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a systematic review and modelling analysis

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# Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis



Davies Adeloye\*, Peige Song\*, Yajie Zhu, Harry Campbell, Aziz Sheikh, Igor Rudan, on behalf of NIHR RESPIRE Global Respiratory Health Unit†



## Summary

**Background** Chronic obstructive pulmonary disease (COPD) is an increasingly important cause of morbidity, disability, and mortality worldwide. We aimed to estimate global, regional, and national COPD prevalence and risk factors to guide policy and population interventions.

**Methods** For this systematic review and modelling study, we searched MEDLINE, Embase, Global Health, and CINAHL, for population-based studies on COPD prevalence published between Jan 1, 1990, and Dec 31, 2019. We included data reported using the two main case definitions: the Global Initiative for Chronic Obstructive Lung Disease fixed ratio (GOLD; FEV<sub>1</sub>/FVC<0.7) and the lower limit of normal (LLN; FEV<sub>1</sub>/FVC<LLN). We employed a multilevel multivariable mixed-effects meta-regression approach to generate the age-specific and sex-specific prevalence of COPD in 2019 for high-income countries (HICs) and low-income and middle-income countries (LMICs) according to the World Bank definition. Common risk factors for GOLD-COPD were evaluated using a random-effects meta-analysis.

**Findings** We identified 162 articles reporting population-based studies conducted across 260 sites in 65 countries. In 2019, the global prevalence of COPD among people aged 30–79 years was 10.3% (95% CI 8.2–12.8) using the GOLD case definition, which translates to 391.9 million people (95% CI 312.6–487.9), and 7.6% (5.8–10.1) using the LLN definition, which translates to 292.0 million people (219.8–385.6). Using the GOLD definition, we estimated that 391.9 million (95% CI 312.6–487.9) people aged 30–79 years had COPD worldwide in 2019, with most (315.5 million [246.7–399.6]; 80.5%) living in LMICs. The overall prevalence of GOLD-COPD among people aged 30–79 years was the highest in the Western Pacific region (11.7% [95% CI 9.3–14.6]) and lowest in the region of the Americas (6.8% [95% CI 5.6–8.2]). Globally, male sex (OR 2.1 [95% CI 1.8–2.3]), smoking (current smoker 3.2 [2.5–4.0]; ever smoker 2.3 [2.0–2.5]), body-mass index of less than 18.5 kg/m<sup>2</sup> (2.2 [1.7–2.7]), biomass exposure (1.4 [1.2–1.7]), and occupational exposure to dust or smoke (1.4 [1.3–1.6]) were all substantial risk factors for COPD.

**Interpretation** With more than three-quarters of global COPD cases in LMICs, tackling this chronic condition is a major and increasing challenge for health systems in these settings. In the absence of targeted population-wide efforts and health system reforms in these settings, many of which are under-resourced, achieving a substantial reduction in the burden of COPD globally might remain a difficult task.

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## Introduction

With population ageing, urbanisation, and their related risks, chronic respiratory diseases will continue to be an increasingly important cause of morbidity and mortality. Chronic obstructive pulmonary disease (COPD) has increasingly been identified as a major cause of death worldwide.<sup>1</sup> Substantial variation in onset, progression, and lung function trajectories at different life stages across populations limits understanding of COPD-predisposing factors.<sup>2</sup> However, tobacco smoking and exposure to indoor air pollution (including from biomass combustion), ambient air pollution, and occupational pollutants have been reported as leading risk factors in most settings.<sup>3</sup>

Although efforts to address risk factors and improve vaccination (influenza and pneumococcal vaccines) and oxygen supply are crucial to reducing global COPD mortality,<sup>3</sup> misdiagnosis and misclassification of the disease due to limited clinical skills and knowledge of the disease, poor access to spirometry, and a lack of consensus on both clinical and epidemiological case definitions also need to be addressed.<sup>4,5</sup> Clinicians, respiratory experts, and epidemiologists have described the scarcity of representative estimates of COPD burden as a global challenge that could limit the implementation of cost-effective evidence-based strategies in the coming years.<sup>6</sup>

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### Research in context

#### Evidence before this study

We searched PubMed for studies published until Dec 31, 2019, on the global prevalence of chronic obstructive pulmonary disease (COPD) using the terms (“chronic obstructive pulmonary disease” OR “bronchitis, chronic” OR “pulmonary emphysema” OR “copd”) AND (“morbidity” OR “prevalence” OR “risk factors”) AND (global OR world\*). Our searches identified 3475 studies. Varying case definitions, diagnostic criteria, and approaches to study design across world regions are largely responsible for existing uncertainties on the prevalence of COPD. The Burden of Obstructive Lung Disease initiative and Global Burden of Disease collaborators have pioneered efforts in collecting country-specific population data on the prevalence of, and risk factors for, COPD and providing updates on global estimates of deaths and disability-adjusted life years due to COPD, with reported global cases ranging from 299.4 million (269.0–330.0) in 2017, to 212.3 million (200.4–225.1) in 2019. In our previous study that included population-based studies providing spirometry-based prevalence rates of COPD, we reported that there were 384 million COPD cases in 2010, translating to a global prevalence of 11.7% (8.4–15.0). We have added a risk-factor model to current estimates.

#### Added value of this study

This study provides, to our knowledge, the first global and regional estimates based on the Global Initiative for Chronic Obstructive Lung Disease fixed ratio (GOLD;  $FEV_1/FVC < 0.7$ ) and

the lower limit of normal (LLN;  $FEV_1/FVC < LLN$ ). The number of studies, countries, and study sites covered, and restriction to people aged 30–79 years, for which most data were available, provide high confidence in the representativeness of our estimates. We estimated that the global prevalence of COPD was 10.3% in 2019, accounting for 391.9 million cases among people aged 30–79 years, on the basis of the GOLD definition, and 7.6%, accounting for 292.0 million cases, using the LLN definition. Most cases were in low-income and middle-income countries (LMICs; 315.5 million [246.7–399.6]; 80.5%), although prevalence was slightly higher in high-income countries (HICs). Male sex, smoking, body-mass index of less than 18.5 kg/m<sup>2</sup>, biomass exposure, and occupational exposure to dust or smoke were all substantial risk factors for COPD.

#### Implications of all the available evidence

LMICs account for more than three-quarters of global COPD cases. HICs still have higher prevalence than LMICs, which might be explained by differences in age distribution between populations. With increased life expectancy in the majority of LMICs, the prevalence of COPD in these countries is set to increase. With limited health information systems and clinical and research capacities, the likelihood of an underestimation in these settings cannot be ruled out. These findings highlight the need to prioritise actions to tackle COPD in LMICs to achieve significant reductions in the global burden of COPD.

In the past two decades, the Burden of Obstructive Lung Disease (BOLD) initiative<sup>7</sup> and Global Burden of Disease (GBD) collaborators<sup>8</sup> have pioneered efforts to collect country-specific population-based data on the prevalence of, and risk factors for, COPD, providing updates on global estimates of deaths, prevalence, and disability-adjusted life years (DALYs). Whereas the BOLD initiative is based on standardised and tested methods for conducting COPD surveys in the general population, the GBD collaborators have combined data from various sources in complex statistical models. Different COPD spirometry definitions have been adopted over the years by different groups. The ratio of forced expiratory volume in one second ( $FEV_1$ ) to forced vital capacity (FVC) of less than lower limit of normal (LLN;  $FEV_1/FVC < LLN$ ) has been adopted by the European Respiratory Society and the American Thoracic Society.<sup>9</sup> However, the Global Initiative on Obstructive Lung Disease (GOLD) recommended the use of a fixed ratio ( $FEV_1/FVC < 0.7$ ), together with exposure to noxious fumes or gases and respiratory symptoms.<sup>10</sup> The LLN criterion is increasingly used in epidemiological studies, as the fixed-ratio criterion in the GOLD definition might lead to underdiagnosis in younger people and overdiagnosis in elderly people.

