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Global and regional estimates of COPD prevalence: Systematic review and meta–analysis

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Background
The burden of chronic obstructive pulmonary disease (COPD) across many world regions is high. We aim to estimate COPD prevalence and number of disease cases for the years 1990 and 2010 across world regions based on the best available evidence in publicly accessible scientific databases.

Methods
We conducted a systematic search of Medline, EMBASE and Global Health for original, population–based studies providing spirometry–based prevalence rates of COPD across the world from January 1990 to December 2014. Random effects meta–analysis was conducted on extracted crude prevalence rates of COPD, with overall summaries of the meta–estimates (and confidence intervals) reported separately for World Health Organization (WHO) regions, the World Bank's income categories and settings (urban and rural). We developed a meta–regression epidemiological model that we used to estimate the prevalence of COPD in people aged 30 years or more.

Findings
Our search returned 37 472 publications. A total of 123 studies based on a spirometry–defined prevalence were retained for the review. From the meta–regression epidemiological model, we estimated about 227.3 million COPD cases in the year 1990 among people aged 30 years or more, corresponding to a global prevalence of 10.7% (95% confidence interval (CI) 7.3%–14.0%) in this age group. The number of COPD cases increased to 384 million in 2010, with a global prevalence of 11.7% (8.4%–15.0%). This increase of 68.9% was mainly driven by global demographic changes. Across WHO regions, the highest prevalence was estimated in the Americas (13.3% in 1990 and 15.2% in 2010), and the lowest in South East Asia (7.9% in 1990 and 9.7% in 2010). The percentage increase in COPD cases between 1990 and 2010 was the highest in the Eastern Mediterranean region (118.7%), followed by the African region (102.1%), while the European region recorded the lowest increase (22.5%). In 1990, we estimated about 120.9 million COPD cases among urban dwellers (prevalence of 13.2%) and 106.3 million cases among rural dwellers (prevalence of 8.8%). In 2010, there were more than 230 million COPD cases among urban dwellers (prevalence of 13.6%) and 153.7 million among rural dwellers (prevalence of 9.7%). The overall prevalence in men aged 30 years or more was 14.3% (95% CI 13.3%–15.3%) compared to 7.6% (95% CI 7.0%–8.2%) in women.

Conclusions
Our findings suggest a high and growing prevalence of COPD, both globally and regionally. There is a paucity of studies in Africa, South East Asia and the Eastern Mediterranean region. There is a need for governments, policy makers and international organizations to consider strengthening collaborations to address COPD globally.

Electronic supplementary material: The online version of this article contains supplementary material.
In a follow-up to the 2011 United Nations (UN) high-level political declaration on non-communicable diseases (NCDs) [1], the World Health Assembly, in 2012, endorsed a new health goal (the “25 by 25 goal”), which focuses on reduction of premature deaths from COPD and other NCDs by 25% by the year 2025 [2]. Despite this initiative, experts have reported that COPD remains a growing [3], but neglected global epidemic [4]. The World Health Organization (WHO) estimated that there were about 62 million people with moderate to severe COPD in 2002, with the total number of COPD cases predicted to increase to about 200 million in 2010 [5,6]. According to the 2010 Global Burden of Disease (GBD) study, COPD was responsible for about 5% of global disability-adjusted life years – DALYs (76.7 million) – and 5% of total deaths (2.9 million) [7,8]. COPD is currently rated the fourth most common specific cause of death globally and predicted to be the third by 2030, in the absence of interventions that address the risks – especially tobacco smoking, exposures to combustion products of biomass fuels and environmental pollution [9,10].

The burden of COPD has been reported to be high in some high-income countries (HIC), particularly due to high prevalence of smoking in these settings [11]. For example, between years 2000 and 2010, about 4%–10% of adults were diagnosed with non-reversible and progressive airway obstruction (a basic feature of COPD) in population-based surveys across many European countries, with smoking indicated as a major risk [12]. The WHO has estimated that in many HIC up to 73% of COPD deaths are related to tobacco smoking [6]. The European Union (EU) reported that the direct cost from COPD was over 38.6 billion Euros in 2005, representing about 3% of total health care expenditure [13,14]. In the United States (US), over 2.7 million adults were estimated to have COPD in 2012, with about 135,000 deaths reported [15]. In 2010, the US government spent nearly US$ 49.9 billion on COPD, including 29.5 billion spent on direct health care, 8.0 billion on indirect morbidity and 12.4 billion on indirect mortality costs, respectively [15].

