Occupational exposure to knee loading and the risk of osteoarthritis of the knee, meniscal knee lesions and pre-patellar bursitis

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1. Summary

Background:

Osteoarthritis of the knee is prevalent in workers over 45 years of age and is considered to be related to knee straining activities at work such as kneeling, squatting, climbing stairs and lifting. These activities are also considered a risk factor for meniscal lesions and pre-patellar bursitis. It is unclear if there is an exposure dose-response relation for these three diseases.

Objective:

The objective of this review is to assess the exposure dose-response relation between kneeling, squatting, climbing stairs, and lifting at work and knee osteoarthritis, meniscal lesions and pre-patellar bursitis.

Methods:

We included cohort and case-control studies that measured exposure to kneeling, squatting, climbing stairs or lifting at work and the risk of osteoarthritis of the knee, meniscal lesions or pre-patellar bursitis. We first searched PubMed, Embase and Web of Science for systematic reviews. We then also conducted a search for primary studies limited to the time period after the last systematic review was published. Two researchers independently assessed if the primary studies included in these reviews fulfilled our inclusion criteria and extracted data from the studies that fulfilled the inclusion criteria.

First, we combined studies based on a dichotomous lowest versus highest exposure in a meta-analysis in RevMan. Then, we calculated an incremental Odds Ratio (OR) per 5000 hours of cumulative exposure to each of the knee straining work activities per study. We pooled these in a random effects meta-analysis with various exposure models. We used sensitivity analysis and subgroup analysis to test the robustness of our findings.

Main results:

We found two cohort and 13 case-control studies that measured the effect on osteoarthritis, two case-control studies on meniscal lesions and no studies on bursitis. All studies used questionnaires to assess exposure. We considered all but one study at high risk of bias.

For exposure to kneeling and squatting, the OR of lowest versus highest exposure for osteoarthritis of the knee was 1.70 (95% Confidence Interval (95% CI) 1.35 to 2.13, 12 studies, very low quality evidence).

For a log-linear exposure dose-response model of kneeling or squatting, the OR per 5000 hours of exposure was 1.26 (95% CI 1.17 to 1.35, five studies, moderate quality evidence). A quadratic dose-response model fitted the data better than the log-linear model. Sensitivity analyses did not change our conclusions. There were no substantial differences between subgroups.

Exposure to kneeling increased the risk of meniscal lesions compared to no kneeling but this was based on two studies with a high risk of bias only.

Conclusions:

There is moderate quality evidence that longer cumulative exposure to kneeling or squatting at work leads to a higher risk of osteoarthritis of the knee. There was insufficient evidence to establish this for squatting or kneeling alone, climbing stairs or lifting. For meniscal lesions, the effects of exposure may be similar. For bursitis, there is no evidence because there are no studies. Consensus about

exposure measurement metrics and more objective exposure measurement would increase the quality of the evidence.

2. Opsummering

Baggrund

En 45-årig arbejdsmand fremviser en udtalt grad af osteoarthritis i knæet, som vurderes til at hænge sammen med knæbelastende arbejdsopgaver som f.eks. knæle, sidde på hug, gå på trapper og løfte. Denne form aktivitet anses også for at udgøre en risiko i forbindelse med menisklæsioner og præpatellarbursitis. Det er ikke fastlagt, om der foreligger en sammenhæng mellem eksponering og disse tre lidelser.

Formål

Formålet med denne gennemgang er at vurdere sammenhængen mellem eksponering ved at knæle, sidde på hug, gå på trapper samt løfte i forbindelse med arbejdet og osteoarthritis i knæet, menisklæsioner samt præpatellarbursitis.

Metoder

Vi medtog undersøgelser af kohorte- og case-kontrol, som målte eksponering ved at knæle, sidde på hug, gå på trapper eller løfte i forbindelse med arbejdet og risikoen for osteoarthritis i knæet, menisklæsioner eller præpatellarbursitis. Vi søgte først efter systematiske gennemgange i PubMed, Embase og Web of Science. Vi foretog også en søgning efter primærstudier for et begrænset tidsrum, dvs. perioden efter offentliggørelsen af den sidste systematiske gennemgang. To forskere vurderede uafhængigt, om de primærstudier, der blev medtaget i disse gennemgange, opfyldte vores inklusionskriterier og uddrog de data, der opfyldte disse kriterier.

Vi sammenkørte først studier, der var baseret på en opdeling mellem dem, der var hhv. mindst og mest eksponeret ved disse bevægelser, i en metaanalyse i RevMan. Vi udregnede derefter en stigende odds-ratio (OR) for hver 5.000 timers arbejde i alt med bevægelserne for hver bevægelsestype pr. studie. Disse blev derefter samlet i en metaanalyse over tilfældige effekter ud fra forskellige modeller over bevægelseseksponeringen. Vi gjorde brug af sensitivitetsanalyse og undergruppeanalyse for at afprøve, hvor holdbare fundene var.

Hovedresultater

Vi fandt frem til to kohorte- og 13 case-kontrol studier, der målte effekten på osteoarthritis, to case-kontrol studier, der vedrørte menisklæsion, og ingen vedrørende bursitis. Ved alle studierne blev der anvendt spørgeskemaer til at vurdere bevægelseseksporingen. Vi anså alle undtagen et studie for at være karakteriseret af stor risiko for bias.

Hvad angår eksponering ved at knæle og sidde på hug var OR for den mindste hhv. største eksponering ved ostearthritis i knæet 1,70 (95 % konfidensinterval (95 % CI) 1,35 til 2,13, 12 studier, evidens af meget ringe kvalitet).

Med en log-linear model for eksponering ved at knæle og sidde sammenholdt med reaktion var OR for hver 5.000 timers eksponering 1,26 (95 % CI 1,17 til 1,35, fem studier, evidens af moderat kvalitet). En kvadratisk model for sammenhængen mellem eksponering og bevægelserne fandt bedre anvendelse på dataene end den log-lineære model. Sensitivitetsanalyser ændrede ikke på vores konklusioner. Der var ikke væsentlige forskelle mellem undergrupperne.

Eksponering for at knæle øgede risikoen for menisklæsioner sammenlignet med ikke at knæle, men dette byggede udelukkende på to studier med stor risiko for bias.

Konklusioner

Der er evidens af moderat kvalitet på, at længere akkumuleret eksponering ved at knæle eller sidde på hug på arbejde medfører en større risiko for osteoarthritis i knæet. Der var utilstrækkelig med evidens til at fastlægge dette for udelukkende at sidde på knæ eller knæle, gå på trapper eller løfte. For menisklæsioner kan der være en lignende effekt af eksponeringen. For bursitis er der ikke nogen evidens, da der ikke forelå nogen studier. Koncensus om målemetrik for eksponering og mere objektive eksponeringsmålinger ville kunne øge kvaliteten af evidensen.

3. Background

Description of the condition

Knee Osteoarthritis

Degenerative diseases of the knee like osteoarthritis are very prevalent. In a general American adult population the prevalence of knee osteoarthritis was estimated at 14%. The causes of knee osteoarthritis are not well known. Several risk factors have been reported. Age is the most prominent risk factor with prevalence rates doubling with increasing age.[1] Being overweight is considered a risk factor either through mechanical stress on the joint or through metabolic processes as part of the metabolic syndrome [2]. Misalignment of the knee joint as a result of either valgus or varus deformity is also considered to lead to osteoarthritis of the knee [3]. Wide geographical variation of the incidence of knee osteoarthritis points to a genetic component [1]. Gender forms a possible risk factor with studies reporting higher prevalence of knee osteoarthritis in women [1]. Playing sports at higher levels poses a risk for osteoarthritis either directly or through additional injuries of the joint and related structures [4]. Finally, work activities that increase pressure on the articular cartilage of the joint are considered risk factors by most authors. Occupational activities that are implied as mechanical stressors are lifting, kneeling, squatting, and climbing stairs [5-10].

Even though the associations between these risk factors and knee osteoarthritis have been generally accepted, the evidence base to support these claims is still thin.

Management of knee osteoarthritis is symptomatic as the disease process cannot be reversed but also directed at the prevention of progression. Patients are prescribed NSAIDs to reduce pain by reducing the inflammatory response [3]. An important step is to try to get patients to lose weight usually with a physical exercise program which decreases the mechanical stress on the knee joint surfaces. In addition, physical exercise through either non-weight or weight-bearing activities has been shown to improve symptoms [11]. Finally, when the disease leads to an increased level of disability and pain, total knee replacement is an option to decrease especially pain symptoms and thus to improve the functional limitations. The relatively few alternatives for treatment and the irreversibility of the disease, stress the necessity of preventive efforts. Therefore, knowledge of causal associations between exposures at work that can be ameliorated and knee outcomes are even more important because this might be one of the few ways to prevent damage to the knee.

Lesions of meniscus of the knee

In a very similar way, lesions of the menisci of the knee have been associated with the same risk factors as mentioned above for knee osteoarthritis [12]. There is discussion if meniscal lesions are just part of the same degenerative process as osteoarthritis or that they have a place of their own [13]. Studies show that after removal of menisci the risk of osteoarthritis increases four fold [14]. One aspect that makes meniscal lesions different from osteoarthritis is their more direct association with injuries leading to direct trauma [12]. The management approach has changed in recent years with conservative treatment being favoured over surgical treatment. These are all good reasons to also take meniscus lesions as a primary health outcome for the review as well as knee osteoarthritis.

Bursitis of the knee

Prepatellar bursitis is a frequently occurring condition, with an annual incidence of 10/100,000, predominantly affecting male patients (80%) aged 40-60 years. Approximately one third of the cases are septic and two thirds of the cases are non-septic [15].

Since long bursitis of the knee has been recognized as an occupational disease in occupations that require kneeling at work, especially in miners [9]. Miners have to do their work kneeling when the mine gallery does not leave enough space to work standing. In addition to kneeling, their work requires shovelling of loads while kneeling, which further increases the mechanical pressure on the knee. Kneepads have been developed to disperse the pressure on the skin and the knee region over a larger area but their efficacy is not clear [16]. We will also take bursitis of the knee as a primary outcome for reviewing.

Anatomy of the knee

The healthy knee joint allows us to move the lower leg toward the back of the thigh (flexion) and back (extension) and a rotation of the lower leg without hip rotation when the knee is bent. The joint is involved when walking, climbing, standing, and kneeling and has to support the body's full weight.

Two joints and three bones build the knee, the thighbone (femur), the shin bone (tibia) and the kneecap (patella). The main joint is between femur and tibia, the second joint is between patella and femur. The articulate surfaces of the bones are covered with cartilage that has the ability to compress when loaded and expand when unloaded. The bone structure does not provide a socket that would hold the bones in place. The most important structures that control the stability of the knee while standing and moving are the ligaments and muscles. Inside the knee are two special types of ligaments between the femur (thighbone) and the tibia (shin bone), called menisci. Besides supporting the stability of the knee due to the C-form and wedged shape, the menisci spread the forces from the weight of the body over a larger area on the femur and tibia and form a buffer between the bones. Around the joint is the synovial capsule. This tissue produces the synovial fluid. The synovial fluid lubricates the articular surfaces, allowing them to move without adhesion and abrasion and on the other hand transports nutrients to the cartilage. The cartilage is sponge like and soaked in synovial fluid, that will be squeezed out when the knee is loaded and soaked back by the cartilage when the knee is unloaded. Cartilage is avascular and nutrients reach the cells mainly by diffusion from the synovial fluid [17]. Around the knee joint are many fluid filled sacks (bursae) located that function as gliding surfaces to reduce the friction between different tissues (e.g. bones, muscles, and ligaments).

Description of the exposure and how it might affect the knee

While standing and moving the knee joint is loaded by different types of forces, for example gravity (weight), acceleration (from the lower leg and foot), tension (from the ligaments and muscles), and friction (between the surfaces). Forces are vectors and therewith have a magnitude and a direction. These can be described as a push or a pull, causing an object to move or to be deformed. Forces working at a distance to a rotating point result in moments.

The direction and amplitude of forces and moments inside the knee are highly dependent on the type of movement or position. With more knee flexion the same knee moment will lead to higher contact forces between patella and femur given geometrical considerations. In vivo measurements of forces and moments with instrumented knee implants in five subjects measured highest average peak resultant forces between tibia and femur in percent of body weight during descending stairs (346% BW), followed by stair ascending (316 % BW), level walking (261% BW), one legged stance (259% BW), knee bending /squatting (253% BW), and two legged stance (107% BW) [18]. The same study did not measure the exposure to lifting, but forces may most likely be higher when adding weight.

Relevant knee loading activities and positions for this review are kneeling, squatting, climbing stairs or ladders, and lifting weight. Most of these activities are not different from everyday activities. However, in the work environment the knee joint can be exposed to knee loading activities for a longer period of time and more frequently. For example professional floor layers spend at least half of their working time kneeling or in other knee straining activities [19 20].

How higher mechanical stress exactly leads to knee osteoarthritis, bursitis or meniscal lesions is not exactly known. The biomechanical theory is that mechanical stress leads to an overburdening of the joint surface, the bursa and the menisci with micro-fractures or other signs of wear-out as a result. The body's ability to repair these micro-fractures or to recover from constant pressure and continuous movements is apparently insufficient and leads to the signs of osteoarthritis, bursitis and meniscal lesions. A supporting argument of this theory is that during high mechanical stress moments the water content in the cartilage decreases, making it more vulnerable to damage as it loses its flexibility. In addition, the loss of articular cartilage in osteoarthritis is considered to be genetic. The level of cell activity to synthesize and destruct cartilage components is based on the individual gene matrix. If the level of activity is imbalanced this will result in cartilage loss and lead to osteoarthritis.

Why it is important to do this review

The following three knee diseases have been listed as occupational disease after sufficient exposure to occupational knee demanding activities:

- Knee osteoarthritis after exposure to kneeling or squatting at work
- Prepatellar bursitis after exposure to pressure on the knee at work
- Meniscal lesions of the knee after exposure to squatting positions at work

Exposure to knee demanding work is an important occupational exposure. It seems that sufficient reviews are available to draw reliable conclusions about a basic association. A new systematic appraisal of the literature will provide current knowledge on:

- Exposure: Even though a link between work demands and knee strain has been established, the quantification and categorisation of the mechanical exposure remains a problem. This project will propose a better exposure description.
- Effect: Even though an effect of the mechanical exposure on the development of the three disease outcomes seems established, an exposure dose-response relation is missing in all reviews. This project aims at finding whether there is evidence for the presence of such an exposure dose-response relationship.

4. Objectives

To summarize the available evidence on the association between the occupational activities kneeling, squatting, climbing on ladders or stairs or lifting on the one hand and knee-osteoarthritis, pre-patellar bursitis and meniscal lesions of the knee on the other hand.

Furthermore, to examine the possible dose-response relationship between the exposures to kneeling, squatting, climbing on ladders or stairs, or lifting at work on the one hand and knee osteoarthritis on the other hand.

5. Methods

We formulated the following criteria that had to be fulfilled in order to include primary studies.

Inclusion criteria

Type of studies

We included any cohort study that compared the risk or severity of the outcome in the exposed participants with the risk or severity in the less or unexposed participants.

We also included case-control studies that included participants with knee osteoarthritis, knee bursitis or meniscal lesions (cases) and participants without or with less severe outcomes (controls) and that compared the exposure between them.

Type of participants

Participants had to be exposed to knee load at the workplace. We excluded professional athletes as the exposure is different from work related knee-loading activities. Jumping and pivoting plays a much bigger role than kneeling and climbing ladders or stairs and knee problems may predominately be injury related.

Type of exposures

We only included studies that measured the following activities or that measured work tasks that involve the following activities: climbing stairs or ladders, working in kneeling or squatted positions, or lifting weights. We included both self-reports or researcher observations to measure the knee load based on work tasks (e.g. floor laying) or activities (e.g. climbing stairs). The exposure had to be measured in at least two categories (exposed and less/non-exposed).

We excluded studies that used job titles only as exposure. This was done to reduce exposure measurement bias. Job titles may not represent the actual knee load and would limit the interpretation of the effect of knee loading activities on the outcomes.

Type of comparison

We included any comparison of different levels of exposure, or exposed compared to non-exposed.

Type of outcome measures

We included all incidence and severity outcomes of knee osteoarthritis, meniscal lesions, and bursitis of the knee.

We included studies only if they reported the use of x-ray, arthroscopy, or indicated that the diagnosis was made by a physician. We excluded studies that used biomarkers and proxy measures as these may not represent the actual health outcome and may have limited the interpretation of the results.

We included severity outcomes if the study reported the use of appropriate imaging techniques to measure the outcome (e.g. joint space measurements via x-ray). We also included studies that used validated scales to measure the severity of the disease, like patient reported pain or function scores (e.g. The Western Ontario and McMaster University Osteoarthritis Index (WOMAC), or Oxford-12 knee score (OKS)).

Type of Confounders

We included studies on osteoarthritis, knee bursitis and meniscal lesions only if they at least adjusted for age as a confounder.

Searching and including studies

Searches

We performed two different searches. First, we searched three electronic databases (Embase, Web of Science and PubMed) for systematic reviews on heavy work load and one or more of our adverse health outcomes. We developed a sensitive search in PubMed applying search terms for the exposure and the outcome. We then translated the search strategy to Embase and Web of Science. We used the filter for systematic reviews that is developed by the Cochrane Work Review group. We first searched for reviews in PubMed in the beginning of March 2015 and later in all three databases in the beginning of May 2015 to locate all published reviews on the topic from the earliest record. We used the reviews to locate all available primary studies that could fulfil our inclusion criteria.

Then, we searched PubMed in the beginning of July to locate more recent studies that have not been covered by the search strategy of the included reviews. The latest included review was published in 2013. We therefore included a time filter searching from date of publication in 2012 up to date.

Additionally, we searched non-electronic sources (references of included studies and reviews) for finding systematic reviews and primary studies for knee osteoarthritis, meniscal lesions and bursitis.

Selection of studies

Two reviewers independently checked the fulfilment of the inclusion criteria. Initially, we screened titles and abstracts and excluded studies that obviously did not fulfil the inclusion criteria. Of the remaining references we obtained the full text and assessed them for eligibility applying the same inclusion criteria. We resolved disagreements by discussion or by a third reviewer.

Data extraction

Primary studies:

Two reviewers independently extracted data from the primary studies. We collected information about the following:

- General study characteristics: design, funding, country, data source (database or self-collected), time span covered by the data, and confounders adjusted for
- Participants: source of participants, demographics (mean age, gender, BMI, injuries, type of work), inclusion and exclusion criteria set by study authors, number of participants enrolled in the study and number of participants analysed
- Exposure: Type of exposure, exposure measure, measurement technique, and exposure categories
- Outcome: name, definition, and measurement technique (diagnostic tests used),
- Study results: Number of participants, mean and standard deviations, adjusted and crude risk rations and odds ratios, mean differences and standard error, and p values

Risk of bias assessment

We adapted a checklist for assessing the quality of observational studies as developed by Shamliyan [21 22]

We drew up an ideal study for assessing the effect of occupational knee loading and the three main outcomes. We used this ideal study to assess the risk of bias for study designs in how much they departed from this ideal. We distinguished between studies with a high risk of bias and studies with a low risk of bias.

