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Association between Weight or Body Mass Index and Hand Osteoarthritis: A Systematic Review

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Abstract

Objective:

To investigate the association between weight or Body Mass Index (BMI) and the development of hand osteoarthritis (OA).

Methods:

Systematic review of observational studies. Medical databases were searched up to April 2008. Articles which presented data on the association between weight and hand OA were selected. The qualities of these studies were then assessed by two independent reviewers using a 19 criteria scoring system. Using the mean scores of all studies as cut-off value, the studies were deemed as high- or low- quality. Study quality and study designs were combined to determine the level of evidence using best-evidence synthesis which consisted of five levels of evidence.

Results:

From the 25 studies included, two had cohort, three case-control and 20 cross-sectional study designs. Fifteen studies were considered as high-quality studies. Of these high-quality studies, one cohort, two case-control and seven cross-sectional studies showed a positive association between weight or BMI and hand OA. Based on three high-quality studies with preferred study designs (one cohort and two case-control) with a positive association, the level of evidence of the association between overweight and developing hand OA is moderate. The approximate risk ratio of this association is 1.9.

Conclusion:

Weight or BMI is associated with hand OA development. The level of evidence of published studies is moderate according to best-evidence synthesis. Further high-quality cohort or case-control studies are needed to elucidate the role of weight in hand OA.

Introduction

Osteoarthritis (OA) is the most common joint disease. Its etiology is largely unknown and no disease-modifying treatment exists.(1) Overweight is recognized as a risk factor for developing knee OA. Being overweight increases the mechanical forces across weight-bearing joints and leads to OA.(2) Whether this is the sole explanation, is challenged by some studies that showed that overweight is also associated with hand OA of non-weight-bearing joints, like hand joints.

In a recommendation for the diagnosis of hand OA by a task force of the European League Against Rheumatism, obesity was described as a risk factor for hand OA.(3) This was based only on four studies. However, in two narrative reviews (1;4) the association of overweight and hand OA was inconsistent, but narrative reviews have some shortcomings like potential selective inclusion of papers without systematic quality assessment of selected studies.(5) Furthermore, since the latest narrative review, several new studies on this topic have been published.

To summarize data on the association between weight and hand OA development which would give more insight in the etiology of OA and give consideration whether prevention of overweight and loosing weight could be a preventive treatment of hand OA, we performed a systematic review of available studies.

Material and Methods

Identification of studies

Together with a medical librarian we searched medical databases up to April 2008 for studies with data on the association between weight or Body Mass Index (BMI) and hand OA (Appendix I, online supplemental file). No language restriction was applied. Additional articles were searched on the reference lists of identified articles and in Google Scholar.

Inclusion and exclusion criteria

Two reviewers, EY, a PhD student, and MK, a senior rheumatologist, independently read abstracts of all retrieved references for obvious exclusions and subsequently read the full text of remaining references. Studies with: (i.) data on the association between weight or BMI and hand OA; (ii.) participants suffering from clinical or radiographic or self-reported hand OA, were included. Hand OA was defined as involvement of at least one hand joint. Reviews, abstracts, letters to the editor, case reports, case series and studies investigated other musculoskeletal disease than OA, were excluded. In case of multiple publications of the same patient population, the publication with the largest study population was selected.

Data extraction

Following data were extracted: (i.) study population (patient characteristics, population size, gender, and age) (ii.) exposure (weight (kilograms) or BMI (kg/m^2) or other methods) (iii.) outcome (methods of assessment of hand OA, reproducibility, blinding).

(iv.) potential confounders (age, gender, smoking, hormone therapy, workload) (v.) association size (relative risk (RR) or odds ratio (OR)).

Assessment of study quality

The same reviewers independently evaluated the quality of the studies using 19 criteria based on previous systematic reviews in the area of musculoskeletal disorders (6;7) with a modification to evaluate studies on the association between weight and hand OA (Appendix II, online supplemental file). When the criterion was met in the article, '1' was given; otherwise '0'. A '0' was also given when no information about the specific criterion mentioned in the article. Differences were solved by discussion. Maximum scores obtainable were 16 for cohort and case-control studies, and 13 for cross-sectional studies. Total scores per study were calculated as percentage of maximum obtainable scores.

Rating the level of evidence

We generated a Forest plot and summarized the evidence using the best-evidence synthesis based on the guidelines on systematic review of the Cochrane Collaboration Back Review Group.(8) This system is a method to summarize evidence in observational studies where the study population, the assessment of exposure and outcomes, and the data analyses are heterogenic.(7) It has five levels of evidence (Table 1). It puts more weight on studies with a prospective cohort design where exposure truly precedes outcomes. The next preferred designs are case-control and cross-sectional, respectively. The mean of the quality scores of all studies was used to classify studies as high or low quality.

Table 1: Best-evidence synthesis used in this review (8).

Strong	General consistent findings were presented in multiple high-quality cohort studies
Moderate	One high-quality cohort study and at least two high-quality case-control studies, or when at least three high-quality case-control studies show general consistent findings
Limited	General consistent findings were found in a single cohort study, or in maximum two case-control studies, or in multiple cross-sectional studies
Conflicting,	Less than 75% of the studies reported consistent findings
No evidence	No study could be found

Publication bias

Publication bias was investigated by generating a Funnel plot. The association size of weight or BMI and developing hand OA on the horizontal axis was plotted against study population size on the vertical axis. Asymmetry in the Funnel plot suggests publication bias.(9) We determined symmetry visually.

Results

Literature flow

From 472 identified references 27 were selected based on in- and exclusion criteria (Figure 1).(10-36) Additional search resulted in another 6 articles.(37-42) Seven articles were excluded (11;17;25;27;32;35;41) due to overlap in study population. One study was represented by two publications (20;21), further referred to as (20). In total, 25 studies were included: two cohort (13;36), one case-control (30) and 20 cross-sectional studies (10;12;15;16;18-20;22-24;26;28;31;33;34;37-40;42). Two studies (14;29) resembled a case-control design.

Characteristics of included studies (Appendix III, online supplemental file)

Eight studies investigated only women (13;14;18;23;30;34;37;38) and one (22) only men Hand OA was diagnosed using radiographic criteria in 21 studies (12-16;18;20;22-24;26;28;30;33;34;36-40;42); 18 of them used radiographic criteria only and three (18;30;39) used radiographic *and* clinical criteria. Clinical criteria only were used in two studies (10;31), one of them (10) used the American College of Rheumatism criteria for hand OA. In two studies (19;29), hand OA was self-reported by the patients.

