The prevalence of Rheumatoid Arthritis: A systematic review of population-based studies.

Al Mutairi KB[1, 2], Nossent JC [2, 3], Preen DB[4], Keen HI [2, 5], Inderjeeth CA[2, 3]

1 King Fahd Specialist Hospital, Burydah, Saudi Arabia.

2 School of Medicine, The University of Western Australia, Perth, Western Australia, Australia.

3 Department of Rheumatology, Sir Charles Gairdner Hospital, Perth, Western Australia, Australia.

4 School of Population and Global Health, Faculty of Health and Medical Sciences, University of Western Australia, Perth, Western Australia, Australia.

5 Fiona Stanley Hospital, Murdoch, Western Australia 6009 Australia.

The email address of the corresponding first author
Khalid Bander D Almutairi,
ORCID ID: https://orcid.org/0000-0002-9246-7294
Email: khalid.almutairi@research.uwa.edu.au

Disclosure statement
The authors have declared no conflicts of interest.

Key Indexing Terms:
Rheumatoid arthritis; Prevalence; Registries; Epidemiology, Database.

Short Running Head: Systematic Review

Word count: 3500

Address:
C/O Professor Charles Inderjeeth
The University of Western Australia
Faculty of Health and Medical Sciences
School of Medicine
35 Stirling Highway
Perth WA 6009 Australia

Abstract

Objectives

To estimate the prevalence of Rheumatoid Arthritis (RA) from international population-based studies and investigate the influence of prevalence definition, data sources, classification criteria and geographical area on RA prevalence.

Methods

A search of ProQuest, MEDLINE, Web of Science, and EMBASE was undertaken to include population-based studies investigating RA prevalence between 1980 and 2019. Studies were reviewed using the Joanna Briggs Institute approach for the systematic review and Preferred Reporting Items for Systematic Reviews guidelines.

Results

Sixty studies met the inclusion criteria. There was a wide range of point-prevalence reported (0.00% - 2.70%) with a mean 0.56% (S.D= 0.51) between 1986 and 2014 and period-prevalence 0.51% (S.D= 0.35) between 1955 and 2015.. RA point- and period-prevalence was higher in urban settings than rural settings, (0.69% vs 0.48%) and (0.54% vs 0.25%), respectively. The RA diagnosis validated by rheumatologists yielded the highest period-prevalence of RA and was observed in linked databases (0.80%, S.D=0.1).

Conclusion

The literature reports a wide range of point- and period- prevalence based on population forms and method of data collection, but average point- and period-prevalence of RA were 51/10,000 and 56/10,000, respectively. Higher urban vs rural prevalence may be biased by poor case finding with less health care or reflect risk environment. The population database studies were more consistent than sampling studies, and linked databases in different continents appeared to provide a consistent estimate of RA period-prevalence and confirming the high value of rheumatologist diagnosis as classification criteria.

 Word count: 243

Word count limit 250 words

Introduction

Rheumatoid arthritis (RA) is a heterogeneous disease with partially unknown aetiology (1, 2). The reported worldwide RA prevalence varies widely, and it is unclear whether this is due to inconsistencies in defining populations; methodologies used to identify RA patients including data sources, sample sizes, variation with date of data collection; or the employed RA classification criteria (2). Alternatively, this may be a true reflection of the impact of different risk factors over time across jurisdictions, including age, sex distribution, socioeconomic differences, ethnogenetic differences, or exposure to risk factors in a population for the development of autoimmune-mediated disease such as RA (2, 3).

Hence, it will be clinically useful to investigate the prevalence of RA at the national and international level to shed further light on possible genetic and environmental factors that would potentially improve our knowledge about the aetiology of the disease (4).

A systematic review of RA prevalence data could assist in such planning (5) and also with decision making regarding the most efficient use of available resources (6). Two systematic reviews have examined the prevalence of RA in the last three decades (7, 8). One by Alamanos et al. (7) was limited by the selection of studies based on the revised 1987 American Rheumatism Association (ARA) classification criteria only, while Rudan et al. (8) investigated the regional RA prevalence in studies from low-to-middle–income countries published between 2000 and 2010.. However, to our best knowledge, there are yet no systematic reviews or meta-analyses based on published population-based studies or those that have investigated the influence of prevalence methodology on the estimates of RA prevalence.

This review aimed to describe the international point- and period-prevalence of RA based on currently published population-based study estimates and describe the implications of using different data sources, RA classification criteria, and geographical population settings to estimate the prevalence of RA.

Method

Study design

A systematic literature review was performed using the Joanna Briggs Institute guidelines for conducting a systematic review of prevalence data (5) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (9). A study list of key terminology, corresponding definitions, and PRISMA checklist can be found in Supplemental Data file 1 and Supplemental Table 1.

Study selection

Timeframe

The timeframe of the search was publication from 1 January 1980 through 26 June 2019. The timeframe was chosen to estimate and account for changes in trends in reporting prevalence data due to major revisions of RA classification criteria that have affected the reported incidence and prevalence (10, 11).

Inclusion criteria
Types of studies

We included case-control studies, cross-sectional studies, and prospective or retrospective cohort studies in our search strategy.

