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# Occupational risk in knee osteoarthritis: a systematic review and meta-analysis of observational studies

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## Abstract

**Objectives—**To assess the association between occupational exposures and knee osteoarthritis (OA).

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Professor Hunter provides consulting advice for Pfizer, Lilly, TLC bio and Merck Serono. Professor Arden reports grants from Merck, personal fees from Merck, Flexion, Regeneron and Pfizer/Lilly outside the submitted work. Professor Cooper reports personal fees from Alliance for Better Bone Health, Amgen, Eli Lilly, GSK, Medtronic, Merck, Novartis, Pfizer, Roche, Servier, Takeda and UCB. All the other authors have no conflicts of interest to disclose.

**Author Contributions:**
Dr Wang and Dr Perry had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors take responsibility in concept and design; acquisition, analysis, or interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis; and administrative, technical, or material support.

**No Patient and Public Involvement (PPI)**
There were no funds or time allocated for PPI. We have invited patients to help us develop our dissemination strategy.


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**Methods—**We systematically searched for observational studies that examined the relationship between occupational exposures and, knee OA and total knee replacement (TKR). Four databases were searched until Oct 1st, 2019. Two reviewers independently assessed study quality using the Newcastle-Ottawa Scale and evidence quality using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. Subgroup meta-analyses were conducted for important study characteristics and each type of occupational exposure. Odds ratios (OR) and 95% confidence intervals (CI) were estimated for meta-analysis using random-effects models.

**Results—**Eighty eligible studies were identified including 25 case-control (total study participants: N=20,505), 36 cross-sectional (N=139,463) and 19 cohort studies (N=16,824,492). Synthesis of 71 studies suggested increased odds of knee OA (OR: 1.52; 95%CI: 1.37, 1.69), which combined different physically demanding jobs and occupational activities, compared to sedentary occupations and/or low exposure groups. Odds of knee OA were greater in males, industry-based studies and studies assessing lifetime occupational exposures. There were 9 specific job titles that were associated with knee OA, including farmers, builders, metal workers and floor layers. Occupational lifting, kneeling, climbing, squatting and standing were all associated with a higher odds of knee OA compared to sedentary workers, respectively.

**Conclusions—**Heavy physically demanding occupations and occupational activities were associated with increased odds of knee OA; as supported by moderate-quality evidence. Specifically, agricultural and construction sectors which typically involve heavy lifting, frequent climbing, prolonged kneeling, squatting and standing carried increased odds of knee OA.

### Keywords

Knee Osteoarthritis; Occupation; Epidemiology; Meta-analysis

## Introduction

Knee osteoarthritis (OA) is a highly prevalent, chronic condition and one of the leading contributors to loss of work and disability(1). The understanding of prevalent, modifiable risk factors is essential for OA prevention. In the general working population, an important domain for disease prevention and management is the workplace. Many studies have examined the relationship between physically demanding occupations such as farming(2), mining(3), and floor laying(4) and the onset of knee OA. The underlying mechanistic links between occupations and knee OA are believed to be biomechanical with excessive knee forces generated during strenuous work tasks(5, 6). Several papers have identified frequent workplace kneeling, squatting and heavy lifting as risk factors for development and progression of knee OA(7–9). However, few studies have quantitatively synthesised the evidence(8, 9) and no systematic review has compared the disease outcomes according to specific job titles.

With rising longevity and the aging population, longer work-life has become more common in industrialised countries. Exposure time to occupational activities is also prolonged which might increase the risk of OA development. Up-to-date evidence is essential to inform workplace regulators and insurers about specific activities that may be problematic and to

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identify targeted industrial sectors for developing tailored OA preventive strategies. The impetus for greater public attention to workplace health is important for the aging of workforces and facilitating policy changes in many countries that push for longer employment trajectories(10). To provide an updated synthesis of the available data and to identify specific populations at risk of knee OA, we conducted a systematic review and meta-analysis exploring the relationship between multiple occupational exposures (i.e. job titles, job categories, occupational activities) and knee OA (including TKR) using data from all available and relevant observational studies.

## Methods

This review was conducted in accordance with the meta-analysis of observational studies in epidemiology (MOOSE)(11) and Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines(12). *A priori* protocol following standard Cochrane and PRISMA protocol(13) guidelines is available at PROSPERO: CRD42018107747.

### Literature search

We conducted a systematic search of MEDLINE, EMBASE, CINAHL and Web of Science, to identify relevant studies without language or time restrictions until Oct 1st, 2019. Search strategies were developed in consultation with a librarian (Appendix 1). An additional hand search was performed in the references of included publications; to include articles potentially missed by the systematic search. Only published studies were included. When relevant information was unavailable, efforts were made (emails and calls) to contact corresponding authors.

### Study selection and inclusion/exclusion criteria

Observational studies (i.e. case-control, cross-sectional and cohort studies) of occupational exposures and, symptomatic and radiographic knee OA were selected by two independent authors (XW and TAP); a third author (DJH) was consulted in cases of disagreement. Occupational exposures included broad job categories according to the levels of physical workload (e.g. heavy physical, sedentary), specific job titles (e.g. farmer, secretary) and workplace activities (e.g. bending). Radiographic knee OA was defined when only radiographic criteria were used (e.g. Kellgren-Lawrence grade(14), Osteoarthritis Research Society International classification score(15)). Symptomatic knee OA included any diagnosis (with/without radiographic verification) that took knee pain into account, such as TKR due to OA, knee symptoms identified using validated questionnaires (e.g. Western Ontario and McMaster Universities Osteoarthritis Index(16), Nordic Musculoskeletal questionnaire(17)) and diagnosis by a doctor or after clinical examinations (e.g. American College of Rheumatology criteria(18)). When radiographic and symptomatic measures were both reported, we chose the symptomatic outcome to calculate the overall risk. Studies reporting males and females separately were treated as two studies (in subgroup analyses). Studies with adjusted and/or unadjusted risk estimates and an appropriate measure of prevalence were included. Studies were also included where there was enough data to calculate unadjusted OR and 95%CI(19).