Study quality assessment
The two reviewers agreed on 305 (90%) of 340 criteria (Appendix IV, online supplemental file). The disagreements were solved in a single meeting and mostly concerned assessment of hand OA (criteria 9 and 10). The mean of quality scores was 63%.

The participation rates in most studies were lower than 80% (criterion 5). One cohort study had limitations in the assessment of hand OA (criteria 9 and 10) and the follow-up (criteria 14 and 15). Two case-control studies had limitations in the assessment of hand OA (criterion 10). Moreover, two of three case-control studies had potential selection bias, being sampling bias (items 2 and 5). This bias was also commonly seen in cross-sectional studies.

Associations shown in included studies
Hand OA in at least one joint showed a statistically significant positive association with weight in 16 of 25 (64%)studies.(12-16;18;20;26;30;31;33;34;37;38;40;42) The other nine studies showed a non-significant or no association. Fourteen of 25 studies (10;13;14;16;18-20;24;28;30;31;34;36;39) presented association sizes as OR and RR values (Figure 2) giving an estimated pooled risk ratio of 1.9 for the positive association between (over)weight and development of hand OA. Three (15;31;37) of these 16 studies showed a significant positive association in one gender, but a non-significant or no association in the other gender.

Six of nine studies (12;14-16;18;24;39;40;42) investigating distal interphalangeal joints, two of eight (12;14-16;36;39;40;42) studies investigating proximal interphalangeal joints, one of four studies (12;22;40;42) investigating metacarpophalangeal joints and four of 12 studies (12;14-16;20;24;28;33;36;39;40;42) investigating first carpometacarpal joints showed a positive significant association with weight or BMI.
Levels of evidence
The level of evidence for a positive association between weight or BMI and hand OA is moderate. Fifteen of 25 included studies (10;13-16;18;20;24;28;30;31;34;36;39;42) were considered to be of high quality. Of two high-quality cohort studies (13;36) one (13) showed an RR of 3.12 (1.65-5.88); the second showed no association. Both high-quality case-control studies (14;30) reported a positive significant association, with an OR of 1.30(1.06-1.59) (14) and 8.3 (1.2-56.5)(30). Of 11 (10;15;16;18;20;24;28;31;34;39;42) high-quality cross-sectional studies, seven studies (15;16;18;20;31;34;42) reported a positive association.

In a subgroup of studies which used radiographic criteria with or without clinical criteria for hand OA, 13 of 21 studies were deemed as high-quality. Ten (13-16;18;20;30;31;34;42) of these 13 studies showed a positive association and the level of evidence remained moderate. In the subgroup of studies using radiographic criteria only (18 studies; of which 10 with high-quality), seven (13-16;20;34;42) studies showed a positive association, but due to the lack of sufficient number of high quality cohort (only one study) and case-control (only one study) studies, the level was limited. The subgroup of clinical studies (10;31) showed conflicting level of evidence.

Using alternative cut-offs for methodological quality assessment (median or 25^{th} percentile) did not change the results. When using 75^{th} percentile as cut-off, few studies were retained leading to limited level of evidence.

Publication bias
We plotted the association sizes (OR and RRs) against the sample sizes of 14 studies to investigate publication bias (Figure 3). Visually, the plot was asymmetric.

Discussion

This systematic review showed that the evidence for a positive association between weight or BMI and hand OA is moderate. This conclusion is based on three high-quality studies with preferred study designs. Moderate level of evidence did not change for the subgroup of studies investigated hand OA using radiographic criteria. When no best-evidence synthesis was performed, a pooled risk ratio was approximately 1.9, where 64% of published studies showed a positive association between (over)weight and hand OA.

The strength of a systematic review is the use of a focused research question, an extended search strategy and a pre-defined system to evaluate the quality of evidence. Here, we also use qualitative levels of evidence to give a conclusion when a summary of quantity statistic was not appropriate. Yet, this systematic review has some possible limitations which also reflect the limitations of the published studies. The first caveat is the heterogeneities in multiple aspects of the studies, like the definition of BMI, hand OA and study population. Studies categorized BMI in various ways, mainly based on the distribution of study population, such as tertiles and median or BMI as a continuous variable. Preferentially, cut-off of BMI 25 kg/m^2, as World Health Organization definition for overweight could be used.(43) However, this was performed only in a minority of studies. Included studies defined hand OA also in various ways, using radiographic and clinical criteria. Subgroup analysis of studies which used radiograph to make diagnosis of hand OA, however did not change the level of evidence. The level of evidence became conflicting when we performed a subgroup analysis in only two studies defined hand OA using clinical criteria. The lack of clinical studies might reflect the available evidence which suggests that radiography is a better method in defining hand OA in epidemiology studies.(4) Another heterogeneity which can be mentioned here is the study population. Although the most studies used mixed sex, a third of the included studies concerned only females. These heterogeneities lead to difficulties in comparing studies and in summarizing studies quantitatively. The second caveat of this review is the possibility of publication bias. However, when we examine the Funnel plot carefully, the asymmetry is caused by one study with large effect (30) This study also differs to other studies that it used hand OA based on clinical criteria supported by radiograph findings. The third caveat of this review is that theoretically, the criteria we used can influence the outcomes of this review. We used and modified criteria which were previously used in systematic reviews the musculoskeletal field, since no generally accepted set of criteria exist for methodological quality assessment in observational studies,.

The consequence of the moderate level of evidence of an association is that further research is likely to have an important impact.(44) Therefore, future studies, especially well-designed prospective cohort or case-control studies are called for, which should also investigate the etiological mechanisms of the association and temporal relationship between overweight or obesity and hand OA.

The pathogenesis of OA is largely unknown and no disease-modiying treatment exists, hence knowledge on the role of overweight in hand OA is of importance for understanding and treating (hand) OA. The association between overweight and hand OA suggests that also other factors than mechanical forces play a role. Some possible links between overweight and osteoarthritis have been proposed, like metabolic alteration, atherosclerosis and diabetes mellitus.(45) Fat tissues secrete pro-and anti-inflammatory adipo(cyto)kines, like leptin, which was observed in synovial fluid obtained from osteoarthritic joints.(46) Leptin's concentration in advanced osteoarthritic cartilage is significantly correlated with the BMI of the patients, and its level and pattern of expression were related to the grade of cartilage

destruction. Obesity-associated atherosclerosis can also accelerated the OA process by the vascular disease in subchondral bone.(47) Lastly, in diabetes mellitus, advanced glycation end products (AGE) is formed and accumulated. AGE cross-linking damaged collagen network and lead to cartilage changes associated with osteoarthritis. This AGE formation is initiated not only by sugars but also by lipids.(48)

In summary, this is the first systematic review which investigated the association between weight and BMI and hand OA. The association is positive and the level of evidence is moderate. This calls for well-designed studies that further estimate the association as well as its underlying mechanisms.

