

Association between weight or body mass index and hand osteoarthritis: a systematic review

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► Additional data (supplementary appendices I, II, III and IV) are available online only at <http://ard.bmj.com/content/vol69/issue4>

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ABSTRACT

Objective To investigate the association between weight or body mass index (BMI) and the development of hand osteoarthritis.

Methods Systematic review of observational studies. Medical databases were searched up to April 2008. Articles that presented data on the association between weight and hand osteoarthritis 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 a 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 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 osteoarthritis. 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 osteoarthritis is moderate. The approximate risk ratio of this association is 1.9.

Conclusion Weight or BMI is associated with the development of hand osteoarthritis. 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 osteoarthritis.

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

In a recommendation for the diagnosis of hand osteoarthritis by a task force of the European League Against Rheumatism, obesity was described as a risk factor for hand osteoarthritis.³ This was based on only four studies. However, in two narrative reviews⁴ the association of overweight and hand osteoarthritis was inconsistent, but narrative reviews have some shortcomings such as the 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 summarise data on the association between weight and the development of hand osteoarthritis, which would give more insight into the aetiology of osteoarthritis and give consideration as to whether prevention of overweight and losing weight could be a preventive treatment of hand osteoarthritis, 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 osteoarthritis (see supplementary Appendix I, available online only). No language restriction was applied. Additional articles were searched in 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 data on the association between weight or BMI and hand osteoarthritis, participants with clinical, radiographic or self-reported hand osteoarthritis, were included. Hand osteoarthritis was defined as involvement of at least one hand joint. Reviews, abstracts, letters to the editor, case reports, case series and studies investigating other musculoskeletal disease than osteoarthritis, were excluded. In the case of multiple publications of the same patient population, the publication with the largest study population was selected.

Data extraction

The following data were extracted: (1) study population (patient characteristics, population size, gender and age); (2) exposure (weight (kg) or BMI (kg/m²) or other methods); (3) outcome (methods of assessment of hand osteoarthritis, reproducibility, blinding); (4) potential confounders (age, gender, smoking, hormone therapy, workload) and (5) 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

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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 osteoarthritis (see supplementary Appendix II, available online only). When the criterion was met in the article, '1' was given, otherwise '0'. A '0' was also given when no information was given 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 the percentage of maximum obtainable scores.

Rating the level of evidence

We generated a Forest plot and summarised 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 summarise evidence in observational studies in which 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 in which 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.

Publication bias

Publication bias was investigated by generating a funnel plot. The association size of weight or BMI and developing hand osteoarthritis 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 inclusion and exclusion criteria (figure 1).¹⁰⁻³⁶ An additional search resulted in another six articles.³⁷⁻⁴² Seven articles were excluded^{11 17 25 27 32 35 41} as a result of overlap in the study population. One study was represented by two publications,^{20 21} further referred to as reference 20. In total, 25 studies were included: two cohort,^{13 36} one case-control³⁰ 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

The characteristics of the included studies can be seen in supplementary Appendix III, available online only. Eight studies investigated only women^{13 14 18 23 30 34 37 38} and one²² only men. Hand osteoarthritis 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 them¹⁰ used the American College of Rheumatism criteria for hand osteoarthritis. In two studies,^{19 29} hand osteoarthritis was self-reported by the patients.

Study quality assessment

The two reviewers agreed on 305 (90%) of 340 criteria (see supplementary Appendix IV, available online only). The disagreements were solved in a single meeting and mostly concerned the assessment of hand osteoarthritis (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 osteoarthritis (criteria 9 and 10) and the follow-up (criteria 14 and 15). Two case-control studies had limitations in the assessment of hand osteoarthritis (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 osteoarthritis 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 the development of hand osteoarthritis. 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 osteoarthritis 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} one¹³ 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 that used radiographic criteria with or without clinical criteria for hand osteoarthritis, 13 of 21 studies were deemed to be 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 were high quality), seven^{13-16 20 34 42} studies showed a positive association, but because of the lack of a 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 levels of evidence.

