



Sex Differences in Patients with COVID-19: A Retrospective Cohort Study and Meta-analysis

Zhijun Li¹, Lina Feng², Wenyu Cui², Jian Zhang², Yingxin Huang², Yunhong Zhao², Fei Teng², Donglin Wu³, Bonan Cao³, Hui Wang³, Liquan Deng¹*, Qiong Yu¹*

¹Department of Epidemiology and Biostatistics, School of Public Health, Jilin University, Changchun, China; ²Changchun Infectious Hospital, Changchun, China; ³Center for Disease Prevention and Control of Jilin Province, Changchun, China

Abstract

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Introduction

December 2019, the On outbreak of (COVID-19) coronavirus disease caused bv severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in Wuhan, China [1]. The clinical presentations of COVID-19 greatly resembled with viral pneumonia, and patients could be infected both in hospitals and in family or public settings [2]. Previous studies have demonstrated that SARS-CoV-2 has a high homology with severe acute respiratory syndrome coronavirus (SASR-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) that they might have similar clinical characteristics [3], [4]. World Health Organization (WHO) has declared COVID-19 as a public health emergency of international concern and a pandemic successively. As of April 4, 2020, the laboratoryconfirmed cases had climbed above 1 million and deaths over 50,000 all around the world [5]. With the first confirmed case occurred on January 31, 2020 in the US, the number of patient surge rapidly in the US

BACKGROUND: Accumulated evidence revealed that male was much more likely to higher severity and fatality by SARS-CoV-2 infection than female patients, but few studies and meta-analyses have evaluated the sex differences of the infection and progression of COVID-19 patients.

AIM: We aimed to compare the sex differences of the epidemiological and clinical characteristics in COVID-19 patients; and to perform a meta-analysis evaluating the severe rate, fatality rate, and the sex differences of the infection and disease progression in COVID-19 patients.

METHODS: We analyzed clinical data of patients in Changchun Infectious Hospital and Center, Changchun, Northeast China; and searched PubMed, Embase, Web of Science, and Cochrane Library without any language restrictions for published articles that reported the data of sex-disaggregated, number of severe, and death patients on the confirmed diagnosis of adult COVID-19 patients.

RESULTS: The pooled severe rate and fatality rate of COVID-19 were 22.7% and 10.7%. Male incidence in the retrospective study was 58.1%, and the pooled incidence in male was 54.7%.

CONCLUSION: The pooled severe rate in male and female of COVID-19 was 28.2% and 18.8%, the risky of severe and death was about 1.6folds higher in male compared with female, especially for older patients (> 50 y).

and exceeded all reported cases in China and Italy in a short term [6]. Although the detailed data of severity and mortality all over the world were limited, especially in western countries, there were a large variation of severe rate and case-fatality rate of COVID-19 among different population [2], [7], [8], [9], [10].

Timelvidentification of risk factors for the infection and severe or critical cases is of critical importance [11]. Previous studies found that older age, higher d-dimer concentrations, high sequential organ failure assessment (SOFA) score, and pre-existing underlying disease were the potential risk factors for the infections and poor progression and prognosis in COVID-19 patients [12], [13], [14], [15], [16]. Meantime, accumulated evidence revealed that male was much more likely to higher severity and fatality by SARS-CoV-2 infection than female patients [10], [11], [14], [15], [17], [18], [19], but few studies and meta-analyses have evaluated the sex differences of the infection and progression of COVID-19 patients. Therefore, we performed the first retrospective cohort study to compare the sex differences of the epidemiological and clinical characteristics on

COVID-19 patients in Changchun, Northeast China; and a comprehensive meta-analysis to evaluate the severe rate and the sex differences of the infection and disease progression in COVID-19 patients.

Materials and Method

Retrospective cohort study

Data were collected from Changchun Infectious Hospital and Center for Disease Prevention and Control in Jilin Province, Northeast China. All 43 patients were hospitalized from January 20, 2020, to February 14, 2020, and discharged from February 19, 2020, to March 9, 2020. The study was approved by the ethical committee of Jilin University School of Public Health (ethical code: 2020-03-011), and written informed consent was obtained from all cases.

Meta-analysis

We searched and identified all relevant articles through following electronic databases: PubMed, Embase, Web of Science, and Cochrane Library without any language restrictions to limit the language bias (up to April 2020). We also evaluated the reference lists of all identified references for additional relevant studies by manual retrieval. We combined the following search terms: COVID-19, 2019 novel coronavirus, SARS-CoV-2, 2019-nCoV, and novel coronavirus-infected pneumonia. After removing duplicate citations and screening the title and abstracts, we downloaded and assessed the full texts in accordance with the following criteria for eligibility. Two authors (ZJ Li and LQ Deng) independently evaluated the screened articles for eligibility and any disagreements were adjudicated by the third author (Q Yu). The meta-analysis was performed and reported on the basis of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [20].

Any relevant studies that reported the data of sex-disaggregated, number of severe cases on the confirmed diagnosis of adult COVID-19 patients were included in the meta-analysis. The exclusion criteria were described as follows: (1) Data not provided or unavailable or duplication; (2) children or pregnant population; and (3) non-human studies, abstract, case reports, methodological report, review, or meta-analysis. Two authors (Li and Deng) independently performed data extraction and assessed the methodological quality of eligible studies, and any discrepancies were adjudicated by discussion with third author (Yu). The following information was extracted: Author, publication year, study design, date of collection, location, age, total patients, number of severe cases, and sex distribution of COVID-19 patients.

Assessment of risk bias

The quality of eligible studies was assessed using 11-item checklist criteria which recommended for cross-sectional study by Agency for Healthcare Research and Quality (AHRQ). Each item was answered by "Yes" "No" "Unclear," only answered "Yes" that would score 1.

Statistical analysis

All analyses were processed on R 3.6.1 software, and $p \le 0.05$ was considered to be statistically significant. Median with interguartile and the number of illness and its percentages were used to summarize continuous and categorical variables. The Chinese management guideline for COVID-19 (6.0) was used to separate patients into general and severe or critical cases. Mann-Whitney U test, Chi-square test, and Fisher's exact test were used to compare the differences between general and severe or critical cases. All meta-analyses were performed by meta package and metaprop module of R 3.6.1. Heterogeneity among studies were evaluated by l^2 statistics and Q test, the random-effect model was used to compute the pooled results when $l^2 > 50\%$ and p < 0.05 of Q test; otherwise, the fixed-effect model was used. Subgroup analysis, sensitivity analysis, and meta-regression were performed to assess the sources of heterogeneity. Funnel plot asymmetry and peters test were used to evaluate the publication bias among studies.

Results

As of March 9, 2020, 43 patients with SAS-CoV-2 infections were discharged. Baseline of demographic characteristic, clinical features of COVID-19 patients were presented in Table 1. The median of age was 41.0 years and 25 (58.1%) patients were male. Most patients (88.4%) were classified as general pneumonia, 11.6% as critical or severe (Table 1). Age, severity of pneumonia, exposure history, and comorbidities were comparable between female and male (p > 0.05). As for occupation, half of female cases were retired or unemployed and most male (72.0%) were employee or professional technical (p < 0.05). The majority of female were family cluster cases (p < 0.05). Comorbidities were nonsignificant higher in female than that in male. History of hypertension and diabetes in male was higher than female, but COPD, CVD, bronchitis, and asthma in male were lower than female (Table 1). The initial symptoms

Table 1: Baseline of demographic characteristic, clinical features of COVID-19 patients

