| Female | 71.3 | 70.7 |
| Mean age (years) | 61.2 | 59.9 |
| BMI mean study entry | 25.5 | 26.0 |
| BMI mean–age 45 | 23.3 | 23.9 |
| Smoker (ever) | 58.9 | 50.3 |

acute knee injury. These data show that women who have a history of knee injury are over 9.5 times as likely to develop knee OA than are those women who do not have a history of knee injury (risk ratio=9.5; CI=7.2–12.6). Similarly, men who have a history of knee injury are also over nine times more likely to develop knee OA than are those men who do not have a history of knee injury (risk ratio=9.2; CI=6.4–13.4).

Final adjusted analyses simultaneously considered the possible effects of the following factors: age, gender, BMI at study entry, BMI at age 45 years, high risk occupation, smoking status (ever vs never), physical activity, and history of diabetes. History of diabetes, physical activity, and high risk occupation demonstrated only a minute alteration in the point estimate. These co-variates were dropped from the final predictive model. Subjects' self-reported historical BMI at age 25 and age 45 years were available for the analyses. While the historical BMIs (age 25 and 45 years) were highly correlated, the inclusion of a subject's BMI at study entry and their BMI at age 45 years added predictive ability to the final model. Thus BMI at age 25 years was not retained in the final statistical model. As over 98% of the study subjects were white, the predictive model was run both ways: with and without the non-white subjects. The point estimate was identical for each method. Race was not retained in the final predictive model. The final adjusted association between acute knee injury and knee OA held and retained high statistical significance (risk ratio=7.4; CI 5.8–9.4) (Table III). The adjusted gender-stratified risk estimate showed a risk of 7.2 and 8.3 for women and men, respectively (risk ratio=7.2; CI 5.2–9.8 and risk ratio=8.3; CI 5.9–12.9).

Among those contributing person-years to the analysis, 13% of the cohort were considered lost to follow-up. Differences by selected characteristics between those subjects that were lost to follow-up and those that were not lost were examined (Table IV). Differences in lost to follow-up by the exposure classification knee injury, reflected a 9.3% difference (2.2% lost and 11.5% not lost). Furthermore, those lost from the study were older (61.2 vs 59.9 years, respectively), had similar BMIs, but displayed a higher percentage of smokers compared to those not lost (58.9% vs 50.3%, respectively). We assessed the impact of considering various factors in the proportional hazards model analyses (Table IV). When considering the influence of age, gender, BMI, BMI at 45 years, smoking, diabetes, high risk occupation, and physical activity, risk estimates ranged from 7.20–8.29.

## Discussion

The results of this epidemiological investigation indicate that those individuals with a history of acute knee injury are more likely to develop knee OA than are those individuals who do not have a history of acute knee injury. While only a clinical trial would serve to identify a causal relationship between an exposure and an outcome (clearly inappropriate for this exposure), the current prospective cohort study enabled investigators to address four of the causal criteria[17]:

(1) The strength of the association between acute knee injury and the development of knee OA indicates that those who have had an acute knee injury are seven times more likely to develop knee OA than are those individuals who do not have a previous knee injury. This association remained highly statistically significant after eliminating the influence of the aforementioned confounding factors (*P*-value 0.0001).
(2) These findings are consistent with previous epidemiological studies, noting a heightened risk for OA of the knee among those with a history of acute knee injury. While some studies have reported lower risk estimates for this association[4], other studies have reflected a far greater risk[3,5]. This may be, in part, attributable to differences in exposure definition. The current study categorized exposure based on the following two questions: '*Have you ever had a fractured knee?*' or, '*Have you ever had a severe twisting of either knee with resultant sprain or swelling lasting more than two weeks?*' If other studies classified individuals as exposed if they had more severe acute injuries (relative to the current study definition), this may have produced a higher risk estimate, assuming there is an association between injury and subsequent OA. Our study subjects may have interpreted the term 'fractured knee' in an inexact manner as it encompasses a wide spectrum concerning extent of injury. As our exposure was self-reported based on the aforementioned questions, we were unable to classify and differentiate those who sustained knee injuries which involved the knee joint surface directly and those that did not. Had such a distinction been afforded by these data, it is unproven but possible that we may have generated two separate risk estimates: one suggesting a reduced risk among those *without* a history of direct joint surface damage, relative to a heightened risk among those *with* such a history.
(3) The prospective cohort design was able to clearly establish the temporal relationship between knee injury and the subsequent development of radiologically confirmed knee OA. Although the Clearwater Osteoarthritis Study accepted individuals into the study regardless of their OA status at enrollment, only those participants who were free from disease at study entry were selected for the current investigation.