Analysis

Adjustment for confounding

We considered four possible confounders for studies measuring knee osteoarthritis and meniscal lesion based on existing literature [1 2 4]. The confounders were age, gender, BMI, and injuries. For studies measuring knee bursitis only two of those risk factors (age and BMI) were considered important confounders.

We planned to adjust the effect estimates from studies that had not adjusted for gender, injury or obesity (BMI) differences if data was available following the methods described by Greenland [23 24]. However, this was not done due to lack of sufficient data in the included studies.

Dealing with missing data

If required data for the analysis was missing from the articles, we contacted the study authors for additional information. If they could not be reached we tried to calculate the missing data from the available statistics. Previous research indicates no clear pattern between increasing exposure and the development of the three disease outcomes. Therefore we assumed and tested for a linear relationship between the natural logarithm of RR and increasing exposure. We decided to use a cumulative exposure level for the analysis. An exposure of 5000 cumulative hours was used as a dose that would be sufficient to increase the risk of an adverse outcome. This is equivalent to about 5 years of 4 hours of exposure per day.

Data synthesis

First, we performed a meta-analyses of the studies based on a no-exposure or least exposure versus yes-exposure or maximum exposure comparison. For studies that used various levels of exposure, we compared the lowest versus the highest exposure categories. We calculated log RRs and their Standard Errors (SE) for this comparison and combined these with the general inverse variance method available in RevMan using a random effects model.

Then, where possible, we calculated a cumulative dose in a standardized way as cumulative lifetime hours of kneeling or squatting, meters climbed or kilos lifted. Next, for each study, we assigned a dose per exposure category following the methods described by Il'yasova [25]. With these assigned doses we calculated an exposure dose-response curve for each individual study following Orsini and Greenland [26].

We then combined the odds ratios per 5000 hours of exposure per study for each disease outcome separately. This was done using the most adjusted natural logarithms of the relative risks as input for a random effects meta-analysis in RevMan. We also used the more accurate method of general least squares for trend estimation (glst) meta-regression as described by Orsini and Greenland [26].

We used three exposure models (linear with logRR, splines, and quadratic) to calculate the risk per 5000 hours increase of lifetime exposure. We tested different exposure dose-response models by means of splines and a quadratic model using the web-based R-version by Crippa & Orsini (https://alecri.shinyapps.io/dosresmeta/). In the various models, we centred the exposure towards zero by subtracting the exposure values of the reference category from the other categories. This was done to adjust for the non-zero exposure in the reference categories.

Assessment of reporting biases

We avoided language and publication bias by including studies in any language and of any publication status. We assessed publication bias by using a funnel plot and applying Egger's test to the included studies.

Subgroup analysis and investigation of heterogeneity

We assessed statistical heterogeneity by means of the I^2 statistic. We took an I^2 value of up to 25% as low, values between 25% and 75% as moderate, and values over 75% as high degrees of heterogeneity respectively.

We assessed the studies for similarity of participants, exposure and outcome measurement and grouped for the meta-analysis accordingly. At first, we intended to organize studies in subgroups by job, occupation or industry. However, almost all studies included multiple occupations and it was not possible to separate these. Instead, we decided to build subgroups based on the variations between studies in the exposure definition (e.g. kneeling, or kneeling and squatting) and the adjustment for confounding. We also evaluated if there was an effect of study year by organizing studies in the following time-periods: before 2000, 2000-2004, 2005-2009, and 2010-2014.

Sensitivity analysis

We included a sensitivity analysis for the quality of the studies by excluding high-risk studies from the meta-analysis in case of more than one high quality study.

We also evaluated how sensitive our results were to assumptions made about the cumulative level of exposure to knee load. To be able to combine studies we calculated a common measure of cumulative lifetime exposure because not all studies used the same metric. This meant that we had to make assumptions about the number of hours per day that workers would be kneeling or about the number of working weeks/years participants had been working. We calculated exposure based on a lightest workload scenario and based on a heaviest workload scenario and compared the results of the meta-analyses based on these different scenarios.

Strength of causality of the evidence and GRADE

We used the approach of the Danish Occupational Medicine Association to grade the strength of causality. In addition, we used the GRADE approach to assess the overall quality of evidence.

6. Results

Search

The search strategy yielded 286 references to systematic reviews in the three databases altogether. From these we selected 50 to be assessed full-text. This resulted in 24 systematic reviews that fulfilled our inclusion criteria. From these reviews, we extracted 38 separate primary studies that we assessed full-text. We excluded 21 of these. This resulted in 19 articles that fulfilled our inclusion criteria.

The additional search for primary studies published after 2012 resulted in 439 references. Of these, we excluded 429 in the title and abstract stage and assessed 10 full-text. After full-text assessment, we did not include any additional studies.

Thus, from both the systematic reviews and the complementary search for primary studies, we located 19 articles that fulfilled our inclusion criteria. Three articles reported data on one study [27-29]. This resulted in 17 included studies.

Five studies reported the results for male and female gender separately. We included these as separate studies in the analyses, which is denoted with –f- or –m- after the study id. Therefore, of the 17 included studies, we have 22 studies or study-arms in the analyses.

Description of included studies

Study design

Of the included studies, fifteen were case control studies and two were cohort studies [30 31] (Table 3).

Outcome

Two cohort and thirteen case control studies measured the effect of the exposure on knee osteoarthritis and two case control studies measured the effect on meniscal lesions of the knee [32 33]. None of the included studies measured the effect on pre-patellar knee bursitis.

Outcome measure, definition and measurement technique

The case control studies defined cases of knee osteoarthritis in the following ways:

- Kellgren and Lawrence scale (table 3 appendix) minimally grade 2 [27 34],
- Kellgren and Lawrence scale grade 2 or 3 [35],
- Kellgren and Lawrence scale grade 3 minimally [36-39].
- minimum changes visible on the radiograph: sclerosis, osteophytes, and joint space narrowing [40 41]
- knee prosthetic surgery [42-45]

Knee osteoarthritis was measured in the two cohort studies as new cases of knee osteoarthritis or as knee osteoarthritis progression (cartilage loss). New cases of knee osteoarthritis were defined as participants with no knee OA at baseline but who had knee OA at follow-up according to a radiograph in one study [31]. Progression was measured as a change in joint space width between two radiographs of at least -1 measured independently by two physicians on a -4 to +4 scale [30].

Meniscal lesions were measured in two studies as undergoing meniscectomy [33] or as meniscal tear (including acute, degenerative and non-classified tears) [32].

Type of Participants

Number of participants

On average for knee osteoarthritis, the case control studies included 583 (range 74 to 1316) and the cohort studies 274 (range 105 to 424) study participants in the analysis. For meniscal lesions, the average was 478 participants.

Countries

Studies were mainly from Europe with six from the UK, three from Germany, two from Sweden, one each from Finland, the Netherlands, Japan, China and Morocco.

Sex

Five studies reported the results of the analysis separately for males and females [34 36 40 44 45]. Two studies included only female participants [39 43]. Three studies included only male participants [27 33 38]. Five studies included both men and women but reported only one result including both sexes. The percentage of males in these studies was respectively 81% [32], 52% [42], 36% [31], 28% [35], and 27% [37].

One study included both sexes but did not report how many males or females were included [41]. One study did not report any information about the sex of the participants [30].

Age

All case control studies reported that they used controls matched with the age of cases. The exact age band, within which the matching took place, was reported in six studies. Three studies matched within one year [32 33 36], two studies matched within 2 years [35 44], and one study matched within 5 years [42]. Only two of those studies reported the mean age for cases as 40.1 years [32] and 72.7 years [35]. Seven of the eleven studies that did not report the age band matched within reported the mean age or the age range and showed a good agreement between cases and controls.

The age range of included cases was reported in seven case control studies and one of those studies reported the median. One study did not report the age separate for males and females but for all cases included in both study arms. The age range of cases in three studies started below 25 years of age, one study had the starting age of 37 years, and the other three studies had only cases that were above 45 years of age. The maximum age of cases was 59 years in two studies and above 70 years in the other five studies. Only one study reported the median age (71.5 years).

Two studies did not report on age ([31 36]).

Table 1 Characteristics of included studies: ML meniscal lesions of the knee, OA knee osteoarthritis, No studies fulfilled the inclusion criteria for pre-patellar bursitis, nr = not reported

Study ID:	Study design	Out-come	Outcome measure	Country	Study Period	Occu-pation	Age (mean ± sd / range)	gender (% male)	N Partici-pants
Studies on meniscal lesions									
Baker 2002	case control	ML	Arthroscopy, confirmed for the first time	UK	1996-1998	various	40.1 ± ? / 20-59	81.00 %	535
Baker 2003	case control	ML	Arthroscopy, confirmed for the first time	UK	nr	nr	20-59	100.00 %	402
Studies on knee osteoarthritis, case control studies									
Coggon 2000	case control	OA	listed for surgery, graded according to KL scale	UK	1995-1998	nr	47- 93	40%, separate analysis for gender	1036
Cooper 1994	case control	OA	2 or 3 on KL scale	UK	nr	various	72.7 ± ? / 55-90	28.00 %	327
Dawson 2003	case control	OA	listed for knee replacement surgery	UK	nr	nr	50-70	0 %	111
Elsner 1996	case control	OA	changes observed in radiographs	Germany	1989-1993	various	Males: 58% > 55y Females: 59% > 55y	57%, separate analysis for gender	383
Klusmann 2010	case control	OA	≥2 on KL scale or outerbridge scale≥3	Germany	2006-2010	nr	Females: cases 59.6 ± 9.8 controls 54.8 ± 11.8 Males: cases 57.1 ± 11.2, controls 50.9 ± 12.7	41%, separate analysis for gender	1270
Lau 2000	case control	OA	3 or 4 on KL scale	China (Hong-Kong)	1998	nr	n.r.	25%, separate analysis for gender	1316
Manninen 2002	case control	OA	knee arthroplasty	Finland	1992-1993	nr	Male: cases 67.5 ± 5.7 controls: 67.2 ± 5.6 Female:	20%, separate analysis for gender	805

							cases 69.2 ± 5.4 controls 67.1 ± 5.6		
Mounach 2008	case control	OA	≥3 on KL scale	Morocco	2005-2006	various	cases 59.7 ± 8.5 / 37-76, controls 59.7 ± 8.5	27%	190
Seidler 2008	case control	OA	>2 KL scale	Germany	nr	various	25-70	100%	622
Sandmark 2000	case control	OA	knee prosthetic surgery	Sweden	1994	nr	nr	52%	1173
Sahlström 1997	case control	OA	changes observed in radiographs	Sweden	nr	nr	Males: 77 ± ? / 52-96 Female: 72 ± ? /47-96	nr	729
Yoshimura 2004	case control	OA	≥3 on KL scale	Japan	nr	various	Cases and controls 73.3 ± 9.8	0%	186
Yoshimura 2006	case control	OA	≥3 on KL scale	Japan	nr	various	Cases 70.0 ± 6.6 controls 70.1 ± 7.0	100%	74
Studies on knee osteoarthritis, cohort studies									
Schouten 1992	cohort	OA	changes observed in radiographs used as dichotomous outcome (comparing cartilage loss (-1 to -4) to no cartilage loss (0-4)	Netherlands	1988	nr	23% >60y	nr	105
Zhang 2011	cohort	OA	n.r.	UK	1996-2008	nr	nr	36 %	424

Type of work

Most studies included participants with a variety of occupations. Three studies included only participants with paid work [35 36 44], two studies included also housework [34 37]. One study included only jobs that had been held for at least 12 months [33]. Four studies decided to assess only the job that was held longest [27 35 36 39], two studies assessed all jobs each participant ever had [32 40]. Six studies did not report a definition of work or jobs included.

The name of the trades or occupations were only reported in six case control studies of the included seventeen studies. All but one of those studies reported the same trade names for cases and controls but had different numbers of cases and controls per trade. However, in five studies half of the cases and controls had similar jobs. One study did not report the job distribution of cases and controls and only reported some of the occupations in which cases were employed (teaching, nursing, steel erecting, electrical maintenance, roofing and other construction work) [35].

Exposure

Type of exposure

All of the included studies reported the exposure to kneeling, squatting, climbing or lifting as occupational activities. Only two of the included studies reported a definition of the activities. One study defined lifting as lifts with bent knee of objects weighting 15kg or more from one level to another [41]. Another study provided pictures of the work postures [27].

Kneeling and squatting

All but two studies reported on kneeling or squatting. We categorized the studies according to their measurement of exposure as kneeling only, squatting only or combined reporting of kneeling and squatting. Kneeling was included as kneeling only in eleven case-control studies. The same studies included squatting as squatting only (ten studies) or as squatting and knee bending (one study). Three other case control studies combined the exposure to kneeling or squatting and one cohort study combined kneeling, squatting or crawling.

Climbing

Twelve case control studies evaluated the exposure to climbing stairs (nine studies), stairs or ladders (one study), and stairs, ladders, or flights of stairs (one study). One case control study did not specify the exposure of climbing but refers to it later in the discussion section as climbing stairs.

Lifting

All but two of 15 case control studies measured the exposure to lifting and carrying (three studies), lifting only (six studies), and heavy lifting (four studies). One cohort study measured the exposure to heavy lifting.

Other exposure combinations

One case control study expressed the exposure to lifting, carrying, and climbing as light, medium or heavy knee moments. The lowest exposure is defined as ‘walking, sitting and carrying’, medium exposure is ‘lifting with bent knees and carrying, climbing ladders or stairs with or without carrying’, and heavy knee moments are all activities with additional jumping with or without carrying extra load.

One cohort study combined the exposure to kneeling and lifting.

Table 2 Characteristics of included studies: exposure related variables ML meniscal lesions of the knee, OA knee osteoarthritis, No studies fulfilled the inclusion criteria for pre-patellar bursitis, nr=not reported

Study ID:	Study design	Out-come	Exposure(s)	Measurement technique	More than 2 exposure categories
Studies on meniscal lesions					
Baker 2002	case control	ML	K, S, Cst, L or Car	interview at home by research nurse using a structured questionnaire	No
Baker 2003	case control	ML	K, S, Cst, L or Car 10+kg, L or Car 25+kg	questionnaire	No
Studies on knee osteoarthritis, case control studies					
Coggon 2000	case control	OA	K or S, Cst or Cfl or Cl, L	interview	K or S, Cst or Cfl or Cl, L
Cooper 1994	case control	OA	K, S, Cst, HL	interview	No
Dawson2003	case control	OA	K, S, L	interview	K, S, L
Elsner 1996	case control	OA	K, S, HL	questionnaire	No
Klusmann2010	case control	OA	K or S, Cst, L or Car	questionnaire and interview	K or S, L or Car
Lau 2000	case control	OA	K, S, Cst, L >10kg, L >50 kg	interview using standardized and structured questionnaire	L >10kg, L >50kg
Manninnen 2002	case control	OA	K or S, Cst, L	telephone interview	K or S, Cst, L
Mounach 2008	case control	OA	K, S, Cst, HL	questionnaire	No
Seidler 2008	case control	OA	K or S, L or Car	interview	K or S, L or Car
Sandmark 2000	case control	OA	K, S or Kb, Cst, L	questionnaire	K, S or Kb, Cst, L
Sahlström 1997	case control	OA	Knee moments	questionnaire	No
Yoshimura 2004	case control	OA	K, S, Cst, HL	trained interviewer using translated version of British questionnaire (Coggon 2000)	No
Yoshimura2006	case control	OA	K, S, Cst, L	trained interviewer using translated version of British questionnaire (Coggon 2000)	No
Studies on knee osteoarthritis, cohort studies					
Schouten 1992	Cohort	OA	K or S or Cr, HL	questionnaire	K or S or Cr, HL
Zhang 2011	Cohort	OA	K or L	questionnaire	K or L

K = Kneeling, S = Squatting, C = Climbing, Car = Carrying, Cfl = Climbing flights, Cl = Climbing ladders, Cr = Crawling, Cst= Climbing stairs, L = Lifting, HL = Heavy Lifting, DR = Dose Response

Exposure dose categories

Occupational exposure to kneeling, squatting and climbing was measured in eight studies in two categories of yes/no only. Nine studies had more than two exposure dose categories allowing for a dose-response relation (Table 2).

The exposure to lifting was measured in eight studies in yes/no categories and in nine studies in more than two categories allowing for the analysis of a dose-response relation.

Only four studies measured the no or the lowest exposure category as zero exposure. In other studies, the lowest exposure category included some amount of the exposure (Appendix: Table 11).

Kneeling and/or squatting

No exposure to 'kneeling' was defined as zero minutes per total working life time in one study [42]. Other studies defined the lowest exposure category as less than 30min per working day [35], less than 1 hour per working day [32 33 36-39], rarely or almost never (including participants without answers) [40], and as less than 15 years doing work that involves kneeling (for more than 1 hour a day) [43].

None of the studies used a 'zero exposure' category for 'squatting'. The lowest exposure was defined in a similar way as above explained for kneeling in all studies except Sandmark 2000. They defined no exposure to 'squatting or knee bending' on the basis of referents' reports post-assessment (less than 2 minutes in work life for women, zero minutes in work life for men) [42]

No exposure to 'kneeling or squatting' was defined in three studies as "not at all" [45] or zero hours [27 34]. One study defined the lowest exposure as less than 1 year in work that involves more than 1 hour kneeling or squatting per day [44].

Climbing

None of the studies used a 'no exposure' category for climbing. The lowest exposure to climbing was expressed as less than 10 flights of stairs [35], less than 15 flights [36] and less than 30 flights [32 33]. A flight of stairs is usually defined as an uninterrupted series of stairs between floors or landings. Other studies expressed the lowest exposure as less than 30 steps per day [38 39], less than 50 steps per day [37], or decided post-assessment based on the referents' reports as less than 166 steps per lifetime for women and less than 103 steps per lifetime for men [42]. One study defined the lowest exposure as less than 1 year in work that involves climbing ladders or stairs more than 30 times a day [44]. Another study described the lowest exposure as 'not at all or very little' but did not describe what was climbed or how much is 'very little' [45].

Lifting

Definitions of the lowest category included the total sum lifted per working life, the maximum weight of the objects lifted during work, or the years in work involving lifting. One study used a 'no exposure' category defined as zero tons per work life [34]. Others used 'no lifting and carrying' [27], or 'no regular lifting' [45]. One study defined the lowest category as total weight lifted during working life of 0 to 4 kg for women and 0 to 107 kg for men [42]. Other studies defined the lowest category as lifting only objects less than 10 kg [36], less than 10 kg or less than 10 times per week [32 33], between 5 and 20 kg [40], less than 25 kg [35 37-39], less than 1 year in work involving lifting more than 25 kg more than 10 times per week [44] or as less than 24 years doing work that involved lifting [43]. One study measured the exposure to 'lifting heavy objects' as 'low, medium and high' but neither reported the cut off points nor the measure [30].