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Figures List
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Figure 2. Forest plot showing the association sizes (odds ratios (OR) or relative risks (RR)) between (over)weight or BMI with hand osteoarthritis of the studies included, arranged by study design and quality scores (from high to low). The numbers in bracket represents the references. n represents number of study population. For information on the actual association sizes concerning used hand OA phenotype and BMI category see Appendix III (online supplemental file). Labeled with asterisk are studies which presented OR or RR as increase per unit BMI.
Figure 3. Funnel plot showing the relation between association sizes (odds ratios (OR) or relative risks (RR)) and sample size. The numbers represents the references of the studies. When studies presented multiple association sizes, the largest RR or OR concerning a cut-off at BMI 25 kg/m^2 was denoted. If this information were not available, association size of a cut-off at a higher BMI level was used. Preferentially, association sizes for radiographic hand OA and for men and women combined was presented.

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Appendices (online supplemental files)

Appendix I: Search strategies used and search results

	Key Words	Number of Articles	Unique Articles
Pubmed	(obesity OR obese OR overweight OR adiposity OR fat OR BMI OR body mass index OR Body Fat Distribution) AND (osteoarthritis OR arthritis OR arthrosis OR osteoarthrosis OR osteoarthrit* OR arthriti* OR arthros* OR osteoarthros* OR osteoartrit* OR artriti* OR artros* OR osteoartros*) AND (hand OR hands OR Fingers OR finger OR Thumb OR thumbs OR Metacarpus OR Wrist OR wrists OR Hand Deformities OR hand joints OR hand bones OR hand injuries)	306	306
Web of Science	(obes* OR overweight* OR adipos* OR fat OR BMI OR "body mass index") AND (osteoarthr* OR arthriti* OR arthros* OR osteoartr* OR artriti* OR artros*) AND (hand OR hands OR Finger* OR Thumb* OR Metacarp* OR Wrist*)	248	90
CINAHL	(exp Obesity/ OR exp Body Mass Index/ OR Adipose Tissue Distribution/ OR exp Adipose tissue/ OR (obesity OR obese OR overweight OR adiposity OR fat OR BMI OR body mass index).mp) AND (Exp osteoarthritis/ OR exp Arthritis/ OR (osteoarthritis OR arthritis OR arthrosis OR osteoarthrosis OR osteoarthrit* OR arthriti* OR arthros* OR osteoarthros* OR osteoartrit* OR artriti* OR artros* OR osteoartros*).mp) AND (exp hand/ OR exp Hand deformities/ OR exp Hand injuries/ OR Hand	25	6

	surgery/ OR Hand therapy/ OR (hands OR Fingers OR finger OR Thumb OR thumbs OR Metacarpus OR Wrist OR wrists).mp)		
EMBASE	(exp Obesity/ OR exp Adipose Tissue/ OR body fat/ or body mass/ OR Body Fat Distribution/ OR (obesity OR obese OR overweight OR adiposity OR fat OR BMI OR body mass index OR Body Fat Distribution).mp) AND (Osteoarthritis/ OR exp Arthritis/ OR (osteoarthrit* OR arthriti* OR arthros* OR osteoarthros* OR osteoartrit* OR artriti* OR artros* OR osteoartros*).mp) AND (exp Hand/ OR (hand OR hands OR Fingers OR finger OR Thumb OR thumbs OR Metacarpus OR Wrist OR wrists).mp)	266	70
Hand Search and Google Scholar			6
			478

Appendix II: Explanation of the criteria used for assessment of methodological quality of included studies.

Item	Criteria	Applicable for
Study population: Definition of Study population		
1.	**Sufficient description of characteristics of study groups** *A '1' is given when a paper describes at least setting and time period of the study, ages of the patients (and its range) and man: woman ratio.*	C/CC/CS
Study Population: Selection Bias		
2.	**Selected at time point before disease was present** *A '1' is given when patients were included before the outcome (hand OA) was present.*	C
	Selected at uniform point *A '1' is given when case and control were selected at the same time point concerning disease.*	CC/CS
3.	**Clear description of selection of study subjects.** *When a paper described how the study subjects were selected from the population level to the study level, a '1' will be given.*	C/CC/CS
4.	**Cases and controls were drawn from the same population.** *This is to exclude the possibility of selection bias.*	CC
5.	**Participation rate ≥ 80% for study groups.** *Eighty per cent was an arbitrary margin chosen to determine the quality of the selection of study subjects.*	C/CC/CS
Assessment of overweight as risk factor		
6.	**Weight was measured identical for cases and controls.**	CC
7.	**Weight was assessed prior to outcome.** *In the sequence of assessing, when weight was measured before hand OA was diagnosed, a '1' will be given. In most studies where*	C/CC/CS

	diagnosis of hand OA was made based on radiograph, a '1' will also be given.	
Assessment of the outcome: Hand Osteoarthritis		
8.	**Presence of hand OA was according to valid definition (1-3) and the classification was standardized.(4-6)** *ACR criteria (4) did not request radiographic findings in making a diagnosis of hand OA, whereas EULAR recommendation (3) proposed that multiple features on hand radiographs is adequate to make a diagnosis hand OA. A '1' will than given for a study which used ACR criteria or standardized radiological criteria for hand OA, like those from Kellgren and Lawrence (7), Kallman (5) and OARSI(8).*	C/CC/CS
9.	**Hand OA assessment was blinded** *A '1' is given if the observers when making a diagnosis (by reading patient's chart) or reading the radiograph did not aware of patients' weigh or body composite.*	C/CC/CS
10.	**Presence of hand OA was assessed reproducibly** *A '1' is given if hand OA was assessed repeatedly at least in a subgroup, whether by the same observer or different observers.*	C/CC/CS
11.	**Hand OA was assessed identical in cases and controls** *A '1' is given if assessment of hand OA status was the same in controls as in cases.*	CC
Follow-up		
12.	**Prospective study design was used** *A '1' is given when a study measured the exposure (weight in this case) before the outcomes hand OA. Cross-sectional study will always scored '0' on this item.*	C/CC/CS
13.	**Follow up time ≥ 3 years** *Three years are arbitrary margin to say about the acceptable duration of follow-up.*	C

