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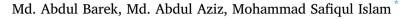
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Review article

Impact of age, sex, comorbidities and clinical symptoms on the severity of COVID-19 cases: A meta-analysis with 55 studies and 10014 cases



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ABSTRACT

Purpose: Severe acute respiratory coronavirus 2 (SARS-CoV-2) cases are overgrowing globally and now become a pandemic. A meta-analysis was conducted to evaluate the impact of age, sex, comorbidities, and clinical characteristics on the severity of COVID-19 to help diagnose and evaluate the current outbreak in clinical decision-making.

Methods: PubMed, ScienceDirect, and BMC were searched to collect data about demographic, clinical characteristics, and comorbidities of COVID-19 patients. Meta-analysis was conducted with Review Manager 5.3. Publication bias was assessed using Egger's test and Begg-Mazumdar's rank correlation.

Results: Fifty-five studies were included in this meta-analysis, including 10014 patients with SARS-CoV-2 infection. Male cases and cases with an age of \geq 50 years (OR = 2.41, p < 0.00001; RR = 3.36, p = 0.0002, respectively) were severely affected by SARS-CoV-2. Patients having age \geq 65 years are not associated (p = 0.110) with the severity of COVID-19. Presence of at least one comorbidity or hypertension, diabetes, cerebrovascular disease, cardiovascular diseases, respiratory disease, malignancy, chronic kidney disease and chronic liver diseases individually increased the severity of COVID-19 cases significantly (OR = 3.13, p < 0.00001; OR = 2.35, p < 0.00001; OR = 2.42, p < 0.00001; OR = 3.78, p < 0.00001; OR = 3.33, p < 0.00001; OR = 2.58, p < 0.00001; OR = 2.32, p < 0.00001; OR = 2.27, p = 0.0007; OR = 1.70, p = 0.003, respectively). Clinical manifestation such as fever, cough, fatigue, anorexia, dyspnea, chest tightness, hemoptysis, diarrhea and abdominal pain (OR = 1.68, p = 0.0001; OR = 1.41, p = 0.004; OR = 1.26, p = 0.03; OR = 2.38, p < 0.0001; OR = 4.30, p < 0.00001; OR = 2.11, p = 0.002; OR = 4.93, p < 0.0001; OR = 1.35, p = 0.03; OR = 2.38, p = 0.008, respectively) were significantly associated with the severity of cases. No association of severity was found with myalgia, pharyngalgia, nausea, vomiting, headache, dizziness and sore throat (p > 0.05). No publication bias was found in case of age (\geq 50 years, age \geq 65 years), comorbidities and clinical manifestations. *Conclusions:* Males patients and elderly or older patients (age >50 years) are at higher risk of developing severity.

whereas comorbidities and clinical manifestations could significantly affect the prognosis and severity of COVID-19.

1. Introduction

The evolving coronavirus disease 2019 (COVID-19), caused by the novel coronavirus (2019-nCoV) or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged from Wuhan, Hubei Province, China in late December 2019, declared global pandemic from the World Health Organization (WHO) on 11th March 2020 due to its worldwide potential and deathly outcomes [1, 2]. This deadly infection is mainly transmitting through large respiratory droplets of affected people during coughing or sneezing, though the virus's presence has also been traced

from stool and urine of infected individuals [3]. The most common COVID-19 patients' symptoms are fever, dry cough, fatigue, nasal congestion, myalgia, sore throat, and diarrhea, whereas the comorbidities are diabetes, hypertension, respiratory disease, cardiovascular disease, malignancy and others [4, 5, 6].

Most coronaviruses can infect different animals, including humans. At present, there are seven classes of coronaviruses that have been isolated from humans, including α -coronaviruses (229E and NL63), β -coronaviruses (OC43), Middle East Respiratory Syndrome Coronavirus (MERS-CoV), HKU1, and Severe Acute Respiratory Syndrome Coronavirus

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(SARS-CoV) [7, 8, 9]. SARS-CoV2 was isolated from the lower respiratory tract of patients suffering from pneumonia in Wuhan, and it was named as 2019-nCoV [10]. The International Committee on the Taxonomy of Viruses (ICTV), on the other hand, officially renamed it SARS-CoV-2 [10, 11]. It is very similar to the genome sequences of previously identified coronaviruses, most importantly, to the SARS-CoV [12, 13]. So, this novel coronavirus has been classified as a β -coronavirus which can be transmitted into humans.

Currently, more than 213 countries and territories have confirmed the infection of this contagious virus. The infection rate is rising globally, as confirmed by the WHO, according to an exponential trend. As of May 29, 2020, approximately 5,962,944 confirmed cases of COVID-19 were identified with a total death of 363,905 (6.10%) patients worldwide [14]. Accordingly, countries across the world have undertaken rapid regulatory and migratory activities in response to the COVID-19 attack to control major patient outbreaks and to level the demand for increased hospital beds, testing facilities, oxygen and mechanical ventilation supports while protecting the most vulnerable one from infection, including elderly or older people with comorbidities to reduce their mortalities [15]. However, severe patients need more intensive care that is somehow lacking in most of the countries.

The current knowledge about the characteristics of novel coronavirus is still limited, and this is transmitting rapidly. To understand both the situation and the seriousness of the disease, health workers and researchers have made remarkable efforts concerning new coronavirus infected patients. The healthcare providers have proposed numerous recommendations for overcoming both diagnostic and therapeutic challenges as there are no approved drugs for protecting this assailable population from contagious viral exposure. Moreover, as there are no established vaccines, researchers are trying to develop vaccines to tackle this pandemic [16, 17].

The global outbreak of highly contagious coronavirus has led the nations' medical, psychological, and socio-economic conditions to a challenging situation that they never thought before. COVID-19 portrays probably one of the greatest threats in this century that the countries have to tackle. Therefore, scientists are trying to understand the pathogenesis, clinical implications, and develop novel preventive strategies. To date, researches on this pandemic have produced many scientific results on the clinicopathological findings that are not consistent. We analyzed relevant data from published articles to conduct the present meta-analysis to identify epidemiological attributes, clinical features, the frequency of comorbidities, severity of the infection, the correlation of age, sex, comorbidities, clinical manifestations with the severity of COVID-19 cases for more accurate and precise outcomes. We hope this study will help the existing clinical practices on the prevention, treatment, and management of the pandemic.

2. Methods

2.1. Literature search strategy

The present meta-analysis was carried out following the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The relevant studies written in any language were systematically searched on PubMed, ScienceDirect and BMC Journal database from January 1, 2020, to May 23, 2020. EndNote X 7.0 software was

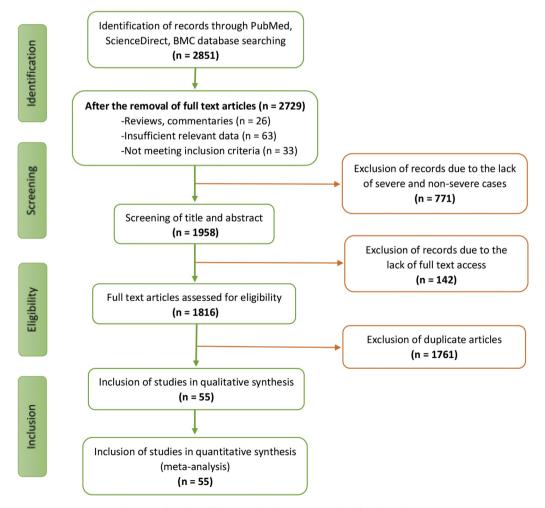


Figure 1. Flow chart illustrating the literature search and study selection.

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Table 1. Baseline characteristics of included studies.

Study ID	Year	Country	Study Design	Sample Size	Male (%)	Median Age/ Mean ± SD	Follow-up/Observation period/Data collection period, days
Aggarwal S	2020	USA	retrospective study	16	12 (75%)	67/65.5	36
Bi X	2020	China	retrospective study	113	64 (56.6%)	46	25
Cai Q	2020	China	retrospective study	298	145 (48.66%)	47.5	55
Cai Y	2020	China	retrospective study	7	5 (71.43%)	60.29	
Chen G	2020	China	retrospective study	21	17 (81%)	56	
Chen X	2020	China	retrospective study	48	37 (77.1%)	64.6 ± 18.1	19
Chen Q	2020	China	single center retrospective observational study	145	79 (54.5%)	47.5	71
Chu J	2020	China	single center retrospective observational study	54	36 (66.7%)	39	35
Colaneri M	2020	Italy	retrospective study	44	28 (63.64%)	67.5	13
		•					
Deng Q	2020	China	retrospective study	112	57 (50.9%)	65.0	45
Feng Y	2020	China	multi-center retrospective study	476	271 (56.9%)	53.0	46
Ferguson J	2020	USA	retrospective study	72	38 (52.8%)	60.4	29
Gao Y	2020	China	retrospective study	43	26 (60.47%)	44.08	10
Guan WJ	2020	China	retrospective study	1099	637 (57.96%)	47.0	49
He R	2020	China	retrospective study	204	79 (38.73%)	49.0	34
Hong KS	2020	South Korea	Descriptive Study	98	38 (38.8%)	$\textbf{55.4} \pm \textbf{17.1}$	90
Huang C	2020	China	prospective study	41	30 (73%)	49.0	17
Huang Q	2020	China	multi-center retrospective study	54	28 (51.9%)	41.0	24
Huang R	2020	China	multi-center retrospective study	202	116 (57.4%)	44.0	19
Jiang Y	2020	China	single center retrospective study	60	35 (58.33%)	41	17
Ketcham SW	2020	China	retrospective study	13	13 (100%)	61.0	46
Lei S	2020	China	retrospective study	34	14 (41.2%)	55.0	36
Li K	2020	China	retrospective study	83	44 (53%)	45.5	60
Li K	2020	China	retrospective study	69	40 (57.97%)	48.5	60
Li X	2020	China	retrospective study	548	279 (50.9%)	60.0	37
Li YK	2020	China	retrospective study	25	13 (52%)	61	51
Liang W	2020	China	retrospective study	1590	904 (57.4%)	48.9	26
Liu F	2020	China	retrospective study	140	49 (35.0%)	65.5	54
Liu J	2020	China	retrospective single-center study	40	15 (37.5%)	48.7 ± 13.9	19
Liu Z	2020	China	retrospective study	72	39 (54.2%)	$\textbf{46.2} \pm \textbf{15.9}$	28
Lodigiani C	2020	Italy	retrospective study	388	264 (68%)	66.0	57
Lv Z	2020	China	retrospective cohort study	354	175 (49.44%)	62.0	24
Lyu P	2020	China	retrospective study	51	29 (56.86%)	54 ± 17	40
Pan L	2020	China	descriptive, cross-sectional, multicenter study	103	37 (35.92%)	48.2	60
Peng YD	2020	China	retrospective study	112	53 (47.32%)	62.0	26
Pereira MR	2020	USA	retrospective study	90	53 (59%)	57.0	20
Shi Y	2020	China	retrospective study	487	259 (53.2%)	46.0	15
Sun L	2020	China	retrospective study	55	31 (56.4%)	44.0	26
Tian S	2020	China	retrospective study	262	127 (48.5%)	47.5	20
Wan S	2020	China	retrospective study	135	72 (53.3%)	47	16
Wang D	2020	China	retrospective single-center study	138	75 (54.3%)	56	34
Wang R	2020	China	single-center, retrospective, descriptive study	125	54 (43.2%)	38.76 ± 13.80	29
Wang F	2020	China	retrospective study	28	21 (75.0%)	68.6 ± 9.0	24
Wu J	2020	China	retrospective study	280	151 (53.93%)	43.12 ± 19.02	31
Xie H	2020	China	retrospective study	79	44 (55.7%)	60.0	21
Xie J	2020	China	retrospective study	56	24 (42.86%)	56.5	10
Xiong F	2020	China	retrospective study	131	75 (57.3%)	63.3	70
Yang AP	2020	China	retrospective study	93	56 (60%)	$\textbf{46.4} \pm \textbf{17.6}$	28
Yang P	2020	China	retrospective study	133	72 (54.14%)	50.60	90
Yang Y	2020	China	retrospective study	50	29 (58%)	62.0	39
Yao Q	2020	China	retrospective study	108	43 (39.8%)	52.0	12
Yu X	2020	China	descriptive study	333	172 (51.7%)	56.0	26
	2020	China	descriptive study	140	71 (50.7%)	57.0	18
Zhang JJ	2020	China	retrospective study	140 96	71 (50.7%) 58 (60%)	57.0	61
Zheng S						1111	

Study Name	Апу сотю	rbidity (%)	Hyperte	nsion (%)	Diabe	tes (%)	Cerebrovascu	ar discase (%)	Cardiovascul	ar discase (%)	Respiratory	disease (%)	Malignz	mcy (%)	Chronic kid	ney disease	Chronic li	ver disease
	Severe	Non-severe	Severe	Non-severe	Severe	Non-severe	Severe	Non-severe	Severe	Non-severe	Severe	Non-severe	Severe	Non-severe	Severe	Non-severe	Severe	Non-severe
Aggarwal S			37.5	75	25	37.5	12.5	12.5	62.5	25	12.5	12.5	12.5	12.5	37.5	37.5		
Cai Q			37.93	10.42	13.79	4.17			22.41	5							13.79	8.33
Chen G	45.45	20	36.36	10	18.18	10												
Chen Q			20.93	12.75	16.28	6.86					0	5.88	0	5.88	2.33	1.96	9.3	1.96
Chen X			36.36	10	29.63	19.05	14.81	9.52	22.22	9.52	3.7	4.76	3.7	4.76				
Colaneri M	76.47	55.56	29.41	37.04	5.88	22.22			35.29	18.52	0	7.41	0	7.41			5.88	3.7
Deng Q			35.82	21.43	20.9	8.93			16.42	7.14	4.48	1.79	4.48	1.79				
Feng Y	58.06	37.78	32.26	20.74	13.71	9.09	7.26	2.27	13.71	5.97	11.29	2.27	11.29	2.27	1.61	0.57		
Ferguson J	71.43	54.9	52.38	29.41	47.62	19.61	4.76	1.96	4.76	7.84	19.05	29.41	19.05	29.41	9.52	13.73		
Gao Y			40	25	40	3.57			6.67	7.14	20	0	20	0				
Guan WJ	38.73	20.95	23.7	13.39	16.18	5.72	2.31	1.19	5.78	1.84	3.47	0.65	3.47	0.65	1.73	0.54	0.58	2.38
He R			37.68	7.41	11.59	5.93	10.14	0.74	7.25	0	1.45	1.48	1.45	1.48			0	1.48
Hong KS			38.46	29.41	23.08	7.06	0	2.35	0	12.94	0	2.35	0	2.35			0	1.18
Huang C	38.46	28.57	15.38	14.29	7.69	25			23.08	10.71	7.69	0	7.69	0				
Huang Q			33.33	13.73	66.67	5.88	33.33	3.92	33.33	13.73	0	3.92	0	3.92			0	7.84
Huang R	39.13	25.7	8.7	15.08	34.78	6.15	4.35	1.12	4.35	2.23	4.35	3.35	4.35	3.35			0	2.23
Jiang Y			12.5	7.69	0	1.92					0	1.92	0	1.92			0	3.85
Ketcham SV			100	71.43	66.67	71.43			66.67	14.29	6.67	0			66.67	100		
Lei S	80	42.11	60	21.05	40	10.53	13.33	0	40	5.26	16	1.72	6.67	0	6.67	0		
Li K	44	6.9	8	5.17	28	0			4	0	15.38	6.98	16	1.72	-			
Li S			34.62	18.6	19.23	6.98			11.54	2.33	5.95	2.15	15.38	6.98			11.54	0
Li X			38.66	22.22	19.33	11.11			10.41	2.15	44.44	6.25	5.95	2.15	2.23	1.43	0.74	1.08
Li YK			11.11	6.25	11.11	0			11.11	18.75	9.16	0.82	44.44	6.25				
Liang W	58.78	22.07	40.46	14.8	23.66	6.79	9.92	3.15	9.92	3.15	12.12	11.21	9.16	0.82	4.58	1.03	2.29	1.71
Liu F			66.67	38.32	66.67	31.78			39.39	20.56	6.67	0	12.12	11.21				
Lin J	53.85	25.93	38.46	3.7	30.77	7.41				44.07						45.0		
Lodigiani C		00.04	44.26	47.71	18.03	23.55			11.48 5.44	14.37 4.35	4.67	174	4.07		14.75	15.9		
Lv Z	31.38	33.91	21.34	20	10.88	7.83	12.82	0	20.51	4.35	1.67 7.69	1.74 0	1.67 7.69	1.74 0				
Lyu P Pan L							12.82	U	35.14	15.15	13.51	3.03	13.51	3.03				
Peng YD			62.5	85.42					62.5	54.17	13.51	3.03	13.51	3.03				
Pereira MR			70.37	58.73	51.85	42.86			02.5	54.17	22.22	17.46	22.22	17.46	70.37	60.32		
Shi Y			53.06	16.67	14.29	5.02			8.16	1.6	66.66	17.40	22.22	17.40	4.08	1.14	4.08	4.57
Sun L	53.33	25	40	5	13.33	7.5			6.67	0	6.67	7.5	6.67	7.5	6.67	0	13.33	2.5
Wan S	72.22	37.25	10	9.47	22.5	3.16			15	1.05	12.5	0	12.5	0	0.07		2.5	1.05
Wang D		07120	58.33	21.57	22.22	5.88			25	10.78	8.33	0.98	8.33	0.98	5.56	1.96	210	1.05
Wang F	71.43	50	71.43	35.71	71.43	35.71	14.29	14.29	28.57	0	7.14	7.14	7.14	7.14	0.00	2.00		
WuJ							51.81	7.11	51.81	7.11	4.82	1.52	4.82	1.52			4.82	1.52
Xie H			14.29	19.61	14.29	19.61			7.14	9.8					2.41	0.51		
Xie J			17.65	4.55	5.88	4.55											0	4.55
Xiong F					16.67	24.75			83.33	64.36	3.33	3.96	3.33	3.96			13.33	9.9
Yang AP	87.5	42.03	66.67	10.14	54.17	11.59			37.5	5.8					33.33	2.9	33.33	23.19
Yang P			83.82	92.31	72.06	95.38			91.18	100	94.12	100	94.12	100	97.06	100	100	98.46
Yang Y	72.22	28.57	36	8.43	16.67	0			47.22	14.29	5.56	0	5.56	0	5.56	0	5.56	0
Yao Q	52	14.46	34.62	17.92	12	2.41			8	2.41	0	3.61	0	3.61			4	1.2
Yu X			66.67	10.14	19.23	7.49			30.77	5.21	7.69	0.98	7.69	0.98				
Zhang JJ	79.31	53.66	37.93	24.39	13.79	10.98			6.9	3.66	6.9	0	6.9	0	3.45	0	6.9	4.88
Zheng S			41.89	18.18	13.51	4.55			9.46	0	5.41	0	5.41	0	1.35	0	2.7	4.55
Zhou Y			32.56	7.43	13.95	4.64	0	1.24	16.28	0.62	6.98	2.17	6.98	2.17	6.98	0.31	9.3	1.24
Average	51.14	25.99	36.47	19.52	21.19	9.73	11.83	2.51	18.76	7.14	9.5	3.34	7.62	2.74	10.63	4.27	8.78	4.13

Figure 2. Comorbidities of COVID-19 cases of the included studies

employed to exclude duplicate studies. The following keywords are used in search alone or in combination: 'clinical characteristics of COVID-19', 'severity of COVID-19', 'clinical outcome', 'death or clinical features', 'comorbidities of COVID-19', 'signs and symptoms of SARS-CoV-2' There was no country limitation to identify the studies and search was limited to humans, but only online literature was included. We have reviewed reference lists of included articles to identify missing studies.

2.2. Inclusion and exclusion criteria

The criteria need to be satisfied for inclusion studies are below:

1) Only study samples with confirmed COVID-19 infection; 2) Studies with age, sex, clinical signs & symptoms, comorbidities, disease severity, deaths, and survival as primary outcomes; 3) Cohort studies and case-control studies; 4) No language and geographical restriction; 5) Study with human samples; 6) Studies with sufficient data to calculate OR and 95% CI.

The criteria for exclusion are as follows:

1) Expert opinions, reviews, letters, and commentaries; 2) Studies with children and pregnant women case; 3) Overlapping or duplicate publications; 4) Irrelevant information for data extraction; 5) Animal studies.



Figure 3. Clinical symptoms of COVID-19 cases of the included studies

Table 2. Results of the meta-analysis of the sex, age, comorbidity and clinical manifestation.

Overall Parameter	Individual Parameter	*OR or RR	95% CI	p value	I^2
Sex	Sex	2.41	1.93-3.02	< 0.00001	67%
Age	Age≥50 vs. age<50	3.36	1.79-6.30	0.0002	89%
	Age≥65 vs. age<65	0.79	0.59–1.06	0.11	88%
Comorbidity	Any comorbidity	3.13	2.26-4.32	< 0.00001	64%
	Hypertension	2.35	1.83-3.02	< 0.00001	66%
	Diabetes	2.42	1.84-3.19	< 0.00001	58%
	Cerebrovascular disease	3.78	2.22-6.43	< 0.00001	35%
	Cardiovascular disease	3.33	2.47-4.47	< 0.00001	47%
	Respiratory disease	2.58	1.76-3.77	< 0.00001	33%
	Malignancy	2.32	1.63-3.32	< 0.00001	9%
	Chronic kidney disease	2.27	1.41-3.65	0.0007	32%
	Chronic liver disease	1.70	1.19-2.42	0.003	0%
	Overall	2.59	2.31-2.89	< 0.00001	49%
Symptoms	Fever	1.68	1.29-2.19	0.0001	54%
	Cough	1.41	1.11-1.77	0.004	63%
	Fatigue	1.26	1.03-1.55	0.03	36%
	Anorexia	2.38	1.60-3.54	< 0.0001	0%
	Myalgia	1.30	0.98-1.71	0.07	58%
	Dyspnea	4.30	2.98-6.22	< 0.00001	79%
	Chest tightness	2.11	1.30-3.42	0.002	72%
	Sputum production	1.35	1.00-1.82	0.05	55%
	Hemoptysis	4.93	2.43-10.02	< 0.0001	0%
	Pharyngalgia	0.91	0.30-2.74	0.87	69%
	Diarrhea	1.35	1.03-1.78	0.03	30%
	Nausea	1.26	0.48-3.31	0.64	86%
	Vomiting	1.48	0.97-2.25	0.07	24%
	Abdominal pain	2.38	1.25-4.52	0.008	0%
	Headache	1.19	0.83-1.72	0.34	48%
	Dizziness	1.40	0.87-2.28	0.17	22%
	Sore throat	1.60	0.88-2.91	0.12	66%
	Overall	1.62	1.46-1.79	< 0.00001	68%

2.3. Data extraction

Two investigators (MAB and MAA) independently extracted data with the inclusion criteria. They separately performed the literature search, evaluation, and data extraction to an excel database. Regarding the disagreements of the studies that emerged during the process were resolved by another investigator (MSI). Rayyan QCRI, a systematic review web app, was used to select the studies [18]. Data extraction included the author's name, country, age, sex, number of participants, comorbidities, clinical symptoms, and severe and nonsevere cases.

2.4. Methodological quality assessment

'Newcastle-Ottawa Scale (NOS)' was utilized for observational cohort studies to determine the methodological quality of the included studies, as described elsewhere [19]. Any disagreement between investigators was settled through discussion.

2.5. Statistical analysis, heterogeneity, and publication bias

The data analyses were performed by Microsoft Excel and Review Manager 5.3 (RevMan 5.3, the Cochrane Collaboration, Oxford, United Kingdom) software. Review Manager 5.3 was utilized to evaluate the heterogeneity (χ 2 and I²) between studies, and heterogeneity in the forest plot was evaluated, applying both the Cochran's chi-square Q-test

and I² statistic. p < 0.1 or I² > 50% indicated the presence of statistically significant heterogeneity. Accordingly, I² values of 25%, 50%, and 75% represented low, moderate, and high heterogeneity. To determine any significant variations in risk across the studies for each parameter, we conducted a sensitivity analysis by omitting studies one-by-one in a certain order. The random-effect model was selected throughout the analysis. Publication biases were evaluated by the funnel plot along with Egger's regression test and Begg-Mazumdar's rank correlation. The level of significance selected for publication bias was p < 0.05, and the values higher than this were predicted as no publication bias.

3. Results

3.1. Study selection and quality assessment

Initially, 2851 articles were identified from three databases (PubMed, ScienceDirect, BMC) during the initial retrieval. A total of 1761 records were excluded because of duplication. Then, 771 articles were removed after reading the title and abstract, and 142 were excluded from the remaining 319 articles for various reasons. In the end, 55 full-text studies involving 10014 COVID-19 patients were included in this meta-analysis based on the detailed assessment and inclusion criteria (Figure 1) [20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30], [31, 32, 33, 34, 35, 36, 37, 38, 39, 40], [41, 42, 43, 44, 45, 46, 47, 48, 49, 50], [51, 52, 53, 54, 55, 56, 57, 58, 59, 60], [61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74]. It was

Table 3. Publication	n bias w	as examined	by	Egger's	linear	regression	test	and
Begg and Mazumda	r's rank c	orrelation te	st.					

