Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Asthma in patients with coronavirus disease 2019

A systematic review and meta-analysis

Li Shi, BM [*]; Jie Xu, MBBS [*]; Wenwei Xiao, MBBS [*]; Ying Wang, MBBS [*]; Yuefei Jin, MD, PhD [*]; Shuaiyin Chen, MD, PhD [*]; Guangcai Duan, MD, PhD [*]; Haiyan Yang, MD, PhD [*]; Yadong Wang, MD, PhD [†]

[*] Department of Epidemiology, College of Public Health, Zhengzhou University, Zhengzhou, People's Republic of China
[†] Department of Toxicology, Henan Center for Disease Control and Prevention, Zhengzhou, People's Republic of China

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ABSTRACT

Background: It is unclear whether asthma has an influence on contracting coronavirus disease 2019 (COVID-19) or having worse outcomes from COVID-19 disease.
Objective: To explore the prevalence of asthma in patients with COVID-19 and the relationship between asthma and patients with COVID-19 with poor outcomes.
Methods: The pooled prevalence of asthma in patients with COVID-19 and corresponding 95% confidence interval (CI) were estimated. The pooled effect size (ES) was used to evaluate the association between asthma and patients with COVID-19 with poor outcomes.
Results: The pooled prevalence of asthma in patients with COVID-19 worldwide was 8.3% (95% CI, 7.6-9.0) based on 116 articles (119 studies) with 403,392 cases. The pooled ES based on unadjusted effect estimates revealed that asthma was not associated with reduced risk of poor outcomes in patients with COVID-19 (ES, 0.91; 95% CI, 0.78-1.06). Similarly, the pooled ES based on unadjusted effect estimates revealed that asthma was not associated with the reduced risk of mortality in patients with COVID-19 (ES, 0.88; 95% CI, 0.73-1.05). However, the pooled ES based on adjusted effect estimates indicated that asthma was significantly associated with reduced risk of mortality in patients with COVID-19 (ES 0.80, 95% CI 0.74-0.86).
Conclusion: The pooled prevalence of asthma in patients with COVID-19 was similar to that in the general population, and asthma might be an independent protective factor for the death of patients with COVID-19, which suggests that we should pay high attention to patients co-infected asthma and COVID-19 and take locally tailored interventions and treatment. Further well-designed studies with large sample sizes are required to verify our findings.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel betacoronavirus, caused the coronavirus disease 2019 (COVID-19), which has posed huge challenges to global public health. To date (data as of September 28, 2020), more than 32.7 million confirmed cases and more than 991,000 deaths have been reported worldwide.[1] The continuous increase of confirmed cases and related clinical studies has led to a greater understanding of COVID-19. Many comorbidities have been identified as risk factors for patients with COVID-19 with poor outcomes, such as diabetes, hypertension, malignancies, cardiovascular diseases, and chronic obstructive pulmonary disease, which can help clinicians identify patients with poor prognosis at an early

Reprints: Haiyan Yang, MD, PhD, Department of Epidemiology, College of Public Health, Zhengzhou University, No. 100 of Science Avenue, Zhengzhou 450001, People's Republic of China;
Yadong Wang, MD, PhD, Department of Toxicology, Henan Center for Disease Control and Prevention, No. 105 of South Nongye Road, Zhengzhou 450016, People's Republic of China; *E-mail addresses:* yhy@zzu.edu.cn or wangyd76@163.com.
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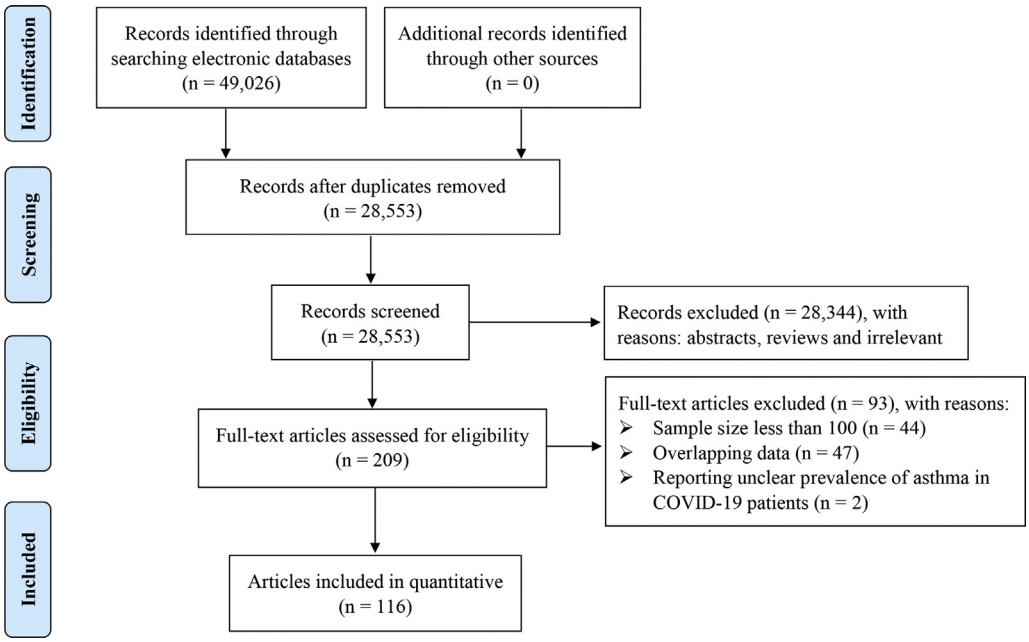

Figure 1. Study selection. COVID-19, coronavirus disease 2019.

stage and thus contribute to the control and prevention of COVID-19.[2]

Asthma, a common chronic disease, can be exacerbated by viral respiratory infections,[3] which has recently attracted considerable attention of researchers focused on COVID-19. Nevertheless, the prevalence of asthma in patients with COVID-19 and the association between asthma and patients with COVID-19 with poor outcomes remains highly controversial. Zhang et al[4] identified particularly low prevalence of asthma (0.3%) among 289 patients with COVID-19 in Wuhan, which was significantly lower than local population asthma prevalence (4.2%).[5] Conversely, Latz et al[6] pointed out that patients with asthma accounted for up to 26.9% of included patients with COVID-19 in the state of Massachusetts. In addition, the studies conducted by Yehia et al[7] and Siso-Almirall et al[8] indicated that asthma was not a predictive comorbidity for death of patients with COVID-19. However, Almazeedi et al[9] reported that asthma was associated with an increased risk of death in patients with COVID-19, whereas Hernandez-Galdamez et al[10] and Santos et al[11] found that asthma was a protective factor of death.