Meanwhile, it has been estimated that despite a high prevalence of COPD in some HIC, 90% of COPD deaths still occur in low- and middle-income countries (LMIC) [4] and 40% of these deaths are attributable to smoking [6]. The burden in LMIC has been comparatively high owing to relatively low COPD awareness, challenges with COPD diagnosis and increased exposures to additional risk factors, especially combustion products of biomass fuels [16]. Salvi and colleagues reported that about 3 billion people globally are exposed to smoke from biomass fuel, compared to 1 billion people who smoke tobacco globally [17]. In many developing countries COPD is neglected by governments, physicians, experts and the pharmaceutical industry, although it’s been identified as an important public health problem [4].

In the last two decades, the Burden of Obstructive Lung Disease (BOLD) initiative has been collecting country-specific data on the prevalence, risk factors and socioeconomic burden of COPD, using standardized and tested methods for conducting COPD surveys in the general population [18]. This is expected to provide governments of many nations with country-specific evidence on which to develop COPD policy [18]. As noted above, this initiative is yet to take a full effect in many LMIC [19]. In addition, spirometry (the gold standard for COPD diagnosis) is not widely available in many LMIC [16]. Even when it is there, professionals in LMIC are often not being trained properly on how to use spirometers or interpret spirometry results. There is concern that COPD burden has been underestimated, owing to over-reliance on doctor’s diagnosis, with many diagnoses not being based on spirometry and international diagnostic guidelines [20]. The lack of routine COPD data collation and effective health information management system in many LMIC also implies that these settings could have been grossly under-represented in global burden of COPD estimates [11].

Some global and regional estimates of COPD burden have been published [1,21–23]. However, despite the fact that COPD is now prevalent in both HIC and LMIC, experts have raised concerns that reliable estimates of COPD prevalence are still few in many parts of the world. Moreover, many of the estimates are based on varying definitions and diagnostic criteria of COPD [9]. Also, some of the current estimates were reported before the BOLD surveys in several countries, thereby failing to account for the additional epidemiological data from the BOLD surveys. There is a need for a revised and updated estimate of COPD prevalence across world regions. We conducted a systematic review of COPD prevalence based on spirometry data across world regions. Our aim was to provide global and regional prevalence rates of COPD that could facilitate adequate policy response in these regions.

**METHODS**

**Search strategy and selection criteria**

After identifying relevant Medical Subject Headings (MeSH), we conducted a systematic search of Medline, EMBASE and Global Health for studies estimating the prevalence of COPD globally from January 1990 to December 2014. We also searched Google Scholar for unpublished studies. Reference lists of retained publications were further hand-searched for studies omitted in our initial searches (see search terms in Tables s1–3 in Online Supplementary Document).
We included original population–based (cohort or cross–sectional) studies conducted worldwide. The retained studies provided estimates of the prevalence and number of cases of COPD and/or relevant population–based information from which COPD prevalence could be estimated. We excluded studies that had unclear study designs and methodologies, conducted before 1990, on non–human subjects, and that were reviews, viewpoints or editorials. No language restrictions were applied.

Case definitions

Based on an understanding of the diagnosis of COPD as reported by respiratory physicians, we included only studies that were based on spirometry, as these have been shown to be consistent with the diagnosis of COPD worldwide [24,25]. However, it is important to note that experts may still not fully agree on the spirometry–based definition that best defines COPD [26]. In 2001, the Global initiative on Obstructive Lung Disease (GOLD) recommended using the ratio of forced expiratory volume in one second (FEV₁) to forced vital capacity (FVC) that is less than 70% in the diagnosis of COPD (FEV₁/FVC<70%) [25,27]. This diagnostic criterion was also endorsed by the American Thoracic Society (ATS) and the European Respiratory Society (ERS) in 2004 [28]. It has been acknowledged that this criterion is simple and independent of reference equations [26]. However, the use of a fixed FEV₁/FVC ratio has been debated from a number of perspectives [29–32], which we summarized in the discussion (see later). For the current study, we selected studies that used case definitions for COPD as shown in detail in Table 1.

