The global burden of adolescent and young adult cancer in 2019: a systematic analysis for the Global Burden of Disease Study 2019

*GBD 2019 Adolescent and Young Adult Cancer Collaborators**

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*Collaborators are listed at the end of the Article

Correspondence to: Dr Elysia Alvarez, Department of Pediatrics, Division of Pediatric Hematology/Oncology, University of California Davis School of Medicine, Sacramento, CA 95817, USA
elalvarez@ucdavis.edu

Summary

Background In estimating the global burden of cancer, adolescents and young adults with cancer are often overlooked, despite being a distinct subgroup with unique epidemiology, clinical care needs, and societal impact. Comprehensive estimates of the global cancer burden in adolescents and young adults (aged 15–39 years) are lacking. To address this gap, we analysed results from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019, with a focus on the outcome of disability-adjusted life-years (DALYs), to inform global cancer control measures in adolescents and young adults.

Methods Using the GBD 2019 methodology, international mortality data were collected from vital registration systems, verbal autopsies, and population-based cancer registry inputs modelled with mortality-to-incidence ratios (MIRs). Incidence was computed with mortality estimates and corresponding MIRs. Prevalence estimates were calculated using modelled survival and multiplied by disability weights to obtain years lived with disability (YLDs). Years of life lost (YLLs) were calculated as age-specific cancer deaths multiplied by the standard life expectancy at the age of death. The main outcome was DALYs (the sum of YLLs and YLDs). Estimates were presented globally and by Socio-demographic Index (SDI) quintiles (countries ranked and divided into five equal SDI groups), and all estimates were presented with corresponding 95% uncertainty intervals (UIs). For this analysis, we used the age range of 15–39 years to define adolescents and young adults.

Findings There were 1·19 million (95% UI 1·11–1·28) incident cancer cases and 396 000 (370 000–425 000) deaths due to cancer among people aged 15–39 years worldwide in 2019. The highest age-standardised incidence rates occurred in high SDI (59·6 [54·5–65·7] per 100 000 person-years) and high-middle SDI countries (53·2 [48·8–57·9] per 100 000 person-years), while the highest age-standardised mortality rates were in low-middle SDI (14·2 [12·9–15·6] per 100 000 person-years) and middle SDI (13·6 [12·6–14·8] per 100 000 person-years) countries. In 2019, adolescent and young adult cancers contributed 23·5 million (21·9–25·2) DALYs to the global burden of disease, of which 2·7% (1·9–3·6) came from YLDs and 97·3% (96·4–98·1) from YLLs. Cancer was the fourth leading cause of death and tenth leading cause of DALYs in adolescents and young adults globally.

Interpretation Adolescent and young adult cancers contributed substantially to the overall adolescent and young adult disease burden globally in 2019. These results provide new insights into the distribution and magnitude of the adolescent and young adult cancer burden around the world. With notable differences observed across SDI settings, these estimates can inform global and country-level cancer control efforts.

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Introduction

Adolescents and young adults represent a heterogenous population consisting of individuals aged 15–39 years.[1–3] This formative time in life is unique, with several physical, emotional, and psychosocial changes, and with individuals potentially beginning or advancing their careers, higher education, relationships, and having children. The definitions and cutoffs of the age range for adolescents and young adults vary, but this age group is generally described as a subpopulation that is in transition between childhood and older adulthood.[1]

Adolescents and young adults develop cancers commonly found and treated in the paediatric population as well as the more common carcinomas seen in adults.[4,5] Additionally, some cancers are more prevalent in this age group than in younger or older individuals, such as Hodgkin lymphoma and gonadal germ cell tumours.[6,7] As a consequence, from a health-care delivery perspective, adolescent and young adult patients with cancer might struggle to find care that is optimal for both their cancer type and their age-related treatment needs.[1] Additionally, adolescent and young adult patients often face social and financial challenges, which might result in inequities

Research in context

Evidence before this study

Adolescents and young adults with cancer represent a transition population within the cancer continuum between children and older adults. As adolescents and young adults with cancer are treated by a variety of specialists, their unique epidemiology and clinical care needs are often overlooked. Although improvements in survival for children and adults with cancer are reported in high-income countries, less incremental progress has been observed among adolescents and young adults. Added complexities of cancer in this age group include the potential impact of a cancer diagnosis on starting or caring for their families and careers, access to care, diagnostic delays, and abandonment of therapy—issues that exist globally. Previous work assessing the global burden of adolescent and young adult cancer has focused on incidence and mortality, and has occasionally used a more restrictive age range than presented in this study. International adolescent and young adult cancer incidence patterns across time have been reported with data from Cancer Incidence in Five Continents reports, and national-level estimates have been reported from select, primarily high-income, countries. These publications have begun to raise awareness of adolescents and young adults as a distinctive population within the oncology community globally. However, to our knowledge, no previous publication has incorporated the impact of morbidity or done a comparative analysis of cancer within the broader context of the adolescent and young adult disease burden. We searched PubMed for English-language research articles describing the global burden of adolescent and young adult cancers between Jan 1, 2010, and Feb 1, 2021, using the terms "adolescent and young adult or adolescent or young adult or AYA" and "oncology or cancer or neoplasm or tumor or malignancy" and "global or worldwide or international" and "incidence or mortality or morbidity or burden or prevalence or survival", and identified no additional comprehensive adolescent and young adult global cancer estimate reports.

Added value of this study

We share for the first time, the formal global analysis of the cancer burden in individuals aged 15–39 years in 2019, using disability-adjusted life-years (DALYs) estimated by the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019. GBD 2019 is a valuable global health resource used to inform government health policy decisions around the world when comprehensive data might be absent. The global burden of cancer in terms of mortality and DALYs is substantial in the adolescent and young adult population. The global distribution of the adolescent and young adult cancer burden is unique, reflecting the shift from cancers that primarily affect children (eg, acute lymphoblastic leukaemia) to those that primarily affect adults (eg, carcinomas), and including cancers that occur most often in adolescents and young adults (eg, testicular cancers). Although high Socio-demographic Index (SDI) countries had the highest age-standardised incidence rates, they also had the lowest age-standardised mortality rates when compared to non-high SDI (low, low-middle, middle, and high-middle SDI) countries.

Implications of all the available evidence

The relative burden of deaths and DALYs due to adolescent and young adult cancer is high globally, concentrated primarily in non-high SDI settings. These estimates are crucial for comparing the burden of cancer to other causes of deaths and DALYs in adolescents and young adults and might be used to inform health policy and resource allocation priorities. Focus on adolescents and young adults as a distinct cancer population in the development of cancer control programmes is crucial to improving outcomes.

in access to appropriate care, timely diagnosis, and treatment.[1,3,8] Although adolescents and young adults have not seen the same improvements in cancer survival as younger and older cohorts for certain cancers, including acute myeloid leukaemia and soft tissue sarcomas,[9] this population has not historically been a major focus of cancer control programmes and research development.[10] Instead, based on historical precedent, adolescents and young adults are often grouped with adult patients in clinical care and clinical trials, and, as a consequence, comprehensive assessments of the cancer burden and epidemiological patterns in this age group are largely unknown or unreported in many settings.[1]

Previous studies have reported on global cancer incidence and mortality patterns of adolescents and young adults.[4,5,11] One study used incidence and mortality estimates from GLOBOCAN 2012 for individuals aged 20–39 years, another reported incidence and mortality estimates from GLOBOCAN 2018 for individuals aged 15–39 years, and a third study reported international cancer incidence trends in individuals aged 15–39 years using data from the Cancer Incidence in Five Continents series, a publication comprising data from a subset of countries around the world with high-quality population-based cancer registries.[4,5,11] However, global differences in measures that incorporate both morbidity and mortality due to adolescent and young adult cancers remain unexplored. Consideration of more comprehensive disease burden metrics is especially relevant in adolescents and young adults, whose disease burden might put a strain on their evolving careers and families.[1,12]

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) is the only global disease burden estimation framework that provides estimates of disability-adjusted life-years (DALYs) for cancer as a metric to complement incidence and mortality data. DALYs are a key measure of disease burden that include both fatal and non-fatal impacts of disease, and are used in the

development of national and global health policy.[13] GBD estimates disease burden for more than 300 diseases and injuries, allowing for comparative analyses with other causes of morbidity and mortality in adolescents and young adults. To our knowledge, no formal GBD analysis has previously been done of the global burden of cancer in the adolescent and young adult population. In this study, we aimed to analyse and report adolescent and young adult cancer burden estimates, using the most encompassing definition of adolescents and young adults (ie, individuals aged 15–39 years),[2,3] with a focused analysis on DALY estimates. DALYs represent an important comprehensive assessment of cancer burden in this distinctive population, adding to existing estimates of disease burden with more classic measures, and are crucial to informing cancer control strategies that address health disparities and inequities in this population.

Methods

GBD study overview

GBD was established to provide global disease burden metrics that are comprehensive and comparable over time. Estimates produced include incidence, prevalence, mortality, years of life lost (YLLs), years lived with disability (YLDs), and DALYs, measures that can each be used to describe different aspects of the adolescent and young adult cancer burden. Estimates are generated for each disease and injury and are reported by age group, sex, location, and year. Each GBD iteration replaces the previous round of GBD estimates for the entire estimated time series, so that updates to data and methods in the new GBD round are applied consistently across time. The present analysis was based on GBD 2019 estimates.[13,14] GBD 2019 was done in accordance with the Guideline for Accurate and Transparent Health Estimates Reporting (appendix pp 5, 6).[15] Data sources used in GBD 2019 are available online and are further outlined in the appendix (p 10). This manuscript was produced as part of the GBD Collaborator Network and in accordance with the GBD Protocol. Analyses were completed with Python (versions 3.6.2 and 3.6.7), Stata (version 13), and R (versions 3.5.0 and 3.4.1).

Definitions

Although the definition of the age range for adolescents and young adults varies, particularly in the upper age limit,[12,16,17] we used the age range of 15–39 years in this study, since this is the most encompassing age range definition recommended in oncology, is endorsed by the US National Cancer Institute and the AYA Working Group of the European Society for Medical Oncology and the European Society for Paediatric Oncology,[3] and allows for comparability with other studies on adolescent and young adult cancer.[1] Individuals aged 15–39 years have also experienced the least progress in survival outcomes in most countries.[11] Data for this age range are available online with the GBD Results Tool and for subsets of this age range with the GBD Compare data visualisation tool or GBD Results Tool. As there are differences in the preferred age range used to define adolescents and young adults around the world, results of the narrower age range of 15–29 years are presented in the appendix (pp 115–122).

All malignant cancer types, as defined in the tenth revision of the International Classification of Diseases, chapter II (Neoplasms),[18] were categorised into 32 cancer groups in this analysis, called causes in GBD and this Article. Non-melanoma skin cancers were excluded, since they are not a major cause of mortality in this age range. The cause "other malignant neoplasms" in GBD includes estimates for cancers not included in any other GBD cancer cause, such as bone cancers and soft tissue sarcomas (see appendix p 11 for more details about cancer mapping). The adolescent and young adult age group was compared to children (aged 0–14 years) and older adults (aged ≥40 years) in specific analyses. The focus of this analysis was on global and regional estimates, although GBD 2019 also produces estimates at the national and, for select countries, subnational level. National and subnational estimates are available in the GBD Compare and GBD Results tools online. Select results are presented by quintiles of the Socio-demographic Index (SDI; countries ranked and divided into five equal SDI groups), which is a composite measure of income per capita, total fertility rate (age <25 years), and average educational fulfilment (for those aged ≥15 years), and is a useful summary measure of a country's overall social and economic development that allows for analyses of disease burden patterns across different resource contexts (appendix p 56).[14] All cancer rates were reported per 100 000 person-years. The GBD world population standard was used for the calculation of age-standardised rates (appendix p 56).

Estimation of cancer burden

The GBD cancer estimation process begins with a focus on mortality. Data sources include vital registration systems, verbal autopsies, and population-based cancer registration systems. Some cancer registries report incidence only; therefore, mortality-to-incidence ratios (MIRs) were used to convert cancer registry incidence data to estimates of mortality, increasing data availability in locations that might not have mortality data, but have active cancer registries. Using a spatiotemporal Gaussian process regression, MIRs were modelled for all combinations of age, sex, year, and location with incidence data from cancer registries and mortality data from cancer registries or high-quality vital statistics registries (elaborated in the appendix pp 25, 26).[13] Estimates of mortality obtained with MIRs were combined with vital registration and verbal autopsy mortality data and used as inputs in cancer type and sex-specific Cause of Death Ensemble models (CODEm).[19] The CODEm methodology uses all available mortality data to select the optimal model or models on the basis of out-of-sample predictive

See Online for appendix

For the **data sources used in GBD 2019** see http://ghdx.healthdata.org/gbd-2019

For the **GBD Results Tool** see http://ghdx.healthdata.org/gbd-results-tool

For the **GBD Compare data visualisation** see https://vizhub.healthdata.org/gbd-compare/

	DALYs, thousands (95% UI)	Age-standardised DALY rate per 100 000 (95% UI)	Incidence, thousands (95% UI)	Age-standardised incidence rate per 100 000 (95% UI)	Mortality, thousands (95% UI)	Age-standardised mortality rate per 100 000 (95% UI)
Global	23 500 (21 900–25 200)	782·2 (730·8–838·1)	1190 (1110–1280)	39·7 (36·9–42·6)	396 (370–425)	13·2 (12·3–14·1)
SDI quintiles						
High SDI quintile	2020 (1940–2110)	564·3 (542·8–590·1)	213 (195–235)	59·6 (54·5–65·7)	33·4 (32·2–34·7)	9·2 (8·9–9·6)
High-middle SDI quintile	4520 (4200–4840)	801·4 (745·8–857·8)	302 (277–329)	53·2 (48·8–57·9)	76·6 (71·1–82·2)	13·4 (12·4–14·3)
Middle SDI quintile	7780 (7190–8410)	810·1 (748·4–876·6)	369 (339–401)	38·3 (35·1–41·6)	132 (122–143)	13·6 (12·6–14·8)
Low-middle SDI quintile	5970 (5420–6530)	836·7 (760·1–915·5)	209 (188–229)	29·4 (26·5–32·2)	101 (91·4–110)	14·2 (12·9–15·6)
Low SDI quintile	3190 (2770–3630)	781·1 (678·2–890·0)	101 (86·3–115)	25·0 (21·4–28·7)	53·5 (46·5–60·9)	13·3 (11·6–15·2)
Cancers						
Breast cancer	2490 (2260–2720)	82·1 (74·4–89·8)	170 (154–186)	5·6 (5·1–6·1)	43·1 (39·1–47·3)	1·4 (1·3–1·6)
Brain and CNS cancer	1750 (1380–1940)	58·4 (46·2–64·9)	61·5 (48·2–69·1)	2·1 (1·6–2·3)	29·1 (23·0–32·3)	1·0 (0·8–1·1)
Colon and rectum cancer	1630 (1510–1760)	53·9 (49·9–58·1)	76·1 (70·2–82·9)	2·5 (2·3–2·7)	28·4 (26·2–30·5)	0·9 (0·9–1·0)
Stomach cancer	1570 (1450–1700)	52·0 (47·8–56·2)	49·0 (45·0–53·1)	1·6 (1·5–1·8)	27·9 (25·7–30·2)	0·9 (0·8–1·0)
Cervical cancer	1560 (1 320–1780)	51·4 (43·5–58·7)	119 (99·6–135)	3·9 (3·3–4·5)	27·2 (22·9–31·1)	0·9 (0·8–1·0)
Tracheal, bronchus, and lung cancer	1390 (1270–1510)	45·8 (42·0–50·0)	32·6 (29·7–35·5)	1·1 (1·0–1·2)	24·8 (22·7–27·0)	0·8 (0·7–0·9)
Non-Hodgkin lymphoma	1280 (1190–1380)	42·8 (39·8–46·4)	52·4 (47·0–58·7)	1·8 (1·6–2·0)	20·8 (19·3–22·6)	0·7 (0·6–0·8)
Liver cancer	1050 (938–1160)	34·6 (31·0–38·4)	25·4 (22·7–28·4)	0·8 (0·8–0·9)	18·6 (16·6–20·7)	0·6 (0·5–0·7)
Other leukaemia	949 (791–1080)	32·0 (26·6–36·4)	28·8 (23·8–32·8)	1·0 (0·8–1·1)	15·3 (12·7–17·4)	0·5 (0·4–0·6)
Acute lymphoid leukaemia	766 (634–844)	26·1 (21·7–28·8)	38·7 (32·2–43·2)	1·3 (1·1–1·5)	11·7 (9·64–12·9)	0·4 (0·3–0·4)
Acute myeloid leukaemia	748 (678–858)	25·2 (22·9–28·9)	20·2 (18·2–22·8)	0·7 (0·6–0·8)	12·2 (11·0–14·0)	0·4 (0·4–0·5)
Lip and oral cavity cancer	580 (520–644)	19·2 (17·2–21·3)	29·4 (26·3–32·7)	1·0 (0·9–1·1)	10·0 (9·00–11·1)	0·3 (0·3–0·4)
Ovarian cancer	529 (443–602)	17·6 (14·7–20·0)	35·8 (30·5–41·0)	1·2 (1·0–1·4)	8·90 (7·46–10·1)	0·3 (0·2–0·3)
Hodgkin lymphoma	508 (432–600)	17·1 (14·5–20·2)	33·4 (29·9–40·5)	1·1 (1·0–1·4)	8·09 (6·85–9·52)	0·3 (0·2–0·3)
Pancreatic cancer	421 (387–463)	13·9 (12·8–15·3)	9·40 (8·59–10·3)	0·3 (0·3–0·3)	7·61 (6·98–8·39)	0·3 (0·2–0·3)
Nasopharynx cancer	363 (334–394)	12·1 (11·1–13·1)	28·6 (25·3–32·3)	0·9 (0·8–1·1)	6·08 (5·60–6·65)	0·2 (0·2–0·2)
Testicular cancer	349 (319–383)	11·7 (10·6–12·8)	57·4 (51·6–65·1)	1·9 (1·7–2·2)	5·35 (4·92–5·84)	0·2 (0·2–0·2)
Oesophageal cancer	344 (308–382)	11·3 (10·1–12·6)	8·09 (7·27–8·97)	0·3 (0·2–0·3)	6·21 (5·57–6·90)	0·2 (0·2–0·2)
Chronic myeloid leukaemia	295 (261–335)	9·8 (8·7–11·2)	9·20 (8·34–10·2)	0·3 (0·3–0·3)	4·96 (4·39–5·62)	0·2 (0·1–0·2)
Malignant skin melanoma	259 (216–318)	8·6 (7·2–10·5)	37·3 (30·5–46·4)	1·2 (1·0–1·5)	4·25 (3·55–5·21)	0·1 (0·1–0·2)
Other pharynx cancer	245 (211–276)	8·1 (7·0–9·1)	7·10 (6·26–7·92)	0·2 (0·2–0·3)	4·36 (3·76–4·91)	0·1 (0·1–0·2)
Kidney cancer	239 (220–264)	7·9 (7·3–8·8)	21·1 (19·3–23·3)	0·7 (0·6–0·8)	4·02 (3·69–4·43)	0·1 (0·1–0·1)
Thyroid cancer	191 (168–214)	6·4 (5·6–7·1)	46·8 (40·6–51·7)	1·6 (1·3–1·7)	2·85 (2·52–3·17)	0·1 (0·1–0·1)
Gallbladder and biliary tract cancer	133 (113–147)	4·4 (3·7–4·9)	3·84 (3·29–4·26)	0·1 (0·1–0·1)	2·39 (2·03–2·66)	0·1 (0·1–0·1)
Larynx cancer	128 (118–140)	4·2 (3·9–4·6)	4·21 (3·88–4·58)	0·1 (0·1–0·2)	2·25 (2·06–2·47)	0·1 (0·1–0·1)
Bladder cancer	124 (113–137)	4·1 (3·7–4·5)	14·1 (12·6–15·8)	0·5 (0·4–0·5)	2·05 (1·85–2·28)	0·1 (0·1–0·1)
Uterine cancer	110 (85·1–124)	3·6 (2·8–4·1)	19·4 (15·8–22·0)	0·6 (0·5–0·7)	1·81 (1·39–2·04)	0·1 (0·0–0·1)
Multiple myeloma	95·6 (74·3–107)	3·2 (2·5–3·5)	2·93 (2·26–3·34)	0·1 (0·1–0·1)	1·68 (1·31–1·88)	0·1 (0·0–0·1)
Chronic lymphoid leukaemia	61·4 (52·8–69·4)	2·0 (1·8–2·3)	4·26 (3·65–4·88)	0·1 (0·1–0·2)	1·01 (0·872–1·14)	0·0 (0·0–0·0)
Mesothelioma	56·4 (44·1–67·9)	1·9 (1·5–2·2)	1·47 (1·15–1·79)	0·0 (0·0–0·1)	0·990 (0·777–1·20)	0·0 (0·0–0·0)
Prostate cancer	54·3 (47·2–66·1)	1·8 (1·6–2·2)	5·47 (4·78–6·55)	0·2 (0·2–0·2)	0·876 (0·757–1·06)	0·0 (0·0–0·0)
Other malignant neoplasms	3230 (2920–3530)	109·1 (98·8–119·4)	141 (130–154)	4·8 (4·4–5·2)	51·5 (46·6–56·2)	1·7 (1·6–1·9)

Estimates are for individuals aged 15–39 years, both sexes combined. Values in parentheses are 95% uncertainty intervals (UIs). Rates are reported per 100 000 person-years. Cancer types are listed in order of global DALY burden, with the exception of "other malignant neoplasms", which are listed last. Other malignant neoplasms are cancers without a detailed GBD cause separately listed. Other leukaemia included leukaemias not otherwise specified. Non-melanoma skin cancers were not included in this analysis. SDI categories do not sum precisely to the global total as GBD 2019 does not provide separate estimates for all locations globally and an adjustment factor is made between all estimated locations, which have corresponding SDI values, and the global estimate. DALYs=disability-adjusted life years. UI=uncertainty interval. GBD=Global Burden of Diseases, Injuries, and Risk Factors Study. SDI=Socio-demographic Index.

