

Global, regional, and national incidence of six major immune-mediated inflammatory diseases: findings from the global burden of disease study 2019

GBD 2019 IMID Collaborators^a



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Summary

Background The causes for immune-mediated inflammatory diseases (IMIDs) are diverse and the incidence trends of IMIDs from specific causes are rarely studied. The study aims to investigate the pattern and trend of IMIDs from 1990 to 2019.

Methods We collected detailed information on six major causes of IMIDs, including asthma, inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis, psoriasis, and atopic dermatitis, between 1990 and 2019, derived from the Global Burden of Disease study in 2019. The average annual percent change (AAPC) in number of incidents and age standardized incidence rate (ASR) on IMIDs, by sex, age, region, and causes, were calculated to quantify the temporal trends.

Findings In 2019, rheumatoid arthritis, atopic dermatitis, asthma, multiple sclerosis, psoriasis, inflammatory bowel disease accounted 1.59%, 36.17%, 54.71%, 0.09%, 6.84%, 0.60% of overall new IMIDs cases, respectively. The ASR of IMIDs showed substantial regional and global variation with the highest in High SDI region, High-income North America, and United States of America. Throughout human lifespan, the age distribution of incident cases from six IMIDs was quite different. Globally, incident cases of IMIDs increased with an AAPC of 0.68 and the ASR decreased with an AAPC of -0.34 from 1990 to 2019. The incident cases increased across six IMIDs, the ASR of rheumatoid arthritis increased (0.21, 95% CI 0.18, 0.25), while the ASR of asthma (AAPC = -0.41), inflammatory bowel disease (AAPC = -0.72), multiple sclerosis (AAPC = -0.26), psoriasis (AAPC = -0.77), and atopic dermatitis (AAPC = -0.15) decreased. The ASR of overall and six individual IMID increased with SDI at regional and global level. Countries with higher ASR in 1990 experienced a more rapid decrease in ASR.

Interpretation The incidence patterns of IMIDs varied considerably across the world. Innovative prevention and integrative management strategy are urgently needed to mitigate the increasing ASR of rheumatoid arthritis and upsurging new cases of other five IMIDs, respectively.

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Keywords: Immune-mediated inflammatory disease; Incidence; Global burden of disease study; Trend

Introduction

Immune-mediated inflammatory diseases (IMIDs) encompass a heterogeneous group of disorders affecting various organs and tissues, including the skin (psoriasis [PsO] and atopic dermatitis [AD]), and the joints (rheumatoid arthritis [RA] and psoriatic arthritis [PsA], internal lumen (inflammatory bowel disease [IBD] and

asthma) and white matter and gray matter (multiple sclerosis [MS]).¹ Patients with IMID have a higher likelihood of developing another IMID and often present with comorbidities, such as cardiovascular, psychiatric, and peripheral artery disorders.^{2–6} The evolving understanding of the shared underlying pathogenesis of these clinically diverse diseases has led to a transition from

*Corresponding author. Department of Rheumatology and Immunology, Sichuan Provincial People's Hospital, School of Medicine, University of Electronic Science and Technology of China, Chengdu, China.

E-mail address: dongze_wu@163.com (D. Wu).

^aCollaborators are listed at the end of the Article.

Research in context

Evidence before this study

We conducted a systematic search of the Medline and EMBASE databases from their inception to January 9, 2023, using the keywords “immune-mediated inflammatory disease”, “incidence”, “trend”, “trend analysis”, “rheumatoid arthritis”, “atopic dermatitis”, “asthma”, “multiple sclerosis”, “inflammatory bowel disease”, and “psoriasis”. Although the burden of immune-mediated inflammatory diseases (IMIDs) is increasing globally, few studies have focused on the most up-to-date incidence trends of IMIDs on a global scale. Most studies have been limited to a single cause, country, or population, or have considered the trend by a single factor. To our knowledge, a comprehensive analysis of the pattern and trends of IMID incidence has not been reported. Therefore, this study aims to fill this gap by providing a comprehensive and up-to-date assessment of the global burden of six major IMIDs, including asthma, inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis, psoriasis, and atopic dermatitis, from 1990 to 2019.

Added value of this study

Our study presents a comprehensive analysis of the temporal trends of IMIDs by gender, age, cause, region, and country, and their association with the socio-demographic index (SDI) across the world. Our findings reveal a wide variation in the incidence of IMIDs, and the age-standardized rate (ASR) of overall and six individual IMIDs increased with SDI across 21

Global Burden of Disease regions and 204 countries and territories. Globally, the number of incident cases of IMIDs increased, while the age-standardized rate decreased from 1990 to 2019. Throughout human lifespan, the age distribution of incident cases from six IMIDs was quite different. Among the six IMIDs studied, incident cases increased, and the ASR of rheumatoid arthritis increased, while the ASR of asthma, inflammatory bowel disease, multiple sclerosis, psoriasis, and atopic dermatitis decreased. We identified several at-risk populations for increasing trends in patients with IMIDs, including those with rheumatoid arthritis, people aged 60 years or older, and those from high-income countries. Our study provides valuable insights into the global burden of IMIDs and can inform future public health policies aimed at reducing their impact.

Implications of all the available evidence

The magnitude of incident cases of IMIDs has increased significantly over the past few decades. As a result, there is an urgent need for an integrative management strategy to address the increasing ASR of rheumatoid arthritis and the upsurge in new cases of the other five IMIDs studied. Furthermore, future analyses of IMID trends should also consider the potential impact of the COVID-19 pandemic on incidence rates. One Health after the COVID-19 pandemic is an opportunity to focus efforts and resources on IMIDs, which can strengthen multisectoral coordination mechanisms.

organ-based to molecular-based classification, which was initiated by insights into associated key immune and inflammatory pathways and the development of cytokine targeted therapy, including monoclonal and bispecific antibodies, small interfering RNA (siRNA) therapeutics and chimeric antigen receptor (CAR)-T cell therapy.⁷⁻⁹

Over the past three decades, there has been a remarkable increase in human life expectancy and healthy life expectancy.¹⁰ Higher life expectancy at age 70 has led to a greater proportion of years spent in ill health at that age.¹¹ Healthcare access and quality disparities persist worldwide, the Healthcare Access and Quality Index increased globally from 1990 to 2019, low-SDI countries had a significantly lower overall index of 30.7 compared to high-SDI countries with an index of 83.4.¹² In 2019, the median physician density was ten times higher in high-SDI countries compared to low-SDI countries.¹³ Given that IMIDs represent a significant health concern, a refined trend analysis of IMIDs will aid in identifying and addressing the underlying causes of disparities in the diagnosis, treatment, and management of these diseases.

The Global Burden of Diseases (GBD), Injuries, and Risk Factors Study provided a systematic approach to

assess the burden of IMIDs in 204 countries and territories, offering a unique opportunity to understand the underlying trends across the past three decades.¹⁴ In this study, we focused primarily on six major IMIDs, chosen due to the emergence of novel drugs and treatment strategies over the past few decades. Given the evolving healthcare needs of patients with IMIDs over their lifespan and medical advancements, this study aimed to i) estimate the pattern and trend of IMIDs incidence across the lifespan, ii) identify the global, regional, and national trends in IMIDs incidence from 1990 to 2019, and iii) determine the driving forces behind these trends.

Methods

Data sources

The GBD 2019 study is the most comprehensive and up-to-date source of epidemiological data, providing estimates for 369 diseases and injuries across 204 countries and territories from 1990 to 2019.^{14,15} Using standardized tools and a Bayesian framework, the study provides a detailed estimation of the incidence of IMIDs across all regions of the world. The accompanying GBD 2019 publications describe the data inputs, processing, synthesis, and final models used to estimate the disease

burden of IMIDs.^{14,15} The GBD 2019 synthesizes a great number of input sources to estimate the incidence of IMIDs. The Data Input Sources Tool in Global Health Data Exchange (<http://ghdx.healthdata.org/gbd-2019/data-input-sources>) provides access to input sources for specific GBD components, causes and risks, and locations. The estimates and methods used in this study are publicly available from the Institute for Health Metrics and Evaluation website, including the GBD Compare tool (<https://vizhub.healthdata.org/gbd-compare/>) and the GBD Results Tool (<http://ghdx.healthdata.org/gbd-results-tool>).

Data collection

Annual incident cases and age standardized incidences of IMIDs from 1990 to 2019, by sex, region, country, and cause (asthma, IBD, MS, RA, psoriasis, AD), were collected from the Global Health Data Exchange (GHDx) query tool (<https://vizhub.healthdata.org/gbd-results/>). Data from a total of 204 countries and territories were categorized into 5 regions in terms of socio-demographic index (SDI), including low, low-middle, middle, high-middle, and high and were separated into 21 regions in terms of geography.

Socio-demographic index

The SDI is a composite index of socio-demographic development status strongly correlated with health outcomes, which is the geometric mean of 0–1 indices of total fertility rate in those under 25 years old, mean education for those age 15 years or older, and lag-distributed income per capita.¹⁰

Statistical analysis

The study aimed to analyze the patterns and trends of major IMIDs using age-standardized incidence rate (ASR) and incident cases. The temporal trend was evaluated using a join-point regression model, and the average annual percent change (AAPC) was calculated for the study period. An increasing trend was determined if both the AAPC estimate and the lower boundary of its 95% confidence interval (CI) were >0, while a decreasing trend was established if both the AAPC estimate, and the upper boundary of its 95% CI were <0. Otherwise, the ASR was considered stable over time. The join-point analysis of entire range (1990–2019), and three segment ranges (1990–1999, 2000–2009, 2010–2019) were used to reflect the full and local trend of IMIDs. To investigate the factors influencing AAPCs, the association between AAPCs and ASRs (1990) and SDI (2019) was assessed at the national level. All statistical analyses were conducted using Join-point Regression Program (Version 4.8.0.1, Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute).¹⁶ A significance level of $p < 0.05$, at a two-tailed level, was used to determine statistical significance.

Ethics statement

This study was produced as part of the GBD Collaborator Network and in accordance with the GBD Protocol (IHME ID 4239-GBD2019-042,022). For GBD studies, a waiver of informed consent was reviewed and approved by the Institutional Review Board of the University of Washington (<https://www.healthdata.org/gbd/2019>).

Role of the funding source

The funders of this study had no role in study design, data collection, data analysis, data interpretation, and writing of the manuscript.

Results

The age effect on incidence of overall immune-mediated inflammatory disease

Throughout human lifespan, the age distribution of incident cases from six IMIDs was quite different (sTable S1, Fig. 1A and B). Most incident cases were observed in individuals under the age of 25 for AD, in the age group of 20–59 years for IBD, in individuals aged 15–54 years for MS, among adults aged 30–69 years for RA, in individuals under the age of 69 for psoriasis. MS and RA did not affect children under the age of 5, while AD and asthma most frequently affected children under the age of 5. The age-specific rate was highest among children under the age of 5, decreased with age, but increased again for individuals over the age of 80 for asthma and AD, increasing with age and plateauing at 40–44 years for IBD, increased rapidly, peaked at 25–29 years, and quickly turned to a decrease for MS, slowly increased, peaked at 65–69 years, and quickly turned to a decrease for RA, slowly increased, peaked at 55–55 years, and slowly turned to a decrease for psoriasis (sTable S2, sFigure S1, sFigure S2).

Throughout human lifespan, the AAPC of overall IMIDs new cases decreased with age, the AAPC of overall IMIDs incidence rate increased before 10 years, decreased during 10–65 years, reached nadir at 65–69 years, then turned to increase (sTable S1, Fig. 1C and D). Specifically, the AAPC of incident cases attributable to six individual IMIDs universally increased with age (sFigure S3). In contrast, the AAPC of incidence rate decreased with age, reached trough at 65–69 years, and turn to increase for asthma; fluctuant decrease with age for inflammatory bowel disease; fluctuant decrease with age, reached trough at 50–54 years, then turned to increase for MS; remained stale between 10 and 79 years, then turn to decrease for RA; slowly decrease, reached trough at 40–44 years, then turned to increase for psoriasis; fluctuant increase with age, peaked at 50–54 years, slightly decrease, reached trough at 75–79 years, then turn to increase for AD (sTable S2, sFigure S4).

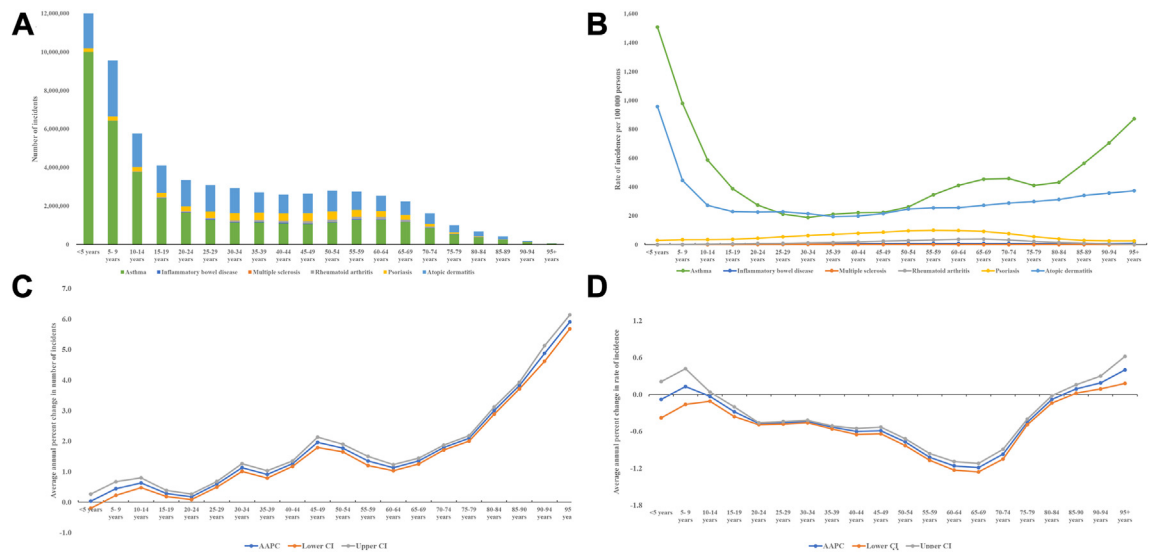


Fig. 1: Cross sectional and longitudinal trend of incidence attributable to overall immune-mediated inflammatory diseases throughout human lifespan. The number of incident cases attributable to overall immune-mediated inflammatory diseases throughout human lifespan in 2019 (A), The rate of incidence attributable to overall immune-mediated inflammatory diseases throughout human lifespan in 2019 (B), The average annual percent change in number of incident cases attributable to overall immune-mediated inflammatory diseases throughout human lifespan, 1990–2019 (C), The average annual percent change in rate of incidence attributable to overall immune-mediated inflammatory diseases throughout human lifespan, 1990–2019 (D).

Global and regional incidence of overall immune-mediated inflammatory disease

In 2019, the global incidence of overall IMIDs was approximately 67,586,168 cases, with an ASR of 908.69 per 100,000 population. Throughout 5 SDI regions, 21 GBD region and 204 countries, the highest ASR was found in the High SDI region, High-income North America, United States of America, and the highest incident cases were recorded in Middle SDI region, South Asia, China, respectively (Table 1).

From 1990 to 2019, the global incident cases increased with an AAPC of 0.68, but the ASRs decreased with an AAPC of -0.34. The ASRs decreased in all five SDI regions from 1990 to 2019, with the quickest decline in the Low-middle SDI region (AAPC = -0.27). Across the regional and national region, the most rapid increase of ASR was observed in High-income North America (AAPC = 0.21) and Oman (AAPC = 0.55), the most rapid increases of incident cases were Western Sub-Saharan Africa (AAPC = 2.59) and Qatar (AAPC = 5.83) (Table 1, Fig. 2C and D, sFigure S5, sTable S3).

Incidence of six immune-mediated inflammatory disease according to gender and proportion

Compared with males, females have more than twice likelihood to develop RA, have modestly higher likelihood to develop AD, have comparable possibility to develop asthma, have more considerable likelihood to develop MS, have similar possibility to develop psoriasis, has slight lower likelihood to IBD. (sFigure S6). In

1990 and 2019, RA, AD, asthma, MS, psoriasis, IBD accounted for 1.02%, 34.32%, 57.53%, 0.07%, 6.53%, 0.53% and 1.59%, 36.17%, 54.71%, 0.09%, 6.84%, 0.60% of overall new IMIDs cases, respectively. In 2019, this proportion exceeded 2.51% for RA in South Asia, comprised as much as 0.27% for MS in certain high-SDI regions, such as Western Europe, reached 1.70% for IBD in Central Europe (Table 1, Fig. 3).

Incidence of six immune-mediated inflammatory disease according to global, SDI and GBD region

From 1990 to 2019, the global ASR significantly increased for RA (AAPC = 0.21), albeit the ASRs significantly decreased for AD (AAPC = -0.15), asthma (AAPC = -0.41), MS (AAPC = -0.26), psoriasis (AAPC = -0.77), IBD (AAPC = -0.32). Among the six IMIDs, the global new cases increased the fastest for RA (AAPC = 2.22), followed by MS (AAPC = 1.21), IBD (AAPC = 1.11), AD (AAPC = 0.84), psoriasis (AAPC = 0.81), asthma (AAPC = 0.53) (Table 1).

The ASR increased across 5 SDI regions for RA, decreased in four out of five SDI regions for AD except for High-middle SDI, was only decreased in the High-middle SDI region for MS, generally decreased across the 5 SDI regions for asthma and psoriasis, increased fastest in middle SDI regions for IBD. The incident cases generally increased across the five SDI regions for RA, AD, MS, psoriasis, IBD, increased in all five regions except High-middle SDI for asthma (sTable S4).

