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Global, regional, and national burden of chronic obstructive pulmonary disease and its attributable risk factors from 1990 to 2021: an analysis for the Global Burden of Disease Study 2021

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Abstract

Background Chronic obstructive pulmonary disease (COPD) continues to be a significant issue, leading to premature death or reduced quality of life. It's important to assess the current burden of COPD and its risk factors on a geographical basis to guide health policy.

Methods Data on the prevalence, deaths, and disability-adjusted life years (DALYs) related to COPD, and riskattributable burden were obtained from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021 database. The relationship between COPD DALYs and the sociodemographic index (SDI) was estimated using Smoothing Splines models.

Results Between 1990 and 2021, the changes were -1.46% (95% uncertainty interval [UI] -3.36% to 0.39%) in agestandardized prevalence, -37.12% (-43.37% to -27.68%) in mortality, and -36.98% (-42.37% to -28.54%) in DALYs rate. In 2021, a total of 213.39 million prevalent cases of COPD were estimated. The age-standardized prevalence of COPD increased with age and was more common in males. The age-standardized COPD DALYs had a reversed U-shaped relationship with SDI at the regional level, with the highest burden at an SDI of about 0.45. At the global level, smoking had the highest influence on COPD DALYs, accounting for 34.8%, followed by ambient particulate matter pollution (22.2%), household air pollution from solid fuels (19.5%), and occupational particulate matter, gases, and fumes (15.8%).

Conclusions The overall burden of COPD has been increasing despite improvements in some rates since 1990. It's crucial to focus on interventions such as smoking cessation and addressing environmental and occupational exposures.

Keywords Chronic obstructive pulmonary disease, Global burden of disease, Epidemiology, Risk factors

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Background

Chronic obstructive pulmonary disease (COPD) is a heterogeneous lung condition that includes chronic respiratory symptoms such as dyspnea, cough, and expectoration. These symptoms are caused by issues in the airways (bronchitis, bronchiolitis), alveoli (emphysema), and/or pulmonary vessels. COPD is usually a progressive condition and is diagnosed using spirometry and objective evidence of structural or physiological pulmonary dysfunction [1, 2].

The World Health Organization (WHO) and the Global Burden of Disease (GBD) Study predicted that the prevalence of COPD would increase in the future due to continued exposure to COPD-related risk factors and the aging populations worldwide [3, 4]. However, the current burden of COPD is not consistently represented due to differences in survey methods, diagnostic criteria, and analytical approaches used in different studies. Therefore, it is important to obtain the most up-to-date estimation of COPD burden using the latest data available from GBD 2021, which defines COPD in line with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification and gathers information on COPD prevalence, incidence, remission, and severity from various sources such as literature, hospital claims, and global research studies [5, 6].

It is also important to regularly update the burden of COPD attributable to different risks. COPD can be caused by factors such as tobacco smoking, biomass exposure, occupational exposures, or other causes, and may present with different clinical features and progressions [7–13]. Different treatment approaches, both pharmacological and non-pharmacological, may be beneficial for these various causes [14].

In order to provide evidence for future COPD policy development, it is necessary to update the burden estimates and its attributable risk factors, stratified by age and sex. This will help us determine if there has been a decrease in the gender-burden gap and if the ranking of risk factors has changed. Although GBD 2019 previously provided insights into the COPD burden, a comprehensive update is needed to support evidence-based policy decisions [3].

Methods

Aims

The purpose of this study was to provide updated estimates of COPD prevalence, deaths, and disabilityadjusted life years (DALYs) based on data from the GBD 2021 database. We would analyze trends from 1990 to 2021 and compared estimates across age and sex groups. The relationship between COPD DALYs and the sociodemographic index (SDI) would be examined. The burden of COPD caused by various risk factors such as smoking, air pollution, and temperature would be also estimated.

Overview and data source

Information on COPD prevalence, deaths, and DALYs was obtained from the Global Health Data Exchange (https://vizhub.healthdata.org/gbd-results/) (GHDx) [15]. In GBD 2021, COPD is defined according to the GOLD classification, based on the ratio of forced expiratory volume in 1 s (FEV₁) to forced vital capacity (FVC) after bronchodilation, with a ratio of (FEV₁/FVC)<0.7 on spirometry. The International Classification of Disease and Injuries (ICD)-10 codes associated with COPD include J41, J42, J43, J44, and J47. There are different case definitions for COPD, such as GOLD Pre-bronchodilation, Lower Limit of Normal (LLN) Post-bronchodilation, LLN Pre-bronchodilation, and European Respiratory Society guidelines. These are used to assess whether an individual has COPD. The most recent comprehensive review of the literature on COPD was conducted for GBD 2016, and data from the literature that matched the case definitions mentioned above were extracted. The detailed case definition and sources of data for COPD can be found in Table S1.