Table: **Adolescent and young adult cancer burden globally and by SDI quintile in 2019**

validity (appendix p 28). Cause-specific mortality estimates were then scaled to independently modelled all-cause mortality with CoDCorrect to ensure consistency.[13]

Incidence estimates were obtained by dividing the mortality estimates by the corresponding MIR for each cancer type. Survival estimates based on MIRs were used to model 10-year prevalence for each cancer cause (appendix pp 50, 51). Prevalence for each cancer cause was divided into distinct phases of cancer treatment to estimate YLDs. For cohorts that survived beyond 10 years

from diagnosis, two phases were estimated for the 10-year time period after diagnosis: diagnosis or treatment; and remission. After the 10-year period, the disability risk was returned to the baseline of the general population without a cancer diagnosis. For cohorts that did not survive beyond 10 years from diagnosis, two additional phases were estimated: the metastatic or disseminated phase; and the terminal phase. YLD estimates were generated by multiplying each phase prevalence by a phase-specific disability weight, representative of the health loss magnitude associated with a specified health outcome. Disability weights are measured on a scale of 0 (full health) to 1 (equivalent to death; appendix p 55). YLLs were calculated as the standard life expectancy at the age of death multiplied by age-specific cancer deaths.[14] DALY estimates were the sum of the YLD and YLL estimates. Proportional DALYs for each cancer cause and 5-year age group were calculated as the mean of 1000 proportion draws of the absolute number of DALYs for each cancer cause and age group divided by the total number of cancer DALYs within the same age group. Proportional DALYs for each SDI were calculated as the mean of 1000 proportion draws of the absolute number of DALYs for each cancer cause within each SDI quintile and divided by the total number of DALYs in each SDI quintile (appendix p 56). An additional analysis was done to identify the proportion of adolescent and young adult cancer cases covered by the WHO Global Initiative for Childhood Cancer (appendix p 56). Further detailed descriptions of the methods are provided in the appendix (pp 7–57) and in GBD 2019 summary publications.[13,14]

Uncertainty analysis

Final point estimates are reported with 95% uncertainty intervals (UIs). 95% UIs are 95% ranges calculated as the range from the 2·5th to the 97·5th percentile on the basis of the distribution of 1000 draws at each GBD cancer estimation step, with uncertainty propagated through each step (appendix p 57).

Role of the funding source

The funders of this study had no role in the design of the GBD cancer estimation process, collection or analysis of data, interpretation of results, or in the writing of this manuscript.

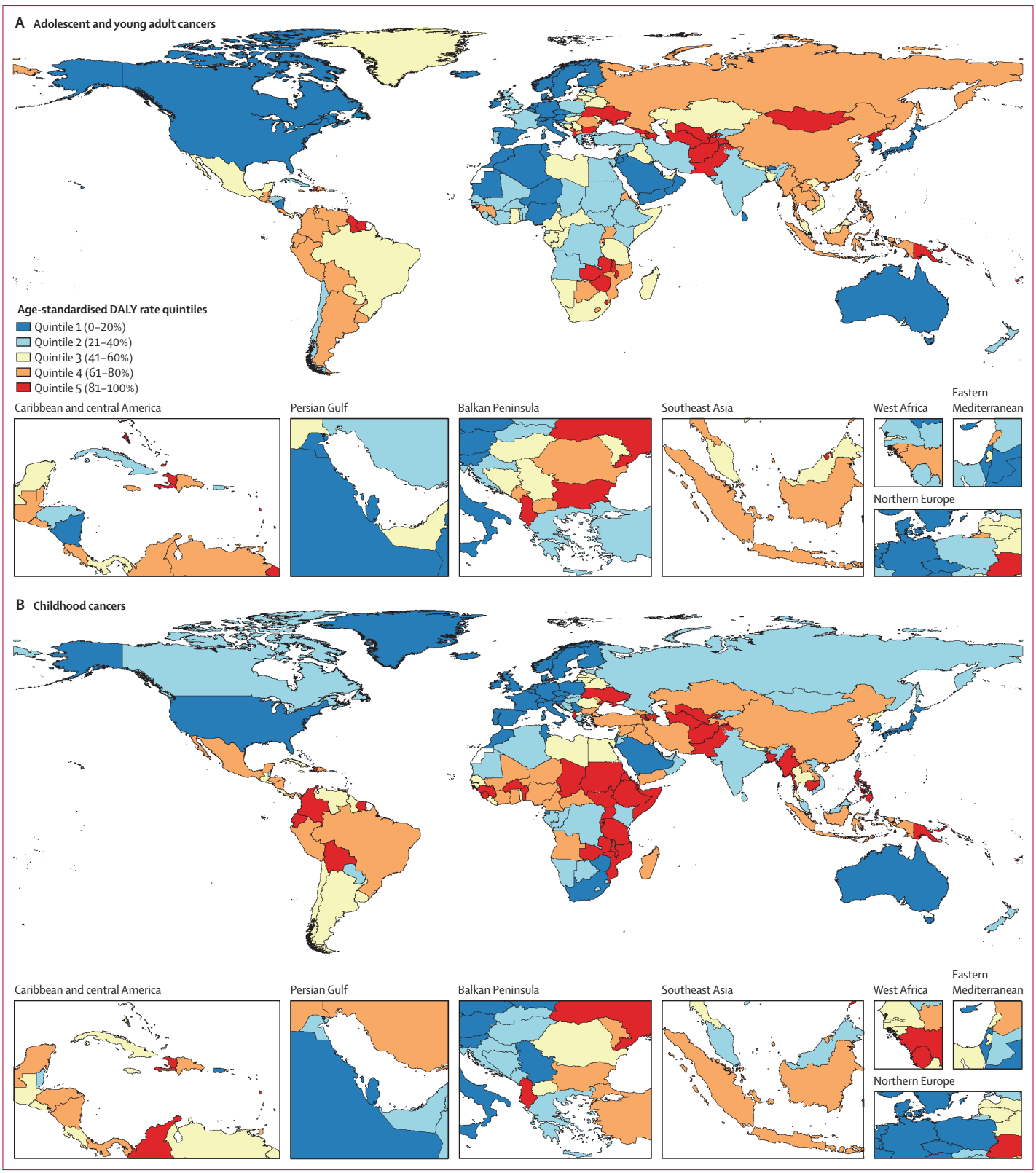
Results

There were an estimated 1·19 million (95% UI 1·11–1·28) incident cancer cases and 396 000 (370 000–425 000) deaths among individuals aged 15–39 years worldwide in 2019 (table). The highest age-standardised incidence rates were seen in high SDI (59·6 [54·5–65·7] per 100 000 person-years) and high-middle SDI (53·2 [48·8–57·9] per 100 000 person-years) countries, while the highest age-standardised mortality rates from cancer in adolescents and young adults were seen in middle SDI (13·6 [12·6–14·8] per 100 000 person-years) and low-middle SDI (14·2 [12·9–15·6] per 100 000 person-years) regions. Adolescent and young adult cancers contributed 23·5 million (21·9–25·2) DALYs to the global burden of disease in 2019 (table), of which 2·7% (1·9–3·6) came from YLDs and 97·3% (96·4–98·1) from YLLs (appendix p 79). The majority (91·4% [91·0–91·8]) of the worldwide absolute adolescent and young adult cancer DALY burden is concentrated in non-high SDI (low, low-middle, middle, and high-middle SDI) quintiles. Overall, high SDI settings have the highest age-standardised incidence rate (59·6 [54·5–65·7] per 100 000 person-years), but the lowest age-standardised DALY rate (564·3 [542·8–590·1] per 100 000 person-years). Breast cancer (10·6% [10·0–11·2]), followed by brain and CNS cancer (7·4% [6·0–8·0]), colon and rectum cancer (7·0% [6·6–7·3]), and stomach cancer (6·7% [6·5–7·0]) were the four greatest contributors to the DALY burden globally for both sexes combined, of separately categorised cancers (appendix p 81). If leukaemias were considered as a single group, given that they are treated by haematologist-oncologists and have a similar diagnostic approach, rather than as individual leukaemia subtypes, leukaemias would be the largest categorised cancer group contributing to the global cancer DALY burden (12·0% [10·9–12·8]), greater than that of breast cancer. The "other malignant neoplasms" category, the aggregated cancer cause category for cancers not separately estimated in the GBD framework, comprised the highest proportion of the adolescent and young adult cancer DALY burden globally (13·7% [12·8–14·5]; appendix p 81). A focused analysis of individuals aged 15–29 years is provided in the appendix (pp 115–122).

For more on the **WHO Global Initiative for Childhood Cancer** see https://www.who.int/publications/m/item/global-initiative-for-childhood-cancer

The greatest burden of cancer in adolescents and young adults in 2019, as represented by age-standardised DALY rates, was concentrated in parts of Asia, southern sub-Saharan Africa, and South America (figure 1A; appendix p 84). The distribution of DALYs due to cancer in adolescents and young adults is distinct from that of children (figure 1B) and older adults (figure 1C). The geographical pattern of age-standardised DALY rate quintiles for adolescent and young adult cancer was similar to the geographical pattern of childhood cancers in high SDI countries and resembled the distribution of adult cancer in low and middle SDI countries (figure 1).

Of all age groups, individuals aged 35–39 years had the largest contribution to the adolescent and young adult global cancer DALYs (8·4 million [95% UI 7·8–9·0], with corresponding DALY rates of 1547·6 [1441·3–1658·0] per 100 000 person-years; figure 2A). The proportion of DALYs attributed to leukaemias declined with increasing age across the adolescent and young adult population (26·7% [24·8–28·8] of total age group DALYs, corresponding to 0·64 million [0·56–0·72] DALYs in those aged 15–19 years *vs* 6·2% [5·6–6·7] of total age group DALYs, corresponding to 0·52 million [0·46–0·58] DALYs in those aged



(Figure 1 continues on next page)

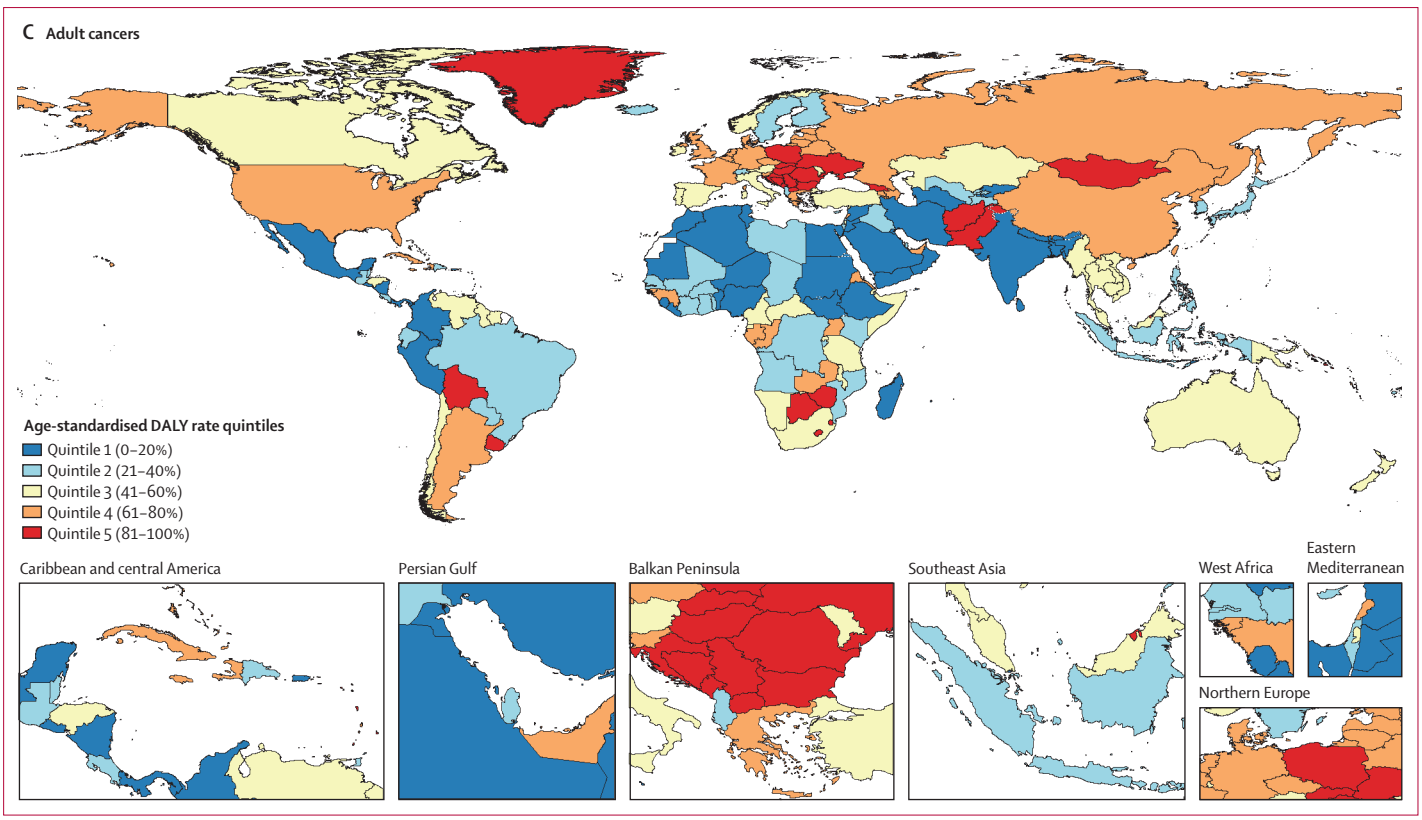


Figure 1: **Global map of age-standardised DALY rates for both sexes combined in 2019, categorised by age-standardised DALY rate quintiles, excluding non-melanoma skin cancers, for malignant adolescent and young adult cancers (A), malignant childhood cancers (B), and malignant adult cancers (C)**

Quintiles are based on age-standardised DALY rates per 100 000 person-years. For adolescent and young adult cancers (age 15–39 years), quintile 1 (0–20%) corresponds to less than 597 DALYs per 100 000 person-years, quintile 2 (21–40%) corresponds to 597 to less than 729 DALYs per 100 000 person-years, quintile 3 (41–60%) corresponds to 729 to less than 833 DALYs per 100 000 person-years, quintile 4 (61–80%) corresponds to 833 to less than 1010 DALYs per 100 000 person-years, and quintile 5 (81–100%) corresponds to 1010 or more DALYs per 100 000 person-years. For childhood cancers (age 0–14 years), quintile 1 (0–20%) corresponds to less than 250 DALYs per 100 000 person-years, quintile 2 (21–40%) corresponds to 250 to less than 311 DALYs per 100 000 person-years, quintile 3 (41–60%) corresponds to 311 to less than 396 DALYs per 100 000 person-years, quintile 4 (61–80%) corresponds to 396 to less than 495 DALYs per 100 000 person-years, and quintile 5 (81–100%) corresponds to 495 or more DALYs per 100 000 person-years. For adult cancers (age ≥40 years), quintile 1 (0–20%) corresponds to less than 6680 DALYs per 100 000 person-years, quintile 2 (21–40%) corresponds to 6680 to less than 7390 DALYs per 100 000 person-years, quintile 3 (41–60%) corresponds to 7390 to less than 8580 DALYs per 100 000 person-years, quintile 4 (61–80%) corresponds to 8580 to less than 9890 DALYs per 100 000 person-years, and quintile 5 (81–100%) corresponds to 9890 or more DALYs per 100 000 person-years. There are several geographical locations (shown in white) where estimates are not available (eg, Western Sahara and French Guiana) as they were not modelled locations in GBD 2019. DALY=disability-adjusted life-year. GBD=Global Burden of Diseases, Injuries, and Risk Factors Study.

35–39 years; appendix p 107). The proportion of DALYs attributed to carcinomas increased with increasing age across the adolescent and young adult population (18·1% [17·3–19·3] of total age group DALYs in those aged 15–19 years, corresponding to 0·43 million [0·40–0·47] DALYs *vs* 73·6% [72·7–75·2] of total age group DALYs, corresponding to 6·2 million [5·7–6·6] DALYs in those aged 35–39 years; figure 2B; appendix p 107). There was a notable proportion of "other malignant neoplasms" across the adolescent and young adult population, which was highest in those aged 15–19 years (30·6% [28·6–32·2] of total age group DALYs, corresponding to 0·73 million [0·65–0·81] DALYs), and lowest in those aged 35–39 years (7·1% [6·5–7·5] of total age group DALYs, corresponding to 0·59 million [0·54–0·65] DALYs; figure 2B). In direct comparisons of the proportional DALY burden for the 15–29-year age group with that of the 30–39-year age group, there is a transition in the predominant cause from leukaemias and lymphomas to carcinomas, especially breast and cervical cancer (appendix p 122).

When assessed by SDI quintile, age-standardised DALY rates and the proportional DALY burden varied by cancer type (figure 3). Individuals in the high SDI quintile had a lower age-standardised DALY rate (564·3 [95% UI 542·8–590·1] DALYs per 100 000 person-years; figure 3A) than other SDI quintiles. Estimates of the proportion of the DALY burden due to cervical cancer increased with decreasing SDI quintile, having the lowest proportional burden in the high SDI setting (4·1% [3·7–4·4]; figure 3B) and the highest burden in the low SDI setting (12·1% [10·4–14·4]; figure 3B). The adolescent and young adult cancer burden attributed to brain and CNS cancer was highest in the high SDI (10·7% [8·8–11·6]) and high-middle SDI (9·0% [7·2–9·7]) quintiles, compared to the low-middle SDI (6·1%

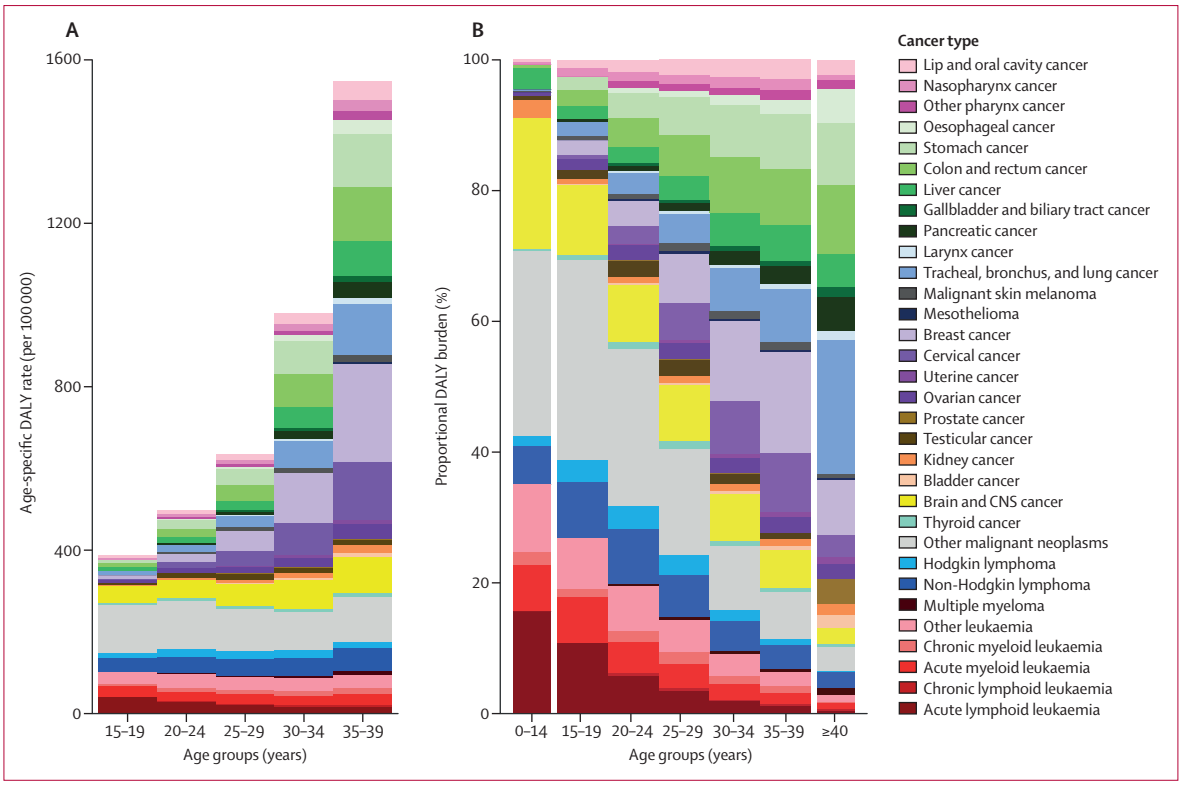


Figure 2: **Global age-specific DALY rates (A) and proportional DALY burden (B) of adolescent and young adult cancer types by age group, in 2019, for both sexes combined**

Rates are expressed per 100 000 person-years. "Other malignant neoplasms" comprise all malignancies without a separate GBD cause category listed; this category does not include non-melanoma skin cancers and myelodysplastic or myeloproliferative neoplasms, which are separate GBD cause categories not included in this analysis. Other leukaemia included leukaemias not otherwise specified. DALY=disability-adjusted life-year. GBD=Global Burden of Diseases, Injuries, and Risk Factors Study.

