ORIGINAL ARTICLE

# Asthma in Adult Patients with COVID-19
## Prevalence and Risk of Severe Disease

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## Abstract

**Rationale:** Health outcomes of people with coronavirus disease (COVID-19) range from no symptoms to severe illness and death. Asthma, a common chronic lung disease, has been considered likely to increase the severity of COVID-19, although data addressing this hypothesis have been scarce until very recently.

**Objectives:** To review the epidemiologic literature related to asthma's potential role in COVID-19 severity.

**Methods:** Studies were identified through the PubMed (MEDLINE) and medRxiv (preprint) databases using the search terms "asthma," "SARS-CoV-2" (severe acute respiratory syndrome coronavirus 2), and "COVID-19," and by cross-referencing citations in identified studies that were available in print or online before December 22, 2020.

**Measurements and Main Results:** Asthma prevalence data were obtained from studies of people with COVID-19 and regional health statistics. We identified 150 studies worldwide that allowed us to compare the prevalence of asthma in patients with COVID-19 by region, disease severity, and mortality. The results of our analyses do not provide clear evidence of increased risk of COVID-19 diagnosis, hospitalization, severity, or mortality due to asthma.

**Conclusions:** These findings could provide some reassurance to people with asthma regarding its potential to increase their risk of severe morbidity from COVID-19.

**Keywords:** asthma; SARS-CoV-2; COVID-19; disease severity; mortality

Coronavirus disease (COVID-19) emerged in Wuhan City, Hubei Province, China, as a pneumonia of unknown origin, and it was declared an international public health emergency in February of 2020 (1). Shortly thereafter, in March of 2020, the World Health Organization (WHO) declared that the situation had escalated to pandemic status. As of January 1, 2021, there have been over 83 million confirmed cases of COVID-19 worldwide and over 1.8 million deaths attributed to the pandemic (2).

Health outcomes of individuals infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, range from the lack of any symptoms to severe illness and death (3).

In addition to advanced age, suspected risk factors for developing severe illness due to SARS-CoV-2 infection include the presence of comorbidities, such as cardiovascular disease, obesity, certain malignancies, and diabetes (3). Asthma is a highly prevalent chronic inflammatory disease of the airways that afflicts over 330 million people worldwide (4). Because SARS-CoV-2 is primarily a respiratory virus, people with asthma are apprehensive that they may be at increased risk of acquiring COVID-19 and suffer poorer outcomes. Among younger patients hospitalized with COVID-19 in the United States, obesity, asthma, and diabetes were the most common comorbidities (5). The CDC and WHO have each stated that people with asthma are more vulnerable to

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Data Availability: Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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## At a Glance Commentary

**Scientific Knowledge on the Subject:** People with asthma are considered to be more vulnerable to becoming severely ill with coronavirus disease (COVID-19). However, many aspects of COVID-19 pathophysiology are under investigation, and the relationship between asthma and COVID-19 severity is unclear.

**What This Study Adds to the Field:** We used prevalence data from 150 studies conducted worldwide to assess whether asthma increases the risk of morbidity and severity of COVID-19. The results of our analyses do not provide clear evidence of increased risk of COVID-19 diagnosis, hospitalization, severity, or mortality due to asthma.

becoming severely ill with COVID-19 (6, 7). These statements are consistent with the chronic inflammation and airways dysfunction characterizing asthma, and the increased frequency and severity of respiratory infections in patients with asthma, such as is the case with influenza (8). In fact, the human rhinovirus, the most common cause of the common cold, is a potent trigger of asthma exacerbations (9). However, many aspects of COVID-19 pathophysiology remain unclear, and emerging data from epidemiologic studies have not consistently supported an increased risk of COVID-19 severity in people with asthma. Given these uncertainties, we used prevalence data from studies conducted worldwide to assess whether susceptibility to COVID-19 diagnosis, hospitalization, or severity are altered in people with asthma.

## Methods

Studies included in this article were identified by searching the PubMed (MEDLINE) and medRxiv (preprint) databases, using the search terms "asthma," "SARS-Cov-2," and "COVID-19," and by cross-referencing citations in identified studies that were available in print or online before December 22, 2020 (Figure 1). We did not consider studies that focused on pediatric cases, those that excluded patients without asthma, those that excluded symptomatic patients, those that examined asthma inseparably from chronic obstructive pulmonary disease (COPD), those that analyzed patients who were COVID-19 positive inseparably from individuals who were COVID-19 negative, or those with a study population that largely overlapped that of another published study. In this way, we identified 150 studies that examined the prevalence of asthma in approximately 1 million people with confirmed COVID-19 in more than 30 countries. Given the marked geographic variation in reported asthma prevalence, we performed analyses by region, and in some regions where a large number of studies were conducted (United States, New York City, Mexico, Europe, South Korea, and China), we sought estimates of asthma prevalence in general populations to interpret published data in their regional context.