In view of the above-mentioned studies, a systematic and quantitative meta-analysis to explore the prevalence of asthma in patients with COVID-19 and the relationship between asthma and patients with COVID-19 with poor outcomes would be of paramount importance.

Methods

Search Strategy and Selection Criteria

We conducted a systematical search of PubMed, Web of Science, and EMBASE databases to recognize eligible studies published from inception to September 18, 2020, using the following terms and keywords: “asthma” or “respiratory diseases” or “comorbidities” or “clinical” AND “novel coronavirus” or “nCoV” or “2019-nCoV” or “COVID-19” or “coronavirus” or “severe acute respiratory syndrome coronavirus 2” or “SARS-CoV-2.” The literature search was not restricted by language. The reference lists of all pertinent studies and reviews were sifted to identify other eligible studies. In addition, when publications with overlapping data were found, only the articles with the larger sample size or more complete analysis were included. EndNote (version X9.0, Thomson ResearchSoft, Stanford, Connecticut) was used for the management of literature. Our analyses were carried out on September 20, 2020, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement (eTable 1).[12]

Inclusion criteria were the following: (1) all patients enrolled in articles were diagnosed as having COVID-19; and (2) articles clearly reported the number of patients with co-infection of asthma and COVID-19.

Exclusion criteria were as follows: (1) abstracts, reviews, meta-analysis, and errata; (2) studies with the sample size fewer than 100 patients; (3) articles with overlapping data; and (4) articles reporting unclear prevalence of asthma in patients with COVID-19.

Data Extraction and Quality Assessment

Notably, 2 researchers (Li Shi and Wenwei Xiao) respectively reviewed all literatures according to the inclusion and exclusion criteria and excerpted the following information: author, location or country, study design, total number of patients, age, sex, settings, the number of patients co-infected asthma and COVID-19, and the number of patients with asthma with poor outcomes (eg, patients diagnosed with having severe or critical COVID-19, or admitted to intensive care unit [ICU], or required mechanical ventilation [MV], or died). Any conflicts were resolved by group discussion.

The quality of the enrolled studies was evaluated by 2 independent researchers using the Agency for Healthcare Research and Quality score checklist.[13] The quality of the studies was graded as low (0-3), moderate (4-7), or high (8-11), according to the corresponding range of scores.

Statistical Analysis

All statistical analyses were carried out using R (version 3.6.3, R Foundation for Statistical Computing, Vienna, Austria) and Stata (version SE 12.1, StataCorp, College Station, Texas). A meta-analysis of the included studies was done with the metaprop command in R to calculate the pooled prevalence of asthma in patients with COVID-19. Furthermore, a meta-analysis of the included studies was done with the metan command in Stata to evaluate the risk of having poor outcomes in patients with COVID-19 and asthma co-

