




EPIDEMIOLOGICAL SCIENCE

Global, regional and national burden of rheumatoid arthritis 1990–2017: a systematic analysis of the Global Burden of Disease study 2017

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Handling editor Josef S Smolen

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/annrheumdis-2019-215920>).

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Received 26 June 2019

Revised 21 August 2019

Accepted 22 August 2019

Published Online First

11 September 2019

ABSTRACT

Objectives To provide the level and trends of prevalence, incidence and disability adjusted life years (DALYs) for rheumatoid arthritis (RA) in 195 countries from 1990 to 2017 by age, sex, Socio-demographic Index (SDI; a composite of sociodemographic factors) and Healthcare Access and Quality (an indicator of health system performance) Index.

Methods Data from the Global Burden of Diseases, Injuries, and Risk Factors study (GBD) 2017 were used. GBD 2017 modelled the burden of RA for 195 countries from 1990 to 2017, through a systematic analysis of mortality and morbidity data to estimate prevalence, incidence and DALYs. All estimates were presented as counts and age-standardised rates per 100 000 population, with uncertainty intervals (UIs).

Results Globally, the age-standardised point prevalence and annual incidence rates of RA were 246.6 (95% UI 222.4 to 270.8) and 14.9 (95% UI 13.3 to 16.4) in 2017, which increased by 7.4% (95% UI 5.3 to 9.4) and 8.2% (95% UI 5.9 to 10.5) from 1990, respectively. However, the age-standardised rate of RA DALYs per 100 000 population was 43.3 (95% UI 33.0 to 54.5) in 2017, which was a 3.6% (95% UI –9.7 to 0.3) decrease from the 1990 rate. The age-standardised prevalence and DALY rates increased with age and were higher in females; the rates peaked at 70–74 and 75–79 age groups for females and males, respectively. A non-linear association was found between age-standardised DALY rate and SDI. The global age-standardised DALY rate decreased from 1990 to 2012 but then increased and reached higher than expected levels in the following 5 years to 2017. The UK had the highest age-standardised prevalence rate (471.8 (95% UI 428.9 to 514.9)) and age-standardised incidence rate (27.5 (95% UI 24.7 to 30.0)) in 2017. Canada, Paraguay and Guatemala showed the largest increases in age-standardised prevalence rates (54.7% (95% UI 49.2 to 59.7), 41.8% (95% UI 35.0 to 48.6) and 37.0% (95% UI 30.9 to 43.9), respectively) and age-standardised incidence rates (48.2% (95% UI 41.5 to 55.1), 43.6% (95% UI 36.6 to 50.7) and 36.8% (95% UI 30.4 to 44.3), respectively) between 1990 and 2017.

Conclusions RA is a major global public health challenge. The age-standardised prevalence and incidence rates are increasing, especially in countries such as Canada, Paraguay and Guatemala. Early identification and treatment of RA is vital especially

Key messages

What is already known about this subject?

- No updated global study on rheumatoid arthritis (RA) has been published after 2010.

What does this study add?

- Globally, the age-standardised point prevalence and annual incidence rates of RA increased by 7.4% (95% uncertainty interval (UI) 5.3 to 9.4) and 8.2% (95% UI 5.9 to 10.5) from 1990, respectively.
- The global age-standardised disability adjusted life year rate decreased from 1990 to 2012 but then increased and reached higher than expected levels in the following 5 years to 2017.
- The UK had the highest age-standardised prevalence and incidence rates in 2017.
- Canada, Paraguay and Guatemala showed the largest increases in age-standardised prevalence and incidence rates between 1990 and 2017.

How might this impact on clinical practice or future developments?

- Early identification and treatment of RA is vital especially among females, in order to reduce the burden and disability associated with this condition and to provide appropriate care for this community.

among females, in order to reduce the ongoing burden of this condition. The quality of health data needs to be improved for better monitoring of disease burden.

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic auto-immune disease. Symmetrical inflammatory polyarthritis is the primary clinical manifestation, usually beginning in the small joints of the hands and the feet, spreading later to the larger joints.¹ A number of national studies have examined prevalence, incidence and mortality of RA^{2–4}; however, there is a lack of a comprehensive global study. In 2016, the WHO estimated the years lived with disability (YLD), years of life lost (YLL) and disability



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To cite: Safiri S, Kolahi AA, Hoy D, et al. *Ann Rheum Dis* 2019;**78**:1463–1471.

adjusted life years (DALYs) of RA by age, sex and country⁵ but no paper has been published in this regard. Recently, Sebbag and colleagues reported the global burden of musculoskeletal disease for 2000, 2010 and 2015 using aforementioned WHO database but they have not specifically focused on RA and their estimates rely on 2015 data.⁶ An analysis utilising the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2010 reported global and regional burden of RA in terms of prevalence and DALYs,⁷ but national-level estimates were not provided. Association of burden of RA with sociodemographic status of countries was not examined in that study. Another study was conducted on GBD 2013 musculoskeletal data combined and were only reported for Eastern Mediterranean region.⁸ Overall, no updated global study on RA has been published after 2010. Hence, in the present study, we examined the data from GBD 2017 for global, regional and national prevalence, incidence and DALY in terms of counts and age-standardised rates from 1990 to 2017 by age, sex, Socio-demographic Index (SDI; a composite of sociodemographic factors) and Healthcare Access and Quality (HAQ; an indicator of health system performance) Index to provide comprehensive and comparable analysis of RA burden.

METHODS

Overview

GBD 2017, conducted by Institute of Health Metrics and Evaluation (IHME), involved 195 countries, seven super-regions and 21 regions from 1990 to 2017.⁹ Three hundred and fifty-four diseases and injuries, 282 causes of death and 84 risk factors were systematically analysed in the GBD 2017 study. The general methodology of GBD 2017 and its main changes compared with previous years have been described in previous publications.^{9–12} The additional information on fatal and non-fatal estimates can be found at <https://vizhub.healthdata.org/gbd-compare/> and <http://ghdx.healthdata.org/gbd-results-tool>. Methods were developed by and most analyses reported here were conducted at IHME.

