Key points

- Globally, there is large variation in the prevalence of COPD, with 10–95% under-diagnosis and 5–60% over-diagnosis (table 1) due to differences in the definition of diagnosis used, and the unavailability of spirometry in rural areas of low- and middle-income countries where the prevalence of COPD is likely to be high.

- In order to be diagnosed with COPD, patients must have a combination of symptoms with irreversible airflow obstruction defined by a post-bronchodilator FEV_1/FVC ratio of <0.7 or below the fifth centile of the lower limit of normal (LLN), and with a history of significant exposure to a risk factor. Repeat spirometry is recommended if the ratio is between 0.6 and 0.8.

- Not performing spirometry is the strongest predictor for an incorrect diagnosis of COPD; however, additional factors, such as age, gender, ethnicity, self-perception of symptoms, co-existent asthma, and educational awareness of risk factor by patients and their physician, are also important.

- COPD can be associated with inhalation of noxious particles other than smoking tobacco.

Educational aims

- To summarise the global prevalence of over- and under-diagnosis of COPD.

- To highlight the risk factors associated with the under- and over-diagnosis of COPD.

- To update readers on the key changes in the recent progress made regarding the correct diagnosis of COPD.

Terence Ho[1,5], Ruth P. Cusack[2,5], Nagendra Chaudhary[3,5], Imran Satia[2,5], Om P. Kurmi[4,5]

✉ kurmio@mcmaster.ca

🐦 @omkurmi

in www.linkedin.com/in/omkurmi

Review

Under- and over-diagnosis of COPD: a global perspective

Globally, chronic obstructive pulmonary disease (COPD) is the fourth major cause of mortality and morbidity and projected to rise to third within a decade as our efforts to prevent, identify, diagnose and treat patients at a global population level have been insufficient. The European Respiratory Society and American Thoracic Society, along with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy document, have highlighted key pathological risk factors and suggested clinical treatment strategies in order to reduce the mortality and morbidity associated with COPD. This review focuses solely on issues related to the under- and over-diagnosis of COPD across the main geographical regions of the world and highlights some of the associated risk factors. Prevalence of COPD obtained mainly from epidemiological studies varies greatly depending on the clinical and spirometric criteria used to diagnose COPD, *i.e.* forced expiratory volume in 1 s to forced vital capacity ratio <0.7 or 5% below the lower limit of normal, and this subsequently affects the rates of under- and over-diagnosis. Although under-utilisation of spirometry is the major reason, additional factors such as exposure to airborne pollutants, educational level, age of patients and language barriers have been widely identified as other potential risk factors. Co-existent diseases, such as asthma, bronchiectasis, heart failure and previously treated tuberculosis, are reported to be the other determinants of under- and over-diagnosis of COPD.

Introduction

Chronic obstructive pulmonary disease (COPD) is a major chronic disease, highly prevalent in the ageing population exposed to tobacco smoke and airborne pollutants [1], and is currently the fourth leading cause of morbidity and deaths worldwide [2], accounting for around 3 million deaths globally. The current 2019 Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy document defines COPD as "a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases." Exposure to noxious particles and gases has been recognised as another risk factor, other than smoking, that may contribute to obstructive airway disease. In a global context, other risk factors, such as exposure to airborne pollutants from household fuel burning, occupation and ambient sources, need to be considered [3, 4].

Our current strategy to diagnose individuals states that patients must have symptoms and

🐦 @ERSpublications
COPD is a major cause of morbidity and mortality, but misdiagnosis of COPD is a huge problem worldwide. Its main causes are under-utilisation of spirometry and lack of uniformity in diagnosis criteria, particularly in resource poor settings. http://ow.ly/KfP330nonkh

obstructive airflow limitation with a prior history of exposure to a known risk factor. In the absence of symptoms and/or physiological confirmation, the definition is not met. This potentially leaves many patients misdiagnosed, which may lead to negative impacts both at the individual and population levels.

The presence of symptoms can be assessed easily, but care must be taken of those patients who may under- or over-perceive their symptoms and those with the presence of comorbidities that could present with similar symptoms. The former can potentially leave patients under-diagnosed, whilst the latter may cause over-diagnosis leading to potentially excessive treatment, given that the treatment algorithm in the GOLD strategy is to offer inhaler therapy based on the modified Medical Research Council breathlessness scale, COPD assessment test score and exacerbation frequency using the ABCD tool.

The correct performance and interpretation of spirometry remains an issue of contention, more often in resource-poor settings of low- and middle-income countries (LMICs). Regular calibration of the spirometer is recommended, as failing to do so may lead to either under- or over-diagnosis of COPD. Traditionally, the presence of a post-bronchodilator forced expiratory volume in 1 s (FEV_1) to forced vital capacity (FVC) ratio of <0.7 has been used to diagnose COPD; however, current European Respiratory Society (ERS)/American Thoracic Society guidelines recommend the use of a post-bronchodilator FEV_1/FVC less than the fifth centile of the lower limit of normal (LLN), although this is mainly used in epidemiological research rather than daily clinical practice [5]. Many studies using the fixed ratio cut-off have reported over-diagnosis of COPD in the elderly and under-diagnosis in younger individuals (<40–45 years), particularly amongst those who are asymptomatic [6, 7]. The 2019 GOLD strategy preferred the use of the ratio, but recommended repeat spirometry testing if the value is between 0.6 and 0.8, due to the variability and the increase in positive predictive value of COPD if the value is less than 0.6 [8]. Given the challenges of performing single post-bronchodilator spirometry in LMICs in a primary care setting, the recommendation of repeating spirometry in borderline cases globally is a major challenge.

The proportion of under-diagnosis of COPD is likely to be high in LMICs for a number of reasons: limited access to healthcare, asymptomatic younger individuals, under-reporting of symptoms, and lack of knowledge about risk factors and hence under-reporting to a physician. Furthermore, under-diagnosis could also occur due to manifestations of respiratory symptoms (*e.g.* breathlessness) in individuals with other existing comorbidities, such as congestive heart failure. In contrast, patients with the presence of other comorbidities, such as asthma, bronchiectasis and post-tuberculosis, may present with respiratory symptoms and may be diagnosed with COPD based on a history of exposure to noxious particles, hence leading to over-diagnosis.

The objective of this current literature review focuses on the global prevalence and risk factors for the diagnosis of COPD and the potential reasons for under- and over-diagnosis separated into geographical regions of interest: North America/Europe/Oceania; Africa; Central and South America; South-East Asia; and the Middle East and South Asia (table 1). Under-diagnosis was defined as those individuals with or without symptoms and chronic airflow obstruction (AFO) who were not yet diagnosed with COPD or those with presence of other comorbidities but symptoms common to COPD wrongly labelled for another disease. Over-diagnosis was defined as those who were labelled as COPD but without the associated symptoms of COPD or evidence of AFO or symptoms of other diseases labelled as COPD. Here, the term over-diagnosis is only meant to refer to correct diagnosis of COPD and may not be associated with increase in morbidity or mortality during their life-time.