Table 1
Baseline Characteristics of the Included Studies

Author	Study design	Location or country	Sample size	Male (%)	Age (y)	Settings (%)	Asthma (%)	Poor outcomes (%)[a]	Quality score
America									
Adrish et al[17]	Retrospective	US	469	279 (59.5)	N/R	Inpatient (100)	83 (17.7)	N/R	6
Agarwal et al[18]	Retrospective	US	404	297 (73.5)	61 (median)	Inpatient/Outpatient	25 (6.2)	N/R	7
Argyropoulos et al[19]	Retrospective	US	205	108 (52.7)	N/R	Inpatient (19.5) Outpatient (80.5)	26 (12.7)	N/R	6
Arshad et al[20]	Retrospective	US	2541	1298 (51.1)	63.7 (mean)	Inpatient (100)	251 (9.9)	N/R	9
Bajaj et al[21]	Retrospective	US	108	37 (34.3)	61.3 (mean)	Inpatient (100)	9 (8.3)	N/R	6
Broadhurst et al[22]	Cross-sectional	US	436	239 (50.1)[b]	54.7 (mean)	Inpatient (100)	53 (12.2)	15 (10.8)[b]	4
Capone et al[23]	Retrospective	US	102	55 (53.9)	63.3 (mean)	Inpatient (100)	12 (11.8)	12 (11.8)	6
Chachkhiani et al[24]	Retrospective	US	250	113 (45.2)	60 (mean)	Inpatient (100)	39 (15.6)	N/R	7
Chhiba et al[25]	Retrospective	US	1526	718 (47.1)	N/R	Inpatient (55.9) Outpatient (44.1)	220 (14.4)	8 (11.1)	7
Cummings et al[26]	Prospective	US	257	171 (66.5)	62 (median)	Inpatient (100)	21 (8.2)	21 (8.2)	7
Enzmann et al[27]	Retrospective	US	150	85 (56.7)	56 (median)	N/R	27 (18.0)	N/R	5
Fox et al[28]	Retrospective	US	355	181 (51.0)	66.2 (mean)	Inpatient (100)	27 (7.6)	N/R	7
Garg et al[29]	Retrospective	US	178	N/R	N/R	Inpatient (100)	27 (17.0)[b]	N/R	6
Garibaldi et al[30]	Retrospective	US	832	443 (51.7)	63 (median)	Inpatient (100)	79 (9.5)	24 (7.9)	9
Gavin et al[31]	Retrospective	US	140	72 (51.4)	60 (mean)	Inpatient (100)	15 (10.7)	1 (5.6)	8
Gayam et al[32]	Retrospective	US	408	231 (56.6)	67 (median)	Inpatient (100)	54 (13.2)	16 (12.1)	7
Gottlieb et al[33]	Retrospective	US	8673	4045 (46.6)	41 (median)	Inpatient (17.1) Outpatient (82.9)	736 (8.5)	N/R	7
Goyal et al[34]	Retrospective	US	1687	1004 (59.5)	66.5 (median)	Inpatient (100)	159 (9.4)	N/R	7
Gupta et al[35]	Retrospective	US	2215	1436 (64.8)	60.5 (mean)	Inpatient (100)	258 (11.6)	70 (8.9)	8
Haberman et al[36]	Prospective	US	103	29 (28.2)	52.7 (mean)	Inpatient (26.2) Outpatient (73.8)	15 (14.6)	N/R	6
Hernandez-Galdamez et al[10]	Cross-sectional	Mexico	211003	115441 (54.7)	45.7 (mean)	Inpatient (31.0) Outpatient (69.0)	5854 (2.8)	533 (2.1)	7
Jehi et al[37]	Retrospective	US	2852	1372 (48.1)	N/R	Inpatient (20.4) Outpatient (79.6)	389 (13.6)	N/R	6
			1684	738 (43.8)	N/R	Inpatient (22.3) Outpatient (77.7)	262 (15.6)	N/R	
Keller et al[38]	Retrospective	US	1806	965 (53.4)	62.2 (mean)	Inpatient (100)	344 (19.0)	N/R	9
Kim et al[39]	Ambispective	US	867	473 (54.6)	56.9 (mean)	N/R	91 (10.5)	10 (8.3)	9
Ko et al[40]	Retrospective	US	5416	2847 (52.6)	N/R	N/R	702 (13.0)	N/R	8
Krishnan et al[41]	Retrospective	US	152	95 (62.5)	66 (mean)	Inpatient (100)	25 (16.4)	16 (17.4)	6
Lara et al[42]	Retrospective	US	121	N/R	64 (median)	Inpatient (54.5) Outpatient (45.5)	10 (8.3)	3 (15.0)	6
Latz et al[6]	Retrospective	US	1289	417 (32.4)	N/R	Inpatient (37.5) Outpatient (62.5)	347 (26.9)	N/R	7
Lovinsky-Desir et al[43]	Retrospective	US	1298	762 (58.7)	N/R	Inpatient (100)	163 (12.6)	9 (8.2)	8
Maatman et al[44]	Retrospective	US	109	62 (56.9)	61 (mean)	Inpatient (100)	16 (14.7)	16 (14.7)	7
Magagnoli et al[45]	Retrospective	US	807	772 (95.7)	N/R	Inpatient (100)	40 (5.0)	N/R	7
Magleby et al[46]	Retrospective	US	678	414 (61.1)	N/R	Inpatient (100)	62 (9.1)	N/R	7
McCarthy et al[47]	Retrospective	US	247	143 (57.9)	61 (median)	Inpatient (100)	29 (11.7)	11 (9.8)	7
Mikami et al[48]	Retrospective	US	6493	3538 (54.5)	59 (median)	Inpatient (55.1) Outpatient (42.9)	271 (4.2)	31 (3.8)	6
Moll et al[49]	Retrospective	US	210	101 (48.1)	62.2 (mean)	Inpatient (100)	35 (16.7)	15 (14.7)	6
Mughal et al[50]	Retrospective	US	129	81 (62.8)	63 (median)	Inpatient (100)	3 (2.3)	2 (6.7)	6
Mukherjee et al[51]	Retrospective	US	137	99 (72.3)	59 (mean)	Inpatient (100)	11 (8.0)	11 (8.0)	8
Nakeshbandi et al[52]	Retrospective	US	504	263 (52.2)	68 (median)	Inpatient (100)	41 (8.1)	N/R	8
Ng et al[53]	Retrospective	US	10482	6239 (59.5)	N/R	Inpatient (100)	859 (8.2)	N/R	9
Ortizz-Brizuela et al[54]	Prospective	Mexico	309	183 (59.2)	43 (median)	Inpatient (45.3) Outpatient (54.7)	9 (2.9)	0 (0.0)	9
Ramachandran et al[55]	Retrospective	US	145	79 (54.5)	N/R	Inpatient (100)	23 (15.9)	N/R	8
Richardson et al[56]	Retrospective	US	5700	3437 (60.3)	63 (median)	Inpatient (100)	479 (9.0)	N/R	8
Robilotti et al[57]	Retrospective	US	423	212 (50.1)	N/R	Inpatient (42.6) Outpatient (57.4)	43 (10.2)	N/R	6
Santos et al[11]	Retrospective	Brazil	21408	12667 (59.2)	N/R	Inpatient (100)	488 (5.7)[b]	488 (5.7)[b]	7
Shady et al[58]	Ambispective	US	371	249 (67.1)	57 (median)	Inpatient (100)	42 (11.4)[b]	N/R	6
Shah et al[59]	Retrospective	US	522	218 (41.8)	63 (median)	Inpatient (100)	68 (13.0)	11 (12.0)	6
Silver et al[60]	Retrospective	US	249	110 (44.2)	59.6 (mean)	Inpatient (100)	49 (20.0)	N/R	8
Singer et al[61]	Retrospective	US	1651	892 (54.0)	50 (mean)	Inpatient (45.0) Outpatient (55.0)	106 (6.4)	N/R	6
Sinha et al[62]	Retrospective	US	255	161 (63.1)	59 (median)	Inpatient (100)	29 (11.4)	N/R	8
Skipper et al[63]	RCT	US and Canada	212	89 (42.0)	41 (median)	Outpatient (100)	28 (13.2)	N/R	9
			211	96 (45.5)	39 (median)	Outpatient (100)	20 (9.5)	N/R	
Smith et al[64]	Retrospective	US	184	98 (53.3)	64.4 (mean)	Inpatient (100)	18 (9.8)	N/R	6
Somers et al[65]	Retrospective	US	154	102 (66.2)	58 (mean)	Inpatient (100)	31 (20.1)	31 (20.1)	9
Souza et al[66]	Cross-sectional	Brazil	197	92 (46.7)	N/R	N/R	1 (0.5)	1 (0.5)	5
Suleyman et al[67]	Retrospective	US	463	204 (44.1)	57.5 (mean)	Inpatient (76.7) Outpatient (23.3)	73 (15.8)	19 (13.5)	8
Tartof et al[68]	Retrospective	US	6916	3111 (45.0)	49 (median)	N/R	1273 (18.4)	44 (21.4)	8
Tenforde et al[69]	Cross-sectional	US	350	165 (47.1)	43 (median)	Inpatient (22.6) Outpatient (77.4)	55 (15.7)	N/R	7

(*continued on next page*)

Table 1 (*continued*)

