



Obstructive lung diseases burden and COVID-19 in developing countries: a perspective

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Purpose of review

Asthma and chronic obstructive pulmonary disease (COPD) are widely prevalent disorders, and important contributors to morbidity and mortality, in both developing and developed countries. It is conjectured that these obstructive lung diseases may have had more deleterious effects in developing nations during the 2019 coronavirus disease (COVID-19) pandemic. We provide an evidence-based perspective on the relationship between asthma/COPD prevalence and COVID-19 burden, and the impact of comorbid asthma/COPD on selected COVID-19 outcomes and healthcare utilization, with special reference to developing countries.

Recent findings

Developing countries with higher COPD (but not asthma) prevalence appear to have higher COVID-19 related mortality. Patients with asthma (but not COPD) in developing countries may be less likely to acquire COVID-19. Published literature suggests that the overall impact of comorbid asthma or COPD on adverse COVID-19 outcomes may be broadly similar between developed and developing nations.

Summary

There is paucity of information on interaction between asthma/COPD and COVID-19 in developing countries. Limited data suggest minor differences between developed and developing nations. In view of inadequacies in healthcare preparedness and delivery in several developing countries, there is a need to generate quality evidence to assess impact of obstructive lung diseases and COVID-19 on each other.

Keywords

asthma, chronic obstructive pulmonary disease, COVID-19, mortality, prevalence

INTRODUCTION

The ongoing 2019 coronavirus disease (COVID-19) pandemic results from infection with the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). At the time of undertaking this review, the global burden of COVID-19 exceeded 225 million (about 2.9% of the world population) [1]. Currently, the USA, a developed country, contributed maximum to this case load (more than 42 million people affected), followed by India, a developing country (more than 33 million people affected). On the basis of these estimates, about 12.5% of the U.S. population, and about 2.4% of the Indian population can be considered to have had proven COVID-19 disease [1]. It is widely assumed that the officially reported figures on COVID-19 are an underestimate, more so from the developing nations. Although a relatively younger population in lower-income countries might decrease the overall risk of adverse COVID-19 outcomes, but a limited health system capacity and a

much closer inter-generational contact likely negates this benefit [2]. The inadequate health infrastructure in most developing countries is also more likely to get overwhelmed in face of the large COVID-19 burden. The overall health and economic consequences from COVID-19 are therefore expected to be far greater for the developing nations.

Chronic respiratory diseases are associated with greater use of healthcare resources, significant morbidity and higher risk of death [3]. Asthma and chronic obstructive pulmonary disease (COPD) are the two most important chronic respiratory diseases

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KEY POINTS

- There is relative paucity of information regarding interactions between asthma/COPD and COVID-19 in developing countries.
- Patients with asthma (but not COPD) in developing countries may be less likely to acquire COVID-19.
- The overall impact of comorbid asthma or COPD on adverse COVID-19 outcomes may be broadly similar between developing and developed countries.

of public health significance. The prevalence of both disorders shows great regional variability, although they are relatively more prevalent in high-income countries [3]. COPD contributes much more to global mortality and morbidity than asthma [3]. Although south Asian countries show comparatively lower prevalence than other geographic regions, their mortality and morbidity attributable to asthma and COPD remain much higher than the rest of world [3].

The interactions between obstructive lung diseases (both asthma and COPD) and COVID-19 have been examined in several studies and systematic reviews. A recent systematic review of 150 studies reported a much higher summary asthma prevalence among COVID-19 patients in the USA (11.0%) as compared to Europe (7.6%) or Asia (1.9%) [4[•]]. However, in contrast to patients hospitalized with influenza, COVID-19 inpatients had a much lower prevalence of underlying asthma [5]. Nonetheless, asthma appears to have at best a marginal impact on adverse clinical outcomes such as severe COVID-19, need for hospitalization, ICU admission or mortality [4[•],6]. COPD, on the contrary, significantly worsens clinical outcomes among COVID-19 patients by a magnitude much larger than that for asthma [7[•],8–11]. Despite this, the prevalence of COPD might be lower than asthma among patients with COVID-19, and some reviews with a limited number of studies suggest wide variability in estimates with summary prevalence of around 2–3% [8,12,13].