Table V
*Adjusted risk ratios*: knee OA and acute knee injury*

| Factors associated with OA | Risk ratio | 95% CI |
|---|---|---|
| Age | 8.29† | 6.62–10.39 |
| Age, gender | 8.17† | 6.51–10.24 |
| Age, gender, BMI | 7.24† | 5.76–9.10 |
| Age, gender, BMI, BMI at 45 | 7.21† | 5.71–9.10 |
| Age, gender, BMI, BMI at 45, smoking | 7.43† | 5.85–9.44 |
| Age, gender, BMI, BMI at 45, smoking, diabetes | 7.31† | 5.79–9.22 |
| Age, gender, BMI, BMI at 45, smoking, high risk occupation | 7.20† | 5.71–9.09 |
| Age, gender, BMI, BMI at 45, smoking, physical activity | 7.23† | 5.72–9.13 |

*Adjusted risk estimates examined knee OA and knee injury including selected potential confounders. CI=Confidence interval.
†=*P*-value<0.0001.

The major strength of this study was the collection of serial radiographs for all participants beginning at study entry, allowing us to determine pre-existing disease among the study subjects. A limited number of epidemiological studies have been able to examine this relationship prospectively.

(4) These study findings note a risk factor for OA that has biologic plausibility. Animal model studies have previously demonstrated that acute joint injury causes OA[18]. Major trauma to the knee has the potential for damage to the articular hyaline cartilage and also for changes in the biomechanics.

As with any prospective study losses to follow-up can present a concern to a study's validity. At this time, the data pertaining to the reasons for losses to follow-up among the Clearwater Osteoarthritis Study participants are not available electronically. A surrogate marker was employed for categorizing those participants as either active or lost to follow-up. As stated previously, subjects are asked to present for biennial check-ups. A study subject was noted lost to follow-up if data records noted they were over 18 months past due for their last exam. Using this method of classification, 13% of the cohort were considered lost to follow-up. The difference in lost to follow-up by knee injury was 9.3% (Table IV). Although these two groups differed with respect to knee injury, the following should be noted. Those that were considered *lost* to follow up did not include any individuals who were diagnosed with knee OA during the study period, as once a participant had developed the outcome of interest, they were no longer 'at risk' for becoming lost to follow up. If a history of knee injury, in fact, shares a causal relationship with knee OA, one could speculate such a difference (9.3%) could in part support this strong association. Additionally, differences were minimal considering gender, age, BMI and occupational risk. A higher percentage of those subjects classified as having a history of smoking and those with a history of diabetes were lost to follow-up. It should be noted again that the group selected for the current investigation had completed four or more of their biennial exams at our institute. It is suggested that a sizable portion of the explanation for the moderate loss to follow-up is attributable to following a cohort of individuals that had already demonstrated a commitment to study participation.

The implications for these study findings are diverse. Primary prevention efforts could include measures to reduce the likelihood of trauma to the knee. Clearly, this can have broad applications, spanning from vehicular safety practices to safety measures implemented and/or reinforced in the work and home environments. As the etiology of OA continues to be elucidated, those with a history of knee injury perhaps benefit from avoiding a commonly implicated risk factor for knee OA, high BMI.