Other exposure combinations

One study assessed 'kneeling or lifting' and the lowest exposure was defined as 'never' [31].

One study assessed 'kneeling, squatting, crawling' and the exposure dose categories were divided post-assessment into three parts based on tertiles [30].

Another study measured 'lifting or climbing' and the lowest exposure was 'no lifting, only sitting, walking, carrying' [41].

Assessment of exposure

None of the studies used a proven reliable assessment of exposure for example based on production figures or observations but all asked participants by questionnaire to report about the duration and intensity of their activities.

In eight studies, the participants were asked to report, for an average working day, either the cumulative hours or minutes of kneeling per day. One of those studies used the pre-specified categories: "not at all", "less than 2 hours", "from 2 to 4 hours", and "more than 4 hours" a day [45]. Four studies reported the exposure either as cumulative hours per work life or as cumulative years in work that included kneeling. One study measured the exposure to kneeling as 'almost never', 'rarely', 'often', 'almost always'. One study did not report the measure [30].

Squatting was measured in the same way as kneeling using the same categorization of exposure. One study measured the lifelong cumulative number of squats during all working days[42].

Climbing was measured either as number of flights of stairs per day, steps per day, steps per week, or years working in jobs that included climbing. One study measured the lifelong cumulative number of steps during average working days [46]. One study did not count the steps, flights, or stairs but measured the exposure to climbing as 'not at all, very little, or much' [45].

The exposure to lifting was measured in kg per average working day, per average working week, or for the whole work lifetime, as the cumulative kg lifted or as the kg lifted multiplied by 2.5 seconds per lifting act and by 1 second per meter carried. The data was summed and expressed as the total number of kg*hours per work lifetime. Another exposure measure in one study was lifting "never", "sometimes", and if more than sometimes as cumulative tons lifted. Two studies assessed the exposure in years working in jobs that included lifting. Two studies did not report how the outcome was measured [30 41].

Table 3 Characteristics of included studies: ML meniscal lesions of the knee, OA knee osteoarthritis, No studies fulfilled the inclusion criteria for pre-patellar bursitis, nr=not reported

Study ID:	**Study design**	**Out-come**	**Outcome measure**	**Country**	**Study Period**	**Occup ation**	**Age (mean ± sd / range)**	**gender (% male)**	**N Participants**
Studies on meniscal lesions									
Baker 2002	case control	ML	Arthroscopy, confirmed for the first time	UK	1996-1998	various	40.1 ±? / 20-59y	81.00 %	535
Baker 2003	case control	ML	Arthroscopy, confirmed for the first time	UK	nr	nr	20-59	100.00 %	402
Studies on knee osteoarthritis, case control studies									
Coggon 2000	case control	OA	surgery (listed for surgery graded according to KL scale)	UK	1995-1998	nr	47- 93	40%, separate analysis for males/ females	1036
Cooper 1994	case control	OA	2 or 3 on KL scale	UK	nr	various	72.7 ±? / 55-90	28.00 %	327
Dawson 2003	case control	OA	surgery (listed for knee replacement surgery according to primary idiopathic OA diagnosis by physician within the preceding 12 month)	UK	nr	nr	50-70	0 %	111
Elsner 1996	case control	OA	changes observed in radiographs (knee joint	Germany	1989-1993	various	Males: 58% > 55y	57%, separate analysis for males/ females	383

			space narrowing, sclerosing, osteophytes on x-ray)				Female: 59% > 55y		
Klusmann 2010	case control	OA	≥2 on KL scale or outer bridge scale≥3	Germany	2006-2010	nr	Females: cases 59.6 ± 9.8 controls 54.8 ± 11.8 Males: cases 57.1 ± 11.2, controls 50.9 ± 12.7	41%, separate analysis for males/ females	1270
Lau 2000	case control	OA	3 or 4 on KL scale	China (Hong-Kong)	1998	nr	n.r.	25%, separate analysis for males/ females	1316
Manninen 2002	case control	OA	surgery (undergone knee arthroplasty)	Finland	1992-1993	nr	Male: cases 67.5 ± 5.7 controls: 67.2 ± 5.6 Female: cases 69.2 ± 5.4 controls 67.1 ± 5.6	20%, separate analysis for males/ females	805
Mounach 2008	case control	OA	≥3 on KL scale	Morocco	2005-2006	various	Cases 59.7 ± 8.5 / 37-76y, controls 59.7 ± 8.5	27%	190
Seidler 2008	case control	OA	>2 KL scale	Germany	nr	various	25-70	100%	622
Sandmark 2000	case control	OA	surgery (if lead to a knee prosthetic surgery)	Sweden	1994	nr	nr	52%	1173
Sahlström 1997	case control	OA	changes observed in radiographs (of non-weight-bearing joints (sclerosis, osteophytes, joint space narrowing))	Sweden	nr	nr	Males: 77 ±? / 52-96y Female: 72 ±? / 47-96y	nr	729
Yoshimura 2004	case control	OA	≥3 on KL scale	Japan	nr	various	Cases and controls 73.3 ± 9.8	0%	186

Yoshimura 2006	case control	OA	≥3 on KL scale	Japan	nr	various	Cases 70.0 ± 6.6 controls 70.1 ± 7.0	100%	74
Studies on knee osteoarthritis, cohort studies									
Schouten 1992	cohort	OA	changes observed in radiographs (change in joint space width between two radiographs mean score of -1 or lower was considered to indicate cartilage loss (on a +4 to -4 scale); used as dichotomous outcome measure (comparing cartilage loss (-1 to -4) to without cartilage loss (0-4)))	Netherlands	1988	nr	23% >60y	nr	105
Zhang 2011	cohort	OA	n.r.	UK	1996-2008	nr	nr	36 %	424

Measurement period of the time at risk

The duration for the occupational exposure measurement ranged in studies from a minimum of 12 years medium duration to over the entire life time. Four studies measured the exposure either for the last 12 years (medium, range 7 to 12 years) [31], during the period 15 to 50 years of age [42], until the age of 49 [45], or over three 15 year age periods (25-39, 40-54 and 55-70 years) [41]. Seven studies measured the exposure for the entire lifetime.

The other six studies have an unknown time of follow-up. Studies only reported assessment of the exposure either for the job longest held, the job at the birthday preceding the onset of the case's symptoms, or for the job at the time the case's symptoms began (Table 11 appendix).

Risk of Bias

Risk of bias was assessed separately for cohort and case control studies because of the different ways of assessing the risk of bias for these study types.

For case control studies, risk of bias was considered most important for assessment of exposure, assessment of the outcome, confounders, attrition and errors in the analysis. There was one study that scored a low risk of bias for all these items [27]. Three studies fulfilled almost all requirements for low risk of bias but failed in one out of the five important dimensions [34 35 44] (Table 4). Other studies failed to meet any of the criteria and scored a high risk of bias for all dimensions. Seven studies scored a low risk of bias in the exposure assessment, which means that at least five out of seven subcategories had to be low risk of bias. However the exposure assessment for all studies was subjective and still not proven reliable, as no study used an objective exposure assessment such as direct observation or production data that could lead to a more reliable assessment of the exposure.

Overall this left us with almost all case-control studies at a high risk of bias (Table 4). This means that the methodological quality in future studies, in our view, still can be substantially improved and it might be that this yields different results than we have now.

For a more detailed analysis we refer to the appendix with a full overview of all sub-items (Table 13).

Table 4 Risk of bias for case control studies

Category / CC study ID	*Coggon 2000*	*Cooper 1994*	*Elsner 1996*	*Lau 2000*	*Manninen 2002*	*Seidler 2008*	*Sandmark 2000*	*Klussmann 2010*	*Mounach 2008*	*Dawson 2003*	*Sahlström 1997*	*Yoshimura 2004*	*Yoshimura 2006*	*Baker 2002*	*Baker 2003*
Funding and Conflict of Interest	low	high	high	low	unclear	High	unclear	low	high	unclear	high	unclear	unclear	unclear	high
Outcome Assessment	low	low	high	high	unclear	Low	high	low	high	high	low	unclear	unclear	high	low
Exposure Assessment	high	low	high	low	low	Low	low	high	high	high	high	high	high	low	low
Confounding factors	low	low	high	high	low	Low	low	low	low	high	high	high	unclear	low	high
Attrition bias	low	high	high	high	high	Low	low	low	high	high	low	high	high	high	high
Analysis	low	low	low	high	low	Low	high	low	high	low	high	high	high	high	low
Overall	high	high	high	high	high	Low	high	high	high	high	high	high	high	high	high

The overall risk of bias in the two cohort studies was also high (Table 5). The occupational risk was only a minor issue in these general population studies. Important domains with a high risk of bias in these studies is the assessment of the exposure and the high number of non-respondents.

Table 5 Risk of bias for cohort studies

Category / Cohort study ID	*Schouten 1992*	*Zhang 2011*
Funding and Conflict of interest	unclear	Unclear
Outcome Assessment	low	Low
Exposure Assessment	high	High
Confounding factors	low	Low
Attrition bias	high	High
Analysis	low	Unclear
Overall	high	High

7. Results – knee osteoarthritis

Exposed vs. Unexposed

Kneeling or ‘kneeling or squatting’ versus no kneeling or ‘kneeling or squatting’

We included 12 of the 13 case control studies in the meta-analysis that compared kneeling or ‘kneeling and squatting’ to no kneeling or no ‘kneeling and squatting’. Yoshimura 2006 could not be included because no results were reported [38]. Exposure to knee loading at work resulted in an Odds Ratio (OR) of 1.7 with a 95% Confidence Interval (95%CI) of 1.35 to 2.13 (Figure 1) with moderate heterogeneity (I^2 = 49%) of the results across studies.

Analysis by subgroup of the type and number of confounders adjusted for did show differences between the subgroups. The subgroup with least adjustment (age and gender, 3 studies) yielded an OR of 1.27 (95% CI 0.96 to 1.67) and the subgroup with most adjustment (age, gender, BMI and injuries, 6 studies) yielded an OR of 2.11 (95% CI 1.60 to 2.78).

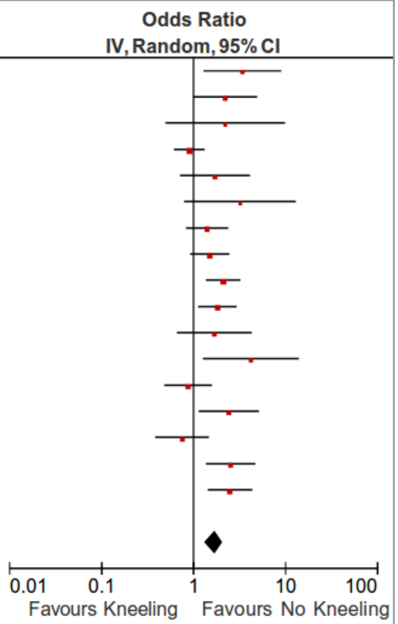
Analysis by gender for those studies that measured the risk in both genders, did not reveal a statistical significant or relevant difference between men (OR 1.93, 95% CI 1.50 to 2.47) and women (OR 1.62, 95% CI 1.10 to 2.39) in five studies [34 36 40 44 45]. Heterogeneity across studies was much higher among women (I^2 = 55 %) than among men (I^2 = 0 %).

We did not run a subgroup analysis by risk of bias, as all but one study [27] were at high risk of bias.

Figure 1 Case-control studies that measured the effect of kneeling (yes/no) on knee osteoarthritis (N=12) (b=both sexes, f=female, m=male)

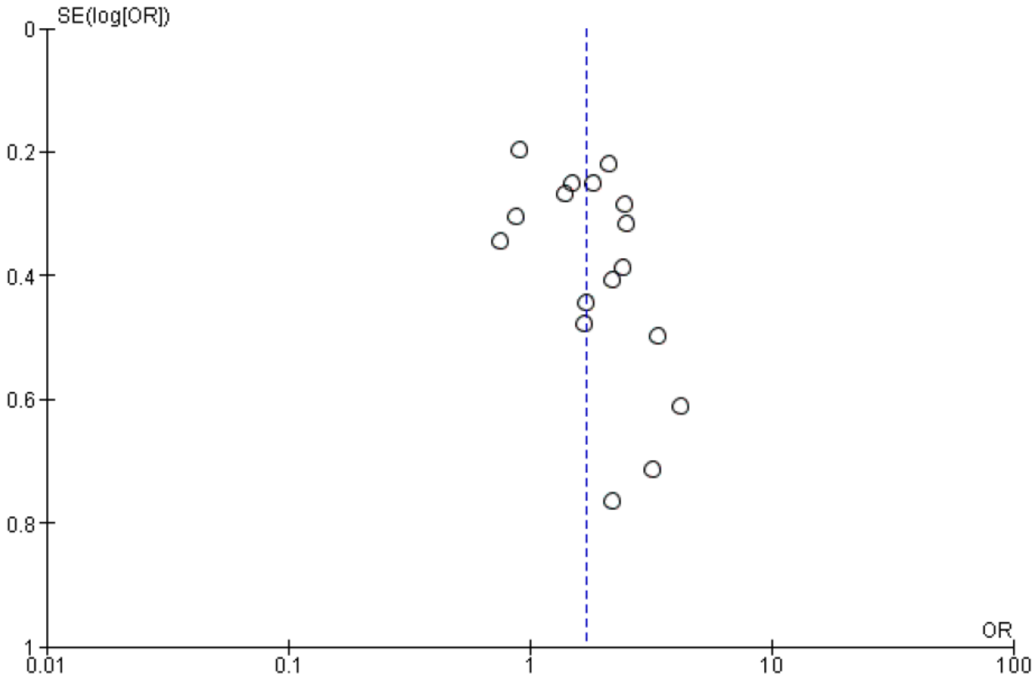
Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Year
Cooper 1994b	1.22378	0.49641	3.9%	3.40 [1.29, 9.00]	1994
Elsner 1996m	0.78846	0.40752	5.0%	2.20 [0.99, 4.89]	1996
Elsner 1996f	0.78846	0.76347	2.0%	2.20 [0.49, 9.82]	1996
Lau 2000f	-0.10536	0.19724	9.6%	0.90 [0.61, 1.32]	2000
Coggon 2000m	0.53063	0.44464	4.5%	1.70 [0.71, 4.06]	2000
Coggon 2000f	1.16315	0.71125	2.2%	3.20 [0.79, 12.90]	2000
Lau 2000m	0.33647	0.26781	7.8%	1.40 [0.83, 2.37]	2000
Sandmark 2000f	0.40547	0.25021	8.2%	1.50 [0.92, 2.45]	2000
Sandmark 2000m	0.74194	0.21874	9.0%	2.10 [1.37, 3.22]	2000
Manninen 2002f	0.59333	0.24935	8.2%	1.81 [1.11, 2.95]	2002
Manninen 2002m	0.51879	0.47691	4.1%	1.68 [0.66, 4.28]	2002
Dawson 2003f	1.43031	0.6106	2.8%	4.18 [1.26, 13.83]	2003
Yoshimura 2004f	-0.13926	0.30393	7.0%	0.87 [0.48, 1.58]	2004
Seidler 2008m	0.87547	0.38626	5.4%	2.40 [1.13, 5.12]	2008
Mounach 2008b	-0.28768	0.34337	6.2%	0.75 [0.38, 1.47]	2008
Klussmann 2010f	0.92426	0.31714	6.7%	2.52 [1.35, 4.69]	2010
Klussmann 2010m	0.90422	0.28563	7.4%	2.47 [1.41, 4.32]	2010
Total (95% CI)			**100.0%**	**1.70 [1.35, 2.13]**	

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 31.51$, df = 16 (P = 0.01); $I^2 = 49\%$
Test for overall effect: Z = 4.54 (P < 0.00001)



We assessed publication bias with a funnel plot in which the effect sizes for kneeling (yes/no) are plotted against 1/variance of the studies. This plot reveals that the less precise, smaller studies have more positive results and small studies with negative or no difference results seem to be missing. The Egger test resulted in a bias coefficient of 2.25 (p = 0.033) which is also an indication that small studies overestimate the effect or that negative small studies are missing.

Figure 2 Funnel Plot of kneeling studies (yes/no), OR against precision (sample size)

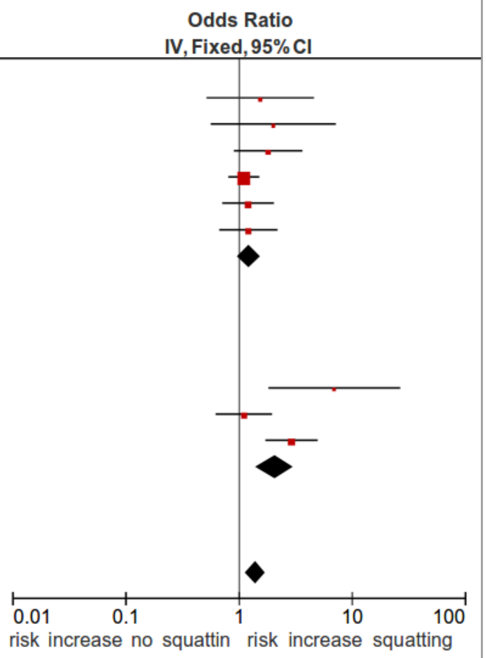


Squatting versus no Squatting

For the exposure squatting versus no squatting the results of the meta-analysis of ten case control studies were similar to the exposure of kneeling and kneeling or squatting with an OR of 1.41 (95%

CI 1.16 to 1.70) with high heterogeneity across studies (I^2 = 53 %). The subgroup analysis showed a significant difference between the four studies without adjustment for BMI and the two studies with an adjustment for BMI. The studies without adjustment showed a smaller effect of the exposure.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
2.6.1 squatting only; age gender				
Dawson 2003f	0.42527	0.55884	3.1%	1.53 [0.51, 4.57]
Elsner 1996f	0.69315	0.6519	2.3%	2.00 [0.56, 7.18]
Elsner 1996m	0.58779	0.35709	7.5%	1.80 [0.89, 3.62]
Lau 2000f	0.09531	0.16036	37.2%	1.10 [0.80, 1.51]
Lau 2000m	0.18232	0.26781	13.3%	1.20 [0.71, 2.03]
Yoshimura 2004f	0.18232	0.30363	10.4%	1.20 [0.66, 2.18]
Subtotal (95% CI)			**73.8%**	**1.23 [0.98, 1.54]**
Heterogeneity: Chi² = 2.35, df = 5 (P = 0.80); I² = 0%				
Test for overall effect: Z = 1.80 (P = 0.07)				
2.6.2 squatting only; age gender bmi				
Cooper 1994b	1.93152	0.6851	2.0%	6.90 [1.80, 26.42]
Sandmark 2000f	0.09531	0.29405	11.1%	1.10 [0.62, 1.96]
Sandmark 2000m	1.06471	0.27005	13.1%	2.90 [1.71, 4.92]
Subtotal (95% CI)			**26.2%**	**2.06 [1.42, 3.00]**
Heterogeneity: Chi² = 9.27, df = 2 (P = 0.010); I² = 78%				
Test for overall effect: Z = 3.79 (P = 0.0002)				
Total (95% CI)			**100.0%**	**1.41 [1.16, 1.70]**
Heterogeneity: Chi² = 17.03, df = 8 (P = 0.03); I² = 53%				
Test for overall effect: Z = 3.49 (P = 0.0005)				
Test for subgroup differences: Chi² = 5.42, df = 1 (P = 0.02), I² = 81.5%				



Lifting versus no lifting

The results of lifting versus no lifting showed an OR of 1.69 (95%CI 1.43 to 2.00, I^2 = 51 %) in twelve case control studies that measured this exposure.