[5·0–6·9]) and low SDI (5·2% [4·0–6·2]) quintiles. The proportion of adolescent and young adult cancers that were in the "other malignant neoplasms" category was highest in the low SDI quintile (20·1% [18·7–22·2]) and lowest in the high-middle SDI quintile (9·9% [9·5–10·6]).

The top five causes by absolute DALY burden in females globally in 2019 were breast cancer (2·46 million [95% UI 2·23–2·70] DALYs), cervical cancer (1·56 million [1·32–1·78] DALYs), "other malignant neoplasms" (1·35 million [1·21–1·51] DALYs), stomach cancer (732 000 [653 000–814 000] DALYs), and brain and CNS cancer (722 000 [536 000–827 000] DALYs; figure 4; appendix pp 66–69). The five cancers with the highest absolute DALY burden in males were "other malignant neoplasms" (1·88 million [1·64–2·12] DALYs); brain and CNS cancer (1·03 million [0·76–1·19] DALYs); colon and rectum cancer (973 000 [887 000–1 070 000] DALYs); tracheal, bronchus, and lung cancer (856 000 [766 000–952 000] DALYs); and stomach cancer (842 000 [767 000–928 000] DALYs; figure 4; appendix pp 62–65). In 2019, females had a higher overall incidence of cancer than males globally (686 000 [622 000–751 000] *vs* 509 000 [469 000–549 000] incident cancer cases), but had similar absolute mortality (202 000 [184 000–222 000] *vs* 194 000 [179 000–209 000] deaths; appendix pp 62, 66, 82–83). Breast and cervical cancer combined made up a substantial proportion of the DALY burden globally in females (33·6% [32·3–35·1]). Among the non-sex-specific cancer causes, males had higher absolute DALYs globally in 24 of 27 cancer groups, representing a 13·7% (3·5–25·1) overall higher absolute number of DALYs than females.

Rankings of the burden of absolute DALYs and deaths due to adolescent and young adult cancer compared to other diseases in individuals aged 15–39 years, both globally and by SDI quintile, are shown in figure 5. Adolescent and young adult cancer had the tenth highest DALY burden globally (23·5 million [95% UI 21·9–25·2] DALYs; figure 5A) among 22 causes of DALYs at this level in the GBD hierarchy. The inter-category rankings show that cancer ranks higher than other prominent causes of DALYs in high, high-middle, and middle SDI quintiles, compared to low-middle and low SDI quintiles. In adolescents and young adults, deaths from cancer ranked fourth globally (396 000 [370 000–425 000]; figure 5B), among 21 causes of death at this level in the GBD hierarchy, with a higher intra-SDI-quintile ranking in high, high-middle, and middle SDI regions, compared to low-middle and low SDI regions. In comparison, deaths due to cancer ranked 11th globally in those younger than

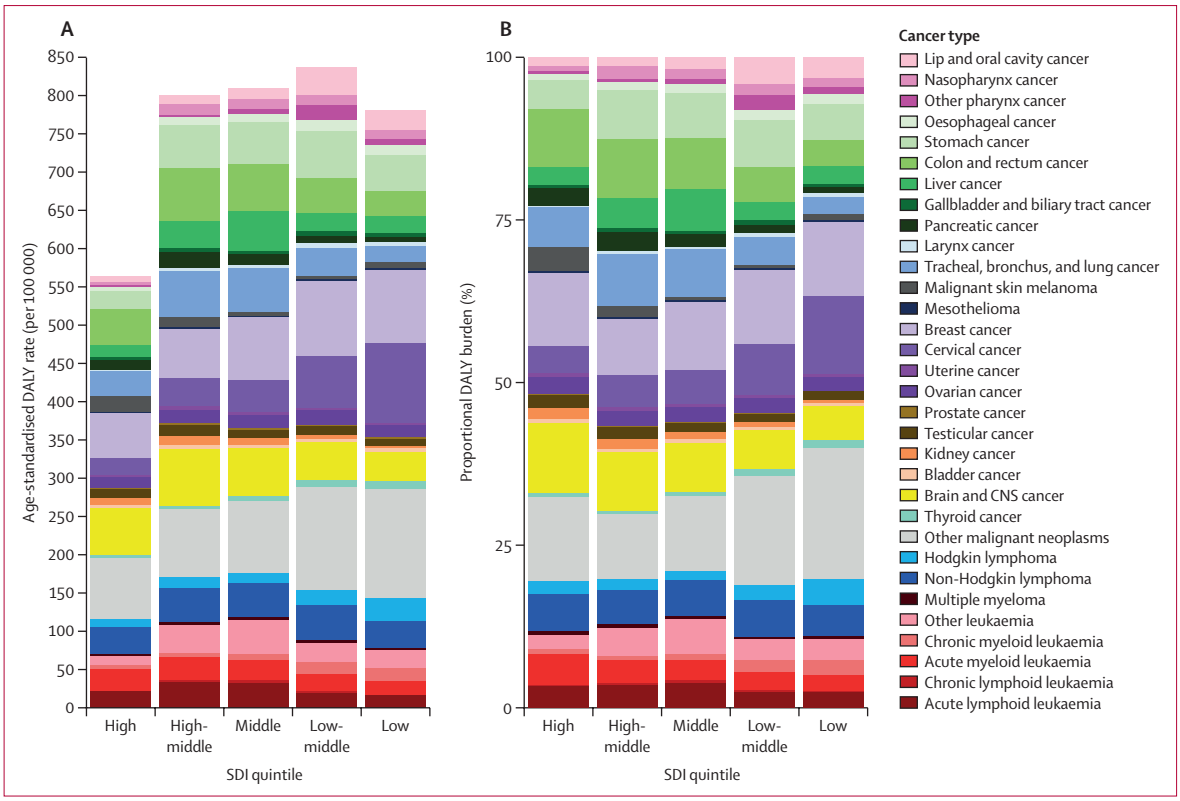


***Figure 3*: Age-standardised DALY rates (A) and proportional adolescent and young adult cancer DALY burden (B) by Socio-demographic Index, in 2019, for both sexes combined**

Rates are expressed per 100 000 person-years. "Other malignant neoplasms" comprise all malignancies without a separate GBD cause category listed; this category does not include non-melanoma skin cancers and myelodysplastic or myeloproliferative neoplasms, which are separate GBD cause categories not included in this analysis. Other leukaemia included leukaemias not otherwise specified. DALY=disability-adjusted life-year. GBD=Global Burden of Diseases, Injuries, and Risk Factors Study. SDI=Socio-demographic Index.

15 years and second in those older than 39 years (appendix pp 105, 106). In 2019, deaths due to cancer in the adolescent and young adult population were lower than those estimated for transport injuries and cardiovascular and circulatory diseases, but higher than those estimated for HIV/AIDS and sexually transmitted infections, respiratory infections and tuberculosis, and unintentional injuries (figure 5B). More detailed findings are summarised in the appendix (pp 62–114). An additional analysis showed that 8·6% (95% UI 8·2–9·1) of all adolescent and young adult cancer cases are included in the WHO Global Initiative for Childhood Cancer (appendix p 56).

Discussion

In our analysis of adolescent and young adult cancer, based on data from GBD 2019, we show, to the best of our knowledge, for the first time that the global burden of adolescent and young adult cancer is substantial in terms of DALYs, a measure that is frequently used by governments to inform policy and resource allocation needs. From a descriptive perspective, the age-standardised distribution of adolescent and young adult DALYs was unique compared to both childhood and adult cancers, reflecting an expected but ill-described transition from childhood to adult cancer epidemiological patterns.[20–22] Additionally, when the overall disease burden is studied cross-sectionally within the age range encompassing adolescents and young adults, the global burden of cancer contributed more DALYs to the global disease burden than some high-profile communicable diseases such as HIV/AIDS and sexually transmitted infections. This comparison of cancer with other leading causes of global mortality and DALYs in adolescents and young adults has not been previously documented. These results highlight that cancer is an important contributor to premature death and the disease burden in adolescents and young adults globally, even when compared with some communicable diseases that that are the focus of more active global funding, research, and advocacy efforts.[1,23] The findings also underscore the need to develop a global strategy to address the cancer burden in this population, which should include the integration of adolescent and young adult cancer into overall cancer control planning and universal health coverage plans.[24]

Because of the substantial burden of adolescent and young adult cancers globally, with the majority of DALYs occurring on the lower end of the SDI spectrum, broader

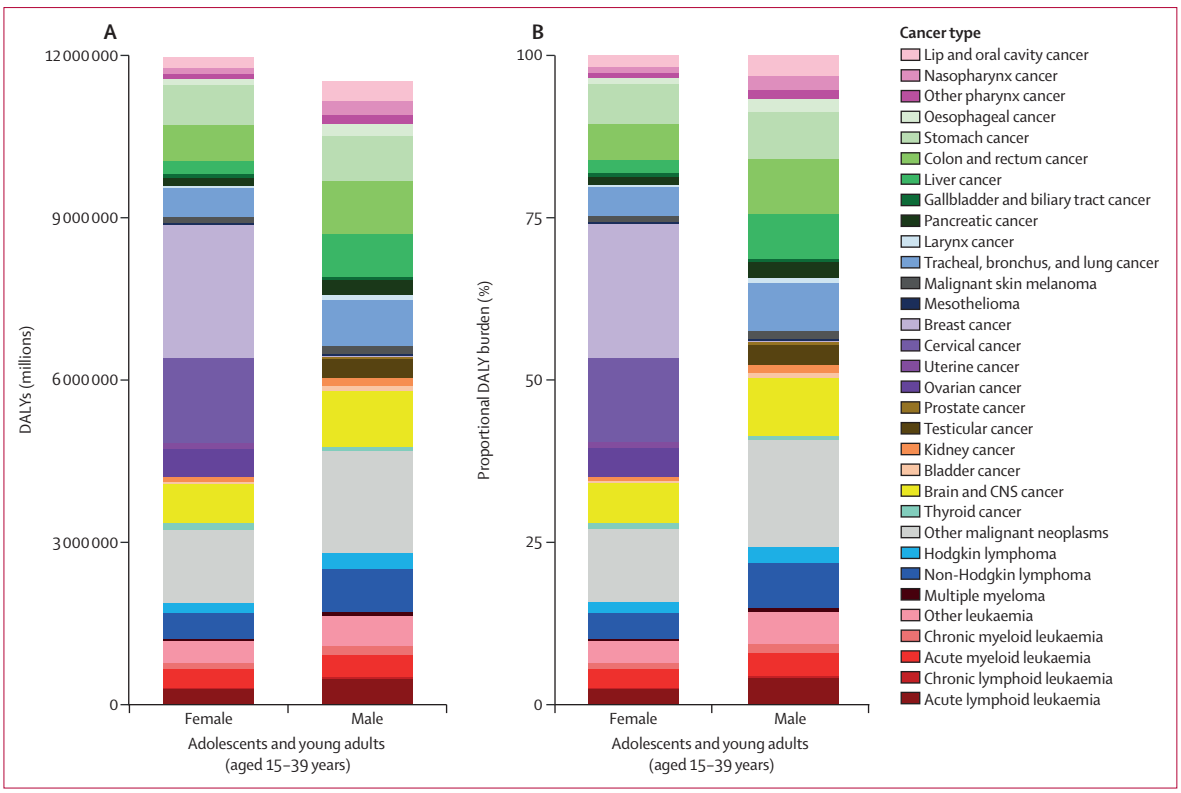


Figure 4: **Global absolute (A) and proportional (B) adolescent and young adult cancer DALY burden by sex in 2019**
Other malignant neoplasms comprise all malignancies without a separate GBD cause category listed; this category does not include non-melanoma skin cancers and myelodysplastic or myeloproliferative neoplasms, which are separate GBD cause categories not included in this analysis. Other leukaemia included leukaemias not otherwise specified. DALY=disability-adjusted life-year. GBD=Global Burden of Diseases, Injuries, and Risk Factors Study.

attention to the unique determinants driving cancer outcomes in this age range is needed.[5] In 2017, the World Health Assembly accepted the global cancer challenge resolution, which stated the importance of including children and adolescents in the development of cancer control programmes.[8] The World Health Assembly noted in particular that these populations often experience delays and difficulties in accessing care. Unfortunately, the resolution did not address the unique needs of young adults separately, thus reinforcing a gap in current global cancer control paradigms. There is an opportunity for advocates to directly address this gap, petitioning member states and developing an amendment specific to adolescents and young adults by emphasising the barriers faced by these patients.

The psychosocial challenges adolescents and young adults face is an important issue since these challenges are truly unique across the age spectrum and require resources and skills that are often not available to cancer treatment teams.[25] The age range of adolescents and young adults encompasses their formative years in life and spans the time from completing education, to possibly starting a career and raising children, and potentially contributing to society more broadly. A cancer diagnosis during these years can have a considerable impact on individuals' future life trajectory through major stressors, including feelings of isolation, anxiety and depression, concerns about infertility, discontinuing schooling or work, and financial hardship.[1,12,26–28] Efforts to mitigate the issues distinct to this age group have resulted in the formation of organisations to help support adolescent and young adult patients with cancer. However, although these oncology advocacy efforts focused on adolescents and young adults have been successful in creating awareness campaigns and implementing adolescent and young adult programmes at cancer centres, these efforts have largely been limited to high-income countries.[29] These initiatives need to be expanded globally, particularly in low SDI settings—which carry a disproportionate burden of adolescent and young adult cancer DALYs—with appropriate local knowledge and champions.

The array of cancer types is also unique in adolescents and young adults compared to children and adults. Even what seems to be the same cancer is often biologically different in adolescents and young adults than in patients of other age groups and thereby might benefit from a different approach to therapy.[6] For these and other reasons, survival improvements in adolescent and young adult patients with cancer have lagged behind those of children and adults for several cancer types.[9] Delivery of cancer care to adolescents and young adults should be

A

	Absolute DALYs, millions (95% UI)	Global rank	High SDI rank	High-middle SDI rank	Middle SDI rank	Low-middle SDI rank	Low SDI rank
Mental disorders	56·5 (41·0–74·8)	1	1	1	1	1	1
Self-harm and interpersonal violence	40·5 (37·8–43·4)	2	6	3	4	2	4
Musculoskeletal disorders	39·4 (27·3–52·6)	3	2	2	2	6	13
Other non-communicable diseases	37·5 (27·3–51·8)	4	4	4	5	3	5
Transport injuries	35·7 (32·1–38·7)	5	7	5	3	4	7
Neurological disorders	30·5 (10·8–60·4)	6	5	7	7	9	10
Cardiovascular diseases	29·8 (27·6–32·1)	7	11	8	6	5	9
Unintentional injuries	29·7 (25·9–34·3)	8	8	6	8	8	12
Respiratory infections and tuberculosis	24·3 (21·6–27·1)	9	17	13	11	7	2
Adolescent and young adult cancers	**23·5 (21·9–25·2)**	**10**	**9**	**9**	**9**	**13**	**15**
HIV/AIDS and sexually transmitted infections	23·3 (18·3–30·4)	11	19	16	10	11	3
Substance use disorders	19·8 (15·3–25·0)	12	3	10	15	19	22
Digestive diseases	19·3 (17·1–22·1)	13	13	12	12	10	14
Maternal and neonatal disorders	18·4 (16·3–20·6)	14	15	17	16	12	6
Skin and subcutaneous diseases	15·5 (10·1–23·1)	15	10	11	13	17	19
Diabetes and kidney diseases	13·2 (11·4–15·2)	16	14	15	14	16	18
Enteric infections	12·0 (8·74–16·5)	17	20	20	21	14	11
Neglected tropical diseases and malaria	10·8 (7·65–14·6)	18	22	21	20	18	8
Nutritional deficiencies	10·3 (6·95–14·5)	19	18	19	19	15	16
Sense organ diseases	10·1 (6·52–14·8)	20	16	14	17	20	21
Chronic respiratory diseases	9·04 (7·59–10·8)	21	12	18	18	21	20
Other infectious diseases	6·57 (5·89–7·34)	22	21	22	22	22	17

B

	Absolute deaths (95% UI)	Global rank	High SDI rank	High-middle SDI rank	Middle SDI rank	Low-middle SDI rank	Low SDI rank
Self-harm and interpersonal violence	599 000 (559 000–641 000)	1	1	1	2	1	3
Transport injuries	505 000 (451 000–550 000)	2	2	2	1	3	5
Cardiovascular diseases	456 000 (420 000–494 000)	3	5	4	3	2	6
Adolescent and young adult cancers	**396 000 (370 000–425 000)**	**4**	**4**	**3**	**4**	**7**	**8**
HIV/AIDS and sexually transmitted infections	357 000 (271 000–480 000)	5	13	7	5	5	2
Respiratory infections and tuberculosis	321 000 (292 000–354 000)	6	11	8	7	4	1
Unintentional injuries	321 000 (285 000–351 000)	7	6	5	6	6	10
Digestive diseases	245 000 (224 000–267 000)	8	7	6	8	8	9
Maternal and neonatal disorders	161 000 (140 000–184 000)	9	16	15	11	9	4
Enteric infections	140 000 (93 600–207 000)	10	17	16	12	10	7
Diabetes and kidney diseases	127 000 (117 000–138 000)	11	9	10	9	11	13
Substance use disorders	95 100 (88 300–102 000)	12	3	9	16	17	18
Neglected tropical diseases and malaria	93 600 (54 000–152 000)	13	21	17	14	13	11
Other infectious diseases	87 600 (78 400–98 700)	14	14	14	13	12	12
Other non-communicable diseases	82 800 (74 100–92 900)	15	8	11	10	14	14
Chronic respiratory diseases	58 000 (52 500–64 100)	16	12	13	15	15	15
Neurological disorders	51 700 (47 100–57 700)	17	10	12	17	16	16
Nutritional deficiencies	12 200 (10 500–14 200)	18	19	20	19	18	17
Musculoskeletal disorders	11 100 (9000–13 300)	19	15	18	18	19	19
Skin and subcutaneous diseases	4940 (3450–5740)	20	18	19	20	20	20
Mental disorders	199 (176–257)	21	20	21	21	21	21

***Figure 5*: Ranking of absolute DALYs (A) and deaths (B) due to cancer compared to other disease groups in adolescents and young adults in 2019, for both sexes combined, globally and by SDI**

Disease rank assigned by total absolute DALYs (A) or absolute deaths (B) globally in 2019 in the adolescent and young adult age group (15–39 years), with 1 representing the highest rank. Values in parentheses are 95% uncertainty intervals (UIs). Colour intensity is proportional to rank number (from 1 denoted by dark red to 22 [or 21 in panel B] denoted by dark green). Cancers comprise all malignant neoplasms, excluding non-melanoma skin cancers. Panels A and B included different causes because some causes do not have mortality estimated in this age range. Other non-communicable diseases comprise congenital birth defects; urinary diseases and male infertility; gynaecological diseases; haemoglobinopathies and haemolytic anaemias; endocrine, metabolic, blood, and immune disorders; and oral disorders. Other infectious diseases comprise meningitis, encephalitis, diphtheria, whooping cough, tetanus, measles, varicella and herpes zoster, acute hepatitis, and other unspecified infectious diseases. DALY=disability-adjusted life-year. SDI=Socio-demographic Index.

prioritised and optimised, especially in non-high SDI settings, where the majority of DALYs are reported. At present, adolescent and young adult patients often do not have an obvious health-care home and are frequently grouped into adult oncology service programmes because of age restrictions in paediatric wards or facilities.[12,16,30] Where a patient receives care has important clinical and policy ramifications, as there is evidence of improvement in survival outcomes for some cancer types (eg, acute lymphoblastic leukaemia) when adolescents and young adults are treated according to paediatric protocols, which are often complex and might be unavailable in adult cancer centres.[31,32] Furthermore, treatment by specialised adolescent and young adult oncology teams has been associated with improved survival of adolescents and young adults with cancer in some high-income countries, possibly as a result of access to cancer expertise, clinical trials, and multidisciplinary care.[33] Although access to these centres and programmes is not currently possible in many settings, most adolescent and young adult patients with cancer might benefit from a multidisciplinary treatment approach involving close collaboration between paediatric and medical oncologists.

