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Effect of asthma, COPD, and ACO on COVID-19: A systematic review and meta-analysis

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Abstract

Introduction

The prevalence of asthma, chronic obstructive pulmonary disease (COPD), and asthma-COPD overlap (ACO) in patients with COVID-19 varies, as well as their risks of mortality. The present study aimed to assess the prevalence of asthma, COPD, and ACO as comorbidities, and to determine their risks of mortality in patients with COVID-19 using a systematic review and meta-analysis.

Methods

We systematically reviewed clinical studies that reported the comorbidities of asthma, COPD, and ACO in patients with COVID-19. We searched various databases including PubMed (from inception to 27 September 2021) for eligible studies written in English. A meta-analysis was performed using the random-effect model for measuring the prevalence of asthma, COPD, and ACO as comorbidities, and the mortality risk of asthma, COPD, and ACO in patients with COVID-19 was estimated. A stratified analysis was conducted according to country.

Results

One hundred one studies were eligible, and 1,229,434 patients with COVID-19 were identified. Among them, the estimated prevalence of asthma, COPD, and ACO using a meta-analysis was 10.04% (95% confidence interval [CI], 8.79–11.30), 8.18% (95% CI, 7.01–9.35), and 3.70% (95% CI, 2.40–5.00), respectively. The odds ratio for mortality of pre-existing asthma in COVID-19 patients was 0.89 (95% CI, 0.55–1.4; $p = 0.630$), while that in pre-existing COPD in COVID-19 patients was 3.79 (95% CI, 2.74–5.24; $p<0.001$). France showed the highest prevalence of asthma followed by the UK, while that of COPD was highest in the Netherlands followed by India.

Competing interests: The authors have declared that no competing interests exist.

Conclusion

Pre-existing asthma and COPD are associated with the incidence of COVID-19. Having COPD significantly increases the risk of mortality in patients with COVID-19. These differences appear to be influenced by the difference of locations of disease pathophysiology and by the daily diagnosis and treatment policy of each country.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first detected in Wuhan, China [1], and it is the causative agent of the coronavirus disease 2019 (COVID-19) pandemic [2]. As many as 50% of patients have reported having at least one comorbidity with COVID-19 [3]. Among them, the highest prevalent comorbidity was hypertension (21.1%), followed by diabetes (9.7%), cardiovascular disease (8.4%), and respiratory system disease (1.5%) [3]. However, the prevalence of asthma, as a comorbidity of patients with COVID-19, has been reported to vary from 1.10% [4] to 36.3% [5]. Additionally, the prevalence of chronic obstructive pulmonary disease (COPD) in COVID-19 ranges from 0.70% [6] to 70.60% [7] and that of asthma-COPD overlap (ACO) ranges from 0.40% [8] to 29.40% [7]. Previous reports have indicated that the global prevalence of asthma in adults is estimated to be 4.3% [9], that of COPD is estimated to be 12.16% [10], and that of ACO ranges from 0.9% to 11.1% [11]. While some studies have reported that asthma, COPD, and ACO are related to an increase in the mortality rate of COVID-19 [12, 13], some studies have reported that they may not be risk factors or may not increase the mortality of COVID-19 [14–17]. However, studies on detailed examinations of the prevalence and risk of mortality of asthma, COPD, and ACO in patients with COVID-19 are still lacking.

Therefore, this study aimed to systematically review and integrate the data from studies with various results on the prevalence of asthma, COPD, and ACO in patients with COVID-19. We also aimed to determine the mortality risks of asthma, COPD, and ACO in patients with COVID-19.

Methods

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement and the statement by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group [18–20].

Search strategy

Two investigators (Y.U. and T.M.) independently searched for eligible studies in PubMed, the Cochrane Library, and MedRxiv from inception to 27 September 2021. We used the following key words: "asthma" OR "asthmatic" OR "COPD" OR "Chronic Obstructive Lung" OR "Chronic Obstructive Pulmonary Disease" OR "chronic bronchitis" OR "pulmonary emphysema" OR "pulmonary disease" OR "Chronic Obstructive" OR "Chronic Obstructive Airway Disease" OR "COAD" OR "Chronic Obstructive Lung Disease" OR "Chronic Airflow Obstruction" OR "Obstructive Lung Disease" OR "Obstructive pulmonary Disease" OR "Lung Disease" OR "ACO" OR "asthma-COPD overlap" OR "Asthma-chronic obstructive pulmonary disease overlap syndrome" OR "Asthma and chronic obstructive pulmonary disease overlap syndrome" OR "asthma-COPD overlap syndrome" OR "asthma-COPD" OR "ACOS" OR

"mixed asthma-COPD phenotype" OR "Asthma combined with COPD" OR "coexistence of asthma and COPD" OR "coexistence of asthma and COPD" OR "COPD with asthmatic features" OR "overlap of asthma-COPD" AND "COVID-19" OR "novel coronavirus" OR "new coronavirus" OR "emerging coronavirus" OR "2019-nCoV" OR "SARS-CoV-2" OR "COVID" OR "coronavirus" OR "nCov" OR "coronavirus disease 2019" OR "coronavirus 2019". We also reviewed the reference lists of eligible studies using Google Scholar and performed a manual search to ensure that all appropriate studies were included.

Eligibility criteria and outcome measures

Studies fulfilling the following selection criteria were included in the meta-analysis: (1) randomized, clinical trials, observational studies, and case series involving >20 patients written in English; and (2) patients with positive laboratory-confirmed SARS-CoV-2 infection who had asthma, COPD, or ACO as comorbidities. The exclusion criteria were as follows: (1) systematic reviews, (2) reviews, (3) animal experimental reports, (4) ≤20 patients in case series, (5) insufficient or incomplete data, (6) unpublished articles, and (7) pediatrics reports.

Data extraction

Two reviewers (Y.U. and T.M.) extracted the data independently. Articles that were retrieved in the search were stored in a citation manager. After removing redundant articles, titles, and abstracts, full-text articles were then investigated. We extracted the following data: study design, observational period, study site, and inclusion/exclusion criteria of each study. Outcome variables were extracted into predesigned data collection forms. We verified the accuracy of the data by comparing the collection of each investigator, and any discrepancies were resolved through discussion.

Level of evidence

The level of evidence was determined using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework, which classifies the level of evidence for each outcome on the basis of the risk of bias, imprecision, inconsistency, indirectness, and publication bias [21]. The authors classified the evidence level for each eligible study in accordance with the revised grading system for recommendation in the evidence-based guideline [22] (S1 Table).

Data analysis. In the meta-analysis, we estimated the odds ratios (ORs) or the proportions of patients for primary outcome variables with 95% confidence intervals (CIs) using the random-effects model (generic inverse variance method). To assess the proportions of the outcome variables in patients with COVID-19, the standard error was calculated using the Agresti-Coull method [23]. Heterogeneity among the original studies was evaluated using the I^2 statistic [24]. Publication bias was examined using a funnel plot. For all analyses, significant levels were two-tailed, and $p<0.01$ was considered significant. All statistical tests were performed using Review Manager (RevMan) ver. 5.4.1 (Cochrane Collaboration, Copenhagen, Denmark) [25].

Ethics approval and consent to participate. The institutional review board and patient consent were not required because of the review nature of this study.

Results

Study selection and characteristics

Of the 2005 references screened, 101 studies reported the outcome variables (Fig 1).

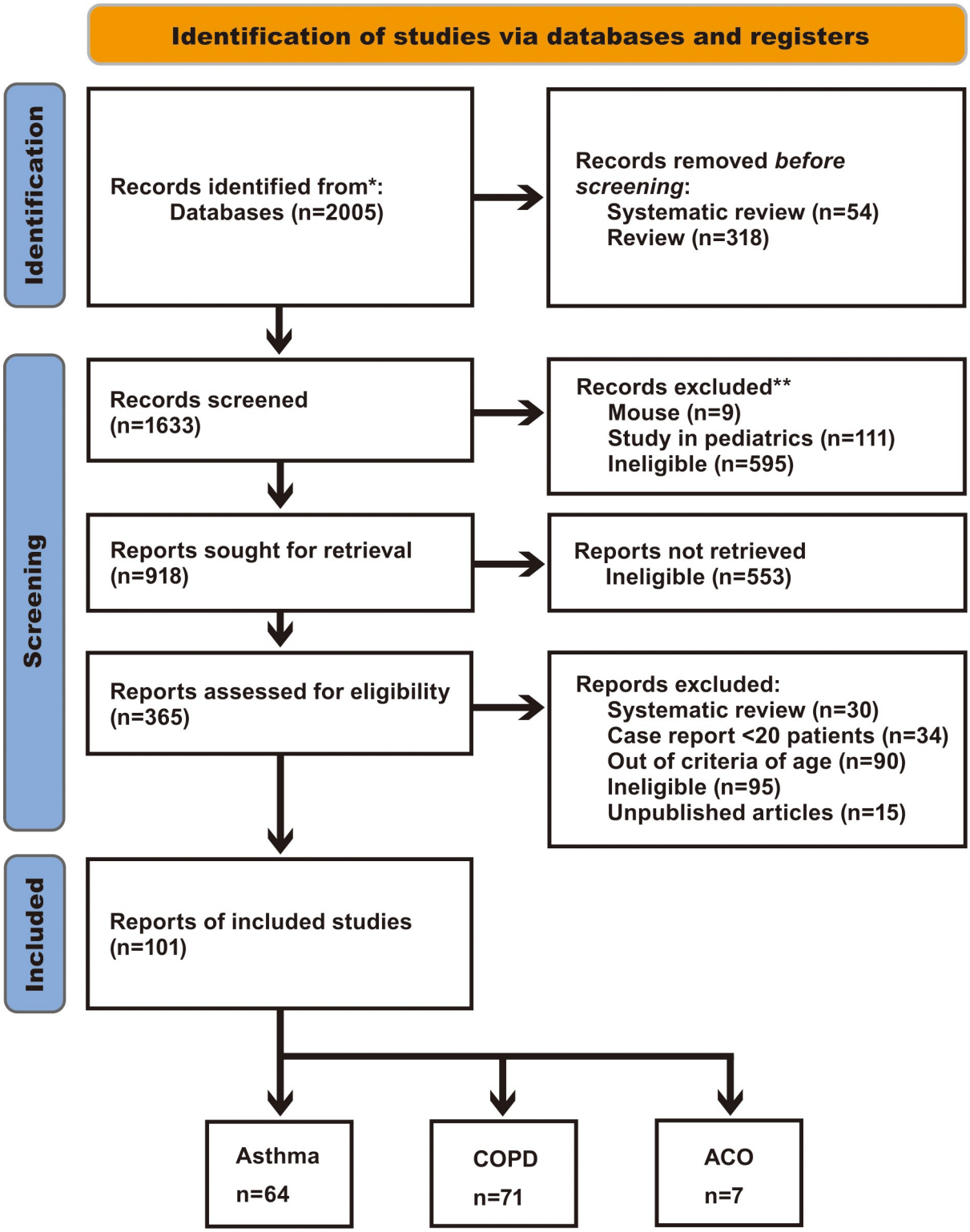

Fig 1. PRISMA flow diagram. N indicates the number of articles.

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We analyzed 64 studies on asthma, 71 on COPD, and 7 on ACO. Thirty-three studies were duplicated for asthma and COPD, two for asthma and ACO, and four for asthma, COPD, and ACO. Table 1 shows the characteristics of the included studies.

Table 1. The characteristics of the included studies.

Study, year	Country	Observational period	Study Design	No. of participants	Sex-Male, n (%)	Age, Median (IQR) or mean±SD, years	Severity of COVID-19, n (%)	Standard of the evidence level
Zhang JJ, 2020 [26]	China	Jan.16-Feb.3, 2020	-	140	71 (50.7)	57 (range, 25–87)	Nonsevere 82 Severe 58	2-
Wang L, 2020 [27]	China	Jan.1-Feb.6, 2020	Retrospective single-center study	339	166	69 (65–76)	Moderate100(29.5) severe159(46.9) critical80(23.6)	2-
Bhatraju PK, 2020 [28]	USA	Feb.24-Mar.9, 2020	-	24	15 (63)	64±18		2-
Turan O, 2021 [29]	Turkey	Mar-Aug, 2020	Multicenter, retrospective cohort study	1069	634	>18		2-
Barrasa H, 2020 [30]	Spain	Mar.4-Mar.31, 2020	-	48	27 (56)	63 (12)≥18		2-
Mahdavinia M, 2020 [31]	USA	Mar.12-Apr.3 2020	-	935	417	≥18		2-
Li P, 2020 [32]	China	Jan.31-Feb.20, 2020	-	204	100	68 (64–75) Range, 60–95	Mild 64.7%, severe 33.3%, critical 2%	2-
Lian J, 2020 [33]	China	Jan.17-Feb.12, 2020	retrospective	136	58	68.28±7.314	Mild 102, severe 22, critical 12	2-
Iaccarino G, 2020 [34]	Italy	Mar.9-Apr.9, 2020	Cross-sectional, multicenter, observational study	1591	64%	66.5±0.4 range18-101		2-
Toussie D, 2020 [35]	USA	Mar.10-Mar.26, 2020	Retrospective study	338	210 (62)	39 (31–45) Between 21 and 50	Low chest radiograph severity score 0–1:202 2–6:136	2-
Argenziano M, 2020 [36]	USA	Mar.1-Apr.5, 2020	Retrospective case series	1000	596	Emergency department55 (40–69) In hospital 64 (51–77) ICU, 62 (52–72)		2-
Cummings MJ, 2020 [37]	USA	Mar.2-Apr.1, 2020	Prospective cohort study	257 critical	171 (67)	62 (51–72)		2-
Zhu Z, 2020 [38]	USA	Mar.16 2020-	Population-based prospective cohort study	641	288 (45)	56±8 Aged 40–69		2-
Grandbastien M, 2020 [39]	France	Mar.4-Apr.6, 2020	Monocentric, retrospective, cohort study	106	66 (62.3)	63. 5(54.2–72.0)		2-
Yao Y, 2020 [40]	China	-Mar.10, 2020	Retrospective, multicenter, cohort study	171	92 (53.8)	50.5±15.2	Severe 71(41.5), critical 29(17.0)	2-
Lieberman-Cribbin W, 2020 [41]	USA	Feb.29-Apr.24, 2020	-	6245	49%	57		2-