The SDI is a composite measure of development status. It is calculated as the geometric mean of three indices, which range from 0 to 1, representing the total fertility rate among women under 25, mean education for individuals aged 15 and above, and lag distributed income per capita. A location with an SDI of 0 represents the minimum level of development relevant to health, while an SDI of 1 indicates the maximum level theoretically achievable [6]. The SDI values can be found on the GHDx website (at https://ghdx.healthdata.org/gbd-2021).

The percentage of COPD DALYs attributable to various risk factors, such as smoking, ambient particulate matter pollution, household air pollution from solid fuels, occupational particulate matter, gases, and fumes, ambient ozone pollution, low temperature, secondhand smoke, and high temperature, was obtained from GHDx. The definitions of these factors and their relative risk for COPD are documented in a previous study and can be found in Table S1 [15].

Statistical analyses

The main tool used for modeling COPD is called disease model-Bayesian meta-regression (DisMod-MR) version 2.1. A remission rate of zero was set because individuals do not fully recover once they have COPD; the symptoms are only managed. The maximum incidence rate is set at 0.0002 before age 15 and 0.0005 before age 30 to prevent inflated estimates in age groups with limited or no primary data. The covariates selected for the model have a directional relationship with COPD, and their directions were chosen based on the strength of the evidence.

The standard Cause of Death Ensemble modeling (CODEm) approach was used to estimate deaths attributable to COPD. Separate models were conducted for male and female mortality, with the age range for both models set at 15 to 95+years. A series of adjustments to data that do not completely match the case definition was made.

Different diagnoses often lead to different estimates of COPD. Similarly, claims data are subject to biases. Claims data are often systematically lower than survey data, probably due to selection bias with regard to socioeconomic status. The data is adjusted to correct any biases using a logit-transformation method called metaregression—Bayesian, regularized, trimmed (MR-BRT). This method involves a logit-transformation process that corrects biases in the data by comparing overlapping data points from different case definitions and study designs. By transforming the data into logit space, calculating the difference in logits, and applying a random effects metaregression, a pooled logit difference is obtained. This difference is then used to adjust all data points, with new estimates and standard errors calculated to account for between-study differences. This ensures a more reliable and consistent estimation of COPD prevalence across various data sources.

All results were reported with 95% uncertainty intervals (95% UI). These intervals were calculated by sampling 1000 draws at each computational step and combining uncertainty from various sources such as input data, corrections for measurement error, and estimates of residual non-sampling error. This study compared results for both global and 21 regional levels based on age and sex. It also examined the relationship between COPD burden and SDI for 21 regions, as well as 204 countries and territories, using Smoothing Splines models. The data were analyzed using R version 4.0.5 (http://CRAN.R-project.org, R Foundation, Vienna, Austria).

Results

Global level

In 2021, a total of 213.39 (95% UI 194.87 to 233.98) million prevalent cases of COPD were estimated, with an age-standardized prevalence of 2,512.86 (95% UI 2,293.93 to 2,748.52) per 100,000, a change of -1.46% (-3.36% to 0.39%) since 1990. A higher total number of female COPD patients and a higher age-standardized prevalence of male COPD patients were observed from 1990 to 2021 (Figure S1). The estimated number of deaths attributed to COPD was 3,719.94 (95% UI 3,347.91 to 4,084.22) thousand, with an age-standardized mortality of 45.22 (95% UI 40.61 to 49.70) per 100,000, a decrease of 37.12% (27.68% to 43.37%) since 1990. The number of DALYs for COPD was estimated to be 79.78 (95% UI 74.03 to 86.01) Page 3 of 11

million, with an age-standardized DALYs rate of 940.66 (95% UI 871.48 to 1014.59) per 100,000, a decrease of 36.98% (28.54% to 42.37%) since 1990 (Table 1).

Regional level

The number of prevalent cases of COPD increased from 100.54 million in 1990 to 213.39 million in 2021 (Table S2). In 2021, the highest number of prevalent cases were reported in East Asia (52.09, 95%UI 46.32 to 58.80 unit: million), South Asia (43.77, 95%UI 39.58 to 47.76), and Western Europe (23.65, 95%UI 21.53 to 25.86). The number of deaths from COPD increased from 2.50 million in 1990 to 3.72 million in 2021, and the number of DALYs for COPD increased from 56.86 million in 1990 to 79.78 million in 2021 (Table S3 and Table S4). In 2021, East Asia, South Asia, and Southeast Asia had the highest number of deaths (1.32, 95%UI 1.08 to 1.57; 1.23, 95%UI 1.10 to 1.38; and 0.23, 95%UI 0.20 to 0.26; unit: million, respectively) and DALYs (24.39, 95%UI 20.76 to 28.63; 28.01, 95%UI 25.40 to 30.94; and 5.56, 95%UI 4.98 to 6.21; unit: million, respectively) (Table 1).