Types of participants

Studies were 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 (12) and the United Nations data repository (13); (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.

Exclusion criteria
We excluded 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 volunteer participants or participants with self-reported RA diagnosis without clinical confirmation; (e) comprised RA prevalence studies from outpatient clinics, residential homes, or hospitals; (f) were published in a language other than English; (g) comprised non-research papers including letters and editorials, narrative, systematic and seminar reviews, case studies, series were reporting cases or abstracts; (h) included capture-recapture studies or disease model studies.

Search strategy
A literature search was conducted by the first author according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 recommendations to locate studies in relevant databases, including ProQuest, MEDLINE (Ovid), Web of Science, and EMBASE (Ovid). The results of each search were loaded into EndNote Volume X.8 (Clarivate Analytics, PA, USA). Medical Subject Headings and the keywords were used in the search machines were peer-reviewed between first author, senior supervising author (CI) and senior librarian (SB). Different keywords were chosen, and the search was conducted using 'AND' and 'OR' in the search section of the databases (Table 1 & Supplemental Table 2). Reference lists from retrieved studies were used to identify more studies and were selected based on the systematic review inclusion criteria.

Risk of bias assessment and data extraction
The research articles selected for systematic review were evaluated using the Hoy et al. tool for risk of bias of prevalence studies (14). The details of the risk bias assessment method and data extraction are presented in Supplemental Data file 4 & Supplemental Table 3.

Selection measure:

Report the studies that provided adequate information to calculate point- and/or period-prevalence for RA. We also assumed the prevalence rate of RA to be constant over the study period. Also, report studies that included a description of secondary outcomes, including the type of prevalence method used, RA classification criteria, type of data sources, and geographic population settings, were included.

Data synthesis

We calculated prevalence by dividing the number of RA cases by the total number of participants, which was then expressed as a percentage. Data analysis included a comparison of the prevalence of RA between countries and continents. In this study, we applied descriptive statistical analysis using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA, Version 25) for the analyses.

Results

Search results

Our keywords-based search yielded a total of 1821 citations (Figure 1) from ProQuest (n = 650), Medline (n = 588), Web of Science (n = 468) and EMBASE (n = 115). After reviewing the title and abstract and removing duplicates, 143 studies remained for further evaluation. Of these, 86 articles were excluded due to discordance with the inclusion criteria (Supplemental Data file 5), resulting in 57 studies included for the full review. In addition, 20 records were included by manual research references from all accepted studies, and only three studies from them met the inclusion criteria. The final selection for the prevalence of RA consisted of 60 population-based studies. Six of these studies have multiple cohorts, and each cohort was recognised separately during analysis (Supplemental Table 4). The total number of cohort studies analysed was 67.

Characteristics of the population-based studies

The 60 population-based studies were conducted in 41 countries (Table S3). Nearly half the studies were conducted in Europe (n = 25, 42%), followed by Asia (n= 22, 37%) and North America (eight studies, 13%). Three studies (5%) were conducted in Africa, and two (3%) were conducted in South America. No studies meeting the inclusion criteria were identified from Oceania.

Risk bias assessment

The risk bias assessment of the included published studies was low in 53 studies (88.3%), moderate in seven studies (11.7%), and there was no high-risk of bias across studies (Supplemental Data file 7 & Supplemental Table 5).

The study participants

The study had 212,335,171 total participants in 67 cohort. A total of 49 (73.1%) cohort studies were based on population cumulative sampling with an overall total of 221,329 participants, ranging from 300 to 26,709 people (mean = 4517, S.D = 4422). In the remaining 18 (26.9%) studies, the RA prevalence was estimated based on larger population database studies, including 212,113,842 total participants, ranging from 18,300 to 49.4 million people (Supplemental Table 6).

Prevalence methods

The point-prevalence method was reported in 32 cohort studies (47.8%) and the period-prevalence method was reported in 35 cohort studies (52.2%) (Table 2).

The point-prevalence method was more common among sampling population cohort studies, while period-prevalence was more common among larger population database cohort studies (Supplemental Table 7).

Data sources
The Population-based survey (P.B.SU) was the most frequently used data source (n = 46, 68.6%), with administrative data in 14 cohort studies (20.9%). Register and linked data were used in three (4.5%) and four cohort studies (6%), respectively.

Classification criteria
The most common diagnostic RA classification criteria were the revised ARA criteria 1987 (15) (n = 37, 55.2%), followed by verified clinical diagnosis by a doctor (n = 19, 28.4%), and then the modified ARA criteria 1987 (16) (n = 7, 10.4%). Two studies used the modified 1987 ARA criteria as reference criteria in parallel with ARA criteria 1956 (17) and Rome criteria 1961 (18) and revised ARA criteria 1987 (19, 20). Both studies results were identified more RA patients using the modified 1987 ARA criteria compared with other existing criteria. The potential disadvantage of the ARA criteria 1956 was included patients with osteoarthritis, while the Rome criteria 1961 and revised ARA criteria 1987 were failed to recognised cases of mild RA. The ARA criteria 1956 (17) and Rome criteria 1961 (18) were used in three cohort studies (4.5%) (21, 22) and one study (1.5%) (23), respectively. Although 21 cohort studies were reported after the ACR/EULAR 2010 criteria (11) were published, none used these criteria. The continent-specific estimates for studies were estimated in this review using the most common classification criteria (Table 3).