Characteristics	Total (n = 43)	Female (n = 18) (%)	Male (n = 25) (%)	p value
lge, median(IQR), y	41.0 (33.0-52.0)	41.0 (30.0–53.0)	42.0 (33.0-85.0)	0.730
Severity				1.000
General	38 (88.4)	16 (88.9)	22 (88.0)	
Critical or severe	5 (11.6)	2 (11.1)	3 (12.0)	
Dccupation	. ,			0.012
Agricultural worker	2 (4.7)	2 (11.1)	0	
Employee	19 (44.2)	4 (22.2)	15 (60.0)	
Professional technical	6 (14.0)	3 (16.7)	3 (12.0)	
Retired	9 (20.9)	5 (27.8)	4 (16.0)	
Self-employed	3 (7.0)	0	3 (12.0)	
Unemployed	4 (9.3)	4 (22.2)	0	
Exposure history	4 (5.5)	+ (22.2)	0	0.680
	7 (16.2)	2(11,1)	F (20.0)	0.000
Exposure to Wuhan	7 (16.3)	2 (11.1) 16 (88.9)	5 (20.0)	
Exposure to confirmed or suspected people	36 (83.7)	. ,	20 (80.0)	0.004
Cluster patients	35 (81.4)	16 (88.9)	19 (76.0)	0.284
Single case	8 (18.6)	2 (11.1)	6 (24.0)	0.013
Family cluster	28 (65.1)	16 (88.9)	12 (48.0)	
Working cluster	7 (16.3)	0	7 (28.0)	
omorbidities	22 (51.2)	10 (55.6)	12 (48.0)	0.760
Hypertension	7 (16.3)	2 (11.1)	5 (20.0)	0.680
Diabetes	5 (11.6)	1 (5.6)	4 (16.0)	0.380
Malignancy	3 (7.0)	2 (11.1)	1 (4.0)	0.562
Hypothyroidism	3 (7.0)	3 (16.7)	0	-
Chronic obstructive pulmonary disease	2 (4.7)	2 (11.1)	0	
Coronary heart disease	2 (4.7)	1 (5.6)	1 (4.0)	-
Bronchitis	2 (4.7) 2 (4.7)	0	2 (8.0)	-
Neurodegenerative disease	2 (4.7) 2 (4.7)		0	-
8		2 (11.1)		-
Asthma	1 (2.3)	1 (5.6)	0	-
ymptoms				
Fever	33 (76.7)	14 (77.8)	19 (76.0)	0.892
Highest temperature, °C	38.0 (37.3–38.4)	37.9 (37.1–38.4)	38.0 (36.9–38.4)	0.961
Cough	35 (81.4)	16 (88.9)	19 (76.0)	0.284
Expectoration	31 (72.1)	12 (66.7)	9 (36.0)	0.047
Myalgia or fatigue	23 (53.5)	9 (50.0)	14 (56.0)	0.736
Chest tightness	20 (46.5)	9 (50.0)	11 (44.0)	0.763
Nasal congestion or sneezing	15 (34.9)	5 (27.8)	10 (40.0)	0.782
Diarrhea	8 (18.6)	1 (5.6)	7 (28.0)	0.111
Nausea or vomiting	8 (18.6)	3 (16.7)	5 (20.0)	0.782
ncubation period, median(IQR), d		9.0 (5.8–12.0)		
	8.0 (5.0-11.0)	9.0 (5.6–12.0)	7.0 (4.0–11.0)	0.459
Dinset of illness to, median(IQR), d		50(0000)		0.440
Hospital admission	6.0 (2.0-8.0)	5.0 (2.0–6.0)	6.0 (3.0–9.0)	0.143
Discharge	22.0 (18.0–24.0)	22.5 (16.0–24.0)	22.0 (18.0–28.0)	0.387
ouration of viral shedding, median(IQR), d	19.0 (14.0–22.0)	19.0 (12.0–21.2)	19.0 (15.0–25.2)	0.393
lospitalization time, median(IQR), d	17.0 (11.0–20.0)	18.0 (10.8–20.0)	17.0 (11.0–21.0)	0.961
aboratory results				
White blood cell count, ×109/L	5.3 (4.1–6.4)	4.0 (3.1–6.3)	5.8 (5.0–7.1)	0.005
Neutrophil count, ×109/L	3.7 (2.8-4.9)	2.9 (1.6-4.5)	4.0 (3.4–5.1)	0.008
Lymphocyte count, ×109/L	1.1 (0.8–1.6)	1.1 (0.8–1.5)	1.0 (0.8–1.7)	0.790
Monocyte count, ×109/L	0.3 (0.2–0.5)	0.26 (0.19–0.32)	0.30 (0.27–0.60)	0.031
Haemoglobin, g/L	144 (130–157)	133.0 (126.0–143.5)	151.5 (139.5–159.5)	0.002
C-reactive protein, mg/L	10.9 (2.5–33.4)	11.5 (2.4–24.0)	10.5 (3.2–63.6)	0.626
				0.020
Platelet count, ×109/L	183 (161–223)	180.0 (163.0–211.5)	201.0 (159.2–240.0)	
Prothrombin time, s	12.0 (11.6–12.9)	11.8 (11.3–12.7)	12.6 (11.7–13.3)	0.104
Activated partial thromboplastin time, s	32.6 (30.5–35.4)	32.2 (26.0–33.8)	34.7 (30.6–36.4)	0.158
Fibrinogen, g/dl	2.2 (2.0–3.5)	2.2 (1.9–3.6)	2.2 (2.0-3.6)	0.601
Thrombin time, s	15.8 (15.2–16.7)	16.2 (15.3–20.9)	15.7 (15.0–16.4)	0.327
Alanine aminotransferase, U/L	25.0 (19.0-45.0)	28.0 (19.7–47.5)	24.0 (19.0-44.0)	0.931
Aspartate aminotransferase, U/L	26.0 (22.0-32.0)	26.5 (24.0-35.5)	23.0 (21.0-31.5)	0.153
Albumin, g/L	44.2 (42.0-46.1)	44.3 (42.4–44.9)	44.2 (41.4-46.4)	0.905
Total bilirubin, mmol/L	7.9 (6.7–10.4)	6.9 (6.0–7.8)	8.8 (7.6–11.3)	0.006
Cholinesterase, U/L	7575 (6084–9029)	6898.5 (5600.8–8958.8)	7899.0 (6711.0–9071.5)	0.207
Creatine, µmol/L	69.2 (62.1–77.3)	61.0 (55.8–67.6)	76.3 (69.2–80.4)	< 0.00
Creatine kinase, U/L	79 (12–24)	71.0 (54.0–96.5)	109.0 (65.5–157.0)	0.047
Creatine kinase–MB, U/L	16 (12–24)	17.5 (11.8–24.2)	15.0 (12.0–23.0)	0.521
Lactate dehydrogenase, U/L	210 (185–269)	220.0 (184.0–263.0)	210 (182.5–285.0)	0.730
Myoglobin, ng/mL	69.7 (20.3–118.6)	24.4 (19.2–72.4)	26.8 (21.4–153.4)	0.151
Glucose, mmol/L	6.5 (5.7-8.0)	6.4 (5.6-7.6)	6.6 (5.9-8.5)	0.233
Cardiac troponin I, pg/mL	1.7 (1.2–7.4)	1.6 (1.2–3.7)	1.8 (1.2–8.4)	0.415
CT imaging features			· /	

were mainly fever, couth, expectoration, myalgia or fatigue, and chest tightness, but the expectoration in female was higher than in male (p < 0.05). Median incubation period in female (9 days) was non-significant longer than that in male (7 days).

The serum WBC, neutrophil count, monocyte count, hemoglobin, total bilirubin, creatine, and creatine kinase were higher in male than that in female (p < 0.05) (Table 1). Leukopenia only occurred in 6 cases (33.3%) of female. C-reactive protein was elevated in 10 cases (55.6%) in female and 15 (60.0%) in male (Table 1). Lymphopenia occurred in 7 cases (38.9%) of female

and 10 (40.0%) of male, aspartate aminotransferase was increased in each 3 cases of female (16.7%) and of male (12.0%), and lactate dehydrogenase was increased in 12 cases (66.7%) of female and 16 (64.0%) of male (Table 1). The typical CT findings of COVID-19 patients were bilateral distribution of patchy shadows or ground glass opacity, and no significant differences between female and male (p > 0.05). Complication of leukopenia in female was higher than in male (p < 0.05), but there were no significant differences on treatment between female and male (p > 0.05) (Supplementary data: Table S1).

Meta-analysis

The detailed inclusion and exclusion steps of the potentially relevant articles are presented in Figure 1. Finally, a total of 76 studies involving 90,475 patients were included in analyzing the proportion of male in patients with COVID-19, including our current retrospective study. The characteristics and quality assessment results of eligible studies are summarized in Supplementary data: Table S2. The pooled male proportion of COVID-19 patients was 54.7% (95% CI: 0.522-0.572, $l^2 = 96.9\%$), which was slightly higher than female (Supplementary data: Figure S1). Subgroup analyses suggested that the pooled morbidity of older male patients (>50-year) was 58.0% (95% CI: 0.532-0.628, $l^2 = 97.8\%$) and 51.5% (95% CI: 0.489-0.541, $l^2 = 89.9\%$) in ≤50-year patients.

Thirty-two articles were in analyzing the severe rate of patients, 21 in each male and female. The pooled severe rate and case-fatality rate of COVID-19 were 22.7% (95% CI: 0.195–0.259) and 10.7% (95% CI: 0.092-0.122, l^2 = 98.8%) (Figures 2 and 3).

The pooled severe rate in male and female of COVID-19 was 28.2% (95%CI: 0.23-0.333, $l^2 = 86.7\%$) and 18.8% (95%CI: 0.149-0.226, $l^2 = 78.6\%$), correspondingly (Figure 4). Subgroup analyses showed that the severe rate and case-fatality rate of older patients (> 50 y) (30.4%, 95%CI: 0.248-0.36, $l^2 = 94.0\%$;

20.5%) were significant higher than younger patients (16.7, 95%CI: 0.134–0.200, $l^2 = 93.9\%$; 1.3%).

Twenty-one studies involving 4213 patients and 12 studies involving 53,695 cases were included analyzing the sex differences of the disease severity and mortality of COVID-19 patients (Table 2) [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]. The pooled risk of disease severity and mortality in male was statistically significant higher than in female (OR: 1.60, 95% CI: 1.37–1.87, $I^2 = 25\%$; OR: 1.57, 95%CI: 1.42–1.74, $I^2 = 34\%$), respectively (Table 3, Figure 5).

Subgroup analyses suggested that the severe risky of older male patients had 1.94 folds higher compared with female. However, the mortality risky of younger male patients had 1.7 folds higher compared with female. Sensitivity analyses by omitting one individual study every time showed that there was no study significantly affected the pooled results (Figure S2-S7). In the meta-regression, there were significant correlation between age and log odds of sex and disease severity and mortality of COVID-19 patients (disease severity-correlation coefficient: 0.013, p = 0.001 and mortality-correlation coefficient: -0.02, p = 0.029) (Figure 6). In addition, there was no publication bias in the study, all that indicated that the results were credible in the meta-analyses (Figure S8-S13).

