

Original Article

The Escalating Global Burden of motor neuron disease: spatiotemporal trends among older adults, affected factors, and future projections

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Abstract: Objective: Motor Neuron Disease (MND) is an increasing social health issue, in the cases of adults above 50 years of age, which requires the examination of its multidimensional burden, the spatiotemporal patterns, and the factors that contribute to it. Methods: We estimated age-standardized prevalence (ASPR), incidence (ASIR), mortality (ASMR), disability-adjusted life years (ASDR), and years lived with disability (ASYLDs) and years of life lost (ASYLLs) in adults aged 50 and older based on Global Burden of Disease (GBD) data 1990-2021. The correlation between Socio-demographic Index (SDI) and disease burden was sought through the analysis of correlation; the relationship between temporal changes and the gave way to joinpoint regression and the Bayesian age-period-cohort (BAPC) models to determine future disease burden. Results: The number of MND cases and age-standardized rates (ASRs) increased substantially over the period 1990-2021 with YLLs making up over 95 percent of DALYs. The highest burden was 75-84 years, with the males having a skewed burden. There were positive relationships between SDI where high-SDI regions (such as Australasia, North America, Western Europe) had the greatest burdens. The burdens were highest in Finland, Ireland and Sweden; the smallest countries recorded steep increases in Lithuania and Costa Rica. The analysis of joinpoint showed that global ASIR on the increase (1995-2005) then decreased (2019-2021), high-SDI areas recorded consistent growth. BAPC forecasted the increase in the number of cases even after minimal decrease in ASRs by 2040. Interpretation: The problem of the increasing burden of MND fueled by the aging population and negative prognosis highlights the inequalities between the strata in terms of SDI. The ability to treat increases the burdens in high-income regions. The focus on surveillance, fair prevention, and resources distribution is important. The paper has emphasized the importance of international cooperation to help reduce disparities associated with SDI and maximize interventions.

Keywords: Global Burden, motor neuron disease, spatiotemporal dynamics, aging population

Introduction

Motor neuron disease (MND) is a life-threatening neurodegenerative disorder characterized by progressive muscle weakness. Its pathological process affects the upper limbs, lower limbs, medulla oblongata (which controls speech and swallowing functions), and respiratory muscle groups. The clinical subtypes are amyotrophic lateral sclerosis (ALS), spinal muscular atrophy, hereditary spastic paraplegia, primary lateral sclerosis, progressive myopathy, and pseudo brachial palsy [1, 2]. This dis-

ease advances through painless progressive paralysis, which usually begins with one side muscles when slowly evolving to other sides muscles [3]. Their mechanisms underlying remain incompletely understood [4], but existing scholarly research has concluded that the etiology of MND is caused by the multi-factorial interplay between genetic vulnerability, exposure elements of the environment and time [5]. Although researches have pointed out that repairing damaged mitochondrial DNA genes can be expected to alleviate the progression of MND [6], clinical management still mainly

focuses on symptom control. It has been shown that ALS patients tend to succumb to respiratory failure in three years of developing the symptoms [7], and the prognosis of the miscellaneous forms of MND is just as bleak, with the ensuing socioeconomic burden of this condition seriously affecting the quality of life of the patient and their surroundings [1].

Globally, more than 60,000 cases were reported in 2021, representing a 74.54% increase compared with 1990. MND have low prevalence and incidence, but cause severe disability with a high fatality rate, with an uneven distribution among affected individuals and a heavy concomitant burden imposed on family and social support systems [8]. Over the past years, the worldwide disease policy of MND has only risen with both the total number of cases and age-standardized rates (ASRs) pronouncedly surging in both males and the aged. Areas which have increased Socio-Demographic Index (SDI), e.g. the high-income North America, Western Europe, Oceania and high-income Asia-Pacific regions, have some of the most highly burdensome patterns in terms of MND prevalence, incidence, and disability-adjusted life years (DALYs) [9]. Regarding the global context, the most rapidly ageing populations are in low- and middle-income countries, the public health burden of the mentioned disease in these regions is likely to increase even more [10]. Consequently, a systematic study of the relevant features of spatiotemporal development of the global disease burden of MND is highly important in developing accurate prevention and intervention measures.

The existing epidemiological studies on MND, utilizing Global Burden of Disease (GBD) study, are still limited. Logroscino et al. investigated the age-sex distribution features of global and regional disease burden based on the GBD 2016 data [2]; Park et al. studied the temporal changes in DALYs with the help of GBD 2019 data [9]. Nevertheless, the current research still requires enhancement of analytical aspects and the depth of methodology. Consequently, the paper presented a systematic examination of the epidemiological burden of MND in the world between 1990 and 2021 preceding its GBD 2021 data by examining the age-standardized prevalence (ASPR), incidence (ASIR), mortality (ASMR), disability-adjusted life years

(ASDR), years lived with disability (ASYLDs), and years of life lost (ASYLLs). We, further, applied the joinpoint regression analysis to disclose the shifts in the trends of the age-standardized rates, employed the correlation analysis study to examine the connection between the burden of disease and SDI, and forecasted the disease trends in the coming 20 years by using Bayesian age-period-cohort (BAPC) modeling.

We intend to use this research as the basis of providing the scientific basis of preventing and controlling global MND outbreaks, facilitating the adoption of stratified intervention measures to different regions and populations and effectively alleviate the global health burden associated with MND.

Material and methods

Data acquisition and download

The data on MND was obtained in the 2021 GBD database [11]. The current paper was devoted to the examination of the MND-related indicators, including prevalence, incidence, mortality, DALYs, YLDs, YLLs, and ASRs with 95% uncertainty intervals (UI). Developed in 2015 by the Institute for Health Metrics and Evaluation (IHME), SDI is a holistic metric crafted to gauge the developmental status of nations and regions, with a focus on the interplay between social progress and population health outcomes. In the 2021 GBD study, a total of 204 countries and territories were categorized into five distinct SDI tiers, namely low, low-middle, middle, high-middle and high [12]. In the research, trends in the disease burden of MND were assessed by using descriptive statistics to examine the data at the global, regional, and national levels between 1990 and 2021. Also, age stratified analyses were conducted (50 to 95+ years, 5-year age group) and sex stratified analyses were conducted to examine the spatio-temporal imbalance by demographics and SDI quintile.

Correlation analysis

Pearson correlation analysis and curve fitting were applied to determine the relationship between SDI and disease burden among 204 countries in the world in 2021 in order to study factors behind the change in disease burden [13].

Joinpoint regression analysis

The joinpoint regression model [Joinpoint Trend Analysis Software]. Surveillance Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, Version 4.9.1.0-April 2022. Those were obtained by applying: Joinpoint Regression Program (cancer.gov) to identify time changes in MND burden on the global and five SDI levels. It is a model of identifying important inflections in time-series data and describes trends within a particular period through annual percentage changes (APCs). Moreover, average annual percentage changes (AAPCs) have been computed to take a recap of the general trends within the study period.

Projection analysis

This paper estimated changes in MND burden by using systematic analysis of MND burden trajectories, and forecasting 2021 to 2040 changes in MND burden globally. The INLA-BAPC model was used with the help of which the marginal posterior distributions are directly approximated [14].

Results

Global trends

Global information on disease burden revealed that the disease burden of MND was on the rise between 1990 and 2021, especially in adults. This age group (50 and above) has the highest burden of the disease. The examination of the overall cases rates showed the steady increase in the overall prevalent cases, incident cases, deaths, DALY, YLDs, and YLLs statistics. The number of deaths showed the most significant growth and increased three times: 12,589.46 to 35,653.69, which is a growth by 183%. The total DALYs also rose considerably, with the value changing to 303,687.51 to 822,092.48 (**Table 1**).

Following age-standardization, there were positive changes in all indicators. ASMR had the most significant increase with the estimated percentage change (EAPC) of 0.87. The ASDR also rose sharply, changing 34.85 to 42.78 with an EAPC raising 0.80 (**Table 1**). The ASRs of the rest of the indicators had consistent overall upward trends whereas EAPCs were

positive. It is worth mentioning that YLLs contributed to more than 95% of DALYs (**Table 1**).

Correlation analysis

In 2021, a correlation analysis was made of 204 countries in the world in relation to the ASRs of all the epidemiological indicators, which revealed that higher SDI positively affected the ASRs, which meant a greater health burden. ASPR, ASIR, ASMR, ASDR, ASYLDs, and ASYLLs all resulted in *p*-values less than 0.01 with correlation coefficients (*R*) of 0.56, 0.51, 0.61, 0.62, 0.56 and 0.62 respectively (**Figure 1A-F**). SDI was positively related to the health burden of MND.

Global trends by SDI

The stratified analysis of 32 regions (global, 5 SDI regions and 26 sub-regions) showed that epidemiology of MND did differ significantly across regions in 1990 to 2021. The five SDI region evaluation revealed that the six epidemiological indicators were differentiated in gradients in ASRs (**Table 1**).

The absolute cases of all six indicators per region of SDI have all been on upward trends with differences in the trends in ASRs. In the year 2021, high-SDI areas reported the most prevalent data and ASRs of all indicators, with 92,267.61 cases, which are more than 65 percent of the worldwide values. Products of ASPR, ASIR, ASMR, ASDR, ASYLLs and ASYLDs also rose directly in relationship to increasing SDI (**Table 1**). By analyzing the data from 1990 to 2021, it was found that except for the EAPC of ASIR and YLDs in the low SDI region which decreased, the rest all increased. The EAPCs of ASIR (0.71), ASPR (0.90) and ASYLDs (0.43) were the highest in high-SDI regions. Regions with middle SDI recorded the largest EAPC of ASDR (4.26). ASMR (5.52) and ASYLLs (5.33) had the highest EAPCs in the Low-SDI regions (**Table 1**). In combination, the number of cases rose in all SDI regions, high-SDI regions had the largest all-age totals and ASRs and in most SDI regions, EAPCs were increasing except among the isolated indicators in the low-SDI regions.

Regional level

The trends in the period between 1990 and 2021 were significantly dissimilar in 26 sub-

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Table 1. The numbers, ASRs, and EAPC for ASR of the six epidemiological indicators of MND in the global and regions in 1990 and 2021

	All-age numbers (95% UI)		ASR (95% UI)		EAPC for ASR (95% CI)
	1990	2021	1990	2021	
Prevalence					
Global	59363.80 (41699.12-80549.06)	140020.23 (103554.52-184567.36)	6.96 (4.89-9.44)	7.36 (5.44-9.70)	0.44 (0.32-0.55)
High SDI	41202.61 (29915.19-54636.86)	92267.61 (5595.38-117040.64)	17 (12.3-22.62)	20.5 (15.83-26.01)	0.90 (0.78-1.03)
High-middle SDI	11125.81 (7366.42-15706.83)	27132.8 (1413.04-37312.2)	5.06 (3.35-7.15)	6.12 (4.26-8.42)	0.73 (0.60-0.85)
Middle SDI	4396.45 (2459.94-7131.66)	13925.17 (480.21-21237.05)	1.93 (1.08-3.13)	2.28 (1.37-3.47)	0.68 (0.62-0.74)
Low-middle SDI	1903.33 (1030.8-3144.06)	5087.07 (201.59-8054)	1.42 (0.77-2.35)	1.6 (0.92-2.54)	0.51 (0.44-0.57)
Low SDI	686.9 (370.1-1136.88)	1499.79 (72.61-2450.06)	1.4 (0.75-2.31)	1.36 (0.75-2.22)	-0.05 (-0.13-0.03)
Andean Latin America	96.71 (56.2-151.88)	370.45 (232.91-548.3)	2.17 (1.26-3.41)	2.86 (4.24-1.8)	1.18 (1.1-1.26)
Australasia	931.53 (653.54-1270.27)	2985.65 (2096.99-4076.84)	18.08 (12.65-24.69)	25.56 (34.89-17.94)	1.2 (1.09-1.3)
Caribbean	167.78 (100.32-257.1)	503.28 (328.67-722.37)	3 (1.79-4.6)	4.21 (6.04-2.75)	1.31 (1.23-1.38)
Central Asia	234.1 (129.39-378.72)	390.07 (220.42-623.46)	2.23 (1.23-3.59)	2.14 (3.41-1.21)	0.01 (-0.12-0.14)
Central Europe	1183.68 (718.93-1789.51)	2367.98 (1553.3-3363.22)	3.57 (2.16-5.41)	5.05 (7.18-3.3)	1.33 (1.27-1.39)
Central Europe, eastern Europe, and central Asia	3135.4 (1828.6-4896.82)	5750.88 (3688.55-8305.97)	2.96 (1.72-4.61)	4.03 (5.83-2.57)	1.37 (1.26-1.49)
Central Latin America	447.65 (261.6-694.38)	1992.88 (1285.56-2904.63)	2.47 (1.45-3.84)	3.57 (5.2-2.31)	1.47 (1.39-1.55)
Central Sub-Saharan Africa	67.97 (35.59-114.32)	154.99 (81.52-261.01)	1.42 (0.75-2.38)	1.3 (2.18-0.69)	-0.25 (-0.33 - -0.17)
East Asia	4192.8 (2364.57-6774.18)	11924.45 (6883.23-18694.78)	2.16 (1.21-3.49)	2.35 (3.69-1.36)	0.26 (0.18-0.34)
Eastern Europe	1717.62 (983.33-2733.25)	2992.83 (1901.05-4357.67)	2.75 (1.57-4.37)	3.88 (5.64-2.45)	1.6 (1.42-1.77)
Eastern Sub-Saharan Africa	233.63 (121.59-394.18)	497.81 (258.91-834.56)	1.47 (0.77-2.48)	1.38 (2.31-0.72)	-0.23 (-0.32 - -0.14)
High-income	46676.9 (33887.76-61910.34)	105333.34 (80952.49-133966.33)	17.82 (12.88-23.69)	22.72 (28.89-17.45)	1.06 (0.94-1.18)
High-income Asia Pacific	4125.68 (2763.13-5724.86)	10765.91 (7549.11-14567.43)	9.09 (6.09-12.62)	11.61 (15.77-8.08)	0.81 (0.6-1.03)
High-income North America	15317.13 (11082.16-20375.45)	35140.36 (28588.67-42748.46)	20.48 (14.75-27.29)	24.31 (29.55-19.78)	1.29 (1.04-1.53)
Latin America and Caribbean	1301.28 (778.84-1996.7)	5539.23 (3612.12-7961.23)	2.7 (1.62-4.15)	4.03 (5.79-2.63)	1.58 (1.5-1.66)
North Africa and Middle East	1021.49 (606.32-1570.53)	3113.15 (1951.54-4616.06)	2.7 (1.6-4.15)	3.05 (4.52-1.92)	0.53 (0.49-0.56)
Oceania	10.14 (5.87-16.21)	23.13 (12.95-37.51)	1.6 (0.92-2.55)	1.41 (2.28-0.79)	-0.57 (-0.66 - -0.48)
South Asia	1532.38 (808.41-2566.02)	4626.61 (2579.77-7422.8)	1.2 (0.63-2.01)	1.42 (2.27-0.79)	0.65 (0.57-0.73)
Southeast Asia	815.48 (436.7-1351.57)	2251.02 (1259.96-3632.48)	1.46 (0.78-2.42)	1.51 (2.44-0.85)	0.13 (0.05-0.2)
Southeast Asia, east Asia, and Oceania	5018.41 (2822.41-8132.04)	14198.61 (8182.86-22361.04)	2 (1.12-3.24)	2.16 (3.4-1.24)	0.24 (0.16-0.32)
Southern Latin America	573.5 (358.21-851.77)	1787.44 (1221.41-2461.3)	5.66 (3.53-8.41)	9.48 (13.06-6.47)	1.72 (1.6-1.84)
Southern Sub-Saharan Africa	102.66 (54.7-170.07)	204.66 (110.73-337.63)	1.8 (0.96-2.99)	1.67 (2.75-0.9)	-0.24 (-0.34 - -0.14)
Sub-Saharan Africa	677.95 (363.16-1120.6)	1458.41 (788.89-2387.77)	1.5 (0.8-2.47)	1.4 (2.3-0.76)	-0.18 (-0.26 - -0.1)
Tropical Latin America	589.14 (353.54-904.13)	2672.62 (1750.56-3838.79)	2.95 (1.77-4.52)	4.69 (6.73-3.07)	1.83 (1.73-1.94)
Western Europe	25729.06 (18768.89-33837.36)	54653.99 (40567.04-71698.31)	20.35 (14.77-26.83)	28.06 (36.86-20.8)	1.14 (1.04-1.24)
Western Sub-Saharan Africa	273.68 (151.3-444.9)	600.95 (336.52-969.98)	1.43 (0.79-2.34)	1.37 (2.21-0.76)	-0.07 (-0.15-0)
Incidence					
Global	19399.22 (14611.01-24825.98)	45159.88 (35371.81-55871.48)	2.26 (1.70-2.88)	2.37 (1.86-2.93)	0.26 (0.20-0.33)
High SDI	11903.08 (9359.27-14493.47)	26932.77 (21909.7-31914.62)	4.9 (3.84-5.99)	5.94 (4.81-7.06)	0.71 (0.66-0.76)
High-middle SDI	3626.46 (2540.9-4886.68)	8376.92 (6263.19-10708.66)	1.63 (1.14-2.19)	1.88 (1.41-2.41)	0.59 (0.49-0.70)
Middle SDI	2242.87 (1345.22-3374.94)	6163.42 (4161.47-8573.02)	0.98 (0.59-1.48)	1.01 (0.68-1.4)	0.21 (0.13-0.28)

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Low-middle SDI	1114.4 (650.18-1708.45)	2652.64 (1690.39-3839.33)	0.83 (0.48-1.27)	0.9 (0.54-1.36)	0.11 (0.04-0.17)
Low SDI	495.57 (288.63-765.08)	997.28 (595.72-1505.74)	1 (0.58-1.55)	0.83 (0.53-1.2)	-0.37 (-0.46 - -0.28)
Andean Latin America	45.9 (28.66-67.6)	176.91 (125.99-235.42)	1.03 (0.65-1.52)	1.37 (1.82-0.98)	1.21 (1.13-1.3)
Australasia	386.73 (312.71-460.97)	1146.24 (935.87-1368.06)	7.42 (5.98-8.89)	9.65 (11.57-7.85)	0.93 (0.86-1)
Caribbean	78.77 (50.93-111.97)	245.71 (186.91-309.39)	1.41 (0.91-2)	2.06 (2.59-1.57)	1.45 (1.36-1.54)
Central Asia	91.86 (51.71-144.56)	144.21 (84.06-221.27)	0.87 (0.49-1.37)	0.78 (1.2-0.45)	-0.39 (-0.46 - -0.32)
Central Europe	437.4 (283.4-622.73)	859.1 (638.87-1100.67)	1.3 (0.83-1.85)	1.82 (2.35-1.35)	1.28 (1.22-1.35)
Central Europe, eastern Europe, and central Asia	1152.05 (714.05-1693.52)	2184.79 (1591.15-2865.49)	1.07 (0.66-1.57)	1.52 (2-1.1)	1.49 (1.38-1.61)
Central Latin America	203.78 (129.53-293.87)	954.87 (709.05-1230.58)	1.13 (0.72-1.63)	1.72 (2.21-1.28)	1.67 (1.58-1.76)
Central Sub-Saharan Africa	51.63 (28.47-81.91)	117.87 (65.79-185.76)	1.08 (0.6-1.71)	0.99 (1.55-0.55)	-0.32 (-0.42 - -0.21)
East Asia	2090.42 (1272.83-3122.39)	4500.53 (2788.34-6638.77)	1.07 (0.65-1.6)	0.88 (1.3-0.55)	-0.72 (-0.84 - -0.6)
Eastern Europe	622.78 (377.5-927.35)	1181.48 (860.28-1550.73)	0.97 (0.59-1.46)	1.52 (2-1.1)	1.9 (1.75-2.05)
Eastern Sub-Saharan Africa	187.46 (102.67-299.44)	361.46 (198.91-573.41)	1.19 (0.65-1.89)	1 (1.59-0.56)	-0.6 (-0.72 - -0.49)
High-income	13238.32 (10396.63-16148.11)	30088.93 (24338.69-35779.77)	5.03 (3.94-6.17)	6.44 (7.68-5.19)	0.89 (0.83-0.94)
High-income Asia Pacific	1191.4 (870.62-1543.15)	2929.64 (2231.7-3657.98)	2.63 (1.93-3.41)	3.05 (3.85-2.29)	0.58 (0.5-0.66)
High-income North America	4630.69 (3660.15-5598.92)	11461.45 (9600.72-13295)	6.08 (4.78-7.4)	7.82 (9.1-6.53)	0.91 (0.83-0.99)
Latin America and Caribbean	635.15 (418.02-890.79)	2842.14 (2188.46-3566.93)	1.32 (0.87-1.85)	2.07 (2.59-1.6)	1.77 (1.67-1.88)
North Africa and Middle East	425.97 (270.35-614.63)	1197.72 (818.93-1640.99)	1.12 (0.71-1.62)	1.17 (1.6-0.8)	0.21 (0.17-0.25)
Oceania	6.52 (4.06-9.53)	13.82 (8.36-20.82)	1.01 (0.63-1.47)	0.82 (1.24-0.5)	-0.79 (-0.89 - -0.7)
South Asia	912.84 (524.05-1411.3)	2313.85 (1423.28-3424.3)	0.71 (0.41-1.1)	0.7 (1.04-0.43)	0.05 (-0.03-0.12)
Southeast Asia	458.58 (260.9-715.77)	1057.13 (625-1603.51)	0.82 (0.47-1.28)	0.7 (1.07-0.42)	-0.51 (-0.61 - -0.41)
Southeast Asia, east Asia, and Oceania	2555.52 (1535.79-3837.43)	5571.48 (3429.1-8258.94)	1.02 (0.61-1.53)	0.84 (1.24-0.52)	-0.68 (-0.8 - -0.56)
Southern Latin America	209.8 (142.08-288.42)	604.02 (465.37-750.98)	2.05 (1.39-2.83)	3.19 (3.98-2.46)	1.42 (1.3-1.55)
Southern Sub-Saharan Africa	52.38 (29.89-81.99)	97.6 (56.5-150.52)	0.92 (0.52-1.44)	0.79 (1.23-0.46)	-0.51 (-0.64 - -0.39)
Sub-Saharan Africa	479.38 (277.51-743.84)	960.98 (565.14-1476.18)	1.05 (0.61-1.64)	0.92 (1.42-0.54)	-0.46 (-0.56 - -0.35)
Tropical Latin America	306.71 (209.37-420.11)	1464.66 (1151.77-1797.91)	1.54 (1.05-2.1)	2.57 (3.16-2.03)	2.04 (1.91-2.16)
Western Europe	6819.7 (5355.38-8322.51)	13947.59 (10954.46-16947.08)	5.41 (4.24-6.63)	7.17 (8.75-5.61)	1.01 (0.95-1.07)
Western Sub-Saharan Africa	187.91 (116.79-279.87)	384.05 (243.17-563.6)	0.98 (0.61-1.47)	0.87 (1.29-0.55)	-0.37 (-0.45 - -0.29)
Deaths					
Global	12589.46 (11788.86-13224.24)	35653.69 (32033.86-39005.18)	1.51 (1.41-1.59)	1.89 (1.69-2.07)	0.87 (0.73-1.00)
High SDI	10092.99 (10454.72-9558.72)	23540.63 (21168.05-25501.37)	4.11 (3.89-4.25)	5.06 (4.58-5.46)	0.88 (0.73-1.04)
High-middle SDI	1850.14 (2097.02-1621.64)	7956.85 (6944.95-9032.77)	0.84 (0.74-0.95)	1.79 (1.56-2.03)	2.36 (2.17-2.55)
Middle SDI	569.68 (672.33-442.25)	3471.63 (2979.27-4036.24)	0.25 (0.19-0.29)	0.57 (0.49-0.66)	2.52 (2.37-2.68)
Low-middle SDI	65.92 (90.73-52.77)	628.15 (526.95-741.38)	0.05 (0.04-0.07)	0.2 (0.17-0.24)	4.77 (4.66-4.89)
Low SDI	2.23 (5.14-0.93)	23.5 (8.02-46.72)	0 (0-0.01)	0.02 (0.01-0.04)	5.52 (5.11-5.92)
Andean Latin America	0.72 (0.38-1.39)	135.32 (96.36-179.83)	0.02 (0.01-0.03)	1.05 (0.75-1.4)	13.98 (11.42-16.59)
Australasia	334.47 (299.76-369.8)	898.21 (761.49-1034.7)	6.39 (5.73-7.07)	7.48 (6.37-8.61)	0.62 (0.34-0.91)
Caribbean	2.2 (1.9-2.8)	193.37 (159.31-231.18)	0.04 (0.03-0.05)	1.63 (1.34-1.95)	10.83 (7.49-14.28)
Central Asia	1.36 (0.96-2.1)	18.06 (15.38-21.13)	0.01 (0.01-0.02)	0.09 (0.08-0.11)	8.04 (7.08-9.01)
Central Europe	214.26 (202.57-227.32)	1002.02 (903.68-1113.75)	0.62 (0.59-0.66)	2.07 (1.87-2.3)	4.32 (3.99-4.65)

