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Review

The effect of osteoarthritis definition on prevalence and incidence estimates: a systematic review

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S U M M A R Y

Objective: To understand the differences in prevalence and incidence estimates of osteoarthritis (OA), according to case definition, in knee, hip and hand joints.
Method: A systematic review was carried out in *PUBMED* and *SCOPUS* databases comprising the date of publication period from January 1995 to February 2011. We attempted to summarise data on the incidence and prevalence of OA according to different methods of assessment: self-reported, radiographic and symptomatic OA (clinical plus radiographic). Prevalence estimates were combined through meta-analysis and between-study heterogeneity was quantified.
Results: Seventy-two papers were reviewed (nine on incidence and 63 on prevalence). Higher OA prevalences are seen when radiographic OA definition was used for all age groups. Prevalence meta-analysis showed high heterogeneity between studies even in each specific joint and using the same OA definition. Although the knee is the most studied joint, the highest OA prevalence estimates were found in hand joints. OA of the knee tends to be more prevalent in women than in men independently of the OA definition used, but no gender differences were found in hip and hand OA. Insufficient data for incidence studies didn't allow us to make any comparison according to joint site or OA definition.
Conclusions: Radiographic case definition of OA presented the highest prevalences. Within each joint site, self-reported and symptomatic OA definitions appear to present similar estimates. The high heterogeneity found in the studies limited further conclusions.

Introduction

In the group of musculoskeletal diseases, osteoarthritis (OA) is thought to be the most prevalent[1,2]. The WHO Scientific Group on Rheumatic Diseases estimates that 10% of the world's population who are 60 years or older have significant clinical problems that can be attributed to OA[3]. Since incidence and prevalence increase with age, longer life expectancy will result in an increase of OA in the future[3,4].

OA can be defined as a condition characterized by focal areas of loss of articular cartilage within the synovial joints, associated with hypertrophy of the bone (osteophytes and subchondral bone sclerosis) and thickening of the capsule[5,6]. Epidemiological research in OA faces some specific problems: different possible affected joint sites with different pathologic patterns, the difficulty of making a correct diagnosis, with unclear signs and symptoms and the need for a radiographic examination for clinical confirmation[7,8]. Additionally, a large proportion of people with radiographic evidence of OA have no symptoms or disability[9] and it is unclear whether such people should be considered as having OA[5]. These difficulties have led to the existence of several definitions of OA that may indeed explain part of the heterogeneity in OA estimates[10–12].

Radiographic OA, symptomatic OA and self-reported OA are the most commonly used case definitions[3]. Radiographic definition considers only pathophysiological joint signs present on radiographic images[13]. Several radiographic scoring systems exist [e.g., Kellgren–Lawrence (KL) scale, Joint space width method, Croft index, American college of rheumatology criteria]. The KL score of 2–4 is still the most widely used criteria in radiographic OA[14],

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considering: grade 0, none: no features of OA; grade 1, doubtful: questionable osteophytes or questionable joint space narrowing; grade 2, minimal: definitive small osteophytes, little/mild joint space narrowing; grade 3, moderate: definitive moderate osteophytes, joint space narrowing of at least 50%; grade 4, severe: joint space impaired severely, cysts and sclerosis of subchondral bone[15]. Symptomatic definition considers OA cases when both radiographic and joint symptoms related to the pathology (i.e., pain, stiffness and loss of function) are present[16]. Additionally, we can also find studies based on self-reported information about previous diagnosis of OA[17].

Because early diagnosis and appropriate management can minimize the effect of OA, clinicians and public health planners should be aware of the prevalence and incidence of OA[18]. Although it is likely that OA definition can influence prevalence and incidence estimates, it is important to understand which other factors can contribute to the different estimates, especially age, gender and anatomic joint site. The aim of this study was to understand the differences in prevalence and incidence estimates of OA, according to case definition, in knee, hip and hand joints, through a systematic review of the literature.

Methods

Data collection

A systematic literature review was carried out on *PUBMED* and *SCOPUS* databases. Several combinations of terms and expressions were tried, including both *MeSH* and free text terms. By analysing the articles retrieved from each combination, we chose as final search expression: (osteoarthritis OR osteoarthrosis OR osteoarthroses OR arthritis OR arthrosis OR joint diseases) AND (prevalence OR incidence) AND (knee OR hip OR hand). The search was restricted to studies published between January 1995 and February 2011. We limited our search to "Humans" and to publications in English, Spanish, French or Portuguese. Additionally, we performed a manual search in the reference lists provided by the identified papers. We used the *PRISMA* (Preferred Reporting Items of Systematic reviews and Meta-Analyses)[19] and the *MOOSE* (Guidelines for Meta-Analyses and Systematic Reviews of Observational Studies)[20] guidelines in the planning and execution of this study.

Eligibility criteria

The eligibility of studies was assessed using standardized inclusion and exclusion criteria. We included papers, in the dates of publication and languages earlier described, with cross-sectional or longitudinal methodologies that evaluated prevalence or incidence, using self-reported, radiographic (X-ray) and symptomatic (clinical plus radiographic) definitions of OA in both genders, without age limitations, for the knee, hip or hands joints. Papers were, in a first step, analysed according to their title and abstract and only those considered deemed irrelevant for the study purpose were excluded (in case of any doubt papers were fully analysed).

In a second stage, full text papers were analysed. We excluded papers with other languages, that presented no original data; articles related with OA pathophysiology, *in vitro*, or genetic studies; articles on OA treatment/therapy and methodological papers about questionnaires or instruments on OA. We also excluded papers that evaluated other forms of arthritis, other joint sites, papers based on other definitions beside self-reported, radiographic or symptomatic OA. Furthermore we excluded duplicated data, studies using sub-groups or specific populations, populations with previous injury or pathology and all papers without results on prevalence or incidence of OA (or without data to calculate them).

When several radiographic definitions were used in the same study we selected data from the most commonly used definition (preferably KL $\geq$ 2 to allow a better comparison, if available). For hand OA, we only included studies that presented an overall prevalence or incidence value for hand OA, normally defined as OA in any hand joint. When the same data was published in more than one paper, we selected the paper with the most detailed description. Further description can be seen in Fig. 1.

Assessment of methodological quality

Different instruments to assess methodological quality have been developed; based on a recent systematic review[21] we used the methodological scoring system described by Loney *et al.*[22] to evaluate the studies included. We chose this instrument because it is specific for studies that estimate the prevalence and/or incidence of a health problem. Reviewers classified studies according to eight methodological items (one-point for each item covered) with a maximum score of eight points. Item number 4 (Are objective, suitable and standard criteria used for measurement of the health outcome?) was considered positive for all studies since it was a previous inclusion criteria.

Data extraction and analysis

We analysed studies according to OA definition and joint studied. Search results were screened by two independent reviewers according to eligibility criteria, further analysis was undertaken in cases of doubt in any screening stage and conflicts were resolved by consensus discussion. Prevalence was considered as the number of existing cases and incidence considered the new cases of disease in a population within the time frame of each study. Papers were analysed by reviewers, who systematically extracted the information about joint site(s), OA definition, authors, year of publication, study population and results. If prevalence estimates and 95% confidence intervals (CIs) were not described, but enough data was available, estimates were calculated using EPinfo version 3.5.1.

Because a normal distribution is mandatory for the pooling of data, *logit* transformation was applied and weighted by inverse variance of *logit* transformed prevalence. Pooled prevalence estimates were computed by the DerSimonian–Laird method assuming a random-effects model[23]. Between-study heterogeneity was quantified through the I^2 statistics. The I^2 statistic describes the percentage of variation across studies that is due to heterogeneity rather than chance[24]. Stratified analyses were carried out according to population (hospital or population based), sex and age (<45, 45–59 and $\geq$60). The minimum age in each study was used as an indicator of age sample. The *Mann–Whitney* test was used for independent samples comparisons. These analyses were conducted with STATA®, version 9.2[25].

Results

We found 7558 papers, of which 1091 were duplicated references from databases; secondly, 6467 were assessed for both title and abstract; we excluded 6141 which were not relevant for our study purpose, and three studies for which we could not obtain the complete article[26–28]. There remained 323 articles that were fully analysed. In this phase, a further 45 were included from the reference lists of the papers chosen for study.

Of the total 368 fully analysed articles, we excluded 296 (Fig. 1). Finally, for this review we included 72 articles.