Author	Study design	Location or country	Sample size	Male (%)	Age (y)	Settings (%)	Asthma (%)	Poor outcomes (%)[a]	Quality score
Twigg et al[70]	Retrospective	US	242	141 (58.3)	59.6 (mean)	Inpatient (100)	34 (14.0)	34 (14.0)	7
Vaughn et al[71]	Retrospective	US	1705	885 (51.9)	64.7 (median)	Inpatient (100)	215 (12.6)	N/R	7
Yao et al[72]	Retrospective	US	242	138 (57.0)	N/R	Inpatient (100)	28 (11.6)	N/R	7
Yehia et al[7]	Retrospective	US	11210	5583 (49.8)	61 (median)	Inpatient (100)	628 (5.6)	N/R	8
Zhao et al[73]	Retrospective	US	641	384 (59.9)	60 (median)	Inpatient (100)	41 (6.9)[b]	16 (8.2)	8
Zuniga-Moya et al[74]	Retrospective	Honduras	877	538 (61.3)	N/R	Inpatient (25.1) Outpatient (74.9)	31 (3.5)	3 (7.9)	10
Asia									
Almazeedi et al[9]	Retrospective	Kuwait	1096	888 (81.0)	41 (median)	Inpatient (100)	43 (3.9)	4 (21.1)	9
Alsofayan et al[75]	Retrospective	Saudi Arabia	1519	825 (54.3)	N/R	N/R	54 (4.9)[b]	N/R	5
Asghar et al[76]	Retrospective	Pakistan	100	69 (69.0)	52.6 (mean)	Inpatient (100)	2 (2.0)	N/R	6
Gao et al[77]	Retrospective	China	2877	1470 (51.1)	N/R	Inpatient (100)	22 (0.8)	N/R	10
Huang et al[78]	Retrospective	China	336	182 (54.2)	43 (median)	Inpatient (100)	5 (1.5)	N/R	7
Li et al[79]	Ambispective	China	548	279 (50.9)	60 (median)	Inpatient (100)	5 (0.9)	3 (1.1)	8
Lian et al[80]	Retrospective	China	232	109 (47.0)	N/R	Inpatient (100)	4 (1.7)	3 (3.3)	6
Liu et al[81]	Retrospective	China	104	63 (60.6)	42 (medina)	Inpatient (100)	12 (11.5)	6 (20.0)	7
Mao et al[82]	Retrospective	China	188	94 (50.0)	46 (mean)	Inpatient (100)	2 (1.1)	N/R	9
Ozger et al[83]	Retrospective	Turkey	175	74 (42.3)	N/R	Inpatient (100)	9 (5.1)	N/R	5
Pan et al[84]	Retrospective	China	996	465 (46.7)	N/R	Inpatient (100)	12 (1.2)	N/R	7
Satici et al[85]	Retrospective	Turkey	681	347 (51.0)	56.9 (mean)	Inpatient (100)	43 (6.3)	1 (1.8)	7
Song et al[86]	Retrospective	China	961	500 (52.0)	63 (median)	Inpatient (100)	22 (2.3)	1 (0.4)	7
Sy et al[87]	Retrospective	Philippines	530	373 (70.4)	48.9 (mean)	N/R	21 (4.0)	N/R	8
Tezcan et al[88]	Retrospective	Turkey	408	188 (46.1)	54.3 (mean)	Inpatient (100)	32 (7.8)	N/R	5
Trabulus et al[89]	Retrospective	Turkey	336	192 (57.1)	55 (mean)	Inpatient (100)	20 (6.0)	1 (2.3)	7
Tsou et al[90]	Retrospective	Taiwan	100	44 (44.0)	44 (median)	Inpatient (100)	3 (3.0)	N/R	5
Wang et al[91]	Retrospective	China	123	60 (48.8)	68 (median)	Inpatient (100)	1 (0.8)	0 (0.0)	6
Yang et al[92]	Retrospective	Korea	7340	2970 (40.5)	47.1 (mean)	Inpatient (100)	725 (9.9)	N/R	8
Yu et al[93]	Retrospective	China	142	81 (57.0)	61.9 (mean)	Inpatient (100)	1 (0.7)	N/R	8
Zhang et al[4]	Retrospective	China	289	154 (53.3)	57 (median)	Inpatient (100)	1 (0.3)	1 (0.8)	8
Zhou et al[94]	Retrospective	China	110	60 (54.5)	57.7 (mean)	Outpatient (100)	1 (0.9)	N/R	7
Europe									
Alkundi et al[95]	Retrospective	UK	232	145 (62.5)	70.5 (mean)	Inpatient (100)	6 (2.6)	0 (0.0)	6
Avdeev et al[96]	Retrospective	Russia	1307	N/R	N/R	Inpatient (100)	23 (1.8)	23 (1.8)	3
Azoulay et al[97]	Retrospective	France	379	292 (77.0)	66 (median)	Inpatient (100)	23 (6.1)[b]	23 (6.1)[b]	7
Barillari et al[98]	Cross-sectional	Italy	294	147 (50.0)	42.1 (mean)	Inpatient (16.3) Outpatient (83.7)	18 (6.1)	N/R	4
Barroso et al[99]	Retrospective	Spain	189	N/R	N/R	Inpatient (100)	11 (5.8)	N/R	6
Berenguer et al[100]	Retrospective	Spain	4035	2433 (61.0)	70 (median)	Inpatient (100)	299 (7.5)[b]	69 (6.2)[b]	10
Beurnier et al[101]	Prospective	France	768	N/R	N/R	Inpatient (100)	37 (4.8)	N/R	5
Cellina et al[102]	Retrospective	Italy	246	170 (69.1)	63 (mean)	Inpatient (100)	10 (4.1)	N/R	8
Docherty et al[103]	Prospective	UK	20133	12068 (59.9)	72.9 (median)	Inpatient (100)	2540 (14.5)[b]	N/R	9
Fang et al[104]	Retrospective	UK	100	60 (60.0)	N/R	Inpatient (100)	11 (11.0)	N/R	9
Ferrando et al[105]	Prospective	Spain and Andorra	742	504 (68.1)[b]	64 (median)	Inpatient (100)	19 (2.6)	19 (2.6)	10
Fond et al[106]	Retrospective	France	1092	593 (54.3)	62.5 (median)	Inpatient (100)	71 (6.5)	N/R	8
Garcia-Pachon et al[107]	Retrospective	Spain	376	192 (51.1)	54 (median)	Inpatient (42.0) Outpatient (58.0)	10 (2.7)	N/R	4
Grandbastien et al[108]	Retrospective	France	106	66 (62.3)	63.5 (median)	Inpatient (100)	23 (21.7)	N/R	7
Helms et al[109]	Prospective	France	140	100 (71.4)	62 (median)	Inpatient (100)	5 (3.6)	5 (3.6)	10
Ierardi et al[110]	Retrospective	Italy	234	70 (30.0)	61.6 (mean)	Inpatient (100)	10 (4.3)	N/R	5
Joseph et al[111]	Retrospective	France	100	70 (70.0)	59 (median)	Inpatient (100)	8 (8.0)	N/R	7
Lechien et al[112]	Retrospective	Europe[c]	702	206 (29.3)	40.3 (median)	N/R	42 (6.0)	N/R	6
Lendorf et al[113]	Retrospective	Denmark	111	67 (60.4)	68 (median)	Inpatient (100)	12 (10.8)	2 (10.0)	8
Lenti et al[114]	Retrospective	Italy	100	79 (79.0)	70 (median)	Inpatient (100)	6 (6.0)	N/R	7
Lombardi et al[115]	Retrospective	Italy	1043	704 (67.5)	N/R	Inpatient (100)	20 (1.9)	N/R	5
Lund et al[116]	Retrospective	Denmark	9236	3892 (42.1)	50 (median)	N/R	629 (6.8)	N/R	8
Maguire et al[117]	Retrospective	UK	224	124 (55.4)	N/R	Inpatient (100)	46 (20.5)	4 (7.7)	8
Martinez-Del Rio et al[118]	Retrospective	Spain	921	500 (54.3)	78 (mean)	Inpatient (100)	39 (4.2)	9 (3.6)	8
Perez-Guzman et al[119]	Retrospective	UK	614	382 (62.2)	69 (median)	Inpatient (100)	56 (9.1)	N/R	7
Poblador-Plou et al[120]	Retrospective	Spain	771	407 (52.8)	84.2 (mean)	N/R	25 (3.2)	25 (3.2)	6
Sapey et al[121]	Retrospective	UK	2217	1290 (58.2)	73 (median)	Inpatient (100)	439 (19.8)	143 (18.6)	8
Siso-Almirall et al[8]	Retrospective	Spain	322	161 (50.0)	56.7 (mean)	Inpatient (49.1) Outpatient (50.9)	13 (4.0)	2 (3.6)	7
Middle East									
Jalili et al[122]	Retrospective	Iran	28981	16361 (56.5)	57.3 (mean)	Inpatient (100)	573 (2.0)	141 (2.5)	7
Others[c]									
COVIDSurg Collaborative[123]	Retrospective	Countries	1128	605 (53.6)	N/R	Inpatient (100)	78 (7.0)[b]	21 (7.8)	9
Mato et al[124]	Retrospective	Countries	198	125 (63.1)	70.5 (median)	Inpatient (89.9) Outpatient (10.1)	12 (6.1)[b]	7 (10.8)	7
Olender et al[125]	RCT	Countries	298	182 (61.1)	N/R	Inpatient (100)	42 (14.1)	N/R	8
	Retrospective	Countries	816	490 (60.0)	N/R	Inpatient (100)	90 (11.0)	N/R	