GBD of motor neuron disease

Central Europe, eastern Europe, and central Asia	378.25 (320.59-455.44)	2946.8 (2722.99-3206.24)	0.34 (0.29-0.41)	2.01 (1.86-2.19)	5.88 (5.52-6.24)
Central Latin America	115.42 (109.71-121.02)	896.22 (774.83-1028.01)	0.65 (0.62-0.68)	1.62 (1.4-1.86)	3 (2.85-3.16)
Central Sub-Saharan Africa	0.29 (0.14-0.58)	0.29 (0.14-0.75)	0.01 (0-0.01)	0 (0-0.01)	-4.04 (-5.16 - -2.89)
East Asia	741.2 (428.01-968.75)	2870.15 (1876.73-3865.65)	0.37 (0.22-0.48)	0.56 (0.36-0.75)	0.49 (0.05-0.92)
Eastern Europe	162.63 (110.89-237.38)	1926.72 (1751.64-2123.87)	0.25 (0.17-0.36)	2.44 (2.22-2.69)	7.2 (6.55-7.86)
Eastern Sub-Saharan Africa	0.49 (0.21-0.93)	0.53 (0.3-1.24)	0 (0-0.01)	0 (0-0)	-3.32 (-4.16 - -2.47)
High-income	11039.1 (10456.55-11417.45)	26139.08 (23347.49-28490.4)	4.14 (3.92-4.28)	5.4 (4.87-5.86)	1.07 (0.9-1.24)
High-income Asia Pacific	980.27 (925.28-1023.84)	3190.13 (2735.33-3537.14)	2.18 (2.06-2.28)	3.04 (2.65-3.34)	1.1 (0.96-1.25)
High-income North America	3800.9 (3567.61-3957.66)	9019.19 (8206.04-9585.13)	4.9 (4.62-5.1)	6.12 (5.58-6.5)	0.8 (0.47-1.13)
Latin America and Caribbean	328.56 (312.41-342.57)	2804.21 (2539.69-3081.12)	0.69 (0.65-0.72)	2.05 (1.86-2.26)	3.76 (3.57-3.95)
North Africa and Middle East	62.25 (25.79-137.18)	513.27 (306.21-826.63)	0.17 (0.07-0.37)	0.53 (0.31-0.85)	4.21 (3.93-4.49)
Oceania	0.13 (0.07-0.19)	0.19 (0.1-0.32)	0.02 (0.01-0.03)	0.01 (0.01-0.02)	-2.5 (-3.29 - -1.7)
South Asia	20.37 (8.52-48.63)	264.73 (128.74-409.76)	0.02 (0.01-0.04)	0.08 (0.04-0.13)	5.23 (5.04-5.42)
Southeast Asia	16.58 (7.91-26.69)	110.48 (72.61-153.47)	0.03 (0.01-0.05)	0.07 (0.05-0.1)	3 (2.85-3.14)
Southeast Asia, east Asia, and Oceania	757.9 (436.01-992.06)	2980.81 (1958.9-3988.78)	0.29 (0.17-0.38)	0.45 (0.29-0.6)	0.57 (0.15-0.99)
Southern Latin America	27.66 (25.34-30.02)	558.14 (487.19-637.63)	0.27 (0.25-0.29)	2.92 (2.55-3.34)	6.42 (4.8-8.06)
Southern Sub-Saharan Africa	1.86 (0.88-3.41)	1.81 (0.87-3.41)	0.03 (0.01-0.06)	0.02 (0.01-0.03)	-3.06 (-3.55 - -2.56)
Sub-Saharan Africa	3.04 (0.99-4.76)	4.79 (2.98-7.9)	0.01 (0-0.01)	0 (0-0.01)	-2.13 (-2.73 - -1.53)
Tropical Latin America	210.23 (197.03-222.62)	1579.31 (1433.81-1721.29)	1.06 (0.99-1.13)	2.78 (2.52-3.04)	3.48 (3.38-3.59)
Western Europe	5895.79 (5563.97-6163.14)	12473.41 (10905.1-13966.32)	4.58 (4.33-4.78)	6.1 (5.38-6.8)	1.26 (1.1-1.42)
Western Sub-Saharan Africa	0.4 (0.24-0.57)	2.16 (1.41-3.21)	0 (0-0)	0 (0-0.01)	2.39 (2.04-2.75)
DALYs					
Global	303687.51 (286285.25-319761.60)	822092.48 (750353.33-894084.82)	34.85 (32.78-36.71)	42.78 (38.99-46.55)	0.80 (0.68-0.91)
High SDI	235351.88 (225144.21-243325.96)	554048.51 (473781.72-554048.51)	97.93 (93.77-101.23)	117.44 (108.39-125.62)	0.80 (0.66-0.94)
High-middle SDI	49143.84 (42937.6-55891.57)	220036.58 (170750.6-220036.58)	21.57 (18.86-24.49)	43.36 (38.14-49.19)	2.12 (1.96-2.28)
Middle SDI	16617.6 (12918.15-19668.42)	107900.5 (79822.81-107900.5)	6.87 (5.37-8.12)	14.71 (12.68-17.1)	2.24 (2.08-2.41)
Low-middle SDI	2151.41 (1704.58-2872.55)	20377.41 (14639.81-20377.41)	1.56 (1.24-2.08)	5.31 (4.49-6.25)	4.26 (4.18-4.34)
Low SDI	207.44 (116.19-343.4)	1584.53 (472.91-1584.53)	0.41 (0.23-0.69)	0.83 (0.42-1.4)	2.38 (2.08-2.68)
Andean Latin America	40.13 (25.03-63.37)	3557.2 (2529.88-4716.48)	0.89 (0.55-1.4)	27.21 (36.06-19.38)	11.92 (9.95-13.93)
Australasia	7640.17 (6879.4-8414.32)	19271.22 (16626.75-22043.94)	148.69 (133.9-163.65)	169.48 (193.6-146.75)	0.56 (0.31-0.81)
Caribbean	90.37 (71.39-119.15)	4838.34 (4006.86-5758.98)	1.6 (1.26-2.12)	40.53 (48.25-33.56)	9.58 (6.75-12.49)
Central Asia	89.94 (61.28-130.56)	580.1 (492.89-682.49)	0.82 (0.55-1.2)	2.9 (3.43-2.46)	5.16 (4.48-5.84)
Central Europe	5978.16 (5653.69-6355.84)	24632.62 (22325.24-27214.18)	17.3 (16.35-18.41)	53.18 (58.62-48.29)	4.08 (3.76-4.4)
Central Europe, eastern Europe, and central Asia	11105.9 (9317.92-13330.86)	75798.81 (70392.15-81972.64)	9.95 (8.35-11.95)	52.6 (56.85-48.87)	5.49 (5.15-5.82)
Central Latin America	3172.68 (3017.29-3329.26)	23710.72 (20572.45-27148.2)	17.08 (16.22-17.93)	41.88 (47.95-36.34)	2.95 (2.8-3.1)
Central Sub-Saharan Africa	22.4 (13.18-36.63)	41.68 (23.54-70.93)	0.45 (0.26-0.73)	0.34 (0.57-0.19)	-1.05 (-1.32 - -0.78)
East Asia	21831.13 (12858.45-28316.77)	79473.28 (53201.09-107474.78)	10.45 (6.19-13.56)	15.15 (20.48-10.14)	0.39 (-0.04-0.82)
Eastern Europe	5037.79 (3455.13-7197.08)	50586.1 (46207.42-55482.35)	7.61 (5.23-10.87)	65.09 (71.4-59.47)	6.69 (6.1-7.29)
Eastern Sub-Saharan Africa	62.69 (35.26-104.65)	121.58 (66.56-205.19)	0.39 (0.22-0.65)	0.33 (0.56-0.18)	-0.63 (-0.78 - -0.49)
High-income	258128.13 (246985.02-266454.61)	569010.4 (519103.61-614113.31)	99.44 (95.27-102.61)	125.81 (135.26-115.58)	0.97 (0.82-1.13)

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High-income Asia Pacific	24648.4 (23414.56-25753.94)	62500.17 (55174.73-68562.73)	53.99 (51.24-56.44)	66.09 (72.17-59.08)	0.67 (0.53-0.81)
High-income North America	88464.81 (83982.45-91997.46)	205096.8 (190139.02-216338.4)	119.27 (113.52-123.94)	143.98 (151.69-133.83)	0.71 (0.44-0.98)
Latin America and Caribbean	8962.92 (8577.96-9354.52)	72101.7 (65701.91-79044.42)	18.12 (17.31-18.93)	51.82 (56.82-47.2)	3.6 (3.43-3.77)
North Africa and Middle East	1915.28 (917.05-3906.89)	13911.42 (8549.07-21973.84)	4.88 (2.33-10.02)	13.43 (21.2-8.25)	3.77 (3.5-4.04)
Oceania	5.63 (3.75-8.05)	10.06 (6.21-15.19)	0.86 (0.56-1.24)	0.6 (0.91-0.37)	-1.58 (-2 --1.16)
South Asia	883.83 (467.98-1686.19)	7912.35 (4417.91-11844.84)	0.67 (0.36-1.28)	2.35 (3.51-1.32)	4.1 (3.89-4.31)
Southeast Asia	633.33 (378.8-953.47)	3424.9 (2380.86-4629.7)	1.08 (0.65-1.63)	2.2 (2.97-1.53)	2.3 (2.2-2.4)
Southeast Asia, east Asia, and Oceania	22470.08 (13276.96-29164.24)	82908.25 (55843.49-111341.04)	8.32 (4.94-10.8)	12.09 (16.21-8.14)	0.44 (0.03-0.84)
Southern Latin America	820.47 (739.45-909.98)	13674.86 (12050.38-15480.41)	7.99 (7.2-8.87)	73.14 (82.72-64.49)	6.03 (4.52-7.56)
Southern Sub-Saharan Africa	64.76 (25.37-105.56)	84.6 (48.4-140.88)	1.11 (0.44-1.82)	0.69 (1.14-0.39)	-2 (-2.34 --1.67)
Sub-Saharan Africa	221.36 (129.75-345.49)	449.56 (279.16-694.58)	0.48 (0.28-0.75)	0.42 (0.65-0.26)	-0.63 (-0.83 --0.43)
Tropical Latin America	5659.74 (5334.96-5978.72)	39995.43 (36665.58-43426.01)	27.38 (25.76-28.95)	69.32 (75.28-63.48)	3.31 (3.21-3.41)
Western Europe	136554.28 (130064.8-142205.58)	268467.35 (239628.29-297829.33)	110.11 (105.02-114.6)	141.97 (157.02-127.6)	1.13 (0.97-1.29)
Western Sub-Saharan Africa	71.5 (42.36-114.52)	201.7 (128.88-300.45)	0.37 (0.21-0.59)	0.43 (0.65-0.27)	0.55 (0.42-0.68)
YLDs					
Global	12603.16 (7870.58-18629.29)	29651.31 (19242.77-42788.42)	1.48 (0.92-2.18)	1.56 (1.01-2.25)	0.43 (0.32-0.55)
High SDI	8745.82 (5595.38-12802.38)	19511.14 (13039-27578.81)	3.61 (2.3-5.31)	4.338 (2.89-6.15)	0.89 (0.77-1.02)
High-middle SDI	2362.81 (1413.04-3597.48)	5760.32 (3580.89-8605.88)	1.08 (0.64-1.64)	1.3 (0.81-1.94)	0.72 (0.60-0.85)
Middle SDI	933.94 (480.21-1604.59)	2957.74 (1628.56-4841.05)	0.41 (0.21-0.7)	0.48 (0.27-0.79)	0.68 (0.62-0.74)
Low-middle SDI	404.33 (201.59-704.87)	1080.68 (571.33-1812.64)	0.3 (0.15-0.53)	0.34 (0.18-0.57)	0.51 (0.44-0.57)
Low SDI	145.91 (72.61-253.99)	318.61 (161.47-551.88)	0.3 (0.15-0.52)	0.29 (0.15-0.5)	-0.05 (-0.13-0.03)
Andean Latin America	20.54 (11-34.54)	78.66 (44.57-125.6)	0.46 (0.25-0.77)	0.61 (0.97-0.34)	1.18 (1.1-1.25)
Australasia	197.77 (123.13-295.24)	633.06 (397.35-943.54)	3.84 (2.38-5.74)	5.42 (8.11-3.39)	1.19 (1.09-1.3)
Caribbean	35.63 (19.56-58.21)	106.86 (62.72-164.9)	0.64 (0.35-1.04)	0.89 (1.38-0.53)	1.31 (1.23-1.38)
Central Asia	49.73 (25.4-85.52)	82.88 (42.88-140.39)	0.47 (0.24-0.81)	0.45 (0.77-0.24)	0.01 (-0.11-0.14)
Central Europe	251.44 (139.9-407.54)	502.77 (296.78-773.49)	0.76 (0.42-1.23)	1.07 (1.66-0.63)	1.33 (1.27-1.39)
Central Europe, eastern Europe, and central Asia	666.07 (358.79-1106.97)	1221.21 (709.83-1909.94)	0.63 (0.34-1.04)	0.86 (1.34-0.5)	1.37 (1.26-1.49)
Central Latin America	95.1 (50.8-157.71)	423.19 (243.87-662.5)	0.53 (0.28-0.87)	0.76 (1.19-0.44)	1.47 (1.39-1.55)
Central Sub-Saharan Africa	14.44 (7.02-25.8)	32.92 (15.88-58.28)	0.3 (0.15-0.54)	0.28 (0.49-0.13)	-0.25 (-0.33 --0.17)
East Asia	890.68 (465.46-1521.07)	2532.97 (1355.54-4235.9)	0.46 (0.24-0.78)	0.5 (0.84-0.27)	0.26 (0.18-0.34)
Eastern Europe	364.9 (191.78-613.77)	635.56 (365.91-1002.8)	0.58 (0.31-0.98)	0.82 (1.3-0.47)	1.6 (1.42-1.77)
Eastern Sub-Saharan Africa	49.62 (23.94-88.62)	105.75 (50.7-188.21)	0.31 (0.15-0.56)	0.29 (0.52-0.14)	-0.23 (-0.32 --0.14)
High-income	9908.04 (6329.81-14523.42)	22283.73 (14878.63-31704.72)	3.78 (2.41-5.56)	4.81 (6.87-3.2)	1.05 (0.93-1.17)
High-income Asia Pacific	876.19 (527-1320.01)	2285.77 (1424.92-3356.92)	1.93 (1.16-2.91)	2.46 (3.64-1.53)	0.81 (0.6-1.03)
High-income North America	3252.65 (2076.73-4798.09)	7454.83 (5126.5-10309.62)	4.35 (2.76-6.44)	5.16 (7.13-3.54)	1.28 (1.04-1.53)
Latin America and Caribbean	276.4 (150.93-453.07)	1176.18 (684.21-1822.91)	0.57 (0.31-0.94)	0.86 (1.32-0.5)	1.58 (1.5-1.66)
North Africa and Middle East	217.01 (118.84-356.02)	661.3 (378.11-1045.6)	0.57 (0.31-0.94)	0.65 (1.02-0.37)	0.53 (0.49-0.56)
Oceania	2.15 (1.15-3.64)	4.91 (2.55-8.45)	0.34 (0.18-0.57)	0.3 (0.51-0.16)	-0.57 (-0.66 --0.48)
South Asia	325.55 (159.38-574.07)	982.95 (508.49-1670.49)	0.25 (0.12-0.45)	0.3 (0.51-0.16)	0.65 (0.57-0.73)
Southeast Asia	173.24 (85.88-302.97)	478.23 (245.5-821.77)	0.31 (0.15-0.54)	0.32 (0.55-0.16)	0.13 (0.05-0.2)

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Southeast Asia, east Asia, and Oceania	1066.07 (552.96-1825.65)	3016.11 (1605.05-5069)	0.42 (0.22-0.73)	0.46 (0.77-0.24)	0.24 (0.16-0.32)
Southern Latin America	121.81 (69.28-193.68)	379.49 (231.95-568.16)	1.2 (0.68-1.91)	2.01 (3.02-1.23)	1.72 (1.6-1.84)
Southern Sub-Saharan Africa	21.8 (10.89-38.24)	43.48 (21.87-75.62)	0.38 (0.19-0.67)	0.35 (0.62-0.18)	-0.24 (-0.34 - -0.13)
Sub-Saharan Africa	144 (71.65-250.92)	309.83 (154.46-538.41)	0.32 (0.16-0.55)	0.3 (0.52-0.15)	-0.18 (-0.26 - -0.1)
Tropical Latin America	125.13 (68.82-204.64)	567.45 (331.27-870.7)	0.63 (0.34-1.02)	1 (1.53-0.58)	1.83 (1.73-1.93)
Western Europe	5459.62 (3520.51-7951.89)	11530.58 (7557.05-16687.78)	4.32 (2.77-6.31)	5.93 (8.62-3.87)	1.13 (1.03-1.22)
Western Sub-Saharan Africa	58.13 (29.48-99.79)	127.68 (66.16-217.87)	0.3 (0.15-0.52)	0.29 (0.5-0.15)	-0.07 (-0.15-0)
YLLs					
Global	291084.35 (273689.09-306067.84)	792441.17 (720979.82-863009.66)	33.38 (31.31-35.11)	41.22 (37.44-44.92)	0.81 (0.70-0.93)
High SDI	226606.06 (216791.82-233668.53)	496827.02 (455306.99-533173.69)	94.32 (90.32-97.23)	113.1 (104.28-120.97)	0.80 (0.65-0.94)
High-middle SDI	46781.03 (40633.76-53523.96)	188245.32 (165021.67-213754.34)	20.49 (17.82-23.41)	42.06 (36.85-47.77)	2.18 (2.01-2.36)
Middle SDI	15683.66 (12049.16-18564.01)	89754.76 (76849.63-104946.7)	6.46 (4.99-7.63)	14.23 (12.19-16.61)	2.32 (2.14-2.49)
Low-middle SDI	1747.08 (1387.78-2435.01)	16233.23 (13630.72-19194.33)	1.26 (1-1.74)	4.97 (4.17-5.88)	4.74 (4.63-4.85)
Low SDI	61.53 (26.2-139.91)	622.72 (212.46-1231.42)	0.12 (0.05-0.27)	0.54 (0.19-1.08)	5.33 (4.94-5.72)
Andean Latin America	19.59 (10.36-38.38)	3478.54 (2455.56-4639.05)	0.43 (0.23-0.83)	26.61 (35.47-18.81)	13.79 (11.26-16.37)
Australasia	7442.41 (6700.74-8208.31)	18638.16 (15991.9-21396.05)	144.86 (130.42-159.65)	164.06 (188.04-141.3)	0.54 (0.28-0.79)
Caribbean	54.74 (46.98-70.9)	4731.48 (3904.09-5650.2)	0.97 (0.83-1.25)	39.63 (47.34-32.7)	10.8 (7.45-14.25)
Central Asia	40.21 (28.43-61.9)	497.21 (423.14-581.44)	0.35 (0.24-0.53)	2.45 (2.86-2.08)	7.66 (6.72-8.61)
Central Europe	5726.72 (5422.96-6069.78)	24129.85 (21846.73-26715.81)	16.54 (15.67-17.53)	52.1 (57.55-47.26)	4.17 (3.83-4.5)
Central Europe, eastern Europe, and central Asia	10439.82 (8775.26-12630.55)	74577.61 (69204.3-80680.19)	9.32 (7.85-11.28)	51.75 (55.94-48.04)	5.63 (5.29-5.97)
Central Latin America	3077.58 (2934.52-3224.02)	23287.53 (20140.88-26734.25)	16.55 (15.77-17.34)	41.13 (47.21-35.57)	2.99 (2.83-3.14)
Central Sub-Saharan Africa	7.96 (3.74-15.8)	8.76 (4.35-22.13)	0.15 (0.07-0.29)	0.06 (0.16-0.03)	-3.69 (-4.79 - -2.58)
East Asia	20940.44 (12021.84-27366.52)	76940.31 (50454.13-104465.95)	10 (5.76-13.06)	14.65 (19.88-9.6)	0.39 (-0.06-0.84)
Eastern Europe	4672.89 (3158.09-6803.06)	49950.55 (45580.41-54823.7)	7.02 (4.76-10.23)	64.27 (70.54-58.66)	6.86 (6.26-7.48)
Eastern Sub-Saharan Africa	13.07 (5.73-24.75)	15.82 (9.36-35.26)	0.08 (0.03-0.14)	0.04 (0.09-0.02)	-3 (-3.82 - -2.17)
High-income	248220.09 (237528.48-255565.81)	546726.67 (497759.64-590563.38)	95.66 (91.66-98.44)	121 (130.17-110.97)	0.97 (0.81-1.13)
High-income Asia Pacific	23772.2 (22569.48-24772.07)	60214.4 (52806.33-66194.8)	52.06 (49.37-54.28)	63.62 (69.6-56.55)	0.67 (0.51-0.82)
High-income North America	85212.16 (80941.38-88360.19)	197641.98 (183019.37-208569.2)	114.92 (109.47-119.06)	138.82 (146.32-128.93)	0.69 (0.42-0.97)
Latin America and Caribbean	8686.52 (8303.16-9038.06)	70925.52 (64559.6-77845.98)	17.54 (16.74-18.26)	50.97 (55.95-46.37)	3.65 (3.47-3.83)
North Africa and Middle East	1698.27 (713.69-3695.94)	13250.12 (7914.59-21343.3)	4.31 (1.8-9.45)	12.78 (20.58-7.63)	4.02 (3.73-4.31)
Oceania	3.47 (2-5.16)	5.14 (2.8-8.79)	0.53 (0.29-0.79)	0.3 (0.51-0.16)	-2.37 (-3.16 - -1.57)
South Asia	558.28 (231.99-1338.4)	6929.39 (3329.56-10796.63)	0.42 (0.17-1)	2.05 (3.19-0.99)	5.15 (4.95-5.35)
Southeast Asia	460.09 (217.47-741.28)	2946.68 (1923.56-4121.23)	0.77 (0.37-1.24)	1.88 (2.62-1.23)	2.85 (2.7-3.01)
Southeast Asia, east Asia, and Oceania	21404.01 (12240.08-28012.83)	79892.13 (52635.85-107741.46)	7.89 (4.53-10.33)	11.63 (15.66-7.65)	0.45 (0.02-0.87)
Southern Latin America	698.66 (641.72-756.74)	13295.37 (11663.19-15125.92)	6.79 (6.23-7.36)	71.12 (80.85-62.43)	6.29 (4.69-7.92)
Southern Sub-Saharan Africa	42.96 (8.48-76)	41.13 (19.02-78.93)	0.73 (0.15-1.29)	0.33 (0.63-0.16)	-3.3 (-3.86 - -2.74)
Sub-Saharan Africa	77.35 (26.67-119.27)	139.73 (89.56-226.11)	0.16 (0.06-0.26)	0.12 (0.2-0.08)	-1.65 (-2.28 - -1)
Tropical Latin America	5534.61 (5212.21-5849.28)	39427.97 (36106.95-42865.64)	26.75 (25.14-28.3)	68.32 (74.29-62.5)	3.34 (3.23-3.44)
Western Europe	131094.66 (124830.55-136461.83)	256936.76 (228493.13-285890.61)	105.79 (100.9-110.05)	136.04 (150.88-121.88)	1.13 (0.97-1.29)
Western Sub-Saharan Africa	13.37 (7.98-18.73)	74.03 (48.68-109.95)	0.06 (0.04-0.09)	0.14 (0.2-0.09)	2.6 (2.23-2.97)