Table 1 Best-evidence synthesis used in this review⁸

Strong	Generally 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 generally consistent findings
Limited	Generally 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

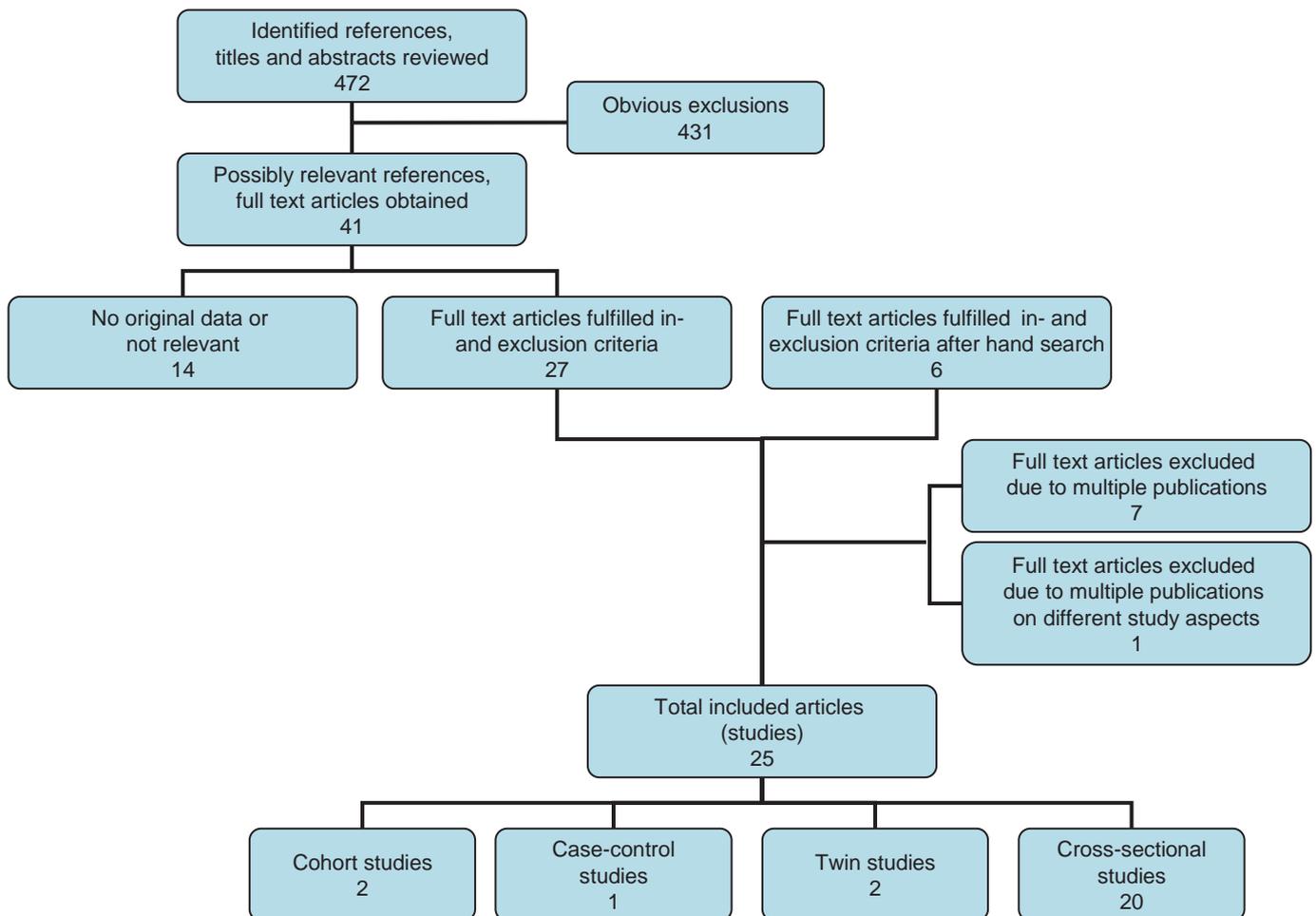


Figure 1 Results of the literature search.

