Supplementary Material

Arthritis as a risk factor for carpal tunnel syndrome: A meta-analysis

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Table S1. Quality assessment of the included studies

Type of domain	Criteria definition	Classification (potential for bias)
Selection bias	Sampling method of the study population, representativeness (response rate, difference between responders and non-responders)	Low: Target population defined as representative of the general population or subgroup of the general population (specific age group, women, men, specific geographic area, and specific occupational group) and response rate is above 80%. Moderate: Target population defined as somewhat representative of the general population, a restricted subgroup of the general population, response rate 60%-79%. High: Target population defined as self-referred/ volunteers, or response rate less than 60%.
Performance bias	Valid and reliable assessment of exposure	Low: Arthritis was diagnosed by a physician. For rheumatoid arthritis based on known diagnostic criteria, and for osteoarthritis confirmed by imaging. Moderate: Arthritis was assessed by patient medical record, or for osteoarthritis by clinical diagnosis not confirmed by imaging. High: Self-reported arthritis.
Detection bias	Clear definition of outcome Standard method for outcome assessment	Low: The outcome was defined by symptoms and nerve conduction studies. Moderate: The outcome was assessed by symptoms and clinical diagnosis.
Confounding	Matching two groups Stratification Statistical analysis	Low: Controlled for most of the potential confounders. Moderate: Controlled for some of the potential confounders, particularly age and sex. High: Controlled for less than two confounders.
Attrition bias	Withdrawal and dropout rates Size of missing data	Low: Follow-up participation rate of more than 80%, or missing data of less than 20%. Moderate: Follow-up participation rate of 60%-79%, or missing data of 20%-40%. High: Follow-up participation rate of less than 60%, or missing data of more than 40%.

Table S2. Studies included in the meta-analysis on the association between arthritis and carpal tunnel syndrome

Author, year and country	Study population	Age range (years)	Gender	Sample size (in analysis)	Arthritis	Outcome	Assessment of quality: Risk of bias					Results	Adjustment for other covariates
							Selection	Performance	Detection	Confounding	Attrition		
Carpal tunnel syndrome													
Cohort studies													
Evanoff 2013, USA (1)	Occupational population (8 employers and three apprentice programs)	Mean age 30.6 ± 10.5	Both, 35.6% female	711	Self-reported arthritis (osteoarthritis or rheumatoid arthritis)	Symptoms and nerve conduction studies	High	High	Low	High	Moderate	Estimated RR 1.045 (CI 0.26-4.12)	Unadjusted
Harris-Adamson 2013, USA (2)	Occupational population (manufacturing, services, agriculture, trade and construction workers). Pooled six cohort studies	18 or older, mean age 30.8–43.4	Both, 47% were females	3375	Self-reported rheumatoid arthritis	Symptoms + clinical diagnosis and nerve conduction study	Moderate	High	Low	Moderate	Low	Unadjusted RR 1.66 (0.60-3.69). Adjusted RR 1.13 (0.50-2.57)	Age, sex and body mass index
Garg 2012, USA (3)	Occupational population (10 diverse production facilities)	18.7–68.1, mean 41.2 ± 11.7	Both, 63.4% were female	429	Symptoms and clinical signs of rheumatoid/ inflammatory arthritis, or osteoarthritis	Symptoms and nerve conduction study	High	Moderate	Low	Low for arthritis and high for osteoarthritis	Low	Unadjusted RR 3.8 (CI 1.47–9.79) for arthritis. Adjusted RR 3.66 (CI 1.32–10.16) for arthritis. Unadjusted RR 2.2 (CI 0.92–5.33) for osteoarthritis	Age, strain index score (continuous variable), gardening, body mass index, depressive symptoms, and number of other musculoskeletal disorders
Gell 2005, USA (4)	Industrial and clerical work sites	19-69, mean age 38.8 in CTS cases and 38.3 in subjects without CTS	Both 69% women	432	Self-reported rheumatoid arthritis	Symptoms + nerve conduction study, or self-reported	Moderate	High	Low	High	High	Estimated RR 1.74 (0.22-13.42)	Unadjusted

