

Asthma and COVID-19

Scientific brief

19 April 2021



Background

People with asthma (PWA) generally are considered at higher risk from respiratory infections, as is seen annually with influenza. At the outset of the COVID-19 pandemic, PWA were widely assumed to be at increased risk from COVID-19. However, as data emerged throughout 2020, the association between asthma and COVID-19 appeared less clear (1).

A rapid systematic review was undertaken to inform this scientific brief. The review set out to assess the available peer-reviewed literature regarding whether PWA are at increased risk of infection with the virus that causes COVID-19, and/or of experiencing complications or death. In particular, the review set out to analyse evidence on the following questions.

- Is asthma associated with increased risk of acquiring SARS-CoV-2 and COVID-19 disease?
- Is asthma associated with hospitalization with COVID-19?
- Is asthma associated with the severity of COVID-19 outcomes?

Methods

A protocol for the rapid review was documented in advance of evidence retrieval and data analysis. Searches included the Cochrane COVID-19 study register, Embase, MEDLINE and LitCOVID on 8 October 2020 for published literature or literature accepted for publication but not yet published, in any language. Two reviewers screened titles and abstracts, and full texts of selected references, according to the following inclusion criteria:

- population: people diagnosed with asthma, with no limitations by age, disease severity or duration
- exposure: SARS-CoV-2 infection
- comparator: people without asthma
- outcome: rates of SARS-CoV-2 infection and COVID-19 disease: confirmed/suspected infection; hospitalization; admission to intensive care unit (ICU); death.

Where reported, data were also extracted on the specified outcomes where broken down by asthma medication, age, ethnicity, body mass index (BMI) and comorbidities. Systematic reviews were included, with data extracted and quality assessed in duplicate. Primary studies judged to be of sufficient quality according to pre-specified criteria were also included to capture more up-to-date evidence than was included in the systematic reviews. The full rapid review, including methods used, has been published (2).

Review of the evidence

Six systematic reviews addressed at least one of the pre-specified questions. The most recent search date was June 2020. Only one of the reviews was judged to be free of critical weaknesses (that is, judged to have at least four critical weaknesses by AMSTAR-2 criteria); this review (16) focused on mortality outcomes only. A further 13 cohort studies were judged to be of sufficient quality to be included in this evidence summary.

Is asthma associated with increased risk of acquiring COVID-19 or with hospitalization with COVID-19?

None of the included reviews were able to conclude with any certainty whether asthma was associated with increased risk of infection with SARS-CoV-2.

Due to the nature of SARS-CoV-2 testing, particularly early in the pandemic, most studies that looked at COVID-19 prevalence were in hospitalized cohorts; two reviews reported data on asthma prevalence within this context. Broadhurst et al. (3) charted the proportion of PWA among patients hospitalized with COVID-19 against each study site's asthma prevalence and found the proportions were similar across all studies, concluding that asthma prevalence among those hospitalized with COVID-19 appeared similar to population asthma prevalence. This was significantly lower than asthma prevalence in those hospitalized for influenza using four-year aggregate data, but the authors caution that it is possible that reporting of comorbidities was inconsistent across studies. Morais-Almeida et al. (4) reported asthma prevalence in those hospitalized with COVID-19 ranging from 0.3% to 17.9% (median 8.6%) but did not formally compare this to asthma rates in the community. Neither of two reviews in paediatric populations (5,6) concluded that children with asthma were at increased risk from COVID-19, although data were scarce.

Four primary studies compared COVID-19 rates in PWA to those in people without asthma. In three (7–10), data suggested an increased infection rate in PWA compared with people without asthma; this difference was statistically significant in two, although the magnitude of the increased risk was moderate, and in one case the estimates included the possibility of no meaningful difference.

Is asthma associated with severity of COVID-19 outcomes?

ICU admission

One review (Castro-Rodriguez et al. (6)) looked at risk of paediatric intensive care unit (PICU) admission with COVID-19 but found very little data. In the one study they included that reported this outcome, of 46 children hospitalized with COVID-19, no differences in proportions admitted to general floor versus PICU were found. One review (Morais-Almeida et al. (4)) evaluated ICU admission. Of the three studies they included that reported data on this outcome in more than 200 participants, none clearly signalled an increased risk of ICU admission in PWA with COVID-19, but the authors did not conduct formal analyses. None of the five that included primary studies testing for an association between asthma and admission to the ICU with COVID-19 (8,11–14) detected a statistically significant association, but in all cases the results were very imprecise, due in part to relatively limited samples.

