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ORIGINAL ARTICLE

Is There an Association Between a History of Running and Symptomatic Knee Osteoarthritis? A Cross-Sectional Study From the Osteoarthritis Initiative

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Objective. **Regular physical activity, including running, is recommended based on known cardiovascular and mortality benefits. However, controversy exists regarding whether running can be harmful to knees. The purpose of this study is to evaluate the relationship of running with knee pain, radiographic osteoarthritis (OA), and symptomatic OA.**

Methods. **This was a retrospective cross-sectional study of Osteoarthritis Initiative participants (2004–2014) with knee radiograph readings, symptom assessments, and completed lifetime physical activity surveys. Using logistic regression, we evaluated the association of history of leisure running with the outcomes of frequent knee pain, radiographic OA, and symptomatic OA. Symptomatic OA required at least 1 knee with both radiographic OA and pain.**

Results. **Of 2,637 participants, 55.8% were female, the mean ± SD age was 64.3 ± 8.9 years, and the mean ± SD body mass index was 28.5 ± 4.9 kg/m^2; 29.5% of these participants ran at some time in their lives. Unadjusted odds ratios of pain, radiographic OA, and symptomatic OA for those prior runners and current runners compared to those who never ran were 0.83 and 0.71 (P for trend = 0.002), 0.83 and 0.78 (P for trend = 0.01), and 0.81 and 0.64 (P for trend = 0.0006), respectively. Adjusted models were similar, except radiographic OA results were attenuated.**

Conclusion. **There is no increased risk of symptomatic knee OA among self-selected runners compared with nonrunners in a cohort recruited from the community. In those without OA, running does not appear to be detrimental to the knees.**

INTRODUCTION

Controversy exists regarding the question of whether running is harmful to the knee (1). Chronic mechanical overloading could physically damage structures within the knee. Alternatively, runners generally have a lower body mass index compared to nonrunners (2), which could be protective against knee osteoarthritis (OA). Addressing the question of whether running increases the risk for knee OA is relevant, as US Department of Health and Human Services 2008 physical activity guidelines include an option to participate in vigorous-intensity aerobic activity for 75 minutes per week, with running as an example of this type of activity (1). This

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Significance & Innovations

- Increased physical activity reduces the risk for cardiovascular disease and all-cause mortality. Based on a review of existing studies, running, a common form of leisure-time physical activity, may be associated with knee osteoarthritis (OA).
- In the Osteoarthritis Initiative, a cohort with standardized questionnaires and radiographs, we addressed the question of whether running increases the risk of knee OA.
- In those without OA, running does not appear to be detrimental to the knees.

recommendation is based on overwhelming evidence that increased physical activity reduces the risk of cardiovascular disease and all-cause mortality (3–6).

In the Osteoarthritis Initiative (OAI; a cohort of people recruited from the community irrespective of their running status), more than 2,000 participants completed a survey of exposure to leisure-time physical activities. Standardized radiographs and questionnaires were administered to these participants, allowing for the assessment of radiographic knee OA and symptomatic knee OA in accordance with uniform definitions in these participants. This cross-sectional study provided a unique opportunity to evaluate, in a setting in which the highest-quality clinical and radiographic assessments of knee OA were obtained, the relationship of the history of leisure running with knee pain, radiographic OA, and symptomatic OA in a broad range of people who ran at some point in their lives and compare them to those who never ran. Based on the existing literature, we hypothesized that a history of leisure running may increase the risk of knee symptoms and radiographic knee OA, even at lower levels (for a breakdown of the existing literature, see Supplementary Table 1, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.22939/abstract).

MATERIALS AND METHODS

Study design. This is a cross-sectional study nested within the OAI, a prospective multicenter observational study of knee OA including men and women ages 45 to 79 years old at the time of enrollment (2004–2006) who had no evidence of knee OA and were not deemed to be at high risk; or were at high risk of developing symptomatic knee OA; or had prevalent symptomatic knee OA. The 4 clinical sites were Memorial Hospital of Rhode Island (Pawtucket, Rhode Island), Ohio State University (Columbus, Ohio), the University of Pittsburgh (Pittsburgh, Pennsylvania), and the University of Maryland/Johns Hopkins University (Baltimore, Maryland).

We studied OAI participants who completed a modified version of the Historical Physical Activity Survey instrument at the 96-month visit (the only time point at which this instrument was used in this cohort) and who had knee-specific pain data and/or knee radiographic readings at the 48-month visit (the latest time point with the greatest number of readings and data points available) or at a visit proximate to that visit. Approval was obtained from the institutional review board at each participating OAI site and at Baylor College of Medicine. Each participant provided written informed consent.

Historical Physical Activity Survey instrument. Between September 12, 2012, and October 31, 2014, participants were asked to complete a self-administered modified version of the Historical Physical Activity Survey instrument (7), prior to their OAI 96-month visit. At the time of the clinic visit, if the survey was incomplete, participants were invited to complete the survey with assistance from the clinic staff.