North America, Europe, Australia and New Zealand

Epidemiology of COPD

Published studies from high-income countries have reported a large variation in prevalence and incidence of COPD, both within a country and also among different countries [9]. These variations are likely due to inherent population differences between geographic regions, but also could be related to a host of factors, including the sampling method, the specific populations studied, and the multitude of criteria used to define COPD.

Data from the USA is primarily derived from the National Health and Nutrition Examination Survey (NHANES). Prevalence estimates in the USA range from 10.2–20.9% [10–12], with TILERT *et al.* [12] demonstrating that the observed variability in their study could be explained by the spirometric criteria applied. The Burden of Obstructive Lung Diseases (BOLD) study reported a prevalence of 19.6% at its US site, similar to the NHANES, using the GOLD definition of COPD [13]. Prevalence of self-reported but physician-diagnosed COPD in Canada and Australia ranged from 8.5% to 18% [11, 14], similar to the US estimates, but with the BOLD and COLD studies reporting rates of 19.3% and 17.4% for Canada, respectively, and 19.2% in Australia [13, 15].

In Europe, the prevalence of COPD ranged from 3% in the Netherlands [16] to 26.1% in Austria [17] when adhering to the GOLD criteria. Much like North America, a variety of spirometric criteria have been applied, with pre-bronchodilator spirometry associated with relatively higher estimates (compared to post-bronchodilator recommended by GOLD), and FEV_1/FVC defined by the lower limit

Table 1 *Prevalence, under- and over-diagnosis of COPD*

Continent	Country	Gender M:F	Age years	Prevalence (self-reported)	Prevalence (spirometry)	Under-diagnosis	Over-diagnosis	Year of data collection
North America	USA	55:45 [12] 57:43 [14] 48:52 [24] 96:4 [42]	40–79 [12] 55–75 [14] ≥45 [24]	18% [14]	10–21% [12]	12% [24]	48% [42]	1988–1994 [24] 2001 [14] 2003–2007 [42] 2007–2010 [12]
	Canada	45:55 [15]	≥40	8.9%	17%	14%	5.1%	2007–2011
Europe	Austria	55:45 [22]	≥40		26%	95% [17]		2004–2006
	Finland	51:49 [37]	21–70		5.4–9.4%		60%	1995–1996
	Italy	47:53 [21] 49:51 [39]	≥14 [21] >25 [39]	2.8% [21]	11–18% [39]			1998–1991 [39] 2009 [21]
	Netherlands	48:52 [16]	≥40		3%			2000–2007
	Norway	50:50 [30] 38:62 [43]	47–78 [30] ≥40 [43]		9% [30]	66% [30]	26% [43]	1992–1993 [30] 2009–2010 [43]
	Spain	47:53 [35]	40–80		10.2%	73%		2006–2007
	Sweden	48:52 [22]	≥40	12%	10–16%	71%		2004–2006
	Austria	55:45 [22]	≥40		26%	95%		2004–2006
	Finland	51:49 [37]	21–70		5.4–9.4%		60%	1995–1996
Oceania	Australia	53:47 [44]	>55 [44]		19% [13]		31% [44]	2008 [44]
Africa	Nigeria	39:61 [51]	≥40	0.3%	7.7%			
	Malawi	39:61 [53] 42.1:57.9 [52]	≥30 ≥18		13.6% 4.3%			
	Cameroon	0:100 [54]	≥40		1.6%			2012
	Uganda	49.5:50.5 [50]	≥30		16.2%			2012
	South Africa	48:52 [57] 37:63 [87]	≥55 ≥40	11.2%	23.8%			2012
South America	Mexico	39.8:60.2 [63]	40–84	6.03%	20.6%	86.2%	40%	2008
	Peru	49.3:50.7 [62] 49.2:50.8 [88]	≥35 ≥35	0.4% 0.1%	6% 4.8%			2010

(Continued)

Table 1 Continued

Continent	Country	Gender M:F	Age years	Prevalence (self-reported)	Prevalence (spirometry)	Under-diagnosis	Over-diagnosis	Year of data collection
South America (cont.)	Brazil	60.3:39.7 [64] 82.6:17.4 [70]	≥40 15–63	19% 5.1%	31.5% 1.1%	71.4%	14.6%	2011
South-East Asia	China	49.7:50.3 [71] 49.8:50.2 [72, 73] 41:59 [74] 49.6:50.4 [75]	≥35 [71] ≥40 [73]		5.9% [71] 8.2% [72, 73] (male 7.3%; female 6.4%) [74] (overall 13.6%; male 19.0%; female 8.1%) [75]	70% without CB; 30% with CB [72] (overall 88.8%; male 86.2%; female 90.7%) [74]	Urban 81%; rural 62.2% [74] (male 67.7%; female 73.7%) [74]	2000–2001 [71] 2003 [72] 2004–2008 [74] 2014–2015 [75]
	Hong Kong#	NA [76]	≥30		3.5%			2000
	Singapore#	NA [76]	≥30		3.5%			2000
	Thailand#	NA [76]	≥30		5.0%			2000
	Vietnam#	NA [76]	≥30		6.7%			2000
	Malaysia#	NA [76]	≥30		4.7%			2000
	Indonesia#	NA [76]	≥30		5.6%			2000
	Philippines#	NA [76]	≥30		6.3%			2000
	Taiwan#	NA [76]	≥30		5.4%			2000
	South Korea#	NA [76]	≥30		5.9%	36.9% [77]		2000
	Japan#	NA [76]	≥30		6.1%			2000
The Middle East and South Asia	Abu Dhabi	55:45 [78]	40–80		3.7%			
	India	51.6:48.4 [80] 50.2:49.8 [82]	17–64 [79] >35 [80] >30 [81] ≥40 [83]	CB 12.5% [79] 1.1–10% [82]	4.1% [80] 2.44% [81] 5.7–17.3% [83] 4.2% (crude) to 5.5% age-standardised [84]			2007 [81] 2014 [83] 2016 [84]
	Bangladesh	45.7:54.3 [85]	≥40		13.5% (GOLD) and 10.3% (LLN)			2011–2012

#: prevalence estimated. M: males; F: females; NA: not available; CB: chronic bronchitis.

of normal (LLN) associated with underestimation, particularly in the younger population. Three different studies from Denmark demonstrate the variation in prevalence estimates; 17.4% using pre-bronchodilator spirometry [18], 12% using GOLD criteria [19], and 3.9% using FEV_1/FVC <LLN and FEV_1 <80%; [20]. Similar variation has been reported using physician diagnoses with 2.8% in Italy [21], 12% in Sweden [22], and 6.2% in a combined survey of eight European cities [23].