Geographic population settings
Most studies were performed in a mixed (urban and rural) setting (n = 30, 44.8%), while studies restricted to urban settings (n = 25, 37.3%) were more frequent than rural studies (n = 12, 17.9%). In Europe, the most commonly reported environmental area was a mixed setting (n = 19, 73.1%), with remaining cohort studies conducted in urban areas (n = 6, 23.1%) and a rural area (n = 1, 3.8%). In contrast, in Asia, mixed settings were less reported (n = 7, 26.9%) than urban areas (n = 11, 42.3%) and rural areas (n = 8, 30.8%).

Synthesis of results
There was a high level of heterogeneity (I^2= 99.9%) between included studies, due to differences in data sources, diagnostic criteria, region, and geographic settings. The review findings are categorised and presented as a narrative synthesis on different sources, methodology and populations, which highlights the potential factors that may affect the RA prevalence estimates.

Review findings

Point-prevalence estimates of RA

The mean point-prevalence of RA was 0.56% (S.D = 0.51), ranging from 0.00% to 2.70%, based on studies from various countries between 1986 and 2014 (Figure 2 & Supplemental Table 8). The highest reported mean point-prevalence was in North America (1.46%), followed by Africa (0.80%), Europe (0.53%), South America (0.46%) and Asia (0.34%). Country-specific point-prevalence was highest in Cuba (2.70%), followed by Lesotho (1.80%) and Lithuania (0.92%). The lowest point-prevalence was seen in Nigeria (0.00%), followed by Thailand (0.12%) and Iran (0.19%).

Period-prevalence estimates of RA
The mean period-prevalence of RA was 0.51% (S.D = 0.35), ranging from 0.05% to 1.90%, across countries between 1955 and 2015 (Figure 3 & Supplemental Table 9). The highest mean period-prevalence was reported in North America (0.69%), followed by Europe (0.60%), Asia (0.34%) and South America (0.19%). Country-specific period-prevalence estimates were highest in Finland (1.90%), followed by Lebanon (1.00%) and Poland (0.90%), while the lowest period-prevalence was reported in Taiwan (0.09%), Philippines (0.17%) and Yugoslavia (0.18%).

Population sampling methodology
The highest point- and period-prevalence in sampling population studies were 2.70% and 1.90%, respectively. In contrast, the highest point- and period-prevalence based on the larger population databases studies were 0.80% and 0.90%, respectively. The mean point and period-prevalence, based on sampling population studies were 0.56% and 0.57%, respectively. In contrast, the mean point- and period-prevalence based on the population database studies were 0.60% and 0.44%, respectively.

Data sources
The P.B.SU was used most frequently for both point- and period-prevalence studies (Supplemental Table 10-11). The highest mean point-prevalence of RA using administrative data (0.8%) was reported from Finland (24). The highest mean period-prevalence of RA (0.8%, S.D = 0.1) was reported in three cohort studies using linked data, two conducted in Canada (25, 26) and one conducted in Sweden (27), which are linked using rheumatology clinics, emergency departments, and inpatient facilities datasets. The mean point-prevalence of RA (0.8%) was higher than the period-prevalence when using administrative data (mean = 0.40%, S.D = 0.28). The lowest mean period-prevalence of RA among data sources was in administrative data.

RA classification criteria
The revised 1987 criteria were usually applied in both point- and period-prevalence studies; the mean point- and period-prevalence were 0.61% and 0.42%, respectively. The highest point-prevalence of RA was observed for ARA criteria 1956 (0.76%) based on three cohort studies: one conducted in Lesotho (21) and two in urban and rural areas of Indonesia (22). In contrast, the highest period-prevalence of RA was observed when doctors verified the clinical diagnosis (0.65%).

Geographic settings

Urban and mixed populations were commonly surveyed in point- and period-prevalence studies rather than rural populations. The point-prevalence of RA was higher in urban settings (0.69%) than rural (0.54%) and mixed areas (0.45%), and when incorporating geography, the point-prevalence was highest in urban areas of North America (1.80%) (Cuba and Mexico), while the lowest point-prevalence was observed in the mixed populations of Asia (Saudi Arabia (0.22%) and Oman (0.36%).

The period-prevalence of RA was higher in mixed populations (0.57%) than urban (0.48%) and rural areas (0.25%) with the highest period-prevalence in the urban areas of North America (0.92%), namely Canada (0.90% and 0.80%) and the USA (1.07%), while the lowest (0.22%) was reported in an urban area of South America, namely Argentina (0.19%).

Discussion

The worldwide average point- and period-prevalence of RA were 0.51% and 0.56%, respectively, more than double the overall prevalence reported by Cross et al. (0.24%) based on the global estimate of the burden of disease in 2010 (28). Cross et al. used a modelling method to estimate the missing RA prevalence data values for five regions, including Oceania which have led to an underestimation of the true RA prevalence.