Case definition and data sources

As stated in many epidemiological studies, RA is a systemic autoimmune disorder that causes pain and swelling of the joints. While RA is known to affect internal organs in addition to the joints, these extra-articular effects are not factored into the disability weights (DW) used in GBD. The reference case definition for RA is based on the 1987 guidelines by the American College of Rheumatology (ACR 1987),¹³ which explain seven diagnostic criteria (1. morning stiffness, 2. arthritis of three or more joint areas, 3. symmetric arthritis, 4. arthritis of hand, 5. rheumatoid nodules, 6. serum rheumatoid factor and 7. radiographic changes), of which four need to be satisfied for a diagnosis. Criteria 1 through 4 must have been present for at least 6 weeks.^{9,13}

A comprehensive systematic review was conducted on RA prevalence, incidence and mortality in GBD 2010 and updated in GBD 2017. Studies with the following characteristics were excluded: (a) non-representative, (b) non-population-based, (c) inadequate primary data on epidemiological parameters, (d) studying a specific type of RA, for example, seropositive RA and (e) reviews. Finally, prevalence (site-years=499), incidence (site-years=151) and other, including remission (site-years=20), were estimated through literature studies included in GBD 2017. Notably, a site-year is a unique combination of location and calendar year and is defined as a country or other subnational geographical unit contributing data in a given year. Also, the

number of countries with data was quite small globally, and these numbers were different for estimating the prevalence (n=42), incidence (n=14) and other (n=9). The number of GBD regions with data was higher for prevalence (n=16), compared with incidence (n=6) and other (n=5). In addition, USA claims data for 2000, and 2010–2014 by US state and Taiwan claims for 2016 were included. It is worth mentioning that hospital inpatient data were not used as it was assumed, they would not be representative of true prevalence.⁹

Data used to estimate RA mortality included vital registration, verbal autopsy, and China disease surveillance data from the cause of death database. Outlier criteria were to exclude data points that were (1) implausibly high or low relative to global or regional patterns, (2) substantially conflicted with established age or temporal patterns, or (3) significantly conflicted with other data sources based from the same locations or locations with similar characteristics that is, SDI.

Disease model

GBD 2017 methods included the standard Cause of Death Ensemble model, which was applied to estimate deaths due to RA. The list of covariates used for the RA model can be found in the appendix methods section of previously published GBD 2017 paper.¹⁰ RA prevalence, incidence and mortality data were analysed within the IHME Bayesian meta-regression tool DisMod-MR 2.1 for modelling and calculation of estimates by pooling the available heterogeneous data to adjust for methodological differences and check for internal consistency.

IHME prior settings in the DisMod-MR 2.1 model included setting remission to 0.009–0.021, which is the assumed remission rate for natural disease (ie, drug-free) remission, and it was assumed that there was no incidence or prevalence of RA before the age of 5 years.⁹ Data from all sources were re-extracted to better reflect the range of case definitions. ACR 1987 criteria¹³ was set as the reference, with other definitions including Rome 1961,¹⁴ American Rheumatology Association 1958,¹⁵ or European League against Rheumatism¹⁶ criteria identified with a single study covariate 'non-ACR_1987'. Additional study covariates were created for studies using administrative health system data sources; for studies covering regional rather than (sub)-nationally representative populations; and for claims data. R software V3.5.2 was used to generate figures of the final estimates of prevalence and incidence rates from data available from ghdx.healthdata.org/gbd-results-tool.

Severity and YLD

The International Classification of Diseases version 10 codes were used for RA (M05-M06.9, M08.0-M08.89) with three sequelae (severity levels) where each sequela had specific DW ranging from 0.11 to 0.58 (see online supplementary table 1). GBD 2013 European Disability Weights Measurement Study and GBD 2010 Disability Weights Measurement Study were used as the sources of DW values. More details are described in previous GBD studies.^{9,17} Medical Expenditure Panel Surveys were used to specify the proportion of each of the severity levels in patients with RA.⁹ Then, these proportions were used to split the overall prevalence of RA into the severity categories. Finally, the prevalence of each severity category was multiplied by severity-specific DWs to calculate YLDs.

Compilation of results

The YLLs were calculated by multiplying the number of deaths in an age group by the remaining life expectancy in that age

group, taken from the GBD standard life table. DALYs were then calculated as the sum of YLLs and YLDs. Uncertainty was propagated by sampling 1000 draws at each computational step, combining uncertainty from multiple sources such as input data, corrections of measurement error and estimates of residual non-sampling error. Uncertainty intervals (UIs) were defined as the 25th and 975th values of the ordered draws. We examined the shape of association of RA burden in terms of DALYs with SDI and HAQ for 21 regions and 195 countries using the Smoothing Splines models.¹⁸ SDI is a composite indicator of lag-dependent income per capita; that is gross domestic product per capita that has been smoothed over the preceding 10 years, average years of schooling for the population older than 15 years of age, and total fertility rate under the age of 25. It ranges from 0 (less developed) to 1 (most developed). HAQ is an indicator of health system performance and reflects personal HAQ for 195 countries and is calculated based on amenable mortality, that is, deaths from causes that should not occur in the presence of effective medical care. This index ranged from 0 (worst-performing health systems) to 100 (best-performing health systems). Additional details for HAQ have been presented previously.¹⁹

RESULTS

Global level

The present study found that globally there were 19 965 115 (95% UI 17 990 489 to 21 955 673) prevalent cases of RA, with an age-standardised prevalence rate of 246.6 per 100 000 (95% UI 222.4 to 270.8), which increased by 7.4% (95% UI 5.3 to 9.4) between 1990 and 2017. Also, RA was responsible for 1 204 599 (95% UI 1 071 090 to 1 331 694) incident cases globally with an age-standardised incidence rate of 14.9 (95% UI 13.3 to 16.4), an increase of 8.2% (95% UI 5.9 to 10.5) between 1990 and 2017 (table 1).

The global age-standardised DALY rate showed a decreasing trend from 1990 to 2012 but increased and reached higher levels in the following 5 years. Moreover, RA accounted for 3.4 million (95% UI 2.6 to 4.4) DALYs at the global level, with an age-standardised rate of 43.3 (95% UI 33.0 to 54.5) DALYs per 100 000 population. The age-standardised DALY rate reduced by 3.6% (95% UI -9.7 to 0.3) from 1990 to 2017 (table 1).

Regional level

At the regional-level, the age-standardised prevalence of RA was found to be highest in high-income North America (377.6 (95% UI 356.4 to 400.2)), Western Europe (346.8 (95% UI 314.4 to 378.3)) and the Caribbean (338.9 (95% UI 304.6 to 374.1)). In contrast, Southeast Asia (100.9 (95% UI 89.9 to 112.2)), Oceania (135.3 (95% UI 120.9 to 150.8)) and Western Sub-Saharan Africa (135.7 (95% UI 120.6 to 151.6)) showed the lowest age-standardised rates (table 1).