Most studies reporting information on the prevalence and outcomes of obstructive lung diseases in COVID-19 patients have been conducted in the USA, Europe or China. There is little published data on this subject from the developing world. A modelling study suggested that chronic respiratory diseases increase population COVID-19 mortality in India, a developing nation with high COVID-19 burden, by 1.88% relative to England, a developed nation [14]. Our review attempts to fill this

knowledge gap. We provide an evidence-based perspective on the relationship between asthma/COPD prevalence and COVID-19 burden, variations in prevalence of comorbid asthma/COPD among COVID-19 patients, impact of comorbid asthma/COPD on selected COVID-19 outcomes and health-care utilization by asthma/COPD patients during the COVID-19 pandemic, with special reference to developing countries.

LITERATURE SEARCH AND DATA COLLECTION

We queried the PubMed database using the search string [(‘chronic obstructive pulmonary disease’ OR COPD OR asthma OR ‘chronic respiratory disease’) AND (COVID-19 OR SARS-CoV-2)]. We identified 1928 publications indexed till 31 July 2020, without imposing any geographic, temporal or linguistic restrictions. We searched for studies reporting data on prevalence or outcomes of comorbid asthma/COPD among COVID-19 patients, or those describing patterns of healthcare usage by asthma/COPD patients during the COVID-19 pandemic. We looked at two commonly reported clinical outcomes: COVID-19 severity, described by a composite of patients needing hospital admission or having severe COVID-19 disease defined as per the prevalent WHO or another guidance, and mortality. On the basis of a review of titles and abstracts, we excluded 1327 articles not focusing on COVID-19 or chronic respiratory diseases; autopsy, radiologic, experimental or modelling studies; narrative and systematic reviews; and clinical guidelines, case reports, editorials, letters to editor and comments. We reviewed the full text of remaining publications to assess eligibility for inclusion in this review. We excluded multicountry studies, articles not reporting outcomes of interest, studies reporting data from highly specific patient populations (e.g. cancer patients, patients on dialysis or patients in ICUs) and those summarizing information from 100 COVID-19 patients or less. In all, 310 studies met our inclusion criteria. We also hand-searched the bibliographies of recent reviews and key articles and identified 138 additional relevant publications. Finally, 448 studies were considered for data-synthesis, of which 397 provided prevalence and/or outcome data, and 51 reported information regarding healthcare resource utilization (Tables S1 and S2 of online supplement, <http://links.lww.com/COPM/A29>). Prevalence of asthma/COPD was computed as the proportion of COVID-19 patients having comorbid asthma/COPD in each study. We constructed 2 x 2 contingency tables for each study reporting patient outcome data and

calculated the relative risk (RR) and corresponding 95% confidence interval (95% CI) for each outcome of interest for COVID-19 patients with comorbid asthma/COPD, as compared to those without (Table S1 of online supplement, <http://links.lww.com/COPM/A29>). RRs were pooled across studies to generate summary estimates using random effects models.

In the absence of any universally accepted definition for a developing country, we adopted the World Bank approach (based on per capita gross national income) for the current 2022 fiscal year. Low-income and lower-middle-income economies were categorized as developing nations, and the other high-income or upper-middle-income economies as developed nations [15]. We acquired the national asthma and COPD prevalence rates from estimations projected for various countries by the Global Burden of Disease (GBD) collaborators [16]. We also queried the Worldometer database to obtain cumulative COVID-19 burden estimates for different countries [1].

COVID-19 BURDEN AND PREVALENCE OF OBSTRUCTIVE LUNG DISEASES

We noted wide variability in COVID-19 burden, and asthma/COPD prevalence, estimates across both developed and developing countries. The median COVID-19 prevalence in the general population of developed nations was 6.4% [interquartile range

(IQR) 2.7–9.5]. The prevalence was much lower for developing countries (median 0.4%, IQR 0.2–1.3) (Table 1). Similarly, the mortality rates from COVID-19 (per million population) were also lower for the developing countries than for developed countries (median 67.5, IQR 20.2–272.7 vs. median 972.0, IQR 335.2–1759.7). The median prevalence of asthma and COPD in the developed countries were 4.1% (IQR 3.2–5.8) and 2.7% (IQR 1.5–4.4), respectively. The median prevalence of both disorders in the developing nations were relatively lower at 3.1% (IQR 2.5–4.1) and 1.1% (IQR 1.0–1.7), respectively (Table 1).