We calculated the overall prevalence of asthma in study populations, as well as the prevalence of asthma in people hospitalized and not hospitalized with COVID-19. Among hospitalized patients, we compared the prevalence of asthma according to categories of COVID-19 severity and mortality. The severity of COVID-19 was categorized in various ways in previous studies. When studies dichotomized hospitalized (still living) patients as having "severe" versus "not severe" COVID-19, we abstracted asthma prevalence data into those same categories in our analyses, even though the underlying criteria for such classification may have varied among those studies. Other studies dichotomized patients as requiring "ICU" versus "no ICU," which was our primary measure of COVID-19 severity. Secondary measures of severity included requiring "invasive mechanical ventilation" versus "no invasive mechanical ventilation," "critical" versus "not critical," or having COVID-19 that "progressed" versus "stabilized." We considered people in the first category to have "severe" COVID-19 and those in the second to have "not severe" disease.

### Statistical Methods

A series of meta-analyses using the Freeman-Tukey transformation were performed to establish the pooled proportion of asthma in people with COVID-19 overall in the examined studies and according to hospitalization, COVID-19 severity, COVID-19 positivity, and mortality. The weighted final proportion was calculated for each meta-analysis. Cochran's $Q$ test was used to test for heterogeneity of effects across the reported results in the studies. Random-effects models were used for each meta-analysis. Forest plots were produced to provide a visual depiction of the meta-analysis findings.

A separate series of meta-analyses were conducted to produce the weighted pooled prevalence ratio (PR) of asthma for hospitalized versus nonhospitalized participants, those with severe COVID-19 versus nonsevere COVID-19, COVID-19–positive versus COVID-19–negative participants, and those who died versus survived, as defined above. The heterogeneity of the treatment effects in each model was accounted for using Mantel-Haenszel analyses to generate the pooled PR for the random-effects models. The meta-analyses associated with pooled prevalence and PR were performed using scistat.com (MedCalc Software).

Finally, a meta-analysis was performed to test for a pooled effect associated with adjusted odds ratios from studies in which confounding variables were taken into account when testing for associations between asthma and COVID-19 mortality. That analysis was performed using the "metan" function in Stata (StataCorp).

## Results

Among the studies that were included in our analysis (Figure 1), we analyzed the prevalence of asthma in people with COVID-19 by geographic region, severity, and mortality.

### Asthma Prevalence by Geographic Region

North American studies were conducted in the United States, Canada, and Mexico (*see* Table E1 in the online supplement). The pooled prevalence for asthma in 63 studies conducted in the United States ($n = 351{,}728$) (5, 10–71) was 11.0% (95% confidence interval [CI], 9.8–12.3%). In 19 studies conducted in the New York City region ($n = 50{,}256$) (10–28), the pooled prevalence for asthma was 8.7% (95 % CI, 7.3–10.2%). In five studies conducted in Mexico ($n = 409{,}800$) (72–76), the pooled prevalence was 2.9% (95 % CI, 2.8–3.1%). In 31 studies conducted in Europe ($n = 203{,}978$) (70, 77–106), the pooled prevalence was 7.6% (95 % CI, 6.0–9.4%). Asian studies were conducted primarily in

China and South Korea. In 11 studies conducted in China ($n = 4{,}050$) (107–117), the pooled prevalence was 1.9% (95 % CI, 0.4–4.4%). In nine studies conducted in South Korea ($n = 37{,}938$) (70, 118–125), the pooled prevalence was 5.4% (95 % CI, 2.3–9.6%). Data regarding asthma prevalence in people with COVID-19 in Canada (126), Brazil (127–129), India (130, 131), Bangladesh (132, 133), the Philippines (134), Japan (135, 136), Africa (137–140), Iran (141, 142), Kuwait (143), Turkey (144–146), Israel (147–149), and Saudi Arabia (150) were relatively sparse, making them difficult to characterize by country, but they were generally within the range of the prevalences reported above.

### Asthma Prevalence by Severity of COVID-19

Twenty-six studies provided data on the prevalence of asthma in people who were hospitalized with COVID-19 and those who were deemed well enough to be sent home with the disease (Tables 1 and E1 and E2 and Figure 2) (12, 20, 23, 27, 31, 32, 34, 35, 37, 39, 43, 50, 51, 53, 54, 56, 59, 73–75, 86, 89, 121, 147, 148, 151). The prevalence of asthma in these two groups was 10.0% (95% CI, 8.0–12.2%) and 9.5% (95% CI, 8.0–11.0%), respectively. The pooled PR for hospitalized individuals versus those not hospitalized was 1.06 (95% CI, 0.94–1.19; $P = 0.37$).