GBD of motor neuron disease

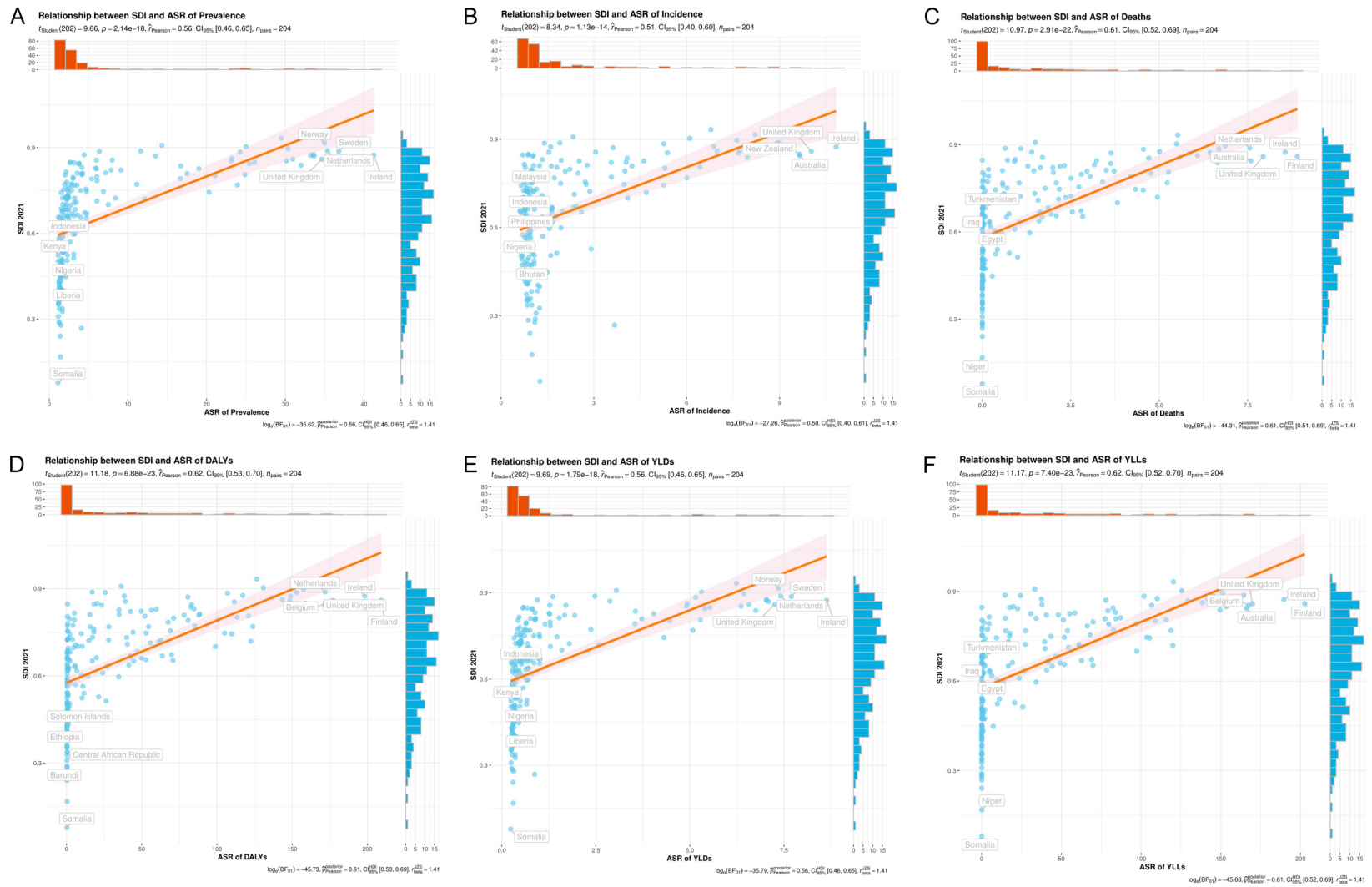


Figure 1. Relationship between ASPR (A), ASIR (B), ASMR (C), ASDR (D), ASYLDs (E), and ASYLLs (F) and SDI levels in MND from 1990 to 2021.

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regions. Australasia, High-income North America, and Western Europe had the largest age-standardized epidemiological indicators, with the other five indicators low in Sub-Saharan Africa (except ASIR). The lowest ASIRs were recorded in Oceania, South Asia and few other parts of Southeast Asia (**Table 1**).

Over the years 1990 to 2021, the EAPCs of ASPR in Tropical Latin America, Southern Latin America, and Eastern Europe are the highest, and so is the same with ASYLDs. ASIR had the greatest EAPCs in tropical Latin America, Eastern Europe, and Central Latin America. This was highest in EAPCs of ASMR and ASYLLs, and the same pattern was showing in Andean Latin America, the Caribbean and Central Asia. The highest EAPCs in relation to ASDR were in Andean Latin America, Caribbean and Eastern Europe. On the other hand, other regions including Oceania, Central Sub-Saharan Africa, Southern Sub-Saharan Africa, and Eastern Sub-Saharan Africa recorded negative EAPC, which means that they have deteriorating epidemiological indicators (**Table 1**). In general, significant differences were found in regional disease burden, and the majority of the regions showed an increasing pattern in epidemiological measures.

National level

The results of a study of 204 countries across the world demonstrated the disparity among countries, with the majority of them recording increased tendencies in the number of cases and ASRs of epidemiological indicators. The highest age-standardized epidemiological indicators in all countries were in high-income countries in 2021, including Finland, Ireland, Sweden, Netherlands, and the United Kingdom (**Figure 2A-F**). Comparison of EAPC data from 1990 to 2021 indicated the highest growth trends in ASPR in Lithuania, Costa Rica and Poland. Incremental ASIR changes were seen in Lithuania, Costa Rica and Barbados. Ecuador, Georgia and Kyrgyzstan realized the greatest changes on the ASMR in a relative term and this is the same condition with the ASDR and ASYLLs. The most significant change in ASYLDs was observed in Lithuania, Costa Rica as well as Poland. On the other hand, there was decreased epidemiological indicators in the countries of American Samoa, Guam as well as

Burundi. The trajectories of the epidemiological indicators change at the national level were in line with the SDI divisions and geographical regions and were generally upward moving (**Table 2**).

Global trends by age and sex

This paper was based on the epidemiological features of MND among 10 age groups with 50 and above to more than 95 years. The data analysis in 2021 revealed that the majority of epidemiological indicators were typical of an inverted U shape as age increases. Peaks of prevalence and incidence were 75-79 years (**Figure 3A, 3B; Table 3**) and tendency was similar in mortality (**Figure 3C; Table 3**). In the case of DALYs, the highest value among men was between 75 and 79 years and among women between 70 and 74 years (**Figure 3D; Table 3**). The trends of YLDs were consistent with ASPR (**Figure 3E; Table 3**), and the trends of YLLs were consistent with ASDR (**Figure 3F; Table 3**). A comparison between the 2021 and 1990 data revealed that majority of epidemiological data had been on the increase across various 10 age groups of 50 years and above. The most significant differences in prevalence, incidence, and YLDs could be observed in the age group 90-95, the most significant differences in mortality and YLL were observed in the age group 70-74, and the most significant differences in DALY were noted in the age group 95+ (**Table 3**). According to the findings, there is an initial growth and subsequent decline of each indicator of MND with age. Most age categories of 50 years and above recorded an upward pattern in epidemiology indicators within the years 1990 and 2021.

A sex-stratified analysis was done and showed gender disparity in the epidemiology of MND. All six indicators stood higher among males as compared to females at all ages across the world and the size of the difference between the genders had a trend of ever-increasing and then gradually lowering as the age advanced. The highest disparities between the sexes in prevalence and mortality were in 85-89 age group, highest disparities in incidence and YLDs in 90-94 age group and highest disparities in DALYs and YLLs in 80-84 age group (**Figure 3A-F; Table 4**). The greatest gender difference was observed in high-SDI areas

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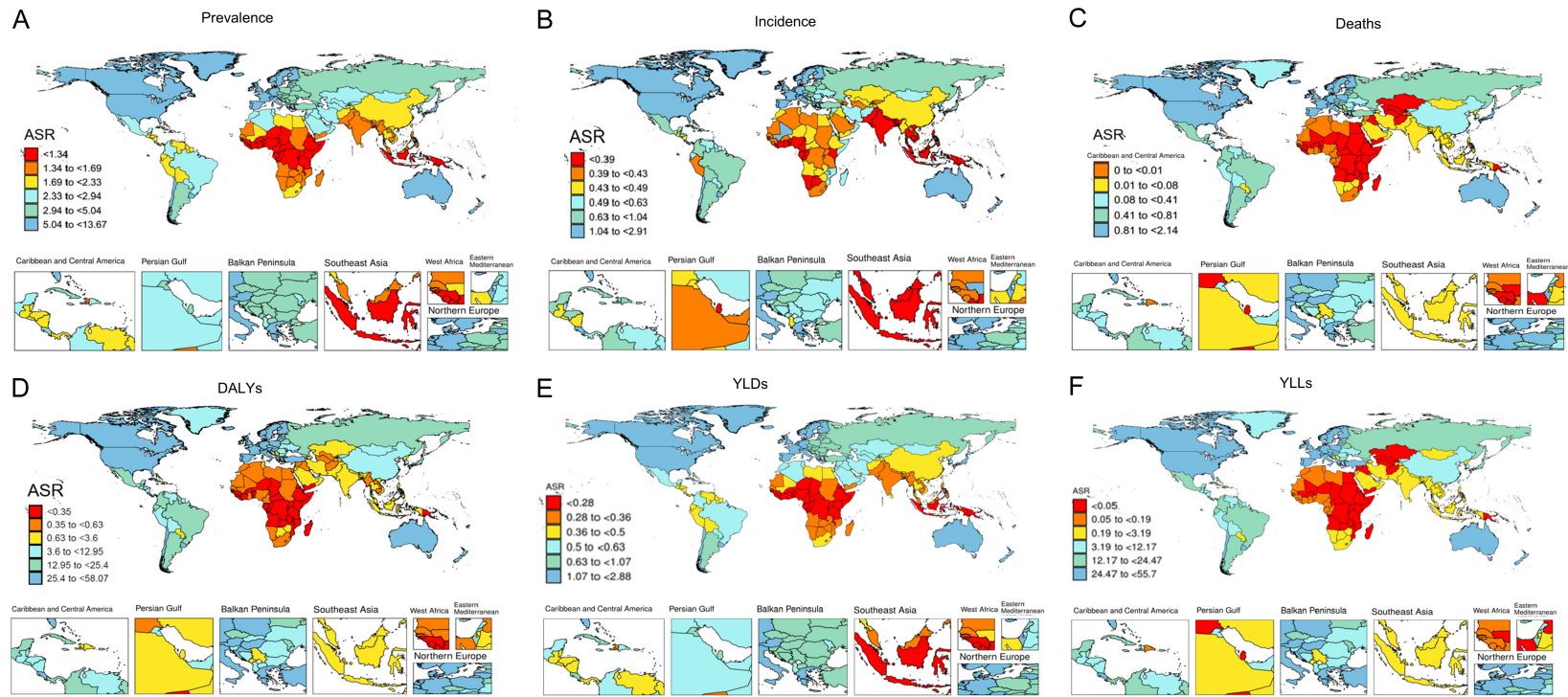


Figure 2. ASPR (A), ASIR (B), ASMR (C), ASDR (D), ASYLDs (E), and ASYLLs (F) for global MND in 2021.

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Table 2. The counts, ASRs, and EAPC for ASR of the six epidemiological indicators of MND in 204 countries in 1990 and 2021

Countries	Prevalence			Incidence			Deaths		
	ASR-1990	ASR-2021	EAPC for ASR (95% CI)	ASR-1990	ASR-2021	EAPC for ASR (95% CI)	ASR-1990	ASR-2021	EAPC for ASR (95% CI)
Afghanistan	1.84	1.66	-0.24 (-0.32 - -0.15)	1.14	1.00	-0.49 (-0.61 - -0.37)	0.00	0.00	9.05 (8.04-10.06)
Albania	2.94	3.14	0.34 (0.26-0.42)	1.01	0.92	-0.28 (-0.36 - -0.21)	0.12	0.22	2.67 (2.42-2.92)
Algeria	2.43	2.32	-0.09 (-0.15 - -0.03)	0.83	0.75	-0.37 (-0.45 - -0.29)	0.00	0.01	6.79 (6.36-7.22)
American Samoa	2.47	1.72	-1.38 (-1.51 - -1.26)	1.27	0.83	-1.71 (-1.88 - -1.54)	0.05	0.01	-6.87 (-7.9 - -5.84)
Andorra	26.71	33.65	0.88 (0.84-0.92)	6.65	8.35	0.86 (0.82-0.9)	4.81	5.85	1.18 (0.96-1.41)
Angola	1.69	1.63	-0.04 (-0.1-0.02)	1.18	1.01	-0.58 (-0.69 - -0.48)	0.01	0.00	-3.46 (-4.3 - -2.61)
Antigua and Barbuda	2.95	3.99	1.13 (1.09-1.17)	1.32	1.93	1.48 (1.42-1.54)	0.04	1.78	10.94 (7.55-14.43)
Argentina	5.29	8.44	1.54 (1.42-1.66)	1.90	2.87	1.3 (1.17-1.42)	0.17	2.51	7.87 (5.8-9.98)
Armenia	2.21	2.2	0.15 (0.04-0.26)	0.79	0.71	-0.42 (-0.49 - -0.35)	0.11	0.37	3.8 (3.05-4.56)
Australia	17.74	25.45	1.24 (1.13-1.35)	7.30	9.65	0.98 (0.9-1.06)	6.27	7.59	0.73 (0.44-1.01)
Austria	15.18	23.12	1.47 (1.33-1.62)	3.62	5.39	1.41 (1.27-1.56)	3.08	4.71	1.83 (1.64-2.01)
Azerbaijan	2.13	2.07	0.1 (-0.06-0.26)	0.80	0.70	-0.55 (-0.66 - -0.45)	0.00	0.03	6.86 (6.19-7.54)
Bahamas	3.32	4.16	0.91 (0.83-1)	1.36	1.81	1.12 (1.05-1.19)	0.02	2.01	12.26 (8.58-16.06)
Bahrain	2.35	2.31	-0.02 (-0.07-0.04)	0.82	0.74	-0.33 (-0.41 - -0.24)	0.01	0.02	1.01 (0.62-1.4)
Bangladesh	1.39	1.48	0.21 (0.15-0.28)	0.74	0.68	-0.29 (-0.35 - -0.22)	0.01	0.05	6.38 (6.25-6.51)
Barbados	3.63	6.9	1.96 (1.72-2.21)	1.74	3.98	2.54 (2.27-2.81)	0.08	4.34	12.62 (9.09-16.27)
Belarus	4.3	6.08	1.3 (1.23-1.37)	1.66	2.49	1.36 (1.22-1.51)	0.42	2.51	5.68 (5.07-6.29)
Belgium	26.39	30.14	0.45 (0.4-0.5)	7.51	7.66	0.06 (-0.06-0.17)	10.52	7.36	0.96 (0.04-1.88)
Belize	2.6	2.75	0.22 (0.18-0.26)	1.30	1.29	0.08 (0.02-0.14)	0.02	0.92	11.74 (7.97-15.65)
Benin	1.38	1.32	-0.12 (-0.19 - -0.05)	0.91	0.82	-0.36 (-0.44 - -0.28)	0.00	0.00	0.21 (-0.06-0.48)
Bermuda	8.37	9.13	0.28 (0.23-0.33)	3.32	3.57	0.2 (0.15-0.24)	0.11	1.65	8 (5.5-10.56)
Bhutan	1.53	1.68	0.32 (0.26-0.37)	0.75	0.68	-0.34 (-0.41 - -0.27)	0.01	0.04	7.76 (7.55-7.97)
Bolivia (Plurinational State of)	2.37	3.29	1.3 (1.22-1.37)	1.39	1.94	1.35 (1.26-1.44)	0.02	0.54	11.33 (10.17-12.51)
Bosnia and Herzegovina	2.82	3.22	0.5 (0.41-0.6)	1.18	1.06	-0.42 (-0.52 - -0.32)	0.52	1.08	2.88 (2.68-3.08)
Botswana	1.71	1.71	-0.03 (-0.1-0.03)	0.96	0.82	-0.53 (-0.62 - -0.44)	0.03	0.01	-5.44 (-5.92 - -4.96)
Brazil	2.93	4.72	1.88 (1.77-1.98)	1.54	2.60	2.08 (1.94-2.21)	1.09	2.84	3.47 (3.37-3.58)
Brunei Darussalam	4.06	4.24	0.31 (0.25-0.38)	1.31	1.24	-0.07 (-0.15-0.01)	0.88	1.46	2 (1.86-2.14)
Bulgaria	2.84	2.83	0.05 (-0.03-0.13)	1.07	0.97	-0.38 (-0.48 - -0.29)	0.20	0.58	3.99 (3.73-4.26)
Burkina Faso	1.35	1.32	-0.06 (-0.14-0.01)	0.98	0.88	-0.33 (-0.42 - -0.24)	0.00	0.00	0.19 (-0.02-0.41)
Burundi	1.35	1.25	-0.25 (-0.31 - -0.19)	1.14	1.11	-0.11 (-0.19 - -0.02)	0.00	0.00	-6.22 (-7.2 - -5.23)
Cabo Verde	1.86	1.8	-0.09 (-0.15 - -0.03)	0.97	0.80	-0.68 (-0.78 - -0.59)	0.00	0.00	2.61 (2.47-2.74)
Cambodia	1.38	1.4	0.05 (-0.03-0.12)	0.95	0.81	-0.59 (-0.69 - -0.49)	0.01	0.02	2.41 (2.26-2.56)
Cameroon	1.32	1.23	-0.22 (-0.29 - -0.15)	0.85	0.78	-0.35 (-0.42 - -0.28)	0.00	0.00	0.91 (0.64-1.19)
Canada	25.45	33.21	0.97 (0.9-1.04)	7.07	8.81	0.78 (0.71-0.84)	5.42	6.43	0.51 (0.24-0.77)
Central African Republic	1.29	1.16	-0.31 (-0.37 - -0.24)	1.22	1.14	-0.22 (-0.32 - -0.13)	0.00	0.00	-5.09 (-5.78 - -4.4)
Chad	1.43	1.39	-0.02 (-0.08-0.04)	1.03	0.93	-0.35 (-0.44 - -0.25)	0.00	0.00	1.39 (1.17-1.62)
Chile	6.69	11.15	1.79 (1.67-1.9)	2.42	3.57	1.4 (1.31-1.49)	0.58	3.41	3.97 (2.98-4.96)