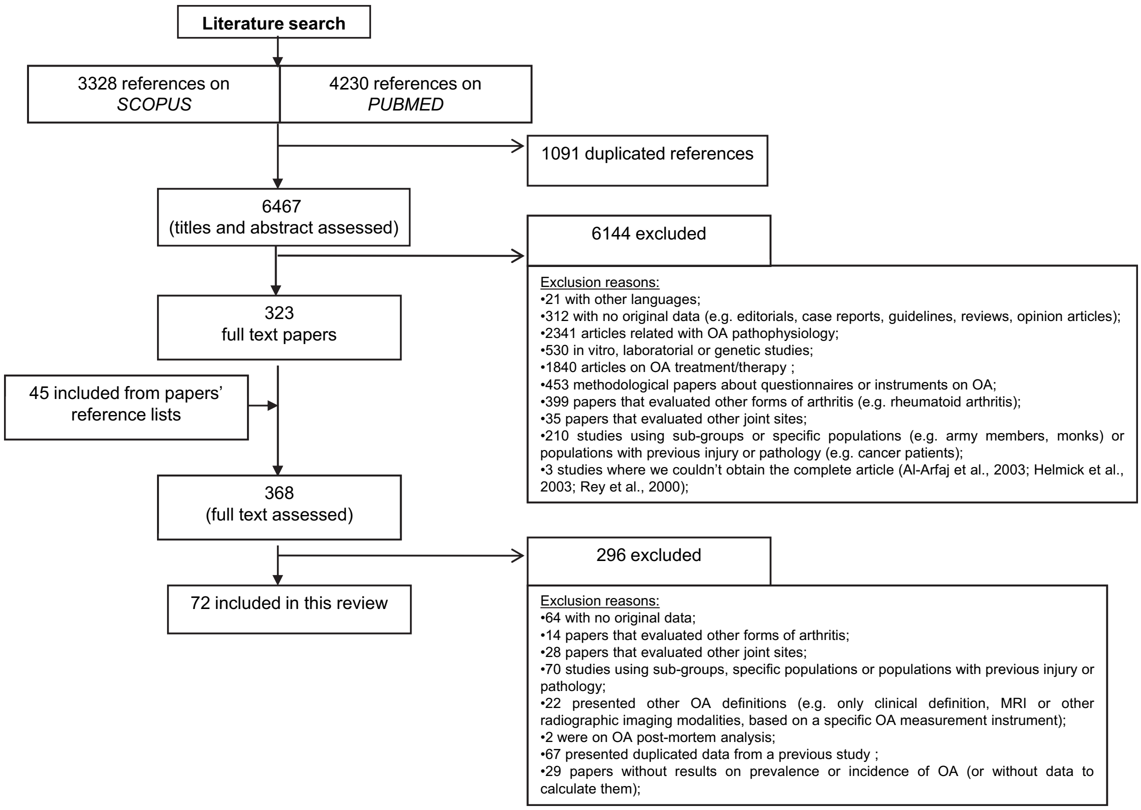

Fig. 1. Flow diagram on literature search.

Assessment of methodological quality results

The potential range of our score of quality was 0–8 and the overall mean score for methodological quality of studies included in the analysis regarding prevalence was 5.9 ± 0.9 and 6.9 ± 0.8 for incidence studies. As far as prevalence is concerned, the mean score of studies according to the joint site evaluated was: 6.0 ± 0.8 for knee, 5.7 ± 1.1 for hip and 5.7 ± 0.8 for hand. No subgroup analysis was made for incidence due to the small number of studies addressing this issue. The proportion of studies that met each criterion and the total score are presented in Table I. Lower scores were found for items 7 (CIs and subgroup analysis) and 8 (study subjects description) both in prevalence and incidence studies.

In order to better organize the contents according to OA case definition we present each joint site in one table. Prevalence papers on OA presented data for knee ($n = 45$; Table II), hip ($n = 27$; Table III) and hand ($n = 20$; Table IV). Only nine papers presented data on the incidence of OA, with data for knee ($n = 7$), hip ($n = 4$) and hand ($n = 3$) (Table V).

Prevalence

Radiographic definition is the most widely used criteria, and was present in 58% of prevalence studies. Self-reported diagnosis was, in general, the least commonly used, and generally in younger populations. Analysing OA prevalence meta-analysis (95% CIs) by sex and joint site, we can see that the hand is the joint site with highest OA prevalence and the hip is the joint with the lowest prevalence. Similar estimates were found by sex both for hand and hip OA, but regarding knee OA women presented higher prevalence values than men ($P < 0.01$) (Table VI).

To understand the influence of hospital based studies we made a sensitivity analysis regarding this variable. Only two hospital based data were found for knee, three for hand and 10 for hip. So,

Table I
Methodological quality evaluation of the studies included

Methodological quality item	Prevalence studies (item compliance)				Incidence studies (item compliance)
	Knee	Hip	Hand	Overall	Overall
1. Random sample or whole population	97.7%	89.7%	100%	95.6%	100%
2. Unbiased sampling frame	97.7%	96.6%	88.9%	95.6%	88.9%
3. Adequate sample size (>300 subjects)	93.2%	93.1%	77.8%	90.1%	100%
4. Measures were the standard*	100%	100%	100%	100%	100%
5. Outcomes measured by unbiased assessors	97.7%	86.2%	94.4%	93.4%	100%
6. Adequate response rate (70%), refusers described	61.4%	55.2%	66.7%	60.4%	66.7%
7. CIs, subgroup analysis	13.6%	3.4%	5.6%	8.8%	55.6%
8. Study subjects described	38.6%	44.8%	38.9%	40.7%	77.8%
Total score (min 0–max 8) [Mean ± standard deviation (SD)]	6.0 ± 0.8	5.7 ± 1.1	5.7 ± 0.8	5.9 ± 0.9	6.9 ± 0.8

* One-point score attributed to all studies.