Abbreviations: N/R, not (clearly) reported; RCT, randomized controlled trial; UK, United Kingdom; US, United States.

[a]The prevalence of asthma in patients with coronavirus disease 2019 with poor outcomes.

[b]Data missing for patients.

[c]Patients were collected from multiple countries of different regions.

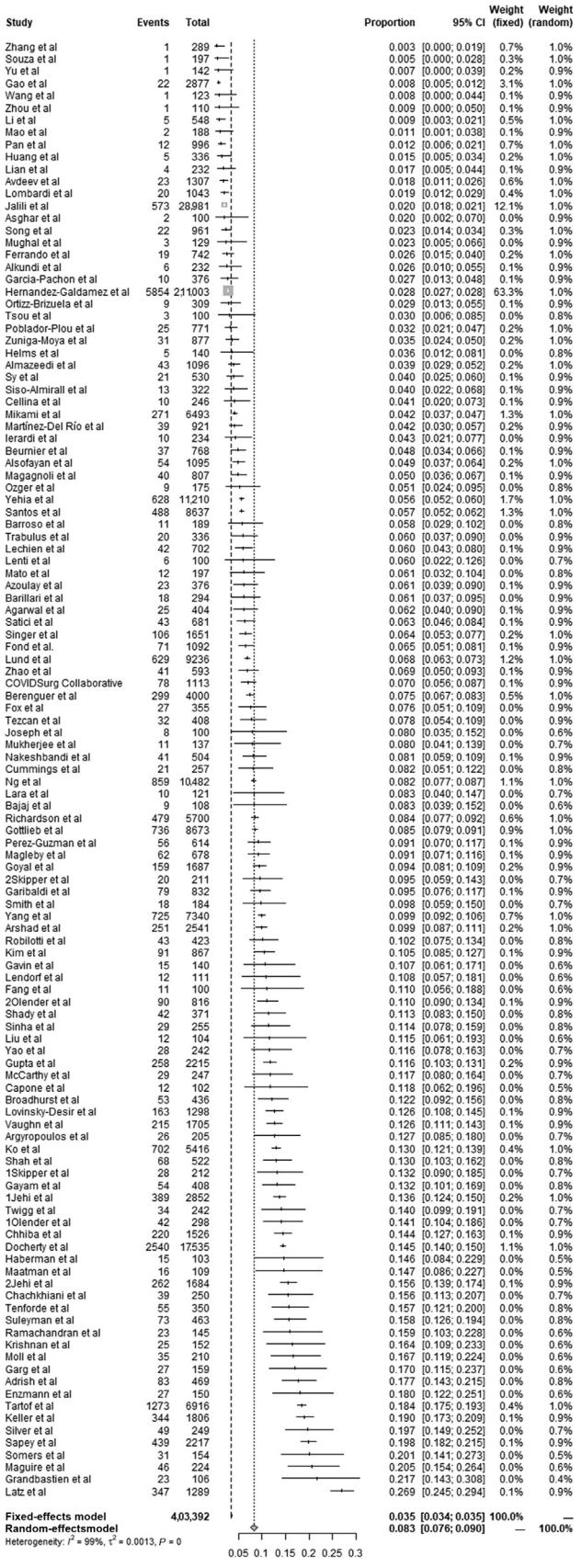

Figure 2. Forest plot of the pooled prevalence of asthma in patients with COVID-19 on a basis of 119 studies. CI, confidence interval; COVID-19, coronavirus disease 2019.

infection. Considering the influence of various factors such as sex, age, and other comorbidities on the risk of mortality in patients with COVID-19,[2] the pooled effect size (ES) and corresponding 95% confidence interval (CI) were calculated on the basis of the studies reporting the adjusted effect estimates. The χ^2-based Q test (represented as χ^2 and P values) and I^2 statistic were applied to evaluate the heterogeneity among studies.[14] If I^2 was less than 50% or P was greater than .05, we used the fixed-effects model. Otherwise, the random-effects model was chosen. Considering the obvious heterogeneity of our analysis, subgroup and meta-regression analyses were conducted to investigate possible factors that caused heterogeneity. The factors that we investigated were sample size, study design, region, settings, and quality score. Publication bias was examined by Begg test and Egger test.[15,16] P values less than .05 were regarded as statistically significant.