(*Continued*)

Table 1. (Continued)

Study, year	Country	Observational period	Study Design	No. of participants	Sex-Male, n (%)	Age, Median (IQR) or mean±SD, years	Severity of COVID-19, n (%)	Standard of the evidence level
Wang J, 2020 [42]	China	Jan.24-Feb.23, 2020	Retrospective study	307	156 (50.8)	57.65±15.754	Mild/moderate 259 (84.6) Severe/critical 48 (15.6)	2-
Aggarwal A, 2020 [43]	India	Apr.10-Apr.30, 2020	Retrospective, single-center case series	32	19 (59.4)	54. 5 (46.25–60)	Severe 24 Non-severe 8	2-
Caminati M, 2020 [44]	Italy	Mar.1-Apr.30, 2020	-	Brescia20 Verona6	Brescia8 Verona3	Brescia41-77 (mean 61.5) Verona55-79 (69.3)		2-
Bello-Chavolla OY, 2020 [4]	Mexico	-June.3, 2020	Population-based statistics	20804	12257 (58.9)	≥ 60		2-
Bravi F, 2020 [45]	Italy	-Apr.24, 2020	Case-control, retrospective study	1603	47.3%	58.0 (20.9) All adults	Mild957 Severe454 Very severe/ lethal192	2-
Song J, 2021 [46]	China	Feb.1-Mar.6 2020	Retrospective observational study	961	500 (52.0)	63 (49–70)	Nonsevere719(74.8) Severe242(25.2)	2-
Wang L, 2020 [47]	USA	Mar .3-June.8, 2020	-	1827	595	54 (37–66)	Hospitalized 565, Non-hospitalized 1262	2-
Canevelli M, 2020 [48]	Italy	Feb.21-Apr.29, 2020	-	2687	1807	Natives 78.3±10.8 Migrants 71.1±13.1		2-
De Vito A, 2020 [49]	Italy	Mar.8-Apr.8, 2020	Retrospective, monocentric study	87	56 (64.4)	72 (62.5–83.5)		2-
Atkins JL, 2020 [50]	UK	Mar.16-Apr.26, 2020	-	507	311	74.3 (4.5) Aged 65 and older		2-
Zhao Z, 2020 [51]	USA	Mar.9-Apr.20, 2020	Retrospective study	641	Died 53 (64.6), ICU admission136 (69.7) General admission222 (55.8)	Died 77 (66–85) ICU admission 60 (50–70) General admission 58 (46–71)		2-
Pérez-Sastré MA, 2020 [52]	Mexico	Feb.28-June.21, 2020	-	159017	(52.2)	≥20		2-
Guner R, 2020 [53]	Turkey	Mar.10-Apr.10, 2020	-	222	132 (59.5)	50.6±16.5 (18–93)	Mild172 Critical50	2-
Somani SS, 2020 [54]	USA	Feb.27-Apr.12	Retrospective cohort study	2864	1663	≥18		2-
Yang JM, 2020 [55]	Korea	Jan.1-May.15, 2020	Propensity-score-matched nationwide cohort	7430	2970 (40.5)	49.0±19.9		2-
Campioli CC, 2020 [56]	USA	Feb.1-May.15, 2020	Retrospective study	251	103 (41.0)	53 (27) adult		2-
He Y, 2020 [57]	China	Jan.20-Apr.12020	-	336	201 (59.8)	65 (50–77)	severe	2-
Mushtaq J, 2021 [58]	Italy	Feb.25-Apr.9, 2020	Retrospective single-center study	697	465 (66.7)	62 (52–75)		2-
Goel N, 2020 [59]	India	May.8-July.3, 2020	Retrospective observational study	35	20 (57.1)	46±17	Symptomatic 29 (82.9%), asymptomatic 6 (17.1%)	2-

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Table 1. (Continued)

Study, year	Country	Observational period	Study Design	No. of participants	Sex-Male, n (%)	Age, Median (IQR) or mean±SD, years	Severity of COVID-19, n (%)	Standard of the evidence level
Brendish NJ, 2020 [60]	UK	Mar.20-Apr.29, 2020	Prospective, interventional, non-randomised study	352	202 (57.4)	68 (50–80)		2-
Ioannou GN, 2020 [61]	USA	Feb.28-May.14, 2020	Longitudinal cohort study	10131	9221 (91.0)	63.6 (16.2) ≥18		2-
Xiong Q, 2021 [62]	China	-Mar.1, 2020	Longitudinal study	538	245 (45.5)	52.0 (41.0–62.0) From 20 to 80	General 331(61.5), severe 180(33.5), critical 27(5)	2-
Seaton RA, 2020 [63]	UK	Apr.20-30, 2020	-	531	274 (51.6)	72(61–82) Range25-104		2-
Abrams MP, 2020 [64]	USA	Mar.1-Apr.3, 2020	cohort	133	74 (55.6)	81.0 (70.5–88.0)	Arrhythmic death11 Nonarrhythmic death122	2-
Akpinar G, 2021 [65]	Turkey	Mar.1-May.31, 2020	Retrospective cross-sectional design	88	46	48.0±17.3		2-
Schiavone M, 2021 [66]	Italy	Feb.23-Apr.1, 2020	Retrospective study	844	521 (61.7)	63.4±16.1		2-
Calmes D, 2020 [67]	Belgium	Mar.18-Apr.17 2020	-	596	294	≥35		2-
Rial MJ, 2021 [68]	Spain	Mar-June, 2020	Multicenter retrospective cohort	35	14	≥20		2-
Robinson LB, 2020 [69]	USA	Mar.8-Apr.27, 202	Matched cohort study	403	191	≥18		2-
Cates J, 2020 [70]	USA	Mar.1-Mar.31, 2020	-	3948	3710 (94.0)	70 (61–77)		2-
Şanlı DET, 2020 [71]	Turkey	Mar.11-Apr.11, 2020	Local institutional reveiw	102	73 (72)	48.62±14.42 Ranging 19–94		2-
Hussein MH, 2020(USA) [72]	USA	Mar.15-June.9, 2020	Multi-center retrospective study	502	238	Mean age 60.7 ≥18	qSOFA score, CURB65 score	2-
Liao SY, 2021 (USA) [5]	USA	Mar.11-June.23, 2020	Prospective observational study	113	53 (47)	50±16		2-
Tabarsi P, 2021 [73]	Iran	?	Randomized controlled trial	84	65	IVIg, 54.29±12.85 Control group, 52.47±14.49 Between 18 and 65	All severe patients	1-
Lee SC, 2020 [74]	Korea	Jan.20-May.27 2020	Retrospective cohort study	7272	2927	≥20	Non-severe, severe	2-
Jiang Y, 2020 [75]	China	Jan.30-Mar.8, 2020	Retrospective observational study	281	143	≥60		2-
Xiao J, 2020 [76]	China	Dec.25, 2019-Feb.16, 2020	Retrospective single-center study	243	105 (43.2)	47.0 (range20-89)	Moderate203, severe/critical 40	2-
Signes-Costa J, 2021 [77]	Spain	Mar.23-May.5, 2020	Retrospective, multicenter, cohort study	5847	3432	65.1±16.6		2-

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Table 1. (Continued)

Study, year	Country	Observational period	Study Design	No. of participants	Sex-Male, n (%)	Age, Median (IQR) or mean±SD, years	Severity of COVID-19, n (%)	Standard of the evidence level
Bello-Chavolla OY, 2020 [78]	Mexico	Mar.16-Aug.17, 2020	-	3007	Non-severe1227 (50.5) Severe403 (70.1)	Non-severe 44 (33–55) Severe 56 (47–66)	Non-severe2432 Severe 575	2-
Lokken EM, 2020 [79]	USA	Jan.21-Apr.17, 2020	Retrospective study	46	0 Pregnant women	29 (26–34)		2-
Gómez Antúnez M, 2021 [80]	Spain	Mar 2020	Retrospective cohort study	10420	5893 (56.7)	69 (55–79)		2-
Ferastraoaru D, 2021 [8]	USA	Mar.14-Apr.27, 2020	Retrospective study	4558	(31.8)	Asthma 60.5±17.07		2-
Monterrubio-Flores E, 2021 [81]	Mexico	Feb.28-July.31, 2020	-	406966	216908 (53.2)	≥20		2-
Mortaz E, 2021 [82]	Iran	Apr.10-May.9, 2020	retrospective observational study	29	17	54.45±2.536 (range, 32–79)		2-
Değerli E, 2021 [83]	Turkey	Mar.23-Oct.23, 2020	Retrospective study	45	23 (51)	60.3±15.65		2-
Laake JH, 2020 [84]	Norway	Mar.10-June.19, 2020	National cohort	217	162	63 (54.2–72.2)		2-
Lee SC, 2021 [85]	Korea	Jan.20-May.27, 2020	Retrospective cohort study	4610	1710	≥40		2-
Jungo S, 2021 [86]	France	Apr.1-Apr.29, 2020	-	79	37 (46.8)	44 (36–53) Range, 21–86	COVID-19-related phenotypes 68(86.1)	2-
Cao L, 2021 [87]	USA	Mar-Sep, 2020	Prospectively collected cohort	343	192	>18		2-
Fong WCG, 2021 [88]	UK	Mar.1-May.31, 2020	retrospective	6638(with, w/o covid)	3079 (46.4)	65 (42–79)		2-
Jongbloed M, 2021 [89]	Netherland	Feb.28-Apr.1, 2020	Retrospective cohort study	303	195 (64)	72±12		2-
Artero A, 2021 [90]	Spain	Mar.1-May.28, 2020	Multicenter retrospective cohort study	10238	5924 (57.9)	66.6±16.2		2-
Ho KS, 2021 [91]	USA	Mar.7-June.7, 2020	Retrospective multicenter cohort study	10523	5707	58.35±18.81		2-
Yoshida Y, 2021 [92]	USA	Feb.27-July.15, 2020	Retrospective case series	776	365 (47.3)	60.5 (16.1) >18		2-
Nanda S, 2021 [93]	USA	Jan.1-May.23, 2020	retrospective	1169	575 (49.2)	43.9 (17.6) [range18.0–99.0]		2-
De Vito A, 2021 [94]	Italy	Apr.9-May.31, 2020	Observational retrospective cohort study	264	99 (37.5)	81.93±10.11	Symptomatic 132 Asymptomatic 132	2-
Rodriguez C, 2021 [95]	France	Mar.9-30, 2020	-	104	59	Outpatient 50 (range, 19–87) Hospitalized 61 (31–82) ICU, 68 (33–90)		2-
Garibaldi BT, 2021 [96]	USA	Mar.4-Aug.29, 2020	Retrospective comparative effectiveness research	2299	1193 adults	All remdesivir, 60 (46–69) All control, 60 (44–74)		2-

(*Continued*)

Table 1. (Continued)

Study, year	Country	Observational period	Study Design	No. of participants	Sex-Male, n (%)	Age, Median (IQR) or mean±SD, years	Severity of COVID-19, n (%)	Standard of the evidence level
Giovannetti G, 2021 [97]	Italy	May.18-July.25, 2020	Prospective observational study	38	27 (71.1)	60.6 (10.4) Between 18 and 75	Mild11(28.9) Moderate11(28.9) Severe3(7.9)	2-
Khan MS, 2021 [98]	USA	Jan.1-June.15, 2020	Retrospective, observational cohort study	470	224 (47.7)	≥18		2-
Tsai S, 2021 [99]	USA	Feb.24-Nov.25, 2020	Retrospective cohort	8308	0 All women	50.69±12.80 Adult		2-
Lobelo F, 2021 [100]	USA	Mar.3-Oct.29, 2020	Retrospective cohort	5721	2416 (42.2)	44.8 (15.7) ≥18		2-
Chatterjee A, 2021 [101]	Netherland	Mar.1-July.1, 2020	Retrospective study	2337	Non-mortality1078 (60.9) Mortality393 (69.2)	Non-mortality, 65 (55–75) Mortality, 77 (70–83)	Non-mortality1769 Mortality568	2-
Yordanov Y, 2021 [102]	France	Mar.9-Aug.11, 2020	Prospective cohort	7320	2301 (31.5)	43.0±13.9		2-
Riou M, 2021 [103]	France	June-Dec, 2020	descriptive	81	59 (73)	61 (51–68)	Mild-to-moderate 21, severe 15, critical 45	2-
Wei W, 2021 [104]	USA	June.1-Dec.9, 2021	Retrospective study	206741	85228	46.7 (17.8) ≥18	-	2-
Hou X, 2021 [105]	China	Jan.28-Feb.25, 2020	Single-center retrospective cohort study	113	61 (54)	55.1±14.2	Severe113	2-
Valverde-Monge M, 2021 [106]	Spain	Jan.31-Apr.17, 2020	Retrospective analysis	2539	1275	NCRD 61.1±19.3, CRD 71.4±14.8	-	2-
Cosio BG, 2021 [107]	Spain	Mar.15-Apr.30, 2020	Case-control study	52	48 (92.3)	72.96±10.75	-	2-
Adir Y, 2021 [108]	Israel	Mar.1-Dec.7, 2020	Case-control study	8242	4343	43.3±20.4	Moderate, severe	2-
Sen P, 2021 [7]	USA	Mar.8-Sap.16, 2020	-	1288	499 (38.8)	63.7 (15.2)≥35	-	2-
Chandel A, 2021 [6]	USA	Mar.1-June.9, 2020	Multicenter retrospective observational study	272	180	57±13	-	2-
Chaudhary S, 2021 [109]	USA	Mar.15-May.10, 2020	Single-center retrospective observational study	128	71	68 (61–75.5) All adult	-	2-
Williamson EJ, 2020 [110]	UK	Feb.1-May.6, 2020	Cohort study	10926	6126 (0.07)	≥18	-	2-
Abayomi A, 2021 [111]	Nigeria	Feb.27-Jul.6, 2020	Retrospective cohort study	2075	1379	40 (32–50) Range18-98	Mild/asymptomatic 1179, moderate 743, severe 107, critical 42	2-
Liu YH, 2021 [112]	China	Feb.10-Apr.10, 2020	Cross-sectional study	1539	738 (47.95)	69 (66–75)	Severe238 Non-severe1301	2-
Munblit D, 2021 [113]	Russia	Dec.2-Jan.14, 2020	Longitudinal cohort study	1358	675	57 (47–67)	Mild841(61.9) Moderate479(35.3) Severe38(2.8)	2-