There was no significant change in COVID-19 burden (both prevalence and mortality) in either developed or developing countries, with change in national asthma prevalence estimates (Fig. 1). On the contrary, countries with higher population prevalence of COPD also reported higher national COVID-19 burden. The relative increase in cumulative COVID-19 cases with rising national COPD prevalence was similar in both developed and developing nations, despite seemingly lower COPD prevalence estimates in the latter. However, developing countries appeared to have far greater COVID-19-related mortality with rising national COPD prevalence, as compared to the developed countries (Fig. 1). Overall, the patterns in developing countries look like those in developed countries, despite the differences in national burdens of COVID-19 and obstructive lung diseases.

Table 1. Comparison of summary estimates of COVID-19 and obstructive lung diseases from developing and developed countries

	Developing countries	Developed countries
National COVID-19 burden, median (IQR)		
Prevalence (%)	0.38 (0.15–1.34)	6.39 (2.74–9.49)
Mortality (per million)	67.5 (20.2–272.7)	972.0 (335.2–1759.7)
National prevalence of obstructive lung diseases, median (IQR)		
Asthma (%)	3.13 (2.49–4.07)	4.06 (3.20–5.76)
Chronic obstructive pulmonary disease (%)	1.12 (0.96–1.67)	2.69 (1.50–4.40)
Prevalence of comorbid obstructive lung diseases among COVID-19 patients, median (IQR)		
Asthma (%)	2.02 (1.92–3.45)	8.49 (4.19–12.56)
Chronic obstructive pulmonary disease (%)	3.63 (1.78–7.89)	6.00 (3.14–10.35)
Summary relative risk (95% CI) of severe COVID-19/ hospitalization among COVID-19 patients having comorbid obstructive lung diseases		
Asthma	1.21 (1.17–1.25)	1.16 (1.08–1.25)
Chronic obstructive pulmonary disease	1.48 (1.30–1.69)	2.02 (1.82–2.23)
Summary relative risk (95% CI) of mortality among COVID-19 patients having comorbid obstructive lung diseases		
Asthma	1.01 (0.80–1.28)	0.86 (0.80–0.93)
Chronic obstructive pulmonary disease	2.69 (1.56–4.62)	2.20 (1.98–2.43)

95% CI, 95% confidence interval; IQR, interquartile range.