Under-diagnosis of COPD

Despite the ease of access to spirometry in high-income countries, problems arise because of insufficient utilisation of testing, particularly in general practice, or testing not strictly adhering to the guidelines; this forms the basis of under-diagnosis. When spirometry is measured in empirically diagnosed populations, the degree of underestimation varies with the criterion applied. This holds true in the USA, where NHANES and NHANES III reported under-diagnosis rates of 12–72% [24, 25]. Pre-bronchodilator spirometry and a fixed FEV_1/FVC ratio revealed that approximately 70% of individuals with AFO do not have a concurrent physician diagnosis [25]. However, with the inclusion of post-bronchodilator testing (GOLD criteria), approximately 50% of individuals are under-diagnosed [26]. AFO based on the LLN criteria led to a reduced under-diagnosis rate of 12% [24]. Similar under-diagnoses rates have been reported from Canada, ranging from 14% to 70% in the COLD and CanCOLD studies (using GOLD criteria [15, 27]), to 82% (using pre-bronchodilator spirometry and a fixed FEV_1/FVC ratio [28]). However, in the CanCOLD study, LLN-defined AFO did not necessarily lead to a lower estimation of under-diagnosis, as would be expected, with the study reporting a rate of 26% [29]. For individual European countries, the estimates of under-diagnosis using GOLD criteria from randomly sampled populations were generally greater, ranging from 66% in Norway [30] to 95% in Austria [17]. A meta-analysis including North American and European studies reported that under-diagnosis was present in greater than 90% of cases [9].

Within this multi-continental region, patient characteristics, including sex, age, self-perceived health status and FEV_1 impairment were associated with under-diagnosis. Interestingly, separate cohorts from different countries demonstrated that both younger patients [31–33] and older patients [6] were prone to under-diagnosis. Mixed results were also seen with respect to gender, where females were less likely to have a diagnosis in cohorts from Europe [16, 33, 34], but males were less likely in Canada [6]. Preserved quality-of-life scores and a mild to moderate degree of lung function impairment also predicted under-diagnosis in multiple countries [25, 30, 33, 35]. Other factors associated with under-diagnosis include: either

being asymptomatic or presence of mild respiratory symptoms [33]; belonging to a racial or ethnic minority [25]; co-diagnosis of asthma [6]; and presence of lower overall comorbidity [6, 25].

The criteria for diagnosis of AFO can also contribute to under-diagnosis in different age groups. As expected, concurrently applying AFO defined by the LLN *versus* fixed ratio criteria led to lower prevalence estimates in Switzerland (8% *versus* 15.2% [36]) Canada (12% *versus* 17% [28]) and the USA (10.2% *versus* 14.2% [12]). In Europe, many studies over the past decade using the British Thoracic Society and ERS criteria, result in an underestimation compared with GOLD criterion; studies from Sweden and Finland reported almost half the prevalence estimates [37, 38]. The prevalence of COPD in Italy was 11% using the ERS criterion but increased to 18.3% when the GOLD criterion was used [39].

Over-diagnosis of COPD

Most studies examining the prevalence of over-diagnosis used electronic medical registry data in primary care cohorts applying GOLD criteria. Within North America, rates ranged from 16.4% in Canada [40] to 42.5% in the USA [41]. Random sampling of a Canadian population revealed that over-diagnosis occurred in 5.1% of cases [15]. Another large North American study of US veterans demonstrated that overestimation occurred in 48% [42]. European countries also exhibited a significant degree of over-diagnosis and variability, with the lowest estimate from Norway at 25.8% [43], and the highest from Finland at 60% [37]. Similar overestimates (31–42%) were reported by Australian studies [44, 45].

The diagnosis of COPD without spirometry testing is common and unquestionably contributes to the majority of over-diagnosis [46]. This occurs often in the setting of advancing age [17, 47], nonsmokers [6], male sex, higher education levels, and symptoms of chronic bronchitis and other comorbidities [47]. Over-diagnosis is also more common in the setting of elevated body mass index [44, 48] and having an older primary care provider [6]. In addition, the specific spirometry protocol ordered can also influence the results, particularly if regular calibration of equipment is not done. Exclusion of post-bronchodilator spirometry provides an estimate for obstructive lung disease in general, and thus overestimates the prevalence of COPD [25], particularly where prevalence of other obstructive diseases such as asthma is significantly high. Applying a fixed FEV_1/FVC <0.7 rather than the LLN to older populations also leads to an increase in prevalence, as reported by Swiss (15.2% *versus* 8% [36]) and Swedish (16.2% *versus* 10% [22]) studies.

Furthermore, a clinician's reliance on a single spirometry outcome can also lead to overestimation, given the instability demonstrated in serial tests. In fact, in two large cohorts from the USA and Canada, a spirometric diagnosis of COPD was overturned

in 12–27% of individuals. The only predisposing factor for diagnostic reversal was smoking cessation during the 5-year follow-up period [8].

Africa

Epidemiology of COPD

COPD has been poorly studied in Africa, particularly in sub-Saharan countries. An autopsy study performed in Uganda in 1974 reported emphysema was found in 23.5% of lungs [49]. A study in 2012 from rural Ugandan communities reported that the prevalence of spirometry-defined COPD using the GOLD criterion in people older than 30 years of age was 16·2% [50]. The main risk factors were previous smoking history, non-Bantu ethnicity and exposure to biomass fuel for cooking or heating purposes.

However, the prevalence of chronic AFO has differed widely, not only among different countries, but also between different communities within a country. The prevalence of chronic AFO was 7.7% in Ile-Ife in a Nigerian population aged 40 years and over [51] although only 0.3% of people reported a diagnosis of chronic bronchitis, emphysema or COPD. A population-based study in Malawi reported that 4.3% of men and 4.1% of women had post bronchodilator obstruction when spirometry was performed [52].

In many African countries, use of solid fuel (biomass and coal) and paraffin for cooking and heating is quite common and the majority of small-scale cross-sectional studies have reported that it is an independent risk factor for COPD. Self-reported biomass exposure is more common in an African neighbourhood than smoking, particularly among the rural communities, and has an incidence of up to 85.2% [52]. Wood smoke has previously been shown to contribute to reduced lung function in rural Africa, particularly in nonsmoking women [53, 54].

The low prevalence of COPD is thought to be due to a younger population and lower smoking rates than developed countries [55]. Sub-Saharan smoking rates have ranged between 9.2% and 29% for men and 0.7% and 4.0% for women [52, 55].

Under- or over-diagnosis

There is very limited information on the prevalence of under- and over-diagnosis of COPD in Africa. A report by Chan-Yeung et al. [55] in 2004 reported that epidemiological data regarding the prevalence of COPD in a large part of Africa is patchy or localised with reports in local languages only. They reported that prevalence studies require the administration of questionnaires in several languages within the same country with high illiteracy rates, at a higher cost and with the limited availability of spirometry devices. Furthermore, the misdiagnosis of COPD in African communities could also be due to high unfamiliarity with the term "COPD". A qualitative study in rural Ugandan communities found that among the general public, there was poor knowledge on the risk of tobacco and biomass smoke on respiratory health, and the term COPD was almost unknown [56].