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Studies focused on elite sports or injury-induced OA were excluded as they were more likely to be focused on post-traumatic OA phenotypes rather than primary OA. We also excluded studies reporting general arthritis/musculoskeletal pain or mixed OA combing the knee with other joints, unless knee data were reported separately. Studies of persons with a mean age <30 years or studies of persistent pain that were not clearly defined were also excluded. In cases of multiple publications from a single study/cohort sample, we used the most up-to-date information.

### Data extraction

English language data were extracted and coded by two reviewers (XW, TAP) using a standardised form including author name, year of publication, sample size, age, sex and body mass index (BMI), occupation status, duration of follow-up (cohort study only) and outcome measures. Data from one Chinese and one German article were translated by other team members.

### Quality of methodology

Two reviewers (XW, TAP) independently assessed the quality of the included studies using the Newcastle-Ottawa Scale (NOS), as recommended by the Cochrane Collaboration(20). The NOS consists of eight items grouped into three categories: selection, comparability of cohorts, outcome and follow-up. A star system, ranging from 0 (low) to 9 (high), was used to score the quality of the respective studies with a score ≥7 considered as ‘good quality’ (21). Disagreements were resolved through discussion or consultation with a third reviewer (DJH).

### Quality of evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) was used to summarize the quality of evidence for risk of bias, publication bias, imprecision, inconsistency, indirectness and magnitude of effect(22). The quality/certainty of evidence was graded as high, moderate, low, or very-low.

### Data analysis

We calculated the summary estimates using inverse variance weighted random-effects meta-analysis because of the presumed heterogeneity across studies. Individual and summary estimates were presented as ORs and 95%CI in forest plots. When a single study reported multiple levels of exposures (e.g. moderate and intensive levels), ORs derived from all levels of exposures were pooled to give one overall OR per study. Because there were fewer studies reporting occupational activities than job categories/titles, when data from multiple exposures were available, we chose results of job categories/titles to calculate the overall risk to align with the rest of the studies. Subgroup meta-analyses were conducted for important study characteristics as previously defined in the protocol (e.g. study design, setting, region, OA disease definition etc.) and for each type of occupational exposure (i.e. job titles, job categories and occupational activities) as previously described.

Heterogeneity was quantified using the $I^2$ statistic and Cochran Q test. An $I^2$ value <25%, 25%-75% and >75% were considered as low, moderate and high heterogeneity respectively(19). Publication bias was assessed visually by funnel plots and formally by Egger's test(19). Meta-regression analyses were performed using random-effects modelling to identify continuous study-level factors (e.g. age, BMI, female sex and study quality) that may have modified the associations and contributed to heterogeneity(19). Sensitivity analyses were performed using fixed-effects models and excluding small sample size studies (N<1000). A P-value<0.05 was considered to be statistically significant. Statistical analyses were performed using STATA V.14.

# Results

## Study characteristics

We identified a total of 80 eligible studies (Figure 1) including 25 case-control studies, 36 cross-sectional studies and 19 cohort studies. Characteristics of the included studies are summarised in Table 1. Mean age across the included studies was 56.6 years, ranging from 18 to 98 years. Sixteen studies exclusively examined males whilst six examined females, but the mean overall percentage of females was 44.5%. Detailed individual study information, including sample size, demographics, exposures, comparators, adjustments and full references are presented in Appendix 2.

The average methodological quality across the included studies was low (mean score=5 out of 9, see Appendix 3). There were 19 studies (24%) that scored ≥7 out of 9. However, 8 studies were graded two or three, suggesting a higher risk of bias. Significant publication biases were found in case-control (bias=1.82; P=0.001) and cross-sectional (bias=1.23; P<0.001) studies, as well as studies conducted in a hospital setting (bias=1.07, P<0.001). These findings were consistent with the funnel plots (Appendix 4).

The overall quality of evidence was rated as "moderate" across cohort studies due to evidence of considerable heterogeneity and, "very-low" in cross-sectional and case-control studies due to the existence of risk of bias, substantial heterogeneity and publication bias (Appendix 5).

## Meta analyses

Studies that reported knee OA prevalence (as percentages only)(23–26), incident ratios(27) or hazards ratios(28–31) were not included in the meta-analyses. Synthesis of the remaining 71 studies (total number of participants=951,345) yielded overall occupational odds of knee OA of 1.52 (95%CI: 1.37, 1.69); see the forest plot presented in Figure 2. This is a composite of different physically demanding jobs and work-related physical activities compared to people in sedentary, low physical workload jobs or not exposed to those activities. There was evidence of statistically significant heterogeneity across all studies ($I^2$=94.4%, P<0.0001). Meta-regression of the main results suggested that study quality may have contributed to the level of heterogeneity (P<0.05; Appendix 6). Similar results were found using fixed-effect models and in studies with small sample (Appendix 7).