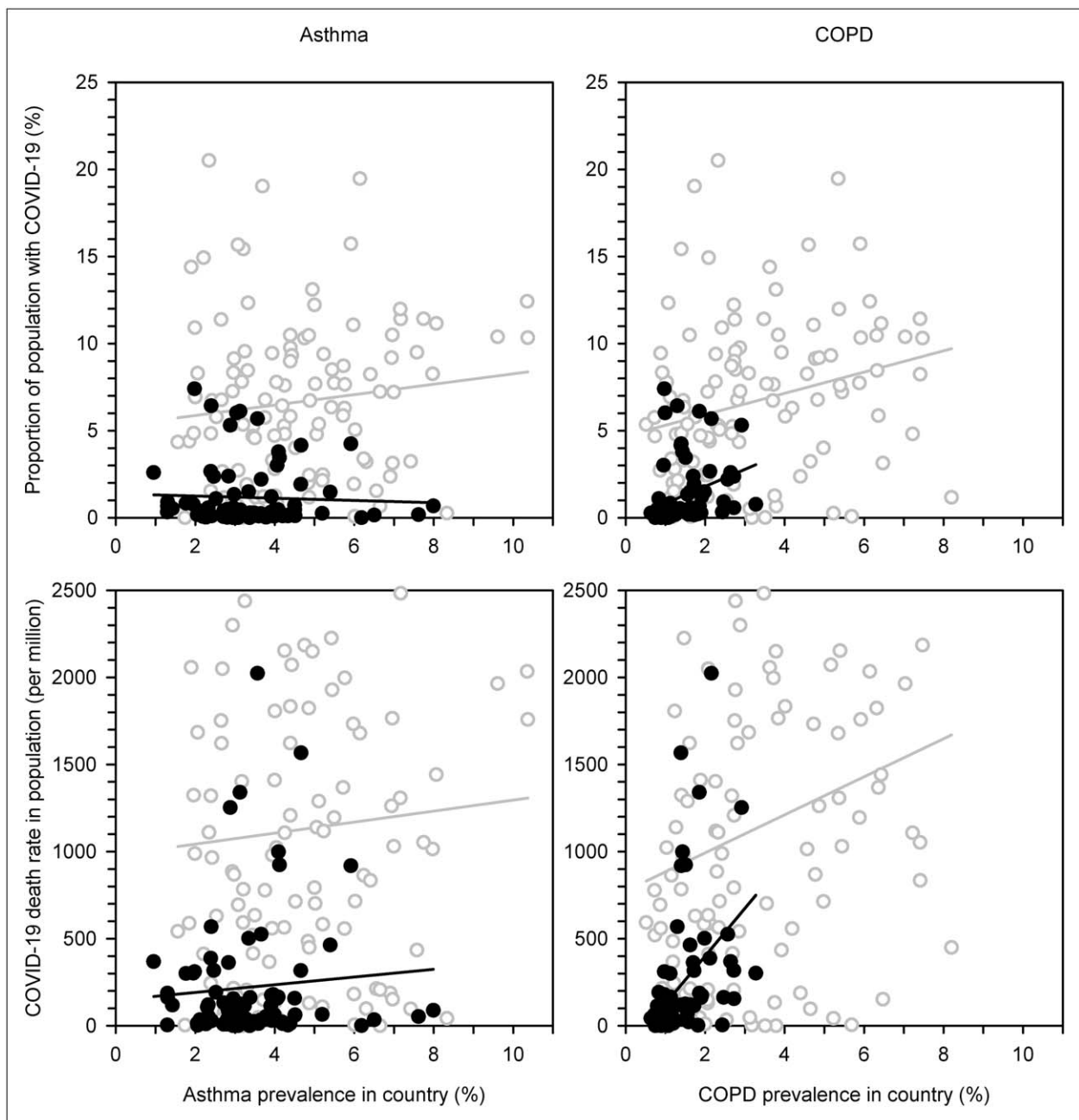


FIGURE 1. Scatterplot summarizing the relationship between national COVID-19 burden, and the corresponding national prevalence of asthma or chronic obstructive pulmonary disease (COPD), in developed (hollow grey circles) and developing (solid black circles) countries. Results from linear regression of data are depicted through straight lines in each graph.

Clinical implications

A previous study reporting information from 93 countries had also suggested that COVID-19 case-fatality rates were relatively higher in countries with higher COPD prevalence, and in countries with a relatively higher per capita gross domestic product (GDP) [17]. The steeper trajectory of the relationship between COPD prevalence and COVID-19-related mortality in developing nations (Fig. 1) is difficult

to explain but could be related to differences in level of comorbidities among patients, or to inequalities in distribution of healthcare resources. Differences between asthma and COPD on a national level suggest that asthma (unlike COPD) may not be a significant risk factor for either acquiring COVID-19 or leading to adverse clinical outcomes from COVID-19, in both developed and developing countries.

COMORBID OBSTRUCTIVE LUNG DISEASES AMONG COVID-19 PATIENTS

From our literature review, we identified 279 and 307 publications providing data on proportion of COVID-19 patients having comorbid asthma or COPD, respectively. Of these, only 22 studies [16 (5.7%) on asthma and 14 (4.6%) on COPD] reported on information from a developing country (Table S1 of online supplement, <http://links.lww.com/COPM/A29>) [18–39]. Among studies from developing countries providing data on asthma or COPD, seven (43.8%) and five (35.7%), respectively, were conducted in Iran [18,20,21,25,28–30,35,36].