Nkosi et al. [57] performed a cross sectional study with face to face interviews to assess the relationship between mine dumps and chronic respiratory disease in a community in South Africa. The prevalence of self-reported chronic bronchitis was 13.4% and that of emphysema was 5.6%.

Sub-Saharan Africa has the greatest proportion of the world's population living with HIV, while having a low proportion of smokers, thus it was hypothesised that HIV may contribute to COPD in this population, and thus be an under-recognised risk factor. However, a case–control study in Cameroon between 2012 and 2013 showed the prevalence of COPD was 5.2% (24/461) in HIV-positive participants and 5% (23/461) in HIV-negative participants, with no statistical correlation between HIV status and increased prevalence of COPD [58].

Previous pulmonary tuberculosis has also been associated with increased prevalence in chronic bronchitis and airflow limitation. A prior history of tuberculosis was associated with an irreversible AFO irrespective of smoking history, and could result in the over-diagnosis of COPD [59, 60].

Central and South America

Epidemiology of COPD

The prevalence of smoking in Central and South America is high, with a median prevalence of 30%, contributing significantly to the burden of respiratory diseases [61]. Studies have assessed the prevalence of COPD in a small number of cities across the region and COPD prevalence has ranged from 7.8% to 19.7%; however, more widespread studies, representative of the different communities in different countries (including isolated areas) have not been performed to date [61]. In Peru, a study of four separate resource-poor areas showed an overall prevalence of 6.0% for COPD, despite a low daily smoking rate of 3.3% [62].

Under- or over-diagnosis

A case-finding study in Mexico in patients with risk factors for COPD reported 20% prevalence of COPD [63]. Of the patients who had a clinical diagnosis of COPD from their family physician, 40% had normal spirometry, while only 13.8% with chronic AFO had been diagnosed clinically with COPD. Queiroz et al. [64] studied 200 patients to understand the potential risk factors for COPD in primary care centres in South Brazil. Based on the results of spirometry (15% of patients), they reported that 71.4% of patients were under-diagnosed for COPD, and 14.6% were over-diagnosed.

Jaganath *et al.* [62] found that in four different areas of Peru, COPD was not fully explained by smoking, and also reported that biomass exposure and tuberculosis were attributable risk factors, particularly in women. A retrospective spirometry and clinical study of 170 patients in Brazil assessed the contribution of risk factors including wood smoke and tobacco exposure [65]. They reported that patients with tobacco smoke had more severe COPD; however, 19.4% of participants had been exposed to wood smoke over a long period, and 85.3% were women. These results are consistent with a study of Mexican Mayan women that showed biomass smoke exposure was associated with more air trapping but less emphysema than tobacco smoke exposure [66]. Women with biomass exposure presented with fewer symptoms than those with tobacco smoke exposure. Thus, exposure to biomass fuel, particularly in nonsmoking women in rural areas, may be underestimated as a risk factor for COPD and may lead to an under-diagnosis. Furthermore, a study from Colombia suggested that replacing biomass fuel with natural gas could reduce the prevalence of severe obstructive lung disease and could be an important public health intervention [67].

Occupational exposure is associated with around 15% of total COPD; however, this has been poorly studied in Central and South America [57, 68, 69]. A study of pig farmers in Brazil showed a prevalence of chronic bronchitis of 5.1% in workers aged more than 40 years [70]. In addition, there was a higher prevalence of chronic bronchitis associated with the use of disinfectants, and significant increase in dyspnoea due to the use of ammonia [68].

South-East Asia

Epidemiology of COPD

The prevalence of COPD in China in population-based surveys ranges from 3.9% to 13.7% in different regions of China. The crude prevalence of COPD was significantly higher in men than in women (7.2–12.4% *versus* 4.7–5.1%), and in rural areas than in urban areas (4.4–8.8% *versus* 6.7–7.8%) [71–73]. A population-based cohort of more than half a million participants from 10 different regions of China reported that the prevalence of COPD based on pre-bronchodilator lung function test (using LLN criteria) was 7.3% in men (range 2.5–18.2%) and 6.4% in women (1.5–18.5%) [74]. The prevalence of COPD was higher in rural areas compared to urban areas for both men (9.2% *versus* 4.8%; p<0.001) and women (7.7% *versus* 4.8%; p<0.001). A recent study of 66752 Chinese individuals older than 40 years of age reported an overall prevalence of COPD of 13.6%, with significant difference between men and women (19.0% *versus* 8.1%; p<0.0001), highest in southwest China (20.2%) and lowest in central China (10.2%) [75]. The difference in prevalence between genders was mainly attributed to smoking status between
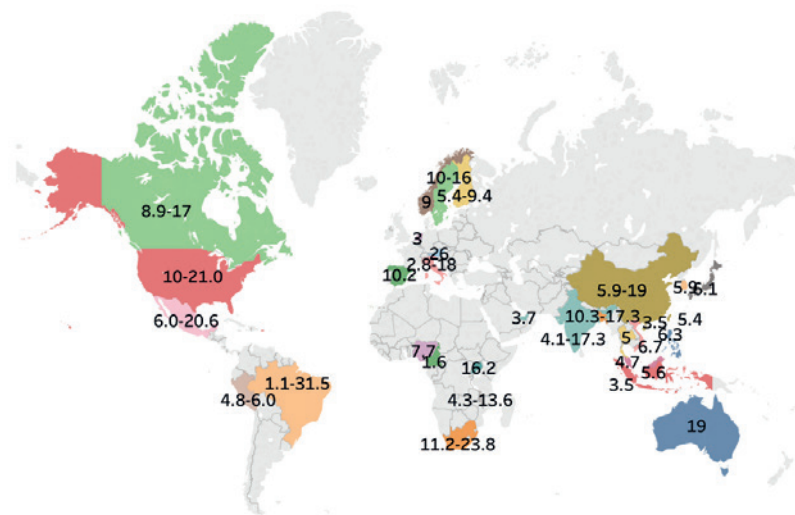
Figure 1 *Prevalence (%) of COPD in different countries. The prevalence data is based on narrative review and not systematic review of all the literature.*

men and women (current smokers 58.2% *versus* 4.0%, respectively). Prevalence data from many other South-East Asian countries are still sparse. COPD prevalence estimates vary widely in Asian countries, with 3.5% in Hong Kong and Singapore, 6.7% in Vietnam, 4.7% in Malaysia, 5% in Thailand, 5.6% in Indonesia, 6.3% in the Philippines, 5.4% in Taiwan, 5.9% in South Korea and 6.1% in Japan [76].

Under- or over-diagnosis of COPD

The prevalence of under-diagnosis in China is greater than that in Western countries. A study from 10 different regions in China reported that the physician correctly diagnosed 11.2% of those with AFO; under-diagnosis was highest (96.7%) among the 30–39 years age group and lowest (81.1%) in those older than 70 years [74]. The prevalence of COPD was higher in rural areas compared to urban areas for both men (9.2% *versus* 4.8%; p<0.001) and women (7.7% *versus* 4.8%; p<0.001). Another population-based study from China sampled 20245 adults and reported an overall prevalence of 8.2% of persistent AFO. Among those who had post-bronchodilator AFO (FEV1/FVC <0.70), only 35% had a previous physician diagnosis of COPD, suggesting that 65% of subjects with chronic AFO in China remain undiagnosed [73].