We could not include Yoshimura 2006 and one study arm of Klussman 2010 in the meta-analysis. The studies did not report the results for men as “the correlation was not significant”[34] or the occupational activity was “not associated with increased risk of knee OA” [38]. We made a sensitivity analysis with five studies that reported results for both genders separately and the subgroup difference was statistically not significant (p=0.39).

Climbing stairs or ladders versus no climbing stairs or ladders

The results for climbing ladders resulted in an OR of 1.55 (95% CI 1.25 to 1.91) in the seven studies that could be included in the meta-analysis. The heterogeneity was I^2 = 68 %. Two studies could not be included in the meta-analysis because the results were not reported [34 38]. Both studies reported that no correlation or no significant correlation was found. There were no statistically significant differences in the effect of the exposure between studies with and studies without adjustment for confounding.

Exposure combinations

One cohort studies combined the exposure to kneeling, squatting and crawling. The study reported a non-significant OR of 0.31 (95% CI 0.09 to 1.04) for workers that kneel, squat, or crawl compared to workers that do not [30].

The second cohort study combined the exposure to kneeling and lifting and found an OR of 1.35 [31].

One case control study compared the exposure of medium and heavy knee moments to light knee moments and found an odds ratio of 1.10 (95% CI 0.70 to 1.80) [41].

Dose-Response analysis

Kneeling or squatting

Seven studies (eleven study arms) reported more than two exposure categories for the exposure to kneeling, kneeling or squatting, or kneeling, squatting, crawling (Table 6).

Table 6 Exposure categories (maximum 5) for kneeling and squatting (including kneeling, kneeling or squatting, and kneeling, squatting, crawling) from all studies with more than two exposure categories and per study arm

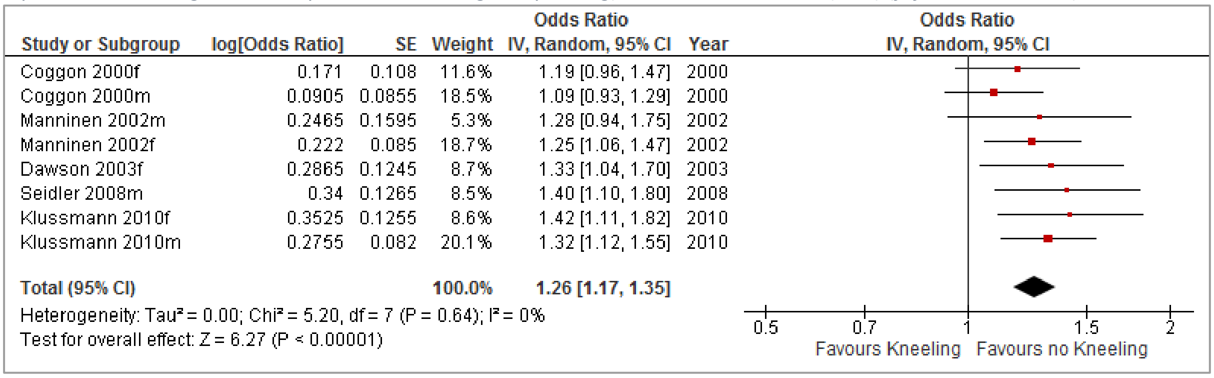
Type	**Study ID**	**1st**	**2nd**	**3rd**	**4th**	**5th**	**Comments**
K	Dawson 2003f (CC) [43]	<15 yrs spent doing work that involved kneeling	between >=15 and <26yrs spent doing work that involved kneeling	>=26 yrs spent doing work that involved kneeling			adjusted for age, gender
K or S	Coggon 2000f (CC) [44]	>1hr per day in total for less than 1yr	>1hr per day in total for 1 to less than 10 yrs	>1hr per day in total for 10 to less than 20 yrs	>1hr per day in total for 20 or more years		adjusted for age, gender, bmi, injuries
K or S	Coggon 2000m (CC) [44]	>1hr per day in total for less than 1yr	>1hr per day in total for 1 to less than 10 yrs	>1hr per day in total for 10 to less than 20 yrs	>1hr per day in total for 20 or more years		adjusted for age, gender, bmi, injuries
K or S	Klussmann 2010f (CC) [34]	no	<3,542 hours/life	3,542 to 8,934 hours/life	>8,934 hours/life		post-assessment, adjusted for age, gender, bmi
K or S	Klussmann 2010m (CC) [34]	no	<3,574 hours/life,	>3,574 =<12244 hours/life,	>12,244 hours per life		post-assessment, adjusted for age, gender, bmi
K or S	Manninen 2002f (CC) [45]	not at all	"less than 2 hours" per day	"from 2 to 4 hours" and "more than 4 hours per day			adjusted for age, gender, bmi, injuries
K or S	Manninen 2002m (CC) [45]	not at all	"less than 2 hours" per day	"from 2 to 4 hours" and "more than 4 hours per day			adjusted for age, gender, bmi, injuries

K	Sandmark 2000f (CC) [42], Sandmark 2000m (CC) [42]	no or low	medium	high			post-assessment, exact doses of lifelong sum (minutes) n.r., adjusted for age, gender, bmi
K or S	Seidler 2008m (CC) [27]	no	0-870 hrs/life	870-4757 hrs/life	4757 - 10800 hrs/life	>= 10.800 hrs/life	post-assessment, adjusted for age, gender, bmi
K or S or Cr	Schouten 1992 (C) [30]	low	medium	high			post-assessment, exact doses n.r., adjusted for age, gender, bmi

K = kneeling, S = squatting, CR = crawling, (C) = cohort study, (CC) = case control study, post-assessment = Study authors divided the exposure into dose categories based on participants values retrieved from the questionnaire/interviews, n.r. = not reported by study authors

Five case control studies with eight study arms reported sufficient information to be included in the exposure dose-response analysis (Figure 4, Table 7, Figure 5,). One case control and one cohort study did not report the exact doses to calculate the risk per 5000 hours [30 42].

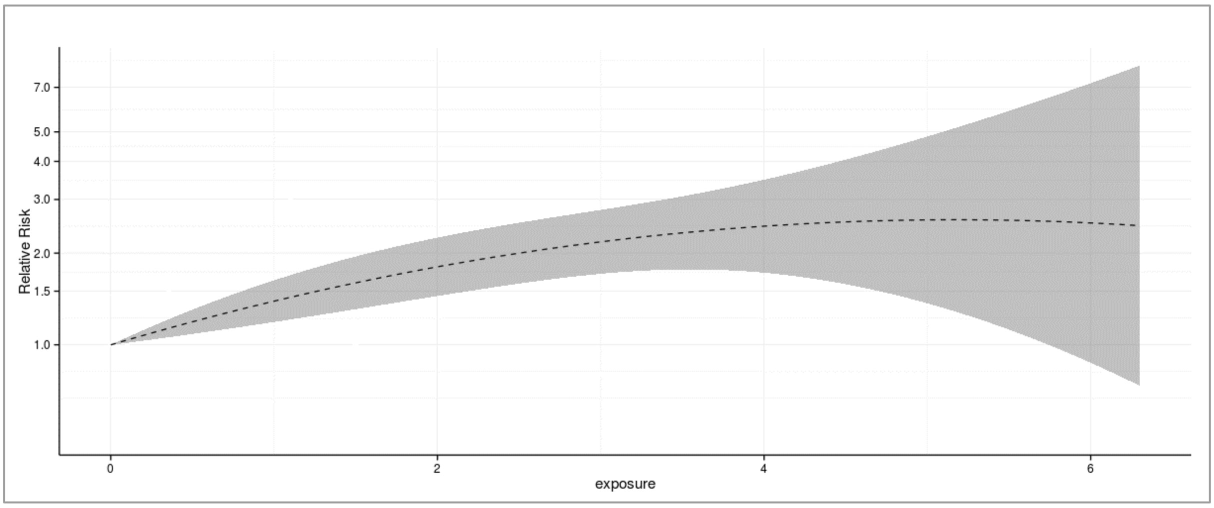
Figure 3: Meta-analysis of (log-linear model exposure dose-response) ORs per 5000 hours of lifetime exposure (including the exposure to kneeling and the exposure to kneeling or squatting), case-control studies (N=8) (f=female, m=male)



The results from the log-linear model show an increased risk per increased exposure to kneeling or squatting for all eight study arms, of which five were statistical significant (Figure 4). The combined ORs of the case control studies per 5000 hours of lifetime kneeling or squatting at work yielded an OR of 1.26 (95% CI 1.17 to 1.35). This means a 26% increase in the risk of knee osteoarthritis per 5000 hours increase of kneeling or squatting. The overall risk of bias was high in all but one study [27] (Table 4). The sub-group analysis showed that the difference in the effects of kneeling or squatting among females (OR = 1.28, 95% CI 1.15 to 1.42) compared to males (OR = 1.25 95% CI 1.11 to 1.40) were statistical non-significant. In the sensitivity analysis with the assumptions that led to the lowest possible exposure level, the slopes became a little bit steeper with an OR of 1.33 (95% CI 1.22 to 1.33) compared to the highest possible exposure level, when the slopes became gentler with an OR of 1.22 (95% CI 1.15 to 1.30).

The results from the quadratic model show that the risk is at maximum around 24 500 lifetime hours of kneeling or squatting at work and then decreases again (Figure 5).

Figure 4 Exposure dose-response results from the quadratic model showing the relative risk and 95% CI of knee osteoarthritis per unit of exposure (1= 5000 hours) (including the exposure to kneeling and kneeling or squatting)



The table below shows the hours kneeled during one person's work lifetime and the corresponding predictions of the risk. Due to the smaller numbers in the higher exposure ranges, the confidence intervals are wider. Compared to the linear model, the risks seem to be lower in the higher exposure ranges.

Table 7: Prediction model for the risk of knee osteoarthritis based on quadratic exposure response model for kneeling

Dose Hours Kneeling at work during Lifetime	**OR**	**95% CI Lower Bound**	**95% CI Upper Bound**
0	1	1	1
1900	1.14	1.06	1.23
4150	1.32	1.15	1.52
6350	1.5	1.25	1.8
8600	1.69	1.37	2.08
10800	1.87	1.49	2.34
13050	2.04	1.62	2.57
15250	2.2	1.72	2.8
17500	2.33	1.77	3.07
19750	2.44	1.73	3.43
21950	2.52	1.62	3.91
24200	2.56	1.44	4.55
26400	2.57	1.23	5.37
28650	2.55	1.01	6.43
31200	2.47	0.76	8.02

The funnel plot and the Egger test for the effects in the five studies for which we had exposure dose-response data, did not reveal strong publication bias and the bias coefficient in the Egger test was 1.70 (p=0.255).

According to GRADE and the Danish Occupational Medicine Criteria the effect of kneeling at work on knee osteoarthritis is based on moderate quality evidence. That means it is possible but not likely that better quality evidence will change the estimate of the effect.

Squatting and climbing

We could not perform a separate dose response analysis for climbing. Four studies reported more than two exposure categories but none of the studies reported enough information to calculate the exposure dose based on the measure of stairs or meters climbed at work per lifetime.

Only one study reported results for a dose-response analysis for squatting separately [43]. Four other studies (seven study arms) reported the results of the combined exposure to kneeling and squatting and are included in the former analysis about kneeling (see paragraph above). Because there were no studies that measured a dose-response or that could be separated from the kneeling exposure, we refrained from drawing conclusion for squatting only.

Lifting

Three case control studies reported more than two exposure categories for lifting. We performed a dose-response analysis with two studies with four study arms [44 45] . We left out the study that reported the dose as kilogramhours per lifetime for which we could not transform the measure into a reliable dose as kilograms lifted per lifetime [27]. The other study used a measurement unit that included 'sometimes' and tons per life and we could only calculate the exact dose for two out of four exposure categories.

None of the studies showed a clear dose response with incremental OR varying from 0.99 to 1.01.

When applying the Danish Occupational Medicine criteria (DOM) we come to a result of insufficient evidence of a causal association between lifting and knee osteoarthritis. For GRADE we also came to a level of low quality evidence because we could not upgrade the level of evidence based on a dose response relation.

8. Results - Meniscal Lesions

The two studies that measured the effect of kneeling on meniscal lesions were by the same author and had comparable results with a pooled estimate of OR = 2.31 (95% CI 1.55 to 3.45) [32 33].

The same two studies found an effect of squatting (OR = 2.01, 95% CI 1.34 to 3.03), climbing stairs (OR = 2.24, 95% CI 1.56 to 3.22) and lifting (OR = 1.83, 95% CI 1.28 to 2.62).

The studies did not report more than two exposure categories. Therefore, we could not perform a dose-response analysis.

The overall risk of bias for those studies was high (Table 4).

9. Results – Pre-patellar bursitis

We did not find studies for bursitis that fulfilled our minimum inclusion criteria.

10. Results - Quality of the evidence

Danish Occupational Medicine Criteria (DOM)

We considered our findings as moderate evidence for an effect of kneeling on knee osteoarthritis, and a lack of evidence for an effect of lifting because of the small number of studies that could be used and a high risk of bias.

Table 8 Quality of the evidence according to the Danish Occupational Medicine Criteria - for the evidence on the dose-response analysis

	Several	Chance?	Bias?	Confounding	Overall

	studies +				judgement
Knee Osteoarthritis					
Kneeling	yes	unlikely	possible	unlikely	++
Lifting	2 only	unclear	possible	unlikely	0

+++ strong evidence of a causal association

++ moderate evidence of a causal association

+ limited evidence of a causal association

0 insufficient evidence of a causal association

- evidence suggesting lack of a causal association

GRADE

We assessed the quality of the evidence for each exposure and each outcome separately. We only assessed the quality of the evidence for studies that included a dose-response relation because that is the main research question of this review.

The quality assessment according to GRADE is summarized in the tables below. We started off at a low level of quality as these are all observational studies as per GRADE. For kneeling, we downgraded one level because of high risk of bias in the included studies. We upgraded two levels because of a strong dose-response relation and because of an unlikely influence of confounding. This brought us to moderate quality evidence for effect of kneeling at work on knee osteoarthritis risk.

Table 9 Grading of evidence in terms of high, moderate and low

Start: Low Quality	Risk of Bias	Consistency	Directness	Precision	Publication Bias	Downgrading
Knee Osteoarthritis						
Kneeling	High	I^2=0%	Yes	Yes	Not Observed	1 level because of RoB
Lifting	High	Consistent results	Yes	Yes	Not Applicable	1 level because of RoB

Table 10 Grading of evidence in terms of high, moderate and low - overall judgement

	Dose response	Unlikely confounding	Magnitude big	Upgrading	Overall judgement
Knee Osteoarthritis					
Kneeling	Yes	Yes	No	2 levels because of DR and unlikely confounding	Moderate
Lifting	No	Yes	No	1 level because of	Low

				unlikely confounding	

For lifting, there were only two studies that could be combined because of the use of different metrics in the exposure assessment. However, none of the studies showed a clear dose response. Therefore we could not upgrade the level of evidence because of the existence of a dose response relation. This brought us to a level of low quality evidence for the effect of lifting on knee osteoarthritis.

For the other exposures and outcomes, there were no studies that measured a dose-response or that could be separated from the kneeling exposure. We concluded that there was no evidence of a dose response effect on knee osteoarthritis or meniscal lesions

11. Discussion

Summary of the main results

Knee Osteoarthritis

A meta-analysis of 12 case control studies showed a higher risk of developing knee osteoarthritis in workers that are exposed to kneeling or squatting at work compared to workers that are less or not exposed (yes/no) with an OR of 1.70 (95% CI 1.35 to 2.13). All included studies adjusted for at least age and gender but still the risk of bias was considered high for all but one study. One cohort study at high risk of bias found no statistical significant increased risk for workers exposed to kneeling, squatting or crawling versus unexposed workers (OR 0.31, 95 % CI 0.09 to 1.04). The meta-analyses of studies that measured exposure to squatting, climbing, and lifting (yes versus no) resulted in similar risk estimates as for kneeling.

The meta-analysis of studies that evaluated an exposure dose-response relationship for kneeling resulted in an increased risk per unit of exposure increase. Assuming a linear relationship, the OR was 1.26 (95%CI 1.17 to 1.35) per 5000 hours exposure to kneeling or squatting. Assuming a quadratic relationship, there was a similar risk increase of knee osteoarthritis per 5000 hours lifetime exposure to kneeling or squatting. The goodness of fit test showed that the quadratic model fitted the data better. The model showed the maximum risk at around 24500 lifetime hours of kneeling or squatting at work (OR 2.56 95% CI 1.27 to 5.37) after which it decreases. This amount of exposure can refer to several different exposure scenarios. One realistic scenario for 24500 lifetime hours could be eighteen years of kneeling every workday for 4 hours, which occurs in occupations such as floor laying. After eighteen years the risk decreases and is lower than 26%. The tests for publication bias were not significant but this can be due to the small number of studies included in the analysis (N=5).

The exposure dose-response analysis for lifting showed no risk increase per 5000 lifetime hours of lifting at work (OR 1.00, 95% CI 1.00 to 1.01; log-linear model). Studies of exposure to climbing did not provide enough information to calculate the exposure dose.

We judged the evidence for the exposure dose-response for kneeling of moderate quality according to the criteria of the DSOM and GRADE. The quality of the evidence for the exposure to lifting was insufficient according to the DSOM and low according to GRADE. The similarity of the results of the two judgement systems strengthens our findings and conclusions.

There were no differences between subgroups that measured exposure differently or that adjusted for more confounders. A larger effect was visible when the studies were adjusted for BMI and injuries in addition to age and gender. This is however difficult to interpret as the number of studies per subgroup was very small (one to three studies). Subgroup analyses of gender, and year of publication did not show significant differences.

Our results were robust to variation in assumptions because sensitivity analyses for exposure - worst and best case scenarios- did not considerably change the results.

Meniscal lesions

The risk of meniscal lesions due to the exposures to kneeling (OR 2.31, 95% CI 1.55 to 3.45), squatting (OR 2.01, 95% CI 1.34 to 3.03), climbing (OR 2.24, 95% CI 1.56 to 3.22), and lifting (OR 1.83, 95% CI 1.28 to 2.62) resulted in effects similar to those found for osteoarthritis, but this was based on two case-control studies only. There was not enough data to conduct a dose-response analysis.

Bursitis

We did not find any studies that fulfilled our inclusion criteria for bursitis.