Of the 71 studies, gender specific data were available in 29 studies for males and 18 studies for females (Figure 2). Increased odds of knee OA were found across both genders. Assessment of industry-based study samples yielded higher ORs than hospital and

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community-based studies (Table 2). The odds of knee OA were by up to 20% higher in studies assessing lifetime accumulated occupational exposures (OR: 1.65, 95% CI: 1.30, 2.09) compared to studies of longest-held or current jobs (OR: 1.45, 95% CI: 1.31, 1.60). However, these differences were not statistically significant. The associations between occupational exposures and knee OA were similar across study designs, OA definitions, methodological quality and geographic regions. Similar results were also observed across unadjusted and adjusted analyses (Table 2).

**i Job categories—**Seventeen studies reported broad job categories by levels of physically demand based on authors' own criteria; no details of included job titles were provided (Table 3). Compared to other categories (e.g. sedentary, low-physical activity), heavy physical occupations carried an increased, pooled odds for knee OA of 1.65 (95%CI: 1.43, 1.91). A pooled OR of 1.47 was found from five studies that investigated the association between knee OA and light and/or moderate occupational physical activity. There were also four studies that investigated risk of knee OA in sedentary occupations; no statistically significant relationship was reported.

**ii Detailed job titles—**Subgroup meta-analyses were conducted for 23 specific occupations; where there was sufficient data to allow pooling (Table 3). Eight studies assessed the relationship between agricultural, forestry and fishery industry work and risk of knee OA respectively which yielded incremental odds of 1.94 (95%CI: 1.56, 2.42) with no evidence of heterogeneity. In studies of agricultural workers (predominately farming), statistically significant higher odds (1.64; 95%CI: 1.33, 2.01) of knee OA was found. When stratifying by gender, odds of knee OA was higher in male farmers than female farmers (Figure 3). Heterogeneity did not reach levels of statistical significance in females ($I^2$=0%) but was significant in males ($I^2$=81.3%). Table 3 also shows statistically significant higher odds of knee OA in 76,648 male construction workers and/or builders with no evidence of heterogeneity. Five studies reported statistically significant higher odds of knee OA in 13,567 male metal workers (e.g. metal sheet processers, furnacemen and blacksmiths). Floor-layers, bricklayers and carpenters had ~2.5 times increased odds of knee OA compared to sedentary workers.

Statistically significantly higher odds of knee OA were found in miners (mainly coal miners) with an OR of 1.47 (95%CI: 1.11, 1.95). Cleaners, craftsmen and service workers also had a statistically significant increased odds of knee OA. Three studies reported that full-time housework was statistically significantly associated with increased odds of knee OA. All of the remaining occupations, such as commerce, forestry or fishery workers, machine operators, plumbers, electricians, technicians, postmen etc., were not found to be statistically significantly associated with knee OA (Table 3).

**iii Major occupational activities—**Across 30 studies, 40 occupational activities were reported. We focused on the seven most commonly reported activities; these included kneeling, squatting, lifting, climbing, standing, walking and sitting (Table 3). Activities beyond those listed here, such as bending, jumping, crawling or combinational activities, were not included due to the limited number of studies per activity category.

There were large variations across studies in the definitions of workplace activities; in particular, duration and intensity of the activity. In general, the amount of time for kneeling and squatting was ≥30 mins/day and for standing and walking this was equal to ≥2hours/day. The exposed group usually lifted 10-50kg at least once a week and climbed 15-50 flights/day. The pooled results showed that each of these respective workplace physical activities was associated with increased odds of knee OA compared to non-exposed workers or those exposed to the lowest level possible. An inverse association was found between sitting time and knee OA. There was substantial heterogeneity across all meta-analyses ($I^2$>50%). (Table 3).

## Discussion

### Principal findings

Our meta-analyses, of 71 studies with over 950,000 participants, investigated a variety of occupational exposures and showed that, compared to sedentary (or low-levels of physical activity), heavy physical workload contributed to overall increased odds of knee OA of up to 52%. Quality of evidence was rated as moderate in cohort studies and, very-low in case-control and cross-sectional studies due to evidence of substantial heterogeneity and publication bias. A potential source of heterogeneity may have been due to a high risk of study bias. We observed similar findings across different study designs, regions, levels of study quality and OA definitions. More so, males tended to have higher odds of knee OA compared to females, although the difference was not statistically significant. This is probably because males are more likely to be exposed to heavy workload, which is reflected in a large number of exclusively male studies (32–34). Also, the odds of the disease seem to be higher in participants recruited from industries than communities or hospitals. A possible selection bias might exist as jobs with the highest odds were likely to be recruited and reported. Compared to previous systematic reviews of occupation and knee OA(7, 8), our study is the most comprehensive including an increased number of relevant occupational exposures and sample size.

Our findings are largely consistent with previous systematic reviews which reported that occupational lifting, climbing, kneeling and squatting were all associated with a higher risk of knee OA(8, 9). Our review has further suggested that prolonged standing and walking also contributed to knee OA. In contrast, sitting seemed to be protective. These findings, however, have not been confirmed in other studies and should be interpreted with caution due to the large variations in study designs, assessments of exposure and study populations.

