

# INPLASY

## Prevalence of Osteoporosis in Rheumatoid Arthritis: Protocol for Systematic Review and Meta-analysis

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### ADMINISTRATIVE INFORMATION

**Support** - Australian Rheumatology Association, and Arthritis & Osteoporosis WA.

**Review Stage at time of this submission** - Completed but not published.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY2023120023

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 December 2023 and was last updated on 06 December 2023.

### INTRODUCTION

**Review question / Objective** Estimate the global prevalence of osteoporosis in RA patients, identify associated risk factors, and determine high-risk RA patients who require preventive osteoporosis treatment.

**Rationale** Rheumatoid Arthritis (RA) patients have a risk of developing osteoporosis, which increases morbidity, mortality rates, and healthcare costs. There is limited data on the prevalence of osteoporosis and associated risk factors in RA.

**Condition being studied** Osteoporosis is a commonly co-existing comorbidity and well-documented extra-articular manifestation in patients with rheumatoid arthritis (RA), which is more prevalent than in the general population [1]. The prevalence of osteoporosis among people with

RA varies from 21% to 70% [2]. In particular, the prevalence of lumbar osteoporosis in RA patients ranges from 12.3% to 38.9%, while hip osteoporosis ranges from 6.3% to 36.3% [3]. Despite advancements in the management of RA, which include synthetic disease-modifying antirheumatic drugs (DMARDs) and biological agents, the prevalence of osteoporosis remains persistent in RA.

### METHODS

**Search strategy** A search will be undertaken of the electronic databases, including MEDLINE, Scopus, ProQuest Central, Web of Science, EMBASE, CINAHL, and Google Scholar, using the relevant medical subject heading search terms and keywords: prevalence OR trend OR rate OR epidemiology OR Frequency OR Percentage OR Effect AND RA OR "Rheumatoid arthritis AND

Osteoporosis\* OR "Bone Loss" OR Osteopenia OR "Bone density" OR "Bone mineral density" OR Fracture OR "Bone mass" OR "Osteoporotic fractures" Osteoporosis\* OR "Bone Loss" OR Osteopenia OR "Bone density" OR "Bone mineral density" OR Fracture OR "Bone mass" OR "Osteoporotic fractures".

**Participant or population** A population-based study will be defined as a study that included the entire adult populations with clinically verified RA and osteoporosis.

**Intervention** Not applicable.

**Comparator** Not applicable.

**Study designs to be included** The review will include all type of population-based studies: nested case-control studies, cross-sectional studies, and prospective or retrospective cohort studies.

**Eligibility criteria** Studies will be included if they met the following inclusion criteria: (a) the participants were representative of the adult populations based on country reference populations using the World Health Organisation and the United Nations data repository; (b) the participants had clinically verified RA or met one of the published RA classification sets; (c) residents in a defined country; or (d) lived in defined geographic population settings. We will exclude population-based studies that (a) had participants aged under 16 years; (b) only presented prevalence estimates based on subsets of a population or communities by age range, sex, or ethnicity; (c) had fewer than 300 participants; (d) were published in a language other than English; (e) comprised non-research papers including letters and editorials, narrative, systematic and seminar reviews, case studies, series were reporting cases or abstracts; (f) included capture-recapture studies or disease model studies.

**Information sources** Medical Subject Headings and the keywords will be used in the search machines and will be peer-reviewed by first author, senior supervising author and senior librarian. Different keywords will be chosen, and the search will be conducted using 'AND' and 'OR' in the search section of the databases.

**Main outcome(s)** The timeframe will be selected from 1 January 1980 through 15 Jul 2023 to estimate and account for changes in trends in reporting prevalence data due to significant revisions of osteoporosis classification criteria that

may have affected the reported incidence and prevalence.

**Additional outcome(s)** We conducted a search in several databases (MEDLINE, Scopus, ProQuest Central, Web of Science, EMBASE, CINAHL, and Google Scholar) to estimate the global prevalence of osteoporosis in RA populations. We also evaluated the influence of geographical location, prevalence methods, and osteoporosis diagnostic criteria on prevalence estimates from 1980 to 2023.

**Data management** The study information (such as authors, year, and country where the study was conducted) will be initially recorded. All the information related to participants, such as the source population size and sample size of those who participated in the study, will be extracted. In the methodology section, the method used to measure RA prevalence, such as point- or period-prevalence and osteoporosis classification criteria, will be outlined. The data sources such as administrative databases, linked data, medical records, register data, and the population-based survey will also be extracted. Authors of the primary studies will be contacted if any information is missing or unclear.

**Quality assessment / Risk of bias analysis** The research articles selected for systematic review and meta-analysis will be evaluated using the Hoy et al. tool for risk of bias in prevalence studies.

**Strategy of data synthesis** The RA prevalence will be calculated by dividing the number of RA cases by the total number of participants, which will then be expressed as a percentage. Data analysis will be included as a comparison of the prevalence of RA between countries and continents. Pooled estimates of the prevalence of RA in population-based studies will be calculated using the random-effects meta-analysis model due to the anticipated heterogeneity that is expected from the difference in methodological approach, geographical location, diagnostic criteria, data sources and geographic settings. Statistical analyses will be performed using R with 'meta' packages of R.

**Subgroup analysis** We also evaluated the influence of geographical location, prevalence methods, and diagnostic criteria on prevalence estimates from 1980 to 2023.

**Sensitivity analysis** To assess the robustness of our results, a sensitivity analysis of the pooled estimates of osteoporosis prevalence will be pooled based on influence analyses, including

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leave-one-out analyses, risk of bias assessment for studies, influential outliers and residual analyses. A cut-off value of z-score >2 in absolute value was considered a potential outlier and verified through the Baujat plot.

**Language restriction** English.

**Country(ies) involved** Australia, Saudi Arabia.

**Other relevant information** None.

**Keywords** epidemiology; osteoporosis prevalence; rheumatoid arthritis; risk factors.

**Dissemination plans** We will disseminate our findings via publications in open-access peer-reviewed journals and present at national and international conferences.

#### **Contributions of each author**

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