In the questionnaire, participants were asked to review 37 leisure-time physical activities, including "jogging or running (outdoor or indoor treadmill or track)." Then participants were asked to identify all activities they performed for at least 20 minutes within a given day at least 10 times in their lives during 4 age periods: 12–18, 19–34, 35–49, and ≥50 years old. Then they identified the 3 most frequently performed activities during those age periods. Additional questions ascertained the number of years, months per year, and bouts per month the participants engaged in those activities, in order to provide an estimate of bouts of an activity per age period. Similar questions regarding walking as a leisure-time activity were administered.

Individuals indicating running or jogging as a top-3 activity were defined as runners in those age periods. "Any history of running" included people who were runners in at least one age period. We also asked people whether they participated in the activity at a competitive level. To accommodate incorporation of this instrument within the OAI, the instrument was given as a self-administered questionnaire, a deviation from the original instrument, similar to what was done by Chasan-Taber previously (8). Other modifications were implemented to limit response burden, including the use of ordinal categories for each of the frequency/duration selections and limiting comments to the 3 activities most frequently undertaken in each age period. Not included in the original version was the question of whether they had participated at a competitive level or not (dichotomous question), and we included walking as an activity of interest for all age ranges, which was also new.

Knee radiographs. Weight-bearing, bilateral, fixed-flexion, posteroanterior radiographs of knees were obtained at the 48-

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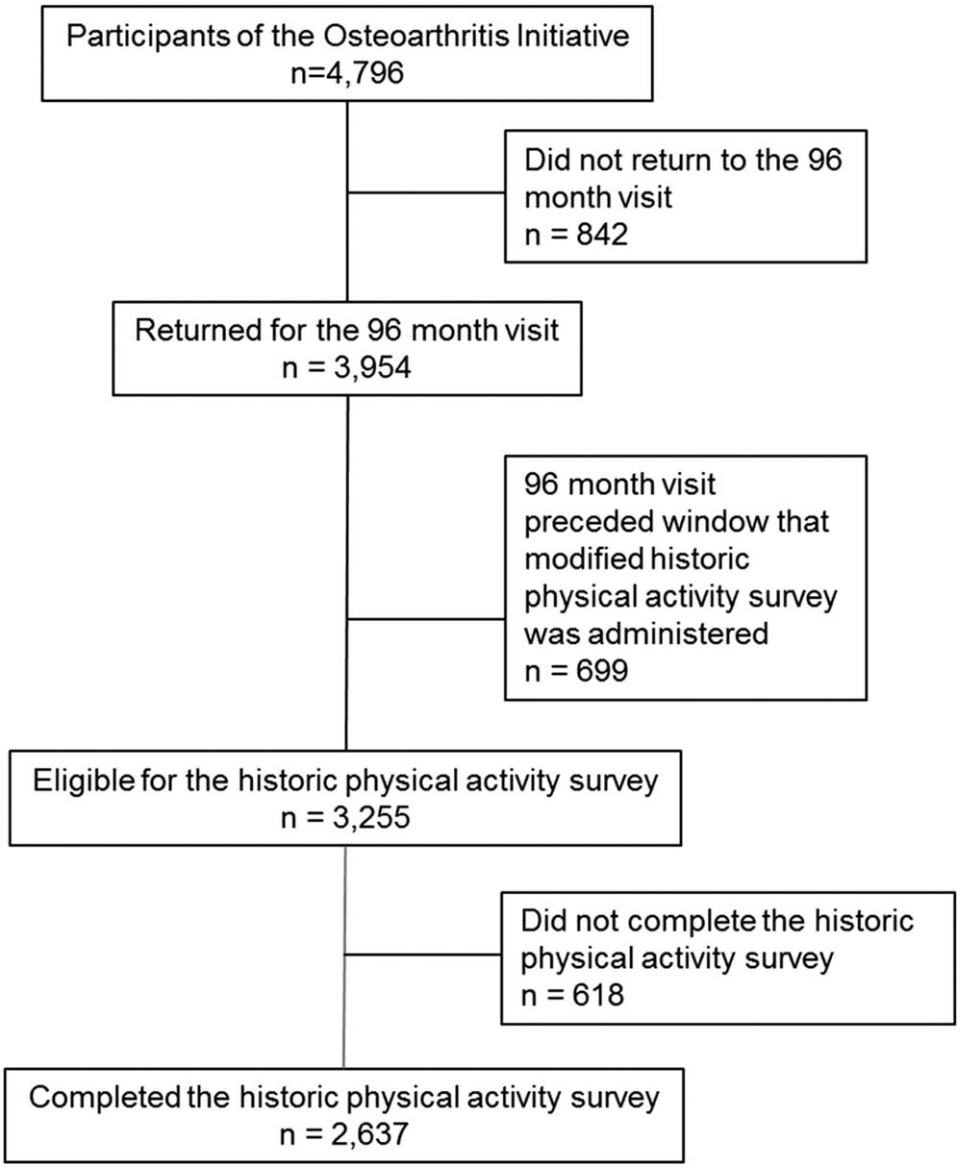

Figure 1. Flow diagram of participants who completed the modified Historical Physical Activity Survey.

month visit, the most current OAI visit with the largest number of radiographic readings at the time of this analysis. Central readers (9) scored for overall radiographic severity using Kellgren/Lawrence (K/L) grades (0–4) based on the Osteoarthritis Research Society International Atlas (10). If the 48-month visit readings were not available, readings from the most proximate radiographs available (at the baseline, 12-, 24-, or 36-month visit) were used instead. The reliability for these readings (read-reread) was substantial (11) (weighted kappa for intrarater reliability 0.71 [95% confidence interval 0.55–0.87]) (12).

