Risks of infection, hospital and ICU admission, and death from COVID-19 in people with asthma: systematic review and meta-analyses

Afolarin Otunla,¹ Karen Rees,² Paddy Dennison,³ Richard Hobbs,⁴ Jana Suklan,⁵ Ella Schofield,¹ James Gunnell,¹ Alexandra Migliu,¹ Jamie Hartmann-Boyce ⚫ ⁴

Abstract

Objectives To determine if and to what degree asthma may predispose to worse COVID-19 outcomes in order to inform treatment and prevention decisions, including shielding and vaccine prioritisation.

Design Systematic review and meta-analysis.

Setting Electronic databases were searched (October 2020) for clinical studies reporting at least one of the following stratified by asthma status: risk of infection with SARS-CoV-2; hospitalisation, intensive care unit (ICU) admission or mortality with COVID-19.

Participants Adults and children who tested positive for or were suspected to have COVID-19.

Main outcome measures Main outcome measures were the following stratified by asthma status: risk of infection with SARS-CoV-2; hospitalisation, ICU admission or mortality with COVID-19. We pooled odds ratios (ORs) and presented these with 95% confidence intervals (CI). Certainty was assessed using GRADE (Grading of Recommendations, Assessment, Development and Evaluations).

Results 30 (n=112 420) studies were included (12 judged high quality, 15 medium, 3 low). Few provided indication of asthma severity. Point estimates indicated reduced risks in people with asthma for all outcomes, but in all cases the evidence was judged to be of very low certainty and 95% CIs all included no difference and the possibility of increased risk (death: OR 0.90, 95% CI 0.72 to 1.13, I²=58%; hospitalisation: OR 0.95, 95% CI 0.71 to 1.26; ICU admission: OR 0.96, 95% CI 0.75 to 1.24). Findings on hospitalisation are also limited by substantial unexplained statistical heterogeneity. Within people with asthma, allergic asthma was associated with less COVID-19 risk and concurrent chronic obstructive pulmonary disease was associated with increased risk. In some studies, corticosteroids were associated with increased risk, but this may reflect increased risk in people with more severe asthma.

Conclusions Though absence of evidence of a clear association between asthma and worse outcomes from COVID-19 should not be interpreted as evidence of absence, the data reviewed indicate that risks from COVID-19 in people with asthma, as a whole, may be less than originally anticipated.

Introduction

The SARS-CoV-2 pandemic has affected over 158 million people worldwide, with at least 3.28 million deaths due to COVID-19 as of 9 May 2021.¹ At the start of the pandemic, people with asthma (PWA) were assumed to be at increased risk from COVID-19, as respiratory viral infections are well

SUMMARY BOX

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT?

⇒ At the beginning of the pandemic, it was assumed that people with asthma (PWA) would be at increased risk of poor outcomes with COVID-19.

⇒ This was contradicted by early primary studies, which reported that PWA represented a lower proportion of those with COVID-19 admitted to hospital than seen in the general population.

⇒ Systematic reviews and meta-analyses on this topic have generated conflicting conclusions, with some finding an association between asthma and poor COVID-19 outcomes while others do not. Analysis of the quality of these reviews reveals significant pitfalls, ranging from incomplete risk of bias reporting to inadequate justification for exclusion of individual studies.

WHAT ARE THE NEW FINDINGS?

⇒ This systematic review is one of the largest to date on the effects of asthma on the risk of poor COVID-19 outcomes, covering a large number of studies across multiple continents.

⇒ Pooled results showed that, overall, asthma was not associated with severe COVID-19 outcomes, but evidence was judged to be of very low certainty.
known to cause severe adverse outcomes in patients with established asthma through stimulation of exacerbation episodes.3

Early, large-scale case series provided evidence to the contrary, reporting that PWA made up a lower proportion of patients with COVID-19 admitted to hospital than seen in the general population.4–5 These findings birthed a myriad of hypothesised immunopathological mechanisms to explain this apparent reduction in susceptibility to severe COVID-19.6–7 More recent epidemiological studies have further complicated our understanding of the association between COVID-19 and asthma, with some suggesting an association while others do not.8–15 It is important for PWA, their carers, healthcare providers and policymakers to understand if and to what degree asthma may predispose to worse COVID-19 outcomes. Such information impacts both treatment and prevention decisions, including shielding and vaccine prioritisation.

The ambiguity of primary evidence combined with the clear importance of determining the relationship between COVID-19 and asthma has resulted in a number of systematic reviews on the subject.16–18 Analysis of the quality of these reviews reveals significant pitfalls, ranging from incomplete risk of bias reporting to inadequate justification for exclusion of individual studies. This is reflected in the scientific brief on asthma and COVID-19 released by the WHO, in which only one of six systematic reviews on the subject were judged to be free of ‘critical weakness’ using the AMSTAR-2 (A MeaSurement Tool to Assess systematic Reviews-2) ratings for critical domains.19 The single high-quality review identified through the WHO scientific brief focused on mortality and concluded that there was insufficient evidence to draw firm conclusions.18 The review contained published literature up to 8 June 2020, and further studies have since emerged. In addition, no systematic reviews of sufficient quality have examined whether PWA are more likely to be infected with COVID-19 or be hospitalised or admitted to intensive care with COVID-19 than people without asthma.

We therefore conducted a comprehensive systematic review and meta-analysis of published literature to determine whether asthma is a risk factor for worse outcomes in both adults and children with COVID-19, focusing on the specific endpoints of infection, hospitalisation, intensive care unit (ICU) admission and mortality. We also investigated whether, within PWA, asthma medication, severity, comorbidity, age and ethnicity affected COVID-19 outcomes.

Methods
Search strategy
This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and incorporates the PRISMA-Equity extension designed for systematic reviews with a focus on health equity.20 We were commissioned by the WHO to conduct a rapid review on this topic, the protocol for which was specified and made publicly available before review conduct.21 This review follows on from that work; our WHO review did not include statistical synthesis, and therefore following the WHO rapid review, we posted a new protocol outlining our synthesis plans, results from which are presented here (https://osf.io/c9ed6t/).

We searched Medline, Embase, LitCOVID and the Cochrane study register on 8 October 2020 for COVID-19 clinical studies, published or accepted for publication but not yet published, in any language. We included any type of clinical study (randomised controlled trials, cohort studies, cross-sectional studies, case reports and series, and case–control studies) that reported the number of adults or children with asthma (as determined by the investigators) and COVID-19 (either confirmed with RT-PCR test or suspected), and specified at least one of the following outcomes stratified by asthma status: risk of infection; hospitalisation status; ICU admission status; mortality. Studies were excluded if they did not report any of our prespecified outcomes in PWA and COVID-19. The full search strategy is outlined in online supplemental appendix 1 (pp 2–4). Two reviewers independently screened titles and abstracts, and full texts of selected references, with discrepancies resolved by discussion or referral to a third reviewer. Where grey literature was identified, we contacted the authors where it was unclear if grey literature had been accepted for publication; if it had been (ie, had been subject to peer review) then we included it in our review. Non-peer-reviewed publications were excluded, as specified in advance.

Two reviewers independently assessed methodological quality using the Newcastle-Ottawa Scale (NOS) for cohort and cross-sectional studies. The NOS consists of three domains across which 9 points are available (9 for cohort studies, 6 for cross-sectional studies): selection of study groups (4 points), comparability of groups (2 points) and ascertainment of exposure and outcomes (3 points).22 We considered a score of 1–3 stars as low quality, 4–6 as medium quality and 7–9 as high quality. We also rated the certainty of the evidence according to the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) approach,23 which we present in a summary of findings (table 1). Two reviewers independently extracted data on patient characteristics and clinical outcomes using a bespoke extraction form which was piloted before use to facilitate efficient extraction of data. Any discrepancies were resolved by discussion. When a study presented patients with asthma as a percentage of total population, we estimated the number based on the given percentage.

Data analysis
We performed meta-analyses using the Cochrane Review Manager V.5.4 platform to determine the risk of infection with SARS-CoV-2,24 hospitalisation with COVID-19, ICU admission with COVID-19 and risk of mortality from COVID-19 in PWA versus those without asthma, presenting results as ORs with 95% CIs. We used prevalence of asthma in patients with COVID-19 as a proxy for risk of infection, although we appreciate this is significantly limited by lack of widespread random testing. In each meta-analysis, we fitted a random effects model using the inverse-variance method, using ORs as reported within the study or calculated based on data provided in accordance with the Cochrane Handbook.25 When producing the prevalence meta-analysis, we used prevalence ratios and calculated the 95% CIs in accordance with the Cochrane Handbook. When studies reported both adjusted and unadjusted estimates, we used the adjusted estimates and

SUMMARY BOX

HOW MIGHT IT IMPACT CLINICAL PRACTICE IN THE FORESEEABLE FUTURE?
⇒ Evidence suggests that PWA are not at increased risk of acquiring SARS-CoV-2 compared with those without asthma, and have similar, if not slightly improved, clinical outcomes with COVID-19.
⇒ However, absence of evidence should not be interpreted as evidence of absence, and further high-quality primary studies are required to reinforce this conclusion.
performed subgroup analysis to compare adjusted and unadjusted values. We assessed heterogeneity using the Cochrane $I^2$ value, and used their suggested thresholds for moderate, substantial and considerable heterogeneity. We undertook sensitivity analyses removing studies at high risk of bias. The following prespecified subgroup analyses were performed: outcomes by mean/median age (up to 60 years and 60 years and above), by mean/median body mass index (BMI) (less than and greater than 30), by ethnicity (less than and greater than 50% white), by asthma severity (as defined by each study), by asthma medication and by adjustment status (studies where the effect size was adjusted for factors including age, sex, BMI and comorbidities compared with studies which did not adjust at all). We visually inspected the funnel plots for all comparisons with over 10 studies for possible publication bias. In meta-analyses with less than 10 studies, we performed Egger analysis.

We narratively report results from studies that could not be included in meta-analysis. We were also interested to know whether asthma medication, severity, comorbidity, age and ethnicity affected COVID-19 outcomes in PWA. We narratively report results from studies assessing the extent to which different characteristics within PWA predispose to our outcomes of interest, using effect direction plots.

**Results**

A total of 824 articles were identified from the search of databases. The selection process is presented in a PRISMA flow diagram (figure 1). After initial screening based on titles and abstracts, 97 articles remained for full text evaluation. Full text analysis produced a total of 30 studies which met the inclusion criteria, 25 of which had sufficient data to be included in meta-analysis.

Of the 30 studies included, totalling 112,420 people who tested positive for or were suspected to have COVID-19, there were 24 cohort studies (22 conducted retrospectively and 2 conducted prospectively) and 6 cross-sectional analyses. All were published after peer review and no preprints were included in the analyses. Sample sizes ranged from 106 to 81,490 people, with median sample size $n=1043$ and IQR=7145 (445-7590). Studies were from North and South America (12), Europe (14) and Asia (4). The majority of studies used adult (18+) cohorts (19), six studies used mixed paediatric and adult cohorts and one study used a paediatric cohort. The remaining studies did not report sufficiently detailed age data to determine whether children were included. Only one study included people with suspected but unconfirmed SARS-CoV-2; this study reported only on prevalence and was not included in meta-analyses. We assessed studies for possible overlap to ensure participants were not being double counted in our analyses; studies were conducted in different cohorts (eg, different hospitals) with no overlap identified.

Using the NOS, 12 studies were rated as high quality, 15 studies as medium quality and 3 studies as low quality (overall NOS scores for each study can be seen in online supplemental table 1, scores for individual domains can be seen in online supplemental appendix 1, online supplemental table 2). A summary of included studies is presented in online supplemental table 1.

**Outcomes**

**Prevalence**

Twenty-one studies reported prevalence of asthma in those suffering from COVID-19. The estimated prevalence of asthma in patients with COVID-19 ranged from 0.32% to 25.8% (median 9.14% and IQR 11.15 (3.05-14.2)). We included all of these studies in meta-analysis. Data were highly heterogeneous. The pooled prevalence of the 21 studies was 9.38% (95% CI 7.38% to 11.38%, $I^2=99\%$, n=81,294). Among these studies, there was some asymmetry to the funnel plot, raising the possibility of publication bias (online supplemental figure 1). Overall, this evidence was judged to be of very low certainty due to unexplained statistical heterogeneity and possible publication bias.