(*Continued*)

Table 1. (Continued)

Study, year	Country	Observational period	Study Design	No. of participants	Sex-Male, n (%)	Age, Median (IQR) or mean±SD, years	Severity of COVID-19, n (%)	Standard of the evidence level
Sandoaval M, 2021 [114]	USA	Mar.1-Dec.7, 2020	Retrospective registry-based chart reveiw	1853	704(38.0)	24 (21–27) From 18 to 29	-	2-
Lokken EM, 2021 [115]	USA	Mar.1-June.30, 2020	Multicenter retrospective cohort study	240	0 (pregnant woman)	28 (24–34)	Mild218(90.8) Severe18(7.5) Critical4(1.7)	2-
Cataño-Correa JC, 2021 [116]	Colombia	Mar-Aug, 2020	-	399	235(58.9)	>18	-	2-
Meza D, 2021 [117]	USA	Feb.2021	-	387008	COPD 3949, no COPD 126324	COPD 70.5, no COPD 57.9 Aged over 35	-	2-
Sun Y, 2021 [118]	China	Feb.2-Mar.25, 2020	Retrospective study	268	139(51.9)	57.75 (67–73) Range, 20–88	Severe 96 Non-severe 172	2-
Fernández-Martínez NF, 2021 [119]	Spain	Mar.1-Apr.15, 2020	Observational longitudinal study	968	530(55)	67 (55–77)	-	2-
Cosma S, 2021 [120]	Italy	Sep.20-Jan.9, 2020	Case-control study	21	0	≥18	-	2-
Chudasama YV, 2021 [121]	UK	Mar.16-July.26, 2020	-	1706	981(57.5)	68 (range48-85)	severe	2-

IQR, Interquartile range; SD, Standard deviation; NCRD, non-chronic respiratory disease; CRD, chronic respiratory disease

https://doi.org/10.1371/journal.pone.0276774.t001

In the 101 included studies, we identified 1,229,434 patients with COVID-19, and 32,301, 10,827, and 818 had asthma, COPD, and ACO, respectively, as the comorbidities. Among the studies, there were 34 reports from USA, 14 from China, 10 from Italy, 8 from Spain, 6 from the UK, 5 from Turkey, 4 from Mexico, 3 from Korea, 2 from the Netherlands, 2 from Iran, and 1 each from Israel, Nigeria, Russia, Norway, and Columbia. The study designs were 52 retrospective studies, 7 prospective studies, 1 population-based statistics, 2 matched cohort studies, 4 longitudinal cohort studies, 2 local institutional reviews, 1 randomized, controlled trial, 2 nation cohort studies, 1 descriptive study, 3 case–control studies, 2 cross-sectional studies, and 24 with an unknown design. The total number of male patients was 616,380 and that of female patients was 737,188. Among the studies, the severity of patients with COVID varied from asymptomatic to a critical condition.

Frequency of asthma, COPD, and ACO in patients with COVID-19

The overall prevalence of asthma, COPD, and ACO was estimated, and their forest plots are shown in Figs 2–4, respectively.

Among the eligible patients with COVID-19, the prevalence of asthma, COPD, and ACO was 10.04% (95% CI, 8.79–11.30) for asthma (Fig 2), 8.18% (95% CI, 7.01–9.35) for COPD (Fig 3), and 3.70% (95% CI, 2.40–5.00) for ACO (Fig 4). In the stratified analysis, the frequencies of asthma in different countries are shown in Table 2, and their forest plots are shown in S1 Fig.

With regard to the frequency of asthma, France showed a rate of 13.50% (95% CI, 9.08–17.92), which was the highest, followed by 13.45% in the UK (95% CI, 11.23–15.66). The frequency of COPD in patients with COVID-19 was the highest in the Netherlands at 17.00% (95% CI, 12.96–21.04), followed by India at 11.34% (95% CI, 3.24–19.44). The frequency of

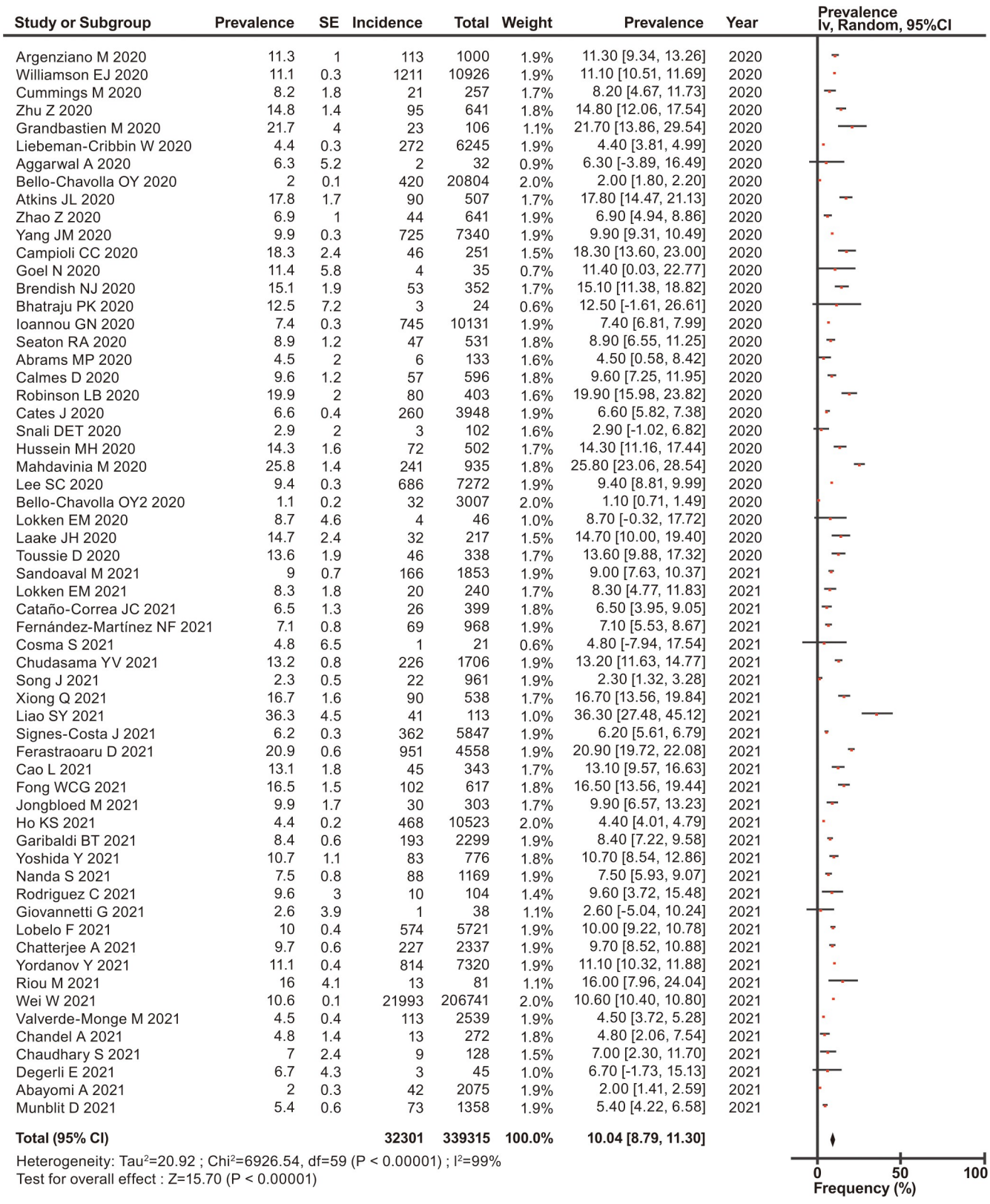


Fig 2. Forest plots of the prevalence of asthma in patients with COVID-19.

https://doi.org/10.1371/journal.pone.0276774.g002

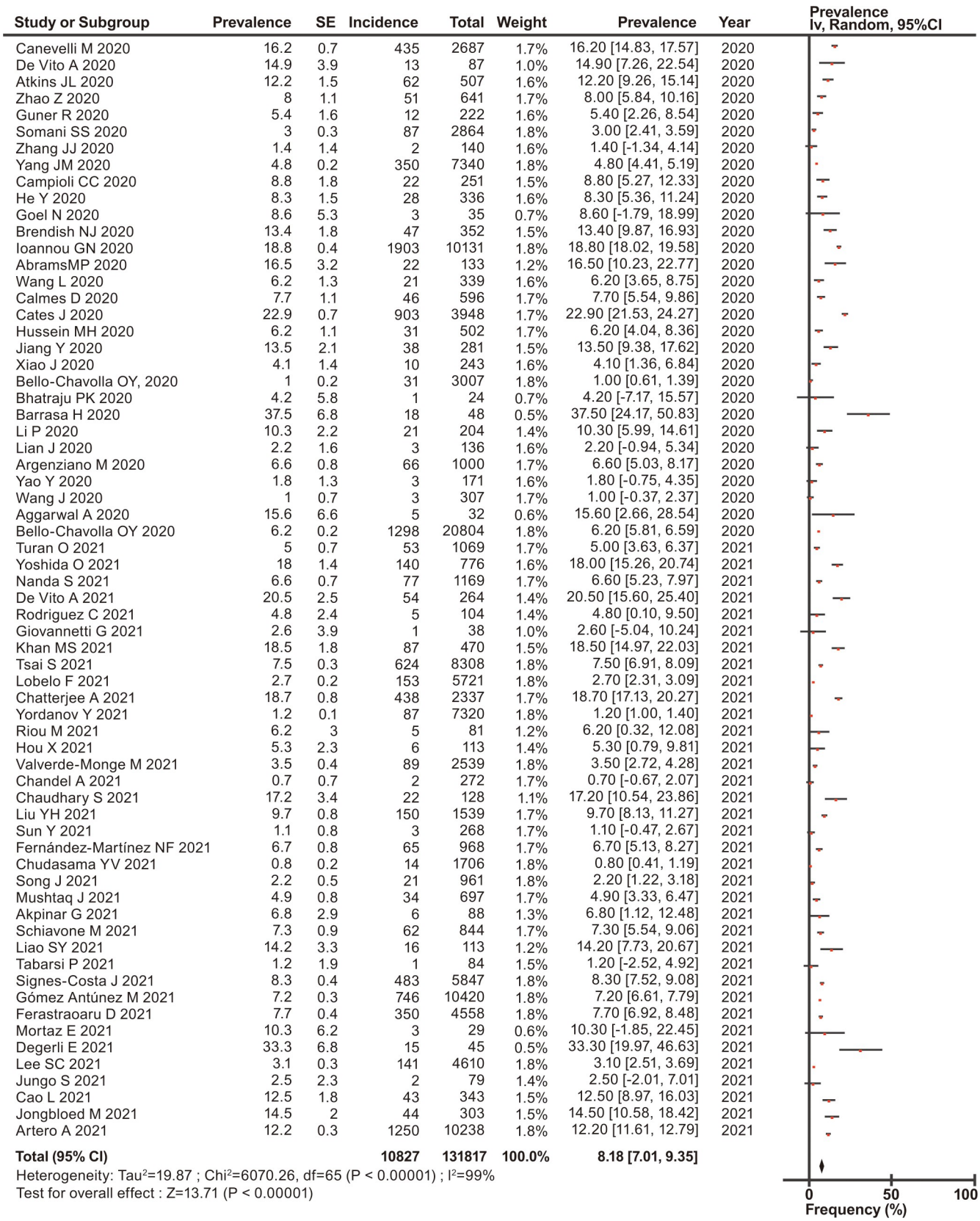


Fig 3. Forest plots of the prevalence of COPD in patients with COVID-19.

https://doi.org/10.1371/journal.pone.0276774.g003

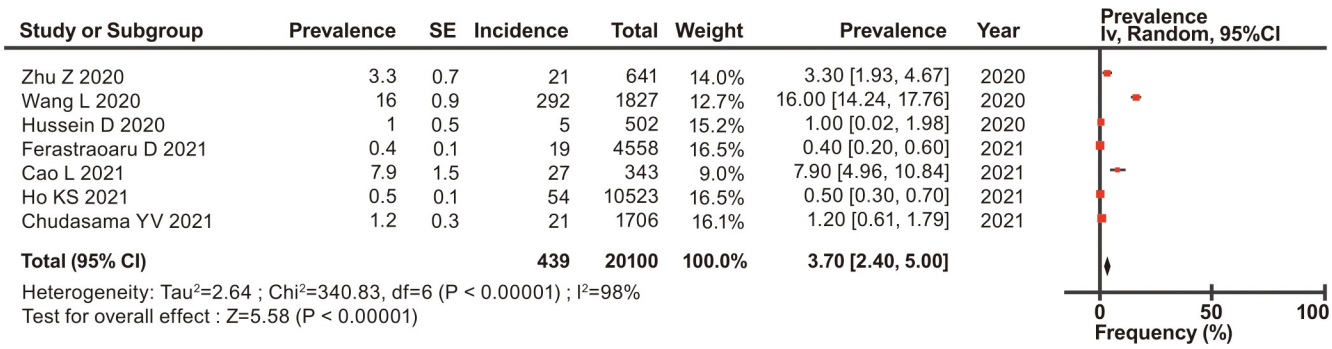


Fig 4. Forest plots of the prevalence of ACO in patients with COVID-19.

https://doi.org/10.1371/journal.pone.0276774.g004

ACO on the USA and the UK was 4.24% (95% CI, 2.74–5.73) and 1.20% (95% CI, 0.61–1.79), respectively. The forest plots of these data are shown in supplementary figures (S1 Fig).