	1990	2019	1990-1999	2000-2009	2010-2019	1990-2019
	N (95%CI)	N (95% CI)	AAPC (95% CI)	AAPC (95% CI)	AAPC (95% CI)	AAPC (95% CI)
Age standardized rate						
Overall	1013.74 (888.58-1169.42)	908.69 (786.07-1057.33)	-0.91 (-0.96, -0.87)	-0.28 (-0.37, -0.19)	0.19 (-0.17, 0.54)	-0.34 (-0.46, -0.22)
Male	936.49 (807.69-1098.63)	844.27 (717.13-1004.97)	-0.90 (-0.96, -0.84)	-0.13 (-0.33, 0.06)	0.11 (-0.26, 0.48)	-0.29 (-0.43, -0.15)
Female	1092.27 (966.58-1243.79)	973.24 (851.86-1115.20)	-0.93 (-0.97, -0.90)	-0.39 (-0.50, -0.27)	0.20 (0.11, 0.29)	-0.38 (-0.43, -0.33)
Cause						
Asthma	580.09 (474.68-715.04)	504.28 (400.64-633.26)	-1.47 (-1.55, -1.40)	-0.32 (-0.58, -0.07)	0.54 (0.05, 1.02)	-0.41 (-0.59, -0.23)
Inflammatory bowel disease	6.10 (5.35-6.96)	4.97 (4.43-5.59)	-1.65 (-1.71, -1.59)	-0.16 (-0.29, -0.03)	-0.32 (-0.39, -0.26)	-0.72 (-0.77, -0.67)
Multiple sclerosis	0.80 (0.70-0.90)	0.74 (0.65-0.83)	-0.68 (-0.71, -0.65)	-0.12 (-0.13, -0.11)	0.00 (-0.03, 0.03)	-0.26 (-0.27, -0.24)
Rheumatoid arthritis	12.21 (11.13-13.38)	13.00 (11.83-14.27)	0.27 (0.23, 0.31)	0.41 (0.40, 0.42)	-0.08 (-0.19, 0.02)	0.21 (0.18, 0.25)
Psoriasis	72.24 (69.70-74.72)	57.78 (55.76-59.71)	-0.72 (-0.72, -0.71)	-0.76 (-0.76, -0.75)	-0.84 (-0.85, -0.83)	-0.77 (-0.78, -0.76)
Atopic dermatitis	342.30 (327.04-358.42)	327.91 (312.76-343.67)	-0.04 (-0.06, -0.03)	-0.15 (-0.16, -0.14)	-0.27 (-0.28, -0.27)	-0.15 (-0.16, -0.14)
SDI region						
High SDI	1505.32 (1289.94-1773.48)	1441.66 (1225.91-1685.83)	-1.09 (-1.20, -0.98)	0.31 (0.20, 0.41)	0.24 (0.15, 0.33)	-0.14 (-0.21, -0.08)
High-middle SDI	1013.46 (878.70-1180.79)	931.65 (794.68-1094.39)	-0.61 (-0.84, -0.38)	-0.60 (-0.74, -0.45)	0.61 (0.32, 0.89)	-0.23 (-0.37, -0.09)
Middle SDI	965.01 (839.49-1123.07)	903.46 (775.97-1062.31)	-0.69 (-0.74, -0.65)	-0.38 (-0.43, -0.32)	0.40 (-0.05, 0.84)	-0.23 (-0.37, -0.09)
Low-middle SDI	843.92 (744.71-963.28)	766.86 (672.61-884.99)	-0.90 (-0.97, -0.84)	0.00 (-0.17, 0.17)	0.04 (-0.33, 0.42)	-0.27 (-0.41, -0.14)
Low SDI	859.27 (741.80-999.00)	798.54 (682.39-936.25)	-0.64 (-0.72, -0.56)	-0.06 (-0.14, 0.02)	0.07 (-0.19, 0.34)	-0.22 (-0.31, -0.13)
GBD region						
East Asia	894.11 (774.31-1047.27)	843.98 (726.72-1002.12)	-1.09 (-1.21, -0.98)	-0.77 (-0.91, -0.62)	1.12 (-0.44, 2.71)	-0.26 (-0.76, 0.24)
Southeast Asia	1137.98 (1007.04-1297.84)	1110.15 (974.02-1281.29)	-0.30 (-0.33, -0.27)	0.01 (-0.04, 0.05)	0.04 (-0.03, 0.11)	-0.10 (-0.13, -0.07)
Oceania	1312.62 (1158.42-1477.09)	1194.09 (1060.93-1340.98)	-0.11 (-0.14, -0.08)	-0.60 (-0.63, -0.57)	-0.22 (-0.28, -0.16)	-0.32 (-0.35, -0.29)
Central Asia	1116.28 (961.86-1299.42)	1077.72 (915.85-1273.98)	-0.16 (-0.18, -0.13)	-0.35 (-0.41, -0.30)	0.19 (0.14, 0.23)	-0.11 (-0.14, -0.09)
Central Europe	1011.85 (871.77-1191.64)	895.63 (746.27-1085.60)	-0.37 (-0.45, -0.30)	-0.69 (-0.73, -0.65)	-0.13 (-0.22, -0.03)	-0.42 (-0.46, -0.37)
Eastern Europe	998.65 (841.63-1192.99)	803.47 (658.87-977.26)	-0.68 (-0.80, -0.57)	-1.54 (-1.66, -1.42)	0.16 (-0.04, 0.36)	-0.73 (-0.82, -0.64)
High-income Asia Pacific	1466.17 (1281.85-1695.46)	1168.98 (995.26-1378.25)	-1.18 (-1.33, -1.03)	-1.43 (-1.54, -1.32)	0.29 (0.18, 0.40)	-0.84 (-0.91, -0.76)
Australasia	1338.01 (1138.99-1551.76)	1164.09 (984.84-1379.40)	0.24 (-0.01, 0.50)	-1.70 (-1.84, -1.55)	-0.07 (-0.19, 0.05)	-0.49 (-0.60, -0.38)
Western Europe	1353.20 (1210.93-1519.95)	1229.29 (1072.90-1402.16)	-0.70 (-0.97, -0.43)	-0.24 (-0.28, -0.21)	-0.09 (-0.29, 0.11)	-0.34 (-0.44, -0.23)
Southern Latin America	1255.43 (1101.48-1453.59)	1263.50 (1076.81-1496.65)	0.12 (0.00, 0.23)	0.00 (-0.01, 0.01)	0.00 (-0.01, 0.01)	0.03 (-0.01, 0.06)
High-income North America	1826.13 (1487.93-2270.75)	1911.37 (1603.78-2271.19)	-1.82 (-2.03, -1.61)	1.47 (1.32, 1.62)	0.69 (0.55, 0.82)	0.21 (0.10, 0.31)
Caribbean	1355.04 (1125.45-1626.43)	1283.19 (1060.07-1549.93)	-0.29 (-0.31, -0.28)	-0.29 (-0.31, -0.28)	0.12 (0.02, 0.22)	-0.17 (-0.20, -0.13)
Andean Latin America	1293.82 (1042.51-1583.94)	1118.89 (903.69-1402.55)	-0.68 (-0.73, -0.63)	-1.09 (-1.13, -1.06)	0.37 (0.31, 0.43)	-0.51 (-0.54, -0.48)
Central Latin America	982.24 (810.15-1192.05)	845.25 (673.58-1055.32)	-1.05 (-1.19, -0.92)	-0.66 (-0.78, -0.54)	0.25 (0.21, 0.28)	-0.53 (-0.59, -0.47)
Tropical Latin America	1476.43 (1178.40-1839.26)	1341.33 (1049.19-1666.04)	-0.48 (-0.66, -0.30)	-0.94 (-1.02, -0.87)	0.55 (0.35, 0.75)	-0.34 (-0.44, -0.25)
North Africa and Middle East	897.41 (768.64-1049.74)	851.41 (718.70-1007.79)	-0.29 (-0.32, -0.26)	-0.47 (-0.49, -0.45)	0.31 (0.22, 0.39)	-0.18 (-0.21, -0.15)
South Asia	733.14 (649.63-827.25)	672.56 (596.87-760.22)	-1.57 (-2.02, -1.13)	0.85 (0.19, 1.51)	-0.28 (-0.57, 0.00)	-0.34 (-0.61, -0.07)
Central Sub-Saharan Africa	816.85 (695.52-958.17)	741.82 (627.48-883.02)	-0.34 (-0.35, -0.33)	-0.49 (-0.57, -0.40)	-0.14 (-0.19, -0.09)	-0.33 (-0.36, -0.30)
Eastern Sub-Saharan Africa	943.32 (793.17-1131.35)	852.92 (708.08-1030.73)	-0.57 (-0.64, -0.50)	-0.48 (-0.50, -0.46)	0.06 (0.00, 0.13)	-0.34 (-0.37, -0.31)
Southern Sub-Saharan Africa	779.75 (633.85-944.95)	709.23 (576.11-868.27)	0.35 (-0.07, 0.76)	-3.54 (-4.77, -2.31)	3.28 (2.74, 3.83)	-0.06 (-0.53, 0.41)
Western Sub-Saharan Africa	789.05 (666.42-944.59)	715.11 (599.63-870.18)	-0.65 (-0.98, -0.32)	-0.41 (-0.47, -0.35)	0.00 (-0.20, 0.20)	-0.36 (-0.48, -0.23)
Number of incident cases						
Overall	55,906,499 (48,383,433-65,460,874)	67,586,168 (58,788,402-77,980,783)	0.13 (0.09, 0.17)	0.75 (0.63, 0.88)	1.13 (0.90, 1.37)	0.68 (0.59, 0.77)
Male	26,180,219 (22,235,358-31,447,992)	31,442,524 (26,888,533-37,097,214)	0.05 (-0.01, 0.11)	0.85 (0.67, 1.03)	1.07 (0.74, 1.41)	0.68 (0.55, 0.80)
Female	29,726,280 (26,136,610-34,237,346)	36,143,644 (31,908,458-40,987,243)	0.17 (0.14, 0.20)	0.67 (0.64, 0.70)	1.23 (1.14, 1.32)	0.68 (0.65, 0.72)

(Table 1 continues on next page)

	1990	2019	1990-1999	2000-2009	2010-2019	1990-2019
	N (95%CI)	N (95% CI)	AAPC (95% CI)	AAPC (95% CI)	AAPC (95% CI)	AAPC (95% CI)
(Continued from previous page)						
<i>Cause</i>						
Asthma	32,163,213 (25,752,792-40,513,127)	36,979,267 (29,601,976-45,928,112)	-0.52 (-0.60, -0.45)	0.61 (0.38, 0.84)	1.48 (1.04, 1.91)	0.53 (0.37, 0.70)
Inflammatory bowel disease	293,572 (257,425-336,651)	404,552 (360,521-456,478)	0.43 (0.30, 0.56)	1.67 (1.62, 1.71)	1.27 (1.21, 1.34)	1.11 (1.06, 1.16)
Multiple sclerosis	41,854 (36,306-47,445)	59,345 (51,818-66,943)	1.14 (1.10, 1.17)	1.36 (1.35, 1.37)	1.11 (1.08, 1.14)	1.21 (1.20, 1.23)
Rheumatoid arthritis	567,463 (519,417-621,415)	1,074,391 (975,502-1,179,332)	2.31 (2.28, 2.34)	2.47 (2.46, 2.48)	1.84 (1.75, 1.93)	2.22 (2.19, 2.25)
Psoriasis	3,653,236 (3,527,023-3,778,791)	4,622,594 (4,458,904-4,780,771)	0.98 (0.97, 1.00)	0.85 (0.84, 0.85)	0.61 (0.60, 0.63)	0.81 (0.80, 0.82)
Atopic dermatitis	19,187,161 (18,290,469-20,163,445)	24,446,018 (23,339,682-25,569,146)	0.93 (0.89, 0.97)	0.86 (0.86, 0.87)	0.72 (0.70, 0.74)	0.84 (0.82, 0.86)
<i>SDI region</i>						
High SDI	11,308,057 (9,894,762-13,026,205)	12,088,206 (10,695,628-13,675,720)	-0.87 (-0.96, -0.77)	0.79 (0.65, 0.93)	0.69 (0.60, 0.78)	0.25 (0.18, 0.32)
High-middle SDI	11,390,468 (9,919,040-13,277,351)	11,576,149 (10,234,863-13,168,363)	-0.38 (-0.61, -0.15)	-0.29 (-0.39, -0.19)	1.03 (0.82, 1.24)	0.09 (-0.02, 0.21)
Middle SDI	17,217,439 (14,695,850-20,511,806)	20,163,835 (17,515,593-23,332,662)	0.22 (-0.01, 0.46)	0.30 (0.20, 0.41)	1.29 (1.07, 1.50)	0.59 (0.47, 0.70)
Low-middle SDI	10,430,368 (9,006,974-12,270,814)	13,307,082 (11,596,864-15,359,307)	0.47 (0.42, 0.52)	1.26 (1.10, 1.41)	0.87 (0.58, 1.16)	0.90 (0.79, 1.01)
Low SDI	5,522,262 (4,623,631-6,700,074)	10,402,167 (8,603,854-12,719,419)	2.01 (1.93, 2.10)	2.69 (2.57, 2.81)	2.04 (1.74, 2.33)	2.25 (2.15, 2.36)
<i>GBD region</i>						
East Asia	10,690,192 (9,252,978-12,581,924)	11,270,729 (10,033,558-12,788,729)	-0.26 (-0.85, 0.34)	-0.58 (-0.84, -0.32)	1.83 (1.37, 2.29)	0.28 (0.00, 0.56)
Southeast Asia	5,520,353 (4,796,120-6,444,135)	7,160,601 (6,320,548-8,165,612)	0.91 (0.86, 0.95)	1.03 (0.96, 1.10)	0.74 (0.65, 0.83)	0.88 (0.84, 0.92)
Oceania	88,198 (75,687-102,467)	162,617 (142,217-186,085)	2.53 (2.48, 2.57)	1.72 (1.65, 1.78)	2.25 (2.09, 2.41)	2.15 (2.10, 2.21)
Central Asia	878,383 (742,184-1,047,408)	1,019,637 (864,469-1,210,312)	-0.38 (-0.50, -0.26)	0.17 (-0.09, 0.43)	1.83 (1.78, 1.89)	0.53 (0.44, 0.63)
Central Europe	1,207,366 (1,049,354-1,402,317)	869,178 (755,103-1,000,998)	-1.15 (-1.26, -1.05)	-1.53 (-1.58, -1.49)	-0.67 (-0.80, -0.53)	-1.14 (-1.20, -1.09)
Eastern Europe	2,162,990 (1,846,212-2,545,314)	1,382,432 (1,179,409-1,627,520)	-2.27 (-2.51, -2.04)	-2.37 (-2.46, -2.29)	0.20 (-0.03, 0.43)	-1.51 (-1.63, -1.39)
High-income Asia Pacific	2,258,416 (1,988,004-2,583,898)	1,691,690 (1,513,016-1,891,154)	-1.07 (-1.16, -0.97)	-1.86 (-1.96, -1.75)	0.01 (-0.06, 0.08)	-1.03 (-1.09, -0.98)
Australasia	243,038 (209,273-278,595)	286,422 (249,096-330,809)	1.00 (0.84, 1.16)	-0.31 (-0.41, -0.20)	1.01 (0.95, 1.06)	0.57 (0.50, 0.64)
Western Europe	4,763,790 (4,308,445-5,272,713)	4,565,937 (4,109,690-5,053,466)	-0.69 (-0.87, -0.51)	0.24 (0.13, 0.35)	-0.03 (-0.11, 0.05)	-0.19 (-0.26, -0.11)
Southern Latin America	633,000 (553,280-736,366)	775,180 (671,334-903,964)	0.79 (0.62, 0.95)	0.58 (0.51, 0.64)	0.82 (0.76, 0.87)	0.72 (0.66, 0.78)
High-income North America	4,662,400 (3,905,771-5,676,648)	5,910,905 (5,129,336-6,821,981)	-1.17 (-1.45, -0.89)	2.25 (2.05, 2.44)	1.17 (1.00, 1.34)	0.85 (0.71, 0.99)
Caribbean	524,424 (432,880-632,393)	557,437 (464,673-667,717)	0.22 (0.18, 0.27)	0.01 (-0.03, 0.04)	0.36 (0.10, 0.62)	0.19 (0.11, 0.27)
Andean Latin America	627,462 (495,373-777,248)	711,504 (575,085-893,222)	0.23 (0.14, 0.31)	-0.52 (-0.60, -0.45)	1.82 (1.75, 1.89)	0.44 (0.39, 0.49)
Central Latin America	1,926,142 (1,547,193-2,378,778)	1,998,679 (1,604,735-2,490,472)	0.14 (-0.10, 0.38)	-0.13 (-0.22, -0.04)	0.45 (0.42, 0.48)	0.13 (0.05, 0.21)
Tropical Latin America	2,534,797 (1,993,882-3,218,798)	2,557,679 (2,044,355-3,124,198)	-0.01 (-0.17, 0.14)	-0.54 (-0.61, -0.48)	0.72 (0.56, 0.87)	0.01 (-0.07, 0.09)
North Africa and Middle East	3,496,870 (2,902,019-4,224,006)	5,108,802 (4,286,740-6,082,702)	1.39 (1.31, 1.46)	1.02 (0.99, 1.05)	1.59 (1.49, 1.69)	1.32 (1.28, 1.36)
South Asia	8,465,092 (7,460,147-9,802,521)	11,614,829 (10,330,682-13,169,438)	-0.02 (-0.48, 0.43)	2.61 (1.95, 3.28)	0.65 (0.37, 0.93)	1.07 (0.79, 1.34)
Central Sub-Saharan Africa	574,128 (463,728-704,268)	1,163,850 (945,928-1,431,971)	2.50 (2.47, 2.52)	2.55 (2.52, 2.58)	2.36 (2.32, 2.41)	2.47 (2.45, 2.49)
Eastern Sub-Saharan Africa	2,337,638 (1,878,499-2,929,628)	4,284,839 (3,413,453-5,375,525)	1.98 (1.84, 2.13)	2.12 (2.07, 2.16)	2.28 (2.14, 2.41)	2.12 (2.05, 2.19)
Southern Sub-Saharan Africa	450,736 (356,336-561,184)	554,527 (447,968-685,629)	1.91 (1.42, 2.39)	-3.15 (-4.52, -1.75)	4.57 (3.98, 5.17)	1.01 (0.48, 1.55)
Western Sub-Saharan Africa	1,861,085 (1,503,020-2,320,718)	3,938,693 (3,155,961-4,963,753)	2.39 (2.26, 2.52)	2.99 (2.87, 3.11)	2.49 (2.46, 2.53)	2.59 (2.52, 2.65)

Table 1: The incident cases and age-standardized rate of incidence attributable to immune-mediated inflammatory diseases according to gender, cause, socio-demographic index regions, global burden of disease regions, and its temporal trends from 1990 to 2019.

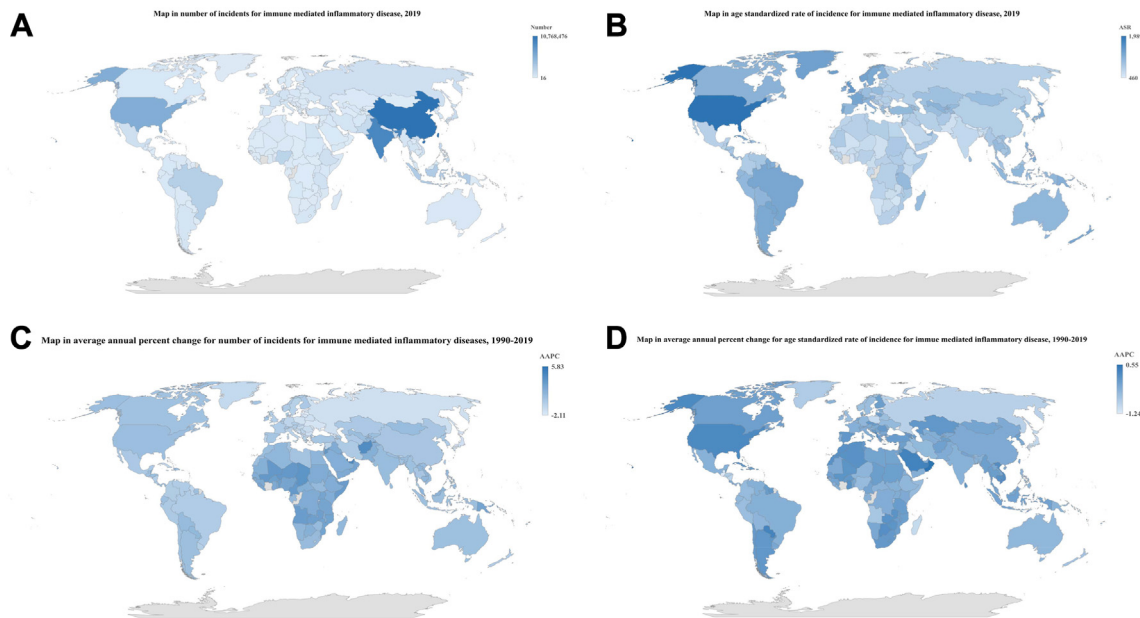


Fig. 2: The global map of incidence attributable to overall immune-mediated inflammatory diseases in 204 countries and territories for both sexes combined. The global map in number of incident cases attributable to overall immune-mediated inflammatory diseases, 2019 (A). The global map in age standardized rate of incidence attributable to overall immune-mediated inflammatory diseases, 2019 (B). The global map in average annual percent change in number of incident cases attributable to overall immune-mediated inflammatory diseases, 1990–2019 (C). The global map in average annual percent change in age standardized rate of incidence attributable to overall immune-mediated inflammatory diseases, 1990–2019 (D).