To improve outcomes in this unique population, a new approach to global cancer control in adolescents and young adults is required. Faced with similar challenges for children and adolescents, the recently launched WHO Global Initiative for Childhood Cancer provides one implementation framework for addressing gaps in access and care. This initiative includes adolescents up to 19 years of age, bridging the lowest ages included in adolescent and young adult oncology, and at least one cancer that predominantly occurs in adolescents and young adults—Hodgkin lymphoma—is an index cancer in this initiative. Although this is excellent news for the younger bounds of the adolescent and young adult spectrum, the Global Initiative for Childhood Cancer initiative covers only 8·6% (95% UI 8·2–9·1) of all adolescent and young adult cancer cases, and the unique needs of and potential synergies with adolescent and young adult cancer care are not specifically addressed. A dedicated initiative similar to the Global Initiative for Childhood Cancer is unlikely in the near future. Therefore, integration of adolescent and young adult cancer policies within WHO cancer initiatives such as the Global Initiative for Childhood Cancer and the WHO Cervical Cancer Elimination Initiative, a cancer that comprises approximately 10·0% (8·5–10·9) of adolescent and young adult cancer cases globally, could be prioritised in the short term. A strategy to integrate specific objectives of relevance to the adolescent and young adult population in these initiatives would immediately cover almost one-fifth of adolescent and young adult cancer cases and provide a template for future global cancer initiatives. Potential areas for collaboration could include integration of human papillomavirus (HPV) vaccination efforts into the Global Initiative for Childhood Cancer, an as-yet untapped opportunity, and inclusion of policies specific to adolescent and young adult patients in the WHO technical packages, such as provisions for referrals and access to expert adolescent and young adult cancer care and appropriate treatment regimens, psychosocial support, and universal health coverage to reduce financial hardship. Intentional collaboration with other WHO cancer initiatives could facilitate progress in both areas and highlight other potential areas of synergy for improving cancer outcomes in adolescents and young adults.

For more on the **WHO Cervical Cancer Elimination Initiative** see https://www.who.int/initiatives/cervical-cancer-elimination-initiative

The adolescent and young adult cancer burden estimates presented in this study also underscore the limitations of GBD and possible opportunities to improve future assessments of the global adolescent and young adult cancer burden.[34] The classification of adolescent and young adult cancers in this study is based on the GBD cancer cause list, which has historically focused on cancers occurring in adulthood. As such, GBD 2019 did not differentiate some of the most common adolescent and young adult cancer types, such as soft tissue sarcomas and bone tumours. These cancers contribute to the substantial proportion of "other malignant neoplasms" in this age range, cancers that do not have their own individual GBD cancer causes. Many of the rarer cancers that fall into this "other malignant neoplasms" category rely on complex multidisciplinary therapy (eg, provided by medical, radiation, and surgical oncologists), and resource allocation could be improved if their global burden was accurately known.[5] Future studies should use the recently updated recommendations for classification of adolescent and young adult cancers to better characterise the cancer burden in this age group and minimise the number of cancer types falling into the "other malignant neoplasms" category.[34] Additionally, the quality of the data obtained, especially from low-resource settings, might cause challenges due to underestimates or miscategorisation of less common cancer types.[10] For instance, there was an observed decrease in the proportion of adolescent and young adult cancer DALYs due to brain and CNS cancers across the SDI spectrum, with the lowest proportion in low SDI settings. As many lower SDI countries do not have population-based cancer registries or robust referral mechanisms, the data upon which these estimates are drawn might be subject to underdiagnosis, misdiagnosis, or under-reporting. Therefore, results in lower SDI settings should be interpreted with caution. However, these modelled results provide a useful contribution towards determining the global burden of adolescent and young adult cancer, especially in regions where such data do not exist or are scarce. An additional limitation of the present analysis is that SDI was applied at the national level, but within-country socio-economic status can vary greatly. Improving global adolescent and young adult cancer burden estimates must be rooted in capacity-building efforts that consider the local context, to ensure identification of

incident cancer cases and deaths in the adolescent and young adult population, as well as expansion of and support for population-based cancer registration systems. Another potential limitation of the present analysis is the current approach to YLD estimation, which accounts for only 10 years after cancer diagnosis. Previous studies have shown that late effects, such as cardiomyopathy, can affect the adolescent and young adult population beyond the 10-year cutoff point.[25,35] This limits the ability to determine the long-term chronic disease burden and competing risks for survivors in this population, which have the potential to be substantial. Additionally, the experience of disability for survivors of childhood cancer might be different to that of the general population. Thus, GBD 2019 might be underestimating the YLDs and DALYs associated with cancer in adolescents and young adults, and future efforts might be needed to identify ways to account for this limitation. Finally, this study focused on estimates from 2019, and thus did not incorporate the direct and indirect effects of the COVID-19 pandemic on the global adolescent and young adult cancer burden. This will be an important area of consideration in future studies as the data become available.

This report of the adolescent and young adult cancer burden from GBD 2019 identified a considerable burden of DALYs due to cancer in the global adolescent and young adult population. The absolute mortality burden in adolescents and young adults is highest in non-high SDI settings, underscoring the need for a global effort to improve outcomes in this population, with collaboration at the regional and country levels, as well as between governments, institutions, academic societies, and patient advocacy and non-profit organisations. Efforts to comprehensively estimate the global burden of cancer in adolescents and young adults are a crucial first step.[10,21] Adolescent and young adult oncology has historically been less prioritised than cancer disciplines in younger and older patients. Increased awareness of the burden of cancer in this population could lead to targeted interventions for improved outcomes.

Contributors

Please see the appendix (pp 127–133) for more detailed information about individual author contributions to the research, divided into the following categories: managing the estimation or publication process; 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; development of 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 overall research enterprise. Members of the core Institute for Health Metrics and Evaluation (IHME) research team (Lisa Force, Christina Fitzmaurice, Jonathan Kocarnik, Weijia Fu, Franny Dean, James Harvey, Rixing Xu, Alyssa Pennini, and Kelly Compton) for this topic area had full access to the underlying data used to generate estimates presented in this Article. All other authors had access to, and reviewed, estimates as part of the GBD and research evaluation process, which includes additional stages of internal IHME and external formal collaborator review. The corresponding author had final responsibility for the decision to submit the manuscript for publication.

GBD 2019 Adolescent and Young Adult Cancer Collaborators

Elysia M Alvarez*, Lisa M Force*, Rixing Xu, Kelly Compton, Dan Lu, Hannah Jacqueline Henrikson, Jonathan M Kocarnik, James D Harvey, Alyssa Pennini, Frances E Dean, Weijia Fu, Martina T Vargas, Theresa H M Keegan, Hany Ariffin, Ronald D Barr, Yana Arturovna Erdomaeva, D Sanjeeva Gunasekera, Yetunde O John-Akinola, Tyler G Ketterl, Tezer Kutluk, Marcio Henrique Malogolowkin, Prashant Mathur, Venkatraman Radhakrishnan, Lynn Ann Gloeckler Ries, Carlos Rodriguez-Galindo, Garik Barisovich Sagoyan, Iyad Sultan, Behzad Abbasi, Mohsen Abbasi-Kangevari, Zeinab Abbasi-Kangevari, Hedayat Abbastabar, Michael Abdelmasseh, Sherief Abd-Elsalam, Amir Abdoli, Haimanot Abebe, Aidin Abedi, Hassan Abidi, Hassan Abolhassani, Hiwa Abubaker Ali, Eman Abu-Gharbieh, Basavaprabhu Achappa, Juan Manuel Acuna, Isaac Akinkunmi Adedeji, Oyelola A Adegboye, Qorinah Estiningtyas Sakilah Adnani, Shailesh M Advani, Muhammad Sohail Afzal, Mohamad Aghaie Meybodi, Bahman Ahadinezhad, Bright Opoku Ahinkorah, Sajjad Ahmad, Sepideh Ahmadi, Muktar Beshir Ahmed, Tarik Ahmed Rashid, Yusra Ahmed Salih, Wajeeha Aiman, Gizachew Taddesse Akalu, Hanadi Al Hamad, Fares Alahdab, Abdulhadi A AlAmodi, Fahad Mashhour Alanezi, Turki M Alanzi, Adugnaw Zeleke Alem, Dejene Tsegaye Alem, Yosef Alemayehu, Fadwa Naji Alhalaiqa, Robert Kaba Alhassan, Saqib Ali, Gianfranco Alicandro, Vahid Alipour, Syed Mohamed Aljunid, Motasem Alkhayyat, Sunitha Alluri, Nihad A Almasri, Sadeq Ali Al-Maweri, Sami Almustanyir, Rajaa M Al-Raddadi, Nelson Alvis-Guzman, Edward Kwabena Ameyaw, Saeed Amini, Hubert Amu, Robert Ancuceanu, Catalina Liliana Andrei, Tudorel Andrei, Fereshteh Ansari, Alireza Ansari-Moghaddam, Davood Anvari, Anayochukwu Edward Anyasodor, Jalal Arabloo, Morteza Arab-Zozani, Ayele Mamo Argaw, Muhammad Arshad, Judie Arulappan, Armin Aryannejad, Zatollah Asemi, Mohammad Asghari Jafarabadi, Mohammad Reza Atashzar, Prince Atorkey, Alok Atreya, Sameh Attia, Avinash Aujayeb, Marcel Ausloos, Leticia Avila-Burgos, Atalel Fentahun Awedew, Beatriz Paulina Ayala Quintanilla, Alemu Degu Ayele, Solomon Shitu Ayen, Mohammed A Azab, Sina Azadnajafabad, Hiva Azami, Mohammadreza Azangou-Khyavy, Amirhossein Azari Jafari, Ghasem Azarian, Ahmed Y Azzam, Saeed Bahadory, Jianjun Bai, Atif Amin Baig, Jennifer L Baker, Maciej Banach, Till Winfried Bärnighausen, Francesco Barone-Adesi, Fabio Barra, Amadou Barrow, Huda Basaleem, Abdul-Monim Mohammad Batiha, Masoud Behzadifar, Niguss Cherie Bekele, Rebuma Belete, Uzma Iqbal Belgaumi, Arielle Wilder Bell, Alemshet Yirga Berhie, Devidas S Bhagat, Akshaya Srikanth Bhagavathula, Nikha Bhardwaj, Pankaj Bhardwaj, Sonu Bhaskar, Krittika Bhattacharyya, Vijayalakshmi S Bhojaraja, Sadia Bibi, Ali Bijani, Antonio Biondi, Setognal Birara, Tone Bjørge, Obasanjo Afolabi Bolarinwa, Srinivasa Rao Bolla, Archith Boloor, Dejana Braithwaite, Hermann Brenner, Norma B Bulamu, Katrin Burkart, Maria Teresa Bustamante-Teixeira, Nadeem Shafique Butt, Zahid A Butt, Florentino Luciano Caetano dos Santos, Chao Cao, Yin Cao, Giulia Carreras, Ferrán Catalá-López, Francieli Cembranel, Ester Cerin, Raja Chandra Chakinala, Promit Ananyo Chakraborty, Vijay Kumar Chattu, Pankaj Chaturvedi, Akhilanand Chaurasia, Prachi P Chavan, Odgerel Chimed-Ochir, Jee-Young Jasmine Choi, Devasahayam J Christopher, Dinh-Toi Chu, Michael T Chung, Joao Conde, Vera Marisa Costa, Omar B Da'ar, Omid Dadras, Saad M A Dahlawi, Xiaochen Dai, Giovanni Damiani, Emanuele D'Amico, Lalit Dandona, Rakhi Dandona, Parnaz Daneshpajouhnejad, Amira Hamed Darwish, Ahmad Daryani, Fernando Pio De la Hoz, Sisay Abebe Debela, Takele Gezahegn G Demie, Getu Debalkie Demissie, Zeleke Geto Demissie, Edgar Denova-Gutiérrez, Meseret Derbew Molla, Rupak Desai, Abebaw Alemayehu Desta, Deepak Dhamnetiya, Samath Dhamminda Dharmaratne, Mandira Lamichhane Dhimal, Meghnath Dhimal, Mostafa Dianatinasab, Mojtaba Didehdar, Mengistie Diress, Shirin Djalalinia, Huyen Phuc Do, Saeid Doaei, Fariba Dorostkar, Wendel Mombaque dos Santos, Thomas M Drake, Michael Ekholuenetale, Iman El Sayed, Maysaa El Sayed Zaki,

Maha El Tantawi, Hassan El-Abid, Mostafa Ahmed Elbahnasawy, Iffat Elbarazi, Hala Rashad Elhabashy, Muhammed Elhadi, Shaimaa I El-Jaafary, Daniel Berhanie Enyew, Ryenchindorj Erkhembayar, Babak Eshrati, Sharareh Eskandarieh, Mohammed Faisaluddin, Jawad Fares, Umar Farooque, Abidemi Omolara Fasanmi, Wafa Fatima, José Miguel P Ferreira de Oliveira, Simone Ferrero, Lorenzo Ferro Desideri, Getahun Fetensa, Irina Filip, Florian Fischer, James L Fisher, Masoud Foroutan, Takeshi Fukumoto, Peter Andras Gaal, Mohamed M Gad, Piyada Gaewkhiew, Silvano Gallus, Tushar Garg, Teferi Gebru Gebremeskel, Belete Negese Belete Gemeda, Tamiru Getachew, Mansour Ghafourifard, Seyyed-Hadi Ghamari, Ahmad Ghashghaee, Fariba Ghassemi, Nermin Ghith, Ali Gholami, Jamshid Gholizadeh Navashenaq, Syed Amir Gilani, Themba G Ginindza, Abraham Tamirat Gizaw, James C Glasbey, Amit Goel, Mahaveer Golechha, Pouya Goleij, Davide Golinelli, Sameer Vali Gopalani, Giuseppe Gorini, Houman Goudarzi, Bárbara Niegia Garcia Goulart, Ayman Grada, Mohammed Ibrahim Mohialdeen Gubari, Maximiliano Ribeiro Guerra, Avirup Guha, Bhawna Gupta, Sapna Gupta, Veer Bala Gupta, Vivek Kumar Gupta, Rasool Haddadi, Nima Hafezi-Nejad, Alemayehu Hailu, Arvin Haj-Mirzaian, Rabih Halwani, Randah R Hamadeh, Mitiku Teshome Hambisa, Sajid Hameed, Samer Hamidi, Shafiul Haque, Sanam Hariri, Josep Maria Haro, Ahmed I Hasaballah, S M Mahmudul Hasan, Seyedeh Melika Hashemi, Treska S Hassan, Soheil Hassanipour, Simon I Hay, Khezar Hayat, Sultan H Hebo, Golnaz Heidari, Mohammad Heidari, Brenda Yuliana Herrera-Serna, Claudiu Herteliu, Demisu Zenbaba Heyi, Kamal Hezam, Michael K Hole, Ramesh Holla, Nobuyuki Horita, Md Mahbub Hossain, Mohammad Bellal Hossain, Mohammad-Salar Hosseini, Mostafa Hosseini, Ali Hosseinzadeh, Mehdi Hosseinzadeh, Mihaela Hostiuc, Sorin Hostiuc, Mowafa Househ, Mohamed Hsairi, Junjie Huang, Nawfal R Hussein, Bing-Fang Hwang, Segun Emmanuel Ibitoye, Olayinka Stephen Ilesanmi, Irena M Ilic, Milena D Ilic, Kaire Innos, Lalu Muhammad Irham, Rakibul M Islam, Sheikh Mohammed Shariful Islam, Nahlah Elkudssiah Ismail, Gaetano Isola, Masao Iwagami, Louis Jacob, Farhad Jadidi-Niaragh, Vardhmaan Jain, Mihajlo Jakovljevic, Roksana Janghorban, Amirreza Javadi Mamaghani, Shubha Jayaram, Ranil Jayawardena, Seyed Behzad Jazayeri, Rime Jebai, Ravi Prakash Jha, Tamas Joo, Nitin Joseph, Farahnaz Joukar, Mikk Jürisson, Billingsley Kaambwa, Ali Kabir, Leila R Kalankesh, Feroze Kaliyadan, Zul Kamal, Ashwin Kamath, Himal Kandel, Sitanshu Sekhar Kar, Ibraheem M Karaye, Amirali Karimi, Bekalu Getnet Kassa, Joonas H Kauppila, Phillip M Kemp Bohan, Andre Pascal Kengne, Amene Abebe Kerbo, Mohammad Keykhaei, Yousef Saleh Khader, Himanshu Khajuria, Nastaran Khalili, Neda Khalili, Ejaz Ahmad Khan, Gulfaraz Khan, Maseer Khan, Md Nuruzzaman Khan, Moien AB Khan, Javad Khanali, Maryam Khayamzadeh, Omid Khosravizadeh, Jagdish Khubchandani, Roba Khundkar, Min Seo Kim, Yun Jin Kim, Adnan Kisa, Sezer Kisa, Katarzyna Kissimova-Skarbek, Ali-Asghar Kolahi, Jacek A Kopec, Rajasekaran Koteeswaran, Sindhura Lakshmi Koulmane Laxminarayana, Ai Koyanagi, Nuworza Kugbey, G Anil Kumar, Nithin Kumar, Alexander Kwarteng, Carlo La Vecchia, Qing Lan, Iván Landires, Savita Lasrado, Paolo Lauriola, Caterina Ledda, Sang-woong Lee, Wei-Chen Lee, Yeong Yeh Lee, Yo Han Lee, James Leigh, Elvynna Leong, Bingyu Li, Jiarui Li, Ming-Chieh Li, Stephen S Lim, Xuefeng Liu, Stany W Lobo, Joana A Loureiro, Alessandra Lugo, Raimundas Lunevicius, Hassan Magdy Abd El Razek, Muhammed Magdy Abd El Razek, Morteza Mahmoudi, Azeem Majeed, Alaa Makki, Shilpa Male, Mohammad-Reza Malekpour, Reza Malekzadeh, Ahmad Azam Malik, Mohammed A Mamun, Navid Manafi, Fariborz Mansour-Ghanaei, Borhan Mansouri, Mohammad Ali Mansournia, Santi Martini, Seyedeh Zahra Masoumi, Clara N Matei, Manu Raj Mathur, Colm McAlinden, Ravi Mehrotra, Walter Mendoza, Ritesh G Menezes, Alexios-Fotios A Mentis, Tuomo J Meretoja, Amanual Getnet Mersha, Mohamed Kamal Mesregah, Tomislav Mestrovic, Junmei Miao Jonasson, Bartosz Miazgowski, Irmina Maria Michalek, Ted R Miller, Alemu Basazin Mingude, Seyyedmohammadsadeq Mirmoeeni, Hamed Mirzaei, Sanjeev Misra, Prasanna Mithra, Karzan Abdulmuhsin Mohammad, Mokhtar Mohammadi, Seyyede Momeneh Mohammadi, Abdollah Mohammadian-Hafshejani, Reza Mohammadpourhodki, Arif Mohammed, Shafiu Mohammed, Teroj Abdulrahman Mohammed, Nagabhishek Moka, Ali H Mokdad, Mariam Molokhia, Sara Momtazmanesh, Lorenzo Monasta, Mohammad Ali Moni, Ghobad Moradi, Yousef Moradi, Maliheh Moradzadeh, Rahmatollah Moradzadeh, Paula Moraga, Shane Douglas Morrison, Ebrahim Mostafavi, Amin Mousavi Khaneghah, Christine Mpundu-Kaambwa, Sumaira Mubarik, Lillian Mwanri, Ashraf F Nabhan, Shankar Prasad Nagaraju, Chie Nagata, Mohsen Naghavi, Mukhammad David Naimzada, Luigi Naldi, Vinay Nangia, Atta Abbas Naqvi, Sreenivas Narasimha Swamy, Aparna Ichalangod Narayana, Biswa Prakash Nayak, Vinod C Nayak, Javad Nazari, Sabina Onyinye Nduaguba, Ionut Negoi, Serban Mircea Negru, Seyed Aria Nejadghaderi, Samata Nepal, Sandhya Neupane Kandel, Haruna Asura Nggada, Cuong Tat Nguyen, Chukwudi A Nnaji, Hamed Nosrati, Hasti Nouraei, Ali Nowroozi, Virginia Nuñez-Samudio, Vincent Ebuka Nwatah, Chimezie Igwegbe Nzoputam, Bogdan Oancea, Oluwakemi Ololade Odukoya, Ayodipupo Sikiru Oguntade, In-Hwan Oh, Andrew T Olagunju, Tinuke O Olagunju, Babayemi Oluwaseun Olakunde, Mojisola Morenike Oluwasanu, Emad Omar, Ahmed Omar Bali, Sokking Ong, Obinna E Onwujekwe, Doris V Ortega-Altamirano, Nikita Otstavnov, Stanislav S Otstavnov, Bilcha Oumer, Mayowa O Owolabi, Mahesh P A, Alicia Padron-Monedero, Jagadish Rao Padubidri, Keyvan Pakshir, Adrian Pana, Anamika Pandey, Shahina Pardhan, Fatemeh Pashazadeh Kan, Maja Pasovic, Jenil R Patel, Siddhartha Pati, Sanjay M Pattanshetty, Uttam Paudel, Renato B Pereira, Mario F P Peres, Arokiasamy Perianayagam, Maarten J Postma, Hadi Pourjafar, Akram Pourshams, Akila Prashant, Thejodhar Pulakunta, Mirza Muhammad Fahd Fahd Qadir, Mohammad Rabiee, Navid Rabiee, Amir Radfar, Raghu Anekal Radhakrishnan, Ata Rafiee, Alireza Rafiei, Sima Rafiei, Fakher Rahim, Shadi Rahimzadeh, Mosiur Rahman, Muhammad Aziz Rahman, Amir Masoud Rahmani, Aashish Rajesh, Vajiheh Ramezani-Doroh, Kamal Ranabhat, Priyanga Ranasinghe, Chythra R Rao, Sowmya J Rao, Sina Rashedi, Mahsa Rashidi, Mohammad-Mahdi Rashidi, Goura Kishor Rath, David Laith Rawaf, Salman Rawaf, Lal Rawal, Reza Rawassizadeh, Mohammad Sadegh Razeghinia, Misganu Teshoma Regasa, Andre M N Renzaho, Maryam Rezaei, Negar Rezaei, Nima Rezaei, Mohsen Rezaeian, Aziz Rezapour, Sahba Rezazadeh-Khadem, Abanoub Riad, Ligia Estefania Rios Lopez, Jefferson Antonio Buendia Rodriguez, Luca Ronfani, Gholamreza Roshandel, Godfrey M Rwegerera, Maha Mohamed Saber-Ayad, Siamak Sabour, Basema Saddik, Erfan Sadeghi, Saeid Sadeghian, Umar Saeed, Amirhossein Sahebkar, KM Saif-Ur-Rahman, S Mohammad Sajadi, Sarvenaz Salahi, Sana Salehi, Marwa Rashad Salem, Hamideh Salimzadeh, Abdallah M Samy, Juan Sanabria, Francesco Sanmarchi, Arash Sarveazad, Brijesh Sathian, Monika Sawhney, Susan M Sawyer, Mete Saylan, Ione Jayce Ceola Schneider, Abdul-Aziz Seidu, Mario Šekerija, Endalew Gemechu Sendo, Sadaf G Sepanlou, Allen Seylani, Kenbon Seyoum, Feng Sha, Omid Shafaat, Masood Ali Shaikh, Erfan Shamsoddin, Mohammed Shannawaz, Rajesh Sharma, Sara Sheikhbahaei, Adithi Shetty, B Suresh Kumar Shetty, Pavanchand H Shetty, Jae Il Shin, Reza Shirkoohi, K M Shivakumar, Parnian Shobeiri, Soraya Siabani, Migbar Mekonnen Sibhat, Sudeep K Siddappa Malleshappa, Negussie Boti Sidemo, Diego Augusto Santos Silva, Guilherme Silva Julian, Achintya Dinesh Singh, Jasvinder A Singh, Jitendra Kumar Singh, Surjit Singh, Abiy H Sinke, Yitagesu Sintayehu, Valentin Yurievich Skryabin, Anna Aleksandrovna Skryabina, Lee Smith, Ahmad Sofi-Mahmudi, Mohammad Sadegh Soltani-Zangbar, Suhang Song, Emma Elizabeth Spurlock, Paschalis Steiropoulos, Kurt Straif, Ranjeeta Subedi, Mu'awiyyah Babale Sufiyan, Rizwan Suliankatchi Abdulkader, Saima Sultana, Viktória Szerencsés, Miklós Szócska, Seidamir Pasha Tabaeian, Rafael Tabarés-Seisdedos, Mohammadreza Tabary, Takahiro Tabuchi, Hooman Tadbiri, Majid Taheri, Amir Taherkhani, Ken Takahashi, Mircea Tampa, Ker-Kan Tan, Vivian Y Tat, Ahmad Tavakoli, Abdelghani Tbakhi, Arash Tehrani-Banihashemi, Mohamad-Hani Temsah, Fisaha Haile Tesfay, Bekele Tesfaye, Jarnail Singh Thakur, Rekha Thapar, Aravind Thavamani, Arulmani Thiyagarajan, Nihal Thomas, Ruoyan Tobe-Gai, Munkhsaikhan Togtmol, Seyed Abolfazl Tohidast, Hamid Reza Tohidinik,