						surgery due to CTS since the time of the initial screening.							
Werner 2005, USA (5)	Automobile assembly workers	Mean age 48.4	Both	189	Self-reported rheumatoid arthritis	Symptoms and nerve conduction study, or surgery for CTS	High	High	Low	High	Low	RR of confirmed incident cases 1.065 (CI 0.066-17.165)	Unadjusted
Case control studies													
Coggon 2013, UK (6)	Cases were CTS patients and controls were patients attended the accident and emergency department	20-64	Both, 68% were women	1230 (457 cases neurophysiologically confirmed and 773 controls)	Self-reported rheumatoid arthritis/other arthritis	Symptoms + nerve conduction study	High	High	Low	Moderate	Low	Estimated OR 1.06 (CI 0.70-1.61) for any arthritis. OR 1.3 (CI 0.8-2.3) for rheumatoid arthritis	Frequency matched by age and sex. Adjusted for sex, age and ethnicity.
Karadag 2012, Turkey (7)	Consecutive patients with rheumatoid arthritis and healthy controls from a check-up unit	24-76, mean age 50.9 ± 12.6 for RA patients and 46.7 ± 12.6 for control group	Both	145 (100 patients with rheumatoid arthritis and 45 healthy controls)	Rheumatoid arthritis diagnosed using the American College of Rheumatology 1987 criteria	Symptoms + clinical diagnosis + nerve conduction study + ultrasonography	High	Low	Low	High	Low	Prevalence of CTS was 17% in RA patients and 4.4% in control group. Estimated OR 4.40 (CI 0.97-19.95)	Unadjusted. No statistically significant differences in age, sex, BMI and history of diabetes or hypothyroidism between two groups.
Tseng 2012, Taiwan (8)	Population of a national insurance claim (covers 96% of the country). CTS cases were a random sample of 1 million	20% ≤19, 69% 20-59 and 11% 60 or older	Both	47406 (15802 cases and 31604 controls)	Rheumatoid arthritis based on an ICD code	CTS based on an ICD code. Nerve conduction study was performed for 47.9% of cases	Low	Moderate	Moderate	Low	Low	Unadjusted OR 3.65 (3.22–4.13). Adjusted OR 2.21 (1.94–2.52)	Age, sex, occupation, urbanization, income, uremia, vitamin B6 deficiency, hypothyroidism, obesity, diabetes, gout,

						and 6.13% operated because of CTS							hypertension, and acromegaly
Geoghegan 2004, UK (9)	General practice population	Age range for cases 16-96. Mean age for cases 46. Age not reported for controls.	Both	16955 (3391 cases and 13564 controls)	Physician diagnosed rheumatoid arthritis based on ICD codes. Physician diagnosed osteoarthritis of the wrist or carpus based on ICD codes	CTS recorded using an ICD code	Low	Moderate	Moderate	Moderate	Low	Unadjusted OR 3.31 (2.34–4.67) for rheumatoid arthritis. Adjusted OR 2.23 (1.57–3.17) for rheumatoid arthritis. Unadjusted OR 2.62 (2.29–2.99) for osteoarthritis. Adjusted OR 1.89 (1.65–2.17) for osteoarthritis.	Matched by age, sex, general practice, and date of diagnosis. OR adjusted for mean annual consultation rates
Ferry 2000, UK (10)	General practice population	Mean age 41.9 for both groups	Female	2528 (1264 cases and 1264 controls)	Rheumatoid arthritis, unspecified arthritis, or osteoarthritis based on CD codes	CTS recorded using an ICD code	Moderate	Moderate	Moderate	Moderate	Low	Estimated unadjusted OR 1.71 (CI 1.01-2.90) for any arthritis. Estimated adjusted OR 1.45 (CI 0.82-2.55) for any arthritis. Unadjusted OR 1.50 (0.76-2.95) for rheumatoid arthritis. Adjusted OR 1.31 (0.63-2.70) for rheumatoid arthritis.	Matched by age. Adjusted for arm fracture, osteoarthritis, rheumatoid arthritis, unspecified arthritis, fibrosis, neck pain, tennis elbow, brachial neuralgia, limb pain, and joint pain.