Meanwhile, the challenges from varying case definitions, diagnostic criteria, and approaches to clinical

and epidemiological studies across world regions have been reported in previous studies, largely responsible for existing uncertainties on the prevalence of COPD. In a 2015 analysis of data from 27 countries, more than 80% of COPD cases identified from spirometry were undiagnosed, particularly in sub-Saharan Africa, and most prominently among men, young adults, and never smokers.<sup>11</sup> In another study, between one-third and two-thirds of physician-diagnosed COPD cases were found not to have the disease after spirometry and further clinical evaluation, with many primary care physicians likely to change a previous diagnosis of COPD on a reassessment of patients.<sup>12</sup> A high misdiagnosis-related burden of COPD limits disease understanding and presents a major challenge to the response across health-care systems.<sup>13</sup>

Given these considerations, we have updated the methods used in our previous study<sup>14</sup> by carefully considering important risk factors across world regions in our model. In that study, we only estimated global and regional prevalence and cases of COPD from studies based on spirometry and showed there were 384 million cases in 2010, translating to a global prevalence of 11.7% (8.4–15.0).<sup>14</sup> We have now estimated global, regional, and national estimates of COPD prevalence and risk factors using the two main definitions—GOLD and LLN—to

provide up-to-date global evidence to guide policy and population interventions.

## Methods

### Search strategy and selection criteria

For our systematic review, we searched MEDLINE, Embase, Global Health, and CINAHL for population-based studies published between Jan 1, 1990, and Dec 31, 2019, using various combinations of Medical Subject Headings (MeSH) terms on COPD and epidemiology (appendix p 3). We ran additional searches on Google Scholar using the same search terms and date restrictions. Reference lists of included papers and related systematic reviews on COPD were further hand-searched for additional studies that were not identified in our main search. No language or geographical restrictions were applied.

We included population-based studies that had quantified prevalence estimates of COPD in the general adult population (aged 18 years or older), defined COPD as airflow limitation not fully reversible via spirometry using post-bronchodilator FEV<sub>1</sub>/FVC ratio of less than 0.7 (GOLD-COPD) or less than lower limit of normal (LLN-COPD), and reported COPD prevalence based on two previous points. We excluded studies that were not population based, that were derived from administrative data, or that were conducted in a subpopulation that was not representative of the general population, as well as studies that did not estimate the prevalence of COPD, studies with unclear or inconsistently applied definitions of COPD, and reviews, case reports, viewpoints, or opinion-based articles.

DA and PS extracted data independently. Discrepancies in selection of studies and data extraction were resolved by consensus or following discussions with IR. We extracted the following data from all included studies using a purpose-built data collection form: first author, year of publication, date of investigation, investigation site, country and region of investigation site (African region, region of the Americas, South-East Asian region, European region, Eastern Mediterranean region, and Western Pacific region, as designated by WHO; and high-income countries [HICs] and low-income and middle-income countries [LMICs], as designated by the World Bank), setting of investigation site (urban or rural), study design, definition and diagnostic method of COPD, sample size, mean age of participants, proportion of female participants, and number of COPD cases. When available, stratified prevalence data were abstracted by age group, sex, setting, and geographical location. In case of censored age range, the upper or lower limit of age range was imputed using the same width as reported in other age groups in the same article. Finally, we extracted risk factors, their definitions, and the corresponding odds ratios (ORs) from articles that explored COPD risks using multivariable logistic regressions.

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,<sup>15</sup> and the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER).<sup>16</sup> No ethics approval was sought for this study, as all data were from publicly available publications.

### Data analysis

We estimated the prevalence of COPD defined by GOLD and LLN criteria at global, regional, and national levels, and reported them separately.

For modelling of the global prevalence of GOLD-COPD and LLN-COPD, a hierarchical dataset was constructed (ie, multiple datapoints from the same articles). We first used a multilevel multivariable mixed-effects meta-regression approach to assess the age-adjusted effects of cluster-level variables—namely, proportion of women, setting (rural and urban), year of investigation, and WHO region. As a rule, at least 20 datapoints should be available for each variable in each model.<sup>17</sup>

We controlled for clustering of multiple datapoints from the same investigation and from the same country by adding study identification and country identification as random effects. This modelling was done separately for HICs and LMICs. Prevalence was calculated as  $p = (\text{COPD cases}) / (\text{study sample})$ , where  $p$  is prevalence. Due to varying estimates and outliers from different studies and their impact on the distribution of the overall dataset, prevalence was stabilised with the logit link as follows:

$$\text{logit}(p) = \ln\left(\frac{p}{1-p}\right) = \ln(\text{odds}) = a + \beta_1 * x_1 + \beta_2 * x_2 + \dots + u_i$$

Based on the result of age-adjusted models and the fact that age, sex, and year of investigation were our main variables of interest, we constructed the following model to estimate the age-specific, sex-specific, and year-specific prevalence of GOLD-COPD:

$$\begin{aligned} \text{logit}(\text{GOLD-COPD}) = & a + \beta_1 * \text{Age} \\ & + \beta_2 * \text{proportion of women} \\ & + \beta_3 * \text{investigation year} + u_i \end{aligned}$$

Due to limited data points covering the whole timespan (1990–2019), we constructed only the age-specific and sex-specific prevalence of LLN-COPD:

$$\begin{aligned} \text{logit}(\text{LLN-COPD}) = & a + \beta_1 * \text{Age} \\ & + \beta_2 * \text{proportion of women} + u_i \end{aligned}$$

To estimate the number of people with GOLD-COPD and LLN-COPD worldwide in 2019, the number of people affected by COPD in HICs and LMICs was generated by multiplying the estimated prevalence (age-specific, sex-specific, and year-specific prevalence of GOLD-COPD,

See Online for appendix

and age-specific and sex-specific prevalence of LLN-COPD) by the corresponding world population data in 2019, obtained from the UN Population Division.<sup>18</sup> To provide robust estimates, we restricted prevalence and

numbers of cases to the age range of 30–79 years, where most informative datapoints were available. The global number of COPD cases was then calculated by adding cases in HICs and LMICs.

We also estimated the regional number of people with COPD in 2019. Due to data availability, we were able to estimate regional COPD cases using the GOLD criteria only. To address geography and income simultaneously, the world was classified into ten different World Bank–WHO (WB–WHO) regions: HICs in the region of the Americas, European region, Eastern Mediterranean region, and Western Pacific region, and LMICs in the African region, region of the Americas, South-East Asia region, European region, Eastern Mediterranean region, and Western Pacific region (appendix p 10). Using a risk factor-based model, the global number of people with GOLD-COPD in 2019 was distributed into the ten WB–WHO regions. Four major risk factors—namely, current smoking, underweight, use of biomass fuel, and rural residence—were included in the risk factor-based model (appendix pp 4–5). Similarly, numbers of GOLD-COPD cases were estimated for the 201 countries and territories in 2019 using prevalence of the four risk factors and their meta-ORs.

A sensitivity analysis of global GOLD-COPD prevalence estimates based on studies using post-bronchodilatory spirometry was conducted, because not all studies provided this measure, which normally excludes the possibility of a reversible airflow limitation (COPD is primarily irreversible).