Pain assessment. At the 48-month visit (contemporaneous with the radiographs described above), participants were asked to self-report knee-specific pain: "During the last 12 months, have you had pain, aching, or stiffness in or around your right/left knee on most days for at least one month? By most days, we mean more than half the days of a month." If the 48-month visit responses were not available, the responses from most proximate prior in-person visit (baseline, 12-, 24-, or 36-month visit) were used instead.

Covariates. Date of birth and date of the 48-month visit were used to calculate participant ages. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2), measured at the 36-month OAI visit, the closest visit to the 48-month visit where both height and weight were measured. If the BMI was missing at the 36-month visit, the BMI from the most proximate annual visit was used instead. History of knee injuries and total knee replacements (TKRs)

Table 1. Characteristics of those with no history of running, any history of running, all participants, and those excluded from these analyses*

Participant characteristics	Nonrunners (n = 1,859)	Runners (n = 778)	All (n = 2,637)	OAI group 1 (n = 699)†	OAI group 2 (n = 618)‡
Age, years	65.3 ± 9.0	62.0 ± 8.4	64.3 ± 8.9	65.4 ± 8.5	67.0 ± 9.4
Male sex, %	36.7	62.2	44.2	32.5	38.8
BMI, kg/m^2	28.8 ± 5.0	27.9 ± 4.7	28.5 ± 4.9	28.7 ± 5.1	29.1 ± 5.2
Frequent knee symptoms, %§	41.1	35.1	39.3	50.4	48.5
Radiographic OA, %§	58.8	53.5	57.3	65.7	62.9
Symptomatic OA, %§	29.4	22.8	27.4	37.0	38.7
TKR, %§	4.6	2.6	4.0	7.0	6.2
Prior injury, %§	47.2	53.0	48.9	55.5	47.6

* Values are the mean ± SD unless otherwise indicated. OAI = Osteoarthritis Initiative; BMI = body mass index; OA = osteoarthritis; TKR = total knee replacement.
† OAI participants seen at the 96-month visit before September 12, 2012, who did not complete the Historic Physical Activity Survey.
‡ OAI participants eligible for the Historic Physical Activity Survey but who did not complete the questionnaire.
§ In at least 1 knee.

were self-reported at baseline and at all annual visits up to the 48-month visit. All publicly available data were accessed from the OAI website (http://oai.epi-ucsf.org/datarelease/).

Statistical analysis. Using logistic regression, we evaluated the association of any history of running as well as during 4 age periods: ages 12–18, 19–34, 35–49, and ≥50 years with the prevalence of radiographic OA, frequent knee pain, and symptomatic OA. All outcome definitions were person-based definitions. Radiographic OA was defined as a K/L grade >2 in at least 1 knee. Frequent knee pain was defined by answering affirmative to the knee pain question regarding at least 1 knee. Symptomatic radiographic OA was defined as having at least 1 knee with both radiographic OA and frequent knee pain. Because we were interested in an assessment of ever having had knee OA symptoms or radiographic evidence of knee OA related to running exposure, those with a history of TKR were classified as having all 3 outcomes.

If participants had 1 knee with the outcome of interest, they were classified as having the outcome, even if data from the contralateral knee were missing. If participants had 1 knee without the outcome of interest and the data for the contralateral knee were missing, those participants were excluded from the analyses. For each of the 4 age ranges and any history of running, we looked at the exposure to running in 2 ways: first, by dichotomizing those who were runners versus nonrunners and, second, by examining 4 groups (nonrunners and low, medium, and high levels of runners based on tertiles of running bouts).

We performed the analyses unadjusted and then adjusted for age, sex, BMI, prior knee injury, and leisure-time physical activities that were statistically significantly associated with running (to account for activities correlated with running). The leisure-time physical activity variables were binary variables if they occurred less frequently than in 33% of the cohort; if they were more common than 33%, they were included as tertiles of participation for the particular activity. We tested whether there was an interaction between running with injury and running with BMI. Participants missing the Historical Physical Activity Survey were excluded from the analyses.

To evaluate the differential effect of prior running and current running on the outcomes of radiographic OA, knee pain, and symptomatic OA, we categorized participants as never runners, prior runners, and current runners and tested this exposure with the 3 outcomes. Never runners were those who did not identify running as a top-3 activity in any age period. Prior runners were those who identified running as a top-3 activity in at least 1 of the 3 younger periods but not during the age >50 period. Current runners were those who identified running as a top-3 activity during the age ≥50 period. A significant value for the Cochran-Armitage trend test indicated a dose response. All analyses were performed using SAS, version 9.4. *P* values less than 0.05 were considered statistically significant.