Forty-two studies provided data on asthma prevalence among living patients hospitalized with COVID-19 according to disease severity (Tables 1 and E1 and E2 and Figure 3) (11, 12, 16, 18, 19, 28, 31–34, 37, 41, 45, 48, 56, 59, 73–75, 86, 87, 98–100, 102–104, 110, 111, 113–115, 121, 130, 132, 135, 136, 142–144, 150, 151). The prevalence of asthma in patients with "severe" and "not severe" COVID-19 was 8.7% (95% CI, 6.9–10.7%) and 9.1% (95% CI, 7.8–10.5%), respectively. The pooled PR for asthma according to COVID-19 severity was 1.18 (95% CI, 0.98–1.42; $P = 0.07$).

We examined the prevalence of asthma in 43 studies that provided data from patients who either died of COVID-19 or survived (Tables 1 and E1 and E2 and Figure 4) (13, 15, 18, 20, 21, 23, 25, 30–33, 37, 46, 53, 61, 67, 74, 77, 81, 82, 85, 88, 97, 98, 102, 105, 106, 118, 119, 121, 129, 133, 134, 141–146, 151–154). The prevalence of asthma in these two groups was 6.8% (95% CI, 5.7–8.0%) and 8.4% (95% CI, 7.2–9.8%), respectively. The pooled PR for asthma among patients who died of COVID-19 versus those who survived was 0.85 (95 % CI, 0.71–1.01; $P = 0.07$). The majority of these meta-analyses yielded statistically significant heterogeneity indices related to the pooled effects (Table E2).

### Studies That Adjusted Relative Measures of Association for Confounding Factors

Multivariable modeling was used in a subset of 24 studies of asthma and COVID-19 mortality (13, 17, 24, 29, 46, 58, 74, 76, 78, 82, 90, 98, 105, 118, 119, 124, 127, 143, 146, 152, 155–158), with adjustment for such factors as age, sex, ethnicity/race, education, and various comorbidities. These studies showed meta-odds ratio = 0.82 (95% CI, 0.79–0.85; $P < 0.001$), albeit with significant heterogeneity ($I^2 = 59.1\%$; 95% CI, 29.7–72.9) (Table E2).

### Asthma Prevalence in People Testing Positive versus Negative for SARS-CoV-2

Seventeen studies compared asthma prevalence among people with suspected COVID-19 who subsequently tested positive for SARS-CoV-2 with those who tested negative ($n = 1{,}828{,}284$) (17, 21, 27, 37, 38, 47, 49, 55, 73, 79, 80, 125, 126, 128, 144, 147, 149). Asthma prevalence was significantly lower among people who tested positive (7.8%; 95 % CI, 5.1–11.1%) than among those who tested negative (10.2%; 95 % CI, 7.5–13.3%) (Table E2). One of these studies compared asthma prevalence among people