In order to provide a more contextualised view, we compared asthma prevalence in each study population to prevalence in the general population of the country in which the study was based (figure 2).

We looked to clinical study setting (whether hospital based or community based) as a potential driving force behind the observed heterogeneity. However, high heterogeneity was maintained in subgroup analysis stratifying studies based on whether their cohorts were hospital based, community based or mixed ($I^2=99\%$ in both hospital and mixed subgroups; test for subgroup differences $I^2=55\%$, online supplemental figure 2).

Further subgroup analysis provided evidence that BMI (test for subgroup differences $I^2=60.4\%$, online supplemental figure 3) and ethnicity (test for subgroup differences $I^2=94.9\%$, online supplemental figure 4) may have contributed to some of the variation. This was a contrast to subgroup analysis by age (online supplemental figure 5), where no subgroup differences were apparent ($I^2=0\%$).

| Table 1 | Summary of findings: risks of infection, hospital and ICU admission, and death from COVID-19 in people with asthma compared with people without asthma |
|---|---|---|---|
| Outcome | Number of participants (studies) | Relative effect (95% CI) | Certainty |
| Prevalence: as a proxy for risk of infection | 83,294 (21 observational studies) | PP: 9.38% (7.38 to 11.38) | Very low* |
| Mortality | 62,521 (15 observational studies) | OR: 0.9 (0.72 to 1.13) | Very low† |
| Hospitalisation | 25,065 (9 observational studies) | OR: 0.95 (0.71 to 1.26) | Very low‡ |
| ICU admission | 13,092 (9 observational studies) | OR: 0.96 (0.75 to 1.24) | Very low§ |

*Downgraded two levels due to unexplained statistical heterogeneity, one level due to possible publication bias (skewed funnel plot). †Downgraded one level due to unexplained statistical heterogeneity, downgraded one level due to imprecision (wide CIs). ‡Downgraded two levels due to unexplained statistical heterogeneity, downgraded one level due to imprecision (wide CIs). §Downgraded one level due to imprecision (wide CIs).
Evidence synthesis

We performed sensitivity analyses to assess risk of bias by removing high risk of bias studies (0–3 on the NOS). Niquini et al were the only high risk of bias study reporting prevalence outcomes, with removal leading to a slight increase in pooled prevalence from 9.38 (95% CI 7.38 to 11.38, I²=99%, n=83,294) to 9.81 (95% CI 7.92 to 11.71, I²=99%, n=51,332), and no impact on heterogeneity.45

Mortality
Mortality data were reported by 15 studies. A meta-analysis of data from 13 of these studies was conducted to evaluate the association between asthma and risk of mortality in patients with COVID-19 (figure 3). The pooled effect estimate demonstrated that asthma was associated with slightly reduced odds of mortality (OR 0.90, 95% CI 0.72 to 1.13, I²=58%, n=62,521), although CIs were wide and incorporated no difference as well as increased risk. The funnel plot analysis of these studies did not suggest publication bias (online supplemental figure 6). There was no high risk of bias studies within this outcome, therefore we did not perform a sensitivity analysis. We judged this finding to be of very low certainty due to unexplained statistical heterogeneity and imprecision (wide CIs).

Subgroup analyses by age (online supplemental figure 7) and comparing adjusted versus unadjusted estimates (online supplemental figure 8) did not explain the moderate heterogeneity observed. However, there was some evidence that both BMI (test for subgroup differences I²=85%) and ethnicity (test for subgroup differences I²=77%) may explain some of the variation. In the three studies where the majority of the cohort had a BMI of 30 or over, asthma was associated with an increased odds of mortality, with CIs excluding no difference (OR 1.24, 95% CI 1.0 to 1.53, n=29,51) (figure 3), but the majority of studies did not provide BMI data. In the five studies where the majority of the cohort was of non-white ethnicity, asthma was associated with a reduced odds of mortality, with CIs excluding no difference (OR 0.75, 95% CI 0.60 to 0.93, n=41,894) (online supplemental figure 9). Again, the majority of studies did not report data on ethnicity.

The two studies not included in the meta-analysis (Abrams et al and Beurnier et al) were excluded due to the fact that neither reported mortality rates in people without asthma, and thus no OR could be extracted or calculated.28 32 However, through utilisation of mortality rates reported in hospitalised patients without asthma in other large-scale studies over a similar time period, the data can still be interpreted narratively. Abrams et al reported a mortality rate (percentage of PWA who died from COVID-19) of 4.5% in New York City (NYC) hospitals, which is lower than the 32.1% mortality rate (percentage of people who died from COVID-19) in NYC hospitals reported by Thompson et al.52 Beurnier et al reported an in-hospital mortality rate (percentage of PWA who died from COVID-19) of 8.1% in Paris, France, which was lower than that in hospital mortality rate (percentage of people who

Figure 1 PRISMA diagram of study flow

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### Figure 2

Prevalence of asthma in COVID-19 patients. Blue squares indicate population prevalence of asthma for comparison.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>N/A</th>
<th>Total</th>
<th>Weight</th>
<th>Prevalence IV, Random, 95% CI</th>
<th>Prevalence IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>France</strong></td>
<td></td>
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<tr>
<td>Beurnier (France)</td>
<td>37</td>
<td>768</td>
<td>5.0%</td>
<td>4.80 [3.29, 6.31]</td>
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<tr>
<td>Grandbastien (France)</td>
<td>25</td>
<td>106</td>
<td>2.9%</td>
<td>21.70 [13.85, 29.55]</td>
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<tr>
<td>France Reference</td>
<td></td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>60</td>
<td>874</td>
<td>7.8%</td>
<td>12.79 [9.37, 16.33]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: TAU^2 = 134.49; CHI^2 = 17.18, df = 1 (P &lt; 0.0001); I^2 = 94%</td>
<td>Test for overall effect: Z = 1.52 (P = 0.13)</td>
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<tr>
<td><strong>USA</strong></td>
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<tr>
<td>Adrich (USA)</td>
<td>83</td>
<td>469</td>
<td>4.4%</td>
<td>17.70 [14.25, 21.15]</td>
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</tr>
<tr>
<td>Broadhurst (USA)</td>
<td>53</td>
<td>436</td>
<td>4.6%</td>
<td>12.80 [9.13, 15.27]</td>
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</tr>
<tr>
<td>Chiba (USA)</td>
<td>220</td>
<td>1,526</td>
<td>4.9%</td>
<td>14.40 [12.34, 16.16]</td>
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<tr>
<td>Lieberman–Cribbin (USA)</td>
<td>618</td>
<td>11,405</td>
<td>5.1%</td>
<td>4.35 [4.02, 5.58]</td>
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<tr>
<td>Lovinsky-Desir (USA)</td>
<td>163</td>
<td>1,298</td>
<td>4.9%</td>
<td>12.60 [10.79, 14.41]</td>
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<tr>
<td>Mahdavinia (USA)</td>
<td>241</td>
<td>935</td>
<td>4.6%</td>
<td>25.80 [23.00, 28.60]</td>
<td></td>
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<tr>
<td>Tousie (USA)</td>
<td>46</td>
<td>338</td>
<td>4.3%</td>
<td>14.00 [10.30, 17.70]</td>
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</tr>
<tr>
<td>Wang (USA)</td>
<td>219</td>
<td>1,027</td>
<td>4.9%</td>
<td>13.10 [11.55, 14.65]</td>
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<tr>
<td>Ko (USA)</td>
<td>702</td>
<td>5,416</td>
<td>5.0%</td>
<td>13.00 [12.10, 13.90]</td>
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<tr>
<td>USA Reference</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>2,365</td>
<td>23,653</td>
<td>42.8%</td>
<td>14.08 [9.91, 18.24]</td>
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<tr>
<td>Heterogeneity: TAU^2 = 39.20; CHI^2 = 595.86, df = 8 (P &lt; 0.0001); I^2 = 96%</td>
<td>Test for overall effect: Z = 6.62 (P &lt; 0.00001)</td>
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<td><strong>Korea</strong></td>
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<tr>
<td>Choi (Korea)</td>
<td>218</td>
<td>7,590</td>
<td>5.1%</td>
<td>2.90 [2.52, 3.28]</td>
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<tr>
<td>Kim (Korea)</td>
<td>70</td>
<td>2,200</td>
<td>5.1%</td>
<td>3.20 [2.46, 3.94]</td>
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<tr>
<td>Korea Reference</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>288</td>
<td>9,790</td>
<td>10.2%</td>
<td>2.96 [2.63, 3.30]</td>
<td></td>
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<tr>
<td>Heterogeneity: TAU^2 = 0.00; CHI^2 = 0.51, df = 1 (P = 0.48); I^2 = 0%</td>
<td>Test for overall effect: Z = 17.29 (P &lt; 0.00001)</td>
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<tr>
<td><strong>Spain</strong></td>
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<tr>
<td>Barroso (Spain)</td>
<td>11</td>
<td>189</td>
<td>4.5%</td>
<td>5.80 [4.47, 7.13]</td>
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<tr>
<td>Garcia-Pachon (Spain)</td>
<td>10</td>
<td>376</td>
<td>4.9%</td>
<td>2.70 [0.94, 4.46]</td>
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<tr>
<td>Lemus-Calderon (Spain)</td>
<td>577</td>
<td>6,310</td>
<td>5.1%</td>
<td>9.14 [8.43, 9.83]</td>
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<td>Spain Reference</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>598</td>
<td>6,875</td>
<td>14.4%</td>
<td>5.93 [5.02, 10.66]</td>
<td></td>
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<td>Heterogeneity: TAU^2 = 16.27; CHI^2 = 46.34, df = 2 (P &lt; 0.0001); I^2 = 96%</td>
<td>Test for overall effect: Z = 2.46 (P = 0.01)</td>
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<td><strong>UK</strong></td>
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<tr>
<td>Atkins (UK)</td>
<td>90</td>
<td>507</td>
<td>4.5%</td>
<td>17.60 [14.29, 20.91]</td>
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<td>UK Reference</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>90</td>
<td>507</td>
<td>4.5%</td>
<td>17.60 [14.29, 20.91]</td>
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<td>Heterogeneity: Not applicable</td>
<td>Test for overall effect: Z = 10.41 (P &lt; 0.00001)</td>
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<td>Lombardi (Italy)</td>
<td>20</td>
<td>1,043</td>
<td>5.1%</td>
<td>1.92 [1.09, 2.75]</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>20</td>
<td>1,043</td>
<td>5.1%</td>
<td>1.92 [1.09, 2.75]</td>
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<tr>
<td>Heterogeneity: Not applicable</td>
<td>Test for overall effect: Z = 4.52 (P &lt; 0.00001)</td>
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<td><strong>Norway</strong></td>
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<tr>
<td>Nystad (Norway)</td>
<td>515</td>
<td>7,632</td>
<td>5.1%</td>
<td>6.75 [6.19, 7.31]</td>
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<td>Norway Reference</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>515</td>
<td>7,632</td>
<td>5.1%</td>
<td>6.75 [6.19, 7.31]</td>
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<tr>
<td>Heterogeneity: Not applicable</td>
<td>Test for overall effect: Z = 23.50 (P &lt; 0.00001)</td>
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<tr>
<td><strong>Brazil</strong></td>
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<tr>
<td>Niquini (Brazil)</td>
<td>395</td>
<td>31,094</td>
<td>5.1%</td>
<td>0.32 [0.26, 0.38]</td>
<td></td>
</tr>
<tr>
<td>Brazil Reference</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>395</td>
<td>31,094</td>
<td>5.1%</td>
<td>0.32 [0.26, 0.38]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Not applicable</td>
<td>Test for overall effect: Z = 10.13 (P &lt; 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>China</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Song (China)</td>
<td>22</td>
<td>961</td>
<td>5.0%</td>
<td>2.30 [1.35, 3.25]</td>
<td></td>
</tr>
<tr>
<td>China Reference</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>22</td>
<td>961</td>
<td>5.0%</td>
<td>2.30 [1.35, 3.25]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Not applicable</td>
<td>Test for overall effect: Z = 4.76 (P &lt; 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>4,953</td>
<td>82,429</td>
<td>100.0%</td>
<td>9.38 [7.38, 11.38]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: TAU^2 = 20.41; CHI^2 = 3570.06, df = 20 (P &lt; 0.00001); I^2 = 99%</td>
<td>Test for overall effect: Z = 9.20 (P &lt; 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: CHI^2 = 887.80, df = 8 (P &lt; 0.00001); I^2 = 99.1%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Evidence synthesis