Completeness and applicability of the results

Studies included participants from a variety of occupations including both blue and white collar workers. No group clearly stood out and the findings can probably be applied to all occupations. The results apply both to men and women. However the age of the included participants was quite high and it is unclear how well the findings apply to younger workers. It is also unclear if the findings apply to workers outside Europe, as no studies from Africa, America, or Australia, and only two studies from Asia met our inclusion criteria.

Because we included no studies on knee bursitis we don't know if there is an effect of the exposure.

We are confident that the most relevant studies have been identified because we searched multiple databases to locate studies and also translated non English studies as far as possible.

We located one study that could be possibly included but we could not retrieve the full text before the end of the project [47] . For another study, we did not manage the translation from Turkish to English in time. However, we do not think that these studies would have changed our overall conclusions.

Quality of the evidence

We applied strict inclusion criteria in order to find better studies and to exclude studies with unclear exposure. However, even these better quality studies were still considered to be at high risk of bias. All studies relied on self-reports to measure the exposure over a period that had either been many years ago or lasted 35 to 60 years or longer. Recall bias is likely in such situations.

Furthermore, when estimating the effect of a specific exposure, only two studies [27 34] adjusted for other occupational knee straining activities and adjusted e.g. for squatting when estimating the effect of kneeling. This could explain why the results for different knee straining exposures across studies were similar. In future studies, more reliable exposure measurements are needed. This is possible either via observation or with modern measurement instruments like direct instrumented data collection systems for knee angles.

In case control studies, the power to detect an OR that is significantly different from the value of one, depends on the magnitude of the OR and the proportion exposed among the controls. A study with 80% power to detect an OR of 1.5 and with 40% exposed controls would need a sample size of 384 cases and 384 controls. There was only one study that met this sample size requirement. This could be the reason that there was a strong suspicion of publication bias for the analysis of the yes/no exposure to kneeling.

Potential biases in the review process

We prevented language bias by searching for references and including studies irrespective of the language of the publication but most of our studies came from reviews. Primary studies before 2011 were located indirectly through screening the references included in other reviews. This could have caused language bias. However, eight reviews (33%) did not apply any language restrictions or restricted the search to a minimum of three European languages (Table 17, appendix). Therefore, we don't think we have missed important information that could have changed our conclusions.

We prevented reporting bias by including all reports of the same sample as a single study.

A major problem in a dose-response meta-analysis is the assumption about the nature of the relation between the exposure and the risk. We tested not only a linear relationship but also a relation based on splines and one based on a quadratic function. There is no consensus on how to choose the best model. Some use the model with the narrower confidence interval others use a goodness of fit test. We choose the model with the best fit to the data. To our knowledge this is the first time the nature of the relationship has been explored and our findings should be tested in future primary studies.

In the absence of prior evidence, we made certain assumptions to be able to pool the data from various studies and to have still meaningful results. We checked the influence of our assumptions with sensitivity analyses based on a best and a worst-case scenario. Even though there were differences between the two, the direction and magnitude of the effect size remained largely the same.

We excluded studies that only used job titles and no information on kneeling, squatting, climbing, or lifting at work. We also excluded studies that used a job exposure matrix (JEM) because the exposure assessments in these JEMs is based on expert judgement and not on observations or measurements. We do not believe that an expert judgement of exposure to occupational knee straining activities provides more valid results than self-reports. This is also supported by van der Beek en Frings-Dresen in their review of methods to assess exposure in studies of ergonomic epidemiology [48]. It has been argued that self-reports suffer from recall bias because a worker with a knee disease would overestimate the exposure to knee straining activities and that experts' ratings provide a more objective measure of the exposure. To our knowledge, there are no studies available that compared self-reports to experts' ratings for kneeling at work. Therefore, we concluded that studies with a JEM could add valuable results only if the JEM is based on objective measurements and quantifies the exposure. We excluded three studies that used a JEM-like classification system. None of those studies used a JEM based on objective measurements. One study [49] developed a JEM based on subjective measurements from two earlier studies, both of which are included in this review [33 44]. The other two studies used expert ratings to assign an exposure dose category to a job title [50 51]. All three JEM studies found some relation between knee load and knee osteoarthritis but none of them calculated an exposure dose-response. Therefor the exclusion of those studies has not biased the exposure dose-response results of this review.

We only included studies that used physician-diagnosed outcomes, validated scales or radiographs. Some argue that pain would be a better outcome, because those with knee-straining activities at work would be more likely to visit a doctor and have a higher likelihood to become cases. This could artificially increase the risk of disease due to the exposure. However, a visit to the doctor would also occur because of limitations in everyday activities like walking or shopping. Therefore, we don't believe that this would inflate the risk due to occupational activities. Moreover, pain is a non-specific outcome that can have various reasons and does not measure the disease that we are interested in.

We excluded case-control studies that did not use incident cases but compared a group of cases at one moment in time with controls. For knee osteoarthritis, it is unclear how important the use of incident cases is, compared to prevalent cases. Since we had sufficient better quality studies, we do not think that the exclusion of these studies has biased the results of our review.

Comparison with other reviews

We do not know of any other reviews that assessed a dose response relation. Those reviews that assessed the relationship between knee load and knee osteoarthritis, generally came to a positive conclusion. Given the implication of publication bias, these conclusions probably overestimate the real effect because studies with negative findings are missing.

Implications for practice and research

There is moderate quality evidence that every 5000 hours of exposure to kneeling at work increase the risk of knee osteoarthritis with 26%. The effect is significant even for shorter cumulative exposures such as 1900 lifetime hours. This indicates that prevention efforts are warranted in all occupations involving kneeling. Interventions for prevention of the adverse effects of kneeling such as spacing of activities and cushioning of the knee should be evaluated because their preventive effects on knee osteoarthritis, knee bursitis and meniscal lesions are unknown.

There is evidence to suggest a similar risk of meniscal lesions after exposure to kneeling but this is based on only two studies at high risk of bias.

We found no evidence on bursitis. This does not mean that such an effect does not exist, but simply that no studies were found.

It appears that the effect of the exposure does not vary by sex.

In future research that would provide us with better knowledge on kneeling and osteoarthritis than existing studies, researchers should use more objective measurements of kneeling, squatting, climbing and lifting with a longitudinal follow up. When JEMs are to replace direct measurements, these should be validated with direct observations, log data of tasks or production data that include a certain activity, like square-meters/day of floor laid. Novel measurement techniques may allow worksite measurements. This will prevent recall bias and that findings can be applied to the working population. Case control studies should include at least 384 cases and 384 controls.

We still need studies on the effect of kneeling and related exposures on meniscal lesions and bursitis.

12. References

1. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis and rheumatism 2008;**58**(1):26-35 doi: 10.1002/art.23176.
2. Visser AW, de Mutsert R, le Cessie S, et al. The relative contribution of mechanical stress and systemic processes in different types of osteoarthritis: the NEO study. Annals of the rheumatic diseases 2014 doi: 10.1136/annrheumdis-2013-205012.
3. Hiligsmann M, Cooper C, Guillemin F, et al. A reference case for economic evaluations in osteoarthritis: An expert consensus article from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Seminars in arthritis and rheumatism 2014 doi: 10.1016/j.semarthrit.2014.06.005.
4. Gouttebarge V, Inklaar H, Backx F, et al. Prevalence of osteoarthritis in former elite athletes: a systematic overview of the recent literature. Rheumatology international 2014 doi: 10.1007/s00296-014-3093-0. E-pub 2014 Jul 19.
5. McWilliams DF, Leeb BF, Muthuri SG, et al. Occupational risk factors for osteoarthritis of the knee: a meta-analysis. Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society 2011;**19**(7):829-39 doi: 10.1016/j.joca.2011.02.016.
6. Palmer KT. Occupational activities and osteoarthritis of the knee. British Medical Bulletin 2012;**102**:147-70 doi: 10.1093/bmb/lds012.
7. Jensen LK. Knee osteoarthritis: influence of work involving heavy lifting, kneeling, climbing stairs or ladders, or kneeling/squatting combined with heavy lifting. Occupational and Environmental Medicine 2008;**65**(2):72-89 doi: 10.1136/oem.2007.032466. E-pub 2007 Jul 18
8. Jensen LK, Eenberg W. Occupation as a risk factor for knee disorders. Scandinavian Journal of Work, Environment & Health 1996;**22**(3):165-75
9. Sharrard WJ. Pressure effects on the knee in kneeling miners. Annals of the Royal College of Surgeons of England 1965;**36**:309-24.
10. Reid CR, Bush PM, Cummings NH, et al. A review of occupational knee disorders. Journal of Occupational Rehabilitation 2010;**20**(4):489-501. doi: 10.1007/s10926-010-9242-8.
11. Tanaka R, Ozawa J, Kito N, et al. Efficacy of strengthening or aerobic exercise on pain relief in people with knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. Clinical Rehabilitation 2013;**27**(12):1059-71 doi: 10.1177/0269215513488898. Epub 2013 Jul 4.
12. Snoeker BA, Bakker EW, Kegel CA, et al. Risk factors for meniscal tears: a systematic review including meta-analysis. The Journal of Orthopaedic and Sports Physical Therapy 2013;**43**(6):352-67 doi: 10.2519/jospt.2013.4295. Epub 2013 Apr 29
13. Lohmander LS, Englund PM, Dahl LL, et al. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. The American Journal of Sports Medicine 2007;**35**(10):1756-69 doi: 10.1177/0363546507307396. Epub 2007 Aug 29.
14. Papalia R, Del Buono A, Osti L, et al. Meniscectomy as a risk factor for knee osteoarthritis: a systematic review. British medical bulletin 2011;**99**:89-106 doi: 10.1093/bmb/ldq043. Epub 2011 Jan 19.
15. Baumbach SF, Lobo CM, Badyine I, et al. Prepatellar and olecranon bursitis: literature review and development of a treatment algorithm. Archives of Orthopaedic and Trauma Surgery 2014;**134**(3):359-70 doi: 10.1007/s00402-013-1882-7. Epub 2013 Dec 5.
16. Porter WL, Mayton AG, Moore SM. Pressure distribution on the anatomic landmarks of the knee and the effect of kneepads. Applied Ergonomics 2010;42(1):106-13. doi: 10.1016/j.apergo.2010.05.007. Epub 2010 Jun 15.
17. O'Hara BP, Urban, J. P., & Maroudas, A. Influence of cyclic loading on the nutrition of articular cartilage. Annals of the Rheumatic Diseases 1990:49(7), 536–39.

18. Kutzner IH, B.; Graichen, F.; Bender, A.; Rohlmann, A.; Halder A., Beier, A.; Bergmabb G. Loading of the knee joint during activities of daily living measured in vivo in five subjects. Journal of Biomechanics 2010;43(11):2164-73. doi: 10.1016/j.biomech 2010.03.046. .
19. Kivimäki J, Riihimäki H, Hänninen K. Knee disorders in carpet and floor layers and painters. Scandinavian Journal of Work, Environment & Health 1992;18(5):310-16.
20. Jensen LK, Mikkelsen S, Loft I, et al. Work-related knee disorders in floor layers and carpenters. Journal of Occupational and Environmental Medicine 2000;42(8):835–42.
21. Shamliyan T KR, Ansari MT, Raman G, Berkman ND, Grant M, , Janes G MM, Moher D, Nasser M, Robinson KA, Segal JB, Tsouros S. Development of the Quality Criteria To Evaluate Nontherapeutic Studies of Incidence, Prevalence, or Risk Factors of Chronic Diseases: Pilot Study of New Checklists. Methods Research Report AHRQ Publication No 11-EHC008-EF Agency for Healthcare Research and Quality, 2011.
22. Shamliyan TA, Kane RL, Ansari MT, et al. Development quality criteria to evaluate nontherapeutic studies of incidence, prevalence, or risk factors of chronic diseases: pilot study of new checklists. Journal of clinical epidemiology 2011;64(6):637-57. doi: 10.1016/j.jclinepi.2010.08.006. Epub 2010 Nov 11.
23. Greenland S. Chapter 16 Applications of stratified analysis methods. In: Rothman K GS, Lash LT, ed. Modern epidemiology. third ed. Philadelphia, USA: Lippincott Williams and Wilkins, 2008.
24. Greenland S, Lash T. Chapter 19 Bias analysis. In: Rothman K GS, Lash LT, ed. Modern epidemiology. third ed. Philadelphia, USA: Lippincott Williams and Wilkins, 2008.
25. Il'yasova D, Hertz-Picciotto I, Peters U, et al. Choice of exposure scores for categorical regression in meta-analysis: a case study of a common problem. Cancer Causes and Control 2005;16(4):383-8. doi: 10.1007/s10552-004-5025-x.
26. Orsini N, Bellocco R, Greenland S. Generalize least squares for trend estimation of summarized dose-response data. The Stata Journal 2006;**6**(1):40-57
27. Seidler A, Bolm-Audorff U, Abolmaali N, et al. The role of cumulative physical work load in symptomatic knee osteoarthritis - a case-control study in Germany. Journal of Occupational Medicine and Toxicology 2008;3:14. doi: 10.1186/1745-6673-3-14. Epub 2008 Jul 14.
28. Seidler A, Bolm-Audorff U, Abolmaali N, et al. Correction: The role of cumulative physical work load in symptomatic knee osteoarthritis - a case-control study in Germany (Seidler et al. 2008). Journal of Occupational Medicine and Toxicology 2012;7(1):21. doi: 10.1186/1745-6673-7-21. Epub 2012 Oct 10.
29. Vrezas I, Elsner G, Bolm-Audorff U, et al. Case-control study of knee osteoarthritis and lifestyle factors considering their interaction with physical workload. International Archives of Occupational and Environmental Health 2010;83(3):291-300. doi: 10.1007/s00420-009-0486-6.

Int Arch Occup Environ Health (2010) 83:713 DOI 10.1007/s00420-010-0536-0

Erratum to: Case–control study of knee osteoarthritis and lifestyle factors considering their interaction with physical workload. Ilias Vrezas • Gine Elsner • Ulrich Bolm-Audorff • Nasreddin Abolmaali • Andreas Seidler. Published online: 6 May 2010 Springer-Verlag 2010 Erratum to: Int Arch Occup Environ Health (2010) 83:291–300 DOI 10.1007/s00420-009-0486-6.

30. Schouten JS, van den Ouweland FA, Valkenburg HA. A 12 year follow up study in the general population on prognostic factors of cartilage loss in osteoarthritis of the knee. Annals of the Rheumatic diseases 1992;51(8):932-7
31. Zhang W, McWilliams DF, Ingham SL, et al. Nottingham knee osteoarthritis risk prediction models. Annals of the Rheumatic diseases 2011;70(9):1599-604. doi: 10.1136/ard.2011.149807. Epub 2011 May 25.

32. Baker P, Coggon D, Reading I, et al. Sports injury, occupational physical activity, joint laxity, and meniscal damage. The Journal of Rheumatology 2002;29(3):557-63.
33. Baker P, Reading I, Cooper C, et al. Knee disorders in the general population and their relation to occupation. Occupational and Environmental Medicine 2003;60(10):794-7. doi:10.1136/oem.60.10.794.
34. Klussmann A, Gebhardt H, Nubling M, et al. Individual and occupational risk factors for knee osteoarthritis: results of a case-control study in Germany. Arthritis Research & Therapy 2010;12(3):R88. doi: 10.1186/ar3015. Epub 2010 May 14.
35. Cooper C, McAlindon T, Coggon D, et al. Occupational activity and osteoarthritis of the knee. Annals of the Rheumatic Diseases 1994;53(2):90-3.
36. Lau EC, Cooper C, Lam D, et al. Factors associated with osteoarthritis of the hip and knee in Hong Kong Chinese: obesity, joint injury, and occupational activities. American Journal of Epidemiology 2000;152(9):855-62.
37. Mounach A, Nouijai A, Ghozlani I, et al. Risk factors for knee osteoarthritis in Morocco. A case control study. Clinical Rheumatology 2008;27(3):323-6. doi: 10.1007/s10067-007-0709-8. Epub 2007 Aug 16.
38. Yoshimura N, Kinoshita H, Hori N, et al. Risk factors for knee osteoarthritis in Japanese men: a case-control study. Modern Rheumatology 2006;16(1):24-9. doi: 10.1007/s10165-005-0450-6.
39. Yoshimura N, Nishioka S, Kinoshita H, et al. Risk factors for knee osteoarthritis in Japanese women: heavy weight, previous joint injuries, and occupational activities. The Journal of Rheumatology 2004;31(1):157-62.
40. Elsner G, Nienhaus A, Beck W. [Knee joint arthroses and work-related factors]. Sozial- und Praventivmedizin 1996;41(2):98-106.
41. Sahlstrom A, Montgomery F. Risk analysis of occupational factors influencing the development of arthrosis of the knee. European Journal of Epidemiology 1997;13(6):675-9.
42. Sandmark H, Hogstedt C, Vingard E. Primary osteoarthrosis of the knee in men and women as a result of lifelong physical load from work. Scandinavian Journal of Work, Environment & Health 2000;26(1):20-5.
43. Dawson J, Juszczak E, Thorogood M, et al. An investigation of risk factors for symptomatic osteoarthritis of the knee in women using a life course approach. Journal of Epidemiology and Community Health 2003;**57**(10):823-30
44. Coggon D, Croft P, Kellingray S, et al. Occupational physical activities and osteoarthritis of the knee. Arthritis and Rheumatism 2000;43(7):1443-9. doi: 10.1002/1529-0131(200007)43:7<1443::aid-anr5>3.0.co;2-1.
45. Manninen P, Heliovaara M, Riihimaki H, et al. Physical workload and the risk of severe knee osteoarthritis. Scandinavian Journal of Work, Environment & Health 2002;28(1):25-32. doi:10.5271/sjweh.643.
46. Sandmark H. Musculoskeletal dysfunction in physical education teachers. Occupational and Environmental Medicine 2000;57(10):673-7. doi:10.1136/oem.57.10.673.
47. Liu Q, Niu J, Ke Y, et al. Natural history and risk factors of radiographic knee osteoarthritis: Wuchuan osteoarthritis study. Osteoarthritis and Cartilage 2015;**23**:A183
48. van der Beek AJ, Frings-Dresen MH. Assessment of mechanical exposure in ergonomic epidemiology. Occupational and Environmental Medicine 1998;**55**(5):291-9
49. Martin KR, Kuh D, Harris TB, et al. Body mass index, occupational activity, and leisure-time physical activity: an exploration of risk factors and modifiers for knee osteoarthritis in the 1946 British birth cohort. BMC Musculoskeletal Disorders 2013;**14**:219 doi: 10.1186/1471-2474-14-219.
50. Felson DT, Hannan MT, Naimark A, et al. Occupational physical demands, knee bending, and knee osteoarthritis: results from the Framingham Study. The Journal of Rheumatology 1991;**18**(10):1587-92.