Our study is the first to examine the association between occupation and knee OA by specific job titles. We conducted sub-group meta-analyses of 23 occupations and found statistically significant higher odds of knee OA in 13 physically demanding jobs; such as agricultural workers, builders and construction workers, miners, cleaners and service workers. Compared to sedentary (or low physically active) workers, agricultural workers had up to 64% increased odds of knee OA. These occupations frequently involve severe knee flexion whilst weeding, feeding, harvesting and lifting(35, 36). Despite the ongoing changes in the scale of farming operations and machinery, physical practices in farming remain unchanged; including those most likely to cause injuries(37). While many agricultural tasks vary among different farming systems(38), the development of tailored and practical ergonomic solutions for specific tasks warrant further investigation. Similarly, a 63% increased odds of knee OA was observed in builders and floor layers. It has been shown that floor layers kneel and squat for a large proportion of their working time, especially during gluing and filling, thereby generating high external knee forces(6, 39). The prevalence of patellofemoral radiological changes and prepatellar, infrapatellar bursitis, however, do not seem to increase in floor layers(40–42). Due to the cross-sectional nature of these studies, causality cannot be determined for which longitudinal studies are needed.

Light to moderate manual job titles, including service workers, houseworkers and cleaners, have rarely been investigated in knee OA leaving significant knowledge and practice gaps. We have shown that houseworkers have up to 93% increased odds of developing knee OA. This is consistent with a previous study that reported that female ‘homemakers’ had up to 92% increased prevalence of lower extremity pain(43). The biomechanical features of housework resemble those of tasks performed by paid workers in care-giving, food preparation and cleaning(44). Housemakers often engage in prolonged standing activities and frequently perform household tasks such as mopping/cleaning which involve frequent bending, kneeling and squatting. Cleaners frequently engage in awkward knee postures and repetitive tasks and movements(45) that mirror many household tasks. These working areas require special attention, especially for unpaid full-time housewives or carers.

## Limitations

Overall, there was evidence of a high risk of bias and heterogeneity across many of the included studies. Most of the occupation-related studies relied on self-reported, retrospective occupation status over a period of 10 to 50 years making recall bias very likely. Over 10% of studies collected current occupation as the main exposure without providing detailed employment time; which could have biased the pooled results. In addition, due to the lack of standardised instruments and classification for occupation status focusing on lower limbs, there was substantial heterogeneity and missingness in the overall pooled results thus our findings should be interpreted with caution. We focused on load-bearing and knee strain-related factors on the biomechanical causal pathway. We acknowledge that there are other occupational factors such as machine vibration, improper body positioning and psychological stress at work that may contribute to the development of knee OA though we were unable to assess such factors due to too few studies reporting these occupational exposures. Lastly, we assessed, in accordance with routinely used assessment criteria, the NOS for the assessment of study quality. We acknowledge that there are limitations to this approach including a lack of weighting on specific items among the risk of bias criteria.

## Conclusions and future implications

Our systematic review found that physically demanding occupations and activities carried increased odds of knee OA among, in particular, agricultural and construction workers. These findings reinforce the importance of occupational exposures in OA, beyond its roles of musculoskeletal injury, and these data should be carried forward to help develop preventions and inform policy in occupational health.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.


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### Significance and innovations

- Prevalence of knee OA has been associated with work-related repetitive joint movements and excess knee load but little is known of the relationship between specific job titles and risk of knee OA; especially light to moderate physically demanding occupations.
- Increased odds of knee OA were found in agriculture workers, construction workers, miners, service workers, houseworkers and cleaners who typically perform high levels of lifting, kneeling, climbing, squatting and standing, compared to sedentary occupations.
- This evidence could help inform workplace regulators and insurers by identifying people, who are frequently involved in specific work activities, that may be susceptible to joint disorders and, it could also help identify targeted industrial sectors which might need tailored prevention strategies for knee OA.