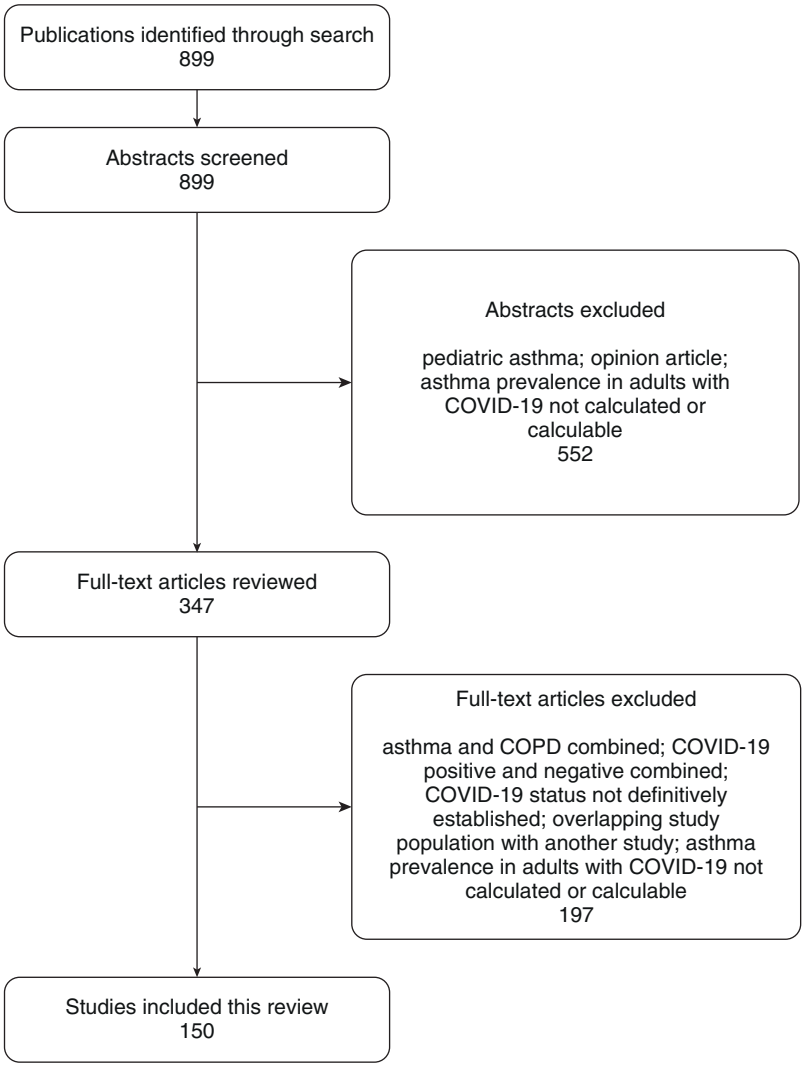


**Figure 1.** Literature acquisition flow diagram. COPD = chronic obstructive pulmonary disease; COVID-19 = coronavirus disease.

**Table 1.** Summary of Asthma Prevalence Data by Measures of COVID-19 Severity

| | Hospital Admission* | | COVID-19 Severity† | | COVID-19 Survival‡ | |
|---|---|---|---|---|---|---|
| | Hospitalized | Not Hospitalized | Severe | Not Severe | Died | Survived |
| Asthma prevalence, % | 10.0 (8.0–12.2) | 9.5 (8.0–11.0) | 9.9 (7.8–12.3) | 8.2 (7.0–10.0) | 7.1 (5.6–8.8) | 8.6 (7.0–10.3) |
| Pooled prevalence ratio | 1.06 (0.94–1.19); $P = 0.37$ | | 1.18 (0.98–1.42); $P = 0.07$ | | 0.89 (0.77–1.02); $P = 0.09$ | |

*Definition of abbreviation*: COVID-19 = coronavirus disease.
Numbers in the parentheses are 95% confidence intervals.
*Hospitalization: 26 studies, $n = 385,737$.
†Severity (among patients who survived during the study period): 42 studies, $n = 180,770$.
‡Mortality: 43 studies, $n = 311,732$.