High-income North America (3,298.88) and South Asia (3,019.10) had the highest age-standardized prevalence of COPD, with more than 3,000 cases per 100,000 people. The lowest age-standardized prevalence was reported in Southern Latin America (1,482.66) and High-income Asia Pacific (1527.27). Oceania (118.21), South Asia (101.63), and East Asia (72.20) had an age-standardized point mortality (per 100,000) greater than the global level for COPD, while High-income Asia Pacific (6.68) had the lowest. Oceania (2,351.49), South Asia (2,049.22), and East Asia (1,217.69) also had an age-standardized DALYs rate (per 100,000) greater than the global level for COPD, while High-income Asia Pacific (182.14) had the lowest. Age-standardized prevalence, mortality, and DALYs rate by sex are shown in Figure S2 to Figure S4.

From 1990 to 2021, Australasia (-23.13%), High-income Asia Pacific (-12.65%), and Eastern Europe (-11.44%) experienced a decline of more than 10% in age-standardized COPD prevalence, while Caribbean (19.41%) and North Africa and Middle East (19.44%) experienced an increase of about 20%. Age-standardized deaths for COPD increased in Caribbean (7.41%) and High-income North America (13.73%), while there was a decrease of over 50% in East Asia (-67.95%), Eastern Europe (-67.23%), and High-income Asia Pacific (-52.84%). Caribbean (10.72%) and High-income North America (4.66%) also had an increase in age-standardized DALYs for COPD, while East Asia (-67.62%), Eastern Europe (-58.88%), and High-income Asia Pacific (-41.58%) experienced the greatest decrease (Table 1). The percent change in age-standardized prevalence, mortality, and DALYs rates by sex is shown in Figure S5 to Figure S7.

Table 1 Prevalence, deaths, and disability adjusted life years for chronic obstructive pulmonary disease in 2021, and percentage change in age-standardized rates per 100 000, by Global Burden of Disease region, from 1990 to 2021