51. Riyazi N, Rosendaal FR, Slagboom E, et al. Risk factors in familial osteoarthritis: the GARP sibling study. Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society 2008;**16**(6):654-9 doi: 10.1016/j.joca.2007.10.012.
52. Aghili MM, Asilian H, Poursafa P. Evaluation of musculoskeletal disorders in sewing machine operators of a shoe manufacturing factory in Iran. JPMA The Journal of the Pakistan Medical Association 2012;**62**(3 Suppl 2):S20-5
53. Allen KD, Chen JC, Callahan LF, et al. Racial differences in knee osteoarthritis pain: potential contribution of occupational and household tasks. The Journal of Rheumatology 2012;**39**(2):337-44 doi: 10.3899/jrheum.110040.
54. Apold H, Meyer HE, Nordsletten L, et al. Risk factors for knee replacement due to primary osteoarthritis, a population based, prospective cohort study of 315,495 individuals. BMC Musculoskeletal Disorders 2014;**15**:217 doi: 10.1186/1471-2474-15-217.
55. Bieleman HJ, Reneman MF, Drossaers-Bakker KW, et al. Prognostic factors for sustained work participation in early osteoarthritis: a follow-up study in the Cohort Hip and Cohort Knee (CHECK). Journal of Occupational Rehabilitation 2013;**23**(1):74-81 doi: 10.1007/s10926-012-9384-y.
56. Bieleman A. The 5 year course of physical work capacity in people with early OA: A longitudinal study in the check cohort. Annals of the Rheumatic Diseases 2013;**72**
57. Chen JC, Linnan L, Callahan LF, et al. Workplace policies and prevalence of knee osteoarthritis: the Johnston County Osteoarthritis Project. Occupational and Environmental Medicine 2007;**64**(12):798-805 doi: 10.1136/oem.2006.030148.
58. Cheng Y, Macera CA, Davis DR, et al. Physical activity and self-reported, physician-diagnosed osteoarthritis: is physical activity a risk factor? J Clin Epidemiol 2000;**53**(3):315-22
59. Cooper C, Snow S, McAlindon TE, et al. Risk factors for the incidence and progression of radiographic knee osteoarthritis. Arthritis and Rheumatism 2000;**43**(5):995-1000 doi: 10.1002/1529-0131(200005)43:5<995::aid-anr6>3.0.co;2-1.
60. D'Souza JC, Werner RA, Keyserling WM, et al. Analysis of the Third National Health and Nutrition Examination Survey (NHANES III) using expert ratings of job categories. American Journal of Industrial Medicine 2008;**51**(1):37-46 doi: 10.1002/ajim.20512.
61. Du H, Chen SL, Bao CD, et al. Prevalence and risk factors of knee osteoarthritis in Huang-Pu District, Shanghai, China. Rheumatology International 2005;**25**(8):585-90 doi: 10.1007/s00296-004-0492-7.
62. Enderlein G, Kasch J. [Modeling of dose-response relations in exposure-related changes of the locomotor system]. Zeitschrift fur die gesamte Hygiene und ihre Grenzgebiete 1989;**35**(4):215-8
63. Ezzat AM, Cibere J, Koehoorn M, et al. Cumulative occupational physical load as risk factor for knee osteoarthritis. Arthritis and Rheumatism 2012;**64**:S473-S74
64. Gholami J, Mansournia MA, Davatchi F, et al. Are daily physical activities risk factors for knee osteoarthritis? International Journal of Rheumatic Diseases 2015 doi: 10.1111/1756-185x.12604.
65. Hart DJ, Doyle DV, Spector TD. Incidence and risk factors for radiographic knee osteoarthritis in middle-aged women: the Chingford Study. Arthritis and Rheumatism 1999;**42**(1):17-24 doi: 10.1002/1529-0131(199901)42:1<17::aid-anr2>3.0.co;2-e.
66. Herquelot E, Bodin J, Petit A, et al. Incidence of Chronic and Other Knee Pain in Relation to Occupational Risk Factors in a Large Working Population. The Annals of Occupational Hygiene 2015 doi: 10.1093/annhyg/mev010.
67. Hwang BY, Kim SJ, Lee SC, et al. Risk factors for medial meniscus posterior root tears. Arthroscopy - Journal of Arthroscopic and Related Surgery 2012;**28**(6):e19-e20
68. Ingham SL, Zhang W, Doherty SA, et al. Incident knee pain in the Nottingham community: a 12-year retrospective cohort study. Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society 2011;**19**(7):847-52 doi: 10.1016/j.joca.2011.03.012.

69. Jacobs JJ, Jevsevar DS, Brown GA, et al. AAOS Osteoarthritis Guideline: transparency and credibility. Arthroscopy : the Journal of Arthroscopic & Related Surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association 2014;**30**(6):656-8 doi: 10.1016/j.arthro.2014.03.002.
70. Jones GT, Harkness EF, Nahit ES, et al. Predicting the onset of knee pain: results from a 2-year prospective study of new workers. Annals of the Rheumatic Diseases 2007;**66**(3):400-6 doi: 10.1136/ard.2006.057570.
71. Jonsson H, Olafsdottir S, Sigurdardottir S, et al. Incidence and prevalence of total joint replacements due to osteoarthritis in the elderly: Risk factors and factors associated with late life prevalence. The AGES-Reykjavik study. Osteoarthritis and Cartilage 2015;**23**:A189
72. Kohatsu ND, Schurman DJ. Risk factors for the development of osteoarthrosis of the knee. Clinical Orthopaedics and Related Research 1990(261):242-6
73. Le Manac'h AP, Ha C, Descatha A, et al. Prevalence of knee bursitis in the workforce. Occupational Medicine (Oxford, England) 2012;**62**(8):658-60 doi: 10.1093/occmed/kqs113.
74. Muraki S, Oka H, Akune T, et al. Association of occupational activity with joint space narrowing and osteophytosis in the medial compartment of the knee: the ROAD study (OAC5914R2). Osteoarthritis and Cartilage 2011
75. Namali H, Fonseka P, Gunathilake N. Risk factors for knee osteoarthritis in community dwelling older adults in Sri Lanka. Internal Medicine Journal 2011;**41**:38
76. Ratzlaff CR, Koehoorn M, Cibere J, et al. Is lifelong knee joint force from work, home, and sport related to knee osteoarthritis? International Journal of Rheumatology 2012;**2012**:584193 doi: 10.1155/2012/584193.
77. Sigurdardottir S, Olafsdottir S, Aspelund T, et al. Total joint replacement due to osteoarthritis: The effect of occupational history, education and physical activity. the ages-reykjavik study. Osteoarthritis and Cartilage 2013;**21**:S164
78. Toivanen AT, Heliovaara M, Impivaara O, et al. Obesity, physically demanding work and traumatic knee injury are major risk factors for knee osteoarthritis--a population-based study with a follow-up of 22 years. Rheumatology (Oxford, England) 2010;**49**(2):308-14 doi: 10.1093/rheumatology/kep388.
79. Eva V, Lars A, Evy F, et al. Disability pensions due to musculo-skeletal disorders among men in heavy occupations. A case-control study. Scandinavian Journal of Social Medicine 1992;**20**(1):31-6
80. Nauwald G. [Incidence of occupational knee joint diseases in elderly pipe-fitters in the ship-building industry]. Beitrage zur Orthopadie und Traumatologie 1986;**33**(3):124-8

13. Appendix

Table 11 Definition of lowest and highest exposure categories as described by study authors, including all studies and outcomes per type of exposure

Kneeling including: kneeling (K), kneeling or squatting (K or S) and squatting or kneeling or crawling (K or S or Cr)						
Studies on meniscal lesions, case control studies						
Study ID	**Exposure type**	**Measurement unit**	**No exposure / lowest exposure category**	**Exposure / highest exposure category**	**Measurement period**	**Comments**
Baker 2002b	K	hrs/day	<1h in total per day	>1h in total per day	average working day in the job at the time the cases symptoms begun	
Baker 2003m	K	hrs/day	<1h in total per day	>1h in total per day	average working day in the job at the birthday preceding the onset of the cases symptoms	
Studies on knee osteoarthritis, case control studies						
Study ID	**Exposure type**	**Measurement unit**	**No exposure / lowest exposure category**	**Exposure / highest exposure category**	**Measurement period**	**Comments**
Coggon 2000f, Coggon 2000m	K or S	hrs/day	>1hr per day in total for less than 1yr	>1hr per day in total for 20 or more yrs	lifetime	

Cooper 1994b	K	min per day	<30min per day	>30min per day	average working day during paid job longest hold	
Dawson2003f	K	years working	<15yrs spent doing work that involved kneeling	>=26yrs spent doing work that involved kneeling	lifetime	
Elsner 1996f, Elsner 1996m	K	yes or no / lifetime	rarely or almost never over entire work lifetime or no information given	almost always or often over entire work lifetime	lifetime	
Klusmann2010f	K or S	cumulative hours / life housework	no	>8,934 hrs/life	lifetime	post-assessment
Klusmann 2010m	K or S	cumulative hours / life housework	no	>12244 hrs per life	lifetime	post-assessment
Lau 2000f, Lau 2000m	K	hrs/day	<1 hr/day during the main job	>=1 hr/day during the main job	average working day during paid job longest hold before the onset of cases symptoms	
Manninen 2002f, Manninen 2002m	K or S	cumulative hrs/average workday, choices were "not at all", "less than 2 hours", "from 2 to 4 hours", and "more than 4 hours" a day	not at all	“from 2 to 4 hours” and “more than 4 hours per day’’	average working day until age 49	
Mounach 2008b	K	hrs/day	<1h/day during average working week	>=1h/day during average working week	average working day during the entire lifetime	
Sandmark 2000f, Sandmark 2000m	K	min/work life	no or low (0 min)	high (170–1264 min)	lifelong sum (minutes) of average working days during the period 15 to 50 years of age	post-assessment, N of exposed controls per categpry n.r. (OR in meta-analysis)
Seidler 2008m	K or S	total hrs kneeling	no	>= 10.800 hrs/life	lifetime	post-assessment
Yoshimura 2004f	K	hrs/day	<1hr/day	>=1hrs/day	average working day during job longest hold	
Yoshimura 2006m	K	hrs/day	<1 hr/day	≥ 1 hrs/day	average working day during job longest hold	Results n.r.

Studies on knee osteoarthritis, cohort studies

Study ID	**Exposure type**	**Measurement unit**	**No exposure / lowest exposure category**	**Exposure / highest exposure category**	**Measurement period**	**Comments**
Schouten 1992	K or S or Cr	n.r.	low	high	lifetime	post-assesment, N of participants per exposure category n.r., one study only

						(no meta/analysis)
Squatting including: squatting (S) and squatting or knee bending (S or Kb)						
Studies on meniscal lesions, case control studies						
Study ID	**Exposure type**	**Measurement unit**	**No exposure / lowest exposure category**	**Exposure / highest exposure category**	**Measurement period**	**Comments**
Baker 2002b	S	total hrs/day	<1h in total per day	>1h in total per day	average working day in the job at the time the cases symptoms begun	
Baker 2003m	S	**hrs/day**	<1h in total per day	>1h in total per day	**average working day in the job at the birthday preceding the onset of the case symptoms**	
Studies on knee osteoarthritis, case control studies						
Study ID	**Exposure type**	**Measurement unit**	**No exposure / lowest exposure category**	**Exposure / highest exposure category**	**Measurement period**	**Comments**
Cooper 1994b	S	min/day	<30min per day	>30min per day	average working day during paid job longest hold	
Dawson2003	S	total numbers of yrs	<15yrs doing work that involved kneeling	>=27yrs doing work that involved squatting	lifetime	
Elsner 1996f, Elsner 1996m	S	yes = almost always or often; no = rarely or almost never or no answer	rarely or almost never over entire work lifetime or no information given	almost always or often over entire work lifetime	lifetime	
Lau 2000f, Lau2000m	S	hrs/day	<1hr/day during main job	>=1hr/day during main job	average working day during paid job longest hold before the onset of case symptoms	
Mounach 2008b	S	yes or no / week	?	?	average working week during the entire lifetime	Results n.r.
Sandmark 2000f, Sandmark 2000m	S or Kb	N/life	Females: 0-2 N; Males: 0 N	Females: 59-236 N; Males: 70-312 N	lifelong sum (N) of average working days during the period 15 to 50 years of age	Post-assessment, N of exposed controls per category n.r. (OR in meta-analysis)
Yoshimura 2004f	S	hrs/day	<1hr/day	>=1hrs/day	average working day during job longest hold	
Yoshimura 2006m	S	hrs/day	<1 hr/day	≥ 1 hr/day	average working day during job longest hold	Results n.r.

Climbing including climbing (C), climbing stairs (Cst), and climbing ladders, stairs or flights (Cl,st,fl)

Studies on meniscal lesions, case control studies

Study ID	Exposure type	Measurement unit	No exposure / lowest exposure category	Exposure / highest exposure category	Measurement period	Comments
Baker 2002b	Cst	flights/day	<30 flights of stairs per day	>30 flights of stairs per day	average working day in the job at the time the case symptoms begun	
Baker 2003m	Cst	flights/day	<30 flights of stairs per day	>30 flights of stairs per day	average working day in the job at the birthday preceding the onset of the case symptoms	

Studies on knee osteoarthritis, case control studies

Study ID	Exposure type	Measurement unit	No exposure / lowest exposure category	Exposure / highest exposure category	Measurement period	Comments
Coggon 2000f, Coggon 2000m	Cl,st,fl	frequency/workday * yrs working	>30 times/day for less than 1yr	>30 times/day for 20 or more yrs	lifetime	
Cooper 1994b	Cst	flights/workday	<10 flights per day	>10 flights per day	average working day during paid job longest hold	
Klusmann2010f, Klusmann2010m	Cst	n.r.	n.r.	n.r.	lifetime	Results n.r. (“No correlation found“)
Lau2000f, Lau2000m	Cst	flights/workday	<15 flights/day during main job	>=15 flights/day during main job	average working day during paid job longest hold before the onset of cases symptoms	
Manninen2002f, Manninen2002m	C	n.r.	not at all or very little	much	until age 49	
Mounach 2008b	Cst	yes or no/work week	<50 steps/day during average working week	>=50 steps/day during average working week	average working week during the entire lifetime	
Sandmark 2000	Cst	Steps/work life	no or low	high	lifelong sum of average working days during the period 15 to 50 years of age	Post-assessment, N of controls per category n.r. (OR used in meta-analysis)
Yoshimura 2004f	Cst	steps/work day	<30 steps/day	>=30 steps/day	average working day during job longest hold	
Yoshimura2006m	Cst	steps/work day	<30 steps/day	≥ 30 steps/day	average working day during job longest hold	Results n.r.

Lifting including: lifting (L), heavy lifting (HL) and lifting or carrying (L or Ca)

Studies on meniscal lesions, case control studies

Study ID	Exposure type	Measurement unit	No exposure / lowest exposure category	Exposure / highest exposure category	Measurement period	Comments
Baker 2002b	L or Ca	kg*frequency/work week	3 exposure types: <10+kg or < 10 times per week; <20+kg or < 10 times per week; <50+kg or < 10 times per week	3 exposure types: 10+kg > 10 times per week; 20+kg > 10 times per week; 50+kg > 10 times per week	average working week in the job at the time the cases symptoms begun	We used the comparison with the no-exposure category that was closest to zero (10+kg) for the meta-analysis.
Baker 2003m	L or Ca	kg*frequency/work week	2 exposure types: <10+kg or < 10 times per week; <20+kg or < 10 times per week	2 exposure types: 10+kg > 10 times per week; 20+kg > 10 times per week	average working week in the job at the birthday preceding the onset of the cases symptoms	We used the comparison with the no-exposure category that was closest to zero (10+kg) for the meta-analysis.

Studies on knee osteoarthritis, case control studies

Study ID	Exposure type	Measurement unit	No exposure / lowest exposure category	Exposure / highest exposure category	Measurement period	Comments
Coggon 2000f, Coggon2000m	L	kg/life (kg*frequency per work week / yrs working)	>= 25kg >10 times/week less than 1 yr	>= 25kg >10 times/week for 20 or more yrs	lifetime	
Cooper 1994	HL	kg/work day	<25kg per day	>25kg per day	average working day during paid job longest hold	
Dawson2003	L	total numbers of yrs working	<24yrs spent doing work that involved lifting	>33yrs spent doing work that involved lifting	lifetime	
Elsner 1996f, Elsner 1996m	HL	yes or no / work lifetime; (yes = almost always or often, no = rarely or almost never or no answer)	3 exposure types: no lifting 5-20kg; no lifting >20kg; no lifting heavy tools	3 exposure types: yes lifting 5-20kg; yes lifting >20kg; yes lifting heavy tools	lifetime	We used the comparison with the no-exposure category that was closest to zero (5-20kg) for the meta-analysis.
Klusmann 2010f	L or Ca	tons/work life	No	≥1,088 tons/life	lifetime	Post-assessment
Klusmann 2010m	L or Ca	tons/work life	No	≥2.214 tons/life	lifetime	Post-assessment, results n.r. (no correlation found)
Lau2000f, Lau 2000m	L	kg * frequency/work week	2 exposure types: <10 kg , <50kg	2 exposure types: >10kg >10times/week; >50kg >10 times/week	average working week during paid job longest hold before the onset of cases symptoms	We used the comparison with the no-exposure category that was closest to zero (>10kg) for the meta-analysis.
Manninen 2002f, Manninen 2002m	L	Kg/work life (mean weight times number of lifts per day	low (no regular lifting),	high (≥100000kg)	lifelong sum of average working days until age 49	Post-assessment

		times lifelong sum of working days, for each occupation)				
Mounach 2008	HL	Yes or no / work week	lifting weights <25kg/week	lifting weights >25kg/week	average working week during the entire lifetime	
Sandmark 2000f, Sandmark 2000m	L	Kg/work life (kg times frequency per average working day times sum of working days)	no or low (exact doses not reported)	high (exact doses not reported)	15 to 50 yrs of age	Post-assessment, N of controls per category n.r. (OR used in meta-analysis)
Seidler 2008m	L or Ca	Kilogramhours (lifted kg at work times 2.5 s per lifting act, carried kg at work times 1 s per meter carried)	no lifting or carrying	>=37.000 kilogramhours/ life	lifetime	
Yoshimura 2004f	HL	kg*frequency / work week	<25kg or ≤1 time/week	>25kg > 1 time/week	average working week during job longest hold	
Yoshimura2006m	L	Yes or No /work week	<25kg≤1 time/week	>25kg ≥ 1 time/week	average working week during job longest hold	Results n.r.
Studies on knee osteoarthritis, cohort studies						
Study ID	**Exposure type**	**Measurement unit**	**No exposure / lowest exposure category**	**Exposure / highest exposure category**	**Measurement period**	**Comments**
Schouten 1992	HL	n.r.	low (no definition)	high (no definition)	lifetime	One study only, no meta-analysis
Other exposure combinations including Lifting or climbing ladders or stairs (L or CL,st) and kneeling or lifting (K or L)						
Studies on knee osteoarthritis, case control studies						
Study ID	**Exposure type**	**Measurement unit**	**No exposure / lowest exposure category**	**Exposure / highest exposure category**	**Measurement period**	**Comments**
Sahlström 1997	Knee moment	kg per ? (n.r.)	Light knee moment = sitting, walking, carrying	Medium and heavy knee moment: Medium = work including weight-bearing knee bending (lifting with bend knees, climbing stairs or ladders with/without carrying objects); Heavy = activities with additional jumping with/without carrying objects (activities are: sitting, walking,	Over 3 age periods of 15 yrs each (25-39, 40-54 and 55-70 yrs)	one study only, no meta-analysis

				carrying, lifting with bend knees and carrying, climbing stairs and ladders)		
Studies on knee osteoarthritis, cohort studies						
Study ID	**Exposure type**	**Measurement unit**	**No exposure / lowest exposure category**	**Exposure / highest exposure category**	**Measurement period**	**Comments**
Zhang 2011	K or L	0=never, 1=seldom, 2=sometimes, 3=often, 4=always at work	never	always	12 yrs	one study only, no meta-analysis