The reported RA prevalence was between 1.9% and 2.7% in Australian populations based on P.B.SU studies without clinical verification (29, 30). Although the validity of self-reported diagnosis varied between 7% and 96% based on confirmation methods (31), Cross et al. estimated an RA prevalence of 0.09% in male and 0.25% in female patients in Oceania, which was 10-times lesser than the reported RA prevalence in Australia (29, 30). Moreover, these results were contrary to the highest reported prevalence of RA (6.6%) among Australian populations aged ≥75 years (29), especially given the sizeable ageing population of 4.6 million in Oceania (32).

Although the period-prevalence method presumably captures more RA cases than the point-prevalence method, the highest RA prevalence was reported in point-prevalence studies that used the sampling population studies. The main limitation of sampling population studies is that they are affected by sampling frame, sampling size, and subjects' participation (33).

A Cuban study (34) which reported the highest RA prevalence (2.7%) was potentially confounded by small sample size (n=300), which may not be representative of the true population because of potential sampling errors (34). We may speculate the highest prevalence of RA in Cuba may also be confounded by higher prevalence rate of smoking and tobacco use in Cuba (36.6%) especially when compared with other Latin-American countries such as Argentina (16.7%), Brazil (12.1%), and Mexico (7.7%) (35), where smoking is one of the risk factors for developing RA (36).

The prevalence rates of RA in a population increase with the age of the participants in that sample (86). Absence of RA cases in the Nigerian study may be confounded owing to the

different age structure of the selected samples (n=2000), where 80% of the sample subjects were young adults because of lower life expectancy (45 years) (37), while the highest prevalence of arthritis was reported in the age group of 60–69 years (86).

The lowest period-prevalence was observed in larger population database studies. An underestimation of the prevalence of rheumatic diseases was observed in population database studies with the prevalence estimate variations being related to the length of the observation period and data source accuracy (38). Ng et al. reported this phenomenon as an administration data limitation to presenting true prevalence for rare diseases (39).

Although the P.B.SU was the more common data collection method using the point-prevalence method in included studies, most administrative data studies used period-prevalence method to estimate RA prevalence. Categorising different data sources was to enable judgment of comparability to estimate RA prevalence and their impact on the mean point- and period-prevalence of RA. The higher mean and lowest S.D of period-prevalence estimates in the studies using linked data suggests that they are superior to other data sources to capture cases of RA over time. This may be because of RA diagnosis confirmed by rheumatologists and additional multiple sources of case ascertainment from different health care settings. Therefore, linked data is the preferred data source to estimate RA prevalence with improved case ascertainment, as RA is challenging to diagnose and classify over time without expert opinion.

In the absence of a gold standard for the diagnosis of RA, various RA classification criteria have been developed over time where doctor diagnosis or expert opinions were often used as the preferred diagnostic approach (40). However, these classification criteria do not cover the full spectrum of disease in RA and elsewhere, and doctor diagnosis is heavily influenced by training, experience, and preferences (41).

Based on the clinical diagnosis, the mean period-prevalence of RA was 0.65% vs. a mean point-prevalence of 0.39%. Moreover, there is a significant discrepancy in the identification of RA between primary care physicians and rheumatologists. In Della Rossa et al's 2010 study, the pattern of RA diagnosis among primary care physicians was showed less reliability (69%) of RA cases that were confirmed later by rheumatologists, with a high degree of heterogeneity (42).

The absence of RA in Nigeria may reflect the rheumatologist –to-population ratio of 0.012 per 100,00 resulting in the absence of diagnosis rather than absence of disease. The current sample was screened by medical students rather than trained professionals (43). Although diagnosed RA cases were zero, there were three inflammatory polyarthritis cases in the cohort with one meeting the revised 1987 criteria.

The impact of ARA 1956 criteria on estimated point-prevalence rates was detected in the present study, which indicates that ARA 1956 criteria has low sensitivity to missing inactive RA (10). Furthermore, the specificity for detection of active RA cases was low and included patients with joint inflammation given that osteoarthritis cases too met the ARA 1956 criteria because of the poor specificity of the criteria (20). Two studies used the modified 1987 ARA criteria in parallel with revised 1987 ARA (19, 20). The results illustrate the enhanced

sensitivity of modified 1987 ARA criteria compared with ARA criteria 1956 and Rome criteria 1961 and revised 1987 criteria. There were revisions of RA classification criteria over time, but the latest ACR/EULAR 2010 criteria still have not been used to estimate RA prevalence to date. An important characteristic of the ACR/EULAR 2010 criteria over previous criteria is the inclusion of anti-citrullinated protein antibodies and exclusion item (no better alternative diagnosis), which has improved the diagnostic accuracy of classification criteria (44, 45). However, there is no data to confirm or refute this assumption at this stage.

In Saraux et al. study (45), although agreement between all RA classification criteria was poor (κ = 0.09-0.43), the rheumatologist diagnosis with >50% certainty after two years of follow-up agreed with ACR/EULAR 2010, confirming the high value of rheumatologist diagnosis as classification criteria (45) which consistent with our review findings.