	Prevalence	(95% UI)		Deaths (95	% UI)		DALYs (95% UI)		
	No, in mil- lion (95% Ul)	ASRs per 100 000 (95% UI)	Percentage change in ASRs from 1990 to 2021	No, in mil- lion (95% Ul)	ASRs per 100 000 (95% UI)	Percentage change in ASRs from 1990 to 2021	No, in million (95% UI)	ASRs per 100 000 (95% UI)	Percentage change in ASRs from 1990 to 2021
Global	213.39 (194.87 to 233.98)	2512.86 (2293.93 to 2748.52)	-1.46 (-3.36 to 0.39)	3.72 (3.35 to 4.08)	45.22 (40.61 to 49.7)	-37.12 (-43.37 to -27.68)	79.78 (74.03 to 86.01)	940.66 (871.48 to 1014.59)	-36.98 (-42.37 to -28.54)
East Asia	52.09 (46.32 to 58.8)	2484.43 (2224.88 to 2771.41)	-9.85 (-14.59 to -5.77)	1.32 (1.08 to 1.57)	72.2 (59.32 to 85.26)	-67.95 (-74.24 to -60.2)	24.39 (20.76 to 28.63)	1217.69 (1043.87 to 1422.79)	-67.62 (-73.56 to -60.32)
Southeast Asia	13.66 (12.17 to 15.27)	2136.77 (1904.59 to 2396.24)	1.2 (-1.19 to 3.56)	0.23 (0.2 to 0.26)	43.14 (38.24 to 48.54)	-28.31 (-39.04 to -2.65)	5.56 (4.98 to 6.21)	914.73 (822.27 to 1016.35)	-27.15 (-36.76 to -4.98)
Oceania	0.2 (0.18 to 0.21)	2492.77 (2275.04 to 2748.51)	-5.81 (-9.24 to -2.48)	0.01 (0 to 0.01)	118.21 (96.32 to 144.59)	-18.06 (-35.44 to 6.4)	0.16 (0.13 to 0.19)	2351.49 (1931.26 to 2854.06)	-19.46 (-36.93 to 5.81)
Central Asia	1.78 (1.61 to 1.98)	2258.77 (2029.8 to 2508.18)	-1.87 (-6.54 to 2.8)	0.01 (0.01 to 0.02)	21.27 (19.12 to 23.46)	-41.44 (-46.91 to -35.23)	0.39 (0.35 to 0.42)	498.6 (452.01 to 546.1)	-38.57 (-44.13 to -32.34)
Central Europe	5.18 (4.68 to 5.71)	2427.25 (2209.94 to 2672.32)	3.53 (-1.06 to 8.53)	0.04 (0.03 to 0.04)	16.03 (14.7 to 17.22)	-47.71 (-51.51 to -44.2)	0.92 (0.85 to 0.98)	413.12 (382.55 to 444.56)	-39.19 (-43.01 to -35.75)
Eastern Europe	7.08 (6.22 to 7.98)	2125.62 (1896.41 to 2381.92)	-11.44 (-14.67 to -8.55)	0.04 (0.04 to 0.05)	11.72 (10.79 to 12.62)	-67.23 (-69.62 to -64.92)	1.12 (1.04 to 1.21)	324.42 (301.04 to 350.1)	-58.88 (-61.5 to -56.22)
High-in- come Asia Pacific	7.29 (6.34 to 8.31)	1527.27 (1344.7 to 1724.48)	-12.65 (-16.27 to -8.58)	0.04 (0.04 to 0.05)	6.68 (5.7 to 7.37)	-52.84 (-56.34 to -48.45)	0.96 (0.84 to 1.07)	182.14 (162.64 to 202.95)	-41.58 (-44.75 to -37.51)
Australasia	0.85 (0.75 to 0.97)	1580.64 (1411.47 to 1793.95)	-23.13 (-28.96 to -15.06)	0.01 (0.01 to 0.01)	18.89 (16.66 to 20.42)	-35.78 (-41.33 to -30.94)	0.21 (0.19 to 0.23)	376.2 (343.09 to 400.39)	-38.37 (-42.43 to -34.49)
Western Europe	23.65 (21.53 to 25.86)	2590.99 (2375.15 to 2818.23)	-3.37 (-6.09 to -0.27)	0.21 (0.18 to 0.22)	17.82 (15.74 to 18.92)	-27.73 (-31.63 to -25.02)	3.89 (3.55 to 4.14)	390.81 (361.46 to 415.88)	-24.88 (-27.31 to -22.8)
Southern Latin America	1.29 (1.14 to 1.44)	1482.66 (1320.77 to 1654.03)	-4.68 (-12.12 to 3.96)	0.02 (0.02 to 0.02)	22.53 (20.53 to 24.07)	-16.33 (-22.08 to -10.66)	0.39 (0.36 to 0.41)	436.03 (405.72 to 461.73)	-21.34 (-26.29 to -16.57)
High- income North America	21.49 (20.38 to 22.54)	3298.88 (3132.14 to 3451.88)	5.88 (0.56 to 12.71)	0.21 (0.19 to 0.23)	29.89 (26.2 to 31.63)	13.73 (7.7 to 17.06)	4.95 (4.58 to 5.22)	736.05 (685.79 to 776.49)	4.66 (1.34 to 7.41)
Caribbean	1.01 (0.92 to 1.12)	1888.04 (1704.73 to 2076.77)	19.41 (12.95 to 26.35)	0.01 (0.01 to 0.01)	19.85 (17.47 to 22.49)	7.41 (-5.2 to 21.66)	0.24 (0.21 to 0.27)	439.53 (388.88 to 499.3)	10.72 (-1.21 to 25)
An- dean Latin America	0.98 (0.87 to 1.1)	1658.68 (1461.64 to 1874.88)	8.53 (-1.73 to 20.04)	0.01 (0.01 to 0.01)	13.4 (10.93 to 16.29)	-31.06 (-44.04 to -13.59)	0.15 (0.13 to 0.18)	261.42 (222.3 to 306.62)	-30.34 (-41.28 to -16.16)
Central Latin America	5.46 (4.93 to 6.05)	2221.43 (1999.23 to 2453.11)	10.95 (6.91 to 15.12)	0.06 (0.05 to 0.07)	26.92 (23.7 to 29.64)	-24.67 (-31.07 to -18.26)	1.23 (1.12 to 1.35)	512.35 (462.65 to 560.08)	-22.47 (-28.17 to -16.38)
Tropi- cal Latin America	6.44 (5.7 to 7.22)	2546.83 (2252.36 to 2847.04)	-0.76 (-3.69 to 1.98)	0.06 (0.06 to 0.07)	26.32 (23.44 to 27.99)	-41.04 (-44.14 to -38.38)	1.4 (1.3 to 1.48)	554.73 (513.83 to 585.11)	-37.02 (-39.58 to -34.58)
North Africa and Middle East	11.42 (10.3 to 12.69)	2512.32 (2248.38 to 2803.61)	19.44 (14.93 to 23.7)	0.09 (0.08 to 0.1)	26.37 (23.19 to 29.31)	-27.11 (-36.93 to -5.37)	2.53 (2.31 to 2.8)	599.18 (546.07 to 658.22)	-24.59 (-33.63 to -7.68)

Table 1 (continued)