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

Publication bias

We plotted the association sizes (OR and RR) 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 osteoarthritis is moderate. This conclusion is based on three high-quality studies with preferred study designs. A moderate level of evidence did not change for the subgroup of studies investigating hand osteoarthritis using radiographic criteria. When no best-evidence synthesis was performed, a pooled risk ratio was approximately 1.9, in which 64% of published studies showed a positive association between (over)weight and hand osteoarthritis.

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, such as the definition of BMI, hand osteoarthritis and study population. Studies categorised BMI in various ways, mainly based on the distribution of the study population, such as tertiles and median or BMI as a continuous variable. Preferentially, the cut-off of BMI is 25 kg/m², as the World Health Organization definition for overweight could be used.⁴³ However, this was the case in only a minority of studies. Included studies also defined hand osteoarthritis in various ways, using radiographic and clinical criteria. Subgroup analysis of studies that used radiography to make a diagnosis of hand osteoarthritis, however, did not change the level of evidence. The level of evidence became conflicting when we performed a subgroup analysis in only two studies defining hand osteoarthritis using clinical criteria. The lack of clinical studies might reflect the available evidence, which suggests that radiography is a better method of defining hand osteoarthritis in epidemiology studies.⁴ Another heterogeneity that should be mentioned here is the study population. Although most studies used a mixed sex population, a third of the included studies concerned only women. These heterogeneities lead to difficulties in comparing studies and in summarising 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

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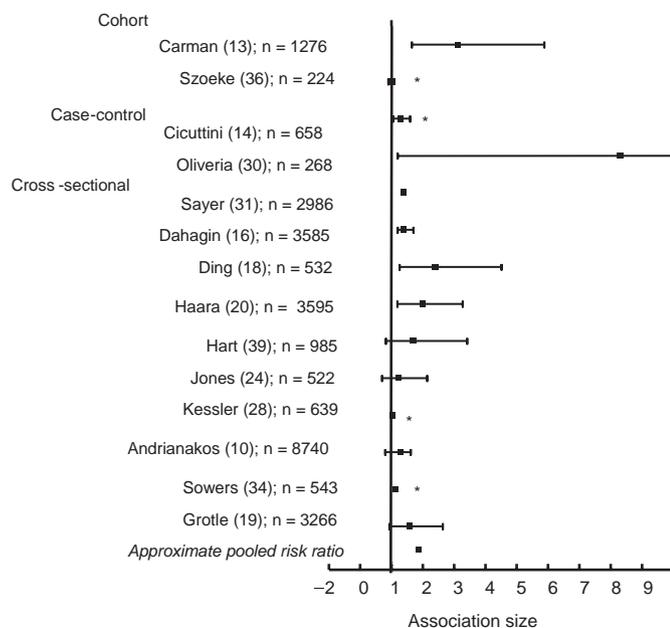


Figure 2 Forest plot showing the association sizes (odds ratios (OR) or relative risks (RR)) between (over)weight or body mass index (BMI) with hand osteoarthritis of the studies included, arranged by study design and quality scores (from high to low). The numbers in parentheses represent the references. n Represents number of study population. For information on the actual association sizes concerning used hand osteoarthritis phenotype and BMI category see supplementary Appendix III (available online only). Studies labelled with an asterisk are those that presented OR or RR as an increase per unit BMI.

a large effect.³⁰ That study also differs from other studies in that it used hand osteoarthritis based on clinical criteria supported by radiographic findings. The third caveat of this review is that theoretically the criteria we used can influence the outcomes of the review. We used and modified criteria that were previously used in systematic reviews of the musculoskeletal field, because 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 aetiological mechanisms of the association and temporal relationship between overweight or obesity and hand osteoarthritis.