RESULTS

Of 4,796 OAI participants enrolled in the OAI database, 842 did not return for the 96-month visit (Figure 1). There were 699 participants whose visits preceded the window during which the modified Historical Physical Activity Survey instrument was administered and therefore did not complete the survey. In total, of the 3,255 eligible to participate, 2,637 (80%) completed the modified Historic Physical Activity Survey (Figure 1). Those who did not complete the lifetime historical physical activity question tended to be older, female, more likely to have radiographic OA and knee pain, and more likely to have a history of TKR and injury. All but one participant who completed the physical activity survey had 48-month visit radiographs (99.9%; 2,636 of 2,637). The remaining participant did not have radiographic readings available from any visits. Frequent knee pain assessments were available for 2,617 participants at the 48-month visit (99.2%; 2,617 of 2,637). From the 36-month, 24-month, 12-month, and baseline visits, 9, 1, 7, and 3 knee pain assessments, respectively, were carried forward.

Table 2. Odds ratios of prevalent frequent knee pain for runners compared to nonrunners, with low, medium, and high running activity levels*

Running time period	Prevalence of frequent knee pain, %	Unadjusted OR (95% CI)	Adjusted OR (95% CI)†
Any history of running			
Nonrunners (n = 1,859)	41.1	Ref.	Ref.
Runners (n = 778)	35.1	0.78 (0.65–0.92)	0.80 (0.66–0.97)
Low (n = 261)	34.9	0.77 (0.59–1.01)	0.75 (0.57–1.00)
Medium (n = 258)	39.2	0.92 (0.71–1.20)	0.93 (0.70–1.24)
High (n = 259)	31.3	0.65 (0.49–0.86)	0.71 (0.53–0.97)
P for trend		0.003	0.03
Ages 12–18 years			
Nonrunners (n = 2,379)	39.7	Ref.	Ref.
Runners (n = 258)	35.7	0.84 (0.64–1.10)	0.88 (0.66–1.18)
Low (n = 100)	34.0	0.78 (0.51–1.19)	0.88 (0.57–1.38)
Medium (n = 78)	34.6	0.80 (0.50–1.29)	0.83 (0.50–1.37)
High (n = 80)	38.8	0.96 (0.61–1.52)	0.93 (0.57–1.50)
P for trend		0.4	0.5
Ages 19–34 years			
Nonrunners (n = 2,242)	40.0	Ref.	Ref.
Runners (n = 395)	35.4	0.82 (0.66–1.03)	0.79 (0.62–1.01)
Low (n = 129)	35.7	0.83 (0.57–1.20)	0.85 (0.58–1.25)
Medium (n = 149)	40.3	1.01 (0.72–1.42)	0.97 (0.68–1.39)
High (n = 117)	29.1	0.61 (0.41–0.92)	0.55 (0.36–0.84)
P for trend		0.05	0.02
Ages 35–49 years			
Nonrunners (n = 2,212)	40.3	Ref.	Ref.
Runners (n = 425)	34.1	0.77 (0.62–0.95)	0.83 (0.66–1.05)
Low (n = 122)	33.6	0.75 (0.51–1.10)	0.73 (0.49–1.09)
Medium (n = 132)	42.4	1.10 (0.76–1.56)	1.21 (0.83–1.76)
High (n = 171)	28.1	0.58 (0.41–0.82)	0.66 (0.46–0.96)
P for trend		0.008	0.1
Ages >50 years			
Nonrunners (n = 2,304)	40.2	Ref.	Ref.
Runners (n = 333)	33.0	0.73 (0.58–0.93)	0.81 (0.63–1.05)
Low (n = 105)	37.1	0.88 (0.59–1.32)	0.86 (0.57–1.31)
Medium (n = 121)	33.9	0.76 (0.52–1.12)	0.90 (0.60–1.35)
High (n = 107)	28.0	0.58 (0.38–0.89)	0.66 (0.42–1.01)
P for trend		0.05	0.07

* OR = odds ratio; 95% CI = 95% confidence interval.
† Adjusted for age, sex, body mass index, all leisure-time physical activities that significantly correlate with running during the relevant time frame, and prior knee injury.

In total, 2,637 participants were included. Of these, 55.8% were female, the mean ± SD age was 64.3 ± 8.9 years, and the mean ± SD BMI was 28.5 ± 4.9 kg/m^2 (Table 1). Of the 2,637 participants, 634 were from the progression cohort (had symptomatic OA at the baseline visit), 1,899 were from the incidence cohort (did not have symptomatic OA at baseline but were at high risk of developing symptomatic OA during followup), and 104 were from the nonexposed control group (did not have symptomatic OA at baseline and were not considered to be at high risk of developing symptomatic OA during followup). There were 778 participants (29.5%) who ran at some point in their lives; of those, 48.6%, 28.8%, 15.3%, and 7.3% identified running in 1, 2, 3, and 4 of the age ranges, respectively. Seventy-five percent reported at least 250 bouts of running in their lives, 50% ran at least 800 bouts, and 25% ran at least 2,000 bouts. Only a very small percentage of overall participants in each time frame indicated that they ran competitively (2–5%). From the lowest to highest BMI tertile, 35.1%, 28.3%, and 25.0% had any history of running.