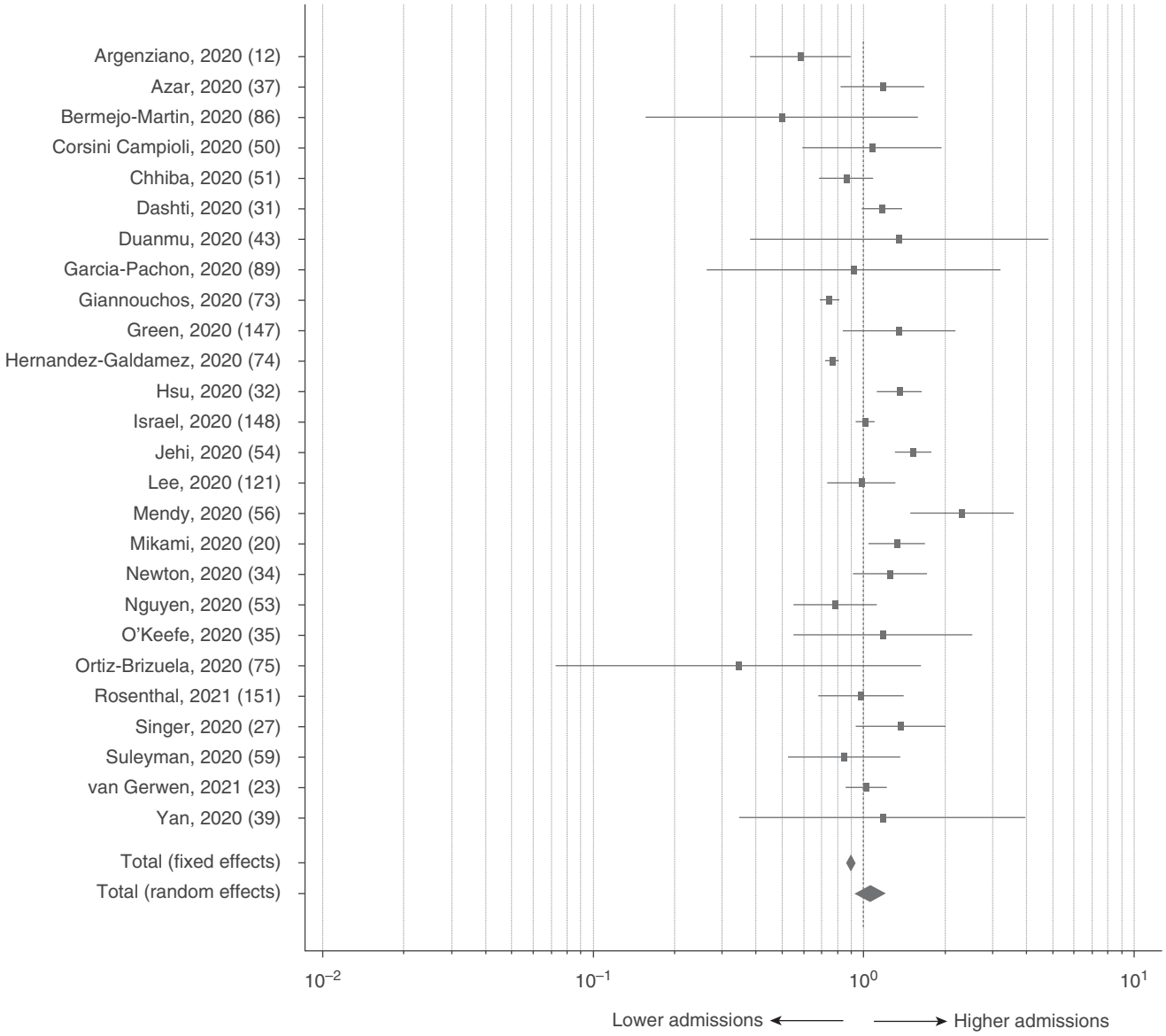


**Figure 2.** Prevalence ratios of asthma in hospitalized versus not hospitalized patients with COVID-19; pooled prevalence ratio = 1.06 (95% confidence interval, 0.94–1.19; $P = 0.37$). COVID-19 = coronavirus disease.

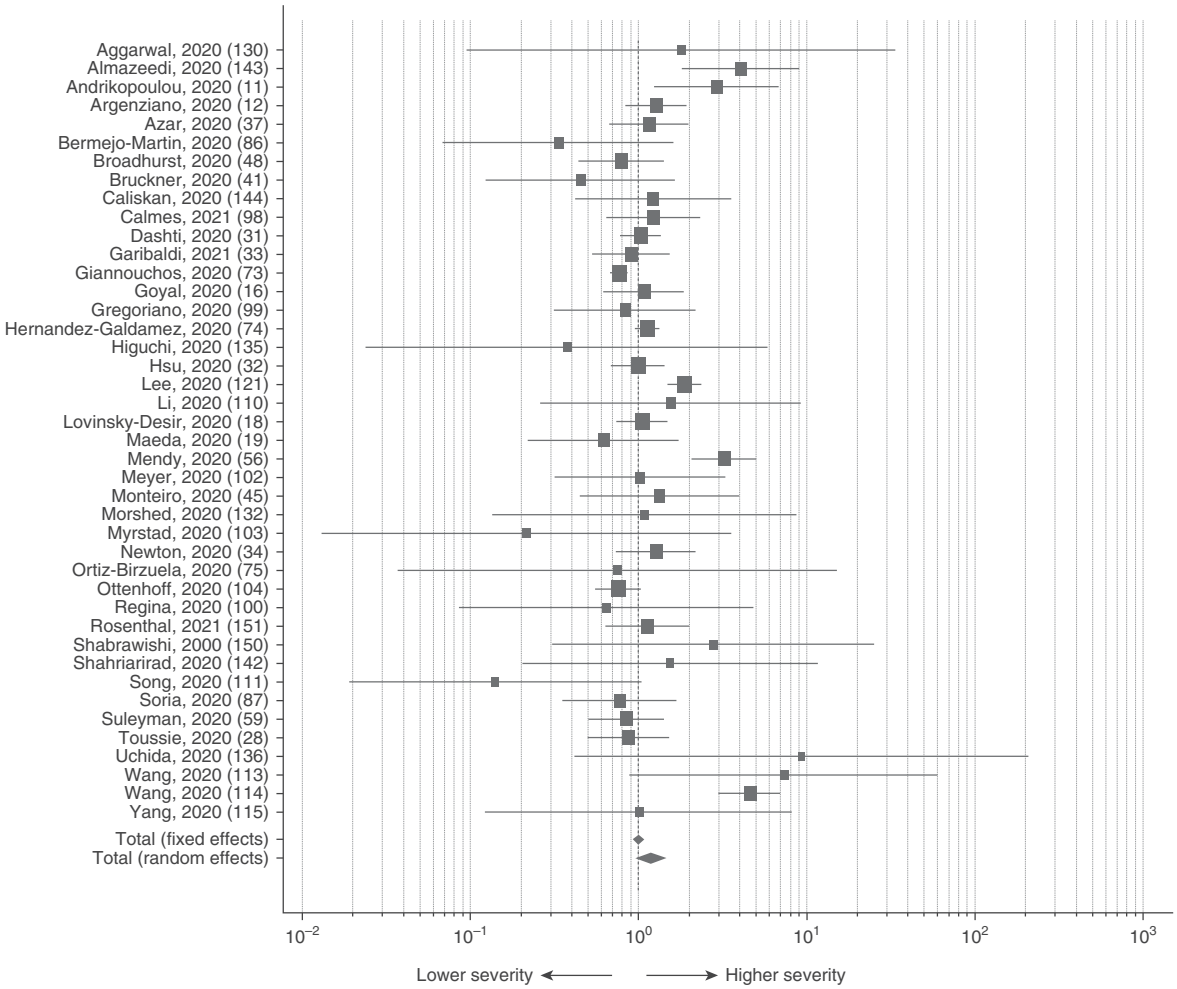


**Figure 3.** Prevalence ratios of asthma in "severe" versus "not severe" patients hospitalized with COVID-19; pooled prevalence ratio = 1.18 (95% confidence interval, 0.98–1.42; $P = 0.07$). COVID-19 = coronavirus disease.