The point- and period-prevalence of RA in urban settings were higher than in rural areas. The reason for lower rural prevalence is unclear and may be multifactorial and reflect socioeconomic differences, lifestyle and environmental risk associated with urban living or simply patient migration to be closer to health care.

Strengths
To the best of our knowledge, this is the first systematic review summarising available published peer-reviewed population-based studies on the prevalence of RA. We used both point- and period-prevalence and assessed methodology based on multiple data sources, RA classification criteria and geographical settings, which strengthens this review. Moreover, we applied stringent inclusion criteria and clear definitions with robust assessment for bias and heterogeneity.

Limitations
Limitations of this review include the small sample sizes in some studies. Furthermore, the non-representation from the South Pacific region may interfere with generalisability to this region. The continental data also may be biased due to the dominance of studies from Europe and Asia and the limited studies from Africa and South America. The study findings do not permit any causal interpretations due to measurement variability.

Conclusion
The average point- and period-prevalence of RA were 51/10,000 and 56/10000, respectively. Variation occurred in RA point- and period-prevalence across countries and continents related to different methodological approaches and possibly different genetic and environmental risk factors. The RA prevalence in urban areas was higher than in rural areas suggesting environmental factors may be important in development RA. The mean RA period-prevalence was more consistent in population database studies than in sampling population studies. Linked databases appear to provide the best estimate of RA period-prevalence using multiple sources of case ascertainment, especially when rheumatologists likely confirm RA clinical diagnosis.

(3500 words) 3500 words limit.

Ethical consideration

This systematic review relies solely on data obtained from published research literature and therefore obtaining institutional ethical approval was not required.

Figures

Figure 1: PRISMA flow diagram for prevalence studies of rheumatoid arthritis.

Figure 2: Adult point-prevalence of rheumatoid arthritis (1986-2014).

Figure 3: Adult period-prevalence of rheumatoid arthritis (1955-2015).

Tables

Table 1: Keywords used to identify relevant studies.

Table 2: Overall mean of the continental prevalence of rheumatoid arthritis.

Table 3: Overall mean of the continental point- and period-prevalence of rheumatoid arthritis using different classification criteria.

Supplementary data

Supplementary Data file 1: Definitions.

Supplementary Data file 2: PRISMA 2009 checklist.

Supplementary Data file 3: Search strategy and sample search terms.

Supplementary Data file 4: Risk of bias assessment method and data extraction.

Supplementary Data file 5: Excluded studies and reasons for exclusion.

Supplementary Data file 6: Included studies in the systematic review.

Supplementary Data file 7: Risk bias assessment results.

Supplementary Data file 8: (Supplemental Tables 6-11).

References

1.   Tobon GJ, Youinou P, Saraux A. The environment, geo-epidemiology, and autoimmune disease: Rheumatoid arthritis. J Autoimmun 2010;35:10-4.

2.   Shapira Y, Agmon-Levin N, Shoenfeld Y. Geoepidemiology of autoimmune rheumatic diseases. Nat Rev Rheumatol 2010;6:468-76.

3.   Carmona L, Cross M, Williams B, Lassere M, March L. Rheumatoid arthritis. Best Pract Res Clin Rheumatol 2010;24:733-45.

4.   Carmona L, Villaverde V, Hernandez-Garcia C, Ballina J, Gabriel R, Laffon A. The prevalence of rheumatoid arthritis in the general population of spain. Rheumatology (Oxford) 2002;41:88-95.

5.   Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. Int J Evid Based Healthc 2015;13:147-53.

6.   Gomersall JS, Jadotte YT, Xue Y, Lockwood S, Riddle D, Preda A. Conducting systematic reviews of economic evaluations. International journal of evidence-based healthcare 2015;13:170-8.

7.	Alamanos Y, Voulgari PV, Drosos AA. Incidence and prevalence of rheumatoid arthritis, based on the 1987 american college of rheumatology criteria: A systematic review. Semin Arthritis Rheum 2006;36:182-8.

8.	Rudan I, Sidhu S, Papana A, Meng SJ, Xin-Wei Y, Wang W, et al. Prevalence of rheumatoid arthritis in low- and middle-income countries: A systematic review and analysis. J Glob Health 2015;5:010409.

9.	Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The prisma statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. PLoS Med 2009;6:e1000100.

10.	MacGregor AJ. Classification criteria for rheumatoid arthritis. Baillieres Clin Rheumatol 1995;9:287-304.

11.	Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, et al. 2010 rheumatoid arthritis classification criteria: An american college of rheumatology/european league against rheumatism collaborative initiative. Arthritis Rheum 2010;62:2569-81.

12.	Global health observatory data repository. Geneva: World Health Organisation; 2016 [updated 2016; cited]; Available from: http://apps.who.int/gho/data/node.country.country-CUB?lang=en.

13.	The united nations data repository. New York: United Nations; 2016 [updated 2016; cited]; Available from: http://data.un.org/Data.aspx?d=POP&f=tableCode:26.

14.	Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: Modification of an existing tool and evidence of interrater agreement. J Clin Epidemiol 2012;65:934-9.

15.	Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The american rheumatism association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315-24.