A study in China recruited 25627 subjects, of whom 20245 (79%) completed questionnaires and performed acceptable spirometry, reported that 1668 subjects (8.2%) had COPD. Among those who had COPD, only 589 (35.3%) reported a history of chronic bronchitis. Among those with AFO and without chronic bronchitis, about 92% were under-diagnosed, compared to 54% those who were symptomatic. Hence, COPD without symptoms of chronic bronchitis is often referred to as "silent", due to their lack of symptoms and under-reporting to the

physician and thus are usually under-diagnosed [72]. A study from Korea showed that 36.9% of COPD patients did not show any respiratory symptoms [77].

It is likely that the use of clinical definitions of COPD based on current symptoms and exposure history and under use of spirometry, particularly in rural areas, have led to the majority of under- and over-diagnosis of COPD. Furthermore, lack of awareness about risk factors other than smoking among physicians had led to delayed diagnosis and interventions for patients with COPD [26].

The Middle East and South Asia

Epidemiology of COPD

A cross-sectional survey in a random sample of individuals 40–80 years old in Abu Dhabi, showed the prevalence of COPD to be 3.7%, with no difference, however, between gender [78].

Around 40 years ago, the prevalence of chronic bronchitis in an industrial town in India was reported to be 12.5% and around five times higher in smokers compared to nonsmokers [79]. Thereafter, many studies have reported COPD prevalence as low as 2.0–4.1% [80, 81]. A study in 2011 conducted in different states of India estimated the self-reported prevalence of chronic bronchitis at 3.5% in India (ranging from 1.1% in Mumbai to 10% in Trivandrum) [82]. The BOLD study in 2014 used standardised spirometry and reported overall COPD prevalence estimates of 5.7%, 6.0% and 17.3% in Pune, Mumbai and Srinagar for males and 6.8%, 7.6% and 14.8% for females, respectively [83]. A recent global burden of diseases study in India reported a 29.2% increase in crude prevalence of COPD from 3.2% in 1990 to 4.2% in 2016; however, the age-standardised prevalence decreased by 5% during the same period (5.8% to 5.5%) [84]. The percentage of total deaths attributed to COPD in India was 8.7% (males 8.7% and females 8.6%) in 2016 and disability adjusted life-years 4.8% (males 5.2% and females 4.4%).

In Bangladesh, the prevalence of COPD was 13.5% by GOLD definition criteria and 10.3% by LLN criteria. The prevalence of COPD was higher among rural than urban residents and in males than females. More than half of the COPD cases were stage II COPD by both criteria. Mild cases (stages I and II) were overestimated by the GOLD fixed criteria, but more severe cases (stages III and IV) were similarly classified [85].

Under- and over-diagnosis

There is a lack of data from the Middle East and South Asia on under- and over-diagnosis of COPD, similar to that from the Africa region. However, under-diagnosis of COPD in the region are likely to
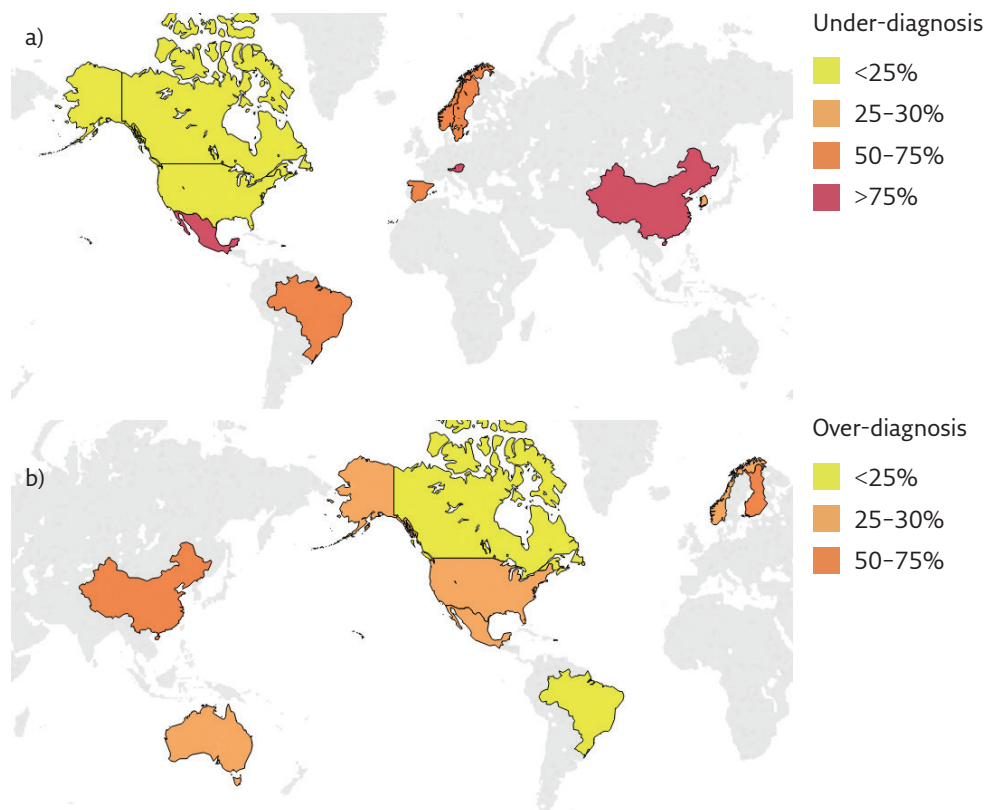
Figure 2 *a) Under- and b) over-diagnosis of COPD.*

be due to the lack of the availability of spirometry, lack of awareness of hazards of various risk factors of COPD, such as exposure to biomass fuel, a low level of education and lack of awareness of the healthcare provider, particularly those in rural areas, who are often semi-skilled [86].

Conclusions

This review on the global assessment of misdiagnosis of COPD has identified large variations in the prevalence of COPD across different geographical regions, ranging between 3% and 21% (figure 1). Estimation of the true burden of COPD will remain a challenge unless a more uniform approach to diagnosis of COPD is adopted by all regions where the associated risk factors are common. One of the major reasons for the huge variation in COPD prevalence is the different criteria used to define COPD. The vast majority of data on under- and over-diagnosis of COPD has been generated from the developed world, whilst very limited or poor quality data is available from LMICs (figure 2). Access to healthcare and under-utilisation of spirometry remains a large global challenge. Although spirometry is recommended for confirmatory diagnosis of COPD, its uniformity of use for test procedures, regular maintenance and calibration remain global challenges. Furthermore, the use of different reference values for lung function, *i.e.* country-specific or Global Lung Function Initiative (GLI) values, remains a hotly debated area but one that is beyond the scope of this review. Additional risk factors for misdiagnosis include age, gender, ethnicity, self-perception of symptoms, co-existent disease, and educational awareness of risk factors, both for the patients and their physicians, are also important.