who tested positive for SARS-CoV-2 with that among remaining members of their large cohort, who were not tested (79). In that study, asthma prevalence was higher in those who tested positive (13.2% vs. 11.5%). The pooled PR for asthma prevalence in these 17 studies was 0.74 (95% CI, 0.68–0.81; $P < 0.001$).

## Discussion

The questions addressed in our analyses are among those that would seem most meaningful to people who have asthma in a time of high respiratory-related morbidity and mortality from a novel infectious disease of unclear etiology, one for which there is limited treatment. The public health significance of these questions is underscored by the high worldwide prevalence of asthma and the relatively rapid appearance in the literature of many studies addressing aspects of the association between asthma and COVID-19. However, the results and conclusions presented here should be viewed in light of the likelihood that the results of many additional relevant studies will be available in the near future.

### Does Asthma Increase the Risk of Contracting Morbid COVID-19?

The prevalence of asthma in study populations diagnosed with COVID-19 can be compared with that among regional general populations, possibly suggesting whether patients with asthma are more likely than average to be negatively affected by SARS-CoV-2. In 63 U.S.-based studies, for example, the prevalence of asthma in people with COVID-19 was 11.0%, approximately 43% higher than the estimated 7.7% of adults with asthma in the general U.S. population, including adults over age 65 (159). This suggests the possibility that individuals with asthma may be more likely than individuals without asthma to be diagnosed with COVID-19 in the United States. In 19 studies conducted in the New York City region, however, the prevalence of asthma in patients with COVID-19 was 8.7%, which is approximately the same as the 8.8% estimated prevalence among adults in New York City (160). In 31 studies conducted in Europe, the prevalence of asthma in patients with COVID-19 was 7.6%, which is 7% lower than the estimated 8.2% prevalence among adults in Europe (161). Likewise, the pooled prevalence of asthma in studies of people with COVID-19 conducted in Mexico (2.9%), Korea (5.4%), and China (1.9%) is similar to, or lower than, estimates from general population surveys in those countries (162–164).