Parameters	p-value (Egger's test_)	p-value (Begg-Mazumdar's test)
Sex	0.063	0.126
Age (\geq 50 vs. <50 years)	0.116	0.835
Age (≥65 vs. <65 years)	0.926	0.891
Any comorbidity	0.300	0.600
Hypertension	0.953	0.992
Diabetes	0.872	0.754
Cerebrovascular disease	0.207	0.656
Cardiovascular disease	0.731	0.683
Respiratory diseases	0.085	0.654
Malignancy	0.334	0.218
Chronic kidney disease	0.542	1.000
Chronic liver disease	0.751	0.779
Fever	0.035	0.819
Cough	0.125	0.977
Fatigue	0.638	0.657
Anorexia	0.208	0.805
Myalgia	0.793	0.563
Dyspnoea	0.803	0.780
Chest tightness	0.122	0.324
Sputum production	0.813	0.513
Haemoptysis	0.424	0.608
Pharyngalgia	0.675	0.543
Diarrhea	0.305	0.762
Nausea	0.304	0.742
Vomiting	0.287	0.472
Abdominal pain	0.684	0.677
Headache	0.914	0.235
Dizziness	0.164	0.531
Sore throat	0.474	0.625

also found that most of these studies (n = 49) were based in China, although three studies were identified from the USA, two studies were from Italy, and one study from South Korea was included. The quality of most included studies was of high quality (score ranges between 6-8) assessed by the Newcastle Ottawa scale. Only two studies being of

moderate quality (score 5), as shown in Supplementary Table S1. The baseline characteristics of all studies are presented in Table 1, and other results are presented in Figures 2, 3 and Tables 2, 3.

3.2. Effect of sex on disease severity

Among the 10014 patients, 2469 were severe or critical cases, 7545 were nonsevere patients. Males (62.83%) were found more than females (37.17%) in severe cases (Figure 4), whereas the males were 53.04%, and 46.6% were female in nonsevere cases. Significant heterogeneity was found when compared the severity among the male and female COVID-19 patients ($I^2 = 67\%$, p < 0.00001). The random-effect model was used in the meta-analysis, and the results showed that the proportion of severe patients in the males was significantly higher than the females and male patients showed 2.41 times more risk of the development severe COVID-19 than female patients (male Vs. female 59.67% vs. 40.33%, OR = 2.41, 95%CI = 1.93–3.02, p < 0.00001) (Table 2, Figure 5.

3.3. Effect of age on the severity

Studies that provided only median or mean age were excluded from the analysis of the association of severity with age. Among the 55 studies, the severe patients of 8 studies were categorized as age \geq 50 years (73.09%) and <50 years (26.91%), whereas 12 studies were categorized as age \geq 65 years (43.36%) and <65 years (56.64%) (Figure 6). A higher significant heterogeneity also found in both age \geq 50 vs. age<50 years (I² = 89%, p < 0.00001) and age \geq 65 vs. age<65 (I² = 88%, p < 0.00001) groups. COVID-19 patients with age \geq 50 years showed statistically significant 3.36 times more risk of severity in comparison with age below 50 years (age \geq 50 years Vs. age<50 years, RR = 3.36; 95% CI = 1.79–6.30, p = 0.0002) whereas patients with age \geq 65 years showed 0.79 times risk compared to severe patients age below 65 years (age \geq 65 years, RR = 0.79; 95% CI = 0.59–1.06, p = 0.110) (Table 2, Figure 7).

3.4. Effect of comorbidity on the disease severity

The prevalence of comorbidities including the presence of at least one comorbidity, hypertension, diabetes, cerebrovascular disease, cardio-vascular diseases, respiratory disease, malignancy, chronic kidney disease and chronic liver disease in severe and non-severe COVID-19 patients of the included studies is shown in Figures 2, 8 and Table 2.

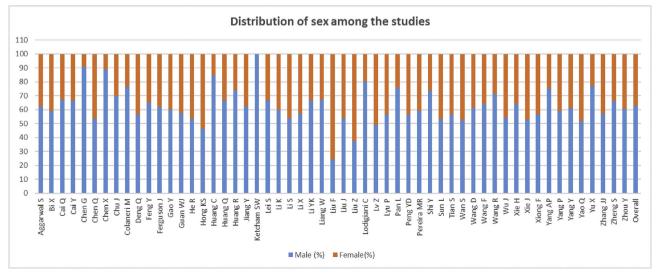


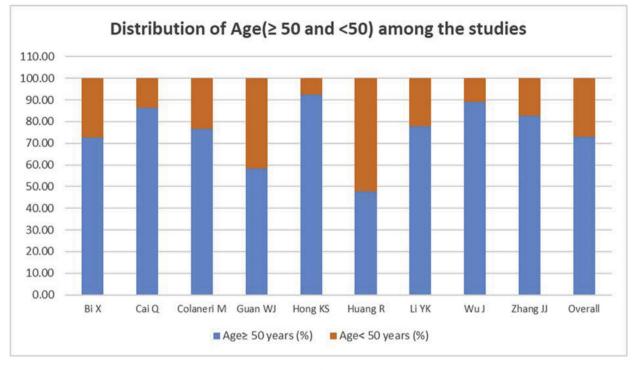
Figure 4. Distribution of sex of included studies to analyze the effect of sex on for the severity of COVID-19.

Study or Subgroup	Male Se Events	Total	Female S Events		Weight	Odds Ratio M-H, Random, 95% CI	Odds Ratio M-H, Random, 95% Cl
Aggarwal S	5	8	3	8	0.9%	2.78 [0.37, 21.03]	
BiX	13	22	9	22	1.7%	2.09 [0.63, 6.94]	
CaiQ	39	58	19	58	2.5%	4.21 [1.94, 9.15]	
Cai Y	2	3	1	3	0.4%	4.00 [0.13, 119.23]	
Chen Q	23	43	20	43	2.3%	1.32 [0.57, 3.09]	
Chu J	30	43	13	43	2.2%	5.33 [2.12, 13.37]	
Colaneri M	13	43	4	43	1.3%	10.56 [2.17, 51.53]	
Deng Q	38	67	29	67	2.6%		
-						1.72 [0.87, 3.40]	
Feng Y	81	124	43	124	2.9%	3.55 [2.10, 5.99]	
Ferguson J	13	21	8	21	1.7%	2.64 [0.76, 9.18]	
Gao Y	9	15	6	15	1.4%	2.25 [0.52, 9.70]	
Guan WJ	100	173	73	173	3.1%	1.88 [1.22, 2.88]	
He R	37	69	32	69	2.7%	1.34 [0.68, 2.61]	
Hong KS	6	13	7	13	1.3%	0.73 [0.16, 3.43]	
Huang C	11	13	2	13	0.8%	30.25 [3.59, 254.73]	
Huang Q	2	3	1	3	0.4%	4.00 [0.13, 119.23]	
Huang R	17	23	6	23	1.6%	8.03 [2.15, 29.94]	
Jiang Y	5	8	3	8	0.9%	2.78 [0.37, 21.03]	
Lei S	10	15	5	15	1.3%	4.00 [0.88, 18.26]	+
Li K	15	25	10	25	1.9%	2.25 [0.73, 6.98]	
LiS	14	26	12	26	1.9%	1.36 [0.46, 4.05]	
LiX	153	269	116	269	3.2%	1.74 [1.24, 2.45]	
Li YK	6	- 9	3		1.0%	4.00 [0.56, 28.40]	
Liang W	88	131	43	131	2.9%	4.19 [2.50, 7.01]	
Liu F	8	33	25	33	1.9%	0.10 [0.03, 0.32]	
LiuJ	7	13	25	13	1.3%		
						1.36 [0.29, 6.36]	
Liu Z	3	8	5	8	0.9%	0.36 [0.05, 2.73]	
Lodigiani C	49	61	12	61	2.3%	16.67 [6.83, 40.72]	
Lv Z	117	239	122	239	3.2%	0.92 [0.64, 1.32]	
Lyu P	22	39	17	39	2.2%	1.67 [0.68, 4.10]	
Pan L	28	37	9	37	2.0%	9.68 [3.35, 28.00]	
Peng YD	9	16	7	16	1.5%	1.65 [0.41, 6.68]	
Pereira MR	16	27	11	27	1.9%	2.12 [0.71, 6.27]	
Shi Y	36	49	13	49	2.2%	7.67 [3.13, 18.80]	
Sun L	8	15	7	15	1.4%	1.31 [0.31, 5.48]	
Tian S	26	46	20	46	2.4%	1.69 [0.74, 3.85]	
Wan S	21	40	19	40	2.3%	1.22 [0.51, 2.94]	
Wang D	22	36	14	36	2.2%	2.47 [0.96, 6.37]	· · · · ·
Wang F	10	14	4	14	1.2%	6.25 [1.21, 32.21]	
Wang R	16	25	9	25	1.8%	3.16 [1.00, 10.03]	
WuJ	45	83	38	83	2.8%	1.40 [0.76, 2.58]	
Xie H	18	28	10	28	1.9%	3.24 [1.09, 9.67]	
Xie J	18	34	16	34	2.1%	1.27 [0.49, 3.28]	
	18	34 30					
Xiong F			13	30	2.0%	1.71 [0.62, 4.75]	
Yang AP Yang D	18	24	6	24	1.6%	9.00 [2.44, 33.24]	
Yang P	40	68	28	68	2.6%	2.04 [1.03, 4.04]	
Yang Y	22	36	14	36	2.2%	2.47 [0.96, 6.37]	
Yao Q	13	25	12	25	1.9%	1.17 [0.39, 3.56]	
Yu X	20	26	6	26	1.6%	11.11 [3.06, 40.37]	
Zhang JJ	33	58	25	58	2.5%	1.74 [0.84, 3.63]	+
Zheng S	49	74	25	74	2.6%	3.84 [1.94, 7.59]	
ZhouY	26	43	17	43	2.3%	2.34 [0.99, 5.55]	<u>├</u> ───
		-					
Total (95% CI)		2425		2425	100.0%	2.41 [1.93, 3.02]	◆
Total events	1447		978)001); I² =		

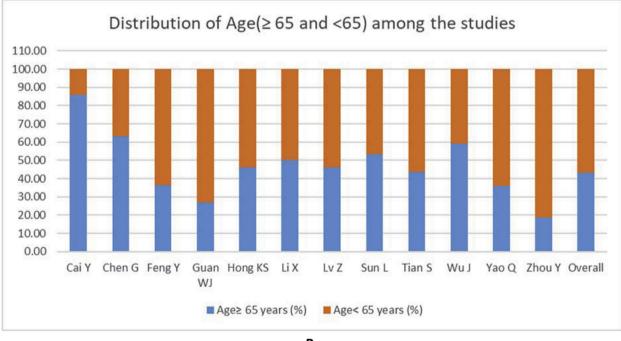
Figure 5. Meta-analysis for the effect of sex on the severity of COVID-19 cases. Forest plots depict the comparison of the incidences of male and female in severe and nonsevere patients.

Among the different comorbidities, 51.14% of severe COVID-19 cases had at least one comorbidity and patients having at least one comorbidity had 3.13 times more risk of severe illness than nonsevere patients (severe

vs. nonsevere: 51.14 vs. 25.99: OR = 3.13, 95% CI = 2.26–4.32, $p<0.00001,\ I^2=64\%).$ A total of 36.47 % of severe patients had hypertension as comorbidity, and the severity of illness was found 2.35 times



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Figure 6. Distribution of age A. \geq 50 Vs. < 50 years and B. \geq 65 and < 65 years among the included studies to analyze the effect of age on for the severity of COVID-19.

higher in COVID-19 cases having preexisting hypertension (severe vs. nonsevere: 36.47% vs. 19.52%, OR = 2.35, 95% CI = 1.83–3.02, $p<0.00001, I^2=66\%$). The proportion of severe illness in cerebrovascular

disease (severe vs. nonsevere: 11.83% vs. 2.51%) and cardiovascular disease (severe vs. nonsevere: 18.76% vs. 7.14%) was also higher than the non-severe patients and the disease severity are strongly associated

	Age≥ 50 y	ears	Age<50 y	ears		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Bi X	16	22	6	22	11.7%	2.67 [1.29, 5.53]	
Cai Q	50	58	8	58	12.0%	6.25 [3.26, 11.99]	
Colaneri M	13	17	4	17	10.8%	3.25 [1.33, 7.97]	
Guan WJ	95	163	68	163	13.6%	1.40 [1.12, 1.75]	
Hong KS	12	13	1	13	6.2%	12.00 [1.81, 79.40]	
Huang R	11	23	12	23	12.4%	0.92 [0.51, 1.64]	
Li YK	7	9	2	9	8.8%	3.50 [0.98, 12.48]	
WuJ	74	83	9	83	12.2%	8.22 [4.42, 15.31]	
Zhang JJ	48	58	10	58	12.4%	4.80 [2.70, 8.54]	
Total (95% CI)		446		446	100.0%	3.36 [1.79, 6.30]	•
Total events	326		120				
Heterogeneity: Tau ² =	0.75; Chi ² =	= 72.56,	df = 8 (P <	0.0000	1); l² = 89	%	0.01 0.1 1 10 100
Test for overall effect:	Z= 3.77 (P	= 0.000	2)				Favours [experimental] Favours [control]

А

	≥ 65 ye	ars	<65 ye	ars		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Cai Y	6	7	1	7	2.1%	6.00 [0.95, 37.76]	
Chen G	17	27	10	27	8.0%	1.70 [0.96, 3.01]	⊢
Feng Y	45	124	79	124	10.3%	0.57 [0.44, 0.74]	
Guan WJ	44	163	119	163	10.3%	0.37 [0.28, 0.48]	
Hong KS	6	13	7	13	6.4%	0.86 [0.40, 1.86]	
Li X	135	269	134	269	10.9%	1.01 [0.85, 1.19]	+
Lv Z	110	239	129	239	10.8%	0.85 [0.71, 1.02]	
Sun L	8	15	7	15	6.8%	1.14 [0.56, 2.35]	_
Tian S	20	46	26	46	9.2%	0.77 [0.51, 1.17]	
WuJ	49	83	34	83	10.0%	1.44 [1.05, 1.97]	
Yao Q	9	25	16	25	7.7%	0.56 [0.31, 1.02]	
Zhou Y	8	43	35	43	7.4%	0.23 [0.12, 0.43]	_ -
Total (95% CI)		1054		1054	100.0%	0.79 [0.59, 1.06]	•
Total events	457		597				
Heterogeneity: Tau ² =	0.20; Chi	² = 88.0)8, df = 11	I (P < 0	.00001);	I² = 88%	
Test for overall effect:	Z=1.58 (P = 0.1	1)				0.01 0.1 1 10 100 Favours [experimental] Favours [control]

Figure 7. Meta-analysis for the effect of age on the severity of COVID-19 cases. Forest plots depict the comparison of the incidences of A) age \geq 50 vs. age<50 years B) age \geq 65 vs. age<65 years in severe patients.

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with preexisting cerebrovascular and cardiovascular diseases (cerebrovascular disease: OR = 3.78, 95% CI = 2.22–6.43, p < 0.00001, I² = 35%; cardiovascular disease: OR = 3.33, 95% CI = 2.47–4.47, p < 0.00001, I² = 47%). Preexisting diabetes (severe vs. nonsevere: 21.19% vs. 9.73%), respiratory disease (severe vs. nonsevere: 9.50% vs. 3.34%) and malignancy (severe vs. nonsevere: 7.62% vs. 2.74%) also significantly increased the severity of COVID-19 cases (diabetes: OR = 2.42, 95% CI = 1.84–3.19, p < 0.00001, I² = 58%; respiratory disease: OR = 2.58, 95% CI = 1.76–3.77, p < 0.00001, I² = 33%; malignancy: OR = 2.32, 95% CI = 1.63–3.32, p < 0.00001, I² = 9%). Chronic liver disease (CLD, severe vs. nonsevere: 10.63% vs. 4.27%) were also found as risk factors for increasing the severity of COVID-19 (CLD: OR = 1.70, 95% CI = 1.19–2.42, p = 0.003, I² = 0; CKD: OR = 2.27, 95% CI = 1.41–3.65, p = 0.0007, I² = 32%).

3.5. Effect of clinical symptoms on the disease severity

Fever, cough, fatigue, anorexia, myalgia, dyspnea, chest tightness, sputum production, hemoptysis, pharyngalgia, diarrhea, nausea, vomiting, abdominal pain, headache, dizziness and sore throat were reported in 47, 46, 37, 8, 34, 40, 22, 25, 4, 7, 39, 17, 18, 9, 27, 10 and 13 studies, respectively. The percentages of these symptoms in severe and nonsevere

COVID-19 cases are presented in Figure 3 and Table 2, and forest plots are presented in Figure 9. The most prevalent clinical symptoms were fever (81.73%), cough (65.41%) and dyspnea (51.50%) followed by fatigue (38.34%), sputum production (35.10%), anorexia (31.23%), chest tightness (25.62%), myalgia (24.91%), diarrhea (18.35%), headache (16.20%), sore throat (13.78%), dizziness (12.26%), pharyngalgia (12.12%), nausea (8.27%), vomiting (6.53%), abdominal pain (5.48%) and hemoptysis (3.17) in the severe patients.

Regarding the clinical manifestations, fever (OR = 1.68, 95% CI = 1.29–2.19, p = 0.0001, I² = 54%), cough (OR = 1.41, 95% CI = 1.11–1.77, p = 0.004, I² = 63%), fatigue (OR = 1.26, 95% CI = 1.03–1.55, p = 0.03, I² = 36%), anorexia (OR = 2.38, 95% CI = 1.60–3.54, p < 0.0001, I² = 0%), dyspnea (OR = 4.30, 95% CI = 2.98–6.22, p < 0.00001, I² = 79%), chest tightness (OR = 2.11, 95% CI = 1.30–3.42, p = 0.002, I² = 72%), hemoptysis (OR = 4.93, 95% CI = 2.43–10.02, p < 0.0001, I² = 0), diarrhea (OR = 1.35, 95% CI = 1.03–1.78, p = 0.03, I² = 30%) and abdominal pain (OR = 2.38, 95% CI = 1.25–4.52, p = 0.008, I² = 0%) are significantly associated with the severity of COVID-19 cases compared to nonsevere cases whereas myalgia (OR = 1.30, p = 0.07), pharyngalgia (OR = 0.91, p = 0.87), nausea (OR = 1.26, p = 0.64), vomiting (OR = 1.48, p = 0.07), headache (OR = 1.19, p = 0.34), dizziness (OR = 1.40, p = 0.17) and sore throat (OR = 1.60, p = 0.12) are not associated with increased risk of severity of

Events	Total	Events	Total	Weight	Odds Ratio M-H, Random, 95% Cl	M-H, Random, 95% CI
5	11	2	10	0.3%	3 33 [0 47 23 47]	
					and the second sec	
						1220
46		44				
	1015		2022	10.5%	3.13 [2.20, 4.32]	-
			(D	0041	0.400	
			(P < 0.0	001); l² =	64%	
= 6.91 (F	- < 0.00	001)				
-	-	-	-	0.00	0.00 10 00 1 7 1	
				0.2%	5.14 [0.46, 56.90]	
5		10	27	0.4%	0.71 [0.19, 2.61]	
24	67	12	56	0.7%	2.05 [0.91, 4.60]	
40	124	73	352	0.9%	1.82 [1.15, 2.87]	
11	21	15	51	0.5%	2.64 [0.93, 7.52]	
6	15	7	28	0.4%	2.00 [0.52, 7.65]	
41	173	124	926	0.9%	2.01 [1.35, 2.99]	
26	69	10	135	0.7%	7.56 [3.37, 16.95]	
5	13	25	85	0.5%		
						100
						÷.
					0.28 [0.09, 0.91]	
					1.67 [0.63, 4.39]	
26	49	73	438	0.8%	5.65 [3.06, 10.45]	
6	15	2	40	0.3%	12.67 [2.18, 73.44]	
4	40	9	95	0.5%	1.06 [0.31, 3.67]	
21	36	22	102	0.7%	5.09 [2.26, 11.48]	
10	14	5	14	0.3%	4.50 [0.91, 22.15]	+
4	28	10	51	0.4%	0.68 [0.19, 2.42]	
6	34	1	22	0.2%	4.50 [0.50, 40.26]	
16	24	7	69	0.5%	17.71 [5.59, 56.15]	
57	68	60	65	0.5%		
14	2081	24	6669	21.8%	2.35 [1.83, 3.02]	
	2001		0005	21.070	2.00 [1.03, 5.02]	
759		1302				
	5 13 72 167 5 9 121 77 75 8 26 10 21 26 13 46 518 26 10 21 26 13 46 518 26 10 21 26 13 46 3 22 4 9 4 5 21 10 21 26 13 46 3 22 4 9 4 5 21 10 21 26 11 21 26 10 21 26 10 21 26 10 21 26 10 21 26 10 21 26 10 21 26 10 21 26 10 21 26 10 22 4 9 4 21 20 10 22 4 9 29 104 1 53 22 57 10 10 126 27 27 10 125 277 510 10 192 6 41 10 192 6 41 10 192 6 41 10 104 10 192 6 41 100 104 10 104 10 104 10 104 10 104 10 104 10 104	5 11 13 17 72 124 15 21 67 173 5 13 9 23 12 15 11 7 7 131 7 13 75 239 8 15 26 36 10 14 21 24 26 36 10 14 21 24 26 36 10 14 21 24 26 36 13 25 40 14 9 43 4 11 5 13 2 33 2 13 3 8 22 58 4 11 5 13 2 13 1 23 1 3	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	5 11 2 10 0.3% 13 17 15 27 0.4% 72 124 133 352 0.9% 15 21 28 51 0.5% 67 173 194 926 0.9% 5 13 8 28 0.4% 9 23 46 179 0.6% 12 15 8 19 0.3% 11 25 4 58 0.4% 76 239 39 115 0.9% 8 15 10 40 0.5% 26 36 38 102 0.7% 101 14 7 14 0.3% 113 25 12 83 0.6% 46 58 44 82 0.7% 1013 3655 10.5% 518 950 .26; Chi ² = 49.71, df = 18 (P < 0.0001); P =	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

Figure 8. Meta-analysis for the effect of comorbidities on the severity of COVID-19 cases. Random effect model for any comorbidity, hypertension, diabetes, cerebrovascular disease, cardiovascular disease, respiratory disease, malignancy, chronic kidney disease and chronic liver disease.

3.1.3 Diabetes						
Aggarwal S	2	8	3	8	0.2%	0.56 [0.06, 4.76]
Cai Q	8	58	10	240	0.6%	3.68 [1.38, 9.79]
Chen G	2 7	11	1	10	0.2%	2.00 [0.15, 26.19]
Chen Q Chen X	8	43 27	7 4	102 21	0.5% 0.4%	2.64 [0.86, 8.05] 1.79 [0.46, 7.02]
Colaneri M	1	17	6	27	0.4%	0.22 [0.02, 2.00]
Deng Q	14	67	5	56	0.5%	2.69 [0.90, 8.02]
Feng Y	17	124	32	352	0.8%	1.59 [0.85, 2.98]
Ferguson J	10	21	10	51	0.5%	3.73 [1.24, 11.20]
Gao Y	6	15	1	28	0.2%	18.00 [1.90, 170.34]
Guan WJ	28	173	53	926	0.8%	3.18 [1.95, 5.19]
He R	8	69	8	135	0.5%	2.08 [0.75, 5.81]
Hong KS	3	13	6 7	85	0.4%	3.95 [0.85, 18.32]
Huang C Huang Q	1 2	13 3	3	28 51	0.2% 0.2%	0.25 [0.03, 2.28] 32.00 [2.22, 461.54]
Huang R	8	23	11	179	0.2%	8.15 [2.84, 23.34]
Jiang Y	Ō	8	1	52	0.1%	2.02 [0.08, 53.77]
Ketcham SW	4	6	5	7	0.2%	0.80 [0.08, 8.47]
Lei S	6	15	2	19	0.3%	5.67 [0.94, 34.03]
Li K	7	25	0	58	0.1%	47.43 [2.58, 870.76]
LIS	5	26	3	43	0.4%	3.17 [0.69, 14.60]
LiX	52	269	31	279	0.9%	1.92 [1.19, 3.10]
LiYK	1	9	0	16	0.1%	5.82 [0.21, 158.82]
Liang W Liu F	31 22	131 33	99 34	1459 107	0.9% 0.7%	4.26 [2.71, 6.69] 4.29 [1.87, 9.85]
Liu J	4	13	2	27	0.3%	5.56 [0.86, 35.71]
Lodigiani C	11	61	77	327	0.7%	0.71 [0.35, 1.44]
Lv Z	26	239	9	115	0.7%	1.44 [0.65, 3.18]
Pereira MR	14	27	27	63	0.6%	1.44 [0.58, 3.55]
Shi Y	7	49	22	438	0.6%	3.15 [1.27, 7.81]
Sun L	2	15	3	40	0.3%	1.90 [0.28, 12.65]
WanS	9	40	3	95	0.4%	8.90 [2.27, 34.99]
Wang D	8	36	6	102	0.5%	4.57 [1.46, 14.28]
Wang F Xie H	10 4	14 28	5 10	14 51	0.3% 0.4%	4.50 [0.91, 22.15] 0.68 [0.19, 2.42]
Xie J	2	34	1	22	0.4%	1.31 [0.11, 15.40]
Xiong F	5	30	25	101	0.5%	0.61 [0.21, 1.76]
Yang AP	13	24	8	69	0.5%	9.01 [3.03, 26.80]
Yang P	49	68	62	65	0.4%	0.12 [0.03, 0.45]
Yang Y	6	36	0	14	0.1%	6.18 [0.33, 117.33]
Yao Q	3	25	2	83	0.3%	5.52 [0.87, 35.13]
Yu X Zhang Ll	5	26	23	307	0.5%	2.94 [1.01, 8.52]
Zhang JJ Zheng S	8 10	58 74	9 1	82 22	0.6% 0.2%	1.30 [0.47, 3.59] 3.28 [0.40, 27.17]
Zhou Y	6	43	15	323	0.6%	3.33 [1.22, 9.11]
Subtotal (95% CI)		2147		6699	19.0%	2.42 [1.84, 3.19]
Total events	455		652			
Heterogeneity: Tau ² = 0).41; Chi²	= 104.69	9, df = 44	(P < 0.0	10001); I²:	= 58%
Test for overall effect: Z	= 6.32 (F	° < 0.000	01)			
3.1.4 Cerebrovascular	diegaeg					
Aggarwal S	uisease 1	8	1	8	0.1%	1.00 [0.05, 19.36]
Chen X	4	27	2	21	0.1%	1.65 [0.27, 10.02]
Feng Y	9	124	8	352	0.6%	3.37 [1.27, 8.93]
Ferguson J	1	21	1	51	0.1%	2.50 [0.15, 41.94]
Guan WJ	4	173	11	926	0.5%	1.97 [0.62, 6.26]
He R	7	69	1	135	0.2%	15.13 [1.82, 125.64]
Hong KS	0	13	2	85	0.1%	1.24 [0.06, 27.20]
Huang Q	1	3	2	51	0.1%	12.25 [0.76, 198.63]
Huang R	1	23	2	179	0.2%	4.02 [0.35, 46.20]
Lei S	2	15	0	19	0.1%	7.22 [0.32, 162.68]
Liang W Lyu P	13 5	131 39	46 0	1459 12	0.8% 0.1%	3.38 [1.78, 6.44] 3.99 [0.21, 77.41]
Wang F	2	14	2	14	0.1%	1.00 [0.12, 8.31]
WuJ	43	83	14	197	0.7%	14.05 [7.02, 28.11]
Zhou Y	0	43	4	323	0.1%	0.82 [0.04, 15.42]
Subtotal (95% CI)		786		3832	4.3%	3.78 [2.22, 6.43]
Total events	93		96			
Heterogeneity: Tau ² = 0	1.30° Chiž	= 21.57	df = 14 (P = 0.09	$11 \mathbf{F} = 359$	6