Different studies reported great variability in the proportion of COVID-19 patients having asthma or COPD (Table S1 of online supplement, <http://links.lww.com/COPM/A29>). For instance, 121 studies on COVID-19 patients from the USA, a developed country, reported asthma prevalence ranging between 2.0 and 29.8%, and 99 studies reported COPD prevalence ranging from 1.0 to 22.9%. Studies in developing countries described 0.6–8.9% COVID-19 patients as having asthma, and 0.3–12.0% patients as having COPD. In general, studies from developing countries reported a lower prevalence of comorbid asthma or COPD as compared to studies from developing countries (Table 1).

The prevalence of COPD among COVID-19 patients was marginally or substantially higher than the corresponding national prevalence in most (174, 59.4%) studies from developed countries (Fig. 2). Similarly, the prevalence of COPD among COVID-19 patients was marginally or substantially higher than the corresponding national prevalence in most (14, 85.7%) studies from developing countries. The prevalence of asthma among COVID-19 patients was also marginally or substantially higher than the corresponding national prevalence in most (153, 68.2%) studies from developed countries. In contrast, the prevalence of asthma among COVID-19 patients was marginally or substantially lower than the corresponding national prevalence in most (12, 75.0%) studies from developing countries (Fig. 2).

Clinical implications

We cannot draw any firm conclusions from these observations because studies from developing countries were few and had enrolled a variable number of patients in diverse clinical settings. Nevertheless, it seems that asthmatic individuals in developing countries may be less likely to acquire COVID-19 as compared to asthmatic individuals in developed countries. In contrast, COPD patients in both

developed and developing countries are more likely to acquire COVID-19.

OBSTRUCTIVE LUNG DISEASES AND COVID-19 OUTCOMES

We also evaluated whether the presence of comorbid asthma or COPD altered the risk of adverse COVID-19 outcomes differently in developed and developing nations. From our literature review, we could identify 62 studies providing data on comorbid asthma and COVID-19 severity (of which two were from developing countries), 70 studies providing data on comorbid COPD and COVID-19 severity (of which two were from developing countries), 76 studies providing data on comorbid asthma and COVID-19 mortality (of which five were from developing countries) and 101 studies providing data on comorbid COPD and COVID-19 mortality (of which six were from developing countries) (Table S1 of online supplement, <http://links.lww.com/COPM/A29>). Overall, we found only nine studies conducted in developing nations that describe either or both of our selected COVID-19 outcomes with reference to asthma or COPD [22,26–28,30,34–36,38].

The RR of severe COVID-19 or hospitalization for COVID-19 patients also having asthma varied widely between 0.18 and 3.87 across studies, with most (37, 59.7%) reporting values above 1.0 (implying higher risk for asthmatics) (Fig. 3). Summary RRs were 1.16 (1.08–1.25) and 1.21 (95% CI 1.17–1.25) for data from developed (60 studies) and developing (two studies) countries. This suggests that that COVID-19 patients with comorbid asthma are marginally more likely have severe COVID-19 or require hospitalization as compared to COVID-19 patients without asthma, in both developing and developed countries (Table 1).

The RR of mortality for COVID-19 patients also having asthma varied widely between 0.22 and 6.53 across studies, with most (57, 75.0%) reporting values below 1.0 (implying lower risk for asthmatic individuals) (Fig. 3). Summary RRs were 0.86 (0.80–0.93) and 1.01 (95% CI 0.80–1.28) for data from developed (71 studies) and developing (five studies) countries. This suggests that that COVID-19 patients with comorbid asthma in developed countries are less likely to die as compared to COVID-19 patients without asthma, while the limited data from developing countries are equivocal (Table 1).