Data extraction, synthesis of results and analysis

All extracted data were stored in Microsoft Excel file format. A parallel search and extraction was conducted by three independent reviewers (SC, CL and CB). Any disagreement between the three reviewers over article inclusion, exclusion and/or data extraction for the current study was resolved through re-review of their work and agreement between their two supervisors (DA and IR). We did not calculate Kappa statistics for the agreement between all reviewers because it was not amenable to straightforward computation and interpretation in this two-stage extraction process, which was based on a mix of independent review and collaborative re-review. Also, we did not make any attempts to contact the authors of studies that were rejected based on unclear reporting. Data were abstracted systematically on sample size, mean age, number of COPD cases, and the respective age– and sex– specific prevalence rates. These were classified into WHO regions, the World Bank's income categories, and study setting (urban, rural or mixed). For studies conducted on the same study site, population or cohort, the first chronologically published study was selected, and all additional data from other studies were included in the selected paper. All extracted information from the retained studies is available in Table s4 in Online Supplementary Document.

A random effect meta–analysis (DerSimonian and Laird method) was conducted on extracted crude prevalence rates of COPD [33]. Overall summaries of the meta–estimates (and confidence intervals) were reported separately for the WHO regions, the World Bank's income categories, and study settings, all expressed as percentages.

We developed a meta–regression epidemiological model and applied this on crude prevalence rates of COPD. In this model, mean ages corresponding to each prevalence rate were plotted on the x–axis (independent variable) and crude prevalence rates were plotted on the y–axis (dependent variable). We accounted for variation in sample sizes from each data point and controlled for year of publication to generate estimates of COPD prevalence for the years 1990 and 2000, respectively. The best fit was then used in our model and the equation generated from the fitted line was applied to the respective midpoints of the United Nations (UN) 5–year age–group population estimates for the years 1990 and 2010, respectively (United Nations, 2013).

Table 1. Basic characteristics of the studies retained for the analyses (a total of 140 study sites from 123 studies)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Study sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO regions:</td>
<td></td>
</tr>
<tr>
<td>AFRO</td>
<td>6</td>
</tr>
<tr>
<td>AMRO</td>
<td>13</td>
</tr>
<tr>
<td>EMRO</td>
<td>7</td>
</tr>
<tr>
<td>EURO</td>
<td>64</td>
</tr>
<tr>
<td>SEARO</td>
<td>6</td>
</tr>
<tr>
<td>WPRO</td>
<td>42</td>
</tr>
<tr>
<td>Income category:</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>87</td>
</tr>
<tr>
<td>Low and middle</td>
<td>53</td>
</tr>
<tr>
<td>Settings:</td>
<td></td>
</tr>
<tr>
<td>Mixed*</td>
<td>52</td>
</tr>
<tr>
<td>Urban</td>
<td>63</td>
</tr>
<tr>
<td>Rural</td>
<td>25</td>
</tr>
<tr>
<td>Study period:</td>
<td></td>
</tr>
<tr>
<td>1990–1999</td>
<td>24</td>
</tr>
<tr>
<td>2000–2009</td>
<td>94</td>
</tr>
<tr>
<td>2010–present</td>
<td>22</td>
</tr>
<tr>
<td>COPD case definitions:</td>
<td></td>
</tr>
<tr>
<td>FEV₁/FVC&lt;70%</td>
<td>130</td>
</tr>
<tr>
<td>FEV₁/FVC&lt;LLN</td>
<td>8</td>
</tr>
<tr>
<td>FEV₁/FVC&lt;75%</td>
<td>1</td>
</tr>
<tr>
<td>FEV₁/FVC&gt;65%</td>
<td>1</td>
</tr>
</tbody>
</table>

COPD – chronic obstructive pulmonary disease, FEV₁ – forced expiratory volume, FVC – forced vital capacity, LLN – lower limit of normal
*Studies presenting a joint COPD estimate for urban and rural settings.
ally and in the WHO regions. A detailed description of our model has been explained in our previous study where we estimated the burden of COPD in Africa [34]. All analyses were conducted in Stata 13.1 (Stata Corp LP, College Station, Texas, USA).