16.	MacGregor A, Bamber S, Silman A. A comparison of the performance of different methods of disease classification for rheumatoid arthritis. Results of an analysis from a nationwide twin study. The Journal of rheumatology 1994;21:1420-6.

17.	Ropes MW, Bennett GA, Cobb S, Jacox R, Jessar RA. Proposed diagnostic criteria for rheumatoid arthritis: Report of a study conducted by a committee of the american rheumatism association. Ann Rheum Dis 1957;16:118.

18.	Kellgren JH. Diagnostic criteria for population studies. Bull Rheum Dis 1962;13:291.

19.	Cimmino MA, Parisi M, Moggiana G, Mela GS, Accardo S. Prevalence of rheumatoid arthritis in italy: The chiavari study. Ann Rheum Dis 1998;57:315-8.

20.	Simonsson M, Bergman S, Jacobsson LT, Petersson IF, Svensson B. The prevalence of rheumatoid arthritis in sweden. Scand J Rheumatol 1999;28:340-3.

21.	Moolenburgh JD, Valkenburg HA, Fourie PB. A population study on rheumatoid arthritis in lesotho, southern africa. Ann Rheum Dis 1986;45:691-5.

22.	Darmawan J, Muirden KD, Valkenburg HA, Wigley RD. The epidemiology of rheumatoid arthritis in indonesia. Br J Rheumatol 1993;32:537-40.

23.	Shichikawa K, Inoue K, Hirota S, Maeda A, Ota H, Kimura M, et al. Changes in the incidence and prevalence of rheumatoid arthritis in kamitonda, wakayama, japan, 1965–1996. Ann Rheum Dis 1999;58:751-6.

24.	Hakala M, Pöllänen R, Nieminen P. The ara 1987 revised criteria select patients with clinical rheumatoid arthritis from a population based cohort of subjects with chronic rheumatic diseases registered for drug reimbursement. The Journal of rheumatology 1993;20:1674-8.

25.	Jean S, Hudson M, Gamache P, Bessette L, Fortin PR, Boire G, et al. Temporal trends in prevalence, incidence, and mortality for rheumatoid arthritis in quebec, canada: A population-based study. Clin Rheumatol 2017;36:2667-71.

26.   Widdifield J, Paterson JM, Bernatsky S, Tu K, Thorne JC, Ahluwalia V, et al. The rising burden of rheumatoid arthritis surpasses rheumatology supply in ontario. Can J Public Health 2013;104:e450-5.

27.   Neovius M, Simard JF, Askling J, group As. Nationwide prevalence of rheumatoid arthritis and penetration of disease-modifying drugs in sweden. Ann Rheum Dis 2011;70:624-9.

28.   Cross M, Smith E, Hoy D, Carmona L, Wolfe F, Vos T, et al. The global burden of rheumatoid arthritis: Estimates from the global burden of disease 2010 study. Ann Rheum Dis 2014;73:1316-22.

29.   Australian Institute of Health and Welfare. Rheumatoid arthritis. Canberra: AIHW; 2019 [updated 2019; cited]; Available from: https://www.aihw.gov.au/reports/chronic-musculoskeletal-conditions/rheumatoid-arthritis/contents/what-is-rheumatoid-arthritis.

30.   Cunningham J. Socioeconomic disparities in self-reported arthritis for indigenous and non-indigenous australians aged 18-64. Int J Public Health 2011;56:295-304.

31.   Walitt BT, Constantinescu F, Katz JD, Weinstein A, Wang H, Hernandez RK, et al. Validation of self-report of rheumatoid arthritis and systemic lupus erythematosus: The women's health initiative. The Journal of rheumatology 2008;35:811-8.

32.   He W, Goodkind D, Kowal PR. An aging world: 2015. 2016.

33.   Hammer GP, du Prel J-B, Blettner M. Avoiding bias in observational studies: Part 8 in a series of articles on evaluation of scientific publications. Deutsches Arzteblatt international 2009;106:664-8.

34.   Reyes Llerena GA, Guibert Toledano M, Hernandez Martinez AA, Gonzalez Otero ZA, Alcocer Varela J, Cardiel MH. Prevalence of musculoskeletal complaints and disability in cuba. A community-based study using the copcord core questionnaire. Clin Exp Rheumatol 2000;18:739-42.

35.   World Health Organisation. Who global report on trends in tobacco smoking 2015.; 2015 Contract No.: Document Number|.

36.   Sugiyama D, Nishimura K, Tamaki K, Tsuji G, Nakazawa T, Morinobu A, et al. Impact of smoking as a risk factor for developing rheumatoid arthritis: A meta-analysis of observational studies. Ann Rheum Dis 2010;69:70-81.

37.   The World Bank. Nigeria: Life expectancy at birth, total (years). 2017 [updated 2017; cited]; Available from: https://data.worldbank.org/indicator/SP.DYN.LE00.IN?locations=NG.-NG.

38.   Ward MM. Estimating disease prevalence and incidence using administrative data: Some assembly required. The Journal of rheumatology 2013;40:1241-3.