	Prevalence	e (95% UI)		Deaths (95% UI)			DALYs (95% UI)		
	No, in mil- lion (95% Ul)	ASRs per 100 000 (95% UI)	Percentage change in ASRs from 1990 to 2021	No, in mil- lion (95% Ul)	ASRs per 100 000 (95% UI)	Percentage change in ASRs from 1990 to 2021	No, in million (95% UI)	ASRs per 100 000 (95% UI)	Percentage change in ASRs from 1990 to 2021
South Asia	43.77 (39.58 to 47.76)	3019.1 (2729.72 to 3298.67)	3.02 (0.9 to 4.72)	1.23 (1.1 to 1.38)	101.63 (90.55 to 114.34)	-11.27 (-25.19 to 14.84)	28.01 (25.4 to 30.94)	2049.22 (1862.71 to 2268.73)	-15.47 (-27.1 to 5.86)
Central Sub-Saha- ran Africa	1.15 (1.03 to 1.29)	1930.5 (1703.4 to 2184.23)	10.23 (4.41 to 15.72)	0.02 (0.01 to 0.02)	42.82 (29.63 to 65.02)	-18.17 (-37.34 to 5.85)	0.5 (0.37 to 0.66)	975.91 (720.5 to 1344.93)	-15.19 (-32.85 to 4.54)
Eastern Sub-Saha- ran Africa	3.33 (2.96 to 3.69)	1658.85 (1469.54 to 1852.14)	4.88 (1.24 to 8.4)	0.04 (0.03 to 0.05)	29.91 (24.41 to 35.14)	-29.29 (-39.44 to -14.81)	1.19 (0.99 to 1.36)	713.24 (593 to 816.07)	-25.68 (-34.58 to -13.19)
Southern Sub-Saha- ran Africa	1.24 (1.09 to 1.38)	2127.98 (1882.89 to 2384.97)	1.75 (-1.11 to 4.54)	0.02 (0.02 to 0.02)	34.78 (31.93 to 37.34)	-7.01 (-21.83 to 4.47)	0.48 (0.44 to 0.52)	864.13 (800.37 to 929.92)	-3.63 (-14.11 to 4.99)
Western Sub-Saha- ran Africa	4.03 (3.58 to 4.48)	1749.91 (1540.55 to 1959.17)	11.99 (9.42 to 15.18)	0.03 (0.03 to 0.04)	22.07 (19.45 to 25.05)	-22.63 (-34.47 to -2.48)	1.13 (1.01 to 1.26)	567.27 (510.78 to 631.22)	-16.81 (-28.37 to -0.01)

ASRs=age-standardized rates, DALYs=disability adjusted life years, 95% UI=95% uncertainty intervals



Fig. 1 Age-standardized prevalence of chronic obstructive pulmonary disease per 100 000 population in 2021

National level

The age-standardized prevalence of COPD varied from 922.56 to 3445.29 per 100,000 in 2021 across 204 countries and territories. The United States of America (3445.29, 95%UI 3263.49 to 3602.42), the United Kingdom (3270.26, 95%UI 2957.04 to 3570.38), and Turkey (3146.68, 95%UI 2861.31 to 3477.82) had the highest prevalence, while Singapore (922.56, 95%UI 805.95 to 1060.47), Cabo Verde (1001.29, 95%UI 872.55 to 1138.04), and Chile (1213.70, 95%UI 1060.34 to 1388.75) had the lowest (Fig. 1 & Table S2). Country specific age-standardized mortality for COPD ranged from 2.74 to 156.82 per 100,000 people in 2021, with Papua New Guinea (156.82,

95%UI 123.55 to 197.43), Nepal (146.13, 95%UI 116.66 to 182.46), and India (108.39, 95%UI 94.73 to 122.39) having the highest estimates, and Kuwait (2.74, 95%UI 2.24 to 3.28), Japan (5.84, 95%UI 4.93 to 6.33), and Montenegro (5.87, 95%UI 4.63 to 7.15) having the lowest (Figure S8 & Table S3). The national age-standardized DALYs rate of COPD ranged from 146.48 to 3004.36 per 100,000 people in 2021, with Papua New Guinea (3004.36, 95%UI 2404.29 to 3732.82), Nepal (2836.01, 95%UI 2275.31 to 3485.04), and India (2171.16, 95%UI 1953.69 to 2422.39) having the highest estimates, and Singapore (146.48, 95%UI 131.42 to 161.67), Japan (155.76, 95%UI 137.62

to 174.26), and Kuwait (160.46, 95%UI 138.49 to 185.65) having the lowest (Figure S9 & Table S4).