Musliu Adetola Tolani, Daniel Nigusse Tollosa, Mathilde Touvier, Marcos Roberto Tovani-Palone, Eugenio Traini, Bach Xuan Tran, Mai Thi Ngoc Tran, Jaya Prasad Tripathy, Biruk Shalmeno Tusa, Gebresilasea Gendisha Ukke, Irfan Ullah, Saif Ullah, Krishna Kishore Umapathi, Bhaskaran Unnikrishnan, Era Upadhyay, Tolassa Wakayo Ushula, Marco Vacante, Sahel Valadan Tahbaz, Shoban Babu Varthya, Massimiliano Veroux, Paul J Villeneuve, Francesco S Violante, Vasily Vlassov, Giang Thu Vu, Yasir Waheed, Ning Wang, Paul Ward, Adisu Birhanu Weldesenbet, Yi Feng Wen, Ronny Westerman, Andrea Sylvia Winkler, Befikadu Legesse Wubishet, Suowen Xu, Seyed Hossein Yahyazadeh Jabbari, Lin Yang, Sanni Yaya, Vahid Yazdi-Feyzabadi, Taklo Simeneh Yazie, Sisay Shewasinad Yehualashet, Alex Yeshaneh, Yigizie Yeshaw, Birhanu Wubale Yirdaw, Naohiro Yonemoto, Mustafa Z Younis, Zabihollah Yousefi, Chuanhua Yu, Ismaeel Yunusa, Vesna Zadnik, Mazyar Zahir, Telma Zahirian Moghadam, Mohammad Zamani, Maryam Zamanian, Hamed Zandian, Fariba Zare, Mikhail Sergeevich Zastrozhin, Anasthasia Zastrozhina, Jianrong Zhang, Zhi-Jiang Zhang, Arash Ziapour, Mohammad Zoladl, Christopher J L Murray, Christina Fitzmaurice, Archie Bleyer†, and Nickhill Bhakta†.

* co-first authors

† co-senior authors

Affiliations

Department of Pediatrics (E M Alvarez MD, M H Malogolowkin MD), Department of Internal Medicine (T H M Keegan PhD), University of California Davis, Sacramento, CA, USA; Department of Health Metrics Sciences, School of Medicine (L M Force MD, K Burkart PhD, X Dai PhD, Prof R Dandona PhD, Prof S D Dharmaratne MD, Prof S I Hay DSc, Prof S S Lim PhD, A H Mokdad PhD, Prof M Naghavi MD, Prof C J L Murray DPhil), Division of Pediatric Hematology-Oncology (L M Force MD), Institute for Health Metrics and Evaluation (L M Force MD, R Xu BS, K Compton BS, D Lu MA, H J Henrikson BA, J M Kocarnik PhD, J D Harvey BS, A Pennini MSc, F E Dean BA, W Fu MSc, M T Vargas MLS, K Burkart PhD, X Dai PhD, Prof L Dandona MD, Prof R Dandona PhD, Prof S D Dharmaratne MD, Prof S I Hay DSc, Prof S S Lim PhD, A H Mokdad PhD, Prof M Naghavi MD, M Pasovic MEd, E E Spurlock MPH, Prof C J L Murray DPhil, C Fitzmaurice MD), Department of Pediatrics (T G Ketterl MD), Division of Hematology (C Fitzmaurice MD), University of Washington, Seattle, WA, USA; Department of Dermatology (A Grada MD), Department of Computer Science (R Rawassizadeh PhD), Boston University, Boston, MA, USA; Department of Paediatrics (Prof H Ariffin MD), University of Malaya Medical Centre (Prof H Ariffin MD), University of Malaya, Kuala Lumpur, Malaysia; Department of Pediatrics (Prof R D Barr MD), Department of Psychiatry and Behavioural Neurosciences (A T Olagunju MD), Department of Pathology and Molecular Medicine (T O Olagunju MD), McMaster University, Hamilton, ON, Canada; Oncology Department (Y A Erdomaeva MD), Children Republican Clinical Hospital, Ulan-Ude, Russia; Department of Paediatrics (D S Gunasekera MD), National Cancer Institute, Maharagama, Sri Lanka; Department of Health Promotion and Education (Y O John-Akinola PhD, S E Ibitoye MPH, M M Oluwasanu PhD), Department of Epidemiology and Medical Statistics (M Ekholuenetale MSc), Faculty of Public Health (M Ekholuenetale MSc), Department of Community Medicine (O S Ilesanmi PhD), Department of Medicine (Prof M O Owolabi DrM), University of Ibadan, Ibadan, Nigeria; Division of Pediatric Hematology/Oncology (T G Ketterl MD), Seattle Children's Hospital, Seattle, WA, USA; Pediatric Oncologist Department of Surgery No. 2 (Tumors of Thoracoabdominal Localization) (G B Sagoyan MD), N.N. Blokhin National Medical Research Center of Oncology, Moscow, Russia; Department of Pediatric Oncology (Prof T Kutluk MD), Hacettepe University, Ankara, Turkey; National Centre for Disease Informatics and Research (P Mathur PhD), Indian Council of Medical Research, Bengaluru, India; Department of Medical Oncology (Prof V Radhakrishnan MD), Cancer Institute (W.I.A), Chennai, India; RiesSearch LLC, Rockville, MD, USA (L A G Ries MS); Department of Global Pediatric Medicine (Prof C Rodriguez-Galindo MD, N Bhakta MD), Department of Oncology (Prof C Rodriguez-Galindo MD, N Bhakta MD), St. Jude Children's Research Hospital, Memphis, TN, USA; Pediatric Services (I Sultan MD), Department of Cell Therapy and Applied Genomics (A Tbakhi MD), King Hussein Cancer Center, Amman, Jordan; Department of Pediatrics (I Sultan MD), Department of Physiotherapy (Prof N A Almasri PhD), University of Jordan, Amman, Jordan; Uro-oncology Research Center (B Abbasi MD), Non-communicable Diseases Research Center (Z Abbasi-Kangevari BSc, A Aryannejad MD, S Azadnajafabad MD, M Azangou-Khyavy MD, S Ghamari MD, M Keykhaei MD, J Khanali MD, M Malekpour MD, S Momtazmanesh MD, M Rashidi MD, N Rezaei PhD, S Rezazadeh-Khadem MD), Advanced Diagnostic and Interventional Radiology Research Center (H Abbastabar PhD), Research Center for Immunodeficiencies (H Abolhassani PhD, Prof N Rezaei PhD), Experimental Medicine Research Center (A Aryannejad MD), Iranian Research Center for HIV/AIDS (IRCHA) (O Dadras DrPH), Multiple Sclerosis Research Center (S Eskandarieh PhD), Department of Ophthalmology (Prof F Ghassemi MD), School of Medicine (N Hafezi-Nejad MD, S Hashemi MD, A Karimi, N Khalili MD, N Khalili MD, A Nowroozi BMedSc), Digestive Diseases Research Institute (S Hariri MD, Prof R Malekzadeh MD, Prof A Pourshams MD, H Salimzadeh PhD, S G Sepanlou MD), Department of Epidemiology and Biostatistics (Prof M Hosseini PhD, M Mansournia PhD), Pediatric Chronic Kidney Disease Research Center (Prof M Hosseini PhD), Students' Scientific Research Center (SSRC) (M Keykhaei MD), Metabolomics and Genomics Research Center (F Rahim PhD), Department of Cardiology (S Rashedi MD), Endocrinology and Metabolism Research Institute (N Rezaei PhD), Cancer Research Center (R Shirkoohi PhD), Cancer Biology Research Center (R Shirkoohi PhD), Faculty of Medicine (P Shobeiri MD), Department of Pharmacology (M Zahir MD), Tehran University of Medical Sciences, Tehran, Iran; Reproductive Biomedicine Research Center (B Abbasi MD), Royan Institution, Isfahan, Iran; Social Determinants of Health Research Center (M Abbasi-Kangevari MD, Z Abbasi-Kangevari BSc, M Azangou-Khyavy MD, S Ghamari MD, J Khanali MD, A Kolahi MD, M Rashidi MD), School of Advanced Technologies in Medicine (S Ahmadi PhD), Department of Community Nutrition (S Doaei PhD), Department of Pharmacology (A Haj-Mirzaian MD), Obesity Research Center (A Haj-Mirzaian MD), Department of Parasitology (A Javadi Mamaghani PhD), Department of Health & Community Medicine (A Kolahi MD), School of Medicine (S Nejadghaderi MD), Department of Epidemiology (S Sabour PhD), Medical Ethics and Law Research Center (M Taheri PhD), Shahid Beheshti University of Medical Sciences, Tehran, Iran (M Khayamzadeh MD); Department of Surgery (M Abdelmasseh MD, Prof J Sanabria MD), Marshall University, Huntington, WV, USA; Department of Tropical Medicine (S Abd-Elsalam PhD), Department of Pediatrics (A H Darwish MD), Tanta University, Tanta, Egypt; Zoonoses Research Center (A Abdoli PhD), Jahrom University of Medical Sciences, Jahrom, Iran; Master of Public Health in Reproductive Health (H Abebe MPH), Department of Midwifery (A Yeshaneh MSc), Wolkite University, Wolkite, Ethiopia; Department of Neurosurgery (A Abedi MD), Keck School of Medicine (A Abedi MD), Department of Radiology (S Salehi MD), University of Southern California, Los Angeles, CA, USA; Laboratory Technology Sciences Department (H Abidi PhD), Yasouj University, Yasuj, Iran; Department of Biosciences and Nutrition (H Abolhassani PhD), Karolinska University Hospital, Huddinge, Sweden; Department of Computer Science (M Hosseinzadeh PhD), Diplomacy and Public Relations Department (A Omar Bali PhD), University of Human Development, Sulaymaniyah, Iraq (Prof H Abubaker Ali PhD); Clinical Sciences Department (E Abu-Gharbieh PhD, Prof R Halwani PhD, M M Saber-Ayad MD), College of Medicine (Prof R Halwani PhD), Mass Communication Department (A Makki PhD), Sharjah Institute for Medical Research (B Saddik PhD), University of Sharjah, Sharjah, United Arab Emirates; Department of Internal Medicine (B Achappa MD, A Boloor MD), Department of Community Medicine (N Joseph MD, N Kumar MD, P Mithra MD, R Thapar MD), Department of Obstetrics and Gynaecology (A Shetty MS), Department of Forensic Medicine and Toxicology (Prof B K Shetty MD, P H Shetty MD), Kasturba Medical College (Prof B Unnikrishnan MD), Manipal Academy of Higher Education, Mangalore, India; Department of Epidemiology and

Population Health (Prof J M Acuna MD), Khalifa University, Abu Dhabi, United Arab Emirates; FIU Robert Stempel College of Public Health & Social Work (Prof J M Acuna MD), Department of Epidemiology (R Jebai MPH), Florida International University, Miami, FL, USA; Department of Sociology (I A Adedeji PhD), Olabisi Onabanjo University, Ago-Iwoye, Nigeria; Division of Public Health and Tropical Medicine (O A Adegboye PhD), James Cook University, Towsville, QLD, Australia; Faculty of Medicine (Q E S Adnani PhD), Universitas Padjadjaran (Padjadjaran University), Bandung, Indonesia; Terasaki Institute for Biomedical Innovation, Los Angeles, CA, USA (S M Advani PhD); School of Medicine (S M Advani PhD), Georgetown University, Washington, DC, USA; Department of Life Sciences (M S Afzal PhD), University of Management and Technology, Lahore, Pakistan; Department of Medicine (M Aghaie Meybodi MD), Rutgers University, Newark, NJ, USA; Social Determinants of Health Research Center (B Ahadinezhad PhD, O Khosravizadeh PhD, S Rafiei PhD), Research Institute for Prevention of Non-Communicable Diseases (B Ahadinezhad PhD, O Khosravizadeh PhD), Qazvin University of Medical Sciences, Qazvin, Iran; The Australian Centre for Public and Population Health Research (ACPPHR) (B O Ahinkorah MPH, E K Ameyaw MPhil), School of Health (S Siabani PhD), University of Technology Sydney, Sydney, NSW, Australia; Department of Health and Biological Sciences (S Ahmad PhD), Abasyn University, Peshawar, Pakistan; Department of Epidemiology (M B Ahmed MPH), Department of Health, Behavior and Society (A T Gizaw MPH), Department of Dietetics and Nutrition (T W Ushula MSc), Jimma University, Jimma, Ethiopia; Australian Center for Precision Health (M B Ahmed MPH), University of South Australia, Adelaide, SA, Australia; Department of Computer Science and Engineering (T Ahmed Rashid PhD), University of Kurdistan Hewler, Erbil, Iraq; Database Technology Department (Y Ahmed Salih PhD), College of Informatics (Y Ahmed Salih PhD), Sulaimani Polytechnic University, Sulaymaniyah, Iraq; Department of Neurology (W Aiman MD), Nishtar Medical University, Multan, Pakistan; Department of Microbiology, Immunology and Parasitology (G T Akalu MSc), Public Health Department (T G Demie MPH), St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia; Department of Microbial, Cellular and Molecular Biology (G T Akalu MSc), Department of Surgery (A F Awedew MD), College of Health Sciences (E G Sendo PhD), School of Nursing and Midwifery (E G Sendo PhD), Addis Ababa University, Addis Ababa, Ethiopia; Geriatric and Long Term Care Department (H Al Hamad MD, B Sathian PhD), Rumailah Hospital (H Al Hamad MD), Hamad Medical Corporation, Doha, Qatar; Mayo Evidence-based Practice Center (F Alahdab MSc), Mayo Clinic Foundation for Medical Education and Research, Rochester, MN, USA; Department of Epidemiology and Biostatistics (A A AlAmodi MS), Department of Health Policy and Management (Prof M Z Younis PhD), Jackson State University, Jackson, MS, USA; Health Information Management and Technology Department (T M Alanzi PhD), Environmental Health Department (S M A Dahlawi PhD), Forensic Medicine Division (Prof R G Menezes MD), Pharmacy Practice Department (A Naqvi PhD), Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia (F M Alanezi PhD); Department of Epidemiology and Biostatistics (A Z Alem MPH, Y Yeshaw MPH), Institute of Public Health (G D Demissie MPH), Department of Biochemistry (M Derbew Molla MSc), Department of Surgical Nursing (A A Desta MSc), Department of Human Physiology (M Diress MSc), School of Medicine (A G Mersha MD), Department of Midwifery (B W Yirdaw MSc), University of Gondar, Gondar, Ethiopia; Department of Nursing (D T Alem MSc), Debre Markos University, Debremarkos, Ethiopia; Department of Midwifery (Y Alemayehu MSc, B Oumer MPH, G G Ukke MSc), Department of Biomedical Science (T Getachew MSc), Department of Public Health (S H Hebo MPH), Arba Minch College of Health Science (B Oumer MPH), School of Public Health (N B Sidemo MPH), College of Medicine and Health Science (N B Sidemo MPH), Arba Minch University, Arba Minch, Ethiopia; Faculty of Nursing (F N Alhalaiqa PhD, Prof A M Batiha PhD), Philadelphia University, Amman, Jordan; Psychological Sciences Association, Amman, Jordan (F N Alhalaiqa PhD); Institute of Health Research (R K Alhassan PhD), Department of Population and Behavioural Sciences (H Amu PhD), University of Health and Allied Sciences, Ho, Ghana; Department of Information Systems (S Ali PhD), Department of Maternal and Child Health (J Arulappan DSc), Sultan Qaboos University, Muscat, Oman; Department of Pathophysiology and Transplantation (G Alicandro PhD), Università degli Studi di Milano (University of Milan), Milan, Italy; Cystic Fibrosis Center (G Alicandro PhD), Fondazione IRCCS Ospedale Maggiore Policlinico (IRCCS "Ca' Granda Maggiore Policlinico" Hospital Foundation), Milan, Italy; Health Management and Economics Research Center (V Alipour PhD, J Arabloo PhD, A Ghashghaee BSc, A Rezapour PhD), Department of Health Economics (V Alipour PhD), Department of Medical Laboratory Sciences (F Dorostkar PhD), Preventive Medicine and Public Health Research Center (B Eshrati PhD, A Tehrani-Banihashemi PhD), Student Research Committee (A Ghashghaee BSc), Minimally Invasive Surgery Research Center (A Kabir MD, S Salahi MD), Colorectal Research Center (A Sarveazad PhD), Department of Internal Medicine (S Tabaeian MD), Trauma and Injury Research Center (M Taheri PhD), Research Center of Pediatric Infectious Diseases (A Tavakoli PhD), Department of Medical Virology (A Tavakoli PhD), Department of Community and Family Medicine (A Tehrani-Banihashemi PhD), Iran University of Medical Sciences, Tehran, Iran (F Pashazadeh Kan BSN); Department of Health Policy and Management (Prof S M Aljunid PhD), Kuwait University, Safat, Kuwait; International Centre for Casemix and Clinical Coding (Prof S M Aljunid PhD), National University of Malaysia, Bandar Tun Razak, Malaysia; Department of Internal Medicine (M Alkhayyat MD, V Jain MD, A D Singh MD), Department of Cardiovascular Medicine (M M Gad MD), Lerner Research Institute (X Liu PhD), Cleveland Clinic, Cleveland, OH, USA; Division of Hematology-Oncology (S Alluri MD), University of Massachusetts Medical School, Springfield, MA, USA; College of Dental Medicine (S A Al-Maweri PhD), Qatar University, Doha, Qatar; Faculty of Dentistry (S A Al-Maweri PhD), Sana'a University, Sanaa, Yemen; College of Medicine (S Almustanyir MD), Alfaisal University, Riyadh, Saudi Arabia; Ministry of Health, Riyadh, Saudi Arabia (S Almustanyir MD); Department of Family and Community Medicine (R M Al-Raddadi PhD, N S Butt PhD), Rabigh Faculty of Medicine (A A Malik PhD), King Abdulaziz University, Jeddah, Saudi Arabia; 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 Health Services Management (S Amini PhD), Khomein University of Medical Sciences, Khomein, Iran; Department of Pharmacy (Prof R Ancuceanu PhD), Department of Cardiology (C Andrei PhD), Department of Internal Medicine (M Hostiuc PhD), Department of Legal Medicine and Bioethics (S Hostiuc PhD), Department of Dermatology (C N Matei PhD, M Tampa PhD), Department of General Surgery (I Negoi PhD), Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; Department of Statistics and Econometrics (Prof T Andrei PhD, Prof M Ausloos PhD, Prof C Herteliu PhD, A Pana MD), Bucharest University of Economic Studies, Bucharest, Romania; Research Center for Evidence Based Medicine (F Ansari PhD), Department of Biostatistics and Epidemiology (Prof M Asghari Jafarabadi PhD), Department of Medical Surgical Nursing (M Ghafourifard PhD), Student Research Committee (M Hosseini MD), Department of Immunology (F Jadidi-Niaragh PhD, M Soltani-Zangbar MSc), Department of Parasitology (A Javadi Mamaghani PhD), School of Management and Medical Informatics (L R Kalankesh PhD), School of Medicine (M Soltani-Zangbar MSc), Tabriz University of Medical Sciences, Tabriz, Iran; Razi Vaccine and Serum Research Institute (F Ansari PhD), Agricultural Research, Education, and Extension Organization (AREEO), Tehran, Iran; Department of Epidemiology and Biostatistics (Prof A Ansari-Moghaddam PhD), Zahedan University of Medical Sciences, Zahedan, Iran; Department of Parasitology (D Anvari PhD), Toxoplasmosis Research Center (Prof A Daryani PhD), Department of Immunology (Prof A Rafiei PhD), Molecular and Cell Biology Research Center (Prof A Rafiei PhD), Department of Environmental Health (Prof Z Yousefi PhD), Mazandaran University of Medical Sciences, Sari, Iran; Department of Parasitology (D Anvari PhD), Iranshahr University of Medical Sciences, Iranshahr, Iran; School of Community Health (A E Anyasodor PhD), Charles Sturt University, Orange, NSW, Australia;