Post-assessment = Study authors divided the exposure into dose categories based on the reported exposure values from participants; OR = odds ratio; n.r. = not reported by study authors, N = number, yrs = years

Table 12 Risk of bias assessment empty form

Domain	Sub-domain	Low=	High=	Unclear=
1) Funding and conflict of interest	Risk of bias due to funding source of study:	no industry involved (Grant/ not-for-profit sponsors)	Industry involved (one or more corporate sponsors)	Not reported
	Risk due to role of funding organization in data analysis and interpretations of the results:	low = study was clearly not affected by sponsors	high = Sponsoring organization participated in data analyses	Not reported
	Risk due to conflict of interest	Reported not having conflict of interest or clear from report/ communication that study not affected by author(s) affiliation	conflict of interest exists (at least one author)	Disclosure not reported
2) Adequate diagnosis of Outcome	Source of outcome data	diagnosed for the purpose of the study OR diagnosis from medical records	diagnosis obtained from administrative databases	not reported
	Severity, degree of the symptoms of the condition	assessed with validated questionnaires, scales or imaging techniques	non-validated questionnaire, scales or imaging techniques	measurement methods not reported
	Validation of outcome measurements	diagnosis made by physician or imaging technique	self-reports	No information about validation
3) Adequate ascertainment of Exposure	Definition of the exposure - general	defined as the following activities: climbing stairs or ladders, working in kneeling or squatted positions, or lifting weights	authors define the exposure as work task not the activity itself OR	knee load is not defined in report (knee load is used as a term without elaboration on what it stands for in the study)

	Definition of the exposure - length of exposure	exposure length or weight(lifting) included in definition and justified (according to consensus/ guidelines) for two out of three dimensions: the episode, day, working life	exposure length or weight(lifting) not included in definition OR arbitrary threshold (no consensus/guideline) AND/OR does include only one of three dimensions: episode, day, working life	knee load is not defined in report (knee load is used as a term without elaboration on what it stands for in the study)
	Measure the exposure - Intensity/dose of exposure	measured as: - cumulative hours on the knees or in squatted position - the cumulative distance climbed on stairs or ladders (as number of steps or meters) - the weight of the object and the cumulative distance lifted either total amount (3,5 hours) or in categories (<2, >2 -<4, >4 hrs)	measured as time in certain work tasks (e.g. 3hr floor laying) OR exposed yes/no categories	unclear risk Intensity/dose assessment is not reported
	Source to measure exposure	data collected for study	data from other sources e.g. archives	

	Measurement methods used for exposure assessment	observations OR combined observations and self-reports	only self-reports	not reported
	Masking of investigators	Assessors were blind to exposure status in cohort studies and to case status in case control studies	not blinded	not reported
	Reliability of exposure estimates- For prospective studies	sufficient inter observer reliability values reported or reference to study showing reliability values	Inter observer reliability not reported	
	Reliability - For case-control studies	The authors used same methods for cases and controls to measure exposure	The authors used different methods to measure exposure in cases and controls	not reported if the same methods were used to measure exposure in cases and controls
4) Confounding factors	Confounding factors that can modify the association between the exposure and **Osteoarthritis/ meniscal lesion**	adjusted for at least three of the following four: age, gender, injuries, obesity (BMI)	adjusted for less then three out of the following four: age, gender, injuries, BMI	not reported
	Confounding factors that can modify the association between the exposure and **Bursitis**	adjusted for obesity (BMI)	not adjusted for obesity (BMI)	not reported
	Measuring of confounding factors	Confounders measured with valid methods like questionaire, objective measures, using archive data	Non-valid methods to measure confounding factors (e.g. BMI via observation)	not reported
5) Attrition bias	Cohort studies - Loss of follow-up	Loss to follow up below 20% in total and not different between the two groups (up to 10%	Total loss to follow up is larger than acceptable (20% or more) OR drop out differs between the groups	not reported

		difference)	by more than 10% OR the reasons for drop out are different for exposed and non-exposed groups	
	Case-control studies - Non response	% non-response was reported for both cases and controls and did not differ	% of nonresponse differed > 10% among cases and controls OR % of nonresponse reported for cases only OR reasons for non-response not reported/ different between cases and controls	not reported
6) Analysis of the study	Analysis of the study - Methods to reduce research specific bias	Authors reported more than one method to reduce bias (standardization, matching, adjustment in multivariate model, stratification, propensity scoring)	Authors did not use methods to reduce bias OR did not justify their choice of statistical models to reduce research specific bias OR Authors attempted to reduce bias in post hoc statistical adjustment	Strategies/ statistical methods to reduce research specific bias not reported
	Dose response analysis	Dose response assessed in analysis	Not assessed (no/yes exposure categories)	not reported
	Reporting of the tested hypothesis	Adjusted estimates presented for all hypothesis tested as per aims	Incomplete/ selective reporting of the tested hypotheses (compared to aim and objectives) AND/OR Crude estimates presented only	Unclear reporting of tested hypothesis
	Precision of the estimates	Estimate value reported with p value and confidence interval	Numeric value of estimates not reported (only p value or significance/non-	Mean only reported without p value or variance (poor reporting)

			significance) (risk of selective reporting)	
	Sample size justification	well justified (calculation)	Justification by authors is incomplete or inaccurate or done as Post-hoc analyses	not reported
Risk of bias per category	1) Funding and conflict of interest		at least one item is high risk of bias	
	2) Adequate diagnosis of Outcome		at least one out of three items is high risk of bias	
	3) Adequate ascertainment of Exposure		as soon as three out of seven items is high risk of bias	
	4) Confounding factors		one out of two items is high risk of bias	
	5) Attrition bias		one out of two items is high risk of bias	
	6) Analysis of the study		as soon as three out of five items is high risk of bias	
Overall risk of bias per study	all six categories		at least one of category 2)-6) is high risk of bias	

Table 13 Risk of bias assessment per study (?=unclear, na=not applicable)

Study ID / RoB Sub-domains	*Baker 2002*	*Baker 2003*	*Coggon 2000*	*Cooper 1994*	*Elsner 1996*	*Lau 2000*	*Manninen 2002*	*Seidler 2008*	*Sandmark 2000*	*Klussmann 2010*	*Mounach 2008*	*Dawson 2003*	*Sahlström 1997*	*Schouten 1992*	*Yoshimura 2004*	*Yoshimura 2006*	*Zhang 2011*
funding source of study:	?	low	low	low	low	low	?	high	low	low	?	low	low	low	low	low	low
role of funding organization in data analysis and interpretations of the results:	?	low	?	low	?	low	?	low	low	low	?	low	low	?	?	?	?
conflict of interest	?	?	?	?	?	low	?	low	?	low	?	?	?	?	?	?	low
Source of outcome data	low	low	low	low	low	low	?	low	low	low	low	low	low	low	?	?	low
Severity, degree of the symptoms of the condition	low	low	low							low	na	high for cases, low for controls	n.a.	low	n.a.	?	low
Validation of outcome measuremen	high	low	low	low	high	high	?	low	high	low	high	high for cases,	low	low	?	?	low

ts												low for controls					
Definition of the exposure - general	low	low	low	low	low	low	low	low	low	low	low	low	?	low	low	low	low
Definition of he exposure - length of exposure	low	low	low	low	high	low	low	low	low	low	low	high	?	high	low	low	high
Measure the exposure - Intensity/dose of exposure	low	low	high	high	high	low	low	low	low	low, except for climbing stairs = high	high	high	?	?	high	high	high
Source to measure exposure	low	low	low	low	low	low	low	low	low	low	low	low	low	low	low	low	low
Measurement methods used for exposure assessment	high	high	high	high	high	high	high	high	high	high	high	high	high	high	high	high	high
Masking of investigators	?	?	?	low	?	?	?	?	?	high	?	?	low	?	?	?	?

Reliability of exposure estimates- prospective studies	na	na	na	na	na	na	na	na	na	na	na	na	na	high	na	na	high
Reliability - case-control studies	low	low	?	low	low	low	low	low	low	low	low	low	low	na	low	low	na
Confounding factors **Osteoarthritis/ meniscal lesion**	na	na	low	low	high	High (k, s, L 50kg+) Low (c, L>10kg)	low	low	low	low	low	high	?	low	high	?	low
Confounding factors **Bursitis**	low	high	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na
Measuring of confounding factors	low	low	low	low	low	low	low	low	low	low	low	low	low	low	low	low	low
Cohort studies - Loss of follow-up	na	na	na	na	na	na	na	na	na	na	n.a.	na	na	high	na	na	high
Case-control studies - Non response	high	?	low	high	high	?	high	low	low	low	?	high	low	na	high	high	n.a.
Analysis of the study - Methods to reduce research specific bias	low	low	low	low	low	High: K, S / Low: Cl and L 10kg	low	low	high	low	high	low	high (logistic regression only)	low	high	?	?

Dose response analysis	high	high	low	high	high	High: Cl, K, S / Low: L	low	low	high	low	high	low	high	low	high	?	?
Reporting of the tested hypothesis	high	low	low	low	low	high	low	low	low	high	high	low	high	low	low	high	high
Precision of the estimates	low	low	low	low	low	low	low	low	high	low	low	low	low	low	low	?	low
Sample size justification	?	?	?	?	?	high	?	low	?	low	?	high	?	?	?	?	high
1) Funding and conflict of interest	?	high	low	high	high	low	?	high	?	low	high	?	high	?	?	?	?
2) Adequate diagnosis of Outcome	high	low	low	low	high	high	?	low	high	low	high	high	low	low	?	?	low
3) Adequate ascertainment of Exposure	low	low	high	low	high	low	low	low	low	high	high	high	high	high	high	high	high
4) Confounding factors	low	high	low	low	high	high	low	low	low	low	low	high	high	low		?	low
5) Attrition bias	high	high	low	high	high	high	high	low	low	low	high	high	low	high	high	high	high
6) Analysis of the study	high	low	low	low	low	high	low	low	high	low	high	low	high	low	high	high	?
all six categories	high	high	high	high	high	high	high	low	high	high	high	high	high	high	high	high	high

Table 14 Degree of evidence of a causal association between an exposure to a specific risk factor and a specific outcome (Danish Occupational Medicine Association Approach)

The following categories are used.	Description of categories:	Comments:
+++ strong evidence of a causal association	A causal relationship is very likely. A positive relationship between exposure to the risk factor and the outcome has been observed in several epidemiological studies. It can be ruled out with reasonable confidence that this relationship is explained by chance, bias or confounding.	The classification does not include a category for which a causal relation is considered as established beyond any doubt. The key criterion is the epidemiological evidence. The likelihood that chance, bias and confounding may explain observed associations are criteria that encompass criteria such as consistency, number of 'high quality' studies, types of design etc. Biological plausibility and contributory information may add to the evidence of a causal association.
++ moderate evidence of a causal association	A causal relationship is likely. A positive relationship between exposure to the risk factor and the outcome has been observed in several epidemiological studies. It cannot be ruled out with reasonable confidence that this relationship can be explained by chance, bias or confounding, although this is not a very likely explanation.	
+ limited evidence of a causal association	A causal relationship is possible. A positive relationship between exposure to the risk factor and the outcome has been observed in several epidemiological studies. It is not unlikely that this relationship can be explained by chance, bias or confounding.	
0 insufficient evidence of a causal association	The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of a causal association.	
- evidence suggesting lack of a causal association	Several studies of sufficient quality, consistency and statistical power indicate that the specific risk factor is not causally related to the specific outcome.	

Figure 5 Flow chart

INSERT FLOW CHART

Table 15 Systematic search strategy for reviews

I. Search for reviews	
PubMed: 03.05.2015	
#1	"workload"[MeSH Terms] OR "workload"[All Fields] OR ("work"[All Fields] AND "load"[All Fields]) OR "work load"[All Fields]
#2	"physical"[All Fields] OR kneeling[All Fields] OR kneel*[tw] OR squatting[All Fields] OR squatt*[tw] OR crawling[All Fields] OR crawl*[tw] OR lifting[Mesh Terms] OR lifting[All Fields] OR lift*[tw] OR ladders[All Fields] OR stairs[All Fields]
#3	miner*[tw] OR Millwright*[tw] OR industr*[tw] OR (oil[All Fields] AND ("Rig"[Journal] OR "rig"[All Fields])) OR pick*[tw] OR boilermaker*[tw] OR installer*[tw] OR landscaper*[tw] OR pipefitter*[tw] OR migrant*[tw] OR "mechanics"[MeSH Terms] OR "mechanics"[tw] OR (("motor vehicles"[MeSH Terms] OR ("motor"[tw] AND "vehicles"[tw]) OR "motor vehicles"[tw] OR "truck"[tw]) AND driver*[tw]) OR (refinery[tw] AND operator[tw]) OR machine*[tw] OR electric*[tw] OR repair*[tw] OR farm*[tw] OR "maintenance"[MeSH Terms] OR "maintenance"[tw] OR "wood"[MeSH Terms] OR "wood"[tw] OR concrete[tw] OR (brick*[tw] AND (layer[tw] OR mason[tw])) OR plumber*[tw] OR "asphalt"[Supplementary Concept] OR "asphalt"[tw] OR rock*[tw] OR (Sheet[tw] AND ("metals"[MeSH Terms] OR "metals"[tw] OR "metal"[tw])) OR Seam*[tw] OR fisherm*[tw] OR waitress*[tw] OR construct*[tw] OR "floors and floorcoverings"[MeSH Terms] OR ("floors"[tw] AND "floorcoverings"[tw]) OR "floors and floorcoverings"[tw] OR (floor*[tw] AND lay*[tw])
#4	"work"[MeSH Terms] OR "work"[All Fields] OR "occupations"[MeSH Terms] OR "occupations"[All Fields] OR "occupation"[All Fields] OR works*[tw] OR work'*[tw] OR worka*[tw] OR worke*[tw] OR workg*[tw] OR worki*[tw] OR workl*[tw] OR workp*[tw] OR occupation*[tw] OR "manpower"[Subheading] OR "manpower"[All Fields]
#5	(#2 OR #3) AND #4
#6	#1 OR #5
#7	"knee"[MeSH Terms] OR "knee"[All Fields] OR "knee joint"[MeSH Terms] OR ("knee"[All Fields] AND "joint"[All Fields]) OR "knee joint"[All Fields] OR "lower extremity"[MeSH Terms] OR ("lower"[All Fields] AND "extremity"[All Fields]) OR "lower extremity"[All Fields] OR ("lower"[All Fields] AND "limb"[All Fields]) OR "lower limb"[All Fields]
#8	("osteoarthritis, knee"[MeSH Terms] OR "osteoarthritis"[All Fields] OR "arthritis"[MeSH Terms] OR "arthritis"[All Fields] OR "arthrosis"[tw]) OR (meniscus[All Fields] OR meniscal[All Fields]) OR "bursitis"[MeSH Terms] OR "bursitis"[All Fields]
#9	#6 AND #7 AND #8
#10	"meta-analysis as topic"[MeSH Terms] OR meta-analysis[pt] OR meta-analysis[tiab] OR review[pt] OR review[tiab] NOT (letter[pt] OR editorial[pt] OR comment[pt]) NOT ("Animals"[Mesh] NOT "Humans"[Mesh])
#11	#9 AND #10
Embase (embase.com): 06.05.2015	
#1	'workload'/de OR 'workload' OR 'work load' OR (work AND load) OR work NEAR/5 load
#2	'physical' OR kneeling OR kneel* OR squatting OR squatt* OR crawling OR crawl* OR 'lifting effort'/de OR 'lifting effort' OR lifting OR ladder* OR stairs
#3	miner* OR millwright* OR industr* OR (oil AND ('rig':jt OR 'rig')) OR pick* OR boilermaker* OR installer* OR landscaper* OR pipefitter* OR migrant* OR 'mechanics'/de OR 'mechanics' OR 'motor vehicle'/de OR 'motor' NEAR/3 'vehicles' OR 'motor vehicles' OR 'truck' NEAR/3 driver* OR refinery NEAR/3 operator* OR machine* OR electric* OR repair* OR farm* OR 'device maintenance'/de OR 'maintenance' OR 'wood'/de OR 'wood' OR concrete OR (brick* AND (layer OR mason)) OR plumber* OR 'asphalt'/de OR 'asphalt' OR rock* OR (sheet AND ('metals' OR 'metal'/de OR 'metal')) OR seam* OR fisherm* OR waitress* OR construct* OR 'building'/de OR ('floors' AND 'floorcoverings') OR 'floors and floorcoverings' OR floor* NEAR/5 lay*
#4	'work'/de OR 'work' OR 'occupation'/de OR 'occupation' OR occupation OR occupations OR work* OR 'manpower'/de OR 'manpower' OR manpower
#5	#2 OR #3
#6	#4 AND #5
#7	#1 OR #6
#8	'knee'/de OR 'knee' OR 'knee joint' OR ('knee' AND 'joint') OR 'leg'/de OR 'leg' OR 'lower extremity' OR ('lower' AND 'extremity') OR 'lower' NEAR/1 'limb' OR 'lower limb'
#9	'knee osteoarthritis'/de OR 'knee osteoarthritis' OR 'osteoarthritis' OR 'arthritis'/de OR 'arthritis' OR 'arthrosis' OR meniscus OR meniscal OR 'bursitis'/de OR 'bursitis'

#10	#7 AND #8 AND #9
#11	'meta analysis (topic)'/de OR 'meta analysis':it OR review:it OR review:ab,ti NOT (letter:it OR editorial:it OR comment:it)
#12	#10 AND #11
#13	#12 NOT ([animals]/lim NOT [humans]/lim)
#14	#13 AND [embase]/lim
#15	#14 NOT [medline]/lim