The pathogenesis of osteoarthritis is largely unknown and no disease-modifying treatment exists, therefore knowledge of the role of overweight in hand osteoarthritis is of importance for understanding and treating (hand) osteoarthritis. The association between overweight and hand osteoarthritis suggests that factors other than mechanical forces also play a role. Some possible links between overweight and osteoarthritis have been proposed, such as metabolic alteration, atherosclerosis and diabetes mellitus.⁴⁵ Fat tissues secrete pro and anti-inflammatory adipo(cyto)kines, such as leptin, which was observed in synovial fluid obtained from osteoarthritic joints.⁴⁶ The concentration of leptin 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 osteoarthritis process by vascular disease in subchondral bone.⁴⁷ Finally, in diabetes mellitus, advanced glycation end-products

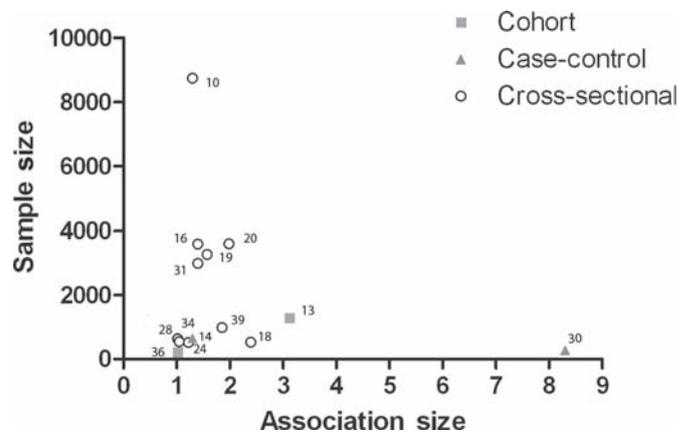


Figure 3 Funnel plot showing the relationship between association sizes (odds ratios (OR) or relative risks (RR)) and sample size. The numbers represent the references of the studies. When studies presented multiple association sizes, the largest RR or OR concerning a cut-off at body mass index (BMI) 25 kg/m² was denoted. If this information was not available, the association size of a cut-off at a higher BMI level was used. Preferentially, association sizes for radiographic hand osteoarthritis and for men and women combined were presented.

(AGE) are formed and accumulated. AGE cross-links the damaged collagen network and leads to cartilage changes associated with osteoarthritis. This AGE formation is initiated by sugars and by lipids.⁴⁸

In summary, this is the first systematic review to investigate the association between weight and BMI and hand osteoarthritis. 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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Competing interests None.

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REFERENCES

- Felson DT, Chaisson CE. Understanding the relationship between body weight and osteoarthritis. *Baillieres Clin Rheumatol* 1997;**11**:671–81.
- Hunter DJ, Felson DT. Osteoarthritis. *BMJ* 2006;**332**:639–42.
- Zhang W, Doherty M, Leeb BF, et al. EULAR evidence based recommendations for the diagnosis of hand osteoarthritis: report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCIIT). *Ann Rheum Dis* 2009;**68**:8–17.
- Hart DJ, Spector TD. Definition and epidemiology of osteoarthritis of the hand: a review. *Osteoarthr Cartil* 2000;**8**(Suppl A):S2–7.
- Cook DJ, Mulrow CD, Haynes RB. Systematic reviews: synthesis of best evidence for clinical decisions. *Ann Intern Med* 1997;**126**:376–80.
- Borghouts JA, Koes BW, Bouter LM. The clinical course and prognostic factors of non-specific neck pain: a systematic review. *Pain* 1998;**77**:1–13.
- Lievse AM, Bierma-Zeinstra SM, Verhagen AP, et al. Influence of obesity on the development of osteoarthritis of the hip: a systematic review. *Rheumatology (Oxford)* 2002;**41**:1155–62.
- van Tulder M, Furlan A, Bombardier C, et al. Updated method guidelines for systematic reviews in the cochrane collaboration back review group. *Spine* 2003;**28**:1290–9.
- Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**:629–34.
- Andrianakos AA, Kontelis LK, Karamitsos DG, et al. Prevalence of symptomatic knee, hand, and hip osteoarthritis in Greece. The ESORDIG study. *J Rheumatol* 2006;**33**:2507–13.
- Bagge E, Bjelle A, Edén S, et al. Factors associated with radiographic osteoarthritis: results from the population study 70-year-old people in Göteborg. *J Rheumatol* 1991;**18**:1218–22.