The age-standardized prevalence for COPD has significantly increased in several countries since 1990, with Saudi Arabia (36.65%, 95%UI 26.63 to 46.60), Morocco (35.32%, 95%UI 24.84 to 45.54), and Egypt (32.35%, 95%UI 23.55 to 41.79) experiencing the largest increases, while Singapore (-36.79%, 95%UI -44.37 to -28.08) showed the largest decrease of more than 30% (Figure S10 & Table S2). In terms of age-standardized mortality for COPD, Norway (100.73%, 95%UI 87.23 to 110.72), Saint Vincent and the Grenadines (71.62%, 95%UI 50.19 to 96.85), and Belize (58.00%, 95%UI 34.75 to 83.85) had the most significant increases of more than 50%, while Singapore (-85.46%, 95%UI -86.80 to -84.40), Belarus (-84.67%, 95% UI -87.25 to -81.70), and Ukraine (-80.87%, 95%UI -85.44 to -75.78) experienced the largest decreases of more than 80% (Figure S11 & Table S3). From 1990 to 2021, Saint Vincent and the Grenadines (60.06%, 95%UI 42.14 to 79.78), Norway (57.21%, 95%UI 49.36 to 64.35), and Belize (50.74%, 95%UI 31.00 to 71.18) had the greatest increase in age-standardized DALYs for COPD, while Singapore (-80.98%, 95%UI -82.63 to -79.23), Belarus (-76.02%, 95%UI -79.40 to -72.07), and Ukraine (-74.00%, 95%UI -78.91 to -68.16) saw the largest decreases since 1990 (Figure S12 & Table S4).

Age and sex pattern

The age-standardized prevalence of COPD increased with age, with the highest rates observed in people over

95 years old. Among males, the prevalence was 44,027.73 (95%UI 37,884.64 to 51,084.59) per 100,000 people, and among females, it was 41,728.01 (95%UI 36,165.54 to 48,351.48) per 100,000 people. The highest number of cases were found in individuals aged 70 to 74 years, with approximately 14 million cases in males and 15 million cases in females (Fig. 2).

The age-standardized mortality for COPD was highest among males aged 90 to 94 years and in females over 95 years, at 2357.79 (95%UI 2039.83 to 2610.24) and 1581.27 (95%UI 1153.76 to 1914.99) per 100,000 people, respectively. There were more COPD-related deaths in males than in females before the age of 90 to 94 years. The highest number of COPD deaths for both males and females was observed in individuals aged 80 to 84 years, totaling 382,747.10 cases and 317,113.93 cases, respectively (Figure S13).

Similarly, the highest age-standardized DALYs for COPD were observed in males aged 90 to 94 years and in females over 95 years, with 22345.83 (95%UI 19515.18 to 24654.34) and 14939.34 (95%UI 11538.17 to 17794.61) per 100,000 people, respectively. There were more DALYs cases for COPD in males than in females before the age of 90 to 94 years. The highest number of COPD DALYs in both males and females was found in individuals aged 70 to 74 years, totaling approximately 8 million cases and 6 million cases, respectively (Figure S14).



Fig. 2 Number of prevalent cases globally and prevalence of chronic obstructive pulmonary disease per 100 000 population, by age and sex in 2021. Boxes indicate prevalent cases with 95% uncertainty intervals for men and women. Lines indicate prevalence rate with 95% uncertainty intervals for men and women

Association with the sociodemographic index

The global burden of COPD, measured in age-standardized DALYs, decreased as the SDI increased (Fig. 3). When examining the regional level, there was a roughly reversed U-shaped relationship between the age-standardized COPD DALYs and SDI, with the highest burden observed at an SDI of about 0.45. South Asia, Oceania, East Asia, and High-income North America had higher age-standardized COPD DALYs from 1990 to 2021 than expected based on their SDI. At the national level, several countries, including Papua New Guinea, Nepal, and India, had a higher than expected burden of COPD in 2021 based on their SDI (Figure S15).

Risk factors

At the global level, certain factors had different levels of influence on COPD DALYs. Smoking had the highest influence, accounting for 34.8%, followed by ambient particulate matter pollution (22.2%), household air pollution from solid fuels (19.5%), occupational particulate matter, gases, and fumes (15.8%), ambient ozone pollution (11.0%), secondhand smoke (7.1%), low temperature (6.2%), and high temperature (0.9%) (Fig. 4).

Household air pollution from solid fuels was the leading risk factor for females, accounting for 21.5% of risk-attributable DALYs globally in 2021 (Figure S16). Smoking was the leading risk factor for males, accounting for 50.7% of risk-attributable DALYs in 2021 (Figure S17). The proportion of COPD DALYs attributable to household air pollution from solid fuels was higher in females than in males every year from 1990 to 2021, with the impact reaching its lowest point in 2021. Conversely, the proportion of COPD DALYs caused by smoking was consistently higher in males than in females throughout the same period, also reaching its lowest impact in 2021 (Figure S18).