Heterogeneity: Tau² = 0.30; Chi² = 21.57, df = 14 (P = 0.09); l² = 35% Test for overall effect: Z = 4.91 (P < 0.00001)

Figure 8. (continued).

garwal S	5	8	2	8	0.2%	5.00 [0.58, 42.80]	
iQ	13	58	12	240	0.6%	5.49 [2.35, 12.81]	
en X	6	27	2	21	0.3%	2.71 [0.49, 15.10]	
laneri M	6	17	5	27	0.4%	2.40 [0.60, 9.64]	
ng Q	11	67	4	56	0.5%	2.55 [0.77, 8.52]	
ngY	17	124	21	352	0.7%	2.50 [1.27, 4.92]	
guson J	1	21	4	51	0.2%	0.59 [0.06, 5.59]	
οY	1	15	2	28	0.2%	0.93 [0.08, 11.16]	
an WJ	10	173	17	926	0.7%	3.28 [1.48, 7.29]	
R	5	69	0	135	0.1%	23.11 [1.26, 424.28]	
ng KS	0	13	11	85	0.1%	0.24 [0.01, 4.32]	
ang C	3	13	3	28	0.3%	2.50 [0.43, 14.54]	
ang Q	1	3	7	51	0.2%	3.14 [0.25, 39.43]	
ang R	1	23	4	179	0.2%	1.99 [0.21, 18.60]	
tcham SW	4	6	1	7	0.1%	12.00 [0.80, 180.97]	
S	6	15	1	19	0.2%	12.00 [1.25, 115.36]	
<	1	25	Ó	58	0.1%	7.16 [0.28, 182.02]	
3	3	26	1	43	0.2%	5.48 [0.54, 55.72]	
(28	269	6	279	0.6%	5.29 [2.15, 12.98]	
ſK	1	9	3	16	0.2%	0.54 [0.05, 6.14]	
ngW	13	131	46	1459	0.8%	3.38 [1.78, 6.44]	
F	13	33	22	107	0.6%	2.51 [1.08, 5.82]	
digiani C	7	61	47	327	0.6%	0.77 [0.33, 1.80]	
Z	13	239	5	115	0.5%	1.27 [0.44, 3.64]	
- I P	8	39	õ	12	0.1%	6.75 [0.36, 125.89]	
nL	13	37	10	66	0.6%	3.03 [1.17, 7.87]	
ng YD	10	16	52	96	0.5%	1.41 [0.47, 4.19]	
iY	4	49	7	438	0.4%	5.47 [1.54, 19.42]	
nL	1	15	Ó	40	0.1%	8.38 [0.32, 217.48]	
in S	6	40	1	95	0.2%	16.59 [1.93, 142.84]	
ing D	9	36	11	102	0.6%	2.76 [1.03, 7.35]	
ing F	4	14	0	14	0.1%	12.43 [0.60, 256.66]	
J	43	83	14	197	0.7%	14.05 [7.02, 28.11]	
H	43	28	5	51	0.3%	0.71 [0.13, 3.91]	
ng F	25	30	65	101	0.5%	2.77 [0.98, 7.86]	10 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
ng AP	25	24	4	69	0.3%	9.75 [2.64, 35.95]	
ng P	62	68	4 65	65	0.4%	0.07 [0.00, 1.33]	
-	17	36	2	14	0.1%		
ng Y DQ	2	25	2	83	0.3%	5.37 [1.05, 27.50] 3.52 [0.47, 26.39]	he and he are a second s
X	2 8	25	16	307	0.2%		
x ang JJ	8	26 58	16	307	0.6%	8.08 [3.05, 21.39]	
-	4	58 74	3 0	82 22	0.4%	1.95 [0.42, 9.07]	
eng S			_			5.00 [0.27, 91.07]	
ou Y btotal (95% CI)	7	43 2186	2	323 6794	0.3% 15.5%	31.21 [6.25, 155.94]	
	44.0	2100	105	0194	15.5%	3.33 [2.47, 4.47]	
al events terogeneity: Tau² = 1	410		485				

Figure 8. (continued).

COVID-19 cases and sputum production is in the marginal line (OR = 1.35, 95% CI = 1.00–1.82, $p=0.05,\,I^2=55\%).$

3.6. Sensitivity and publication bias

Publication bias, checked by Egger's regression test and Begg-Mazumdar's rank correlation, are presented in Table 3 and Supplementary Figure S1–S28. No publication bias was found in case of age, sex, comorbidities and clinical symptoms tested by both Egger's and Begg-Mazumdar's tests (p > 0.05). The sensitivity was analyzed for assessing the stability of the results obtained and the influence of each study by omitting each study one by one for age, sex, comorbidities and clinical symptoms (Supplementary Figure S29-56). No significant effect of any single study on the pooled results was found in the case of age, sex and comorbidities and clinical symptoms.

4. Discussion

The new novel coronavirus (SARS-CoV-2) is the seventh human coronavirus, the third type of zoonotic coronavirus, and has genetically similarity with SARS-CoV (79%) and MERS-CoV (50%) [75, 76]. SARS-CoV-2 receptor-binding domain (RBD) is nearly the same as the RBD of SARS-CoV [77]. COVID-19 is highly contagious, and WHO declared it a global pandemic. A total of 5,962,944 confirmed cases and 363,905 (6.10%) deaths were reported as of May 29, 2020, and COVID-19 has spread to 213 countries and territories across all continents [14]. Moreover, China, Europe, and America sufferer more, and now, the severity decreases in China. Although the number of COVID-19 cases continues to grow worldwide, no specific antiviral treatment has been confirmed to be effective against COVID-19. So, clinical demographical characteristics, clinical manifestation, comorbidities of

3.1.6 Respiratory dise							
Aggarwal S	1	8	1	8	0.1%	1.00 [0.05, 19.36]	
Chen Q Chen X	0 1	43 27	6 1	102 21	0.1% 0.1%	0.17 [0.01, 3.10] 0.77 [0.05, 13.07]	
Colaneri M	0	17	2	21	0.1%	0.29 [0.01, 6.45]	
Deng Q	3	67	1	56	0.1%	2.58 [0.26, 25.50]	
Feng Y	14	124	8	352	0.6%	5.47 [2.24, 13.39]	
Ferguson J	4	21	15	51	0.5%	0.56 [0.16, 1.96]	
Gao Y	3	15	0	28	0.1%	15.96 [0.77, 332.61]	
Guan WJ	6	173	6	926	0.5%	5.51 [1.76, 17.29]	
He R	1	69	2	135	0.2%	0.98 [0.09, 10.98]	
Hong KS	0	13	2	85	0.1%	1.24 [0.06, 27.20]	
Huang C	1	13	0	28	0.1%	6.84 [0.26, 179.78]	
Huang Q	0	3	2	51	0.1%	2.83 [0.11, 71.08]	
Huang R	1	23	6	179	0.2%	1.31 [0.15, 11.40]	
Jiang Y	0	8	1	52	0.1%	2.02 [0.08, 53.77]	
Lei S	1	15	0	19	0.1%	4.03 [0.15, 106.36]	
Li K	4	25	1	58	0.2%	10.86 [1.15, 102.77]	
LiS	4	26	3	43	0.3%	2.42 [0.50, 11.83]	
LiX	16	269	6	279	0.6%	2.88 [1.11, 7.47]	
LI YK	4	9	1	16	0.2%	12.00 [1.07, 134.11]	
Liang W	12	131	12	1459	0.7%	12.16 [5.35, 27.66]	
Liu F	4	33	12	107	0.5%	1.09 [0.33, 3.65]	
Lv Z	4	239	2	115	0.3%	0.96 [0.17, 5.33]	
Lyu P	3	39	0	12	0.1%	2.40 [0.12, 49.72]	
Pan L	5	37	2	66	0.3%	5.00 [0.92, 27.20]	
Pereira MR	6	27	11	63	0.5%	1.35 [0.44, 4.12]	
Sun L	1	15	3	40	0.2%	0.88 [0.08, 9.19]	
Wan S	5	40	0	95	0.1%	29.59 [1.60, 548.98]	
Wang D	3	36	1	102	0.2%	9.18 [0.92, 91.31]	
Wang F	1	14	1	14	0.1%	1.00 [0.06, 17.75]	
Wu J	4	83	3	197	0.4%	3.27 [0.72, 14.97]	
Xiong F	1	30	4	101	0.2%	0.84 [0.09, 7.78]	
Yang P	64	68	65	65	0.1%	0.11 [0.01, 2.07]	•
Yang Y	2	36	0	14	0.1%	2.10 [0.09, 46.54]	
Yao Q	0	25	3	83	0.1%	0.45 [0.02, 9.03]	
Yu X	2	26	3	307	0.3%	8.44 [1.35, 53.00]	
Zhang JJ	4	58	0	82	0.1%	13.62 [0.72, 258.15]	
Zheng S	4	74	0	22	0.1%	2.87 [0.15, 55.43]	
Zhou Y Subtotal (95% CI)	3	43	7	323	0.4%	3.39 [0.84, 13.62]	
		2022		5783	0 5%	2 58 [1 76 3 77]	
	102	2022	102	5783	9.5%	2.58 [1.76, 3.77]	•
Total events	192 1.41: Chiř		193 df = 38				•
Total events Heterogeneity: Tau² = 0	0.41; Chi ^a	² = 56.81	df= 38				•
Total events Heterogeneity: Tau² = 0 Test for overall effect: Z	0.41; Chi ^a	² = 56.81	df= 38				•
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 3.1.7 Malignancy	0.41; Chi ^a (= 4.86 (l	² = 56.81, P < 0.000	, df = 38 101)	(P = 0.03); I² = 339	6	•
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 3.1.7 Malignancy Aggarwal S	0.41; Chi ^a (= 4.86 (l 2	² = 56.81, P < 0.000	, df = 38 101) 1	(P = 0.03 8); I² = 339 0.2%	% 2.33 [0.17, 32.58]	•
Total events Heterogeneity: Tau ^a = 0 Test for overall effect: Z 3.1.7 Malignancy Aggarwal S Cai Q	0.41; Chi ^a (= 4.86 (1 2 2	² = 56.81 P < 0.000 8 58	, df = 38 101) 1 2	(P = 0.03 8 240); I² = 339 0.2% 0.2%	% 2.33 [0.17, 32.58] 4.25 [0.59, 30.83]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q	0.41; Chi ^a (= 4.86 (l 2 2 2 2	² = 56.81, P < 0.000 8 58 43	, df = 38 101) 1 2 1	(P = 0.03 8 240 102); I [≠] = 339 0.2% 0.2% 0.2%	% 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen X	0.41; Chi ^a 2 = 4.86 (l 2 2 2 1	² = 56.81, P < 0.000 8 58 43 27	, df = 38 101) 1 2 1 1	(P = 0.03 8 240 102 21); I ^z = 339 0.2% 0.2% 0.2% 0.1%	% 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen X Colaneri M	0.41; Chi ² 2 = 4.86 (l 2 2 2 1 4	² = 56.81, P < 0.000 8 58 43 27 17	df = 38 001) 1 2 1 1 2 2	(P = 0.03 8 240 102 21 27); I ^z = 339 0.2% 0.2% 0.2% 0.1% 0.3%	% 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07] 3.85 [0.62, 23.85]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen X Colaneri M Feng Y	0.41; Chi ² 2 = 4.86 (l 2 2 2 1 4 7	⁸ = 56.81, P < 0.000 8 58 43 27 17 124	df = 38 001) 1 2 1 1 2 5	(P = 0.03 8 240 102 21 27 352); I ^z = 339 0.2% 0.2% 0.2% 0.1% 0.3% 0.5%	% 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07] 3.85 [0.62, 23.85] 4.15 [1.29, 13.33]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen Q Chen X Colaneri M Feng Y Guan WJ	0.41; Chi ^a 2 = 4.86 (1 2 2 2 1 4 7 3	⁸ = 56.81 P < 0.000 8 58 43 27 17 124 173	, df = 38 001) 1 2 1 1 2 5 7	(P = 0.03 8 240 102 21 27 352 926); I ^z = 339 0.2% 0.2% 0.1% 0.3% 0.5% 0.4%	 % 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07] 3.85 [0.62, 23.85] 4.15 [1.29, 13.33] 2.32 [0.59, 9.05] 	
Total events Heterogeneity: Tau [#] = 0 Test for overall effect: Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen Q Chen X Colaneri M Feng Y Guan WJ He R	0.41; Chi ^a 2 4.86 (1 2 2 2 1 4 7 3 4 4	* = 56.81, P < 0.000 8 58 43 27 17 124 173 69	, df = 38)01) 1 2 1 1 2 5 7 7	(P = 0.03 8 240 102 21 27 352 926 135); ≠ = 339 0.2% 0.2% 0.1% 0.3% 0.5% 0.4% 0.2%	% 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07] 3.85 [0.62, 23.85] 4.15 [1.29, 13.33] 2.32 [0.59, 9.05] 8.25 [0.90, 75.26]	
Total events Heterogeneity: Tau ² = C Test for overall effect: Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen X Colaneri M Feng Y Guan WJ He R Hong KS	0.41; Chi ³ 2 = 4.86 (l 2 2 2 1 4 7 3 4 1	* = 56.81, P < 0.000 8 58 43 27 17 124 173 69 13	, df = 38)01) 1 2 1 1 2 5 7 1 3	(P = 0.03 8 240 102 21 27 352 926 135 85); ≠ = 339 0.2% 0.2% 0.3% 0.3% 0.5% 0.4% 0.2%	% 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07] 3.85 [0.62, 23.85] 4.15 [1.29, 13.33] 2.32 [0.59, 9.05] 8.25 [0.09, 75.26] 2.28 [0.22, 23.71]	
Total events Heterogeneity: Tau [≢] = 0 Test for overall effect: Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen X Colaneri M Feng Y Guan WJ He R Hong KS Huang C	0.41; Chi ³ 2 = 4.86 (1 2 2 2 1 4 7 3 4 1 0	* = 56.81, P < 0.000 8 58 43 27 17 124 173 69 13 13	, df = 38)01) 1 2 1 1 2 5 7 1 3 3 1	(P = 0.03 8 240 102 21 27 352 926 135 85 28); ≠ = 339 0.2% 0.2% 0.3% 0.3% 0.5% 0.4% 0.2% 0.2% 0.1%	% 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07] 3.85 [0.62, 23.85] 4.15 [1.29, 13.33] 2.32 [0.59, 9.05] 8.25 [0.90, 75.26] 2.28 [0.22, 23.71] 0.68 [0.03, 17.80]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen X Colaneri M Feng Y Guan WJ He R Hong KS Huang C Huang R	0.41; Chi ³ 2 = 4.86 (1 2 2 2 4 7 3 4 7 3 4 1 0 0 0	* = 56.81, P < 0.000 8 58 43 27 17 124 173 69 13 13 23 23	, df = 38)01) 1 2 1 1 2 5 7 1 3 3 1 2 2	(P = 0.03 8 240 102 21 27 352 926 135 85 28 179	0.2% 0.2% 0.2% 0.1% 0.3% 0.5% 0.2% 0.2% 0.2% 0.1% 0.1%	 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07] 3.85 [0.62, 23.85] 4.15 [1.29, 13.33] 2.32 [0.59, 9.05] 8.25 [0.90, 75.26] 2.28 [0.22, 23.71] 0.68 [0.03, 17.80] 1.51 [0.07, 32.43] 	
Total events Heterogeneity: Tau [#] = 0 Test for overall effect Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen Q Chen X Colaneri M Feng Y Guan WJ He R Hong KS Huang C Huang R Lei S	0.41; Chi ⁷ 2 = 4.86 (1 2 2 2 1 4 7 3 4 7 3 4 1 0 0 5	* = 56.81 P < 0.000 8 58 43 27 17 124 173 69 13 13 23 15	, df = 38 001) 1 2 1 2 5 7 1 2 5 7 1 3 1 2 4	(P = 0.03 8 240 102 21 27 352 926 135 85 28 179 19); I [≠] = 339 0.2% 0.2% 0.3% 0.5% 0.4% 0.2% 0.1% 0.1% 0.1%	% 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07] 3.85 [0.62, 23.85] 4.15 [1.29, 13.33] 2.32 [0.59, 9.05] 8.25 [0.90, 75.26] 2.28 [0.22, 23.71] 0.68 [0.03, 17.80] 1.51 [0.07, 32.43] 1.88 [0.40, 8.74]	
Total events Heterogeneity: Tau [#] = C Test for overall effect: Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen X Colaneri M Feng Y Guan WJ He R Hong KS Huang C Huang R Lei S Li S	0.41; Chi ⁷ 2 = 4.86 (1 2 2 2 1 4 7 3 4 7 3 4 1 0 0 5 5	* = 56.81, P < 0.000 8 58 43 27 124 173 69 13 13 13 13 13 23 26	, df = 38 001) 1 2 1 1 2 5 7 1 3 3 1 2 4 0	(P = 0.03 8 240 102 21 27 352 926 135 85 28 179 19 43	0.2% 0.2% 0.2% 0.3% 0.5% 0.4% 0.2% 0.4% 0.2% 0.1% 0.4%	% 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07] 3.85 [0.62, 23.85] 4.15 [1.29, 13.33] 2.32 [0.59, 9.05] 8.25 [0.90, 75.26] 2.28 [0.22, 23.71] 0.68 [0.03, 17.80] 1.51 [0.07, 32.43] 1.88 [0.40, 8.74] 5.12 [0.20, 130.38]	
Total events Heterogeneity: Tau [≢] = 0 Test for overall effect: Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen X Colaneri M Feng Y Guan WU He R Hong KS Huang C Huang R Lei S Li S Li X	0.41; Chi ⁷ 2 = 4.86 (1 2 2 2 2 1 4 4 7 3 4 1 0 0 5 1 1 4	* = 56.81, P < 0.000 8 58 43 27 17 124 173 69 13 13 13 23 13 23 26 269	, df = 38)01) 1 2 1 1 2 5 7 1 3 3 1 2 4 0 10	(P = 0.03 8 240 102 21 27 926 135 85 28 179 43 279	0.2% 0.2% 0.2% 0.1% 0.3% 0.5% 0.4% 0.2% 0.1% 0.1% 0.1% 0.1% 0.1%	% 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07] 3.85 [0.62, 23.85] 4.15 [1.29, 13.33] 2.32 [0.59, 9.05] 8.25 [0.90, 75.26] 2.28 [0.22, 23.71] 0.68 [0.03, 17.80] 1.51 [0.07, 32.43] 1.88 [0.40, 8.74] 5.12 [0.20, 130.38] 1.48 [0.64, 3.38]	
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Total events Heterogeneity: Tau [#] = C Test for overall effect Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen X Colaneri M Feng Y Guan WJ He R Hong KS Huang C Huang R Lei S Li S Li S Li S Li S Li S Li S Li S L	0.41; Chi ^P (= 4.86 (1 2 2 2 1 4 7 3 4 7 3 4 1 0 0 5 1 1 4 7 0 0 0 0 0 0 0 0 0 4 3 2 2 3 4 2 2 3 4 2 1 1 7 7 3 2 2 1 1 7 7 3 1 1 7 7 3 1 1 7 7 1 7 8 1 7 1 7 7 1 7 7 7 7 7 7 7	= 56.81, P < 0.000 8 58 43 27 17 124 173 69 13 13 23 26 269 131 13 61 13 13 61 13 39 37 27 49 40 36 83 37 27 40 36 83 33 37 27 40 36 83 37 27 40 36 83 37 27 40 36 83 37 37 27 40 36 83 37 37 37 37 37 37 37 37 37 37 37 37 37	, df = 38 101) 1 2 1 1 2 5 7 1 2 5 7 1 2 5 7 1 3 1 2 4 0 10 11 2 2 3 1 2 4 0 10 11 2 5 7 7 1 3 2 2 4 0 10 11 2 5 7 7 1 3 2 2 4 0 10 11 2 5 7 7 1 3 2 2 4 0 10 11 2 5 7 7 1 3 2 2 4 0 10 11 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 1 2 2 3 1 2 2 3 1 1 2 2 3 1 2 2 3 1 1 2 2 3 1 4 0 10 11 2 2 3 1 4 0 10 11 2 2 3 1 4 0 10 11 2 2 3 1 4 0 10 11 2 2 3 1 4 0 10 1 1 2 2 3 1 1 6 3 1 1 2 2 1 4 0 10 1 1 5 1 1 2 2 3 1 1 4 0 3 1 1 5 1 1 2 2 3 1 1 6 3 0 1 1 6 3 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0	(P = 0.03 8 240 102 21 27 352 926 135 85 179 19 439 1459 27 327 1459 27 327 1459 1459 1459 1459 102 197 102 102 102 102 105 14 85 102 27 327 115 12 66 63 83 95 102 197 22 102 105 127 105 102 107 227 227 227 227 227 227 227 2	0.2% 0.2% 0.2% 0.3% 0.3% 0.4% 0.2% 0.4% 0.2% 0.1% 0.1% 0.4% 0.1% 0.6% 0.1% 0.6% 0.1% 0.4% 0.1% 0.3% 0.1% 0.1% 0.2% 0.1% 0.2% 0.1% 0.2% 0.1% 0.1% 0.2% 0.1% 0.2% 0.1% 0.1% 0.1% 0.1% 0.1% 0.1% 0.1% 0.1	 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07] 3.85 [0.62, 23.85] 4.15 [1.29, 13.33] 2.32 [0.59, 9.05] 8.25 [0.90, 75.26] 2.28 [0.22, 23.71] 0.68 [0.03, 17.80] 1.51 [0.07, 32.43] 1.88 [0.40, 8.74] 5.12 [0.20, 130.38] 1.48 [0.64, 3.38] 7.43 [2.83, 19.51] 0.38 [0.02, 8.45] 0.45 [0.10, 1.95] 0.09 [0.00, 1.99] 0.10 [0.00, 2.55] 1.88 [0.44, 8.00] 18.14 [0.90, 34.72] 6.17 [1.01, 37.87] 7.62 [0.77, 75.63] 2.00 [0.53, 7.54] 1.60 [0.26, 9.74] 2.01 [0.8, 51.70] 3.45 [0.21, 56.85] 0.34 [0.01, 8.59] 1.18 [0.11, 24.2] 17.77 [0.82, 382.97] 0.92 [0.04, 23.34] 	
Total events Heterogeneity: Tau [#] = C Test for overall effect Z 3.1.7 Malignancy Aggarwal S Cai Q Chen Q Chen X Colaneri M Feng Y Guan WJ He R Hong KS Huang C Huang R Lei S Li S Li X Liang W Liu J Lodigiani C Lv Z Lyu P Pan L Pereira MR Shi Y Wan S Wang D Wu J Xie J Xiong F Yang P Yang Y Yang Y Yang S Zheng S Zhou Y	0.41; Chi ^P (= 4.86 (l 2 2 2 2 1 4 7 3 4 1 4 7 3 4 1 0 0 5 1 1 4 7 0 0 0 0 0 4 3 2 0 0 4 3 2 2 1 1 7 7 0 0 1 4 7 7 1 1 4 7 7 1 1 4 7 1 1 4 7 1 1 4 7 1 7 1	= 56.81, P < 0.000 8 58 43 27 17 124 173 69 13 13 23 15 26 269 131 13 61 239 37 27 49 40 36 83 37 27 49 40 36 83 34 30 68 34 30 68 34 30 68 34 30 68 34 30 68 34 30 68 34 30 68 34 30 68 34 30 68 34 30 37 37 39 37 37 37 37 37 39 37 37 37 37 37 37 37 39 37 37 37 37 37 37 37 37 37 37 37 37 37	, df = 38 101) 1 2 1 1 2 5 7 1 2 5 7 1 2 5 7 1 3 1 2 4 0 10 11 2 2 3 1 2 4 0 10 11 2 5 7 1 3 1 2 4 0 10 11 2 5 7 1 3 1 2 5 7 1 3 1 2 5 7 1 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 1 2 5 7 7 1 3 2 2 2 1 1 2 2 2 1 1 2 2 2 1 1 2 2 2 1 1 2 2 2 1 1 2 2 2 1 1 2 2 2 1 1 2 2 2 1 1 2 2 1 1 2 2 2 1 1 2 2 1 1 2 2 1 1 2 2 1 1 5 7 1 3 1 2 2 1 1 5 7 1 3 1 2 2 1 1 5 7 1 1 2 2 1 1 5 7 1 1 2 2 1 1 5 7 1 1 2 2 1 1 5 7 1 1 5 7 1 1 2 2 1 1 6 3 0 1 1 5 1 1 5 1 1 5 1 1 5 1 1 5 1 1 5 1 1 1 5 1 1 1 5 1 1 1 1 5 1 1 1 1 5 1 1 1 1 1 1 1 1 1 1 1 1 1	(P = 0.03 8 240 102 21 27 352 85 28 179 1459 27 327 327 1459 27 327 1459 27 327 1459 27 327 101 66 63 438 95 102 102 102 105 12 66 63 438 95 102 102 102 105 1459 102 102 105 1459 102 105 105 105 105 105 105 105 105); * = 339 0.2% 0.2% 0.3% 0.4% 0.4% 0.2% 0.4% 0.1% 0.4% 0.1% 0.4% 0.1% 0.4% 0.1% 0.4% 0.1% 0.4% 0.1% 0.3% 0.3% 0.2% 0.1% 0.3% 0.2% 0.1% 0.3% 0.2% 0.1% 0.3% 0.2% 0.1% 0.1% 0.3% 0.1% 0.1% 0.3% 0.1% 0.1% 0.1% 0.1% 0.2% 0.1% 0.1% 0.1% 0.1% 0.1% 0.1% 0.1% 0.1	 2.33 [0.17, 32.58] 4.25 [0.59, 30.83] 4.93 [0.43, 55.84] 0.77 [0.05, 13.07] 3.85 [0.62, 23.85] 4.15 [1.29, 13.33] 2.32 [0.59, 9.05] 8.25 [0.90, 75.26] 2.28 [0.22, 23.71] 0.68 [0.31, 17.80] 1.51 [0.07, 32.43] 1.88 [0.40, 8.74] 5.12 [0.20, 130.36] 1.48 [0.64, 3.38] 7.43 [2.83, 19.51] 0.38 [0.02, 8.45] 0.45 [0.10, 1.95] 0.68 [0.44, 8.00] 18.14 [0.90, 364.27] 6.17 [1.01, 37.87] 7.62 [0.77, 75.63] 2.00 [0.53, 7.54] 1.60 [0.26, 9.74] 2.01 [0.8, 51.70] 3.45 [0.21, 56.85] 0.34 [0.01, 8.59] 1.18 [0.11, 12.42] 17.77 [0.82, 382.97] 0.92 [0.04, 23.34] 2.47 [0.10, 61.62] 2.32 [1.63, 3.32] 	

Heterogeneity: Tau² = 0.09; Chi² = 34.10, df = 31 (P = 0.32); l² = 9% Test for overall effect: Z = 4.64 (P < 0.00001)

Figure 8. (continued).