The age-standardised incidence rates were also found to be highest in high-income North America (22.5 (95% UI 20.9 to 24.1)), South Asia (20.7 (95% UI 18.4 to 22.9)) and Western Europe (20.4 (95% UI 18.3 to 22.4)); whereas, Southeast Asia (6.2 (95% UI 5.5 to 6.9)), Oceania (7.9 (95% UI 7.0 to 8.9)) and Western Sub-Saharan Africa (8.5 (95% UI 7.5 to 9.5)) showed the lowest rates (table 1).

The regional-level age-standardised prevalence and incidence estimates for all GBD 2017 regions have been presented by sex in online supplementary figure 1.

This study also found that the percentage change in age-standardised prevalence rates during 1990–2017 was not similar across the GBD 2017 regions. East Asia (25% (95% UI 22 to

29)), high-income North America (19% (95% UI 14 to 25)) and Western Sub-Saharan Africa (14% (95% UI 11 to 17)) showed the most increasing significant trends, while Southern Sub-Saharan Africa (-12% (95% UI -15 to -8)), high-income Asia-Pacific (-7% (95% UI -10 to -4)) and Eastern Sub-Saharan Africa (-5% (95% UI -8 to -2)) showed decreasing significant trends (table 1 and online supplementary figure 2). The number of prevalent cases was found to be doubled from 1990 (10 226 042 (95% UI 9 320 195 to 11 179 199)) to 2017 (19 965 114 (95% UI 17 990 489 to 21 955 673)) but the contribution of GBD 2017 regions was different (see online supplementary figure 3).

East Asia (26% (95% UI 23 to 30)), high-income North America (22% (95% UI 18 to 28)) and North Africa and Middle East (13% (95% UI 10 to 15)) had the top statistically significant increasing trends in age-standardised incidence rates whereas statistically significant decreasing trend was found in Southern Sub-Saharan Africa (-11% (95% UI -14 to -8)), high-income Asia-Pacific (-10% (95% UI -14 to -7)) and Eastern Sub-Saharan Africa (-9% (95% UI -12 to -6)) (table 1 and online supplementary figure 2). The number of incident cases was also found to be doubled from 1990 (650 269 (95% UI 589 738 to 711 375)) to 2017 (1 204 599 (95% UI 1 071 089 to 1 331 694)) with differing contribution of GBD 2017 regions (see online supplementary figure 3).

The top three statistically significant increasing trends in age-standardised DALY rate belonged to high-income North America (13% (95% UI 8 to 18)), Western Sub-Saharan Africa (10% (95% UI 1 to 18)) and Tropical Latin America (9% (95% UI 5 to 13)). Southern Sub-Saharan Africa (-29% (95% UI -35 to -22)), high-income Asia-Pacific (-28% (95% UI -34 to -23)) and Eastern Sub-Saharan Africa (-24% (95% UI -35 to -15)) were considered to have statistically decreasing trend in age-standardised DALY rate among GBD 2017 regions (table 1).

National level

Age-standardised prevalence rate of RA ranged from 91 to 471 cases per 100 000 population. The UK (471.8 (95% UI 428.9 to 514.9)), Trinidad and Tobago (404.4 (95% UI 362.6 to 446.6)) and Barbados (402.6 (95% UI 361.1 to 445.3)) had the three highest age-standardised prevalence rates in 2017, whereas Indonesia (91.1 (95% UI 81.1 to 101.8)), Timor-Leste (91.4 (95% UI 81.5 to 102.4)) and Sri Lanka (97.2 (95% UI 85.9 to 109.6)) showed the lowest rates (figure 1 and online supplementary table 2).

Age-standardised incidence rates varied from 5.6 to 27.5 cases per 100 000 population. UK (27.5 (95% UI 24.7 to 30.0)), Ireland (23.7 (95% UI 21.0 to 26.4)) and Sweden (23.4 (95% UI 21.0 to 25.8)) showed the highest age-standardised incidence rates in 2017; in contrast, Indonesia (5.6 (95% UI 4.9 to 6.3)), Timor-Leste (5.7 (95% UI 5.1 to 6.4)) and Sri Lanka (5.9 (95% UI 5.2 to 6.7)) had the lowest rates (figure 2 and online supplementary table 3).

The percentage change in age-standardised prevalence rates from 1990 to 2017 differed substantially between countries, with Canada (54.7% (95% UI 49.2 to 59.7)), Paraguay (41.8% (95% UI 35.0 to 48.6)) and Guatemala (37.0% (95% UI 30.9 to 43.9)) showing the largest increases. In contrast, South Africa (-16.6% (95% UI -20.3 to -13.0)) Sweden (-15.7% (95% UI -19.9 to -11.4)) and Burundi (-15.6% (95% UI -19.5 to -11.1)) showed decreasing trends (see online supplementary table 2).

The percentage change in age-standardised incidence rates (from 1990 to 2017) also differed between countries. The largest

Table 1 Prevalent cases, incident cases and DALYs for rheumatoid arthritis in 2017 for both sexes and percentage change of age-standardised rates by Global Burden of Disease (GBD) region (generated from data available from: ghdx.healthdata.org/gbd-results-tool/)