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China	2.13	2.31	0.28 (0.19-0.37)	1.06	0.86	-0.73 (-0.86 - -0.6)	0.37	0.55	0.43 (-0.01-0.88)
Colombia	2.39	4.02	2.09 (1.98-2.21)	1.09	1.99	2.45 (2.31-2.6)	0.84	2.09	3.28 (3-3.56)
Comoros	1.8	1.66	-0.28 (-0.35 - -0.21)	1.18	1.08	-0.33 (-0.41 - -0.24)	0.00	0.00	-4 (-4.69 - -3.29)
Congo	1.32	1.25	-0.15 (-0.21 - -0.09)	0.97	0.88	-0.4 (-0.5 - -0.31)	0.01	0.01	-3.7 (-4.51 - -2.88)
Cook Islands	2.65	2.22	-0.78 (-0.87 - -0.68)	1.25	0.87	-1.41 (-1.52 - -1.3)	0.03	0.02	-1.11 (-1.29 - -0.93)
Costa Rica	3.23	7.52	2.61 (2.34-2.89)	1.49	4.09	3.04 (2.65-3.43)	1.22	3.83	3.85 (3.41-4.28)
Coted'Ivoire	1.37	1.29	-0.21 (-0.29 - -0.13)	0.87	0.79	-0.32 (-0.4 - -0.24)	0.00	0.00	0.08 (-0.11-0.28)
Croatia	4.45	6.05	1.26 (1.18-1.34)	1.56	2.22	1.34 (1.27-1.42)	1.44	2.80	2.95 (2.66-3.24)
Cuba	3.21	4.77	1.46 (1.39-1.54)	1.42	2.35	1.74 (1.61-1.87)	0.04	2.55	12.26 (8.57-16.07)
Cyprus	13.72	16.73	0.74 (0.66-0.82)	3.66	4.08	0.46 (0.41-0.51)	3.02	3.63	0.47 (0.24-0.69)
Czechia	4.51	5.9	1.09 (1.02-1.15)	1.45	1.94	1.15 (1.08-1.23)	1.32	2.32	2.7 (2.29-3.11)
Democratic People's Republic of Korea	3.01	2.67	-0.41 (-0.5 - -0.31)	1.52	1.35	-0.43 (-0.55 - -0.31)	0.20	0.19	0.01 (-0.19-0.22)
Democratic Republic of the Congo	1.36	1.2	-0.4 (-0.48 - -0.31)	1.06	0.99	-0.24 (-0.35 - -0.14)	0.01	0.00	-4.33 (-5.73 - -2.9)
Denmark	25.52	30.35	0.59 (0.5-0.67)	6.95	7.62	0.31 (0.25-0.36)	5.04	6.86	0.91 (0.73-1.09)
Djibouti	1.83	1.71	-0.25 (-0.33 - -0.18)	1.16	1.07	-0.32 (-0.41 - -0.24)	0.00	0.00	-4.62 (-5.25 - -3.98)
Dominica	2.77	4.73	1.86 (1.71-2.01)	1.42	2.75	2.32 (2.13-2.51)	0.05	2.18	11.53 (8.89-14.24)
Dominican Republic	2.72	3.72	1.35 (1.22-1.47)	1.28	1.67	1.28 (1.12-1.44)	0.01	0.01	1.65 (0.1-3.23)
Ecuador	1.96	3.18	2.05 (1.9-2.2)	0.93	1.64	2.39 (2.21-2.57)	0.00	1.95	25.77 (18.43-33.58)
Egypt	1.86	1.92	0.18 (0.13-0.23)	0.93	0.84	-0.28 (-0.34 - -0.21)	0.02	0.00	-16.41 (-19.05 - -13.67)
El Salvador	2.24	2.19	-0.06 (-0.12-0)	1.11	0.96	-0.47 (-0.55 - -0.39)	0.13	0.40	3.8 (3.65-3.95)
Equatorial Guinea	1.34	1.44	0.44 (0.29-0.59)	1.02	0.77	-1.11 (-1.25 - -0.97)	0.01	0.01	-0.02 (-0.46-0.41)
Eritrea	1.61	1.54	-0.22 (-0.3 - -0.13)	1.36	1.19	-0.42 (-0.52 - -0.32)	0.00	0.00	-3.27 (-3.81 - -2.71)
Estonia	3.62	3.81	0.29 (0.22-0.36)	1.13	1.05	-0.24 (-0.31 - -0.17)	1.22	3.24	4.56 (1.74-7.44)
Eswatini	1.73	1.67	-0.14 (-0.2 - -0.07)	1.06	0.92	-0.46 (-0.56 - -0.37)	0.03	0.01	-3.6 (-3.99 - -3.2)
Ethiopia	1.29	1.24	-0.12 (-0.26-0.01)	1.17	0.95	-0.71 (-0.88 - -0.53)	0.00	0.00	-3.27 (-4.24 - -2.29)
Fiji	1.66	1.64	-0.1 (-0.16 - -0.03)	0.97	0.87	-0.38 (-0.46 - -0.3)	0.00	0.01	4.82 (3.89-5.76)
Finland	34.09	30.95	-0.39 (-0.59 - -0.19)	9.09	6.98	-1.02 (-1.22 - -0.81)	6.93	8.91	0.97 (0.86-1.09)
France	24.12	32	0.99 (0.92-1.06)	6.42	7.96	0.75 (0.7-0.8)	5.43	6.65	0.86 (0.77-0.96)
Gabon	1.5	1.38	-0.26 (-0.33 - -0.2)	0.87	0.79	-0.35 (-0.43 - -0.26)	0.01	0.01	-3.94 (-4.65 - -3.22)
Gambia	1.48	1.36	-0.26 (-0.33 - -0.18)	0.95	0.87	-0.31 (-0.41 - -0.22)	0.00	0.00	1.21 (0.95-1.48)
Georgia	2.27	2.35	0.39 (0.2-0.57)	0.77	0.81	0.22 (0.18-0.27)	0.01	0.61	21.38 (18.2-24.64)
Germany	17.68	25.02	1.28 (1.19-1.36)	4.52	6.10	1.13 (1.06-1.19)	4.11	5.49	1.35 (1.1-1.61)
Ghana	1.35	1.33	-0.03 (-0.09-0.03)	0.88	0.77	-0.43 (-0.51 - -0.36)	0.00	0.01	2.04 (1.73-2.34)
Greece	9.54	16.67	2.13 (1.93-2.33)	2.17	4.00	2.33 (2.15-2.51)	1.52	4.19	3.37 (3.26-3.49)
Greenland	17.38	19.02	0.42 (0.34-0.51)	5.11	4.62	-0.28 (-0.39 - -0.16)	1.19	1.29	0.79 (0.63-0.95)
Grenada	2.44	2.95	0.49 (0.38-0.61)	1.38	1.65	0.33 (0.17-0.49)	0.04	1.65	11.54 (8.27-14.91)
Guam	5.26	2.03	-3.99 (-4.45 - -3.53)	2.82	0.78	-5.34 (-5.95 - -4.74)	0.41	0.01	-13.6 (-14.97 - -12.22)
Guatemala	2.16	2.09	-0.07 (-0.14 - -0.01)	1.17	1.04	-0.38 (-0.46 - -0.3)	0.17	0.43	3.12 (2.86-3.38)
Guinea	1.36	1.28	-0.24 (-0.32 - -0.16)	0.94	0.85	-0.32 (-0.4 - -0.24)	0.00	0.00	1.3 (1.16-1.44)
Guinea-Bissau	1.28	1.19	-0.28 (-0.35 - -0.21)	1.00	0.90	-0.37 (-0.45 - -0.29)	0.00	0.00	0.59 (0.42-0.76)

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Guyana	1.77	2.46	1.22 (1.17-1.28)	1.25	1.64	1.13 (1.06-1.21)	0.03	1.70	11.75 (8.45-15.16)
Haiti	2.05	2.11	0.2 (0.15-0.24)	1.42	1.49	0.28 (0.23-0.33)	0.03	0.28	7.84 (6.96-8.72)
Honduras	2.26	3.1	1.3 (1.22-1.38)	1.27	1.80	1.46 (1.36-1.56)	0.24	1.00	4.92 (4.76-5.09)
Hungary	3.96	5.4	1.29 (1.2-1.38)	1.52	2.08	1.29 (1.2-1.39)	1.34	3.05	3.44 (3.13-3.76)
Iceland	27.35	33.59	0.75 (0.71-0.8)	6.00	6.86	0.5 (0.46-0.53)	4.21	5.01	0.89 (0.66-1.12)
India	1.16	1.41	0.76 (0.68-0.85)	0.70	0.70	0.1 (0.03-0.18)	0.02	0.09	5.12 (4.88-5.36)
Indonesia	1.17	1.16	-0.04 (-0.13-0.06)	0.72	0.61	-0.55 (-0.67 - -0.44)	0.02	0.05	1.86 (1.63-2.09)
Iran (Islamic Republic of)	2.56	2.73	0.3 (0.25-0.36)	0.96	0.91	-0.19 (-0.25 - -0.13)	0.05	0.18	4.68 (4.53-4.82)
Iraq	2.42	2.29	-0.06 (-0.14-0.02)	1.01	0.87	-0.58 (-0.68 - -0.49)	0.00	0.00	5.02 (4.89-5.16)
Ireland	27.07	41.25	1.55 (1.5-1.59)	7.61	10.83	1.36 (1.3-1.41)	6.60	8.56	1.16 (1.02-1.29)
Israel	14.23	17.53	0.73 (0.68-0.78)	3.73	4.24	0.48 (0.45-0.52)	2.91	3.73	0.8 (0.66-0.94)
Italy	16	24.87	1.46 (1.26-1.66)	4.16	6.42	1.48 (1.37-1.6)	3.04	5.26	1.89 (1.58-2.2)
Jamaica	2.88	3.32	0.59 (0.54-0.64)	1.34	1.51	0.6 (0.52-0.67)	0.03	1.87	12.67 (8.85-16.63)
Japan	9.76	13.52	1.08 (0.87-1.28)	2.82	3.62	0.92 (0.86-0.98)	2.40	3.65	1.39 (1.25-1.53)
Jordan	2.4	2.31	-0.04 (-0.1-0.02)	0.91	0.82	-0.42 (-0.51 - -0.32)	0.05	0.14	4.45 (3.97-4.94)
Kazakhstan	2.56	2.49	0.03 (-0.08-0.15)	0.94	0.81	-0.56 (-0.64 - -0.47)	0.00	0.00	4.7 (1.69-7.81)
Kenya	1.35	1.14	-0.62 (-0.76 - -0.49)	0.96	0.74	-0.92 (-1.08 - -0.75)	0.00	0.00	-2.36 (-3.1 - -1.6)
Kiribati	2.65	3.13	0.65 (0.6-0.69)	2.48	2.91	0.63 (0.59-0.67)	0.42	0.77	2.07 (1.88-2.26)
Kuwait	3.41	3.2	-0.2 (-0.23 - -0.17)	0.99	0.87	-0.52 (-0.56 - -0.48)	0.97	0.71	0.4 (-1.63-2.46)
Kyrgyzstan	2.07	1.93	-0.16 (-0.28 - -0.03)	0.81	0.76	-0.23 (-0.3 - -0.16)	0.00	0.35	21.11 (17.71-24.62)
Lao People's Democratic Republic	1.51	1.56	0.1 (0.02-0.17)	1.01	0.84	-0.65 (-0.74 - -0.55)	0.01	0.02	3.58 (3.42-3.73)
Latvia	3.36	4.15	1.07 (0.94-1.2)	1.10	1.34	0.98 (0.83-1.12)	0.24	3.17	9.91 (8-11.87)
Lebanon	2.53	2.45	-0.01 (-0.06-0.04)	0.91	0.81	-0.38 (-0.46 - -0.31)	0.13	0.37	4.51 (4.18-4.85)
Lesotho	1.7	1.62	-0.18 (-0.26 - -0.1)	1.19	1.00	-0.59 (-0.69 - -0.49)	0.01	0.00	-3.61 (-4.06 - -3.16)
Liberia	1.28	1.16	-0.2 (-0.29 - -0.12)	0.90	0.83	-0.32 (-0.41 - -0.23)	0.00	0.00	0.5 (0.09-0.91)
Libya	2.45	2.1	-0.41 (-0.47 - -0.36)	0.79	0.73	-0.23 (-0.33 - -0.13)	0.00	0.01	9.08 (8.61-9.55)
Lithuania	3.62	8.01	2.89 (2.69-3.09)	1.19	3.06	3.28 (2.95-3.61)	1.36	5.58	4.85 (3.5-6.21)
Luxembourg	21.17	24.26	0.43 (0.32-0.55)	5.22	5.26	-0.01 (-0.11-0.09)	4.16	4.56	0.75 (0.55-0.96)
Madagascar	1.95	1.79	-0.27 (-0.34 - -0.2)	1.40	1.25	-0.4 (-0.48 - -0.31)	0.00	0.00	-5.09 (-6.02 - -4.15)
Malawi	1.64	1.53	-0.23 (-0.3 - -0.17)	1.32	1.17	-0.43 (-0.53 - -0.34)	0.00	0.00	-3.48 (-4.28 - -2.66)
Malaysia	1.51	1.55	0.07 (0.02-0.13)	0.74	0.65	-0.44 (-0.52 - -0.36)	0.05	0.08	0.81 (0.59-1.04)
Maldives	1.55	1.69	0.32 (0.27-0.36)	0.78	0.74	-0.15 (-0.22 - -0.08)	0.16	0.68	4.71 (4.26-5.16)
Mali	3.84	4.1	0.22 (0.17-0.26)	3.69	3.67	-0.04 (-0.1-0.02)	0.00	0.00	1.09 (0.81-1.38)
Malta	16	21.04	0.94 (0.9-0.99)	4.56	5.30	0.56 (0.53-0.59)	3.83	4.76	0.73 (0.54-0.92)
Marshall Islands	1.55	1.37	-0.51 (-0.57 - -0.45)	1.14	0.94	-0.76 (-0.83 - -0.69)	0.01	0.01	-0.33 (-0.67-0.02)
Mauritania	1.74	1.66	-0.13 (-0.19 - -0.07)	1.00	0.90	-0.4 (-0.49 - -0.3)	0.00	0.00	0.37 (-0.01-0.75)
Mauritius	2.05	2.22	0.29 (0.24-0.35)	0.96	0.92	-0.07 (-0.15-0)	0.22	2.36	8.76 (6.06-11.52)
Mexico	2.54	3.58	1.41 (1.32-1.49)	1.13	1.66	1.59 (1.49-1.69)	0.71	1.62	2.53 (2.35-2.71)
Micronesia (Federated States of)	1.45	1.34	-0.33 (-0.38 - -0.28)	1.09	0.96	-0.51 (-0.58 - -0.45)	0.01	0.01	-1.46 (-1.7 - -1.22)
Monaco	12.07	14.33	0.63 (0.57-0.69)	2.14	2.33	0.35 (0.29-0.41)	0.77	1.50	2.4 (1.99-2.81)

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Mongolia	2.09	2.33	0.49 (0.42-0.57)	1.00	0.96	-0.1 (-0.14 - -0.06)	0.16	0.23	0.74 (0.49-0.99)
Montenegro	3.16	3.04	-0.04 (-0.13-0.05)	1.09	0.97	-0.44 (-0.54 - -0.34)	0.03	0.06	2.93 (2.81-3.05)
Morocco	2.18	2.1	-0.11 (-0.16 - -0.05)	0.98	0.84	-0.5 (-0.59 - -0.4)	0.00	0.00	8.57 (8-9.15)
Mozambique	1.7	1.67	-0.04 (-0.11-0.03)	1.47	1.24	-0.63 (-0.72 - -0.53)	0.00	0.00	-2.97 (-3.79 - -2.14)
Myanmar	1.59	1.69	0.23 (0.15-0.32)	1.04	0.86	-0.73 (-0.83 - -0.62)	0.01	0.03	3.16 (3.1-3.22)
Namibia	1.74	1.7	-0.06 (-0.12-0)	0.95	0.84	-0.47 (-0.56 - -0.38)	0.03	0.01	-4.45 (-4.98 - -3.92)
Nauru	1.63	1.35	-0.73 (-0.87 - -0.58)	1.09	0.90	-0.79 (-0.86 - -0.73)	0.03	0.02	-2.79 (-3.44 - -2.13)
Nepal	1.43	1.49	0.14 (0.07-0.21)	0.81	0.73	-0.31 (-0.38 - -0.23)	0.00	0.04	7.89 (7.5-8.28)
Netherlands	27.24	35.35	0.93 (0.86-1.01)	7.30	8.98	0.74 (0.69-0.79)	5.88	7.56	0.9 (0.73-1.08)
New Zealand	19.75	26.08	0.98 (0.88-1.07)	8.04	9.64	0.66 (0.62-0.7)	7.01	6.88	0.12 (-0.24-0.48)
Nicaragua	2.35	2.31	0.02 (-0.04-0.08)	1.10	1.02	-0.25 (-0.31 - -0.19)	0.13	0.38	4 (3.65-4.36)
Niger	1.49	1.43	-0.11 (-0.19 - -0.04)	1.06	1.00	-0.17 (-0.27 - -0.08)	0.00	0.00	-0.09 (-0.34-0.16)
Nigeria	1.25	1.15	-0.15 (-0.26 - -0.05)	0.77	0.64	-0.64 (-0.78 - -0.51)	0.00	0.01	3.41 (2.96-3.86)
Niue	2.29	2.08	-0.37 (-0.42 - -0.33)	1.28	1.04	-0.83 (-0.91 - -0.75)	0.03	0.02	-1.45 (-1.62 - -1.27)
North Macedonia	2.83	2.84	0.08 (0-0.16)	1.05	0.97	-0.27 (-0.36 - -0.17)	0.37	0.70	2.45 (2.19-2.71)
Northern Mariana Islands	2.13	1.97	-0.36 (-0.46 - -0.27)	0.83	0.77	-0.24 (-0.31 - -0.17)	0.02	0.01	-1.99 (-3.41 - -0.55)
Norway	28.12	34.99	0.83 (0.75-0.91)	7.21	8.20	0.49 (0.46-0.52)	5.84	7.13	0.59 (0.4-0.79)
Oman	2.44	2.85	0.66 (0.56-0.75)	1.05	1.21	0.55 (0.45-0.64)	0.01	0.15	10.03 (9.51-10.55)
Pakistan	1.32	1.38	0.23 (0.16-0.3)	0.74	0.70	-0.09 (-0.17 - -0.01)	0.01	0.08	5.82 (5.44-6.2)
Palau	2.21	1.84	-0.75 (-0.82 - -0.68)	1.37	1.02	-1.16 (-1.24 - -1.08)	0.00	0.01	1.09 (0.97-1.21)
Palestine	2.26	2.14	-0.19 (-0.25 - -0.13)	1.06	0.90	-0.5 (-0.59 - -0.41)	0.06	0.20	4.32 (4.02-4.62)
Panama	2.58	3.45	0.98 (0.94-1.03)	1.07	1.33	0.72 (0.64-0.8)	0.49	1.58	3.88 (3.65-4.1)
Papua New Guinea	1.36	1.29	-0.27 (-0.34 - -0.2)	0.88	0.77	-0.48 (-0.57 - -0.4)	0.00	0.00	-2.62 (-3.33 - -1.9)
Paraguay	3.4	3.27	-0.12 (-0.21 - -0.04)	1.53	1.35	-0.44 (-0.55 - -0.32)	0.06	0.21	4.34 (4.26-4.42)
Peru	2.21	2.58	0.7 (0.63-0.76)	0.98	1.08	0.45 (0.4-0.5)	0.02	0.76	11.89 (10.22-13.58)
Philippines	1.38	1.3	-0.2 (-0.31 - -0.09)	0.76	0.63	-0.61 (-0.73 - -0.48)	0.07	0.08	0.42 (-0.17-1.02)
Poland	3.79	7.18	2.28 (2.14-2.42)	1.41	2.79	2.39 (2.19-2.6)	0.60	3.51	5.73 (4.89-6.59)
Portugal	11.7	20.31	1.92 (1.75-2.09)	2.99	5.26	1.98 (1.82-2.15)	2.40	4.56	2.23 (2.05-2.4)
Puerto Rico	3.77	6	1.76 (1.64-1.87)	1.48	2.53	2.04 (1.92-2.17)	0.06	2.20	10 (6.44-13.69)
Qatar	2.62	2.64	0.17 (0.1-0.23)	0.77	0.70	-0.32 (-0.39 - -0.25)	0.00	0.00	2.59 (1.91-3.28)
Republic of Korea	5.61	6.37	0.36 (0.22-0.51)	1.63	1.40	-0.56 (-0.7 - -0.42)	0.91	1.09	0.66 (-0.02-1.35)
Republic of Moldova	2.53	2.4	-0.1 (-0.21-0.02)	1.04	0.93	-0.38 (-0.46 - -0.3)	0.99	1.48	4.23 (0.88-7.69)
Romania	3.05	3.19	0.26 (0.17-0.36)	1.10	1.02	-0.25 (-0.33 - -0.18)	0.39	1.04	3.44 (3.18-3.69)
Russian Federation	2.71	4.13	1.98 (1.76-2.2)	0.94	1.63	2.42 (2.21-2.64)	0.20	2.96	8.65 (7.83-9.48)
Rwanda	1.29	1.27	-0.02 (-0.1-0.06)	1.08	0.96	-0.43 (-0.52 - -0.34)	0.00	0.00	-4.55 (-5.51 - -3.58)
Saint Kitts and Nevis	2.79	4.67	1.8 (1.72-1.89)	1.49	2.72	2.13 (2.03-2.24)	0.05	2.74	12.22 (8.81-15.74)
Saint Lucia	2.76	4.53	1.81 (1.73-1.9)	1.38	2.44	2.15 (2.04-2.27)	0.06	2.80	10.73 (7.4-14.17)
Saint Vincent and the Grenadines	2.46	3.31	1.18 (1.11-1.24)	1.30	1.77	1.28 (1.19-1.37)	0.07	1.60	8.58 (6.33-10.88)
Samoa	1.89	1.71	-0.41 (-0.46 - -0.36)	1.14	0.93	-0.81 (-0.89 - -0.74)	0.01	0.01	-1.5 (-1.81 - -1.2)
San Marino	13.09	11.64	-0.4 (-0.55 - -0.24)	2.50	1.90	-0.97 (-1.15 - -0.8)	0.78	0.65	0.3 (-0.08-0.69)

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Sao Tome and Principe	1.52	2.26	1.62 (1.51-1.73)	1.02	1.61	1.83 (1.72-1.94)	0.00	0.01	3.71 (3.58-3.83)
Saudi Arabia	2.23	2.15	-0.07 (-0.11 - -0.03)	0.84	0.75	-0.39 (-0.47 - -0.31)	0.03	0.18	5.9 (5.23-6.57)
Senegal	1.55	1.47	-0.16 (-0.23 - -0.08)	0.94	0.85	-0.35 (-0.43 - -0.26)	0.00	0.00	1.28 (0.99-1.57)
Serbia	3.25	3.02	-0.22 (-0.33 - -0.12)	1.22	1.02	-0.77 (-0.9 - -0.65)	0.08	0.18	2.82 (2.65-2.98)
Seychelles	1.97	2.38	0.69 (0.64-0.75)	0.98	1.15	0.62 (0.56-0.69)	0.01	0.03	2.91 (2.41-3.4)
Sierra Leone	1.3	1.21	-0.22 (-0.29 - -0.15)	0.93	0.86	-0.26 (-0.36 - -0.16)	0.00	0.00	1.12 (0.79-1.46)
Singapore	4.74	6	0.85 (0.8-0.91)	1.51	1.55	0.13 (0.1-0.16)	1.83	1.71	-0.09 (-0.36-0.18)
Slovakia	3.4	3.57	0.29 (0.22-0.37)	1.10	1.05	-0.07 (-0.15-0.01)	0.28	0.57	2.75 (2.48-3.01)
Slovenia	4.76	3.78	-0.99 (-1.17 - -0.82)	1.48	1.02	-1.65 (-1.89 - -1.41)	0.57	0.91	1.86 (1.53-2.2)
Solomon Islands	1.32	1.21	-0.41 (-0.48 - -0.33)	1.02	0.88	-0.57 (-0.65 - -0.49)	0.00	0.00	-1.7 (-2.44 - -0.96)
Somalia	1.24	1.11	-0.35 (-0.42 - -0.27)	1.35	1.26	-0.26 (-0.35 - -0.17)	0.00	0.00	-5.59 (-6.29 - -4.87)
South Africa	1.86	1.68	-0.3 (-0.41 - -0.19)	0.89	0.75	-0.59 (-0.74 - -0.44)	0.02	0.01	-4.67 (-5.06 - -4.28)
South Sudan	1.67	1.48	-0.36 (-0.42 - -0.3)	1.13	1.09	-0.19 (-0.29 - -0.1)	0.00	0.00	-5.36 (-6.25 - -4.46)
Spain	16.36	23.91	1.25 (1.1-1.4)	4.20	6.01	1.15 (1.01-1.29)	3.29	5.23	1.51 (1.29-1.74)
Sri Lanka	1.59	1.73	0.29 (0.25-0.33)	0.81	0.74	-0.31 (-0.36 - -0.26)	0.04	0.29	8.39 (7.46-9.32)
Sudan	1.54	1.5	-0.02 (-0.08-0.03)	0.86	0.74	-0.49 (-0.58 - -0.41)	0.00	0.00	9.16 (8.49-9.84)
Suriname	2.21	3	1.24 (1.16-1.31)	1.16	1.60	1.27 (1.2-1.33)	0.02	1.04	10.92 (8.26-13.65)
Sweden	30.42	36.79	0.77 (0.54-1)	7.25	8.91	0.75 (0.67-0.84)	5.33	6.68	0.89 (0.63-1.16)
Switzerland	27.05	29.49	0.3 (0.26-0.34)	6.86	6.78	-0.04 (-0.07 - -0.02)	5.76	5.52	0.34 (0.11-0.56)
Syrian Arab Republic	2.4	2.23	-0.18 (-0.24 - -0.11)	1.01	0.88	-0.45 (-0.54 - -0.36)	0.00	0.00	6.24 (5.79-6.69)
Taiwan (Province of China)	3.14	4.44	0.07 (-0.44-0.59)	1.21	1.61	-0.39 (-0.99-0.21)	0.77	1.40	1.47 (0.99-1.95)
Tajikistan	2.01	1.81	-0.25 (-0.41 - -0.1)	0.84	0.77	-0.38 (-0.46 - -0.29)	0.00	0.01	5.97 (5.36-6.58)
Thailand	1.94	1.98	0.01 (-0.05-0.07)	0.87	0.75	-0.51 (-0.6 - -0.42)	0.02	0.08	3.93 (3.58-4.27)
Timor-Leste	1.43	1.41	0.03 (-0.02-0.07)	0.85	0.73	-0.59 (-0.7 - -0.48)	0.01	0.01	2.75 (2.56-2.95)
Togo	1.31	1.22	-0.22 (-0.3 - -0.15)	0.91	0.83	-0.32 (-0.4 - -0.23)	0.00	0.00	0.48 (0.23-0.73)
Tokelau	1.67	1.53	-0.34 (-0.39 - -0.28)	1.04	0.84	-0.81 (-0.89 - -0.73)	0.02	0.02	-1.19 (-1.45 - -0.94)
Tonga	1.99	1.85	-0.33 (-0.4 - -0.26)	1.06	0.90	-0.63 (-0.71 - -0.55)	0.01	0.01	-1.18 (-1.54 - -0.82)
Trinidad and Tobago	2.49	3.53	1.34 (1.24-1.44)	1.24	1.72	1.14 (1.03-1.26)	0.05	2.09	11.06 (7.53-14.71)
Tunisia	2.59	2.51	-0.07 (-0.13 - -0.01)	0.95	0.81	-0.51 (-0.6 - -0.43)	0.00	0.01	6.63 (6.27-6.99)
Turkey	4.63	6.08	1.04 (0.99-1.09)	1.83	2.37	1.02 (0.97-1.07)	0.73	2.16	4.03 (3.75-4.32)
Turkmenistan	2.01	2.29	0.62 (0.48-0.76)	0.80	0.83	0.17 (0.14-0.2)	0.00	0.00	0.61 (-1.33-2.59)
Tuvalu	1.48	1.32	-0.54 (-0.62 - -0.47)	1.09	0.86	-0.93 (-1.02 - -0.85)	0.01	0.01	-0.45 (-0.71 - -0.19)
Uganda	1.34	1.3	-0.1 (-0.16 - -0.04)	1.09	0.93	-0.58 (-0.67 - -0.49)	0.00	0.00	-2.09 (-2.74 - -1.43)
Ukraine	2.48	2.41	0.1 (-0.03-0.23)	0.91	0.91	0.09 (0.02-0.17)	0.21	0.58	2.55 (1.84-3.28)
United Arab Emirates	2.72	2.72	0.02 (-0.03-0.08)	0.82	0.89	0.29 (0.25-0.33)	0.40	0.93	4.48 (3.69-5.27)
United Kingdom	24.49	34.64	1.27 (1.18-1.36)	7.16	10.03	1.24 (1.18-1.29)	6.03	7.94	1.3 (0.97-1.64)
United Republic of Tanzania	1.57	1.52	-0.09 (-0.16 - -0.02)	1.12	0.99	-0.5 (-0.59 - -0.4)	0.00	0.00	-3.72 (-4.52 - -2.92)
United States of America	4.53	7.86	1.32 (1.04-1.6)	2.17	4.04	0.92 (0.83-1)	0.68	2.00	0.83 (0.49-1.17)
United States Virgin Islands	19.97	23.22	1.9 (1.67-2.13)	5.98	7.70	2.2 (1.99-2.4)	4.86	6.08	3.42 (2.42-4.44)
Uruguay	6.1	12.16	2.16 (1.97-2.35)	2.40	4.70	2.05 (1.83-2.28)	0.31	4.95	7.43 (5.56-9.32)