												Unadjusted OR for osteoarthritis of spine 2.49 (CI 1.76-3.44).	
												Adjusted OR for osteoarthritis of spine 2.16 (CI 1.52-3.06).	
												Unadjusted OR for unspecified osteoarthritis 1.60 (CI 1.10-2.32).	
												Adjusted OR for unspecified osteoarthritis 1.23 (CI 0.82-1.85).	
												Estimated unadjusted OR for any osteoarthritis 2.04 (CI 1.36-3.07).	
												Estimated adjusted OR for any osteoarthritis 1.70 (CI 1.10-2.62)	
de Krom 1990, Netherlands (11)	Cases were CTS cases from general population or outpatient clinic and controls were a random sample of general population	25-74	Both	629 (156 cases and 473 controls)	Self-reported physician diagnosed rheumatism	Symptoms + nerve conduction study	Moderate	High	Low	High	Low	OR 0.38 (0.11-1.30)	Unadjusted
Barnes 1967, UK (12)	Cases were a random sample of RA patients	Not reported	Both	65 (45 rheumatoid)	Rheumatoid arthritis diagnosed	Symptoms + clinical diagnosis +	Moderate	Low	Low	Moderate	Low	33.3% of RA patients and 0% of controls had CTS	Matched by age and sex.

	attending the departments of Physical Medicine and Rheumatology at the London Hospital. Controls were a random sample of patients attending for non-inflammatory arthritic conditions other than neck and upper limbs.			arthritis patients and 20 controls)	using the American Rheumatism Association 1958 criteria (classic or definite cases with positive rheumatoid factor)	nerve conduction study						defined by symptoms and clinical diagnosis and nerve conduction study. Estimated OR 20.84 (CI 1.18-367.95).	
												53.3% of RA patients and 15.0% of controls had CTS defined by clinical diagnosis. Estimated OR 6.48 (CI 1.66-25.23)	
Cross-sectional studies													
Eleftheriou 2012, Greece (13)	Workers of a data entry and processing unit	Mean age 45.2 ± 9.46	Both, 83.6% were female	461	Self-reported rheumatoid arthritis	CTS diagnosed by a physician (including surgery for CTS)	Moderate	High	Moderate	High	Low	Prevalence ratio 2.32 (0.67-7.89)	Unadjusted
Shin 2012, South Korea (14)	A random sample of elderly population	66-96, mean age 75 ± 7	Both	368	Basal joint osteoarthritis of the thumb based on x-ray, a Kellgren and Lawrence grade of 2 or higher	Symptoms and nerve conduction study	Moderate	Low	Low	High	High	Estimated prevalence ratio 1.52 (CI 0.75-3.09)	Unadjusted
Burt 2011, USA (15)	Occupational population (hospital and manufacturing workers or clerks)	19-68, mean age 41.2 ± 10.7	Both, 44.1% were female	455	Self-reported arthritis	Symptoms + nerve conduction study	Moderate	High	Low	Moderate	Low	Estimated unadjusted prevalence ratio 1.98 (CI 1.20-3.26). Reported adjusted OR 2.03 (CI 1.02–4.04)	Sex, occupational hand activity level, blood pressure

Raigani 2009, Iran (16)	Patients with upper extremity disorders	Not reported	Both, 86% were female	1000 (250 with CTS and 750 with other upper extremity disorders)	Self-reported arthritis (any condition)	Symptoms + clinical diagnosis + nerve conduction study	Moderate	High	Low	High	Low	Prevalence of rheumatologic disease was 2% in CTS cases and 1.2% in healthy group. Estimated prevalence ratio 1.67 (CI 0.56--4.93)	Unadjusted
Maghsoudipour 2008, Iran (17)	Occupational population (auto factories)	Mean age in patient group 29.85, in healthy group 27.95	Both 304 men and 91 women	395	Self-reported rheumatologic disease	Symptoms + clinical diagnosis + nerve conduction study.	Moderate	High	Low	High	Low	Prevalence of rheumatologic disease was 0% in CTS cases and 0.3% (1 case) in healthy group. Estimated prevalence ratio 2.42 (CI 0.10--58.7).	Unadjusted
Melchior 2006, France (18)	Occupational population (manual workers)	20-59, mean age 38 ± 10	Both	2656 (1549 men and 1107 women)	Self-reported arthritis (rheumatoid, other inflammatory or degenerative arthritis)	Symptoms + clinical diagnosis	Low	High	Moderate	Moderate	Low	No exposed cases in women with arthritis. Prevalence ratio 2.06 (0.29--14.36) for men.	Sex-specific. Adjusted for age
Atroshi 1999, Sweden (19)	General population	25-74	Both, 54% were females	2466	Self-reported rheumatoid arthritis	Symptoms + clinical diagnosis + nerve conduction study	Low	High	Low	High	Low	Prevalence ratio 2.37 (0.75-7.43)	Unadjusted
Atcheson 1998, USA (20)	Patients with upper extremity disorders were referred by a worker	25-54	Both	297	Physician diagnosed inflammatory arthritis based on known	Symptoms + clinical diagnosis	High	Low	Moderate	High	Low	Estimated prevalence ratio 1.745 (0.92--3.31) for arthritis.	Unadjusted