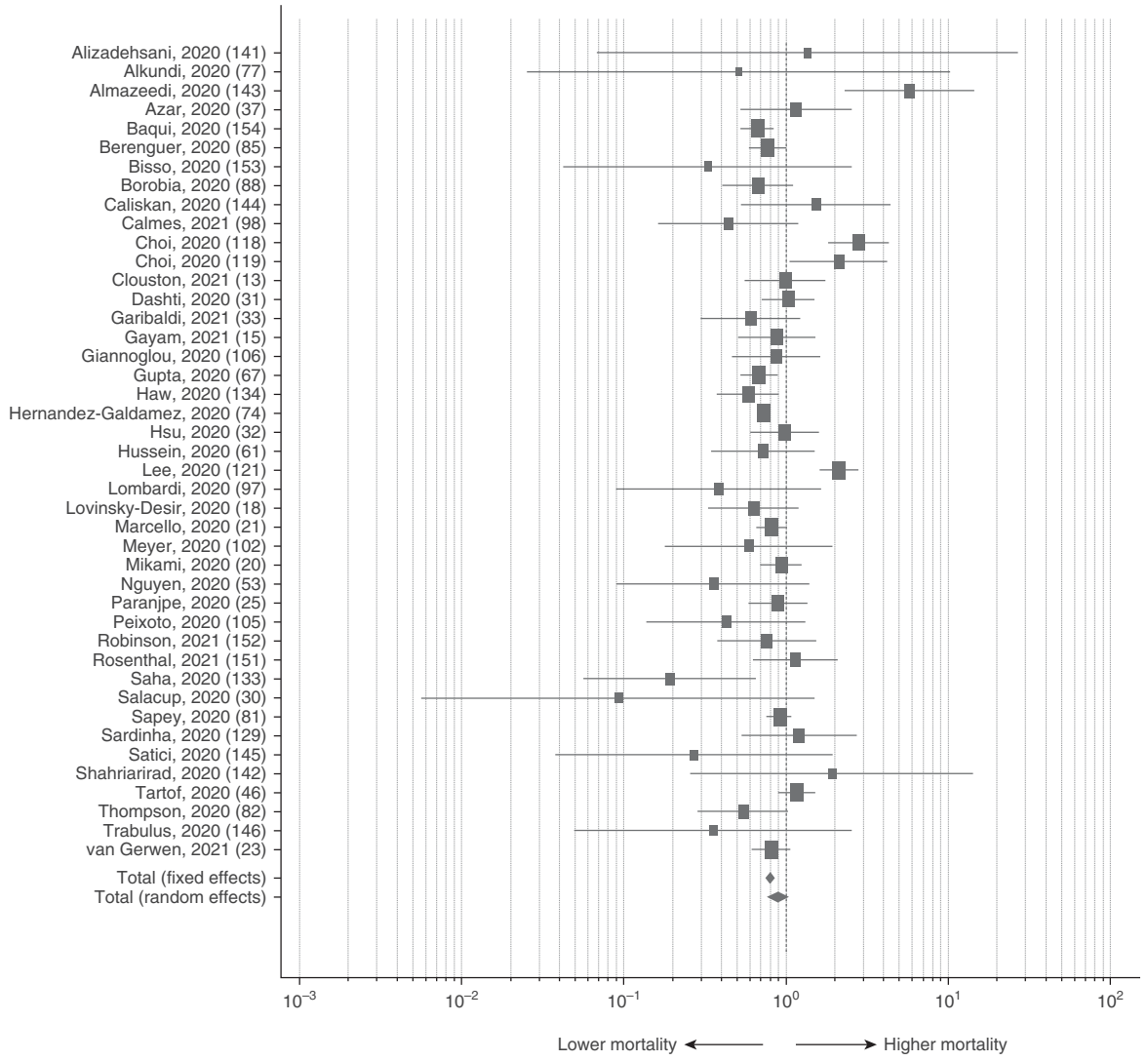


**Figure 4.** Prevalence ratios of asthma by survival status ("died" vs. "survived") in patients hospitalized with COVID-19; pooled prevalence ratio = 0.89 (95% confidence interval, 0.77–1.02; $P = 0.09$). COVID-19 = coronavirus disease.

Comparisons of asthma prevalence in studies of people with morbid COVID-19 with that in general population surveys are problematic, with population estimates varying among samples and over time, and with generally no standardization for such factors as age, sex, race/ethnicity, and the methods by which asthma was diagnosed. At best, such comparisons using data from the studies we reviewed crudely suggest that there are no obvious trends toward higher asthma prevalence in study populations afflicted with COVID-19 compared with regional general populations.

In our review, 17 studies compared asthma prevalence among people with suspected COVID-19 who subsequently tested positive with those who tested negative. In those studies, investigators classified patients' asthma status using standardized electronic health records within the same hospital or health system. The results do not support an increased risk of COVID-19 morbidity in people with asthma; rather, they suggest the possibility of a moderate decreased risk.

### Does Asthma Increase the Severity of COVID-19?

Asthma prevalence was compared among people hospitalized with COVID-19 and ambulatory patients; among surviving hospitalized patients with "severe" and "nonsevere" COVID-19; and among those surviving and not surviving the disease. None of these comparisons showed strong or statistically significant differences. Unlike studies comparing asthma prevalence among study populations with that among local populations, these pooled PRs related to COVID-19 hospitalization, severity, and mortality were based on asthma prevalence assessed similarly among study participants with the same disease, COVID-19, underlying their visit to the same hospitals during the same time periods. Furthermore, our analysis of 24 studies that adjusted asthma's association with mortality for factors such as age, sex, ethnicity/race, and education, does not suggest that an appreciable harmful effect of asthma on COVID-19 severity was masked by confounding. Of course, in the latter studies, there is still potential bias from confounding by other factors.

Several other studies relating asthma to COVID-19 severity have been conducted that were not included in our analyses. A case series of 1,827 adults with laboratory-confirmed

COVID-19 in Boston, Massachusetts (data not included in our analyses because all participants had asthma), showed similar COVID-19 severity and mortality risks when compared with all patients with COVID-19 in the Mass General Brigham system during the same time period (165). Likewise, a cohort of patients with severe asthma and COVID-19 in Italy showed a hospitalization rate similar to that in the general Italian population (166). In Spain, a survey of the medical records of 71,192 patients with asthma showed 1.4% had been diagnosed with COVID-19 (167), considerably lower than the approximately 4% diagnosis in the Spanish population (168). Investigators at the CDC used data from the national Veterans Health Administration to compare asthma prevalence in 3,948 hospitalized patients with COVID-19 (March 1 to May 31, 2020) with that in 5,453 hospitalized patients with influenza (October 1, 2018, to February 1, 2020) (66). The prevalence of asthma in patients with COVID-19 (6.9%) was significantly lower than that in patients with influenza (10.5%). Similarly, the prevalence of asthma in patients hospitalized with COVID-19 (14.3%) was lower than that among patients hospitalized with influenza (27.3%) during the same time period in Finland, although the study was small and statistical significance for this difference was lacking (169). A multivariable analysis using data from electronic health records of over 17 million adults with suspected COVID-19 in London, England, in the National Health Service database, showed a hazard ratio of death for "asthma with no recent use of oral corticosteroids" of 0.99 (95% CI, 0.93–1.05), whereas the estimate for "asthma with recent use of oral corticosteroids" was 1.13 (95% CI, 1.01–1.26) (170). That study analyzed "suspected" cases of COVID-19 that were not necessarily diagnostically confirmed and therefore may include false positives. Although the possibility of effect modification by oral corticosteroid use is of interest, a recent systematic review (171), in agreement with recent mechanistic data (172), found that "there is no evidence to support the withdrawal of ICS [inhaled corticosteroids] in patients treated with these drugs, and to do so is likely to be harmful." Overall, these data, together with those discussed above, do not support a clear increased risk of COVID-19 severity among most people with asthma.