Results

Study Selection

Initially, 49,026 records were retrieved by our search strategy. By deleting duplicates of original retrieved articles, 28,553 related articles were obtained. A total of 209 articles that reported the prevalence of asthma in patients with COVID-19 were yielded after reading the titles and abstracts. Subsequently, 44 articles were excluded because of a sample size less than 100, 47 articles were eliminated owing to the potential duplicate patients, and 2 articles were removed because they reported unclear prevalence of asthma in patients with COVID-19 (eTable 2). Ultimately, 116 articles (119 studies)[4,6-11,17-125] with 403,392 patients with COVID-19 passed multiple screening (Fig 1).

Study Characteristics

All patients in enrolled articles were diagnosed with having COVID-19 (eTable 3). The main characteristics of the enrolled studies are found in Table 1. The included studies were from different countries and regions around the world, of which 64 from the Americas, 28 from Europe, 22 from Asia, 1 from the Middle East, and 4 from other countries. In terms of the study design, 101 were retrospective studies, 7 prospective studies, 5 cross-sectional studies, and 3 each ambispective studies and randomized controlled trials. Through qualitative assessment, 47 studies were of high quality, 71 studies of moderate quality, and the remaining 1 study of low quality (eTable 4).

The Pooled Prevalence of Asthma in Patients With COVID-19

The estimated prevalence of asthma in patients with COVID-19 ranged from 0.3% to 26.9%. By combining 119 studies (a total of 403,392 patients) reporting the data of patients with co-infection of asthma and COVID-19, the pooled prevalence of asthma in patients with COVID-19 was 8.3% (95% CI, 7.6-9.0; random-effects model) and heterogeneity was obvious ($\chi^2 = 9311.76$; $P < .01$; $I^2 = 98.7\%$) (Fig 2). Therefore, we conducted subgroup and meta-regression analyses to explore the possible factors that caused heterogeneity according to sample size, study design, region, settings, and quality score (Table 2 and eFigs 1-5). The pooled prevalence of asthma among patients with COVID-19 was 3.3% (95% CI, 1.9-4.6; $\chi^2 = 712.56$, $P < .01$; $I^2 = 97.1\%$) in Asia, 11.1% (95% CI, 9.9-12.3; $\chi^2 = 5466.42$, $P < .01$; $I^2 = 98.8\%$) in the Americas, 7.0% (95% CI, 5.0-9.0; $\chi^2 = 1608.20$, $P < .01$; $I^2 = 98.3\%$) in Europe, and 9.4% (95% CI, 6.2-12.5; $\chi^2 = 18.82$, $P < .01$; $I^2 = 84.1\%$) in other countries. Only 1 study was completed in the Middle East, and the prevalence of asthma in patients with COVID-19 was 2.0% (95% CI, 1.8-2.1). The results of univariate meta-regression revealed that region ($P < .001$) might be a factor caused by heterogeneity, whereas no significant differences

Table 2
Subgroup Analysis and Meta-Regression

Variables	No. of studies	Meta-regression			Subgroup analysis		Heterogeneity		
		Tau^2	*t* value	*P* value	Pooled ES (95% CI)	*P* value	I^2 (%)	χ^2	*P* value
Sample size (continuous)		0.0018	−1.52	.131					
≥500	53				0.081 (0.072-0.091)	<.01	99.4	8339.83	<.01
<500	66				0.088 (0.075-0.100)	<.01	93.2	962.03	<.01
Settings (continuous)		0.0018	−0.96	.337					
Inpatient	85				0.082 (0.073-0.092)	<.01	98.5	5633.00	<.01
Outpatient	3				0.077 (0.000-0.157)	<.01	94.2	34.41	<.01
Others	31				0.090 (0.073-0.107)	<.01	99.1	3475.58	<.01
Region		0.0015	—	*<.001*					
Asia	22	—	0.45	.656	0.033 (0.019-0.046)	<.01	97.1	712.56	<.01
Americas	64	—	2.22	*.029*	0.111 (0.099-0.123)	<.01	98.8	5466.42	<.01
Europe	28	—	1.30	.197	0.070 (0.050-0.090)	<.01	98.3	1608.20	<.01
Middle East	1	—	—	—	0.020 (0.018-0.021)	<.01	—	—	—
Others	4	—	1.52	.132	0.094 (0.062-0.125)	<.01	84.1	18.82	<.01
Study design		0.0019	−0.08	.936					
Prospective/RCT	10				0.086 (0.042-0.130)	<.01	98.4	549.08	<.01
Others	109				0.082 (0.076-0.089)	<.01	98.6	7491.52	<.01
Quality score		0.0019	−0.51	.610					
High	46				0.088 (0.073-0.103)	<.01	98.9	4017.89	<.01
Moderate/low	73				0.079 (0.072-0.086)	<.01	98.1	3855.35	<.01

Abbreviations: CI, confidence interval; ES, effect sizes; RCT, randomized controlled trial.
Italic value indicates statistical significance.

were observed in sample size ($P = .131$), settings ($P = .337$), study design ($P = .936$), or quality score ($P = .610$).

The Association Between Asthma and the Poor Outcomes of Patients With COVID-19

Poor outcomes included severe or critical illness, ICU admission, requirement of MV, or death. A total of 40 studies comprising 274,395 patients reported the data on asthma in patients with COVID-19 with poor outcomes and patients with COVID-19 without poor outcomes (eTable 5). The pooled results revealed that asthma was not significantly associated with the reduced risk of poor outcomes in COVID-19 (ES, 0.91; 95% CI, 0.78-1.06; $\chi^2 = 90.97$, $P < .001$; $I^2 = 57.1\%$; random-effects model) based on unadjusted effect estimates (Fig 3).