Of the 21 geographical regions, the most significant increase in ASR was observed in Andean Latin America (AAPC = 1.36) for RA, in Eastern Europe (AAPC = 0.07) for AD, in High-income North America (AAPC = 0.37) for asthma, in Australasia (AAPC = 1.05) for MS, in East Asia (AAPC = 2.48) for IBD. The ASR of psoriasis unanimously decreased among the 21 regions, with the highest decrement observed in North Africa and the Middle East (AAPC = -0.90). The incident cases increased across 21, 18, 12, 21, 19, 21 regions for RA, AD, asthma, MS, psoriasis, IBD, with highest increase in Andean Latin America (AAPC = 3.91), Western Sub-Saharan Africa (AAPC = 2.82), Western Sub-Saharan Africa (AAPC = 2.51), Western Sub-Saharan Africa (AAPC = 3.61), Eastern Sub-Saharan Africa (AAPC = 2.42), Central Sub-Saharan Africa (AAPC = 3.90), respectively (sTable S5, sFigure S7, sFigure S8).

Incidence of six immune-mediated inflammatory disease according to countries and territories

At the national level, the highest ASR of RA, AD, asthma, MS, psoriasis, IBD were observed in Ireland, Mongolia, United States of America, Sweden, France, Canada, while the highest incident cases were recorded in India, China, India, United States of America, China, United States of America for RA, AD, asthma, MS,

psoriasis, IBD, respectively. The fastest increasing trend in ASR of RA, AD, asthma, MS, IBD were Peru (AAPC = 1.43), Kenya (AAPC = 0.16), Oman (AAPC = 0.93), Taiwan (Province of China) (AAPC = 1.55), Taiwan (Province of China) (AAPC = 3.20), respectively. The ASR of psoriasis remained stable in Japan and Somalia but decreased in other 202 countries and territories from 1990 to 2019. The most significant decline in ASR was observed in Equatorial Guinea (AAPC = -1.66). The most significant increase of new cases across six IMIDs was observed in Qatar (AAPC: RA = 8.32, AD = 5.85, asthma = 5.68, MS = 8.82, psoriasis = 6.14, IBD = 8.24) (sTable S6, sFigure S9–S12).

The association between ASR, SDI and AAPC

In 2019, the ASR of overall IMIDs increased with the SDI across 21 regions and 204 countries and territories (Fig. 4A and B). This increasing trend was also observed for six individual IMIDs at the regional and global levels (sFigure S13, sFigure S14).

From 1990 to 2019, countries with higher ASR in 1990 showed a more rapid decrease in ASR of overall IMIDs for an ASR below 1600 per 100,000 (Fig. 4-C). The ASR of IMIDs in 1990 reflects the disease reservoir at baseline, while the SDI in 2019 can serve as a surrogate for the level and availability of healthcare in each

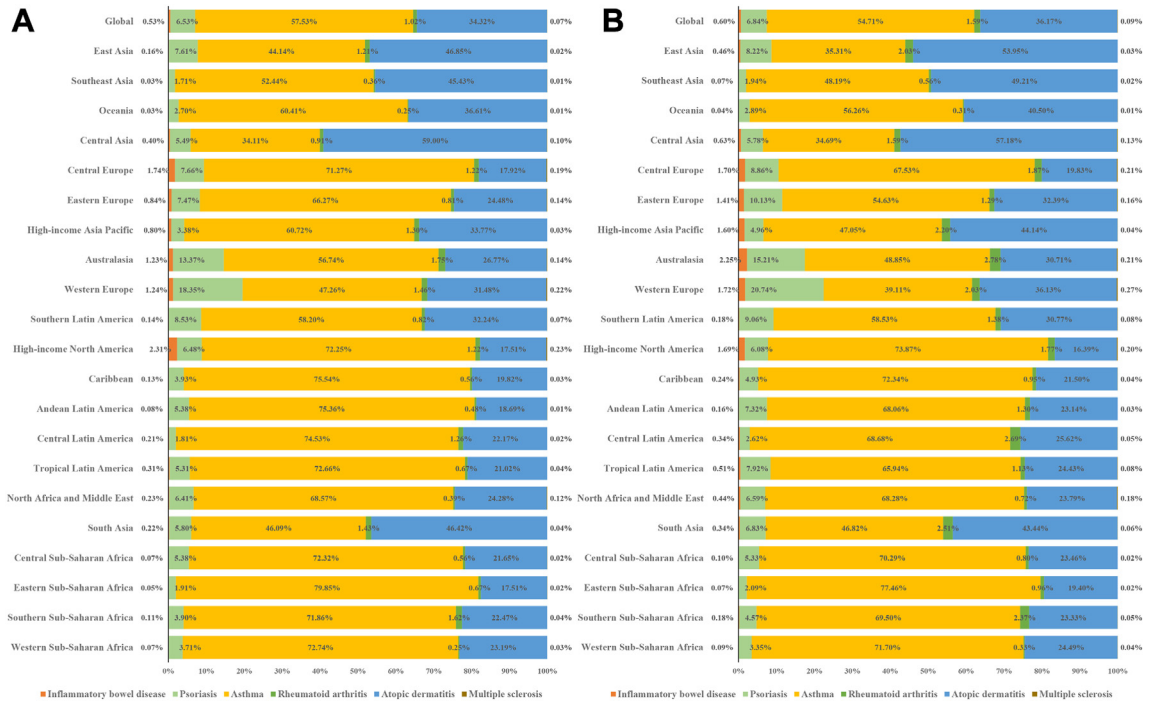


Fig. 3: Contribution of incident cases from six individual to overall immune-mediated inflammatory diseases, both sexes, globally and by region, 1990 and 2019. Contribution of incident cases from six individual to overall immune-mediated inflammatory diseases, both sexes, globally and by region, 1990 (A), Contribution of incident cases from six individual to overall immune-mediated inflammatory diseases, both sexes, globally and by region, 2019 (B).

country. This decreasing trend was also found in four IMIDs, with the most notable being RA. However, the trend was reversed in psoriasis and MS (sFigure S15).

Throughout all regions and countries, those with higher SDI have experienced a more rapid increase in ASR of overall IMIDs from 1990 to 2019 (Fig. 4D). The SDI in 2019 serves as a surrogate for the level and availability of healthcare in each country. A similar increasing trend was also found for IBD, MS, and psoriasis, while a reverse trend was observed for asthma, RA, and AD at the global level (sFigure S16).

Discussion

This study provides a comprehensive estimation of the incidence of IMIDs and investigates their temporal trend by gender, age, SDI, and global-regional-national levels for the first time. The magnitude of incident cases of IMIDs increased, probably driven by population growth and ageing, societal development, interaction between genetic and environmental factors. The global population has risen from 5.3 billion in 1990 to 7.7 billion in 2019, the population aged 70–79 years increased by 115.4%, aged 80–94 years increased by 164.7%, and ≥95 years increased by 363.7%, respectively.¹¹

The ideal efforts to prevent the onset or redirect the course of IMIDs should focus on modifying environmental or behavioral factors.¹⁷ The accumulation of environmental exposures and lifestyle factors that can trigger genetic predisposition underlying immune response over time.^{18–20} Exposure to environmental air pollution above the threshold for human protection was associated with a 10% higher risk of developing IMIDs.²¹ The hygiene hypothesis postulates that the increase in the incidence of IMIDs was caused by the reduced exposure to infectious agents, probably explains the rising development of IMID’s in low-middle-SDI countries, where there has been a steady decline in microbes and parasites over the past thirty years.²² For example, exposure to agricultural farming and poultry is associated with the asthma-protective effect in the rural area.²³ Indeed, hygiene hypothesis cannot fully explain autoimmunity, there is no strong evidence linking the hygiene hypothesis to rheumatoid arthritis.²⁴ In addition, industrial PM2.5 associated with the risk of systemic autoimmune rheumatic diseases and air pollution may be a trigger factor for psoriasis flare.^{25,26} However, the impact of lifestyle changes in preventing the development of systemic autoimmunity in rheumatoid arthritis, such as smoking cessation, dietary changes, weight reduction, has been partially established.²⁷

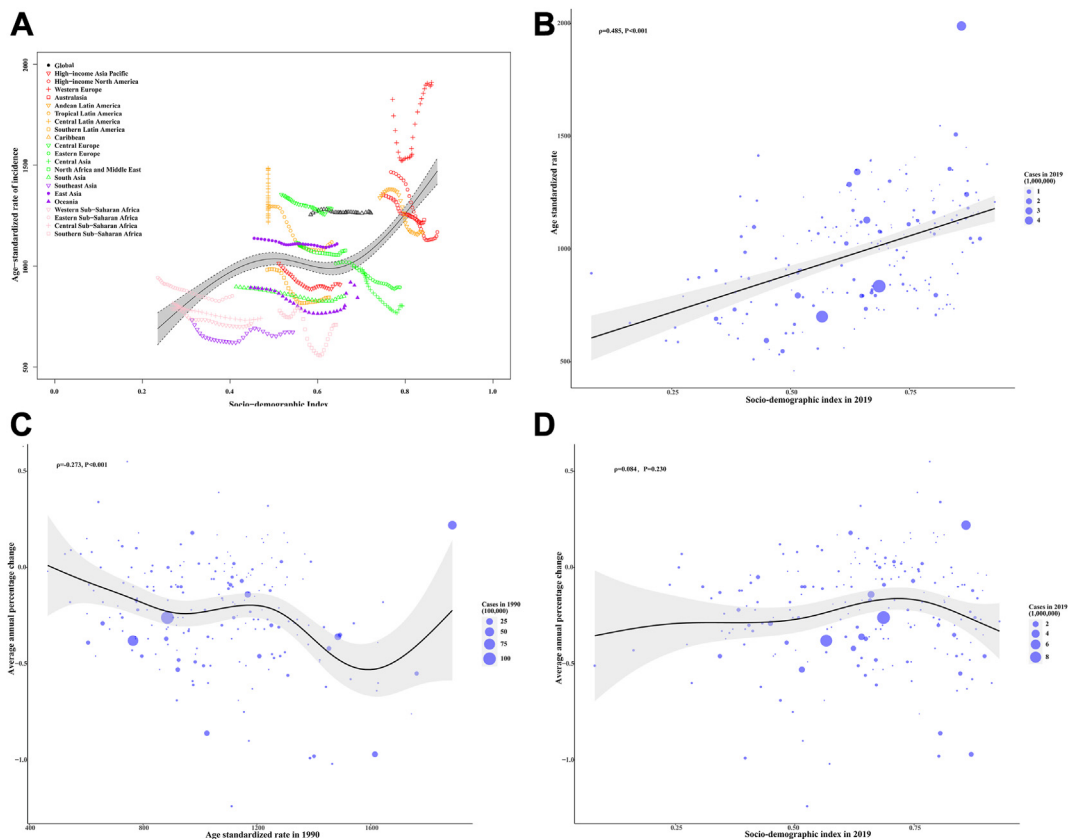


Fig. 4: The association between age standardized rate of incidence, socio-demographic index, average annual percent change across global burden of disease regions and countries and territories. Age standardized rate of incidence attributable to overall immune-mediated inflammatory diseases per 100,000 persons for socio-demographic index by 21 global burden of disease regions, 2019 (A). Black line represents expected values based on socio-demographic index and disease rates across 21 global burden of disease regions; each point shows observed age standardized rate of incidence for specified global burden of disease region in 2019. Age standardized rate of incidence attributable to overall immune-mediated inflammatory diseases per 100,000 persons for socio-demographic index by 204 countries and territories, 2019 (B). Black line represents expected values based on socio-demographic index and disease across 204 countries and territories, each point shows observed age standardized rate of incidence for specified country in 2019. The correlation between average annual percent change and age standardized rate of incidence attributable to overall immune-mediated inflammatory in 1990 across 204 countries and territories (C). The size of circle is increased with the incident cases of immune-mediated inflammatory diseases. The ρ indices and p values were derived from Pearson correlation analysis. The correlation between average annual percent change and socio-demographic index attributable to overall immune-mediated inflammatory in 2019 across 204 countries and territories (D). The size of circle is increased with the incident cases of immune-mediated inflammatory diseases. The ρ indices and p values were derived from Pearson correlation analysis.

Furthermore, the rise in overweight and obesity has paralleled the increase in the incidence of IMIDs, which might be explained by the overstimulation of T lymphocytes by nutrient- and energy-sensing pathways and loss of self-tolerance by metabolic overload.²⁸

Preventive strategy is urgently needed to address the rising ASR of RA. Currently available treatment did not shown to prevent the development of RA in individuals at high risk, early treatment with rituximab and abatacept only delayed onset of full-blown RA.²⁹ Similarly, the TREAT EARLIER study found that early intervention with methotrexate and glucocorticoid treatment did not prevent the development of clinical arthritis.³⁰ Ongoing investigations into preventive interventions that

interfere with altered activation of the adaptive immune system, such as ARIAA (EudraCT 2014-000555-93) and APIPPRA (EudraCT 2013-003413-18), may provide further insight into the feasibility of preventing RA in the future.^{31,32}

A reoriented management strategy and more targeted drugs are needed to control the disease burden from the rapid increase in incident cases of IMIDs as traditional therapeutic modalities, including biologic and small-molecule therapies, is not a concern in patients with IMIDs. New methods are urgently needed to choose tailored formulation and frequency of administration with the highest probability of acceptance and to limit unnecessary use of medication.^{33–35} The Allergic

March story tell us which subtype of AD are at risk progresses to asthma, which might be enhanced when allergic sensitization presents at early life,^{36,37} long term study was needed to investigate whether the new biologics that interact with classic type 2 inflammatory process truly interrupt the atopic march.³⁸ The 2021 asthma recommendation from the Global Initiative for Asthma (GINA) emphasizes the use of symptoms and side-effect preventive modifiers instead of relying on side-effect prone and regular use of relievers.³⁹ Whether modern steroid-sparing anti-inflammatory treatments are disease modifiers remain controversy as the therapeutic effect of allergen immunotherapy is modest and therapeutic effects of biologics targeting IgE, IL-5, IL-4, IL-13 are maintained in adults with established asthma.^{40–42} Although biologic agents can be effective add-on therapies for patients with type 2–high severe asthma, no biologic drugs are currently available for type 2–low severe asthma.⁴³ However, the recent success of tezepelumab, which targets the epithelial alarmin thymic stromal lymphopoietin, is an encouraging development.⁴⁴

Appropriate disease-modifying therapies should be considered in patients with MS and comorbid autoimmune diseases due to the autoimmunity partially overlap with other autoimmune mediated disorders.⁴⁵ More innovative therapies are needed to prevent neurodegeneration and reverse structural damage.⁴⁶ The domain-driven treatment approach aims to address all active domains of psoriatic disease and related conditions.⁴⁷ Larger and longer trials are needed to assess the comparative efficacy and safety of tapinarof (1%) and roflumilast cream (0.3%) in patients with skin psoriasis,^{48,49} While head-to-head trials have shown dual blockade of IL-17A and IL-17F to be superior to biologic targeting IL-17A, IL-12/23, TNF- α in patients with psoriasis, further data is required to confirm whether this finding replicated in patients with PsA.^{50,51} Considering the potential benefits of small molecules over monoclonal antibodies, the next leap forward in treating psoriasis and PsA might be small molecule modulators targeting IL-17A/IL-17RA.⁵² Exciting preliminary data confirms this leap, as deucravacitinib demonstrated superiority over apremilast in patients with psoriasis,⁵³ and upadacitinib was superior to adalimumab in patients with PsA.⁵⁴ Although currently available therapeutic armamentarium resulting in somewhat durable remission in patients with ulcerative colitis, the treatment goal of corticosteroid-free clinical remission was hardly achieved with biologic and small-molecule therapies targeting TNF- α , 4 β 7 integrin, JAK, S1P, TYK2, etc.⁵⁵ Although the effect on small bowel lesions remain unclear, risankizumab represents a promising and favorable option for patients with Crohn's disease who still have unmet needs.⁵⁶

Emerging novel therapeutic modality opens a window on exit strategies of biologic therapy as both

patients and clinicians hope to avoid the undesirable consequences of long-term biologic therapy. Effective improvement in AD have been observed in mesenchymal stem cell (MSC) based therapy, although more research is needed to determine optimal dosages, ideal administration routes and standard methods.⁵⁷ A phase 1/2a single-arm study showed that intravenous infusions of umbilical cord mesenchymal stem cells were could partially be effective in treating psoriasis.⁵⁸ Autologous haemopoietic stem cell transplantation (aHSCT), allogeneic neural stem-cell-based therapy, and CAR-Tregs targeting myelin oligodendrocyte glycoprotein were effective for inducing remissions of active relapsing remitting MS, although long follow-ups and head-to-head comparisons with the most effective disease-modifying treatments are necessary to understand how to position them for the management of patients with aggressive MS.^{59–62} Novel vaccines that prevent EBV infection or targeting EBV would be expected to prevent most new cases or represent a novel treatment strategy for MS.⁶³ Although the failure of Seres Therapeutics' microbiome-based candidate SER-287 in ulcerative colitis casting a shadow over the emerging field,⁶⁴ more data on functional effects of individual and groups of microbes on the mucosal immune system might lead to new microbiota-based therapies.^{65,66} Local treatment with adipose-derived mesenchymal stem cells (Cx601) added on to established treatments for Crohn's disease represents a novel and minimally invasive alternative for complex perianal fistulas.^{67,68} The long-term efficacy and time frame for retreatment are currently being investigated in the INSPIRE trial (EUPAS24267).⁵⁵

Future analyses of the IMIDs should prioritize examining the direct and indirect effects of the COVID-19 pandemic. While the pandemic threatens healthcare access and quality gains achieved at all ages, it poses a particularly grave risk to older individuals who account for most COVID-19 deaths.⁶⁹ However, the pandemic has also catalyzed innovation in the provision of health care, including an expansion in the use of telemedicine.⁷⁰ Recent data strongly suggest that patients with IMID require a third SARS-CoV-2 vaccination, future study should ascertain whether fourth and beyond doses should be given as new boosters become available.^{71,72} Immunocompromising therapies for IMIDs, such as TNF- α inhibitors, are not associated with a significantly greater risk of SARS-CoV-2 or severe sequelae and may even be associated with a lower risk of adverse COVID-19 outcomes.^{73,74} In addition to the impact of immunomodulatory medications that were used in severe cases of COVID-19, on the developing, recurring, or improving the IMIDS, it is necessary to capture the trends at different stages of the pandemic. For example, there may be a surge in incidents as the post-COVID-19 era progresses and diagnoses return to normal levels. The increased attention to One Health after the COVID-

19 pandemic is an opportunity to focus efforts and resources on IMIDs, which can strengthen multisectoral coordination mechanisms at national, regional, and global levels.^{75,76}

The previous analyses of the GBD study have highlighted its limitations.^{11,15} The major limitation of the analysis of the incidence of six IMIDs is the sources vary substantially and out-of-sample modelling data where primary data are not available. Although the data for the modelling on the incidence of IMIDs comes from scientific literature, national surveys, claims data, data were excluded if they violated established regional trends and age distributions, if they led to overestimation of sub-national pseudo-random effects and poor model fit. The GBD study tried to include all available data to modeling the global-regional-national incidence of IMIDs but part data were marked as outliers and excluded if they were implausibly high or low relative to global or regional patterns, substantially conflicted with established age or temporal patterns, significantly conflicted with other data sources conducted from the same locations or locations with similar socio-demographic index. Five additional limitations have been identified. Firstly, the current estimates of the incidence of IMIDs do not reflect the impact of the COVID-19 pandemic. Secondly, underreporting of IMID incidence in low- and middle-income countries may occur due to inadequate reporting mechanisms and infrastructure in some regions. However, the incidence rates of some countries may have been overestimated as they were based on data from major cities. Thirdly, the study does not include a comprehensive list of IMIDs, such as systemic lupus erythematosus, scleroderma, and primary Sjogren's syndrome, Muckle Wells syndrome. Fourthly, the physician density, healthcare access, the quality of medical training might influence the diagnosis of different IMIDs, especially the incidence of IMIDs might overestimate in developed countries and underestimate in developing countries. Fifthly, as inpatients with IMIDs are severely affected patients, further analysis of inpatient data with IMIDs could reflect refractory disease burden and difference of disease burden between inpatient and outpatient.