RESULTS

Systematic review

Our search returned 37,472 publications: 10,828 in Medline, 24,265 in EMBASE and 2,379 in Global Health. A further three studies were included from other sources (Google Scholar and hand–searching reference list of relevant publications). 23,457 studies remained after removing duplicates. After screening titles for relevance (studies estimating the burden of COPD) 21,762 studies were excluded. We therefore assessed 1,694 full–text papers. After applying the quality criteria, 1,566 studies were excluded. This is because 934 articles did not provide prevalence data on COPD, population figures or relevant estimates from which prevalence can be calculated; further 325 articles did not specify study designs; and 307 studies were not based on spirometry and/or clarify COPD case definitions. A total of 128 studies were retained for the review, with 123 providing quantitative data for a total of 140 study settings (see Figure 1 for the PRISMA flow diagram of study selection).

Study characteristics

The retained studies [23,26,35–155] were conducted across 140 locations spread across the six regions of the WHO (see Table s4 in Online Supplementary Document). European (EURO) and Western Pacific (WPRO) regions had the highest number of studies with 64 and 42 study sites, respectively. This was followed by the American region (AMRO) with 15 study sites. Eastern Mediterranean region (EMRO) had seven study sites, while the African region (AFRO) and South East Asia region (SEARO) each had six study sites (Table 1). Five studies were conducted in multiple sites. They included the BOLD study [40], European Community of Respiratory Health Survey (ECRHS) [113], the PLATINO study in Latin America [23] and two other studies in Europe [61,89].

A total of 52 countries were represented, with China contributing the largest number of studies (22 in total). The mean age across studies was 54.1 years, ranging from 32 to 74 years. The total population from all studies was 8,775,662. The COPD survey guidelines employed across selected studies included GOLD, ATS, ATS/ERS and the British Thoracic Society (BTS) (see Table s4 in Online Supplementary Document). However, COPD diagnosis was based on the diagnostic criterion of FEV1/FVC<70% in 92.2% of all retained studies (see Table 1 and Table s4 in Online Supplementary Document for detailed explanation of characteristics of selected studies).
Meta-estimates from crude COPD prevalence rates

Forest plots were used to give a visual assessment of the pooled crude prevalence along with 95% confidence intervals of COPD by WHO regions, by study settings, and by the World Bank income category (Figures 2-4). We used the I²-statistic to evaluate heterogeneity in COPD prevalence between the retained studies. From the random effects meta-analysis, a prevalence of 11.4% (CI: 10.8%–12.0%) was estimated globally in people aged ≥30 years (Figure 2). The overall prevalence was higher among men (14.3%; CI: 13.3%–15.3%) than women (7.6%; CI: 7.0%–8.2%) (Table 2).

Among the WHO regions, AMRO region had the highest prevalence (14.1%; CI: 11.4%–16.7%), followed by EMRO (13.2%; CI: 8.8%–17.7%) and EURO (12.0%; CI: 10.7%–13.2%). AFRO had an estimated prevalence of 10.6% (CI: 6.1%–15.1%) and WPRO of 10.0% (CI: 9.0%–11.0%). SEARO had the lowest prevalence of 7.8% (CI: 5.3%–10.4%) (Figure 2 and Table 2).

Across most settings, urban dwellers had higher COPD prevalence rates (13.2%; CI: 11.8%–14.7%) than rural populations (10.2%; 8.2%–12.2%) (Figure 3 and Table 2). An analysis according to the World Bank’s income categories revealed that the prevalence was higher in high-income countries (HIC): 12.0% (CI: 11.0%–13.0%), compared to 10.6% (CI: 9.5%–11.6%) in LMIC (Figure 4 and Table 2).

Modelled estimates of COPD prevalence and number of cases

The initial meta-regression analysis showed a significant effect of mean age and the year of study on estimated COPD prevalence rates. We therefore controlled for these effects in the model (Figure 5 and Table 3) [34]. From the model based on meta-regression we estimated about 227.3 million COPD cases in the year 1990 among people aged 30 years or more, corresponding to the global prevalence of 10.7% (7.3%–14.0%) in this age group. However, the number increased to 384 million COPD cases in 2010, corresponding to the global prevalence of 11.7% (8.4%–15.0%). This is an increase of 68.9% and it is driven mainly by the global demographic changes over the 20–year period (Table 4).

Based on the UN percentage of people living in urban areas in 1990 (43.0%) and 2010 (51.6%) [156], we estimated the global population in these regions in those two years.