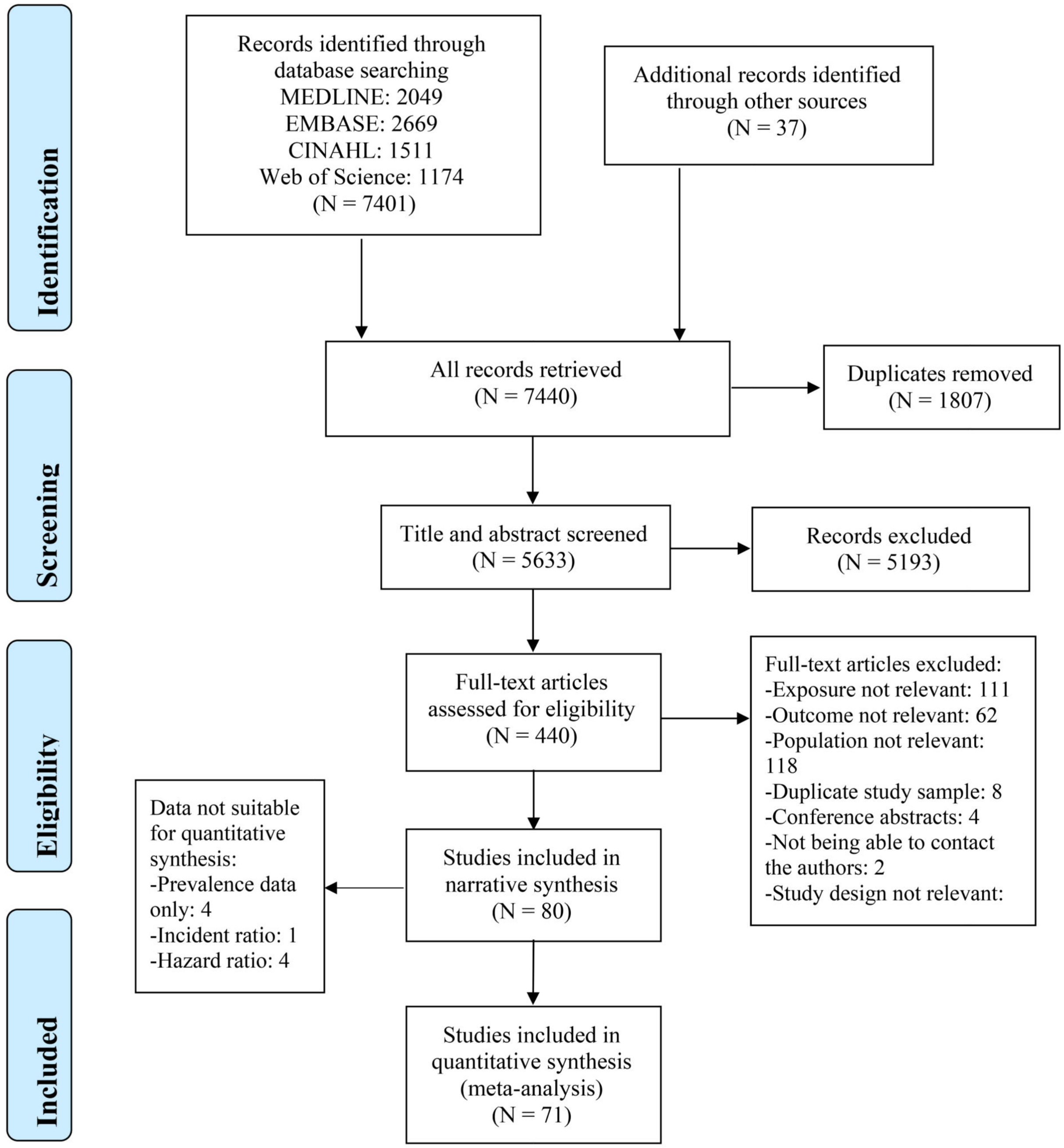


**Figure 1.**
PRISMA flowchart of study selection.

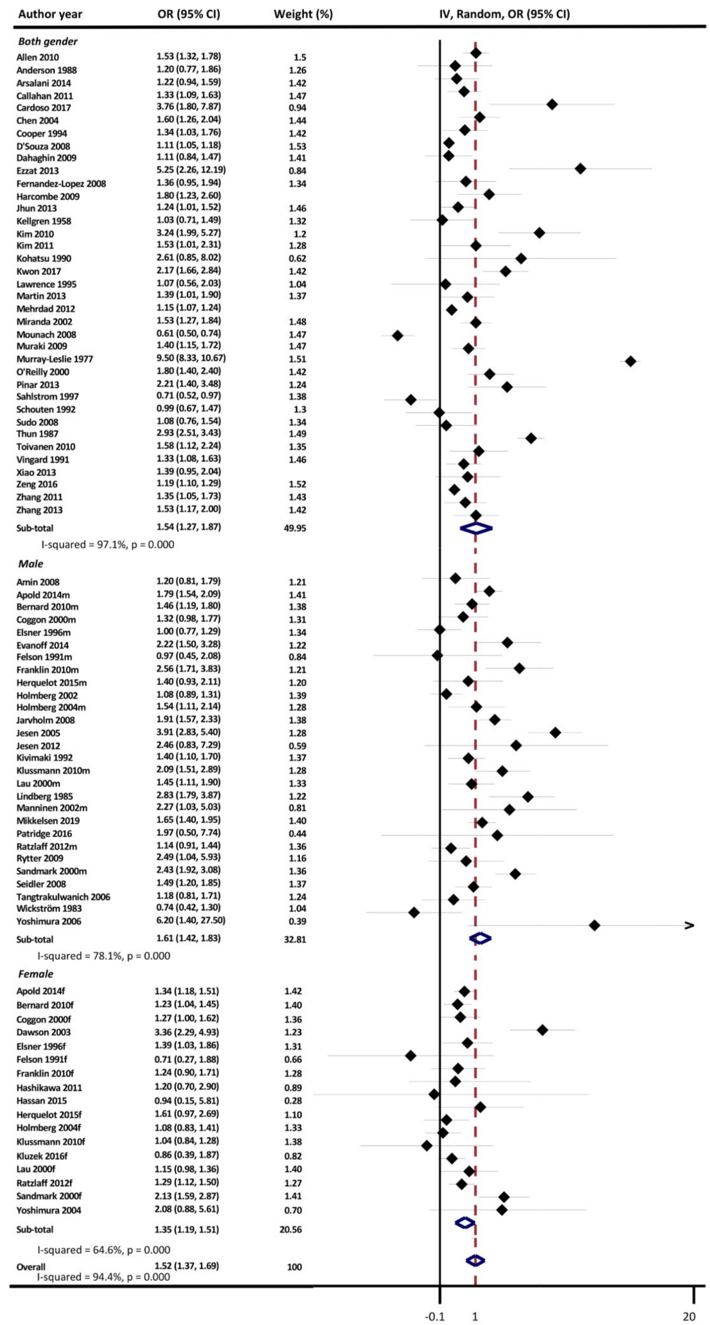


**Figure 2.**

Forest plot showing odds of knee osteoarthritis in all occupational exposures grouped by gender with sub-totals showed for males, females and both sexes. The square data markers indicate odds ratios (ORs) from primary studies, with sizes reflecting the statistical weight of the study using random-effects meta-analysis. The horizontal lines indicate 95% confident intervals (CIs). The blue diamond data markers represent the subtotal and overall OR and 95%CI. The vertical dashed line shows the summary effect estimate and the solid line shows the line of no effect (OR = 1).