	Prevalence (95% UI)			Incidence (95% UI)			DALYs (95% UI)		
	Counts (2017)	Age-standardised rates (2017)	Percentage change in age-standardised rates between 1990 and 2017	Counts (2017)	Age-standardised rates (2017)	Percentage change in age-standardised rates between 1990 and 2017	Counts (2017)	Age-standardised rates (2017)	Percentage change in age-standardised rates between 1990 and 2017
Global	19 965 115 (17 990 489 to 673)	246.6 (222.4 to 270.8)	7.4 (5.3 to 9.4)	1 204 599 (1 071 090 to 1 331 694)	14.9 (13.3 to 16.4)	8.2 (5.9 to 10.5)	3 492 036 (2 658 460 to 4 414 818)	43.3 (33 to 54.5)	-3.6 (-9.7 to 0.3)
High-income Asia-Pacific	592 474 (530 417 to 654 202)	187.1 (167.4 to 206.2)	-7.2 (-10.3 to -4.1)	29 557 (25 963 to 33 128)	11.2 (9.9 to 12.4)	-10.3 (-13.8 to -7.1)	101 012 (76 168 to 1 279 22)	30.4 (22.3 to 39.1)	-28.2 (-34.4 to -22.9)
High-income North America	1 954 937 (1 837 944 to 616)	377.6 (356.4 to 400.2)	18.9 (13.9 to 24.5)	105 426 (96 864 to 113 713)	22.5 (20.9 to 24.1)	22.2 (17.5 to 27.7)	301 847 (225 327 to 384 825)	57.6 (42.5 to 73.6)	13.3 (8.1 to 18.1)
Western Europe	2 357 945 (2 135 893 to 2 578 942)	346.8 (314.4 to 378.3)	8 (4.8 to 11.1)	118 352 (105 064 to 131 272)	20.4 (18.3 to 22.4)	7.3 (3.9 to 10.9)	356 870 (259 769 to 463 315)	51.5 (36.9 to 67.2)	-4.5 (-10 to 0)
Australasia	108 716 (97 003 to 121 072)	268.2 (238.7 to 297)	4.4 (-2.2 to 11)	6060 (5347 to 6772)	16.5 (14.7 to 18.4)	2.4 (-5.1 to 9.3)	17 932 (13 401 to 22 908)	43.2 (31.8 to 55.7)	-12 (-19.9 to -4)
Andean Latin America	178 171 (160 962 to 196 538)	313.5 (283.2 to 345.9)	6.2 (2.1 to 10.6)	10 656 (9567 to 11 804)	18.2 (16.3 to 20.1)	2.8 (-1.5 to 7.1)	28 123 (20 233 to 36 630)	49.7 (36 to 64.5)	-7 (-14.6 to -0.4)
Tropical Latin America	676 815 (605 733 to 754 902)	281.6 (251.9 to 313.8)	11.6 (8.8 to 14.2)	38 636 (33 960 to 43 375)	16.1 (14.2 to 18)	8 (4.8 to 10.9)	103 214 (74 615 to 134 983)	43 (31.2 to 56.3)	8.9 (5 to 12.6)
Central Latin America	624 874 (565 265 to 688 015)	254.6 (230 to 279.9)	4.6 (1.7 to 7.6)	39 013 (34 971 to 43 048)	15.5 (13.9 to 17.1)	-3 (-6.3 to 0.4)	124 065 (97 205 to 154 064)	51 (40.1 to 63.2)	-10.4 (-15.4 to -6.1)
Southern Latin America	217 872 (195 209 to 2 603)	283.9 (255.1 to 311.7)	3.6 (-0.8 to 8.5)	13 377 (11 090 to 13 651)	16.9 (15.1 to 18.6)	1.8 (-2.7 to 7)	36 371 (27 270 to 46 577)	47.2 (35.2 to 60.6)	-6.8 (-13.3 to -0.6)
Caribbean	170 721 (153 068 to 188 256)	338.9 (304.6 to 374.1)	10.3 (6.8 to 13.9)	9 499 (8428 to 10 601)	19.2 (17 to 21.4)	7.9 (4.1 to 11.5)	26 314 (18 897 to 34 224)	52.3 (37.6 to 67.9)	2.8 (-4.2 to 9)
Central Europe	406 849 (361 770 to 452 447)	226.9 (202.3 to 251.3)	4.7 (1 to 8.4)	20 799 (18 241 to 23 395)	13.3 (11.8 to 14.8)	3.6 (-0.1 to 7.7)	62 355 (45 539 to 80 198)	34.5 (25 to 44.6)	-6.2 (-11.9 to -1.1)
Eastern Europe	644 432 (570 685 to 718 332)	207.5 (185.2 to 230.5)	4.1 (1.7 to 6.4)	34 028 (29 461 to 38 599)	12.1 (10.7 to 13.5)	4.8 (2.4 to 7.2)	105 205 (79 075 to 134 521)	33.9 (25.4 to 43.5)	-2.8 (-6.6 to 0.7)
Central Asia	178 222 (158 760 to 198 150)	213.8 (191 to 236.8)	6.3 (3.5 to 9.1)	11 218 (9889 to 12 566)	12.7 (11.2 to 14.1)	7.6 (4.7 to 10.7)	29 748 (22 044 to 38 260)	35.6 (26.4 to 45.4)	-3 (-9.1 to 3.5)
North Africa and Middle East	1 315 587 (1 171 457 to 1 473 984)	259.3 (230.6 to 289.7)	13.3 (10.6 to 16.1)	83 695 (73 497 to 94 434)	15 (13.2 to 16.9)	12.8 (10.2 to 15.5)	186 728 (129 598 to 249 177)	36.7 (25.5 to 48.5)	6 (-1 to 11.6)
South Asia	840 760 (4 340 681 to 5 383 020)	323.7 (289.7 to 358.5)	2 (-0.8 to 4.8)	33 161 (295 195 to 366 416)	20.7 (18.4 to 22.9)	2.3 (-0.6 to 5.1)	979 798 (757 468 to 1 201 710)	69.7 (54.3 to 84.9)	-5.6 (-16.9 to 1.7)
Southeast Asia	658 609 (584 675 to 736 927)	100.9 (89.9 to 112.2)	9.8 (6.5 to 13)	41 886 (36 798 to 47 257)	6.2 (5.5 to 6.9)	5.3 (1.9 to 8.6)	114 176 (85 908 to 145 679)	17.9 (13.6 to 22.6)	-15.4 (-23.6 to -6.9)
East Asia	3 972 614 (3 535 309 to 4 422 987)	194.8 (173.9 to 216.1)	25.2 (22 to 28.5)	232 716 (2 03 851 to 2 61 978)	11.8 (10.4 to 13.1)	26.4 (23.1 to 29.6)	709 970 (5 331 29 to 9 002 331)	35.1 (26.4 to 44.3)	3.9 (-10.2 to 11.8)
Oceania	12 115 (10 742 to 13 659)	135.3 (120.9 to 150.8)	8.6 (5.2 to 12)	826 (729 to 930)	7.9 (7 to 8.9)	8.3 (5 to 11.8)	2305 (1703 to 3038)	25.7 (19.1 to 33.7)	7.8 (-1.9 to 18.6)
Western Sub-Saharan Africa	333 819 (294 662 to 375 452)	135.7 (120.6 to 151.6)	13.9 (10.8 to 17.1)	24 519 (21 667 to 27 531)	8.5 (7.5 to 9.5)	12.2 (9 to 15.4)	55 004 (40 010 to 71 924)	22.9 (17 to 29.6)	9.8 (0.8 to 18.3)
Eastern Sub-Saharan Africa	421 220 (379 258 to 467 912)	212 (190.9 to 233.1)	-4.8 (-7.9 to -1.8)	33 425 (30 086 to 36 797)	14.5 (13 to 16.1)	-8.8 (-11.7 to -5.8)	94 182 (74 288 to 117 235)	51.6 (41 to 63)	-24.5 (-34.6 to -14.6)
Central Sub-Saharan Africa	501 288 (134 719 to 166 777)	219 (197.8 to 242.3)	-4 (-8.3 to 0.3)	11 077 (9956 to 12 257)	13.5 (12.1 to 15)	-5.6 (-9.8 to -1.5)	29 915 (22 826 to 38 220)	45.9 (35.2 to 58.2)	-20.1 (-31.1 to -8.5)
Southern Sub-Saharan Africa	148 235 (132 691 to 164 329)	231.1 (207.6 to 256.9)	-11.7 (-15.1 to -8.3)	9675 (8639 to 10 760)	13.9 (12.4 to 15.5)	-10.8 (-13.8 to -7.6)	26 901 (20 342 to 34 074)	42.6 (32.5 to 53.5)	-28.9 (-34.9 to -21.6)