Social Determinants of Health Research Center (M Arab-Zozani PhD), Medical Toxicology & Drug Abuse Research Center (M Rezaei MD), Birjand University of Medical Sciences, Birjand, Iran; Madda Walabu University Goba Referral Hospital (A M Argaw MSc), Department of Public Health (D Z Heyi MPH), School of Health Sciences (D Z Heyi MPH, K Seyoum MSc), Department of Midwifery (K Seyoum MSc), Madda Walabu University, Robe, Ethiopia; College of Allied Health Sciences (M Arshad PhD), Khyber Medical University, Timergara Lower Dir, Pakistan; Research Center for Biochemistry and Nutrition in Metabolic Diseases (Z Asemi PhD, H Mirzaei PhD), Kashan University of Medical Sciences, Kashan, Iran; Department of Biostatistics and Epidemiology (Prof M Asghari Jafarabadi PhD), Department of Anatomical Sciences (S Mohammadi PhD), Faculty of Pharmacy (H Nosrati PhD), Zanjan University of Medical Sciences, Zanjan, Iran; Department of Immunology (M R Atashzar PhD), School of Medicine (M R Atashzar PhD), Fasa University of Medical Sciences, Fasa, Iran; School of Medicine and Public Health (P Atorkey MPhil, M T Hambisa MPH, A G Mersha MD, D N Tollosa PhD), Research Centre for Generational Health and Ageing (B Wubishet MPH), University of Newcastle, Newcastle, NSW, Australia; Hunter New England Population Health, Wallsend, NSW, Australia (P Atorkey MPhil); Department of Forensic Medicine (A Atreya MD), Lumbini Medical College, Palpa, Nepal; Department of Oral and Maxillofacial Surgery (S Attia MSc), Justus Liebig University of Giessen, Giessen, Germany; Northumbria HealthCare NHS Foundation Trust (A Aujayeb MBBS), National Health Service (NHS) Scotland, Newcastle upon Tyne, UK; School of Business (Prof M Ausloos PhD), University of Leicester, Leicester, UK; Center for Health Systems Research (L Avila-Burgos ScD), Center for Nutrition and Health Research (E Denova-Gutiérrez DSc), Health Systems Research Center (D V Ortega-Altamirano DrPH), National Institute of Public Health, Cuernavaca, Mexico; The Judith Lumley Centre (B Ayala Quintanilla PhD), School of Nursing and Midwifery (M Rahman PhD), La Trobe University, Melbourne, VIC, Australia; San Martin de Porres University, Lima, Peru (B Ayala Quintanilla PhD); Department of Midwifery (A D Ayele MSc, B G Kassa MSc), Department of Pharmacy (T S Yazie MSc), Debre Tabor University, Debre Tabor, Ethiopia; Department of Midwifery (S S Ayen MSc), Wolkite University, wolkite, Ethiopia; Department of Neurosurgery (M A Azab MD), Department of Neurology (Prof H R Elhabashy MD, S I El-Jaafary MD), Cairo University, Cairo, Egypt; Department of Medical-Surgical Nursing (H Azami MSc), Department of Environmental Health Engineering (G Azarian PhD), Department of Pharmacology and Toxicology (R Haddadi PhD), Department of Midwifery (S Masoumi PhD), Department of Health Management and Economics (V Ramezani-Doroh PhD), Research Center for Molecular Medicine (A Taherkhani PhD), Hamadan University of Medical Sciences, Hamadan, Iran; School of Medicine (A Azari Jafari MD, S Mirmoeeni MD), Department of Epidemiology (A Hosseinzadeh DrPH), Shahroud University of Medical Sciences, Shahroud, Iran (F Zare MSc); Faculty of Medicine (A Y Azzam MBBCh), October 6 University, 6th October City, Egypt; Department of Parasitology (S Bahadory PhD), Tarbiat Modares University, Tehran, Iran; Department of Parasitology (S Bahadory PhD), Dietary Supplements and Probiotic Research Center (H Pourjafar PhD), Alborz University of Medical Sciences, Karaj, Iran; Department of Epidemiology and Biostatistics (J Bai BA, S Mubarik MS, Prof C Yu PhD), School of Health Sciences (J Bai BA), School of Medicine (Z Zhang PhD), Wuhan University, Wuhan, China; Unit of Biochemistry (A A Baig PhD), Universiti Sultan Zainal Abidin (Sultan Zainal Abidin University), Kuala Terengganu, Malaysia; Center for Clinical Research and Prevention (J L Baker PhD), Bispebjerg University Hospital, Frederiksberg, Denmark; Department of Hypertension (Prof M Banach PhD), Medical University of Lodz, Lodz, Poland; Polish Mothers' Memorial Hospital Research Institute, Lodz, Poland (Prof M Banach PhD); Heidelberg Institute of Global Health (HIGH) (Prof T W Bärnighausen MD), Heidelberg University, Heidelberg, Germany; T.H. Chan School of Public Health (Prof T W Bärnighausen MD), Department of Global Health and Social Medicine (A W Bell MSW), Harvard University, Boston, MA, USA; Department of Translational Medicine (F Barone-Adesi PhD), University of Eastern Piedmont, Novara, Italy; Academic Unit of Obstetrics and Gynecology (F Barra MD), Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI) (Prof S Ferrero PhD), University Eye Clinic (L Ferro Desideri MD), University of Genoa, Genoa, Italy; Department of Public & Environmental Health (A Barrow MPH), University of The Gambia, Brikama, The Gambia; Epidemiology and Disease Control Unit (A Barrow MPH), Ministry of Health, Kotu, The Gambia; School of Public Health and Community Medicine (Prof H Basaleem PhD), Aden College, Aden, Yemen; Social Determinants of Health Research Center (M Behzadifar PhD), Lorestan University of Medical Sciences, Khorramabad, Iran; Department of Public health (N C Bekele MPH), Department of Biomedical Science (Z G Demissie MSc), Wollo University, Dessie, Ethiopia; Department of Medical Laboratory Sciences (R Belete MSc), Department of Health Informatics (D B Enyew MSc), School of Public Health (M T Hambisa MPH, A B Weldesenbet MPH), Haramaya University, Harar, Ethiopia; Department of Oral Pathology and Microbiology (U I Belgaumi MD), Public Health Dentistry Department (Prof K M Shivakumar PhD), Krishna Institute of Medical Sciences "Deemed To Be University", Karad, India; Department of Social Services (A W Bell MSW), Tufts Medical Center, Boston, MA, USA; School of Nursing (A Y Berhie MSc), University of Gondar, Bahir Dar, Ethiopia; Department of Forensic Chemistry (D S Bhagat PhD), Government Institute of Forensic Science, Aurangabad, India; Department of Social and Clinical Pharmacy (A S Bhagavathula PharmD), Charles University, Hradec Kralova, Czech Republic; Institute of Public Health (A S Bhagavathula PharmD, I Elbarazi DrPH), Department of Medical Microbiology & Immunology (Prof G Khan PhD), Family Medicine Department (M A Khan MSc), United Arab Emirates University, Al Ain, United Arab Emirates; Department of Anatomy (Prof N Bhardwaj MD), Department of Community Medicine and Family Medicine (P Bhardwaj MD), School of Public Health (P Bhardwaj MD), Department of Surgical Oncology (Prof S Misra MCh), Department of Pharmacology (S Singh DM, S B Varthya MD), All India Institute of Medical Sciences, Jodhpur, India; Neurovascular Imaging Laboratory (S Bhaskar PhD), NSW Brain Clot Bank, Sydney, NSW, Australia; Department of Neurology and Neurophysiology (S Bhaskar PhD), South West Sydney Local Heath District and Liverpool Hospital, Sydney, NSW, Australia; Department of Statistical and Computational Genomics (K Bhattacharyya MSc), National Institute of Biomedical Genomics, Kalyani, India; Department of Statistics (K Bhattacharyya MSc), University of Calcutta, Kolkata, India; Department of Anatomy (V S Bhojaraja MD), Manipal University College Melaka, Melaka, Malaysia; Institute of Soil and Environmental Sciences (S Bibi PhD, S Ullah PhD), University of Agriculture, Faisalabad, Faisalabad, Pakistan; Social Determinants of Health Research Center (A Bijani PhD), Student Research Committee (M Zamani MD), Babol University of Medical Sciences, Babol, Iran; Department of General Surgery and Medical-Surgical Specialties (Prof A Biondi PhD, Prof G Isola PhD, M Vacante PhD), Department of Medical, Surgical Sciences and Advanced Technologies (E D'Amico MD, Prof M Veroux PhD), Clinical and Experimental Medicine (C Ledda PhD), University of Catania, Catania, Italy; Department of Public Health (S Birara MPH), Samara University, Samara, Ethiopia; Department of Global Public Health and Primary Care (Prof T Bjørge PhD, A Hailu PhD), University of Bergen, Bergen, Norway; Cancer Registry of Norway, Oslo, Norway (Prof T Bjørge PhD); Discipline of Public Health Medicine (O A Bolarinwa MSc, T G Ginindza PhD), University of KwaZulu-Natal, Durban, South Africa; Department of Biomedical Sciences (S Bolla PhD), Nazarbayev University, Nur-Sultan City, Kazakhstan; Department of Epidemiology (D Braithwaite PhD), University of Florida, Gainesville, FL, USA; Cancer Population Sciences Program (D Braithwaite PhD), University of Florida Health Cancer Center, Gainesville, FL, USA; Division of Clinical Epidemiology and Aging Research (Prof H Brenner MD), German Cancer Research Center, Heidelberg, Germany; Flinders Health and Medical Research Institute (N B Bulamu PhD), Health Economics Unit (B Kaambwa PhD), College of Medicine and Public Health (B Kaambwa PhD, Prof P Ward PhD), Health and Social Care Economics Group (C Mpundu-Kaambwa PhD), Southgate Institute for Health and Society (F H Tesfay PhD), Flinders University, Adelaide, SA, Australia; Department of Public Health