GBD of motor neuron disease

Uzbekistan	2.02	1.95	-0.03 (-0.15-0.09)	0.91	0.78	-0.54 (-0.61 - -0.46)	0.00	0.00	10.03 (9.22-10.85)
Vanuatu	1.57	1.44	-0.36 (-0.43 - -0.29)	1.07	0.93	-0.57 (-0.65 - -0.48)	0.00	0.00	-1.46 (-2.07 - -0.85)
Venezuela (Bolivarian Republic of)	2.44	3.1	1.02 (0.94-1.1)	1.13	1.56	1.23 (1.17-1.28)	0.43	1.34	3.71 (3.12-4.3)
Viet Nam	1.66	1.79	0.29 (0.23-0.34)	0.92	0.82	-0.38 (-0.45 - -0.31)	0.02	0.05	2.83 (2.69-2.98)
Yemen	1.53	1.4	-0.2 (-0.26 - -0.13)	0.86	0.77	-0.41 (-0.51 - -0.31)	0.00	0.00	10.52 (9.82-11.23)
Zambia	1.7	1.61	-0.15 (-0.22 - -0.07)	1.27	1.08	-0.63 (-0.73 - -0.52)	0.00	0.00	-3.45 (-4.38 - -2.5)
Zimbabwe	1.54	1.51	-0.11 (-0.18 - -0.05)	0.97	0.99	0.12 (0.07-0.17)	0.08	0.08	-0.45 (-0.96-0.06)

Countries	DALYs			YLDs			YLLs		
	ASR-1990	ASR-2021	EAPC for ASR (95% CI)	ASR-1990	ASR-2021	EAPC for ASR (95% CI)	ASR-1990	ASR-2021	EAPC for ASR (95% CI)
Afghanistan	0.4	0.40	0.13 (0.01-0.25)	0.39	0.35	-0.24 (-0.32 - -0.15)	0.01	0.05	8.87 (7.89-9.87)
Albania	3.69	6.09	2.28 (2.07-2.5)	0.62	0.67	0.34 (0.26-0.42)	3.06	5.42	2.6 (2.35-2.85)
Algeria	0.54	0.63	0.62 (0.53-0.71)	0.52	0.49	-0.09 (-0.15 - -0.03)	0.02	0.13	6.8 (6.39-7.21)
American Samoa	1.6	0.51	-4.88 (-5.55 - -4.2)	0.52	0.37	-1.38 (-1.5 - -1.26)	1.07	0.14	-8.21 (-9.36 - -7.05)
Andorra	118.46	136.49	0.98 (0.77-1.19)	5.66	7.10	0.85 (0.81-0.9)	112.80	129.39	0.99 (0.77-1.21)
Angola	0.49	0.41	-0.66 (-0.83 - -0.49)	0.36	0.35	-0.04 (-0.1-0.02)	0.13	0.07	-3.16 (-3.99 - -2.33)
Antigua and Barbuda	1.71	44.31	9.6 (6.76-12.53)	0.63	0.85	1.13 (1.09-1.17)	1.08	43.46	10.82 (7.43-14.31)
Argentina	5.39	62.85	7.33 (5.41-9.3)	1.12	1.79	1.54 (1.42-1.66)	4.26	61.05	7.79 (5.7-9.91)
Armenia	3.65	10.39	3.39 (2.68-4.11)	0.47	0.47	0.15 (0.04-0.26)	3.18	9.93	3.64 (2.88-4.41)
Australia	145.35	171.47	0.66 (0.41-0.91)	3.77	5.40	1.23 (1.13-1.34)	141.58	166.08	0.64 (0.39-0.9)
Austria	75.59	111.59	1.7 (1.52-1.88)	3.22	4.91	1.47 (1.33-1.62)	72.36	106.68	1.71 (1.52-1.9)
Azerbaijan	0.59	1.11	2.9 (2.55-3.24)	0.45	0.44	0.1 (-0.05-0.26)	0.14	0.67	6.64 (5.98-7.3)
Bahamas	1.19	52.13	10.5 (7.54-13.53)	0.70	0.88	0.91 (0.83-0.99)	0.48	51.24	12.12 (8.45-15.92)
Bahrain	0.87	0.93	0.4 (0.24-0.55)	0.50	0.49	-0.02 (-0.07-0.04)	0.37	0.44	0.91 (0.5-1.32)
Bangladesh	0.49	1.62	3.93 (3.72-4.13)	0.29	0.31	0.21 (0.15-0.28)	0.19	1.30	6.27 (6.15-6.39)
Barbados	2.71	105.05	11.58 (8.43-14.83)	0.77	1.46	1.96 (1.72-2.21)	1.94	103.58	12.52 (9-16.16)
Belarus	12.39	67.57	-10.81 (-11.88 - -9.72)	0.91	1.29	1.3 (1.23-1.37)	11.48	66.28	5.42 (4.75-6.09)
Belgium	203.22	173.75	5.27 (4.64-5.91)	5.59	6.36	0.44 (0.39-0.49)	197.63	167.39	1.15 (0.36-1.95)
Belize	1	24.06	1.12 (0.36-1.88)	0.55	0.58	0.22 (0.18-0.26)	0.44	23.47	11.76 (8-15.66)
Benin	0.35	0.34	9.68 (6.78-12.66)	0.29	0.28	-0.12 (-0.19 - -0.05)	0.05	0.06	0.23 (-0.06-0.53)
Bermuda	4.44	42.54	-0.06 (-0.13-0.01)	1.78	1.94	0.28 (0.23-0.33)	2.67	40.60	7.97 (5.45-10.54)
Bhutan	0.45	1.41	6.7 (4.68-8.76)	0.33	0.36	0.32 (0.26-0.38)	0.13	1.05	7.61 (7.41-7.81)
Bolivia (Plurinational State of)	1.13	14.27	4.11 (3.93-4.3)	0.50	0.70	1.3 (1.22-1.37)	0.63	13.57	11.16 (10.01-12.33)
Bosnia and Herzegovina	14.35	28.02	9.43 (8.6-10.27)	0.60	0.68	0.5 (0.41-0.6)	13.75	27.34	2.7 (2.51-2.89)
Botswana	0.99	0.49	2.63 (2.44-2.82)	0.36	0.36	-0.03 (-0.1-0.03)	0.62	0.12	-6.09 (-6.59 - -5.59)
Brazil	27.99	70.79	-2.82 (-3.12 - -2.52)	0.62	1.00	1.87 (1.77-1.98)	27.37	69.78	3.33 (3.23-3.44)
Brunei Darussalam	21.57	35.02	3.31 (3.2-3.41)	0.86	0.90	0.31 (0.25-0.38)	20.70	34.12	1.95 (1.82-2.09)
Bulgaria	5.72	15.67	1.9 (1.77-2.04)	0.60	0.60	0.05 (-0.03-0.13)	5.12	15.07	4.02 (3.75-4.3)
Burkina Faso	0.32	0.31	3.77 (3.51-4.03)	0.29	0.28	-0.06 (-0.14-0.01)	0.03	0.03	0.25 (0.02-0.48)
Burundi	0.37	0.28	-0.03 (-0.1-0.04)	0.29	0.27	-0.25 (-0.31 - -0.19)	0.08	0.02	-6.08 (-7.04 - -5.11)
Cabo Verde	0.44	0.49	-1.01 (-1.17 - -0.85)	0.39	0.38	-0.09 (-0.15 - -0.03)	0.05	0.11	2.67 (2.54-2.79)

GBD of motor neuron disease

Cambodia	0.58	0.86	0.35 (0.3-0.41)	0.29	0.30	0.05 (-0.03-0.12)	0.29	0.56	2.25 (2.1-2.41)
Cameroon	0.38	0.42	1.33 (1.22-1.44)	0.28	0.26	-0.22 (-0.29 - -0.15)	0.10	0.16	1.08 (0.79-1.36)
Canada	127.36	148.79	0.2 (0.08-0.31)	5.41	7.04	0.96 (0.89-1.03)	121.95	141.75	0.4 (0.17-0.64)
Central African Republic	0.38	0.28	0.42 (0.2-0.65)	0.27	0.25	-0.31 (-0.37 - -0.24)	0.11	0.03	-4.81 (-5.48 - -4.14)
Chad	0.33	0.34	-1.17 (-1.31 - -1.02)	0.30	0.30	-0.02 (-0.08-0.04)	0.03	0.04	1.33 (1.11-1.55)
Chile	16.08	85.12	0.12 (0.06-0.18)	1.42	2.37	1.78 (1.67-1.9)	14.66	82.75	3.83 (2.88-4.79)
China	10.33	14.85	3.74 (2.83-4.66)	0.45	0.49	0.28 (0.19-0.37)	9.88	14.36	0.33 (-0.12-0.79)
Colombia	22.06	52.78	0.33 (-0.11-0.77)	0.51	0.85	2.09 (1.98-2.21)	21.55	51.92	3.19 (2.9-3.49)
Comoros	0.47	0.39	3.17 (2.88-3.46)	0.38	0.35	-0.28 (-0.35 - -0.21)	0.09	0.04	-3.64 (-4.32 - -2.96)
Congo	0.58	0.41	-0.75 (-0.87 - -0.64)	0.28	0.26	-0.15 (-0.21 - -0.09)	0.30	0.15	-3.27 (-4.06 - -2.48)
Cook Islands	1.1	0.82	-1.49 (-1.83 - -1.15)	0.56	0.47	-0.78 (-0.87 - -0.68)	0.54	0.35	-1.75 (-1.97 - -1.53)
Costa Rica	31.03	98.89	-1.23 (-1.37 - -1.09)	0.69	1.60	2.61 (2.33-2.89)	30.34	97.30	3.89 (3.46-4.32)
Coted'Ivoire	0.36	0.36	3.87 (3.44-4.29)	0.29	0.27	-0.21 (-0.29 - -0.13)	0.07	0.09	0.2 (0.01-0.39)
Croatia	37.38	71.17	-0.12 (-0.2 - -0.03)	0.94	1.28	1.26 (1.18-1.34)	36.43	69.88	2.87 (2.58-3.15)
Cuba	1.68	63.64	2.83 (2.55-3.11)	0.68	1.01	1.46 (1.39-1.54)	0.99	62.62	12.29 (8.57-16.13)
Cyprus	63.42	82.79	10.96 (7.8-14.21)	2.91	3.55	0.74 (0.66-0.82)	60.51	79.23	0.75 (0.48-1.03)
Czechia	35.61	59.64	0.75 (0.48-1.02)	0.96	1.25	1.09 (1.02-1.15)	34.66	58.39	2.57 (2.16-2.99)
Democratic People's Republic of Korea	6.18	5.97	2.54 (2.13-2.94)	0.64	0.57	-0.41 (-0.5 - -0.31)	5.54	5.40	-0.01 (-0.21-0.19)
Democratic Republic of the Congo	0.43	0.30	-0.05 (-0.23-0.13)	0.29	0.25	-0.4 (-0.48 - -0.31)	0.14	0.05	-4.01 (-5.38 - -2.62)
Denmark	126.61	157.51	-1.18 (-1.48 - -0.87)	5.42	6.44	0.58 (0.5-0.67)	121.19	151.08	0.67 (0.49-0.85)
Djibouti	0.51	0.40	0.67 (0.49-0.85)	0.39	0.36	-0.25 (-0.33 - -0.18)	0.12	0.04	-4.41 (-5.03 - -3.79)
Dominica	1.77	52.84	-0.91 (-1.05 - -0.77)	0.59	1.00	1.86 (1.71-2.01)	1.18	51.83	11.37 (8.75-14.05)
Dominican Republic	0.73	1.08	10.55 (8.21-12.93)	0.58	0.79	1.35 (1.22-1.47)	0.15	0.29	1.71 (0.19-3.26)
Ecuador	0.44	49.86	1.4 (0.89-1.92)	0.42	0.68	2.05 (1.9-2.19)	0.02	49.18	25.63 (18.31-33.41)
Egypt	0.88	0.42	16.92 (12.94-21.05)	0.40	0.41	0.18 (0.13-0.23)	0.48	0.01	-16.46 (-19.13 - -13.71)
El Salvador	3.93	10.86	-3.64 (-4.37 - -2.9)	0.48	0.47	-0.06 (-0.12-0)	3.46	10.39	3.81 (3.66-3.95)
Equatorial Guinea	0.42	0.49	3.52 (3.4-3.65)	0.28	0.31	0.44 (0.29-0.59)	0.14	0.18	0.38 (-0.04-0.79)
Eritrea	0.43	0.37	0.42 (0.36-0.49)	0.34	0.33	-0.22 (-0.3 - -0.13)	0.09	0.05	-3.04 (-3.57 - -2.51)
Estonia	33.81	83.17	-0.68 (-0.79 - -0.57)	0.77	0.81	0.29 (0.22-0.36)	33.04	82.36	4.3 (1.51-7.16)
Eswatini	1.02	0.57	4.11 (1.53-6.76)	0.37	0.36	-0.14 (-0.2 - -0.07)	0.65	0.21	-4.13 (-4.56 - -3.7)
Ethiopia	0.33	0.29	-2.25 (-2.51 - -1.99)	0.27	0.26	-0.12 (-0.26-0.01)	0.06	0.03	-3.08 (-4.02 - -2.14)
Fiji	0.44	0.64	-0.51 (-0.69 - -0.33)	0.35	0.35	-0.1 (-0.16 - -0.03)	0.09	0.29	5.12 (3.97-6.28)
Finland	165.93	209.24	1.62 (1.19-2.04)	7.22	6.57	-0.38 (-0.58 - -0.19)	158.71	202.67	0.93 (0.81-1.05)
France	130.54	156.24	0.88 (0.77-0.99)	5.12	6.75	0.98 (0.91-1.05)	125.41	149.49	0.82 (0.72-0.92)
Gabon	0.65	0.45	0.83 (0.73-0.93)	0.32	0.29	-0.26 (-0.33 - -0.2)	0.33	0.16	-3.58 (-4.27 - -2.88)
Gambia	0.37	0.38	-1.66 (-1.95 - -1.37)	0.31	0.29	-0.26 (-0.33 - -0.19)	0.05	0.09	1.34 (1.04-1.63)
Georgia	0.64	17.29	0.05 (-0.05-0.15)	0.48	0.50	0.39 (0.2-0.57)	0.15	16.79	21.25 (18.08-24.5)
Germany	101.03	130.83	14.89 (12.73-17.09)	3.75	5.31	1.28 (1.19-1.36)	97.28	125.52	1.25 (1.03-1.46)
Ghana	0.4	0.51	1.25 (1.04-1.45)	0.29	0.28	-0.03 (-0.09-0.03)	0.11	0.23	2.19 (1.88-2.5)
Greece	35.8	100.60	0.77 (0.62-0.92)	2.03	3.54	2.13 (1.93-2.33)	33.78	97.06	3.53 (3.41-3.66)

GBD of motor neuron disease

Greenland	33.01	34.90	3.47 (3.35-3.59)	3.69	4.04	0.42 (0.34-0.51)	29.32	30.86	0.66 (0.5-0.81)
Grenada	1.61	42.51	0.63 (0.49-0.78)	0.52	0.63	0.49 (0.38-0.61)	1.09	41.89	11.56 (8.41-14.8)
Guam	10.82	0.59	10.52 (7.78-13.33)	1.12	0.43	-3.99 (-4.44 - -3.53)	9.70	0.16	-14.71 (-16.02 - -13.37)
Guatemala	4.76	11.58	3.05 (2.8-3.29)	0.46	0.44	-0.08 (-0.14 - -0.01)	4.30	11.13	3.25 (2.98-3.51)
Guinea	0.33	0.34	0.02 (-0.06-0.1)	0.29	0.27	-0.24 (-0.32 - -0.17)	0.04	0.07	1.36 (1.21-1.51)
Guinea-Bissau	0.34	0.35	-0.06 (-0.14-0.03)	0.27	0.25	-0.28 (-0.35 - -0.21)	0.07	0.10	0.63 (0.46-0.81)
Guyana	1.23	44.67	10.85 (7.93-13.85)	0.38	0.52	1.22 (1.17-1.27)	0.86	44.15	11.79 (8.48-15.21)
Haiti	1.22	7.65	6.63 (5.97-7.28)	0.44	0.45	0.2 (0.15-0.24)	0.78	7.20	7.81 (6.95-8.69)
Honduras	6.86	26.40	4.71 (4.56-4.86)	0.48	0.66	1.3 (1.22-1.38)	6.38	25.74	4.86 (4.7-5.02)
Hungary	37.04	80.82	3.26 (2.96-3.56)	0.84	1.15	1.29 (1.2-1.38)	36.20	79.67	3.3 (2.99-3.61)
Iceland	102.18	117.12	0.72 (0.51-0.92)	5.81	7.03	0.7 (0.65-0.75)	96.37	110.09	0.72 (0.5-0.93)
India	0.71	2.48	4.12 (3.88-4.37)	0.25	0.30	0.76 (0.68-0.85)	0.46	2.18	5.06 (4.81-5.3)
Indonesia	0.89	1.50	1.32 (1.15-1.49)	0.25	0.25	-0.04 (-0.13-0.06)	0.64	1.25	1.67 (1.44-1.91)
Iran (Islamic Republic of)	1.6	4.70	3.82 (3.7-3.94)	0.54	0.58	0.3 (0.24-0.36)	1.05	4.12	4.73 (4.56-4.91)
Iraq	0.52	0.50	-0.01 (-0.09-0.07)	0.51	0.49	-0.06 (-0.14-0.02)	0.00	0.01	4.98 (4.83-5.13)
Ireland	156.26	198.24	1.06 (0.93-1.2)	5.74	8.63	1.49 (1.45-1.53)	150.51	189.61	1.05 (0.91-1.18)
Israel	69.32	87.93	0.76 (0.62-0.9)	3.02	3.72	0.73 (0.68-0.78)	66.30	84.21	0.76 (0.61-0.91)
Italy	78.55	121.00	1.5 (1.22-1.77)	3.40	5.28	1.46 (1.26-1.66)	75.15	115.72	1.5 (1.22-1.78)
Jamaica	1.35	47.20	11.01 (7.8-14.33)	0.61	0.70	0.59 (0.53-0.64)	0.74	46.50	12.63 (8.79-16.61)
Japan	59.72	80.71	0.99 (0.85-1.14)	2.07	2.87	1.08 (0.87-1.28)	57.65	77.84	0.99 (0.83-1.15)
Jordan	1.72	3.98	3.54 (3.13-3.95)	0.51	0.49	-0.04 (-0.1-0.02)	1.21	3.49	4.38 (3.89-4.87)
Kazakhstan	0.56	0.60	0.27 (0.06-0.47)	0.54	0.53	0.03 (-0.08-0.15)	0.02	0.07	4.63 (1.49-7.87)
Kenya	0.39	0.31	-0.92 (-1.12 - -0.72)	0.29	0.24	-0.62 (-0.76 - -0.49)	0.10	0.07	-1.89 (-2.6 - -1.17)
Kiribati	11.94	21.31	2.01 (1.82-2.21)	0.56	0.66	0.64 (0.6-0.69)	11.37	20.64	2.07 (1.86-2.28)
Kuwait	26.5	18.17	0.15 (-1.74-2.09)	0.72	0.68	-0.2 (-0.23 - -0.17)	25.77	17.48	0.18 (-1.83-2.24)
Kyrgyzstan	0.51	10.02	13.09 (11.07-15.15)	0.44	0.41	-0.16 (-0.28 - -0.03)	0.07	9.61	20.96 (17.57-24.45)
Lao People's Democratic Republic	0.52	0.89	1.78 (1.65-1.91)	0.32	0.33	0.1 (0.02-0.17)	0.20	0.56	3.43 (3.29-3.58)
Latvia	7.07	84.78	9.32 (7.68-10.99)	0.71	0.88	1.07 (0.94-1.2)	6.36	83.90	9.75 (7.84-11.69)
Lebanon	3.88	9.82	3.93 (3.63-4.22)	0.54	0.52	-0.01 (-0.06-0.04)	3.35	9.30	4.31 (3.99-4.64)
Lesotho	0.65	0.43	-1.45 (-1.64 - -1.27)	0.36	0.34	-0.18 (-0.26 - -0.1)	0.29	0.09	-4.2 (-4.67 - -3.73)
Liberia	0.33	0.31	-0.05 (-0.17-0.07)	0.27	0.25	-0.2 (-0.29 - -0.12)	0.06	0.07	0.62 (0.19-1.05)
Libya	0.54	0.72	1.15 (1-1.31)	0.52	0.45	-0.42 (-0.47 - -0.36)	0.02	0.27	9.13 (8.69-9.57)
Lithuania	37.03	148.27	4.69 (3.39-6.01)	0.77	1.70	2.89 (2.69-3.09)	36.26	146.57	4.73 (3.4-6.08)
Luxembourg	101.14	106.95	0.62 (0.41-0.83)	4.50	5.16	0.43 (0.32-0.55)	96.64	101.80	0.63 (0.41-0.84)
Madagascar	0.51	0.41	-0.78 (-0.92 - -0.64)	0.41	0.38	-0.27 (-0.34 - -0.2)	0.10	0.03	-4.73 (-5.65 - -3.81)
Malawi	0.42	0.36	-0.59 (-0.69 - -0.48)	0.35	0.33	-0.23 (-0.3 - -0.17)	0.07	0.03	-3.19 (-3.97 - -2.4)
Malaysia	1.69	2.27	0.62 (0.43-0.81)	0.32	0.33	0.07 (0.02-0.13)	1.37	1.94	0.73 (0.5-0.96)
Maldives	4.48	17.07	4.35 (3.94-4.76)	0.33	0.36	0.32 (0.27-0.36)	4.15	16.71	4.5 (4.07-4.94)
Mali	0.85	0.92	0.25 (0.2-0.31)	0.81	0.87	0.22 (0.17-0.26)	0.04	0.05	0.94 (0.63-1.26)
Malta	90.7	113.40	0.77 (0.6-0.94)	3.40	4.47	0.95 (0.9-0.99)	87.30	108.93	0.76 (0.58-0.94)
Marshall Islands	0.56	0.50	-0.83 (-1 - -0.65)	0.33	0.29	-0.51 (-0.57 - -0.45)	0.24	0.21	-1.27 (-1.64 - -0.9)