							1
3.1.8 Chronic kidney di	sease						
Aggarwal S	3	8	3	8	0.2%	1.00 [0.13, 7.57]	
Chen Q	1	43	2	102	0.2%	1.19 [0.11, 13.49]	
Feng Y	2	124	2	352	0.2%	2.87 [0.40, 20.59]	
Ferguson J	2	21	7	51	0.3%	0.66 [0.13, 3.48]	
Guan WJ	3	173	5	926	0.4%	3.25 [0.77, 13.73]	
Ketcham SW	4	6	7	7	0.1%	0.12 [0.00, 3.11]	+
Lei S	1	15	0	19	0.1%	4.03 [0.15, 106.36]	
Li X	6	269	4	279	0.4%	1.57 [0.44, 5.62]	
Liang W	6	131	15	1459	0.6%	4.62 [1.76, 12.12]	- 184
Lodigiani C	9	61	52	327	0.7%	0.92 [0.43, 1.97]	
Pereira MR	19	27	38	63	0.6%	1.56 [0.59, 4.11]	
Shi Y	2	49	5	438	0.3%	3.69 [0.70, 19.52]	
Sun L	1	15	0	40	0.1%	8.38 [0.32, 217.48]	
Wang D	2	36	2	102	0.2%	2.94 [0.40, 21.69]	
Wu J	2	83	1	197	0.2%	4.84 [0.43, 54.12]	
Yang AP	8	24	2	69	0.3%	16.75 [3.24, 86.58]	
Yang P	66	68	65	65	0.1%	0.20 [0.01, 4.31]	
Yang Y	2	36	0	14	0.1%	2.10 [0.09, 46.54]	
Zhang JJ	2	58	0	82	0.1%	7.30 [0.34, 154.96]	
Zheng S	1	74	0	22	0.1%	0.92 [0.04, 23.34]	
Zhou Y	3	43	1	323	0.2%	24.15 [2.45, 237.74]	•
Subtotal (95% CI)		1364		4945	5.7%	2.27 [1.41, 3.65]	-
Total events	145		211				
Heterogeneity: Tau ² = 0.				(P = 0.0)	3); I² = 329	6	
Test for overall effect: Z	= 3.37 (P = 0.000	7)				
3.1.9 Chronic liver dise	260						
		60	20		0.00	4 70 10 70 4 001	· · · · · · · · · · · · · · · · · · ·
Cai Q	8	58	20	240	0.6%	1.76 [0.73, 4.22]	
Chen Q Colonori M	4 1	43	2	102 27	0.3%	5.13 [0.90, 29.14]	
Colaneri M Cuon Wil	1	17	1		0.1%	1.63 [0.09, 27.84]	
Guan WJ He R	0	173 69	22 2	926 135	0.2% 0.1%	0.24 [0.03, 1.78]	
Hong KS	0	13	1	85	0.1%	0.38 [0.02, 8.11] 2.09 [0.08, 53.90]	
Huang Q	0	3	4	51	0.1%	1.51 [0.07, 34.04]	
Huang R	0	23	4	179	0.1%	0.83 [0.04, 15.91]	
Jiang Y	Ő	8	2	52	0.1%	1.19 [0.05, 26.97]	
LiS	3	26	õ	43	0.1%	12.96 [0.64, 261.66]	
LIX	2	269	3	279	0.3%	0.69 [0.11, 4.16]	
Liang W	3	131	25	1459	0.5%	1.34 [0.40, 4.51]	
ShiY	2	49	20	438	0.4%	0.89 [0.20, 3.92]	
Sun L	2	15	1	40	0.2%	6.00 [0.50, 71.73]	
Wan S	1	40	1	95	0.1%	2.41 [0.15, 39.51]	
Wu J	4	83	3	197	0.4%	3.27 [0.72, 14.97]	
Xie J	0	34	1	22	0.1%	0.21 [0.01, 5.33]	←
Xiong F	4	30	10	101	0.5%	1.40 [0.41, 4.83]	<u> </u>
Yang AP	8	24	16	69	0.6%	1.66 [0.60, 4.58]	
Yang P	68	68	64	65	0.1%	3.19 [0.13, 79.63]	
Yang Y	2	36	0	14	0.1%	2.10 [0.09, 46.54]	
Yao Q	1	25	1	83	0.1%	3.42 [0.21, 56.69]	
Zhang JJ	4	58	4	82	0.4%	1.44 [0.35, 6.03]	
Zheng S	2	74	1	22	0.2%	0.58 [0.05, 6.75]	
Zhou Y	4	43	4	323	0.4%	8.18 [1.97, 34.02]	•
Subtotal (95% CI)		1412		5129	6.2%	1.70 [1.19, 2.42]	•
Total events	124		212				
Heterogeneity: Tau ² = 0.				(P = 0.7)	2); I² = 0%		
Test for overall effect: Z	= 2.95 (I	P = 0.003)				
Total (05% Ch		44054		10404	100.00	2 50 52 24 2 201	
Total (95% CI)		14954		49481	100.0%	2.59 [2.31, 2.89]	•
Total events	2844		4265	0.01-1		17 4000	
Heterogeneity: Tau ² = 0.				52 (INOT 6	estimable)	r = 49%	0.01 0.1 1 10 100
Test for overall effect: Z		•		0 /P - 0	10) 12 - 01	7 404	Favours [experimental] Favours [control]
Test for subgroup differ	ences. (201 = 12.	79, ui≃	0 (F = 0.	12], (*= 3	7.470	

Figure 8. (continued).

COVID-19 patients are more important to early detection and isolation as well as minimize the spread of the disease, severity, and death rate. In this meta-analysis, we retrospectively analyzed clinical data from patients with COVID-19. So, we completed a systemic meta-analysis. In this meta-analysis, we retrieved 55 independent studies from January 1, 2020, to May 24, 2020, which reported age, sex, severity, comorbidity, clinical symptoms, and different outcomes on 10014 patients with COVID-19 distributed across four countries.

In our study, we observed that males are more likely to be infected by COVID-19 and going to severe conditions (OR = 2.41, p < 0.00001) than

	Sever	e	Nonse	/ere		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
4.1.1 Fever							
Aggarwal S	8	8	7	8	0.1%	3.40 [0.12, 96.70]	
BiX	12	22	35	91	0.3%	1.92 [0.75, 4.91]	
CaiQ	53	58	165	240	0.3%	4.82 [1.85, 12.54]	
Cai Y	2	3	3	4	0.1%	0.67 [0.02, 18.06]	
Chen G	10	11	10	10	0.1%	0.33 [0.01, 9.16]	
Chen Q	39	43	70	102	0.3%	4.46 [1.47, 13.53]	
Chu J	27	43	9	11	0.2%	0.38 [0.07, 1.96]	
Colaneri M	17	17	23	27	0.1%	6.70 [0.34, 132.82]	
Deng Q	62	67	36	56	0.3%	6.89 [2.38, 19.93]	
Feng Y	113	124	277	352	0.4%	2.78 [1.42, 5.43]	
Ferguson J	16	21	37	51	0.3%	1.21 [0.37, 3.93]	
Guan WJ	82	173	391	926	0.5%	1.23 [0.89, 1.71]	
He R	56	69	90	135	0.4%	2.15 [1.07, 4.34]	
Hong KS	8	13	54	85	0.3%	0.92 [0.28, 3.05]	
Huang C	13	13	27	28	0.1%	1.47 [0.06, 38.60]	
Huang Q	3	3	38	51	0.1%	2.45 [0.12, 50.67]	
Huang R	20	23	136	179	0.3%	2.11 [0.60, 7.44]	
Jiang Y	7		36	52	0.2%	3.11 [0.35, 27.42]	
Ketcham SW	5	6	7	7	0.1%	0.24 [0.01, 7.21]	· · · · · · · · · · · · · · · · · · ·
Lei S	15	15	16	19	0.1%	6.58 [0.31, 137.91]	
LiK	22	25	50	58	0.3%	1.17 [0.28, 4.85]	
LiS	25	26	34	43	0.2%	6.62 [0.79, 55.66]	
LiX	228	269	248	279	0.4%	0.70 [0.42, 1.15]	
LiYK	220	203	15	16	0.1%	1.84 [0.07, 49.90]	
	114	131	1237	1459	0.1%		
Liang W Liu F	21	33	69	1409	0.4%		
	13	33 13	23	27		0.96 [0.43, 2.17]	
Liu J	13	13			0.1%	5.17 [0.26, 103.58]	
Liu Z		39	57	64	0.1%	2.22 [0.12, 42.45]	
Lyu P Bon J	39		11	12	0.1%	10.30 [0.39, 270.39]	
Pan L Bana XD	37	37	57	66	0.1%	12.39 [0.70, 219.29]	
Peng YD	16	16	85	96	0.1%	4.44 [0.25, 79.07]	
Pereira MR	13	27	50	63	0.3%	0.24 [0.09, 0.64]	
Sun L	13	15	32	40	0.2%	1.63 [0.30, 8.70]	
Tian S	37	46	178	216	0.4%	0.88 [0.39, 1.97]	
Wan S	34	40	86	95	0.3%	0.59 [0.20, 1.79]	
Wang D	36	36	100	102	0.1%	1.82 [0.09, 38.73]	
Wang F	14	14	12	14	0.1%	5.80 [0.25, 132.56]	
WuJ	83	83	154	197	0.1%	47.02 [2.86, 773.51]	
Xie H	24	28	32	51	0.3%	3.56 [1.07, 11.84]	
Xie J	25	34	17	22	0.3%	0.82 [0.23, 2.87]	
Xiong F	22	30	46	101	0.4%	3.29 [1.34, 8.08]	
Yang P	40	68	51	65	0.4%	0.39 [0.18, 0.84]	
Yang Y	33	36	9	14	0.2%	6.11 [1.22, 30.57]	
Yao Q	19	25	61	83	0.3%	1.14 [0.40, 3.23]	
Zhang JJ	51	58	59	82	0.4%	2.84 [1.13, 7.16]	
Zheng S	68	74	17	22	0.3%	3.33 [0.91, 12.24]	
Zhou Y	25	43	132	323	0.4%	2.01 [1.05, 3.83]	-
Subtotal (95% CI)		2003		6151	11.1%	1.68 [1.29, 2.19]	●
Total events	1637		4389				
Heterogeneity: Tau² =	: 0.34; Chi ^z	= 100.1	10, df = 46	6 (P < 0.	00001); I²	= 54%	
Test for overall effect:	Z = 3.85 (F	P = 0.00	01)				

Figure 9. Meta-analysis for the effect of clinical symptoms on the severity of COVID-19 cases. Random effect model for fever, cough, fatigue, anorexia, myalgia, dyspnea, chest tightness, sputum production, hemoptysis, pharyngalgia, diarrhea, nausea, vomiting, abdominal pain, headache, dizziness and sore throat.

females. A similar finding was also reported earlier in some other studies [78, 79]. A study conducted in Spain reported that men are more vulnerable than women because of their irresponsible attitude toward the risk of COVID-19 pandemic [80]. Another Spanish study revealed that the severity and case fatality rate (CFR) are higher in males and old aged people [81]. Moreover, a higher resistance in females is observed, which might be due to female sex hormones, whereas men have lower resistance because of high expression ACE2 receptor to which coronavirus binds easily [82]. Studies also showed that ACE2 expression, decreased B cell and NK cell-specific transcripts, male hormones, and increased NF- κ B inhibitor are responsible for the higher viral load in men [83, 84, 85]. According to the data published by Global Health 50/50 presents that men are dying at a more consistent rate than women [86].

Besides, the lifestyle of men, including smoking, leads to high viral load and high severity [87]. A systemic review and meta-analysis also suggested that current smokers are at greater risk than former or non-smokers [88]. One study reported a positive hazard ratio (HR) in the COVID-19 related deaths for current smokers (HR = 1.14, 95%Cl = 1.05-1.23) in a model adjusted for demographic age and sex, whereas a lower HR was found in a fully adjusted model (HR = 0.89, 95%Cl = 0.82-0.97) [89].

Elderly or older people in both sexes (\geq 50 years) are more susceptible to SARS-CoV-2, which may be associated with a higher frequency of severity (age \geq 50 years vs. age<50 years, RR = 3.36; 95% CI = 1.79–6.30, p = 0.0002). We did not find any significant association of age \geq 65 years with COVID-19 severity. Although we did not find any

4.1.2 Cough							
-	7	8	7	8	0.1%	1 00 00 05 10 261	
Aggarwal S Bi X	13	22	53	91	0.1%	1.00 [0.05, 19.36]	
CaiQ	27	58	78	240	0.3%	1.04 [0.40, 2.67]	
Cai Q Cai Y	1	58 3	/8	240		1.81 [1.01, 3.24]	· · · · · · · · · · · · · · · · · · ·
			з 9		0.1%	0.17 [0.01, 4.51]	,
Chen G	7	11		10	0.1%	0.19 [0.02, 2.15]	
Chen Q	38	43	80 3	102	0.3%	2.09 [0.74, 5.94]	
Chu J Colonori M	14 5	43 17	_	11 27	0.2%	1.29 [0.30, 5.61]	
Colaneri M	47	67	10		0.3%	0.71 [0.19, 2.61]	
Deng Q Form V			32	56	0.4%	1.76 [0.84, 3.71]	
Feng Y	49	124	220	352	0.5%	0.39 [0.26, 0.60]	
Ferguson J	14	21	28	51	0.3%	1.64 [0.57, 4.75]	
Guan WJ	122	173	623	926	0.5%	1.16 [0.82, 1.66]	T
He R	33	69	51	135	0.4%	1.51 [0.84, 2.71]	
Hong KS	6	13	52	85	0.3%	0.54 [0.17, 1.76]	
Huang C	11	13	20	28	0.2%	2.20 [0.40, 12.23]	
Huang Q	3	3	29	51	0.1%	5.34 [0.26, 108.70]	
Huang R	17	23	103	179	0.3%	2.09 [0.79, 5.55]	
Jiang Y	5	8	29	52	0.2%	1.32 [0.29, 6.12]	
Ketcham SW	4	6	6	7	0.1%	0.33 [0.02, 5.03]	
Lei S	9	15	9	19	0.3%	1.67 [0.42, 6.56]	
LiK	24	25	41	58	0.2%	9.95 [1.24, 79.55]	
LiS	20	26	20	43	0.3%	3.83 [1.29, 11.42]	
LiX	203	269	212	279	0.5%	0.97 [0.66, 1.44]	
LIYK	6	9	11	16	0.2%	0.91 [0.16, 5.20]	
Liang W	93	131	959	1459	0.5%	1.28 [0.86, 1.89]	<u>+-</u>
Liu F	17	33	46	107	0.4%	1.41 [0.64, 3.08]	
Liu J	11	13	22	27	0.2%	1.25 [0.21, 7.51]	
Liu Z	5	8	29	64	0.2%	2.01 [0.44, 9.14]	
Lyu P	20	39	2	12	0.2%	5.26 [1.02, 27.21]	
Peng YD	12	16	64	96	0.3%	1.50 [0.45, 5.02]	
Pereira MR	14	27	39	63	0.4%	0.66 [0.27, 1.65]	
Sun L	9	15	17	40	0.3%	2.03 [0.61, 6.79]	
Tian S	25	46	95	216	0.4%	1.52 [0.80, 2.87]	+
Wan S	35	40	67	95	0.3%	2.93 [1.04, 8.24]	
Wang D	21	36	61	102	0.4%	0.94 [0.43, 2.04]	
Wang F	12	14	11	14	0.2%	1.64 [0.23, 11.70]	
WuJ	83	83	114	197	0.1%	121.79 [7.45, 1991.48]	
Xie H	20	28	36	51	0.3%	1.04 [0.38, 2.88]	
Xie J	15	34	12	22	0.3%	0.66 [0.22, 1.93]	
Xiong F	20	30	29	101	0.4%	4.97 [2.07, 11.89]	
Yang P	29	68	39	65	0.4%	0.50 [0.25, 0.99]	
Yang Y	24	36	11	14	0.2%	0.55 [0.13, 2.33]	
Yao Q	19	25	65	83	0.3%	0.88 [0.31, 2.52]	
Zhang JJ	45	58	45	82	0.4%	2.85 [1.34, 6.06]	
Zheng S	42	74	12	22	0.3%	1.09 [0.42, 2.85]	
Zhou Y	30	43	85	323	0.4%	6.46 [3.22, 12.96]	·
Subtotal (95% CI)		1966		6085	13.6%	1.41 [1.11, 1.77]	◆
Total events	1286		3589				
Heterogeneity: Tau ² =	0.32; Chi ²	= 120.33	3, df = 49	5 (P < 0.0)0001); I ^z	= 63%	
Test for overall effect:	Z = 2.88 (F	P = 0.004)				

Figure 9. (continued).

association of age (\geq 65 years) with COVID-19 severity, the age \geq 50 years group also included some patients with \geq 65 years of age. It was thought that elderly or older people are more susceptible to severity for weak immunity and other organ dysfunction. Elderly or older people and a higher frequency of comorbidities patients are more susceptible to SARS-CoV-2 [78,90].

Among 10014 COVID-19 patients, 51.14% had at least one comorbidity in severe groups, and other most common comorbidities in severe cases are hypertension (36.47%), diabetes (21.19%), cardiovascular disease (18.76%), cerebrovascular disease (11.83%) and chronic kidney disease (10.63%). All the preexisting comorbidities are associated with the increased severity in the COVID-19 cases (p < 0.05) in our current meta-analysis. Any comorbidity is a crucial factor in poor prognosis. Diseases such as hypertension, diabetes, respiratory system disease, cardiovascular disease, and their susceptibility conditions are higher risk

of severe illness or death [78, 91, 92, 93]. Some articles also reported an association of hypertension and other cardiovascular diseases with COVID-19 [94,95]. Innate immunity response, macrophage, and lymphocyte function are decreased in the presence of comorbidities, which may be more susceptible to the pathogenesis of COVID-19 [96]. A metabolic disorder, inflammation, and infection are induced by diabetes, whereas chronic liver disease was reported to be associated with COVID-19 [97,98]. The presence of respiratory diseases develops acute respiratory distress syndromes (ARDS). Furthermore, a study reported that diabetes, smoking, and heart disease were mainly responsible for MERS-CoV illness [99]. The expression of ACE2 receptors is increased in some comorbid conditions like hypertension and diabetes, and SARS-CoV-2 attacks cells through ACE2 receptors. Therefore, comorbidities increase the severity of COVID-19 cases [90].

							I
4.1.3 Fatigue							
Aggarwal S	5	8	3	8	0.2%	2.78 [0.37, 21.03]	
Cai Q	3	58	10	240	0.3%	1.25 [0.33, 4.71]	
Cai Y	0	3	2	4	0.1%	0.14 [0.00, 4.47] 🕈	· · · · · · · · · · · · · · · · · · ·
Chen G	10	11	7	10	0.1%	4.29 [0.37, 50.20]	
Chen Q	21	43	38	102	0.4%	1.61 [0.78, 3.30]	
Chu J	5	43	4	11	0.2%	0.23 [0.05, 1.08]	
Colaneri M	0	17	2	27	0.1%	0.29 [0.01, 6.45]	
Ferguson J	5	21	21	51	0.3%	0.45 [0.14, 1.41]	
Guan WJ	69	173	350	926	0.5%	1.09 [0.78, 1.52]	
He R	13	69	33	135	0.4%	0.72 [0.35, 1.47]	
Huang C Huang Q	7	13 3	11 22	28 51	0.3%	1.80 [0.48, 6.81]	
-	3 7	23	37	179	0.1% 0.3%	9.18 [0.45, 186.85]	
Huang R Ketcham SW	4	23	12	52	0.3%	1.68 [0.64, 4.38] 3.33 [0.72, 15.37]	
Lei S	12	15	13	19	0.2%	1.85 [0.38, 9.08]	
LiS	14	26	12	43	0.2%	3.01 [1.09, 8.35]	
LiX	130	269	128	279	0.5%	1.10 [0.79, 1.54]	
LIYK	4	203	13	16	0.2%	0.18 [0.03, 1.14]	
Liang W	45	131	539	1459	0.5%	0.89 [0.61, 1.30]	
Liu F	10	33	11	107	0.3%	3.79 [1.44, 10.01]	<u> </u>
Liu J	8	13	14	27	0.3%	1.49 [0.39, 5.72]	
Liu Z	1	.0		64	0.1%	0.87 [0.10, 7.96]	
Lyu P	12	39	5	12	0.3%	0.62 [0.16, 2.36]	
PanL	26	37	28	66	0.4%	3.21 [1.36, 7.56]	
Peng YD	9	16	62	96	0.3%	0.71 [0.24, 2.06]	
Pereira MR	5	27	20	63	0.3%	0.49 [0.16, 1.48]	
Sun L	4	15	10	40	0.3%	1.09 [0.28, 4.21]	
Tian S	15	46	54	216	0.4%	1.45 [0.73, 2.89]	
Wan S	19	40	25	95	0.4%	2.53 [1.17, 5.47]	
Wang D	29	36	67	102	0.4%	2.16 [0.86, 5.44]	
Wang F	10	14	8	14	0.2%	1.88 [0.39, 9.01]	
Xie J	7	34	9	22	0.3%	0.37 [0.11, 1.23]	
Xiong F	18	30	41	101	0.4%	2.20 [0.96, 5.04]	<u> </u>
Yao Q	8	25	20	83	0.3%	1.48 [0.56, 3.95]	
Zhang JJ	39	58	51	82	0.4%	1.25 [0.62, 2.53]	
Zheng S	8	74	1	22	0.2%	2.55 [0.30, 21.55]	
Zhou Y	2	43	24	323	0.2%	0.61 [0.14, 2.67]	
Subtotal (95% CI)		1531		5175	10.6%	1.26 [1.03, 1.55]	•
Total events	587		1716				
Heterogeneity: Tau ² = 0			df = 36	(P = 0.02	2); I² = 36%		
Test for overall effect: Z	= 2.22 (F	P = 0.03)					
4.1.4 Anorexia							
Chen G	26	12	26	400	0.40	2 00 14 25 5 04	
	26	43	36	102	0.4%	2.80 [1.35, 5.84]	
He R	5	69	7	135	0.3%	1.43 [0.44, 4.68]	
Huang Q	1	3	12	51	0.1%	1.63 [0.14, 19.52]	
Lei S Cum I	3	15	2	19	0.2%	2.13 [0.31, 14.73]	
Sun L	3	15	4	40	0.2%	2.25 [0.44, 11.52]	
Wang D Wang E	24	36	31	102	0.4%	4.58 [2.04, 10.31]	
Wang F Zhang JJ	9 8	14 58	8 9	14 82	0.2% 0.3%	1.35 [0.29, 6.18] 1.30 [0.47, 3.59]	
Subtotal (95% CI)	0	253	9	545	0.3% 2.1%	2.38 [1.60, 3.54]	•
Total events	79	200	109	040	2.17/0	F100 [1100] 0104]	•
Heterogeneity: Tau ² = 0		= 5.41 o		= 0.61)	I² = 0%		
Test for overall effect: Z				0.01),	0.0		
. Serier ereran eneor. 2	4.20 (0.000	.,				

Figure 9. (continued).