Table II
Knee prevalence studies included in this review

Joint site	OA definition	Author	Publ. year	Country	Sample size	*n* women	*n* men	Age range	Mean age (±SD)	Prevalence women (95% CI) %	Prevalence men (95% CI) %	Crude overall prevalence (95% CI) %	Method. quality score (0–8)
Knee	Self-reported	Carmona *et al.*[29]	2001	Spain	2192†	1178	1014	≥20	–	14.0 (12.1–16.0)‡	5.7 (4.4–7.3)‡	10.2 (8.5–11.9)	6
		Picavet *et al.*[2]	2003	Netherlands	7818†	3878	3940	≥25	–	13.6 (12.1–5.1)	10.1 (8.6–11.6)	11.8‡ (11.1–12.6)‡	6
		Costa *et al.*[30]	2004	Portugal	1238†	787	451	≥18	–	14.2 (11.8–6.9)	5.9 (3.9–8.6)	11.1 (9.4–13.1)	5
		Haq *et al.*[31]	2005	Bangladesh	5160†	2578	2582	≥15	–	10.1‡ (9.0–11.3)‡	7.4‡ (6.4–8.4)‡	8.7‡ (8.0–9.5)‡	6
		Grotle *et al.* a)[32]	2008	Norway	3266†	1796	1470	24–76	–	7.9 (6.7–9.2)	6.3 (5.1–7.6)	7.1 (6.3–8.0)	7
		Tukker *et al.*[33]	2009	Netherlands	3664†	2024	1640	≥25	54.6	16.5 (14.9–18.2)‡	13.0 (11.4–14.7)‡	15.0 (13.8–16.1)‡	6
	Radiographic	Hochberg *et al.*[34]	1996	USA	898†	351	547	≥20	–	28.5 (24.0–33.4)‡	31.6 (27.8–35.6)‡	30.4 (27.5–33.5)‡	6
		Odding *et al.*[35]	1998	Netherlands	2895†	1739	1156	55–93	68.6 ± 7.5	29.1 (27.0–31.2)	16.3 (14.2–18.4)	24 (22.5–25.6)‡	7
		Shiozaki *et al.*[36]	1999	Japan	1463†	858	605	54–79	–	29.7 (27.6–31.9)‡	10.9 (9.2–12.8)‡	21.9 (20.5–23.5)‡	6
		Cvijetiae *et al.*[37]	2000	Croatia	610†	306	304	≥45	–	9.9 (6.8–13.5)‡	4.3 (2.4–7.0)‡	7.1 (5.2–9.3)‡	5
		Sowers *et al.*[38]	2000	USA	1053†	1053	0	42–52	–	14.2 (11.8–16.6)	–	14.2 (11.8–16.6)	7
		Zhang *et al.*[6]	2001	China	1781†	1051	730	≥60	–	42.8 (39.8–45.8)‡	21.5 (18.6–24.6)‡	34.1 (31.9–36.3)‡	7
		Yoshida *et al.*[39]	2002	Japan	358†	358	0	63–89	–	46.8 (41.8–52.1)‡	–	46.8 (41.8–52.1)‡	6
		Yoshida *et al.*[39]	2002	USA	815†	815	0	63–89	–	35.0 (31.8–38.3)‡	–	35.0 (31.8–38.3)‡	6
		Al-Arfaj *et al.*[40]	2002	Saudi Arabia	300*	133	167	40–75	–	60.9 (52.4–68.9)‡	53.3 (45.7–60.8)‡	56.7 (51.0–62.2)‡	5
		Du *et al.*[41]	2005	China	2093†	1199	894	≥62	–	47.1 (44.3–50)	40.6 (37.4–43.9)‡	44.6 (42.5–46.8)‡	5
		Szoeke *et al.*[42]	2006	Australia	224†	224	0	≥45	59.9±2.5	21.9‡ (16.8–27.6)‡	–	21.9‡ (16.8–27.6)‡	5
		Dillon *et al.*[43]	2006	USA	2415†	1271	1144	≥60	–	42.1 (38.2–46.0)	31.2 (26.4–35.9)	37.4 (35–39.8)	7
		Janssen & Mark[44]	2006	Canada	2323†	1219	1104	≥20	70.6 ± 9.5	50.4 (47.6–53.2)‡	43.5 (40.6–46.4)‡	47.4 (45.4–49.4)‡	6
		Tamm *et al.*[45]	2008	Estonia	160*	101	59	34–55	–	–	–	63.8 (56.1–70.9)‡	4
		Sudo *et al.*[46]	2008	Japan	596†	392	204	65–98	73.6	36.5 (31.8–41.3)‡	17.7 (12.9–23.3)‡	30.0 (26.5–33.8)‡	6
		Jordan *et al.*[47]	2007	USA	3068†	1906	1162	≥45	–	31.0 (29.2–32.8)	23.7 (22–25.5)	27.8 (26.5–29.2)	7
		Miura[48]	2008	Japan	450†	325	125	24–87	–	31.1(26.2–36.3)‡	23.2 (16.4–31.2)‡	28.9 (24.8–33.2)‡	5
		Kang *et al.*[49]	2009	China	1025†	520	505	≥50	58.8 ± 8	29.6 (16.4–23.2)‡	10.3 (7.9–13.2)‡	15.1 (13.0–17.4)‡	6
		Oka *et al.*[50]	2009	Japan	719†	449	270	≥60	72.1 ± 6.3	78.6(74.6–82.2)‡	57.8 (51.8–63.6)‡	70.8 (67.4–74.0)‡	6
		Muraki *et al.*[51]	2009	Japan	1471†	940	531	≥50	68.4 ± 9.2	61.2 (58–64.2)‡	45.6 (41.4–49.8)‡	55.6 (53.0–58.1)‡	6
		Bergink *et al.*[15]	2009	Netherlands	1248†	728	520	≥55	66.2 ± 6.7	–	–	6.5 (5.2–8.0)‡	5
		Laxafoss *et al.*[52]	2010	Denmark	3784†	2347	1437	22–93	–	14.2 (12.8–15.6)‡	12.1 (10.5–13.9)‡	13.4 (12.3–14.5)‡	8
		Ding *et al.*[53]	2010	Tasmania	806†	385	411	51–81	61.8 ± 7.1	69.6 (65.0–74.0)‡	64.5 (59.8–69.0)	67.0 (63.7–70.2)‡	6
		Kim *et al.*[54]	2010	Korea	504†	274	230	50–89	70.2 ± 8.0	54.7 (48.8–60.6)	16.5 (12.1–21.7)‡	37.3 (33.2–41.6)‡	5
		Cho[55]	2011	Korea	696†	398	298	≥65	71.7 ± 5.3	53.8 (48.9–58.7)‡	17.1 (12.8–21.4)‡	38.1 (34.5–41.7)‡	6
	Symptomatic	Shiozaki *et al.*[36]	1999	Japan	1463†	858	605	54–79	–	19.5 (17.7–21.5)‡	8.8 (7.3–10.5)‡	15.1 (13.8–16.4)‡	6
		Zhang *et al.*[6]	2001	China	1781†	1051	730	≥60	–	15.0 (13.0–17.3)‡	5.6 (4.1–7.5)‡	11.1‡ (9.8–12.7)‡	7
		Du *et al.*[41]	2005	China	2093†	1199	894	≥62	–	9.8 (8.3–11.6)‡	3.7 (2.6–5.1)‡	7.2 (6.1–8.3)‡	5
		Kacar *et al.*[56]	2005	Turkey	655†	306	349	≥50	59.7 ± 8.3	22.5 (18.1–27.5)‡	8.0 (5.5–11.2)‡	14.8 (12.2–17.7)‡	6
		Salaffi *et al.*[57]	2005	Italy	2155†	1151	1004	18–91	–	–	–	5.4 (3.4–8.0)‡	5
		Dillon *et al.*[43]	2006	USA	2394†	1261	1133	≥60	–	13.6 (11.3–15.9)	10.0 (7.0–13.0)	12.1 (10.6–13.5)	7
		Andrianakos *et al.*[58]	2006	Greece	8740†	4269	4471	19–99	47.0 ± 17.7	8.6 (7.5–9.5)‡	3.2 (2.7–3.7)‡	6.3 (5.8–6.8)	7
		Zeng *et al.*[59]	2006	China	2188†	1139	1049	35–64	–	15.4 (13.4–17.5)‡	6.6 (5.2–8.2)‡	11.2 (9.9–12.5)‡	7
		Jordan *et al.*[47]	2007	USA	3068†	1906	1162	≥45	–	18.7 (17.3–20.2)	13.5 (12.2–14.8)‡	16.4 (15.4–17.6)	7
		Quintana *et al.*[60]	2008	Spain	7577†	4264	3313	60–89	–	14.9 (13.8–16.0)‡	8.7 (7.8–9.7)‡	12.2 (11.5–12.9)‡	6
		Sudo *et al.*[46]	2008	Japan	596†	392	204	65–98	73.6	26.7 (22.6–31.3)‡	10.7 (7.1–15.6)‡	21.2 (18.0–24.6)‡	6
		Roux *et al.*[61]	2008	France	1380†	–	–	40–75	58.3	–	–	7.6 (6.4–8.8)	5
		Kang *et al.*[49]	2009	China	1025†	520	505	≥50	58.0 ± 8.0	14.2 (11.4–17.4)‡	6.9 (5.0–9.4)‡	10.6 (8.9–12.6)‡	6
		Kim *et al.*[54]	2010	Korea	504†	274	230	50–89	70.2 ± 8.0	38.0 (32.4–44.8)‡	7.4 (4.5–11.3)‡	24.2 (20.4–27.9)‡	5

* Hospital based study.
† Population based study.
‡ Calculated based on data presented in the paper.