14.	**No difference in withdrawal in both groups**	C
15.	**Information on completers vs. withdrawals**	C
Analysis and Data Presentation		
16.	**Weight distribution was given** *A '1'is given if the paper describes the distribution of weight or BMI of the study population.*	C/CC/CS
17.	**Sufficient information on association sizes were given**	C/CC/CS
18.	**Appropriate analysis techniques were used**	C/CC/CS
19.	**Adjusted for at least age and gender**	C/CC/CS

Appendix III. Details of the studies included, in order of study design hierarchy and their quality score

First Author, Publication year (reference number)	Study Population	Hand OA Phenotype	Adjusted for	Results[1]	Quality score[2]
Cohort studies					
Carman, 1994 (9)	General population from Tecumseh, USA (Tecumseh Community Health Study) n=588 males and 688 females. Age at follow-up: 50-74 years. Follow-up duration: 23 years.	Radiographic (K&L)	Age, gender and smoking.	OA in any hand joint: Ideal weight, RR 1.0 (index) ≥ 20% above ideal weight, RR 3.12 (1.65-5.88)	88
Szoeke, 2006 (10)	Females from general population in Melbourne (Melbourne Women's Midlife Health Project) n = 224 Mean age at follow up: 59 years. Follow-up duration: 11 years.	Radiographic (OARSI)	Age, gender, hormone therapy, physical activity, smoking	Osteophytes or JSN in any hand joint: OA per unit BMI (kg/m^2) increase, RR 1.02 (0.9-1.1)	75
Case-control studies					

Cicuttini, 1996 (11)	Female twins from 2 sources of volunteers: twin registers and twins recruited by phone in London, UK. Case: osteophytes on radiograph (n=78 for DIP, 43 for PIP and 82 for 1st CMC) Control: sib pairs with no radiolographic OA Mean age: 58 years.	Radiographic (Kallman)	Gender, menopausal status, age of menopause, hysterectomy, use of hormone replacement therapy, smoking, physical activity	OA per unit BMI (kg/m^2) increase: DIP, OR 1.07 (0.91 to 1.25) PIP, OR 1.15 (0.9 to 1.45) 1st CMC, OR 1.30 (1.06 to 1.59)	88
Oliveria, 1999 (12)	Females from general practice in Worchester USA (Fallon Community Health Plan) Case: hand OA (n = 39) Control: females, matched by closest date of birth (n = 39) Mean age 61 years.	Clinical (ACR) , supported by radiographic OA featrures	Age, gender, estrogen therapy, smoking, number of Fallon health contacts	OA in any hand joint: BMI ≤ 23.80, OR 1 BMI 23.81 – 28.60, OR 5.4 (0.9 to 31.3) BMI > 28.6, OR 8.3 (1.2 to 56.5)	75
Kujala, 1999 (13)	Finnish Twin Cohort, Finland 73 twins discordant for hand OA Age: 39-66 years.	Self-reported physican-based	Age, gender	'No differences in BMI among twin pairs discordant for finger OA'	44

Cross-sectional studies

Sayer, 2003 (14)	General population followed since their birth in England, Scotland and Wales. n = 1467 males and 1519 females Cross- sectional analysis at age of 53 years	Clinical (Heberden's, Bouchard's nodes, squaring at 1st CMC)	Age, gender, height, social class	OA in any hand joint, men: Weight ≤74 kg, OR 1 Weight >91.8, OR 1.4 'increasing OR with increasing adult weights'	77
Dahagin, 2007 (15)	General population of Ommoord, the Netherlands (Rotterdam Study) n = 1499 males and 2086 females Mean age: 66 years.	Radiographic (K&L)	Age, gender, smoking	OA in two of three groups (DIP, PIP, 1st CMC) hand joints: BMI <27.4, OR 1 BMI >27.4, OR 1.4 (1.2 to 1.7)	77
Ding, 2008 (16)	Female dentists and teacher in Helsinki, Finland. n=532 Mean age: 54 years.	Radiographic (modified K&L) and clinical (pain)	Age, gender, occupation, hand-loading leisure-time activities, occupation	Symptomatic OA in DIP joint: BMI <25, OR 1 (index) BMI 25-26.9, OR 1.62 (0.83 to 3.15) BMI≥ 27, OR 2.39 (1.26 to 4.51)	77
Haara, 2003 and Haara, 2004 (17)	General population of Finland from 69 municipalities. n = 1560 males and 2035 females Age: older than 30 years.	Radiographic (K&L)	Age, gender, educational level, smoking, workload	OA in any hand joint (except CMC): BMI ≤20, OR 0.50 (0.31-0.83) BMI 20-24.9, OR 1 (index) BMI 25.0-29.9 OR 1.17 (0.96-1.43) BMI 30-34.9, OR 1.78 (1.37-2.33)	77

				BMI ≥35, OR 1.98 (1.19-3.27) OA in 1st CMC joint: BMI 20.0-24.9, OR 1 (index) BMI 35, OR ±2	
Hart, 1993 (18)	Females from a large general practice in Chingford, near London, UK (The Chingford Study) n=985 Mean age: 54 years .	Radiographic (K&L) and clinical (pain and stiffness)	Age and gender	BMI < 23.4, OR 1 (index) OA in DIP joint: BMI 23.4 – 26.4, OR 1.64 (0.84 to 3.21) BMI > 26.4, OR 1. 71 (0.88 to 3.33) OA in PIP joint: BMI 23.4 – 26.4, OR 1.19 (0.39 to 3.62) BMI > 26.4, OR 0.71 (0.22 to 2.29) OA in CMC joint: BMI 23.4 – 26.4, OR1.68 (0.88 to 3.21) BMI > 26.4, OR 1. 85 (0.96 to 3.56)	77
Jones, 2002 (19)	Patients with OA and their family in Tasmania, Australia. n = 174 males and 348 females Mean age males: 53 years, females: 57 years.	Radiographic (OARSI) or clinical (Heberden's nodes)	Age, gender, and family effects	BMI < 25, OR 1 Radiographic OA in DIP joint: BMI ≥ 25, OR 1.22 (0.70 to 2.14) Radiographic OA in CMC joint: BMI ≥ 25, OR 0.99 (0.54 to 1.52)	77