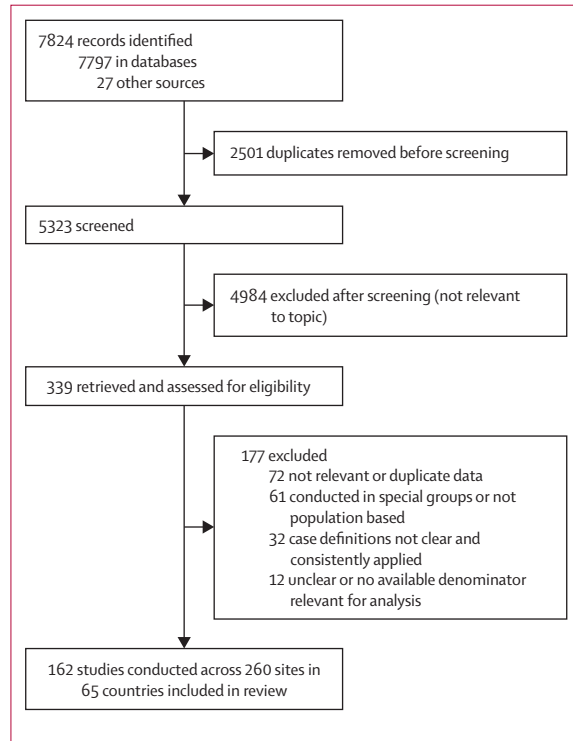


Figure 1: Study selection

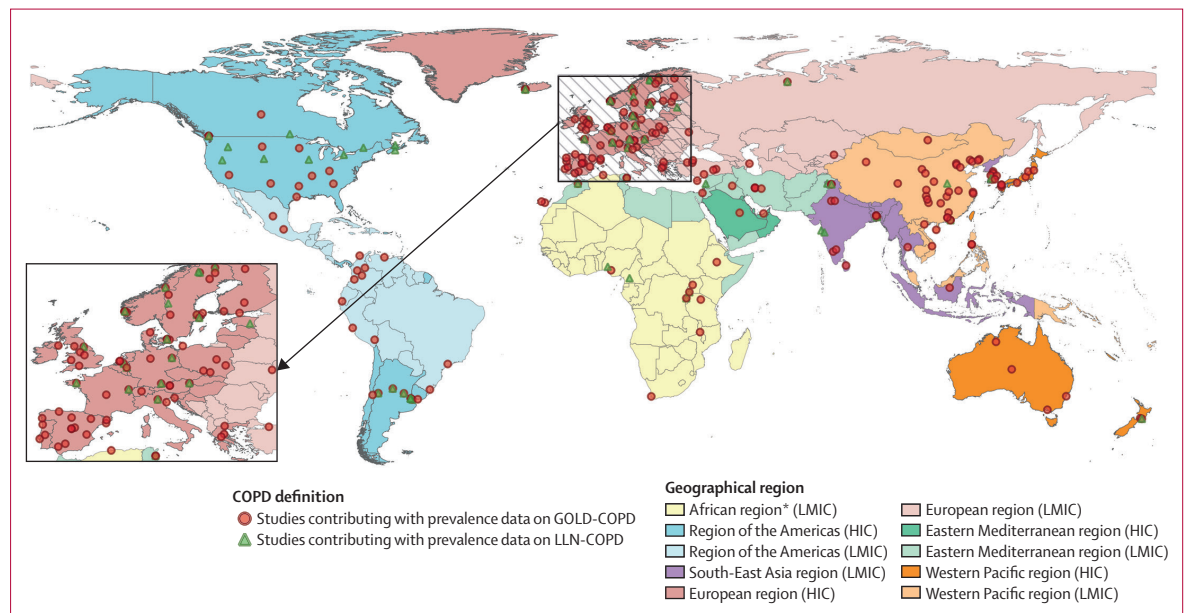


Figure 2: Contributing data sources across world regions

COPD=chronic obstructive pulmonary disease. GOLD=Global Initiative on Obstructive Lung Disease. HICs=high-income countries. LLN=lower limit of normal. LMICs=low-income and middle-income countries. \*Seychelles is a high-income country according to the latest World Bank income classification, but classified into the low-income and middle-income African region because of its relatively small population size. GOLD-COPD is defined as  $FEV_1/FVC < 0.7$ , whereas LLN-COPD is defined as  $FEV_1/FVC < LLN$ .

	Prevalence of COPD in men (95% CI)			Prevalence of COPD in women (95% CI)			Overall prevalence of COPD (95% CI)		
	HICs	LMICs	Worldwide	HICs	LMICs	Worldwide	HICs	LMICs	Worldwide
<b>GOLD-COPD</b>									
30–34 years	4.0% (3.4–4.7)	5.7% (4.3–7.5)	5.4% (4.2–7.1)	2.0% (1.7–2.4)	2.1% (1.6–2.8)	2.1% (1.6–2.8)	3.0% (2.6–3.6)	4.0% (3.0–5.2)	3.8% (2.9–5.0)
35–39 years	5.2% (4.4–6.1)	7.3% (5.6–9.6)	7.0% (5.4–9.0)	2.6% (2.2–3.1)	2.8% (2.1–3.7)	2.8% (2.1–3.6)	3.9% (3.3–4.7)	5.1% (3.9–6.7)	4.9% (3.8–6.3)
40–44 years	6.7% (5.7–7.9)	9.4% (7.2–12.2)	8.9% (6.9–11.4)	3.4% (2.9–4.1)	3.6% (2.7–4.8)	3.6% (2.8–4.7)	5.1% (4.3–6.0)	6.5% (5.0–8.5)	6.3% (4.9–8.1)
45–49 years	8.6% (7.3–10.1)	12.0% (9.2–15.4)	11.4% (8.9–14.4)	4.5% (3.8–5.3)	4.7% (3.6–6.2)	4.7% (3.6–6.0)	6.6% (5.6–7.7)	8.3% (6.4–10.8)	8.0% (6.3–10.2)
50–54 years	11.0% (9.4–12.8)	15.1% (11.8–19.2)	14.3% (11.3–18.0)	5.8% (4.9–6.8)	6.1% (4.6–7.9)	6.0% (4.7–7.7)	8.4% (7.2–9.8)	10.6% (8.2–13.6)	10.2% (8.0–12.8)
55–59 years	14.0% (12.1–16.2)	18.9% (14.9–23.8)	17.9% (14.3–22.1)	7.5% (6.4–8.8)	7.8% (6.0–10.2)	7.7% (6.0–9.9)	10.7% (9.2–12.5)	13.3% (10.4–16.9)	12.8% (10.1–15.9)
60–64 years	17.6% (15.3–20.2)	23.4% (18.7–29.0)	22.0% (17.8–26.9)	9.6% (8.2–11.2)	10.0% (7.7–12.9)	9.9% (7.8–12.5)	13.5% (11.7–15.6)	16.5% (13.0–20.8)	15.8% (12.7–19.5)
65–69 years	21.9% (19.1–25.0)	28.6% (23.1–34.9)	27.0% (22.1–32.4)	12.2% (10.5–14.2)	12.7% (9.8–16.3)	12.6% (10.0–15.7)	16.9% (14.6–19.4)	20.3% (16.2–25.2)	19.5% (15.8–23.7)