Any history of running was associated with less frequent knee pain (Table 2) in the unadjusted and adjusted models compared to those who never ran. Those who had any history of running had lower odds of both radiographic OA and symptomatic OA compared to those who did not run (Table 3 and Table 4) in the unadjusted models, but these were no longer significant in models adjusted for age, sex, BMI, all leisure-time physical activities that significantly correlated with running during the relevant time frame, and prior knee injury. All 3 outcomes were least common in current runners and most common in never runners, except in the fully adjusted model evaluating radiographic OA (Table 5). There was no interaction between running and either injury or BMI for any of the 3 outcomes (data not shown).

Table 3. Odds ratios of prevalent radiographic knee OA in runners compared to nonrunners, with low, medium, and high running activity levels*

Running time period	Prevalence of radiographic OA, %	Unadjusted OR (95% CI)	Adjusted OR (95% CI)†
Any history of running			
Nonrunners (n = 1,859)	58.8	Ref.	Ref.
Runners (n = 777)	53.5	0.81 (0.68–0.96)	0.95 (0.78–1.16)
Low (n = 261)	54.4	0.84 (0.65–1.09)	0.95 (0.72–1.26)
Medium (n = 258)	55.4	0.87 (0.67–1.13)	0.98 (0.73–1.32)
High (n = 258)	50.8	0.72 (0.56–0.94)	0.92 (0.69–1.24)
P for trend		0.009	0.6
Ages 12–18 years			
Nonrunners (n = 2,379)	57.9	Ref.	Ref.
Runners (n = 257)	51.4	0.77 (0.59–0.99)	1.05 (0.78–1.40)
Low (n = 99)	48.5	0.69 (0.46–1.02)	0.98 (0.63–1.51)
Medium (n = 78)	48.7	0.69 (0.44–1.09)	1.01 (0.61–1.65)
High (n = 80)	57.5	0.98 (0.63–1.55)	1.18 (0.73–1.93)
P for trend		0.2	0.6
Ages 19–34 years			
Nonrunners (n = 2,242)	58.3	Ref.	Ref.
Runners (n = 394)	51.5	0.76 (0.62–0.94)	0.95 (0.75–1.21)
Low (n = 129)	52.7	0.80 (0.56–1.14)	0.98 (0.67–1.44)
Medium (n = 149)	51.7	0.77 (0.55–1.07)	1.00 (0.69–1.44)
High (n = 116)	50.0	0.72 (0.49–1.04)	0.86 (0.57–1.30)
P for trend		0.01	0.6
Ages 35–49 years			
Nonrunners (n = 2,212)	58.3	Ref.	Ref.
Runners (n = 424)	51.9	0.77 (0.63–0.95)	0.91 (0.73–1.16)
Low (n = 122)	56.6	0.93 (0.65–1.35)	1.06 (0.71–1.57)
Medium (n = 132)	55.3	0.89 (0.62–1.26)	1.03 (0.70–1.50)
High (n = 170)	45.9	0.61 (0.44–0.83)	0.75 (0.53–1.06)
P for trend		0.003	0.2
Ages >50 years			
Nonrunners (n = 2,303)	57.9	Ref.	Ref.
Runners (n = 333)	52.6	0.81 (0.64–1.01)	0.96 (0.74–1.23)
Low (n = 105)	56.2	0.93 (0.63–1.38)	1.09 (0.71–1.67)
Medium (n = 121)	54.5	0.87 (0.60–1.26)	1.11 (0.75–1.66)
High (n = 107)	46.7	0.64 (0.43–0.94)	0.71 (0.47–1.08)
P for trend		0.02	0.4

* OA = osteoarthritis; OR = odds ratio; 95% CI = 95% confidence interval.
† Adjusted for age, sex, body mass index, all leisure-time physical activities that significantly correlate with running during the relevant time frame, and prior knee injury.

DISCUSSION

Our findings show that a history of leisure-time running is not associated with increased odds of prevalent knee pain, radiographic OA, or symptomatic OA. In fact, for knee pain, there was a dose-dependent inverse association with running, with runners having less knee pain. With no interaction between running and history of injury or BMI, those with and without knee injury or with higher or lower BMIs did not have a differential association between running and OA. This was an observational study where people chose whether or not they wanted to run; therefore there is always the possibility that people stopped running because they had knee pain. Thus we cannot comment on the influence of compulsory running on overall knee health. This cohort was not recruited based on elite running status, making these findings potentially more applicable to a broader population than many prior studies (Supplementary Table 1). Frequent knee pain and symptomatic OA were observed least commonly in current runners and most commonly in never runners in all models, which suggests that running cessation is not more harmful than never running at all. Running does not appear to be detrimental from a knee health perspective.