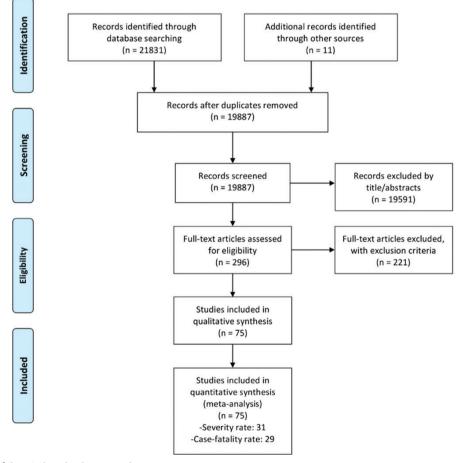


Figure 1: Flowchart of the study selection procedure

Study	Events	Total			Proportion	95%-CI	Weight (fixed)	Weight (random)
Cai QX et al	58	298			0.19	[0.15; 0.24]	0.4%	3.6%
Cao JL et al	18	102		_	0.18	[0.11; 0.26]	0.2%	3.2%
Chen C et al	24	150			0.16	[0.11; 0.23]	0.2%	3.4%
Chen G et al	11	21			0.52	[0.30; 0.74]	0.0%	1.4%
Chen J et al	22	249	→ → ::		0.09	[0.06; 0.13]	0.7%	3.7%
Chen L et al	14	29			0.48	[0.29; 0.67]	0.0%	1.7%
China CDC	8255	44672	-		0.18	[0.18; 0.19]	65.9%	3.9%
Dong XC et al	62	135			0.46	[0.37; 0.55]	0.1%	3.0%
Goyal P et al	130	393		<u> </u>	0.33	[0.28; 0.38]	0.4%	3.6%
Guan W et al	173	1099			0.16	[0.14; 0.18]	1.8%	3.8%
Huang C et al	13	41			0.32	[0.18; 0.48]	0.0%	2.2%
Jin X et al	64	651	+		0.10	[0.08; 0.12]	1.6%	3.8%
Lei SQ et al	15	34			0.44	[0.27; 0.62]	0.0%	1.9%
Li KH et al	25	83			0.30	[0.21; 0.41]	0.1%	2.8%
Liu W et al	8	78			0.10	[0.05; 0.19]	0.2%	3.3%
Livngston E et al	6731	22512			0.30	[0.29; 0.31]	23.9%	3.9%
Peng YD et al	16	112			0.14	[0.08; 0.22]	0.2%	3.3%
Qian GQ et al	9	91	i		0.10	[0.05; 0.18]	0.2%	3.4%
Shi HS et al	3	81	!!		0.04	[0.01; 0.10]	0.5%	3.6%
Shi Y et al	49	487	::		0.10	[0.08; 0.13]	1.2%	3.8%
Tian S et al	46	262			0.18	[0.13; 0.23]	0.4%	3.6%
Wan SX et al	40	135	÷	+	0.30	[0.22; 0.38]	0.1%	3.2%
Wang DW et al	36	138	++	+	0.26	[0.19; 0.34]	0.2%	3.2%
Wu CM et al	84	201			0.42	[0.35; 0.49]	0.2%	3.3%
Wu J et al	3	80	II		0.04	[0.01; 0.11]	0.5%	3.6%
Xie HS et al	28	79			0.35	[0.25; 0.47]	0.1%	2.7%
Xu YH et al	13	50		+	0.26	[0.15; 0.40]	0.1%	2.5%
Yao N et al	22	40			0.55	[0.38; 0.71]	0.0%	2.0%
Zhang GQ et al	55	221			0.25	[0.19; 0.31]	0.3%	3.4%
Zhang JJ et al	58	140		—— · ——	0.41	[0.33; 0.50]	0.1%	3.1%
Zhao W et al	14	101			0.14	[0.08; 0.22]	0.2%	3.3%
Current study	5	43		-	0.12	[0.04; 0.25]	0.1%	2.9%
_								
Fixed effect model		72808	ė.			[0.21; 0.21]	100.0%	
Random effects model			<	>	0.23	[0.20; 0.26]		100.0%
Heterogeneity: $I^2 = 98\%$, τ	$e^2 = 0.0070$, <i>p</i> < 0.0						
			0.1 0.2	0.3 0.4 0.5 0.6 0.7				

Figure 2: The pooled severity rate of COVID-19 patients

Study	Events	Total	Proportion	95%-CI	Weight (fixed)	Weight (random)
Arentz M et al	11	21	0.52	[0.30; 0.74]	0.0%	0.4%
Cai QX et al	3	298	0.01	[0.00; 0.03]	0.9%	5.1%
Cao JL et al	17	102	· 0.17	[0.10; 0.25]	0.0%	2.4%
Chen C et al	11	150	0.07	[0.04; 0.13]	0.1%	3.7%
Chen NS et al	11	99	- 0.11	[0.06; 0.19]	0.0%	2.8%
Chen T et al	113	274	0.41	[0.35; 0.47]	0.0%	2.9%
Cheng JL et al	11	1079	0.01	[0.01; 0.02]	3.1%	5.2%
China CDC	1023	44672	0.02	[0.02; 0.02]	57.9%	5.3%
Dong XC et al	3	135	0.02	[0.00; 0.06]	0.2%	4.6%
Guan W et al	15	1099	0.01	[0.01; 0.02]	2.4%	5.2%
Guo T et al	43	187	0.23	[0.17; 0.30]	0.0%	2.8%
Huang C et al	6	41		[0.06; 0.29]		1.4%
KIDS	22	4212	0.01	[0.00; 0.01]	23.5%	5.3%
Lei SQ et al	7	34	0.21	[0.09; 0.38]	0.0%	1.0%
Liu K et al	16	137	- 0.12	[0.07; 0.18]	0.0%	3.1%
Livngston E et al	1625	22512	0.07	[0.07; 0.08]	9.7%	5.3%
Peng YD et al	17	112		[0.09; 0.23]		2.6%
Ruan QR et al	68	150	0.45	[0.37; 0.54]	0.0%	2.1%
Tang N et al	21	183	- 0.11	[0.07; 0.17]	0.1%	3.5%
Tian S et al	3	262	0.01	[0.00; 0.03]	0.7%	5.1%
Wan SX et al	1	135	0.01	[0.00; 0.04]	0.5%	5.0%
Wang DW et al	6	138	0.04	[0.02; 0.09]	0.1%	4.1%
Wu CM et al	44	201	 0.22	[0.16; 0.28]	0.0%	3.0%
Yang XB et al	32	52	0.62	[0.47; 0.75]	0.0%	1.0%
Yuan ML et al	10	27	0.37	[0.19; 0.58]	0.0%	0.6%
Zhang GQ et al	12	221	0.05	[0.03; 0.09]	0.1%	4.4%
Zhou F et al	54	191	0.28	[0.22; 0.35]	0.0%	2.7%
Goyal P et al	40	393	0.10	[0.07; 0.14]	0.1%	4.4%
Richardson S et al	553	2634	+ 0.21	[0.19; 0.23]	0.5%	5.0%
Fixed effect model		79751	0.02	[0.02; 0.03]	100.0%	
Random effects mode			0.11	[0.09; 0.12]		100.0%
Heterogeneity: $I^2 = 99\%$,	$\tau^2 = 0.0011$, p = 0				
,			0.2 0.3 0.4 0.5 0.6 0.7			