We summarized 17 clinical symptoms in our meta-analysis among them we found the significant association of fever (81.73%, OR = 1.68, p = 0.0001), cough (65.41%, OR-1.41, p = 0.004), fatigue (38.34%, OR = 1.26, p = 0.03), anorexia (31.23%, OR = 2.38, p < 0.0001), dyspnea (51.50%, OR = 4.30, p < 0.00001), chest tightness (25.62%, OR = 2.11, p = 0.002), hemoptysis (3.17%, OR = 4.93, p < 0.0001), diarrhea (18.35%, OR = 1.35, p = 0.03), abdominal pain (5.48%, OR = 2.38, p = 0.008) with the severity of COVID-19 cases.

We observed no association of COVID-19 severity with myalgia (24.91%, OR = 1.30, p = 0.07), sputum production (35.10%, OR = 1.35, p = 0.05), pharyngalgia (12.12%, OR = 0.91, p = 0.87), nausea (8.27%,

OR = 1.26, p = 0.64), vomiting (6.53%, OR = 1.48, p = 0.07), headache (16.20%, OR = 1.19, p = 0.34), dizziness (12.26%, OR = 1.40, p = 0.17), and sore throat (13.78%, OR = 1.60, p = 0.12). SARS-CoV-2 binds with the ACE-2 receptor, causing diffuse alveolar damage and lymphocytic infiltration in both lungs and may cause several respiratory tract symptoms [100]. Several clinical researchers found that the common clinical manifestations of COVID-19 patients are fever, cough, headache, fatigue, myalgia, nausea, diarrhea, and sputum [101]. Diarrhea has been found in the Middle East respiratory syndrome coronavirus (MERS-COV) patients (up to 30%) [102]. A recent study showed that SARS-CoV-2 was detected in stool samples of patients with abdominal symptoms [103]. There also