Prevalence of death in patients with COVID-19 and asthma or COPD

Forest plots of the prevalence of death in patients with COVID-19 and asthma or COPD are shown in Fig 5A and 5B.

Among 4,980 patients with asthma and COVID-19, the prevalence of death was 10.17% (95% CI, 7.38–12.97) (Fig 5A). Among 10,525 patients with COPD and COVID-19, the prevalence of death was 40.60% (95% CI, 32.02–49.17) (Fig 5B).

Risk of mortality due to COVID-19 in patients with asthma or COPD

The risk to mortality due to COVID-19 in patients with asthma or COPD was estimated and it is shown in forest plots in Fig 6.

The risk of mortality in pre-existing asthma in COVID-19 patients was not significant (OR, 0.89; 95% CI, 0.55–1.43; $p = 0.630$) (Fig 6A). However, the risk of mortality in pre-existing COPD in COVID-19 patients was significant (OR, 3.79; 95% CI, 2.74–5.24; $p<0.001$) (Fig 6B).

Table 2. Estimated frequencies of asthma, COPD, and ACO in patients with COVID-19 according to countries.

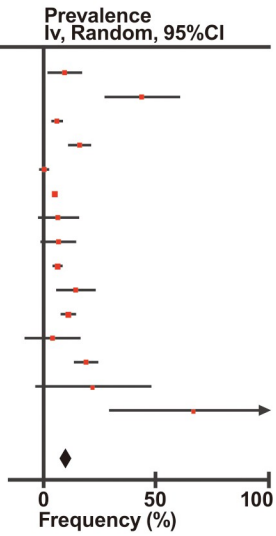
	Asthma			COPD			ACO		
Country	No. of studies	No. of patients	Estimated frequency (95% CI)	No. of studies	No. of patients	Estimated frequency (95% CI)	No. of studies	No. of patients	Estimated frequency (95% CI)
USA	28	26692	11.14 (9.55–12.73)	19	4600	10.48 (7.56–13.40)	6	418	4.24 (2.74–5.73)
Mexico	2	452	1.57 (0.69–2.45)	2	1329	3.60 (-1.50–8.70)	-	-	-
UK	6	1729	13.45 (11.23–15.66)	3	123	8.69 (-0.83–18.22)	1	21	1.20 (0.61–1.79)
Italy	3	28	0.10 (0.09-.011)	6	599	11.09 (5.64–16.54)	-	-	-
Spain	3	544	5.83 (4.44–7.23)	6	2651	8.84 (5.77–11.91)	-	-	-
France	4	860	13.50 (9.08–17.92)	4	99	2.60 (0.33–4.88)	-	-	-
Netherland	2	257	9.72 (8.61–10.83)	2	482	17.00 (12.96–21.04)	-	-	-
Turkey	2	6	3.58 (0.02–7.13)	4	86	8.23 (3.47–12.98)	-	-	-
Iran	-	-	-	2	4	3.84 (-4.25–11.93)	-	-	-
India	2	6	8.57 (0.98–16.16)	2	8	11.34 (3.24–19.44)	-	-	-
China	2	112	9.42 (-4.69–23.53)	13	309	4.93 (2.89–6.96)	-	-	-
Korea	2	1411	9.65 (9.16–10.14)	2	491	3.96 (2.30–5.63)	-	-	-

https://doi.org/10.1371/journal.pone.0276774.t002

a.

Study or Subgroup	Prevalence	SE	Incidence	Total	Weight	Prevalence Iv, Random, 95%CI	Year
Hussein MH, 2020	9.7	3.7	7	72	6.3%	9.70 [2.45, 16.95]	2020
Laake JH, 2020	43.8	8.3	14	32	2.3%	43.80 [27.53, 60.07]	2020
Lee SC, 2020	6.4	0.9	44	686	10.5%	6.40 [4.64, 8.16]	2020
Lieberman-Cribbin W, 2020	16.5	2.3	45	272	8.6%	16.50 [11.99, 21.01]	2020
Mahdavinia M, 2020	0.8	0.8	2	241	10.6%	0.80 [-0.77, 2.37]	2020
Wang L, 2020	5.4	0.5	98	1827	10.9%	5.40 [4.42, 6.38]	2020
Zhao Z, 2020	6.8	4.4	3	44	5.4%	6.80 [-1.82, 15.42]	2020
Calmes D, 2020	7	3.8	4	57	6.2%	7.00 [-0.45, 14.45]	2020
Ferastraoaru D, 2021	6.9	0.8	66	951	10.6%	6.90 [5.33, 8.47]	2021
Fernández-Martínez NF, 2021	14.5	4.3	10	69	5.5%	14.50 [6.07, 22.93]	2021
Ho KS, 2021	11.5	1.5	54	468	9.8%	11.50 [8.56, 14.44]	2021
Song J, 2021	4.5	6.2	1	22	3.6%	4.50 [-7.65, 16.65]	2021
Chatterjee A, 2021	19.4	2.6	44	227	8.1%	19.40 [14.30, 24.50]	2021
Chaudhary S, 2021	22.2	12.9	2	9	1.1%	22.20 [-3.08, 47.48]	2021
Degerli E, 2021	66.7	18.9	2	3	0.5%	66.70 [29.66, 103.74]	2021
Total (95% CI)			**396**	**4980**	**100.0%**	**10.17 [7.38, 12.97]**	

Heterogeneity: Tau²=18.43 ; Chi²=143.66, df=14 (P < 0.00001) ; I²=90%
Test for overall effect : Z=7.14 (P < 0.00001)



b.

Study or Subgroup	Prevalence	SE	Incidence	Total	Weight	Prevalence Iv, Random, 95%CI	Year
He Y, 2020	78.6	7.7	22	28	5.5%	78.60 [63.51, 93.69]	2020
Jiang Y, 2020	78.9	6.6	30	38	5.8%	78.90 [65.96, 91.84]	2020
Wang L, 2020	52.4	10	11	21	4.9%	52.40 [32.80, 72.00]	2020
Zhao Z, 2020	29.4	6.2	15	51	5.9%	29.40 [17.25, 41.55]	2020
Calmes D, 2020	34.8	6.8	16	46	5.7%	34.80 [21.47, 48.13]	2020
Artero A, 2021	40.2	1.4	502	1250	6.6%	40.20 [37.46, 42.94]	2021
Chatterjee A, 2021	30.1	2.2	132	438	6.6%	30.10 [25.79, 34.41]	2021
Chaudhary S, 2021	54.5	9.8	12	22	5.0%	54.50 [35.29, 73.71]	2021
Degerli E, 2021	86.7	9.4	13	15	5.1%	86.70 [68.28, 105.12]	2021
De Vito A, 2021	33.3	6.2	18	54	5.9%	33.30 [21.15, 45.45]	2021
Fernández-Martínez NF, 2021	38.5	5.9	25	65	5.9%	38.50 [26.94, 50.06]	2021
Gómez Antúnez M 2021	38.3	1.8	286	746	6.6%	38.30 [34.77, 41.83]	2021
Khan MS, 2021	23	4.5	20	87	6.2%	23.00 [14.18, 31.82]	2021
Lee SC, 2021	19.1	3.3	27	141	6.4%	19.10 [12.63, 25.57]	2021
Meza D, 2021	14.9	0.4	1107	7449	6.7%	14.90 [14.12, 15.68]	2021
Song J, 2021	47.6	10	10	21	4.9%	47.60 [28.00, 67.20]	2021
Turan O, 2021	13.2	4.8	7	53	6.2%	13.20 [3.79, 22.61]	2021
Total (95% CI)			**2253**	**10525**	**100.0%**	**40.60 [32.02, 49.17]**	

Heterogeneity: Tau²=287.15 ; Chi²=728.00, df=16 (P < 0.00001) ; I²=98%
Test for overall effect : Z=9.28 (P < 0.00001)

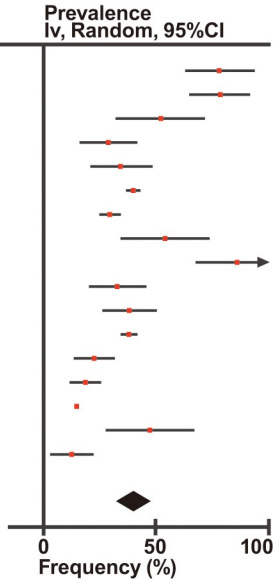


Fig 5. Forest plots of the prevalence of death a) in patients with asthma and COVID-19 and b) in patients with COPD and COVID-19.

https://doi.org/10.1371/journal.pone.0276774.g005

Discussion

The present systematic review and meta-analysis on 101 studies showed that pre-existing asthma and COPD affected the incidence of COVID-19, and asthma had a greater effect than COPD. However, pre-existing asthma did not have a significant effect on mortality in patients with COVID-19, while patients with COPD had a 3.8-fold increased risk of mortality among COVID-19 cases. Among patients with COVID-19, the highest prevalence of asthma was observed in France followed by the UK, while the highest prevalence of COPD was observed in the Netherlands followed by India. The various prevalence of these disease in each county indicates the importance of daily clinical control of asthma, COPD, and ACO for preventing and reducing the severity of COVID-19.

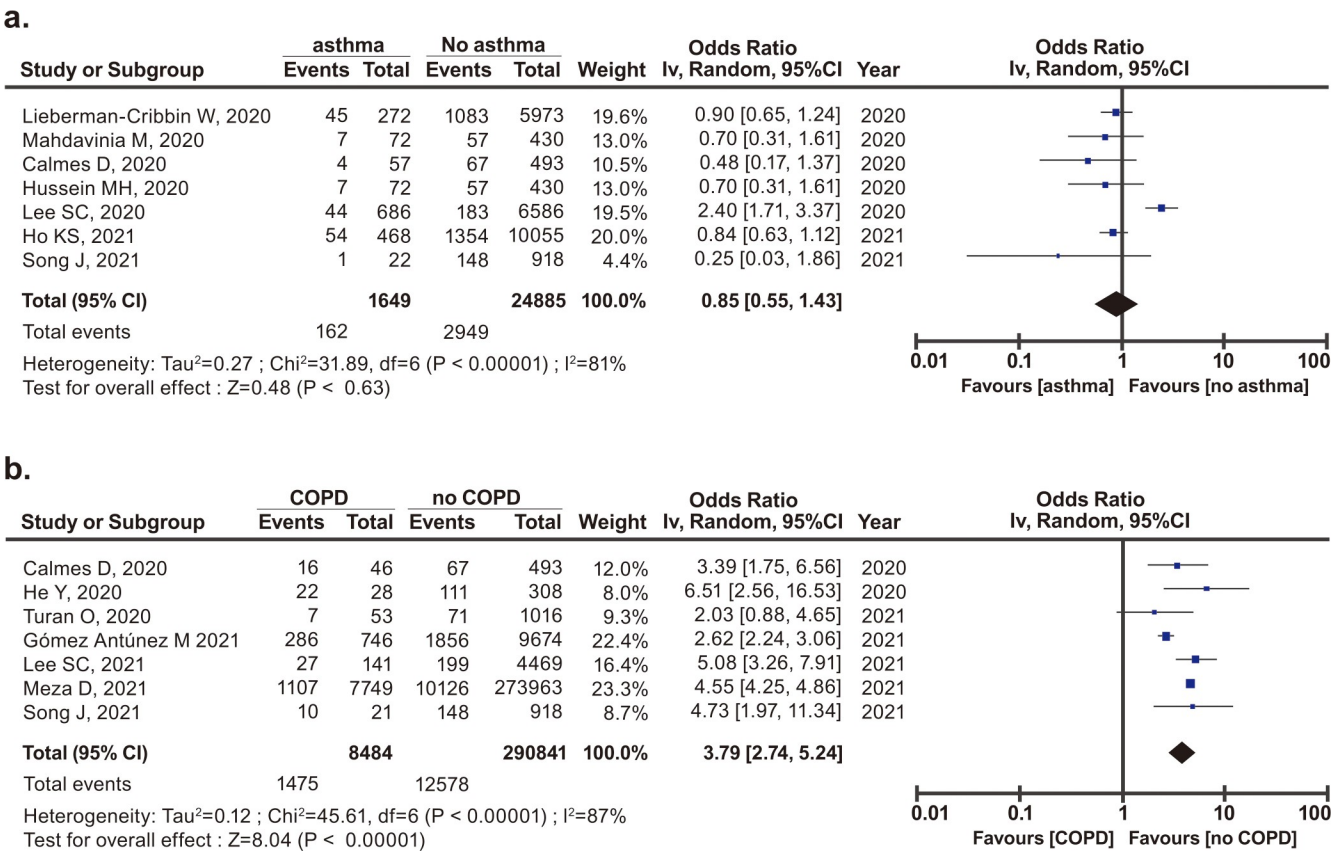


Fig 6. Forest plots of the risk of mortality in patients with COVID-19 and a) asthma or b) COPD.