Figure 3: The pooled case-fatality rate of COVID-19 patients

					Weight	Weight
Study	Events Total		Proportion	95%-CI	(fixed)	(random)
Cai QX et al	39 145		0.27	[0.20; 0.35]	5.2%	5.5%
Cao JL et al	12 53	<u> </u>	0.23	[0.12; 0.36]	2.1%	4.8%
Chen C et al	18 84		0.21	[0.13; 0.32]	3.5%	5.3%
Chen G et al	10 17		0.59	[0.33; 0.82]	0.5%	2.7%
Goyal P et al	92 238		0.39	[0.32; 0.45]	7.1%	5.7%
Guan W et al	100 637		0.16	[0.13; 0.19]		6.1%
Huang C et al	11 30			[0.20; 0.56]	0.9%	3.6%
Lei SQ et al	5 14			[0.13; 0.65]	0.4%	2.5%
Li KH et al	15 44			[0.20; 0.50]	1.4%	4.2%
Peng YD et al	9 53			[0.08; 0.30]	2.7%	5.0%
Shi Y et al	36 259			[0.10; 0.19]	15.3%	6.0%
Tian S et al	26 127			[0.14; 0.29]	5.5%	5.6%
Wan SX et al	21 72			[0.19; 0.41]	2.5%	4.9%
Wang DW et al	22 75			[0.19; 0.41]	2.6%	5.0%
Wu CM et al	60 128			[0.38; 0.56]	3.6%	5.3%
Xie HS et al	18 44			[0.26; 0.57]		4.1%
Xu YH et al Zhang GO et al	7 29 35 108			[0.10; 0.44]	1.1% 3.5%	3.9% 5.3%
Zhang GQ et al Zhang JJ et al	33 71			[0.24; 0.42] [0.35; 0.59]	3.5% 2.0%	5.3% 4.7%
Zhao W et al	8 56			[0.35, 0.59]		4.7% 5.2%
Current study	3 25			[0.03; 0.26]	3.2% 1.7%	4.5%
Current study	5 25		0.12	[0.03, 0.31]	1.770	4.5%
Fixed effect model	2309	\$	0.22	[0.21; 0.24]	100.0%	
Random effects model		\diamond		[0.23; 0.33]		100.0%
Heterogeneity: $I^2 = 87\%$, τ		.01		,,		
		0.2 0.4 0.6	0.8			
а						
a		0.2 0.1 0.0	0.0		Weight	Weight
a Study	Events Total		Proportion	95%-CI	Weight (fixed)	Weight (random)
Study Cai QX et al	19 153		Proportion	95%–Cl [0.08; 0.19]		
Study Cai QX et al Cao JL et al	19 153 6 49		Proportion 0.12		(fixed)	(random) 6.6% 5.3%
Study Cai QX et al Cao JL et al Chen C et al	19 153 6 49 6 66		Proportion 0.12 0.12 0.09	[0.08; 0.19] [0.05; 0.25] [0.03; 0.19]	(fixed) 8.6% 2.8% 4.9%	(random) 6.6% 5.3% 6.1%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al	19 153 6 49 6 66 1 4		Proportion 0.12 0.12 0.09 0.25	[0.08; 0.19] [0.05; 0.25] [0.03; 0.19] [0.01; 0.81]	(fixed) 8.6% 2.8% 4.9% 0.1%	(random) 6.6% 5.3% 6.1% 0.8%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al	19 153 6 49 6 66 1 4 38 155		Proportion 0.12 0.12 0.09 0.25 0.25	[0.08; 0.19] [0.05; 0.25] [0.03; 0.19] [0.01; 0.81] [0.18; 0.32]	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1%	(random) 6.6% 5.3% 6.1% 0.8% 6.1%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al	19 153 6 49 6 66 1 4 38 155 73 459		Proportion 0.12 0.12 0.09 0.25 0.25 0.16	[0.08; 0.19] [0.05; 0.25] [0.03; 0.19] [0.01; 0.81] [0.18; 0.32] [0.13; 0.20]	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al	19 153 6 49 6 66 1 4 38 155 73 459 2 11		Proportion 0.12 0.12 0.09 0.25 0.25 0.16 0.18	[0.08; 0.19] [0.05; 0.25] [0.03; 0.19] [0.01; 0.81] [0.18; 0.32] [0.13; 0.20] [0.02; 0.52]	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al	19 153 6 49 6 66 1 4 38 155 73 459 2 11 10 20		Proportion 0.12 0.12 0.09 0.25 0.25 0.16 0.18 0.50	[0.08; 0.19] [0.05; 0.25] [0.03; 0.19] [0.01; 0.81] [0.18; 0.32] [0.13; 0.20] [0.02; 0.52] [0.27; 0.73]	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1% 2.2%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al	19 153 6 49 6 66 1 4 38 155 73 459 2 11 10 20 10 39		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 - 0.50 0.26	[0.08; 0.19] [0.05; 0.25] [0.03; 0.19] [0.01; 0.81] [0.18; 0.32] [0.13; 0.20] [0.02; 0.52] [0.27; 0.73] [0.13; 0.42]	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 0.5% 1.3%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1% 2.2% 3.9%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al Peng YD et al	19 153 6 49 6 66 1 4 38 155 73 459 2 11 10 20 10 39 7 59		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 - 0.50 0.26 0.12	[0.08; 0.19] [0.05; 0.25] [0.03; 0.19] [0.01; 0.81] [0.18; 0.32] [0.13; 0.20] [0.02; 0.52] [0.27; 0.73] [0.13; 0.42] [0.05; 0.23]	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 0.5% 1.3% 3.5%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1% 2.2% 3.9% 5.6%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al Peng YD et al Shi Y et al	191536496661438155734592111020103975913228		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 - 0.50 0.26 0.12 0.06	[0.08; 0.19] [0.05; 0.25] [0.03; 0.19] [0.01; 0.81] [0.18; 0.32] [0.13; 0.20] [0.02; 0.52] [0.27; 0.73] [0.13; 0.42] [0.05; 0.23] [0.03; 0.10]	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 0.5% 1.3% 3.5% 26.0%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1% 2.2% 3.9% 5.6% 7.2%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al Peng YD et al Shi Y et al Tian S et al	19 153 6 49 6 66 1 4 38 155 73 459 2 11 10 20 10 39 7 59 13 228 20 135		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 0.50 0.26 0.12 0.06 0.15	[0.08; 0.19] [0.05; 0.25] [0.03; 0.19] [0.01; 0.81] [0.18; 0.32] [0.13; 0.20] [0.02; 0.52] [0.27; 0.73] [0.13; 0.42] [0.05; 0.23] [0.03; 0.10] [0.09; 0.22]	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 0.5% 1.3% 3.5% 26.0% 6.6%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1% 2.2% 3.9% 5.6% 7.2% 6.4%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al Peng YD et al Shi Y et al Tian S et al Wan SX et al	191536496661438155734592111020103975913228201351963		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 0.26 0.12 0.06 0.15 0.30	$\begin{bmatrix} 0.08; 0.19 \\ [0.05; 0.25] \\ [0.03; 0.19] \\ [0.01; 0.81] \\ [0.18; 0.32] \\ [0.13; 0.20] \\ [0.02; 0.52] \\ [0.27; 0.73] \\ [0.13; 0.42] \\ [0.05; 0.23] \\ [0.03; 0.10] \\ [0.09; 0.22] \\ [0.19; 0.43] \end{bmatrix}$	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 1.3% 3.5% 26.0% 6.6% 1.8%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1% 2.2% 3.9% 5.6% 7.2% 6.4% 4.6%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al Peng YD et al Shi Y et al Tian S et al Wan SX et al Wang DW et al	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 0.18 0.26 0.12 0.06 0.15 0.30 0.22	$\begin{bmatrix} 0.08; 0.19 \\ [0.05; 0.25] \\ [0.03; 0.19] \\ [0.01; 0.81] \\ [0.18; 0.32] \\ [0.13; 0.20] \\ [0.02; 0.52] \\ [0.27; 0.73] \\ [0.13; 0.42] \\ [0.05; 0.23] \\ [0.03; 0.10] \\ [0.09; 0.22] \\ [0.19; 0.43] \\ [0.13; 0.34] \end{bmatrix}$	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 0.5% 1.3% 3.5% 26.0% 6.6% 1.8% 2.2%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1% 2.2% 3.9% 5.6% 7.2% 6.4% 4.6% 4.9%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al Peng YD et al Shi Y et al Tian S et al Wan SX et al Wang DW et al Wu CM et al	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 0.50 0.26 0.12 0.06 0.15 0.30 0.22 0.24	$ \begin{bmatrix} 0.08; 0.19 \\ 0.05; 0.25 \\ 0.03; 0.19 \\ 0.01; 0.81 \\ 0.18; 0.32 \\ 0.13; 0.20 \\ 0.02; 0.52 \\ 0.27; 0.73 \\ 0.13; 0.42 \\ 0.05; 0.23 \\ 0.03; 0.10 \\ 0.09; 0.22 \\ 0.19; 0.43 \\ 0.13; 0.34 \\ 0.16; 0.34 \\ \end{bmatrix} $	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 1.3% 3.5% 26.0% 6.6% 1.8% 2.2% 3.3%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1% 2.2% 3.9% 5.6% 7.2% 6.4% 4.6% 4.9% 5.6%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al Peng YD et al Shi Y et al Tian S et al Wan SX et al Wang DW et al Wu CM et al Xie HS et al	$\begin{array}{cccccccccccccccccccccccccccccccccccc$		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 - 0.50 0.12 0.06 0.12 0.06 0.15 0.30 0.22 0.24 0.29	[0.08; 0.19] [0.05; 0.25] [0.03; 0.19] [0.01; 0.81] [0.18; 0.32] [0.13; 0.20] [0.02; 0.52] [0.27; 0.73] [0.13; 0.42] [0.05; 0.23] [0.03; 0.10] [0.09; 0.22] [0.19; 0.43] [0.13; 0.34] [0.16; 0.34] [0.15; 0.46]	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 1.3% 3.5% 26.0% 6.6% 1.8% 2.2% 3.3% 1.1%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1% 2.2% 3.9% 5.6% 7.2% 6.4% 4.6% 4.9% 5.6% 3.6%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al Peng YD et al Shi Y et al Tian S et al Wan SX et al Wang DW et al Wu CM et al Xie HS et al Xu YH et al	$\begin{array}{cccccccccccccccccccccccccccccccccccc$		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 0.50 0.26 0.12 0.06 0.15 0.30 0.22 0.24 0.29 0.29	$ \begin{bmatrix} 0.08; 0.19 \\ 0.05; 0.25 \\ 0.03; 0.19 \\ 0.01; 0.81 \\ 0.18; 0.32 \\ 0.13; 0.20 \\ 0.02; 0.52 \\ 0.27; 0.73 \\ 0.13; 0.42 \\ 0.05; 0.23 \\ 0.03; 0.10 \\ 0.09; 0.22 \\ 0.19; 0.43 \\ 0.13; 0.34 \\ 0.13; 0.34 \\ 0.15; 0.46 \\ 0.11; 0.52 \\ \end{bmatrix} $	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 1.3% 3.5% 26.0% 6.6% 1.8% 2.2% 3.3% 1.1% 0.6%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1% 2.2% 3.9% 5.6% 7.2% 6.4% 4.6% 4.9% 5.6% 3.6% 2.6%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al Peng YD et al Shi Y et al Tian S et al Wan SX et al Wang DW et al Wu CM et al Xie HS et al Xu YH et al Zhang GQ et al	$\begin{array}{cccccccccccccccccccccccccccccccccccc$		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 0.50 0.26 0.12 0.06 0.15 0.30 0.22 0.24 0.29 0.29 0.18	$ \begin{bmatrix} 0.08; 0.19 \\ 0.05; 0.25 \\ 0.03; 0.19 \\ 0.01; 0.81 \\ 0.18; 0.32 \\ 0.13; 0.20 \\ 0.2; 0.52 \\ 0.27; 0.73 \\ 0.13; 0.42 \\ 0.05; 0.23 \\ 0.03; 0.10 \\ 0.09; 0.22 \\ 0.19; 0.43 \\ 0.13; 0.34 \\ 0.16; 0.34 \\ 0.15; 0.46 \\ 0.11; 0.52 \\ 0.11; 0.26 \\ \end{bmatrix} $	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 1.3% 3.5% 26.0% 6.6% 1.8% 2.2% 3.3% 1.1% 0.6% 4.8%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1% 2.2% 3.9% 5.6% 7.2% 6.4% 4.6% 4.9% 5.6% 3.6% 2.6% 6.0%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al Peng YD et al Shi Y et al Tian S et al Wan SX et al Wang DW et al Wu CM et al Xie HS et al Xu YH et al	$\begin{array}{cccccccccccccccccccccccccccccccccccc$		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 0.50 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.22 0.24 0.29 0.29 0.29 0.30	$ \begin{bmatrix} 0.08; 0.19 \\ 0.05; 0.25 \\ 0.03; 0.19 \\ 0.01; 0.81 \\ 0.18; 0.32 \\ 0.13; 0.20 \\ 0.2; 0.52 \\ 0.27; 0.73 \\ 0.13; 0.42 \\ 0.05; 0.23 \\ 0.03; 0.10 \\ 0.09; 0.22 \\ 0.13; 0.34 \\ 0.13; 0.34 \\ 0.16; 0.34 \\ 0.15; 0.46 \\ 0.11; 0.52 \\ 0.11; 0.26 \\ 0.25; 0.49 \\ \end{bmatrix} $	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 1.3% 3.5% 26.0% 6.6% 1.8% 2.2% 3.3% 1.1% 0.6% 4.8% 1.8%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.2% 3.9% 5.6% 7.2% 6.4% 4.6% 4.6% 3.6% 3.6% 2.6% 6.0% 4.6%
Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al Peng YD et al Shi Y et al Tian S et al Wan SX et al Wang DW et al Wu CM et al Xie HS et al Xu YH et al Zhang GQ et al Zhang JJ et al	$\begin{array}{cccccccccccccccccccccccccccccccccccc$		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 0.50 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.29 0.29 0.29 0.29 0.18 0.36 0.36 0.13	$ \begin{bmatrix} 0.08; 0.19 \\ 0.05; 0.25 \\ 0.03; 0.19 \\ 0.01; 0.81 \\ 0.18; 0.32 \\ 0.13; 0.20 \\ 0.2; 0.52 \\ 0.27; 0.73 \\ 0.13; 0.42 \\ 0.05; 0.23 \\ 0.03; 0.10 \\ 0.09; 0.22 \\ 0.19; 0.43 \\ 0.13; 0.34 \\ 0.16; 0.34 \\ 0.15; 0.46 \\ 0.11; 0.52 \\ 0.11; 0.26 \\ \end{bmatrix} $	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 1.3% 3.5% 26.0% 6.6% 1.8% 2.2% 3.3% 1.1% 0.6% 4.8%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.1% 2.2% 3.9% 5.6% 7.2% 6.4% 4.6% 4.9% 5.6% 3.6% 2.6% 6.0%
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Study Cai QX et al Cao JL et al Chen C et al Chen G et al Goyal P et al Guan W et al Huang C et al Lei SQ et al Li KH et al Peng YD et al Shi Y et al Tian S et al Wan SX et al Wang DW et al Xu YH et al Xie HS et al Xu YH et al Zhang GQ et al Zhang JJ et al Current study Fixed effect model	19 153 6 49 6 66 1 4 38 155 73 459 2 11 10 20 10 39 7 59 13 228 20 135 19 63 14 63 24 99 10 35 6 21 20 113 25 69 6 45 2 18		Proportion 0.12 0.09 0.25 0.25 0.16 0.18 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.25 0.16 0.13 0.12 0.25 0.25 0.16 0.12 0.25 0.25 0.16 0.12 0.25 0.16 0.12 0.25 0.25 0.16 0.12 0.25 0.25 0.16 0.12 0.25 0.25 0.16 0.12 0.26 0.12 0.26 0.12 0.25 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.26 0.12 0.29 0.29 0.29 0.18 0.29 0.29 0.18 0.29 0.18 0.29 0.18 0.29 0.18 0.30 0.21 0.29 0.18 0.30 0.21 0.29 0.18 0.36 0.13 0.11 0.30 0.13 0.11 0.36 0.13 0.11 0.36 0.13 0.11 0.36 0.13 0.11 0.18 0.36 0.13 0.11 0.18 0.36 0.13 0.11 0.11 0.11 0.18 0.29 0.11 0.11 0.11 0.11 0.11 0.11 0.11 0.11 0.11 0.11 0.11 0.11 0.11	[0.08; 0.19] [0.05; 0.25] [0.03; 0.19] [0.01; 0.81] [0.18; 0.32] [0.13; 0.20] [0.02; 0.52] [0.27; 0.73] [0.13; 0.42] [0.05; 0.23] [0.03; 0.10] [0.09; 0.22] [0.19; 0.43] [0.13; 0.34] [0.15; 0.46] [0.11; 0.52] [0.11; 0.26] [0.25; 0.49] [0.05; 0.27] [0.01; 0.35] [0.13; 0.16]	(fixed) 8.6% 2.8% 4.9% 0.1% 5.1% 21.0% 0.5% 1.3% 3.5% 26.0% 6.6% 1.8% 2.2% 3.3% 1.1% 0.6% 4.8% 1.8% 2.4% 1.1%	(random) 6.6% 5.3% 6.1% 0.8% 6.1% 7.1% 2.2% 3.9% 5.6% 7.2% 6.4% 4.6% 4.6% 4.6% 5.6% 3.6% 2.6% 6.0% 3.7%