UI, uncertainty interval.

Age-standardised prevalence rate (per 100,000), both sexes 2017

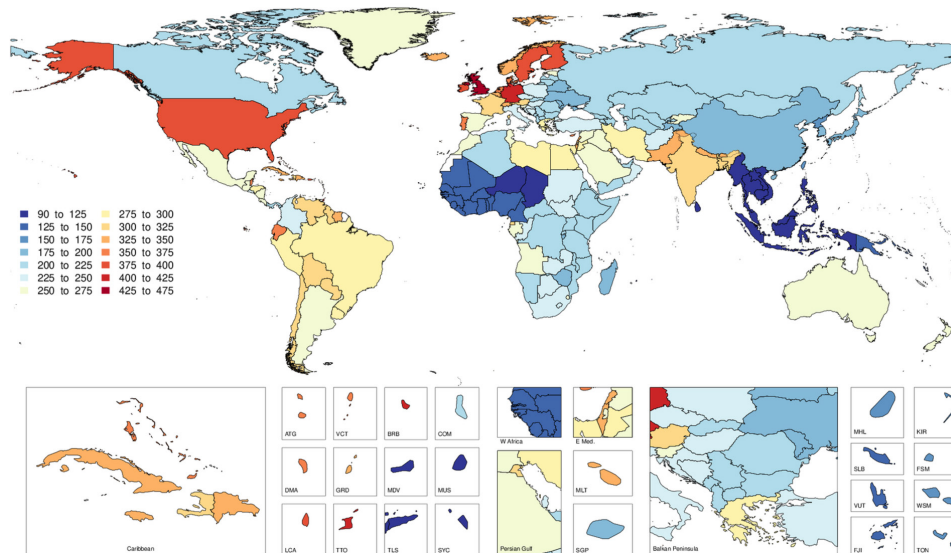


Figure 1 Age-standardised prevalence rate of rheumatoid arthritis per 100 000 population in 2017, by country. ATG, Antigua and Barbuda; BRB, Barbados; COM, Comoros; DMA, Dominica; FJI, Fiji; FSM, Federated states of Micronesia; GRD, Grenada; KIR, Kiribati; LCA, Saint Lucia; MDV, Maldives; MHL, Marshall Islands; MLT, Malta; MUS, Mauritius; SGP, Singapore; SLB, Solomon Islands; SYC, Seychelles; TLS, Timor-Leste; TON, Tonga; TTO, Trinidad and Tobago; VCT, Saint Vincent and the Grenadines; VUT, Vanuatu; WSM, Samoa (generated from data available from ghdx.healthdata.org/gbd-results-tool/).

increases were seen in Canada (48.2% (95% UI 41.5 to 55.1)), Paraguay (43.6% (95% UI 36.6 to 50.7)) and Guatemala (36.8% (95% UI 30.4 to 44.3)). The largest decreases during this period were found in Burundi (−17.0% (95% UI −21.1 to −12.5)), Ethiopia (−16.6% (95% UI −20.1 to −13.6)) and Sweden (−16.2% (95% UI −20.3 to −11.9)) (see online supplementary table 3). The national-level detailed information on DALYs due to RA can be found in online supplementary table 4.

Age and sex patterns

Globally, age-standardised prevalence rate was higher in females and increased with age, peaking at 70–74 and 75–79 age groups among females and males, respectively in 2017. Also, the number of prevalent cases increased with age and peaked in the 60–64 age group for both males and females; after this age, the trend declined (figure 3). In 2017, the global age-standardised

Age-standardised incidence rate (per 100,000), both sexes 2017

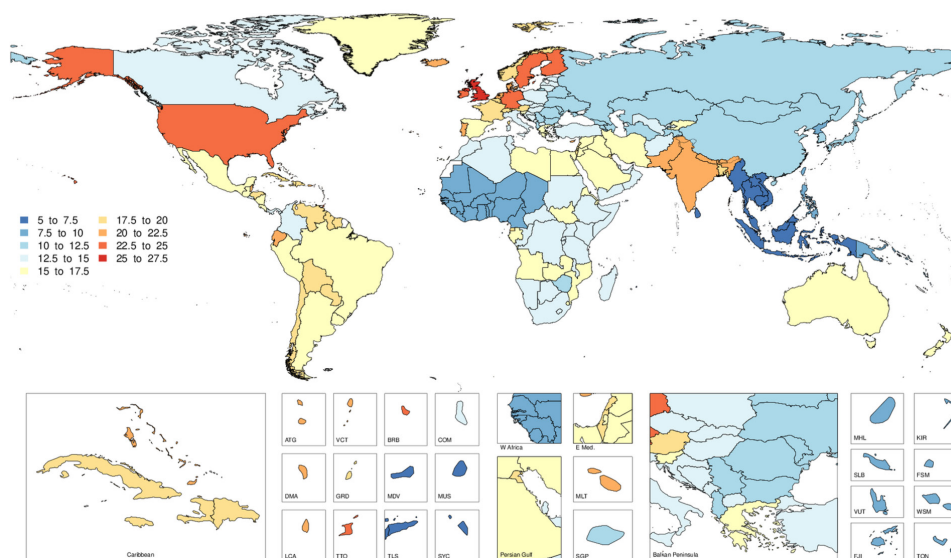


Figure 2 Age-standardised incidence rate of rheumatoid arthritis per 100 000 population in 2017, by country. ATG, Antigua and Barbuda; BRB, Barbados; COM, Comoros; DMA, Dominica; FJI, Fiji; FSM, Federated states of Micronesia; GRD, Grenada; KIR, Kiribati; LCA, Saint Lucia; MDV, Maldives; MHL, Marshall Islands; MLT, Malta; MUS, Mauritius; SGP, Singapore; SLB, Solomon Islands; SYC, Seychelles; TLS, Timor-Leste; TON, Tonga; TTO, Trinidad and Tobago; VCT, Saint Vincent and the Grenadines; VUT, Vanuatu; WSM, Samoa (generated from data available from: ghdx.healthdata.org/gbd-results-tool/).