Evidence synthesis

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Asthma</th>
<th>Non-Asthma</th>
<th>Odds Ratio</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Death</td>
<td>Survival</td>
<td>Death</td>
<td>Survival</td>
</tr>
<tr>
<td></td>
<td>Weight</td>
<td>IV, Random, 95% CI</td>
<td>Weight</td>
<td>IV, Random, 95% CI</td>
</tr>
<tr>
<td>16.1.1 No BMI data</td>
<td>Atkins (UK)</td>
<td>8</td>
<td>212</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td>Chirba (USA)</td>
<td>17</td>
<td>211</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Lemus–Calderon (Spain)</td>
<td>21</td>
<td>556</td>
<td>229</td>
</tr>
<tr>
<td></td>
<td>Liebermann-Cribbin (USA)</td>
<td>45</td>
<td>227</td>
<td>1083</td>
</tr>
<tr>
<td></td>
<td>Lombardi (Italy)</td>
<td>2</td>
<td>18</td>
<td>231</td>
</tr>
<tr>
<td></td>
<td>Lovinsky-Desir (USA)</td>
<td>9</td>
<td>154</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td>Santos (Brazil)</td>
<td>488</td>
<td>1750</td>
<td>8149</td>
</tr>
<tr>
<td></td>
<td>Song (China)</td>
<td>1</td>
<td>21</td>
<td>158</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>591</td>
<td>3146</td>
<td>10225</td>
<td>37979</td>
</tr>
</tbody>
</table>

Test for overall effect: Z = 3.15 (P = 0.002)

16.1.2 BMI 30+

Barroso (Spain) | 2 | 239 | 16 | 678 | 1.8% | 1.69 [0.34, 8.36] | 1.69 [0.34, 8.36] |

Mahdvina (USA) | 2 | 9 | 22 | 167 | 2.1% | 2.56 [0.57, 11.50] | 2.56 [0.57, 11.50] |

Wang (USA) | 98 | 1729 | 637 | 13578 | 16.8% | 1.21 [0.97, 1.50] | 1.21 [0.97, 1.50] |

Subtotal (95% CI) | 102 | 1977 | 675 | 14423 | 20.7% | 1.24 [1.00, 1.53] | 1.24 [1.00, 1.53] |

Test for overall effect: Z = 1.94 (P = 0.05)

16.1.3 BMI <30

Kim (Korea) | 9 | 57 | 127 | 1850 | 4.3% | 1.66 [0.62, 4.42] | 1.66 [0.62, 4.42] |

Subtotal (95% CI) | 9 | 57 | 127 | 1850 | 4.3% | 1.66 [0.62, 4.42] | 1.66 [0.62, 4.42] |

Test for overall effect: Z = 1.01 (P = 0.31)

Total (95% CI) | 702 | 5183 | 11027 | 54252 | 100.0% | 0.90 [0.72, 1.13] | 0.90 [0.72, 1.13] |

Test for overall effect: Z = 0.90 (P = 0.37)

Heterogeneity: Tau² = 0.07; Chi² = 28.38, df = 12 (P = 0.005); I² = 58%

Test for subgroup differences: Chi² = 13.33, df = 2 (P = 0.001), I² = 85.0%

Figure 3 COVID-19 mortality in people with asthma compared to people without asthma, subgrouped by mean/median BMI. BMI, body mass index.

died from COVID-19 of 16.9% recorded by Gaudart et al across a similar time period.5)

Hospitalisation

Nine studies reported hospitalisation in PWA with COVID-19. Meta-analysis revealed that asthma was associated with a slight reduction in odds of hospitalisation with COVID-19 (OR 0.95, 95% CI 0.71 to 1.26, n=25065, I²=94%) (figure 4), although CIs incorporated no difference as well as increased risk. Statistical heterogeneity was high, with some studies showing statistically significantly reduced risk and others showing statistically significant increases in risk. Egger analysis of these studies did not suggest publication bias (test for funnel plot asymmetry, p=0.384). There was no high risk of bias studies within this outcome, therefore we did not perform a sensitivity analysis. We judged this finding to be of very low certainty due to unexplained statistical heterogeneity and imprecision (wide CIs).

There was no evidence that ethnicity, BMI or whether studies presented adjusted or unadjusted estimates explained the heterogeneity observed (I²=0% for all tests for subgroup differences, online supplemental figures 10–12). There was also little evidence that sample age affected heterogeneity (I²=10.8%, figure 4).

Figure 4 COVID-19 hospitalisation in PWA compared to people without asthma, subgrouped by age (mean/median age was less than 60 compared to studies which did not report age data; no studies had mean/median age >60).
**Evidence synthesis**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Asthma (ICU Admission)</th>
<th>Non–Asthma (ICU Admission)</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>23.3.1 Non–white</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lovinsky–Desir (USA)</td>
<td>34</td>
<td>129</td>
<td>231</td>
<td>904</td>
<td>39.5%</td>
</tr>
<tr>
<td>Mahdavinia (USA)</td>
<td>23</td>
<td>218</td>
<td>46</td>
<td>648</td>
<td>22.3%</td>
</tr>
<tr>
<td>Tousse (USA)</td>
<td>23</td>
<td>218</td>
<td>46</td>
<td>648</td>
<td>4.7%</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>57</td>
<td>347</td>
<td>277</td>
<td>1552</td>
<td>66.5%</td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 2 (P = 0.83); I² = 0%</td>
<td>Test for overall effect: Z = 0.37 (P = 0.71)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **23.3.2 No ethnicity data** |                        |                             |        |                              |                              |
| Barroso (Spain)           | 2                      | 9                           | 30     | 158                          | 2.6%                         |
| Broadhurst (USA)          | 15                     | 38                          | 124    | 259                          | 11.8%                        |
| Choi (Korea)              | 7                      | 211                         | 208    | 7194                         | 10.3%                        |
| Grandbastien (France)     | -                      | -                           | -      | -                            | -                            |
| Kim (Korea)               | 5                      | 61                          | 120    | 1857                         | 4.8%                         |
| Subtotal (95% CI)         | 29                     | 319                         | 482    | 9496                         | 33.5%                        |
| Heterogeneity: Tau² = 0.00; Chi² = 1.05, df = 4 (P = 0.90); I² = 0% | Test for overall effect: Z = 1.02 (P = 0.31) |

**Figure 5** COVID-19 ICU admission rates in PWA compared to people without asthma, subgrouped by ethnicity (majority of the cohort (over 50%) was of white ethnicity compared to where the minority of the cohort (50% or less) was of white ethnicity). ICU, intensive care unit.

**ICU admission**

Data on ICU admissions were reported by nine studies. Meta-analysis of eight of these studies demonstrated that asthma was associated with a slight reduction in odds of ICU admission with COVID-19 (OR 0.96, 95% CI 0.75 to 1.24, n=13,092, I²=0%) (figure 5), but ICS included no difference and increased risk. There was no evidence of statistical heterogeneity. Egger analysis of these studies did not suggest publication bias (test for funnel plot asymmetry, p=0.6142). There was no high risk of bias studies within this outcome, therefore we did not perform a sensitivity analysis. We also judged this finding to be of very low certainty due to unexplained statistical heterogeneity and imprecision (wide CIs).

There was no evidence of subgroup differences based on age, BMI or whether studies presented adjusted or unadjusted estimates (I²=0% for subgroup differences in all cases, online supplemental figures 13–15). There was little evidence of subgroup difference by ethnicity (I²=7.5%, figure 5).

The study not included in the meta-analysis (Chhiba et al) did not report ICU admission in people without asthma, and thus no OR could be extracted. However, through utilisation of national ICU admission data, the data can still be interpreted narratively. Chhiba et al reported that 8.6% of PWA hospitalised with COVID–19 were admitted to ICU in the US. This is lower than the national average rate of ICU admission in people hospitalised with COVID–19; 32%.54

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

Very few studies were sufficiently powered to detect a difference by subgroups within PWA. Data regarding our prespecified characteristics reported in more than one study can be found in table 2.

Data on inhaled corticosteroid (ICS) use were not consistent across studies, but the largest study of the type found high-dose ICS was associated with higher risk of COVID–19 mortality when compared with short-acting beta agonist (SABA).49 A second study using the same data set found OCS (oral corticosteroid) use was also associated with greater risk in PWA; no other studies evaluated OCS use. With the exception of the one study comparing ICS to SABA,49 no significant associations were found between SABA and long-acting beta agonist and disease outcomes. Three studies reported on allergic asthma, reporting reduced prevalence9,12 and hospitalisation17 compared with non-allergic counterparts. Two studies investigated the importance of comorbid chronic obstructive pulmonary disease (COPD), finding it was associated with increased hospitalisation, ICU admission, mortality18 and prevalence.27 Only one study reported on ethnicity,18 with univariate analyses using white ethnicity as a reference group finding that all other ethnic groups had higher risks of hospitalisation. The association was statistically significant for Black and Asian groups and remained so in an age-stratified multivariate logistic regression. Only one study looked at BMI.18 Kim et al found that the association between asthma and mortality increased in those with BMI ≤25; it was unclear if this association was statistically significant.

Regarding the influence of asthma medication on COVID–19 outcomes in PWA, where associations were detected, it was unclear if these were due to mechanisms of the medications themselves, or due to the association between prescriptions for these medications and asthma severity.35 People with allergic asthma seem to be at lower risk of severe outcomes from COVID–19 than those with non–allergic asthma,37 but again more data are needed to confirm this. People with COPD and asthma appear at higher risk from severe COVID–19 outcomes than PWA who do not have COPD.18 In PWA, risk from COVID–19 appears to increase with age,18 38 43 as in the general population.

**Discussion**

Our systematic review contains 30 studies and to the best of our knowledge is one of the largest to date on the effects of asthma on the risk of poor COVID–19 outcomes, covering a large number of studies across multiple continents. Whether PWA are at increased risk of infection or severe outcomes from COVID–19 remains unclear, with point estimates reporting a slightly reduced risk for hospitalisation, ICU admission and death with COVID–19 in PWA compared with people without asthma, but 95% CIs encompassing no difference as well as moderately increased and moderately decreased risks. Our results revealed a 9.38% prevalence of asthma in those who tested positive for COVID–19, similar to the prevalence of...
Evidence synthesis

### Table 2: Data from primary studies on whether COVID-19 outcomes in PWA differ based on subgroup characteristics

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Age</th>
<th>Medication</th>
<th>Asthma severity/type/ comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bozeki and Winterstein33</td>
<td>Hospitalisation: ↑ Montelukast</td>
<td>ICU admission: ↑ ICS</td>
<td></td>
</tr>
<tr>
<td>Chhiba et al49</td>
<td>ICU admission: ↑ ICS, ↓ LABA, ↓ SABA, ↓ LAMA</td>
<td>Mortality: ↑ ICS, ↑ SABA, ↑ LAMA</td>
<td></td>
</tr>
<tr>
<td>Choi et al49</td>
<td>ICU admission: ↑ ICS, ↓ LABA, ↓ SABA, ↓ LAMA</td>
<td>Mortality: ↑ ICS, ↑ SABA, ↑ LAMA</td>
<td></td>
</tr>
<tr>
<td>Kim et al49</td>
<td>Mortality Association between asthma and mortality ↑ with increasing age</td>
<td>ICU admission: ↓ Allergic asthma (compared with non-allergic asthma)</td>
<td></td>
</tr>
<tr>
<td>Keswani et al49</td>
<td>Mortality compared with SABA: ↑ Low/medium-dose ICS, ↑ High-dose ICS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mahdavinia et al47</td>
<td>OR for association between asthma and hospitalisation ↑ with increasing age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang et al47</td>
<td>Increasing age: ↑ Hospitalisation, ↑ ICU admission, ↓ Mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Williamson et al</td>
<td>Mortality: ↓ OCS (oral corticosteroid) use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang et al47</td>
<td>↓ Allergic asthma (compared with non-allergic asthma)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhu et al47</td>
<td>↓ Allergic asthma (compared with non-allergic asthma)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Evidence synthesis

The use of ICS in COVID-19 has been subject to intense scrutiny, due to their potential to both reduce antiviral immunity juxtaposed with evidence suggesting they may reduce replication of SARS-CoV-2.48 50 Though some high-quality studies in our review find that corticosteroids are associated with worse outcomes, these are likely confounded, with Schultz stating that the harmful association could be explained by health differences not recorded in the OpenSAFELY database from which information was obtained, most notably, asthma severity.49 They reported an incomplete assessment of exacerbation history, a confounding variable which post hoc analysis demonstrated had one of the greatest impacts on effect size. This, combined with the fact that ICS use will be higher in people with more severe disease, suggests that ICS use does not influence the likelihood of severe COVID-19.