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Mauritania	0.48	0.50	0.02 (-0.1-0.15)	0.37	0.35	-0.13 (-0.19 - -0.07)	0.11	0.15	0.47 (0.07-0.86)
Mauritius	6.14	61.51	8.3 (5.82-10.84)	0.43	0.47	0.29 (0.24-0.35)	5.70	61.04	8.67 (5.96-11.46)
Mexico	18.77	42.46	2.53 (2.36-2.7)	0.54	0.76	1.41 (1.32-1.49)	18.23	41.70	2.56 (2.39-2.73)
Micronesia (Federated States of)	0.59	0.47	-1.11 (-1.26 - -0.97)	0.31	0.29	-0.33 (-0.38 - -0.28)	0.28	0.19	-2.08 (-2.37 - -1.79)
Monaco	20.13	36.38	2.14 (1.77-2.51)	2.56	3.04	0.63 (0.56-0.69)	17.57	33.33	2.31 (1.9-2.72)
Mongolia	5.11	6.87	0.58 (0.33-0.82)	0.44	0.49	0.49 (0.42-0.57)	4.67	6.38	0.59 (0.32-0.86)
Montenegro	1.34	1.99	1.67 (1.58-1.77)	0.67	0.65	-0.04 (-0.13-0.05)	0.66	1.35	2.83 (2.69-2.96)
Morocco	0.48	0.56	0.58 (0.48-0.67)	0.46	0.45	-0.1 (-0.16 - -0.05)	0.01	0.11	8.55 (7.98-9.12)
Mozambique	0.42	0.39	-0.31 (-0.4 - -0.22)	0.36	0.36	-0.04 (-0.11-0.03)	0.06	0.03	-2.7 (-3.5 - -1.88)
Myanmar	0.66	1.13	1.87 (1.81-1.93)	0.34	0.36	0.23 (0.15-0.32)	0.32	0.77	3.01 (2.95-3.07)
Namibia	0.95	0.52	-2.34 (-2.66 - -2.02)	0.37	0.36	-0.06 (-0.12-0)	0.58	0.16	-5.02 (-5.6 - -4.43)
Nauru	0.94	0.57	-2.1 (-2.51 - -1.68)	0.35	0.29	-0.73 (-0.87 - -0.58)	0.59	0.28	-3.22 (-3.86 - -2.58)
Nepal	0.41	1.23	3.92 (3.57-4.27)	0.30	0.32	0.14 (0.07-0.21)	0.11	0.91	7.85 (7.45-8.26)
Netherlands	141.26	171.81	0.76 (0.59-0.95)	5.78	7.41	0.89 (0.81-0.96)	135.48	164.40	0.76 (0.57-0.94)
New Zealand	165.52	158.94	0.06 (-0.27-0.39)	4.19	5.53	0.97 (0.88-1.07)	161.32	153.41	0.03 (-0.31-0.37)
Nicaragua	3.73	10.25	3.71 (3.41-4.01)	0.50	0.49	0.02 (-0.04-0.08)	3.23	9.75	4.01 (3.67-4.35)
Niger	0.33	0.32	-0.11 (-0.19 - -0.04)	0.32	0.30	-0.11 (-0.19 - -0.04)	0.02	0.02	-0.11 (-0.37-0.15)
Nigeria	0.33	0.41	0.94 (0.75-1.14)	0.26	0.24	-0.15 (-0.26 - -0.05)	0.06	0.17	3.71 (3.24-4.17)
Niue	1.08	0.80	-1.31 (-1.44 - -1.18)	0.49	0.44	-0.37 (-0.42 - -0.33)	0.60	0.36	-2.21 (-2.43 - -1.98)
North Macedonia	10.13	18.09	2.27 (2.02-2.53)	0.60	0.60	0.08 (0-0.16)	9.53	17.48	2.37 (2.1-2.64)
Northern Mariana Islands	0.78	0.56	-1.48 (-2.16 - -0.79)	0.45	0.42	-0.36 (-0.46 - -0.27)	0.33	0.15	-3.42 (-4.85 - -1.96)
Norway	142.68	167.13	0.48 (0.31-0.66)	5.96	7.36	0.8 (0.72-0.88)	136.72	159.77	0.47 (0.29-0.65)
Oman	0.81	4.29	6.71 (6.29-7.14)	0.52	0.61	0.66 (0.56-0.75)	0.29	3.68	9.8 (9.28-10.32)
Pakistan	0.58	2.19	4.28 (4.1-4.45)	0.28	0.29	0.23 (0.16-0.3)	0.30	1.90	5.75 (5.37-6.13)
Palau	0.59	0.55	-0.35 (-0.4 - -0.3)	0.47	0.39	-0.75 (-0.82 - -0.68)	0.12	0.16	0.86 (0.73-0.99)
Palestine	2.04	5.39	3.59 (3.34-3.84)	0.48	0.45	-0.19 (-0.25 - -0.13)	1.56	4.94	4.22 (3.93-4.51)
Panama	12.77	40.45	3.83 (3.62-4.04)	0.55	0.73	0.98 (0.94-1.02)	12.22	39.72	3.91 (3.69-4.13)
Papua New Guinea	0.34	0.30	-0.64 (-0.77 - -0.52)	0.29	0.27	-0.27 (-0.34 - -0.2)	0.05	0.03	-3.55 (-4.25 - -2.85)
Paraguay	2.17	5.69	3.37 (3.32-3.43)	0.72	0.70	-0.12 (-0.21 - -0.04)	1.45	5.00	4.29 (4.2-4.38)
Peru	1.02	19.77	10.18 (8.92-11.46)	0.47	0.55	0.69 (0.63-0.76)	0.55	19.23	11.69 (10.04-13.36)
Philippines	2.09	2.33	0.27 (-0.27-0.82)	0.29	0.28	-0.2 (-0.31 - -0.09)	1.80	2.05	0.33 (-0.3-0.95)
Poland	17.14	88.59	5.36 (4.55-6.19)	0.80	1.52	2.28 (2.13-2.42)	16.34	87.07	5.46 (4.62-6.31)
Portugal	58.24	109.67	2.18 (1.99-2.37)	2.49	4.31	1.92 (1.75-2.09)	55.76	105.35	2.19 (2-2.38)
Puerto Rico	2.33	56.50	9.05 (5.95-12.24)	0.80	1.27	1.76 (1.64-1.87)	1.53	55.22	10.05 (6.49-13.73)
Qatar	0.6	0.64	0.38 (0.31-0.46)	0.56	0.56	0.17 (0.1-0.23)	0.05	0.08	2.48 (1.79-3.17)
Republic of Korea	22.58	25.62	0.47 (-0.2-1.14)	1.19	1.35	0.36 (0.22-0.51)	21.39	24.27	0.47 (-0.25-1.2)
Republic of Moldova	27.24	39.99	3.91 (0.91-6.99)	0.54	0.51	-0.1 (-0.21-0.02)	26.70	39.48	4.24 (0.9-7.69)
Romania	11.2	28.14	3.26 (3-3.52)	0.65	0.68	0.26 (0.17-0.36)	10.55	27.46	3.38 (3.11-3.65)
Russian Federation	5.95	78.23	8.16 (7.41-8.92)	0.58	0.88	1.98 (1.76-2.2)	5.38	77.35	8.39 (7.62-9.17)
Rwanda	0.35	0.30	-0.66 (-0.84 - -0.48)	0.27	0.27	-0.02 (-0.1-0.06)	0.08	0.03	-4.32 (-5.25 - -3.38)

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Saint Kitts and Nevis	1.92	69.06	11.04 (8.14-14.02)	0.59	0.99	1.8 (1.72-1.88)	1.33	68.07	12.14 (8.76-15.62)
Saint Lucia	2.08	69.87	9.93 (6.96-12.98)	0.59	0.96	1.81 (1.73-1.9)	1.50	68.91	10.77 (7.43-14.22)
Saint Vincent and the Grenadines	2.14	41.44	8.15 (6.08-10.27)	0.52	0.70	1.18 (1.11-1.24)	1.62	40.73	8.67 (6.39-11)
Samoa	0.69	0.54	-1.08 (-1.22 - -0.93)	0.40	0.36	-0.41 (-0.46 - -0.36)	0.29	0.18	-2.19 (-2.55 - -1.84)
San Marino	20.07	17.06	0.27 (-0.07-0.61)	2.78	2.47	-0.4 (-0.55 - -0.24)	17.29	14.59	0.35 (-0.03-0.74)
Sao Tome and Principe	0.39	0.69	2.1 (1.99-2.21)	0.32	0.48	1.62 (1.51-1.73)	0.07	0.21	3.67 (3.52-3.81)
Saudi Arabia	1.2	5.18	4.96 (4.45-5.47)	0.47	0.46	-0.07 (-0.11 - -0.03)	0.73	4.72	6.04 (5.37-6.71)
Senegal	0.39	0.42	0.16 (0.06-0.25)	0.33	0.31	-0.16 (-0.23 - -0.09)	0.06	0.11	1.37 (1.07-1.67)
Serbia	2.8	5.26	2.34 (2.2-2.48)	0.69	0.64	-0.22 (-0.33 - -0.12)	2.11	4.62	2.87 (2.7-3.04)
Seychelles	0.76	1.29	1.83 (1.59-2.07)	0.42	0.51	0.69 (0.63-0.75)	0.34	0.78	2.78 (2.29-3.26)
Sierra Leone	0.32	0.32	0.02 (-0.08-0.12)	0.28	0.26	-0.22 (-0.29 - -0.15)	0.04	0.06	1.27 (0.93-1.61)
Singapore	44.07	39.06	-0.22 (-0.47-0.04)	1.01	1.27	0.85 (0.8-0.91)	43.06	37.78	-0.25 (-0.51-0.02)
Slovakia	8.24	15.52	2.55 (2.3-2.79)	0.72	0.76	0.3 (0.22-0.37)	7.51	14.77	2.7 (2.43-2.96)
Slovenia	15.89	23.34	1.58 (1.25-1.9)	1.01	0.80	-0.99 (-1.16 - -0.82)	14.88	22.54	1.7 (1.37-2.04)
Solomon Islands	0.33	0.29	-0.7 (-0.85 - -0.55)	0.28	0.26	-0.41 (-0.48 - -0.33)	0.05	0.04	-2.57 (-3.36 - -1.78)
Somalia	0.29	0.24	-0.6 (-0.69 - -0.51)	0.26	0.24	-0.35 (-0.42 - -0.28)	0.03	0.01	-5.27 (-5.94 - -4.6)
South Africa	0.93	0.49	-2.47 (-2.73 - -2.2)	0.39	0.36	-0.3 (-0.41 - -0.19)	0.54	0.13	-5.28 (-5.73 - -4.83)
South Sudan	0.43	0.33	-0.83 (-0.91 - -0.76)	0.36	0.31	-0.36 (-0.42 - -0.3)	0.07	0.02	-5.15 (-6.05 - -4.25)
Spain	83.52	123.78	1.26 (1.06-1.46)	3.47	5.08	1.25 (1.1-1.4)	80.05	118.71	1.26 (1.06-1.46)
Sri Lanka	1.42	7.62	7.35 (6.53-8.17)	0.34	0.37	0.29 (0.25-0.33)	1.08	7.26	8.27 (7.37-9.19)
Sudan	0.33	0.38	0.48 (0.39-0.56)	0.33	0.32	-0.02 (-0.08-0.03)	0.01	0.06	9.04 (8.37-9.72)
Suriname	1.09	27.32	9.85 (7.58-12.17)	0.47	0.64	1.24 (1.16-1.31)	0.62	26.69	10.9 (8.24-13.62)
Sweden	130.68	152.86	0.73 (0.46-1)	6.43	7.70	0.74 (0.51-0.96)	124.25	145.16	0.73 (0.46-1.01)
Switzerland	135.24	126.47	0.24 (0.01-0.48)	5.74	6.23	0.29 (0.25-0.32)	129.50	120.24	0.24 (-0.01-0.49)
Syrian Arab Republic	0.53	0.58	0.44 (0.38-0.51)	0.51	0.47	-0.18 (-0.24 - -0.11)	0.02	0.11	6.18 (5.73-6.62)
Taiwan (Province of China)	21.18	38.42	1.44 (0.98-1.91)	0.67	0.94	0.07 (-0.44-0.59)	20.52	37.48	1.49 (1-1.97)
Tajikistan	0.5	0.71	1.46 (1.19-1.73)	0.43	0.39	-0.25 (-0.41 - -0.1)	0.07	0.32	5.94 (5.34-6.54)
Thailand	0.93	2.42	2.82 (2.52-3.13)	0.41	0.42	0.01 (-0.05-0.07)	0.52	2.00	3.99 (3.63-4.34)
Timor-Leste	0.45	0.65	1.2 (1.1-1.29)	0.30	0.30	0.03 (-0.02-0.07)	0.15	0.35	2.68 (2.47-2.89)
Togo	0.34	0.35	-0.04 (-0.13-0.05)	0.28	0.26	-0.22 (-0.3 - -0.15)	0.07	0.09	0.6 (0.35-0.85)
Tokelau	0.84	0.62	-1.22 (-1.39 - -1.06)	0.36	0.33	-0.34 (-0.39 - -0.28)	0.48	0.29	-2 (-2.28 - -1.71)
Tonga	0.69	0.59	-0.92 (-1.09 - -0.75)	0.42	0.39	-0.33 (-0.4 - -0.26)	0.27	0.20	-1.93 (-2.32 - -1.53)
Trinidad and Tobago	1.68	54.54	10.12 (7.02-13.32)	0.53	0.75	1.34 (1.24-1.43)	1.15	53.79	11.1 (7.56-14.75)
Tunisia	0.57	0.67	0.61 (0.55-0.67)	0.55	0.53	-0.07 (-0.13 - -0.01)	0.02	0.14	6.62 (6.27-6.97)
Turkey	19.68	55.77	3.86 (3.58-4.14)	0.98	1.29	1.04 (0.99-1.09)	18.69	54.48	3.95 (3.67-4.24)
Turkmenistan	0.46	0.49	0.58 (0.4-0.76)	0.43	0.49	0.62 (0.48-0.76)	0.03	0.01	0.47 (-1.53-2.5)
Tuvalu	0.53	0.46	-0.9 (-1.07 - -0.74)	0.31	0.28	-0.54 (-0.62 - -0.47)	0.21	0.18	-1.44 (-1.78 - -1.1)
Uganda	0.34	0.32	-0.36 (-0.46 - -0.26)	0.28	0.28	-0.1 (-0.16 - -0.04)	0.06	0.04	-1.93 (-2.57 - -1.28)
Ukraine	7.35	18.15	2.22 (1.54-2.9)	0.53	0.51	0.1 (-0.02-0.23)	6.82	17.64	2.31 (1.6-3.02)
United Arab Emirates	10.46	20.36	3.52 (2.77-4.28)	0.58	0.58	0.02 (-0.03-0.08)	9.88	19.78	3.64 (2.86-4.42)

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United Kingdom	144.33	177.09	1.04 (0.72-1.35)	5.20	7.25	1.22 (1.13-1.31)	139.14	169.84	1.03 (0.71-1.35)
United Republic of Tanzania	0.43	0.37	-0.6 (-0.75 - -0.46)	0.33	0.32	-0.09 (-0.16 - -0.02)	0.09	0.04	-3.39 (-4.18 - -2.59)
United States of America	17.53	143.39	0.74 (0.46-1.02)	0.96	1.67	1.32 (1.04-1.6)	16.56	48.02	0.72 (0.44-1.01)
United States Virgin Islands	118.5	49.69	3.34 (2.38-4.31)	4.24	4.93	1.9 (1.67-2.12)	114.26	138.46	3.4 (2.41-4.4)
Uruguay	8.95	122.51	7.05 (5.29-8.84)	1.30	2.58	2.16 (1.97-2.35)	7.65	119.92	7.33 (5.47-9.22)
Uzbekistan	0.43	0.44	0.19 (0.05-0.34)	0.43	0.42	-0.03 (-0.15-0.09)	0.00	0.03	9.8 (8.96-10.65)
Vanuatu	0.41	0.35	-0.67 (-0.79 - -0.55)	0.33	0.31	-0.36 (-0.43 - -0.29)	0.08	0.05	-2.32 (-2.97 - -1.67)
Venezuela (Bolivarian Republic of)	11.48	34.72	3.6 (3.02-4.18)	0.52	0.66	1.02 (0.94-1.1)	10.96	34.06	3.67 (3.07-4.28)
Viet Nam	0.93	1.71	2.02 (1.95-2.1)	0.35	0.38	0.29 (0.23-0.34)	0.58	1.33	2.71 (2.57-2.85)
Yemen	0.33	0.34	0.28 (0.23-0.34)	0.32	0.30	-0.2 (-0.26 - -0.13)	0.00	0.05	10.43 (9.74-11.12)
Zambia	0.48	0.40	-0.71 (-0.91 - -0.51)	0.36	0.34	-0.15 (-0.22 - -0.07)	0.12	0.06	-3.07 (-3.99 - -2.13)
Zimbabwe	2.13	2.15	-0.48 (-0.93 - -0.02)	0.33	0.32	-0.12 (-0.18 - -0.05)	1.81	1.83	-0.55 (-1.09 - -0.01)

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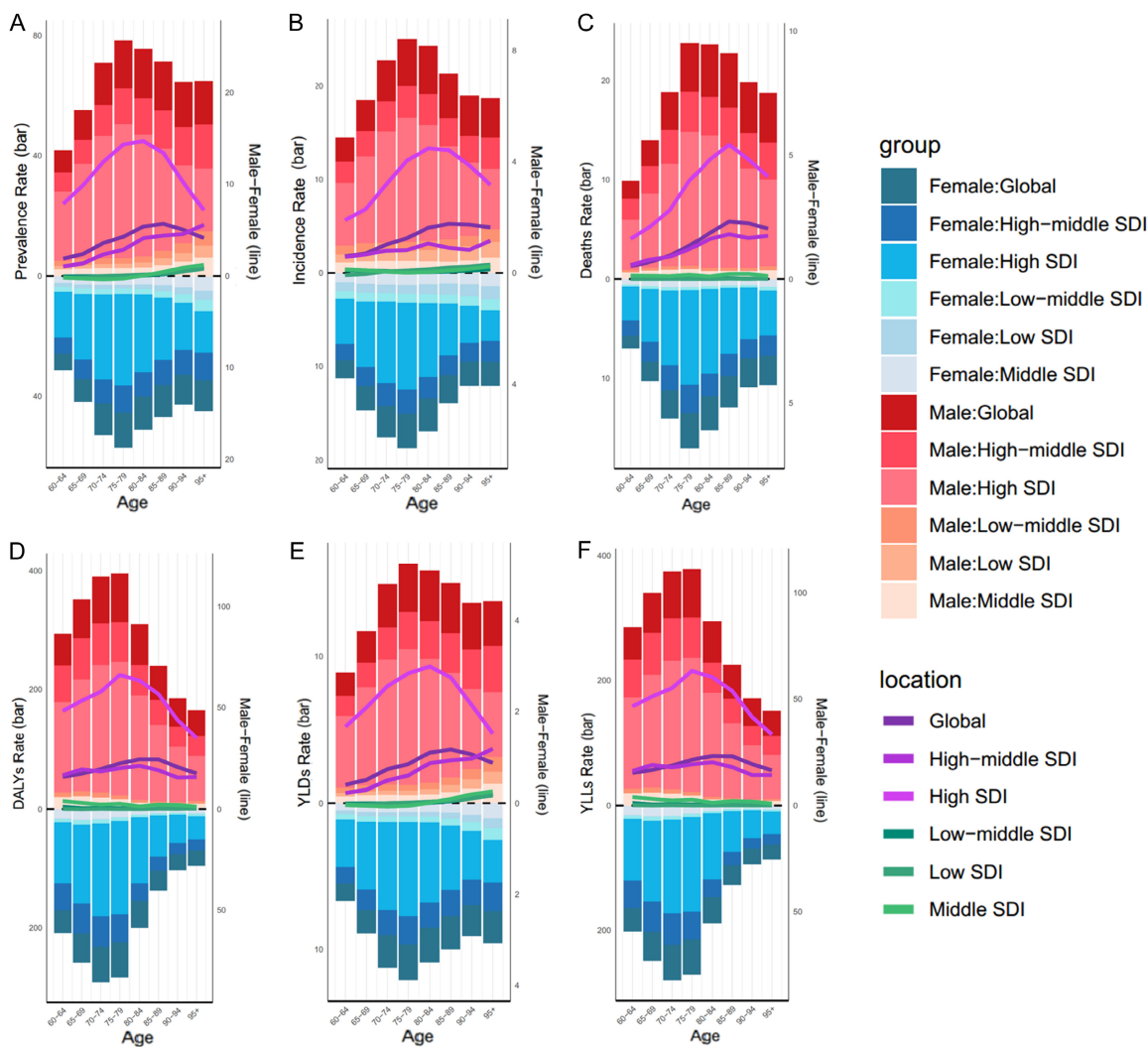


Figure 3. The bar chart displayed the prevalence (A), incidence (B), deaths (C), DALYs (D), YLDs (E), and YLLs (F) rates for males and females across global and 5 SDI regions in 8 age groups (60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-95, and 95+ years) in 2021. The line graph illustrated the difference between male and female rates (male rate minus female rate).

where males had higher values than females in all the age groups but slightly females had higher values in the 5-9 age category on DALYs, deaths, and YLLs. Low-SDI areas had the least gender differences (Table 4). The results do not only explain the gender inequality in the burden of MND but also the further implication of sex-stratified analysis is that the distributions of MND among males and females of all age groups, but not onwards, exhibit peaks at a particular age range.