70–74 years	26.9% (23.7–30.5)	34.5% (28.2–41.3)	32.1% (26.8–37.9)	15.5% (13.4–17.9)	16.0% (12.5–20.3)	15.8% (12.7–19.6)	20.8% (18.2–23.7)	24.5% (19.7–30.0)	23.4% (19.2–28.0)
75–79 years	32.6% (28.9–36.6)	40.8% (34.0–48.0)	38.0% (32.2–44.0)	19.4% (16.8–22.3)	20.0% (15.7–25.0)	19.8% (16.1–24.1)	25.3% (22.2–28.6)	29.2% (23.8–35.2)	27.8% (23.2–32.9)
Overall (30–79 years)	12.8% (11.1–14.7)	14.4% (11.3–18.0)	14.1% (11.3–17.4)	7.4% (6.4–8.7)	6.2% (4.8–8.1)	6.5% (5.1–8.2)	10.1% (8.7–11.7)	10.3% (8.0–13.0)	10.3% (8.2–12.8)
<b>LLN-COPD</b>									
30–34 years	7.8% (6.4–9.5)	3.0% (2.1–4.3)	3.7% (2.7–5.0)	5.8% (4.7–7.1)	3.0% (2.1–4.3)	3.4% (2.5–4.7)	6.9% (5.6–8.3)	3.0% (2.1–4.3)	3.6% (2.6–4.9)
35–39 years	8.4% (6.9–10.2)	3.8% (2.7–5.3)	4.5% (3.4–6.1)	6.2% (5.1–7.6)	3.8% (2.7–5.3)	4.2% (3.1–5.7)	7.4% (6.1–8.9)	3.8% (2.7–5.3)	4.4% (3.2–5.9)
40–44 years	9.1% (7.5–11.0)	4.7% (3.4–6.5)	5.5% (4.1–7.3)	6.7% (5.5–8.1)	4.8% (3.4–6.5)	5.1% (3.8–6.8)	7.9% (6.5–9.6)	4.7% (3.4–6.5)	5.3% (4.0–7.1)
45–49 years	9.8% (8.1–11.7)	5.9% (4.3–8.0)	6.6% (5.0–8.7)	7.2% (6.0–8.7)	5.9% (4.3–8.1)	6.2% (4.6–8.2)	8.5% (7.0–10.3)	5.9% (4.3–8.1)	6.4% (4.8–8.5)
50–54 years	10.5% (8.7–12.6)	7.3% (5.4–9.9)	8.0% (6.0–10.4)	7.8% (6.4–9.4)	7.4% (5.4–10.0)	7.5% (5.6–9.9)	9.1% (7.6–11.0)	7.4% (5.4–10.0)	7.7% (5.8–10.2)
55–59 years	11.2% (9.3–13.5)	9.1% (6.7–12.3)	9.6% (7.3–12.5)	8.4% (6.9–10.1)	9.2% (6.8–12.3)	9.0% (6.8–11.9)	9.8% (8.1–11.8)	9.2% (6.7–12.3)	9.3% (7.0–12.2)
60–64 years	12.1% (10.0–14.4)	11.3% (8.3–15.1)	11.5% (8.7–15.0)	9.0% (7.4–10.8)	11.3% (8.4–15.2)	10.8% (8.1–14.2)	10.5% (8.7–12.6)	11.3% (8.3–15.2)	11.1% (8.4–14.6)
65–69 years	12.9% (10.8–15.5)	13.8% (10.2–18.6)	13.6% (10.3–17.8)	9.7% (8.0–11.6)	13.9% (10.3–18.7)	12.9% (9.7–16.9)	11.2% (9.3–13.5)	13.9% (10.2–18.6)	13.2% (10.0–17.3)
70–74 years	13.9% (11.5–16.6)	16.9% (12.4–22.6)	15.9% (12.1–20.7)	10.4% (8.6–12.5)	17.0% (12.5–22.8)	15.0% (11.3–19.6)	12.0% (10.0–14.4)	17.0% (12.4–22.7)	15.4% (11.7–20.1)
75–79 years	14.8% (12.4–17.7)	20.5% (14.9–27.4)	18.5% (14.0–24.0)	11.2% (9.2–13.4)	20.6% (15.0–27.6)	17.3% (13.0–22.7)	12.8% (10.6–15.3)	20.5% (15.0–27.5)	17.9% (13.5–23.3)
Overall (30–79 years)	10.6% (8.8–12.7)	7.1% (5.2–9.6)	7.8% (5.9–10.2)	8.0% (6.6–9.7)	7.4% (5.4–10.0)	7.5% (5.6–9.9)	9.3% (7.7–11.2)	7.2% (5.3–9.8)	7.6% (5.8–10.1)