We recommend four areas of work that need priority in future research. Firstly, it should incorporate how intercept interventions impact the incidence of new cases. Secondly, it should explore the reasons behind these epidemiological transitions. Thirdly, it is vital to train health care providers in the use of up-to-date therapeutics. Finally, it should prioritize investments and cost-effective healthcare to address the substantial unmet healthcare needs.

Contributors

Dongze Wu, Yingzhao Jin, Cui Guo, and Lai-shan Tam had full access to all the data in the study and directly accessed and verified the underlying data reported in the manuscript. All authors had access to, reviewed estimates, and agree to submit the manuscript. Please see appendix

(Authors' contributions) for more detailed information about individual author contributions to the research, divided into the following categories: managing the overall research enterprise; writing the first draft of the manuscript; primary responsibility for applying analytical methods to produce estimates; primary responsibility for seeking, cataloguing, extracting, or cleaning data; designing or coding figures and tables; providing data or critical feedback on data sources; developing methods or computational machinery; providing critical feedback on methods or results; drafting the manuscript or revising it critically for important intellectual content; and managing the estimation or publications process.

Data sharing statement

Data used for the analyses are publicly available from the Institute of Health Metrics and Evaluation (<http://www.healthdata.org/>; <http://ghdx.healthdata.org/gbd-results-tool>).

Declaration of interests

K Abuabara reports grants or contracts from Pfizer and Cosmetique Internacional SNC to their institution, University of California San Francisco; consulting fees from TARGET RWE; outside the submitted work. S Bhaskar reports leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid, with the Rotary Club or Sydney as Board Director and Chair of Youth, with Rotary District 9675 as Chair of Diversity, Equity and Inclusion, and with Global Hub Health Germany as Founding Member and Co-manager, all outside the submitted work. R Buchbinder reports grants from Australian National Health and Medical Research Council (NHMRC), Arthritis Australia, Cabrini Foundation, HCF Foundation, Australian Department of Health to their institution; royalties or licenses from UptoDate as personal payments for a chapter on plantar fasciitis; all outside the submitted work. A K Demetriades reports leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid, with European Association of Neurosurgical Societies (EANS) as President and with Global Neuro Foundation as Board Member, all outside the submitted work. I Filip and A Radfar report payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Avicenna Medical and Clinical Research Institute. T Fukumoto reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from AbbVie, Eli Lilly, Sanofi, Pfizer, Maruho, Novartis, Taiho, Sun Pharma, UCB, and Janssen Pharma, all outside the submitted work. C Herteliu reports a research grant from Romanian Ministry of Research Innovation and Digitalization, MCID, for project titled "Enhancing institutional performance through development of infrastructure and transdisciplinary research ecosystem within socio-economic domain—PERFECTIS," project number ID-585-CTR-42-PFE-2021, outside the submitted work. N Ismail reports leadership or fiduciary role in other board, society, committee or advocacy group, unpaid, with the Malaysian Academy of Pharmacy as council member and bursar, outside the submitted work. K Krishan reports non-financial support from UGC Centre of Advanced Study, CAS II, Department of Anthropology, Panjab University, Chandigarh, India, outside the submitted work. V Shivarov reports a pending Bulgarian patent for Possible SARS-CoV-2 preimmune epitopes; stock or stock options in ICON PLC through restricted stock units; other financial interests from PRAHS/ICON PLC through their salary; all outside the submitted work. C R Simpson reports research grants from MBIE (NZ), HRC (NZ), Ministry of Health (NZ), MRC (UK), HDRUK, and CSO (UK) to their institution, all outside the submitted work. J A Singh reports consulting fees from Crealta/Horizon, Medisys, Fidia, PK Med, Two Labs Inc., Adept Field Solutions, Clinical Care Options, Clearview Healthcare Partners, Putnam Associates, Focus Forward, Navigant Consulting, Spherix, MedIQ, Jupiter Life Science, UBM, Trio Health, Medscape, WebMD, Practice Point Communications, the National Institutes of Health, and the American College of Rheumatology all as personal payments; payment or honoraria for speakers' bureaus from Simply Speaking; support for attending meetings or travel from the steering committee of OMER-ACT; unpaid participation on a Data Safety Monitoring Board or

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Collaborators

Dongze Wu^{*,†}, Yingzhao Jin^{*,†}, Yuhang Xing^{*,†}, Melsew Dagne Abate, Mohammadreza Abbasian, Mohsen Abbasi-Kangevari, Zeinab Abbasi-Kangevari, Foad Abd-Allah, Michael Abdelmasseh, Mohammad-Amin Abdollahifar, Deldar Morad Abdulah, Aidin Abedi, Vida Abedi, Hassan Abidi, Richard Gyan Aboagye, Hassan Abolhassani, Katrina Abuabara, Morteza Abyadeh, Isaac Yeboah Addo, Kayode Nelson Adeniji, Abiola Victor Adepoju, Miracle Ayomikun Adesina, Qorinah Estiningtyas Sakilah Adnani, Mohsen Afarideh, Shahin Aghamiri, Antonella Agodi, Anurag Agrawal, Constanza Elizabeth Aguilera Arriagada, Aqeel Ahmad, Danish Ahmad, Sajjad Ahmad, Sohail Ahmad, Ali Ahmadi, Ali Ahmed, Ayman Ahmed, Janardhana P Aithala, Abdullateef Abiodun Ajadi, Marjan Ajami, Mostafa Akbarzadeh-Khiavi, Fares Alahdab, Mohammad T AlBatineh, Sharifullah Alemi, Adel Ali Saeed Al-Gheethi, Liaqat Ali, Sheikh Mohammad Alif, Joseph Uy Almazan, Sami Almustanyir, Jaber S Alqahtani, Ibrahim Alqasmi, Ihsan Ullah Khan Altaf, Nelson Alvis-Guzman, Nelson J Alvis-Zakzuk, Yaser Mohammed Al-Worafi, Hany Aly, Reza Amani, Hubert Amu, Ganiyu Adeniyi Amusa, Catalina Liliana Andrei, Adnan Ansar, Hossein Ansariyani, Anayochukwu Edward Anyasodor, Jalal Arabloo, Reza Arefnezhad, Judie Arulappan, Mohammad Asghari-Jafarabadi, Tahira Ashraf, Jamila Abdulhamid Atata, Seyyed Shamsadin Athari, Daniel Atlaw, Maha Moh'd Wahbi Atout, Avinash Aujayeb, Asma Tahir Awan, Haleh Ayatollahi, Sina Azadnajafabad, Ahmed Y Azzam, Alaa Badawi, Ashish D Badiye, Sara Bagherieh, Atif Amin Baig, Beriuh Bantie Bantie, Martina Barchitta, Mainak Bardhan, Suzanne Lyn Barker-Collo, Francesco Barone-Adesi, Kavita Batra, Nebiyu Simegnew Bayileyeegn, Amir Hossein Behnoush, Uzma Iqbal Belgauami, Maryam Bemanalizadeh, Isabela M Bensenor, Kebede A Beyene, Akshaya Srikanth Bhagavathula, Pankaj Bhardwaj, Sonu Bhaskar, Ajay Nagesh Bhat, Saied Bitaraf, Veera R Bitra, Archith Bolor, Kaustubh Bora, João Silva Botelho, Rachele Buchbinder, Daniela Calina, Luis Alberto Cámara, Andre F Carvalho, Jeffrey Shi Kai Chan, Vijay Kumar Chattu, Endeshaw Chekol Abebe, Fatemeh Chichagi, Sungchul Choi, Tzu-Chieh Chou, Dinh-Toi Chu, Kaleb Coberly, Vera Marisa Costa, Rosa A S Couto, Natália Cruz-Martins, Omid Dadrás, Xiaochen Dai, Giovanni Damiani, Ana Maria Dascalu, Mohsen Dashti, Sisay Abebe Debela, Robert Paul Dellavalle, Andreas K Demetriades, Alemayehu Anley Demlash, Xinlei Deng, Hardik Dineshbhai Desai, Rupak Desai, Syed Masudur Rahman Dewan, Sourav Dey, Samath Dhamminda Dharmaratne, Daniel Diaz, Mahmood Dibas, Ricardo Jorge Dinis-Oliveira, Mengstie Diress, Thanh Chi Do, Duy Khanh Doan, Masoud Dodangeh, Milad Dodangeh, Deepa Dongarwar, John Dube, Arkadiusz Marian Dzedzic, Abdelaziz Ed-Dra,

Hisham Atan Edinur, Negin Eissazadeh, Michael Ekholuenetale, Temitope Cyrus Ekundayo, Noha Mousaad Elemam, Muhammed Elhadi, Ahmed O Elmehra, Omar Abdelsadek Abdou Elmeligy, Mehdi Emamverdi, Theophilus I Emeto, Hawi Leul Esayas, Habitu Birhan Eshetu, Farshid Etaee, Adeniya Francis Fagbamigbe, Shahriar Faghani, Ildar Ravisovich Fakhriyev, Ali Fatehizadeh, Mobina Fathi, Alireza Feizkhan, Ginenus Fekadu, Mohammad Fereidouni, Seyed-Mohammad Fereshtehnejad, João C Fernandes, Pietro Ferrara, Getahun Fetensa, Irina Filip, Florian Fischer, Behzad Foroutan, Masoud Foroutan, Takeshi Fukumoto, Balasankar Ganesan, Belete Negese Belete Gemed, Seyyed-Hadi Ghamari, MohammadReza Ghasemi, Maryam Gholamalizadeh, Tiffany K Gill, Richard F Gillum, Mohamad Goldust, Mahaveer Golechha, Pouya Goleji, Davide Golinelli, Houman Goudarzi, Shi-Yang Guan, Yang Guo, Bhawna Gupta, Veer Bala Gupta, Vivek Kumar Gupta, Rasool Haddadi, Najah R Hadi, Rabih Halwani, Shafiqul Haque, Ikramul Hasan, Reza Hashempour, Amr Hassan, Treska S Hassan, Sara Hassanzadeh, Mohammed Bheser Hassen, Johannes Haubold, Khezir Hayat, Golnaz Heidari, Mohammad Heidari, Reza Heidari-Soureshjani, Claudiu Herteliu, Kamran Hessami, Kamal Hezam, Yuta Hiraike, Ramesh Holla, Mohammad-Salar Hosseini, Hong-Han Huynh, Bing-Fang Hwang, Segun Emmanuel Ibitoye, Irena M Ilic, Milena D Ilic, Arad Iranmehr, Farideh Iravanpour, Nahlah Elkudssiah Ismail, Masao Iwagami, Chidozie C D Iwu, Louis Jacob, Morteza Jafarinia, Abdollah Jafarzadeh, Kasra Jahankhani, Haitham Jahrami, Mihajlo Jakovljevic, Elham Jamshidi, Chinmay T Jani, Manthan Dilipkumar Janodia, Sathish Kumar Jayapal, Shubha Jayaram, Jayakumar Jeganthan, Jost B Jonas, Abel Joseph, Nitin Joseph, Charity Ehimwenma Joshua, Vaishali K, Billingsley Kaambwa, Ali Kabir, Zubair Kabir, Vidya Kadashetti, Feroze Kaliyadan, Fatemeh Kalroozi, Vineet Kumar Kamal, Amit Kandel, Himal Kandel, Srikanta Kanungo, Jafar Karami, Ibraheem M Karaye, Hanie Karimi, Hengameh Kasraei, Sina Kazemian, Sewnet Adem Kebede, Leila Keikavooosi-Arani, Mohammad Keykhaei, Yousef Saleh Khader, Himanshu Khajuria, Faham Khamesipour, Ejaz Ahmad Khan, Imteyaz A Khan, Maseer Khan, Md Jobair Khan, Moien AB Khan, Muhammad Arslan Khan, Haitham Khatabbeh, Moawiah Mohammad Khatabbeh, Sorour Khateri, Hamid Reza Khayat Kashani, Min Seo Kim, Adnan Kisa, Sezer Kisa, Hyun Yong Koh, Pavel Kolkhir, Oleksii Korzh, Ashwin Laxmikant Kotnis, Parvaiz A Koul, Ai Koyanagi, Kewal Krishan, Mohammed Kuddus, Vishnuthethertha Vishnuthethertha Kulkarni, Narend Kumar, Satyajit Kundu, Om P Kurmi, Carlo La Vecchia, Chandrakant Lahariya, Tri Laksono, Judit Lám, Kamaluddin Latief, Paolo Lauriola, Basira Kankia Lawal, Thao Thi Thu Le, Trang Thi Bich Le, Munjae Lee, Seung Won Lee, Wei-Chen Lee, Yo Han Lee, Jacopo Lenzi, Miriam Levi, Wei Li, Virendra S Ligade, Stephen S Lim, Guang Liu, Xuefeng Liu, Erand Llanaj, Chun-Han Lo, Vanessa Sintra Machado, Azzam A Maghazachi, Mansour Adam Mahmoud, Tuan A Mai, Azeem Majeed, Pantea Majma Sanaye, Omar Mohamed Makram, Elaheh Malakan Rad, Kashish Malhotra, Ahmad Azam Malik, Iram Malik, Tauqeer Hussain Mallhi, Deborah Carvalho Malta, Mohammad Ali Mansourmia, Lorenzo Giovanni Mantovani, Miquel Martorell, Sahar Masoudi, Seyede Zahra Masoumi, Yasith Mathangasinghe, Elezebeth Mathews, Alexander G Mathioudakis, Andrea Maugeri, Mahsa Mayeli, John Robert Carabeo Medina, Gebrekiros Gebremichael Meles, José João Mendes, Ritesh G Menezes, Tomislav Mestrovic, Irmina Maria Michalek, Ana Carolina Micheletti Gomide Nogueira de Sá, Ephrem Tesfaye Mihretie, Le Huu Nhat Minh, Reza Mirfakhraie, Erkin M Mirrakhimov, Awoke Misganaw, Ashraf Mohamadkhani, Nouh Saad Mohamed, Faezeh Mohammadi, Soheil Mohammadi, Salahuddin Mohammed, Shafiq Mohammed, Syam Mohan, Anita Mohseni, Ali H Mokdad, Sara Montazmanesh, Lorenzo Monasta, Mohammad Ali Moni, Md Moniruzzaman, Yousef Moradi, Negar Morovatdar, Ebrahim Mostafavi, Parsa Mousavi, George Duke Mukoro, Admir Mulita, Getaneh Baye Mulu, Efrén Murillo-Zamora, Fungai MUSAIGWA, Ghulam Mustafa, Sathish Muthu, Firzan Nainu, Vinay Nangia, Sreenivas Narasimha Swamy, Zuhair S Natto, Perumalsamy Navaraj, Biswa Prakash Nayak, Athare Nazri-Panjaki, Hadush Negash, Mohammad Hadi Nematollahi, Dang H Nguyen, Hau Thi Hien Nguyen, Hien Quang Nguyen, Phat Tuan Nguyen, Van Thanh Nguyen, Robina Khan Niazi, Taxiarchis Konstantinos Nikolouzakakis, Lawrence Achilles Nnyanzi,