4.1.5 Myalgia							
CaiY	1	3	1	4	0.1%	1.50 [0.06, 40.63]	
Chen G	5	11	3	10	0.2%	1.94 [0.32, 11.76]	
	7	43	13	102			
Chen Q					0.3%	1.33 [0.49, 3.61]	
Chu J	2	43	1	11	0.1%	0.49 [0.04, 5.93]	
Feng Y	17	124	38	352	0.4%	1.31 [0.71, 2.42]	
Ferguson J	13	21	19	51	0.3%	2.74 [0.96, 7.80]	
Guan WJ	30	173	134	926	0.5%	1.24 [0.80, 1.91]	
He R	6	69	14	135	0.3%	0.82 [0.30, 2.25]	
Hong KS	3	13	34	85	0.3%	0.45 [0.12, 1.76]	
	7						
Huang C		13	11	28	0.3%	1.80 [0.48, 6.81]	
Huang Q	3	3	6	51	0.1%	49.00 [2.26, 1060.89]	
Huang R	3	23	18	179	0.3%	1.34 [0.36, 4.96]	
_ei S	6	15	5	19	0.2%	1.87 [0.44, 7.98]	
ικ	5	25	10	58	0.3%	1.20 [0.36, 3.96]	
Li S	14	26	12	43	0.3%	3.01 [1.09, 8.35]	
JX	49	269	62	279	0.5%	0.78 [0.51, 1.19]	
.i YK	4	9	13	16	0.2%	0.18 [0.03, 1.14]	
iang W	19	131	215	1459	0.4%	0.98 [0.59, 1.63]	
Liu F	4	33	9	107	0.3%		
						1.50 [0.43, 5.23]	
.iu J	8	13	7	27	0.3%	4.57 [1.12, 18.73]	
.iu Z	1	8	6	64	0.1%	1.38 [0.14, 13.20]	
Pan L	7	37	8	66	0.3%	1.69 [0.56, 5.11]	
eng YD	9	16	62	96	0.3%	0.71 [0.24, 2.06]	
		27	18	63	0.3%		
ereira MR	4					0.43 [0.13, 1.44]	
lun L	3	15	7	40	0.2%	1.18 [0.26, 5.31]	
Van S	19	40	25	95	0.4%	2.53 [1.17, 5.47]	———
Vang D	12	36	36	102	0.4%	0.92 [0.41, 2.05]	
VuJ	43	83	28	197	0.4%	6.49 [3.61, 11.68]	
(ie J	3	34	1	22	0.1%	2.03 [0.20, 20.89]	
′ang P	48	68	57	65	0.4%	0.34 [0.14, 0.83]	
′ang Y	22	36	5	14	0.3%	2.83 [0.78, 10.20]	
′ao Q	8	25	20	83	0.3%	1.48 [0.56, 3.95]	
Theng S	13	74	6	22	0.3%	0.57 [0.19, 1.73]	
lhou Y	1	43	13	323	0.2%		
			15			0.57 [0.07, 4.45]	
Subtotal (95% CI) Fotal events	399	1602	917	5194	9.7%	1.30 [0.98, 1.71]	
			df= 33	(P < 0.00	01), F=		
Fest for overall effect:			df= 33	(P < 0.00	01), F=		
Heterogeneity: Tau ² = Fest for overall effect: I.1.6 Dyspnea Aggarwal S	Z = 1.83 (F	P = 0.07)	6	8	0.1%	2.33 [0.17, 32.58]	
Test for overall effect: .1.6 Dyspnea Juggarwal S Cai Y	Z = 1.83 (F 7 0	P = 0.07) 8 3	6 0	8	0.1%	2.33 [0.17, 32.58] Not estimable	
Test for overall effect: .1.6 Dyspnea Juggarwal S Sai Y Shen G	Z = 1.83 (F 7 0 11	P = 0.07) 8 3 11	6 0 0	8 4 10	0.1%	2.33 (0.17, 32.58) Not estimable 483.00 (8.77, 26588.24)	
Test for overall effect: .1.6 Dyspnea Juggarwal S Sai Y Shen G	Z = 1.83 (F 7 0 11 3	P = 0.07) 8 3	6 0	8	0.1%	2.33 [0.17, 32.58] Not estimable	
Test for overall effect: .1.6 Dyspnea Joggarwal S Sai Y Shen G Shen Q	Z = 1.83 (F 7 0 11	P = 0.07) 8 3 11	6 0 0	8 4 10	0.1%	2.33 (0.17, 32.58) Not estimable 483.00 (8.77, 26588.24)	
Test for overall effect: .1.6 Dyspnea Joggarwal S Sai Y Shen G Shen Q Shu J	Z = 1.83 (F 7 0 11 3 2	P = 0.07) 8 3 11 43 43 43	6 0 0 3	8 4 10 102 11	0.1% 0.1% 0.1% 0.2%	2.33 [0.17, 32.58] Notestimable 483.00 [8.77, 26588, 24] 17.72 [0.89, 350.68] 0.13 [0.02, 0.91]	
Test for overall effect: .1.6 Dyspnea (ggarwal S cai Y chen G chen Q chu J colaneri M	Z = 1.83 (F 7 0 11 3 2 4	P = 0.07) 8 3 11 43 43 43 17	6 0 0 3 6	8 4 10 102 11 27	0.1% 0.1% 0.1% 0.2% 0.2%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55]	
est for overall effect: .1.6 Dyspnea ggarwal S sal Y chen G chen Q chu J colaneri M beng Q	Z = 1.83 (F 7 0 11 3 2 4 50	P = 0.07) 8 3 11 43 43 17 67	6 0 0 3 6 13	8 4 10 102 11 27 56	0.1% 0.1% 0.2% 0.2% 0.4%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen Q shu J solaneri M solaneri M song Q eng Y	Z = 1.83 (F 7 0 11 3 2 4 50 59	P = 0.07) 8 3 11 43 43 17 67 124	6 0 0 3 6 13 50	8 4 10 102 11 27 56 352	0.1% 0.1% 0.2% 0.2% 0.4% 0.5%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.88, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen Q shu J solaneri M solaneri M song Q eng Y	Z = 1.83 (F 7 0 11 3 2 4 50	P = 0.07) 8 3 11 43 43 17 67	6 0 0 3 6 13	8 4 10 102 11 27 56	0.1% 0.1% 0.2% 0.2% 0.4%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29]	
est for overall effect: .1.6 Dyspnea ggarwal S cai Y chen G chen Q chu J colaneri M beng Q eng Y erguson J	Z = 1.83 (F 7 0 11 3 2 4 50 59	P = 0.07) 8 3 11 43 43 17 67 124	6 0 0 3 6 13 50	8 4 10 102 11 27 56 352	0.1% 0.1% 0.2% 0.2% 0.4% 0.5%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82]	
Test for overall effect: I.1.6 Dyspnea Iggarwal S Sai Y Shen G Shen Q Shan J Solaneri M Jeng Q Gerguson J Suan WJ	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65	P = 0.07) 8 3 11 43 43 17 67 124 21 173	6 0 3 6 13 50 29 140	8 4 10 102 11 27 56 352 51 926	0.1% 0.1% 0.2% 0.2% 0.4% 0.5% 0.3% 0.5%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.26, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83]	
est for overall effect: .1.6 Dyspnea .ggarwal S .ai Y .hen G .hen Q .hu J .olaneri M .beng Q .eng Y .erguson J .uan WJ .erg	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49	P = 0.07) 8 3 11 43 43 17 67 124 21 173 69	6 0 3 6 13 50 29 140 21	8 4 10 102 11 27 56 352 51 926 135	0.1% 0.1% 0.2% 0.2% 0.4% 0.5% 0.3% 0.5% 0.4%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 13.30 [6.62, 26.73]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen G shen Q shau J olaneri M beng Q eng Y erguson J suan WJ le R long KS	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8	P = 0.07) 8 3 11 43 43 17 67 124 21 173 69 13	6 0 3 13 50 29 140 21 24	8 4 100 102 11 27 56 352 51 926 135 85	0.1% 0.1% 0.2% 0.2% 0.5% 0.5% 0.3% 0.5% 0.3%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.669] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 1.330 [6.62, 26.73] 4.07 [1.21, 13.68]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y Shen G Shen Q Solaneri M Jolaneri M Jeng Q eng Y erguson J Juan WJ le R tong KS tuang C	Z = 1.83 (F 7 0 11 3 2 4 4 50 59 12 65 49 8 8 12	P = 0.07) 8 3 11 43 43 17 67 124 21 173 69 13 13	6 0 3 13 50 29 140 21 24 10	8 4 100 102 11 27 56 352 51 926 135 85 28	0.1% 0.1% 0.2% 0.2% 0.4% 0.5% 0.5% 0.3% 0.5% 0.4% 0.3% 0.1%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 13.30 [6.62, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y Shen G Shen Q Solaneri M Jolaneri M Jeng Q eng Y erguson J Juan WJ le R tong KS tuang C	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8 8 12 85 49 8 12 1	P = 0.07) 8 3 11 43 43 43 17 67 124 21 173 69 13 13 13 3	6 0 3 13 50 29 140 21 24	8 4 10 102 11 27 56 352 51 926 135 85 28 51	0.1% 0.1% 0.2% 0.2% 0.5% 0.5% 0.3% 0.5% 0.3%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.669] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 1.330 [6.62, 26.73] 4.07 [1.21, 13.68]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen Q shu J solaneri M eng Q erg y erg y erg y la an WJ le R long KS luang C luang Q	Z = 1.83 (F 7 0 11 3 2 4 4 50 59 12 65 49 8 8 12	P = 0.07) 8 3 11 43 43 17 67 124 21 173 69 13 13	6 0 3 13 50 29 140 21 24 10	8 4 100 102 11 27 56 352 51 926 135 85 28	0.1% 0.1% 0.2% 0.2% 0.4% 0.5% 0.5% 0.3% 0.5% 0.4% 0.3% 0.1%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 13.30 [6.62, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38]	
est for overall effect: .1.6 Dyspnea ggarwal S ai Y chen G chen G chu J colaneri M veng Q eng Y erguson J avan WJ le R long KS luang C luang Q luang R	Z = 1.83 (F 7 0 111 3 2 4 50 59 12 65 65 49 8 12 12 12 12 65 6 59	P = 0.07) 8 3 11 43 43 17 67 124 21 173 69 13 13 13 3 23	6 0 3 6 13 50 29 140 21 24 10 4 3	8 4 100 102 11 27 56 352 51 926 135 85 28 51 179	0.1% 0.1% 0.2% 0.2% 0.4% 0.5% 0.3% 0.5% 0.4% 0.1% 0.1% 0.3%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.88, 350.68] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen Q shen Q eng Y erguson J suan WJ te R long KS tuang C tuang Q tuang R (etcham SW	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 1 65 6 6	P = 0.07) 8 3 11 43 43 17 67 124 21 173 69 13 13 13 3 23 6	6 0 3 6 13 50 29 140 21 24 10 4 13 5	8 4 100 102 11 27 56 352 51 926 135 85 28 51 179 7	0.1% 0.1% 0.2% 0.2% 0.4% 0.3% 0.5% 0.4% 0.3% 0.1% 0.3% 0.1%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.669] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 13.30 [6.62, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 5.91 [0.23, 151.15]	
est for overall effect: .1.6 Dyspnea ggarwal S sal Y then G then Q then Q then Q eng Y erguson J tean WJ le R tolong KS tuang C tuang R tuang R tuang R	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8 8 12 1 6 6 9	P = 0.07) 8 3 11 43 43 43 17 67 124 21 173 69 13 13 13 3 23 6 15	6 0 3 6 13 50 29 140 24 10 4 13 5 6	8 4 10 102 11 27 56 352 51 926 135 85 28 51 135 28 51 179 7 7 19	0.1% 0.1% 0.2% 0.2% 0.4% 0.3% 0.5% 0.3% 0.3% 0.1% 0.1% 0.1% 0.1%	2.33 [0.17, 32,58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 282] 3.38 [2.37, 4.83] 13.30 [6.62, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 5.91 [0.23, 151.15] 3.25 [0.79, 13.38]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen Q shu J solaneri M eng Q erg V erg V erg V erg V erg S loan WJ le R loan KS luang C luang R luang R luang R luang R letham SW ei S	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 85 49 85 49 8 2 1 6 6 9 7 7	P = 0.07) 8 3 11 43 43 43 17 67 124 21 173 67 124 21 173 13 13 13 3 23 6 15 25	6 0 0 3 50 29 140 21 24 10 4 13 5 6 2	8 4 10 102 11 27 56 352 51 926 135 85 28 51 179 7 7 19 58	0.1% 0.1% 0.2% 0.2% 0.4% 0.5% 0.3% 0.3% 0.3% 0.1% 0.1% 0.3% 0.3% 0.3%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 22, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191 38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 5.91 [0.23, 151.16] 3.25 [0.79, 13.38] 10.89 [2.07, 57.20]	
est for overall effect: .1.6 Dyspnea ggarwal S ai Y chen G chen G chen Q colaneri M veng Q eng Y erguson J uan WJ le R long KS luang C luang Q luang R luang R luang R luang R luang S luang	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 85 49 12 85 49 8 12 1 6 8 12 16 6 9 7 7 7	P = 0.07) 8 3 11 43 43 17 67 124 21 173 69 13 13 13 13 3 23 6 15 25 26	6 0 3 6 13 50 21 21 24 13 5 6 2 1	8 4 10 102 27 56 352 926 135 85 28 51 179 7 19 58 43	0.1% 0.1% 0.2% 0.4% 0.5% 0.5% 0.5% 0.5% 0.4% 0.3% 0.1% 0.1% 0.1% 0.2%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.68] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 1.330 [6.62, 26, 7.3] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 5.91 [0.23, 151.15] 3.25 [0.79, 13.38] 10.98 [2.07, 57, 20] 15.47 [1.78, 134.74]	
est for overall effect: .1.6 Dyspnea ggarwal S ai Y chen G chen G chen Q colaneri M veng Q eng Y erguson J uan WJ le R long KS luang C luang Q luang R luang R luang R luang R luang S luang	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 85 49 85 49 8 2 1 6 6 9 7 7	P = 0.07) 8 3 11 43 43 43 17 67 124 21 173 67 124 21 173 13 13 13 3 23 6 15 25	6 0 0 3 50 29 140 21 24 10 4 13 5 6 2	8 4 10 102 11 27 56 352 51 926 135 85 28 51 179 7 7 19 58	0.1% 0.1% 0.2% 0.2% 0.4% 0.5% 0.3% 0.3% 0.3% 0.1% 0.1% 0.3% 0.3% 0.3%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 22, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191 38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 5.91 [0.23, 151.16] 3.25 [0.79, 13.38] 10.89 [2.07, 57.20]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen Q binon G binon M eng Q erguson J suan WJ le R long KS luang C luang C luang R etcham SW ei S i K	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 1 6 6 9 7 7 7 198	P = 0.07) 8 3 11 43 43 17 67 124 21 173 69 13 13 3 23 6 15 25 26 269	6 0 3 6 13 50 29 140 21 24 10 4 13 5 6 2 1 112	8 4 100 102 111 27 56 352 51 926 135 85 28 51 179 58 51 179 54 32 279	0.1% 0.1% 0.2% 0.4% 0.5% 0.4% 0.3% 0.4% 0.3% 0.4% 0.3% 0.1% 0.3% 0.3% 0.3% 0.2% 0.2%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 13.30 [6.62, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 10.89 [2.07, 57.20] 15.47 [1.78, 134.74] 4.16 [2.90, 5.97]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y Shen G Shen Q Shen Q Solaneri M Jeng Q eng Y erguson J Solan WJ le R Hong K Solang C Huang C Huang R Getcham SW el S J K j K	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8 2 65 49 8 12 6 5 9 7 7 7 7 8 8	P = 0.07) 8 3 11 43 17 67 124 21 173 69 13 13 3 23 6 15 26 269 9	6 0 3 6 13 29 140 21 4 10 4 13 5 6 2 12 11 21 2	8 4 100 102 111 27 56 352 51 926 135 28 51 179 28 51 179 58 43 279 28 43 279 16	0.1% 0.1% 0.2% 0.2% 0.4% 0.3% 0.5% 0.4% 0.3% 0.1% 0.1% 0.3% 0.2% 0.2% 0.2% 0.1%	2.33 [0.17, 32,58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22,29] 5.48 [3.45, 8.70] 1.01 [0.36, 282] 3.38 [2.37, 4.83] 13.30 [6.62, 26,73] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79,77] 4.51 [1.52, 13.38] 5.91 [0.23, 151.15] 3.25 [0.79, 13.38] 10.89 [2.07, 57,20] 15.47 [1.78, 13.474] 4.16 [2.90, 597] 2.67 [0.25, 28,44]	
est for overall effect: .1.6 Dyspnea ggarwal S ai Y chen G chen G chen G chen Q colaneri M veng Q eng Y erguson J erguson J erguson J erguson J erguson J erguson J itang C luang C luang C luang C luang C luang R detcham SW ei S i K i K i X i X i X i X i X i X i X	Z = 1.83 (f 7 0 111 3 2 4 50 59 12 65 49 8 12 65 8 12 1 6 6 9 7 7 198 8 74	P = 0.07) 8 3 11 43 43 43 43 17 124 21 173 69 13 13 23 6 15 26 26 26 26 9 131	6 0 0 3 6 13 50 29 140 21 24 13 5 6 2 1 12 24 13 5 7 24 13 257	8 4 100 102 11 276 352 51 926 135 85 28 915 85 28 51 179 7 7 58 43 279 58 43 2716 1459	0.1% 0.1% 0.2% 0.2% 0.5% 0.3% 0.3% 0.4% 0.3% 0.1% 0.3% 0.1% 0.3% 0.2% 0.2% 0.2% 0.5%	$\begin{array}{c} 2.33 \ [0.17, \ 32.58] \\ \text{Not estimable} \\ 483.00 \ [8.77, \ 26588, 24] \\ 17.72 \ [0.88, \ 350.68] \\ 0.13 \ [0.02, \ 0.91] \\ 1.08 \ [0.25, \ 4.55] \\ 9.73 \ [4.25, \ 22.29] \\ 5.48 \ [3.45, \ 8.70] \\ 1.01 \ [0.36, \ 2.82] \\ 3.38 \ [2.37, \ 4.83] \\ 1.30 \ [6.62, \ 26, \ 7.3] \\ 4.07 \ [1.21, \ 13.68] \\ 21.60 \ [2.44, \ 191.38] \\ 5.88 \ [0.43, \ 79, \ 77] \\ 4.51 \ [1.52, \ 13.38] \\ 5.91 \ [0.23, \ 151.15] \\ 3.25 \ [0.79, \ 13.38] \\ 10.98 \ [2.07, \ 57, \ 20] \\ 15.47 \ [1.78, \ 134.74] \\ 4.16 \ [2.59, \ 4.41] \\ 4.60 \ [5.47, \ 4.18, \ 8.80] \end{array}$	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y ichen G ichen G ichen Q eng Y erguson J ican WJ le R long KS luang C luang C luang Q luang R letcham SW ei S i K i S i K i S i X i y K iang W iu F	Z = 1.83 (f 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 1 6 6 9 7 7 198 8 74 198 8 74 6	P = 0.07) 8 3 11 43 43 17 67 124 21 173 6 13 13 13 13 3 26 15 26 269 9 131 33	6 0 3 6 130 29 140 24 10 4 13 5 6 2 1 112 122 7 3	8 4 100 111 27 56 352 51 926 135 28 51 926 145 28 51 179 7 19 8 43 279 16 1459 107	0.1% 0.1% 0.2% 0.2% 0.5% 0.5% 0.5% 0.3% 0.1% 0.3% 0.1% 0.3% 0.3% 0.2% 0.2%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.669] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 5.91 [0.23, 151.15] 3.25 [0.79, 13.38] 10.89 [2.07, 57.20] 15.47 [1.78, 134.74] 4.16 [2.90, 5.97] 2.67 [0.25, 28.44] 6.07 [4.19, 880] 7.70 [1.81, 32.81]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y ichen G ichen G ichen Q eng Y erguson J ican WJ le R long KS luang C luang C luang Q luang R letcham SW ei S i K i S i K i S i X i y K iang W iu F	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 1 6 6 9 7 7 198 8 74 6 0	P = 0.07) 8 3 11 43 17 67 124 21 173 69 13 13 3 25 26 269 9 131 33 13 13	6 0 0 3 6 13 50 29 140 21 24 13 5 6 2 1 12 24 13 5 7 24 13 257	8 4 100 102 11 276 352 51 926 135 85 28 915 85 28 51 179 7 7 58 43 279 58 43 2716 1459	0.1% 0.1% 0.2% 0.2% 0.5% 0.3% 0.3% 0.4% 0.3% 0.1% 0.3% 0.1% 0.3% 0.2% 0.2% 0.2% 0.5%	$\begin{array}{c} 2.33 \ [0.17, \ 32.58] \\ \text{Not estimable} \\ 483.00 \ [8.77, \ 26588, 24] \\ 17.72 \ [0.88, \ 350.68] \\ 0.13 \ [0.02, \ 0.91] \\ 1.08 \ [0.25, \ 4.55] \\ 9.73 \ [4.25, \ 22.29] \\ 5.48 \ [3.45, \ 8.70] \\ 1.01 \ [0.36, \ 2.82] \\ 3.38 \ [2.37, \ 4.83] \\ 1.30 \ [6.62, \ 26, \ 7.3] \\ 4.07 \ [1.21, \ 13.68] \\ 21.60 \ [2.44, \ 191.38] \\ 5.88 \ [0.43, \ 79, \ 77] \\ 4.51 \ [1.52, \ 13.38] \\ 5.91 \ [0.23, \ 151.15] \\ 3.25 \ [0.79, \ 13.38] \\ 10.98 \ [2.07, \ 57, \ 20] \\ 15.47 \ [1.78, \ 134.74] \\ 4.16 \ [2.59, \ 4.41] \\ 4.60 \ [5.47, \ 4.18, \ 8.80] \end{array}$	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen Q shar M eeng Q erguson J suan WJ le R long KS luang C luang C luang R etcham SW ei S i K i S i X i X i N k iang W lu F iu J	Z = 1.83 (f 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 1 6 6 9 7 7 198 8 74 198 8 74 6	P = 0.07) 8 3 11 43 43 17 67 124 21 173 6 13 13 13 13 3 26 15 26 269 9 131 33	6 0 3 6 130 29 140 24 10 4 13 5 6 2 1 112 122 7 3	8 4 100 111 27 56 352 51 926 135 28 51 926 145 28 51 179 7 19 8 43 279 16 1459 107	0.1% 0.1% 0.2% 0.2% 0.5% 0.5% 0.5% 0.3% 0.1% 0.3% 0.1% 0.3% 0.3% 0.2% 0.2%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 13.30 [6.62, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 10.89 [2.07, 57.20] 15.47 [1.78, 134.74] 4.16 [2.90, 5.97] 2.67 [0.25, 28.44] 6.07 [4.19, 8.80] 7.70 [1.81, 32.81] 0.65 [0.02, 17.16]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen G shu J olaneri M veng Q eng Y erg yson J evan WJ le R long KS tuang C tuang C tuang R detham SW ei S i K i K i S i X i YK iang W tu J i UJ tu J tu J tu Z	Z = 1.83 (f 7 0 111 3 2 4 59 12 65 59 12 65 49 8 12 85 49 8 12 1 6 6 9 7 7 7 198 8 74 6 0 1	P = 0.07) 8 3 11 43 43 43 17 124 21 173 69 13 13 23 6 15 25 26 26 26 9 131 33 13 13 33 13 15 25 26 26 9 131 33 15 25 26 9 131 33 15 25 26 9 131 33 15 25 26 9 131 33 15 25 26 26 9 131 33 15 25 26 26 9 131 33 15 25 26 26 26 9 131 33 25 26 26 26 26 26 26 26 26 26 26	6 0 3 6 13 50 29 140 21 24 13 5 6 2 1 1 12 257 3 1 6	8 4 100 102 11 27 56 352 51 926 135 85 28 51 179 7 7 9 58 43 279 58 43 276 1459 107 27 64	0.1% 0.1% 0.2% 0.2% 0.3% 0.5% 0.3% 0.4% 0.3% 0.4% 0.3% 0.1% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.1%	$\begin{array}{c} 2.33 \ [0.17, \ 32.58] \\ \text{Not estimable} \\ 483.00 \ [8.77, \ 26588.24] \\ 17.72 \ [0.88, \ 350.69] \\ 0.13 \ [0.02, \ 0.91] \\ 1.08 \ [0.25, \ 4.55] \\ 9.73 \ [4.25, \ 22.29] \\ 5.48 \ [3.45, \ 8.70] \\ 1.01 \ [0.36, \ 2.82] \\ 3.38 \ [2.37, \ 4.83] \\ 1.30 \ [6.62, \ 26.73] \\ 4.07 \ [1.21, \ 13.68] \\ 21.60 \ [2.44, \ 191.38] \\ 5.88 \ [0.43, \ 79.77] \\ 4.51 \ [1.52, \ 13.38] \\ 5.98 \ [0.43, \ 79.77] \\ 4.51 \ [1.52, \ 13.38] \\ 10.99 \ [2.07, \ 57.20] \\ 15.47 \ [1.78, \ 134.74] \\ 4.16 \ [2.05, \ 597] \\ 2.67 \ [0.25, \ 28.44] \\ 6.07 \ [4.19, \ 8.80] \\ 7.70 \ [1.81, \ 32.81] \\ 0.65 \ [0.02, \ 17.16] \\ 0.65 \ [0.02, \ 17.16] \\ 0.65 \ [0.02, \ 17.16] \\ 1.38 \ [0.14, \ 13.20] \end{array}$	
est for overall effect: .1.6 Dyspnea gganval S ai Y chen G chen G chen Q chu J colaneri M veng Q eng Y erguson J uan WJ le R long KS luang C luang Q luang Q luang Q luang R lecham SW ei S i K i S i X i X i YK i ang W lu F lu J ju Z yu P	Z = 1.83 (f 7 0 11 3 2 4 50 59 12 85 49 8 12 85 49 8 12 1 6 6 9 7 7 7 198 8 74 6 0 1 11	P = 0.07) 8 3 11 43 43 43 17 67 124 21 173 6 13 13 23 6 15 26 269 9 131 33 13 13 8 39	6 0 0 3 6 50 29 140 24 13 5 6 2 1 112 122 257 3 1 6 1	8 4 100 102 11 27 56 352 51 926 135 85 28 51 179 7 7 19 58 43 279 58 43 279 58 43 279 58 43 279 58 43 279 58 43 279 58 43 279 58 43 27 56 57 57 58 43 27 58 43 27 58 43 27 58 43 27 58 43 27 58 43 27 58 43 27 58 43 27 58 43 27 58 43 27 58 43 27 58 43 27 58 43 27 58 58 57 58 57 58 58 58 58 58 58 58 58 58 58 58 58 58	0.1% 0.1% 0.2% 0.2% 0.5% 0.5% 0.3% 0.1% 0.3% 0.1% 0.3% 0.2% 0.2% 0.2% 0.5% 0.2%	$\begin{array}{c} 2.33 \ [0.17, \ 32.58] \\ \text{Not estimable} \\ 483.00 \ [8.77, \ 26588, \ 24] \\ 17.72 \ [0.89, \ 350, \ 68] \\ 0.13 \ [0.02, \ 0.91] \\ 1.08 \ [0.25, \ 4.55] \\ 9.73 \ [4.25, \ 22.29] \\ 9.73 \ [4.25, \ 22.29] \\ 3.78 \ [2.37, \ 4.83] \\ 1.330 \ [6.62, \ 26, \ 7.3] \\ 4.07 \ [1.21, \ 13.68] \\ 21.60 \ [2.44, \ 191, \ 38] \\ 5.88 \ [0.43, \ 79.77] \\ 4.51 \ [1.52, \ 13.38] \\ 5.89 \ [0.23, \ 151.15] \\ 3.25 \ [0.79, \ 13.38] \\ 10.99 \ [2.07, \ 57, \ 20] \\ 15.47 \ [1.78, \ 134.74] \\ 4.16 \ [2.90, \ 5.97] \\ 2.67 \ [0.25, \ 28.44] \\ 6.07 \ [4.19, \ 8.80] \\ 7.70 \ [1.81, \ 32.81] \\ 0.65 \ [0.02, \ 17.16] \\ 1.38 \ [0.14, \ 13.20] \\ 1.38 \ [0.14, \ 13.2$	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G then G then Q chu J colaneri M veng Q erguson J suan WJ le R loong KS luang C luang Q luang C luang Q luang R setcham SW el S i K i K i S i X i X i X i X i X i y u F eug YD	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 1 65 49 8 12 1 65 49 7 7 7 198 8 74 6 6 0 1 1 13 3	P = 0.07) 8 3 11 43 43 17 67 124 21 173 69 13 13 3 25 26 269 9 131 13 3 3 13 8 33 13 8 33 13 8 31 15 26 26 269 9 13 13 15 26 26 26 26 26 26 26 26 26 26	6 0 3 6 130 29 140 21 24 10 4 13 5 6 2 1 112 257 3 1 122 3 1 10	8 4 100 102 111 27 56 352 51 926 1355 28 51 85 28 51 79 7 19 58 43 279 16 1459 107 27 64 12 96	0.1% 0.1% 0.2% 0.2% 0.5% 0.5% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2%	$\begin{array}{c} 2.33 \ [0.17, \ 32.58] \\ \text{Not estimable} \\ 483.00 \ [8.77, \ 26588.24] \\ 17.72 \ [0.89, \ 350.69] \\ 0.13 \ [0.02, \ 0.91] \\ 1.08 \ [0.25, \ 4.55] \\ 9.73 \ [4.25, \ 22.29] \\ 5.48 \ [3.45, \ 8.70] \\ 1.01 \ [0.36, \ 2.82] \\ 3.38 \ [2.37, \ 4.83] \\ 1.30 \ [6.62, \ 26.73] \\ 1.30 \ [6.62, \ 26.73] \\ 1.30 \ [6.62, \ 26.73] \\ 1.30 \ [6.62, \ 26.73] \\ 1.30 \ [6.62, \ 26.73] \\ 5.88 \ [0.43, \ 79.77] \\ 4.51 \ [1.52, \ 1.38] \\ 5.91 \ [0.23, \ 151.15] \\ 3.25 \ [0.79, \ 13.38] \\ 10.89 \ [2.07, \ 57.20] \\ 15.47 \ [1.78, \ 134.74] \\ 4.16 \ [2.90, \ 5.97] \\ 2.67 \ [0.25, \ 28.44] \\ 6.07 \ [4.19, \ 8.80] \\ 7.70 \ [1.81, \ 32.81] \\ 0.65 \ [0.02, \ 17.16] \\ 1.38 \ [0.14, \ 13.20] \\ 4.32 \ [0.50, \ 37, \ 57] \\ 1.98 \ [0.48, \ 8.18] \\ \end{array}$	
est for overall effect: 1.6 Dyspnea ggarwal S iai Y hen G hen Q hou J volaneri M erg Q erg V erguson J uan WJ le R tong KS luang C luang C luang R etcham SW ei S i K i S i X iai S i X iai S i X i yu P eng YD ereira MR	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 65 49 8 12 1 6 6 9 7 7 198 8 74 6 0 1 1 13 3 17	P = 0.07) 8 3 11 43 17 67 124 21 173 69 13 13 3 25 26 269 9 131 33 13 8 39 16 27	6 0 3 6 130 29 140 21 4 10 4 12 257 3 1 6 257 3 1 6 10 22	8 4 100 102 111 27 56 352 51 926 135 28 51 27 135 28 51 135 28 51 135 28 51 27 135 28 51 135 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 29 51 29 51 29 51 51 51 51 51 51 51 51 51 51 51 51 51	0.1% 0.1% 0.2% 0.2% 0.5% 0.5% 0.3% 0.1% 0.3% 0.1% 0.3% 0.2% 0.2% 0.2% 0.5% 0.2%	$\begin{array}{c} 2.33 \ [0.17, \ 32.58] \\ \text{Not estimable} \\ 483.00 \ [8.77, \ 26588, \ 24] \\ 17.72 \ [0.89, \ 350, \ 68] \\ 0.13 \ [0.02, \ 0.91] \\ 1.08 \ [0.25, \ 4.55] \\ 9.73 \ [4.25, \ 22.29] \\ 9.73 \ [4.25, \ 22.29] \\ 3.78 \ [2.37, \ 4.83] \\ 1.330 \ [6.62, \ 26, \ 7.3] \\ 4.07 \ [1.21, \ 13.68] \\ 21.60 \ [2.44, \ 191, \ 38] \\ 5.88 \ [0.43, \ 79.77] \\ 4.51 \ [1.52, \ 13.38] \\ 5.89 \ [0.23, \ 151.15] \\ 3.25 \ [0.79, \ 13.38] \\ 10.99 \ [2.07, \ 57, \ 20] \\ 15.47 \ [1.78, \ 134.74] \\ 4.16 \ [2.90, \ 5.97] \\ 2.67 \ [0.25, \ 28.44] \\ 6.07 \ [4.19, \ 8.80] \\ 7.70 \ [1.81, \ 32.81] \\ 0.65 \ [0.02, \ 17.16] \\ 1.38 \ [0.14, \ 13.20] \\ 1.38 \ [0.14, \ 13.2$	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen Q solaneri M leng Q eng Y erguson J suan WJ le R tong KS luang C luang R setcham SW ei S i K i S i X i ang W lu F i ang W lu F lu J lu F lu J lu F eng YD ereira MR	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 1 65 49 8 12 1 65 49 7 7 7 198 8 74 6 6 0 1 1 13 3	P = 0.07) 8 3 11 43 43 17 67 124 21 173 69 13 13 3 25 26 269 9 131 13 3 3 13 8 33 13 8 33 13 8 31 15 26 26 269 9 13 13 15 26 26 26 26 26 26 26 26 26 26	6 0 3 6 130 29 140 21 24 10 4 13 5 6 2 1 112 257 3 1 122 3 1 10	8 4 100 102 111 27 56 352 51 926 1355 28 51 85 28 51 79 7 19 58 43 279 16 1459 107 27 64 12 96	0.1% 0.1% 0.2% 0.2% 0.5% 0.5% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2%	$\begin{array}{c} 2.33 \ [0.17, \ 32.58] \\ \text{Not estimable} \\ 483.00 \ [8.77, \ 26588.24] \\ 17.72 \ [0.89, \ 350.69] \\ 0.13 \ [0.02, \ 0.91] \\ 1.08 \ [0.25, \ 4.55] \\ 9.73 \ [4.25, \ 22.29] \\ 5.48 \ [3.45, \ 8.70] \\ 1.01 \ [0.36, \ 2.82] \\ 3.38 \ [2.37, \ 4.83] \\ 1.30 \ [6.62, \ 26.73] \\ 1.30 \ [6.62, \ 26.73] \\ 1.30 \ [6.62, \ 26.73] \\ 1.30 \ [6.62, \ 26.73] \\ 1.30 \ [6.62, \ 26.73] \\ 5.88 \ [0.43, \ 79.77] \\ 4.51 \ [1.52, \ 1.38] \\ 5.91 \ [0.23, \ 151.15] \\ 3.25 \ [0.79, \ 13.38] \\ 10.89 \ [2.07, \ 57.20] \\ 15.47 \ [1.78, \ 134.74] \\ 4.16 \ [2.90, \ 5.97] \\ 2.67 \ [0.25, \ 28.44] \\ 6.07 \ [4.19, \ 8.80] \\ 7.70 \ [1.81, \ 32.81] \\ 0.65 \ [0.02, \ 17.16] \\ 1.38 \ [0.14, \ 13.20] \\ 4.32 \ [0.50, \ 37, \ 57] \\ 1.98 \ [0.48, \ 8.18] \\ \end{array}$	
est for overall effect: .1.6 Dyspnea ggarwal S ai Y chen G chen G chen G chen Q colaneri M veng Q eng Y erguson J avan WJ le R long KS luang C luang C luang Q luang Q luang R detcham SW ei S i K i S i X i X i X i X i X i X i X i X	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 65 49 8 12 1 6 6 9 7 7 198 8 74 6 0 1 1 13 3 17	P = 0.07) 8 3 11 43 17 67 124 21 173 69 13 13 3 25 26 269 9 131 33 13 8 39 16 27	6 0 3 6 130 29 140 21 4 10 4 12 257 3 1 6 257 3 1 6 10 22	8 4 100 102 111 27 56 352 51 926 135 28 51 27 135 28 51 135 28 51 135 28 51 27 135 28 51 135 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 28 51 29 51 29 51 29 51 51 51 51 51 51 51 51 51 51 51 51 51	0.1% 0.1% 0.2% 0.2% 0.5% 0.3% 0.1% 0.3% 0.1% 0.3% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.1% 0.3%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 13.30 [6.62, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 10.89 [2.07, 57.20] 15.47 [1.78, 134.74] 6.07 [4.19, 8.80] 7.70 [1.81, 32.81] 0.65 [0.02, 17.16] 1.38 [0.14, 13.20] 4.32 [0.50, 37.57] 1.98 [0.48, 818] 3.17 [1.24, 8.09]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y ichen G ichen G ichen Q ichen Q eng Y erguson J ican WJ le R ican WJ le R ican SW erguson J ican WJ le R ican SW erguson J ican SW ican	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 85 49 12 85 49 8 12 12 85 49 8 12 12 65 9 7 7 198 8 74 6 0 1 1 13 3 7 7 198 8 74 11 13 2 2 4 59 59 59 59 59 59 59 59 59 59 59 59 59	P = 0.07) 8 3 11 43 43 17 67 124 21 173 6 13 13 13 23 6 15 26 269 9 131 33 13 13 8 39 16 27 15 46	6 0 3 6 130 29 140 24 10 4 13 5 6 2 1 112 257 3 1 6 110 22 1 3	8 4 100 102 111 27 56 352 51 926 135 85 28 51 179 7 19 8 43 279 16 1459 107 27 64 1459 107 27 64 1459 107 27 64 3279 1459 216	0.1% 0.1% 0.2% 0.2% 0.5% 0.5% 0.3% 0.1% 0.3% 0.1% 0.3% 0.2% 0.3% 0.2% 0.2% 0.2% 0.2% 0.5% 0.2% 0.5% 0.2%	$\begin{array}{c} 2.33 \ [0.17, \ 32.58] \\ \text{Not estimable} \\ 483.00 \ [8.77, \ 26588, \ 24] \\ 17.72 \ [0.89, \ 350.68] \\ 0.13 \ [0.02, \ 0.91] \\ 1.08 \ [0.25, \ 4.55] \\ 9.73 \ [4.25, \ 22.29] \\ 9.73 \ [4.25, \ 22.29] \\ 5.48 \ [3.45, \ 8.70] \\ 1.01 \ [0.36, \ 2.82] \\ 3.38 \ [2.37, \ 4.83] \\ 1.30 \ [6.62, \ 26.73] \\ 4.07 \ [1.21, \ 13.68] \\ 21.60 \ [2.44, \ 191, \ 38] \\ 5.88 \ [0.43, \ 79.77] \\ 4.51 \ [1.52, \ 13.38] \\ 5.91 \ [0.23, \ 151.15] \\ 3.25 \ [0.79, \ 13.38] \\ 10.89 \ [2.07, \ 57.20] \\ 15.47 \ [1.78, \ 134.74] \\ 4.16 \ [2.90, \ 5.97] \\ 2.67 \ [0.25, \ 28.44] \\ 6.07 \ [4.19, \ 8.80] \\ 7.70 \ [1.81, \ 32.81] \\ 0.65 \ [0.02, \ 17.16] \\ 1.38 \ [0.14, \ 13.20] \\ 1.38 \ [0.48, \ 8.18] \\ 3.17 \ [1.24, \ 8.09] \\ 6.00 \ [0.50, \ 71.73] \\ 34.35 \ [9.40, \ 125.50] \end{array}$	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen G shen Q chu J colaneri M beng Q erg Y erguson J suan WJ te R long KS tuang C tuang Q tuang C tuang Q tuang R Sectham SW si K i K i K i K i K i K i K i S i X i V vu P tereng YD tereira MR stan S Van S	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 12 65 49 8 12 12 65 49 8 77 7 7 198 8 77 198 8 74 6 0 1 1 1 3 12 7 85 7 12 85 12 85 7 12 85 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 85 12 12 12 85 12 12 12 13 12 12 12 12 12 12 12 12 12 12 12 12 12	P = 0.07) 8 3 11 43 43 17 67 124 21 173 6 13 13 3 25 26 269 9 131 33 13 8 39 16 27 15 46 40	6 0 3 6 130 29 140 21 10 4 13 5 6 2 1 112 257 3 1 6 1 10 22 1 3 0	8 4 100 102 111 27 56 352 51 926 1355 28 51 85 28 51 179 7 19 58 43 279 16 1459 279 16 1459 107 27 64 107 27 64 107 27 64 107 27 64 107 109 55	0.1% 0.1% 0.2% 0.2% 0.2% 0.5% 0.5% 0.3% 0.1% 0.3% 0.3% 0.3% 0.2% 0.1% 0.2% 0.1% 0.2% 0.1% 0.2%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 13.30 [6.62, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 5.91 [0.23, 151.15] 3.25 [0.79, 13.38] 10.89 [2.07, 57.20] 15.47 [1.78, 134.74] 4.16 [2.90, 5.97] 2.67 [0.25, 28.44] 6.07 [4.19, 8.80] 7.70 [1.81, 32.81] 0.65 [0.02, 17.16] 1.38 [0.14, 13.20] 4.32 [0.50, 37.57] 1.98 [0.48, 8.18] 3.17 [1.24, 8.09] 6.00 [0.50, 71.73]	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen G shen G shen Q solaneri M song Q eng Y erguson J souan WJ le R tong KS tuang C tuang C tuang C tuang R cetcham SW ei S tuang R cetcham SW ei S 1X 1/YK iang W Ju F sin L tan S Yan S Yan S Yan S Yan S Yan S	Z = 1.83 (f 7 0 111 3 2 4 59 12 65 49 8 12 65 49 8 12 6 8 12 6 6 9 7 7 7 198 8 74 6 0 1 111 3 7 7 2 15 8 8 74 6 2 1 11 3 7 2 198 8 7 198 8 7 198 8 7 198 8 7 198 8 7 19 19 19 19 19 19 19 19 19 19 19 19 19	P = 0.07) 8 3 11 43 43 43 43 17 124 21 173 69 13 13 23 6 15 26 269 9 131 33 15 25 26 26 9 131 33 8 39 16 27 15 46 40 36 37 15 40 36 37 15 40 37 15 40 37 15 40 37 15 40 37 15 40 37 15 40 37 15 40 37 15 40 15 15 15 15 15 15 15 15 15 15	6 0 0 3 6 13 50 29 140 24 10 4 13 5 6 2 24 13 5 6 2 1 12 257 3 1 6 1 1 2257 3 1 257 3 1 20 20 20	8 4 100 102 11 276 352 51 926 135 85 28 51 179 7 7 19 58 43 279 58 43 279 58 43 279 58 43 276 64 1459 107 7 64 12 95 63 40 216 63 20 216 63 20 216 20 216 20 216 20 20 20 20 20 20 20 20 20 20 20 20 20	0.1% 0.1% 0.2% 0.2% 0.5% 0.3% 0.4% 0.3% 0.1% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2	$\begin{array}{c} 2.33 \ [0.17, \ 32.58] \\ \text{Not estimable} \\ 483.00 \ [8.77, \ 26588.24] \\ 17.72 \ [0.88, \ 350.69] \\ 0.13 \ [0.02, \ 0.91] \\ 1.08 \ [0.25, \ 4.55] \\ 9.73 \ [4.25, \ 22.29] \\ 5.48 \ [3.45, \ 8.70] \\ 1.01 \ [0.36, \ 2.82] \\ 3.38 \ [2.37, \ 4.83] \\ 2.37, \ 4.83 \ [2.37, \ 4.83] \\ 2.30 \ [6.62, \ 26.73] \\ 4.07 \ [1.21, \ 13.68] \\ 21.60 \ [2.44, \ 191.38] \\ 21.60 \ [2.44, \ 191.38] \\ 5.88 \ [0.43, \ 9.77] \\ 4.51 \ [1.52, \ 13.38] \\ 5.98 \ [0.43, \ 9.77] \\ 4.51 \ [1.52, \ 13.38] \\ 10.98 \ [2.07, \ 57.20] \\ 15.47 \ [1.78, \ 134.74] \\ 4.16 \ [2.90, \ 5.97] \\ 2.67 \ [0.25, \ 28.44] \\ 6.07 \ [4.19, \ 8.80] \\ 7.70 \ [1.81, \ 32.81] \\ 0.65 \ [0.02, \ 17.16] \\ 1.38 \ [0.14, \ 13.20] \\ 4.32 \ [0.50, \ 37.57] \\ 1.98 \ [0.48, \ 8.18] \\ 3.17 \ [1.24, \ 8.09] \\ 6.00 \ [0.50, \ 71.73] \\ 3.43 \ [9.40, \ 125.50] \\ 157.04 \ [9.12, \ 270.497] \\ 7.25 \ [3.14, \ 16.76] \end{array}$	
est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen G shen G shen Q solaneri M song Q eng Y erguson J souan WJ le R tong KS tuang C tuang C tuang C tuang R cetcham SW ei S tuang R cetcham SW ei S 1X 1/YK iang W Ju F sin L tan S Yan S Yan S Yan S Yan S Yan S	Z = 1.83 (F 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 12 65 49 8 12 12 65 49 8 77 7 7 198 8 77 198 8 74 6 0 1 1 1 3 17 7 25 18	P = 0.07) 8 3 11 43 43 17 67 124 21 173 6 13 13 3 25 26 269 9 131 33 13 8 39 16 27 15 46 40	6 0 3 6 130 29 140 21 10 4 13 5 6 2 1 112 257 3 1 6 1 10 22 1 3 0	8 4 100 102 111 27 56 352 51 926 1355 28 51 85 28 51 179 7 19 58 43 279 16 1459 279 16 1459 107 27 64 107 27 64 107 27 64 107 27 64 107 109 55	0.1% 0.1% 0.2% 0.2% 0.2% 0.5% 0.5% 0.3% 0.1% 0.3% 0.3% 0.3% 0.2% 0.1% 0.2% 0.1% 0.2% 0.1% 0.2%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 13.30 [6.62, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 5.91 [0.23, 151.15] 3.25 [0.79, 13.38] 10.89 [2.07, 57.20] 15.47 [1.78, 134.74] 4.16 [2.90, 5.97] 2.67 [0.25, 28.44] 6.07 [4.19, 8.80] 7.70 [1.81, 32.81] 0.65 [0.02, 17.16] 1.38 [0.14, 13.20] 4.32 [0.50, 37.57] 1.98 [0.48, 8.18] 3.17 [1.24, 8.09] 6.00 [0.50, 71.73]	
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est for overall effect: .1.6 Dyspnea ggarwal S sai Y shen G shen Q eng Y erguson J beng Q eng Y erguson J buan WJ te R long KS tuang C tuang Q tuang C tuang Q tuang R Cetcham SW ei S i K i S i X i X i J Wang F teng YD tererira MR son S Van S Va	Z = 1.83 (f 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 65 49 8 12 12 65 49 8 12 65 49 8 12 16 6 9 7 7 198 8 8 74 11 13 12 65 49 12 12 65 49 8 12 12 65 49 8 12 12 65 49 8 12 12 65 49 8 12 12 65 49 8 12 12 65 49 8 12 12 65 49 8 12 12 65 49 8 12 16 59 59 59 59 59 59 59 59 59 59 59 59 59	P = 0.07) 8 3 11 43 17 67 124 21 173 69 13 13 13 3 23 6 15 26 269 9 131 33 13 13 3 26 269 9 131 13 3 26 269 9 131 13 3 13 13 3 26 26 269 9 131 33 13 13 13 26 26 269 9 131 33 13 13 26 26 269 9 131 33 13 13 26 26 269 9 131 33 13 13 26 26 269 9 131 33 13 13 26 26 269 9 131 33 13 13 26 26 269 9 131 133 13 13 26 26 269 9 131 133 13 13 26 269 9 131 133 13 27 26 269 9 131 133 13 26 269 9 131 33 13 13 26 269 9 131 133 13 13 26 269 9 131 133 13 26 269 269 131 132 133 133 133 133 13 26 269 9 131 133 13 26 269 269 131 133 133 138 39 16 27 16 27 16 27 16 27 16 26 26 26 26 26 26 26 26 26 2	6 0 0 3 6 130 29 140 21 12 257 3 1 112 257 3 1 6 112 257 3 1 6 10 20 5 67	8 4 100 102 111 27 56 352 51 926 1355 28 51 85 28 51 179 7 19 58 43 279 169 147 107 27 64 145 107 27 64 12 96 63 40 216 95 102	0.1% 0.1% 0.2% 0.2% 0.5% 0.5% 0.3% 0.1% 0.3% 0.3% 0.3% 0.3% 0.2% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2%	$\begin{array}{c} 2.33 \ [0.17, \ 32.58] \\ \text{Not estimable} \\ 483.00 \ [8.77, \ 26588, \ 24] \\ 17.72 \ [0.89, \ 350.69] \\ 0.13 \ [0.02, \ 0.91] \\ 1.08 \ [0.25, \ 4.55] \\ 9.73 \ [4.25, \ 22.29] \\ 9.73 \ [4.25, \ 22.29] \\ 5.48 \ [3.45, \ 8.70] \\ 1.01 \ [0.36, \ 2.82] \\ 3.38 \ [2.37, \ 4.83] \\ 1.30 \ [6.62, \ 26.73] \\ 4.07 \ [1.21, \ 13.68] \\ 21.60 \ [2.44, \ 191, \ 38] \\ 5.88 \ [0.43, \ 79.77] \\ 4.51 \ [1.52, \ 13.38] \\ 5.91 \ [0.23, \ 151.15] \\ 3.25 \ [0.79, \ 13.38] \\ 10.89 \ [2.07, \ 57.20] \\ 15.47 \ [1.78, \ 134.74] \\ 4.16 \ [2.90, \ 5.97] \\ 2.67 \ [0.25, \ 28.44] \\ 6.07 \ [1.49, \ 880] \\ 7.70 \ [1.81, \ 32.81] \\ 0.65 \ [0.02, \ 17.16] \\ 1.38 \ [0.14, \ 13.20] \\ 6.00 \ [0.50, \ 71.73] \\ 3.43 \ [9.40, \ 125.50] \\ 157.04 \ [9.12, \ 2704.97] \\ 7.25 \ [3.14, \ 16.76] \\ 6.60 \ [1.23, \ 55.44] \\ 322.87 \ [1.97, \ 5286.01] \end{array}$	
est for overall effect: .1.6 Dyspnea 	Z = 1.83 (F 7 0 11 3 2 4 50 50 50 12 65 49 8 12 65 49 8 12 12 65 49 8 12 65 49 8 12 13 6 6 9 7 7 7 198 8 74 6 0 1 1 13 12 12 65 49 9 7 7 198 8 7 7 11 13 2 2 50 50 50 50 50 50 50 50 50 50 50 50 50	P = 0.07) 8 3 11 43 43 17 67 124 21 173 69 13 13 3 23 6 15 25 26 269 9 131 33 13 8 39 16 27 15 46 40 36 16 27 15 46 28 33 13 28 33 28 33 28 36 28 28 28 28 28 28 28 28 28 28	6 0 3 6 130 29 140 21 10 4 13 5 6 2 1 112 257 3 1 6 10 222 1 3 0 20 57 24	8 4 100 102 111 27 56 352 51 926 1355 28 51 926 1355 28 51 179 58 43 279 16 1459 107 27 64 127 64 127 64 127 64 127 61	0.1% 0.1% 0.2% 0.2% 0.2% 0.5% 0.5% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.1% 0.3% 0.2% 0.1% 0.2% 0.2% 0.1% 0.2%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 13.30 [6.62, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 10.89 [2.07, 57.20] 15.47 [1.78, 134.74] 4.16 [2.90, 5.97] 2.67 [0.25, 28.44] 6.07 [4.19, 8.80] 7.70 [1.81, 32.81] 0.65 [0.02, 17.16] 1.38 [0.14, 13.20] 4.32 [0.50, 37.57] 1.98 (0.48, 818] 3.17 [1.24, 8.09] 6.00 [0.50, 71.73] 4.35 [9.40, 125.50] 157.04 [9.12, 2704.97] 7.25 [3.14, 16.76] 6.60 [1.23, 35.44] 322.87 [9.72, 5286.01] 1.50 [0.59, 3.80]	
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iest for overall effect: 1.6 Dyspnea yggarwal S sai Y shen G shen G shen Q shen Q eng Y erguson J Suan WJ te R Hong KS Huang C Huang Q Huang Q Huang Q Huang Q Huang W Juang W Juang W Juang W Ji K Ji S JX JX Var S Var S Van S	Z = 1.83 (F 7 0 11 3 2 4 50 50 50 12 65 49 8 12 65 49 8 12 12 65 49 8 12 65 49 8 12 13 6 6 9 7 7 7 198 8 74 6 0 1 1 13 12 12 65 49 9 7 7 198 8 7 7 11 13 2 2 50 50 50 50 50 50 50 50 50 50 50 50 50	P = 0.07) 8 3 11 43 43 17 67 124 21 173 69 13 13 3 23 6 15 25 26 269 9 131 33 13 8 39 16 27 15 46 40 36 16 27 15 46 28 33 13 28 33 28 33 28 36 28 28 28 28 28 28 28 28 28 28	6 0 3 6 130 29 140 21 10 4 13 5 6 2 1 112 257 3 1 6 10 222 1 3 0 20 57 24	8 4 100 102 111 27 56 352 51 926 1355 28 51 926 1355 28 51 179 58 43 279 16 1459 107 27 64 127 64 127 64 127 64 127 61	0.1% 0.1% 0.2% 0.2% 0.2% 0.5% 0.5% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.1% 0.3% 0.2% 0.1% 0.2% 0.2% 0.1% 0.2%	2.33 [0.17, 32.58] Not estimable 483.00 [8.77, 26588.24] 17.72 [0.89, 350.69] 0.13 [0.02, 0.91] 1.08 [0.25, 4.55] 9.73 [4.25, 22.29] 5.48 [3.45, 8.70] 1.01 [0.36, 2.82] 3.38 [2.37, 4.83] 13.30 [6.62, 26.73] 4.07 [1.21, 13.68] 21.60 [2.44, 191.38] 5.88 [0.43, 79.77] 4.51 [1.52, 13.38] 10.89 [2.07, 57.20] 15.47 [1.78, 134.74] 4.16 [2.90, 5.97] 2.67 [0.25, 28.44] 6.07 [4.19, 8.80] 7.70 [1.81, 32.81] 0.65 [0.02, 17.16] 1.38 [0.14, 13.20] 4.32 [0.50, 37.57] 1.98 (0.48, 818] 3.17 [1.24, 8.09] 6.00 [0.50, 71.73] 4.35 [9.40, 125.50] 157.04 [9.12, 2704.97] 7.25 [3.14, 16.76] 6.60 [1.23, 35.44] 322.87 [9.72, 5286.01] 1.50 [0.59, 3.80]	
Test for overall effect: L1.6 Dyspnea (ggarwal S Cai Y Chen G Chen G Chu J Colaneri M Deng Q Terguson J Deng Q Terguson J Duan VUJ He R Hong KS Huang C Huang C Huang R Cetcham SW Lei S Li K Li S Li K Li S Li K Li S Li K Li S Li K Li S D Son L Tan S Vang D Vang D Vang P Vang F Vang C Vang F Vang C Vang C Son L Tan S Vang D Vang P Vang F Vang F Vang F Vang F Vang F Vang P	Z = 1.83 (f 7 0 111 3 2 4 50 59 12 85 59 12 85 49 8 12 12 85 8 12 12 85 8 12 12 85 8 74 6 0 1 11 3 7 7 7 198 8 74 6 0 11 1 3 7 7 198 8 74 6 19 8 7 198 8 7 198 8 7 198 8 7 19 8 8 7 198 8 7 19 8 19 19 19 8 19 19 19 19 19 19 19 19 19 19 19 19 19	P = 0.07) 8 3 11 43 43 43 17 67 124 21 173 69 13 13 23 6 15 26 269 9 131 33 13 8 39 16 27 15 46 40 30 16 17 124 23 6 13 13 13 13 13 13 13 13 13 13	6 0 3 6 13 50 29 140 4 13 5 6 24 13 5 6 2 1 112 257 3 1 6 1 102 257 3 1 6 1 102 257 3 1 6 1 102 257 3 1 102 13 102 140 140 140 140 140 140 140 140 140 140	8 4 100 102 111 276 352 51 926 135 85 28 135 85 28 135 85 28 179 7 7 19 58 43 279 58 43 279 58 43 279 58 43 279 64 129 64 129 63 40 216 51 216 51 926 135 28 117 27 51 926 135 28 117 27 51 926 135 28 117 926 135 28 117 926 135 28 117 926 135 28 117 926 135 28 117 926 135 28 117 926 135 28 117 926 135 28 117 926 135 28 117 926 135 28 117 926 135 28 117 926 135 28 117 926 135 28 117 926 135 28 117 926 117 102 117 117 117 117 117 117 117 117 117 11	0.1% 0.1% 0.2% 0.2% 0.5% 0.3% 0.1% 0.3% 0.1% 0.3% 0.2% 0.2% 0.2% 0.2% 0.2% 0.1% 0.3% 0.1% 0.3% 0.1% 0.3% 0.1% 0.3%	$\begin{array}{c} 2.33 \ [0.17, \ 32.58] \\ \text{Not estimable} \\ 483.00 \ [8.77, \ 26588, \ 24] \\ 17.72 \ [0.89, \ 350.69] \\ 0.13 \ [0.02, \ 0.91] \\ 1.08 \ [0.25, \ 4.55] \\ 9.73 \ [4.25, \ 22.29] \\ 9.73 \ [4.25, \ 22.29] \\ 5.48 \ [3.45, \ 8.70] \\ 1.01 \ [0.36, \ 2.82] \\ 3.38 \ [2.37, \ 4.83] \\ 1.30 \ [6.62, \ 26.73] \\ 4.07 \ [1.21, \ 13.68] \\ 21.60 \ [2.44, \ 191, \ 38] \\ 5.89 \ [0.43, \ 79.77] \\ 4.51 \ [1.52, \ 13.38] \\ 5.91 \ [0.23, \ 151.15] \\ 3.25 \ [0.79, \ 13.38] \\ 10.89 \ [2.07, \ 57.20] \\ 15.47 \ [1.78, \ 134.74] \\ 4.16 \ [2.90, \ 5.97] \\ 2.67 \ [0.25, \ 28.44] \\ 6.07 \ [4.19, \ 8.80] \\ 7.70 \ [1.81, \ 32.81] \\ 0.65 \ [0.02, \ 17.16] \\ 1.38 \ [0.14, \ 13.20] \\ 1.38 \ [0.48, \ 8.18] \\ 3.17 \ [1.24, \ 8.09] \\ 6.00 \ [0.50, \ 71.73] \\ 34.35 \ [9.40, \ 125.50] \\ 157.04 \ [9.12, \ 2704.97] \\ 7.25 \ [3.14, \ 16.76] \\ 6.60 \ [1.23, \ 35.44] \\ 322.87 \ [1.97, \ 5286.01] \\ 1.50 \ (0.59, \ 3.80] \\ 4.32 \ [1.80, \ 10.33] \\ 0.08 \ [0.03, \ 0.20] \end{array}$	
Test for overall effect: L1.6 Dyspnea (xggarwal S Cai Y Chen G Chen G Chu J Colaneri M Deng Q Terguson J Suan VKJ He R Hong KS Huang C Huang Q Huang R Ketcham SW Lei S J K J K J K J K J K J K J K J K	Z = 1.83 (f 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 15 6 6 9 7 7 198 8 74 6 6 9 7 7 198 8 7 12 15 12 12 15 12 12 15 12 12 15 12 12 15 12 12 15 12 12 15 12 12 15 12 15 12 12 15 12 12 15 15 15 15 15 15 15 15 15 15	P = 0.07) 8 3 11 43 43 17 67 124 21 173 6 124 21 173 6 13 13 3 23 6 15 25 26 269 9 131 13 33 13 13 33 13 13 33 13 1	$\begin{array}{c} 6\\ 0\\ 0\\ 0\\ 3\\ 6\\ 130\\ 29\\ 140\\ 21\\ 10\\ 4\\ 13\\ 22\\ 112\\ 257\\ 3\\ 1\\ 10\\ 22\\ 1\\ 3\\ 0\\ 20\\ 5\\ 67\\ 24\\ 19\\ 59\\ 6\end{array}$	8 4 100 102 111 27 56 352 51 926 1352 28 51 926 1352 28 51 926 145 28 51 926 145 28 51 97 7 19 53 279 16 145 107 27 64 216 107 27 64 107 107 107 107 107 107 107 107 107 107	0.1% 0.1% 0.2% 0.2% 0.2% 0.5% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.2% 0.3% 0.2% 0.2% 0.1% 0.2% 0.2% 0.2% 0.2% 0.3% 0.2% 0.3% 0.2%	$\begin{array}{c} 2.33 \ [0.17, 32.58] \\ Not estimable\\ 483.00 \ [8.77, 26588.24]\\ 17.72 \ [0.89, 350.69]\\ 0.13 \ [0.02, 0.91]\\ 1.08 \ [0.25, 4.55]\\ 9.73 \ [4.25, 22.29]\\ 9.73 \ [4.25, 22.29]\\ 5.48 \ [3.45, 8.70]\\ 1.01 \ [0.36, 2.82]\\ 3.38 \ [2.37, 4.83]\\ 13.30 \ [6.62, 26.73]\\ 1.33 \ [6.62, 26.73]\\ 1.33 \ [6.62, 26.73]\\ 1.33 \ [6.62, 26.73]\\ 1.33 \ [6.62, 26.73]\\ 1.33 \ [6.62, 26.73]\\ 1.33 \ [1.52, 13.38]\\ 5.91 \ [0.23, 151.15]\\ 3.25 \ [0.79, 13.38]\\ 10.89 \ [2.07, 57.20]\\ 15.47 \ [1.78, 134.74]\\ 4.16 \ [2.90, 5.97]\\ 2.67 \ [0.25, 28.44]\\ 6.07 \ [4.19, 8.80]\\ 7.70 \ [1.81, 32.81]\\ 0.65 \ [0.02, 17.16]\\ 1.38 \ [0.14, 13.20]\\ 4.32 \ [0.50, 37, 57]\\ 1.98 \ [0.48, 8.18]\\ 3.17 \ [1.24, 8.09]\\ 6.00 \ [0.50, 71.73]\\ 34.35 \ [9.40, 125.50]\\ 157.04 \ [9.12, 2704.97]\\ 7.25 \ [3.14, 16.76]\\ 6.60 \ [1.23, 35.44]\\ 322.87 \ [19.72, 5286.01]\\ 1.50 \ [0.59, 3.80]\\ 4.32 \ [1.80, 0.30, 0.20]\\ 7.22 \ [2.25, 23.14]\\ \end{array}$	
Test for overall effect: L1.6 Dyspnea Siggarwal S Sai Y Chen G Chen G Chen G Chu J Colaneri M Cong K Souan WJ He R Hong KS Huang C Huang C Hu	Z = 1.83 (f 7 0 11 3 2 4 50 59 12 65 49 8 12 65 49 8 12 6 6 9 7 7 198 8 74 6 0 1 11 3 7 2 4 5 9 7 198 8 74 6 0 11 12 65 9 7 198 8 74 198 8 74 198 8 74 198 8 74 11 13 12 12 12 15 12 12 12 15 12 12 15 12 15 12 12 15 12 15 12 15 12 15 12 15 12 15 15 15 15 15 15 15 15 15 15	P = 0.07) 8 3 11 43 43 43 43 43 17 124 21 173 69 13 13 23 6 15 26 269 9 131 33 13 8 39 16 27 15 46 40 27 15 46 40 27 15 46 30 27 15 46 30 27 15 46 30 36 27 15 46 30 30 30 30 30 30 30 30 30 30	$\begin{array}{c} 6\\ 0\\ 0\\ 3\\ 6\\ 13\\ 50\\ 29\\ 140\\ 4\\ 13\\ 5\\ 6\\ 24\\ 13\\ 5\\ 6\\ 2\\ 1\\ 112\\ 257\\ 3\\ 1\\ 6\\ 1\\ 102\\ 2\\ 5\\ 6\\ 7\\ 19\\ 59\\ 6\\ 31\\ \end{array}$	8 4 100 102 111 276 352 51 926 135 85 28 179 7 19 58 43 279 58 43 279 58 43 279 58 43 279 58 43 279 58 43 279 58 43 276 107 27 64 129 963 40 216 51 107 115 58 43 27 51 107 115 58 43 27 51 107 107 107 107 107 107 107 107 107 10	0.1% 0.1% 0.2% 0.2% 0.3% 0.5% 0.3% 0.1% 0.3% 0.1% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3	$\begin{array}{c} 2.33 \ [0.17, \ 32.58] \\ \text{Not estimable} \\ 483.00 \ [8.77, \ 26588.24] \\ 17.72 \ [0.88, \ 350.69] \\ 0.13 \ [0.02, \ 0.91] \\ 1.08 \ [0.25, \ 4.55] \\ 9.73 \ [4.25, \ 22.29] \\ 5.48 \ [3.45, \ 8.70] \\ 1.01 \ [0.36, \ 2.82] \\ 3.38 \ [2.37, \ 4.83] \\ 1.3.30 \ [6.62, \ 2.67] \\ 4.07 \ [1.21, \ 13.68] \\ 21.60 \ [2.44, \ 191.38] \\ 5.88 \ [0.43, \ 9.77] \\ 4.51 \ [1.52, \ 13.38] \\ 5.98 \ [0.43, \ 9.77] \\ 4.51 \ [1.52, \ 13.38] \\ 5.98 \ [0.43, \ 9.77] \\ 4.51 \ [1.52, \ 13.38] \\ 10.98 \ [2.07, \ 57.20] \\ 15.47 \ [1.78, \ 134.74] \\ 4.16 \ [2.90, \ 5.97] \\ 2.67 \ [0.25, \ 2844] \\ 6.07 \ [4.19, \ 8.80] \\ 7.70 \ [1.81, \ 32.81] \\ 0.65 \ [0.02, \ 17.6] \\ 1.38 \ [0.14, \ 13.281] \\ 0.65 \ [0.02, \ 17.6] \\ 3.317 \ [1.24, \ 8.09] \\ 6.00 \ [0.50, \ 71.73] \\ 3.435 \ [9.40, \ 125.50] \\ 157.04 \ [9.42, \ 125.60, \ 11] \\ 1.50 \ [0.59, \ 3.81] \\ 4.32 \ [1.80, \ 10.33] \\ 0.08 \ [0.03, \ 0.20] \\ 1.50 \ [0.59, \ 3.81] \\ 4.32 \ [1.80, \ 10.33] \\ 0.08 \ [0.03, \ 0.21] \\ 1.61 \ [0.58, \ 2.31] \end{array}$	
est for overall effect: 1.1.6 Dyspnea (ggarwal S cai Y chen G chen G chen Q chen Q eng Y erguson J buan WJ He R dong KS Huang C Huang Q Huang C Huang Q Huang R Ketcham SW Lei S J X J X J X J X J X J X J X J X	Z = 1.83 (F 7 0 11 3 2 4 50 50 50 50 50 50 50 50 50 50 50 50 50	P = 0.07) 8 3 11 43 43 17 67 124 21 173 6 124 21 173 6 13 13 3 23 6 15 25 26 269 9 131 13 33 13 13 33 13 13 13 1	$\begin{array}{c} 6\\ 0\\ 0\\ 0\\ 3\\ 6\\ 130\\ 29\\ 140\\ 21\\ 10\\ 4\\ 13\\ 22\\ 112\\ 257\\ 3\\ 1\\ 10\\ 22\\ 1\\ 3\\ 0\\ 20\\ 5\\ 67\\ 24\\ 19\\ 59\\ 6\end{array}$	8 4 100 102 111 27 56 352 51 926 1352 28 51 926 1352 28 51 926 145 28 51 926 145 28 51 97 7 19 53 279 16 145 107 27 64 216 107 27 64 107 107 107 107 107 107 107 107 107 107	0.1% 0.1% 0.2% 0.2% 0.2% 0.5% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.3% 0.2% 0.3% 0.2% 0.2% 0.1% 0.2% 0.2% 0.2% 0.2% 0.3% 0.2% 0.3% 0.2%	$\begin{array}{c} 2.33 \ [0.17, 32.58] \\ Not estimable\\ 483.00 \ [8.77, 26588.24]\\ 17.72 \ [0.89, 350.69]\\ 0.13 \ [0.02, 0.91]\\ 1.08 \ [0.25, 4.55]\\ 9.73 \ [4.25, 22.29]\\ 9.73 \ [4.25, 22.29]\\ 5.48 \ [3.45, 8.70]\\ 1.01 \ [0.36, 2.82]\\ 3.38 \ [2.37, 4.83]\\ 13.30 \ [6.62, 26.73]\\ 1.33 \ [6.62, 26.73]\\ 1.33 \ [6.62, 26.73]\\ 1.33 \ [6.62, 26.73]\\ 1.33 \ [6.62, 26.73]\\ 1.33 \ [6.62, 26.73]\\ 1.33 \ [1.52, 13.38]\\ 5.91 \ [0.23, 151.15]\\ 3.25 \ [0.79, 13.38]\\ 10.89 \ [2.07, 57.20]\\ 15.47 \ [1.78, 134.74]\\ 4.16 \ [2.90, 5.97]\\ 2.67 \ [0.25, 28.44]\\ 6.07 \ [4.19, 8.80]\\ 7.70 \ [1.81, 32.81]\\ 0.65 \ [0.02, 17.16]\\ 1.38 \ [0.14, 13.20]\\ 4.32 \ [0.50, 37, 57]\\ 1.98 \ [0.48, 8.18]\\ 3.17 \ [1.24, 8.09]\\ 6.00 \ [0.50, 71.73]\\ 34.35 \ [9.40, 125.50]\\ 157.04 \ [9.12, 2704.97]\\ 7.25 \ [3.14, 16.76]\\ 6.60 \ [1.23, 35.44]\\ 322.87 \ [19.72, 5286.01]\\ 1.50 \ [0.59, 3.80]\\ 4.32 \ [1.80, 0.30, 0.20]\\ 7.22 \ [2.25, 23.14]\\ \end{array}$	