COPD=chronic obstructive pulmonary disease. GOLD= Global Initiative on Obstructive Lung Disease. HICs=high-income countries. LLN=lower limit of normal. LMICs=low-income and middle-income countries.

**Table 1: Estimated prevalence of COPD in people aged 30–79 years, by age group, world bank region, and sex in 2019**

A subset of included articles additionally investigated potential risk factors for COPD using multivariable analysis. We did a random-effects (DerSimonian and Laird method) meta-analysis of ORs to assess the effects of major risk factors for COPD, including age, sex, smoking status, and body-mass index (BMI).<sup>19</sup> We included only risk factors that shared similar definitions

and had been investigated in at least three separate studies. These were categorised into nine sub-groups: sex, age, smoking, exposure to smoking, biomass, or dust, BMI, past medical history, socioeconomic status, education, and residence. Due to data availability, this was done only for GOLD-COPD and was done separately for HICs and LMICs.

	Men living with COPD, millions (95% CI)			Women living with COPD, millions (95% CI)			Overall number of people with COPD, millions (95% CI)		
	HICs	LMICs	Worldwide	HICs	LMICs	Worldwide	HICs	LMICs	Worldwide
<b>GOLD-COPD</b>									
30–34 years	1.8 (1.5–2.1)	14.9 (11.3–19.5)	16.7 (12.8–21.6)	0.8 (0.7–1.0)	5.4 (4.1–7.2)	6.2 (4.8–8.2)	2.6 (2.2–3.1)	20.3 (15.4–26.7)	22.9 (17.6–29.8)
35–39 years	2.3 (2.0–2.7)	16.8 (12.8–21.9)	19.1 (14.8–24.6)	1.1 (0.9–1.3)	6.2 (4.7–8.2)	7.3 (5.6–9.6)	3.4 (2.9–4.0)	23.0 (17.5–30.1)	26.4 (20.4–34.2)
40–44 years	2.9 (2.5–3.4)	19.1 (14.6–24.7)	22.0 (17.1–28.1)	1.4 (1.2–1.7)	7.2 (5.5–9.6)	8.7 (6.7–11.3)	4.4 (3.7–5.1)	26.3 (20.1–34.3)	30.7 (23.8–39.4)
45–49 years	3.8 (3.2–4.4)	23.3 (18.0–29.9)	27.1 (21.2–34.4)	1.9 (1.6–2.2)	9.1 (6.9–11.9)	11.0 (8.5–14.2)	5.7 (4.8–6.6)	32.4 (24.9–41.9)	38.1 (29.7–48.5)
50–54 years	4.7 (4.0–5.5)	26.9 (20.9–34.1)	31.6 (25.0–39.6)	2.4 (2.1–2.8)	10.9 (8.3–14.2)	13.3 (10.3–17.1)	7.1 (6.1–8.3)	37.7 (29.2–48.4)	44.8 (35.3–56.7)
55–59 years	5.8 (5.0–6.7)	28.2 (22.2–35.4)	34.0 (27.2–42.1)	3.1 (2.6–3.6)	11.9 (9.1–15.4)	15.0 (11.7–19.1)	8.9 (7.6–10.3)	40.0 (31.2–50.8)	48.9 (38.9–61.1)
60–64 years	6.5 (5.7–7.5)	27.7 (22.1–34.4)	34.3 (27.7–41.9)	3.7 (3.2–4.3)	12.4 (9.5–16.1)	16.1 (12.7–20.4)	10.3 (8.8–11.8)	40.2 (31.6–50.4)	50.4 (40.5–62.3)
65–69 years	7.0 (6.1–8.0)	27.4 (22.1–33.4)	34.4 (28.2–41.4)	4.3 (3.7–5.0)	13.2 (10.2–17.0)	17.5 (13.9–21.9)	11.3 (9.8–13.0)	40.6 (32.3–50.3)	51.9 (42.1–63.3)
70–74 years	7.3 (6.4–8.2)	20.4 (16.7–24.4)	27.7 (23.1–32.7)	4.8 (4.1–5.6)	11.1 (8.7–14.1)	15.9 (12.8–19.6)	12.1 (10.6–13.8)	31.5 (25.4–38.5)	43.6 (35.9–52.3)
75–79 years	6.1 (5.4–6.9)	14.4 (12.0–17.0)	20.6 (17.5–23.8)	4.6 (4.0–5.2)	8.9 (7.0–11.2)	13.5 (11.0–16.5)	10.7 (9.4–12.1)	23.4 (19.1–28.2)	34.1 (28.5–40.3)
Overall (30–79 years)	48.2 (41.8–55.5)	219.1 (172.8–274.7)	267.4 (214.6–330.2)	28.2 (24.1–32.8)	96.4 (73.9–124.9)	124.6 (98.0–157.7)	76.4 (65.9–88.3)	315.5 (246.7–399.6)	391.9 (312.6–487.9)
<b>LLN-COPD</b>									
30–34 years	3.5 (2.9–4.3)	7.8 (5.5–11.1)	11.3 (8.4–15.4)	2.4 (1.9–2.9)	7.6 (5.3–10.8)	10.0 (7.3–13.7)	5.9 (4.8–7.2)	15.4 (10.8–21.9)	21.3 (15.7–29.1)
35–39 years	3.8 (3.1–4.6)	8.6 (6.1–12.0)	12.4 (9.2–16.6)	2.6 (2.1–3.2)	8.5 (6.0–11.8)	11.1 (8.2–15.0)	6.4 (5.2–7.7)	17.1 (12.2–23.8)	23.5 (17.4–31.6)
40–44 years	4.0 (3.3–4.8)	9.6 (6.9–13.2)	13.5 (10.2–18.0)	2.8 (2.3–3.4)	9.5 (6.9–13.1)	12.3 (9.2–16.5)	6.8 (5.6–8.2)	19.1 (13.8–26.2)	25.9 (19.4–34.5)
45–49 years	4.3 (3.5–5.1)	11.5 (8.4–15.6)	15.8 (11.9–20.8)	3.1 (2.5–3.7)	11.5 (8.4–15.6)	14.5 (10.9–19.3)	7.3 (6.1–8.8)	23.0 (16.8–31.3)	30.3 (22.8–40.1)
50–54 years	4.5 (3.7–5.4)	13.0 (9.6–17.6)	17.5 (13.3–23.0)	3.3 (2.7–3.9)	13.2 (9.7–17.9)	16.5 (12.4–21.8)	7.7 (6.4–9.3)	26.3 (19.3–35.5)	34.0 (25.7–44.8)
55–59 years	4.7 (3.9–5.6)	13.6 (10.0–18.3)	18.2 (13.9–23.8)	3.5 (2.9–4.2)	14.0 (10.3–18.8)	17.4 (13.2–23.0)	8.1 (6.7–9.8)	27.5 (20.3–37.0)	35.7 (27.0–46.8)
60–64 years	4.5 (3.7–5.4)	13.3 (9.8–17.9)	17.8 (13.6–23.3)	3.5 (2.9–4.2)	14.1 (10.4–19)	17.6 (13.3–23.2)	8.0 (6.6–9.6)	27.5 (20.2–36.8)	35.4 (26.8–46.4)
65–69 years	4.1 (3.4–4.9)	13.2 (9.7–17.8)	17.4 (13.2–22.7)	3.4 (2.8–4.1)	14.5 (10.7–19.5)	17.9 (13.5–23.5)	7.5 (6.2–9.0)	27.8 (20.4–37.2)	35.3 (26.7–46.2)
70–74 years	3.7 (3.1–4.5)	10.0 (7.3–13.4)	13.8 (10.5–17.9)	3.2 (2.7–3.9)	11.8 (8.6–15.8)	15.0 (11.3–19.7)	7.0 (5.8–8.4)	21.8 (16.0–29.2)	28.8 (21.8–37.6)
75–79 years	2.8 (2.3–3.3)	7.2 (5.3–9.7)	10.0 (7.6–13.0)	2.6 (2.2–3.2)	9.2 (6.7–12.3)	11.8 (8.9–15.5)	5.4 (4.5–6.5)	16.5 (12.0–22.0)	21.9 (16.5–28.5)
Overall (30–79 years)	39.8 (33.0–47.8)	107.9 (78.7–146.6)	147.8 (111.7–194.4)	30.3 (25.0–36.6)	114.0 (83.1–154.6)	144.3 (108.1–191.2)	70.1 (58.0–84.5)	221.9 (161.8–301.2)	292.0 (219.8–385.6)

COPD=chronic obstructive pulmonary disease. GOLD= Global Initiative on Obstructive Lung Disease. HICs=high-income countries. LLN=lower limit of normal. LMICs=low-income and middle-income countries. GOLD-COPD is defined as FEV1/FVC<0.7, whereas LLN-COPD is defined as FEV1/FVC<LLN.

**Table 2: Estimated number of COPD cases in people aged 30–79 years, by age group, World Bank region, and sex in 2019**

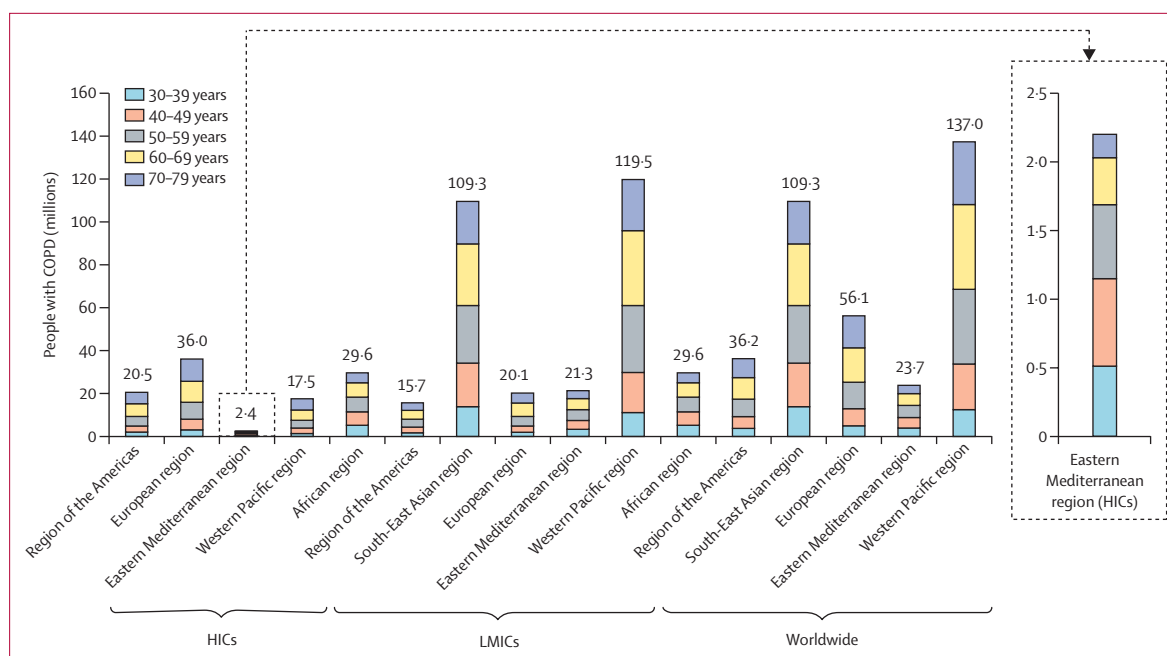
All analyses were conducted with Stata version 14.0 and R version 3.3.0.