Kessler, 2003 (20)	Patients with hip or knee OA severe enough for arthroplasty in Ulm, Germany (Ulm Osteoarthritis Study) n = 242 males and 397 females Median age: 65 years.	Radiographic (OARSI)	Age, gender, physical exertion, and hip or knee OA	OA in two or more IP joints: OA per unit BMI (kg/m^2) increase, OR 1.02 (0.98 to 1.07) OA in at least one of 1st CMC joint: OA per unit BMI (kg/m^2) increase, OR 1.01 (0.96 to 1.06)	77
Van Saase, 1989 (21)	General population of Zoetermeer, near the Hague, the Netherlands 1071 males and 1097 females (n=2168) Age: 45-64 years.	Radiographic (K&L)	Age and gender	♂, association between overweight and OA : DIP ($p \leq 0.001$), MCP ($p \leq 0.001$), 1st CMC ($p \leq 0.15$), wrist ($p \leq 0.29$), PIP ($p \leq 0.001$), CARP ($p \leq 0.06$) ♀, association between overweight and OA: DIP ($p \leq 0.002$), MCP ($p \leq 0.39$), 1st CMC ($p \leq 0.30$), PIP ($p \leq 0.001$), CARP ($p \leq 0.003$), wrist ($p \leq 0.12$)	77
Andrianakos, 2006 (22)	General population of Greece (ESORDIG study). Urban, suburban and rural. n = 4269 males and 4471 females Age: 19 to 99 years old, mean: 47 years.	Clinical (ACR)	Age, gender, education level, occupation, alcohol consumption, cigarette smoking, rural residence, socioeconomic status.	Clinical OA: BMI ≤ 30, OR 1 (index) BMI ≥ 30, OR 1.3 (0.98 to1.8)	69

Cvijetic, 2000 (23)	General population of Zagreb, Croatia n = 304 males and 306 females Mean age male and female: 63 years.	Radiographic (K&L)	Age, gender, duration of postmenopause, cigarette smoking, blood pressure	β values of multiple regression analysis: ♂: DIP: 0.25, p<0.001, PIP: 0.08, 1st CMC: 0.07 ♀: DIP: 0.17, PIP: 0.02, 1st CMC: 0.02	69
Sowers, 2000 (24)	Females from two cohorts: General population of Michigan, USA (Michigan Bone Health Study), n=510 and volunteers from Study of Women's Health Across the Nation, n=543 Age: 27-53 years, median: 44 years	Radiographic (K&L)	Age, gender, previous injury, smoking	OA in any hand joint: OA per unit BMI (kg/m^2) increase, OR 1.05 (1.03 to 1.08)	69
Bergstrom, 1986 (25)	Seventy-year old People Study in Goteborg, Sweden n = 190 males and 162 females Cross-sectional analysis of 70 years (cohort 1), 75 years (cohort 2) and 79 years (cohort 3)	Radiographic (K&L)	Age and gender	DIP, PIP, MCP II-V, MCPI, 1st CMC joints were assessed: ♂: 'BMI was correlated to MCP I and IP I (p< 0.05) but not with other joints' ♀: 'BMI was correlated with DIP (p<0.01) but not with other joints'	62
Kalichman, 2005 (26)	General population of Chuvasa, Russia, (Chuvasha Skeletal Aging). Agricultural. n = 663 males and 605 females Age males: 18-89 years, mean: 46.3 years and	Radiographic (K&L)	Age and gender	Correlation between overweight and OA: 0.11	62

	females 18-90 years, mean: 48.2.				
Grotle, 2008 (27)	General population of Ullensaker, near Oslo, Norway. Rural. n = 1470 males and 1796 females Mean age: 45 years	Self-reported	Age and gender	Self-reported OA: BMI <20, OR 0.70 (0.24 to1.99) BMI 20-25, OR 1 (index) BMI 26-30 OR 1.00 (0.69 to1.48) BMI > 30, OR 1.57 (0.93 to2.64)	46
Hochberg, 1993 (28)	Female volunteers in Baltimore (Baltimore Longitudinal Study of Aging). Middle class n = 317 Mean age: 55 years	Radiographic (K&L)	Age and gender	'all independent variables (age, WHR, % fat) were significantly different across grade of hand OA except BMI'	46
Hochberg, 1991 (29)	Male volunteers in Baltimore (Baltimore Longitudinal Study of Aging). Middle class. n = 888 Mean age: 56 years	Radiographic (K&L)	Age and gender	'the distribution of these residual values were not significantly different by grade of hand osteoarthritis for any of these independent variables (like BMI)'.	46
Sonne-Holm, 2006 (30)	General population of Osterbro, Copenhagen, Denmark (Copenhagen City Health Study). n = 1295 males and 2060 females.	Radiographic (K&L)	Not adjusted	'OA is associated with K&L grade 2 to 3 (p<0.0000)'	38
Acheson, 1975 (31)	General population New Haven, Connecticut, USA.	Radiographic (K&L)	Gender	Difference on the average weight between subjects with OA and without OA.	31

	n = 300 males and 385 females Age: older than 21 years.			♂: 172.13 vs. 171.58 lbs, not significant ♀: 143.96 vs. 134.48, p<0.01	
Kellgren, 1958 (32)	Random sample of general population in Leigh, UK. Urban. n = 204 males and 277 Age: 55-64 years.	Radiographic features	Not adjusted	'DIP OA is associated with overweight males (p <0.01) but no significant association on PIP, 1st CMC, MP and wrists in both sexes.'	31
Engel, 1968 (33)	General population in USA (Health Examination Survey I) n=6672 18-79 years	Radiographic features	Age, gender	Association between Ponderal index (height divided by the cubed root of weight) and hand OA for age groups: ♂: 45-54 yr: p 0.01, 55-64 yr: -, 65-74 yr: p 0.05 ♀: 45-54 yr: p 0.0005, 55-64 yr: -, 65-74 yr: -	23

[1] in parentheses 95% confidence interval, [2] quality score in per cent (%)

Abbreviations: K&L: Kellgren and Lawrence radiographs scoring system, OARSI: Osteoarthritis Research Society International scoring system, ACR: American College of Rheumatology, DIP: distal interphalangeal joints, PIP: proximal interphalangeal joints, MCP: metacarpophalangeal joints, CMC: carpometacarpal joints, 1st CMC: carpometacarpal joints of the thumb, BMI: body mass index.