The Association Between Asthma and the Risk of Mortality in Patients With COVID-19

A meta-analysis of 24 studies reporting the unadjusted ES (eTable 5) and a meta-analysis of 12 studies reporting the adjusted ES (eTable 6) were conducted to evaluate the association between asthma and the risk of mortality in patients with COVID-19, respectively. The pooled results of unadjusted effect estimates revealed that asthma was not significantly associated with the reduced risk of mortality in patients with COVID-19 (ES, 0.88; 95% CI, 0.73-1.05; $\chi^2 = 75.65$, $P < .001$; $I^2 = 69.6\%$; random-effects model) (Fig 4A). However, the pooled results of adjusted effect estimates indicated that asthma was significantly associated with the reduced risk of mortality in patients with COVID-19 (ES, 0.80; 95% CI, 0.74-0.86; $\chi^2 = 16.31$; $P = .13$; $I^2 = 32.6\%$; fixed-effects model) (Fig 4B).

Publication Bias

Significant publication bias was found by Begg test ($P = .038$) and Egger test ($P < .001$) within our analysis (eFig 6).

Discussion

Our quantitative meta-analysis suggested that the pooled prevalence of asthma in patients with COVID-19 worldwide was 8.3%, which was contained in a range (4.3%-8.6%) of the global prevalence rates of asthma.[126] The pooled prevalence of asthma in patients with COVID-19 worldwide (8.3%) was more similar to the global prevalence of wheezing (8.6%) using the least stringent definition of asthma.[126] Considering the obvious heterogeneity of our analysis, we subsequently performed subgroup analysis and meta-regression according to sample size, study design, region, settings, and quality score. The univariate meta-regression implied that region ($P < .001$) might be a potential source of heterogeneity. According to the results of subgroup analysis, the pooled prevalence of asthma among patients with COVID-19 was 3.3%, 11.1%, 7.0%, 2.0%, and 9.4% in Asia, the Americas, Europe, the Middle East, and other countries, respectively, which highlighted the demand for locally tailored interventions and initiatives. Interestingly, Gibson et al[127] reported that the prevalence of asthma in the European population was 4% to 7%. Huang et al[5] identified that the overall prevalence of asthma in 57,779 participants of China was 4.2%. Furthermore, the US Centers for Disease Control and Prevention pointed out that adult self-reported asthma prevalence was 9.2%.[128] All of these evidences indicate that the prevalence of asthma among patients with COVID-19 in different regions and countries seemed to be similar to that of asthma in the general population.

To explore the relationship between asthma and patients with COVID-19 with poor outcomes (including severe or critical illness, ICU admission, requirement of MV, or death), we calculated the pooled unadjusted ES based on 40 studies comprising 274,395 patients. The pooled unadjusted ES was less than 1, which revealed that asthma might be associated with the reduced risk of poor outcomes in patients with COVID-19, although the corresponding 95% CI crossed 1 (ES, 0.91; 95% CI, 0.78-1.06). We hypothesized that the different poor outcomes reported in the included articles and the known factors (such as sex, age, and other comorbidities) influencing the risk of poor outcomes in patients with COVID-19 might contribute to the results.[2,129,130] Therefore, we specifically explored the association between asthma and the risk of mortality in patients with COVID-19 based on the limited data reported by the included articles. Similarly, the pooled unadjusted ES was less than 1, which also revealed that asthma might be significantly associated with the reduced risk of mortality in patients with COVID-19 (ES, 0.88; 95% CI, 0.73-1.05). Considering that this result might be because of the influence of various factors on the risk of mortality in patients with COVID-19, we subsequently calculated