The historical lifetime physical activity questionnaire used in our study was substantially modified compared to the original instrument designed by Kriska et al (7) that has been validated and used to establish links between lifetime physical activity and bone mineral density (7), decreased risk of diabetes (13), and decreased risk of ovarian cancer (14). Importantly, it was a self-administered questionnaire, using a similar strategy as Chasan-Taber et al, which was reproducible and showed that metabolic equivalent hours per week were lowest in the earliest and oldest age periods

Table 4. Odds ratios of prevalent symptomatic knee OA in runners compared to nonrunners, with low, medium, and high running activity levels*

Running time period	Prevalence of radiographic OA, %	Unadjusted OR (95% CI)	Adjusted OR (95% CI)†
Any history of running			
Nonrunners (n = 1,831)	29.6	Ref.	Ref.
Runners (n = 775)	23.5	0.73 (0.61–0.89)	0.81 (0.65–1.00)
Low (n = 260)	22.7	0.70 (0.51–0.95)	0.74 (0.53–1.03)
Medium (n = 258)	27.9	0.92 (0.69–1.23)	0.97 (0.71–1.33)
High (n = 257)	19.8	0.59 (0.43–0.81)	0.71 (0.500–1.02)
P for trend		0.002	0.08
Ages 12–18 years			
Nonrunners (n = 2,350)	28.0	Ref.	Ref.
Runners (n = 256)	25.8	0.89 (0.67–1.20)	1.13 (0.81–1.54)
Low (n = 99)	23.5	0.79 (0.49–1.27)	1.07 (0.65–1.76)
Medium (n = 78)	25.7	0.89 (0.53–1.49)	1.14 (0.66–1.99)
High (n = 80)	28.8	1.04 (0.63–1.70)	1.14 (0.67–1.93)
P for trend		0.7	0.05
Ages 19–34 years			
Nonrunners (n = 2,213)	28.9	Ref.	Ref.
Runners (n = 393)	21.4	0.67 (0.52–0.87)	0.70 (0.53–0.93)
Low (n = 128)	21.9	0.69 (0.45–1.06)	0.75 (0.48–1.17)
Medium (n = 149)	22.8	0.73 (0.49–1.08)	0.77 (0.51–1.17)
High (n = 116)	19.0	0.58 (0.36–0.92)	0.56 (0.34–0.93)
P for trend		0.003	0.01
Ages 35–49 years			
Nonrunners (n = 2,184)	28.9	Ref.	Ref.
Runners (n = 422)	22.3	0.71 (0.55–0.91)	0.82 (0.63–1.07)
Low (n = 121)	23.1	0.74 (0.48–1.15)	0.77 (0.49–1.21)
Medium (n = 132)	28.0	0.96 (0.65–1.42)	1.13 (0.75–1.72)
High (n = 169)	17.2	0.51 (0.34–0.77)	0.63 (0.41–0.98)
P for trend		0.003	0.1
Ages >50 years			
Nonrunners (n = 2,274)	28.8	Ref.	Ref.
Runners (n = 332)	21.1	0.66 (0.50–0.88)	0.81 (0.60–1.09)
Low (n = 105)	24.8	0.82 (0.52–1.28)	0.90 (0.56–1.45)
Medium (n = 121)	20.7	0.65 (0.41–1.01)	0.85 (0.53–1.36)
High (n = 106)	17.9	0.54 (0.33–0.90)	0.66 (0.39–1.12)
P for trend		0.002	0.1

* OA = osteoarthritis; OR = odds ratio; 95% CI = 95% confidence interval.
† Adjusted for age, sex, body mass index, all leisure-time physical activities that significantly correlate with running during the relevant time frame, and prior knee injury.

(8), similar to the observed prevalence of running in our study. The inverse association between BMI and running in our study also lends it construct validity. Using this instrument, we captured activities performed at least 10 times in their lives that were listed as a top-3 activity in at least 1 of 4 age periods to be considered a runner. Arguably, running only 10 times may not be sufficient to classify participants as runners. However, in our study, among those who were identified as runners, 75% reported running at least 250 bouts in their lives, 50% ran at least 800 bouts, and 25% ran at least 2,000 bouts, supporting the idea that most runners ran far more than 10 bouts and were classified correctly. There may have also been some misclassification of runners as nonrunners if people participated in many different leisure-time physical activities and running just did not make the top 3 activities. We addressed this possibility by adjusting for all activities that were correlated with running; notably, this adjustment did not alter any results.

A limitation to our study is that the exposure of interest, running, has been retrospectively ascertained. Since we were interested in the exposure to running over a long duration of time, prospective assessment of this exposure would have been much more expensive and cumbersome than the retrospective ascertainment deployed in this study. Although the assessment of running status may have been influenced by recall bias, since it has not been clear whether running is harmful or protective against knee OA, it is unlikely that the recall bias would be differential in either direction. Notably, our response rate was high, at 81%, but without knowing the distribution of runners among those who did not provide us with data on physical activity, it is difficult to know how inclusion of all nonparticipants would

Table 5. Odds ratios of prevalent frequent knee pain, radiographic OA, and symptomatic OA for prior runners and current runners compared to never runners*