(Prof M T Bustamante-Teixeira PhD, Prof M R Guerra PhD), Federal University of Juiz de Fora, Juiz de Fora, Brazil; School of Public Health and Health Systems (Z A Butt PhD), University of Waterloo, Waterloo, ON, Canada; Al Shifa School of Public Health (Z A Butt PhD), Al Shifa Trust Eye Hospital, Rawalpindi, Pakistan; Institute of Microengineering (F Caetano dos Santos PhD), Federal Polytechnic School of Lausanne, Lausanne, Switzerland; Program in Physical Therapy (C Cao MPH), Department of Surgery (Y Cao MPH), Washington Universtiy in St. Louis, St. Louis, MO, USA; Oncological Network, Prevention and Research Institute (G Gorini MD), Institute for Cancer Research, Prevention and Clinical Network, Florence, Italy (G Carreras PhD); National School of Public Health (F Catalá-López PhD, A Padron-Monedero PhD), Department of Public Health and Mental Health (A Padron-Monedero PhD), Institute of Health Carlos III, Madrid, Spain; Clinical Epidemiology Program (F Catalá-López PhD), Ottawa Hospital Research Institute, Ottawa, ON, Canada; Department of Nutrition (Prof F Cembranel DSc), Department of Physical Education (Prof D A S Silva PhD), Federal University of Santa Catarina, Florianópolis, Brazil; Mary MacKillop Institute for Health Research (Prof E Cerin PhD), Australian Catholic University, Melbourne, VIC, Australia; School of Public Health (Prof E Cerin PhD), University of Hong Kong, Hong Kong, China; Hospitalist Department (R Chakinala MD), Geisinger Health System, Danville, PA, USA; School of Population and Public Health (P A Chakraborty MPH, J A Kopec PhD), University of British Columbia, Vancouver, BC, Canada; Department of Medicine (V Chattu MD), University of Toronto, Toronto, ON, Canada; Saveetha Medical College (V Chattu MD), Saveetha University, Chennai, India; Center for Cancer Epidemiology (Prof P Chaturvedi MD), Department of Head and Neck Surgery (Prof P Chaturvedi MD), Tata Memorial Hospital, Navi Mumbai, India; Department of Oral Medicine and Radiology (A Chaurasia MD), King George's Medical University, Lucknow, India; Department of Epidemiology and Environmental Health (P P Chavan PhD), University at Buffalo, Buffalo, NY, USA; Department of Public Health and Health Policy (O Chimed-Ochir PhD), Hiroshima University, Hiroshima, Japan; Division of Biomedical Informatics (J J Choi PhD), Seoul National University Hospital, Seoul, South Korea; Department of Pulmonary Medicine (Prof D J Christopher MD), Department of Endocrinology, Diabetes and Metabolism (Prof N Thomas PhD), Christian Medical College and Hospital (CMC), Vellore, India; Center for Biomedicine and Community Health (D Chu PhD), VNU-International School, Hanoi, Vietnam; Department of Otolaryngology (M T Chung MD), Wayne State University, Detroit, MI, USA; Nova Medical School (J Conde PhD), Nova University of Lisbon, Lisbon, Portugal; Research Unit on Applied Molecular Biosciences (UCIBIO) (V M Costa PhD), Associated Laboratory for Green Chemistry (LAQV) (J P Ferreira de Oliveira PhD), Laboratory for Process Engineering, Environment, Biotechnology and Energy (LEPABE) (J Loureiro PhD), Department of Chemistry (R B Pereira PhD), University of Porto, Porto, Portugal; Health Systems Management (O B Da'ar PhD), College of Public Health and Health Informatics (O B Da'ar PhD), King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia; School of Public Health (O Dadras DrPH), Walailak University, Nakhon Si Thammarat, Thailand; 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), Harrington Heart and Vascular Institute (A Guha MD), Department of Quantitative Health Science (X Liu PhD), Department of Nutrition and Preventive Medicine (Prof J Sanabria MD), Division of Pediatric Gastroenterology (A Thavamani MD), Case Western Reserve University, Cleveland, OH, USA; Health Policy Research (M R Mathur PhD), Department of Research (A Pandey PhD), Public Health Foundation of India, Gurugram, India (Prof L Dandona MD, Prof R Dandona PhD, G Kumar PhD); India Cancer Research Consortium (Prof R Mehrotra DPhil), Indian Council of Medical Research, New Delhi, India (Prof L Dandona MD); Department of Pathology (P Daneshpajouhnejad MD), Johns Hopkins University School of Medicine, Baltimore, MD, USA; Department of Pathology (P Daneshpajouhnejad MD), Research Institute for Primordial Prevention of Non-Communicable Disease (S Hariri MD), Department of Biostatistics and Epidemiology (E Sadeghi PhD), Department of Radiology and Interventional Neuroradiology (O Shafaat MD), Isfahan University of Medical Sciences, Isfahan, Iran; Department of Public Health (Prof F P De la Hoz PhD), National University of Colombia, Bogota, Colombia; School of Public Health (S Debela MPH), Salale University, Fiche, Ethiopia; Emergency Operating Center (EOC) (T G Demie MPH), Ethiopian Public Health Institute, Addis Ababa, Ethiopia; Division of Cardiology (R Desai MBBS), Atlanta Veterans Affairs Medical Center, Decatur, GA, USA; Department of Community Medicine (D Dhamnetiya MD, R P Jha MSc), Dr. Baba Saheb Ambedkar Medical College & Hospital, Delhi, India; Department of Community Medicine (Prof S D Dharmaratne MD), University of Peradeniya, Peradeniya, Sri Lanka; Policy Research Institute, Kathmandu, Nepal (M L Dhimal PhD); Global Institute for Interdisciplinary Studies, Kathmandu, Nepal (M L Dhimal PhD); Health Research Section (M Dhimal PhD, U Paudel PhD), Nepal Health Research Council, Kathmandu, Nepal (R Subedi MPH); Department of Epidemiology (M Dianatinasab MSc), Maastricht University, Maastricht, Netherlands; Department of Epidemiology (M Dianatinasab MSc), Department of Midwifery (R Janghorban PhD), Non-communicable Disease Research Center (Prof R Malekzadeh MD, S G Sepanlou MD), Department of Medical Mycology and Parasitology (H Nouraei MSc, Prof K Pakshir PhD), Shiraz University of Medical Sciences, Shiraz, Iran; Department of Parasitology and Mycology (M Didehdar PhD), Department of Epidemiology (R Moradzadeh PhD, M Zamanian PhD), Department of Pediatrics (J Nazari MD), Arak University of Medical Sciences, Arak, Iran; Development of Research and Technology Center (S Djalalinia PhD), Ministry of Health and Medical Education, Tehran, Iran; Center of Excellence in Behavioral Medicine (H P Do PhD, G T Vu BA), Nguyen Tat Thanh University, Ho Chi Minh City, Vietnam; School of Health (S Doaei PhD), Gastrointestinal and Liver Diseases Research Center (S Hassanipour PhD, F Joukar PhD, Prof F Mansour-Ghanaei MD), Caspian Digestive Disease Research Center (S Hassanipour PhD, F Joukar PhD, Prof F Mansour-Ghanaei MD), Guilan University of Medical Sciences, Rasht, Iran; Responsabilidade Social (W M dos Santos PhD), Hospital Alemão Oswaldo Cruz (Oswaldo Cruz German Hospital), São Paulo, Brazil; Brazilian Centre for Evidence-based Healthcare (W M dos Santos PhD), Joanna Briggs Institute, São Paulo, Brazil; Department of Clinical Surgery (T M Drake MD), University of Edinburgh, Edinburgh, Scotland; Biomedical Informatics and Medical Statistics Department (I El Sayed PhD), Pediatric Dentistry and Dental Public Health Department (Prof M El Tantawi PhD), Alexandria University, Alexandria, Egypt; Reference Laboratory of Egyptian Universities-Cairo (Prof M El Sayed Zaki PhD), Ministry of Higher Education and Scientific Research, Cairo, Egypt; Direction de L'épidémiologie et la Lutte Contre les Maladies (Directorate of Epidemiology and Diseases Control) (H El-Abid PhD), Ministry of Health, Rabat, Morocco; Department of Microbiology (M A Elbahnasawy PhD), Department of Zoology and Entomology (A I Hasaballah PhD), Al Azhar University, Cairo, Egypt; Faculty of Medicine (M Elhadi MD), University of Tripoli, Tripoli, Libya; Department of International Cyber Education (R Erkhembayar MD), Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; Department of Internal Medicine (M Faisaluddin MD), Rochester General Hospital, Rochester, NY, USA; Department of Neurological Surgery (J Fares MD), Northwestern University, Chicago, IL, USA; Department of Internal Medicine (U Farooque MD), Dow University of Health Sciences, Karachi, Pakistan; Satcher Health Leadership Institute (A O Fasanmi PhD), Morehouse School of Medicine, Atlanta, GA, USA; School of Medicine (A O Fasanmi PhD), Emory University, Atlanta, GA, USA; Department of Public Health (W Fatima PhD), Faculty of Allied Health Sciences (Prof S Gilani PhD), University Institute of Public Health (S Hameed MPH, A A Malik PhD), The University of Lahore, Lahore, Pakistan; Department of Public Health (W Fatima PhD), Afro-Asian Institute, Lahore, Pakistan (Prof S Gilani PhD); Department of Nursing and Midwifery (G Fetensa MSc, M Regasa MSc), Institute of Health Sciences (G Fetensa MSc, M Regasa MSc), Wollega University, Nekemte, Ethiopia; 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 Gerontological Health Services and Nursing Research (F Fischer PhD), Ravensburg-Weingarten University of Applied Sciences, Weingarten, Germany; James Cancer Hospital (J L Fisher PhD), Division of Cardiovascular Medicine (A Guha MD), Ohio State University, Columbus, OH, USA; 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; Health Services Management Training Centre (P A Gaal PhD, T Joo MSc, V Szerencsés MA), Faculty of Health and Public Administration (M Szócska PhD), Semmelweis University, Budapest, Hungary; Department of Applied Social Sciences (P A Gaal PhD), Sapientia Hungarian University of Transylvania, Târgu Mureş, Romania; Gillings School of Global Public Health (M M Gad MD), University of North Carolina Chapel Hill, Chapel Hill, NC, USA; Department of Community Dentistry (P Gaewkhiew PhD), Mahidol University, Ratchathewi, Thailand; Population and Patient Health (P Gaewkhiew PhD), Faculty of Life Sciences and Medicine (M Molokhia PhD), King's College London, London, UK; Department of Environmental Health Sciences (S Gallus DSc, A Lugo PhD), Mario Negri Institute for Pharmacological Research, Milan, Italy; Department of Radiology (T Garg MBBS), King Edward Memorial Hospital, Mumbai, India; Department of Reproductive and Family Health (T G Gebremeskel MPH), Aksum University, Axum, Ethiopia; Department of Nursing (B N B Gemeda MSc), Debre Berhan University, Debre Birhan, Ethiopia; Research Group for Genomic Epidemiology (N Ghith PhD), Technical University of Denmark, Copenhagen, Denmark; Department of Epidemiology and Biostatistics (A Gholami PhD), Noncommunicable Diseases Research Center (A Gholami PhD), Neyshabur University of Medical Sciences, Neyshabur, Iran; Noncommunicable Diseases Research Center (J Gholizadeh Navashenaq PhD), Bam University of Medical Sciences, Bam, Iran; NIHR Global Health Research Unit on Global Surgery (J C Glasbey MSc), University of Birmingham, Birmingham, UK; Department of Gastroenterology (Prof A Goel DM), Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India; 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, F Sanmarchi MD), Department of Medical and Surgical Sciences (Prof F S Violante MD), University of Bologna, Bologna, Italy; Hudson College of Public Health (S V Gopalani MPH), University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; Department of Health and Social Affairs (S V Gopalani MPH), Government of the Federated States of Micronesia, Palikir, Federated States of Micronesia; Department of Respiratory Medicine (H Goudarzi PhD), Center for Environmental and Health Sciences (H Goudarzi PhD), Hokkaido University, Sapporo, Japan; Postgraduate Program in Epidemiology (Prof B N G Goulart DSc), Federal University of Rio Grande do Sul, Porto Alegre, Brazil; Department of Family and Community Medicine (M I M Gubari PhD), University Of Sulaimani, Sulaimani, Iraq; Department of Public Health (B Gupta PhD), Torrens University, Melbourne, VIC, Australia; Toxicology Department (S Gupta MSc), Shriram Institute for Industrial Research, Delhi, India; School of Medicine (V Gupta PhD), Deakin University, Geelong, VIC, Australia; Department of Clinical Medicine (Prof V K Gupta PhD), Macquarie University, Sydney, NSW, Australia; Department of Radiology and Radiological Science (N Hafezi-Nejad MD, O Shafaat MD, S Sheikhbahaei MD), Johns Hopkins University, Baltimore, MD, USA (H Tadbiri MD); Department of Family and Community Medicine (Prof R R Hamadeh PhD), Arabian Gulf University, Manama, Bahrain; School of Health and Environmental Studies (Prof S Hamidi DrPH), Hamdan Bin Mohammed Smart University, Dubai, United Arab Emirates; Research & Scientific Studies Unit (S Haque PhD), Epidemiology Department (M Khan MD), Jazan University, Jazan, Saudi Arabia; Research Unit (J M Haro MD), University of Barcelona, Barcelona, Spain; Biomedical Research Networking Center for Mental Health Network (CiberSAM), Barcelona, Spain (J M Haro MD); Kumudini Women Medical College (S Hasan PhD), University of Dhaka, Tangail, Bangladesh; Department of Epidemiology (S Nejadghaderi MD, S Rashedi MD), Department of Oral Health (E Shamsoddin DDS, A Sofi-Mahmudi DDS), Department of International Studies (P Shobeiri MD), Non-Communicable Diseases Research Center (NCDRC), Tehran, Iran (S Hashemi MD); Research Centre (T S Hassan PhD), Salahaddin University, Erbil, Iraq; Department of Medicine (T S Hassan PhD), Department of Molecular Medicine and Surgery (J H Kauppila MD), Karolinska Institute, Stockholm, Sweden; 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); Community-Oriented Nursing Midwifery Research Center (M Heidari PhD), Department of Epidemiology and Biostatistics (A Mohammadian-Hafshejani PhD), Shahrekord University of Medical Sciences, Shahrekord, Iran; Departamento de Salud Oral (Department of Oral Health) (B Y Herrera-Serna PhD), Universidad Autónoma de Manizales (Autonomous University of Manizales), Manizales, Colombia; 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; Department of Pediatrics (M K Hole MD), University of Texas Austin, Austin, TX, USA; Kasturba Medical College, Mangalore (R Holla MD, A Kamath MD, S Koulmane Laxminarayana MD) Department of Nephrology (Prof S Nagaraju DM), Manipal College of Dental Sciences (Prof A I Narayana PhD, Prof R A Radhakrishnan PhD), Department of Forensic Medicine and Toxicology (Prof V C Nayak MD, J Padubidri MD), Department of Health Policy (S M Pattanshetty MD), Department of Community Medicine (C R Rao MD), Manipal Academy of Higher Education, Manipal, India (A Kamath MD); Department of Pulmonology (N Horita PhD), Yokohama City University, Yokohama, Japan; National Human Genome Research Institute (NHGRI) (N Horita PhD), National Institutes of Health, Bethesda, MD, USA; Social and Environmental Health Research (M Hossain MPH), Nature Study Society of Bangladesh, Khulna, Bangladesh; Department of Health Promotion and Community Health Sciences (M Hossain MPH), Texas A&M University, College Station, TX, USA; Department of Population Sciences (Prof M B Hossain PhD), University of Dhaka, Dhaka, Bangladesh; Institute of Research and Development (M Hosseinzadeh PhD), Duy Tan University, Da Nang, Vietnam; Clinical Legal Medicine Department (S Hostiuc PhD), National Institute of Legal Medicine Mina Minovici, Bucharest, Romania; College of Science and Engineering (Prof M Househ PhD), Hamad Bin Khalifa University, Doha, Qatar; Faculty of Medicine of Tunis (Prof M Hsairi MPH), University Tunis El Manar, Tunis, Tunisia; Jockey Club School of Public Health and Primary Care (J Huang MD), The Chinese University of Hong Kong, Hong Kong, China; Department of Biomolecular Sciences (N R Hussein PhD), University of Zakho, Zakho, Iraq; Department of Occupational Safety and Health (Prof B Hwang PhD), China Medical University, Taichung, Taiwan; Department of Community Medicine (O S Ilesanmi PhD), Department of Medicine (A S Oguntade MSc, Prof M O Owolabi DrM), University College Hospital, Ibadan, Ibadan, Nigeria; Faculty of Medicine (I M Ilic PhD), University of Belgrade, Belgrade, Serbia; Department of Epidemiology (Prof M D Ilic PhD), Department of Global Health, Economics and Policy (Prof M Jakovljevic PhD), University of Kragujevac, Kragujevac, Serbia; Department of Epidemiology and Biostatistics (K Innos PhD), National Institute for Health Development, Tallinn, Estonia; School of Pharmacy (L M Irham BPharm), Taipei Medical University, Taipei, Taiwan; Faculty of Pharmacy (L M Irham BPharm), Ahmad Dahlan University, Yogyakarta, Indonesia; Department of Epidemiology and Preventive Medicine (R M Islam PhD), Monash University, Melbourne, VIC, Australia; Institute for Physical Activity and Nutrition (S Islam PhD), Deakin University, Burwood, VIC, Australia; Sydney Medical School (S Islam PhD), Save Sight Institute (H Kandel PhD), Asbestos Diseases Research Institute (J Leigh MD), University of Sydney, Sydney, NSW, Australia; Department of Clinical Pharmacy (Prof N Ismail PhD), MAHSA University, Bandar Saujana Putra, Malaysia; 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; 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; Institute of Comparative Economic Studies (Prof M Jakovljevic PhD), Hosei University, Tokyo, Japan; Department of Biochemistry (Prof S Jayaram MD), Government Medical College, Mysuru, India; Department of Physiology (R Jayawardena PhD), Department of Pharmacology (P Ranasinghe PhD), University of Colombo, Colombo, Sri Lanka; School of Exercise and Nutrition Sciences (R Jayawardena PhD), School of Public Health and Social Work (M T N Tran PhD, N Wang PhD), Queensland University of Technology, Brisbane, QLD, Australia; Urology Department (S Jazayeri MD), University of Florida, Jacksonville, FL, USA; Department of Community Medicine (R P Jha MSc), Banaras Hindu University, Varanasi, India; Institute of Family Medicine and Public Health (M Jürisson PhD), University of Tartu, Tartu, Estonia; Dermatology Department (F Kaliyadan MD), King Faisal University, Hofuf, Saudi Arabia; Department of Pharmacy (Z Kamal PhD), Shaheed Benazir Bhutto University, Dir Upper, Pakistan; School of Pharmacy (Z Kamal PhD), Shanghai Jiao Tong University, Shanghai, China; Sydney Eye Hospital (H Kandel PhD), South Eastern Sydney Local Health District, Sydney, NSW, Australia; Department of Preventive and Social Medicine (Prof S S Kar MD), Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India; School of Health Professions and Human Services (I M Karaye MD), Hofstra University, Hempstead, NY, USA; Surgery Research Unit (J H Kauppila MD), University of Oulu, Oulu, Finland; Department of Surgery (P M Kemp Bohan MD), Brooke Army Medical Center, San Antonio, TX, USA; Non-Communicable Diseases Research Unit (Prof A P Kengne PhD), Medical Research Council South Africa, Cape Town, South Africa; Department of Medicine (Prof A P Kengne PhD), School of Public Health and Family Medicine (C A Nnaji MPH), University of Cape Town, Cape Town, South Africa; School of Public Health (A A Kerbo PhD), Wolaita Sodo University, Wolaita Sodo, Ethiopia; 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; Department of Epidemiology and Biostatistics (E A Khan MPH), Health Services Academy, Islamabad, Pakistan; Department of Population Science (M Khan PhD), Jatiya Kabi Kazi Nazrul Islam University, Mymensingh, Bangladesh; Primary Care Department (M A Khan MSc), NHS North West London, London, UK; The Iranian Academy of Medical Sciences, Tehran, Iran (M Khayamzadeh MD); Department of Public Health (Prof J Khubchandani PhD), New Mexico State University, Las Cruces, NM, USA; Nuffield Department of Surgical Sciences (R Khundkar MA), The George Institute for Global Health (Prof S Yaya PhD), University of Oxford, Oxford, UK; Department of Genomics and Digital Health (M Kim MD), Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Seoul, South Korea; Public Health Center (M Kim MD), Ministry of Health and Welfare, Wando, South Korea; School of Traditional Chinese Medicine (Y Kim PhD), Xiamen University Malaysia, Sepang, Malaysia; School of Health Sciences (Prof A Kisa PhD), Kristiania University College, Oslo, Norway; Department of Global Community Health and Behavioral Sciences (Prof A Kisa PhD), Department of Medicine (M F Qadir PhD), Tulane University, New Orleans, LA, USA; Department of Nursing and Health Promotion (S Kisa PhD), Oslo Metropolitan University, Oslo, Norway; Department of Health Economics and Social Security (K Kissimova-Skarbek PhD), Jagiellonian University Medical College, Krakow, Poland; Arthritis Research Canada, Richmond, BC, Canada (J A Kopec PhD); Microbiology & Molecular Cell Biology Department (R Koteeswaran MD), Eastern Virginia Medical School, Norfolk, VA, USA; Biomedical Research Networking Center for Mental Health Network (CIBERSAM) (A Koyanagi MD), San Juan de Dios Sanitary Park, Sant Boi de Llobregat, Spain; Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain (A Koyanagi MD); University of Environment and Sustainable Development, Somanya, Ghana (N Kugbey PhD); Department of Biochemistry and Biotechnology (A Kwarteng PhD), Kwame Nkrumah University of Science and Technology, Kumasi, Ghana; Division of Cancer Epidemiology and Genetics (Q Lan PhD), National Cancer Institute, Rockville, MD, USA; Unit of Genetics and Public Health (Prof I Landires MD), Unit of Microbiology and Public Health (V Nuñez-Samudio PhD), Institute of Medical Sciences, Las Tablas, Panama; Department of Public Health (V Nuñez-Samudio PhD), Ministry of Health, Herrera, Panama (Prof I Landires MD); Department of Otorhinolaryngology (S Lasrado MS), Father Muller Medical College, Mangalore, India; Institute of Clinical Physiology (P Lauriola MD), National Research Council, Pisa, Italy; Pattern Recognition and Machine Learning Lab (Prof S Lee PhD), Gachon University, Seongnam, South Korea; The Office of Health Policy & Legislative Affairs (W Lee PhD), Department of Pathology (V Y Tat BS), University of Texas, Galveston, TX, USA; Department of Medicine (Prof Y Lee PhD), School of Medical Sciences (Prof Y Lee PhD), University of Science Malaysia, Kota Bharu, Malaysia; Graduate School of Public Health (Y Lee PhD), Ajou University, Suwon-si, South Korea; Faculty of Science (E Leong PhD), Universiti Brunei Darussalam (University of Brunei Darussalam), Bandar Seri Begawan, Brunei; Department of Sociology (B Li PhD), Shenzhen University, Shenzhen, China; Department of Medical Oncology (J Li MD), Peking Union Medical College, Beijing, China; Department of Health Promotion and Health Education (M Li PhD), National Taiwan Normal University, Taipei, Taiwan; Department of Professional and Medical Education (S W Lobo PhD), Meharry Medical College, Nashville, TN, USA; Department of Biomedical Sciences (S W Lobo PhD), Mercer University, Macon, GA, USA; School of Health (J Loureiro PhD), Polytechnic Institute of Porto, Portugal; Department of General Surgery (Prof R Lunevicius DSc), Liverpool University Hospitals NHS Foundation Trust, Liverpool, UK; Department of Surgery (Prof R Lunevicius DSc), Institute of Population Health Sciences (M R Mathur PhD), Department of International Public Health (V E Nwatah MD), University of Liverpool, Liverpool, UK; Radiology Department (H Magdy Abd El Razek MD), Egypt Ministry of Health and Population, Mansoura, Egypt; Ophthalmology Department (M Magdy Abd El Razek MSc), Ministry of Health & Population, Aswan, Egypt; Radiology and Precision Health Program (M Mahmoudi PhD), Michigan State University, East Lansing, MI, USA; Department of Primary Care and Public Health (Prof A Majeed MD, Prof S Rawaf MD), WHO Collaborating Centre for Public Health Education and Training (D L Rawaf MD), Imperial College London, London, UK; Department of Ophthalmology (S Male DNB), M M Joshi Eye Institute, Hubli, India; Department of Epidemiology (M A Mamun HSC), CHINTA Research Bangladesh, Dhaka, Bangladesh; Department of Public Health and Informatics (M A Mamun HSC), Jahangirnagar University, Dhaka, Bangladesh; Doheny Eye Institute (N Manafi MD), University of California Los Angeles, Los Angeles, CA, USA; Substance Abuse Prevention Research Center (B Mansouri PhD), Department of Health Education and Health Promotion (S Siabani PhD, A Ziapour PhD), Kermanshah University of Medical Sciences, Kermanshah, Iran; Faculty of Public Health (S Martini PhD), Universitas Airlangga (Airlangga University), Surabaya, Indonesia; Indonesian Public Health Association, Surabaya, Indonesia (S Martini PhD); Association of Resident Physicians, Bucharest, Romania (C N Matei PhD); Department of Ophthalmology (C McAlinden PhD), Singleton Hospital, Swansea, UK; Peru Country Office (W Mendoza MD), United Nations Population Fund (UNFPA), Lima, Peru; University Research Institute (A A Mentis MD), National and Kapodistrian University of Athens, Athens, Greece; Breast Surgery Unit (T J Meretoja MD), Helsinki University Hospital, Helsinki, Finland; University of Helsinki, Helsinki, Finland (T J Meretoja MD); Department of Orthopaedic Surgery (M K Mesregah MSc), Menoufia University Faculty of Medicine, Shebin El-Kom, Egypt; Clinical Microbiology and Parasitology Unit (T Mestrovic PhD), Dr. Zora Profozic Polyclinic, Zagreb, Croatia; University Centre Varazdin (T Mestrovic PhD), University North, Varazdin, Croatia; School of Public Health and Community Medicine (J Miao Jonasson PhD), University of Gothenburg, Gothenburg, Sweden; Center for Innovation in Medical Education (B Miazgowski MD), Pomeranian Medical University, Szczecin, Poland (B Miazgowski MD); Woman-Mother-Child Department (I Michalek PhD), Lausanne University Hospital, Lausanne, Switzerland; Pacific Institute for Research & Evaluation, Calverton, MD, USA (T R Miller PhD); School of Public Health (T R Miller PhD), Curtin