**Role of the funding source**

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

**Results**

Our literature searches identified 7824 records published between Jan 1, 1990, and Dec 31, 2019, and 5323 records were screened after removal of duplicates. Following screening for eligibility, 162 articles (of studies covering 260 sites in 65 countries) that reported the prevalence of COPD, risk factors for COPD, or both, in the general



**Figure 3: Number of people with GOLD-COPD by region and age groups in 2019**

COPD=chronic obstructive pulmonary disease. GOLD=Global Initiative on Obstructive Lung Disease. HICs=high-income countries. LMICs=low-income and middle-income countries. GOLD-COPD is defined as  $FEV_1/FVC < 0.7$ .

population were included (figure 1). The geographical locations of the included studies are shown in figure 2, and detailed characteristics of included articles and study sites are provided in the appendix (pp 11–23).

The estimated prevalence of GOLD-COPD generally increased with advancing age and was consistently higher in men than in women. These trends were also observed in our sensitivity analysis based on data using post-bronchodilatory spirometry (appendix pp 6–7).

For GOLD-COPD, we found that prevalence in HICs significantly increased with advancing age, was lower in women, in urban settings, and in the Eastern Mediterranean region than the Western Pacific region, and significantly decreased over time (appendix p 8). In LMICs, the prevalence of GOLD-COPD also increased with advancing age and was lower in women and in urban settings, but was higher in the African region and the Eastern Mediterranean region than in the Western Pacific region (appendix p 8).

The global prevalence of GOLD-COPD in people aged 30–79 years was 10.3% (95% CI 8.2–12.8) in 2019 (table 1). The prevalence was consistently higher in LMICs than in HICs over a broad age range (30–79 years). After considering the demographic characteristics (age, sex, and population distribution) in 2019, the overall prevalence of GOLD-COPD was slightly higher in LMICs (10.3% [8.0–13.0]) than in HICs (10.1% [8.7–11.7]). Worldwide, the prevalence of GOLD-COPD in men aged 30–79 years was more than double that in women in the same age range (14.1% [11.3–17.4] vs 6.5% [5.1–8.2]) in 2019.

Across age and sex groups, the prevalence of LLN-COPD was lower than that of GOLD-COPD (table 1, appendix pp 27–28). The estimated prevalence of LLN-COPD also increased with advancing age, with the trend more pronounced in LMICs. For LLN-COPD, the prevalence in HICs was also lower in women and in rural settings, and decreased over time. In LMICs, the prevalence of LLN-COPD was similar between sexes and significantly increased over time (appendix pp 8–9).

The prevalence of LLN-COPD in people aged 30–79 years was 7.6% (95% CI 5.8–10.1) worldwide in 2019, and was higher in HICs than in LMICs (9.3% [7.7–11.2] vs 7.2% [5.3–9.8]). Overall, no substantial difference between sexes was found, with the prevalence of LLN-COPD being 7.8% (5.9–10.2) in men and 7.5% (5.6–9.9) in women.

Using the GOLD definition, we estimated that 391.9 million (95% CI 312.6–487.9) people aged 30–79 years had COPD worldwide in 2019, with most (315.5 million [246.7–399.6]; 80.5%) living in LMICs. 267.4 million (214.6–330.2; 68.2%) GOLD-COPD cases were in men. With the LLN definition, COPD accounted for 292.0 million (219.8–385.6) people aged 30–79 years in 2019, with most (221.9 million [161.8–301.2]; 76.0%) living in LMICs. LLN-COPD cases were almost evenly distributed between sexes (147.8 million [111.7–194.4] men vs 144.3 million [108.1–191.2] women; table 2).

Due to limited data, we estimated the number of COPD cases (aged 30–79 years) in each WB-WHO region using only the GOLD definition (figure 3, appendix pp 25–26).



	Worldwide	HICs	LMICs
<b>Sex</b>			
Male	2.1 (1.8–2.3)	2.0 (1.7–2.3)	2.2 (1.9–2.5)
Female	0.8 (0.6–1.1)	0.8 (0.6–1.1)	0.7 (0.3–1.4)
<b>Age</b>			
Per 10-year increase in age if <50 years	1.5 (1.3–1.5)	1.5 (1.4–1.6)	1.4 (1.3–1.5)
50–59 years	2.1 (1.8–2.6)	2.0 (1.8–2.3)	2.3 (1.6–3.1)
≥60 years	4.2 (3.1–5.6)	4.7 (3.8–5.8)	3.3 (2.1–5.1)
<b>Smoking status</b>			
Current smoker*	3.2 (2.5–4.0)	3.2 (2.4–4.5)	3.1 (2.2–4.2)
Former smoker	2.1 (1.8–2.4)	1.8 (1.5–2.1)	2.5 (1.7–2.5)
Ever smoker	2.3 (2.0–2.5)	2.1 (1.8–2.4)	2.7 (2.2–3.3)
Per 10-unit increase in pack-years if <20	1.3 (1.2–1.3)	1.2 (1.2–1.3)	1.6 (1.3–2.1)
≥20 pack-years	3.2 (2.1–4.7)	3.4 (2.0–5.9)	2.3 (1.7–3.0)
<b>Exposure</b>			
Second-hand tobacco smoke	1.2 (1.0–1.4)	1.1 (0.8–1.6)	1.2 (0.9–1.5)
Biomass exposure*	1.4 (1.2–1.7)	1.4 (1.2–1.7)	1.5 (1.2–1.8)
Occupational exposure to dust or smoke	1.4 (1.3–1.6)	1.4 (1.2–1.6)	1.5 (1.2–1.8)
<b>BMI</b>			
BMI <18.5 kg/m <sup>2</sup> *	2.2 (1.7–2.7)	2.3 (1.5–3.6)	2.2 (1.7–2.8)
BMI ≥25 kg/m <sup>2</sup>	0.9 (0.8–0.9)	0.9 (0.8–1.0)	0.8 (0.7–1.0)
<b>Past medical history or comorbidity</b>			
Child hospital admission for severe respiratory illness	1.9 (1.5–2.4)	1.7 (1.4–2.1)	1.9 (1.4–2.8)
Family history of obstructive airway disease	1.6 (1.4–1.9)	1.5 (1.1–2.0)	1.7 (1.5–2.0)
Asthma	2.6 (1.6–4.1)	2.5 (1.4–4.3)	3.6 (0.5–24.1)
Tuberculosis	2.8 (1.9–4.0)	3.7 (1.9–7.2)	2.6 (1.7–3.9)
HIV	1.4 (0.2–10.1)	..	1.4 (0.2–10.1)
<b>Socioeconomic status</b>			
Upper class	1.1 (0.8–1.5)	1.2 (0.8–1.7)	1.0 (0.5–2.0)
Middle class	1.2 (1.0–1.4)	1.2 (1.0–1.5)	1.0 (0.8–1.4)
Lower class	1.8 (1.4–2.3)	1.7 (1.4–2.1)	1.8 (1.0–3.2)
<b>Education</b>			
College or higher	0.8 (0.7–0.9)	0.9 (0.7–1.1)	0.8 (0.4–1.4)
Middle or high school	1.1 (0.9–1.2)	1.1 (1.0–1.3)	1.0 (0.8–3.2)
Primary or no education	1.5 (1.0–2.1)	1.6 (1.2–2.1)	1.4 (1.0–2.1)
<b>Residence</b>			
Urban	1.2 (1.0–1.5)	1.3 (1.0–1.7)	1.1 (0.6–2.0)
Rural	1.4 (1.3–1.6)	1.1 (0.8–1.5)	1.5 (1.4–1.7)

Data are OR (95% CI). ORs for binary variable risk factors are compared with those without the risk factor, except for current-smokers, ex-smokers, and ever-smokers (vs non-smokers); BMI <18.5 kg/m<sup>2</sup> and BMI ≥25 kg/m<sup>2</sup> (vs BMI 20–24 kg/m<sup>2</sup>); college or higher and middle-high school (vs no education), and primary or no education (vs high school). HICs=high-income countries. LMICs=low-income and middle-income countries. OR=odds ratio. \*Pooled ORs included in the regional-level and national-level estimates of GOLD-COPD prevalence.