The PRINCIPLE (Platform Randomised trial of INterventions against COVID-19 In older people) trial has recently shown that inhaled budesonide, a common corticosteroid used in asthma management, shortens recovery times in patients with COVID-19 over the age of 50.60 Current guidelines suggest ICS use in PWA should be continued until more evidence is available.61

There were limitations to this systematic review. Some analyses were limited by significant heterogeneity, even when subgrouped by geographical region, age, BMI and study quality. This may be a reflection of the fact that subgroup analyses are a relatively crude tool with which to investigate the cause of heterogeneity, as they rely on study-level aggregates as opposed to individual characteristics, and are thus prone to confounding factors. It would be more informative to look at individual data in a large, well-reported study, the likes of which are not yet available in the literature. The diagnosis of asthma in primary studies was based largely on self-report or physician diagnosis, not using more objective measures such as spirometry or peak flow. This, combined with the tendency for asthma to flip between underdiagnosis and overdiagnosis depending on where you are in the world,62 has the potential to confound results. Furthermore, factors which influence COVID-19 outcomes, such as obesity, may contribute to asthma misdiagnosis and thus further confound the issue, particularly in those studies not reporting on BMI.63 However, the same possible causes of confounding exist in other areas, and yet the lack of consistency observed for the relationship between asthma and COVID-19 is in contrast to other long-term conditions, notably diabetes where available research suggests clear associations of poorer outcomes.64 When we compared unadjusted and adjusted estimates, there was no evidence of difference between the two. If data and reporting in this area improve, future reviews may wish to specify minimal sets of adjustment factors for inclusion.

Incomplete data and reporting bias are also potential issues. We cannot rule out publication bias and the small number of studies contributing to each analysis means methods for testing for publication bias are underpowered in our sample. As prespecified with WHO, we did not include preprints, which may mean some relevant evidence has been overlooked. Most of the studies reported in our review derive their data from hospitals, where multiple biases are possible; for example, studies which find higher rates of COVID-19 hospitalisation in PWA could be because PWA are more likely to contract COVID-19, or because if having contracted COVID-19 PWA are more likely to require hospitalisation or to be referred to hospital as a precautionary measure; studies which find lower
Asthma is not a risk factor for poor COVID-19 outcomes. Given the paucity of data, we cannot conclude that asthma is not a risk factor for poor COVID-19 outcomes independent of asthma severity.

In conclusion, pooled results do not suggest that PWA are at increased risk for acquiring SARS-CoV-2 compared with those without asthma, and suggest that PWA have similar clinical outcomes with COVID-19. However, results were limited by imprecision, a lack of reporting on asthma severity and, in some cases, substantial unexplained statistical heterogeneity. Though the absence of evidence of a clear association between asthma and worse outcomes from COVID-19 should not be interpreted as evidence of absence, particularly given the paucity of data on asthma severity, the data reviewed do give some indication that risks in PWA, as a whole, may be less than originally anticipated. Further high-quality primary studies are required to reinforce and broaden this conclusion in order to facilitate the development of evidence-based shielding and avoidance measures, as well as appropriate vaccination schedules.

Competing interests
None declared.

Patient consent for publication
Not applicable.

Provenance and peer review
Not commissioned; externally peer reviewed.

Data availability statement
Data are available upon reasonable request. Data sharing not applicable as no datasets were generated and/or analysed for this study. All data are from publicly available documents, and references are provided should readers wish to look at original sources.

Supplemental material
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26 9.5.2 identifying and measuring heterogeneity, 2021. Available: https://handbook-5.1.cochrane.org/chapter_9/9_5_2_identifying_and_measuring_heterogeneity.htm


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Appendix
**Supplementary methods**

### Details of search strategy

We searched Medline, Embase, LitCOVID and the Cochrane study register on 8 October 2020 for COVID-19 clinical studies, published or accepted for publication but not yet published, in any language.

The LitCOVID search strategy was as follows: ‘(asthma OR asthmatic) AND (mortality OR death OR deaths OR fatality OR survival OR hospitalized OR hospitalised OR hospitalization OR hospitalisation OR admission OR "intensive care" OR ventilation OR intubation OR recovery OR severe OR severity)’.

The Cochrane COVID-19 Study Register search strategy was as follows: ‘asthma - Diagnostics/Prognostic - Case Series/Case Control/Cohort’, ‘asthma - Epidemiology - Case Series/Case Control/Cohort’.

The Medline search strategy is outlined below.

1. exp Coronavirus/
2. exp Coronavirus Infections/
3. (coronavirus* or corona virus* or OC43 or NL63 or 229E or HKU1 or HCoV* or ncov* or covid* or sars-cov* or sarscov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus*).mp.
4. ((pneumonia or covid* or coronavirus* or corona virus* or ncov* or 2019-ncov or sars*).mp. or exp pneumonia/) and Wuhan.mp.
5. (2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV on nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19) and pandemic*2) or (coronavirus* and pneumonia)).mp.
7. 1 or 2 or 3 or 4 or 5 or 6
8. exp Asthma/
9. asthma*.ti,ab,kw.
10. 8 or 9
11. exp Mortality/
12. exp Hospitalization/
13. Life Support Care/
14. exp Respiration, Artificial/
15. Critical Care/
16. intensive care units/ or respiratory care units/
17. incidence/ or prevalence/ or risk factors/
18. (mortality or death? or fatal* or survival or recovery).ti,ab,kw.
19. ((sever* or serious* or critical*) adj3 (infection* or complication* or ill*)).ti,ab,kw.
20. (hospitali?ed or hospitali?ation*).ti,ab,kw.
21. ((hospital? or patient?) adj2 (admit* or admission* or readmit* or re-admit* or readmission* or re-admission* or discharg*).ti,ab,kw.
22. (life support or intubat* or ventilat*).ti,ab,kw.
23. ((artificial or assist*) adj2 (respiration or breathing)).ti,ab,kw.
24. (critical care or intensive care or itu or icu or ccu).ti,ab,kw.
25. (((prevalence or incidence) and (risk? or factor? or predict*)) or risk factor?).ti,ab,kw.
26. ((positive or negative or confirmed) adj2 case?).ti,ab,kw.
The Embase search strategy is outlined below.
1 exp Coronavirus/
2 exp Coronavirus Infections/
3 (coronavirus* or corona virus* or OC43 or NL63 or 229E or HKU1 or HCoV* or ncov* or covid* or sars-cov* or sarascov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus*).mp.
4 ((pneumonia or covid* or coronavirus* or corona virus* or ncov* or 2019-ncov or sars*).mp. or exp pneumonia/) and Wuhan.mp.
5 (2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarascov2 or sarascov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV on nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19) and pandemic*2) or (coronavirus* and pneumonia)).mp.
6 1 or 2 or 3 or 4 or 5
7 exp Asthma/
8 asthma*.ti,ab,kw.
9 7 or 8
10 exp Mortality/ or mortality risk/
11 survival/ or cause specific survival/ or long term survival/ or overall survival/ or survival factor/ or survival rate/
12 hospital admission/ or hospital discharge/ or hospital readmission/ or hospital utilization/ or hospitalization/
13 intensive care/ or exp artificial ventilation/
14 intensive care unit/ or medical intensive care unit/
15 incidence/ or prevalence/ or risk factor/
16 (mortality or death? Or fatal* or survival or recovery).ti,ab,kw.
17 ((sever* or serious* or critical*) adj3 (infection* or complication* or ill*)).ti,ab,kw.
18 (hospitali?ed or hospitali?ation*).ti,ab,kw.
19 ((hospital? Or patient?) adj2 (admit* or admission* or readmit* or re-admit* or readmission* or re-admission* or 3ntubate3*).ti,ab,kw.
20 (life support or 3ntubate* or ventilat*).ti,ab,kw.
21 ((artificial or assist*) adj2 (respiration or breathing)).ti,ab,kw.
22 (critical care or intensive care or itu or icu or ccu).ti,ab,kw.
23 ((prevalence or incidence) and (risk? Or factor? Or predict*)) or risk factor?).ti,ab,kw.

limit 30 to yrs="2019 -Current"
((positive or negative or confirmed) adj2 case?).ti,ab,kw.
((clinical or physical or patient?) adj2 (presentation or feature? Or characteristic? Or manifestation?)).ti,ab,kw.
(presentation or feature? Or characteristic? Or manifestation?).ti.
10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
6 and 9 and 27
limit 28 to yr="2019 -Current"
## Supplementary table 1. Data extracted from the included studies. Created by the authors.

Abbreviations: NR, Not reported; ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; ICU, intensive care unit; ARB, angiotensin-II receptor blocker; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; HTN, hypertension; CAD, coronary artery disease; DM, Diabetes Mellitus; SABA, short acting beta-agonist; ICS, inhaled corticosteroids.