Figure 4: The pooled severity rate in Male (a) and Female (b) of COVID-19 patients

Table 2: Characteristic of severe and deceased patients with COVID-19

Author	Date	Location	Age	Total patients (M/F)	Severe (M/F)	Mortality (M/F)	Quality
Arentz et al. [21]	Feb 20–Mar 5,2020	USA	70 (IR 43–92)	21 (11/10)	-	11	8
Cai <i>et al.</i> [14]	Jan 11–Feb 6,2020	Shenzhen, China	47 (IQR 33–61)	298 (145/153)	58 (39/19)	3	8
Cao et al. [22]	Jan 3–Feb 1,2020	Wuhan, China	54 (37–67)	102 (53/49)	18 (12/6)	17	6
Chen <i>et al</i> . [23]	Jan–Feb,2020	Wuhan, China	59 (SD 16)	150 (84/66)	24 (18/6)	11	9
Chen <i>et al.</i> [24]	Dec,2019–Jan 27,2020	Wuhan, China	56 (IQR 50–65)	21 (17/4)	11 (10/1)	-	8
Chen <i>et al</i> . [15]	Jan 20–Feb 6,2020	Shanghai, China	51 (IQR 36–64)	249 (126/123)	22	-	9
Chen et al. [25]	Jan 14–Jan 29,2020	Wuhan, China	56 (IR 26–79)	29 (21/8)	14	-	8
Chen <i>et al</i> . [16]	Jan 1–Jan 20,2020	Wuhan, China	55.5 (SD 13.1)	99 (67/32)	-	11	9
Chen <i>et al</i> . [26]	Jan 13–Feb 12,2020	Wuhan, China	62 (IQR 44-77)	274 (171/103)	-	113 (83/30)	9
Cheng et al. [7]	Feb 19,2020	Henan, China	46 (SD 24)	1079 (573/505)	-	11 (7/4)	7
China CDC[8]	Feb 11,2020	China	50	44672 (22981/21691)	8255	1023 (653/370)	8
Dong et al. [27]	Jan 7–Feb 24,2020	Tianjin, China	48.6 (SD 16.8)	135 (72/63)	62	3	8
Goyal et al. [28]	Mar 3–Mar 27.2020	USA	62.2 (IQR 48.6–73.7)	393 (238/155)	130 (92/38)	40	7
Guan et al [2]	Dec 11,2019–Jan 31,2020	China	47 (35–58)	1099 (637/459)	173 (100/73)	15	9
Guo et al [29]	Jan 23–Feb 23,2020	Wuhan, China	58.5 (SD 14.66)	187 (91/96)	,	43	9
Huang et al [19]	Dec 16,2019–Jan 2,2020	Wuhan, China	49 (41–58)	41 (30/11)	13 (11/2)	6	9
Jin et al [30]	Jan 17–Feb 8,2020	Zhejiang, China	45	651 (331/320)	64	_	8
KSID [10]	Jan 19–Mar 2.2020	Korea	43	4212 (1591/2621)	_	22 (13/9)	8
Lei et al [31]	Jan 1–Feb 5,2020	Wuhan, China	55 (IQR 43-63)	34 (14/20)	15 (5/10)	7	9
Li et al [32]	Jan–Feb,2020	Chongging, China	45.5 (SD 12.3)	83 (44/39)	25 (15/10)	-	7
Liu et al [33]	Dec 30,2019–Jan 24,2020	Hubei, China	55 (SD 16)	137 (61/76)	_	16	8
Liu et al [34]	Dec 30,2019–Jan 15,2020	Wuhan, China	38 (IQR 33–57)	78 (39/39)	8	_	9
Livingston et al [9]	Mar 15,2020	Italy	64	22512 (13462/9050)	6731	1625	3
Peng et al [35]	Jan 20–Feb 15,2020	Wuhan, China	62 (IQR 55–67)	112 (53/59)	16 (9/7)	17	8
Qian <i>et al.</i> . [36]	Jan 20–Feb 11.2020	Zhejiang, China	50 (IQR 36.5–57)	91 (37/54)	9	_	7
Ruan et al. [37]	-	Wuhan, China	57.7	150 (102/48)	-	68 (49/19)	6
Richardson et al.[6]	Mar 1–Apr 4,2020	USA	63 (IQR 52–75)	2634 (1499/1135)	_	553 (337/216)	9
Shi et al [3]	50(IQR 36.5–57)	Wuhan, China	49.5 (SD 11)	81 (42/39)	3	-	9
Shi et al [17]	Feb 17,2020	Zhejiang, China	46 (SD 19)	487 (259/228)	3 49 (36/13)	_	6
Tang <i>et al.</i> . [38]	Jan 1–Feb 3,2020	Wuhan, China	54.1 (SD 16.2)	183 (98/85)	43 (30/13)	21 (16/5)	7
Tian <i>et al</i> [39]	Jan 20–Feb 10.2020	Beijing, China	47.5 (1–94)	262 (127/135)	46 (26/20)	3	7
Wan <i>et al.</i> [40]	Jan 23–Feb 8,2020	Chongging, China	47 (IQR 36–55)	135 (72/63)	40 (21/19)	1	8
Wang <i>et al.</i> [40]	Jan 1–Jan 28.2020	Wuhan, China	56 (42–68)	138 (75/63)	36 (22/14)	6	9
Wu et al [13]	Dec 25,2019–Jan 26,2020	Wuhan, China Wuhan, China	50 (42–68) 51 (IQR 43–60)	201 (128/99)	84 (60/24)	44	9
	Jan 22–Feb 14,2020	Jiangsu, China	()	· · · ·	3	44 -	9
Wu et al [42]	Feb 2–Feb 23.2020	Wuhan, China	46.1 (SD 15.42) 60 (IQR48–66)	80 (39/41)		-	8
Xie et al [43]	Jan–Feb,2020	Beijing, China	43.9 (SD 16.8)	79 (44/35) 50 (29/21)	28 (18/10)	-	8 7
Xu et al [44]	-		()		13 (7/6)		9
Yang <i>et al.</i> . [45]	Dec,2019–Jan 26,2020	Wuhan, China	59.7 (SD 13.3)	52 (35/17)	-	32 (21/11)	
Yao <i>et al.</i> . [46]	Jan 12–Feb 21,2020	Shaanxi, China	53.87 (SD 15.84)	40 (25/15)	22	-	7 7
Yuan <i>et al.</i> . [47]	Jan 1–Jan 25,2020	Wuhan, China	60 (IQR 47–69)	27 (12/15)	- EE (2E(20)	10 (4/6)	
Zhang <i>et al.</i> . [18]	Jan 2–Feb 10,2020	Wuhan, China	55 (IQR 39–66.5)	221 (108/113)	55 (35/20)	9 (7/2)	9
Zhang <i>et al.</i> . [48]	Jan 16–Feb 3,2020	Wuhan, China	57 (IR 25–87)	140 (71/69)	58 (33/25)	-	8
Zhao <i>et al.</i> . [49]	-	Hunan, China	44.4 (SD 12.3)	101 (56/45)	14 (8/6)	-	7
Zhou et al [12]	Dec 29–Jan 31,2020	Wuhan, China	56 (IQR 46-67)	191 (119/72)	-	54 (38/16)	9
Current study	Jan 20–Feb 14,2020	Changchun, China	41 (IQR 33–52)	43 (25/18)	5 (3/2)	-	8

Table 3: Meta-analysis on risk of disease severity and mortality patients with COVID-19 between male and female

	Study	Total patients	OR	95%CI	Heterogene	ity	P for pooled	Publication Bias
					$I^{2}(\%)$	P for I ²		
Severity	21	4213	1.604	1.373 - 1.873	25	0.145	< 0.001	0.535
≤ 50 y	10	2596	1.358	1.098 - 1.678	38.0	0.105	0.005	0.885
> 50 y	11	1617	1.942	1.546 - 2.44	0.0	0.742	< 0.001	0.536
Mortality	11	53695	1.571	1.422 – 1.736	34	0.1266	< 0.001	0.678
≥ 50 v	3	49962	1.696	1.494 - 1.926	0.0	0.721	< 0.001	0.910
> 50 y	8	3732	1.382	1.175 – 1.625	33.0	0.164	< 0.001	0.973

Discussion

It has been suggested that gender may play a role in the infection, severe or fatality of COVID-19 patients [11], [13], [15]. This is the first retrospective study to compare the sex differences of the epidemiological and clinical characteristics in COVID-19 patients, we included 43 patients with COVID-19, the morbidity of male (58.1%) was higher than female (41.9%), which was consistent with previous results [6], [15], [26], [31], [48]. There were no significant sex differences on severity, comorbidity, complication, and treatments. Previous studies found that male was more prone to SAS-Cov-2 infection and more severe symptoms [12], [15], [44], but the severity of COVID-19 patients was comparable between males and females in our study, that might be due to the small sample, comparable ages between males and females and mostly general or mild patients. The initial symptoms between female and male were similar that

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were consistent with previous studies [16]. We found that male was more have underlying comorbidities, and higher levels of WBC, neutrophil count, monocyte count, hemoglobin, total bilirubin, creatine, and creatine kinase compared with female. Previous studies suggested that the severity of COVID-19 had a positive correlation with the inflammatory response and cytokine storm [14], [15], [19], [24], [48].