https://doi.org/10.1371/journal.pone.0276774.g006

The COVID-19 pandemic has disproportionately affected people with chronic diseases, such as asthma and COPD, which are the most common respiratory diseases. Generally, viral infection to the respiratory tract is thought to be one of the triggers for the exacerbation of pre-existing diseases [110]. Respiratory viral infection that is initiated in the upper respiratory tract and innate immunity are critical for the initial control of infection at this site [122]. If the innate immune response is inadequate, the infection can spread to the lower respiratory tract, causing pneumonia [123]. Before the COVID-19 pandemic, the reported global prevalence of adult asthma and COPD was 3.5% [9] and 12.16% [10], respectively. However, in patients with COVID-19 in the present study, which assessed studies published after COVID-19 emerged, the prevalence of pre-existing asthma was 10.04% and that of COPD was 8.18%. The prevalence of asthma after COVID-19 emerged was higher than that before the pandemic. These results indicated that asthma affected the incidence of COVID-19. The increased susceptibility of viral infection in the bronchial airway might be caused by pathophysiological impairment in both of these diseases. Especially in asthma, the main involved sites of the bronchial airway are the upper and lower bronchi [124]. In case of COVID-19, more than 80% of patients have mild illness [123], and the locations where mild COVID-19 is involved are similar to those in patients with asthma. Consequently, the number of patients with asthma may have increased as the number and proportion of mild COVID-19 cases increased. This possibility may also explain why the prevalence of pre-existing asthma was higher than that of COPD. In fact, the Omicron variant was associated with a large number of mild COVID-19 cases [125]. Additionally, a previous meta-analysis, which used only data before the Omicron variant emerged,

reported that the prevalence of asthma was similar to that before the COVID-19 pandemic [126]. This result is different from that in the present study, which assessed COVID-19 cases that included infected patients with the Omicron variant. However, a study including hospitalized COVID-19 cases with a history of asthma indicated that none of these patients presented with asthma exacerbation [127]. Owing to the nature of the meta-analysis, we could not evaluate asthma exacerbation after admission among the patients in this study.

The present study showed that pre-existing COPD in patients had a 3.8-fold higher risk of mortality than in those who did not have COPD. The risk of mortality for pre-existing COPD was stronger than that for pre-existing asthma. Unlike asthma, of which the main involved sites are the upper and lower bronchi, the main impaired lesion of COPD extends from the peripheral small airway to alveolar tissues with architectural damage, which can cause the severe illness. These locations of lesions are compatible with those in COVID-19 when the disease severity is moderate to severe. Indeed, patients with COPD have a high risk of mortality in other respiratory infectious diseases, such as influenza [128] and community-acquired pneumonia [129]. A previous study showed that the long-term use of inhaled corticosteroids for controlling asthma is likely to have a beneficial modulatory effect on COVID-19 [130]. This finding suggests that this efficacy is achieved by reducing epithelial damage and improving the T-cell response. Several studies reported a large number of patients who were receiving either inhaled steroids or systemic steroids at the time of COVID-19 diagnosis [55, 127, 131, 132]. However, the effect of inhaled corticosteroids at the early stage of COVID-19 is controversial [133]. The benefit of systemic corticosteroids for patients with asthma may outweigh the risk of severe outcomes in patients with COVID-19 [134]. Systemic corticosteroids are effective for treating bronchial wall inflammation and bronchial spasm. As the result, uncontrolled asthma is associated with increased intensive care unit admission and intensive respiratory support [135], whereas well-controlled asthma does not have an increased risk of COVID-19-related death [136]. The present study showed that the prevalence of pre-existing asthma in COVID-19 cases varied according to the countries. This finding may be partly due to the fact that each country has different treatment policies and guidelines, as well as available medical resources. In addition, owing to the nature of the meta-analysis in which we did not use individual patient data, we were unable to examine the impact on COVID-19 diagnosis according to age, sex, and stage at which therapy was started. These differences may also influence the severity of COVID-19 in different countries. These factors may be also related to the heterogeneity in the results of the meta-analysis in the present study. A large-sample study showed that the contribution of inhaled corticosteroids for patients with COPD to COVID-19-related death was lower than that for patients with asthma [137]. Additionally, the association with mortality was confounded by the presence of other risk factors for severe COVID-19, such as an older age, cardiovascular disease, hypertension, and diabetes mellitus [123], which are common in people with COPD.

ACO has clinical characteristics derived from asthma and COPD. The risk of mortality from ACO in patients with COVID-19 might be significant and as high as that for COPD. However, in the present study, the prevalence of pre-existing ACO was lower than that of asthma and COPD. Our results regarding ACO cannot be properly assessed because of the number of eligible studies, and the countries that reported pre-existing ACO were only from the USA, UK, and China among the eligible studies. These issues might be due to the short history of the concept of ACO and a lack of global recognition. However, even with the small number of eligible studies, the prevalence of ACO was highest in studies from the USA. Additionally, a study in the USA before the COVID-19 pandemic reported that the prevalence of ACO was 1.05% (0.74%–1.37%) [138], while that in the present study was 4.24%. One of the reasons for this discrepancy between studies may be related to the high smoking rate (14%) in

the USA [139–141]. This discrepancy suggests the necessity of considering other cofounding factors for assessing the risk of ACO, such as the rate of smokers and obesity.

Our study has some limitations, including mainly those inherent to the nature of systematic reviews and meta-analyses using observational studies and case series. The eligible studies were limited to articles written in English. The treatment guidelines and available medical resources for COVID-19, and the examined comorbidities may be different according to the different countries, and these could have affected the risk of infection and mortality of COVID-19. The eligible studies were selected from published papers during 1 year and 9 months from the beginning of the COVID-19 pandemic. We were not able to evaluate the change in the risk of COVID-19 caused by the change in SARS-CoV-2 variants and the vaccination availability during this observational period.

Despite these limitations, the present systematic review and meta-analysis of 101 studies suggests the importance of daily clinical management for patients with asthma, COPD, or ACO. Additionally, this study suggests that attention should be paid to the prevention of COVID-19 infection and disease progression, as well as to patients with other high-risk diseases of COVID-19.

Conclusion

The present systematic review and meta-analysis using 101 studies shows that pre-existing asthma and COPD are associated with the incidence of COVID-19. Asthma has a stronger influence on the incidence of COVID-19 than COPD. The presence of COPD as a comorbidity in patients with COVID-19 has a 3.8 times higher risk of mortality, while asthma has no significant effect on COVID-19 related death. These differences appear to be affected by the difference in locations of disease pathophysiology, and by the daily diagnosis and treatment policy of each country.

Supporting information

S1 Checklist.
(DOCX)

S1 Table. Classification standard of the evidence level.
(DOCX)

S1 Fig. Forrest plots for prevalence of asthma among patients with COVID-19.
(PDF)

S2 Fig. Forrest plots for prevalence of COPD among patients with COVID-19.
(PDF)

S3 Fig. Forrest plots for prevalence of ACO among patients with COVID-19.
(PDF)

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References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15; 395(10223):497–506. https://doi.org/10.1016/S0140-6736(20)30183-5 PMID: 31986264
2. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 January 2022 Available at https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—12-january-2022 (Access January 30, 2022)
3. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020 Mar 28; 395 (10229):1054–1062. https://doi.org/10.1016/S0140-6736(20)30566-3 PMID: 32171076
4. Bello-Chavolla OY, González-Díaz A, Antonio-Villa NE, Fermín-Martínez CA, Márquez-Salinas A, Vargas-Vázquez A, et al. Unequal Impact of Structural Health Determinants and Comorbidity on COVID-19 Severity and Lethality in Older Mexican Adults: Considerations Beyond Chronological Aging. J Gerontol A Biol Sci Med Sci. 2021 Feb 25; 76(3):e52–e59. https://doi.org/10.1093/gerona/glaa163 PMID: 32598450
5. Liao SY, Petrache I, Fingerlin TE, Maier LA. Association of inhaled and systemic corticosteroid use with Coronavirus Disease 2019 (COVID-19) test positivity in patients with chronic pulmonary diseases. Respir Med. 2021 Jan; 176:106275. https://doi.org/10.1016/j.rmed.2020.106275 PMID: 33276252
6. Chandel A, Patolia S, Brown AW, Collins AC, Sahjwani D, Khangoora V, et al. High-Flow Nasal Cannula Therapy in COVID-19: Using the ROX Index to Predict Success. Respir Care. 2021 Jun; 66 (6):909–919. https://doi.org/10.4187/respcare.08631 PMID: 33328179
7. Sen P, Majumdar U, Zein J, Hatipoğlu U, Attaway AH. Inhaled corticosteroids do not adversely impact outcomes in COVID-19 positive patients with COPD: An analysis of Cleveland Clinic's COVID-19 registry. PloS One. 2021 Jun 3; 16(6):e0252576. https://doi.org/10.1371/journal.pone.0252576 PMID: 34081722
8. Ferastraoaru D, Hudes G, Jerschow E, Jariwala S, Karagic M, de Vos G, et al. Eosinophilia in Asthma Patients Is Protective Against Severe COVID-19 Illness. J Allergy Clin Immunol Pract. 2021 Mar; 9 (3):1152–1162.e3. https://doi.org/10.1016/j.jaip.2020.12.045 PMID: 33495097
9. Mattiuzzi C, Lippi G. Worldwide asthma epidemiology: insights from the Global Health Data Exchange database. Int Forum Allergy Rhinol. 2020; 10(1):75–80. https://doi.org/10.1002/alr.22464 PMID: 31645084
10. Varmaghani M, Dehghani M, Heidari E, Sharifi F, Moghaddam SS, Farzadfar F. Global prevalence of chronic obstructive pulmonary disease: systematic review and meta-analysis. East Mediterr Health J. 2019 Mar 19; 25(1):47–57. https://doi.org/10.26719/emhj.18.014 PMID: 30919925
11. Leung C, Sin DD. Asthma-COPD Overlap: What Are the Important Questions? Chest. 2021 Oct 6: S0012-3692(21)04078–2. https://doi.org/10.1016/j.chest.2021.09.036 PMID: 34626594
12. Rothe T, Spagnolo P, Bridevaux PO, Clarenbach C, Eich-Wanger C, Meyer F, et al. Diagnosis and Management of Asthma–The Swiss Guidelines. Respiration. 2018; 95(5):364–380. https://doi.org/10.1159/000486797 PMID: 29614508
13. Vogelmeier CF, Román-Rodríguez M, Singh D, Han MK, Rodríguez-Roisin R, Ferguson GT. Goals of COPD treatment: Focus on symptoms and exacerbations. Respir Med. 2020 May; 166:105938. https://doi.org/10.1016/j.rmed.2020.105938 PMID: 32250871
14. Yanagisawa S, Ichinose M. Definition and diagnosis of asthma-COPD overlap (ACO). Allergol Int. 2018 Apr; 67(2):172–178. https://doi.org/10.1016/j.alit.2018.01.002 PMID: 29433946

15. Gao YD, Ding M, Dong X, Zhang JJ, Kursat Azkur A, Azkur D, et al. Risk factors for severe and critically ill COVID-19 patients: A review. Allergy. 2021 Feb; 76(2):428–455. https://doi.org/10.1111/all.14657 PMID: 33185910

16. Wang Y, Chen J, Chen W, Liu L, Dong M, Ji J, et al. Does Asthma Increase the Mortality of Patients with COVID-19?: A Systematic Review and Meta-Analysis. Int Arch Allergy Immunol. 2021; 182 (1):76–82. https://doi.org/10.1159/000510953 PMID: 32961539

17. Guan WJ, Liang WH, Shi Y, Gan LX, Wang HB, He JX, et al. Chronic Respiratory Diseases and the Outcomes of COVID-19: A Nationwide Retrospective Cohort Study of 39,420 Cases. J Allergy Clin Immunol Pract. 2021 Jul; 9(7):2645–2655.e14. https://doi.org/10.1016/j.jaip.2021.02.041 PMID: 33684635

18. Liberati A., Altman D.G., Tetzlaff J., Mulrow C., Gøtzsche P.C., Ioannidis J.P. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ*. 2009;339 b2700. https://doi.org/10.1136/bmj.b2700 PMID: 19622552

19. Stroup D.F., Berlin J.A., Morton S.C., Olkin I., Williamson G.D., Rennie D. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. *J Am Med Assoc*. 2000; 283:2008–2012. https://doi.org/10.1001/jama.283.15.2008 PMID: 10789670

20. Lee SW., Koo MJ. PRISMA 2020 statement and guidelines for systematic review and meta-analysis articles, and their underlying mathematics: Life Cycle Committee Recommendations. Life Cycle. 2022; 2:e9. https://doi.org/10.54724/lc.2022.e9

21. Balshem H, Helfand M, Schünemann HJ, Andrew Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the quality of evidence. Clin Epidemiol. 2011; 64(4):401–6. https://doi.org/10.1016/j.jclinepi.2010.07.015 PMID: 21208779

22. Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. BMJ. 2001 Aug 11; 323(7308):334–6. https://doi.org/10.1136/bmj.323.7308.334 PMID: 11498496

23. Agresti A, Coull BA. Approximate is better than "exact" for interval estimation of binomial proportions. Am Stat. 1998; 52:119–26.

24. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003; 327(7414):557–60. https://doi.org/10.1136/bmj.327.7414.557 PMID: 12958120

25. Review Manager (RevMan) [Computer program] Version 5.4.1 Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2014

26. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020 Jul; 75(7):1730–1741. https://doi.org/10.1111/all.14238 PMID: 32077115

27. Wang L, He W, Yu X, Hu D, Bao M, Liu H, et al. Coronavirus disease 2019 in elderly patients: Characteristics and prognostic factors based on 4-week follow-up. J Infect. 2020 Jun; 80(6):639–645. https://doi.org/10.1016/j.jinf.2020.03.019 PMID: 32240670

28. Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK, et al. Covid-19 in Critically Ill Patients in the Seattle Region—Case Series. N Engl J Med. 2020 May 21; 382(21):2012–2022. https://doi.org/10.1056/NEJMoa2004500 PMID: 32227758

29. Turan O, Arpınar Yigitbas B, Turan PA, Mirici A. Clinical characteristics and outcomes of hospitalized COVID-19 patients with COPD. Expert Rev Respir Med. 2021 Aug; 15(8):1069–1076. https://doi.org/10.1080/17476348.2021.1923484 PMID: 33944643

30. Barrasa H, Rello J, Tejada S, Martín A, Balziskueta G, Vinuesa C, et al; Alava COVID-19 Study Investigators. SARS-CoV-2 in Spanish Intensive Care Units: Early experience with 15-day survival in Vitoria. Anaesth Crit Care Pain Med. 2020 Oct; 39(5):553–561. https://doi.org/10.1016/j.accpm.2020.04.001 PMID: 32278670

31. Mahdavinia M, Foster KJ, Jauregui E, Moore D, Adnan D, Andy-Nweye AB, et al. Asthma prolongs intubation in COVID-19. J Allergy Clin Immunol Pract. 2020 Jul-Aug; 8(7):2388–2391. https://doi.org/10.1016/j.jaip.2020.05.006 PMID: 32417445

32. Li P, Chen L, Liu Z, Pan J, Zhou D, Wang H, et al. Clinical features and short-term outcomes of elderly patients with COVID-19. Int J Infect Dis. 2020 Aug; 97:245–250. https://doi.org/10.1016/j.ijid.2020.05.107 PMID: 32492533

33. Lian J, Jin X, Hao S, Cai H, Zhang S, Zheng L, et al. Analysis of Epidemiological and Clinical Features in Older Patients With Coronavirus Disease 2019 (COVID-19) Outside Wuhan. Clin Infect Dis. 2020 Jul 28; 71(15):740–747. https://doi.org/10.1093/cid/ciaa242 PMID: 32211844

34. Iaccarino G, Grassi G, Borghi C, Ferri C, Salvetti M, Volpe M; SARS-RAS Investigators. Age and Multimorbidity Predict Death Among COVID-19 Patients: Results of the SARS-RAS Study of the Italian

Society of Hypertension. Hypertension. 2020 Aug; 76(2):366–372. https://doi.org/10.1161/HYPERTENSIONAHA.120.15324 PMID: 32564693

35. Toussie D, Voutsinas N, Finkelstein M, Cedillo MA, Manna S, Maron SZ, et al. Clinical and Chest Radiography Features Determine Patient Outcomes in Young and Middle-aged Adults with COVID-19. Radiology. 2020 Oct; 297(1):E197–E206. https://doi.org/10.1148/radiol.2020201754 PMID: 32407255

36. Argenziano MG, Bruce SL, Slater CL, Tiao JR, Baldwin MR, Barr RG, et al. Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: retrospective case series. BMJ. 2020 May 29; 369:m1996. https://doi.org/10.1136/bmj.m1996 PMID: 32471884

37. Cummings MJ, Baldwin MR, Abrams D, Jacobson SD, Meyer BJ, Balough EM, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet. 2020 Jun 6; 395(10239):1763–1770. https://doi.org/10.1016/S0140-6736(20)31189-2 PMID: 32442528

38. Zhu Z, Hasegawa K, Ma B, Fujiogi M, Camargo CA Jr, Liang L. Association of asthma and its genetic predisposition with the risk of severe COVID-19. J Allergy Clin Immunol. 2020 Aug; 146(2):327–329.e4. https://doi.org/10.1016/j.jaci.2020.06.001 PMID: 32522462

39. Grandbastien M, Piotin A, Godet J, Abessolo-Amougou I, Ederlé C, Enache I, et al. SARS-CoV-2 Pneumonia in Hospitalized Asthmatic Patients Did Not Induce Severe Exacerbation. J Allergy Clin Immunol Pract. 2020 Sep; 8(8):2600–2607. https://doi.org/10.1016/j.jaip.2020.06.032 PMID: 32603901

40. Yao Y, Chen W, Wu X, Shen L, Shen L, Fu Y, et al. Clinical characteristics of COVID-19 patients in three consecutive generations of spread in Zhejiang, China. Clin Microbiol Infect. 2020 Oct; 26(10):1380–1385. https://doi.org/10.1016/j.cmi.2020.06.018 PMID: 32593742

41. Lieberman-Cribbin W, Rapp J, Alpert N, Tuminello S, Taioli E. The Impact of Asthma on Mortality in Patients With COVID-19. Chest. 2020 Dec; 158(6):2290–2291. https://doi.org/10.1016/j.chest.2020.05.575 PMID: 32522556

42. Wang J, Zhu X, Xu Z, Yang G, Mao G, Jia Y, et al. Clinical and CT findings of COVID-19: differences among three age groups. BMC Infect Dis. 2020 Jun 22; 20(1):434. https://doi.org/10.1186/s12879-020-05154-9 PMID: 32571228

43. Aggarwal A, Shrivastava A, Kumar A, Ali A. Clinical and Epidemiological Features of SARS-CoV-2 Patients in SARI Ward of a Tertiary Care Centre in New Delhi. J Assoc Physicians India. 2020 Jul; 68(7):19–26. PMID: 32602676

44. Caminati M, Lombardi C, Micheletto C, Roca E, Bigni B, Furci F, et al. Asthmatic patients in COVID-19 outbreak: Few cases despite many cases. J Allergy Clin Immunol. 2020 Sep; 146(3):541–542. https://doi.org/10.1016/j.jaci.2020.05.049 PMID: 32620309

45. Bravi F, Flacco ME, Carradori T, Volta CA, Cosenza G, De Togni A, et al. Predictors of severe or lethal COVID-19, including Angiotensin Converting Enzyme inhibitors and Angiotensin II Receptor Blockers, in a sample of infected Italian citizens. PLoS One. 2020 Jun 24; 15(6):e0235248. https://doi.org/10.1371/journal.pone.0235248 PMID: 32579597

46. Song J, Zeng M, Wang H, Qin C, Hou HY, Sun ZY, et al. Distinct effects of asthma and COPD comorbidity on disease expression and outcome in patients with COVID-19. Allergy. 2021 Feb; 76(2):483–496. https://doi.org/10.1111/all.14517 PMID: 32716553

47. Wang L, Foer D, Bates DW, Boyce JA, Zhou L. Risk factors for hospitalization, intensive care, and mortality among patients with asthma and COVID-19. J Allergy Clin Immunol. 2020 Oct; 146(4):808–812. https://doi.org/10.1016/j.jaci.2020.07.018 PMID: 32735807

48. Canevelli M, Palmieri L, Raparelli V, Punzo O, Donfrancesco C, Lo Noce C, et al; Italian National Institute of Health COVID-19 Mortality Group. COVID-19 mortality among migrants living in Italy. Ann Ist Super Sanita. 2020 Jul-Sep; 56(3):373–377. https://doi.org/10.4415/ANN_20_03_16 PMID: 32959804

49. De Vito A, Geremia N, Fiore V, Princic E, Babudieri S, Madeddu G. Clinical features, laboratory findings and predictors of death in hospitalized patients with COVID-19 in Sardinia, Italy. Eur Rev Med Pharmacol Sci. 2020 Jul; 24(14):7861–7868. https://doi.org/10.26355/eurrev_202007_22291 PMID: 32744714

50. Atkins JL, Masoli JAH, Delgado J, Pilling LC, Kuo CL, Kuchel GA, et al. Preexisting Comorbidities Predicting COVID-19 and Mortality in the UK Biobank Community Cohort. J Gerontol A Biol Sci Med Sci. 2020 Oct 15; 75(11):2224–2230. https://doi.org/10.1093/gerona/glaa183 PMID: 32687551

51. Zhao Z, Chen A, Hou W, Graham JM, Li H, Richman PS, et al. Prediction model and risk scores of ICU admission and mortality in COVID-19. PLoS One. 2020 Jul 30; 15(7):e0236618. https://doi.org/10.1371/journal.pone.0236618 PMID: 32730358

52. Pérez-Sastré MA, Valdés J, Ortiz-Hernández L. Clinical characteristics and severity of COVID-19 among Mexican adults. Gac Med Mex. 2020; 156(5):373–381. English. https://doi.org/10.24875/GMM.M20000424 PMID: 33372930

53. Güner R, Hasanoğlu İ, Kayaaslan B, Aypak A, Kaya Kalem A, Eser F, et al. COVID-19 experience of the major pandemic response center in the capital: results of the pandemic's first month in Turkey. Turk J Med Sci. 2020 Dec 17; 50(8):1801–1809. https://doi.org/10.3906/sag-2006-164 PMID: 32682358

54. Somani SS, Richter F, Fuster V, De Freitas JK, Naik N, Sigel K, et al. Characterization of Patients Who Return to Hospital Following Discharge from Hospitalization for COVID-19. J Gen Intern Med. 2020 Oct; 35(10):2838–2844. https://doi.org/10.1007/s11606-020-06120-6 PMID: 32815060

55. Yang JM, Koh HY, Moon SY, Yoo IK, Ha EK, You S, et al. Allergic disorders and susceptibility to and severity of COVID-19: A nationwide cohort study. J Allergy Clin Immunol. 2020 Oct; 146(4):790–798. https://doi.org/10.1016/j.jaci.2020.08.008 PMID: 32810517

56. Corsini Campioli C, Cano Cevallos E, Assi M, Patel R, Binnicker MJ, O'Horo JC. Clinical predictors and timing of cessation of viral RNA shedding in patients with COVID-19. J Clin Virol. 2020 Sep; 130:104577. https://doi.org/10.1016/j.jcv.2020.104577 PMID: 32777762

57. He Y, Xie M, Zhao J, Liu X. Clinical Characteristics and Outcomes of Patients with Severe COVID-19 and Chronic Obstructive Pulmonary Disease (COPD). Med Sci Monit. 2020 Sep 4; 26:e927212. https://doi.org/10.12659/MSM.927212 PMID: 32883943

58. Mushtaq J, Pennella R, Lavalle S, Colarieti A, Steidler S, Martinenghi CMA, et al. Initial chest radiographs and artificial intelligence (AI) predict clinical outcomes in COVID-19 patients: analysis of 697 Italian patients. Eur Radiol. 2021 Mar; 31(3):1770–1779. https://doi.org/10.1007/s00330-020-07269-8 PMID: 32945968

59. Goel N, Spalgais S, Mrigpuri P, Khanna M, Menon B, Kumar R. Characteristics of COVID-19 at a non-COVID tertiary pulmonary care centre in Delhi, India. Monaldi Arch Chest Dis. 2020 Nov 9; 90(4). https://doi.org/10.4081/monaldi.2020.1568 PMID: 33169599

60. Brendish NJ, Poole S, Naidu VV, Mansbridge CT, Norton N, Borca F, et al. Clinical characteristics, symptoms and outcomes of 1054 adults presenting to hospital with suspected COVID-19: A comparison of patients with and without SARS-CoV-2 infection. J Infect. 2020 Dec; 81(6):937–943. https://doi.org/10.1016/j.jinf.2020.09.033 PMID: 32998038

61. Ioannou GN, Locke E, Green P, Berry K, O'Hare AM, Shah JA, et al. Risk Factors for Hospitalization, Mechanical Ventilation, or Death Among 10131 US Veterans With SARS-CoV-2 Infection. JAMA Netw Open. 2020 Sep 1; 3(9):e2022310. https://doi.org/10.1001/jamanetworkopen.2020.22310 PMID: 32965502

62. Xiong Q, Xu M, Li J, Liu Y, Zhang J, Xu Y, et al. Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. Clin Microbiol Infect. 2021 Jan; 27(1):89–95. https://doi.org/10.1016/j.cmi.2020.09.023 PMID: 32979574

63. Seaton RA, Gibbons CL, Cooper L, Malcolm W, McKinney R, Dundas S, et al. Survey of antibiotic and antifungal prescribing in patients with suspected and confirmed COVID-19 in Scottish hospitals. J Infect. 2020 Dec; 81(6):952–960. https://doi.org/10.1016/j.jinf.2020.09.024 PMID: 32987097

64. Abrams MP, Wan EY, Waase MP, Morrow JP, Dizon JM, Yarmohammadi H, et al., Clinical and cardiac characteristics of COVID-19 mortalities in a diverse New York City Cohort. J Cardiovasc Electrophysiol. 2020; 31(12):3086–3096. https://doi.org/10.1111/jce.14772 PMID: 33022765

65. Akpinar G, Demir MC, Sultanoglu H, Sonmez FT, Karaman K, Keskin BH, et al. The Demographic Analysis of the Probable COVID-19 Cases in Terms of RT-PCR Results and Age. Clin. Lab. 2021 Sep 67:1058–1064 https://doi.org/10.7754/Clin.Lab.2020.200844 PMID: 33865252