Mamoon Noreen, Chimezie Igwegbe Nzopotam, Ogochukwu Janet Nzopotam, Bogdan Oancea, In-Hwan Oh, Hassan Okati-Aliabad, Osaretin Christabel Okonji, Patrick Godwin Okwute, Andrew T Olagunju, Matthew Idowu Olatubi, Isaac Iyinoluwa Olufadewa, Michal Ordak, Nikita Ovtstavnov, Mayowa O Owolabi, Mahesh P A, Jagadish Rao Padubidri, Anton Pak, Reza Pakzad, Raffaele Palladino, Adrian Pana, Ioannis Pantazopoulos, Paraskevi Papadopoulou, Shahina Pardhan, Ashwaghosha Parthasarathi, Ava Pashaei, Jay Patel, Aslam Ramjan Pathan, Shankargouda Patil, Uttam Paudel, Shrikant Pawar, Paolo Pedersini, Umberto Pensato, David M Pereira, Jeevan Pereira, Maria Odete Pereira, Renato B Pereira, Mario F P Peres, Arokiasamy Perianayagam, Simone Perna, Ionela-Roxana Petcu, Parmida Sadat Pezeshki, Hoang Tran Pham, Anil K Philip, Michael A Piradov, Indrashis Podder, Vivek Podder, Dimitri Poddighe, Elton Junio Sady Prates, Ibrahim Qattee, Amir Radfar, Pourya Raee, Alireza Rafiei, Alberto Raggi, Fakher Rahim, Mehran Rahimi, Mahban Rahimifard, Vafa Rahimi-Movaghar, Md Obaidur Rahman, Mohammad Hifz Ur Rahman, Mosiur Rahman, Muhammad Aziz Rahman, Amir Masoud Rahmani, Mohamed Rahmani, Shayan Rahmani, Vahid Rahmani, Premkumar Ramasubramani, Nemanja Rancic, Indu Ramachandra Rao, Sina Rashedi, Ahmed Mustafa Rashid, Nakul Ravikumar, Salman Rawaf, Elrashdy Moustafa Mohamed Redwan, Nazila Rezaei, Negar Rezaei, Nima Rezaei, Mohsen Rezaeian, Daniela Ribeiro, Mónica Rodrigues, Jefferson Antonio Buendia Rodriguez, Leonardo Roeser, Esperanza Romero-Rodriguez, Aly M A Saad, Basema Saddik, Saied Sadeghian, Umar Saeed, Azam Safary, Mahdi Safdarian, Sher Zaman Safi, Amene Saghazadeh, Dominic Sagoe, Fatemeh Saheb Sharif-Askari, Narjes Saheb Sharif-Askari, Amirhossein Sahebkar, Harihar Sahoo, Mohammad Ali Sahraian, Mirza Rizwan Sajid, Sateesh Sakhamuri, Joseph W Sakshaug, Mohamed A Saleh, Leili Salehi, Sana Salehi, Amir Salek Farrokhi, Sara Samadzadeh, Saad Samargandy, Noosha Samiee-far, Abdallah M Samy, Nima Sanadgol, Rama Krishna Sanjeev, Monika Sawhney, Ganesh Kumar Saya, Art Schuermans, Subramanian Senthilkumar, Sadaf G Sepanlou, Yashendra Sethi, Mahan Shafie, Humaira Shah, Izza Shahid, Samiah Shahid, Masood Ali Shaikh, Sadaf Sharfaei, Manoj Sharma, Maryam Shayan, Hatem Samir Shehata, Aziz Sheikh, Jeevan K Shetty, Jae Il Shin, Reza Shirkoobi, Nebiyu Aniley Shitaye, K M Shivakumar, Velizar Shivarov, Parnian Shobeiri, Soraya Siabani, Migbar Mekonnen Sibhat, Emmanuel Edwar Siddiq, Colin R Simpson, Ehsan Sinaei, Harpreet Singh, Inderbir Singh, Javinder A Singh, Paramdeep Singh, Surjit Singh, Md Shahjahan Siraj, Abdullah Al Mamun Sohag, Ranjan Solanki, Solikhah Solikhah, Yonatan Solomon, Mohammad Sadegh Soltani-Zangbar, Jing Sun, Mindy D Szeto, Rafael Tabarés-Seisdedos, Seyed Mohammad Tabatabaei, Mohammad Tabish, Ensiyeh Taheri, Azin Tahvildari, Iman M Talaat, Jacques JL Lukenze Tamuzi, Ker-Kan Tan, Nathan Y Tat, Raziieh Tavakoli Oliaee, Arian Tavasol, Mohamad-Hani Temsah, Pugazhenthana Thangaraju, Samar Tharwat, Nigusie Selomon Tibebe, Jansje Henny Vera Ticoalu, Tala Tillawi, Tenaw Yimer Tiruye, Amir Tiyuri, Marcos Roberto Tovani-Palone, Manjari Tripathi, Guesh Mebrahtom Tsegay, Abdul Rohim Tualeka, Sree Sudha Ty, Chukwudi S Ubah, Saif Ullah, Sana Ullah, Muhammad Umair, Srikanth Umakanthan, Era Upadhyay, Seyed Mohammad Vahabi, Asokan Govindaraj Vaithinathan, Sahel Valadan Tahbaz, Rohollah Valizadeh, Shoban Babu Varthya, Tommi Juhani Vanskari, Narayanaswamy Venketasubramanian, Georgios-Ioannis Verras, Jorge Hugo Villafaña, Vasily Vlassov, Danh Cao Vo, Yasir Waheed, Abdul Waris, Brhane Gebrehiwot Welegebrial, Ronny Westerman, Dakshitha Praneeth Wickramasinghe, Nuwan Darshana Wickramasinghe, Barbara Willekens, Beshada Zerfu Woldegeorgis, Melat Woldeariam, Hong Xiao, Dereje Y Yada, Galal Yahya, Lin Yang, Fereshteh Yazdanpanah, Dong Keon Yon, Naohiro Yonemoto, Yuyi You, Mazyar Zahir, Syed Saoud Zaidi, Moien Zangiabadian, Iman Zare, Mohammad A Zeineddine, Dawit T Zemedikun, Naod Gebrekrstos Zeru, Chen Zhang, Hanqing Zhao, Chenwen Zhong, Magdalena Ziełńska, Mohammad Zoladl, Alimuddin Zumla, Cui Guo*, and Lishan Tam*.

*Joint first authors.

*Joint senior authors.

*Writing authors.

Affiliations

Department of Rheumatology and Immunology (D Wu PhD), Sichuan Provincial People's Hospital, School of Medicine, University of Electronic Science and Technology of China; Department of Medicine & Therapeutics (Y Jin PhD, Prof L Tam MD), Department of Paediatrics (Y Xing PhD), School of Pharmacy (G Fekadu MSc), Jockey Club School of Public Health and Primary Care (C Zhong MD), The Chinese University of Hong Kong, Hong Kong, China; Department of Nursing (M D Abate MSc), Woldia University, Woldia, Ethiopia; Department of Orthopedic Surgery (M Abbasian MD), Postgraduate Medical Education (A O Elmehra PGCert), Maternal Fetal Care Center (K Hessami MD), Department of Health Policy and Oral Epidemiology (Z S Natto DrPH), Division of General Internal Medicine (Prof A Sheikh MD), Harvard University, Boston, MA, USA; Department of Orthopaedic Surgery (M Abbasian MD), Social Determinants of Health Research Center (Z Abbasi-Kangevari BSc, S Ghamari MD), Department of Biotechnology (S Aghamiri PhD), Department of Epidemiology (A Ahmadi PhD), National Nutrition and Food Technology Research Institute (M Ajami PhD), Department of Immunology (H Ansariyia PhD, K Jahankhani MSc), Department of Neurology (M Fathi MD), Department of Medical Genetics (M Ghasemi PhD), Center for Comprehensive Genetic Services (M Ghasemi PhD), Cancer Research Center (M Gholamalizadeh PhD), Department of Health Economics and Statistics (R Hashempour MSc), Functional Neurosurgery Research Center (E Jamshidi PharmD), Department of Neurosurgery (H Khayat Kashani MD), Department of Genetics (R Mirfakhraie PhD), Department of Virology (A Mohseni BSc), Department of Biology and Anatomical Sciences (P Raei PhD), School of Medicine (S Rahmani MD, N Samieefar MD, M Zangiabadian MD), Ophthalmic Research Center (ORC) (M Shayan MD), Department of Dermatology (A Tahvildari MD), Faculty of Medicine (A Tavasol MD), Urology and Nephrology Research Center (M Zahir MD), Shahid Beheshti University of Medical Sciences, Tehran, Iran; Non-communicable Diseases Research Center (M Abbasi-Kangevari MD, Z Abbasi-Kangevari BSc, S Azadnajafabad MD, S Ghamari MD, M Keykhaei MD, S Momtazmanesh MD, P Mousavi MD, S Rahmani MD, N Rezaei MD, N Rezaei PhD), Research Center for Immunodeficiencies (H Abolhassani PhD, Prof N Rezaei PhD, A Saghazadeh MD), Endocrinology and Metabolism Research Center (M Afarideh MD, N Rezaei PhD), School of Medicine (A Behnoush BS, M Mayeli MD, S Mohammadi MD, S Momtazmanesh MD), Department of Pediatric Neurology (M Bemanalizadeh MD), Department of Scientific Research (F Chichagi MD), Interdisciplinary Neuroscience Research Program (S Faghani MD), Department of Neurosurgery (A Iranmehr MD), Immunology Department (J Karami PhD), Department of Medicine (H Karimi MD), Cardiac Primary Prevention Research Center (S Kazemian MD), Department of Cardiac Electrophysiology (S Kazemian MD), Students Scientific Research Center (SSRC) (M Keykhaei MD), Center for Research and Training in Skin Diseases and Leprosy (F Khamesipour PhD), Department of Pediatric Cardiology (Prof E Malakan Rad MD), Department of Epidemiology and Biostatistics (M Mansournia PhD), Digestive Diseases Research Institute (S Masoudi MSc, A Mohamadkhani PhD, S G Sepanlou MD), Department of Internal Medicine (P Pezeshki BMedSc), Department of Public Health (P Pezeshki BMedSc), Pharmaceutical Sciences Research Center (PSRC) (M Rahimifard PhD), Sina Trauma and Surgery Research Center (Prof V Rahimi-Movaghar MD), Department of Cardiology (S Rashedi MD), Multiple Sclerosis Research Center (Prof M Sahraian MD), Department of Neurology (M Shafie MD), Cancer Research Center (R Shirkoobi PhD), Cancer Biology Research Center (R Shirkoobi PhD), Faculty of Medicine (P Shobeiri MD, S Vahabi MD), Department of Pediatric Allergy and Immunology (F Yazdanpanah MD), Tehran University of Medical Sciences, Tehran, Iran (R Heidari-Soureshjani MSc); Department of Neurology (Prof F Abd-Allah MD, A Hassan MD, Prof H S Shehata MD), Faculty of Medicine (A O Elmehra PGCert), Cairo University, Cairo, Egypt; Department of Surgery (M Abdelmasseh MD), Marshall University, Huntington, WV, USA; Department of Small Animal Clinical Sciences (M Abdollahifar PhD), University of Saskatchewan, Saskatoon, SK, Canada; Community and Maternity Nursing Unit (D M Abdulah MPH), University of Duhok, Duhok, Iraq; Department of

Neurosurgery (A Abedi MD), Keck School of Medicine (A Abedi MD), Mark and Mary Stevens Neuroimaging and Informatics Institute (S Salehi MD), University of Southern California, Los Angeles, CA, USA; Department of Public Health Sciences (V Abedi PhD), Pennsylvania State University, Hershey, PA, USA; Biocomplexity Institute (V Abedi PhD), Virginia Tech, Blacksburg, VA, USA; Laboratory Technology Sciences Department (H Abidi PhD), Department of Nursing (M Zoladl PhD), Yasuj University of Medical Sciences, Yasuj, Iran; Department of Family and Community Health (R G Aboagye MPH), Department of Population and Behavioural Sciences (H Amu PhD), University of Health and Allied Sciences, Ho, Ghana; Department of Biosciences and Nutrition (H Abolhassani PhD), Karolinska University Hospital, Huddinge, Sweden; Department of Dermatology (K Abuabara MD), University of California San Francisco, San Francisco, CA, USA; Virginia Commonwealth University, Richmond, VA, USA (M Abyadeh PhD); Centre for Social Research in Health (I Y Addo PhD), University of New South Wales, Sydney, NSW, Australia; Quality and Systems Performance Unit (I Y Addo PhD), Cancer Institute NSW, Sydney, NSW, Australia; Department of Geography Planning and Environment (K N Adeniji MSc), Department of Public Health (C S Ubah MPH), East Carolina University, Greenville, NC, USA; HIV and Infectious Diseases Department (A V Adepoju MD), Jhpiego, Abuja, Nigeria; Adolescent Research and Care (A V Adepoju MD), Adolescent Friendly Research Initiative and Care, Ado Ekiti, Nigeria; Slum and Rural Health Initiative Research Academy (M A Adesina BPT, I I Olufadewa MHS), Slum and Rural Health Initiative, Ibadan, Nigeria; Department of Physiotherapy (M A Adesina BPT), Department of Epidemiology and Medical Statistics (M Ekholuenetale MSc, A F Fagbamigbe PhD), Faculty of Public Health (M Ekholuenetale MSc, I I Olufadewa MHS), Department of Health Promotion and Education (S E Ibitoye MPH), Department of Medicine (Prof M O Owolabi DrM), University of Ibadan, Ibadan, Nigeria; Faculty of Medicine (Q E S Adnani PhD), Universitas Padjadjaran, Bandung, Indonesia; Department of Dermatology (M Afarideh MD), Mayo Clinic, Rochester, MN, USA; Department of Medical and Surgical Sciences and Advanced Technologies "GF Ingrassia" (Prof A Agodi PhD, M Barchitta PhD, A Maugeri PhD), University of Catania, Catania, Italy; Trivedi School of Biosciences (Prof A Agrawal PhD), Ashoka University, Sonapat, India; Section of General Internal Medicine (Prof A Agrawal PhD), Baylor College of Medicine, Houston, TX, USA; Unidad de Emergencia Adulto (C E Aguilera Arriagada MD), Complejo Asistencial Dr. Sótero del Río, Santiago de Chile, Chile; Department of Medical Biochemistry (A Ahmad PhD), Department of Pediatrics (Prof G Mustafa MD), Department of Pharmacology (A R Pathan PhD, M Tabish MPharm), Shaqra University, Shaqra, Saudi Arabia; Health Research Institute (D Ahmad PhD), University of Canberra, Canberra, ACT, Australia; Public Health Foundation of India, Gandhinagar, India (D Ahmad PhD); Department of Health and Biological Sciences (S Ahmad PhD), Abasyn University, Peshawar, Pakistan; Faculty of Pharmacy (S Ahmad MSc), MAHSA University, Kuala Langat, Malaysia; Department of Epidemiology and Biostatistics (A Ahmadi PhD), Community-oriented Nursing Midwifery Research Center (M Heidari PhD), Shahrekord University of Medical Sciences, Shahrekord, Iran; School of Pharmacy (A Ahmed MPhil), Monash University, Bandar Sunway, Malaysia; Department of Pharmacy (A Ahmed MPhil), Quaid I Azam University Islamabad, Islamabad, Pakistan; Institute of Endemic Diseases (A Ahmed MSc), Unit of Basic Medical Sciences (E E Siddig MD), University of Khartoum, Khartoum, Sudan; Swiss Tropical and Public Health Institute (A Ahmed MSc), University of Basel, Basel, Switzerland; Department of Orthopedics (Prof J P Aithala DNB, J Pereira MS), Yenepoya Medical College, Mangalore, India; Department of Veterinary Pathology (A A Ajadi MS), University of Ibadan, Ilorin, Nigeria; Veterinary Pathology (A A Ajadi MS), Stockholm County Council Surveillance and Analysis Centre for Epidemiology and Community Medicine, Ilorin, Nigeria; Department of Food and Nutrition Policy and Planning Research (M Ajami PhD), National Institute of Nutrition, Tehran, Iran; Liver and Gastrointestinal Diseases Research Center (M Akbarzadeh-Khavi PhD), Department of Radiology (M Dashti MD), Research Center for Evidence-Based Medicine (M Hosseini MD), Cardiovascular Research Center (M Rahimi MD), Connective Tissue Diseases Research

Center (A Safary PhD), Department of Immunology (M Soltani-Zangbar MSc), Department of Pediatric Allergy and Immunology (F Yazdanpanah MD), Tabriz University of Medical Sciences, Tabriz, Iran; Evidence-Based Practice Center (F Alahdab MSc), Mayo Clinic Foundation for Medical Education and Research, Rochester, MN, USA; Department of Molecular Biology and Genetics (Prof M T AlBataineh PhD, Prof M Rahmani PhD), Center for Biotechnology (Prof M Rahmani PhD), Khalifa University, Abu Dhabi, United Arab Emirates; Global Health Entrepreneurship (S Alemi PhD), Tokyo Medical and Dental University, Tokyo, Japan; Micropollutant Research Centre (MPRC) (A A S Al-Gheethi PhD), Tun Hussein Onn University of Malaysia (Universiti Tun Hussein Onn Malaysia (UTHM)), Batu Pahat, Malaysia; Camborne School of Mines (A A S Al-Gheethi PhD), University of Exeter, Penryn, UK; Department of Biological Sciences (L Ali PhD), National University of Medical Sciences, Rawalpindi, Pakistan; School of Public Health and Preventive Medicine (S M Alif PhD), School of Public Health and Preventive Medicine (Prof M Asghari-Jafarabadi PhD), Department of Epidemiology and Preventive Medicine (Prof R Buchbinder PhD), Monash University, Melbourne, VIC, Australia; Department of Medicine (J U Almazan PhD), School of Medicine (Prof D Poddighe PhD), Nazarbayev University, Astana, Kazakhstan; College of Medicine (S Almoustanyir MD), Alfaisal University, Riyadh, Saudi Arabia; Ministry of Health, Riyadh, Saudi Arabia (S Almoustanyir MD); Department of Respiratory Care (J S Alqahtani PhD), Prince Sultan Military College of Health Sciences, Dammam, Saudi Arabia; Department of Public Health (I Alqasmi PhD), Saudi Electronic University, Riyadh, Saudi Arabia; Health Department (I Altaf MS), Directorate General of Health Services, Peshawar, Pakistan; Research Group in Hospital Management and Health Policies (Prof N Alvis-Guzman PhD), Universidad de la Costa (University of the Coast), Barranquilla, Colombia; Research Group in Health Economics (Prof N Alvis-Guzman PhD), University of Cartagena, Cartagena, Colombia; Department of Economic Sciences (N J Alvis-Zakzuk MSc), University of the Coast, Barranquilla, Colombia; National Health Observatory (N J Alvis-Zakzuk MSc), National Institute of Health, Bogota, Colombia; Department of Medical Sciences (Prof Y M Al-Worafi PhD), Azal University for Human Development, Sana'a, Yemen; Department of Clinical Sciences (Prof Y M Al-Worafi PhD), University of Science and Technology of Fujairah, Fujairah, United Arab Emirates; Department of Pediatrics (Prof H Aly MD), Lerner Research Institute (X Liu PhD), Cleveland Clinic, Cleveland, OH, USA; Department of Veterinary Pathology (R Amani DVM), Islamic Azad University, Babol, Iran; Health Policy Research Center (R Amani DVM, H Kasraei MD), Department of Anatomy (R Arefnezhad MSc), Maternal Fetal Medicine Research Center (K Hessami MD), Shiraz Neuroscience Research Center (F Iravanpour PhD, M Jafarinia PhD), Non-communicable Disease Research Center (S G Sepanlou MD), Department of Physical Therapy (E Sinaei MSc), Department of Parasitology and Mycology (R Tavakoli Oliaee PhD), Basic Sciences in Infectious Diseases Research Center (R Tavakoli Oliaee PhD), Shiraz University of Medical Sciences, Shiraz, Iran; Department of Medicine (G A Amusa MD), University of Jos, Jos, Nigeria; Department of Internal Medicine (G A Amusa MD), Jos University Teaching Hospital, Jos, Nigeria; Cardiology Department (C Andrei PhD), Ophthalmology Department (A Dascaleu PhD), Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; School of Nursing and Midwifery (A Ansar PhD, M Rahman PhD), La Trobe University, Melbourne, VIC, Australia; Special Interest Group International Health (A Ansar PhD), Public Health Association of Australia, Canberra, ACT, Australia; Reproductive Immunology Research Center (H Ansarinia PhD), Shahid Sadoughi University of Medical Sciences, Yazd, Iran; School of Dentistry and Medical Sciences (A E Anyasodor PhD), Charles Sturt University, Orange, NSW, Australia; Health Management and Economics Research Center (J Arabloo PhD, H Ayatollahi PhD), Department of Health Information Management (H Ayatollahi PhD), School of Medicine (M Dodangeh MD, N Eissazade MD, F Mohammadi MD), Minimally Invasive Surgery Research Center (A Kabir MD), Eye Research Center (H Kasraei MD), Department of Epidemiology and Biostatistics (A Tiyuri MSc), Iran University of Medical Sciences, Tehran, Iran; Department of Maternal and Child Health (J Arulappan DSc), Sultan