Table III
Hip prevalence studies included in this review

Joint site	OA definition	Author	Publ. year	Country	Sample size	*n* women	*n* men	Age range	Mean age (±SD)	Prevalence women (95% CI) %	Prevalence men (95% CI) %	Crude overall prevalence (95% CI) %	Method. quality score (0–8)
Hip	Self-reported	Picavet *et al.*[2]	2003	Netherlands	7818†	3878	3940	≥25	–	9.6 (8.3–10.9)	3.9 (3.0–4.8)	6.7‡ (6.2–7.3)‡	6
		Costa *et al.*[30]	2004	Portugal	1238†	787	451	≥18	–	7.4 (5.7–9.5)	2.2 (1.1–4.2)	5.5 (4.3–7.0)	5
		Grotle *et al.* a)[32]	2008	Norway	3266†	1796	1470	24–76	–	6.2‡ (5.1–7.4)‡	4.6‡ (3.6–5.8)‡	5.5 (4.7–6.3)	7
		Tukker *et al.*[33]	2009	Netherlands	3664†	2024	1640	≥25	54.6	12.3 (10.9–13.8)‡	6.5 (5.4–7.8)‡	9.7 (8.8–10.7)‡	6
	Radiographic	Lau *et al.*[62]	1995	Japan	999*	0	999	65–75	70.0 ± 7.0	–	5.4 (4.1–6.9)‡	5.4 (4.1–6.9)‡	7
		Ali-Gombe *et al.*[63]	1996	Nigeria	63*	0	63	60–75	–	–	7.0 (3.5–12.7)‡	7.0 (3.5–12.7)‡	3
		Danielsson & Lindberg[64]	1997	Sweden	4121*	2410	1711	≥40	–	2.0 (1.5–1.7)‡	1.7 (1.2–2.4)‡	1.9 (1.5–2.3)‡	5
		Hirsch *et al.*[65]	1998	USA	749*	457	292	45–93	–	2.8 (1.6–4.7)‡	4.8 (2.8–7.7)‡	3.6 (2.4–5.1)‡	6
		Odding *et al.*[35]	1998	Netherlands	2895†	1739	1156	55–93	68.6	15.9 (14.2–17.6)	14.1 (16.1–21.1)	15.2 (12–18.4)‡	7
		Yoshimura *et al.*[66]	1998	Britain	1498†	195	1303	60–75	–	4.8 (2.5–6.7)	11 (9.8–12.3)	10.2 (8.8–11.8)‡	7
		Yoshimura *et al.*[66]	1998	Japan	198†	99	99	60–79	–	0	2.0 (0.04–4.0)	1.0 (0.2–3.3)‡	7
		Ingvarsson *et al.*[67]	1999	Iceland	1517*	873	644	≥35	68.0	10.1 (8.2–12.2)‡	12.0 (9.6–14.6)‡	10.8 (9.4–12.5)‡	7
		Inoue *et al.*[68]	2000	France	401*	118	283	20–79	–	2.5 (0.7–6.8)‡	5.7 (3.4–8.8)‡	4.7 (3.0–7.2)‡	4
		Inoue *et al.*[68]	2000	Japan	782*	368	414	20–79	–	3.5 (2–5.8)‡	1.4 (0.6–3.0)‡	2.4 (1.5–3.7)‡	4
		Cvijetiae *et al.*[37]	2000	Croatia	610†	306	304	≥45	–	18.6 (14.6–23.3)‡	27.3 (22.5–32.5)‡	23.0 (19.7–26.4)‡	5
		Goker[69]	2001	Turkey	682*	205	477	25–97	–	9.4(5.8–13.8)‡	12.6 (9.8–15.8)‡	11.7 (9.3–14.2)‡	6
		Nevitt *et al.*[70]	2002	China	1492†	878	614	60–89	–	0.9 (0.4–1.7)‡	1.1 (0.5–2.2)‡	1.0 (0.6–1.6)‡	7
		Jacobsen *et al.*[71]	2004	Denmark	3807†	2359	1448	23–93	–	5.0 (4.2–5.9)‡	10.8 (9.3–12.5)‡	7.2 (6.4–8.1)‡	7
		Goker *et al.*[72]	2005	Turkey	92*	27	65	≥55	64.0 ± 7.0	–	–	14.0 (8.1–22.4)‡	5
		Kim *et al.*[73]	2008	South Korea	580*	290	290	71–95	78.3	0.7 (0.1–2.3)‡	1.7 (0.6–3.8)‡	1.2 (0.5–2.4)‡	4
		Chung *et al.*[74]	2009	Korea	674†	386	288	65–99	71.7 ± 5.3	–	–	13.1 (10.5–15.6)‡	6
		Johnsen *et al.*[75]	2009	Norway	836†	412	424	20–64	–	7.1 (4.9–9.8)‡	6.5 (4.5–9.3)‡	6.8 (5.3–8.7)‡	6
		Ding *et al.*[53]	2010	Tasmania	801†	407	416	51–81	61.8 ± 7.1	46.9 (42.1–51.8)‡	42.9 (38.1–47.8)‡	45.0 (41.5–48.4)‡	6
	Symptomatic	Salaffi *et al.*[57]	2005	Italy	2155†	1151	1004	18–91	57.8 ± 18.4	–	–	1.6 (1.4–1.9)‡	5
		Andrianakos *et al.*[58]	2006	Greece	8740†	4269	4471	19–99	47.0 ± 17.7	1.5 (1.0–1.9)‡	0.3 (0.2–0.5)‡	0.9 (0.7–1.1)	7
		Roux *et al.*[61]	2008	France	1380†	–	–	40–75	58.3	–	–	5.0 (3.9–6.1)	5
		Quintana *et al.*[60]	2008	Spain	7577†	4264	3313	60–89	–	8.0 (7.2–8.8)‡	6.7 (5.9–7.6)‡	7.4 (6.9–8.0)‡	6

* Hospital based study.
† Population based study.
‡ Calculated based on data presented in the paper.

Table IV
Hand prevalence studies included in this review

Joint site	OA definition	Author	Publ. year	Country	Sample size	*n* women	*n* men	Age range	Mean age (±SD)	Prevalence women (95% CI) %	Prevalence men (95% CI)%	Crude overall prevalence (95% CI) %	Method. quality score (0–8)
Hand	Self-reported	Carmona *et al.*[29]	2001	Spain	2192†	1178	1014	≥20	–	9.5 (7.9–11.3)‡	2.3 (1.5–3.3)‡	6.2 (5.9–6.5)	6
		Grotle *et al.* a)[32]	2008	Norway	3266†	1796	1470	24–76	–	5.8‡ (4.8–6.9)‡	2.5‡ (1.8–3.4)‡	4.3 (3.6–5.0)	7
	Radiographic	Sowers *et al.*[38]	2000	USA	1053†	1053	0	42–52	–	20.6 (17.8–23.3)	–	20.6 (17.8–23.3)	7
		Caspi *et al.*[76]	2001	Israel	253*	171	82	≥62§	78.8 ± 8.3	82.5 (76.2–87.6)‡	82.9 (73.6–89.9)‡	82.6 (77.6–86.9)‡	5
		Al-Arfaj *et al.* b)[77]	2002	Saudi Arabia	300*	133	167	40–75	–	36.3 (28.3–44.5)‡	30.3 (23.9–37.8)‡	33.0 (27.9–38.5)‡	4
		Zhang *et al.*[78]	2003	China	2507†	1503	1004	≥60	72.7	47.0 (44.5–49.5)‡	44.5 (41.5–47.6)‡	46.0 (44.0–48.0)‡	6
		Haara *et al.*[79]	2003	Finland	3595†	2035	1560	≥30	–	48.1 (45.9–50.3)‡	44.3 (41.8–46.8)‡	46.5 (44.8–48.1)‡	7
		Dahaghin *et al.*[13]	2005	Netherlands	3906†	2101	1805	≥50	66.6 ± 7.3	67.0 (65.0–69.0)‡	54.8 (52.5–57.1)‡	61.4 (59.8–62.9)‡	6
		Wilder *et al.*[80]	2006	USA	3327†	2302	1025	40–94	62.0 ± 11.0	41.1‡ (39.1–43.1)‡	41.8‡ (38.8–44.8)‡	41.3‡ (39.6–43.0)‡	6
		Toba *et al.*[81]	2006	Japan	551†	551	0	40–89	63.9	74.4 (70.6–78)‡	–	74.4 (70.6–78.0)‡	5
		Szoeke *et al.*[42]	2006	Australia	224†	224	0	≥45	59.9 ± 2.5	45.0‡ (38.7–51.6)‡	–	45.0‡ (38.7–51.6)‡	5
		Kalichman *et al.* a)[82]	2009	Russia	1005†	463	542	18–95	–	35.4 (31.1–39.9)‡	33.6 (29.7–37.6)‡	34.4 (31.5–37.4)‡	5
		Kalichman *et al.* b)[83]	2009	Turkmenistan	704*	427	277	19–90	49.0 ± 17.1	57.2 (52.4–61.8)‡	62.2 (56.3–67.7)‡	59.1 (55.4–62.7)‡	6
		Kalichman *et al.* c)[84]	2010	Russia	899*	481	418	18–60	–	30.9 (27.0–35.2)‡	34.9 (30.5–39.6)‡	32.8 (29.8–35.9)‡	6
		Kalichman *et al.* d)[85]	2010	Russia	1897*	1076	821	18–90	–	54.4 (51.4–57.3)‡	58.1 (54.7–61.4)‡	56.0 (53.7–58.2)‡	6
	Symptomatic	Caspi *et al.*[76]	2001	Israel	253*	171	82	≥62§	78.8 ± 8.3	75.4 (68.6–81.5)‡	80.5 (70.9–88)‡	77.1 (71.6–81.9)‡	5
		Zhang *et al.*[86]	2002	USA	1032†	668	369	71–100	–	26.2 (22.9–29.6)	13.3 (9.8–16.7)	21.6 (19.2–24.2)‡	6
		Zhang *et al.*[78]	2003	China	2507†	1503	1004	≥60	72.7	5.8 (4.7–7.1)‡	3.0 (2.1–4.2)‡	4.7 (3.9–5.6)‡	6
		Salaffi *et al.*[57]	2005	Italy	2155†	1151	1004	18–91	57.8 ± 18.4	–	–	2.0 (1.2–2.9)‡	5
		Andrianakos *et al.*[58]	2006	Greece	8740†	4269	4471	19–99	47.0 ± 17.7	3.4 (2.9–4.0)‡	0.5 (0.3–0.7)‡	2.0 (1.7–2.3)	7

* Hospital based study.
† Population based study.
‡ Calculated based on data presented in the paper.
§ Estimated minimum age (mean age − 2× SD).