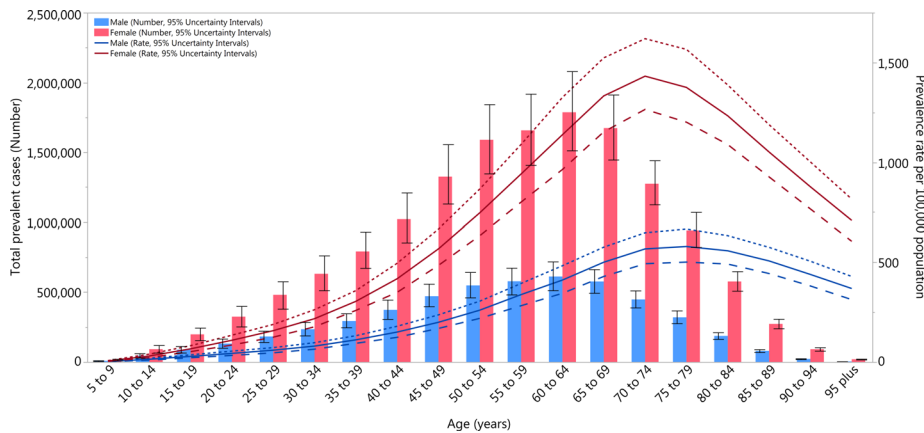


Figure 3 Global number of prevalent cases and prevalence rate of rheumatoid arthritis per 100 000 population by age and sex, 2017; dotted and dashed lines indicate 95% upper and lower uncertainty intervals, respectively

incidence rate was also found to be higher in females and increased with population ageing but there was no statistically significant difference between males and females in the 70+ age groups. The number of incident cases reached the highest level at 50–54 age group then a declining trend was observed to the oldest group (see online supplementary figure 4). The pattern of age-standardised DALY rate by sex across the age groups was relatively similar to the age-standardised prevalence rate (see online supplementary figure 5). Decomposition of DALY rate into YLL and YLD also showed that the YLL rate was significantly lower than YLD up to 70–74 age group. Moreover, it was found 60–64 and 65–69 age groups had the highest number of YLD and YLL, respectively (see online supplementary figure 6).

Burden of RA by SDI and HAQ

At the regional-level, a non-linear association was found between the age-standardised DALY rate and the SDI. The lowest age-standardised DALY rate was seen at an SDI of around 0.43; it then increased and decreased intermittently with SDI improvement (figure 4). In the high-income super region, only high-income North America showed an increasing level during 1990–2017. Despite a declining trend in Western Europe, this region still showed a higher than expected level of age-standardised DALY rate during the measurement period. In the Latin-America super-region, Caribbean and Tropical Latin America showed

increasing trend during 1990–2017 and all regions had higher than expected level of age-standardised DALY rate in the recent 6 years. Central Europe, Eastern Europe, Central Asia, North Africa and Middle East, Southeast Asia, East Asia and Oceania had lower than expected age-standardised DALY rates during 1990–2017. Finally, in the Sub-Saharan Africa super-region, only Western Sub-Saharan Africa showed lower than expected age-standardised DALY rate during 1990–2017 (figure 4).

National-level analysis found there was a non-linear association between age-standardised DALY rate and SDI and the high burden of RA was not limited to the most developed or less developed countries. UK, India, Pakistan, Nepal, Honduras, Barbados, Trinidad and Tobago and many other countries showed much higher than expected level of age-standardised DALY rates. In contrast, Singapore, Malaysia, Sri Lanka, Vietnam, Timor-Leste showed and many other countries showed much lower than expected age-standardised DALY rates (figure 5). The association of age-standardised DALY rates and countries' HAQ also was also non-linear (see online supplementary figure 7).

DISCUSSION

In this paper, we presented the prevalence, incidence and DALY counts and age-standardised rates for RA in 195 countries from 1990 to 2017, as reported in GBD 2017. Globally, there were almost 20 million prevalent cases, 1.2 million incident cases and

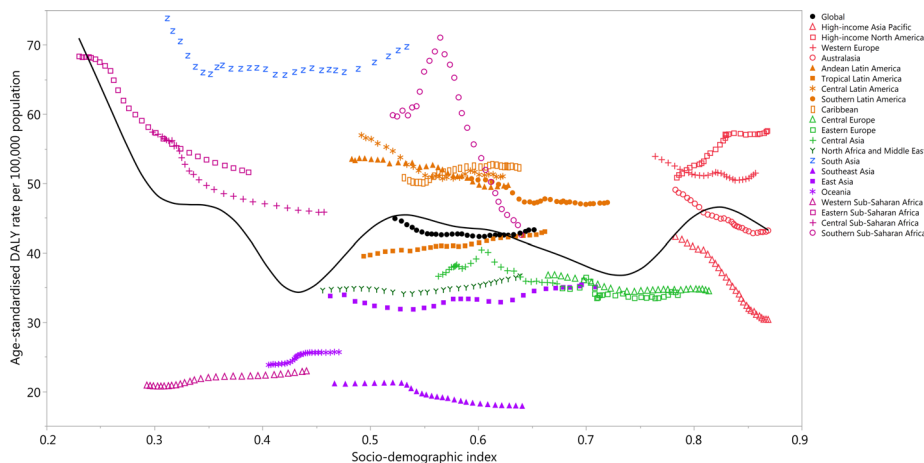


Figure 4 Age-standardised DALY rates for rheumatoid arthritis for 21 Global Burden of Disease (GBD) regions by Socio-Demographic Index (SDI), 1990–2017; expected values based on SDI and disease rates in all locations are shown as the black line. Twenty-eight points are plotted for each GBD region and show observed age-standardised DALY rates from 1990 to 2017 for that region. DALY, disability adjusted life year