66. Schiavone M, Gasperetti A, Mancone M, Curnis A, Mascioli G, Mitacchione G, et al. Oral anticoagulation and clinical outcomes in COVID-19: An Italian multicenter experience. Int J Cardiol. 2021 Jan 15; 323:276–280. https://doi.org/10.1016/j.ijcard.2020.09.001 PMID: 32911000

67. Calmes D, Graff S, Maes N, Frix AN, Thys M, Bonhomme O, et al. Asthma and COPD Are Not Risk Factors for ICU Stay and Death in Case of SARS-CoV2 Infection. J Allergy Clin Immunol Pract. 2021 Jan; 9(1):160–169. https://doi.org/10.1016/j.jaip.2020.09.044 PMID: 33038592

68. Rial MJ, Valverde M, Del Pozo V, González-Barcala FJ, Martínez-Rivera C, Muñoz X, et al. Clinical characteristics in 545 patients with severe asthma on biological treatment during the COVID-19 outbreak. J Allergy Clin Immunol Pract. 2021 Jan; 9(1):487–489.e1. https://doi.org/10.1016/j.jaip.2020.09.050 PMID: 33045398

69. Robinson LB, Fu X, Bassett IV, Triant VA, Foulkes AS, Zhang Y, et al. COVID-19 severity in hospitalized patients with asthma: A matched cohort study. J Allergy Clin Immunol Pract. 2021 Jan; 9(1):497–500. https://doi.org/10.1016/j.jaip.2020.10.021 PMID: 33164794

70. Cates J, Lucero-Obusan C, Dahl RM, Schirmer P, Garg S, Oda G, et al. Risk for In-Hospital Complications Associated with COVID-19 and Influenza—Veterans Health Administration, United States, October 1, 2018-May 31, 2020. MMWR Morb Mortal Wkly Rep. 2020 Oct 23; 69(42):1528–1534. https://doi.org/10.15585/mmwr.mm6942e3 PMID: 33090987

71. Tekcan Şanlı DE, Yıldırım D. A new imaging sign in COVID-19 pneumonia: vascular changes and their correlation with clinical severity of the disease. Diagn Interv Radiol. 2021 Mar; 27(2):172–180. https://doi.org/10.5152/dir.2020.20346 PMID: 33044171

72. Hussein MH, Toraih EA, Attia AS, Burley N, Zhang AD, Roos J, et al. Asthma in COVID-19 patients: An extra chain fitting around the neck? Respir Med. 2020 Dec; 175:106205. https://doi.org/10.1016/j.rmed.2020.106205 PMID: 33217538

73. Tabarsi P, Barati S, Jamaati H, Haseli S, Marjani M, Moniri A, et al. Evaluating the effects of Intravenous Immunoglobulin (IVIg) on the management of severe COVID-19 cases: A randomized controlled trial. Int Immunopharmacol. 2021 Jan; 90:107205. https://doi.org/10.1016/j.intimp.2020.107205 PMID: 33214093

74. Lee SC, Son KJ, Han CH, Jung JY, Park SC. Impact of comorbid asthma on severity of coronavirus disease (COVID-19). Sci Rep. 2020 Dec 11; 10(1):21805. https://doi.org/10.1038/s41598-020-77791-8 PMID: 33311519

75. Jiang Y, Abudurexiti S, An MM, Cao D, Wei J, Gong P. Risk factors associated with 28-day all-cause mortality in older severe COVID-19 patients in Wuhan, China: a retrospective observational study. Sci Rep. 2020 Dec 22; 10(1):22369. https://doi.org/10.1038/s41598-020-79508-3 PMID: 33353956

76. Xiao J, Li X, Xie Y, Huang Z, Ding Y, Zhao S, et al. Maximum chest CT score is associated with progression to severe illness in patients with COVID-19: a retrospective study from Wuhan, China. BMC Infect Dis. 2020 Dec 11; 20(1):953. https://doi.org/10.1186/s12879-020-05683-3 PMID: 33308183

77. Signes-Costa J, Núñez-Gil IJ, Soriano JB, Arroyo-Espliguero R, Eid CM, Romero R, et al; HOPE COVID-19 investigators. Prevalence and 30-Day Mortality in Hospitalized Patients With Covid-19 and Prior Lung Diseases. Arch Bronconeumol. 2021 Apr; 57:13–20. https://doi.org/10.1016/j.arbres.2020.11.012 PMID: 34629634

78. Bello-Chavolla OY, Antonio-Villa NE, Ortiz-Brizuela E, Vargas-Vázquez A, González-Lara MF, de Leon AP, et al. Validation and repurposing of the MSL-COVID-19 score for prediction of severe COVID-19 using simple clinical predictors in a triage setting: The Nutri-CoV score. PLoS One. 2020 Dec 16; 15(12):e0244051. https://doi.org/10.1371/journal.pone.0244051 PMID: 33326502

79. Lokken EM, Walker CL, Delaney S, Kachikis A, Kretzer NM, Erickson A, et al. Clinical characteristics of 46 pregnant women with a severe acute respiratory syndrome coronavirus 2 infection in Washington State. Am J Obstet Gynecol. 2020 Dec; 223(6):911.e1–911.e14. https://doi.org/10.1016/j.ajog.2020.05.031 PMID: 32439389

80. Gómez Antúnez M, Muiño Míguez A, Bendala Estrada AD, Maestro de la Calle G, Monge Monge D, Boixeda R, et al; SEMI-COVID-19 Network. Clinical Characteristics and Prognosis of COPD Patients Hospitalized with SARS-CoV-2. Int J Chron Obstruct Pulmon Dis. 2021 Jan 5; 15:3433–3445. https://doi.org/10.2147/COPD.S276692 PMID: 33447021

81. Monterrubio-Flores E, Ramírez-Villalobos MD, Espinosa-Montero J, Hernandez B, Barquera S, Villalobos-Daniel VE, et al. Characterizing a two-pronged epidemic in Mexico of non-communicable diseases and SARS-Cov-2: factors associated with increased case-fatality rates. Int J Epidemiol. 2021 May 17; 50(2):430–445. https://doi.org/10.1093/ije/dyab008 PMID: 33585901

82. Mortaz E, Bassir A, Dalil Roofchayee N, Dezfuli NK, Jamaati H, Tabarsi P, et al. Serum cytokine levels of COVID-19 patients after 7 days of treatment with Favipiravir or Kaletra. Int Immunopharmacol. 2021 Apr; 93:107407. https://doi.org/10.1016/j.intimp.2021.107407 PMID: 33631512

83. Değerli E, Derin S, Oruç K, Şengül Samancı N, Bedir Ş, Çelik E, et al. The demographic characteristics, prognosis, and relationship with cancer subtypes of hospitalized COVID-19 patients with malignancy: A single-center experience. J Med Virol. 2021 Oct; 93(10):5839–5845. https://doi.org/10.1002/jmv.27123 PMID: 34081337

84. Laake JH, Buanes EA, Småstuen MC, Kvåle R, Olsen BF, Rustøen T, et al. Characteristics, management and survival of ICU patients with coronavirus disease-19 in Norway, March-June 2020. A prospective observational study. Acta Anaesthesiol Scand. 2021 May; 65(5):618–628. https://doi.org/10.1111/aas.13785 PMID: 33501998

85. Lee SC, Son KJ, Han CH, Park SC, Jung JY. Impact of COPD on COVID-19 prognosis: A nationwide population-based study in South Korea. Sci Rep. 2021 Feb 12; 11(1):3735. https://doi.org/10.1038/s41598-021-83226-9 PMID: 33580190

86. Jungo S, Moreau N, Mazevet ME, Ejeil AL, Biosse Duplan M, Salmon B, et al. Prevalence and risk indicators of first-wave COVID-19 among oral health-care workers: A French epidemiological survey.

PLoS One. 2021 Feb 11; 16(2):e0246586. https://doi.org/10.1371/journal.pone.0246586 PMID: 33571264

87. Cao L, Lee S, Krings JG, Rauseo AM, Reynolds D, Presti R, et al. Asthma in patients with suspected and diagnosed coronavirus disease 2019. Ann Allergy Asthma Immunol. 2021 May; 126(5):535–541. e2. https://doi.org/10.1016/j.anai.2021.02.020 PMID: 33639262

88. Fong WCG, Borca F, Phan H, Moyses HE, Dennison P, Kurukulaaratchy RJ, et al. Asthma did not increase in-hospital COVID-19-related mortality in a tertiary UK hospital. Clin Exp Allergy. 2021 Jul; 51 (7):939–941. https://doi.org/10.1111/cea.13855 PMID: 33626216

89. Jongbloed M, Leijte WT, Linssen CFM, van den Hoogen BG, van Gorp ECM, de Kruif MD. Clinical impact of human metapneumovirus infections before and during the COVID-19 pandemic. Infect Dis (Lond). 2021 Jul; 53(7):488–497. https://doi.org/10.1080/23744235.2021.1887510 PMID: 33612055

90. Artero A, Madrazo M, Fernández-Garcés M, Muiño Miguez A, González García A, Crestelo Vieitez A, et al; SEMI-COVID-19 Network. Severity Scores in COVID-19 Pneumonia: a Multicenter, Retrospective, Cohort Study. J Gen Intern Med. 2021 May; 36(5):1338–1345. https://doi.org/10.1007/s11606-021-06626-7 PMID: 33575909

91. Ho KS, Howell D, Rogers L, Narasimhan B, Verma H, Steiger D. The relationship between asthma, eosinophilia, and outcomes in coronavirus disease 2019 infection. Ann Allergy Asthma Immunol. 2021 Jul; 127(1):42–48. https://doi.org/10.1016/j.anai.2021.02.021 PMID: 33647451

92. Yoshida Y, Gillet SA, Brown MI, Zu Y, Wilson SM, Ahmed SJ, et al. Clinical characteristics and outcomes in women and men hospitalized for coronavirus disease 2019 in New Orleans. Biol Sex Differ. 2021 Feb 5; 12(1):20. https://doi.org/10.1186/s13293-021-00359-2 PMID: 33546750

93. Nanda S, Toussaint L, Vincent A, Fischer KM, Hurt R, Schroeder DR, et al. A Midwest COVID-19 Cohort for the Evaluation of Multimorbidity and Adverse Outcomes from COVID-19. J Prim Care Community Health. 2021 Jan-Dec; 12:21501327211010991. https://doi.org/10.1177/21501327211010991 PMID: 33855875

94. De Vito A, Fiore V, Princic E, Geremia N, Panu Napodano CM, Muredda AA, et al. Predictors of infection, symptoms development, and mortality in people with SARS-CoV-2 living in retirement nursing homes. PLoS One. 2021 Mar 16; 16(3):e0248009. https://doi.org/10.1371/journal.pone.0248009 PMID: 33724987

95. Rodriguez C, de Prost N, Fourati S, Lamoureux C, Gricourt G, N'debi M, et al. Viral genomic, metagenomic and human transcriptomic characterization and prediction of the clinical forms of COVID-19. PLoS Pathog. 2021 Mar 29; 17(3):e1009416. https://doi.org/10.1371/journal.ppat.1009416 PMID: 33780519

96. Garibaldi BT, Wang K, Robinson ML, Zeger SL, Bandeen-Roche K, Wang MC, et al. Comparison of Time to Clinical Improvement With vs Without Remdesivir Treatment in Hospitalized Patients With COVID-19. JAMA Netw Open. 2021 Mar 1; 4(3):e213071. https://doi.org/10.1001/jamanetworkopen.2021.3071 PMID: 33760094

97. Giovannetti G, De Michele L, De Ceglie M, Pierucci P, Mirabile A, Vita M, et al. Lung ultrasonography for long-term follow-up of COVID-19 survivors compared to chest CT scan. Respir Med. 2021 May; 181:106384. https://doi.org/10.1016/j.rmed.2021.106384 PMID: 33839587

98. Khan MS, Dogra R, Miriyala LKV, Salman FNU, Ishtiaq R, Patti DK, et al. Clinical characteristics and outcomes of patients with Corona Virus Disease 2019 (COVID-19) at Mercy Health Hospitals, Toledo, Ohio. PLoS One. 2021 Apr 22; 16(4):e0250400. https://doi.org/10.1371/journal.pone.0250400 PMID: 33886663

99. Tsai S, Nguyen H, Ebrahimi R, Barbosa MR, Ramanan B, Heitjan DF, et al. COVID-19 associated mortality and cardiovascular disease outcomes among US women veterans. Sci Rep. 2021 Apr 19; 11 (1):8497. https://doi.org/10.1038/s41598-021-88111-z PMID: 33875764

100. Lobelo F, Bienvenida A, Leung S, Mbanya A, Leslie E, Koplan K, et al. Clinical, behavioural and social factors associated with racial disparities in COVID-19 patients from an integrated healthcare system in Georgia: a retrospective cohort study. BMJ Open. 2021 May 19; 11(5):e044052. https://doi.org/10.1136/bmjopen-2020-044052 PMID: 34011589

101. Chatterjee A, Wu G, Primakov S, Oberije C, Woodruff H, Kubben P, et al. Can predicting COVID-19 mortality in a European cohort using only demographic and comorbidity data surpass age-based prediction: An externally validated study. PLoS One. 2021 Apr 15; 16(4):e0249920. https://doi.org/10.1371/journal.pone.0249920 PMID: 33857224

102. Yordanov Y, Dinh A, Bleibtreu A, Mensch A, Lescure FX, Debuc E, et al; AP-HP/Universities/Inserm COVID-19 research collaboration. Clinical characteristics and factors associated with hospital admission or death in 43 103 adult outpatients with coronavirus disease 2019 managed with the Covidom telesurveillance solution: a prospective cohort study. Clin Microbiol Infect. 2021 Aug; 27(8):1158–1166. https://doi.org/10.1016/j.cmi.2021.04.010 PMID: 33915287