**Table 3: Pooled odds ratios of COPD risk factors by World Bank income category**

In 2019, the Western Pacific region had the largest share of global GOLD-COPD cases (137.0 million [95% CI 109.0–170.8]), whereas the Eastern Mediterranean region had the least (23.7 million [18.7–30.0]). The age group that contributed the most GOLD-COPD cases was 60–69 years in region of the Americas, South-East Asian region, European region, and Western Pacific region, and 50–59 years in the African and Eastern Mediterranean regions (figure 3). The overall prevalence of GOLD-COPD in people aged 30–79 years was highest in Western Pacific region (11.7% [9.3–14.6]) and lowest in region of Americas (6.8% [5.6–8.2]; appendix pp 27–28). The national prevalence of COPD and affected cases were estimated for 201 countries and territories (appendix pp 64–68). The ten countries with the most COPD cases (China, India, Indonesia, USA, Bangladesh, Japan, Pakistan, Russia, Vietnam, and Germany) accounted for 255.4 million (65.2%) of global COPD cases in 2019.

We extracted 28 individual risk factors that were investigated in at least three studies and conducted a random-effects meta-analysis. From the pooled ORs, male sex, smoking (current smoker, former smoker, ever smoker, 10-unit increase in pack years, and >20 pack years), advanced age (per 10-year increase, 50–59 years, >60 years), BMI of less than 18.5 kg/m<sup>2</sup>, childhood hospital admission for severe respiratory disease, family history of obstructive lung disease, history of tuberculosis, biomass exposure, and occupational exposure to dust or smoke were all substantial risk factors for COPD, with significant effect sizes (meta-estimates) globally, and across HICs and LMICs (table 3).

### Discussion

In this systematic review and modelling study, including 162 population based studies across 260 sites in 65 countries, we estimated that the global prevalence of COPD among people aged 30–79 years in 2019 was 10.3% (95% CI 8.2–12.8) using the GOLD case definition, which translates to 391.9 million people (95% CI 312.6–487.9), and 7.6% (5.8–10.1) using the LLN definition, which translates to 292.0 million people (219.8–385.6). Most cases were in LMICs, although prevalence was slightly higher in HICs. Male sex, smoking, body-mass index of less than 18.5 kg/m<sup>2</sup>, biomass exposure, and occupational exposure to dust or smoke were all substantial risk factors for COPD.

This study is the first, to our knowledge, to report the prevalence and number of cases of COPD based on the two widely used case definitions at global, regional, and national levels. We extracted multiple datapoints from all included articles. The resulting hierarchical dataset offers improvements on previous approaches, many of which were based on models of single estimates from individual studies (ie, estimates from mean or median age of the study sample).

Although previous estimates of COPD prevalence have been limited by concerns about representativeness across

different regions, some previous findings are similar to those of this study. One common finding across studies is that the prevalence of COPD is high in many LMICs, reflecting the prevalence of leading risk factors such as tobacco smoking, exposure to biomass smoke, and air pollution.<sup>3,4,6</sup> Our age-standardised estimate of prevalence of LLN-COPD in HICs is higher than that in LMICs; however, in terms of the absolute number of people affected, we estimated that more than 75% of people with COPD aged 30–79 years resided in LMICs, which is probably a reflection of the larger younger populations in these settings. With further population growth and ageing in LMICs, both the absolute number of COPD cases and prevalence are likely to continue to increase.

Some prevalence estimates in previous studies are within the uncertainty intervals reported in this study. For instance, in 2006, from 67 articles conducted across 28 countries, the pooled prevalence of COPD based on spirometry was 8·9%.<sup>20</sup> In a recent review of 60 articles between 2004 and 2015, the prevalence of COPD based on the GOLD definition was estimated to be 12·2% in 2015. Although this prevalence estimate was not age-standardised and the scarcity of data from a wide range of countries meant that regional estimates might not have been representative, it is still within the upper bound of our global estimate.<sup>21</sup> In our previous review based on 123 studies using spirometry-defined estimates, we reported a COPD prevalence of 11·7% worldwide in 2010.<sup>14</sup> In a recent study using geographical information systems technology, the authors noted a probable increase in the global prevalence of GOLD-COPD, with a prevalence of 13·1% (95% CI 10·5–15·9) estimated in 2019.<sup>22</sup> However, the Global Burden of Disease (GBD) chronic respiratory diseases collaborators reported a rather low global prevalence of COPD at 3·9% (95% CI 3·5–4·3), representing 174·5 million cases (95% CI 160·2–180·9) in 2015.<sup>14</sup> Although this estimate was based on people aged 15 years or older, it still appears to be inconsistent with previous global estimates. For example, using a similar approach, the GBD collaborators estimated that there were 251·6 million (242·0–261·1) people with COPD in 2016,<sup>23,24</sup> and 299·4 million (269·0–330·0) in 2017,<sup>25</sup> which are similar estimates to those in our current study. In the GBD 2019 study, estimated global COPD cases were further reduced to 212·3 million (200·4–225·1).<sup>26</sup> Although a major strength of the GBD approach is the combination of various data sources and inclusion of important explanatory variables—particularly sociodemographic index, income per capita, and total fertility rate—it is not clear how different case definitions were accounted for, which could perhaps explain these inconsistencies.

Regional variation in COPD research practices exists, particularly in terms of differences in survey protocols, case ascertainment, analyses, and research outputs. Although these are important considerations in interpreting regional and national estimates, some specific population characteristics across different settings might

further explain regional variation. In this study we estimated the highest prevalence of COPD in people aged 30–79 years to be in the Western Pacific and the South-East Asian regions. This finding might have been driven by the rapid demographic ageing in countries such as China and India. The Western Pacific region and the South-East Asian region also seem to be driving the overall global increase in COPD prevalence. For example, even with reported high levels of underdiagnosis and underuse of spirometry in these settings,<sup>11,12</sup> the highest absolute numbers for COPD cases in 2019 were estimated in the Western Pacific region and the South-East Asian region at 137·0 million and 109·3 million (appendix pp 25–26), respectively. This finding might have been driven by the large populations in these settings. However, the combined effects of smoking and non-smoking risks (particularly underweight and biomass exposure) cannot be ruled out.<sup>27</sup> In China alone, the Global Health Epidemiology Research Group (GHERG) estimated that, between 1990 and 2010, the number of COPD cases increased from 31 million to 52 million.<sup>28</sup> In 2018, the China Pulmonary Health (CPH) study estimated about 99·9 million COPD cases in China,<sup>29</sup> which is similar to the 105·8 million (95% CI 83·1–133·2; appendix p 68) estimated in this study. The Indian state-level collaborators estimated that the total number of COPD cases in India increased from 28 million in 1990 to 55 million in 2016,<sup>30</sup> which is also within the 95% CI of our estimate (68·7 million [53·7–87·0]).