Temporal joinpoint analysis

The aggregate movement in the six global epidemiological indicators have been specified

above. The regression analysis was employed to investigate the critical points of inflection in the time-series data in order to characterize the epidemiological trends in various time periods. However, at the global level, the epidemiological indicators were increasing but their trends were not the same between various time intervals. The most dramatic rise in ASPR happened in the period 1995 to 2004 followed by the most substantial falls in the years 1992 to 1995, 1992 to 1998, 2008 to 2021 (Figure 4A). It had five Join points with the largest one between 1995 and 2005 and between 2019 and 2021 (Figure 4B). The largest rise in ASMR occurred between the years 1997 and 2001, and the largest fall between the years 2012

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Table 3. Rates for six epidemiological indicators of MND across 10 age groups in 1990 and 2021

Age	Prevalence		Incidence		Deaths	
	2021 (95% UI)	1990 (95% UI)	2021 (95% UI)	1990 (95% UI)	2021 (95% UI)	1990 (95% UI)
50-54	3.26 (2.11-4.6)	3.4 (2.08-4.91)	0.99 (0.66-1.38)	1.11 (0.71-1.58)	0.5 (0.46-0.55)	0.42 (0.39-0.46)
55-59	4.41 (3.09-5.85)	4.45 (2.94-6.17)	1.46 (1.06-1.91)	1.53 (1.07-2.07)	0.9 (0.83-0.97)	0.74 (0.69-0.79)
60-64	6.46 (4.85-8.56)	6.34 (4.5-8.7)	2.23 (1.75-2.75)	2.18 (1.68-2.77)	1.54 (1.44-1.66)	1.22 (1.16-1.28)
65-69	8.76 (6.67-11.53)	9.09 (6.69-12.05)	2.94 (2.36-3.65)	2.95 (2.29-3.75)	2.26 (2.09-2.44)	2.01 (1.93-2.1)
70-74	12.17 (9.27-15.79)	10.42 (7.62-13.84)	3.87 (3.19-4.53)	3.39 (2.69-4.07)	3.3 (3.02-3.59)	2.49 (2.38-2.58)
75-79	13.59 (10.73-17.23)	11.85 (8.81-15.55)	4.29 (3.53-4.98)	3.75 (3.01-4.49)	4.19 (3.74-4.6)	3.22 (3.02-3.34)
80-84	13.33 (10.08-17.09)	11.74 (8.4-15.47)	4.19 (3.44-5.03)	3.62 (2.82-4.45)	4.22 (3.5-4.72)	3.1 (2.78-3.28)
85-89	12.85 (9.07-17.02)	11.33 (7.83-15.41)	3.65 (2.92-4.48)	3.08 (2.37-3.89)	4.06 (3.26-4.61)	3.53 (3.03-3.87)
90-95	11.62 (8.1-16.1)	9.6 (6.3-13.75)	3.17 (2.43-4.02)	2.57 (1.84-3.47)	3.64 (2.8-4.17)	2.73 (2.23-3)
95+	11.47 (6.96-16.95)	9.84 (5.61-15.19)	3.01 (1.92-4.4)	2.47 (1.39-4.01)	3.55 (2.57-4.14)	2.19 (1.66-2.45)

Age	DALYs		YLDs		YLLs	
	2021 (95% UI)	1990 (95% UI)	2021 (95% UI)	1990 (95% UI)	2021 (95% UI)	1990 (95% UI)
50-54	19.93 (18.16-21.75)	16.84 (15.64-18.08)	2.44 (1.39-3.91)	0.72 (0.4-1.14)	19.24 (17.44-21.01)	16.12 (14.92-17.38)
55-59	31.02 (28.79-33.58)	25.85 (24.15-27.55)	0.69 (0.41-1.06)	0.95 (0.56-1.47)	30.08 (27.81-32.58)	24.9 (23.16-26.45)
60-64	45.84 (42.77-49.2)	36.55 (34.77-38.46)	0.94 (0.58-1.4)	1.35 (0.83-2)	44.46 (41.43-47.9)	35.2 (33.42-36.98)
65-69	56.69 (52.7-61.3)	50.77 (48.69-52.96)	1.37 (0.88-2)	1.93 (1.29-2.82)	54.83 (50.86-59.18)	48.84 (46.84-50.84)
70-74	68.24 (62.76-74.27)	51.98 (49.7-53.98)	1.86 (1.26-2.7)	2.21 (1.38-3.15)	65.67 (60.14-71.51)	49.77 (47.47-51.56)
75-79	69.41 (62.06-76.14)	53.67 (50.73-55.81)	2.57 (1.68-3.6)	2.51 (1.66-3.57)	66.55 (59.48-73.18)	51.15 (48.05-53.06)
80-84	55.17 (46.1-61.29)	41.2 (36.85-43.6)	2.86 (1.98-3.98)	2.49 (1.6-3.54)	52.36 (43.48-58.61)	38.71 (34.63-40.95)
85-89	42.68 (34.84-48.12)	37.42 (32.22-40.81)	2.81 (1.9-3.9)	2.4 (1.49-3.39)	39.96 (32.1-45.37)	35.01 (30.01-38.31)
90-95	33.78 (26.65-38.61)	25.57 (21.39-28.06)	2.71 (1.71-3.78)	2.04 (1.19-3.16)	31.31 (24.11-35.86)	23.54 (19.24-25.88)
95+	30.98 (23.31-35.94)	19.88 (15.83-22.45)	2.46 (1.51-3.69)	2.09 (1.11-3.49)	28.55 (20.71-33.32)	17.79 (13.5-19.92)

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Table 4. The ASRs of six epidemiological indicators of the Global MND in 2021 by sex

Age	Prevalence		Incidence		Deaths	
	Male (95% UI)	Female (95% UI)	Male (95% UI)	Female (95% UI)	Male (95% UI)	Female(95% UI)
50-54	3.57 (2.36-4.98)	2.96 (1.87-4.22)	4.19 (2.83-5.92)	2.56 (1.57-3.84)	0.61 (0.51-0.68)	0.4 (0.38-0.44)
55-59	4.95 (3.56-6.52)	3.88 (2.65-5.28)	1.14 (0.78-1.54)	0.85 (0.55-1.2)	1.07 (0.93-1.17)	0.73 (0.69-0.81)
60-64	7.41 (5.64-9.68)	5.56 (4.05-7.57)	1.67 (1.25-2.17)	1.25 (0.89-1.67)	1.81 (1.64-1.94)	1.29 (1.19-1.43)
65-69	10 (7.67-12.95)	7.63 (5.72-10.09)	2.54 (2.02-3.1)	1.95 (1.51-2.43)	2.61 (2.38-2.8)	1.93 (1.76-2.18)
70-74	14.06 (10.77-17.96)	10.5 (8.01-13.74)	3.31 (2.67-4.06)	2.61 (2.08-3.26)	3.79 (3.44-4.11)	2.86 (2.52-3.3)
75-79	15.91 (12.56-20.32)	11.66 (9.09-14.92)	4.42 (3.62-5.14)	3.4 (2.79-4)	4.91 (4.43-5.37)	3.58 (3.05-4.15)
80-84	16.44 (12.5-21.01)	11.09 (8.32-14.27)	4.97 (4.12-5.77)	3.72 (3.06-4.36)	5.29 (4.61-5.8)	3.45 (2.66-4.09)
85-89	16.37 (11.74-21.77)	10.72 (7.54-14.06)	5.13 (4.25-6.1)	3.51 (2.83-4.26)	5.49 (4.7-6.03)	3.18 (2.36-3.8)
90-94	14.99 (10.47-20.79)	9.99 (6.95-13.99)	4.74 (3.85-5.82)	2.98 (2.35-3.67)	5.14 (4.19-5.65)	2.91 (2.12-3.5)
95+	14.44 (8.67-21.23)	10.34 (6.24-15.33)	4.34 (3.4-5.39)	2.6 (1.96-3.4)	5.01 (3.83-5.64)	2.99 (2.07-3.63)

Age	DALYs		YLDs		YLLs	
	Male (95% UI)	Female (95% UI)	Male (95% UI)	Male (95% UI)	Female (95% UI)	Male (95% UI)
50-54	23.89 (20.28-26.65)	16 (14.88-17.49)	3.07 (1.76-4.92)	2.2 (1.25-3.57)	23.13 (19.6-25.95)	15.37 (14.33-16.8)
55-59	36.82 (32.35-40.71)	25.4 (23.67-27.76)	0.76 (0.45-1.15)	0.63 (0.36-0.98)	35.77 (31.26-39.25)	24.58 (23.01-27.01)
60-64	53.79 (48.71-57.62)	38.31 (35.48-42.27)	1.05 (0.66-1.57)	0.83 (0.5-1.25)	52.22 (47.27-56)	37.13 (34.36-41.2)
65-69	65.59 (59.87-70.27)	48.54 (44.11-54.6)	1.58 (1.02-2.28)	1.18 (0.75-1.73)	63.47 (57.87-68.06)	46.92 (42.62-52.94)
70-74	78.52 (71.45-85)	59.19 (52.4-67.85)	2.12 (1.45-3.06)	1.62 (1.09-2.36)	75.56 (68.55-81.96)	56.97 (50.07-65.66)
75-79	81.5 (73.9-88.93)	59.38 (51.15-68.43)	2.96 (1.96-4.15)	2.23 (1.43-3.12)	78.19 (70.58-85.43)	56.9 (48.45-65.92)
80-84	69.24 (60.85-75.71)	45.05 (35.35-53.26)	3.32 (2.28-4.62)	2.47 (1.69-3.49)	65.79 (57.41-72.15)	42.7 (32.93-50.67)
85-89	57.7 (49.9-63.4)	33.57 (25.65-39.67)	3.45 (2.33-4.79)	2.35 (1.59-3.28)	54.26 (46.43-59.58)	31.29 (23.24-37.37)
90-94	47.48 (39.41-52.45)	27.16 (20.28-32.3)	3.44 (2.19-4.81)	2.27 (1.43-3.2)	44.3 (36.12-48.71)	25.04 (18.24-30.08)
95+	43.41 (34.08-48.59)	26.21 (19.19-31.51)	3.18 (1.96-4.79)	2.12 (1.28-3.19)	40.35 (30.89-45.42)	24.02 (16.65-29.14)

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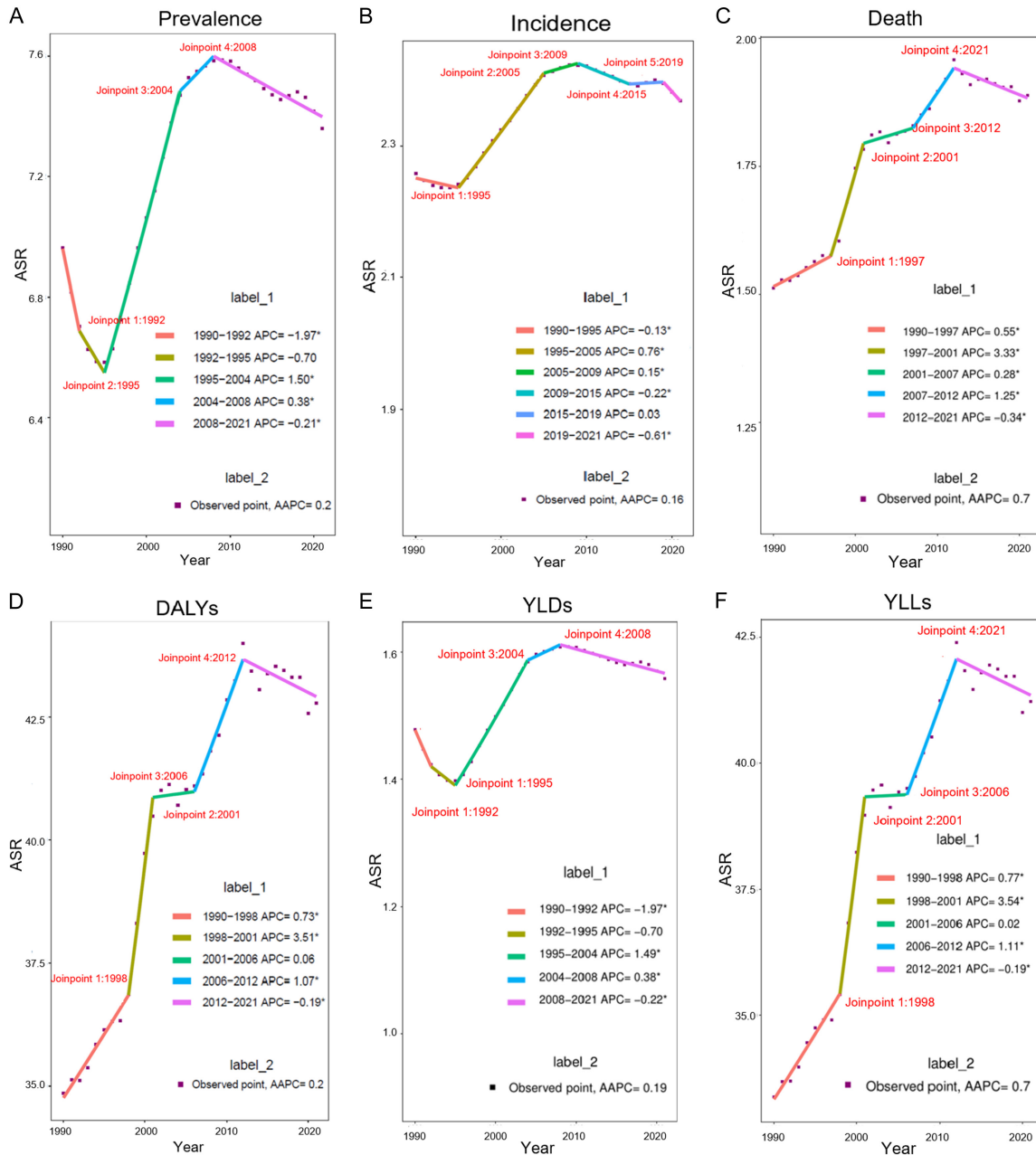


Figure 4. Joinpoint analysis of ASPR (A), ASIR (B), ASMR (C), ASDR (D), ASYLDs (E) and ASYLLs (F) of MND in Global.

and 2021 (**Figure 4C**). ASDR rose the most between 1998 and 2001 and fell between 2012 and 2021 (**Figure 4D**). The trends of the ASYLDs were comparable to the ASMR (**Figure 4E**), whereas the trends of the ASYLLs were comparable to the ASPR (**Figure 4F**). In the analysis of the various SDI regions individually, the ASPR in highly SDI areas experienced a short-term fall during 1990-1995 and then a long-term rise (**Figure 5A**). ASIR continued to increase, with the highest increase being re-

corded between 1995 and 2004 and the increase between 2018 and 2021 tended to reduce (**Figure 5B**). ASMR in high-SDI areas kept growing until 2011, and then it started decreasing (**Figure 5C**). The same thing happened with ASDR (**Figure 5D**). The trends of ASYLDs were consistent to the trends of ASPR (**Figure 5E**), and the same regarding ASYLLs and ASDR (**Figure 5F**). ASPR (**Figure 5A**), ASIR (**Figure 5B**), and ASYLDs (**Figure 5E**) in low-SDI areas had fluctuating and decreasing trends

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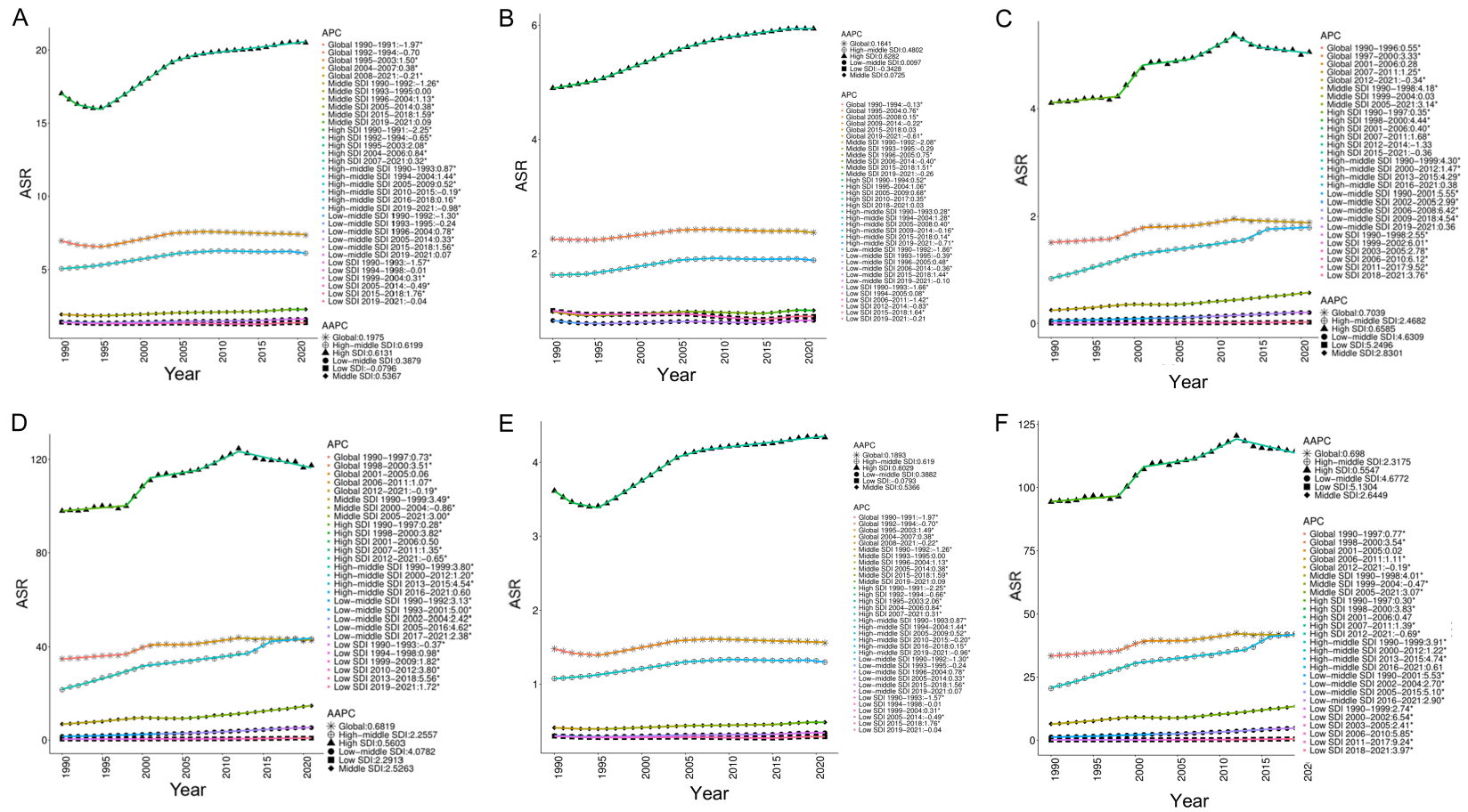


Figure 5. Temporal trends in ASPR (A), ASIR (B), ASMR (C), ASDR (D), ASYLDs (E) and ASYLLs (F) of the burden of MND in globally and in five SDI regions.

with different time nodes, yet all showed the largest growth rate in the years 2015-2019. ASMR (**Figure 5C**), ASDR (**Figure 5D**) and ASYLLs (**Figure 5F**) in mid-high, mid-low, and low-SDI regions rose in all periods of time. Except for the above-mentioned SDI regions and regression analyses, the epidemiological indicators showed fluctuating upward trends across different time periods in different SDI regions (**Table 5**).

The epidemiological statistics indicate that the epidemiology indicators of MND in the world tend to exhibit periodic increasing tendency however, in the recent years, a downward tendency has been noticed. The SDI levels showed differences in regions.

Predictive analysis

Predictions of global trends (2020-2040) show that total prevalent cases, incident cases, deaths, and DALYs are constantly increasing, whereas age-standardized epidemiological indicators will decrease slightly. Projected incident cases will rise from 44,303.06 in 2020 to 67,224.10 in 2040, with ASIR increasing from 4,310.82 to 5,946.64. The prevalent cases will increase from 206,536.14 to 34,687.48 and deaths from 1,253,469.96 to 57,510.51 and the DALYs will rise from 798,145.39 to 1,253,469.96 (**Table 6**). ASPR, ASIR, ASMR, and ASDR have trends that reflect an overall sustained but modest decreases in ASPR and ASIR (**Figure 6A, 6B**) and even slower increases then moderate in the years preceding 2040 (**Figure 6C, 6D**).

Discussion

The number of cases and consequential health burden of MND in the world have been rising progressively with a wide variation in the disease burden across regions. High-SDI locations have seen a continuous positive growth in health burden, possibly because of the following factors: richest locations like Europe and North America might over diagnose more deaths of MND through complicated diagnostic tests; it might extend life produce extra suitable medical interventions, or extensive public health initiatives to reduce socioeconomic strains and burdens. The increase of the accuracy of the death certificate documentation

can also augment the mortality rates [15]. However, low-SDI regions demonstrated declining prevalence and incidences but markedly higher mortality and DALYs. As an example, diagnosis of ALS lacks ALS-specific biomarkers and clinical presentation between ALS and other syndromes, thus it is usually underdiagnosed in Africa. Since access to treatments (e.g., riluzole, nasogastric tube support or ventilation) in these areas is limited, they result in poor prognoses and therefore contribute to mortality and DALYs [16].

It found that there were major sex disparities in all the MND epidemiological variables with males consistently outperforming the females in all age groups but most in the middle aged and the elderly. Males are more susceptible to ALS than females (literature evidence indicates that they are 23 times more susceptible to ALS over a lifetime [17]) and genetic mutations responsible of ALS (e.g. C9orf72 repeat expansions) are expressed age and sex-dependently [18, 19]. The female steroid hormones can enhance ALS survival and decrease the susceptibility [20], whereas males experience faster ageing in the epigenetics due to occupational exposures (e.g. particulate matter, volatile organic compounds, pesticides, metals, and combustion/diesel exhaust) [21], and this can accelerate ageing and ALS onset. All these combines to generate the attenuated symptoms and improved prognoses in females which are manifested by reduced DALYs in women. The results illustrate the need to consider sex specific factors in MND pathophysiology studies and the discrimination of sex sensitive interventions; interventions aimed at eradicating the risk of MND and enhancing survival could benefit males especially on work-related high-risk occupations [22].