<table>
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<th>Study Author(s), year</th>
<th>Design</th>
<th>Country</th>
<th>Setting</th>
<th>Dates of data collection</th>
<th>Reported outcomes</th>
<th>Number with Covid</th>
<th>Number with asthma</th>
<th>Number without asthma</th>
<th>Mean/Median Age (years)</th>
<th>Male gender</th>
<th>Median BMI</th>
<th>Adjusted analysis</th>
<th>NOS Score</th>
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<tbody>
<tr>
<td>Abrams 2020 [28]</td>
<td>Retrospective cohort</td>
<td>USA</td>
<td>Hospital</td>
<td>March 1\textsuperscript{st} – April 3\textsuperscript{rd} 2020</td>
<td>Mortality</td>
<td>133</td>
<td>6</td>
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<td>Adrish 2020 [29]</td>
<td>Retrospective cohort</td>
<td>USA</td>
<td>Hospital</td>
<td>March 1\textsuperscript{st} – March 31\textsuperscript{st} 2020</td>
<td>Prevalence</td>
<td>469</td>
<td>83</td>
<td>386</td>
<td>ACE/ARB: 64.6</td>
<td>ACE/ARB: 56%</td>
<td>ACE/ARB: BMI &gt;30: 41 (45.1%)</td>
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<td>Atkins 2020 [30]</td>
<td>Retrospective cohort</td>
<td>UK</td>
<td>Community and Hospital</td>
<td>March 16\textsuperscript{th} – April 26\textsuperscript{th} 2020</td>
<td>Prevalence Mortality</td>
<td>507</td>
<td>90</td>
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<td>61.3</td>
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<td>Barrosa 2020 [31]</td>
<td>Retrospective cohort</td>
<td>Spain</td>
<td>Hospital</td>
<td>March 1\textsuperscript{st} – March 21\textsuperscript{st} 2020</td>
<td>Prevalence ICU admission Mortality</td>
<td>189</td>
<td>11</td>
<td>178</td>
<td>Asthma: 57.7</td>
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<td>Asthma: 29.9</td>
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<td>Study</td>
<td>Design</td>
<td>Location</td>
<td>Hospital or records</td>
<td>Start Date - End Date</td>
<td>Outcome Measures</td>
<td>Prevalence</td>
<td>Hospitalisation</td>
<td>Mortality</td>
<td>Asthma:</td>
<td>No Asthma:</td>
<td>Age, Sex, BMI, Other Risk Factors</td>
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<tr>
<td>Beurnier 2020</td>
<td>Prospective cohort</td>
<td>France</td>
<td>Hospital</td>
<td>March 15th - April 15th 2020</td>
<td>Prevalence, Mortality</td>
<td>768</td>
<td>37</td>
<td>731</td>
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<td>30%</td>
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<td>Bozek 2020</td>
<td>Retrospective cohort</td>
<td>Poland and Germany</td>
<td>Hospital</td>
<td>March-April 2020</td>
<td>Prevalence, Hospitalisation</td>
<td>5</td>
<td>445</td>
<td>N.A</td>
<td>Montelukast: 64.3</td>
<td>Montelukast: 43.7%</td>
<td>NR</td>
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<td>Broadhurst 2020</td>
<td>Cross-sectional</td>
<td>USA</td>
<td>Hospital</td>
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<td>Prevalence, ICU admission</td>
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<td>53</td>
<td>383</td>
<td>Asthma: 32</td>
<td>Asthma: 34.6</td>
<td>Asthma: 35.7, Yes (Age, Sex, BMI)</td>
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<tr>
<td>Chhiba 2020</td>
<td>Retrospective cohort</td>
<td>USA</td>
<td>Medical records</td>
<td>March 1st - April 30th 2020</td>
<td>Prevalence, Hospitalisation, Mortality</td>
<td>1526</td>
<td>220</td>
<td>1,065</td>
<td>Asthma: &lt;40; 63 (28.6%)</td>
<td>Asthma: 70.9%</td>
<td>NR</td>
<td>Yes (Hospitalisation) (Age, Sex, smoking status, obesity, HTN, DM, CAD, COPD, allergic rhinitis, rhinosinusitis, and immunodeficiency)</td>
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<td>Choi 2020</td>
<td>Retrospective cohort</td>
<td>Korea</td>
<td>Medical Records</td>
<td>January 2017-15th May 2020</td>
<td>7590</td>
<td>218</td>
<td>7372</td>
<td>Asthma: 0–9: 20 (9.2%), 10–19: 6 (2.8%), 20–29: 19 (8.7%), 30–39: 18 (8.2%), 40–49: 25 (11.5%), 50–59: asthma 34 (15.6%), 60–69: 36 (16.5%), 70–84: 60 (27.5%) Non-Asthma: 0–9: 62 (0.8%), 10–19: 343 (4.7%), 20–29: 1,833 (24.9%), 30–39: 758 (10.3%), 40–49: 983 (13.3%), 50–59: 1,468 (19.9%), 60–69: 1,020 (13.8%), 70–84: 6 (11.5%)</td>
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<td>Garcia-Pachon 2020 [35]</td>
<td>Retrospective cohort</td>
<td>Spain</td>
<td>Community and Hospital</td>
<td>March 3rd - April 12th 2020</td>
<td>376</td>
<td>10</td>
<td>366</td>
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<td>51%</td>
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<td>March 4th - April 6th 2020</td>
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<td>Country</td>
<td>Setting</td>
<td>Date</td>
<td>Prevalence</td>
<td>Hospitalisation</td>
<td>Mortality</td>
<td>Admissions</td>
<td>Total (%)</td>
<td>Not reported (%)</td>
<td>Yes (%)</td>
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<td>Keswani 2020 [37]</td>
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<td>USA</td>
<td>Medical Records</td>
<td>NR</td>
<td>1043</td>
<td>265</td>
<td>778</td>
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<tr>
<td>Kim 2020 [38]</td>
<td>Retrospective cohort</td>
<td>Korea</td>
<td>Hospital</td>
<td>Feb 17\textsuperscript{th} - May 19\textsuperscript{th} 2020</td>
<td>2200</td>
<td>70</td>
<td>2130</td>
<td>Total: 56.7</td>
<td>Total: 35.7%</td>
<td>Total: 23.5 (3.4)</td>
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<tr>
<td>Ko 2020 [39]</td>
<td>Cross-sectional analysis</td>
<td>USA</td>
<td>Hospital</td>
<td>March 1\textsuperscript{st} - June 23\textsuperscript{rd} 2020</td>
<td>5416</td>
<td>702</td>
<td>4714</td>
<td>Total: 18-44: 30% 45-64: 40% 65+: 31%</td>
<td>Total: 53%</td>
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<td>Lemus-Calderon 2020 [40]</td>
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<td>Spain</td>
<td>Community and Hospital</td>
<td>July 2020</td>
<td>6310</td>
<td>577</td>
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<td>Total: 41%</td>
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<td>Lieberman-Cribbin 2020 [41]</td>
<td>Retrospective cohort</td>
<td>USA</td>
<td>Hospital</td>
<td>February 29\textsuperscript{th} - April 24\textsuperscript{th} 2020</td>
<td>11405</td>
<td>618</td>
<td>10787</td>
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<td>Total: 49%</td>
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<tr>
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<td>Design/Type</td>
<td>Country</td>
<td>Setting</td>
<td>Date Range</td>
<td>Prevalence</td>
<td>ICU Admissions</td>
<td>Mortality</td>
<td>Prevalence</td>
<td>ICU Admissions</td>
<td>Mortality</td>
<td>Asthma Range</td>
<td>Non-asthma Range</td>
<td>Race, Sex and BMI</td>
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<td>Lombardi 2020 [42]</td>
<td>Retrospective cohort</td>
<td>Italy</td>
<td>Hospital</td>
<td>February 20th-April 20th 2020</td>
<td>1043</td>
<td>20</td>
<td>1023</td>
<td>Total: 14-91 (Range)</td>
<td>Total: 67.5%</td>
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<td>Asthma: 40%</td>
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<td>Lovinsky-Desir 2020 [11]</td>
<td>Retrospective cohort</td>
<td>USA</td>
<td>Hospital</td>
<td>February 11th-May 7th 2020</td>
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<td>163</td>
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<td>Asthma: 51</td>
<td>Non-asthma: 52</td>
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<td>Yes</td>
<td>(Race, Sex and BMI)</td>
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<td>Mahdavinia 2020 [43]</td>
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<td>Medical Records</td>
<td>March 12th-April 3rd 2020</td>
<td>935</td>
<td>241</td>
<td>694</td>
<td>Asthma: 18-49: 138 (57.3%)</td>
<td>Asthma: 33.2%</td>
<td>Asthma: 33.6</td>
<td>Non-asthma: 48.6%</td>
<td>Non-asthma: 31.6</td>
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<td>Matucci 2020 [44]</td>
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<td>Community</td>
<td>April 1st - April 20th 2020</td>
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<td>473</td>
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<td>Brazil</td>
<td>Hospital</td>
<td>February 26th-May 23rd 2020</td>
<td>31962</td>
<td>102</td>
<td>31860</td>
<td>Total: 0-4: 0.8%</td>
<td>0-5: 0.1%</td>
<td>10-19: 0.5%</td>
<td>20-39: 15.7%</td>
<td>40-49: 37.7%</td>
<td>60 or more: 45.2%</td>
<td>NR</td>
<td>No</td>
<td>3</td>
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<th>Design</th>
<th>Country</th>
<th>Period</th>
<th>Prevalence</th>
<th>Mortality</th>
<th>Total: Prevalence Hospitalisation</th>
<th>Total: Mortality</th>
<th>PWA treated with:</th>
<th>NR</th>
<th>Yes</th>
<th>Adjusted for significant variable in the model, both statistically and theoretically</th>
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<td>Norway</td>
<td>Community and Hospital</td>
<td>March 1&lt;sup&gt;st&lt;/sup&gt;-May 13&lt;sup&gt;th&lt;/sup&gt; 2020</td>
<td>7632</td>
<td>515</td>
<td>7117</td>
<td>40+</td>
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<td>(Sex and Age)</td>
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<td>Ruano 2020 [47]</td>
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<td>Spain</td>
<td>Hospital</td>
<td>February-April 2020</td>
<td>29</td>
<td>212</td>
<td>N.A</td>
<td>10</td>
<td>79%</td>
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<td>Santos 2020 [48]</td>
<td>Retrospective cohort</td>
<td>Brazil</td>
<td>Hospital</td>
<td>February 20&lt;sup&gt;th&lt;/sup&gt;-June 2&lt;sup&gt;nd&lt;/sup&gt; 2020</td>
<td>26730</td>
<td>2238</td>
<td>24492</td>
<td>&lt;50: 3119 (14.6%)</td>
<td>51-67: 6763 (31.6%)</td>
<td>68 or more: 11526 (53.8%)</td>
<td>59.2%</td>
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<td>Schultz 2020 [49]</td>
<td>Retrospective cohort</td>
<td>UK</td>
<td>Medical Records</td>
<td>March 1&lt;sup&gt;st&lt;/sup&gt;-May 6&lt;sup&gt;th&lt;/sup&gt; 2020</td>
<td>529</td>
<td>818490</td>
<td>N.A</td>
<td>PWA treated with: SABA: 48.3</td>
<td>Low or Medium ICS: 53.1</td>
<td>High ICS: 55</td>
<td>NR</td>
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<td>Song 2020 [50]</td>
<td>Retrospective cohort</td>
<td>China</td>
<td>Hospital</td>
<td>February 1&lt;sup&gt;st&lt;/sup&gt;-March 6&lt;sup&gt;th&lt;/sup&gt; 2020</td>
<td>961</td>
<td>22</td>
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<td>Total: 63</td>
<td>Total: 52%</td>
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<td>Toussie 2020 [51]</td>
<td>Retrospective cohort</td>
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<td>Hospital</td>
<td>March 10&lt;sup&gt;th&lt;/sup&gt;-March 26&lt;sup&gt;th&lt;/sup&gt; 2020</td>
<td>338</td>
<td>46</td>
<td>292</td>
<td>39</td>
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<td>March 3&lt;sup&gt;rd&lt;/sup&gt;-June 8&lt;sup&gt;th&lt;/sup&gt; 2020</td>
<td>1827</td>
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<td>Retrospective cohort</td>
<td>Korea</td>
<td>Medical Records</td>
<td>January 1&lt;sup&gt;st&lt;/sup&gt;-May 15&lt;sup&gt;th&lt;/sup&gt;</td>
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<td>UK Hospital</td>
<td>March 16th - April 16th, 2020</td>
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<td>Asthma: 56</td>
<td>Yes (age, sex, race, BMI)</td>
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<td>diabetes mellitus, cerebrovascular disease, COPD, hypertension, or chronic kidney disease, Charlson comorbidity index and use of immunosuppressants</td>
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**Supplementary Table 2. Quality assessment of studies using the Newcastle-Ottawa scale.**

<table>
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<th>Study ID</th>
<th>Representativeness of exposed cohort (⋆)</th>
<th>Selection of non-exposed cohort (⋆)</th>
<th>Ascertainment of exposure (⋆)</th>
<th>Demonstration that outcome of interest was not present at start of study (⋆⋆)</th>
<th>Comparability</th>
<th>Assessment of outcome (⋆)</th>
<th>Was follow-up long enough for outcomes to occur (⋆)</th>
<th>Adequacy of follow up of cohorts (⋆)</th>
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**Supplementary Figure 1.** Funnel plot for Prevalence Meta-analysis. Created by the authors.
Supplementary Figure 2. Prevalence of asthma in COVID-19 stratified by clinical setting. Created by the authors.

### 4.3.1.2 Hospital Only

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<th>Weight</th>
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<th>SE</th>
<th>Weight</th>
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<td>1.702382</td>
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<td>5.8</td>
<td>1.702382</td>
<td></td>
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<td>1.702382</td>
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</table>

Subtotal (55% CI) 60.9% [54.2; 64.6]

Heterogeneity: $\tau^2 = 19.59, \chi^2 = 326.58, df = 12$ ($p < 0.00001$), $I^2 = 99$

Test for overall effect: $Z = 6.39$ ($p < 0.00001$)

### 4.3.1.3 Community and Hospital

<table>
<thead>
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<th>SE</th>
<th>Weight</th>
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<th>SE</th>
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<td>17.6</td>
<td>1.691282</td>
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<td>2.9</td>
<td>0.012431</td>
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<td>Gecreter-Hamone (France)</td>
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Subtotal (55% CI) 33.1% [11.3; 64.0]

Heterogeneity: $\tau^2 = 12.33, \chi^2 = 754.59, df = 7$ ($p < 0.00001$), $I^2 = 99$

Test for overall effect: $Z = 6.15$ ($p < 0.00001$)

Total (95% CI) 100.0% [73.5; 119.8]

Heterogeneity: $\tau^2 = 20.41, \chi^2 = 5370.06, df = 26$ ($p < 0.00001$), $I^2 = 99$

Test for overall effect: $Z = 9.28$ ($p < 0.00001$)

Test for subgroup differences: $\chi^2 = 11.2, df = 1$ ($p = 0.001$), $I^2 = 45$

---

Supplementary Figure 3. Asthma prevalence in studies where the mean/median BMI was 30 or greater compared to studies where the mean/median BMI was less than 30. Created by the authors.