Web of Science 06.05.2015

#1	TS=("workload" OR "work load" OR (work AND load) OR (work NEAR load)) Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#2	TS=("physical" OR kneeling OR kneel* OR squatting OR squatt* OR crawling OR crawl* OR "lifting effort" OR lifting OR ladder* OR stairs) Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#3	TS=(miner* OR millwright* OR industr* OR (oil AND "rig") OR pick* OR boilermaker* OR installer* OR landscaper* OR pipefitter* OR migrant* OR "mechanics" OR ("motor" NEAR "vehicles") OR "motor vehicles" OR ("truck" NEAR driver*) OR (refinery NEAR operator*) OR machine* OR electric* OR repair* OR farm* OR "maintenance" OR "wood" OR concrete OR ((brick*) AND (layer OR mason)) OR plumber* OR "asphalt" OR rock* OR ((sheet) AND ("metals" OR "metal")) OR seam* OR fisherm* OR waitress* OR construct* OR "building" OR (("floors") AND ("floorcoverings")) OR "floors and floorcoverings" OR (floor* NEAR lay*)) Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#4	TS=("'work" OR "occupation" OR occupation OR occupations OR work* OR "manpower" OR manpower) Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#5	#2 OR #3 Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#6	#4 AND #5 Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#7	#1 OR #6 Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#8	TS=("knee" OR "knee joint" OR ("knee" AND "joint") OR "leg" OR "lower extremity" OR ("lower" AND "extremity") OR ("lower" NEAR "limb") OR "lower limb") Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#9	TS=("knee osteoarthritis" OR "osteoarthritis"' OR "arthritis" OR "arthrosis" OR meniscus OR meniscal OR "bursitis") Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#10	#7 AND #8 AND #9 Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#11	TS=("meta analysis" OR "review") Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#12	TI=("review") Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#13	#11 OR #12 Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years
#14	#10 AND #12 Indexes=SCI-EXPANDED, SSCI, A&HCI Timespan=All years

II. Search for primary studies

PubMed: 08.09.2015
(same as earlier search excluding review filter and including 2011 publication time limit)

#1	"workload"[MeSH Terms] OR "workload"[All Fields] OR ("work"[All Fields] AND "load"[All Fields]) OR "work load"[All Fields]
#2	"physical"[All Fields] OR kneeling[All Fields] OR kneel*[tw] OR squatting[All Fields] OR squatt*[tw] OR crawling[All Fields] OR crawl*[tw] OR lifting[Mesh Terms] OR lifting[All Fields] OR lift*[tw] OR ladders[All Fields] OR stairs[All Fields]
#3	miner*[tw] OR Millwright*[tw] OR industr*[tw] OR (oil[All Fields] AND ("Rig"[Journal] OR "rig"[All Fields])) OR pick*[tw] OR boilermaker*[tw] OR installer*[tw] OR landscaper*[tw] OR pipefitter*[tw] OR migrant*[tw] OR "mechanics"[MeSH Terms] OR "mechanics"[tw] OR (("motor vehicles"[MeSH Terms] OR ("motor"[tw] AND "vehicles"[tw]) OR "motor vehicles"[tw] OR "truck"[tw]) AND driver*[tw]) OR (refinery[tw] AND operator[tw])

	OR machine*[tw] OR electric*[tw] OR repair*[tw] OR farm*[tw] OR "maintenance"[MeSH Terms] OR "maintenance"[tw] OR "wood"[MeSH Terms] OR "wood"[tw] OR concrete[tw] OR (brick*[tw] AND (layer[tw] OR mason[tw])) OR plumber*[tw] OR "asphalt"[Supplementary Concept] OR "asphalt"[tw] OR rock*[tw] OR (Sheet[tw] AND ("metals"[MeSH Terms] OR "metals"[tw] OR "metal"[tw])) OR Seam*[tw] OR fisherm*[tw] OR waitress*[tw] OR construct*[tw] OR "floors and floorcoverings"[MeSH Terms] OR ("floors"[tw] AND "floorcoverings"[tw]) OR "floors and floorcoverings"[tw] OR (floor*[tw] AND lay*[tw])
#4	"work"[MeSH Terms] OR "work"[All Fields] OR "occupations"[MeSH Terms] OR "occupations"[All Fields] OR "occupation"[All Fields] OR works*[tw] OR work'*[tw] OR worka*[tw] OR worke*[tw] OR workg*[tw] OR worki*[tw] OR workl*[tw] OR workp*[tw] OR occupation*[tw] OR "manpower"[Subheading] OR "manpower"[All Fields]
#5	(#2 OR #3) AND #4
#6	#1 OR #5
#7	"knee"[MeSH Terms] OR "knee"[All Fields] OR "knee joint"[MeSH Terms] OR ("knee"[All Fields] AND "joint"[All Fields]) OR "knee joint"[All Fields] OR "lower extremity"[MeSH Terms] OR ("lower"[All Fields] AND "extremity"[All Fields]) OR "lower extremity"[All Fields] OR ("lower"[All Fields] AND "limb"[All Fields]) OR "lower limb"[All Fields]
#8	("osteoarthritis, knee"[MeSH Terms] OR "osteoarthritis"[All Fields] OR "arthritis"[MeSH Terms] OR "arthritis"[All Fields] OR "arthrosis"[tw]) OR (meniscus[All Fields] OR meniscal[All Fields]) OR "bursitis"[MeSH Terms] OR "bursitis"[All Fields]
#9	#6 AND #7 AND #8
#10	("2011"[Date - Publication] : "3000"[Date - Publication])
#11	#9 AND #10

Embase (embase.com): 08.09.2015

(same as earlier search excluding review filter and including 2011 publication time limit)

#1	'workload'/de OR 'workload' OR 'work load' OR (work AND load) OR work NEAR/5 load
#2	'physical' OR kneeling OR kneel* OR squatting OR squatt* OR crawling OR crawl* OR 'lifting effort'/de OR 'lifting effort' OR lifting OR ladder* OR stairs
#3	miner* OR millwright* OR industr* OR (oil AND ('rig':jt OR 'rig')) OR pick* OR boilermaker* OR installer* OR landscaper* OR pipefitter* OR migrant* OR 'mechanics'/de OR 'mechanics' OR 'motor vehicle'/de OR 'motor' NEAR/3 'vehicles' OR 'motor vehicles' OR 'truck' NEAR/3 driver* OR refinery NEAR/3 operator* OR machine* OR electric* OR repair* OR farm* OR 'device maintenance'/de OR 'maintenance' OR 'wood'/de OR 'wood' OR concrete OR (brick* AND (layer OR mason)) OR plumber* OR 'asphalt'/de OR 'asphalt' OR rock* OR (sheet AND ('metals' OR 'metal'/de OR 'metal')) OR seam* OR fisherm* OR waitress* OR construct* OR 'building'/de OR ('floors' AND 'floorcoverings') OR 'floors and floorcoverings' OR floor* NEAR/5 lay*
#4	'work'/de OR 'work' OR 'occupation'/de OR 'occupation' OR occupation OR occupations OR work* OR 'manpower'/de OR 'manpower' OR manpower
#5	#2 OR #3
#6	#4 AND #5
#7	#1 OR #6
#8	'knee'/de OR 'knee' OR 'knee joint' OR ('knee' AND 'joint') OR 'leg'/de OR 'leg' OR 'lower extremity' OR ('lower' AND 'extremity') OR 'lower' NEAR/1 'limb' OR 'lower limb'
#9	'knee osteoarthritis'/de OR 'knee osteoarthritis' OR 'osteoarthritis' OR 'arthritis'/de OR 'arthritis' OR 'arthrosis' OR meniscus OR meniscal OR 'bursitis'/de OR 'bursitis'
#10	#7 AND #8 AND #9
#11	#10 NOT ([animals]/lim NOT [humans]/lim)
#12	#11 AND [embase]/lim
#13	#12 NOT [medline]/lim

Table 16 Exposure dose definitions for studies with more than two exposure dose categories - definition per study arm

Exposure	study ID	lowest category	2nd	3rd	4th	5th	Comment if categorized post-assessment
kneeling	Dawson2003f	<15yrs spent doing work that involved kneeling	>=15<26yrsyrs spent doing work that involved kneeling	>=26yrs spent doing work that involved kneeling			
kneeling	Sandmark 2000	no or low	medium	high			lifelong sum (min); on the basis of referents' values, lower quartile is low exposure (exact doses not reported)
squatting	Dawson2003f	<=15yrs spent doing work that involved squatting	>15<27 yrs spent doing work that involved squatting	>=27yrs spent doing work that involved squatting			
kneeling or squatting	Coggon 2000f	< 1hr per day or >1hr per day in total for less than 1yr	>1hr per day in total for 1 to less than 10 yrs	>1hr per day in total for 10 to less than 20 yrs	>1hr per day in total for 20 or more years		
kneeling or squatting	Coggon 2000m	>1hr per day in total for less than 1yr	>1hr per day in total for 1 to less than 10 yrs	>1hr per day in total for 10 to less than 20 yrs	>1hr per day in total for 20 or more years		
kneeling or squatting	Klussmann2010f	No	<3,542 hours/life	3,542 to 8,934 hours/life	>8,934 hours/life		based on participants data divided into 0, and three equal parts
kneeling or squatting	Klussmann2010m	No	<3574 hours/life,	>3574 =<12244 hours/life,	>12244 hours per life		based on participants data divided into 0, and three equal parts
kneeling or squatting	Manninen 2002f	not at all	"less than 2 hours" per day	"from 2 to 4 hours" and "more than 4 hours per day			
kneeling or squatting	Manninen 2002m	not at all	"less than 2 hours" per day	"from 2 to 4 hours" and "more than 4 hours per day			
kneeling or squatting	Seidler 2008m	no,	0-870 hrs/life	870-4757 hrs/life	4757 - 10800 hrs/life	>= 10.800 hrs/life	categorized in tertiles based on the distribution of the exposed controls; If less than 20% of the control subjects were non-exposed, the reference category combined non-exposed subjects and subjects in the first exposuretertile, if the highest tertile of exposed control subjects comprised more than 10% of all (exposed plu snon-exposed) control subjects, a high-dose category was generated according to the

							95th percentile of control subjects.
squatting or knee bending	Sandmark 2000	no or low	medium	high			lifelong sum (N); on the basis of referents' values, lower quartile is low exposure (exact doses not reported)
climbing	Coggon 2000f	>30 times/day for less than 1yr	>30 times/day for 1 to less than 10 yrs	>30 times/day for 10 to less than 20 yrs	>30 times/day for 20 or more years		
climbing	Coggon 2000m	>30 times/day for less than 1yr	>30 times/day for 1 to less than 10 yrs	>30 times/day for 10 to less than 20 yrs	>30 times/day for 20 or more years		
climbing	Manninen 2002f	not at all or very little	some	much			
climbing	Manninen 2002m	not at all or very little	some	much			
climbing	Sandmark 2000	no or low	medium	high			lifelong sum(number of steps); on the basis of referents' values, upper quartile is high exposure (exact doses not reported)
lifting	Coggon 2000f	>= 25kg >10 times/week less than 1 yr	>= 25kg >10 times/week for 1 to less than 10 yrs	>= 25kg >10 times/week for 10 to less than 20 yrs	>= 25kg >10 times/week for 20 or more yrs		
lifting	Coggon 2000m	>= 25kg >10 times/week less than 1 yr	>= 25kg >10 times/week for 1 to less than 10 yrs	>= 25kg >10 times/week for 10 to less than 20 yrs	>= 25kg >10 times/week for 20 or more yrs		
lifting	Dawson2003f	<24yrs spent doing work that involved lifting	>24<=33yrs spent doing work that involved lifting	>33yrs spent doing work that involved lifting			
lifting	Klussmann2010f	No	Sometimes	<1,088 tons/life	≥1,088 tons/life		based on participants data divided into 0, and three equal parts
lifting	Klussmann2010m	No	Sometimes	<2,214 tons/life	≥2.214 tons/life		based on participants data divided into 0, and three equal parts
lifting	Lau2000f	no	>10kg/>50kg yes 1-10 times/week	>10kg/>50kg yes >10times/week			
lifting	Lau2000m	no	>10kg/>50kg yes 1-10 times/week	>10kg/>50kg yes >10times/week			

lifting	Manninen 2002f	no regular lifting)	< 100000 kg per life	>= 100000kg per life			
lifting	Manninen 2002m	no regular lifting)	< 100000 kg/life	≥100000kg/life			
lifting	Sandmark 2000	no or low	medium	high			lifelong sum(kg); on the basis of referents' values, upper quartile is high exposure (exact doses not reported)
lifting	Seidler 2008m	no	0-630 kilogramhours / life	630-5120 kilogramhours / life	5120-37.00 kilogramhours / life	>=37.000 kilogramh ours / life	categorized in tertiles based on the distribution of the exposed controls; If less than 20% of the control subjects were non-exposed, the reference category combined non-exposed subjects and subjects in the first exposuretertile, if the highest tertile of exposed control subjects comprised more than 10% of all (exposed plu snon-exposed) control subjects, a high-dose category was generated according to the 95th percentile of control subjects.
kneeling or lifting	Zhang 2011	never over the last 12 years	seldom over the last 12 yrs	sometimes over the last 12 yrs	often over the last 12 yrs	always over the last 12 yrs	
kneeling, squatting, crawling	Schouten 1992	low	medium	high			divided into tertiles based on participants data (when more than one third had a score of 0, the cutoff point was set at 0 and the other cutoff point divided the group with a score of more than 0 into two groups of equal size.) (exact doses not reported)

Table 17 List of excluded studies at fultext stage and reasons for exclusion

Study ID	Topic	Reason for exclusion
Aghili 2012[52]	-	Outcome musculoskeletal disorder
Allen 2012[53]	OA	Cross-sectional study
Apold 2014 [54]	OA	physical activities measured as sedentary, moderate , intermediate and intensive, classification system does not enable a specification of our activities of interest
Bieleman 2013 [55 56]	-	Outcome not of interest (work participation)
Chen 2007 [57]	-	cross-sectional study, no OA, Bursitis, or ML Outcome (pain only)
Cheng 2000 [58]	OA	leisure time physical activity (not occupational knee load)
Cooper 2000 [59]	OA	No occupational knee load exposure measurements
D'Souza 2008 [60]	OA	Cross-sectional study (survey data)
Du 2005 [61]	OA	cross-sectional study, no occupational exposure
Enderlein 1989 [62]	OA	job title only
Ezzat 2012 [63]	OA	Cross-sectional study
Felson 1991	OA	Use of job classification system based on experts' rating, inclusion in the discussion section.
Gholami 2015 [64]	OA	Cross-sectional prevalence of cases
Hart 1999 [65]	OA	no physical workload, not age adjusted
Herquelot 2015 [66]	-	No OA, B, ML specific outcome (pain)
Hwang 2012 [67]	ML	Job title only (no JEM)
Ingham 2011 [68]	-	No OA, Bursitis or ML Outcome (pain)
Jacobs 2014 [69]	OA	No primary study
Jensen 2015	OA	Cross-sectional study, job title only
Jones 2007 [70]	-	not OA, Bursitis or ML Outcome (outcome knee pain only, not measured if knee pain is OA/B/ML)
Jonnsson 2015 [71]	OA	Job title only
Kohatsu 1990 [72]	OA	crude exposure measurement does not enable differentiation between exposure/no exposure to kneeling, squatting, climbing or lifting, no occupational tasks or activities measured, general occupational exposure classified as light, medium, heavy
Le Manac'h 2012 [73]	B	Cross-sectional study
Martin 2013 [49]	OA	Use of job exposure matrix based on subjective measures from two other studies (both of which are included), inclusion in discussion section
Muraki 2011 [74]	OA	Cross-sectional study
Namali 2011 [75]	OA	Cross-sectional design
Ratzlaff 2012 [76]	OA	Cross-sectional design, analysis of joint force exposure,
Sigurdardottir 2013 [77]	OA	Same study population as Johnsson 2015
Toivanen 2010 [78]	OA	crude exposure measurement does not enable differentiation between exposure and no exposure (to kneeling, squatting, climbing or lifting)
Vingard 1992 [79]	OA	exposure measurement based on job titles only
Von Nauwald 1986 [80]	OA, B	job title only

Table 18 Overview of search characteristics from included Reviews (N=24)

Review characteristics	Databases (Dbs) searched													
Review ID	# Dbs	Medline	PubMED	NIOSH-tic	EMBASE	HSE-Line	CINAHL	Cochrane	PsychINFO	Web of Sci	SciDirect	Other (Google Scholar, ERIC, DATASTAR, sportDisc, AMED)	Time Restriction	Language Restrictions
Aluoch 2009	4	x							x			x	not reported	unknown
Cooper 2014	24	x			x		x				x	Web of Know., BSC, AMED, springerlink, IEEE, ASSIA, Westlaw, Lexus, Avery, OnePetro, Construction & Building Abstracts, Construction Information Service, Business Source Complete, JBI Db of SR, Implementation Reports, PROSPERO, Google, Google Scholar, Conference Proceedings, Centre for Reviews and Dissemination, OpenDOAR and international Newsstand	"all years searched"	English only
Cozzensa da Silva 2007	4	x										x	1990-2006	English + several (portugese, spanish)
Ezzat 2014	2	x			x								1946- April 2011	English only
Fransen 2011	4	x		x	x	x							1966-April 2007	English + several (German, Danish, Swedish, Norwegian)
Gaudreault 2013	9	x			x		x	x				AMED, HEALTHSTAR, MANTIS, SCOPUS, Database of Abstracts of Reviews of Effects et ACP Journal Club	Creation of DB- June 2011; Creation of Db-june 2012	English + French
Jensen 2005														unknown
Jensen 2008	4	x		x	x	x							1966-April 2007	English + several (German, Danish, Swedish, Norwegian)
Johnson 2014	2	x	x										1990-2015	English only
Kirkeskov (Jensen) 1996	6	x		x	x	x						x	not reported	English + several (German, Scandinavian languages)

kwon 2012														unknown
Mattioli 2013	1		x										no restriction	no restriction
McMillan 2005	8	x		x	x							x	not reported	unknown
McWilliams 2007	5	x	x	x	x					x		x	1950-July 2010	no restriction
Palmer 2012	2	x			x								1948-2011	English only
Pena 2007													not reported	unknown
Reid 2010	2		x								x	x	1950-2009	English only
Richmond 2013	10	x	x		x		x	x	x	x		x	not reported	unknown
Schouten 2002	2	x			x								2000-2001	no restriction
Silverwood 2015	3	x			x							x	start of DB-Dec 2012	English only
Snoeker 2013	3	x			x			x					1950-Jan 2012	no restriction
Walker-Bone 2002	2	x			x								1966- June 2001	unknown
Weber 2007	1		x									use of search results of two other reviews (Maetzel 1997, Kirkeskov Jensen 1996)	2005	unknown
Vignon 2006		x			x			x						English + French

Table 19 Kellgren and Lawrence scale - https://en.wikipedia.org/wiki/Kellgren-Lawrence_grading_scale

Grade	Description
0	No radiographic features of osteoarthritis
1	Possible joint space narrowing and osteophyte formation
2	Definite osteophyte formation with possible joint space narrowing
3	Multiple osteophytes, definite joint space narrowing, sclerosis and possible bony deformity
4	Large osteophytes, marked joint space narrowing, severe sclerosis and definite bony deformity