The distribution of COPD DALYs attributed to various factors varied by age. COPD DALYs attributed to smoking peaked at the age of 65 to 74 years, accounting for 15.1 to 38.4% of the total. Ambient particulate matter pollution accounted for 18.8 to 22.9% of COPD DALYs, while household air pollution from solid fuels was highest in people aged 30 to 34 years, accounting for 27.6%. Occupational particulate matter, gases, and fumes showed their highest impact in people aged 70 to 74 years, contributing to 17.8% of COPD DALYs. Meanwhile, COPD DALYs attributed to ambient ozone pollution and secondhand smoke ranged from 5.1 to 11.9% and 6.7 to 8.7%, respectively. COPD DALYs attributed to low temperature increased with age, mostly up to 8.3%, and those attributed to high temperature accounted for approximately 1.0% (Figure S19).

Notably, among individuals aged 30 and above, COPD DALYs attributed to smoking ranged from 25.1 to 54.4% in males and from 3.8 to 16.2% in females (Figure S20 & Figure S21).



Fig. 3 Age-standardized disability adjusted life year rates of chronic obstructive pulmonary disease for the 21 Global Burden of Disease regions by sociodemographic index, 1990–2021. Thirty-two points are plotted for each region and show the observed age-standardized disability adjusted life year rates from 1990 to 2021 for that region. Expected values, based on the sociodemographic index and disease rates in all locations, are shown as a solid line. Regions above the solid line represent a higher than expected burden and regions below the line show a lower than expected burden. DALY: disability adjusted life year



Fig. 4 Percentage of disability adjusted life years due to chronic obstructive pulmonary disease attributable to each risk factor for the 21 Global Burden of Disease regions in 2021. DALY: disability adjusted life year

Discussion

This study provided the most recent data on the prevalence, deaths, and DALYs of COPD from 1990 to 2021 using the GBD 2021 database. Although the annual change in age-standardized disease burden rates decreased, the absolute counts for the prevalence, deaths, and DALYs of COPD increased, totaling 213.39 million, 3.72 million, and 79.78 million cases, respectively.

The GBD 2019 reported an age-standardized prevalence rate of COPD at 2.6% [3]. In 2021, we found a prevalence of 2.5% based on GBD 2021, indicating similar results. However, when compared to the Burden of Obstructive Lung Disease (BOLD) program and other large-scale epidemiological studies, which estimated the global prevalence of COPD at 10.3%, our findings appear lower [16, 17]. The disparities between the GBD study and other large-scale epidemiological surveys or metaanalyses of prevalence rates may primarily lie in the use of different definitions of COPD, the inclusion of different variables affecting COPD, and the adoption of different methods to construct predictive models [18]. In addition to including spirometry-based measures, the GBD study also considered hospital claims data and BOLD data, and factored in the impact of the SDI and education in the modeling process [5, 6]. However, since the GBD data is derived from modeling predictions, it may underestimate the actual burden of COPD disease.

The GBD 2017 predicted a COPD-attributable death rate of 42.0 per 100,000, while the GBD 2019 forecasted a slightly higher rate of 42.5 per 100,000 [3, 19]. The GBD 2021 still used the CODEm methodology to estimate deaths attributable to COPD, but adjusted the age range to 15 to 95+years, resulting in a prediction of 45.2 per 100,000. Additionally, there may be 3 million deaths annually due to COPD according to the GOLD guidelines [1]. Based on GBD 2021, our study found that 3.72 million people died from COPD in 2021. Some studies predict that in 2022, COPD will rank third in all-cause mortality, and by 2050, COPD will still be the third leading cause, after ischemic heart disease and stroke [20].

DALYs represent the sum of years lost due to premature mortality and the years lived with disability. The GBD 2019 estimated a COPD DALY rate of 926.1 per 100,000, and GBD 2021 estimated it to be 940.7 per 100,000 [3]. According to the GBD Study, COPD was the primary driver of increased DALYs worldwide, especially in low and middle-income countries [3, 21]. Predictions indicated that in 2022, COPD DALYs will rank sixth, but by 2050, it is expected to rise to the fourth position [20]. The burden of COPD is severe and is often related to a combination of continued exposure to COPD risk factors and the aging of the world's population [18, 22, 23].

Several studies showed that COPD is more common in individuals aged \geq 40 years compared to those <40, and is more prevalent in men than in women [16, 24,

25]. Our research also found that the age-standardized prevalence of COPD increased with age, with a higher age-standardized prevalence in males, but a higher total number of female patients in all age groups. Previous studies examining the burden of COPD in 28 European countries from 2001 to 2019 revealed a 9.7% decrease in the age-standardized prevalence rate for men, while women experienced a 4.3% increase [26]. Previous explanations included the increased life expectancy due to reduced mortality from diseases such as cardiovascular diseases, as well as changes in women's smoking behavior patterns [27]. However, based on the definition of smoking from GBD, we did not observe obvious changes in COPD DALYs caused by smoking between males and females from 1990 to 2021. Further in-depth research is still needed. Additionally, our result showed that COPD mortality and DALYs are generally more severe in males, but studies suggested that this gender-burden gap may decrease, in line with the changing burden of COPD prevalence [26].