Qaboos University, Muscat, Oman; Cabrini Research (Prof M Asghari-Jafarabadi PhD), Cabrini Health, Melbourne, VIC, Australia; University Institute of Radiological Sciences and Medical Imaging Technology (T Ashraf MS), University Institute of Public Health (A A Baig PhD, A A Malik PhD), Biochemistry Department (S Shahid PhD), The University of Lahore, Lahore, Pakistan; Department of Veterinary Pathology (J A Atata PhD), University of Ilorin, Nigeria, Kwara, Nigeria; Department of Immunology (S Athari PhD), Department of Pharmacology (P Majma Sanaye PharmD), Zanjan University of Medical Sciences, Zanjan, Iran; Department of Biomedical Science (D Atlaw MSc), Mada Walabu University, Bale Robe, Ethiopia; Faculty of Nursing (M M W Atout PhD), Philadelphia University, Amman, Jordan; Northumbria HealthCare NHS Foundation Trust, Newcastle upon Tyne, UK (A Aujayeb MBBS); School of Nursing and Health Sciences (A T Awan DrPH), Capella University, Minneapolis, MN, USA; Continuing Education Grant Writing Academy (A T Awan DrPH), University of Nevada, Las Vegas, NV, USA; Department of Neurovascular Research (A Y Azzam MD), Nested Knowledge Inc, Saint Paul, MN, USA; Faculty of Medicine (A Y Azzam MD), October 6 University, 6th of October City, Egypt; Public Health Risk Sciences Division (A Badawi PhD), Public Health Agency of Canada, Toronto, ON, Canada; Department of Nutritional Sciences (A Badawi PhD), Temerty Faculty of Medicine (V Chattu MD), University of Toronto, Toronto, ON, Canada; Department of Forensic Science (A D Badiye PhD), Government Institute of Forensic Science, Nagpur, India; School of Medicine (S Bagherieh BSc, S Hassanzadeh MD), Department of Pediatrics (M Bemanalizadeh MD), Department of Environmental Health Engineering (A Fatehizadeh PhD, E Taheri PhD), Isfahan University of Medical Sciences, Isfahan, Iran; Department of Comprehensive Nursing (B B Bantie MSc), Department of Medical Biochemistry (E Chekol Abebe MSc), Department of Pediatrics and Child Health Nursing (N S Tibebe MSc), Debre Tabor University, Debre Tabor, Ethiopia; Department of Molecular Microbiology and Bacteriology (M Bardhan MD), National Institute of Cholera and Enteric Diseases, Kolkata, India; Department of Molecular Microbiology (M Bardhan MD), Department of Biostatistics (V K Kamal PhD), Indian Council of Medical Research, New Delhi, India; School of Psychology (Prof S L Barker-Collo PhD), University of Auckland, Auckland, New Zealand; Department of Translational Medicine (F Barone-Adesi PhD), University of Eastern Piedmont, Novara, Italy; Department of Medical Education (K Batra PhD), Department of Social and Behavioral Health (Prof M Sharma PhD), University of Nevada Las Vegas, Las Vegas, NV, USA; Department of Surgery (N S Bayileyege MD), Department of Biostatistics (N G Zeru MSc), Jimma University, Jimma, Ethiopia; Non-communicable Diseases Research Center, Tehran, Iran (A Behnoud BS); Department of Oral Pathology and Microbiology (U I Belgaumi MD), Department of Public Health Dentistry (Prof K M Shivakumar PhD), Krishna Institute of Medical Sciences Deemed To Be University, Karad, India; Department of Internal Medicine (I M Bensor PhD), Department of Psychiatry (Prof M F P Peres MD), University of São Paulo, São Paulo, Brazil; School of Pharmacy (K A Beyene PhD), University of Auckland, AUCKLAND, New Zealand; Department of Pharmaceutical and Administrative Sciences (K A Beyene PhD), University of Health Sciences and Pharmacy in St. Louis, St Louis, MI, USA; Department of Health, Human Performance and Recreation (A S Bhagavathula PhD), University of Arkansas, Fayetteville, AR, USA; Department of Community Medicine and Family Medicine (P Bhardwaj MD), School of Public Health (P Bhardwaj MD), Department of Pharmacology (S Singh DM, S B Varthya MD), All India Institute of Medical Sciences, Jodhpur, India; Global Health Neurology Lab (S Bhaskar PhD), NSW Brain Clot Bank, Sydney, NSW, Australia; Department of Neurology and Neurophysiology (S Bhaskar PhD), South West Sydney Local Health District and Liverpool Hospital, Sydney, NSW, Australia; Department of General Medicine (A N Bhat MD, J Jeganathan MD), Department of Internal Medicine (A Boloor MD), Department of Community Medicine (N Joseph MD), Manipal Academy of Higher Education, Mangalore, India; Department of Biostatistics and Epidemiology (Prof S Bitaraf PhD), Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; Faculty of Health Sciences (V R Bitra PhD), University of Botswana, Gaborone, Botswana; Regional Medical

Research Centre North East Region (K Bora MD), Indian Council of Medical Research, Dibrugarh, India; Clinical Research Unit (Prof J S Botelho PhD), Centro de Investigação Interdisciplinar Egas Moniz, Almada, Portugal; Monash Department of Clinical Epidemiology at Cabrini Hospital (Prof R Buchbinder PhD), Cabrini Institute, Melbourne, VIC, Australia; Department of Clinical Pharmacy (Prof D Calina PhD), University of Medicine and Pharmacy of Craiova, Craiova, Romania; Internal Medicine Department (Prof L A Cámara MD), Hospital Italiano de Buenos Aires (Italian Hospital of Buenos Aires), Buenos Aires, Argentina; Board of Directors (Prof L A Cámara MD), Argentine Society of Medicine, Buenos Aires, Argentina; Institute for Mental and Physical Health (A F Carvalho MD), School of Medicine (V Gupta PhD), Deakin University, Geelong, VIC, Australia; Heart Failure and Structural Heart Disease Unit (J Chan MBChB), Cardiovascular Analytics Group, Hong Kong, China; Saveetha Dental College (V Chattu MD), Centre of Molecular Medicine and Diagnostics (COM-Mand) (Prof S Patil PhD), Saveetha University, Chennai, India; College of Medicine (S Choi BSc), Yonsei University, Seoul, South Korea; Department of Public Health (Prof T Chou PhD), Department of Occupational Safety and Health (Prof B Hwang PhD), China Medical University, Taichung, Taiwan; Center for Biomedicine and Community Health (D Chu PhD), VNU-International School, Hanoi, Viet Nam; Institute for Health Metrics and Evaluation (K Coberly BS, X Dai PhD, M Hassen BSc, Prof S S Lim PhD, T Mestrovic PhD, A H Mokdad PhD, D Y Yada MSc), Department of Health Metrics Sciences, School of Medicine (X Dai PhD, Prof S D Dharmaratne MD, Prof S S Lim PhD, A Misganaw PhD, A H Mokdad PhD), University of Washington, Seattle, WA, USA; Research Unit on Applied Molecular Biosciences (UCIBIO) (V M Costa PhD), Department of Chemical Sciences (R A S Couto MD), Institute for Research and Innovation in Health (Prof N Cruz-Martins PhD), Faculty of Medicine (Prof R J Dinis-Oliveira PhD), Associated Laboratory for Green Chemistry (LAQV) (Prof D M Pereira PhD, D Ribeiro PhD), Department of Chemistry (R B Pereira PhD), University of Porto, Porto, Portugal; Therapeutic and Diagnostic Technologies Department (Prof N Cruz-Martins PhD), Cooperativa de Ensino Superior Politécnico e Universitário (Polytechnic and University Higher Education Cooperative), Gandra, Portugal; Global Health and Rehabilitation Section (O Dadrás DrPH), Western Norway University of Applied Sciences, Bergen, Norway; Department of Global Public Health and Primary Care (O Dadrás DrPH), Department of Psychosocial Science (D Sagoe PhD), University of Bergen, Bergen, Norway; IRCCS Istituto Ortopedico Galeazzi (Galeazzi Orthopedic Institute IRCCS) (G Damiani MD), Department of Clinical Sciences and Community Health (Prof C La Vecchia MD), University of Milan, Milan, Italy; Department of Dermatology (G Damiani MD), Department of Quantitative Health Science (X Liu PhD), Department of Neonatology (I Qattee MD), Case Western Reserve University, Cleveland, OH, USA; Ophthalmology Department (A Dascalu PhD), Emergency University Hospital Bucharest, Bucuresti, Romania; School of Public Health (S Debela MPH), Salale University, Fiche, Ethiopia; Department of Dermatology (Prof R P Dellavalle MD), University of Colorado Denver, Aurora, CO, USA; Dermatology Service (Prof R P Dellavalle MD), Department of Veterans Affairs, Aurora, CO, USA; Department of Neurosurgery (A K Demetriades MD), Global Health Governance Programme (J Patel BSc), Centre for Medical Informatics (Prof A Sheikh MD), Usher Institute (Prof C R Simpson PhD), College of Medicine and Veterinary Medicine (G Verras MD), University of Edinburgh, Edinburgh, UK; Department of Neurosurgery (A K Demetriades MD), National Health Service (NHS) Scotland, Edinburgh, UK; Department of Nursing (A A Demlash MSc), Department of Midwifery (H L Esayas MSc), Department of Medical Laboratory Science (M Woldemariam MSc), Arba Minch University, Arba Minch, Ethiopia; Epidemiology Branch (X Deng PhD), National Institute of Health, Durham, NC, USA; Department of Medicine (H D Desai MD), Gujarat Adani Institute of Medical Sciences, Bhuj, India; Division of Cardiology (R Desai MBBS), Atlanta Veterans Affairs Medical Center, Decatur, GA, USA; Department of Pharmacy (S Dewan PhD), University of Asia Pacific, Dhaka, Bangladesh; Pharmacology Department (S Dewan PhD), Center for Life Sciences Research Bangladesh, Dhaka, Bangladesh; Department of Biostatistics and

Epidemiology (S Dey Mphil), Department of Development Studies (Prof A Perianayagam PhD, H Sahoo PhD), International Institute for Population Sciences, Mumbai, India; Department of Community Medicine (Prof S D Dharmaratne MD), University of Peradeniya, Peradeniya, Sri Lanka; Institute for Health Metrics and Evaluation (Prof S D Dharmaratne MD), University of Washington, Seattle, WA (Prof S D Dharmaratne MD), USA; Center of Complexity Sciences (Prof D Diaz PhD), National Autonomous University of Mexico, Mexico City, Mexico; Faculty of Veterinary Medicine and Zootechnics (Prof D Diaz PhD), Autonomous University of Sinaloa, Culiacán Rosales, Mexico; Research Unit (M Dibas MD), Sulaiman Al Rajhi University, Qassim, Saudi Arabia; Sciences Department (Prof R J Dinis-Oliveira PhD), Advanced Polytechnic and University Cooperative, Gandra, Portugal; Department of Human Physiology (M Diress MSc), Department of Health Promotion and Health Behavior (H B Eshetu MPH), University of Gondar, Gondar, Ethiopia; Department of Medicine (T C Do MD), Medical School (H Pham MD), Pham Ngoc Thach University of Medicine, Ho Chi Minh City, Viet Nam; Department of Cardiothoracic Surgery (D K Doan MD), Mayo Clinic, Jacksonville, FL, USA; Department of Biostatistics (M Dodangeh MCom), Independent Consultant, Tehran, Iran; Health Science Center (D Dongarwar MS), Department of Gastrointestinal Medical Oncology (M A Zeineddine MD), University of Texas, Houston, TX, USA; Office of Institutional Analysis (J Dube MA), University of Windsor, Windsor, ON, Canada; Department of Conservative Dentistry with Endodontics (A M Dziejdz DSc), Medical University of Silesia, Katowice, Poland; Higher School of Technology (Prof A Ed-Dra PhD), Sultan Moulay Slimane University, Beni Mellal, Morocco; School of Health Sciences (H A Edinur PhD), University of Science Malaysia (Universiti Sains Malaysia), Kubang Kerian, Malaysia; Department of Biological Sciences (T C Ekundayo PhD), University of Medical Sciences, Ondo, Ondo, Nigeria; Sharjah Institute for Medical Research (N M Elemam PhD, B Saddik PhD), Department of Clinical Sciences (Prof R Halwani PhD, Prof A A Maghazachi PhD, N Saheb Sharif-Askari PhD, Prof I M Talaat PhD), College of Medicine (Prof R Halwani PhD, M A Saleh PhD), Sharjah Institute of Medical Sciences (F Saheb Sharif-Askari PhD), University of Sharjah, Sharjah, United Arab Emirates; Faculty of Medicine (M Elhadi MD), University of Tripoli, Tripoli, Libya; Pediatric Dentistry Department (Prof O A A Elmeligy PhD), Rabigh Faculty of Medicine (A A Malik PhD), Department of Dental Public Health (Z S Natto DrPH), Department of Community Medicine (S Samargandy PhD), King Abdulaziz University, Jeddah, Saudi Arabia; Pediatric Dentistry and Dental Public Health Department (Prof O A A Elmeligy PhD), Pathology Department (Prof I M Talaat PhD), Alexandria University, Alexandria, Egypt; Doheny Eye Institute (M Emamverdi MD), University of California Los Angeles, Los Angeles, CA, USA; Department of Public Health and Tropical Medicine (T I Emeto PhD), Australian Institute of Tropical Health and Medicine (A Pak PhD), James Cook University, Townsville, QLD, Australia; Department of Internal Medicine (F Etae MD), Department of Dermatology (M Goldust MD), Department of Psychiatry (W Li PhD), Department of Genetics (S Pawar PhD), Yale University, New Haven, CT, USA; Institute of Applied Health Sciences (A F Fagbamigbe PhD), University of Aberdeen, Aberdeen, UK; Head of the Laboratory of Experimental Medicine (I R Fakhraiyev PhD), Kazakh National Medical University, Almaty, Kazakhstan; Department of Social Medicine and Epidemiology (A Feizkhah MD), Guilan University of Medical Sciences, Rasht, Iran; Department of Pharmacy (G Fekadu MSc), Department of Nursing (G Fetensa MSc), Wollega University, Nekemte, Ethiopia; Department of Molecular Medicine (M Fereidouni PhD), Cellular and Molecular Research Center (M Fereidouni PhD), Department of Epidemiology and Biostatistics (A Tiyuri MSc), Birjand University of Medical Sciences, Birjand, Iran; Department of Neurobiology, Care Sciences, and Society (S Fereshtehnejad PhD), Department of Medicine (T S Hassan PhD), Karolinska Institute, Stockholm, Sweden; Division of Neurology (S Fereshtehnejad PhD), University of Ottawa, Ottawa, ON, Canada; Center for Biotechnology and Fine Chemistry (J C Fernandes PhD), Catholic University of Portugal, Porto, Portugal; Research Center on Public Health (P Ferrara MD), School of Medicine and Surgery (Prof L G Mantovani DSc), University of Milan Bicocca, Monza, Italy; Psychiatry

Department (I Filip MD), Kaiser Permanente, Fontana, CA, USA; School of Health Sciences (I Filip MD), A.T. Still University, Mesa, AZ, USA; Institute of Public Health (F Fischer PhD), Institute for Allergy (P Kolkhir MD), Charité Medical University Berlin (Charité Universitätsmedizin Berlin), Berlin, Germany; Department of Pharmacology (Prof B Foroutan PhD), Iranshahr University of Medical Sciences, Iranshahr, Iran; Department of Medical Parasitology (M Foroutan PhD), Faculty of Medicine (M Foroutan PhD), Abadan University of Medical Sciences, Abadan, Iran; Department of Dermatology (T Fukumoto PhD), Kobe University, Kobe, Japan; School of Global Health (B Ganesan PhD), Institute of Health & Management, Melbourne, VIC, Australia; Department of Occupational Therapy (B Ganesan PhD), Mahatma Gandhi Occupational Therapy College, Jaipur, India; Department of Nursing (B N B Gameda MSc), Debre Berhan University, Debre Birhan, Ethiopia; Adelaide Medical School (T K Gill PhD), School of Public Health (V Podder HSC), University of Adelaide, Adelaide, SA, Australia; Division of General Internal Medicine (R F Gillum MD), Department of Community and Family Medicine (R F Gillum MD), Howard University, Washington, DC, USA; Department of Health Systems and Policy Research (M Golechha PhD), Indian Institute of Public Health, Gandhinagar, India; Department of Genetics (P Goleij MSc), Sana Institute of Higher Education, Sari, Iran; Department of Biomedical and Neuromotor Sciences (D Golinelli MD, J Lenzi PhD), University of Bologna, Bologna, Italy; Department of Respiratory Medicine (H Goudarzi PhD), Center for Environmental and Health Sciences (H Goudarzi PhD), Hokkaido University, Sapporo, Japan; Department of Epidemiology and Biostatistics (S Guan MD), Anhui Medica University, Hefei, China; Peking University Shenzhen Hospital (Y Guo PhD), Peking University, Shenzhen, China; Department of Public Health (B Gupta PhD), Torrens University Australia, Melbourne, VIC, Australia; Faculty of Medicine Health and Human Sciences (Prof V K Gupta PhD), Macquarie Medical School (Y You PhD), Macquarie University, Sydney, NSW, Australia; Department of Pharmacology and Toxicology (R Haddadi PhD), Department of Midwifery (S Masoumi PhD), Hamadan University of Medical Sciences, Hamadan, Iran; Department of Clinical Pharmacology and Medicine (Prof N R Hadi PhD), University of Kufa, Najaf, Iraq; Research & Scientific Studies Unit (S Haque PhD), Epidemiology Department (M Khan MD), Substance Abuse and Toxicology Research Center (S Mohan PhD), Jazan University, Jazan, Saudi Arabia; Department of Pharmaceutical Technology (I Hasan MPharm), University of Dhaka, Dhaka, Bangladesh; Research Centre (T S Hassan PhD), Salahaddin University, Erbil, Iraq; National Data Management Center for Health (M Hassen BSc, A Misganaw PhD), Ethiopian Public Health Institute, Addis Ababa, Ethiopia; Department of Diagnostic and Interventional Radiology and Neuroradiology (J Haubold MD), Institute of Artificial Intelligence in Medicine (J Haubold MD), University Hospital Essen, Essen, Germany; Institute of Pharmaceutical Sciences (K Hayat MS), University of Veterinary and Animal Sciences, Lahore, Pakistan; Department of Pharmacy Administration and Clinical Pharmacy (K Hayat MS), Xian Jiaotong University, Xian, China; Independent Consultant, Santa Clara, CA, USA (G Heidari MD); Department of Statistics and Econometrics (Prof C Herteliu PhD, I Petcu PhD), Bucharest University of Economic Studies, Bucharest, Romania; School of Business (Prof C Herteliu PhD), London South Bank University, London, UK; Department of Applied Microbiology (K Hezam PhD), Taiz University, Taiz, Yemen; Department of Microbiology (K Hezam PhD), Nankai University, Tianjin, China; Division for Health Service Promotion (Y Hiraike PhD), University of Tokyo, Tokyo, Japan; Kasturba Medical College, Mangalore (R Holla MD), Manipal College of Pharmaceutical Sciences (Prof M D Janodia PhD), Department of Physiotherapy (Prof V K PhD), Department of Pharmacy Management (V S Ligade PhD), Manipal TATA Medical College (M Rahman PhD), Department of Nephrology (I Rao DM), Manipal Academy of Higher Education, Manipal, India; School of Biotechnology (H Huynh BS), Tan Tao University, Long An, Viet Nam; Department of Occupational Therapy (Prof B Hwang PhD), Asia University, Taichung, Taiwan; Faculty of Medicine (I M Ilic PhD), University of Belgrade, Belgrade, Serbia; Department of Epidemiology (Prof M D Ilic PhD), University of Kragujevac, Kragujevac, Serbia; Department of Clinical