Appendix IV. Study quality assessment scores of two reviewers (1: present, 0: absent or no information). Scores solved by discussion are in italics.

	Criteria																				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	Total	Quality score (%)
Cohort																					
Carman (9)	1	***1***	1	na	***0***	na	1	1	0	1	na	1	1	1	1	1	1	1	1	14	88
Szoeke (10)	1	1	1	na	0	na	1	1	1	0	na	1	1	0	0	1	1	1	1	12	75
% paper met the criteria	100	100	100	na	0	na	100	100	50	50	na	100	100	50	50	100	100	100	100		
Case-control																					
Cicuttini (11)	1	0	1	1	1	1	1	1	***1***	***1***	1	***0***	na	na	na	1	1	1	1	14	88
Kujala (13)	***0***	0	1	1	0	1	1	0	***0***	0	1	***0***	na	na	na	0	0	1	1	7	44
Oliveria (12)	1	1	1	1	0	1	1	1	1	0	0	0	na	na	na	1	1	1	1	12	75
% paper met the criteria	67	33	100	100	33	100	100	67	67	33	67	0	na	na	na	67	67	100	100		
Cross-sectional																					
Acheson (31)	0	0	0	na	0	na	***1***	1	0	0	na	0	na	na	na	0	1	0	1	4	31
Andrianakos (22)	1	1	1	na	1	na	0	1	0	1	na	0	na	na	na	0	1	1	1	9	69
Bergstrom (25)	1	***0***	1	na	***0***	na	1	1	1	1	na	***0***	na	na	na	***0***	0	1	1	8	62
Cvijetic (23)	1	0	0	na	0	na	1	1	1	1	na	0	na	na	na	1	1	1	1	9	69
Dahagin (15)	1	0	1	na	0	na	1	1	1	***1***	na	0	na	na	na	1	1	1	1	10	77
Ding (16)	1	0	1	na	0	na	1	1	1	1	na	0	na	na	na	1	1	1	1	10	77
Engel (33)	0	0	0	na	0	na	1	0	0	0	na	0	na	na	na	0	***1***	0	1	3	23
Grotle (27)	1	0	1	na	0	na	0	0	***0***	0	na	0	na	na	na	1	1	1	1	6	46
Haara (17)	***1***	0	1	na	0	na	1	1	1	1	na	0	na	na	na	1	1	1	1	10	77
Hart (18)	1	0	1	na	0	na	1	1	1	1	na	0	na	na	na	1	1	1	1	10	77
Hochberg (29)	1	0	0	na	0	na	1	1	***0***	***0***	na	0	na	na	na	1	1	0	1	6	46
Hochberg (28)	1	0	0	na	0	na	1	1	***0***	***0***	na	0	na	na	na	***1***	1	0	1	6	46
Jones (19)	1	0	***1***	na	0	na	1	1	1	1	na	0	na	na	na	1	1	1	1	10	77
Kalichman (26)	1	0	0	na	0	na	1	1	0	1	na	0	na	na	na	1	1	1	1	8	62
Kellgren (32)	***1***	0	0	na	0	na	1	***1***	0	1	na	0	na	na	na	0	0	0	0	4	31
Kessler (20)	1	0	1	na	1	na	1	1	1	***0***	na	0	na	na	na	1	1	1	***1***	10	77
Sayer (14)	1	1	1	na	***0***	na	1	1	0	1	na	0	na	na	na	***1***	1	1	1	10	77
Sonne-Holm (30)	***1***	0	***0***	na	1	na	0	1	1	1	na	0	na	na	na	0	0	0	***0***	5	38
Sowers (24)	1	0	1	na	0	na	1	1	0	1	na	0	na	na	na	1	1	1	1	9	69
van Saase (21)	1	0	1	na	0	na	***1***	1	1	1	na	0	na	na	na	***1***	1	1	1	10	77
% paper met the criteria	90	10	60	na	15	na	85	90	50	70	na	0	na	na	na	70	85	70	90		

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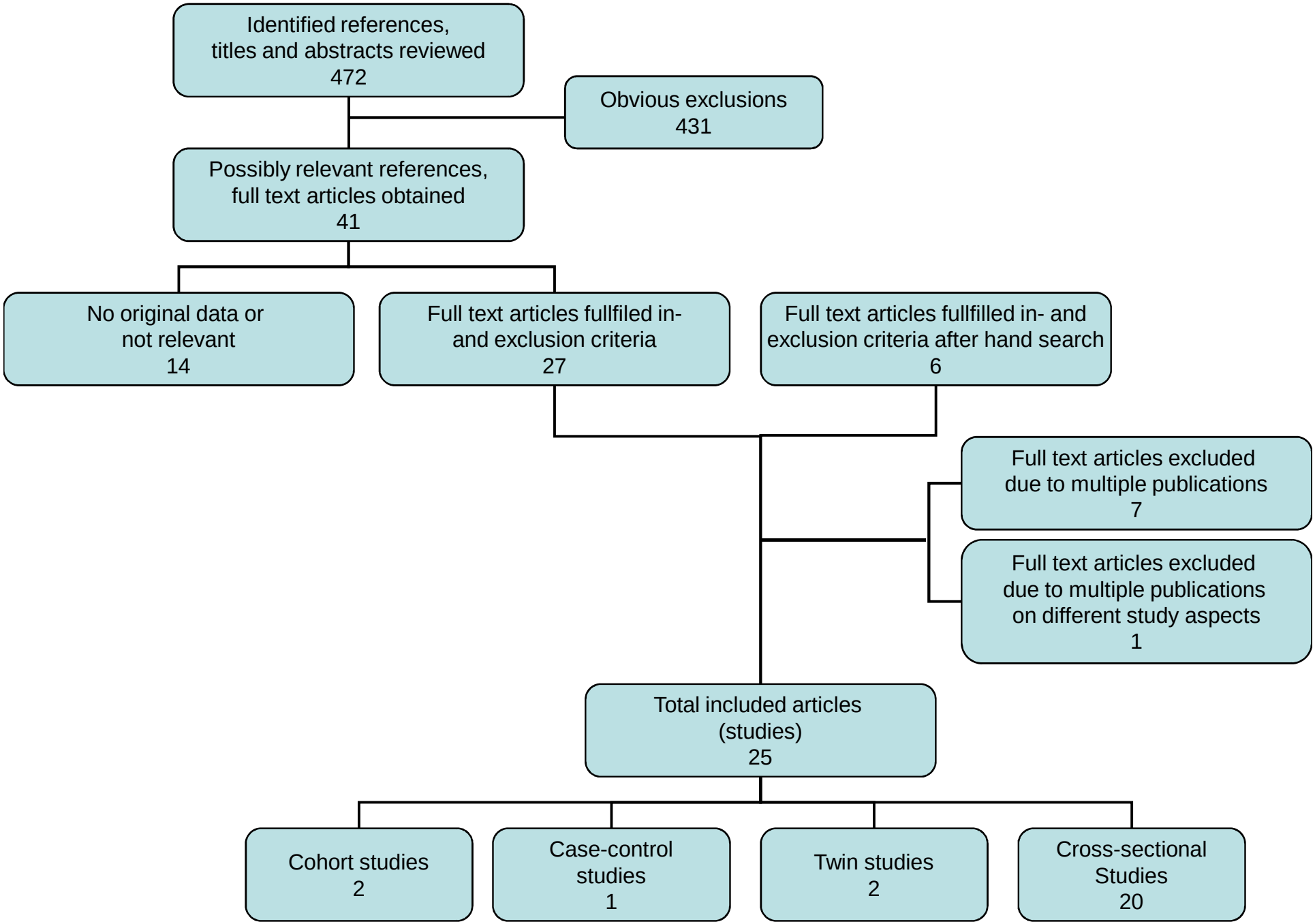