In terms of the relationship between COPD DALYs and the SDI, certain regions, mostly composed of highincome countries, and others predominantly made up of low- and middle-income countries, may have higher COPD DALYs. However, the reasons for this phenomenon could be different. In high-income countries, the increasing problem of an aging population could be the main factor contributing to the high disease burden of COPD. With longer life expectancies and an aging population, the prevalence of COPD is expected to increase due to the accumulation of risk factors over time [1, 28]. In low- and middle-income countries, factors such as higher rates of smoking, environmental pollution, early diagnosis of patients, and insufficient healthcare resources may be the main contributors to the disease burden of COPD [1, 28].

Our results showed that East Asia had a higher agestandardized COPD DALYs from 1990 to 2021 than expected based on its SDI. However, it's noteworthy that this region also had a significant decline in COPDrelated deaths and DALYs during the same period. Taking China as an example, the country implemented various measures over the past 30 years to reduce burden due to COPD. These measures included reducing smoking rates, decreasing the use of fossil fuels to improve air quality, promoting clean energy sources, encouraging environmentally friendly practices, and improving access to quality healthcare for early diagnosis and treatment [28].

Among the various measures, tobacco control is one of the most important. Our results also showed that smoking had the highest influence on the percentage of COPD-related DALYs attributable to each risk factor. Previous studies suggested that compared to non-smokers, smokers may experience more respiratory symptoms, impaired lung function, a greater decline in FEV_1 , and higher mortality [29].

According to the GBD 2019 estimates, occupational exposure to particulate matter, gases, and fumes contributed to 15.6% of the burden impact on COPD DALYs, ranking as the third leading risk factor [3]. However, based on the GBD 2021 estimates, this risk factor contributes to a 15.8% burden impact but is ranked fourth. Household air pollution from solid fuels has taken the place of the third leading risk factor, causing 19.5% of COPD DALYs. In low SDI regions, the global disease burden of COPD due to household air pollution from solid fuels remains significant [30, 31]. In a previous study, a nine-year cohort study was carried out in 12 villages in southern China. The study aimed to enhance kitchen ventilation and encourage the use of clean fuels instead of biomass for cooking. The results showed that the use of clean fuels and improved ventilation were linked to a reduced decline in FEV_1 [32]. Since COPD related to biomass exposure, tobacco smoking, or various other causes may present different clinical features and progressions, and may require different treatments, there are still several knowledge gaps that need to be addressed [14].

Our study presented a comprehensive analysis of the global, regional, and national burden of COPD from 1990 to 2021, using data from the GBD 2021. It contains detailed data on COPD prevalence, mortality, and DALYs, and investigates the impact of various risk factors such as smoking, ambient particulate matter pollution, and household air pollution from solid fuels. However, our study had some limitations, including potential biases in data sources, variations in COPD definitions and diagnostic criteria across studies, and the complex nature of risk factors which might not be entirely captured. Further research is necessary to address knowledge gaps and the dynamic nature of COPD burden and risk factors.

Conclusions

Our study shows that the global burden of COPD varies across regions and countries. Although the age-standardized prevalence, mortality, and DALYs rates have decreased since 1990, the absolute numbers indicate an increasing overall burden of COPD. This study highlights the importance of targeted interventions such as smoking cessation programs and strategies to address environmental and occupational exposures. It also stresses the need for context-specific approaches that consider local risk factors, healthcare infrastructure, and sociodemographic factors. These findings emphasize the necessity of sustained efforts in prevention, early diagnosis, and effective treatment to reduce the burden of COPD and improve public health worldwide.

Abbreviations

BOLD CODEm COPD DALYS DisMod-MR FEV1 FVC GBD GHDX GOLD ICD LLN MR-BRT SDI 95% UI	Burden of Obstructive Lung Disease Cause of Death Ensemble modelling Chronic Obstructive Pulmonary Disease Disability Adjusted Life Years Disease Model-Bayesian Meta-Regression Forced Expiratory Volume in 1 s Forced Vital Capacity Forced Vital Capacity Global Burden of Disease Global Health Data Exchange Global Health Data Exchange Global Initiative for Chronic Obstructive Lung Disease International Classification of Disease and Injuries Lower Limit of Normal Meta-Regression—Bayesian, Regularized, Trimmed Sociodemographic Index 95% Uncertainty Interval World Health Organization
WHO	World Health Organization

Supplementary Information

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Supplementary Material 1

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Author contributions

Z.F.W did the data curation, formal analysis, methodology, software, validation, and visualization, and was a major contributor in writing the manuscript. J.F.L, L.N.L, F.F.H, X.Y.Y, and K.P also did the data curation, validation, and writing the manuscript. Y.G and J.P.Z did the conceptualization, data curation, supervision, validation, and writing the manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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