Pharmacy & Pharmacy Practice (Prof N Ismail PhD), Asian Institute of Medicine, Science and Technology, Kedah, Malaysia; Malaysian Academy of Pharmacy, Puchong, Malaysia (Prof N Ismail PhD); Department of Health Services Research (M Iwagami PhD), University of Tsukuba, Tsukuba, Japan; Department of Non-communicable Disease Epidemiology (M Iwagami PhD), London School of Hygiene & Tropical Medicine, London, UK; School of Health Systems and Public Health (C C D Iwu MPH), University of Pretoria, Pretoria, South Africa; Research and Development Unit (L Jacob MD), Biomedical Research Networking Center for Mental Health Network (CiberSAM), Sant Boi de Llobregat, Spain; Faculty of Medicine (L Jacob MD), University of Versailles Saint-Quentin-en-Yvelines, Montigny-le-Bretonneux, France; Department of Immunology (Prof A Jafarzadeh PhD), Department of Clinical Biochemistry (M Nematollahi PhD), Kerman University of Medical Sciences, Kerman, Iran; Department of Immunology (Prof A Jafarzadeh PhD), Department of Epidemiology and Biostatistics (Prof M Rezaeian PhD), Rafsanjan University of Medical Sciences, Rafsanjan, Iran; College of Medicine and Medical Sciences (H Jahrami PhD), Arabian Gulf University, Manama, Bahrain; Ministry of Health, Manama, Bahrain (H Jahrami PhD); Institute of Advanced Manufacturing Technologies (Prof M Jakovljevic PhD), Peter the Great St. Petersburg Polytechnic University, St. Petersburg, Russia; Institute of Comparative Economic Studies (Prof M Jakovljevic PhD), Hosei University, Tokyo, Japan; Division of Pulmonary Medicine (E Jamshidi PharmD), Lausanne University Hospital (CHUV), Lausanne, Switzerland; Department of Internal Medicine (C T Jani MD), Harvard University, Cambridge, MA, USA; Centre of Studies and Research (S Jayapal PhD), Ministry of Health, Muscat, Oman; Department of Biochemistry (Prof S Jayaram MD), Government Medical College, Mysuru, India; Institute of Molecular and Clinical Ophthalmology Basel, Basel, Switzerland (Prof J B Jonas MD); Department of Ophthalmology (Prof J B Jonas MD), Heidelberg University, Mannheim, Germany; Department of Gastroenterology and Hepatology (A Joseph MD), Stanford University, Stanford, CA, USA; Department of Economics (C E Joshua BSc), National Open University, Benin City, Nigeria; Health Economics Unit (B Kaambwa PhD), College of Medicine and Public Health (B Kaambwa PhD), Flinders University, Adelaide, SA, Australia; School of Public Health (Z Kabir PhD), University College Cork, Cork, Ireland; Department of Oral and Maxillofacial Pathology (V Kadashetti MDS), Krishna Institute of Medical Sciences Deemed to be University, Karad, India; Dermatology Department (F Kaliyadan MD), King Faisal University, Hofuf, Saudi Arabia; department of pediatric nursing, department of research, department of medical student research (F Kalroozii PhD), Aja Medical University, tehran, Iran; Department of Pediatrics (F Kalroozii PhD), Iran University of Medical Sciences, tehran, Iran; Division of Epidemiology and Biostatistics (V K Kamal PhD), National Institute of Epidemiology, Chennai, India; Department of Neurology (A Kandel MD), University at Buffalo, Buffalo, NY, USA; Save Sight Institute (H Kandel PhD, Y You PhD), University of Sydney, Sydney, NSW, Australia; Sydney Eye Hospital (H Kandel PhD), South Eastern Sydney Local Health District, Sydney, NSW, Australia; Regional Medical Research Centre (S Kanungo MD), Indian Council of Medical Research, Bhubaneswar, India; Laboratory Science Department (J Karami PhD), Khomein University of Medical Sciences, Khomein, Iran; School of Health Professions and Human Services (I M Karaye MD), Hofstra University, Hempstead, NY, USA; Department of Epidemiology and Biostatistics (S A Kebede MPH), University of Gondar, Gondar, Faroe Islands; Department of Healthcare Services Management (L Keikavoosi-Arani PhD), Research Center for Health, Safety and Environment (Prof L Salehi PhD), Alborz University of Medical Sciences, Karaj, Iran; Department of Public Health (Prof Y S Khader PhD), Jordan University of Science and Technology, Irbid, Jordan; Amity Institute of Forensic Sciences (H Khajuria PhD, B P Nayak PhD), Amity University, Noida, India; Faculty of Veterinary Medicine (F Khamesipour PhD), Faculty of Veterinary Medicine, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran; Department of Epidemiology and Biostatistics (E A Khan MPH), Health Services Academy, Islamabad, Pakistan; Department of Pediatrics (I A Khan MD), Center for Pharmacoepidemiology and Treatment Science (A Parthasarathi MD), Rutgers University, New Brunswick, NJ,

USA; Department of Rehabilitation Sciences (M Khan MPH), Hong Kong Polytechnic University, Hong Kong, China; Family Medicine Department (M A Khan MSc), United Arab Emirates University, Al Ain, United Arab Emirates; Primary Care Department (M A Khan MSc), NHS North West London, London, UK; Pharmacy Services (M Khan PharmD), The Indus Hospital Health Network and Research Center, Lahore, Pakistan; Faculty of Nursing (H Khatatbeh PhD), Jerash University, Jerash, Jordan; Department of Basic Medical Sciences (M M Khatatbeh PhD), Yarmouk University, Irbid, Jordan; School of Medicine (S Khateri MD), Kurdistan University of Medical Sciences, Sanandaj, Iran; Cardiovascular Disease Initiative (M Kim MD), Broad Institute of MIT and Harvard, Cambridge, MA, USA; School of Health Sciences (Prof A Kisa PhD), Kristiania University College, Oslo, Norway; Department of International Health and Sustainable Development (Prof A Kisa PhD), Tulane University, New Orleans, LA, USA; Department of Nursing and Health Promotion (S Kisa PhD), Oslo Metropolitan University, Oslo, Norway; Department of Neurology (H Koh PhD), Boston Children's Hospital, Boston, MA, USA; Division of Immune-mediated Skin Diseases (P Kolkhir MD), First Moscow State Medical University (Sechenov University), Moscow, Russia; Department of General Practice Family Medicine (Prof O Korzh DSc), Kharkiv National Medical University, Kharkiv, Ukraine; Department of Biochemistry (A L Kotnis PhD), All India Institute of Medical Sciences, Bhopal, India; Department of Internal and Pulmonary Medicine (Prof P A Koul MD), Sheri Kashmir Institute of Medical Sciences, Srinagar, India; San Juan de Dios Sanitary Park, Barcelona, Spain (A Koyanagi MD); Department of Anthropology (Prof K Krishan PhD), Panjab University, Chandigarh, India; Department of Biochemistry (Prof M Kuddus PhD), University of Hail, Hail, Saudi Arabia; Department of Medicine (V V Kulkarni MS), Queensland Health, Brisbane, QLD, Australia; Department of Orthopaedics (Prof N Kumar MS), Medanta Hospital, Lucknow, India; Global Health Institute (S Kundu MPH), North South University, Dhaka, Bangladesh; Department of Nutrition and Food Science (S Kundu MPH), Patuakhali Science and Technology University, Patuakhali, Bangladesh; Faculty of Health and Life Sciences (O P Kurmi PhD), Coventry University, Coventry, UK; Department of Medicine (O P Kurmi PhD), Department of Psychiatry and Behavioural Neurosciences (A T Olagunju MD), McMaster University, Hamilton, ON, Canada; Department of Health Policy and Strategy (Prof C Lahariya MD), Foundation for People-centric Health Systems, New Delhi, India; SD Gupta School of Public Health (Prof C Lahariya MD), Indian Institute of Health Management Research University, Jaipur, India; Department of Physiotherapy (T Laksono MS), Universitas Aisyiyah Yogyakarta, Yogyakarta, Indonesia; Institute of Allied Health Sciences (T Laksono MS), National Cheng Kung University, Tainan, Taiwan; Health Services Management Training Centre (J Lám PhD), Semmelweis University, Budapest, Hungary; NEVES Society for Patient Safety (J Lám PhD), NEVES Society for Patient Safety, Budapest, Hungary; Centre for Family Welfare (K Latief MSE), University of Indonesia, Depok, Indonesia; Department of Global Health and Health Security (K Latief MSE), College of Medicine (L Minh MD), Research Center for Artificial Intelligence in Medicine (L Minh MD), Taipei Medical University, Taipei, Taiwan; International Society Doctors for the Environment, Arezzo, Italy (P Lauriola MD); Clinical Pharmacy and Pharmacy Management (B K Lawal PhD), Kaduna State University, Kaduna, Nigeria; Department of Internal Medicine (T Le MD), Department of General Medicine (V T Nguyen MD), Faculty of Medicine (D C Vo MD), University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Viet Nam (T T Le MD); Department of Medical Humanities and Social Medicine (M Lee PhD), Ajou University School of Medicine, Suwon, South Korea; Medial Research Collaborating Center (M Lee PhD), Ajou University Medical Center, Suwon, South Korea; Department of Precision Medicine (Prof S W Lee MD), Sungkyunkwan University, Suwon-si, South Korea; Department of Internal Medicine (W Lee PhD), University of Texas, Galveston, TX, USA; Department of Preventive Medicine, College of Medicine (Prof Y Lee PhD), Korea University, Seoul, South Korea; Department of Prevention (M Levi PhD), USL Tuscany Center, Firenze, Italy; Department of Health Sciences (M Levi PhD), University of Florence, Florence, Italy; School of Life Sciences (G Liu PhD), University of Technology Sydney,

Ultimo, NSW, Australia; Centre for Inflammation (G Liu PhD), Centenary Institute, Camperdown, NSW, Australia; Department of Molecular Epidemiology (E Llanaj PhD), German Institute of Human Nutrition Potsdam-Rehbrücke, Potsdam, Germany; German Center for Diabetes Research (DZD), München-Neuherberg, Germany (E Llanaj PhD); Department of Internal Medicine (C Lo MD), Kirk Kerkorian School of Medicine, Las Vegas, NV, USA; Clinical Research Unit (Prof V S Machado PhD), Centro de Investigação Interdisciplinar Egas Moniz (Egas Moniz Interdisciplinary Research Center), Monte da Caparica, Portugal; Department of Clinical and Hospital Pharmacy (M A Mahmoud PhD), Taibah University, Al-Madinah Al-Munawwarah, Saudi Arabia; Cardiovascular Research department (T A Mai MSc), Cardiovascular Research Department (H Q Nguyen MD), Methodist Hospital, Merrillville, IL, USA; Department of Primary Care and Public Health (Prof A Majeed MD, R Palladino MD, Prof S Rawaf MD), Imperial College London, London, UK; Center for Health & Nature (O M Makram MD), Houston Methodist Hospital, Houston, TX, USA; Department of Cardiology (O M Makram MD), October 6 University, Cairo, Egypt; Department of Internal Medicine (K Malhotra MBBS), Dayanand Medical College and Hospital, Ludhiana, India; Material Science Programme (I Malik PhD), Indian Institute of Technology Kanpur, Kanpur, India; Department of Clinical Pharmacy (T Mallhi PhD), Jouf University, Sakaka, Saudi Arabia; Department of Maternal and Child Nursing and Public Health (Prof D C Malta PhD, Prof A C Micheletti Gomide Nogueira de Sá MSc, E J S Prates BS), Department of Applied Nursing (Prof M O Pereira PhD), Federal University of Minas Gerais, Belo Horizonte, Brazil; Laboratory of Public Health (Prof L G Mantovani DSc), Istituto Auxologico Italiano IRCCS (Italian Auxological Institute), Milan, Italy; Department of Nutrition and Dietetics (M Martorell PhD), University of Concepcion, Concepción, Chile; Centre for Healthy Living (M Martorell PhD), University of Concepción, Concepción, Chile; Department of Anatomy, Genetics and Biomedical Informatics (Y Mathangasinghe MD), University of Colombo, Colombo, Sri Lanka; Australian Regenerative Medicine Institute (Y Mathangasinghe MD), Monash University, Clayton, VIC, Australia; Department of Public Health and Community Medicine (E Mathews PhD), Central University of Kerala, Kasaragod, India; Division of Infection, Immunity and Respiratory Medicine (A G Mathioudakis PhD), University of Manchester, Manchester, UK; North West Lung Centre (A G Mathioudakis PhD), Manchester University NHS Foundation Trust, Manchester, UK; Department of Epidemiology and Biostatistics (J C Medina MD), University of the Philippines Manila, Manila, Philippines; Department of Global Health (J C Medina MD), University of the Ryukyus, Nishihara, Japan; School of Public Health (G G Meles MPH), Department of Statistics (N G Zeru MSc), Mekelle University, Mekelle, Ethiopia; Clinical Research Unit (Prof J Mendes PhD), Centro de Investigação Interdisciplinar Egas Moniz (Egas Moniz Interdisciplinary Research Center), Monte de Caparica, Portugal; Forensic Medicine Division (Prof R G Menezes MD), Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia; University Centre Varazdin (T Mestrovic PhD), University North, Varazdin, Croatia; Department of Epidemiology (I Michalek PhD), National Cancer Registry (I Michalek PhD), Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland; Department of Medical Physiology (E T Mihretie MSc), Madda Walabu University, Bale Goba, Ethiopia; Internal Medicine Programme (Prof E M Mirrakhimov PhD), Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan; Department of Atherosclerosis and Coronary Heart Disease (Prof E M Mirrakhimov PhD), National Center of Cardiology and Internal Disease, Bishkek, Kyrgyzstan; Molecular Biology Unit (N S Mohamed MSc), Bio-Statistical and Molecular Biology Department (N S Mohamed MSc), Sirius Training and Research Centre, Khartoum, Sudan; Department of Pharmaceutical Sciences (S Mohammed PhD), Notre Dame of Maryland University, Baltimore, MD, USA; Department of Pharmacy (S Mohammed PhD), Mizan-Tepi University, Mizan, Ethiopia; Health Systems and Policy Research Unit (S Mohammed PhD), Ahmadu Bello University, Zaria, Nigeria; Department of Health Care Management (S Mohammed PhD), Technical University of Berlin, Berlin, Germany; Center for Transdisciplinary Research (S Mohan PhD), Saveetha Institute of Medical and Technical Science, Chennai,

India; Clinical Epidemiology and Public Health Research Unit (L Monasta DSc), Burlo Garofolo Institute for Maternal and Child Health, Trieste, Italy; School of Health & Rehabilitation Sciences (M Moni PhD), Mater Research Institute (M Moniruzzaman PhD), Centre for the Business and Economics of Health (A Pak PhD), The University of Queensland, Brisbane, QLD, Australia; Social Determinants of Health Research Center (Y Moradi PhD), Kurdistan University of Medical Sciences, Kurdistan, Iran; Clinical Research Development Unit (N Morovatdar MD), Applied Biomedical Research Center (A Sahebkar PhD), Biotechnology Research Center (A Sahebkar PhD), Department of Medical Informatics (S Tabatabaei PhD), Clinical Research Development Unit (S Tabatabaei PhD), Mashhad University of Medical Sciences, Mashhad, Iran; Department of Medicine (E Mostafavi PhD), Stanford Cardiovascular Institute (E Mostafavi PhD), Stanford University, Palo Alto, CA, USA; Department of Surgery (G D Mukoro MD), Ahmadu Bello University Teaching Hospital, Zaria, Nigeria; Department of Medicine (A Mulita PhD), Democritus University of Thrace, Alexandroupolis, Greece; Department of Pediatrics and Child Health Nursing (G B Mulu MSc), Debre Berhan University, Debre Berhan, Ethiopia; Clinical Epidemiology Research Unit (E Murillo-Zamora PhD), Mexican Institute of Social Security, Villa de Alvarez, Mexico; Postgraduate in Medical Sciences (E Murillo-Zamora PhD), Universidad de Colima, Colima, Mexico; Department of Pathobiology (F Musaigwa PhD), University of Pennsylvania, Philadelphia, PA, USA; Department of Pediatrics & Pediatric Pulmonology (Prof G Mustafa MD), Institute of Mother & Child Care, Multan, Pakistan; Department of Orthopaedics (S Muthu MS), Government Medical College, Dindigul, India; Quality Appraisal Committee (S Muthu MS), Orthopaedic Research Group, Coimbatore, India; Faculty of Pharmacy (F Nainu PhD), Hasanuddin University, Makassar, Indonesia; Suraj Eye Institute, Nagpur, India (V Nangia MD); Mysore Medical College and Research Institute (Prof S Narasimha Swamy MD), Government Medical College, Mysore, India; Department of Zoology (Prof N Perumalsamy PhD), Yadava College, Madurai, India; Department of Zoology (Prof N Perumalsamy PhD), Annai Fathima College, Madurai, India; Department of Health promotion (A Nazri-Panjaki MSc), Health Promotion Research Center (H Okati-Aliabad PhD), Zahedan University of Medical Sciences, Zahedan, Iran; Department of Medical Laboratory Sciences (H Negash MSc), Department of Pharmacy (B G Welegebrail MSc), Adigrat University, Adigrat, Ethiopia; Division of Cardiology (D H Nguyen BS), Massachusetts General Hospital, Boston, MA, USA; Department of Medical Engineering (D H Nguyen BS), University of South Florida, Tampa, FL, USA; Faculty of Medicine (H T H Nguyen MD), Institute for Research and Training in Medicine, Biology and Pharmacy (H T H Nguyen MD), Duy Tan University, Da Nang, Viet Nam; Department of Surgery (P T Nguyen MD), Danang Family Hospital, Danang, Viet Nam; International Islamic University Islamabad, Islamabad, Pakistan (R K Niazi PhD); Department of General Surgery (T K Nikolouzakis PhD), University Hospital of Heraklion, Heraklion, Greece; Laboratory of Toxicology (T K Nikolouzakis PhD), University of Crete, Heraklion, Greece; Center for Public Health (L A Nnyanzi PhD), Teesside University, Middlesbrough, UK; Department of Microbiology and Molecular Genetics (M Noreen PhD), The Women University Multan, Multan, Pakistan; Center of Excellence in Reproductive Health Innovation (CERHI) (C I Nzopotam MPH), University of Benin, Benin City, Nigeria; Department of Physiology (O J Nzopotam PhD), University of Benin, Edo, Nigeria; Department of Physiology (O J Nzopotam PhD), Benson Idahosa University, Benin City, Nigeria; Department of Applied Economics and Quantitative Analysis (Prof B Oancea PhD), University of Bucharest, Bucharest, Romania; Department of Preventive Medicine (I Oh PhD), Kyung Hee University, Dongdaemun-gu, South Korea; School of Pharmacy (O C Okonji MSc), University of the Western Cape, Cape Town, South Africa; Department of Medical Physiology (P G Okwute MSc), Babcock University, Ilisan-Remo, Nigeria; Department of Medical Physiology (P G Okwute MSc), Department of Psychiatry (A T Olagunju MD), University of Lagos, Lagos, Nigeria; Department of Nursing Science (M I Olatubi PhD), Bowen University, Iwo, Nigeria; Department of Pharmacotherapy and Pharmaceutical Care (M Ordak PhD), Department of Applied Pharmacy (M Zielińska PharmD),