Differences in risks of COPD are also observed across population groups. The most important factor underlying variation in COPD prevalence is geographical difference in patterns of tobacco consumption.<sup>31</sup> Even with improved population preventive measures, the high prevalence of ever smokers in HICs has resulted in a high burden of COPD in these settings. By contrast, in LMICs, numbers of active smokers are increasing gradually and effects on respiratory health are beginning to emerge. Across several LMICs, air pollution, occupational exposure, asthma and allergies, severe childhood respiratory infections, and tuberculosis are significant risks. Such risks do not receive sufficient attention from governments, health systems, media, and patients and their families, partly contributing to an increasing burden of COPD in LMICs.<sup>32</sup> This pattern has been reported by the GBD collaborators, with smoking accounting for about 70% of COPD burden in HICs and environmental exposures accounting for about 60% of COPD burden in LMICs.<sup>4</sup>

A significantly higher prevalence of COPD among men than women has long been established, and this was confirmed in our study. However, when income variations were considered, the prevalence of LLN-COPD among women in HICs remained lower than that in men, whereas the prevalence in LMICs was marginally higher among women (7·4%) than among men (7·1%). Higher prevalence estimates among men could arise if affected

women are less likely to participate in community surveys than affected men. Alternative explanations (when using the GOLD-COPD definition) are historic patterns of smoking and occupational exposures in men. Nevertheless, for LLN-COPD, the sex differences were not pronounced.<sup>11</sup>

Although we could not directly account for them in this study, air pollution and biomass smoke are particularly big risk factors for COPD, especially in LMICs.<sup>33</sup> Several cities are experiencing substantial growth in industrial networks and, due to poor geographical and town planning, many are located close to residences. Poor living conditions in densely populated cities such as Lagos, Mumbai, and Dhaka are also contributing to indoor air pollution, and biomass exposure is a leading risk among women across many rural and suburban populations. Indeed, sub-Saharan Africa is perhaps the most affected region in this regard, with more than 90% of rural households depending on biomass fuel for cooking. This use affects many women and has long-term effects on young children, who might develop acute lower respiratory infections.<sup>32</sup>

Underweight (BMI <18.5 kg/m<sup>2</sup>) was a significant risk factor for COPD in our study. Many studies have reported a high prevalence of COPD among people who are underweight, but some have also reported a high COPD prevalence with increasing BMI.<sup>11,34</sup> These findings suggest that people at extreme ends of the weight spectrum have the highest risk and might be further explained by existing comorbidities associated with weight loss or gain.

Although we extracted spirometry-based estimates using the widely used GOLD and LLN criteria, these criteria have their own limitations. Many studies used different protocols, tools, spirometers, and approaches, which contributes to inconsistency in prevalence estimates across countries and significant heterogeneity. These concerns were noted in a recent review of surveys on methods to assess chronic respiratory diseases, which highlighted challenges in maintaining quality-assured spirometry, language and translations, and survey guidelines out of local context, including using appropriate local spirometry values in diagnoses.<sup>35</sup>

Some survey guidelines were also not always clear on the application of pre-bronchodilatory and post-bronchodilatory spirometry values. A post-bronchodilatory measure excludes the possibility of airflow limitation that can be fully overcome by smooth muscle relaxation, as airflow limitation in COPD is primarily irreversible. This is an important consideration when interpreting our estimates, as the chances of potential overdiagnosis and overestimation of the burden of COPD increase with pre-bronchodilatory values.

Prominent international organisations such as the European Respiratory Society and the American Thoracic Society have issued standards for the use of spirometry with necessary guidelines to ensure quality control

in epidemiological surveys; these have been largely maintained in large-scale studies such as the BOLD and PLATINO initiatives;<sup>36</sup> however, several small studies did not grade spirometry procedures and are not likely to adhere to quality measures. This might be particularly true with many procedures where measured FVC is thought to be inadequate, leading to an overestimation of the fixed ratio or LLN, and consequently an underestimation of COPD prevalence.<sup>20</sup> FEV<sub>6</sub> has been proposed as a replacement for FVC, highlighting continued major challenges in the correct diagnosis of COPD.<sup>37</sup>

COPD cases identified in epidemiological studies might not always retain this diagnosis after further examination in clinical settings. Healthy elderly people might meet the GOLD definition of airflow obstruction, but not necessarily COPD, due to the absence of exposure to noxious fumes or gases and respiratory symptoms. Furthermore, not all studies provided a breakdown of COPD prevalence by severity. When provided, staging, reporting, and presentation were inconsistent across both criteria. Without relevant data and detailed evaluation of COPD severity, a substantial number of COPD cases across studies might be overdiagnoses, particularly if a fixed FEV<sub>1</sub>/FVC ratio of more than 0.7 is used.

Appropriate identification of COPD cases might require comprehensive clinical diagnosis over time. Although administrative health records and physician-based or hospital-based reports are important sources of data for comparative analyses, the lack of a clear approach to collation, standardisation, and validation of health reports in many countries restricted their use in this study. Successful incorporation of these data in future estimates might improve the validity of COPD estimates. Although many LMICs have improved their health information systems in the past decade, most are focused on infectious disease notification and are rarely used for chronic diseases such as COPD. Population-based epidemiological studies are also mostly skewed towards infectious diseases in many LMICs. As a result, sub-Saharan Africa, Middle East and North Africa, South Asia, and Latin America jointly contributed to only 24% of all datasets in our study (appendix p 11). This is worrying in areas that contribute to the rising prevalence of COPD globally and impairs provision of the relevant public health response.

Although ambient particulate matter and smoking accounted for more than 70% of DALYs due to COPD,<sup>4</sup> and air pollution and other environmental factors are increasingly becoming major risks for COPD in LMICs,<sup>38</sup> we could not estimate direct risk from ambient air pollution because it was poorly defined across studies. Moreover, although COPD and its severity result from a complex interplay of genetic and environmental factors,<sup>39,40</sup> ethnicity could not be explored in our analysis because prevalence and risk measures by ethnicity were provided mainly by studies in the USA.

Our findings have important implications for policy and research. Smoking remains the single most important risk factor for COPD. Careful characterisation of smoking patterns across different age groups and implementation of strict measures are needed to address this issue. Although understanding of the epidemiology of COPD remains poor in several LMICs, implementation of WHO's Framework Convention for Tobacco Control, which has been ratified by 180 members representing 90% of world population, will be crucial to reduce the global burden of COPD.<sup>41</sup> Efforts should focus on LMICs, where the burden is highest, strict measures to address a gradually growing tobacco industry are not in place, and many young populations are now active smokers. Many countries need to intensify efforts, involving physicians, others health workers, and counselling and support groups, in the management of tobacco dependence, which is evidence-based, particularly for those willing to quit.<sup>42</sup> Given the limitations of data from population-based studies, experts need to work on standardised methods of collating clinical data that would be useful for epidemiological purposes. As a global respiratory health unit, we recommend the inclusion of pack-years in any clinical history of breathlessness or cough. Misdiagnosis of COPD needs to be addressed, particularly through provision and training of health-care providers in the correct use of spirometry. This is especially important in sub-Saharan Africa and South-East Asia, where numbers of undiagnosed cases are highest.<sup>11</sup> Moreover, training and clear guidance should be provided to individualise care in pulmonary rehabilitation, which has been shown to be effective in the treatment of COPD.<sup>43</sup>

COPD is among the most neglected diseases globally, receiving little attention from health-care providers and policy makers despite being a leading contributor to the global burden of disease (both premature mortality and disability).<sup>44</sup> Although the efforts of groups such as the BOLD initiative and PLATINO, and international respiratory organisations such as the European Respiratory Society and the American Thoracic Society have yielded considerable progress in understanding of the global COPD burden, international consensus on the epidemiological definition of COPD and standardised guidelines and data collection for population-based surveys are needed.

#### Contributors

DA, IR, PS, and AS designed study. DA and PS extracted all the data. DA, PS, YZ, and IR conducted data analyses. DA and PS wrote first draft with contributions from IR and HC. IR, HC, and AS reviewed the final draft and checked for important intellectual content. DA and PS verified the underlying data. All authors had full access to all the data in the study and the final responsibility for the decision to submit for publication.

#### Declaration of interests

AS reports grants from health data research (HDR) UK BREATHE Hub, UK Medical Research Council, and UK National Institute for Health Research (NIHR), during the conduct of the study. All other authors declare no competing interests.

#### Data sharing

All datasets are provided in the appendix and metadata are available on the HDR gateway via BREATHE.

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For more on the metadata see <https://web.www.healthdatagateway.org/>

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