### Biological Mechanisms

The presumption that asthma increases the risk of COVID-19 severity and mortality is consistent with the chronic inflammatory infiltration and airways dysfunction characterizing asthma, and the increased frequency and severity of respiratory infections in patients with asthma, such as is the case with influenza (8). The biological mechanisms underlying any protection in people with asthma regarding severe COVID-19 are unknown at this time. It has been suggested that decreased ACE2 (angiotensin-converting enzyme 2) receptor expression may lower the risk of COVID-19 severity and mortality in patients with atopic asthma (173). It has also been suggested that T-helper 2 (Th2) immune response in patients with asthma may counter the inflammation induced by SARS-CoV-2 infection (174). Inhaled corticosteroids, such as budesonide (171) or ciclesonide (175, 176), used by patients with asthma, may reduce the risk of infection or of developing symptoms leading to diagnosis. Biological mechanisms are still speculative, but ciclesonide, for example, may inhibit the replication of SARS-CoV-2 genomic RNA by targeting the viral endonuclease NSP15 (176). The lack of known biological mechanisms notwithstanding, data from the studies included in our analyses do not clearly show an altered risk of COVID-19 morbidity among adults with asthma.

### Limitations

Our study has several limitations. Asthma diagnosis criteria were often not specified, or otherwise varied from self-report to physician diagnosis to use of asthma medication, likely resulting in an unknown degree of misclassification. The type of asthma (atopic, nonatopic) was rarely specified, a limitation given patients with atopic asthma may be less susceptible to increased COVID-19 morbidity (52, 57, 125). The prevalence of asthma in people with COVID-19 also varied greatly across regions, and from sample to sample within regions. Without knowing the reasons for this variation, it is difficult to assess whether or to what extent biased estimates may have influenced our findings. It is possible that certain factors influenced diagnosis patterns, such as increased screening for COVID-19 among people with asthma (177). Certainly, the low estimates of asthma prevalence in the studies conducted in China compared with estimates from other countries and those in the local Chinese populations require explanation. We can speculate that patients with asthma in those study catchment areas tended to stay home due to fear of contracting COVID-19 (178). Lack of chronic airways disease awareness and lack of community spirometric testing are other possible reasons (179).

The majority of the meta-analyses that we performed yielded significant heterogeneity indices related to the pooled effects (Table E2), which may be indicative of the aforementioned biases. This heterogeneity may detract from the generalizability and interpretability of the pooled effects. Nonetheless, these findings may reflect the disparate epidemiological characteristics of COVID-19 in human populations around the world.

Finally, several of the studies included in our analyses were still in preprint (13, 21, 24, 31, 34, 35, 47, 49, 53, 56, 65, 70, 71, 76, 79, 80, 87, 91, 104–106, 115, 126–129, 132, 133, 138–140, 148, 149, 153, 167) and had yet to fully undergo the peer-review process. Whereas early access to study data may facilitate the timely dissemination of information to researchers, policymakers, and the public, the peer-review process helps to ensure the validity of study data and conclusions (180).

In conclusion, whereas patients with asthma are naturally apprehensive about the threat posed by COVID-19, in our review and analysis of the literature, we did not find clear evidence of increased risk of COVID-19 diagnosis, hospitalization, severity, or mortality due to asthma. However, additional studies are needed to clarify these associations, particularly studies with adequate sample size; clearly defined and consistently applied criteria for COVID-19 diagnosis and severity; clearly defined criteria for asthma diagnosis, including phenotype (atopic, nonatopic) and severity; and reliable, accurate data on asthma prevalence in people without COVID-19 who are otherwise comparable on such factors as age, sex, geographic region, and diagnostic methods. Nevertheless, our findings could provide some reassurance to people with asthma regarding its potential to increase their risk of severe consequences of COVID-19. ■

**Author disclosures** are available with the text of this article at www.atsjournals.org.

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