Table V
Incidence studies included in this review

Joint site	OA definition	Author	Publ. year	Country	Sample size	*n* women	*n* men	Age at baseline (years)	Mean age at baseline ±SD	Mean follow-up period (years)	Cumulative incidence %	Annual incidence %	Method. quality score (0–8)
Knee	Self-reported	Grotle *et al.* b)[88]	2008	Norway	1675†	943	732	24–76	41.8 ± 12.9	10	Women 7.3 (95% CI 5.7–9.0); Men 6.2% (95% CI 4.4–7.9)	–	8
		Verweij *et al.*[89]	2009	Netherlands	1678†	–	–	55–85	68.0 ± 8.0	12	27.6%	–	7
	Radiographic	Felson *et al.*[90]	1995	USA	598†	381	217	63–92	70.5 ± 4.9	8	15.6%	Women 2%; Men 1.2%	7
		Hart *et al.*[91]	1999	UK	830†	0	830	≥42§	54.1 ± 5.9	4	12.6%	3.1%	6
		Cooper *et al.*[92]	2000	UK	354†	255	99	≥55	–	5	12.7%	Incidence rates of 2.5%	7
	Symptomatic	Felson *et al.*[90]	1995	USA	598†	381	217	63–92	70.5 ± 4.9	8	–	Women 1%; Men 0.6%	7
		Oliveria *et al.*[93]	1995	USA	1553*	–	–	20–89	–	3.5‡	–	Age and sex adjusted incidence of 0.24 person-year (95% CI 0.22–0.26)	7
Hip	Self-reported	Grotle *et al.* b)[88]	2008	Norway	1675†	943	732	24–76	41.8 ± 12.9	10	Women 5.8% (95% CI 4.3–7.3); Men 3.8% (95% CI 2.4–5.2)	–	8
	Radiographic	Reijman *et al.*[94]	2005	Netherlands	835†	478	375	≥55	65.6 ± 6.5	6.6	9.3%	–	6
		Lane *et al.*[95]	2000	USA	176†	176	0	≥65	70.3 ± 4.7	8	33%	–	6
	Symptomatic	Oliveria *et al.*[93]	1995	USA	1003*	–	–	20–89	–	3.5‡	–	Age and sex adjusted incidence of 0.09 person-year (95% CI 0.75–1)	7
Hand	Self-reported	Grotle *et al.* b)[88]	2008	Norway	1675†	943	732	24–76	41.8 ± 12.9	10	Women 5.6% (95% CI 4.2–7.1); Men 2.5% (95% CI 1.3–3.6)	–	8
	Radiographic	Chaisson *et al.*[96]	1997	USA	751†	496	255	47–76	55.0 ± 5.6	24	83% Women 87%; Men 76%	–	8
	Symptomatic	Oliveria *et al.*[93]	1995	USA	696*	–	–	20–89	–	3.5‡	–	Age and sex adjusted incidence of 0.1 person-year (95% CI 0.9–1.1)	7

* Hospital based study.
† Population based study.
‡ Calculated based on data presented in the paper.
§ Estimated minimum age (mean age − 2× SD).

Table VI
Overall prevalence of knee, hip and hand OA (95% CIs) and heterogeneity by sex and joint site

Joint site	OA prevalence women	OA prevalence men	OA prevalence total
Knee	27.3%* 95% CI [26.9–27.7] $I^2 = 99.3\%$	21.0%* 95% CI [20.5–21.5] $I^2 = 99.7\%$	23.9% 95% CI [23.6–24.2] $I^2 = 99.8\%$
Hip	11.6% 95% CI [11.1–12.1] $I^2 = 99.7\%$	11.5% 95% CI [11.0–12.1] $I^2 = 99.9\%$	10.9% 95% CI [10.6–11.2] $I^2 = 99.8\%$
Hand	43.3% 95% CI [42.6–44.0] $I^2 = 99.1\%$	44.5% 95% CI [43.5–45.5] $I^2 = 99.9\%$	43.3% 95% CI [42.7–42.9] $I^2 = 100\%$

* *P* value<0.01 for gender comparison using *Mann–Whitney* test.

we couldn't compare results by joint sites and definition used. Considering results only by joint site we found a higher prevalence estimate for knee OA from hospital based studies compared to population based studies [49.9 (45.1–54.8) vs 23.7 (23.4–24.0) $P < 0.001$]; in hip, hospital based studies presented lower estimates [7.6 (6.8–8.3)] compared to population based studies [11.4 (11.0–11.8)], $P < 0.001$. In hand similar results were found according to sample base [42.9 (42.2–43.5) for hospital based vs 43.3 (42.7–43.9) for population based; $P = 0.86$]. The overall prevalence in the three joints including both hospital and population studies was similar to the overall prevalence in only population based studies, so we decide to maintain these studies in this review.

According to the results observed in Table VI, and due to the small number of papers, forest graphs were stratified by gender for knee OA (Figs. 2 and 3) but overall representation was done for hip (Fig. 4) and hand (Fig. 5). In general, graphic representations allow us to see that radiographic definition presents higher estimates and that symptomatic definition and self-reported OA definitions tend to present similar results.

To look for the possible effect of age and sex differences according to OA definition we stratified studies according to three age groups using the minimum age (<45, 45–59 and ≥60). Due to the small number of studies for hip and hand, this analysis was only possible for knee OA (Table VII).

Knee OA

Regardless of the definition used, the prevalence ranged from 6.3% in Greece[58] to 70.8% in Japan[50]. Based on self-reported definition we found six studies with estimates which ranged from 7.1% in Norway[32] to 15.0% in The Netherlands[33]. For the knee, a wide range of results were found with radiographic case definition, from 7.1% in Croatia[37], to 70.8% in Japan[50]. Based on symptomatic definition the lowest estimate is found in Italy (5.4%)[57] and the highest 24.2% in Korea[54]. In general, estimates based on radiographic definition present higher estimates than those based on self-reported and symptomatic definitions. However, the populations evaluated were very different as far as age is concerned (Figs. 2, 3 and Table II).

Through sensitivity analysis according with age, we found that radiographic-based studies presented higher estimates both in women and men, and in all age groups. Using symptomatic definition, the prevalence was higher in women in both age groups. Symptomatic definition and self-reported OA definitions presented similar results in the age group below 45 years old, and in both cases were higher in women. Insufficient data for analysis was found for self-reported OA in the age groups 45–59 and ≥60 (Table VII).

Hip OA

The four studies based on self-reported data to estimate hip OA found very similar results: 6.7%[2] and 9.7% in The Netherlands[33], 5.5% in Portugal[30] and in Norway[32]. The 19 studies based on radiographic definition presented estimates ranging from 1.0% both in Japan[66] and China[70] to 45.0% in Tasmania[53]. To investigate hip OA prevalence based on symptomatic definition we only found four studies: 0.9% in Greece (58); 1.6% in Italy[57]; 5.0% in France[61]; and 7.4% in Spain[60] (Fig. 4 and Table III).

Hand OA

The hand was the joint with the lowest number of studies included: two self-reported, 13 on radiographic and five symptomatic definition of OA. Self-reported prevalence for hand OA was estimated to be 6.2% in Spain[29] and 4.3% in Norway[32]. Radiographic definition studies ranged from 20.6% in The USA[38] to 82.6% in Israel[76]. The five studies based on symptomatic definition presented very different estimates: low estimates of 2.0% in Greece[58] and Italy[57]; 4.7% in China[78]; high prevalence of 19.2% in The USA[78] and much higher (77.1%) in Israel[76] (Fig. 5 and Table IV).

Incidence

Only eight papers presented data on the incidence of OA. The small number of studies and the heterogeneity of follow-up periods and measures used to express incidence in the different studies, did not allow us to draw further conclusions or to use any summary data. The most visible fact was that radiographic OA definition presented the higher incidence estimates in all joints (Table V).

Discussion

Our results have to be understood taking into account the high heterogeneity found even within each specific OA definition and joint site, related with the different methodologies and the limited number of studies, which made a more detailed analysis impossible. We evaluated data only for knee, hip and hand joints. However, we are of the opinion that the effect of this is hardly significant since these three locations are thought to be the most prevalent OA joint sites and with most impact in terms of treatment needs and related disability[97].

After analysing the studies reviewed, hand OA estimates showed the highest prevalence compared with other joint sites. In all joint sites considered, it was also evident that there is a tendency for higher prevalence estimates when radiographic definition is used, and studies based on self-reported and symptomatic definitions tend to present more similar estimates. As far as gender is concerned and considering knee OA, prevalence was higher in women than men; however, with regard to hip and hand OA those differences were only approximately 1%, although the limited number of studies must be taken into account.