Runner status	Prevalence of outcome, %	Unadjusted OR (95% CI)	Adjusted OR (95% CI)†
Frequent knee pain			
Never runners (n = 1,859)	41.1	Ref.	Ref.
Prior runners (n = 445)	36.6	0.83 (0.67–1.03)	0.82 (0.65–1.04)
Current runners (n = 333)	33.0	0.71 (0.55–0.90)	0.76 (0.58–0.99)
P for trend		0.002	0.02
Radiographic OA			
Never runners (n = 1,859)	58.8	Ref.	Ref.
Prior runners (n = 444)	54.3	0.83 (0.68–1.03)	0.98 (0.78–1.25)
Current runners (n = 333)	52.6	0.78 (0.61–0.98)	0.91 (0.70–1.19)
P for trend		0.01	0.5
Symptomatic OA			
Never runners (n = 1,859)	29.6	Ref.	Ref.
Prior runners (n = 443)	25.3	0.81 (0.64–1.02)	0.88 (0.67–1.14)
Current runners (n = 332)	21.1	0.64 (0.48–0.84)	0.71 (0.53–0.97)
P for trend		0.0006	0.03

* OA = osteoarthritis; OR = odds ratio; 95% CI = 95% confidence interval.
† Adjusted for age, sex, body mass index, all leisure-time physical activities that significantly correlate with running during the relevant time frame, and prior knee injury.

have impacted the results of our study. Also, although the questionnaire was not administered to all of the participants, approximately half of each of the progression and incidence cohorts responded, and nearly all of the nonexposed controls responded. This is a sample enriched with people who had radiographic OA and symptoms at the time of enrollment. For this reason, it is likely that the prevalence of OA could be overestimated compared to the general population. Also, it may be that the prevalence of running in the general population may be different than what is seen in this group.

In our study we defined our outcomes using 48-month visit measures because this is the time point at which the OAI funded the greatest number of radiographs to be read to date. Consequently, the modified Historical Physical Activity Survey instrument, used to define runner status and administered at the 96-month visit, was administered at a time point after which all outcomes were assessed. However, since the survey required recall over a long period of time and the results were similar during most age groups of running, this limitation did not likely impact the validity of our results.

The directionality of associations in regard to causation observed in cross-sectional studies generally should not be commented upon; however, in the instance of our study, it is unlikely that a diagnosis of OA or symptoms of it caused people to start running. The hypothesized direction of influence was that running would have an effect on OA. It is important to note that because of the cross-sectional nature of this study, we cannot comment on the influence of running in those with preexisting knee OA, as in this study we are only evaluating one point in time. The assumption in our study is that prevalence reflects incident symptoms and disease. The findings from this study support the need for larger longitudinal studies that evaluate the exposure to running, even at lower levels, and its effects on incident and progressive knee OA.

Prior studies (Supplementary Table 1) evaluating the relationship between running and knee OA have mostly focused on those performing at elite or high levels of running (e.g., elite runners [15–18] or members of a running club [19–22]). These studies have been important from the perspective that they have evaluated a high level of the exposure as a risk factor for knee OA. By studying high levels of running, most of these athletes likely limited the type of exercise to running, allowing for a more homogenous group of people who run. A limitation to these studies, however, is that their results are not generalizable to most adults who run less. Those who run less may respond differently to running than the elite athlete. For instance, they may be less skilled at running since they run less and therefore they may incur different biomechanical stresses compared to those who run more. Alternatively, it could have been that elite runners expose their knees to excessive amounts of loading secondary to their high levels of running, which could potentially be harmful to the knee, whereas a lower amount of running conversely may not be harmful. Our study findings add to the existing literature by including a large sample in which we were able to assess the influence of running in people who participated in it for shorter amounts of time and perhaps stopped doing it and to evaluate them with high-quality assessments of symptoms and standardized radiographs. We found that runners in this group were not at a higher risk for symptomatic knee OA.

A high level of loading occurs within the knee during running (23), and runners are prone to knee injury, with injuries in 7–50% of runners, depending on the study (24), which is similar to the rate we observed in our study (Table 1). Intuitively, because of these attributes, it might be expected that runners would be at higher risk for knee OA. Instead, in our study, we did not find an increased risk for knee OA. Perhaps the lower BMI seen in runners compared to nonrunners (2), which was also seen in our study, balances the effects of

running on knee OA. The exact reasons why a higher BMI is a risk factor for knee OA are not entirely clear, but the association of higher BMI with incident knee OA is a consistent finding in epidemiologic studies (25). Running could lead to a healthier lifestyle, or since running is a strenuous exercise that requires repeated flexion and extension of the knee, it could improve proprioception and periarticular muscle strength that may also reduce the risk of knee OA. Irrespective of the biologic pathway, the overall influence of running on knee OA, when taking all the evidence into consideration, does not appear to be harmful. In conclusion, running does not appear detrimental for knee health. People with the lowest BMIs were most likely to identify running as an activity they participated in at some point in their lives. Although we cannot comment on the influence of running in those with preexisting knee OA, among those without OA, running should not be discouraged because of concern of an increased risk for developing knee OA or associated frequent knee pain.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Lo had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Lo.

Acquisition of data. Lo, Eaton, Hochberg, Jackson, Kwoh.