Self-evaluation questions

1. A 45-year-old female smoker with a 20 pack-year smoking history presents to your clinic with persistent respiratory symptoms over the previous 6 months. You perform spirometry which demonstrates a post-bronchodilator FEV_1/FVC ratio of 0.75 and an FEV_1 of 88% predicted. How would you investigate this patient further to diagnose COPD?
   a) No further testing.
   b) Full pulmonary function test
   c) Repeat spirometry in 3 months
   d) Check if the FEV_1/FVC ratio is below the LLN
2. Which of the following is not a known associated risk factor for under- or over-diagnosis of COPD?
   a) Tuberculosis
   b) Age of patient
   c) Use of spirometry
   d) High protein diet
3. Which of the following is not an independent risk factor for COPD?
   a) Exposure to biomass smoke
   b) Tobacco smoke
   c) Alcohol drinking
   d) Diesel fume exposure
4. Compared to the use of FEV_1/FVC ratio of <0.7, the use of 5% below the LLN results in a lower over-diagnosis of COPD in the elderly?
   a) True
   b) False

Affiliations

Terence Ho[1,5], Ruth P. Cusack[2,5], Nagendra Chaudhary[3,5], Imran Satia[2,5], Om P. Kurmi[4,5]

[1]Firestone Institute of Respiratory Health, Division of Respirology, Dept of Medicine, McMaster University, Hamilton, ON, Canada. [2]Division of Respirology, Dept of Medicine, McMaster University, Hamilton, ON, Canada. [3]Dept of Paediatrics, Universal College of Medical Sciences, Bhairahawa, Nepal. [4]Population Health Research Institute, Division of Respirology, Dept of Medicine, McMaster University, Hamilton, ON, Canada. [5]All authors contributed equally.

Conflict of interest

None declared.

References

1. Vos T, Flaxman AD, Naghavi M, *et al.* Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 2163–2196.
2. Lozano R, Naghavi M, Foreman K, *et al.* Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 2095–2128.
3. Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. *Lancet* 2009; 374: 733–743.
4. Eisner MD, Anthonisen N, Coultas D, *et al.* An official American Thoracic Society public policy statement: novel risk factors and the global burden of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2010; 182: 693–718.
5. Swanney MP, Ruppel G, Enright PL, *et al.* Using the lower limit of normal for the FEV_1/FVC ratio reduces the misclassification of airway obstruction. *Thorax* 2008; 63: 1046–1051.

6. Gershon AS, Hwee J, Chapman KR, et al. Factors associated with undiagnosed and overdiagnosed COPD. Eur Respir J 2016; 48: 561–564.

7. Diab N, Gershon AS, Sin DD, et al. Underdiagnosis and overdiagnosis of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2018; 198: 1130–1139.

8. Aaron SD, Tan WC, Bourbeau J, et al. Diagnostic instability and reversals of chronic obstructive pulmonary disease diagnosis in individuals with mild to moderate airflow obstruction. Am J Respir Crit Care Med 2017; 196: 306–314.

9. Halbert RJ, Natoli JL, Gano A, et al. Global burden of COPD: systematic review and meta-analysis. Eur Respir J 2006; 28: 523–532.

10. Fan W, Lee H, Lee A, et al. Association of lung function and chronic obstructive pulmonary disease with American Heart Association's Life's Simple 7 cardiovascular health metrics. Respir Med 2017; 131: 85–93.

11. Mannino DM, Gagnon RC, Petty TL, et al. Obstructive lung disease and low lung function in adults in the United States: data from the National Health and Nutrition Examination Survey, 1988–1994. Arch Intern Med 2000; 160: 1683–1689.

12. Tilert T, Dillon C, Paulose-Ram R, et al. Estimating the US prevalence of chronic obstructive pulmonary disease using pre- and post-bronchodilator spirometry: the National Health and Nutrition Examination Survey (NHANES) 2007–2010. Respir Res 2013; 14: 103.

13. Buist AS, McBurnie MA, Vollmer WM, et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. Lancet 2007; 370: 741–750.

14. Eisner MD, Balmes J, Katz PP, et al. Lifetime environmental tobacco smoke exposure and the risk of chronic obstructive pulmonary disease. Environ Health 2005; 4: 7.

15. Gershon AS, Thiruchelvam D, Chapman KR, et al. Health services burden of undiagnosed and overdiagnosed COPD. Chest 2018; 153: 1336–1346.

16. Afonso AS, Verhamme KM, Sturkenboom MC, et al. COPD in the general population: prevalence, incidence and survival. Respir Med 2011; 105: 1872–1884.

17. Schirnhofer L, Lamprecht B, Vollmer WM, et al. COPD prevalence in Salzburg, Austria: results from the Burden of Obstructive Lung Disease (BOLD) Study. Chest 2007; 131: 29–36.

18. Fabricius P, Lokke A, Marott JL, et al. Prevalence of COPD in Copenhagen. Respir Med 2011; 105: 410–417.

19. Hansen JG, Pedersen L, Overvad K, et al. Praevalensen af kronisk obstruktiv lungesygdom – sekundaerpublikation. [Prevalence of chronic obstructive pulmonary disease – secondary publication]. Ugeskr Laeg 2009; 171: 2986–2988.

20. Colak Y, Afzal S, Nordestgaard BG, et al. Prognosis of asymptomatic and symptomatic, undiagnosed COPD in the general population in Denmark: a prospective cohort study. Lancet Respir Med 2017; 5: 426–434.

21. Cazzola M, Puxeddu E, Bettoncelli G, et al. The prevalence of asthma and COPD in Italy: a practice-based study. Respir Med 2011; 105: 386–391.

22. Danielsson P, Olafsdottir IS, Benediktsdottir B, et al. The prevalence of chronic obstructive pulmonary disease in Uppsala, Sweden – the Burden of Obstructive Lung Disease (BOLD) study: cross-sectional population-based study. Clin Respir J 2012; 6: 120–127.

23. Boutin-Forzano S, Moreau D, Kalaboka S, et al. Reported prevalence and co-morbidity of asthma, chronic bronchitis and emphysema: a pan-European estimation. Int J Tuberc Lung Dis 2007; 11: 695–702.

24. Coultas DB, Mapel D, Gagnon R, et al. The health impact of undiagnosed airflow obstruction in a national sample of United States adults. Am J Respir Crit Care Med 2001; 164: 372–377.

25. Martinez CH, Mannino DM, Jaimes FA, et al. Undiagnosed obstructive lung disease in the United States. Associated factors and long-term mortality. Ann Am Thorac Soc 2015; 12: 1788–1795.

26. Halbert RJ, Isonaka S, George D, et al. Interpreting COPD prevalence estimates: what is the true burden of disease? Chest 2003; 123: 1684–1692.