Differences according to OA definition tend to show similar trends in the different joints. Compared to radiographic definition studies, we found lower prevalence estimates in studies based on symptomatic and self-reported definition studies, but generally these studies were used in younger populations. As is known OA prevalence increases with age[10], and we also found higher prevalence in studies with older populations. To understand if the differences according to OA definition could be explained by age, we stratified studies in three age groups, using the median of the minimum age because it was the age parameter available for almost all studies included. However, specific age differences need to be taken into account in the interpretation of the estimates: in some cases, with a large range of ages, minimum age might not represent the real age of participants; for example the study by Andrianakos *et al.*[58] presents a minimum age of 19, a maximum age of 99 and a mean age of 46.9 years. However, the small number of studies limits our options, and even considering only three age groups, sensitivity analysis was only possible for knee

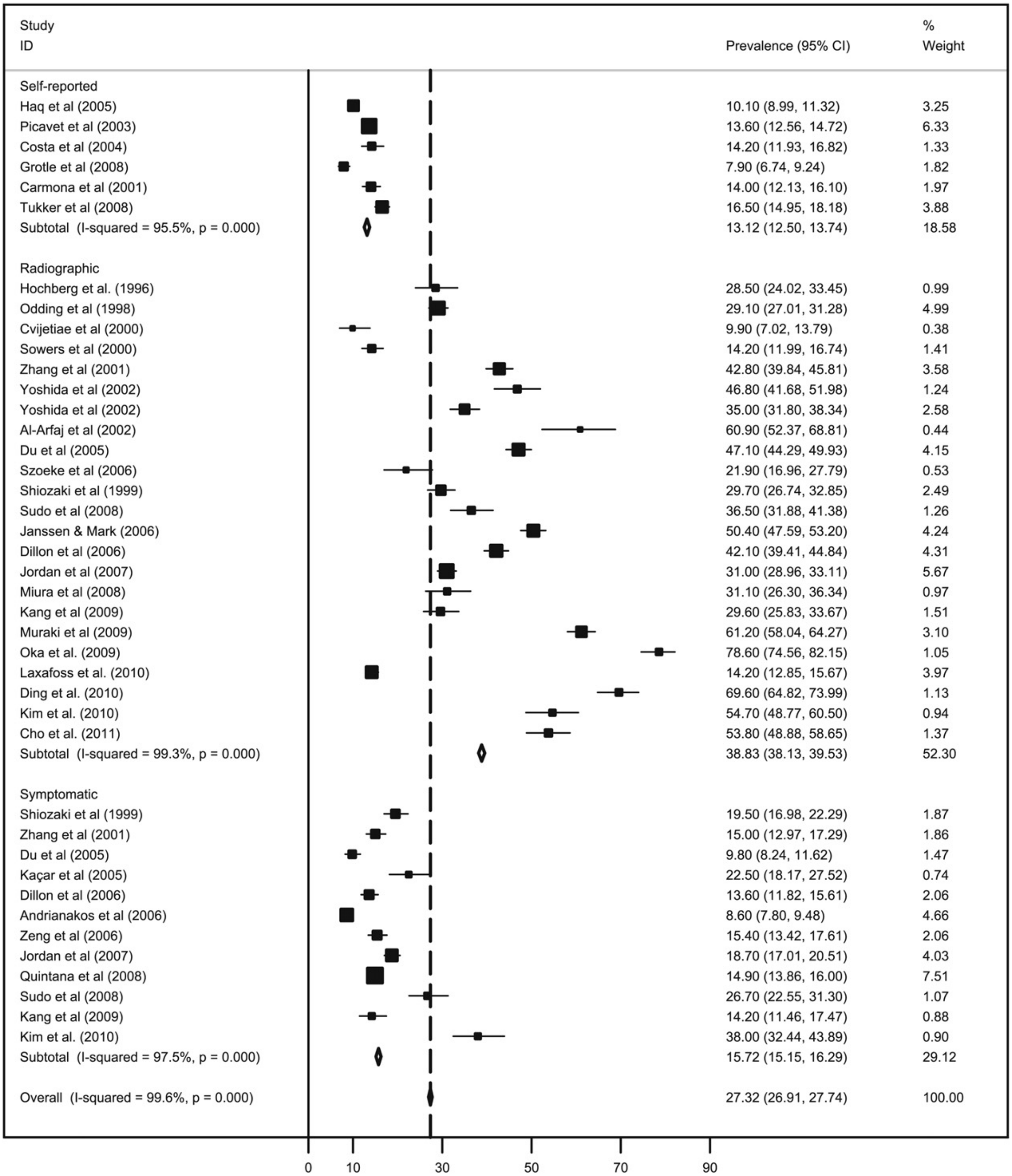

Fig. 2. Forest graph of knee OA prevalence meta-analysis, heterogeneity and 95% CIs by OA definition, in women.

OA. Despite these limitations, the analysis shows a higher prevalence when radiographic definition was used in all age groups and for both genders.

As far as incidence is concerned, data is limited probably because of the problems of defining it and how to determine its onset[96]. In this review the limited number of studies and the use of different incidence measures made any comparison impossible. However, there also seems to be a tendency for radiographic definition to overestimate OA incidence. This can be exemplified by the study by Felson *et al.*[90], where in the same participants OA incidence was twice as high when radiographic definition was used.

Apart from the epidemiological consequences, clinical implications also need to be explored. In this context, the emphasis to radiographic findings should always be given according to patient's physical signs[13,92], self-reported symptoms and disability[16,87,98]. Recent recommendations on knee OA diagnosis[99], state that in adults aged >40 years with usage-related knee pain, only short-lived morning stiffness, functional limitation and one or more typical examination findings (crepitus, restricted movement, bony enlargement), a confident diagnosis can be made without a radiographic examination. Nevertheless, X-rays are an objective instrument for OA pathophysiological findings[79] and people with early

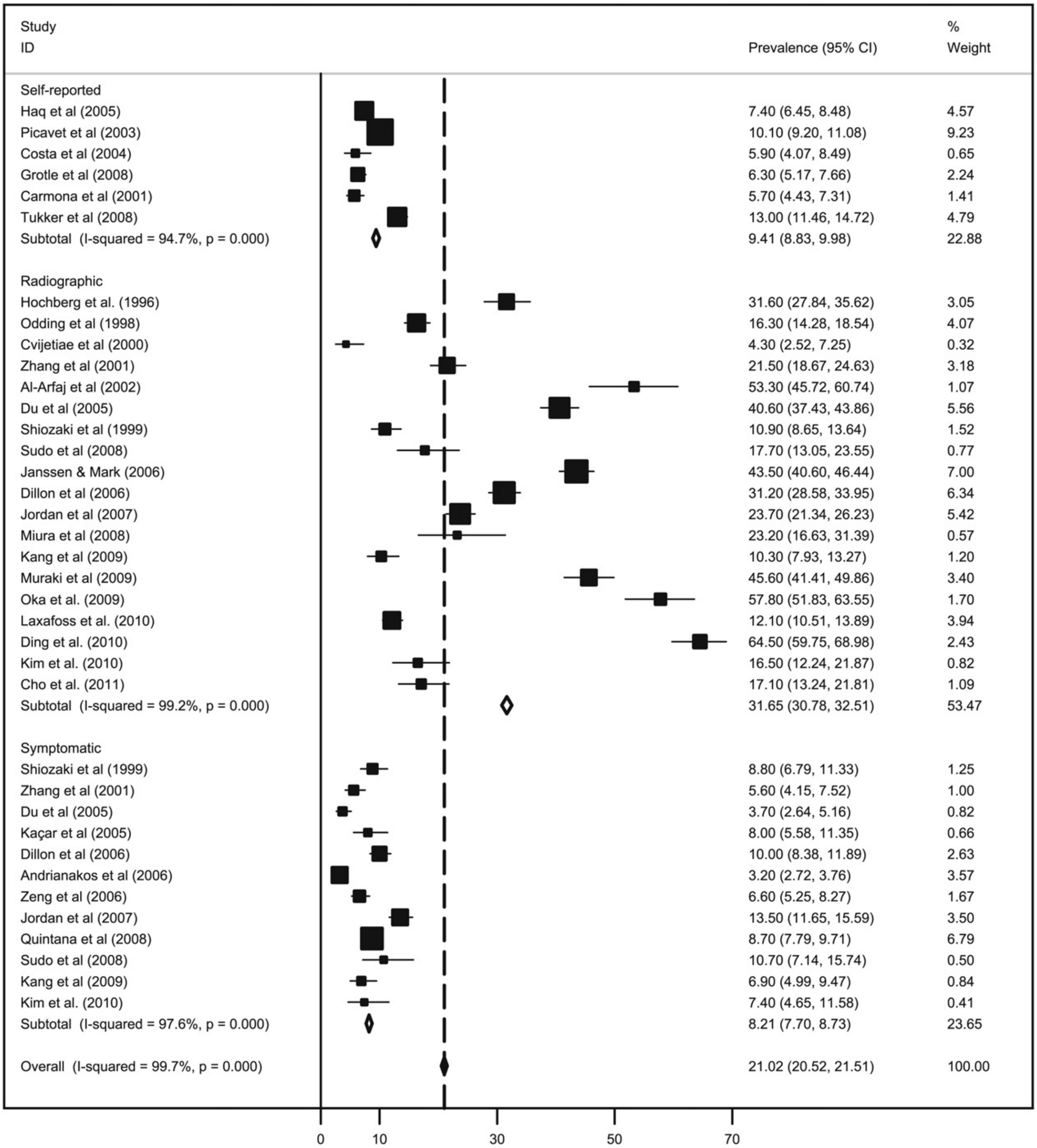

Fig. 3. Forest graph of knee OA prevalence meta-analysis, heterogeneity and 95% CIs by OA definition, in men.

radiographic changes have higher chances of having symptomatic OA in the future[12,13,92].