Analysis and interpretation of data. Lo, Driban, Kriska, McAlindon, Souza, Petersen, Storti, Eaton, Hochberg, Jackson, Kwoh, Nevitt, Suarez-Almazor.

REFERENCES

1. Physical Activity Guidelines Writing Group. 2008 physical activity guidelines for Americans. Washington DC: US Department of Health and Human Services. URL: http://www.health.gov/PAGuidelines/pdf/paguide.pdf.
2. Williams PT. Effects of running and walking on osteoarthritis and hip replacement risk. Med Sci Sports Exerc 2013;45:1292–7.
3. Physical Activity Guidelines Advisory Committee. Physical Activity Guidelines Advisory Committee report, 2008. Washington DC: US Department of Health and Human Services. URL: http://www.health.gov/paguidelines/Report/pdf/CommitteeReport.pdf.
4. Paffenbarger RS Jr., Hyde RT, Wing AL, Lee IM, Jung DL, Kampert JB. The association of changes in physical-activity level and other lifestyle characteristics with mortality among men. N Engl J Med 1993;328:538–45.
5. Blair SN, Kohl HW III, Paffenbarger RS Jr., Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality: a prospective study of healthy men and women. JAMA 1989;262:2395–401.
6. Paffenbarger RS Jr., Hyde RT, Wing AL, Hsieh CC. Physical activity, all-cause mortality, and longevity of college alumni. N Engl J Med 1986;314:605–13.
7. Kriska AM, Sandler RB, Cauley JA, LaPorte RE, Hom DL, Pambianco G. The assessment of historical physical activity and its relation to adult bone parameters. Am J Epidemiol 1988;127:1053–63.
8. Chasan-Taber L, Erickson JB, McBride JW, Nasca PC, Chasan-Taber S, Freedson PS. Reproducibility of a self-administered lifetime physical activity questionnaire among female college alumnae. Am J Epidemiol 2002;155:282–9.
9. Osteoarthritis Initiative. Central reading of knee x-rays for Kellgren and Lawrence grade and individual radiographic features of tibiofemoral knee OA. URL: http://oai.epi-ucsf.org/datarelease/SASDocs/kXR_SQ_BU_descrip.pdf.
10. Altman RD, Gold GE. Atlas of individual radiographic features in osteoarthritis, revised. Osteoarthritis Cartilage 2007;15 Suppl A:A1–56.
11. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159–74.
12. Osteoarthritis Initiative. Project 15 test–retest reliability of semi-quantitative readings from knee radiographs, 2012. URL: https://oai.epi-ucsf.org/datarelease/SASDocs/kXR_SQ_Rel_BU_Descrip.pdf.
13. Kriska AM, Knowler WC, LaPorte RE, Drash AL, Wing RR, Blair SN, et al. Development of questionnaire to examine relationship of physical activity and diabetes in Pima Indians. Diabetes Care 1990;13:401–11.
14. Cottreau CM, Ness RB, Kriska AM. Physical activity and reduced risk of ovarian cancer. Obstet Gynecol 2000;96:609–14.
15. Kujala UM, Kaprio J, Sarna S. Osteoarthritis of weight bearing joints of lower limbs in former elite male athletes. BMJ 1994;308:231–4.
16. Kujala UM, Kettunen J, Paananen H, Aalto T, Battie MC, Impivaara O, et al. Knee osteoarthritis in former runners, soccer players, weight lifters, and shooters. Arthritis Rheum 1995;38:539–46.
17. Kettunen JA, Kujala UM, Kaprio J, Koskenvuo M, Sarna S. Lower-limb function among former elite male athletes. Am J Sports Med 2001;29:2–8.
18. Konradsen L, Hansen EM, Sondergaard L. Long distance running and osteoarthrosis. Am J Sports Med 1990;18:379–81.
19. Lane NE, Bloch DA, Jones HH, Marshall WH Jr., Wood PD, Fries JF. Long-distance running, bone density, and osteoarthritis. JAMA 1986;255:1147–51.
20. Lane NE, Michel B, Bjorkengren A, Oehlert J, Shi H, Bloch DA, et al. The risk of osteoarthritis with running and aging: a 5-year longitudinal study. J Rheumatol 1993;20:461–8.
21. Lane NE, Oehlert JW, Bloch DA, Fries JF. The relationship of running to osteoarthritis of the knee and hip and bone mineral density of the lumbar spine: a 9-year longitudinal study. J Rheumatol 1998;25:334–41.
22. Chakravarty EF, Hubert HB, Lingala VB, Zatarain E, Fries JF. Long distance running and knee osteoarthritis: a prospective study. Am J Prev Med 2008;35:133–8.
23. Bus SA. Ground reaction forces and kinematics in distance running in older-aged men. Med Sci Sports Exerc 2003;35:1167–75.
24. Van Gent RN, Siem D, van Middelkoop M, van Os AG, Bierma-Zeinstra SM, Koes BW. Incidence and determinants of lower extremity running injuries in long distance runners: a systematic review. Br J Sports Med 2007;41:469–80.
25. Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. Osteoarthritis Cartilage 2010;18:24–33.