Joinpoint regression analysis showed the global MND burden rose overall from 1990 to 2021, with all epidemiological indicators declining to varying degrees around 2021. Though the global MND burden keeps mounting, recent changes of the trends may signal strengthened global interventions and advances in MND diagnosis and treatment. Around 2021 in high SDI regions, EAPCs of ASPR and ASYLLs were positive, the EAPC of ASIR was slightly positive, and those of the other three indicators were negative. This pattern may reflect progress in MND

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Table 5. Joinpoint analysis of ASR of the 6 indicators of Global MND by gender

Temporal Joinpoint Analysis of Prevalence, 1990-2021							
Sex	Start Obs	End Obs	Measure	Val	Lower	Upper	P val
Both	1990	2021	AAPC	0.20	0.10	0.30	0
Female	1990	2021	AAPC	0.09	-0.03	0.20	0.14
Male	1990	2021	AAPC	0.29	0.20	0.38	0
Both	1990	1992	APC	-1.97	-2.79	-1.15	0
Both	1992	1995	APC	-0.70	-1.51	0.12	0.09
Both	1995	2004	APC	1.50	1.41	1.58	0
Both	2004	2008	APC	0.38	0.02	0.75	0.04
Both	2008	2021	APC	-0.21	-0.24	-0.17	0
Female	1990	1992	APC	-1.98	-2.89	-1.06	0
Female	1992	1995	APC	-0.73	-1.63	0.18	0.11
Female	1995	2004	APC	1.25	1.16	1.35	0
Female	2004	2008	APC	0.23	-0.18	0.63	0.25
Female	2008	2021	APC	-0.25	-0.29	-0.20	0
Male	1990	1993	APC	-1.74	-2.12	-1.36	0
Male	1993	1996	APC	0.19	-0.57	0.95	0.60
Male	1996	2004	APC	1.75	1.65	1.85	0
Male	2004	2008	APC	0.50	0.16	0.83	0
Male	2008	2021	APC	-0.17	-0.20	-0.14	0
Temporal Joinpoint Analysis of Incidence, 1990-2021							
Sex	Start Obs	End Obs	Measure	Val	Lower	Upper	P val
Both	1990	2021	AAPC	0.16	0.13	0.20	0
Female	1990	2021	AAPC	0.04	0.01	0.07	0.02
Male	1990	2021	AAPC	0.25	0.21	0.30	0
Both	1990	1995	APC	-0.13	-0.20	-0.06	0
Both	1995	2005	APC	0.76	0.73	0.78	0
Both	2005	2009	APC	0.16	0.02	0.29	0.03
Both	2009	2015	APC	-0.22	-0.28	-0.16	0
Both	2015	2019	APC	0.03	-0.10	0.17	0.63
Both	2019	2021	APC	-0.61	-0.88	-0.33	0
Female	1990	1994	APC	-0.50	-0.59	-0.42	0
Female	1994	2005	APC	0.56	0.54	0.58	0
Female	2005	2009	APC	0.02	-0.10	0.15	0.72
Female	2009	2015	APC	-0.36	-0.41	-0.31	0
Female	2015	2019	APC	0.07	-0.05	0.20	0.22
Female	2019	2021	APC	-0.61	-0.86	-0.36	0
Male	1990	1992	APC	-0.27	-0.63	0.10	0.14
Male	1992	1995	APC	0.09	-0.25	0.44	0.58
Male	1995	2005	APC	0.88	0.85	0.91	0
Male	2005	2009	APC	0.29	0.13	0.45	0
Male	2009	2019	APC	-0.08	-0.10	-0.05	0
Male	2019	2021	APC	-0.52	-0.84	-0.20	0
Temporal Joinpoint Analysis of Deaths, 1990-2021							
Sex	Start Obs	End Obs	Measure	Val	Lower	Upper	P val
Both	1990	2021	AAPC	0.70	0.59	0.70	0
Female	1990	2021	AAPC	0.53	0.35	0.53	0
Male	1990	2021	AAPC	0.85	0.71	0.85	0

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Both	1990	1997	APC	0.55	0.39	0.71	0
Both	1997	2001	APC	3.33	2.73	3.93	0
Both	2001	2007	APC	0.28	0.02	0.53	0.04
Both	2007	2012	APC	1.25	0.86	1.655	0
Both	2012	2021	APC	-0.34	-0.48	-0.20	0
Female	1990	1997	APC	0.51	0.31	0.71	0
Female	1997	2002	APC	2.64	2.14	3.13	0
Female	2002	2005	APC	-0.89	-2.44	0.68	0.25
Female	2005	2012	APC	1.02	0.74	1.30	0
Female	2012	2021	APC	-0.51	-0.71	-0.31	0
Male	1990	1997	APC	0.63	0.43	0.84	0
Male	1997	2001	APC	3.69	2.90	4.48	0
Male	2001	2007	APC	0.42	0.12	0.73	0
Male	2007	2012	APC	1.32	0.86	1.78	0
Male	2012	2021	APC	-0.20	-0.37	-0.04	0.02

Temporal Joinpoint Analysis of DALYs, 1990-2021

Sex	Start Obs	End Obs	Measure	Val	Lower	Upper	P val
Both	1990	2021	AAPC	0.68	0.53	0.84	0
Female	1990	2021	AAPC	0.52	0.35	0.70	0
Male	1990	2021	AAPC	0.79	0.60	0.99	0
Both	1990	1998	APC	0.73	0.58	0.88	0
Both	1998	2001	APC	3.51	2.16	4.88	0
Both	2001	2006	APC	0.06	-0.34	0.45	0.76
Both	2006	2012	APC	1.07	0.77	1.36	0
Both	2012	2021	APC	-0.20	-0.35	-0.04	0.02
Female	1990	1997	APC	0.58	0.38	0.79	0
Female	1997	2002	APC	2.17	1.69	2.65	0
Female	2002	2005	APC	-0.82	-2.28	0.66	0.26
Female	2005	2012	APC	0.99	0.73	1.25	0
Female	2012	2021	APC	-0.33	-0.52	-0.15	0
Male	1990	1998	APC	0.77	0.57	0.97	0
Male	1998	2001	APC	3.92	2.14	5.73	0
Male	2001	2007	APC	0.31	-0.02	0.64	0.07
Male	2007	2012	APC	1.20	0.71	1.70	0
Male	2012	2021	APC	-0.11	-0.29	0.07	0.21

Temporal Joinpoint Analysis of YLDs, 1990-2021

Sex	Start Obs	End Obs	Measure	Val	Lower	Upper	P val
Both	1990	2021	AAPC	0.19	0.09	0.29	0
Female	1990	2021	AAPC	0.09	-0.02	0.20	0.12
Male	1990	2021	AAPC	0.26	0.19	0.33	0
Both	1990	1992	APC	-1.97	-2.72	-1.22	0
Both	1992	1995	APC	-0.70	-1.45	0.06	0.07
Both	1995	2004	APC	1.49	1.40	1.57	0
Both	2004	2008	APC	0.38	0.03	0.74	0.04
Both	2008	2021	APC	-0.22	-0.26	-0.18	0
Female	1990	1992	APC	-1.98	-2.84	-1.11	0
Female	1992	1995	APC	-0.73	-1.59	0.14	0.10
Female	1995	2004	APC	1.26	1.16	1.35	0
Female	2004	2008	APC	0.23	-0.18	0.64	0.26

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Female	2008	2021	APC	-0.25	-0.29	-0.21	0
Male	1990	1993	APC	-1.74	-2.01	-1.47	0
Male	1993	1996	APC	0.17	-0.37	0.72	0.51
Male	1996	2004	APC	1.73	1.66	1.81	0
Male	2004	2008	APC	0.46	0.20	0.72	0
Male	2008	2019		-0.16	-0.20	-0.12	0
Male	2019	2021	APC	-0.55	-1.06	-0.03	0.04
Temporal Joinpoint Analysis of YLLs, 1990-2021							
Sex	Start Obs	End Obs	Measure	Val	Lower	Upper	P val
Both	1990	2021	AAPC	0.70	0.54	0.86	0
Female	1990	2021	AAPC	0.55	0.36	0.73	0
Male	1990	2021	AAPC	0.81	0.61	1.02	0
Both	1990	1998	APC	0.77	0.61	0.93	0
Both	1998	2001	APC	3.54	2.13	4.98	0
Both	2001	2006	APC	0.02	-0.38	0.43	0.91
Both	2006	2012	APC	1.11	0.80	1.42	0
Both	2012	2021	APC	-0.19	-0.35	-0.03	0.02
Female	1990	1998	APC	0.75	0.58	0.92	0
Female	1998	2002	APC	2.48	1.72	3.25	0
Female	2002	2005	APC	-0.10	-2.48	0.50	0.18
Female	2005	2012	APC	1.04	0.77	1.31	0
Female	2012	2021	APC	-0.34	-0.53	-0.14	0
Male	1990	1998	APC	0.81	0.60	1.02	0
Male	1998	2001	APC	3.96	2.09	5.86	0
Male	2001	2007	APC	0.28	-0.07	0.63	0.11
Male	2007	2012	APC	1.25	0.73	1.77	0
Male	2012	2021	APC	-0.11	-0.30	0.08	0.24

diagnosis, clinical treatment and mental health interventions in these regions, which reduced mortality, improved survival rates and led to higher ASPR and ASYLLs. In other SDI regions, the ASPR of MND has generally been on the rise from 1990 to 2021. ASIR flattened or even dropped around 2021, yet ASDR and ASYLLs rose, which suggests the lack of appropriate disease screening, diagnosis, and health intervention. A limitation of this study is the potential interpretive bias in the multiple temporal inflection points and associated trend changes identified by joinpoint regression, which may be confounded by external factors. The GBD estimation framework is substantially influenced by periodic methodological updates, expansions of data sources, and the coronavirus disease 2019 (COVID-19) pandemic. Consequently, fluctuations at some temporal inflection points in the present study may not fully reflect the genuine epidemiological dynamics of MND and could contain certain data artifacts. While existing research has confirmed that severe

acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can invade the central nervous system and induce structural and functional brain impairments [23], the association between COVID-19 and MND remains inconclusive. A Scottish cohort study demonstrated that COVID-19 had no significant impact on the new diagnosis rate and mortality of MND in the region before 2020 [24], whereas a US-based study reported a slight increase in MND-related deaths during the COVID-19 pandemic [25]. Additionally, a Mendelian randomization study on European ancestry populations found no definitive causal association between hospital-admitted COVID-19 phenotypes and ALS [23]. At the global level, our analysis revealed a temporal inflection point in MND ASIR in 2019 and inflection points in ASDR and ASYLLs in 2021, with all these indicators showing declining trends following the corresponding inflection points. There is no sufficient evidence to support the notion that COVID-19 imposes a marked adverse effect on MND. At the regional

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Table 6. BAPC prediction for four epidemiological indicators of Global MND from 2020 to 2040

Year	Pred_value (95% UI)	Pred_value (95% UI)
Prevalence		
	Number	ASR
2020	137634.19 (133831.82-141436.57)	7.42 (7.21-7.62)
2021	140104.16 (136220.12-143988.19)	7.36 (7.16-7.57)
2022	144381.16 (138467.24-150295.09)	7.33 (7.02-7.63)
2023	147483.95 (139910.81-155057.08)	7.28 (6.91-7.66)
2024	150658.63 (140668.09-160649.17)	7.24 (6.75-7.72)
2025	153845.23 (140782.43-166908.04)	7.19 (6.58-7.8)
2026	157009.14 (140270.54-173747.73)	7.14 (6.38-7.91)
2027	160138.87 (139127.51-181150.23)	7.1 (6.16-8.03)
2028	163292.19 (137467.92-189116.47)	7.06 (5.93-8.18)
2029	166517.77 (135361.48-197674.07)	7.01 (5.69-8.33)
2030	169780.37 (132776.64-206784.09)	6.97 (5.44-8.5)
2031	173071.31 (129676.46-216466.16)	6.93 (5.18-8.69)
2032	176390.9 (126010.93-226770.88)	6.9 (4.91-8.89)
2033	179814 (121831.42-237796.59)	6.87 (4.63-9.1)
2034	183386.76 (117151.3-249622.22)	6.84 (4.34-9.33)
2035	187051.16 (111901.06-262201.26)	6.81 (4.04-9.57)
2036	190771.95 (106012.79-275531.12)	6.79 (3.74-9.83)
2037	194517.23 (99409.23-289625.22)	6.77 (3.42-10.12)
2038	198365.76 (92099.8-304631.73)	6.76 (3.09-10.42)
2039	202390.04 (84064.37-320715.71)	6.75 (2.75-10.75)
2040	206536.14 (75216.85-337855.43)	6.75 (2.39-11.1)
Incidence		
	Number	ASR
2020	44303.06 (42271.38-46334.74)	2.38 (2.27-2.49)
2021	45214.68 (43129.97-47299.38)	2.37 (2.26-2.48)
2022	46633.73 (44050.97-49216.49)	2.36 (2.23-2.5)
2023	47732.99 (44772.52-50693.46)	2.35 (2.21-2.5)
2024	48857.01 (45344.53-52369.49)	2.34 (2.17-2.51)
2025	49987.02 (45750.58-54223.46)	2.33 (2.13-2.53)
2026	51107.46 (45981.45-56233.48)	2.32 (2.09-2.56)
2027	52206.55 (46032.14-58380.96)	2.31 (2.04-2.59)
2028	53306.59 (45937.6-60675.57)	2.3 (1.98-2.62)
2029	54425.72 (45721.27-63130.17)	2.29 (1.92-2.66)
2030	55550.21 (45371.57-65728.84)	2.28 (1.86-2.7)
2031	56671.06 (44876.6-68465.52)	2.27 (1.79-2.74)
2032	57781.36 (44224.99-71337.72)	2.26 (1.72-2.79)
2033	58908.19 (43439.03-74377.35)	2.25 (1.65-2.84)
2034	60068.47 (42528.7-77608.25)	2.24 (1.58-2.9)
2035	61244.44 (41475.18-81013.71)	2.23 (1.5-2.96)
2036	62421.51 (40260.59-84582.43)	2.22 (1.42-3.02)
2037	63586.53 (38868.83-88304.23)	2.21 (1.34-3.08)
2038	64767.86 (37313.73-92221.98)	2.21 (1.26-3.15)
2039	65986.64 (35598.68-96374.61)	2.2 (1.17-3.23)
2040	67224.1 (33703.03-100745.18)	2.2 (1.09-3.31)
Deaths		
	Number	ASR
2020	34687.48 (32855.2-36519.77)	1.89 (1.79-1.99)
2021	35602.49 (33717.91-37487.07)	1.89 (1.79-1.99)

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2022	36705.12 (34268.63-39141.62)	1.88 (1.75-2)
2023	37636.7 (34664.85-40608.54)	1.87 (1.72-2.02)
2024	38618 (34838.04-42397.95)	1.86 (1.68-2.04)
2025	39633.64 (34794.87-44472.41)	1.86 (1.63-2.08)
2026	40657.88 (34528.91-46786.85)	1.85 (1.57-2.13)
2027	41659.62 (34021.87-49297.37)	1.84 (1.5-2.18)
2028	42671.05 (33314.98-52027.12)	1.84 (1.43-2.24)
2029	43729.72 (32440.59-55018.86)	1.83 (1.36-2.3)
2030	44824.64 (31382.63-58266.65)	1.82 (1.27-2.37)
2031	45940.13 (30115.88-61764.38)	1.82 (1.19-2.45)
2032	47050.2 (28606.19-65494.2)	1.81 (1.1-2.53)
2033	48186.05 (26864.39-69507.71)	1.81 (1.01-2.61)
2034	49381.95 (24893.18-73870.72)	1.81 (0.91-2.71)
2035	50626.68 (22661.57-78591.8)	1.81 (0.8-2.81)
2036	51908.8 (20133.35-83684.25)	1.81 (0.69-2.92)
2037	53206.56 (17264.66-89148.47)	1.81 (0.58-3.04)
2038	54556.83 (14057-95077.69)	1.81 (0.46-3.16)
2039	55995.54 (10592.28-101579.45)	1.82 (0.33-3.3)
2040	57510.51 (6804.84-108688.97)	1.82 (0.21-3.46)
DALYs	Number	ASR
2020	798145.39 (788335.23-807955.56)	42.59 (42.05-43.12)
2021	822030.75 (812067.62-831993.87)	42.78 (42.25-43.31)
2022	833845.46 (786071.39-881619.54)	41.98 (39.57-44.39)
2023	852273.15 (789438.64-915107.66)	41.77 (38.69-44.85)
2024	871322.1 (786452.96-956191.23)	41.58 (37.53-45.63)
2025	890701.9 (777828.77-1003575.04)	41.4 (36.15-46.65)
2026	909947.56 (763643.8-1056251.31)	41.22 (34.58-47.86)
2027	928736.01 (743746.66-1113725.35)	41.04 (32.84-49.23)
2028	947660.01 (718935.52-1176384.49)	40.86 (30.97-50.75)
2029	967357.55 (689767.88-1244947.23)	40.72 (28.99-52.45)
2030	987710.2 (655989.27-1319431.14)	40.61 (26.91-54.3)
2031	1008622.6 (617162.33-1400082.88)	40.52 (24.72-56.32)
2032	1029953.38 (572637.16-1487269.6)	40.45 (22.4-58.51)
2033	1052338.67 (522382.85-1582294.5)	40.42 (19.95-60.89)
2034	1076310.03 (466101.68-1686518.38)	40.44 (17.37-63.5)
2035	1101681.06 (402957.12-1800404.99)	40.51 (14.65-66.36)
2036	1128397.41 (331970.97-1924823.86)	40.62 (11.75-69.49)
2037	1156277.3 (253330.07-2060671.4)	40.79 (8.71-72.93)
2038	1186095.26 (171101.99-2210551.75)	41.02 (5.69-76.73)
2039	1218540.65 (92516.36-2377379.4)	41.33 (2.99-80.96)
2040	1253469.96 (56092.22-2562868.86)	41.71 (1.75-85.67)

level, various indicators have exhibited fluctuations since 2019. The clinical significance of the changes in disease burden indicated by these inflection points awaits verification by more empirical data. Accordingly, we adopted a conservative interpretation of the trend changes at inflection points in this study, clarify-

ing that the observed data fluctuations are the combined result of the inherent dynamic changes of MND and external confounding factors including GBD methodological updates and the COVID-19 pandemic. Furthermore, it should be emphasized that the association between COVID-19 and alterations in MND disease bur-

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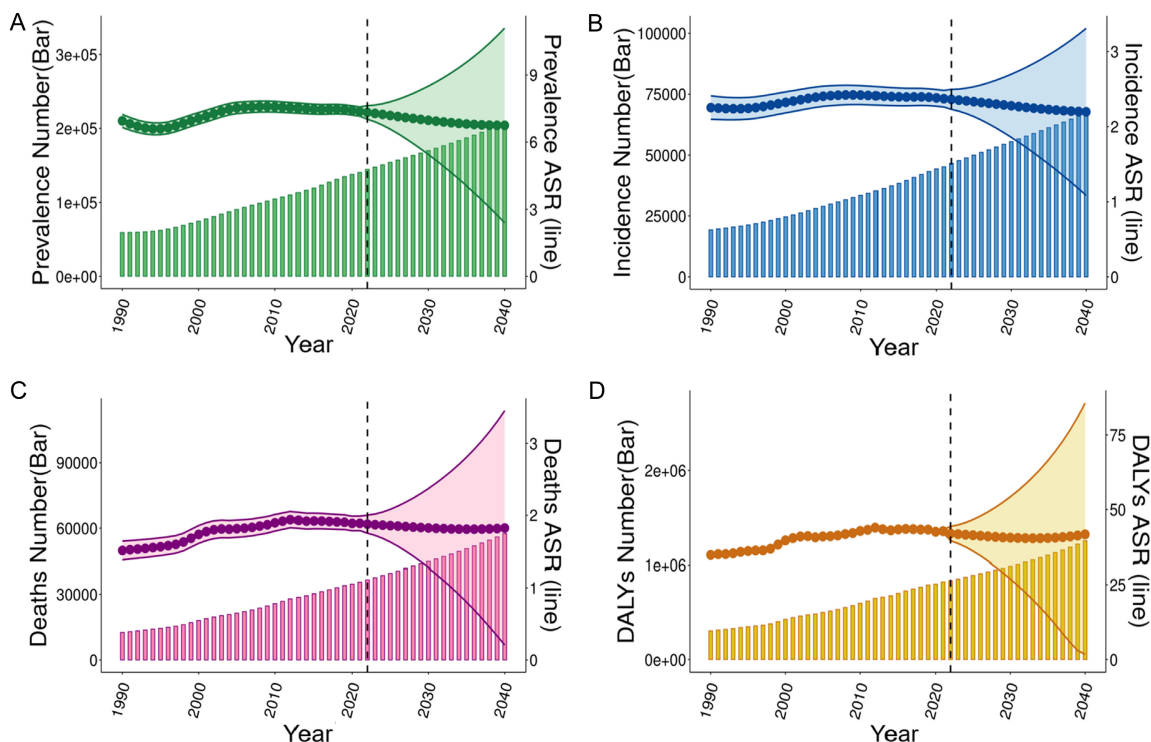


Figure 6. Prediction of ASPR (A), ASIR (B), ASMR (C) and ASDR (D) indicators of MND by BAPC in Global from 2020 to 2040.

den requires further validation by large-sample cohort studies across multiple regions, with such analyses controlling for confounding factors such as methodological updates.

In this study, the researcher has predicted that the overall number of cases of MND incidence, prevalence, mortality, and DALYs in the world will keep increasing between 2020 and 2040. This tendency implies that even though the global public health interventions and treatment efforts became stronger, even the age-standard epidemiological indicators tend to flatten, and despite that, the global burden of the MND continues to rise. The Caribbean area has shown the best upward trend in ASDR which is largely motivated by the exposure to dietary and environmental poisons [26]. All regions except Western Europe and Oceania indicate that the ASDR is increasing with the exception of Western Europe and Oceania where the ASDR is expected to decrease with the time compared to 2020. The reduction in these regions can be contributed by thorough and long-term investigation on the disease [27] and creating of clinical trial networks and shared clinical database assisted by health

organizations [28]. Nevertheless, since the high-SDI areas are associated with the largest number of cases in total, along with inequality and frontier results, these areas will bear more future and improvement possibilities, which will require the emergence of policies, development of MND-related health issues, and innovations in treatment/diagnoses development.

Epidemiological features of MND had been known before in dimensions like sex and region [9] like South Australia [29]. The work that uses the newest database of the GBD 2021 showed the systematic analysis of the disease burden of MND between 1990 and 2021 and was analyzed using correlation analysis, joinpoint analysis, and others. However, this research has its shortcomings. First, this study has an important limitation that multiple neuropathies were classified uniformly based on a single disease type, while the disease subtypes integrated by the GBD framework each have their own unique epidemiological characteristics. The unclear definition of the disease and the significant heterogeneity between subtypes may introduce bias in the interpretation of regional and temporal distribution differences in this study;

especially in regions with a high SDI, the medical diagnostic system is more complete and disease diagnosis is more specific, and the clinical distinction between subtypes is clearer. This uniform classification analysis method has a more obvious deviation from the clinical reality in such regions. This study has explicitly acknowledged this limitation and its potential impact. Future related research should be based on more detailed disease subtype classification standards, conduct stratified analysis by combining the characteristics of each subtype, such as their incidence patterns and population distribution, and include the diagnostic level differences in different SDI regions for correction. This will reduce the bias caused by the disease definition and subtype heterogeneity, and more objectively and accurately reveal the regional and temporal distribution patterns of multiple neuropathies and its subtypes. Second, GBD data is based on national statistical reports, and vague MND diagnostic standards can cause underdiagnosis of the elderly populations. Third, low-SDI areas (e.g., sub-Saharan Africa, Latin America, Southeast Asia) are at risk of missed diagnosis because of low incidence and absence of diagnostic tools and underestimated reported prevalence and incidence. Fourth, the suspects effects of lifestyle, environment, individual risk factors, and genetic mutations [15] on MND were not well investigated in the study and this would call forward studies on the long term effects. Fifth, the intervention strategies are macro-oriented and the precision regional studies should be carried out in the future. Although this research has presented a scientific foundation towards MND prevention and control, research multi-dimensionalization is still necessary in response to this worldwide health issue. Finally, this study conducts scenario estimation based on the BAPC prediction model rather than reaching definite conclusions. The premise is that the current diagnostic level, treatment strategies, and demographic characteristics remain relatively stable. If there are breakthroughs in early diagnosis technologies and targeted therapeutic drugs for MND in the future, the actual disease burden may be lower than the current predicted value.

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Disclosure of conflict of interest

None.

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