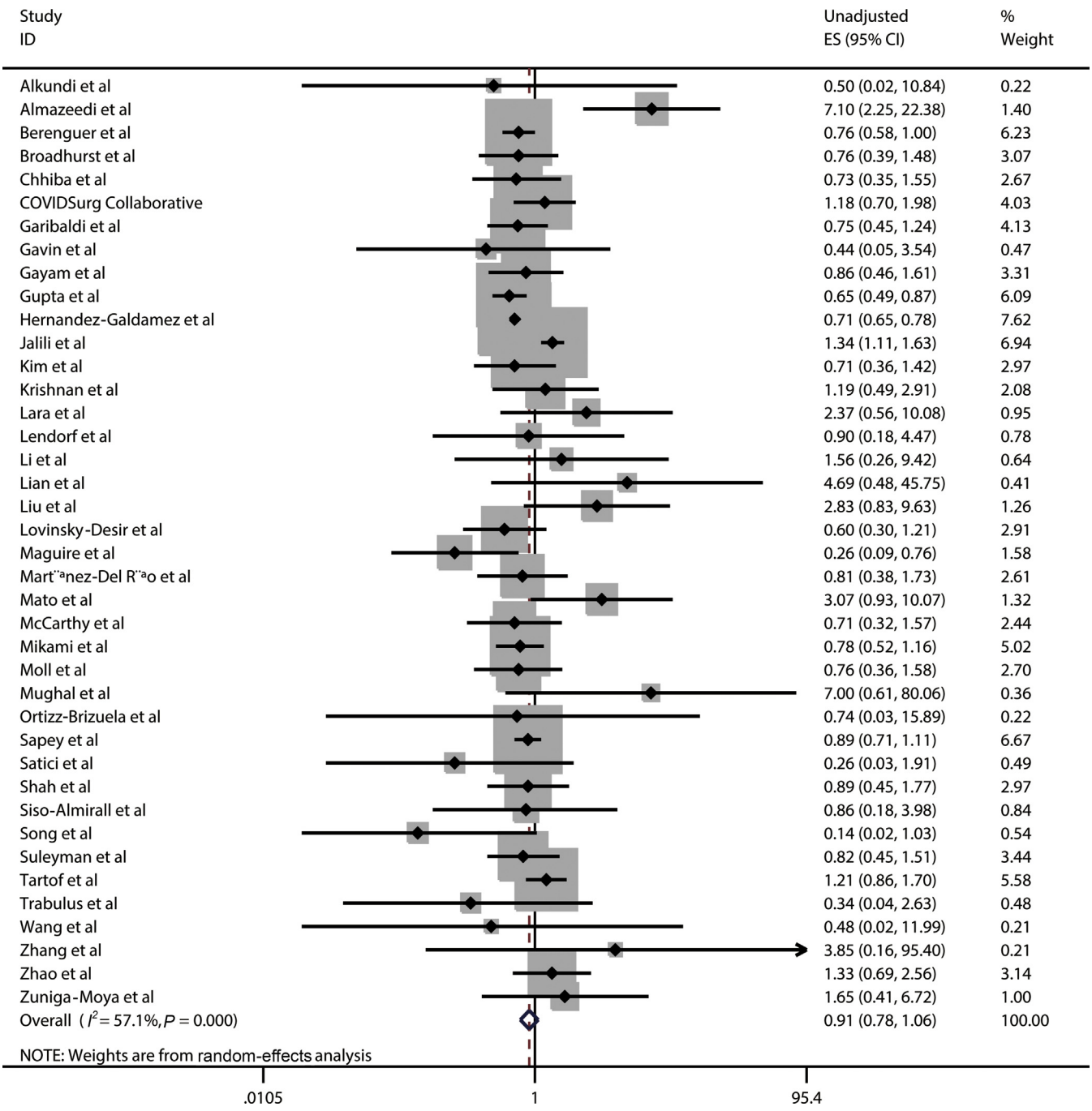

Figure 3. Forest plot of unadjusted ES for the association between asthma and the poor outcomes of patients with COVID-19 on a basis of 40 studies. CI, confidence interval; COVID-19, coronavirus disease 2019; ES, effect size; ID, identification.

the pooled ES on the basis of adjusted effect estimates. The corresponding results suggested that asthma was significantly associated with the reduced risk of mortality in patients with COVID-19 (ES, 0.80; 95% CI, 0.74-0.86). In summary, asthma might be an independent protective factor for death of patients with COVID-19. There are some complicated and multifactorial reasons. One reason is immune response triggered by asthma. Li et al[79] speculated that T_H2 immune response in patients with asthma may counter the inflammation process induced by SARS-CoV-2 infection. Another is the use of inhaled corticosteroids or bronchodilators, which can suppress viral replication and decrease the impact of the inflammatory storm.[131,132]

Several limitations inevitably exist in our meta-analysis. First, most studies we included were retrospective; therefore, the interpretation of our results should be taken with caution because of their inherent limitations. Further well-designed prospective studies with large sample sizes are required to verify our findings. Second, the substantial heterogeneity across the studies should not be ignored, which was why we conducted subgroup analysis and meta-regression, and thus identified the region as a potential source of heterogeneity. Third, in the included studies, the definitions of asthma were not uniform and relatively diverse, including patients' self-report, which might lead to a certain bias. Fourth, we did not carry out statistics and

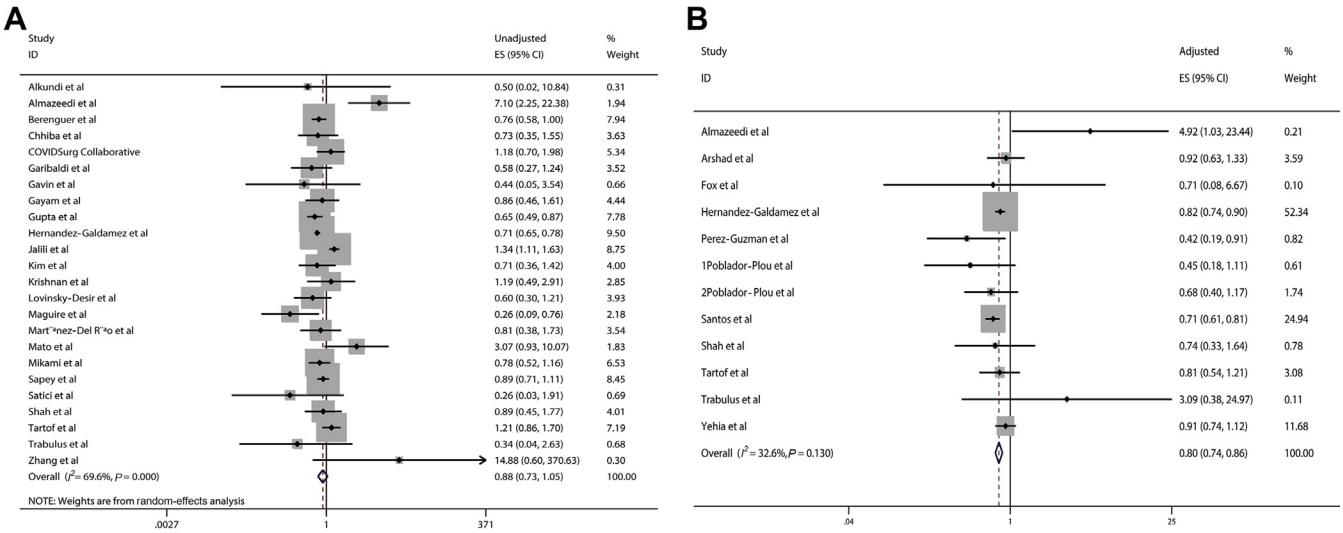

Figure 4. Forest plots of the pooled ES for the relationship between asthma and the risk of mortality in patients with COVID-19. A, The unadjusted ES on a basis of 24 studies. B, The adjusted ES on a basis of 12 studies. CI, confidence interval; COVID-19, coronavirus disease 2019; ES, effect size; ID, identification.

analysis on the use of corticosteroids because of insufficient data provided in the original publications. Fifth, different poor outcomes including severe illness, critical illness, ICU admission, MV, and death were reported in the selected studies; we only specifically explored the association between asthma and the risk of mortality in patients with COVID-19 based on the limited data reported by the included articles. Further subgroup analysis on the relationship between asthma and certain outcomes of patients with COVID-19 should be performed when sufficient data are available. Finally, obvious publication bias was observed in our study, which might be because of the unrecognized duplicate population.

The pooled prevalence of asthma in patients with COVID-19 was similar to that in the general population. Asthma was not associated with the reduced risk of poor outcomes in patients with COVID-19. Interestingly, asthma might be an independent protective factor for the death of patients with COVID-19, which suggests that we should pay high attention to patients with co-infection of COVID-19 and asthma and take locally tailored interventions and treatment. Further well-designed studies with large sample sizes are required to verify our findings.

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Supplementary Data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.anai.2021.02.013.

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