University, Perth, WA, Australia; Department of Nursing (A B Mingude MSc), Department of Pediatrics and Child Health Nursing (S S Yehualashet MSc), Debre Berhan University, Debre Berhan, Ethiopia; Department of Biology (K A Mohammad PhD), Salahaddin University-Erbil, Erbil, Iraq; Department of Information Technology (M Mohammadi PhD), Lebanese French University, Erbil, Iraq; Department of Nursing (R Mohammadpourhodki PhD), Applied Biomedical Research Center (A Sahebkar PhD), Biotechnology Research Center (A Sahebkar PhD), Mashhad University of Medical Sciences, Mashhad, Iran; Department of Biology (A Mohammed PhD), University of Jeddah, Jeddah, Saudi Arabia; Health Systems and Policy Research Unit (S Mohammed PhD), Department of Community Medicine (M B Sufiyan MD), Department of Surgery (M A Tolani FWACS), Ahmadu Bello University, Zaria, Nigeria; Department of Health Care Management (S Mohammed PhD), Technical University of Berlin, Berlin, Germany; Department of Dental Basic Sciences (T A Mohammed MSc), University of Duhok, Duhok, Iraq; Oncology Department (N Moka MD), Appalachian Regional Healthcare, Hazard, KY, USA; Department of Internal Medicine (N Moka MD), University of Kentucky, Lexington, KY, USA; Clinical Epidemiology and Public Health Research Unit (L Monasta DSc, L Ronfani PhD, E Traini MSc), Burlo Garofolo Institute for Maternal and Child Health, Trieste, Italy; Department of Computer Science and Engineering (M Moni PhD), Pabna University of Science and Technology, Pabna, Bangladesh; Social Determinants of Health Research Center (G Moradi PhD, Y Moradi PhD), Department of Epidemiology and Biostatistics (G Moradi PhD), Kurdistan University of Medical Sciences, Sanandaj, Iran; Joint, Bone, Connective tissue, Rheumatology Research Center (JBCRC) (M Moradzadeh PhD), Golestan Research Center of Gastroenterology and Hepatology (GRCGH) (G Roshandel PhD), Golestan University of Medical Sciences, Gorgan, Iran; Computer, Electrical, and Mathematical Sciences and Engineering Division (P Moraga PhD), King Abdullah University of Science and Technology, Thuwal, Saudi Arabia; Section of Plastic Surgery (S D Morrison MD), University of Michigan School of Medicine, Ann Arbor, MI, USA; Department of Medicine (E Mostafavi PhD), Stanford Cardiovascular Institute (E Mostafavi PhD), Stanford University, Palo Alto, CA, USA; Department of Food Science (Prof A Mousavi Khaneghah PhD), University of Campinas (Unicamp), Campinas, Brazil; College of Medicine and Public Health (L Mwanri PhD), Flinders University, Adeaide, SA, Australia; Department of Obstetrics and Gynecology (Prof A F Nabhan PhD), Department of Entomology (A M Samy PhD), Ain Shams University, Cairo, Egypt; Knowledge Translation and Utilization (Prof A F Nabhan PhD), Egyptian Center for Evidence Based Medicine, Cairo, Egypt; Department of Education for Clinical Research (C Nagata PhD), National Center for Child Health and Development, Tokyo, Japan; Laboratory of Public Health Indicators Analysis and Health Digitalization (M Naimzada MD, N Otstavnov BA, S S Otstavnov PhD), Moscow Institute of Physics and Technology, Dolgoprudny, Russia; Experimental Surgery and Oncology Laboratory (M Naimzada MD), Kursk State Medical University, Kursk, Russia; Department of Dermatology (Prof L Naldi MD), San Bortolo Hospital, Vicenza, Italy; GISED Study Center, Bergamo, Italy (Prof L Naldi MD); Suraj Eye Institute, Nagpur, India (V Nangia MD); Discipline of Social & Administrative Pharmacy (A Naqvi PhD), University of Science, Malaysia, Penang, Malaysia; Mysore Medical College and Research Institute (Prof S Narasimha Swamy MD), Government Medical College, Mysore, India; School of Pharmacy (S O Nduaguba PhD), West Virginia University, Morgantown, USA; Department of General Surgery (I Negoi PhD), Emergency Hospital of Bucharest, Bucharest, Romania; Department of Oncology (S Negru MD), Victor Babes University of Medicine and Pharmacy, Timisoara, Romania; Department of Community Medicine (S Nepal MD), Kathmandu University, Palpa, Nepal; Estia Health Blakehurst (S Neupane Kandel BSN), Estia Health, Sydney, NSW, Australia; Department of Histopathology (Prof H A Nggada MD), University of Maiduguri Teaching Hospital, Maiduguri, Nigeria; Department of Human Pathology (Prof H A Nggada MD), University of Maiduguri, Maiduguri, Nigeria; Institute for Global Health Innovations (C T Nguyen MPH), Duy Tan University, Hanoi, Vietnam; South African Medical Research Council, Cape Town, South Africa (C A Nnaji MPH); Joint Ukraine-Azerbaijan International Research and Education Center of Nanobiotechnology and Functional Nanosystems, Baku, Azerbaijan (H Nosrati PhD); Department of Pediatrics (V E Nwatah MD), National Hospital, Abuja, Nigeria; Center of Excellence in Reproductive Health Innovation (CERHI) (C I Nzoputam MPH), University of Benin, Benin City, Nigeria; Administrative and Economic Sciences Department (Prof B Oancea PhD), University of Bucharest, Bucharest, Romania; Department of Community Health and Primary Care (O O Odukoya MSc), University of Lagos, Idi Araba, Nigeria; Department of Family and Preventive Medicine (O O Odukoya MSc), University of Utah, Salt Lake City, UT, USA; Institute of Cardiovascular Science (A S Oguntade MSc), University College London, London, UK; Department of Preventive Medicine (I Oh PhD), Kyung Hee University, Dongdaemun-gu, South Korea; Department of Psychiatry (A T Olagunju MD), University of Lagos, Lagos, Nigeria; Community Prevention and Care Services (B O Olakunde PhD), National AIDS Control Committee, Abuja, Nigeria; Mass Communication Department (E Omar PhD), Ajman University, Dubai, United Arab Emirates; Non-communicable Disease Prevention Unit (S Ong FAMS), Ministry of Health, Bandar Seri Begawan, Brunei; Early Detection & Cancer Prevention Services (S Ong FAMS), Pantai Jerudong Specialist Centre, Bandar Seri Begawan, Brunei; Department of Pharmacology and Therapeutics (Prof O E Onwujekwe PhD), University of Nigeria Nsukka, Enugu, Nigeria; Department of Project Management (S S Otstavnov PhD), Department of Health Care Administration and Economics (Prof V Vlassov MD), National Research University Higher School of Economics, Moscow, Russia; Department of Respiratory Medicine (Prof M P A DNB), Jagadguru Sri Shivarathreeswara Academy of Health Education and Research, Mysore, India; Department of Health Metrics (A Pana MD), Center for Health Outcomes & Evaluation, Bucharest, Romania; Vision and Eye Research Institute (Prof S Pardhan PhD), Faculty of Science and Engineering (L Smith PhD), Anglia Ruskin University, Cambridge, UK; Department of Epidemiology, Human Genetics and Environmental Sciences (J R Patel PhD), The University of Texas Health Science Center at Houston School of Public Health, Dallas, TX, USA; Department of Epidemiology (J R Patel PhD), University of Arkansas for Medical Sciences, Little Rock, AR, USA; SIAN Institute (S Pati PhD), Association for Biodiversity Conservation and Research (ABC), Odisha, India; Department of Biotechnology (S Pati PhD), Academy of Management and Information Technology, Khordha, India; Faculty of Humanities and Social Sciences (U Paudel PhD), Tribhuvan University, Kathmandu, Nepal; Department of Psychiatry (Prof M F P Peres MD), University of São Paulo, São Paulo, Brazil; International Institute for Educational Planning (IIEP) (Prof M F P Peres MD), Albert Einstein Hospital, São Paulo, Brazil; Department of Development Studies (Prof A Perianayagam PhD), International Institute for Population Sciences, Mumbai, India; University Medical Center Groningen (Prof M J Postma PhD), School of Economics and Business (Prof M J Postma PhD), University of Groningen, Groningen, Netherlands; Department of Nutrition and Food Sciences (H Pourjafar PhD), Maragheh University of Medical Sciences, Maragheh, Iran; Department of Biochemistry (Prof A Prashant PhD), Jagadguru Sri Shivarathreeswara University, Mysuru, India; Department of Medical Neuroscience (T Pulakunta MD), Dalhousie University, Halifax, NS, Canada; Biomedical Engineering Department (Prof M Rabiee PhD), Amirkabir University of Technology, Tehran, Iran; Department of Physics (N Rabiee PhD), Sharif University of Technology, Tehran, Iran; College of Medicine (A Radfar MD), University of Central Florida, Orlando, FL, USA; Department of Medicine (A Rafiee MSc), University of Alberta, Edmonton, AB, Canada; Department of Natural Science (S Rahimzadeh MSc), Middlesex University, London, UK; 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 Surgery (A Rajesh MD), University of Texas Health Science Center at San Antonio, San Antonio, TX, USA; Health Emergency Operation Center (K Ranabhat MPH), Ministry of Health & Population,

Kathmandu, Nepal; Central Department of Public Health (K Ranabhat MPH), Institute of Medicine, Kathmandu, Nepal; Department of Oral Pathology (S Rao MDS), Srinivas Institute of Dental Sciences, Mangalore, India; Department of Clinical Science (M Rashidi DVM), Islamic Azad University, Garmsar, Iran; Department of Radiation Oncology (Prof G K Rath MD), All India Institute of Medical Sciences, New Delhi, India; University College London Hospitals, London, UK (D L Rawaf MD); Academic Public Health England (Prof S Rawaf MD), Public Health England, London, UK; School of Health, Medical and Applied Sciences (L Rawal PhD), CQ University, Sydney, NSW, Australia; Department of Immunology and Laboratory Sciences (M Razeghinia MSc), Sirjan School of Medical Sciences, Sirjan, Iran; Department of Immunology (M Razeghinia MSc), HIV/STI Surveillance Research Center, and WHO Collaborating Center for HIV Surveillance (H Tohidinik PhD), Health Services Management Research Center (V Yazdi-Feyzabadi PhD), Department of Health Management, Policy, and Economics (V Yazdi-Feyzabadi PhD), Kerman University of Medical Sciences, Kerman, Iran; School of Medicine (Prof A M N Renzaho PhD), Translational Health Research Institute (Prof A M N Renzaho PhD), Western Sydney University, Campbelltown, NSW, Australia; Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA) (Prof N Rezaei PhD), Universal Scientific Education and Research Network (USERN), Tehran, Iran; Department of Epidemiology and Biostatistics (Prof M Rezaeian PhD), Rafsanjan University of Medical Sciences, Rafsanjan, Iran; Department of Public Health (A Riad DDS), Czech National Centre for Evidence-based Healthcare and Knowledge Translation (A Riad DDS), Masaryk University, Brno, Czech Republic; Departamento de Oncología y Radioterapia (Department of Oncology and Radiotherapy) (L E Rios Lopez BMedSc), Hospital Nacional Edgardo Rebagliati Martins, Lima, Peru; Deparment of Pharmacology and Toxicology (Prof J A B Rodriguez PhD), University of Antioquia, Medellin, Colombia; Department of Internal Medicine (G M Rwegerera MD), University of Botswana, Gaborone, Botswana; Department of Medical Pharmacology (M M Saber-Ayad MD), Public Health and Community Medicine Department (M R Salem MD), Cairo University, Giza, Egypt; Department of Pediatric Neurology (S Sadeghian MD), Golestan Medical, Educational, and Research Centre (S Sadeghian MD), Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; Department of Research and Development (Prof U Saeed PhD), Islamabad Diagnostic Center Pakistan, Islamabad, Pakistan; Biological Production Development (Prof U Saeed PhD), National Institute of Health, Islamabad, Pakistan; Health Systems and Population Studies Division (K Saif-Ur-Rahman MPH), International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh; Department of Public Health and Health Systems (K Saif-Ur-Rahman MPH), Nagoya University, Nagoya, Japan; Department of Phytochemistry (Prof S Sajadi PhD), Soran University, Soran, Iraq; Department of Nutrition (Prof S Sajadi PhD), Cihan University-Erbil, Erbil, Iraq; Advanced Therapy Medicinal Products Department (S Salahi MD), Royan Institution, Tehran, Iran; Faculty of Health & Social Sciences (B Sathian PhD), Bournemouth University, Bournemouth, UK; Department of Public Health Sciences (M Sawhney PhD), University of North Carolina at Charlotte, Charlotte, NC, USA; Department of Paediatrics (Prof S M Sawyer MD), University of Melbourne, Parkville, VIC, Australia; Centre for Adolescent Health (Prof S M Sawyer MD), Murdoch Childrens Research Institute, Parkville, VIC, Australia; Market Access (M Saylan MD), Bayer, Istanbul, Turkey; Department of Health Sciences (I J C Schneider PhD), Federal University of Santa Catarina, Araranguá, Brazil; Department of Population and Health (A Seidu MPhil), University of Cape Coast, Cape Coast, Ghana; College of Public Health, Medical and Veterinary Sciences (A Seidu MPhil), James Cook University, Townsville, QLD, Australia; Department of Medical Statistics, Epidemiology and Medical Informatics (M Šekerija PhD), University of Zagreb, Zagreb, Croatia; Department of Epidemiology and Prevention of Chronic Noncommunicable Diseases (M Šekerija PhD), Croatian Institute of Public Health, Zagreb, Croatia; National Heart, Lung, and Blood Institute (A Seylani BS), National Institute of Health, Rockville, MD, USA; Center for Biomedical Information Technology (F Sha PhD), Shenzhen Institutes of Advanced Technology, Shenzhen, China; Independent Consultant, Karachi, Pakistan (M A Shaikh MD); Non-communicable Diseases Committee (E Shamsoddin DDS), National Institute for Medical Research Development (NIMAD), Tehran, Iran; Symbiosis Medical College for Women (M Shannawaz PhD), Symbiosis International University, Pune, India; University School of Management and Entrepreneurship (R Sharma PhD), Delhi Technological University, Delhi, India; College of Medicine (Prof J Shin MD), Yonsei University, Seoul, South Korea; Department of Pediatrics and Child Health Nursing (M M Sibhat MSc), Dilla University, Dilla, Ethiopia; Department of Hematology-Oncology (S K Siddappa Malleshappa MD), Baystate Medical Center, Springfield, MA, USA; Real World Insights (G Silva Julian MSc), IQVIA, São Paulo, Brazil; 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 Community Medicine & Public Health (J K Singh PhD), Tribhuvan University, Janakpur, Nepal; Program Services Unit (A H Sinke MD), Pathfinder International, Addis Ababa, Ethiopia; Department of Midwifery (Y Sintayehu MSc), Dire Dawa University, Dire Dawa, Ethiopia; Department No.16 (V Y Skryabin MD), Laboratory of Genetics and Genomics (Prof M S Zastrozhin PhD), Moscow Research and Practical Centre on Addictions, Moscow, Russia; Therapeutic Department (A A Skryabina MD), Balashiha Central Hospital, Balashikha, Russia; Cochrane Iran Associate Centre, National Institute for Medical Research Development (NIMAD) (A Sofi-Mahmudi DDS), Iranian Ministry of Health and Medical Education, Tehran, Iran; Taub Institute for Research on Alzheimer's Disease and the Aging Brain (S Song PhD), Columbia University Medical Center, New York, NY, USA; Department of Social and Behavioral Sciences (E E Spurlock MPH), Yale University, New Haven, CT, USA; Department of Medicine (P Steiropoulos MD), Democritus University of Thrace, Alexandroupolis, Greece; Schiller Institute (Prof K Straif PhD), Boston College, Boston, MA, USA; Barcelona Institute for Global Health, Barcelona, Spain (Prof K Straif PhD); National Institute of Epidemiology (R Suliankatchi Abdulkader MD), Indian Council of Medical Research, Chennai, India; Maternal and Child Health (S Sultana MPH), Projahnmo Research Foundation, Dhaka, Bangladesh; 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; Allergy and Critical Care Medicine (M Tabary MD), University of Pittsburgh, Pittsburgh, PA, USA; Cancer Control Center (T Tabuchi MD), Osaka International Cancer Institute, Osaka, Japan; Asbestos Diseases Research Institute, Sydney, NSW, Australia (Prof K Takahashi PhD); Department of Dermato-Venereology (M Tampa PhD), Victor Babes Clinical Hospital of Infectious Diseases and Tropical Diseases, Bucharest, Romania; Department of Surgery (K Tan PhD), National University of Singapore, Singapore, Singapore; Pediatric Intensive Care Unit (M Temsah MD), King Saud University, Riyadh, Saudi Arabia; School of Public Health (F H Tesfay PhD), School of Pharmacy (B Wubishet MPH), Mekelle University, Mekelle, Ethiopia; Department of Nursing (B Tesfaye MSc), Debre Markos University, Debre Markos, Ethiopia; School of Public Health (Prof J S Thakur MD), Post Graduate Institute of Medical Education and Research, Chandigarh, India; Department of Pediatrics (A Thavamani MD), University Hospitals Rainbow Babies & Children's Hospital, Cleveland, OH, USA; Department of Clinical Epidemiology (A Thiyagarajan MPH), Leibniz Institute for Prevention Research and Epidemiology, Bremen, Germany; Department of Social Security Empirical Research (Prof R Tobe-Gai PhD), National Institute of Population and Social Security Research, Tokyo, Japan; General Department of Surgery (M Togtmol MD), National Center of Traumatology and Orthopedics, Ulaanbaatar, Mongolia; Mongolian Burns Association, Ulaanbaatar, Mongolia (M Togtmol MD); Neuromuscular Rehabilitation Research Center (S Tohidast PhD), Semnan University of Medical Sciences, Semnan, Iran; Nutritional Epidemiology Research Team EREN (M Touvier PhD), National Institute for Health and Medical Research INSERM, Paris, France; School of Health, Medicine and Human Biology (M Touvier PhD), Sorbonne Paris Nord University, Bobigny, France; Department of Pathology and Legal Medicine (M R Tovani-Palone PhD),

University of São Paulo, Ribeirão Preto, Brazil; Modestum LTD, London, UK (M R Tovani-Palone PhD); Institute for Risk Assessment Sciences (IRAS) (E Traini MSc), Utrecht University, Utrecht, Netherlands; Department of Health Economics (B X Tran PhD), Faculty of Nursing and Midwifery (M T N Tran PhD), Hanoi Medical University, Hanoi, Vietnam; Department of Community Medicine (J P Tripathy MD), All India Institute of Medical Sciences, Nagpur, India; Department of Epidemiology and Biostatistics (B S Tusa MPH), Haramaya University, Haramaya, Ethiopia; Department of Allied Health Sciences (I Ullah PhD), Iqra National University, Peshawar, Pakistan; Pakistan Council for Science and Technology (I Ullah PhD), Ministry of Science and Technology, Islamabad, Pakistan; Department of Pediatric Cardiology (K Umapathi MD), Rush University, Chicago, IL, USA; Amity Institute of Biotechnology (E Upadhyay PhD), Amity University Rajasthan, Jaipur, India; Clinical Cancer Research Center (S Valadan Tahbaz PhD, S Yahyazadeh Jabbari MD), Milad General Hospital, Tehran, Iran; Department of Microbiology (S Valadan Tahbaz PhD), Faculty of Medicine (M Zahir MD), Islamic Azad University, Tehran, Iran; School of Mathematics and Statistics (Prof P J Villeneuve PhD), Carleton University, Ottawa, ON, Canada; Occupational Health Unit (Prof F S Violante MD), Sant'Orsola Malpighi Hospital, Bologna, Italy; Foundation University Medical College (Prof Y Waheed PhD), Foundation University Islamabad, Islamabad, Pakistan; National Center for Chronic and Noncommunicable Disease Control and Prevention (N Wang PhD), Chinese Center for Disease Control and Prevention, Beijing, China; Key Laboratory of Shaanxi Province for Craniofacial Precision Medicine Research (Y Wen PhD), Stomatological Hospital (College) of Xi'an Jiaotong University, Xi'an, China; Competence Center of Mortality-Follow-Up of the German National Cohort (R Westerman DSc), Federal Institute for Population Research, Wiesbaden, Germany; Institute of Health and Society (Prof A S Winkler PhD), University of Oslo, Oslo, Norway; Department of Neurology (Prof A S Winkler PhD), Technical University of Munich, Munich, Germany; Department of Endocrinology, First Affiliated Hospital (Prof S Xu PhD), University of Science and Technology of China, Hefei, China; Department of Medicine (Prof S Xu PhD), University of Rochester, Rochester, NY, USA; Cancer Epidemiology and Prevention Research (L Yang PhD), Alberta Health Services, Calgary, BC, Canada; Department of Oncology (L Yang PhD), University of Calgary, Calgary, AB, Canada; School of International Development and Global Studies (Prof S Yaya PhD), University of Ottawa, Ottawa, ON, Canada; 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; School of Medicine (Prof M Z Younis PhD), Tsinghua University, Beijing, China; Department of Clinical Pharmacy and Outcomes Sciences (I Yunusa PhD), University of South Carolina, Columbia, SC, USA; Epidemiology and Cancer Registry Sector (Prof V Zadnik PhD), Institute of Oncology Ljubljana, Ljubljana, Slovenia; Social Determinants of Health Research Center (T Zahirian Moghadam PhD, H Zandian PhD), Department of Community Medicine (H Zandian PhD), Ardabil University of Medical Science, Ardabil, Iran; Addictology Department (Prof M S Zastrozhin PhD), Russian Medical Academy of Continuous Professional Education, Moscow, Russia; Peoples' Friendship University of Russia, Moscow, Russia (A Zastrozhina PhD); Department of General Practice (J Zhang MD), University of Melbourne, Melbourne, VIC, Australia; Victorian Comprehensive Cancer Centre, Melbourne, VIC, Australia (J Zhang MD); School of Nursing and Midwifery (M Zoladl PhD), Yasuj University of Medical Sciences, Yasuj, Iran; Department of Radiation Medicine (A Bleyer MD), Oregon Health and Science University, Portland, OR, USA; McGovern Medical School (A Bleyer MD), University of Texas, Houston, TX, USA.

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N Bekele reports participation on a Data Safety Monitoring Board or Advisory Board as Ethical review board member for two years; and leadership or fiduciary role in board, society, committee or advocacy group, paid or unpaid with Wollo University as an unpaid graduate program coordinator for three years, all outside the submitted work. S Bhaskar reports grants or contracts from NSW Ministry of Health, NSW Brain Clot Bank; and leadership or fiduciary role in board, society, committee or advocacy group, paid or unpaid with Rotary Club of Sydney, Australia as Board Director, International Rotary Fellowship of Rotarian Healthcare Professionals (IRFRHP), UK as Board Director, and BMC Neurology as Editorial Board Member, all outside the submitted work. 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C Herteliu reports grants or contracts from Romanian National Authority for Scientific Research and Innovation, CNDS-UEFISCDI, project number PN-III-P4-ID-PCCF-2016-0084, grant title "Understanding and modelling time-space patterns of psychology-related inequalities and polarization" as research team member, and from Romanian National Authority for Scientific Research and Innovation, CNDS-UEFISCDI, project number PN-III-P2-2.1-SOL-2020-2-0351, grant title "Approaches within public health management in the context of COVID-19 pandemic," as project manager, all outside the submitted work. K Innos reports support for the present manuscript from Estonian Research Council, Grant No PRG722. S M S Islam reports grants or contracts from the NHMRC Emerging Leadership Fellowship and the National Heart Foundation of Australia Fellowship, all outside the submitted work. N E Ismail reports leadership or fiduciary role in board, society, committee or advocacy group, paid or unpaid with Malaysian Academy of Pharmacy as an unpaid Council Member, all outside the submitted work. I Karaye reports support for the present manuscript from the Bill and Melinda Gates Foundation, American Lebanese Syrian Associated Charities, and Saint Baldrick's Foundation, all for providing funding, related to their employment at IHME. J Kauppila reports grants or contracts from Sigrid Juselius Foundation, Finnish Cancer Foundation, and Päivikki and Sakari Sohlberg Foundation, all outside the submitted work. T Ketterl reports consulting fees from Fennec Pharmaceuticals, Inc for advisory services, all outside the submitted work. J Kocarnik reports support for the present manuscript from the Bill and Melinda Gates Foundation and American Lebanese Syrian Associated Charities for providing funding, related to their employment at IHME. 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M Šekerija reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Roche and Johnson & Johnson, all outside the submitted work. D A Santos Silva reports support for the present manuscript from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior—Brazil (CAPES) and National Council for Scientific and Technological Development (CNPq), Brazil. D A Santos Silva reports grants or contracts from the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior—Brazil (CAPES)—Finance Code 001 and is supported in part by National Council for Scientific and Technological Development (CNPq), Brazil (302028/2018-8), all outside the submitted work. 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Data sharing

To download the data used in these analyses, please visit the Global Health Data Exchange GBD 2019 website at http://ghdx.healthdata.org/gbd-2019.

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