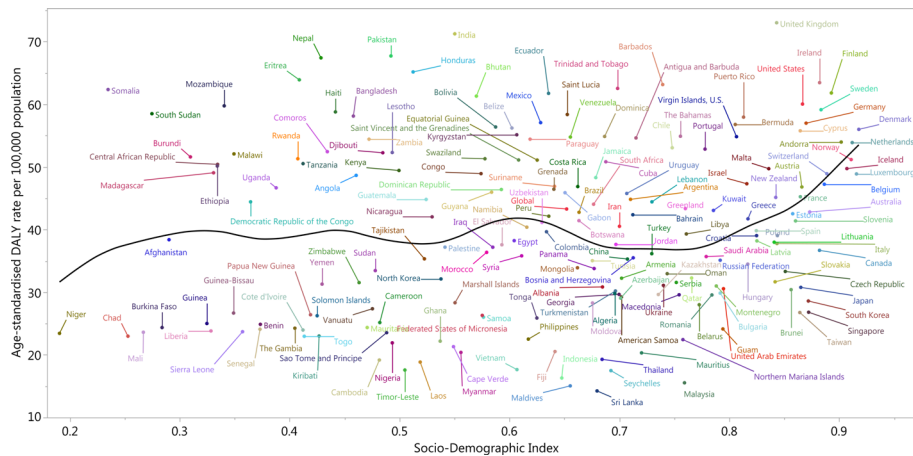


Figure 5 Age-standardised DALY rates of rheumatoid arthritis by 195 countries and Socio-Demographic Index, 2017; expected values are shown as the black line. Each point shows observed age-standardised DALY rate for specified country in 2017. DALY, disability adjusted life year.

3.4 million DALYs. These data serve to highlight the significant, yet under-recognised, global burden of RA.

A previous systematic review on RA prevalence found that regional crude prevalence rates were 400 for Southeast Asia, 370 for the Eastern Mediterranean, 620 for Europe, 1250 for North America, and 420 for the Western Pacific.⁴ While estimates from this review could not be directly compared with the GBD 2017 estimates, it is clear that North America and the Eastern Mediterranean are consistently among the highest regions in terms of prevalence. In GBD 2010,⁷ RA was found to be responsible for 4.8 million DALYs in 2010, which is higher than the updated GBD 2017 estimates. This difference may in part be explained by additional data sources and new methodologies applied in GBD 2017. The global prevalence of RA was similar between GBD 2010 and GBD 2017, at 240 per 100 000 population.⁷ The crude DALYs for RA was higher in 2017 than in GBD 2013 (45.7 vs 37.6).⁸

The GBD 2017 data showed that the age-standardised prevalence and incidence rates have increased during the period 1990 to 2017 but age-standardised DALY rate decreased by 3.6%. An 11.6% increase in crude DALY rate from 1990 to 2013 has been reported⁸; whereas, GBD 2017 found that the crude DALY rate increased by 25% during 1990–2017. Other studies have not investigated the trend of age-standardised rate of prevalence, incidence and DALYS comprehensively and hence, findings cannot be compared.^{20 21}

Differences in incidence and prevalence in regions that are within the same super-region should be noted. South Asia, which includes Bangladesh, India, Nepal, Bhutan and Pakistan, is among the regions with the highest incidence and prevalence of RA, yet South-East Asia, including Cambodia Myanmar and Thailand among others, is among the lowest incidence and prevalence rates globally.

GBD 2017 also showed that age-standardised prevalence and DALY rates were higher in females and increased with age and peaked at 70–74 and 75–79 age groups among females and males, respectively. Moreover, the age-standardised incidence rate was also found to be higher in females and increased with age, but there was no statistically significant difference between males and females in those aged over 70 years. The prevalence rate of RA across age groups was also examined in the previous studies and prevalence rates have reported to be higher in females than males^{4 7 8}; but the association between prevalence rate and age and sex such as the monotonic positive association of prevalence

rate with age found in prior studies⁷ were not similar to the GBD 2017 findings.

It must be noted that the data presented here were primarily derived from modelled data through the processes in DISMOD-MR 2.1. True population-based national data on incidence and prevalence of RA were available from very few countries, thus the present study relies on modelling. As such, these national estimates should be interpreted with caution. Greater inclusion of musculoskeletal conditions, including RA, is encouraged in national health data collections.

To the best of our knowledge, the associations of prevalence, incidence and DALYs due to RA with developing status of region and countries have not been examined in the previous studies and the present study has some important findings. First, the association between burden of RA and SDI should not be assumed to be simplistic and linear; GBD 2017 showed a complex and non-linear association. In fact, burden of RA is not limited to developed or less developed countries and a high burden of RA was reported in countries with various SDI. Second, the global burden of RA has reached higher than expected levels during recent years and awareness of the importance of early identification and treatment should be encouraged in the countries with high incidence, prevalence and DALY rates to reduce future burden. Third, the effectiveness of prevention programmes should not be only judged based on the observed values but also the expected levels in each region and country need to be addressed.

One of the approaches in prevention programme is to focus on risk factors. However, previous observational studies found only smoking to be clearly associated with RA.¹² Although some risk factors such as genetic factors, hormones, stress, obesity, infections, gut bacteria and diet have been studied but the findings have been inconclusive. Smoking, as one of the important risk factors, need to be monitored precisely and specific prevention programme need to be applied in each country. According to a previous study,²² the global age-standardised prevalence of daily smoking decreased by 28.4% and 34.4% in men and women since 1990, respectively. This study also shows the pace of progress as a function of geographies, development status and sex is heterogeneous. Greater success in tobacco control can be achieved through using effective and comprehensive policies introduced in previous papers.^{23 24}

Effective treatment of RA needs a policy and health service response, such as the WHO Global Strategy, which aims to

develop and maintain functional ability that enables well-being in older age. In areas where there is problematic access to specialists, delayed diagnosis of RA may impede the effective treatment of RA and difficulties adhering to treat-to-target principles that aim to prevent RA-related disability by reducing disease activity and achieving remission. Early diagnosis and treatment prevent progression of joint damage in 90% of patients with early RA,²⁵ and increased levels of remission can be gained from effective early treatment with more complex disease modifying and biological drugs that are currently available,²⁵ although with their higher cost, this is primarily in high-income regions. However, greater awareness is needed of RA burden and dissemination of knowledge of the large body of evidence of the important improvements in morbidity and mortality that can be achieved with early clinical diagnosis and treatment with relatively low-cost drugs such as methotrexate.^{26–28} With this early treatment of RA, the adverse consequences and increasing burden of RA can be prevented.