27. Labonte LE, Tan WC, Li PZ, et al. Undiagnosed chronic obstructive pulmonary disease contributes to the burden of health care use. Data from the CanCOLD Study. Am J Respir Crit Care Med 2016; 194: 285–298.

28. Evans J, Chen Y, Camp PG, et al. Estimating the prevalence of COPD in Canada: reported diagnosis versus measured airflow obstruction. Health Rep 2014; 25: 3–11.

29. Johnson KM, Tan WC, Bourbeau J, et al. The diagnostic performance of patient symptoms in screening for COPD. Respir Res 2018; 19: 147.

30. Hvidsten SC, Storesund L, Wentzel-Larsen T, et al. Prevalence and predictors of undiagnosed chronic obstructive pulmonary disease in a Norwegian adult general population. Clin Respir J 2010; 4: 13–21.

31. Artyukhov IP, Arshukova IL, Dobretsova EA, et al. Epidemiology of chronic obstructive pulmonary disease: a population-based study in Krasnoyarsk region, Russia. Int J Chron Obstruct Pulmon Dis 2015; 10: 1781–1786.

32. Lindberg A, Jonsson AC, Ronmark E, et al. Prevalence of chronic obstructive pulmonary disease according to BTS, ERS, GOLD and ATS criteria in relation to doctor's diagnosis, symptoms, age, gender, and smoking habits. Respiration 2005; 72: 471–479.

33. Miravitlles M, Ferrer M, Pont A, et al. Characteristics of a population of COPD patients identified from a population-based study. Focus on previous diagnosis and never smokers. Respir Med 2005; 99: 985–995.

34. Jones RC, Price D, Ryan D, et al. Opportunities to diagnose chronic obstructive pulmonary disease in routine care in the UK: a retrospective study of a clinical cohort. Lancet Respir Med 2014; 2: 267–276.

35. Miravitlles M, Soriano JB, Garcia-Rio F, et al. Prevalence of COPD in Spain: impact of undiagnosed COPD on quality of life and daily life activities. Thorax 2009; 64: 863–868.

36. Bridevaux PO, Probst-Hensch NM, Schindler C, et al. Prevalence of airflow obstruction in smokers and never-smokers in Switzerland. Eur Respir J 2010; 36: 1259–1269.

37. Jyrki-Tapani K, Sovijarvi A, Lundback B. Chronic obstructive pulmonary disease in Finland: prevalence and risk factors. COPD 2005; 2: 331–339.

38. Lindberg A, Bjerg A, Ronmark E, et al. Prevalence and underdiagnosis of COPD by disease severity and the attributable fraction of smoking. Report from the Obstructive Lung Disease in Northern Sweden Studies. Respir Med 2006; 100: 264–272.

39. Viegi G, Pedreschi M, Pistelli F, et al. Prevalence of airways obstruction in a general population: European Respiratory Society versus American Thoracic Society definition. Chest 2000; 117: 339S–345S.

40. Hill K, Goldstein RS, Guyatt GH, et al. Prevalence and underdiagnosis of chronic obstructive pulmonary disease among patients at risk in primary care. CMAJ 2010; 182: 673–678.

41. Ghattas C, Dai A, Gemmel DJ, et al. Over diagnosis of chronic obstructive pulmonary disease in an underserved patient population. Int J Chron Obstruct Pulmon Dis 2013; 8: 545–549.

42. Collins BF, Ramenofsky D, Au DH, et al. The association of weight with the detection of airflow obstruction and inhaled treatment among patients with a clinical diagnosis of COPD. Chest 2014; 146: 1513–1520.

43. Melbye H, Drivenes E, Dalbak LG, et al. Asthma, chronic obstructive pulmonary disease, or both? Diagnostic labeling and spirometry in primary care patients aged 40 years or more. Int J Chron Obstruct Pulmon Dis 2011; 6: 597–603.

44. Walters JA, Walters EH, Nelson M, et al. Factors associated with misdiagnosis of COPD in primary care. Prim Care Respir J 2011; 20: 396–402.

45. Zwar NA, Marks GB, Hermiz O, et al. Predictors of accuracy of diagnosis of chronic obstructive pulmonary disease in general practice. Med J Aust 2011; 195: 168–171.

46. Gershon AS, Guan J, Victor JC, et al. Quantifying health services use for chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2013; 187: 596–601.

47. Pena VS, Miravitlles M, Gabriel R, et al. Geographic variations in prevalence and underdiagnosis of COPD: results of the IBERPOC multicentre epidemiological study. Chest 2000; 118: 981–989.

48. Centurion VP, Huang F, Naureckas ET, *et al.* Confirmatory spirometry for adults hospitalized with a diagnosis of asthma or chronic obstructive pulmonary disease exacerbation. *BMC Pulm Med* 2012; 12: 73.

49. Jones AW, Madda PJ. Necropsy incidence of emphysema in Uganda. *Thorax* 1974; 29: 195–198.

50. van Gemert F, Kirenga B, Chavannes N, *et al.* Prevalence of chronic obstructive pulmonary disease and associated risk factors in Uganda (FRESH AIR Uganda): a prospective cross-sectional observational study. *Lancet Glob Health* 2015; 3: e44–e51.

51. Obaseki DO, Erhabor GE, Gnatiuc L, *et al.* Chronic airflow obstruction in a black African population: results of BOLD Study, Ile-Ife, Nigeria. *COPD* 2016; 13: 42–49.

52. Meghji J, Nadeau G, Davis KJ, *et al.* Noncommunicable lung disease in Sub-Saharan Africa. A community-based cross-sectional study of adults in urban Malawi. *Am J Respir Crit Care Med* 2016; 194: 67–76.

53. Fullerton DG, Suseno A, Semple S, *et al.* Wood smoke exposure, poverty and impaired lung function in Malawian adults. *Int J Tuberc Lung Dis* 2011; 15: 391–398.

54. Mbatchou Ngahane BH, Afane Ze E, Chebu C, *et al.* Effects of cooking fuel smoke on respiratory symptoms and lung function in semi-rural women in Cameroon. *Int J Occup Environ Health* 2015; 21: 61–65.

55. Chan-Yeung M, Ait-Khaled N, White N, *et al.* The burden and impact of COPD in Asia and Africa. *Int J Tuberc Lung Dis* 2004; 8: 2–14.

56. Van Gemert F, Chavannes N, Nabadda N, *et al.* Impact of chronic respiratory symptoms in a rural area of sub-Saharan Africa: an in-depth qualitative study in the Masindi district of Uganda. *Prim Care Respir J* 2013; 22: 300–305.

57. Nkosi V, Wichmann J, Voyi K. Chronic respiratory disease among the elderly in South Africa: any association with proximity to mine dumps? *Environ Health* 2015; 14: 33.

58. Pefura-Yone EW, Fodjeu G, Kengne AP, *et al.* Prevalence and determinants of chronic obstructive pulmonary disease in HIV infected patients in an African country with low level of tobacco smoking. *Respir Med* 2015; 109: 247–254.