 State (c) = (c),
 First
 State (c) = (c),

 Total events
 893
 1003

 Heterogeneity: Tau" = 0.81; Chi" = 177.18, df = 38 (P < 0.00001); I" = 79%</td>

 Test for overall effect: Z = 7.76 (P < 0.00001)</td>

4.1.7 Chest tightness							
Aggarwal S	1	8	0	8	0.1%	3.40 [0.12, 96.70]	
Chen G	8	11	3	10	0.2%	6.22 [0.94, 41.38]	
Chen Q Chu J	26 3	43 43	21 1	102 11	0.4% 0.1%	5.90 [2.71, 12.83] 0.75 [0.07, 8.00]	
Deng Q	59	43	14	56	0.3%	22.13 [8.52, 57.47]	
Feng Y	8	124	13	352	0.4%	1.80 [0.73, 4.45]	
Ferguson J	2	21	6	51	0.2%	0.79 [0.15, 4.27]	
He R	14	69	30	135	0.4%	0.89 [0.44, 1.82]	
Huang Q	0	3	3	51	0.1%	1.98 [0.08, 46.45]	
Jiang Y	2	8	6	52	0.2%	2.56 [0.42, 15.65]	
LIK	4	25	1	58	0.1%	10.86 [1.15, 102.77]	
LiX	76 8	269 33	86 6	279 107	0.5%	0.88 [0.61, 1.28]	
Liu F Liu J	5	33 13	7	27	0.3% 0.3%	5.39 [1.71, 16.94] 1.79 [0.44, 7.32]	
Liu Z	1	8	6	64	0.1%	1.38 [0.14, 13.20]	
Peng YD	4	16	34	96	0.3%	0.61 [0.18, 2.03]	
WanS	3	40	9	95	0.3%	0.77 [0.20, 3.03]	
WuJ	9	83	2	197	0.2%	11.86 [2.50, 56.17]	
Xie J	12	34	8	22	0.3%	0.95 [0.31, 2.92]	
Zhang JJ	24	58	31	82	0.4%	1.16 [0.58, 2.31]	
Zheng S	10	74	2	22	0.2%	1.56 [0.32, 7.73]	
Zhou Y Subtotal (95% CI)	1	43 1093	4	323 2200	0.1% 5.5%	1.90 [0.21, 17.39] 2.11 [1.30, 3.42]	
Total events	280	1055	293	2200	3.3%	2.11[1.30, 3.42]	-
Heterogeneity: Tau ² = 0.7		² = 75 02		(P < 0.00	1001) [.] I ² =	72%	
Test for overall effect: Z =				() 0.00		12.0	
4.1.8 Sputum production							
BiX	7	22	26	91	0.3%	1.17 [0.43, 3.19]	
CaiY	1	3	0	4	0.1%	5.40 [0.15, 188.83]	
Chen G	2	11	3	10	0.2%	0.52 [0.07, 4.00]	
Chu J Feng Y	3 61	43 124	0 100	11 352	0.1% 0.5%	1.99 [0.10, 41.33] 2.44 [1.60, 3.72]	
Ferguson J	3	21	12	51	0.3%	0.54 [0.14, 2.16]	
Guan WJ	61	173	309	926	0.5%	1.09 [0.77, 1.53]	+-
He R	10	69	32	135	0.4%	0.55 [0.25, 1.19]	
Hong KS	2	13	37	85	0.2%	0.24 [0.05, 1.13]	
Huang C	5	13	6	28	0.2%	2.29 [0.54, 9.64]	
Huang Q	3	3	15	51	0.1%	16.48 [0.80, 338.51]	
Lei S	7	15	4	19	0.2%	3.28 [0.73, 14.68]	
LiK	9	25	6	58	0.3%	4.88 [1.51, 15.79]	
Liang W Liu J	52 10	131 13	461 11	1459 27	0.5% 0.2%	1.42 [0.99, 2.06] 4.85 [1.08, 21.76]	
Liu Z	2	8	19	64	0.2%	0.79 [0.15, 4.27]	
Sun L	6	15	6	40	0.3%	3.78 [0.98, 14.56]	
Wan S	7	40	5	95	0.3%	3.82 [1.13, 12.87]	
Wang D	8	36	29	102	0.4%	0.72 [0.29, 1.76]	
Wang F	3	14	4	14	0.2%	0.68 [0.12, 3.83]	
Xie H	7	28	13	51	0.3%	0.97 [0.34, 2.82]	
Xiong F	15	30	23	101	0.4%	3.39 [1.44, 7.96]	
Yang P Yao Q	46 8	68 25	51	65	0.4%	0.57 [0.26, 1.25]	
Zheng S	8 19	25 74	26 7	83 22	0.3% 0.3%	1.03 [0.40, 2.69] 0.74 [0.26, 2.09]	
Subtotal (95% CI)	15	1017	(3944	7.1%	1.35 [1.00, 1.82]	◆
Total events	357		1205				
Heterogeneity: Tau ² = 0.2	4; Chi ^a	= 53.31,	df = 24	(P = 0.00	105); I ² = 5	5%	
Test for overall effect: Z =	1.98 (P = 0.05)					
4.1.9 Hemoptysis							
Feng Y	3	124	2	352	0.2%	4.34 [0.72, 26.28]	
Guan WJ	4	173	6	926	0.2%	3.63 [1.01, 13.00]	
Huang C	1	13	1	28	0.1%	2.25 [0.13, 39.05]	
Liang W	6	131	10	1459	0.3%	6.96 [2.49, 19.45]	
Subtotal (95% CI)		441		2765	0.9%	4.93 [2.43, 10.02]	
Total events	14		19				
Heterogeneity: Tau ² = 0.0				= 0.80);	²=0%		
Test for overall effect: Z =	4.41 (P < 0.000	1)				
4.1.10 Pharyngalgia							
BiX	2	22	8	91	0.2%	1.04 [0.20, 5.27]	
He R	5	69	19	135	0.3%	0.48 [0.17, 1.34]	<u> </u>
Huang Q	1	3	4	51	0.1%	5.88 [0.43, 79.77]	
Lei S	3	15	4	19	0.2%	0.94 [0.18, 5.02]	
Liu J	1	13	4	27	0.1%	0.48 [0.05, 4.78]	
Wan S	0	40	24	95	0.1%	0.04 [0.00, 0.61]	•
Wang D	12	36	12	102	0.4%	3.75 [1.50, 9.39]	
Subtotal (95% CI)	24	198	75	520	1.5%	0.91 [0.30, 2.74]	
Total events Heterogeneity: Tau ² = 1.3	24 7: Chi ^a	2 = 10 21	75 df = 6 (8)· [2 = 60%		
Test for overall effect: Z =			ui – 0 (l	- 0.004	MI - 09%	,	
. cortor oronali cilect. Z =	J (I	= 0.07)					
							ı