<table>
<thead>
<tr>
<th>Table 2. Summary of pooled crude COPD prevalence from selected studies (prevalence expressed in percentages for the population aged 30 years or older)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WHO region:</strong></td>
</tr>
<tr>
<td>World</td>
</tr>
<tr>
<td><strong>WHO region:</strong></td>
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<td></td>
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<td></td>
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<tr>
<td><strong>Study setting:</strong></td>
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<td></td>
</tr>
<tr>
<td><strong>Income category:</strong></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

COPD – chronic obstructive pulmonary disease, CI – confidence interval

*Studies presenting a joint COPD estimate for urban and rural settings.

Figure 2. Overall pooled crude prevalence of COPD by WHO regions.
Our model revealed higher prevalence and number of COPD cases among urban dwellers. In 1990, we estimated about 120.9 million COPD cases among people aged 30 years or more, accounting for a prevalence of 13.2% (10.0%–16.4%). At the same time, rural dwellers had 106.3 million cases, accounting for a prevalence of 8.8% (6.5%–11.1%). By the year 2010, the number of COPD cases among urban dwellers rose to more than 230 million, accounting for a prevalence of 13.6% (11.2%–16.9%), and about 153.7 million cases among rural dwellers, accounting for a prevalence of 9.7% (7.6%–11.8%). The percentage of increase in COPD cases between 1990 and 2010 was higher among urban dwellers than among rural residents (90.5% vs 44.6%, respectively) (Table 5).

DISCUSSION

This study is among the first systematic attempts to estimate the prevalence of COPD across the world regions using spirometry–based data. The estimates presented here are based on the age range starting from 30 years, while many of the previous reviews were based on people aged 40 years or older. An appreciable prevalence of COPD has been reported in younger population groups, adding to uncertainties over the current epidemiological situation globally.

In the current study, we estimated a global prevalence of 10.7% (7.3%–14.0%) in 1990 and 11.7% (8.4%–15.0%) in 2010, corresponding to 227 and 384 million of affected cases in 1990 and 2010, respectively. This estimate is an order of magnitude higher than the one presented in the 2001 World Health Report, estimating a world–wide prevalence of COPD of 10.1 per 1000 population (12.1 per 1000 men and 8.1 per 1000 women) [157]. A 2006 global review conducted by Halbert and colleagues reported a pooled prevalence of 9.2% (7.2–11.0), based on 26 spirometry–based estimates – a figure much closer to our estimates [21]. In the 2005 BOLD study, conducted in 12 sites globally and based on post–bronchodilator FEV1/FVC<70%, the overall prevalence of Stage II or higher COPD was 10.1% (men 11.8% and women 8.5%) [40], which is again much closer to our results. Given that the estimates presented in the 2001 World Health Report were based on doctor’s diagnosis and included all ages, this may explain the departure from spirometry–based estimates. All spirometry–based estimates to date seem to be comparable and may be indicative of the usefulness of spirometry as a gold standard for COPD diagnosis in population–based studies.

The highest COPD prevalence estimated in this study was observed in the American region, with an estimated prevalence of 13.3% and 15.2% in 1990 and 2010, respectively. Moreover, we estimated that 113 million COPD cases should be expected in Western Pacific region in 2010, almost doubling the estimated for 1990 which stood at 60 million. In the South East Asia, we estimated about 66.4 million COPD cases in 2010. Comparing our results to other estimates from previous studies, in the PLATINO multicentre study conducted across five South–American cities, which applied the same survey approach as the 2005 BOLD study, crude prevalence of COPD ranged from 7.8% in Mexico city to 19.7% in Montevideo [23]. A total of 12.2 million COPD cases, corresponding to an overall prevalence of 14.3%, was estimated for the urban population.
A mathematical model derived from prevalence of known COPD risk factors in 12 Asia–Pacific sites estimated about 57 million moderate–to–severe COPD cases in people aged 30 years or more in 2002, which is equivalent to a prevalence of 6.3% in the Asia Pacific region [158]. This figure is considerably larger than the WHO estimate for the region, which stood at 3.9% [157]. In addition, the regional working group reported that the number of COPD cases in China in 2002 should be expected to reach 38.2 million, with a prevalence of 6.5% [158]. This is again about 2.5 times higher than the estimates reported by the WHO [157]. Such differences in the regional pooled prevalence rates reported by separate authors may be linked to heterogeneities arising from differences in survey methodologies, population structure, subject’s age and case identification [159]. Moreover, experts have reported that despite the apparently large burden of COPD in Western Pacific and South East Asia, there are few good epidemiological surveys on COPD in these regions [22]. For example, in a recent review in India, McKay and colleagues reported that they could not identify a single high quality study that provided detailed estimate of COPD prevalence using a relatively standard spirometry-based definition, and were therefore unable to perform a meta–analysis [160]. This was also observed in our study, as there were only three studies retained in India with only two of these providing age– and sex–specific COPD prevalence rates. However, we managed to include several large epidemiological surveys conducted in China, which actually had the highest number of retained studies (22 studies) of all the 52 countries represented (see Table s4 in Online Supplementary Document).