The RR of severe COVID-19 or hospitalization for COVID-19 patients also having COPD varied widely between 0.60 and 9.11 across studies, with only three (4.3%) reporting values below 1.0. This implied an overall higher risk for COPD patients (Fig. 3). Summary RRs were 2.02 (1.82–2.23) and

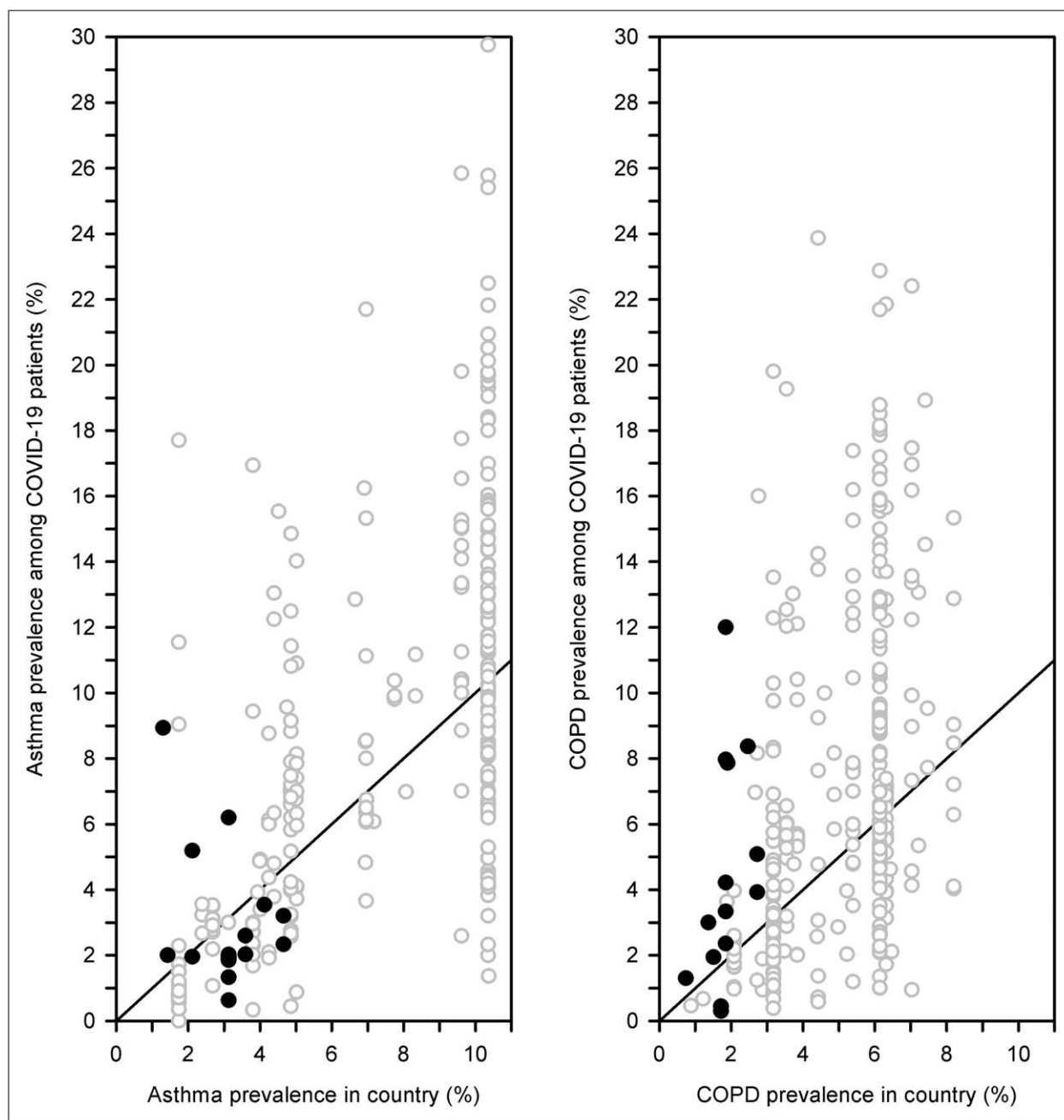


FIGURE 2. Scatterplot summarizing the relationship between prevalence of comorbid asthma or chronic obstructive pulmonary disease (COPD) among COVID-19 patients in individual studies, and the corresponding national prevalence of asthma or COPD, for data from developed (hollow grey circles) and developing (solid black circles) countries. The diagonal line marks the position of equity wherein population prevalence is same as prevalence among COVID-19 patients.