To the best of our knowledge, this comprehensive meta-analysis including the largest cases from December 2019 to April 2020 was the latest to analyze the sex differences of morbidity, and the severe rate of COVID-19 patients. Our meta-analysis results confirmed that sex play an important role in SARS-CoV-2 infection, male of all 90,475 COVID-19 patients showed slightly higher incidence than female. Previous studies have demonstrated that males might be more susceptible to SAS-Cov-2 infection than females, and elder with more underlying comorbidities were associated with the severity of

	Experin	nental	Co	ontrol				Weight	Weight
Study			Events		Odds Rati	o OR	95%-CI		(random)
Cai QX et al	39	145	19	153	l i a	- 2 59	[1.42; 4.75]	5.3%	7.1%
Cao JL et al	12		6	49	1		[0.72; 6.11]	1.9%	2.9%
Chen C et al	18	84	6	66	1		[1.02; 7.32]	2.1%	3.4%
Chen G et al	10		1	4	1		[0.37; 50.20]	0.3%	0.6%
Goyal P et al	92		38	155	1		[1.24; 3.04]	11.0%	10.1%
Guan W et al	100		73	459			[0.71; 1.37]	27.8%	13.4%
Huang C et al	11	30	2	11			[0.47; 14.30]	0.7%	1.3%
Lei SQ et al	5		10	20			[0.14; 2.26]	2.1%	1.8%
Li KH et al	15		10	39	1		[0.58; 3.88]	2.7%	3.6%
Peng YD et al	9	53	7	59			[0.52; 4.41]	2.1%	2.9%
Shi Y et al	36	259	13	228	1.		[1.38; 5.17]	4.6%	6.3%
Tian S et al	26	127	20	135			[0.78; 2.81]	6.0%	6.6%
Wan SX et al	20	72	19	63	1		[0.45; 2.00]		
	22		19	63	11			5.6% 4.2%	5.3%
Wang DW et al	60			99			[0.67; 3.15]		5.0%
Wu CM et al		44	24		1		[1.55; 4.91]	5.6%	7.6%
Xie HS et al Xu YH et al	18 7		10	35 21			[0.67; 4.47]	2.6%	3.6%
Zhang GQ et al			6	113			[0.22; 2.84]	2.1%	2.2%
	35		20		1		[1.19; 4.18]	5.1%	6.7%
Zhang JJ et al	33		25	69			[0.78; 3.01]	5.3%	6.1%
Zhao W et al	8 3	56	6	45			[0.35; 3.39]	2.2%	2.6%
Current study	3	25	2	18		1.09	[0.16; 7.31]	0.8%	1.0%
Fixed effect model		2309		1904		1 60	[1.37; 1.87]	100 0%	
Random effects model		2309		1904			[1.36; 2.01]	100.0%	100.0%
Heterogeneity: $I^2 = 25\%$, τ^2		1 - 0	15			1.05	[1.30, 2.01]		100.078
	- 0.047	+, p = 0	.15		0.1 0.5 1 2	10			
а	Experin	nontal		Control				Weight	Weight
Study			Events	Total	Odds Rat	tio OR	95%_CI		(random)
Study	Lvents	Total	Lvents	Total	Ouus nat		3576-01	(lineu)	(random)
Chen T et al	83	171	30	103	1 +	+ 2.30	[1.36; 3.86]	3.0%	10.1%
Cheng JL et al	7	573		505			[0.45; 5.32]	0.7%	2.3%
China CDC		22981		21691			[1.48; 1.92]	58.4%	33.6%
KIDS	13	1591	9	2621	1		[1.02; 5.61]	1.1%	4.5%
Ruan QR et al	49	102		48			[0.70; 2.83]	2.1%	6.3%
Tang N et al	16	98		85			[1.09; 8.92]	0.7%	3.1%
Xie JF et al	126	126		42		0.12	[0.0%	0.0%
Yang XB et al	21	35		17		- 0.82	[0.25; 2.72]	0.9%	2.4%
Yuan ML et al	4	12		15			[0.15; 3.65]	0.6%	1.4%
Zhang GQ et al	7	108		113			[0.78; 18.95]	0.3%	1.4%
Zhou F et al	38	119		72	4	- 1.64	[0.84; 3.23]	2.1%	6.7%
Richardson S et al	337	1499		1135	-		[1.02; 1.49]		28.4%
Fixed effect model		27415		26447		1 57	[1.42; 1.74]	100.0%	
Random effects model		21410		20447	×		[1.32; 1.93]		100.0%
Heterogeneity: $I^2 = 34\%$, τ^2	$^{2} = 0.0240$	n = 0	13			1.00	[1.02, 1.30]		100.0 /0
	- 0.0240	, p = 0.	.10		0.1 0.5 1 2	2 10			
b									

Figure 5: Risk of Severity (a) and Mortality (b) between male and female in COVID-19

COVID-19 patients [41], [50]. Our study showed that the severe rate and the fatality rate of COVID-19 reached 22.7% and 10.7%, which were higher than the rates of SARS-CoV [51]. The risky of severe and death of COVID-19 in male were significantly higher than female, male has 1.6 folds higher compared with female. Moreover, the risky in older male had 1.94 folds higher compared with female and 1.7 folds higher in younger. It might due to the number of study and limited time so far, data collection of severe or death patients is still incomplete, and most of the studies did not analyzed sex differences in severe or death patients. However, there was significant heterogeneity among eligible studies, which might be potential from age and location of patients. However, the meta-analysis results were stable and reliable that no individual study significantly affects the pooled results after performing subgroup, sensitivity analyses, and meta-regression. Besides, funnel plot asymmetry and peters test results showed that there was no publication bias in our meta-analysis.

Men might be more vulnerable to infection with SARS-CoV-2, and poor progress and outcomes [14], [15], [41]. However, the pathogenesis of

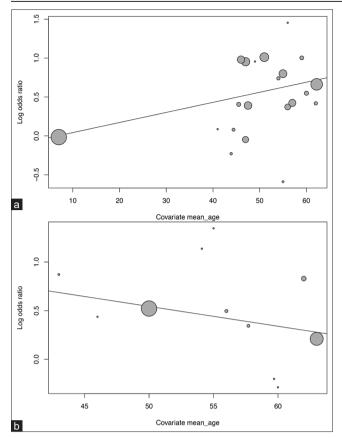


Figure 6: Meta-regression of age and log odds of Sex and Severity (a) or Mortality (b) in COVID-19

sex differences of COVID-19 patients is still unknown. Previous studies have revealed that biological and genetic structure differences, lifestyle, and behavior factors might play a major role for the sex differences of SAS-CoV-2 infection [52]. Previous studies suggested that the innate antiviral immune responses to a variety of virus infections of female was appropriate and greater than male and estrogen would increase the antiviral response of immune cells [16], [24], [53]. Moreover, female have two X-chromosome while male only one, which have encoded many genes that regulate the immune response system [53]. Compared with male, female has better lifestyle and behavior and is more likely to follow public health advice and seek medical attention. Previous studies found that smoking was a risk factor of COVID-19 progression, the prevalence of smoking in severity or death patients was significantly higher than mild or asymptomatic patients [2], [26]. Male smoking prevalence is significantly higher than female, which is the risk factor of many chronic noninfectious diseases. SARA-CoV-2 might directly force bind to ACE2 positive cholangiocytes, which is located on the X-chromosome, and male had higher expression of ACE2 than female [14], [54]. The more underlying comorbidities and higher expression of ACE2 in male patients would prolonged clinical course, cause worse complications and clinical outcomes [24], [55].

Our retrospective cohort study and metaanalysis had several limitations. First, retrospective study results limited by smaller sample, some briefly or incomplete documentation, and not all same laboratory variables were tested in all cases. Second, heterogeneity existed in our meta-analysis, which might relate to large variation of sample variation, different data collection and follow-up time, age, and location of patients. Third, the statistics reported by different countries to estimate overall and sex differences of fatality rate were incomplete and limited, so general conclusions of comparison with fatality rate between different countries should be caution.

Conclusion

The pooled severe rate and fatality rate of COVID-19 were 22.7% and 10.7%. Male incidence in the retrospective study was 58.1%, and the pooled incidence in male was 54.7%. The pooled severe rate in male and female of COVID-19 was 28.2% and 18.8%, the risky of severe and death was about 1.6 folds higher in male compared with female, especially for older patients (> 50 y).

Authors' Contributions

ZJL, LQD, and QY designed the study, ZJL, LNF, and LQD analyzed the data and wrote the first draft. WYC, JZ, YXH, YHZ, FT, DLW, BNC, and HW contributed to analysis and discussion. All authors interpreted the results and wrote the manuscript.