CONCLUSIONS

RA is a major global public health challenge; however, the burden of RA varies geographically. The age-standardised prevalence and incidence rates are overall increasing globally. Increasing population awareness regarding RA, its risk factors and the importance of early diagnosis and treatment with disease modifying agents is warranted to reduce the future burden of this condition. Improving health data for better monitoring of disease burden and health outcomes are strongly suggested.

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Correction notice This article has been corrected since it published Online First. The first and tenth affiliations have been updated.

Acknowledgements We would like to thank Institute for Health Metrics and Evaluation staff and its collaborators who prepared these publicly available data. Also, we would like to thank Social Determinants of Health Research Center of Shahid Beheshti University of Medical Sciences for financial support under reference 19406.

Contributors SS, AAK, LM and MC designed the study. SS, AAK, MAM, AA-H, AA-A and MQ analysed the data and performed the statistical analyses. SS, AAK, DB and MC drafted the initial manuscript. All authors reviewed the drafted manuscript for critical content. All authors approved the final version of the manuscript.

Funding The GBD study is funded by Bill and Melinda Gates Foundation, however these were not involved in any way in the preparation of this

manuscript. The present report was also supported by Social Determinants of Health Research Center, Shahid Beheshti University of Medical sciences, Tehran, Iran (No. 19406).

Disclaimer This study is based on publicly available data and solely reflects the opinion of its authors and not that of the Institute for Health Metrics and Evaluation.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was approved by Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran (IR.SBMU.RETECH.REC.1398.161).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository.

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REFERENCES

- Mathers DSC, Pflieger B. The global burden of rheumatoid arthritis in the year 2000. *Criterion* 2006;1.
- Jean S, Hudson M, Gamache P, *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.
- Won S, Cho S-K, Kim D, *et al*. Update on the prevalence and incidence of rheumatoid arthritis in Korea and an analysis of medical care and drug utilization. *Rheumatol Int* 2018;38:649–56.
- Rudan I, Sidhu S, Papan A, *et al*. Prevalence of rheumatoid arthritis in low- and middle-income countries: a systematic review and analysis. *Journal of Global Health* 2015;5.
- World Health Organization. *Global health estimates 2016: disease burden by cause, age, sex, by country and by region, 2000–2016*. Geneva: World Health Organization, 2018.
- Sebbag E, Felten R, Sage F, *et al*. The world-wide burden of musculoskeletal diseases: a systematic analysis of the World Health Organization burden of diseases database. *Ann Rheum Dis* 2019;78:844–8.
- Cross M, Smith E, Hoy D, *et al*. The global burden of rheumatoid arthritis: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014;73:1316–22.
- Moradi-Lakeh M, Forouzanfar MH, Vollset SE, *et al*. Burden of musculoskeletal disorders in the eastern Mediterranean region, 1990–2013: findings from the Global Burden of Disease study 2013. *Ann Rheum Dis* 2017;76:1365–73.
- James SL, Abate D, Abate KH, *et al*. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease study 2017. *The Lancet* 2018;392:1789–858.
- Roth GA, Abate D, Abate KH, *et al*. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease study 2017. *The Lancet* 2018;392:1736–88.
- Kyu HH, Abate D, Abate KH, *et al*. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease study 2017. *The Lancet* 2018;392:1859–922.
- Stanaway JD, Afshin A, Gakidou E, *et al*. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease study 2017. *The Lancet* 2018;392:1923–94.
- Arnett FC, Edworthy SM, Bloch DA, *et al*. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988;31:315–24.
- Kellgren JH. Diagnostic criteria for population studies. *Bull Rheum Dis* 1962;13:291.
- Ropes MW, Bennett GA, Cobb S, *et al*. Proposed diagnostic criteria for rheumatoid arthritis: report of a study by a Committee of the American Rheumatism Association. *Ann Rheum Dis* 1957;16:118–25.
- Vonkeman HE, van de Laar MAFJ. The new European League Against Rheumatism/American College of Rheumatology diagnostic criteria for rheumatoid arthritis: how are they performing? *Curr Opin Rheumatol* 2013;25:354–9.
- Salomon JA, Haagsma JA, Davis A, *et al*. Disability weights for the Global Burden of Disease 2013 study. *Lancet Glob Health* 2015;3:e712–23.
- Wang Y. *Smoothing splines: methods and applications*. Chapman and Hall/CRC, 2011.
- Fullman N, Yearwood J, Abay SM, *et al*. Measuring performance on the healthcare access and quality index for 195 countries and territories and selected subnational locations: a systematic analysis from the Global Burden of Disease study 2016. *The Lancet* 2018;391:2236–71.

- 20 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.
- 21 Myasoedova E, Crowson CS, Kremers HM, *et al.* Is the incidence of rheumatoid arthritis rising?: results from Olmsted County, Minnesota, 1955–2007. *Arthritis Rheum* 2010;62:1576–82.
- 22 Reitsma MB, Fullman N, Ng M, *et al.* Smoking prevalence and attributable disease burden in 195 countries and territories, 1990–2015: a systematic analysis from the Global Burden of Disease study 2015. *The Lancet* 2017;389:1885–906.
- 23 Pierce JP, White VM, Emery SL. What public health strategies are needed to reduce smoking initiation? *Tob Control* 2012;21:258–64.
- 24 Golechha M. Health promotion methods for smoking prevention and cessation: a comprehensive review of effectiveness and the way forward. *Int J Prev Med* 2016;7:7.
- 25 Aletaha D, Smolen JS. Diagnosis and management of rheumatoid arthritis. *JAMA* 2018;320:1360–72.
- 26 Choi HK, Hernán MA, Seeger JD, *et al.* Methotrexate and mortality in patients with rheumatoid arthritis: a prospective study. *The Lancet* 2002;359:1173–7.
- 27 Lopez-Olivo MA, Siddhanamatha HR, Shea B, *et al.* Methotrexate for treating rheumatoid arthritis. *Cochrane Database of Systematic Reviews* 2014;103.
- 28 Rau R, Herborn G. Benefit and risk of methotrexate treatment in rheumatoid arthritis. *Clin Exp Rheumatol* 2004;22:S83–S94.