<table>
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<th>Study or Subgroup</th>
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<th>Prevalence IV, Random, 95% CI</th>
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<td>Barrett (Spain)</td>
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<td>4.5%</td>
<td>5.00 [2.47, 9.13]</td>
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<td>1.569415</td>
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<td>12.70 [9.13, 15.27]</td>
<td>12.70 [9.13, 15.27]</td>
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<td>1.488589</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 7.82 (P &lt; 0.0001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>100.0%</td>
<td>9.38</td>
<td>7.38, 11.38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 20.41; Chi² = 3570.66, df = 20 (P &lt; 0.0001); I² = 98%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 9.90 (P &lt; 0.0001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Chi² = 2.53, df = 1 (P = 0.11); I² = 60.4%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Supplementary Figure 4. Asthma prevalence in studies where the majority of the cohort (over 50%) was of white ethnicity compared to where the minority of the cohort (50% or less) was of white ethnicity. Created by the authors.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Prevalence</th>
<th>SE</th>
<th>Weight</th>
<th>Prevalence Random, 95% CI</th>
<th>Prevalence IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.1.3 Non-White</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma USA</td>
<td>27.7</td>
<td>1.7938123</td>
<td>4.9%</td>
<td>17.70 (14.25, 21.22)</td>
<td></td>
</tr>
<tr>
<td>China (USA)</td>
<td>16.6</td>
<td>0.097954</td>
<td>4.9%</td>
<td>14.60 (12.64, 16.84)</td>
<td></td>
</tr>
<tr>
<td>Ke (USA)</td>
<td>12.2</td>
<td>0.4999775</td>
<td>5.0%</td>
<td>12.20 (11.38, 13.10)</td>
<td></td>
</tr>
<tr>
<td>Lecithin-Dex (USA)</td>
<td>12.5</td>
<td>0.507893</td>
<td>4.9%</td>
<td>12.50 (10.89, 14.40)</td>
<td></td>
</tr>
<tr>
<td>Manganese-Dex (USA)</td>
<td>25.2</td>
<td>1.408003</td>
<td>4.6%</td>
<td>25.20 (23.09, 28.50)</td>
<td></td>
</tr>
<tr>
<td>Nigarr (Brazil)</td>
<td>0.32</td>
<td>0.025185</td>
<td>5.3%</td>
<td>0.32 (0.27, 0.38)</td>
<td></td>
</tr>
<tr>
<td>Tobacco (USA)</td>
<td>14.6</td>
<td>1.081385</td>
<td>4.6%</td>
<td>14.60 (13.10, 16.27)</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>13.4% (12.02, 15.57)</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity:</td>
<td>Tau² = 9.46, Chi² = 1648.61, df = 6 (P &lt; 0.00001), I² = 99%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 5.57 (P &lt; 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5.1.2 White

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Prevalence</th>
<th>SE</th>
<th>Weight</th>
<th>Prevalence Random, 95% CI</th>
<th>Prevalence IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Song (USA)</td>
<td>16.1</td>
<td>0.755956</td>
<td>4.9%</td>
<td>14.10 (12.55, 14.85)</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>14.10 (12.55, 14.85)</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity:</td>
<td>Tau² = 10.60, Chi² = 2099.97, df = 6 (P &lt; 0.00001), I² = 99%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 16.80 (P &lt; 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5.1.3 Non-ethnicity Data

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Prevalence</th>
<th>SE</th>
<th>Weight</th>
<th>Prevalence Random, 95% CI</th>
<th>Prevalence IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alaborta (Spain)</td>
<td>17.8</td>
<td>1.691286</td>
<td>4.1%</td>
<td>17.80 (14.29, 21.29)</td>
<td></td>
</tr>
<tr>
<td>Barrios (Spain)</td>
<td>5.1</td>
<td>0.980238</td>
<td>4.3%</td>
<td>5.10 (2.67, 9.13)</td>
<td></td>
</tr>
<tr>
<td>Bouhier (France)</td>
<td>6.8</td>
<td>0.712462</td>
<td>10.0%</td>
<td>6.80 (3.23, 10.41)</td>
<td></td>
</tr>
<tr>
<td>Brouhaud (USA)</td>
<td>12.3</td>
<td>1.567415</td>
<td>4.5%</td>
<td>12.30 (10.15, 15.77)</td>
<td></td>
</tr>
<tr>
<td>Che (China)</td>
<td>2.9</td>
<td>0.38614</td>
<td>1.5%</td>
<td>2.90 (2.54, 3.26)</td>
<td></td>
</tr>
<tr>
<td>Garcia-Paredes (Spain)</td>
<td>27.0</td>
<td>0.088523</td>
<td>4.9%</td>
<td>27.00 (23.89, 30.10)</td>
<td></td>
</tr>
<tr>
<td>Grandjean (France)</td>
<td>31.5</td>
<td>0.805866</td>
<td>3.9%</td>
<td>31.50 (28.61, 34.51)</td>
<td></td>
</tr>
<tr>
<td>Kim (South Korea)</td>
<td>2.7</td>
<td>0.375733</td>
<td>3.3%</td>
<td>2.70 (2.10, 3.39)</td>
<td></td>
</tr>
<tr>
<td>Lemos (Colombia)</td>
<td>3.14</td>
<td>0.363233</td>
<td>5.1%</td>
<td>3.14 (2.62, 3.65)</td>
<td></td>
</tr>
<tr>
<td>Lichtenstein-C (Ohio, USA)</td>
<td>4.55</td>
<td>0.296968</td>
<td>4.1%</td>
<td>4.55 (3.84, 5.26)</td>
<td></td>
</tr>
<tr>
<td>Luft (Italy)</td>
<td>3.60</td>
<td>0.348912</td>
<td>5.1%</td>
<td>3.60 (2.86, 4.35)</td>
<td></td>
</tr>
<tr>
<td>Noh (Korea)</td>
<td>0.2</td>
<td>0.028732</td>
<td>5.1%</td>
<td>0.20 (0.16, 0.24)</td>
<td></td>
</tr>
<tr>
<td>Song (South Korea)</td>
<td>1.5</td>
<td>0.351359</td>
<td>5.0%</td>
<td>1.50 (1.11, 1.92)</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>6.7% (6.21, 7.25)</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity:</td>
<td>Tau² = 9.46, Chi² = 776.92, df = 13 (P &lt; 0.00001), I² = 99%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 7.86 (P &lt; 0.00001)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI): 100% 9.3% (7.98, 11.38)

Heterogeneity: Tau² = 24.41, Chi² = 2099.96, df = 13 (P < 0.00001), I² = 99%

Test for overall effect: Z = 19.00 (P < 0.00001)

Test for subgroup differences: Chi² = 95.98, df = 3 (P < 0.00001), I² = 94.9%
### Supplementary Figure 5

Asthma prevalence in studies where the mean/median age was 60 or greater compared to studies where the mean/median age was less than 60. Created by the authors.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Prevalence</th>
<th>SE</th>
<th>Weight</th>
<th>Prevalence</th>
<th>SE</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( % Random, 95% CI)</td>
<td>( % Random, 95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Asthma prevalence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>100.0%</td>
<td>5.3%</td>
<td>11.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>**Intergroup: $\chi^2 = 29.44; df = 20 (P &lt; 0.0001)$</td>
<td>$I^2 = 59$%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>**Test for overall effect: Z = 0.28 (P = 0.80001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3.1.1 Age &gt;60</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrioli (USA)</td>
<td>17.7</td>
<td>1.762182</td>
<td>4.6%</td>
<td>17.70 [14.25, 21.15]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Link (UK)</td>
<td>17.6</td>
<td>1.493282</td>
<td>4.5%</td>
<td>17.60 [14.29, 20.91]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knt (Korea)</td>
<td>3.2</td>
<td>0.373233</td>
<td>5.1%</td>
<td>3.20 [2.46, 3.94]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sena (China)</td>
<td>2.1</td>
<td>0.463959</td>
<td>5.6%</td>
<td>2.10 [1.35, 3.13]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>**Intergroup: $\chi^2 = 21.78; df = 3 (P &lt; 0.0001)$</td>
<td>$I^2 = 59$%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>**Test for overall effect: Z = 4.04 (P &lt; 0.0001)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>3.1.2 Age &lt;60</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bresnana (Spain)</td>
<td>5.8</td>
<td>1.762182</td>
<td>4.5%</td>
<td>5.80 [2.47, 9.13]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chou (France)</td>
<td>4.8</td>
<td>0.771362</td>
<td>5.0%</td>
<td>4.80 [3.79, 5.81]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breadmore (USA)</td>
<td>12.2</td>
<td>1.564115</td>
<td>4.9%</td>
<td>12.20 [9.31, 15.27]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Garcia-Pachon (Spain)</td>
<td>2.7</td>
<td>0.686323</td>
<td>4.9%</td>
<td>2.78 [1.94, 4.64]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grandbasset (France)</td>
<td>21.7</td>
<td>0.868666</td>
<td>2.9%</td>
<td>21.70 [13.61, 29.95]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lennus-Candelier (Spain)</td>
<td>9.1</td>
<td>0.362923</td>
<td>5.1%</td>
<td>9.10 [5.94, 9.85]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lavinsky-Davies (USA)</td>
<td>12.6</td>
<td>0.952895</td>
<td>4.9%</td>
<td>12.60 [10.75, 14.45]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tsuji (USA)</td>
<td>14.1</td>
<td>1.317661</td>
<td>4.3%</td>
<td>14.00 [10.18, 17.79]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang (USA)</td>
<td>13.1</td>
<td>0.789462</td>
<td>4.9%</td>
<td>13.00 [11.13, 14.85]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>**Intergroup: $\chi^2 = 14.11; df = 8 (P &lt; 0.0001)$</td>
<td>$I^2 = 59$%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>**Test for overall effect: Z = 3.18 (P = 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3.1.3 No Age Data</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chiba (Japan)</td>
<td>14.4</td>
<td>0.898754</td>
<td>4.9%</td>
<td>14.40 [12.64, 16.16]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chai (Korea)</td>
<td>2.8</td>
<td>1.029514</td>
<td>5.1%</td>
<td>2.80 [2.52, 3.12]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kiy (Japan)</td>
<td>31.1</td>
<td>1.419575</td>
<td>5.0%</td>
<td>31.00 [22.13, 39.99]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Libesmann-Cribbin (USA)</td>
<td>4.5</td>
<td>0.628648</td>
<td>5.1%</td>
<td>4.55 [4.02, 5.08]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamberts (Japan)</td>
<td>1.9</td>
<td>0.244512</td>
<td>5.1%</td>
<td>1.90 [1.89, 2.75]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mavridou (Greece)</td>
<td>27.8</td>
<td>1.453803</td>
<td>4.9%</td>
<td>27.80 [23.70, 32.60]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nagai (Brazil)</td>
<td>9.2</td>
<td>0.851568</td>
<td>5.1%</td>
<td>9.20 [6.25, 12.12]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nyström (Sweden)</td>
<td>6.7</td>
<td>0.257362</td>
<td>5.1%</td>
<td>6.70 [4.13, 9.73]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>**Intergroup: $\chi^2 = 17.46; df = 7 (P &lt; 0.0001)$</td>
<td>$I^2 = 100$%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>**Test for overall effect: Z = 5.63 (P = 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Supplementary Figure 6.** Funnel plot for Mortality Meta-analysis. Created by the authors.
Supplementary Figure 7. COVID-19 mortality in PWA in studies where the mean/median age was 60 or greater compared to studies where the mean/median age was less than 60. Created by the authors.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Odds Ratio</th>
<th>Odd Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.1.1 No Age Data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chile (USA)</td>
<td>-0.1174107</td>
<td>0.1796149</td>
<td>0.75 [0.35, 1.61]</td>
<td></td>
</tr>
<tr>
<td>China (Korea)</td>
<td>0.27763174</td>
<td>0.3211761</td>
<td>1.32 [0.70, 2.48]</td>
<td></td>
</tr>
<tr>
<td>Lombardy (Italy)</td>
<td>-0.8675646</td>
<td>0.7420266</td>
<td>0.42 [0.23, 0.76]</td>
<td></td>
</tr>
<tr>
<td>Madrid (Spain)</td>
<td>-0.3400972</td>
<td>0.7604454</td>
<td>0.71 [0.53, 0.95]</td>
<td></td>
</tr>
<tr>
<td>Santor (Brazil)</td>
<td>-0.3434148</td>
<td>0.7235464</td>
<td>0.71 [0.52, 0.95]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td>0.71 [0.52, 0.95]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.08; Chi^2 = 7.00; df = 4 (P = 0.14); I^2 = 43%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.81 (P = 0.42)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.1.4 60+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Athens (GRE)</td>
<td>-0.5276227</td>
<td>0.3925238</td>
<td>0.59 [0.33, 0.97]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.28; Chi^2 = 4.05; df = 2 (P = 0.13); I^2 = 51%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.62 (P = 0.54)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.3.5 &lt;60</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barroso (Spain)</td>
<td>0.52672853</td>
<td>0.3156161</td>
<td>1.69 [0.14, 8.36]</td>
<td></td>
</tr>
<tr>
<td>Lemos-Cabral (Spain)</td>
<td>0.09867700</td>
<td>9.8%</td>
<td>0.00 [0.00, 1.00]</td>
<td></td>
</tr>
<tr>
<td>Liebermann-Cribbin (USA)</td>
<td>-0.0618754</td>
<td>0.1805945</td>
<td>13.3%</td>
<td>0.94 [0.66, 1.34]</td>
</tr>
<tr>
<td>Louie-Joy (USA)</td>
<td>-0.51082857</td>
<td>0.3557656</td>
<td>0.60 [0.30, 1.19]</td>
<td></td>
</tr>
<tr>
<td>Wang (USA)</td>
<td>0.13904039</td>
<td>0.1120918</td>
<td>1.16 [0.90, 1.50]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td>1.16 [0.90, 1.50]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.01; Chi^2 = 4.75; df = 4 (P = 0.31); I^2 = 30%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.64 (P = 0.42)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>100.0%</td>
<td>0.00 [0.72, 1.13]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.07; Chi^2 = 28.38; df = 12 (P = 0.00); I^2 = 18%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.90 (P = 0.37)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Supplementary Figure 8. COVID-19 mortality in PWA in adjusted vs unadjusted studies. Created by the authors.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Log(Odds Ratio)</th>
<th>SE</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>20.1.1 Adjusted</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arkansas (U.S.)</td>
<td>-0.5276327</td>
<td>0.29282738</td>
<td>8.8%</td>
<td>0.59 [0.33, 1.05]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choi (Korea)</td>
<td>0.27763174</td>
<td>0.32111761</td>
<td>7.9%</td>
<td>1.32 [0.70, 2.48]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kim (Korea)</td>
<td>0.50864176</td>
<td>0.49908423</td>
<td>4.3%</td>
<td>1.66 [0.62, 4.42]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lieberman-Cribbin (USA)</td>
<td>-0.0618754</td>
<td>0.18069545</td>
<td>13.4%</td>
<td>0.94 [0.66, 1.34]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mahdvoinia (USA)</td>
<td>0.94000726</td>
<td>0.70044514</td>
<td>2.1%</td>
<td>2.30 [0.57, 11.50]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Santos (Brazil)</td>
<td>-0.3424903</td>
<td>0.07234064</td>
<td>18.4%</td>
<td>0.71 [0.62, 0.82]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>54.0%</td>
<td>0.90 [0.67, 1.21]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.06; Chi² = 10.92, df = 5 (P = 0.05); I² = 54%