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Supplementary Tables and Figures

Table S1: Complications and treatments in hospitalization of COVID-19 patients

	Total (n = 43) (%)	Female (n = 18) (%)	Male (n = 25) (%)	p value
Complications				
Liver damage	19 (44.2)	7 (38.9)	12 (48.0)	0.756
Metabolic acidosis	8 (18.6)	5 (27.8)	3 (12.0)	0.247
Hypoxemia	8 (18.6)	4 (22.2)	4 (16.0)	0.701
Respiratory failure	6 (14.0)	2 (11.1)	4 (16.0)	0.648
Leukopenia	6 (14.0)	6 (33.3)	0	0.003
Acute cardiac injury	5 (11.6)	2 (11.1)	3 (12.0)	0.929
Treatment				
Antiviral therapy	43 (100.0)	18 (100.0)	25 (100.0)	-
Lopinavir/ritonavir+ Interferon alpha inhalation	40 (93.0)	17 (94.4)	23 (92.0)	0.756
Antibiotics	36 (83.7)	15 (83.3)	21 (84.0)	0.953
Moxifloxacin	30 (69.8)	12 (66.7)	18 (72.0)	0.747
Moxifloxacin+Xuebijing Injection	13 (30.2)	6 (33.3)	7 (28.0)	0.747
Corticosteroids	23 (53.5)	9 (50.0)	14 (56.0)	0.763
Oxygen therapy	25 (55.8)	11 (61.1)	13 (52.0)	0.756
Traditional Chinese medicine therapy	42 (97.7)	18 (100.0)	24 (96.0)	-

Table S2: The characteristics of eligible studies of COVID-19

Author	Date	Location	Age 70.(ID.40.00)	Total	M/F	Severity	Mortality	Quality
Arentz <i>et al.</i> [1]	February 20-March 5, 2020	USA	70 (IR 43-92)	21	11/10	21	11	8
Bernheim <i>et al.</i> [2]	January 18-February 2, 2020	China Shanahan China	45.3 (SD 15.6)	121	61/60 145/153	-	- 3	9 8
Cai <i>et al.</i> [3]	January 11-February 6, 2020	Shenzhen, China Wuhan, China	47 (IQR 33–61)	298 102	53/49	58 18	3 17	о 6
Cao <i>et al.</i> [4]	January 3-February 1, 2020 January 16-January 29, 2020	Beijing, China	54 (37–67) 34 (IQR 34–48)	13	10/3	10	17	7
Chang <i>et al</i> . [5] Chen <i>et al</i> . [6]	January-February, 2020	Wuhan, China	59(SD 16)	150	84/66	- 24	- 11	9
Chen <i>et al.</i> [7]	December 2019-January 27, 2020	Wuhan, China Wuhan, China	59(3D 10) 56 (IQR 50–65)	21	17/4	24 11	11	8
Chen <i>et al.</i> [8]	January 20-February 6, 2020	Shanghai, China	51 (IQR 36–64)	249	126/123	22	-	9
Chen <i>et al.</i> [9]	January 14-January 29, 2020	Wuhan, China	56 (IR 26–79)	29	21/8	14	-	8
Chen <i>et al.</i> [10]	January 1-January 20, 2020	Wuhan, China	55.5 (SD 13.1)	99	67/32	-	- 11	9
Chen <i>et al.</i> [11]	January 13-February 12, 2020	Wuhan, China	62 (IQR 44–77)	274	171/103	_	113	9
Chen <i>et al.</i> [12]	January 20-February 17, 2020	Zhejiang, China	43 (SD 17.2)	98	52/46	-	-	8
Cheng et al. [13]	February 19, 2020	Henan, China	46 (SD 24)	1079	573/505	-	11	7
hina CDC [14]	February 11, 2020	China	30-69	44672	22981/21691	8255	1023	8
huang <i>et al</i> . [15]	January 18-January 27, 2020	China	51 (SD 14)	21	13/8	-	-	7
ustralia [16]	January 13, 2020	Australia	43 (IR 8–66)	15	9/6	-	-	5
IERC [17]	February 14, 2020	Korea	42.6 (IR 20–73)	28	15/13	-	-	6
ong et al. [18]	January 7-February 24, 2020	Tianjin, China	48.6 (SD 16.8)	135	72/63	62	3	8
asom et al. [19]	January 29-February 24, 2020	UK	42.5 (IR 0.5-76)	68	32/36	-	-	9
ioyal et al. [20]	Mar 3-Mar 27, 2020	USA	62.2 (IQR 48.6-73.7)	393	238/155	130	40	7
rasselli et al. [21]	February 20-March 18, 2020	Italy	63 (IQR 56-70)	1591	1304/287	1591	405/1581	9
uan <i>et al.</i> [22]	December 11-January 31, 2020	China	47 (35–58)	1099	637/459	173	15	9
Guo et al. [23]	January 23-February 23, 2020	Wuhan, China	58.5 (SD 14.66)	187	91/96	-	43	9
uang et al. [24]	December 16, 2019-January 2, 2020	Wuhan, China	49 (41–58)	41	30/11	13	6	9
uang <i>et al.</i> [25]	December 21, 2019-January 28, 2020	Wuhan, China	56.24 (SD 17.14)	34	14/20	-	-	7
in <i>et al.</i> [26]	January 17-February 8, 2020	Zhejiang, China	45	651	331/320	64	-	8
SID [27]	January 19-March 2, 2020	Korea	20-50	4212	1591/2621	-	22	8
ei et al. [28]	January 1-February 5, 2020	Wuhan, China	55 (IQR 43–63)	34	14/20	15	7	9
i et al. [29]	January-February, 2020	Chongging, China	45.5 (SD 12.3)	83	44/39	25	-	7
i et al. [30]	December-January 22, 2020	Wuhan, China	59(IR 15-89)	425	240/185	-	-	9
i et al. [31]	December 28-February 10, 2020	Southwest, China	47 (SD 15)	131	63/68	-	-	8
iu et al. [32]	December 30, 2019-January 24, 2020	Hubei, China	55 (SD 16)	137	61/76	-	16	8
iu <i>et al.</i> [33]	December 30-January 15, 2020	Wuhan, China	38 (IQR 33–57)	78	39/39	8	-	9
ivngston et al. [34]	March 15, 2020	Italy	64	22512	13462/9050	9	1625	3
lizumoto et al. [35]	February 5-February 20, 2020	Japan	-	634	321/313	-	-	8
an <i>et al.</i> [36]	January 12-February 6, 2020	Wuhan, China	40(SD 9)	21	6/15	-	-	8
an <i>et al.</i> [37]	December 30-January 31, 2020	Wuhan, China	44.9 (SD 15.2)	63	33/30	-	-	7
eng et al. [38]	January 20-February 15, 2020	Wuhan, China	62 (IQR 55-67)	112	53/59	16	17	8
ian <i>et al.</i> [39]	January 20-February 11, 2020	Zhejiang, China	50 (IQR 36.5-57)	91	37/54	9	-	7
Richardson et al. [40]	March 1-April 4, 2020	USA	63 (IQR 52–75)	5700	2263/3437	-	553/2634	9
Ruan <i>et al</i> . [41]	-	Wuhan, China	46-70	150	102/48	-	68	6
Shi et al. [42]	December 20-January 23, 2020	Wuhan, China	49.5 (SD 11)	81	42/39	3	-	9
Shi et al. [43]	February 17, 2020	Zhejiang, China	46 (SD 19)	487	259/228	49	-	6
Song et al. [44]	January 20-January 27, 2020	Shanghai, China	49 (SD16)	51	25/26	-	-	8
Sun et al. [45]	January 31, 2020	China	46 (IQR 35-60)	507	281/201	-	-	7
u et al. [46]	January 13-January 31, 2020	Taiwan, China	56.6	10	7/3	-	-	5
un <i>et al.</i> [47]	January 26-February 16, 2020	Singapore	42 (IQR 34–54)	54	29/25	-	-	8
ang <i>et al.</i> [48]	January 1-February 3, 2020	Wuhan, China	54.1 (SD 16.2)	183	98/85	-	21	7
ïan <i>et al.</i> [49]	January 20-February 10, 2020	Beijing, China	47.5 (1–94)	262	127/135	46	3	7
Van <i>et al</i> . [50]	January 23-February 8, 2020	Chongqing, China	47 (IQR 36-55)	135	72/63	40	1	8
Vang <i>et al.</i> [51]	January 1-January 28, 2020	Wuhan, China	56 (42-68)	138	75/63	36	6	9
Vang et al. [52]	January 16-February 17, 2020	Wuhan, China	45 (SD 14)	90	33/57	-	-	7
lu et al. [53]	December 25, 2019-January 26, 2020	Wuhan, China	51 (IQR 43-60)	201	128/99	84	44	9
Vu et al. [54]	January-February, 2020	Chongqing, China	44 (SD 11)	80	42/38	-	-	8
Vu et al. [55]	January 22-February 14, 2020	Jiangsu, China	46.1 (SD 15.42)	80	39/41	3	-	9
Vu et al. [56]	February 9-February 15, 2020	Hubei, China	68 (IQR 53-67)	38	25/13	-	-	9
ie et al. [57]	February 2-February 23, 2020	Wuhan, China	60 (IQR48–66)	79	44/35	28	-	8
(ie <i>et al</i> . [58]	January 21-January 30, 2020	Wuhan, China	70 (IQR 64–78)	168	126/42	-	168	5
u et al. [59]	January 23-February 4, 2020	Guangdong, China	50 (IR 18-86)	90	39/51	-	-	7
u et al. [60]	January 10-January 26, 2020	Zhejiang, China	41 (IQR 32–52)	62	36/27	-	-	8
u et al. [61]	January-February, 2020	Beijing, China	43.9 (SD 16.8)	50	29/21	13	-	7
ang et al. [62]	January 17-February 10, 2020	Zhejiang, China	45.11 (SD 13.35)	149	81/68	-	-	7
ang <i>et al</i> . [63]	December 2019-January 26, 2020	Wuhan, China	59.7 (SD 13.3)	52	35/17	52	32	9
ao <i>et al</i> . [64]	January 12-February 21, 2020	Shaanxi, China	53.87 (SD 15.84)	40	25/15	22	-	7
oung et al. [65]	January 23-February 3, 2020	Singapore	47 (IR 31–73)	18	9/9	-	-	8
uan <i>et al</i> . [66]	January 1-January 25, 2020	Wuhan, China	60 (IQR 47–69)	27	12/15	-	10	7
ha et al. [67]	January 24-February 24, 2020	Wuhan, China	39 (IQR 32–54)	31	20/11	-	-	8
hang et al. [68]	January 2-February 10, 2020	Wuhan, China	55 (IQR 39-66.5)	221	108/113	55	12	9
hang <i>et al</i> . [69]	January 16-February 3, 2020	Wuhan, China	57 (IR 25-87)	140	71/69	58	-	8
hang <i>et al</i> . [70]	January 13-February 26, 2020	Wuhan, China	65 (IQR 56–70)	28	17/11	-	-	8
hang <i>et al.</i> [71]	January 18-February 3, 2020	Beijing, China	36 (IR 15–49)	9	5/4	-	-	6
hang <i>et al.</i> [72]	January 17-February 8, 2020	Zhejiang, China	45.4	645	328/317	-	-	8
hao et al. [73]	-	Hunan, China	44.4 (SD 12.3)	101	56/45	14	-	7
hou et al. [74]	December 29, 2019-January 31, 2020	Wuhan, China	56 (IQR 46–67)	191	119/72	-	54	9
hou et al. [75]	January 16-January 30, 2020	Wuhan, China	52.8 (SD 12.2)	62	39/23	-	-	8
	, ,	,	41 (IQR 33–52)	43	25/18	5		8