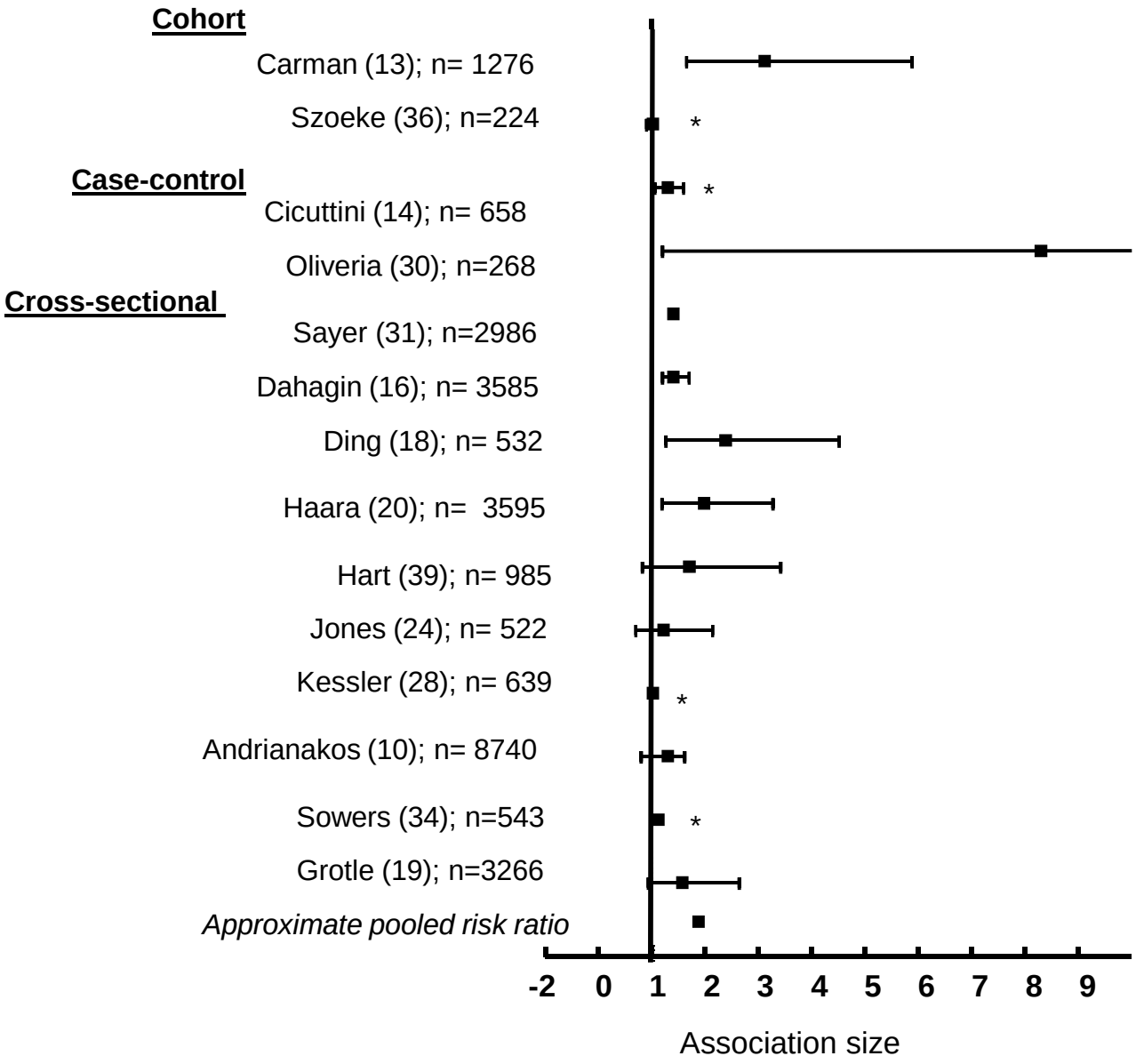

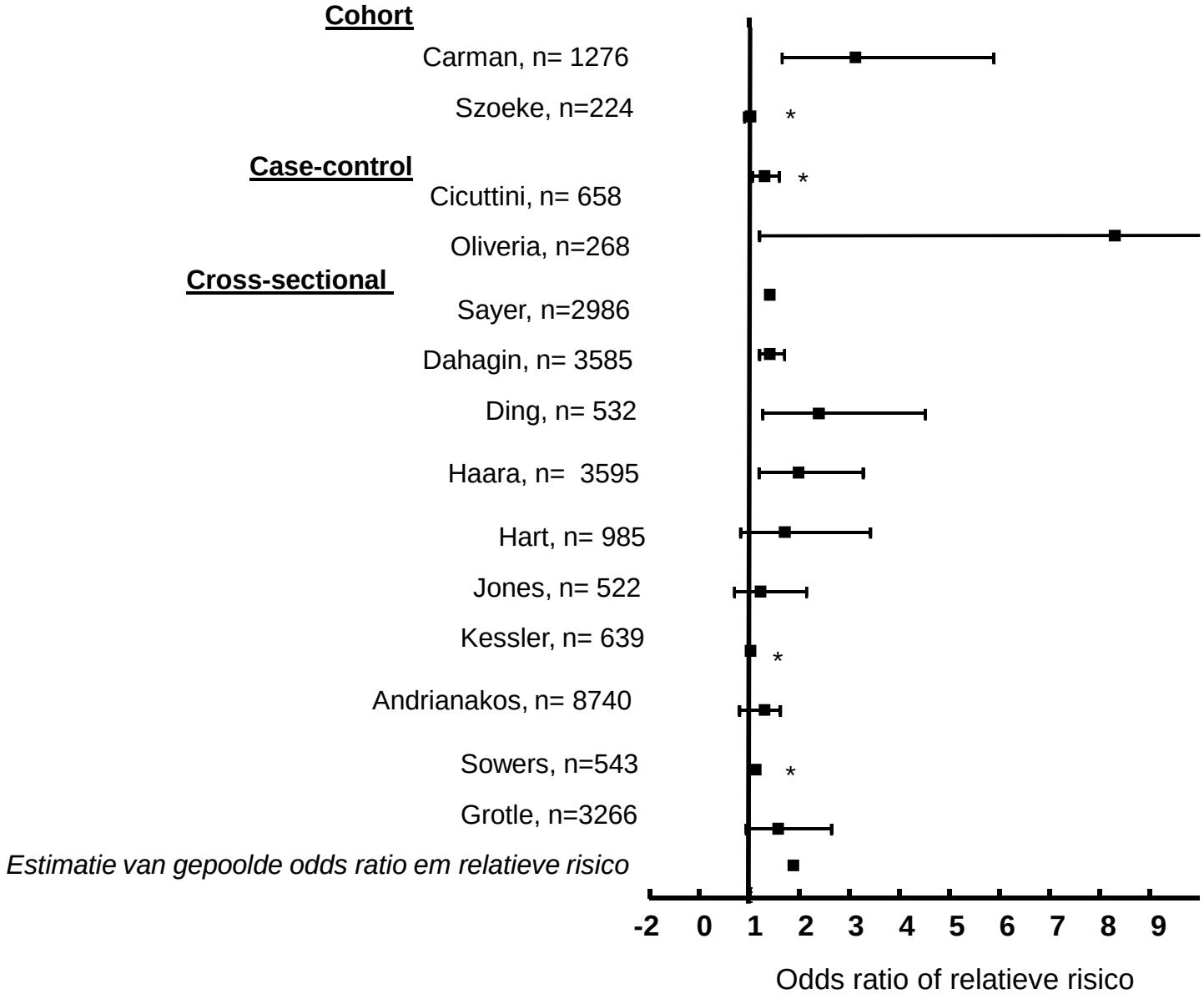

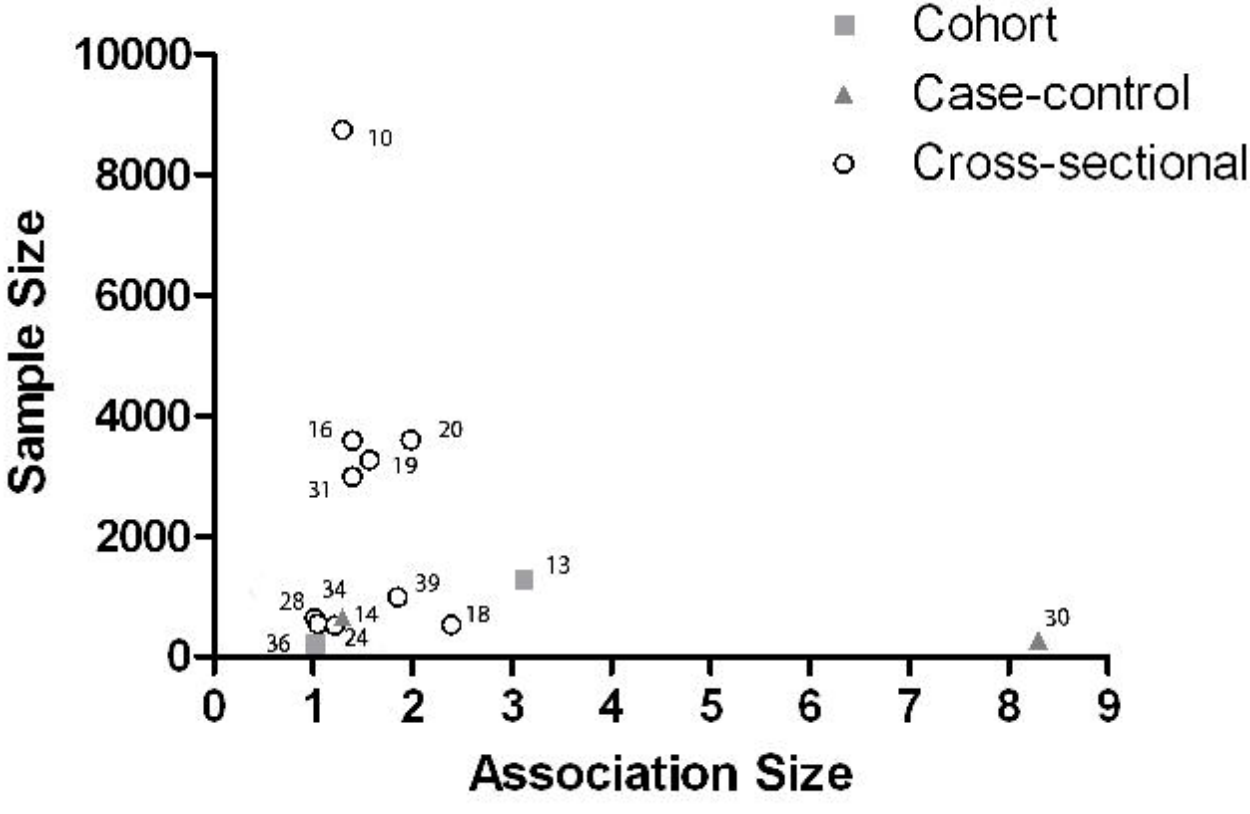
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Case-control
Cross-sectional
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