Medical University of Warsaw, Warsaw, Poland; Laboratory of Public Health Indicators Analysis and Health Digitalization (N Otvastnov BA), Moscow Institute of Physics and Technology, Dolgoprudny, Russia; Department of Medicine (Prof M O Owolabi DrM), University College Hospital, Ibadan, Ibadan, Nigeria; Department of Respiratory Medicine (Prof M P A DNB), Jagadguru Sri Shivarathreeswara Academy of Health Education and Research, Mysore, India; Department of Forensic Medicine and Toxicology (J Padubidri MD), Kasturba Medical College, Mangalore, India; Department of Epidemiology (R Pakzad PhD), Ilam University of Medical Sciences, Ilam, Iran; Department of Public Health (R Palladino MD), University of Naples Federico II, Naples, Italy; Department of Public Health (A Pana PhD), Babes Bolyai University, Cluj Napoca, Romania; Department of Health Metrics (A Pana PhD), Center for Health Outcomes & Evaluation, Bucharest, Romania; Department of Emergency Medicine (I Pantazopoulos PhD), University of Thessaly, Larissa, Greece; Department of Emergency Medicine (I Pantazopoulos PhD), University of Bern, Bern, Switzerland; Department of Science and Mathematics (Prof P Papadopoulou PhD), Deree-The American College of Greece, Athens, Greece; Department of Biophysics (Prof P Papadopoulou PhD), University of Athens, Athens, Greece; Vision and Eye Research Institute (Prof S Pardhan PhD), Anglia Ruskin University, Cambridge, UK; Research Center (A Parthasarathi MD), Allergy Asthma and Chest Center, Mysore, India; School of Nursing (A Pashaei MSc), University of British Columbia, Vancouver, BC, Canada; School of Dentistry (J Patel BSc), University of Leeds, Leeds, UK; Research Consultancy (A R Pathan PhD), Author Gate Publications, Malegaon, India; College of Dental Medicine (Prof S Patil PhD), Roseman University of Health Sciences, South Jordan, UT, USA; Research Section (U Paudel PhD), Nepal Health Research Council, Kathmandu, Nepal; Faculty of Humanities and Social Sciences (U Paudel PhD), Tribhuvan University, Kathmandu, Nepal; Clinical Research Department (P Pedersini MSc, J H Villafañe PhD), IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy; Department of Neurology (U Pensato MD), IRCCS Humanitas Research Hospital, Milan, Italy; International Institute for Educational Planning (IIEP) (Prof M F P Peres MD), Albert Einstein Hospital, São Paulo, Brazil; Department of Biology (Prof S Perna PhD), University of Bahrain, Sakir, Bahrain; School of Pharmacy (A K Philip PhD), University of Nizwa, Nizwa, Oman; Research Center of Neurology, Moscow, Russia (Prof M A Piradov DSc); Department of Dermatology (I Podder MD), College of Medicine and Sagore Dutta Hospital, Kolkata, India; Medical College (V Podder HSC), Tairunnessa Memorial Medical College and Hospital, Gazipur, Bangladesh; Clinical Academic Department of Pediatrics (Prof D Poddighe PhD), University Medical Center (UMC), Astana, Kazakhstan; College of Medicine (A Radfar MD), University of Central Florida, Orlando, FL, USA; Department of Immunology (Prof A Rafiei PhD), Molecular and Cell Biology Research Center (Prof A Rafiei PhD), Mazandaran University of Medical Sciences, Sari, Iran; UO Neurologia, Salute Pubblica e Disabilità (A Raggi PhD), Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy; Department of Anesthesia (F Rahim PhD), Cihan University of Sulaimaniya, Sulaimaniya, Iraq; National Institute of Infectious Diseases (M Rahman PhD), Center for Surveillance, Immunization, and Epidemiologic Research, Tokyo, Japan; Center for Evidence-Based Medicine and Clinical Research, Dhaka, Bangladesh (M Rahman PhD); Department of Population Science and Human Resource Development (M Rahman DrPH), University of Rajshahi, Rajshahi, Bangladesh; School of Nursing and Healthcare Professions (M Rahman PhD), Federation University Australia, Berwick, VIC, Australia; Future Technology Research Center (A Rahmani PhD), National Yunlin University of Science and Technology, Yunlin, Taiwan; Department of Public Health (V Rahmanian PhD), Torbat Jam Faculty of Medical Sciences, Torbat Jam, Iran; Department of Community Medicine (P Ramasubramani MD), Mahatma Gandhi Medical College and Research Institute, Puducherry, India; Centre for Clinical Pharmacology (N Rancic PhD), University of Defence in Belgrade, Belgrade, Serbia; Centre for Clinical Pharmacology (N Rancic PhD), Medical College of Georgia at Augusta University, Belgrade, Serbia; Department of Epidemiology (S Rashedi MD), Department of International Studies (P Shobeiri MD), Non-

Communicable Diseases Research Center (NCDR), Tehran, Iran; Department of Medicine (A M Rashid MD), Jinnah Sindh Medical University, Karachi, Pakistan; Pulmonary Critical Care (N Ravikumar MD), University of Chicago, Chicago, IL, USA; Academic Public Health England (Prof S Rawaf MD), Public Health England, London, UK; Department Biological Sciences (Prof E M M Redwan PhD), King Abdulaziz University, Jeddah, Egypt; Department of Protein Research (Prof E M M Redwan PhD), Research and Academic Institution, Alexandria, Egypt; Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA) (Prof N Rezaei PhD), Network of Interdisciplinarity in Neonates and Infants (NINI) (N Samieefar MD), Universal Scientific Education and Research Network (USERN), Tehran, Iran; Faculty of Agrarian Sciences and Environment (D Ribeiro PhD), University of the Azores, Angra do Heroísmo, Portugal; Department of Geography and Demography (M Rodrigues PhD), University of Coimbra, Coimbra, Portugal; Department of Pharmacology and Toxicology (Prof J A B Rodriguez PhD), University of Antioquia, Medellín, Colombia; Department of Clinical Research (L Roever PhD), Federal University of Uberlândia, Uberlândia, Brazil; Clinical and Epidemiological Research in Primary Care (GICEAP) (E Romero-Rodríguez PhD), Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Cordoba, Spain; Cardiovascular Department (Prof A M A Saad MD), Zagazig University, Zagazig, Egypt; Department of Pediatric Neurology (S Sadeghian MD), Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; Foundation University School of Health Sciences (Prof U Saeed PhD), Foundation University, Islamabad, Pakistan; International Center of Medical Sciences Research (ICMSR), Islamabad, Pakistan (Prof U Saeed PhD); Department of Neurology (M Safdarian MD), Christian-Doppler University Hospital, Salzburg, Austria; Spinal Cord Injury and Tissue Regeneration Center Salzburg (SCI-TReCS) (M Safdarian MD), Paracelsus Medical University, Salzburg, Austria; Faculty of Medicine, Bioscience and Nursing (S Z Safi PhD), MAHSA University, Selangor, Malaysia; Interdisciplinary Research Centre in Biomedical Materials (IRCBM) (S Z Safi PhD), COMSATS Institute of Information Technology, Lahore, Pakistan; Department of Statistics (M R Sajid PhD), University of Gujrat, Gujrat, Pakistan; Clinical Medical Sciences (S Sakhamuri MD), University of the West Indies, St. Augustine, Trinidad and Tobago; Thoracic Department (S Sakhamuri MD), North Central Regional Health Authority, Champ Fleurs, Trinidad and Tobago; Institute for Employment Research (J W Sakshaug PhD), University of Warwick, Coventry, UK; Department of Statistics (J W Sakshaug PhD), Ludwig Maximilians University, Munich, Germany; Faculty of Pharmacy (M A Saleh PhD), Rheumatology and Immunology Unit (S Tharwat MD), Mansoura University, Mansoura, Egypt; Department of Health Education and Promotion (Prof L Salehi PhD), A.C.S. Medical College and Hospital, Karaj, Iran; Department of Immunology (A Salek Farrokhi PhD), Pasteur Institute of Iran, Tehran, Iran; Department of Neurology (S Samadzadeh MD), Charité University Medical Center Berlin, Berlin, Germany; Department of Neurology (S Samadzadeh MD), University of Southern Denmark, Odense, Denmark; Department of Entomology (A M Samy PhD), Medical Ain Shams Research Institute (MARS) (A M Samy PhD), Ain Shams University, Cairo, Egypt; Institute of Neuroanatomy (N Sanadgol PhD), Uniklinik Rhine-Westphalia Technical University of Aachen, Aachen, Germany; Department of Pediatrics (R K Sanjeev MD), Pravara Institute of Medical Sciences, Loni, India; Department of Public Health Sciences (M Sawhney PhD), University of North Carolina at Charlotte, Charlotte, NC, USA; Department of Preventive and Social Medicine (G Saya MD), Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India; Cardiovascular Research Center (A Schuermans BSc), Massachusetts General Hospital, Cambridge, MA, USA; Department of Cardiovascular Sciences (A Schuermans BSc), Katholieke Universiteit Leuven, Leuven, Belgium; Emergency Department (S Senthilkumar MD), Manian Medical Centre, Erode, India; Department of Medicine and Surgery (Y Sethi MBBS), Government Doon Medical College, Dehradun, India; Office of Research and Innovation (H Shah MS), Department of Life Sciences (M Umair PhD), University of Management and Technology, Lahore, Pakistan; Department of Internal Medicine (I Shahid MBBS), Ziauddin University, Karachi, Pakistan; Independent Consultant,

Karachi, Pakistan (M A Shaikh MD); Department of Clinical Review and Safety (S Sharfaei MD), Baim Institute for Clinical Research, Boston, MA, USA; Beth Israel Deaconess Medical Center (S Sharfaei MD), Harvard University, Boston, USA; Schepens Eye Research Institute (M Shayan MD), Harvard Medical School, Boston, MA, USA; Department of Biochemistry (J K Shetty MD), Royal College of Surgeons in Ireland Medical University of Bahrain, Busaiteen, Bahrain; Yonsei University College of Medicine, Seoul, South Korea (Prof J Shin MD); Department of Surgery (N A Shitaye MD), Bahir Dar University, Bahir Dar, Ethiopia; Clinical Immunology and Hematology (V Shivarov PhD), Sofamed University Hospital, Sofia, Bulgaria; Department of Genetics (V Shivarov PhD), Sofia University "St. Kliment Ohridski", Sofia, Bulgaria; Department of Health Education and Health Promotion (S Siabani PhD), Kermanshah University of Medical Sciences, Kermanshah, Iran; School of Health (S Siabani PhD), School of Computing Sciences (Prof J Sun PhD), University of Technology Sydney, Sydney, NSW, Australia; Department of Pediatrics and Child Health Nursing (M M Sibhat MSc), Dilla University, Dilla, Ethiopia; Department of Medical Microbiology and Infectious Diseases (E E Siddig MD), Erasmus University, Rotterdam, Netherlands; School of Health (Prof C R Simpson PhD), Victoria University of Wellington, Wellington, New Zealand; Department of Pulmonary and Critical Care Medicine (H Singh MD), Medical College of Wisconsin, Milwaukee, WI, USA; Chitkara College of Pharmacy (Prof I Singh PhD), Chitkara University, Punjab, India; School of Medicine (Prof J A Singh MD), University of Alabama at Birmingham, Birmingham, AL, USA; Medicine Service (Prof J A Singh MD), US Department of Veterans Affairs (VA), Birmingham, AL, USA; Department of Radiodiagnosis (P Singh MD), All India Institute of Medical Sciences, Bathinda, India; Maternal and Child Health Division (M Siraj MSc), International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh; School of Health and Biomedical Science (A Sohag MSc), Royal Melbourne Institute of Technology (RMIT) University, Melbourne, VIC, Australia; Department of Pathology (R Solanki MD), Ross University School of Medicine, Bridgetown, Barbados; Department of Pathology (R Solanki MD), American University of the Caribbean School of Medicine, Cupecoy, Saint Martin; Faculty of Public Health (S Solikhah DrPH), Universitas Ahmad Dahlan, Yogyakarta, Indonesia; Department of Nursing (Y Solomon MSc), Dire Dawa University, Dire Dawa, Ethiopia; School of Medicine (Prof J Sun PhD), Griffith University, Gold Coast, QLD, Australia; Department of Dermatology (M D Szeto BS), University of Colorado, Aurora, CO, USA; Department of Medicine (Prof R Tabarés-Seisdedos PhD), University of Valencia, Valencia, Spain; Carlos III Health Institute (Prof R Tabarés-Seisdedos PhD), Biomedical Research Networking Center for Mental Health Network (CiberSAM), Madrid, Spain; Department of Epidemiology (J J L Tamuzi MSc), Stellenbosch University, Cape Town, South Africa; Department of Medicine (J J L Tamuzi MSc), Northlands Medical Group, Omuthiya, Namibia; Department of Surgery (K Tan PhD), Yong Loo Lin School of Medicine (Prof N Venketasubramanian MBBS), National University of Singapore, Singapore, Singapore; Department of Economics (N Y Tat MS), Rice University, Houston, TX, USA; Research and Innovation Department (N Y Tat MS), Eventure Medical Innovation, Houston, Texas, USA; Pediatric Intensive Care Unit (M Temsah MD), King Saud University, Riyadh, Saudi Arabia; Department of Pharmacology (P Thangaraju MD), All India Institute of Medical Sciences, Raipur, India; Faculty of Public Health (J H V Ticoalu MPH), Universitas Sam Ratulangi, Manado, Indonesia; Nuffield Department of Primary Care Health Sciences (T Tillawi MD), Oxford University, Oxford, UK; Allied Health and Human Performance (T Y Tiruye PhD), University of South Australia, Adelaide, SA, Australia; Public Health Department (T Y Tiruye PhD), Debre Markos University, Debre Markos, Ethiopia; Saveetha Dental College and Hospitals (M R Tovani-Palone PhD), Saveetha Institute of Medical and Technical Sciences, Chennai, India; SRM College of Pharmacy (M R Tovani-Palone PhD), SRM Institute of Science and Technology (SRMIST), Chennai, India; Department of Neurology (Prof M Tripathi MD), All India Institute of Medical Sciences, Delhi, India; Department of Nursing (G M Tsegay MSc), Aksum University, Aksum, Ethiopia; Department of Occupational Health and Safety (A R Tualeka PhD), Universitas

Airlangga, Surabaya, Indonesia; Department of Pharmacology (S Ty MD), All India Institute of Medical Sciences, Deoghar, India; College of Public Health (C S Ubah MPH), Temple University, Philadelphia, PA, USA; Institute of Soil and Environmental Sciences (S Ullah PhD), University of Agriculture Faisalabad, Faisalabad, Pakistan; Department of Zoology (S Ullah PhD), University of Education Lahore, Lahore, Pakistan; Division of Science and Technology (S Ullah PhD), University of Education, Lahore, Lahore, Pakistan; Medical Genomics Research Department (M Umair PhD), King Abdullah International Medical Research Center, Riyadh, Saudi Arabia; Department of Paraclinical Sciences (S Umakanthan MD), The University of the West Indies, St. Augustine, Trinidad and Tobago; Amity Institute of Biotechnology (E Upadhyay PhD), Amity University, Jaipur, India; College of Health and Sport Sciences (A G Vaithinathan MSc), University of Bahrain, Salmanya, Bahrain; Clinical Cancer Research Center (S Valadan Tahbaz PhD), Milad General Hospital, Tehran, Iran; Department of Microbiology (S Valadan Tahbaz PhD), Islamic Azad University, Tehran, Iran; Urmia University of Medical Sciences, Urmia, Iran (R Valizadeh PhD); UKK Institute, Tampere, Finland (Prof T J Vasankari MD); Faculty of Medicine and Health Technology (Prof T J Vasankari MD), Tampere University, Tampere, Finland; Raffles Neuroscience Centre (Prof N Venkatasubramanian MBBS), Raffles Hospital, Singapore, Singapore; Department of Surgery (G Verras MD), General University Hospital of Patras, Patras, Greece; Department of Health Care Administration and Economics (Prof V Vlassov MD), National Research University Higher School of Economics, Moscow, Russia; Office of Research, Innovation, and Commercialization (Prof Y Waheed PhD), Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan; Gilbert and Rose-Marie Chagoury School of Medicine (Prof Y Waheed PhD), Lebanese American University, Byblos, Lebanon; Department of Biomedical Sciences (A Waris MS), City University of Hong Kong, Hong Kong, China; Competence Center of Mortality-Follow-Up of the German National Cohort (R Westerman DSc), Federal Institute for Population Research, Wiesbaden, Germany; Department of Surgery (D P Wickramasinghe MD), University of Colombo, Colombo 08, Sri Lanka; Department of Community Medicine (N D Wickramasinghe MD), Rajarata University of Sri Lanka, Anuradhapura, Sri Lanka; Department of Neurology (B Willekens PhD), Antwerp University Hospital, Antwerp (Edegem), Belgium; Faculty of Medicine and Health Sciences (B Willekens PhD), University of Antwerp, Antwerp, Belgium; Department of Internal Medicine (B Z Woldegeorgis MD), Wolaita Sodo University, Sodo, Ethiopia; School of Public Health (H Xiao PhD), Zhejiang University, Zhejiang, China; Department of Public Health Science (H Xiao PhD), Fred Hutchinson Cancer Research Center, Seattle, WA, USA; Department of Microbiology and Immunology (G Yahya PhD), Zagazig University, Al Sharkia, Egypt; Department of Cells and Tissues (G Yahya PhD), Molecular Biology Institute of Barcelona, Spanish National Research Council, Barcelona, Spain; Cancer Epidemiology and Prevention Research (L Yang PhD), Alberta Health Services, Calgary, AB, Canada; Department of Oncology (L Yang PhD), University of Calgary, Calgary, AB, Canada; Department of Pediatrics (Prof D Yon MD), Kyung Hee University, Seoul, South Korea; Department of Neuropsychopharmacology (N Yonemoto PhD), National Center of Neurology and Psychiatry, Kodaira, Japan; Department of Public Health (N Yonemoto PhD), Juntendo University, Tokyo, Japan; Department of Pharmaceutics (S Zaidi PhD), Dow University of Health Sciences, Karachi, Pakistan; Research and Development Department (I Zare BSc), Sina Medical Biochemistry Technologies, Shiraz, Iran; School of Population and Global Health (D T Zemedikun PhD), University of Western Australia, Perth, WA, Australia; Institute of Applied Health Research (D T Zemedikun PhD), University of Birmingham, Birmingham, UK; Department of Neurology (C Zhang MD), National Center for Neurological Diseases (C Zhang MD), Capital Medical University, Beijing, China; College of Traditional Chinese Medicine (H Zhao MD), Hebei University, Baoding, China; Department of Infection (Prof A Zumla PhD), University College London, London, UK; NIHR-Biomedical Research Centre (Prof A Zumla PhD), University College London Hospitals, London, UK; Department of Urban Planning and Design (C Guo PhD), University of Hong Kong, Hong Kong Island, China.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.eclinm.2023.102193>.

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