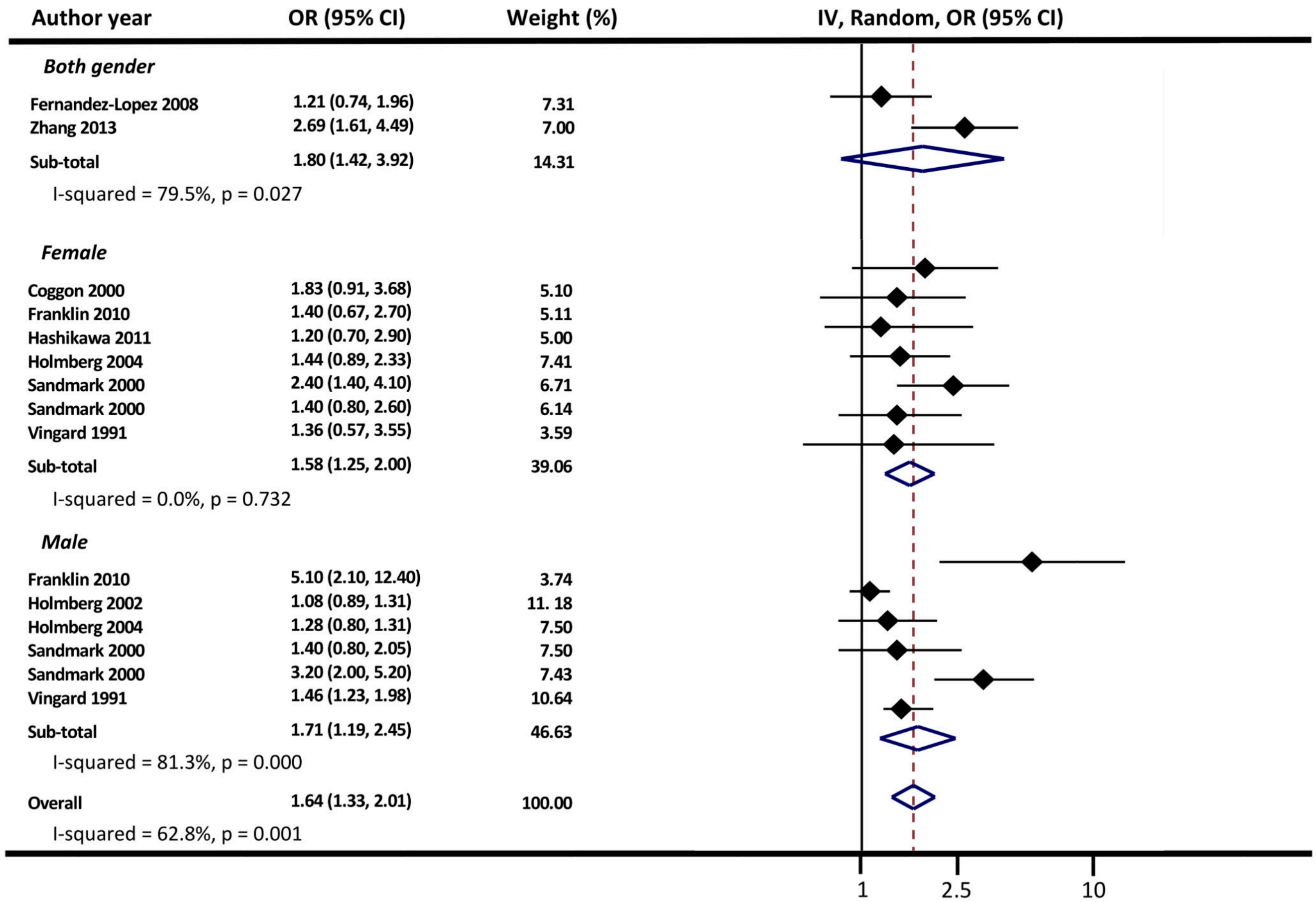


**Figure 3.**

Forest plot showing odds of knee osteoarthritis in people who are working in agriculture. The square data markers indicate odds ratios (ORs) from individual studies, with sizes reflecting the statistical weight of the study using random-effects meta-analysis. The horizontal lines indicate 95%CIs. The blue diamond data markers represent the subtotal and overall OR and 95%CI. The vertical dashed line shows the summary effect estimate and the solid line shows the line of no effect (OR = 1). Reference group is non-agricultural workers. Abbreviations: ROA, radiographic osteoarthritis; SOA symptomatic osteoarthritis.




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## Table 1
## Characteristics of included studies