compensation
administrator

diagnostic
criteria.

Rheumatoid
arthritis
diagnosed
using the
American
College of
Rheumatology
1987 criteria.

Osteoarthritis of
cervical spine
or upper limbs
diagnosed by
symptoms +
physical
examination +
x-ray

Prevalence ratio
1.40 (0.24--8.22)
for rheumatoid
arthritis.

Prevalence ratio
1.396 (0.74--2.63)
for osteoarthritis

Carpal tunnel release

Case control studies

Mattioli 2009, Italy (21)	Cases were a random sample of CTS patients from local hospitals. Controls were a random sample of national health service registries.	18-65	Both	476 (190 cases and 286 controls)	Self-reported rheumatoid arthritis	Operated CTS (symptoms + clinical diagnosis and nerve conduction study)	Moderate	High	Low	Low	Low	Unadjusted OR 2.6 (CI 1.4-4.9). Adjusted OR 2.2 (CI 1.0-4.6).	Age, sex socio- occupational status, BMI, height, alcohol intake, family history of CTS, trigger finger and diabetes mellitus
Geoghegan 2004, UK (9)	General practice population	Age range for cases 16-96. Mean age for cases 46. Age not reported for controls.	Both	16955 (3391 cases and 13564 controls)	Physician diagnosed rheumatoid arthritis based on ICD codes. Physician diagnosed	CTS recorded using an ICD code	Low	Moderate	Moderate	Moderate	Low	OR 2.48 (CI 1.25– 4.94) for rheumatoid arthritis. OR 1.92 (CI 1.50- 2.47) for osteoarthritis	Matched by age, sex, general practice, and date of diagnosis. ORs adjusted for mean annual

					osteoarthritis of the wrist or carpus based on ICD codes								consultation rates
Solomon 1999, USA (22)	Enrollers of Medicare or Medicaid programs. Cases were patients with carpal tunnel release and controls were subjects without such a surgery	45 or older	Both, 81% of cases and 73% of controls were females	4244 (626 cases and 3618 controls)	Any physician- diagnosed inflammatory arthritis (several conditions) or taking anti- rheumatic drugs based on ICD codes	Recorded surgery for CTS based on an ICD code	Moderate	Moderate	Moderate	Moderate	Low	Unadjusted OR 3.1 (2.4-4.1). Adjusted OR 3.1 (2.2-4.2)	Age, sex, race, diabetes, hypothyroidism, haemodialysis, corticosteroid use, and estrogen replacement therapy
Wieslander 1989, Sweden (23)	CTS patients, two types of controls (hospital-based and population- based) controls	20-66	Male	177 (34 cases and 143 controls). 2 hospital controls and 2 population controls for each case	Self-reported rheumatoid arthritis	Operated cases (clinical diagnosis + nerve conduction)	Moderate	High	Low	Moderate	Low	OR 2.25 (0.63- 7.96)	Matched by age and year of operation (for hospital controls)

CI, 95% confidence interval
ICD, International Classification of Diseases
OR, odds ratio
RA, rheumatoid arthritis
RR, risk ratio

Figure S1. Flow chart of the search strategy and selection of studies. CTS, carpal tunnel syndrome

Figure S2. Funnel plot for publication bias in 11 studies on the association between any inflammatory or degenerative arthritis and carpal tunnel syndrome or carpal tunnel release. Five studies reported unadjusted estimates and six reported confounder-adjusted estimates.

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