59. Lam KB, Jiang CQ, Jordan RE, *et al.* Prior TB, smoking, and airflow obstruction: a cross-sectional analysis of the Guangzhou Biobank Cohort Study. *Chest* 2010; 137: 593–600.

60. Sarkar M, Srinivasa Madabhavi I, *et al.* Tuberculosis associated chronic obstructive pulmonary disease. *Clin Respir J* 2017; 11: 285–295.

61. Menezes AM, Victora CG, Perez-Padilla R. The Platino project: methodology of a multicenter prevalence survey of chronic obstructive pulmonary disease in major Latin American cities. *BMC Med Res Methodol* 2004; 4: 15.

62. Jaganath D, Miranda JJ, Gilman RH, *et al.* Prevalence of chronic obstructive pulmonary disease and variation in risk factors across four geographically diverse resource-limited settings in Peru. *Respir Res* 2015; 16: 40.

63. Laniado-Laborin R, Rendon A, Bauerle O. Chronic obstructive pulmonary disease case finding in Mexico in an at-risk population. *Int J Tuberc Lung Dis* 2011; 15: 818–823.

64. Queiroz MC, Moreira MA, Rabahi MF. Underdiagnosis of COPD at primary health care clinics in the city of Aparecida de Goiania, Brazil. *J Bras Pneumol* 2012; 38: 692–699.

65. Moreira MA, Moraes MR, Silva DG, *et al.* Comparative study of respiratory symptoms and lung function alterations in patients with chronic obstructive pulmonary disease related to the exposure to wood and tobacco smoke. *J Bras Pneumol* 2008; 34: 667–674.

66. Camp PG, Ramirez-Venegas A, Sansores RH, *et al.* COPD phenotypes in biomass smoke- *versus* tobacco smoke-exposed Mexican women. *Eur Respir J* 2014; 43: 725–734.

67. Alvis-Guzman N, De la Hoz-Restrepo F, Montes-Farah J, *et al.* Effect of biomass smoke on chronic obstructive pulmonary disease in rural localities of Colombia. *Rev Salud Publica (Bogota)* 2013; 15: 589–600.

68. Mehta AJ, Miedinger D, Keidel D, *et al.* Occupational exposure to dusts, gases, and fumes and incidence of chronic obstructive pulmonary disease in the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults. *Am J Respir Crit Care Med* 2012; 185: 1292–1300.

69. Lopez-Campos JL, Fernandez-Villar A, Calero-Acuna C, *et al.* Occupational and biomass exposure in chronic obstructive pulmonary disease: results of a cross-sectional analysis of the On-Sint Study. *Arch Bronconeumol* 2017; 53: 7–12.

70. Costa M, Teixeira PJ, Freitas PF. Respiratory manifestations and respiratory diseases: prevalence and risk factors among pig farmers in Braco do Norte, Brazil. *J Bras Pneumol* 2007; 33: 380–388.

71. Xu F, Yin X, Zhang M, *et al.* Prevalence of physician-diagnosed COPD and its association with smoking among urban and rural residents in regional mainland China. *Chest* 2005; 128: 2818–2823.

72. Lu M, Yao W, Zhong N, *et al.* Chronic obstructive pulmonary disease in the absence of chronic bronchitis in China. *Respirology* 2010; 15: 1072–1078.

73. Zhong N, Wang C, Yao W, *et al.* Prevalence of chronic obstructive pulmonary disease in China: a large, population-based survey. *Am J Respir Crit Care Med* 2007; 176: 753–760.

74. Kurmi OP, Li L, Smith M, *et al.* Regional variations in the prevalence and misdiagnosis of air flow obstruction in China: baseline results from a prospective cohort of the China Kadoorie Biobank (CKB). *BMJ Open Respir Res* 2014; 1: e000025.

75. Fang L, Gao P, Bao H, *et al.* Chronic obstructive pulmonary disease in China: a nationwide prevalence study. *Lancet Respir Med* 2018; 6: 421–430.

76. Regional COPD Working Group. COPD prevalence in 12 Asia-Pacific countries and regions: projections based on the COPD prevalence estimation model. *Respirology* 2003; 8: 192–198.

77. Chang JH, Lee JH, Kim MK, *et al.* Determinants of respiratory symptom development in patients with chronic airflow obstruction. *Respir Med* 2006; 100: 2170–2176.

78. Al Zaabi A, Asad F, Abdou J, *et al.* Prevalence of COPD in Abu Dhabi, United Arab Emirates. *Respir Med* 2011; 105: 566–570.

79. Joshi RC, Madan RN, Brash AA. Prevalence of chronic bronchitis in an industrial population in North India. *Thorax* 1975; 30: 61–67.

80. Jindal SK, Aggarwal AN, Chaudhry K, *et al.* A multicentric study on epidemiology of chronic obstructive pulmonary disease and its relationship with tobacco smoking and environmental tobacco smoke exposure. *Indian J Chest Dis Allied Sci* 2006; 48: 23–29.

81. Johnson P, Balakrishnan K, Ramaswamy P, *et al.* Prevalence of chronic obstructive pulmonary disease in rural women of Tamilnadu: implications for refining disease burden assessments attributable to household biomass combustion. *Glob Health Action* 2011; 4: 7226.

82. Jindal SK, Aggarwal AN, Gupta D, *et al.* Indian study on epidemiology of asthma, respiratory symptoms and chronic bronchitis in adults (INSEARCH). *Int J Tuberc Lung Dis* 2012; 16: 1270–1277.

83. Burney P, Jithoo A, Kato B, *et al.* Chronic obstructive pulmonary disease mortality and prevalence: the associations with smoking and poverty – a BOLD analysis. *Thorax* 2014; 69: 465–473.

84. India State-Level Disease Burden Initiative CRD Collaborators. The burden of chronic respiratory diseases and their heterogeneity across the states of India: the Global Burden of Disease Study 1990–2016. *Lancet Glob Health* 2018; 6: e1363–e1374.

85. Alam DS, Chowdhury MA, Siddiquee AT, *et al.* Prevalence and determinants of chronic obstructive pulmonary disease (COPD) in Bangladesh. *COPD* 2015; 12: 658–667.

86. KalagoudaMahishale V, Angadi N, Metgudmath V, *et al.* The prevalence of chronic obstructive pulmonary disease and the determinants of underdiagnosis in women exposed to biomass fuel in India – a cross section study. *Chonnam Med J* 2016; 52: 117–122.

87. Buist AS, Vollmer WM, McBurnie MA. Worldwide burden of COPD in high- and low-income countries. Part I. The Burden of Obstructive Lung Disease (BOLD) initiative. *Int J Tuberc Lung Dis* 2008; 12: 703–708.

88. Miele CH, Jaganath D, Miranda JJ, *et al.* Urbanization and daily exposure to biomass fuel smoke both contribute to chronic bronchitis risk in a population with low prevalence of daily tobacco smoking. *COPD* 2016; 13: 186–195.

Suggested answers

1. c.
2. d.
3. c.
4. a.