| Characteristics | Case control studies | Cross sectional studies | Cohort studies | All studies |
|---|---|---|---|---|
| No. of studies | 25 | 36 | 19 | 80 |
| No. of participants | 20,505 | 139,463 | 16,824,492 | 16,984,460 |
| Age (Mean, years) | 57.5 | 57.4 | 53.5 | 56.6 |
| Female (Mean, %) | 42.1 | 48.8 | 42.4 | 44.5 |
| Body mass index (Mean, $kg/m^2$) | 25.4 | 25.9 | 25.7 | 25.7 |
| Newcastle-Ottawa score (Mean) | 6 | 4 | 7 | 5 |
| OA definition | | | | |
| Symptomatic OA | | | | |
| - Clinical diagnosed [a] | 3 | 5 | 9 | 17 |
| - Knee pain [b] | 2 | 10 | 2 | 14 |
| - Knee replacement | 3 | 0 | 4 | 7 |
| Radiographic OA [c] | 7 | 9 | 1 | 7 |
| Symptomatic and radiographic OA | 10 | 12 | 3 | 25 |
| Knee compartment | | | | |
| Tibiofemoral | 14 | 18 | 5 | 37 |
| Tibiofemoral or patellofemoral | 5 | 2 | 0 | 7 |
| Not reported | 6 | 16 | 14 | 36 |
| Main occupation exposure | | | | |
| Job title | 11 | 18 | 8 | 37 |
| Job categories | 0 | 0 | 3 | 3 |
| Occupational activities | 6 | 8 | 4 | 18 |
| Multiple exposures | 8 | 10 | 4 | 22 |
| Employment time | | | | |
| Current | 3 | 13 | 8 | 24 |
| Longest job held | 11 | 11 | 1 | 23 |
| Lifetime | 6 | 3 | 3 | 12 |
| Not reported | 5 | 9 | 7 | 21 |
| Geographic region | | | | |
| Europe | 18 | 10 | 15 | 43 |
| North America | 1 | 8 | 3 | 12 |
| Oriental [d] | 3 | 11 | 1 | 15 |
| Middle East | 2 | 3 | 0 | 5 |
| Rest of the world [e] | 1 | 4 | 0 | 5 |
| Setting | | | | |
| Community | 15 | 23 | 12 | 50 |
| Hospital | 3 | 3 | 1 | 7 |
| Industry | 6 | 8 | 5 | 19 |

| Characteristics | Case control studies | Cross sectional studies | Cohort studies | All studies |
|---|---|---|---|---|
| Other [f] | 1 | 2 | 1 | 4 |

Data presented as number (N) of studies unless otherwise stated.

[a] Clinically diagnosed knee OA consists of a diagnosis made by a clinician, based on physical examinations or knee OA diagnostic criteria (e.g. America College of Rheumatology).

[b] Knee pain defined using validated questionnaires (e.g. Western Ontario and McMaster Universities Osteoarthritis Index, Nordic Musculoskeletal questionnaire).

[c] Radiographic OA defined by Kellgren Lawrence grade ≥2.

[d] ‘Oriental’ countries consisted of East and Southeast Asia, including China, Hong Kong, Singapore, Japan, Korea and Thailand.

[e] ‘Rest of the world’ consisted of India, Morocco, Brazil and Central America.

[f] Other settings consisted of military, religious and government agencies.

## Table 2
### Occupational odds in knee osteoarthritis by different subgroups

| | Subgroups | N of studies/ participants | Summary meta-analysis, OR (95% CI) | Heterogeneity, % (P value) |
|---|---|---|---|---|
| Study design | | | | |
| | Case-control | 25/17,765 | **1.58 (1.18, 2.11)** | 96.9% (<0.01) |
| | Cross-sectional | 32/143,364 | **1.54 (1.38, 1.72)** | 88.4% (<0.01) |
| | Cohort | 14/790,216 | **1.45 (1.32, 1.59)** | 57.6% (<0.01) |
| OA definition criteria [a] | | | | |
| | Symptomatic | 58/11,178,459 | **1.43 (1.34, 1.53)** | 85.8% (<0.01) |
| | Radiographic | 13/39,490 | **1.57 (1.24, 1.98)** | 97.1% (<0.01) |
| Gender | | | | |
| | Male | 29/471,779 | **1.61 (1.42, 1.83)** | 78.7% (<0.01) |
| | Female | 18/174,077 | **1.35 (1.20, 1.51)** | 64.6% (<0.01) |
| Occupational exposure time | | | | |
| | Current job | 19/632,683 | **1.45 (1.30, 1.62)** | 71.4% (<0.01) |
| | Longest-held job | 24/40,381 | **1.45 (1.31, 1.60)** | 77.0% (<0.01) |
| | Lifetime | 13/20,172 | **1.65 (1.30, 2.09)** | 89.8% (<0.01) |
| Region | | | | |
| | Europe | 38/895,716 | **1.56 (1.31, 1.87)** | 96.1% (<0.01) |
| | North America | 10/21,598 | **1.47 (1.19, 1.82)** | 88.1% (<0.01) |
| | Oriental | 14/26,201 | **1.45 (1.27, 1.65)** | 70.7% (<0.01) |
| | Middle East | 5/3,011 | **1.25 (1.04, 1.49)** | 50.1% (0.09) |
| | Rest of the world | 4/4,819 | 1.47 (0.71, 3.04) | 93.7% (<0.01) |
| Setting | | | | |
| | Community | 43/385,536 | **1.38 (1.27, 1.49)** | 78.2% (<0.01) |
| | Hospital | 7/249,758 | **1.39 (1.22, 1.58)** | 79.6% (<0.01) |
| | Industry | 16/315,192 | **1.84 (1.52, 2.24)** | 84.1% (<0.01) |
| Methodological quality | | | | |
| | Low [b] | 55/383,937 | **1.57 (1.37, 1.79)** | 95.5% (<0.01) |
| | High | 16/567,408 | **1.39 (1.19, 1.63)** | 82.6% (<0.01) |
| Confounding | | | | |
| | Unadjusted analysis | 26/31,577 | **1.54 (1.42, 1.67)** | 82.8% (<0.01) |
| | Adjusted analysis | 45/919,768 | **1.44 (1.11, 1.85)** | 97.4% (<0.01) |

Bold values denote statistical significance at the P < 0.05 level.

Subgroup analysis to show if heterogeneity is related to certain study characteristics. The percentage values for heterogeneity were calculated using the $I^2$ test and the P values are from the Cochran Q test.