103. Riou M, MarcoT C, Oulehri W, Enache I, Pistea C, Chatron E, et al. Respiratory follow-up after hospitalization for COVID-19: Who and when? Eur J Clin Invest. 2021 Aug; 51(8):e13603. https://doi.org/10.1111/eci.13603 PMID: 33998683

104. Wei W, Sivapalasingam S, Mellis S, Geba GP, Jalbert JJ. A Retrospective Study of COVID-19-Related Urgent Medical Visits and Hospitalizations After Outpatient COVID-19 Diagnosis in the US. Adv Ther. 2021 Jun; 38(6):3185–3202. https://doi.org/10.1007/s12325-021-01742-6 PMID: 33961213

105. Hou X, Tian L, Zhou L, Jia X, Kong L, Xue Y, et al. Intravenous immunoglobulin-based adjuvant therapy for severe COVID-19: a single-center retrospective cohort study. Virol J. 2021 May 21; 18(1):101. https://doi.org/10.1186/s12985-021-01575-3 PMID: 34020680

106. Valverde-Monge M, Cañas JA, Barroso B, Betancor D, Ortega-Martin L, Gómez-López A, et al. Eosinophils and Chronic Respiratory Diseases in Hospitalized COVID-19 Patients. Front Immunol. 2021 Jun 2; 12:668074. https://doi.org/10.3389/fimmu.2021.668074 PMID: 34149705

107. Cosio BG, Shafiek H, Toledo-Pons N, Iglesias A, Barcelo M, Represas-Represas C, et al. Characterization of COPD Admissions During the First COVID-19 Outbreak. Int J Chron Obstruct Pulmon Dis. 2021 Jun 3; 16:1549–1554. https://doi.org/10.2147/COPD.S312493 PMID: 34113088

108. Adir Y, Humbert M, Saliba W. COVID-19 risk and outcomes in adult asthmatic patients treated with biologics or systemic corticosteroids: Nationwide real-world evidence. J Allergy Clin Immunol. 2021 Aug; 148(2):361–367.e13. https://doi.org/10.1016/j.jaci.2021.06.006 PMID: 34144110

109. Chaudhary S, Benzaquen S, Woo JG, Rubinstein J, Matta A, Albano J, et al. Clinical Characteristics, Respiratory Mechanics, and Outcomes in Critically Ill Individuals With COVID-19 Infection in an Underserved Urban Population. Respir Care. 2021 Jun; 66(6):897–908. https://doi.org/10.4187/respcare.08319 PMID: 33446510

110. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature. 2020 Aug; 584(7821):430–436. https://doi.org/10.1038/s41586-020-2521-4 PMID: 32640463

111. Abayomi A, Osibogun A, Kanma-Okafor O, Idris J, Bowale A, Wright O, et al. Morbidity and mortality outcomes of COVID-19 patients with and without hypertension in Lagos, Nigeria: a retrospective cohort study. Glob Health Res Policy. 2021 Jul 29; 6(1):26. https://doi.org/10.1186/s41256-021-00210-6 Erratum in: Glob Health Res Policy. 2021 Aug 13;6(1):28. PMID: 34325747

112. Liu YH, Wang YR, Wang QH, Chen Y, Chen X, Li Y, et al. Post-infection cognitive impairments in a cohort of elderly patients with COVID-19. Mol Neurodegener. 2021 Jul 19; 16(1):48. https://doi.org/10.1186/s13024-021-00469-w PMID: 34281568

113. Munblit D, Bobkova P, Spiridonova E, Shikhaleva A, Gamirova A, Blyuss O, et al. Incidence and risk factors for persistent symptoms in adults previously hospitalized for COVID-19. Clin Exp Allergy. 2021 Sep; 51(9):1107–1120. https://doi.org/10.1111/cea.13997 PMID: 34351016

114. Sandoval M, Nguyen DT, Vahidy FS, Graviss EA. Risk factors for severity of COVID-19 in hospital patients age 18–29 years. PLoS One. 2021 Jul 30; 16(7):e0255544. https://doi.org/10.1371/journal.pone.0255544 PMID: 34329347

115. Lokken EM, Huebner EM, Taylor GG, Hendrickson S, Vanderhoeven J, Kachikis A, et al; Washington State COVID-19 in Pregnancy Collaborative. Disease severity, pregnancy outcomes, and maternal deaths among pregnant patients with severe acute respiratory syndrome coronavirus 2 infection in Washington State. Am J Obstet Gynecol. 2021 Jul; 225(1):77.e1–77.e14. https://doi.org/10.1016/j.ajog.2020.12.1221 PMID: 33515516

116. Cataño-Correa JC, Cardona-Arias JA, Porras Mancilla JP, García MT. Bacterial superinfection in adults with COVID-19 hospitalized in two clinics in Medellín-Colombia, 2020. PLoS One. 2021 Jul 13; 16(7):e0254671. https://doi.org/10.1371/journal.pone.0254671 PMID: 34255801

117. Meza D, Khuder B, Bailey JI, Rosenberg SR, Kalhan R, Reyfman PA. Mortality from COVID-19 in Patients with COPD: A US Study in the N3C Data Enclave. Int J Chron Obstruct Pulmon Dis. 2021 Aug 13; 16:2323–2326. https://doi.org/10.2147/COPD.S318000 PMID: 34413640

118. Sun Y, Jiang N, Li Z, Li X, Yang B, Si D, et al. A Retrospective Study of 268 Patients with SARS-CoV-2 Infection to Evaluate the Association Between Blood Glucose and Severity of COVID-19 Pneumonia and Patient Mortality. Med Sci Monit. 2021 Aug 7; 27:e932156. https://doi.org/10.12659/MSM.932156 PMID: 34362862

119. Fernández-Martínez NF, Ortiz-González-Serna R, Serrano-Ortiz Á, Rivera-Izquierdo M, Ruiz-Montero R, Pérez-Contreras M, et al. Sex Differences and Predictors of In-Hospital Mortality among Patients with COVID-19: Results from the ANCOHVID Multicentre Study. Int J Environ Res Public Health. 2021 Aug 26; 18(17):9018. https://doi.org/10.3390/ijerph18179018 PMID: 34501608

120. Cosma S, Carosso AR, Cusato J, Borella F, Carosso M, Gervasoni F, et al. Preterm birth is not associated with asymptomatic/mild SARS-CoV-2 infection per se: Pre-pregnancy state is what matters.

PLoS One. 2021 Aug 5; 16(8):e0254875. https://doi.org/10.1371/journal.pone.0254875 PMID: 34351922

121. Chudasama YV, Zaccardi F, Gillies CL, Razieh C, Yates T, Kloecker DE, et al. Patterns of multimorbidity and risk of severe SARS-CoV-2 infection: an observational study in the U.K. BMC Infect Dis. 2021 Sep 4; 21(1):908. https://doi.org/10.1186/s12879-021-06600-y PMID: 34481456

122. Girkin JLN, Maltby S, Bartlett NW. Toll-like receptor-agonist-based therapies for respiratory viral diseases: thinking outside the cell. Eur Respir Rev. 2022 May 4; 31(164):210274. https://doi.org/10.1183/16000617.0274-2021 PMID: 35508333

123. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020 Apr 7; 323(13):1239–1242. https://doi.org/10.1001/jama.2020.2648 PMID: 32091533

124. Jackson DJ, Sykes A, Mallia P, Johnston SL. Asthma exacerbations: origin, effect, and prevention. J Allergy Clin Immunol. 2011 Dec; 128(6):1165–74. https://doi.org/10.1016/j.jaci.2011.10.024 PMID: 22133317

125. Abdullah F, Myers J, Basu D, Tintinger G, Ueckermann V, Mathebula M, et al. Decreased severity of disease during the first global omicron variant covid-19 outbreak in a large hospital in tshwane, south africa. Int J Infect Dis. 2022 Mar; 116:38–42. https://doi.org/10.1016/j.ijid.2021.12.357 PMID: 34971823

126. Han X, Xu J, Hou H, Yang H, Wang Y. Impact of asthma on COVID-19 mortality in the United States: Evidence based on a meta-analysis. Int Immunopharmacol. 2022 Jan; 102:108390. https://doi.org/10.1016/j.intimp.2021.108390 PMID: 34844871

127. Beurnier A, Jutant EM, Jevnikar M, Boucly A, Pichon J, Preda M, et al. Characteristics and outcomes of asthmatic patients with COVID-19 pneumonia who require hospitalisation. Eur Respir J. 2020 Nov 5; 56(5):2001875. https://doi.org/10.1183/13993003.01875-2020 PMID: 32732333; PMCID: PMC7397950.

128. Mulpuru S, Li L, Ye L, Hatchette T, Andrew MK, Ambrose A, et al; Serious Outcomes Surveillance (SOS) Network of the Canadian Immunization Research Network (CIRN). Effectiveness of Influenza Vaccination on Hospitalizations and Risk Factors for Severe Outcomes in Hospitalized Patients With COPD. Chest. 2019 Jan; 155(1):69–78. https://doi.org/10.1016/j.chest.2018.10.044 PMID: 30616737

129. Restrepo MI, Mortensen EM, Pugh JA, Anzueto A. COPD is associated with increased mortality in patients with community-acquired pneumonia. Eur Respir J. 2006 Aug; 28(2):346–51. https://doi.org/10.1183/09031936.06.00131905 PMID: 16611653

130. Baker JR, Mahdi M, Nicolau DV Jr, Ramakrishnan S, Barnes PJ, Simpson JL, et al. Early Th2 inflammation in the upper respiratory mucosa as a predictor of severe COVID-19 and modulation by early treatment with inhaled corticosteroids: a mechanistic analysis. Lancet Respir Med. 2022; 10(6):545–556. https://doi.org/10.1016/S2213-2600(22)00002-9 PMID: 35397798

131. Chhiba KD, Patel GB, Vu THT, Chen MM, Guo A, Kudlaty E, et al. Prevalence and characterization of asthma in hospitalized and nonhospitalized patients with COVID-19. J Allergy Clin Immunol. 2020 Aug; 146(2):307–314.e4. https://doi.org/10.1016/j.jaci.2020.06.010 Epub 2020 Jun 15. PMID: 32554082; PMCID: PMC7295471.

132. Lombardi C, Roca E, Bigni B, Cottini M, Passalacqua G. Clinical course and outcomes of patients with asthma hospitalized for severe acute respiratory syndrome coronavirus 2 pneumonia: A single-center, retrospective study. Ann Allergy Asthma Immunol. 2020 Dec; 125(6):707–709. https://doi.org/10.1016/j.anai.2020.07.029 Epub 2020 Aug 1. PMID: 32745609; PMCID: PMC7395222.

133. Klimek L, Akdis CA, Jutel M, Zuberbier T, Bousquet J. Inhaled corticosteroids in early COVID-19-A tale of many facets. Allergy. 2021; 76(11):3540–3542. https://doi.org/10.1111/all.15041 PMID: 34374091

134. Hasan SS, Capstick T, Zaidi STR, Kow CS, Merchant HA. Use of corticosteroids in asthma and COPD patients with or without COVID-19. Respir Med. 2020 Aug-Sep; 170:106045. https://doi.org/10.1016/j.rmed.2020.106045 PMID: 32843175

135. Huang BZ, Chen Z, Sidell MA, Eckel SP, Martinez MP, et al. Asthma Disease Status, COPD, and COVID-19 Severity in a Large Multiethnic Population. J Allergy Clin Immunol Pract. 2021 Oct; 9(10):3621–3628.e2. https://doi.org/10.1016/j.jaip.2021.07.030 PMID: 34389242

136. Zaki N, Alashwal H, Ibrahim S. Association of hypertension, diabetes, stroke, cancer, kidney disease, and high-cholesterol with COVID-19 disease severity and fatality: A systematic review. Diabetes Metab Syndr. 2020 Sep-Oct; 14(5):1133–1142. https://doi.org/10.1016/j.dsx.2020.07.005 PMID: 32663789

137. Schultze A, Walker AJ, MacKenna B, Morton CE, Bhaskaran K, Brown JP, et al.; OpenSAFELY Collaborative. Risk of COVID-19-related death among patients with chronic obstructive pulmonary

disease or asthma prescribed inhaled corticosteroids: an observational cohort study using the OpenSAFELY platform. Lancet Respir Med. 2020; 8(11):1106–1120. https://doi.org/10.1016/S2213-2600(20)30415-X PMID: 32979987

138. Mendy A, Forno E, Niyonsenga T, Carnahan R, Gasana J. Prevalence and features of asthma-COPD overlap in the United States 2007–2012. Clin Respir J. 2018 Aug; 12(8):2369–2377. https://doi.org/10.1111/crj.12917 PMID: 29873189

139. WHO global report on trends in prevalence of tobacco smoking 2015 9789241564922_eng.pdf; sequence = 1 (who.int) (Accessed February 2, 2022)

140. Chandrupatla SG, Tavares M, Natto ZS. Tobacco Use and Effects of Professional Advice on Smoking Cessation among Youth in India. Asian Pac J Cancer Prev. 2017 Jul 27; 18(7):1861–1867. https://doi.org/10.22034/APJCP.2017.18.7.1861 PMID: 28749122

141. Office for National Statistics. Smoking prevalence in the UK and the impact of data collection changes: 2020. Available at https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/drugusealcoholandsmoking/bulletins/smokingprevalenceintheukandtheimpactofdatacollectionchanges/2020#:~:text=In%20Quarter%201%202020%2C%2013.5,(around%204.9%20million%20people)(Accessed February 4, 2022).