Test for overall effect: Z = 0.71 (P = 0.48)

**20.1.8 Unadjusted**

| Barnett (Spain) | 0.524379 | 0.1558186 | 1.8% | 1.69 [0.34, 8.36] | | |
| Chen (U.S.A) | -0.3147107 | 0.37901149 | 6.4% | 0.73 [0.35, 1.54] | | |
| Leonzio-Calderon (Spain) | 0 | 0.26567201 | 9.8% | 1.00 [0.59, 1.68] | | |
| Lombard (Italy) | -0.967536 | 0.74300064 | 2.2% | 0.18 [0.09, 1.63] | | |
| Lovinsky-Dejean (U.S.A) | -0.5308256 | 0.35570556 | 0.9% | 0.60 [0.30, 1.20] | | |
| Song (China) | -1.2317844 | 0.101532449 | 1.2% | 0.29 [0.04, 1.12] | | |
| Wang (U.S.A) | 0.4503030 | 0.11120518 | 16.8% | 1.21 [0.87, 1.70] | | |
| **Subtotal (95% CI)** | | | | | | |
| | | | 45.1% | 0.91 [0.66, 1.25] | | |

Heterogeneity: Tau² = 0.05; Chi² = 8.86, df = 6 (P = 0.18); I² = 33%

Test for overall effect: Z = 0.57 (P = 0.57)

**Total (95% CI)**

100.0% 0.90 [0.72, 1.13]

Heterogeneity: Tau² = 0.07; Chi² = 28.38, df = 12 (P = 0.005); I² = 58%

Test for overall effect: Z = 0.90 (P = 0.37)

Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.95), I² = 0%
**Supplementary Figure 9.** COVID-19 mortality in people with asthma compared to people without asthma, subgrouped by ethnicity (the majority of the cohort (over 50%) was of white ethnicity compared to where the minority of the cohort (50% or less) was of white ethnicity). Created by the authors.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Odds Ratio IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>24.1.1 Non-white</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chile (USA)</td>
<td>-0.3147107</td>
<td>0.37961194</td>
<td>0.73 (0.33, 1.64)</td>
<td></td>
</tr>
<tr>
<td>Lieberman-Cribbin (USA)</td>
<td>-0.0016748</td>
<td>0.18063945</td>
<td>0.94 (0.66, 1.34)</td>
<td></td>
</tr>
<tr>
<td>Lovinsky-Descarre (USA)</td>
<td>-0.5102856</td>
<td>0.3576356</td>
<td>0.60 (0.30, 1.20)</td>
<td></td>
</tr>
<tr>
<td>Malavolta (USA)</td>
<td>0.04000726</td>
<td>0.76644544</td>
<td>2.18 (0.57, 11.50)</td>
<td></td>
</tr>
<tr>
<td>Santos (Brazil)</td>
<td>0.3424903</td>
<td>0.07244646</td>
<td>1.33 (0.62, 0.03)</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>47.2%</strong></td>
<td><strong>0.77 [0.63, 0.94]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.01; Ch² = 5.05, df = 4 (P = 0.28); P² = 21% Test for overall effect: Z = 2.13 (P = 0.03)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24.1.2 White</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang (USA)</td>
<td>0.19012036</td>
<td>0.1120538</td>
<td>1.21 (0.97, 1.50)</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>16.8%</strong></td>
<td><strong>0.21 [0.97, 1.50]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Not applicable Test for overall effect: Z = 1.73 (P = 0.09)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24.1.3 No Ethnicity data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atkins (UK)</td>
<td>-0.5276327</td>
<td>0.2982738</td>
<td>0.59 (0.33, 1.05)</td>
<td></td>
</tr>
<tr>
<td>Barros (Spain)</td>
<td>0.52477853</td>
<td>0.81568161</td>
<td>1.68 (0.34, 3.86)</td>
<td></td>
</tr>
<tr>
<td>Choi (Korea)</td>
<td>0.17761374</td>
<td>0.2111761</td>
<td>1.10 (0.57, 1.90)</td>
<td></td>
</tr>
<tr>
<td>Kim (Korea)</td>
<td>0.5059176</td>
<td>0.49090825</td>
<td>1.66 (0.62, 4.42)</td>
<td></td>
</tr>
<tr>
<td>Lemus-Calderon (Spain)</td>
<td>0.2656778</td>
<td>0.26570701</td>
<td>1.00 (0.59, 1.68)</td>
<td></td>
</tr>
<tr>
<td>Lombardi (Italy)</td>
<td>0.92759954</td>
<td>0.74727064</td>
<td>2.22 (0.38, 1.63)</td>
<td></td>
</tr>
<tr>
<td>Song (China)</td>
<td>-1.3747441</td>
<td>1.01322401</td>
<td>1.28 (0.04, 2.12)</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>36.0%</strong></td>
<td><strong>0.92 [0.63, 1.35]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.017; Ch² = 8.33, df = 6 (P = 0.22); P² = 28% Test for overall effect: Z = 0.42 (P = 0.67)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>0.99 [0.72, 1.33]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.01; Ch² = 28.33, df = 12 (P = 0.005); P² = 58% Test for overall effect: Z = 0.90 (P = 0.37)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Ch² = 8.89, df = 2 (P = 0.03), I² = 77.5%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Supplementary Figure 10. COVID-19 hospitalisation rates in PWA in adjusted vs unadjusted studies. Created by the authors.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Log(Odds Ratio)</th>
<th>SE</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>7.1.5 Adjusted</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chiba (Japan)</td>
<td>-0.5788</td>
<td>0.0615</td>
<td>0.56 (0.49, 0.63)</td>
</tr>
<tr>
<td>Kaswa (USA)</td>
<td>-0.261</td>
<td>0.315</td>
<td>0.77 (0.57, 1.04)</td>
</tr>
<tr>
<td>Kaswa (USA) (Non-allergic)</td>
<td>0.0226</td>
<td>0.261</td>
<td>0.99 (0.75, 1.31)</td>
</tr>
<tr>
<td>Ko (Korea)</td>
<td>0.5696</td>
<td>0.219</td>
<td>1.77 (1.16, 2.64)</td>
</tr>
<tr>
<td>Nysted (Norway)</td>
<td>0.6151</td>
<td>0.611</td>
<td>1.85 (1.49, 2.29)</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>0.391</td>
<td>1.07 (0.61, 1.84)</td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity</strong></td>
<td></td>
<td></td>
<td>Tau² = 0.38; Cki² = 101.91, df = 4 (p &lt; 0.00001); I² = 98%</td>
</tr>
<tr>
<td><strong>Test for overall effect:</strong></td>
<td>Z = 0.23 (p = 0.82)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**7.1.6 Unadjusted**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Log(Odds Ratio)</th>
<th>SE</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garcia-Pechon (Spain)</td>
<td>-0.08</td>
<td>0.519</td>
<td>0.92 (0.25, 3.34)</td>
</tr>
<tr>
<td>Lemos-Calandron (Spain)</td>
<td>-0.5788</td>
<td>0.89549</td>
<td>0.55 (0.49, 0.61)</td>
</tr>
<tr>
<td>Mahdavi (USA)</td>
<td>0.077</td>
<td>0.1752</td>
<td>1.08 (0.77, 1.52)</td>
</tr>
<tr>
<td>Wang (USA)</td>
<td>-0.151</td>
<td>0.0563</td>
<td>0.86 (0.77, 0.96)</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>0.006</td>
<td>0.79 (0.64, 1.11)</td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity</strong></td>
<td></td>
<td></td>
<td>Tau² = 0.06; Cki² = 31.01, df = 1 (p &lt; 0.00001); I² = 60%</td>
</tr>
<tr>
<td><strong>Test for overall effect:</strong></td>
<td>Z = 1.34 (p = 0.18)</td>
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</tr>
</tbody>
</table>

**Total (95% CI)**

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>160.0%</td>
</tr>
</tbody>
</table>