A management O							
Aggarwal S	0	8	1	8	0.1%	0.29 [0.01, 8.37]	· · · · · · · · · · · · · · · · · · ·
Cai Q	4	58	5	240	0.3%	3.48 [0.90, 13.40]	
Cai Y	1	3	0	4	0.1%	5.40 [0.15, 188.83]	
Chen G	1	11	3	10	0.1%	0.23 [0.02, 2.73]	
Chen Q	16	43	23	102	0.4%	2.04 [0.94, 4.41]	
Chu J Colonori M	3	43	0	11	0.1%	1.99 [0.10, 41.33]	
Colaneri M Ferguson J	2 6	17 21	1 13	27 51	0.1% 0.3%	3.47 [0.29, 41.53] 1.17 [0.38, 3.65]	
Guan WJ	10	173	32	926	0.3%	1.71 [0.83, 3.55]	
He R	5	69	14	135	0.3%	0.68 [0.23, 1.96]	
Huang C	Ō	13	1	28	0.1%	0.68 [0.03, 17.80]	
Huang R	0	23	13	179	0.1%	0.26 [0.02, 4.56]	
Jiang Y	2	8	4	52	0.2%	4.00 [0.60, 26.68]	
Ketcham SW	2	6	4	7	0.1%	0.38 [0.04, 3.61]	
Lei S	1	15	1	19	0.1%	1.29 [0.07, 22.42]	
Li K	2	25	5	58	0.2%	0.92 [0.17, 5.10]	
LIS	3	26	6	43	0.2%	0.80 [0.18, 3.53]	
LiX	85	269	94	279	0.5%	0.91 [0.64, 1.30]	-
Li YK	1	9	4	16	0.1%	0.38 [0.04, 4.00]	
Liang W	5	131	52	1459	0.3%	1.07 [0.42, 2.74]	
Liu F	1	33	4	107	0.1%	0.80 [0.09, 7.46]	
Liu J Liu Z	2 1	13 8	1 1	27 64	0.1% 0.1%	4.73 [0.39, 57.70] 9.00 (0.51, 160, 28)	
Liu∠ Pan L	10	37	25	66	0.1%	9.00 [0.51, 160.28] 0.61 [0.25, 1.46]	
Peng YD	2	16	13	96	0.4%	0.91 [0.19, 4.49]	
Pereira MR	7	27	21	63	0.3%	0.70 [0.26, 1.92]	
Sun L	, O	15	1	40	0.1%	0.85 [0.03, 22.00]	
Wan S	13	40	5	95	0.3%	8.67 [2.83, 26.50]	
Wang D	6	36	8	102	0.3%	2.35 [0.75, 7.31]	
Wang F	4	14	8	14	0.2%	0.30 [0.06, 1.44]	
Wu J	6	83	1	197	0.2%	15.27 [1.81, 128.95]	———•
Xie H	4	28	3	51	0.2%	2.67 [0.55, 12.88]	
Xie J	3	34	5	22	0.2%	0.33 [0.07, 1.55]	
Xiong F	6	30	11	101	0.3%	2.05 [0.69, 6.10]	
Yang P	63	68	54	65	0.3%	2.57 [0.84, 7.85]	
Yang Y	4	36	0	14	0.1%	4.02 [0.20, 79.58]	
Yao Q Zhang JJ	2 9	25 58	6 9	83 82	0.2% 0.3%	1.12 [0.21, 5.91] 1.49 [0.55, 4.02]	
Zhang 55 Zheng S	9 10	74	9	22	0.3%	7.33 [0.41, 130.15]	
Subtotal (95% CI)	10	1646	0	4965	8.4%	1.35 [1.03, 1.78]	•
							÷
	302		452				
Total events Heterogeneity: Tau ^z = 0	0.18; Chi²			(P = 0.04); I² = 30%	•	
Total events Heterogeneity: Tau² = 0 Test for overall effect: Z	0.18; Chi²			(P = 0.04); I²= 30%		
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea	0.18; Chi²			(P = 0.04 8); I² = 30% 0.1%	, 0.15 [0.01, 3.77]	•
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q).18; Chi := 2.17 (F	° = 0.03)	df= 38			0.15 [0.01, 3.77] 1.90 [0.77, 4.71]	·
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J	0.18; Chi ^z := 2.17 (F 0 10 1	P = 0.03) 8 43 43	df = 38 2 14 0	8 102 11	0.1% 0.4% 0.1%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28]	·
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J	0.18; Chi ² := 2.17 (F 0 10 1 2	8 43 43 21	df = 38 2 14 0 15	8 102 11 51	0.1% 0.4% 0.1% 0.2%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22]	· · · · · · · · · · · · · · · · · · ·
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J Guan WJ	0.18; Chi ² := 2.17 (F 0 10 1 2 12	P = 0.03) 8 43 43 21 173	df = 38 2 14 0 15 43	8 102 11 51 926	0.1% 0.4% 0.1% 0.2% 0.4%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q	0.18; Chi ² := 2.17 (F 0 10 1 2 12 0	P = 0.03) 8 43 43 21 173 3	df = 38 2 14 0 15 43 3	8 102 11 51 926 51	0.1% 0.4% 0.1% 0.2% 0.4% 0.1%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q Lei S	0.18; Chi [#] = 2.17 (F 0 10 1 2 12 0 1	e = 0.03) 8 43 43 21 173 3 15	df = 38 2 14 0 15 43 3 2	8 102 11 51 926 51 1459	0.1% 0.4% 0.1% 0.2% 0.4% 0.1%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45] 52.04 [4.46, 607.54]	·
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q Lei S Liang W	0.18; Chi [#] = 2.17 (F 0 10 1 2 12 0 1 7	P = 0.03) 8 43 43 21 173 3 15 15 131	df = 38 2 14 0 15 43 3 2 73	8 102 11 51 926 51 1459 107	0.1% 0.4% 0.2% 0.4% 0.1% 0.1% 0.1%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45] 52.04 [4.46, 607.54] 0.03 [0.01, 0.06]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q Lei S Liang W Liu F	0.18; Chi ⁼ 2.17 (F 0 10 1 2 12 0 1 7 3	e = 0.03) 8 43 43 21 173 3 15 131 33	df = 38 2 14 0 15 43 3 2 73 0	8 102 11 926 51 1459 107 27	0.1% 0.4% 0.1% 0.2% 0.4% 0.1% 0.1% 0.4% 0.1%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45] 52.04 [4.46, 607.54] 0.03 [0.01, 0.06] 6.31 [0.31, 127.75]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q Lei S Liang W Liu F Liu J	0.18; Chi ⁼ 2.17 (F 0 10 1 2 12 0 1 7 3 3 3	9 = 0.03) 8 43 43 21 173 3 15 131 33 13	df = 38 2 14 0 15 43 3 2 73 0 0	8 102 11 51 926 51 1459 107 27 27	0.1% 0.4% 0.2% 0.4% 0.1% 0.1% 0.1% 0.1%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45] 52.04 [4.46, 607.54] 0.03 [0.01, 0.06] 6.31 [0.31, 127.75] 18.33 [0.87, 386.07]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q Lei S Liang W Liu F Liu J Liu J	0.18; Chi ⁼ 2.17 (F 0 10 1 2 12 12 1 7 3 3 3 1	P = 0.03) 8 43 43 21 173 3 15 131 33 13 8	df = 38 2 14 0 15 43 2 73 0 0 0 0	8 102 11 51 926 51 1459 107 27 27 64	0.1% 0.4% 0.2% 0.4% 0.1% 0.1% 0.4% 0.1% 0.1%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45] 52.04 [4.46, 607.54] 0.03 [0.01, 0.06] 6.31 [0.31, 127.75] 18.33 [0.87, 386.07] 25.80 [0.96, 691.66]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q Lei S Liang W Liu F Liu J Liu Z Wang D	0.18; Chi ⁼ 2.17 (F 0 10 1 2 12 0 1 7 3 3 3 1 4	P = 0.03) 8 43 43 21 173 3 15 131 33 13 8 36	df = 38 2 14 0 15 43 2 73 0 0 0 0 10	8 102 11 51 926 51 1459 107 27 27 64 102	0.1% 0.4% 0.1% 0.2% 0.4% 0.1% 0.4% 0.1% 0.1% 0.1% 0.1% 0.3%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45] 52.04 [4.46, 607.54] 0.03 [0.01, 0.06] 6.31 [0.31, 127.75] 18.33 [0.87, 386.07] 25.80 [0.96, 691.66] 1.15 [0.34, 3.92]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q Lei S Liang W Liang W Liu F Liu J Liu Z Wang D Wang F	0.18; Chi ⁼ 2.17 (F 0 10 1 2 12 0 1 7 3 3 3 1 4 2	P = 0.03) 8 43 43 21 173 3 15 131 33 13 8 36 14	df = 38 2 14 0 15 43 2 73 0 0 0 0 10 4	8 102 11 926 51 1459 107 27 27 64 102 14	0.1% 0.4% 0.1% 0.2% 0.4% 0.1% 0.1% 0.1% 0.1% 0.1% 0.1% 0.3% 0.2%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45] 52.04 [4.46, 607.54] 0.03 [0.01, 0.06] 6.31 [0.31, 127.75] 18.33 [0.87, 386.07] 25.80 [0.96, 691.66] 1.15 [0.34, 3.92] 0.42 [0.06, 2.77]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q Lei S Liang W Liu F Liu J Liu Z Wang D Wang F Wu J	0.18; Chi ⁼ 2.17 (F 0 10 1 2 12 0 1 7 3 3 3 1 4	P = 0.03) 8 43 43 21 173 3 15 131 33 13 8 36	df = 38 2 14 0 15 43 2 73 0 0 0 0 10	8 102 11 51 926 51 1459 107 27 27 64 102	0.1% 0.4% 0.1% 0.2% 0.4% 0.1% 0.4% 0.1% 0.1% 0.1% 0.1% 0.3%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45] 52.04 [4.46, 607.54] 0.03 [0.01, 0.06] 6.31 [0.31, 127.75] 18.33 [0.87, 388.07] 25.80 [0.96, 691.66] 1.15 [0.34, 3.92] 0.42 [0.06, 2.77] 7.35 [0.75, 71.72]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q Lei S Liang W Liu F Liu J Liu Z Wang D Wang F Wu J Xiong F	0.18; Chi [≇] 2.17 (F 0 10 1 2 12 0 1 2 12 0 1 7 3 3 1 4 2 3	P = 0.03) 8 43 43 21 173 3 15 131 33 13 8 36 14 83	df = 38 2 14 0 15 43 3 2 73 0 0 0 0 10 4 1	8 102 11 51 926 51 1459 107 27 27 64 102 14 197	0.1% 0.4% 0.1% 0.2% 0.4% 0.1% 0.1% 0.1% 0.1% 0.1% 0.3% 0.2% 0.1%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45] 52.04 [4.46, 607.54] 0.03 [0.01, 0.06] 6.31 [0.31, 127.75] 18.33 [0.87, 386.07] 25.80 [0.96, 691.66] 1.15 [0.34, 3.92] 0.42 [0.06, 2.77]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q Lei S Liang W Liu F Liu J Liu Z Wang D Wang F Wu J Xiong F Zhang JJ	0.18; Chi [≇] 2.17 (F 0 10 1 1 2 12 0 1 7 3 3 1 4 2 3 8	P = 0.03) 8 43 43 21 173 3 15 131 33 13 8 36 14 83 30	df = 38 2 14 0 15 43 3 2 73 0 0 0 0 10 4 1 10	8 102 11 926 51 1459 107 27 27 64 102 14 102 14 197 101 82 22	0.1% 0.4% 0.1% 0.2% 0.4% 0.1% 0.1% 0.1% 0.1% 0.1% 0.3% 0.2% 0.1% 0.3%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45] 52.04 [4.46, 607.54] 0.03 [0.01, 0.06] 6.31 [0.31, 127.75] 18.33 [0.87, 386.07] 25.80 [0.96, 691.66] 1.15 [0.34, 3.92] 0.42 [0.06, 2.77] 7.35 [0.75, 71.72] 3.31 [1.17, 9.36]	
Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q Lei S Liang W Liu F Liu J Liu Z Wang D Wang F Wu J Xiong F Zhang JJ Zheng S	0.18; Chi [≇]	P = 0.03) 8 43 43 21 173 3 15 131 33 13 8 36 14 83 30 58	df = 38 2 14 0 15 43 3 2 73 0 0 10 4 1 10 19	8 102 11 926 51 1459 107 27 64 102 14 197 101 82	0.1% 0.4% 0.1% 0.2% 0.4% 0.1% 0.1% 0.1% 0.1% 0.1% 0.2% 0.1% 0.2% 0.1% 0.3% 0.3%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45] 52.04 [4.46, 607.54] 0.03 [0.01, 0.06] 6.31 [0.31, 127.75] 18.33 [0.87, 386.07] 25.80 [0.96, 691.66] 1.15 [0.34, 3.92] 0.42 [0.06, 2.77] 7.35 [0.75, 71.72] 3.31 [1.17, 9.36] 0.31 [0.11, 0.89]	
Total events Total events Heterogeneity: Tau ² = 0 Test for overall effect: Z 4.1.12 Nausea Aggarwal S Chen Q Chu J Ferguson J Guan WJ Huang Q Lei S Liang W Liu F Liu J Liu J Liu Z Wang D Wang F Wu J Xiong F Zhang JJ Zheng S Subtotal (95% CI) Total events	0.18; Chi [≇]	P = 0.03) 8 43 43 21 173 3 15 131 33 13 8 36 14 83 30 58 74	df = 38 2 14 0 15 43 3 2 73 0 0 10 4 1 10 19	8 102 11 926 51 1459 107 27 27 64 102 14 102 14 197 101 82 22	0.1% 0.4% 0.2% 0.4% 0.1% 0.1% 0.1% 0.1% 0.1% 0.1% 0.1% 0.2%	0.15 [0.01, 3.77] 1.90 [0.77, 4.71] 0.81 [0.03, 21.28] 0.25 [0.05, 1.22] 1.53 [0.79, 2.97] 1.98 [0.08, 46.45] 52.04 [4.46, 607.54] 0.03 [0.01, 0.06] 6.31 [0.31, 127.75] 18.33 [0.87, 386.07] 25.80 [0.96, 691.66] 1.15 [0.34, 3.92] 0.42 [0.06, 2.77] 7.35 [0.75, 71.72] 3.31 [1.17, 9.36] 0.31 [0.11, 0.89] 0.42 [0.07, 2.71]	

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4.1.13 Vomiting						(2) (and the set of the branch of the branch	
Aggarwal S	0	8	2	8	0.1%	0.15 [0.01, 3.77]	· · · · · · · · · · · · · · · · · · ·
Chen Q	3	43	3	102	0.2%	2.48 [0.48, 12.78]	
Ferguson J	0	21	7	51	0.1%	0.14 [0.01, 2.53]	· · · · · · · · · · · · · · · · · · ·
Guan WJ	12	173	43	926	0.4%	1.53 [0.79, 2.97]	
Huang R	1	23	3	179	0.1%	2.67 [0.27, 26.76]	
Jiang Y	1	8	2	52	0.1%	3.57 [0.29, 44.72]	
LiX	20	269	25	279	0.4%	0.82 [0.44, 1.51]	
Liang W	7	131	73	1459	0.4%	1.07 [0.48, 2.38]	—
Liu J	1	13	0	27	0.1%	6.60 [0.25, 173.60]	
Liu Z	1	8	0	64	0.1%	25.80 [0.96, 691.66]	
Pan L	2	37	2	66	0.2%	1.83 [0.25, 13.55]	
Pereira MR	2	27	5	63	0.2%	0.93 [0.17, 5.11]	
Wang D	3	36	1	102	0.1%	9.18 [0.92, 91.31]	
Wang F	1	14	2	14	0.1%	0.46 [0.04, 5.77]	
WuJ	3	83	1	197	0.1%	7.35 [0.75, 71.72]	
Xiong F	8	30	10	101	0.3%	3.31 [1.17, 9.36]	
Zhang JJ	2	58	5	82	0.2%	0.55 [0.10, 2.94]	
Zheng S	2	74	Ō	22	0.1%	1.55 [0.07, 33.53]	
Subtotal (95% CI)	-	1056	Ŭ	3794	3.4%	1.48 [0.97, 2.25]	•
Total events	69		184				•
Heterogeneity: Tau ² = 1		² = 22.45		(P = 0.17)	')· I ² = 249	6	
Test for overall effect: 2							
4.1.14 Abdominal pain			~	400	0.00	0.70/0.45 4.00	
Chen Q	2	43	6	102	0.2%	0.78 [0.15, 4.03]	
Lei S	1	15	0	19	0.1%	4.03 [0.15, 106.36]	
Li K	2	25	5	58	0.2%	0.92 [0.17, 5.10]	
LiX	12	269	4	279	0.3%	3.21 [1.02, 10.08]	
Liu F	1	33	2	107	0.1%	1.64 [0.14, 18.69]	
Liu J	0	13	1	27	0.1%	0.65 [0.02, 17.16]	
Pan L	2	37	0	66	0.1%	9.37 [0.44, 200.47]	
Wang D	3	36	0	102	0.1%	21.42 [1.08, 425.38]	
Zhang JJ	6	58	2	82	0.2%	4.62 [0.90, 23.74]	
Subtotal (95% CI)		529		842	1.4%	2.38 [1.25, 4.52]	◆
Total events	29		20				
Heterogeneity: Tau ² = I				= 0.48);	²=0%		
Test for overall effect: 2	Z = 2.64 (F	P = 0.008	3)				
4.1.15 Headache							
Aggarwal S	2	8	2	8	0.1%	1.00 [0.10, 9.61]	
CaiQ	0	58	5	240	0.1%	0.37 [0.02, 6.71]	
Chen G	1	11	1	10	0.1%	0.90 [0.05, 16.59]	
Chen Q	8	43	16	102	0.1%		
						1.23 [0.48, 3.13]	-
Guan WJ	26	173	124	926	0.5%	1.14 [0.72, 1.81]	
He R	3	69	11	135	0.3%	0.51 [0.14, 1.90]	
Huang C	0	13	3	28	0.1%	0.27 [0.01, 5.62]	
Huang Q	0	3	3	51	0.1%	1.98 [0.08, 46.45]	
Huang R	0	23	12	179	0.1%	0.29 [0.02, 4.98]	
Lei S	5	15	3	19	0.2%	2.67 [0.52, 13.68]	
LIK	3	25	6	58	0.2%	1.18 [0.27, 5.15]	
LiS	5	26	10	43	0.3%	0.79 [0.24, 2.62]	
LIX	25	269	37	279	0.4%	0.67 [0.39, 1.15]	
Liang W	15	131	190	1459	0.4%	0.86 [0.49, 1.51]	
Liu F	0	33	2	107	0.1%	0.63 [0.03, 13.45]	
Liu J	2	13	6	27	0.2%	0.64 [0.11, 3.69]	
Liu Z	1	8	0	64	0.1%	25.80 [0.96, 691.66]	
Sun L	2	15	4	40	0.2%	1.38 [0.23, 8.48]	
Tian S	3	46	14	216	0.3%	1.01 [0.28, 3.66]	
Wan S	11	40	23	95	0.4%	1.19 [0.51, 2.74]	_
Wang D	3	36	6	102	0.2%	1.45 [0.34, 6.15]	
Wang F	2	14	1	14	0.1%	2.17 [0.17, 27.08]	
WuJ	32	83	11	197	0.4%	10.61 [5.00, 22.50]	
Yang P	62	68	62	65	0.2%	0.50 [0.12, 2.09]	
Yang Y	5	36	1	14	0.1%	2.10 [0.22, 19.75]	
Yao Q	0	25	1	83	0.1%	1.08 [0.04, 27.30]	
Zhena S	4	74	, o	22	0.1%	2.87 [0.15, 55.43]	
Subtotal (95% CI)	4	1358	0	4583	5.8%	1.19 [0.83, 1.72]	•
Total events	220		554			the ferred the s	•
Heterogeneity: Tau ² = I		² = 50.24		(P = 0.00)3); ² = 48	3%	

Heterogeneity: Tau² = 0.33; Chi² = 50.24, df = 26 (P = 0.003); l² = 48% Test for overall effect: Z = 0.95 (P = 0.34)

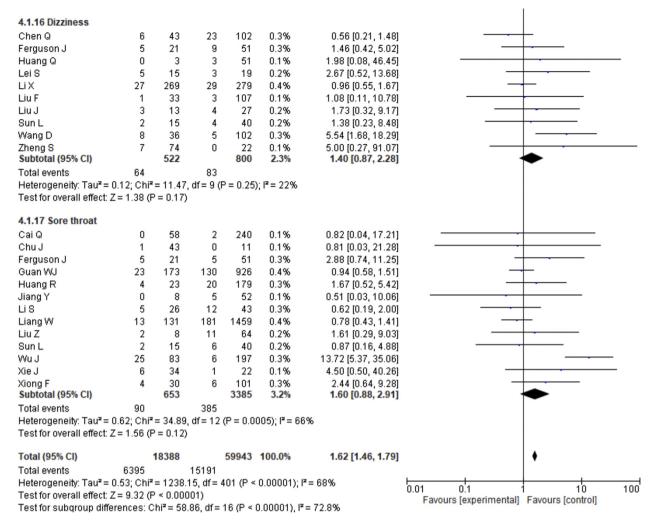


Figure 9. (continued)

found expression of SARS-CoV2 receptor in the GI tract that may be related to GI-related symptoms like diarrhea, nausea and vomiting [104]. Shortness of breath or dyspnea indicates an impaired function of the lung and oxygen deficiency. Therefore, while planning to pay great attention to patients with the respiratory system and dyspnea as the primary symptoms, more attention should also be given to patients with cough, fatigue, anorexia, chest tightness, hemoptysis, diarrhea, abdominal pain, headaches, dizziness, nausea, sputum production and vomiting [78, 79, 105, 106].

Nowadays, many articles have been published on epidemiologic and clinical characteristics, but variations in reporting descriptive data may lead to the misunderstanding of the clinical features of COVID-19. Besides, some meta-analysis is also published. However, these metaanalyses pooled a small number of studies (<30). This is the first meta-analysis with the various studies (55 citations) and the most detailed review and clear proof of the clinical characteristics of COVID-19 patients to date. The quality of the publications included in this study is high, the analysis is rigorous, comprehensive, and the conclusions drawn by this meta-analysis are highly credible. Although this is a novel meta-analysis, there were some limitations to our study. First, the studies included were retrospective. Second, the sample size (7-1590) has a considerable variation among the included studies, leading to high heterogeneity. Third, reports being restricted to China and a few other countries, and our goal is to use the findings of this study to predict patients in general, including other countries and races. Without this limitation, this study analyzed the risk factors for progression to critical illness in COVID-19 patients to help to assess patient status and identify critical patients early. Our findings provide valuable information regarding the association of age, sex, comorbidities and clinical symptoms with the severity of COVID-19. We hope this information will support health care professionals and decisionmakers in the current global pandemic, and more caution, as well as better early intervention, should be taken to improve the prognosis for older patients with respiratory failure. Effective treatment measures should be taken according to age, sex, comorbidities and clinical symptoms as the severity of COVID-19 is associated with these parameters.

5. Conclusions

Nowadays, COVID-19 is an emerging infectious disease and led to a significant health concern globally. Our study found that male patients and elderly or older patients (age≥50 years) are at a higher risk of developing disease severity. Our study also suggests that the presence of at least one or combined comorbidities like hypertension, diabetes, cerebrovascular disease, cardiovascular diseases, respiratory disease, malignancy, chronic kidney disease and chronic liver disease increases the severity of COVID-19. The prevalence of most common clinical symptoms like fever, cough, fatigue, anorexia, dyspnea, chest tightness, hemoptysis, diarrhea and abdominal pain were significantly higher in severe patients, and these are associated with the disease severity. This meta-analysis will

help health care providers make appropriate medical decisions for their patients based on age, sex, comorbidities and clinical symptoms.

Declarations

Author contribution statement

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