In the WHO EURO region, we noted the lowest increase in total number of COPD cases between 1990 and 2010 (22%). This may reflect the reduction in prevalence of smoking in Europe through intensive public health measures and legal regulations. According to the European Health Interview Survey (EHIS), the prevalence of COPD in 2008 among people aged at least 15 years in 16 EU member states ranged from 1.2% to 6.2%, with a mean

Table 4. Summary of overall COPD cases and prevalence rates in people aged 30 years or more (estimates derived from epidemiological model)

<table>
<thead>
<tr>
<th></th>
<th>1990</th>
<th>2010</th>
<th>% increase in COPD cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (millions)</td>
<td>Prevalence (%)</td>
<td>Cases (millions)</td>
</tr>
<tr>
<td>World</td>
<td>227.3</td>
<td>10.7 (7.3–14.0)</td>
<td>384.0</td>
</tr>
<tr>
<td>AFRO</td>
<td>14.1</td>
<td>9.8 (8.9–10.7)</td>
<td>28.5</td>
</tr>
<tr>
<td>AMRO</td>
<td>41.6</td>
<td>13.3 (12.9–13.7)</td>
<td>72.0</td>
</tr>
<tr>
<td>EMRO</td>
<td>13.4</td>
<td>11.8 (10.1–13.5)</td>
<td>29.3</td>
</tr>
<tr>
<td>EURO</td>
<td>54.2</td>
<td>11.8 (11.6–12.0)</td>
<td>66.4</td>
</tr>
<tr>
<td>SEARO</td>
<td>44.5</td>
<td>7.9 (7.5–8.4)</td>
<td>75.1</td>
</tr>
<tr>
<td>WPRO</td>
<td>59.5</td>
<td>9.2 (9.0–9.4)</td>
<td>112.7</td>
</tr>
<tr>
<td>Urban</td>
<td>120.9</td>
<td>13.2 (10.0–16.4)</td>
<td>230.3</td>
</tr>
<tr>
<td>Rural</td>
<td>106.3</td>
<td>8.8 (6.5–11.1)</td>
<td>153.7</td>
</tr>
</tbody>
</table>

COPD – chronic obstructive pulmonary disease

Figure 4. Overall pooled crude prevalence of COPD by World Bank income category.
Table 5. Estimated number of COPD cases (in thousands) and prevalence by 5-year age groups and WHO regions (estimates derived from epidemiological model)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>AFRO</th>
<th>AMRO</th>
<th>EMRO</th>
<th>EURO</th>
<th>SEARO</th>
<th>WPRO</th>
<th>WORLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>2123.771</td>
<td>4795.619</td>
<td>5612.298</td>
<td>7809.886</td>
<td>5211.630</td>
<td>7524.854</td>
<td>9429.498</td>
</tr>
<tr>
<td>2010</td>
<td>4187.729</td>
<td>9175.717</td>
<td>11718.951</td>
<td>15620.986</td>
<td>10699.042</td>
<td>15554.320</td>
<td>22832.208</td>
</tr>
<tr>
<td>% Prevalence</td>
<td>9.79%</td>
<td>11.39%</td>
<td>13.31%</td>
<td>15.19%</td>
<td>11.82%</td>
<td>13.43%</td>
<td>11.83%</td>
</tr>
<tr>
<td>Lower 95% CI</td>
<td>8.92%</td>
<td>10.35%</td>
<td>12.37%</td>
<td>14.34%</td>
<td>10.75%</td>
<td>12.63%</td>
<td>10.73%</td>
</tr>
<tr>
<td>Upper 95% CI</td>
<td>10.67%</td>
<td>12.36%</td>
<td>13.65%</td>
<td>15.54%</td>
<td>11.39%</td>
<td>13.49%</td>
<td>12.03%</td>
</tr>
</tbody>
</table>

Several authors have reported that the epidemiological evidence on COPD in African region is still very limited and that this has affected the estimate of prevalence in the region [16,17]. We estimated a prevalence of about 5% in 2010, amounting to 9 million COPD cases in 1990. This is similar to a recent continent-wide case definition included in the region [16,17]. The prevalence rate may be considerably higher [10,12].