The radiographic evaluation, although it is the most objective measure, presents some reliability and validity limitations[11,71]. Criticism to radiographic grade systems, even for the most widely used radiographic definition in the studies reviewed (KL score $\geq$2), include: inconsistencies in the description of features of OA, the prominence given to osteophytes at all joint sites, and poor inter-rater and between-centre reliability[73,100]. Different radiographic scoring systems can explain some of the variability in the estimates within radiographic studies. For example, it was found in a systematic review of hip radiographic OA that prevalence was higher in studies using KL scale compared to the joint space width[14]. These differences within each radiographic definition were not evaluated in our study.

Symptomatic OA definition considers both clinical symptoms of OA and radiographic changes[87]. Thus, besides the different specific radiographic aspects between studies, symptom evaluation was also different. Some use medical doctor evaluation, questionnaires, interviews or just self-reported symptoms, which could lead to less objectivity and more variability between studies than the variability only due to evaluation of radiographic images. However, when we looked at forest plots, symptomatic definition studies presented less heterogeneity than radiographic studies.

In this review it can be seen that, particularly in knee and hand prevalence studies, the estimates based on self-reported data have

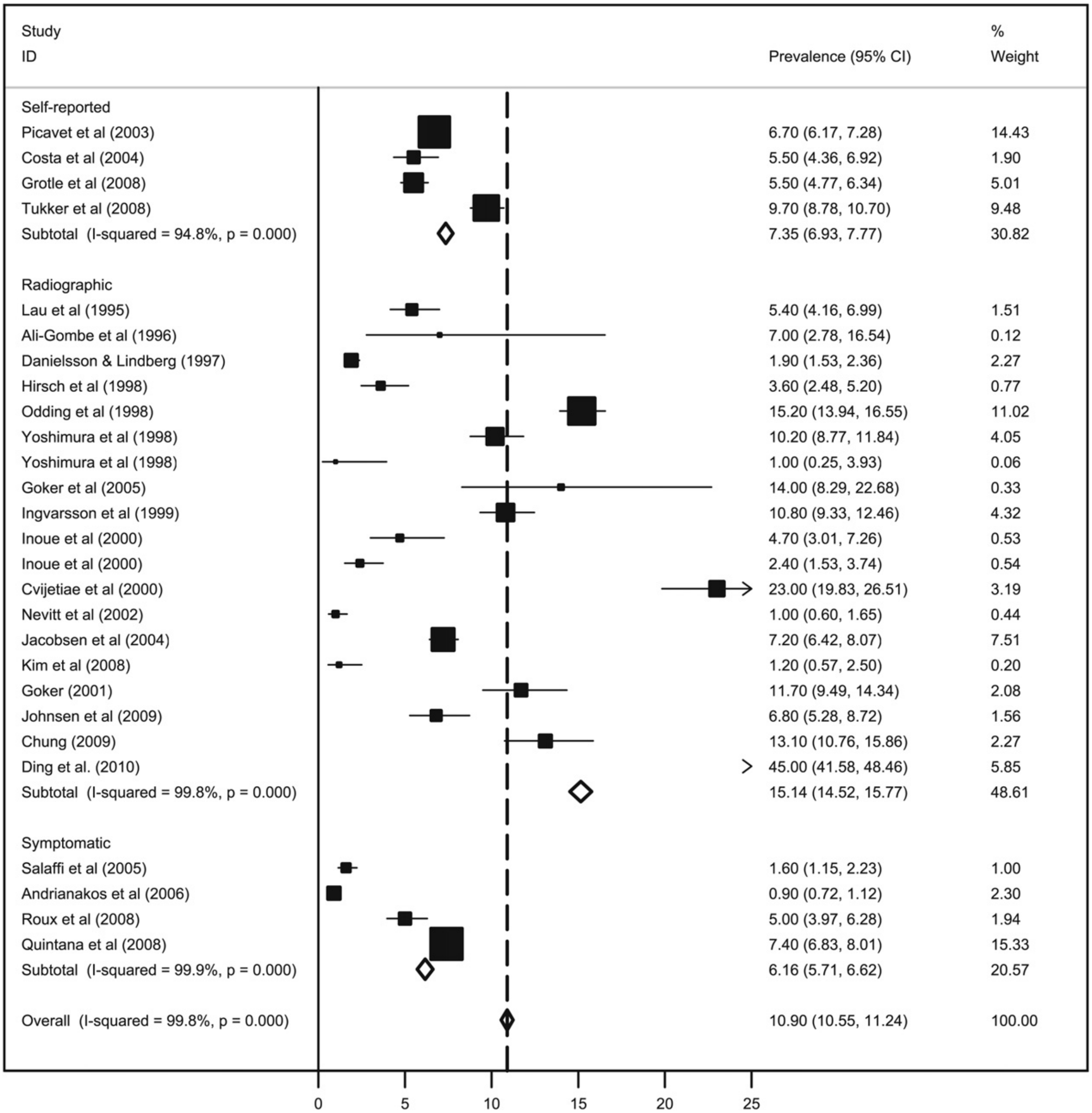

Fig. 4. Forest graph of hip OA prevalence meta-analysis, heterogeneity and 95% CIs by OA definition.

similar results to those with symptomatic case definition. Although we expected that self-reported OA was essentially based on a previous clinical diagnosis which is based on symptomatic and radiographic data, since the demand for a medical diagnosis is primarily determined by symptoms this could explain why these estimates were quite similar. This result was in agreement with Van Minh *et al.*[101] that states that estimates based on several self-reported chronic conditions are accurate when compared with physician diagnoses. However, the use of self-reported information on OA raises questions on the quality of information related with individual's characteristics. Once self-reported OA was based on a previous diagnosis, it is to be expected that all individual characteristics that affect health-care access (for instance, education and socio-economic level) can affect estimates based on self-reported OA[13,30,32], which could partially explain the differences between studies. However, we did not have enough studies or information to analyse this hypothesis.

Several large studies have demonstrated that women have a higher risk of developing OA than men for knee OA[9,58,93] but this is not always seen for the hip and hand[12]. Since women may perceive, evaluate, and act on symptoms differently[102] higher differences between genders could be expected when self-reported and symptomatic definitions were used. Nevertheless, our results in knee OA reveal that this also happened for radiographic estimates, which supports the hypothesis that women suffer from more progressive decline in joint space and loss of cartilage with age[8,9,18]. It would be interesting to evaluate the influence of gender according to the different definitions, in hip and hand, but the small number of studies made this impossible in our analysis.