12. **Bergström G**, Bjelle A, Sundh V, *et al*. Joint disorders at ages 70, 75 and 79 years—a cross-sectional comparison. *Br J Rheumatol* 1986;**25**:333–41.
13. **Carman WJ**, Sowers M, Hawthorne VM, *et al*. Obesity as a risk factor for osteoarthritis of the hand and wrist: a prospective study. *Am J Epidemiol* 1994;**139**:119–29.
14. **Cicuttini FM**, Baker JR, Spector TD. The association of obesity with osteoarthritis of the hand and knee in women: a twin study. *J Rheumatol* 1996;**23**:1221–6.
15. **Cvijetic S**, Campbell L, Cooper C, *et al*. Radiographic osteoarthritis in the elderly population of Zagreb: distribution, correlates, and the pattern of joint involvement. *Croat Med J* 2000;**41**:58–63.
16. **Dahaghin S**, Bierma-Zeinstra SM, Koes BW, *et al*. Do metabolic factors add to the effect of overweight on hand osteoarthritis? The Rotterdam Study. *Ann Rheum Dis* 2007;**66**:916–20.
17. **Davis MA**, Neuhaus JM, Ettinger WH, *et al*. Body fat distribution and osteoarthritis. *Am J Epidemiol* 1990;**132**:701–7.
18. **Ding H**. Association between overweight and dip osteoarthritis among middle-aged Finnish female dentists and teachers. *Obes Res Clin Pract* 2008;**2**:61–8.
19. **Grotle M**, Hagen KB, Natvig B, *et al*. Prevalence and burden of osteoarthritis: results from a population survey in Norway. *J Rheumatol* 2008;**35**:677–84.
20. **Haara MM**, Manninen P, Kröger H, *et al*. Osteoarthritis of finger joints in Finns aged 30 or over: prevalence, determinants, and association with mortality. *Ann Rheum Dis* 2003;**62**:151–8.
21. **Haara MM**, Heliövaara M, Kröger H, *et al*. Osteoarthritis in the carpometacarpal joint of the thumb. Prevalence and associations with disability and mortality. *J Bone Joint Surg Am* 2004;**86-A**:1452–7.
22. **Hochberg MC**, Lethbridge-Cejku M, Plato CC, *et al*. Factors associated with osteoarthritis of the hand in males: data from the Baltimore Longitudinal Study of Aging. *Am J Epidemiol* 1991;**134**:1121–7.
23. **Hochberg MC**, Lethbridge-Cejku M, Scott WW Jr, *et al*. Obesity and osteoarthritis of the hands in women. *Osteoarthr Cartil* 1993;**1**:129–35.
24. **Jones G**, Cooley HM, Stankovich JM. A cross sectional study of the association between sex, smoking, and other lifestyle factors and osteoarthritis of the hand. *J Rheumatol* 2002;**29**:1719–24.
25. **Kalichman L**, Cohen Z, Kobylansky E, *et al*. Interrelationship between bone aging traits and basic anthropometric characteristics. *Am J Hum Biol* 2002;**14**:380–90.
26. **Kalichman L**, Malkin I, Kobylansky E. Association between physique characteristics and hand skeletal aging status. *Am J Phys Anthropol* 2005;**128**:889–95.
27. **Kalichman L**, Kobylansky E. Age, body composition, and reproductive indices as predictors of radiographic hand osteoarthritis in Chuvashian women. *Scand J Rheumatol* 2007;**36**:53–7.
28. **Kessler S**, Stöve J, Puhl W, *et al*. First carpometacarpal and interphalangeal osteoarthritis of the hand in patients with advanced hip or knee OA. Are there differences in the aetiology? *Clin Rheumatol* 2003;**22**:409–13.
29. **Kujala UM**, Leppävuori J, Kaprio J, *et al*. Joint-specific twin and familial aggregation of recalled physician diagnosed osteoarthritis. *Twin Res* 1999;**2**:196–202.