1.48 (95% CI 1.30–1.69) for data from developed (68 studies) and developing (two studies) countries. This suggests that that COVID-19 patients with comorbid COPD are more likely to have severe COVID-19 or require hospitalization as compared to COVID-19 patients without COPD, and this risk might be slightly lower in developed countries based on limited data (Table 1).

The RR of mortality for COVID-19 patients also having COPD varied widely between 0.43 and 12.12 across studies, with only three (3.0%) reporting values below 1.0. This implied an overall higher risk for COPD patients (Fig. 3). Summary RRs were 2.20 (1.98–2.43) and 2.69 (95% CI 1.56–4.62) for data from developed (95 studies) and developing (six studies) countries. This suggests that that COVID-

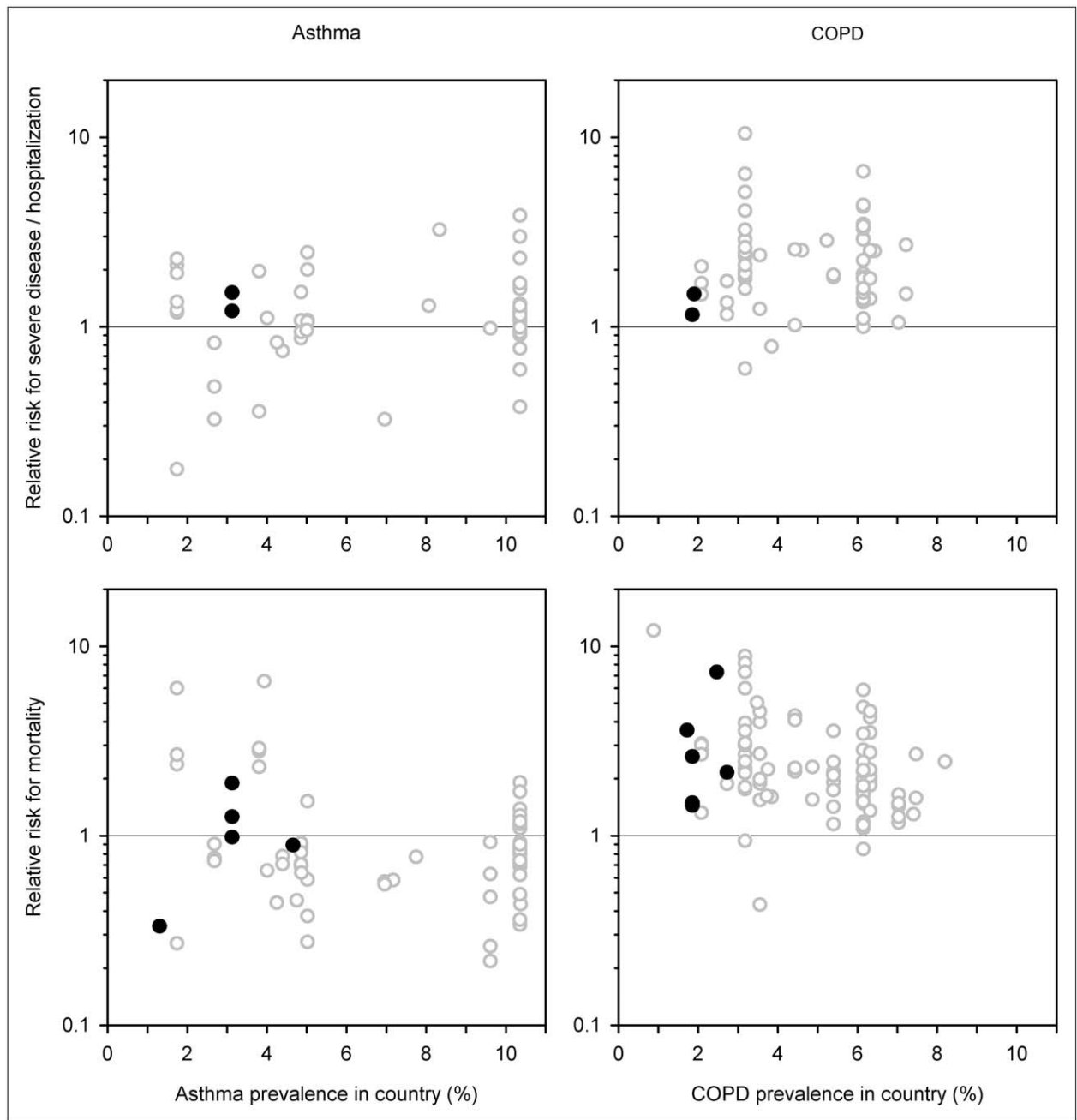


FIGURE 3. Scatterplot summarizing the relationship between relative risk of selected adverse clinical outcomes among COVID-19 patients with comorbid asthma or chronic obstructive pulmonary disease (COPD) in individual studies, and the corresponding national prevalence of asthma or COPD, for data from developed (hollow grey circles) and developing (solid black circles) countries.

19 patients with comorbid COPD are more likely to die as compared to COVID-19 patients without COPD, in both developing and developed countries (Table 1).

Clinical implications

Overall, the impact of comorbid asthma or COPD on COVID-19 outcomes appears similar between

developed and developing countries. There does not appear to be any correlation between this risk and national prevalence of asthma (Fig. 3).

HEALTHCARE UTILIZATION RELATED TO OBSTRUCTIVE LUNG DISEASES

We identified 51 publications describing alterations in patterns of healthcare utilization by patients with

asthma or COPD during the COVID-19 pandemic, mostly from the USA (16, 31.4%) or the UK (8, 15.7%). These studies point to reductions in disease exacerbations, emergency department visits and hospital and ICU admissions among patients with COPD, as well as adult and paediatric asthma (Table S2 of online supplement, <http://links.lww.com/COPM/A29>). Unfortunately, none of these studies reported information from a developing country.

Clinical implications