Another important limitation relates to the differences in case definitions and diagnostic guidelines employed across income countries. Some world regions, especially in LMIC, may contribute to reducing gender differences in COPD in future [1].

Several studies reported that urbanization is an important risk factor for COPD, with over 23 million cases of COPD among global urban dwellers in 2010, accounting for 60% of all COPD cases. The rapid rate of urbanization in many parts of the world, especially in LIC, may contribute to an increasing prevalence in high-income countries with increased tobacco use, among women views suggested that increased tobacco use among women views contribute to reducing gender differences in COPD in future [1].

Similarly, the development of COPD [166], given that the risk profile among men was consistently higher than in women across all world regions, including high-income countries with increasing prevalence in high-income countries and the higher risk of exposure to indoor and outdoor air pollution (such as biomass fuels used for cooking and heating) in low- and middle-income countries can contribute to reducing gender differences in COPD in future [1].

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studies over time. In our analysis, we required spirometry as the standard diagnostic parameter, given the concerns raised over alternative definitions of COPD. Across all retained studies, the definition based on FEV/FVC<70% was used in the large majority of studies, but this still does not address all possible sources of variation in case definition. Some authors even question the use of a fixed FEV1/FVC ratio mainly because it has no statistical basis and because choosing 0.7 as a cut-off point – instead of 0.68 or 0.72, for example – is essentially arbitrary [29]. Experts have argued that this fixed criterion may potentially over-diagnose COPD in the elderly, as lung elasticity decreases with age, which reduces FEV1 more than FVC [30]. Hence, using a fixed ratio can result in under-diagnoses in younger patients, and more frequent diagnoses in the elderly. The use of a lower limit of normal (LLN) has been suggested instead, and this is described as the lower fifth percentile of a reference population [31]. It is calculated by subtracting the standard deviation (multiplied by 1.64) from the mean [31]. However, some studies suggest that LLN may miss subjects with COPD [32]. This variation in COPD diagnosis is especially pertinent in LMICs, where undiagnosed or poorly treated asthma, bronchiectasis, tuberculosis or some other obstructive airway disease may be more prevalent and possibly misdiagnosed as COPD [17]. Even when the FEV/FVC<70% criterion was consistently applied, some studies were based on pre-bronchodilator values, rather than post-bronchodilator values, as recommended by GOLD. In addition, it was often not fully explained how exactly was spirometry performed and what was the protocol. A number of technical issues could have affected the estimates, such as the choice of spirometer, the level of training of the operator, and the process of collection and storage of spirometry measurements. Finally, physicians’ knowledge of guidelines can also pose a barrier to spirometry use in settings where it is available [167].

An additional limitation is associated with the choice of our epidemiological model, which was mainly based on age of the examinees. There are several other important predictors that could have been incorporated into the model if the information was available from the retained studies, including those related to study sites, income levels, smoking, socio-economic determinants of health, occupational exposures and others. However, the studies that we retained would rarely report these important covariates, so we could not use them in our model.

Meanwhile, it is worth noting that most of the studies (83%) included in this review were published after the year 2000, and encouragingly, the number of epidemiological studies focusing on COPD has been steadily increasing over the past two decades. This upward trend provides an indication of an increased awareness and recognition of COPD as a growing global health burden, and the need to strengthen research base and improve and standardize the methods. Our findings suggest a high and growing prevalence of COPD, both globally and regionally, with substantial variation in trends between different world regions. The estimates presented here are consistent with other spirometry-based reviews on the burden of COPD. As with any other public health problem, increased political commitment and funding remains crucial, particularly in LMIC settings. Governments and policymakers must consider strengthening regulations to address occupational and environmental risk factors, regulate tobacco use and improve public awareness. A combined use of patient- and physician targeted educational interventions could also help [168]. The efforts of BOLD, aiming to standardize methodology and definitions, must be supported, and other research entities should strongly consider adopting similar methods or collaborating with BOLD in order to provide epidemiological results that are more comparable in and among populations. It is only through such concerted effort that the current high global COPD burden may be reduced in the coming decades.
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