30. **Oliveria SA**, Felson DT, Cirillo PA, *et al*. Body weight, body mass index, and incident symptomatic osteoarthritis of the hand, hip, and knee. *Epidemiology* 1999;**10**:161–6.
31. **Sayer AA**, Poole J, Cox V, *et al*. Weight from birth to 53 years: a longitudinal study of the influence on clinical hand osteoarthritis. *Arthritis Rheum* 2003;**48**:1030–3.
32. **Solovieva S**, Vehmas T, Riihimäki H, *et al*. Finger osteoarthritis and differences in dental work tasks. *J Dent Res* 2006;**85**:344–8.
33. **Sonne-Holm S**, Jacobsen S. Osteoarthritis of the first carpometacarpal joint: a study of radiology and clinical epidemiology. Results from the Copenhagen Osteoarthritis Study. *Osteoarthr Cartil* 2006;**14**:496–500.
34. **Sowers M**, Lachance L, Hochberg M, *et al*. Radiographically defined osteoarthritis of the hand and knee in young and middle-aged African American and Caucasian women. *Osteoarthr Cartil* 2000;**8**:69–77.
35. **Sowers MF**, Hochberg M, Crabbe JP, *et al*. Association of bone mineral density and sex hormone levels with osteoarthritis of the hand and knee in premenopausal women. *Am J Epidemiol* 1996;**143**:38–47.
36. **Szoeke CE**, Cicuttini FM, Guthrie JR, *et al*. Factors affecting the prevalence of osteoarthritis in healthy middle-aged women: data from the longitudinal Melbourne Women's Midlife Health Project. *Bone* 2006;**39**:1149–55.
37. **Acheson RM**, Collart AB. New Haven Survey of Joint Diseases. XVII. Relationship between some systemic characteristics and osteoarthritis in a general population. *Ann Rheum Dis* 1975;**34**:379–87.
38. **Engel A**. Osteoarthritis and body measurements. *Vital Health Stat* 11 1968;**11**:1–37.
39. **Hart DJ**, Spector TD. The relationship of obesity, fat distribution and osteoarthritis in women in the general population: the Chingford Study. *J Rheumatol* 1993;**20**:331–5.
40. **Kellgren JH**, Lawrence JS. Osteo-arthrosis and disk degeneration in an urban population. *Ann Rheum Dis* 1958;**17**:388–97.
41. **Sowers M**, Zobel D, Weissfeld L, *et al*. Progression of osteoarthritis of the hand and metacarpal bone loss. A twenty-year followup of incident cases. *Arthritis Rheum* 1991;**34**:36–42.
42. **van Saase JL**, van Romunde LK, Cats A, *et al*. Epidemiology of osteoarthritis: Zoetermeer survey. Comparison of radiological osteoarthritis in a Dutch population with that in 10 other populations. *Ann Rheum Dis* 1989;**48**:271–80.
43. **WHO**. Obesity: preventing and managing the global epidemic. Report of a WHO Consultation. WHO Technical Report Series, No. 894. Geneva: World Health Organization, 2000.
44. **Atkins D**, Best D, Briss PA, *et al*. Grading quality of evidence and strength of recommendations. *BMJ* 2004;**328**:1490.
45. **Pottie P**, Presle N, Terlain B, *et al*. Obesity and osteoarthritis: more complex than predicted! *Ann Rheum Dis* 2006;**65**:1403–5.
46. **Dumond H**, Presle N, Terlain B, *et al*. Evidence for a key role of leptin in osteoarthritis. *Arthritis Rheum* 2003;**48**:3118–29.
47. **Conaghan PG**, Vanharanta H, Dieppe PA. Is progressive osteoarthritis an atheromatous vascular disease? *Ann Rheum Dis* 2005;**64**:1539–41.
48. **DeGroot J**. The AGE of the matrix: chemistry, consequence and cure. *Curr Opin Pharmacol* 2004;**4**:301–5.