**Heterogeneity**

- Tau² = 0.16; Cki² = 139.85, df = 8 (p < 0.00001); I² = 94%
- Test for overall effect: Z = 3.31 (p = 0.0001)
- Test for subgroup differences: Cki² = 0.41, df = 1 (p = 0.37), I² = 0%
**Supplementary Figure 11.** COVID-19 hospitalisation rates in studies where the mean/median BMI was 30 or greater compared to studies where the mean/median BMI was less than 30. Created by the authors.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio (IV, Random, 95% CI)</th>
<th>Odds Ratio (IV, Random, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.1.3 No BMI data</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chiba (USA)</td>
<td>-0.5798</td>
<td>0.0635</td>
<td>13.0%</td>
<td>0.56 [0.49, 0.63]</td>
<td></td>
</tr>
<tr>
<td>Garcia-Pachon (Spain)</td>
<td>-0.08</td>
<td>0.059</td>
<td>5.6%</td>
<td>0.92 [0.25, 3.16]</td>
<td></td>
</tr>
<tr>
<td>Keswani (USA)</td>
<td>-0.261</td>
<td>0.151</td>
<td>11.7%</td>
<td>0.77 [0.57, 1.04]</td>
<td></td>
</tr>
<tr>
<td>Keswani (USA) (Non-allergic)</td>
<td>0.0296</td>
<td>0.161</td>
<td>11.5%</td>
<td>1.03 [0.75, 1.41]</td>
<td></td>
</tr>
<tr>
<td>Ko (USA)</td>
<td>0.5696</td>
<td>0.2129</td>
<td>10.4%</td>
<td>1.77 [1.16, 2.68]</td>
<td></td>
</tr>
<tr>
<td>Lemus-Calderon (Spain)</td>
<td>-0.5798</td>
<td>0.0634</td>
<td>13.0%</td>
<td>0.56 [0.49, 0.63]</td>
<td></td>
</tr>
<tr>
<td>Nystad (Norway)</td>
<td>0.6153</td>
<td>0.11</td>
<td>12.4%</td>
<td>1.85 [1.49, 2.29]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td>75.7%</td>
<td>0.95 [0.64, 1.42]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.25; Chi^2 = 127.87, df = 6 (P &lt; 0.000001); I^2 = 96%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.26 (P = 0.00)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.1.4 30+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mahdavinia (USA)</td>
<td>0.077</td>
<td>0.1752</td>
<td>11.2%</td>
<td>1.08 [0.77, 1.52]</td>
<td></td>
</tr>
<tr>
<td>Wang (USA)</td>
<td>-0.151</td>
<td>0.0563</td>
<td>13.3%</td>
<td>0.86 [0.77, 0.96]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td>24.3%</td>
<td>0.91 [0.75, 1.10]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.01; Chi^2 = 1.54, df = 1 (P = 0.22); I^2 = 35%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.01 (P = 0.31)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>100.0%</td>
<td>0.95 [0.71, 1.26]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.16; Chi^2 = 139.85, df = 8 (P &lt; 0.000001); I^2 = 94%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 3.88 (P = 0.04)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Chi^2 = 0.04, df = 1 (P = 0.84); I^2 = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Supplementary Figure 12. COVID-19 hospitalisation rates in studies where the majority of the cohort (over 50%) was of white ethnicity compared to where the minority of the cohort (50% or less) was of white ethnicity. Created by the authors.
**Supplementary Figure 13.** COVID-19 ICU admission rates in studies where the mean/median age was 60 or greater compared to studies where the mean/median age was less than 60. Created by the authors.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio 4, Random, 95% CI</th>
<th>Odds Ratio 4, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No age data</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chile (Korea)</td>
<td>-0.41551544</td>
<td>0.40367583</td>
<td>10.3%</td>
<td>0.66 [0.30, 1.46]</td>
<td></td>
</tr>
<tr>
<td>Madhow (USA)</td>
<td>0.16551444</td>
<td>0.27452537</td>
<td>22.3%</td>
<td>1.18 [0.69, 2.02]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>32.6%</td>
<td>0.95 [0.55, 1.65]</td>
</tr>
<tr>
<td>Heterogeneity: $\tau^2 = 0.05; \chi^2 = 1.42; df = 1 (P = 0.23); I^2 = 2%$</td>
<td>Test for overall effect: $Z = 0.18 (P = 0.86)$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kim (Korea)</td>
<td>0.11332868</td>
<td>0.59029307</td>
<td>4.8%</td>
<td>1.12 [0.38, 3.56]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>4.8%</td>
<td>1.12 [0.38, 3.56]</td>
</tr>
<tr>
<td>Heterogeneity: Not applicable</td>
<td>Test for overall effect: $Z = 0.18 (P = 0.85)$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barros (Spain)</td>
<td>0.09531018</td>
<td>0.80179265</td>
<td>2.6%</td>
<td>1.10 [0.23, 5.30]</td>
<td></td>
</tr>
<tr>
<td>Broadhurst (USA)</td>
<td>-0.37106368</td>
<td>0.37760872</td>
<td>11.8%</td>
<td>0.69 [0.33, 1.45]</td>
<td></td>
</tr>
<tr>
<td>Granbassien (France)</td>
<td>0.0629748</td>
<td>0.65331179</td>
<td>3.9%</td>
<td>1.06 [0.30, 3.83]</td>
<td></td>
</tr>
<tr>
<td>Lovinsky-Desir (USA)</td>
<td>0.0295588</td>
<td>0.20645881</td>
<td>39.5%</td>
<td>1.03 [0.69, 1.54]</td>
<td></td>
</tr>
<tr>
<td>Tousie (USA)</td>
<td>-0.21072103</td>
<td>0.59739944</td>
<td>4.7%</td>
<td>0.81 [0.25, 2.61]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>62.5%</td>
<td>0.94 [0.66, 1.30]</td>
</tr>
<tr>
<td>Heterogeneity: $\tau^2 = 0.00; \chi^2 = 1.00; df = 4 (P = 0.91); I^2 = 0%$</td>
<td>Test for overall effect: $Z = 0.36 (P = 0.72)$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>100.0%</td>
<td>0.96 [0.75, 1.24]</td>
</tr>
<tr>
<td>Heterogeneity: $\tau^2 = 0.00; \chi^2 = 1.51; df = 7 (P = 0.93); I^2 = 0%$</td>
<td>Test for overall effect: $Z = 0.29 (P = 0.77)$</td>
<td>Test for subgroup differences: $\chi^2 = 0.08; df = 2 (P = 0.96); I^2 = 0%$</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Supplementary Figure 14. COVID-19 ICU admission rates in studies where the mean/median BMI was 30 or greater compared to studies where the mean/median BMI was less than 30. Created by the authors.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE Weight</th>
<th>Odds Ratio</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>IV Random</td>
<td>95% CI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>11.1.1.1 No BMI data</td>
<td>-0.4151544</td>
<td>0.03927583</td>
<td>10.36</td>
<td>0.66 [0.30, 1.46]</td>
</tr>
<tr>
<td>Choi (Korea)</td>
<td>0.0629743</td>
<td>0.03531179</td>
<td>3.05</td>
<td>1.06 [0.39, 1.84]</td>
</tr>
<tr>
<td>Levisky-Best (USA)</td>
<td>0.0295344</td>
<td>0.03205383</td>
<td>39.58</td>
<td>1.03 [0.69, 1.54]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>53.73</td>
<td>0.95 [0.67, 1.34]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00, Chi² = 1.00, df = 2 (P = 0.61), I² = 0%
Test for overall effect: Z = -2.60 (P = 0.007)

11.1.2 BMI ≥ 30

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE Weight</th>
<th>Odds Ratio</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>IV Random</td>
<td>95% CI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>Barroso (Spain)</td>
<td>0.00331030</td>
<td>0.00752655</td>
<td>2.63</td>
<td>1.09 [0.52, 2.30]</td>
</tr>
<tr>
<td>Brodustin (USA)</td>
<td>-0.37160616</td>
<td>0.37766872</td>
<td>11.88</td>
<td>0.69 [0.03, 1.45]</td>
</tr>
<tr>
<td>Maldives (USA)</td>
<td>0.20151444</td>
<td>0.27522537</td>
<td>22.28</td>
<td>1.18 [0.69, 2.02]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>36.78</td>
<td>0.99 [0.65, 1.54]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00, Chi² = 1.34, df = 2 (P = 0.51), I² = 0%
Test for overall effect: Z = -2.60 (P = 0.007)

11.1.3 BMI <30

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE Weight</th>
<th>Odds Ratio</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>IV Random</td>
<td>95% CI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>Kim (Korea)</td>
<td>0.1332883</td>
<td>0.00026507</td>
<td>4.88</td>
<td>1.11 [0.35, 3.56]</td>
</tr>
<tr>
<td>Touslee (USA)</td>
<td>-0.21672193</td>
<td>0.59739944</td>
<td>4.78</td>
<td>0.81 [0.25, 2.49]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>0.95</td>
<td>0.95 [0.12, 1.77]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00, Chi² = 0.11, df = 1 (P = 0.70), I² = 0%
Test for overall effect: Z = -6.11 (P = 0.00)

Total (95% CI) 100.00% 0.96 [0.75, 1.24] 0.01 0.1 1 10 160

Heterogeneity: Tau² = 0.00, Chi² = 1.11, df = 7 (P = 0.93), I² = 0%
Test for overall effect: Z = 6.29 (P = 0.00)

Test for subgroup differences: Chi² = 0.00, df = 2 (P = 0.99), I² = 0%
Supplementary Figure 15. COVID-19 ICU admission rates in PWA in adjusted vs unadjusted studies. Created by the authors.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odd Ratio IV, Random, 95% CI</th>
<th>Odd Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>12.1.6 Adjusted</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Broadhurst (USA)</td>
<td>-0.37106368</td>
<td>0.37760872</td>
<td>11.8%</td>
<td>0.69 [0.33, 1.45]</td>
<td></td>
</tr>
<tr>
<td>Choi (Korea)</td>
<td>-0.41551544</td>
<td>0.40367583</td>
<td>10.3%</td>
<td>0.66 [0.30, 1.46]</td>
<td></td>
</tr>
<tr>
<td>Grandbastien (France)</td>
<td>0.0629748</td>
<td>0.65331179</td>
<td>3.9%</td>
<td>1.06 [0.30, 3.83]</td>
<td></td>
</tr>
<tr>
<td>Kim (Korea)</td>
<td>0.11332668</td>
<td>0.59029367</td>
<td>4.8%</td>
<td>1.12 [0.35, 3.54]</td>
<td></td>
</tr>
<tr>
<td>Mahdavinia (USA)</td>
<td>0.16551444</td>
<td>0.27452537</td>
<td>22.3%</td>
<td>1.18 [0.69, 2.02]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>33.2%</td>
<td>0.92 [0.65, 1.31]</td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.00; \chi^2 = 2.24, df = 4 (P = 0.69); I^2 = 0%$
Test for overall effect: $Z = 0.44 (P = 0.66)$

| **12.1.7 Unadjusted**   |                 |      |        |                             |                             |
| Barroso (Spain)         | 0.09531018      | 0.80179265 | 2.6%  | 1.10 [0.23, 5.30]           |                             |
| Lovinsky-Desir (USA)    | 0.02955386      | 0.20645883 | 39.5% | 1.03 [0.69, 1.54]           |                             |
| Toussie (USA)           | -0.21072153     | 0.59739944 | 4.7%  | 0.81 [0.25, 2.61]           |                             |
| Subtotal (95% CI)       |                 |      |        | 48.8% | 1.01 [0.70, 1.46]           |                             |

Heterogeneity: $\tau^2 = 0.00; \chi^2 = 0.16, df = 2 (P = 0.92); I^2 = 0%$
Test for overall effect: $Z = 0.05 (P = 0.96)$

| **Total (95% CI)**      |                 |      |        |                             |                             |
|                        |                 |      | 100.0% | 0.96 [0.75, 1.24]           |                             |

Heterogeneity: $\tau^2 = 0.00; \chi^2 = 2.51, df = 7 (P = 0.93); I^2 = 0%$
Test for overall effect: $Z = 0.29 (P = 0.77)$

Test for subgroup differences: $\chi^2 = 0.11, df = 1 (P = 0.74); I^2 = 0%$