39.   Ng R, Bernatsky S, Rahme E. Observation period effects on estimation of systemic lupus erythematosus incidence and prevalence in quebec. J Rheumatol 2013;40:1334-6.

40.   Banal F, Dougados M, Combescure C, Gossec L. Sensitivity and specificity of the american college of rheumatology 1987 criteria for the diagnosis of rheumatoid arthritis according to disease duration: A systematic literature review and meta-analysis. Ann Rheum Dis 2009;68:1184-91.

41.   Mjaavatten MD, Bykerk VP. Early rheumatoid arthritis: The performance of the 2010 acr/eular criteria for diagnosing ra. Best Pract Res Clin Rheumatol 2013;27:451-66.

42.   Della Rossa A, Neri R, Talarico R, Doveri M, Consensi A, Salvadori S, et al. Diagnosis and referral of rheumatoid arthritis by primary care physician: Results of a pilot study on the city of pisa, italy. Clin Rheumatol 2010;29:71-81.

43.   Al Maini M, Adelowo F, Al Saleh J, Al Weshahi Y, Burmester G-R, Cutolo M, et al. The global challenges and opportunities in the practice of rheumatology: White paper by the world forum on rheumatic and musculoskeletal diseases. Clin Rheumatol 2015;34:819-29.

44.   Aggarwal R, Ringold S, Khanna D, Neogi T, Johnson SR, Miller A, et al. Distinctions between diagnostic and classification criteria? Arthritis Care Res (Hoboken) 2015;67:891-7.

45.   Saraux A, Tobón GJ, Benhamou M, Devauchelle-Pensec V, Dougados M, Mariette X, et al. Potential classification criteria for rheumatoid arthritis after two years: Results from a french multicenter cohort. Arthritis Care Res (Hoboken) 2013;65:1227-34.

Records identified through database searching (n = 1,821)
·ProQuest (650)
·Medline (588)
·Web of Science (468)
·Embase (115)

Records excluded after a review of the title and abstract (n= 1,652)

Potentially relevant results (n =169)
·Medline (56)
·Embase (54)
·Web of Science (34)
·ProQuest (25)

Duplicates removed (n =26)

Manual search of the reference lists of all accepted studies (n=20)

Relevant full-text articles assessed for eligibility (n = 143)

Records excluded (n=17)
Sub-population (9)
Out of scope (1)
Article in Korean (1)
Narrative review (1)
Duplicate (3)
Abstract (2)

Papers initially accepted and met for inclusion criteria (n = 57)

Full-text articles excluded (n = 86)
Exclusion because:
Narrative review (11)
Out of scope (37)
Systematic review (4)
Sub-population (19)
Article in Russian (2)
Article in Chinese (1)
Using secondary data (7)
Study design (3)
Duplicate (1)
RA incidence (1)

Papers accepted and met for inclusion criteria (n = 3)

Studies finally included in the systematic review:
60 Population-based Studies.

Figure1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of search and study selection process for prevalence studies of rheumatoid arthritis (1).

Reference:

1.   Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The prisma statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. PLoS Med 2009;6:e1000100.

PER 100,000
POPULATION

2,250 - 2,700
1,800 - 2,250
900 - 1,800
450 - 900
< 450
No data

FIGURE 2: ADULT POINT-PREVALENCE OF RHEUMATOID ARTHRITIS PER 100,000
POPULATION OF VARIOUS WORLD REGIONS (1986- 2014).

FIGURE 2 ADULT POINT-PREVALENCE OF RHEUMATOID ARTHRITIS PER 100,000 POPULATION OF VARIOUS
WORLD REGIONS (1986- 2014)

PER 100,000
POPULATION

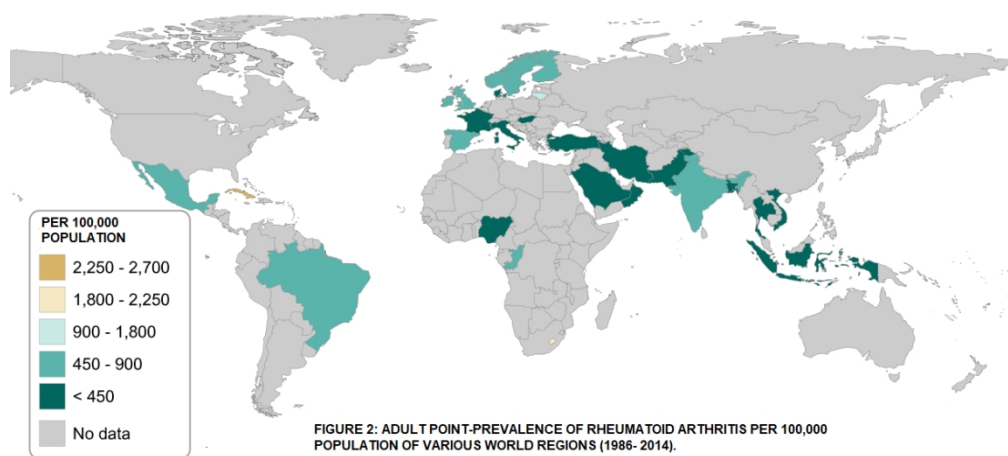|	
	1,800 - 2,250
	1,350 - 1,800
	900 - 1,350
	450 - 900
	< 450
	No data