Mortality

Two reviews looked at whether asthma was associated with death with COVID-19. Morais-Almeida et al. (4) looked at data across studies but did not synthesize these data. In the three studies included in their review with over 200 participants that evaluated death, one found no association, one found PWA were underrepresented in deaths from COVID-19, and one (from the OpenSAFELY cohort) found a higher risk of COVID-19 hospital death in PWA, with a greater risk in those with recent use of an oral corticosteroid. The latter was the only one of these three studies identified as a high-quality primary study in the rapid review (15).

Wang et al. (16) conducted a meta-analysis with data from four studies, including 744 PWA and 8151 people without asthma. They found no significant association between asthma and mortality with COVID-19, but again results were very imprecise, limiting certainty in the evidence. This review was not judged to have any critical weaknesses.

In addition to the OpenSAFELY results presented above, a further six (7,8,11,14,17,18) included primary studies that evaluated associations between asthma and death with COVID-19. Of these, none detected a statistically significantly increased risk of death. One (18) detected a statistically significant reduced odds of death with COVID-19 in PWA.

Do COVID-19 outcomes in PWA differ based on population characteristics?

None of the included reviews evaluated whether outcomes differed based on the population characteristics specified (age, ethnicity, BMI, asthma medication, asthma severity/type, comorbidities).

Ten primary studies investigated at least one of the above characteristics (beyond simply adjusting for them in their analyses). Very few studies included sufficient participants to detect a difference by subgroups within PWA.

Two studies (8,14) found the association between asthma and death with COVID-19 increased with age. As is to be expected from studies in the wider population, risk of mortality rose steeply with age within PWA (19).

Only one study reported on ethnicity. Wang et al. (19) explicitly set out to look at risk factors for hospitalization, intensive care and mortality among patients with asthma and COVID-19. In univariate analyses using white ethnicity as a reference group, all other ethnic groups had higher risks of hospitalization. The association was statistically significant for people from black and Asian communities, and remained so when additional analyses were undertaken, stratified by age. No statistically significant associations with ethnicity were found for ICU or death outcomes; this may reflect lower statistical power for these outcomes.

Only one study looked at BMI. Kim et al. (8) found that the association between asthma and mortality increased in those with BMI ≤ 25 ; it was unclear if this association was statistically significant.

Five studies (11,15,17,19,20) evaluated whether severe outcomes were associated with asthma medication. In adjusted models, only one study found a statistically significant association; Schultze et al. (20) found that high-dose inhaled corticosteroids were associated with higher risk of death from COVID-19 in PWA.

The one study that evaluated asthma severity/type separately from medication use (11) found no association between asthma severity and death with COVID-19. The three studies that evaluated it (9,10,13) found risk of death with COVID-19 was lower in people with allergic asthma compared to non-allergic asthma; the association was statistically significant in one of these studies.

The only comorbidity investigated was chronic obstructive pulmonary disease (COPD). Both studies investigating this (10,19) found risk of severe outcomes was higher in people with asthma and COPD than in people with asthma but no COPD; in one study this association was statistically significant.

Limitations

There is considerable imprecision and inconsistency in existing data. Establishing risk of contracting SARS-CoV-2 and developing COVID-19 remains extremely difficult without widespread community testing programmes that include asymptomatic individuals. Publication and reporting bias may be substantial issues in determining risk of severe outcomes; in primary studies that seek to evaluate risk factors for COVID-19, authors may report only those estimates where statistically significant differences are found.

Conclusions

Whether asthma increases risk of infection or severe outcomes from COVID-19 remains unclear. Systematic reviews do not detect a clear increase in risk. High-quality primary studies report conflicting results in some areas; considerable uncertainty persists. Within PWA with COVID-19, people with comorbid COPD and people with non-allergic (compared to allergic) asthma appear more vulnerable to worse outcomes. Older age and non-white ethnicity also appear to confer greater risk within PWA, as would be expected from data from the general population. Data on medication use is difficult to interpret due to inconsistent findings across primary studies and possible confounding/collinearity between asthma severity and medication prescribed, with some data suggesting an increased risk in people with more severe asthma. Further primary studies and comprehensive meta-analyses are needed.

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WHO continues to monitor the situation closely for any changes that may affect this scientific brief. Should any factors change, WHO will issue a further update. Otherwise, this scientific brief document will expire two years after the date of publication.

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WHO reference number: [WHO/2019-nCoV/Sci_Brief/Asthma/2021.1](https://www.who.int/publications-detail/WHO/2019-nCoV/Sci_Brief/Asthma/2021.1)

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