Some studies tend to present different prevalences according to geographical regions[66,78]. Possible explanations for these differences range from genetic differences, to specific joint morphometry, socio-economic conditions, health-care access or other lifestyle or environmental factors[7,39,66]. Some of these characteristics could be

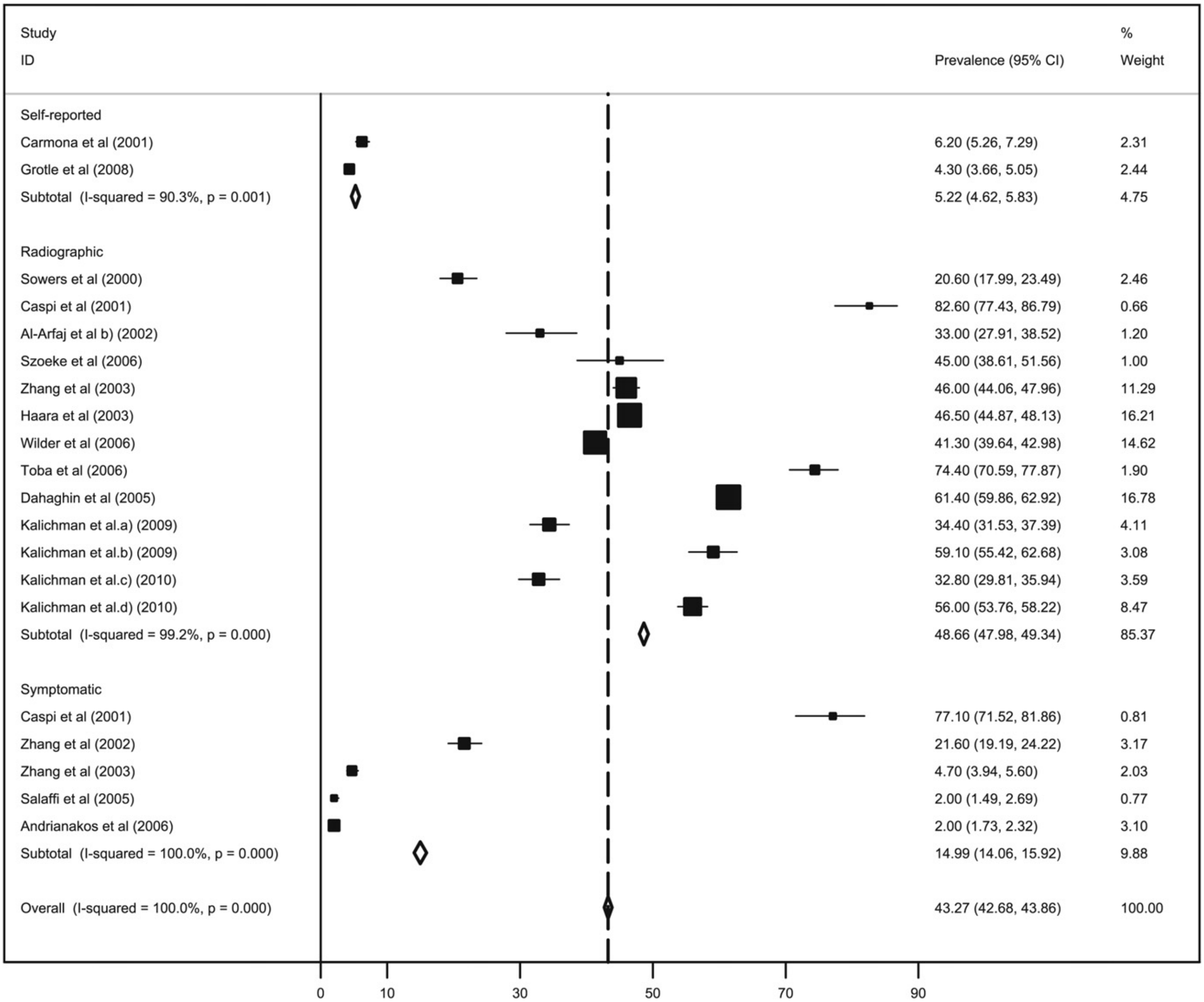

Fig. 5. Forest graph of hand OA prevalence meta-analysis, heterogeneity and 95% CIs by OA definition.

Table VII
Prevalence of knee OA (95% CIs) and heterogeneity by age, sex and OA definition

Knee OA definition		<45*		45–59*		≥60*	
		Women	Men	Women	Men	Women	Men
Self-reported	Number of studies	6	6	0	0	0	0
	Prevalence (95% CI)	13.1% 95% CI [12.5–13.7]	9.4% 95% CI [8.8–10.0]	Insufficient data for analysis	Insufficient data for analysis	Insufficient data for analysis	Insufficient data for analysis
	Heterogeneity	$I^2 = 95.5\%$	$I^2 = 94.7\%$				
Radiographic	Number of studies	9	7	6	6	8	6
	Prevalence (95% CI)	30.5% 95% CI [29.4–31.5]	30.4% 95% CI [29.0–31.7]	41.2% 95% CI [39.9–42.6]	31.3% 95% CI [29.7–32.9]	45.1% 95% CI [43.8–46.3]	33.4% 95% CI [31.9–35.0]
	Heterogeneity	$I^2 = 99.3\%$	$I^2 = 99.4\%$	$I^2 = 99.1\%$	$I^2 = 99.5\%$	$I^2 = 98.1\%$	$I^2 = 97.9\%$
Symptomatic	Number of studies	4	4	4	4	4	4
	Prevalence (95% CI)	13.2% 95% CI [12.4–14.0]	7.6% 95% CI [6.8–8.4]	22.7% 95% CI [20.8–24.6]	8.0% 95% CI [6.6–9.3]	15.7% 95% CI [14.8–16.6]	8.8% 95% CI [8.1–9.6]
	Heterogeneity	$I^2 = 98.3\%$	$I^2 = 99.1\%$	$I^2 = 95.3\%$	$I^2 = 0\%$	$I^2 = 90.5\%$	$I^2 = 81.9\%$
Total	Number of studies	19	17	10	10	12	10
	Prevalence (95% CI)	19.7% 95% CI [19.2–20.2]	17.4% 95% CI [16.8–18.0]	36.9% 95% CI [35.7–38.0]	26.9% 95% CI [25.6–28.1]	33.6% 95% CI [32.8–34.5]	24.3% 95% CI [23.3–25.3]
	Heterogeneity	$I^2 = 99.3\%$	$I^2 = 99.7\%$	$I^2 = 99.1\%$	$I^2 = 99.4\%$	$I^2 = 99.6\%$	$I^2 = 99.6\%$

* Age stratification using the minimum age of the participants in each study.

particularly relevant in studies that use self-reported or symptomatic evaluation. However, in our results, we were unable to obtain enough information to test this hypothesis.

Several limitations can be found in our review and additional methodological strategies should be considered in future studies. There could be a selection bias caused by the inclusion of hospital based studies. We found a higher prevalence of OA for knee and lower for hip among hospital based studies than among population based studies. This difference may be related with differences in selection criteria, however we need to highlight that only two hospital based studies were found for knee. However, hospital based studies represented a small proportion and no effect was found in overall prevalences; so we decided to maintain them, although we highlight the importance of considering this variable in the results interpretation.

An important component of a systematic review is the evaluation of the methodological quality of the studies included. Based on a recent systematic review of these tools[21] we chose the scale developed by Loney *et al.* specifically to measure prevalence and incidence[22] considering a 0–8 range score. We think the overall quality of studies included was good, which increases the value and interpretability of this review, in spite of the high heterogeneity of estimates found.

The extent of heterogeneity in a meta-analysis partly determines the difficulty in drawing overall conclusions[24]. Therefore, in our review no relevance should be given to the pooled prevalence; the most relevant results were found in the figures that clearly showed the similarity between self-reported and symptomatic definitions and the higher prevalence found in studies based on radiographic definitions. We could argue that heterogeneity in the estimates could be explained by OA definition but meta-analysis within studies using the same OA case definition continued to show a high heterogeneity between studies. Heterogeneity in the estimates seems to be related with study design factors, such as different age of populations, and also differences in how each specific OA definition was applied; these differences within OA definitions were not evaluated in this review.

We only used the *PUBMED* and *SCOPUS* databases, which may reduce the number of studies included. However these databases represent a high proportion of the journals covering this issue. We thus believe that we collected a very representative sample of studies published in the period chosen, and it is most likely that the papers not identified, would present similar differences between OA definitions to those presented in this review. Finally, it is also important to take into account that language restriction was used, leading to the exclusion of some studies.

In spite of these limitations, results indicate a tendency for radiographic case definition studies to present higher estimates compared to the self-reported and symptomatic OA definitions; self-reported and symptomatic OA studies tend to present similar estimates. Our review highlights the importance of considering OA definition in the interpretation of epidemiological studies.

Conclusions

The highest OA prevalence estimates were found in hand joints but the knee is the joint most studied. Prevalence of knee OA was higher in women than in men even when studies were stratified by age and by OA definition. In all joints studied, radiographic definition presented the highest prevalence of OA; self-reported and symptomatic OA definitions show similar prevalence estimates. High heterogeneity in the included studies limited further conclusions.

For incidence studies, although results seemed to present analogous implications, the small number of studies made it impossible for us to draw further conclusions.

Author contributions

DP drafted the first version of the manuscript, performed the revision of papers, the statistical analysis and contributed to in the interpretation and discussion; BP performed the statistical analysis and contributed to the interpretation analysis; JA performed the revision of papers and contributed to the discussion of the manuscript; JB and RAS provided significant advice and contributed to the discussion of the manuscript; ER coordinated the manuscript, performed the revision of papers and has contributed to the interpretation and discussion of this review.

All authors read and approved the final manuscript.

Conflict of interest

All authors declare no conflict of interests and disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) this work.

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