FIGURE 3: ADULT PERIOD-PREVALENCE OF RHEUMATOID ARTHRITIS PER 100,000 POPULATION OF VARIOUS WORLD REGIONS (1955- 2015).
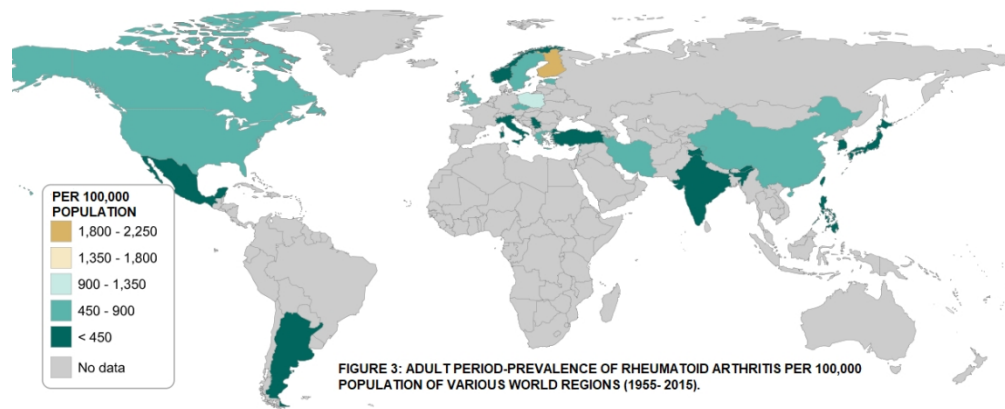
FIGURE 3 ADULT PERIOD PREVALENCE OF RHEUMATOID ARTHRITIS (1955-2015)

Table 1
Keywords used to identify relevant studies

RA		Prevalence		Setting		Data
OR		**OR**		**OR**		**OR**
Rheumatic diseases		Trends		Urban		Administrative data
OR		**OR**		**OR**		**OR**
Rheumatic symptoms		Percentage		Rural		Linked data
OR		**OR**		**OR**		**OR**
Musculoskeletal diseases	**AND**	Rate	**AND**	Community	**AND**	Register
OR		**OR**		**OR**		**OR**
Musculoskeletal conditions		Frequency		Health care		Survey
OR		**OR**		**OR**		
Arthritis		Epidemiology		Population		

RA= Rheumatoid Arthritis.

Table 2: Overall mean of the continental prevalence of rheumatoid arthritis.

Continents	Statistics	RA point-prevalence (%)	RA period-prevalence (%)
North America	Mean	1.46	0.69
	N	3	7
	SD	1.06	0.25
Africa	Mean	0.8	-
	N	3	-
	SD	0.91	-
Europe	Mean	0.53	0.60
	N	12	14
	SD	0.2	0.41
South America	Mean	0.46	0.19
	N	1	1
	SD	-	-
Asia	Mean	0.34	0.34
	N	13	13
	SD	0.19	0.25
Oceania	-	-	-
Total	Mean	0.56	0.51
	N	32	35
	SD	0.51	0.35

RA= Rheumatoid Arthritis.

Table 3: Overall mean of the continental point- and period-prevalence of rheumatoid arthritis using different classification criteria.

Continents	RA classification criteria	RA point- prevalence			RA period- prevalence		
		N	Mean (%)	SD	N	Mean (%)	SD
Africa	ARA criteria 1956	1	1.8	-	-	-	-
	Revised ARA criteria 1987	2	0.3	0.42	-	-	-
	Total	**3**	**0.8**	**0.92**	**-**	**-**	**-**
North America	Revised ARA criteria 1987	3	1.46	1.07	2	0.73	0.47
	Doctor diagnosis	-	-	-	5	0.68	0.19
	Total	**3**	**1.46**	**1.07**	**7**	**0.69**	**0.25**
Europe	Revised ARA criteria 1987	6	0.64	0.23	7	0.46	0.17
	Doctor diagnosis	3	0.44	0.13	5	0.87	0.61
	Modified ARA criteria 1987	3	0.42	0.14	2	0.42	0.13
	Total	**12**	**0.53**	**0.21**	**14**	**0.6**	**0.41**
South America	Revised ARA criteria 1987	1	0.46	.	1	0.19	-
	Total	**1**	**0.46**	**.**	**1**	**0.19**	**-**
Asia	Revised ARA criteria 1987	8	0.37	0.23	7	0.32	0.33
	Modified ARA criteria 1987	1	0.32	.	1	0.49	-
	Doctor diagnosis	2	0.30	0.16	4	0.35	0.17
	ARA criteria 1956	2	0.25	0.07	-	-	-
	Rome criteria 1961	-	-	-	1	0.29	-
	Total	**13**	**0.34**	**0.19**	**13**	**0.34**	**0.26**
Oceania	-	-	-	-	-	-	-
Total of cohort studies		**32**	**0.56**	**0.51**	**35**	**0.51**	**0.35**

RA= Rheumatoid Arthritis.