The changes in healthcare utilization mainly occurred due to lockdown conditions imposed to check COVID-19 spread. Other contributing factors could be related to reduced transmission of other airborne infections because of shielding strategies commonly employed by people with respiratory disorders, potential improvement in air quality due to diminished air pollution, widespread usage of telehealth services and individual changes in healthcare-seeking behaviours and thresholds. However, both the delivery of healthcare, and compliance to social distancing norms, are quite different in the developing world. It is therefore not possible for us to comment if developing countries can expect similar benefits.

FUTURE DIRECTIONS AND CONCLUSION

A major limitation of our review is the paucity of published literature from developing countries regarding interactions between asthma/COPD and COVID-19. Limited data points to only minor differences between developed and developing nations, but uncertainties remain. It is possible that such information is available through local or regional journals that we could not locate through the PubMed database. We used national-level estimates for burden of both COVID-19 and obstructive lung diseases. However, all such estimates suffer from some degree of imprecision. Moreover, they do not reflect variations between regions or subpopulations, especially in large or populous nations. Our categorization of developing and developed nations was based solely on economic criteria as a surrogate, whereas 'development' also has other social, educational, health and technological facets. COVID-19 pandemic has a dynamic character, and our estimates and their importance, as well as the health system responses, are likely to change with time. Most of the studies included for analysis had a retrospective design, and collated data from medical records that were likely completed in an overwhelmed health system. This could have resulted

in both underreporting as well as misclassification of comorbid conditions and health outcomes.

It is well known that the healthcare infrastructure and health delivery in several developing countries has proved quite inadequate in face of the COVID-19 onslaught. Researchers and health programme managers from the developing world need to generate quality evidence from these regions to help determine the impact of COVID-19 and obstructive lung diseases on each other. Such information will be extremely useful to design and implement appropriate mitigation strategies tailored to the requirements of developing countries.

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Conflicts of interest

There are no conflicts of interest.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

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