## Limitations

A possible selection bias may be influencing the results, as the participants are self-selected. If individuals, although initially free of disease, enroll because they think they are at risk of developing OA, then one would expect the prevalence of OA among study participants to exceed that of the general population. However, results from the 1989 population-based Framingham Knee Osteoarthritis Study showed a prevalence of 33% (non-incident cases). The Framingham study consisted of an older population suggestive of higher rates of OA. This figure compares higher than the current study figure of 26.9% (incident cases). Differential recall of exposure between cases and controls can inadvertently introduce bias into a study. If those individuals with knee OA searched their memories harder to recall a previous knee injury, this would have overestimated the association. However, self-exposure classification was established prior to the radiological examination for OA assessment.

Although the sample for this population-based study was not selected using a randomized design, the study participants are similar to the population from which the cases arose. Based on demographic characteristics, we characterized our sample arising from a white, middle to upper socioeconomic class subset of Pinellas County and the surrounding area population. Although recruitment efforts are intended to reach the entire Tampa Bay area community, participation in the COS is associated with membership in specific groups: (1) subjects living in the city of Clearwater (urban dwellers) have a greater chance to be apprised of the study; (2) subjects affiliated with local clubs and organizations have the opportunity to participate in seminars given by the recruitment personnel, or read about the study in the organization's bulletin; (3) among the work force, employees of the city of Clearwater and Pinellas County have been sent personal invitational letters; (4) OA patients attending certain private practice offices of physicians sympathetic to the study would be especially encouraged to participate; (5) relatives or friends of study participants have a greater chance of being involved in the study; and (6) subjects with seasonal residence in the Tampa Bay Region are allowed to participate. Given these factors, the composition of our sample may differ from that

of the source population. An overrepresentation of subjects aged 45 to 54 years was noted, possibly reflecting the fact that many participants are recruited among the Pinellas County and City of Clearwater employees. Analyses also detected a relative under sampling of those 75 years and older. This may be attributable to this segment of the population being perhaps less mobile and having a lower rate of participation in community organizations, where they could be appraised of the study. Educational level is higher among study participants than the average for Tampa Bay. In 2000 it was estimated that 54% of those 25 years or older in the Tampa Bay area were high school graduates Arthritis Foundation, Centers for Disease Control and Prevention, and the Association of State and Territorial Health Offices. National Arthritis Action Plan: A Public Health Strategy 1999: 6., while the proportion of subjects with high school diplomas in our sample is much higher at 96.6%. Based on reported race and educational level, the sample is representative of the white, middle to upper socioeconomic class in the Tampa Bay area.

A limitation of the current study was its inability to quantify the length of time between knee injury and knee OA or censoring. While some subjects may have experienced their injury just prior to study enrollment, others may have sustained the injury many years previously. An induction period between knee injury and subsequent knee OA has not been widely studied. Among those reporting previous knee injuries, it is of interest to know if there is a significant difference in the mean length of time since injury between those who later developed knee OA and those who did not. Because age at knee injury was not collected in the modified *COS History Questionnaire*, this study was unable to quantify such. However, on a limited number of participants with a history of knee injury we had data about the corresponding age at injury ($N$=31). Among those individuals with knee injuries, we compared those who subsequently developed knee OA with those who did not develop knee OA. Among those reporting a knee injury, the mean length of time between injury and those who later developed OA and those who remained disease-free was 26.8 and 28.5 years. Since the time at injury, we had expected to see a longer period of time among those who subsequently developed knee OA compared with those who were censored. Future expansion of these data may afford a better assessment of this potentially contributing factor.

## Future research

Future studies examining this association should investigate the possible role an induction period plays in the causal pathway of knee OA. Greater specificity with regards to the length of time between injury sustained and the subsequent development of OA will add to the existing body of knowledge. Additionally, efforts to standardize of the definition of knee injury will afford future analyses the ability to access the same exposure. Lastly, the role of physical exercise as a possible confounder when evaluating this relationship warrants further research[20]. Surveillance, epidemiology, and prevention research are one of the three major areas of strategy outlined in the 1998 comprehensive public health plan to reducing the burden of arthritis in the United States, entitled, '*The National Arthritis Action Plan: A Public Health Strategy*'. Attention to the aforementioned areas of research will contribute towards meeting this national goal.

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