Reference group is non-exposed workers or those exposed to the lowest level possible.

[a] Symptomatic osteoarthritis defined as symptomatic osteoarthritis with or without radiographic measures. Radiographic osteoarthritis defined as radiographic measures only.

[b] Studies with a Newcastle Ottawa score < 7 were defined as low methodological quality.

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## Table 3

**Subgroup analyses for special occupational exposures**

| | Occupation | Number of studies (participants) | Summary meta-analysis, OR (95% CI) | Heterogeneity, % (Cochran Q, P value) |
|---|---|---|---|---|
| Job categories | | | | |
| | Heavy physical work | 17 (52,984) | **1.65 (1.43, 1.91)** | **76.8% (<0.01)** |
| | Low to moderate physical work | 5 (190,123) | **1.48 (1.23, 1.78)** | **53.5% (0.02)** |
| | Sedentary work | 4 (2,789) | 1.02 (0.80, 1.30) | 4.5% (0.40) |
| Job titles | | | | |
| | Agriculture, forestry and fishery | | | |
| | - Agriculture, forestry and fishery | 8 (4,585) | **1.94 (1.56, 2.42)** | 0.0% (0.84) |
| | - Agriculture | 9 (46,326) | **1.64 (1.33, 2.01)** | **62.8% (<0.01)** |
| | - Forestry | 3 (7,346) | 1.43 (0.99, 2.05) | 0.0% (0.44) |
| | - Fishery | 2 (40,317) | 1.16 (0.84, 1.61) | 48.0% (0.10) |
| | Construction trades | | | |
| | - Building and construction | 8 (76,648) | **1.63 (1.39, 1.92)** | 0.0% (0.42) |
| | - Metal worker | 5 (13,567) | **1.85 (1.25, 2.76)** | 49.9% (0.05) |
| | - Floor- and brick layer | 5 (11,422) | **2.51 (1.79, 3.52)** | **81.2% (<0.01)** |
| | - Carpenter | 4 (43,696) | **2.49 (1.66, 3.74)** | 0.0% (0.45) |
| | - Machine operator | 3 (14,050) | 1.36 (0.97, 1.92) | 0.0% (0.79) |
| | - Plumber | 2 (16,727) | 1.52 (0.60, 3.85) | 60.8% (0.11) |
| | - Electrician | 4 (21,339) | 0.88 (0.59, 1.32) | 0.0% (0.44) |
| | - Technician | 4 (4,121) | 1.31 (0.99, 1.70) | 0.0% (0.26) |
| | Commerce | 6 (10,002) | 1.22 (0.95, 1.57) | 9.7% (0.35) |
| | Healthcare professional | 5 (1,252) | 1.19 (0.96, 1.47) | 29.8% (0.22) |
| | Miner | 4 (2,602) | **1.47 (1.11, 1.95)** | 7.6% (0.36) |
| | Cleaner | 4 (8,722) | **1.51 (1.14, 2.01)** | 14.5% (0.32) |
| | Postman | 4 (3,757) | 1.29 (0.86, 1.94) | 0.0% (0.47) |
| | Painter | 3 (16,027) | 1.60 (0.97, 2.66) | 0.0% (0.70) |
| | Waitress and hairdresser | 3 (7,546) | 1.26 (0.78, 2.03) | 0.0% (0.93) |
| | Housework | 3 (1,608) | **1.93 (1.31, 2.84)** | 0.0% (0.53) |
| | Service worker | 3 (1,749) | **1.79 (1.36, 2.37)** | 1.6% (0.40) |
| | Craftsman | 2 (1,404) | **1.56 (1.17, 2.09)** | 0.0% (0.46) |
| | Driver | 2 (3,732) | 1.67 (0.90, 3.08) | 0.0% (0.49) |
| Occupational activities | | | | |
| | Lifting (>10 kg/day) | 17 (102,813) | **1.39 (1.22, 1.59)** | **76.8% (<0.01)** |
| | Kneeling (>30 mins/day) | 14 (94,762) | **1.29 (1.05, 1.57)** | **85.8% (<0.01)** |
| | Standing (>2 hours/day) | 12 (9,709) | **1.30 (1.09, 1.53)** | **72.4% (<0.01)** |
| | Climbing (>15 flights/day) | 10 (5,653) | **1.49 (1.20, 1.86)** | **73.4% (<0.01)** |
| | Squatting (>30 mins/day) | 10 (6,244) | **1.48 (1.21, 1.81)** | **52.4% (0.02)** |
| | Walking (>2 hours/day, or >2 kms/ day) | 10 (6,097) | **1.23 (1.01, 1.52)** | **68.1% (<0.01)** |

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| Occupation | Number of studies (participants) | Summary meta-analysis, OR (95% CI) | Heterogeneity, % (Cochran Q, P value) |
|---|---|---|---|
| Sitting (>2 hours/day) | 13 (13,996) | **0.77 (0.70, 0.84)** | 35.3% (0.09) |

Bold values denote statistical significance at the P < 0.05 level.

The percentage values for heterogeneity were calculated using the $I^2$ tests and the P values are from the Cochran Q test.

Reference group: non-exposed workers or those exposed to the lowest physical level possible.

For studies (Allen 2000, Callahan 2011, Ezzat 2013, Felson 1991, Jesen 2005, Kim 2010, Kwon 2017, Lawrence 1955, Tangtrakulwanich 2006) that reported radiographic and symptomatic knee osteoarthritis together, only symptomatic knee osteoarthritis outcomes were included in the meta-analysis.