Study	Events	Total		Proportion	95%–CI	Weight (fixed)	Weight (random)
Arentz M et al	11	21		0.52	[0.30; 0.74]	0.0%	0.8%
Bernheim A et al	61	121			[0.41; 0.60]	0.1%	1.4%
Cai QX et al Cao JL et al	145 53	298 102		0.49	[0.43; 0.54] [0.42; 0.62]	0.3% 0.1%	1.6% 1.4%
Chang D et al	10	13			[0.46; 0.95]	0.1%	0.7%
Chen C et al	84	150			[0.48; 0.64]	0.2%	1.5%
Chen G et al	17	21	i		[0.58; 0.95]	0.0%	1.0%
Chen J et al Chen L et al	126 21	249 29			[0.44; 0.57] [0.53; 0.87]	0.3% 0.0%	1.6% 1.0%
Chen NS et al	67	99	·		[0.58; 0.77]	0.1%	1.4%
Chen T et al	171	274	<u>⊨</u>	0.62	[0.56; 0.68]	0.3%	1.6%
Chen ZH et al	52	98			[0.43; 0.63]	0.1%	1.4%
Cheng JL et al China CDC	573 22981	1079 44672			[0.50; 0.56] [0.51; 0.52]	1.2% 47.9%	1.7% 1.8%
Chuang M et al	13	21			[0.38; 0.82]	0.0%	0.8%
Australia	9	15			[0.32; 0.84]	0.0%	0.6%
NERC Dong XC at al	15 72	28 135			[0.34; 0.72]	0.0% 0.1%	0.9% 1.5%
Dong XC et al Easom N et al	32	68			[0.45; 0.62] [0.35; 0.60]	0.1%	1.3%
Goyal P et al	238	393	<u>i</u> —+−	0.61	[0.56; 0.65]	0.4%	1.6%
Grasselli G et al	1304	1591	+		[0.80; 0.84]	2.9%	1.7%
Guan W et al Guo T et al	637 91	1099 187			[0.55; 0.61]	1.2% 0.2%	1.7% 1.5%
Huang C et al	30	41	l		[0.41; 0.56] [0.57; 0.86]	0.2%	1.1%
Huang YH et al	14	34		0.41	[0.25; 0.59]	0.0%	1.0%
Jin X et al	331	651			[0.47; 0.55]	0.7%	1.7%
KSID Lei SQ et al	1591 14	4212 34	*		[0.36; 0.39] [0.25; 0.59]	4.8% 0.0%	1.7% 1.0%
Li KH et al	44	83			[0.25, 0.59]	0.0%	1.3%
Li Q et al	240	425	- 	0.56	[0.52; 0.61]	0.5%	1.7%
Li XM et al	63	131			[0.39; 0.57]	0.1%	1.5%
Liu K et al Liu W et al	61 39	137 78			[0.36; 0.53] [0.38; 0.62]	0.1% 0.1%	1.5% 1.3%
Livngston E et al	13462				[0.59; 0.60]	25.1%	1.8%
Mizumoto K et al	321	634			[0.47; 0.55]	0.7%	1.7%
Pan F et al	6	21			[0.11; 0.52]	0.0%	0.8%
Pan YY et al Peng YD et al	33 53	63 112			[0.39; 0.65] [0.38; 0.57]	0.1% 0.1%	1.2% 1.4%
Qian GQ et al	37	91	l		[0.30; 0.51]	0.1%	1.4%
Richardson S et al	2263	5700	+		[0.38; 0.41]	6.4%	1.8%
Ruan QR et al Shi HS et al	102 42	150 81			[0.60; 0.75]	0.2%	1.5%
Shi Y et al	259	487			[0.40; 0.63] [0.49; 0.58]	0.1% 0.5%	1.3% 1.7%
Song FX et al	25	51			[0.35; 0.63]	0.1%	1.1%
Su YJ et al	281	507			[0.51; 0.60]	0.5%	1.7%
Sun KY et al Sun Y et al	7 29	10 54			[0.35; 0.93] [0.40; 0.67]	0.0% 0.1%	0.5% 1.2%
Tang N et al	98	183			[0.46; 0.61]	0.1%	1.5%
Tian S et al	127	262	<u></u>		[0.42; 0.55]	0.3%	1.6%
Wan SX et al	72	135			[0.45; 0.62]	0.1%	1.5%
Wang DW et al Wang YH et al	75 33	138 90			[0.46; 0.63] [0.27; 0.47]	0.1% 0.1%	1.5% 1.4%
Wu CM et al	128	201			[0.57; 0.70]	0.2%	1.6%
Wu J et al	42	80			[0.41; 0.64]	0.1%	1.3%
Wu J et al	39	80			[0.37; 0.60]	0.1%	1.3%
Wu P et al Xie HS et al	25 44	38 79			[0.49; 0.80] [0.44; 0.67]	0.0% 0.1%	1.1% 1.3%
Xie JF et al	126	168	i ——		[0.68; 0.81]	0.1%	1.6%
Xu X et al	39	90		0.43	[0.33; 0.54]	0.1%	1.3%
Xu XW et al	36	62			[0.45; 0.70]	0.1%	1.2%
Xu YH et al Yang WJ et al	29 81	50 149			[0.43; 0.72] [0.46; 0.63]	0.1% 0.2%	1.1% 1.5%
Yang XB et al	35	52	÷		[0.53; 0.80]	0.1%	1.2%
Yao N et al	25	40		0.62	[0.46; 0.77]	0.0%	1.1%
Young BE et al	9	18			[0.26; 0.74]	0.0%	0.7%
Yuan ML et al Zha L et al	12 20	27 31			[0.25; 0.65] [0.45; 0.81]	0.0% 0.0%	0.9% 1.0%
Zhang GQ et al	108	221			[0.42; 0.56]	0.2%	1.6%
Zhang JJ et al	71	140		0.51	[0.42; 0.59]	0.2%	1.5%
Zhang L et al	17	28			[0.41; 0.78]	0.0%	0.9%
Zhang MQ et al Zhang XL et al	5 328	9 645			[0.21; 0.86] [0.47; 0.55]	0.0% 0.7%	0.4% 1.7%
Zhao W et al	56	101			[0.45; 0.65]	0.1%	1.4%
Zhou F et al	119	191			[0.55; 0.69]	0.2%	1.5%
Zhou SC et al	39 25	62 43			[0.50; 0.75]	0.1%	1.2%
Current study	20	43		0.58	[0.42; 0.73]	0.0%	1.1%
Fixed effect model		90475	6		[0.53; 0.54]	100.0%	
Random effects model Heterogeneity: $I^2 = 97\%$, τ		n = 0		0.55	[0.52; 0.57]		100.0%
Heterogeneity: $I^- = 97\%$, t	= 0.0090	, p = 0	0.2 0.4 0.6 0.8				
L							

Figure S1: The pooled morbidity of male with COVID-19

Study					Proportion	95%–CI
Omitting Cai QX et al				<u> </u>	0.23	[0.20; 0.26]
Omitting Cao JL et al				- + -	0.23	[0.20; 0.26]
Omitting Chen C et al					0.23	[0.20; 0.26]
Omitting Chen G et al					0.22	[0.19; 0.26]
Omitting Chen J et al					0.23	[0.20; 0.27]
Omitting Chen L et al						[0.19; 0.26]
Omitting China CDC						[0.19; 0.28]
Omitting Dong XC et al				+		[0.19; 0.25]
Omitting Goyal P et al						[0.19; 0.26]
Omitting Guan W et al						[0.20; 0.26]
Omitting Huang C et al				<u> </u>		[0.19; 0.26]
Omitting Jin X et al						[0.20; 0.26]
Omitting Lei SQ et al						[0.19; 0.26]
Omitting Li KH et al				<u> </u>		[0.19; 0.26]
Omitting Liu W et al				_		[0.20; 0.26]
Omitting Livngston E et al				- <u></u>		[0.19; 0.25]
Omitting Peng YD et al						[0.20; 0.26]
Omitting Qian GQ et al				<u> </u>		[0.20; 0.26]
Omitting Shi HS et al				· ·		[0.20; 0.27]
Omitting Shi Y et al						[0.20; 0.26]
Omitting Tian S et al						[0.20; 0.26]
Omitting Wan SX et al						[0.19; 0.26]
Omitting Wang DW et al				_		[0.19; 0.26]
Omitting Wu CM et al						[0.19; 0.25]
Omitting Wu J et al						[0.20; 0.27]
Omitting Xie HS et al						[0.19; 0.26]
Omitting Xu YH et al						[0.19; 0.26]
Omitting Yao N et al						[0.19; 0.25]
Omitting Zhang GQ et al				·**********************		[0.19; 0.26]
Omitting Zhang JJ et al						[0.19; 0.25]
Omitting Zhao W et al						[0.20; 0.26]
Omitting Current study				:	0.23	[0.20; 0.26]
Random effects model		1			0.23	[0.20; 0.26]
	-0.2 -0.1	0	0.1	0.2		

Figure S2: Sensitivity analysis of pooled severe rate in COVID-19

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Study			Proportion	95%–Cl
Omitting Arentz M et al			0.10	[0.09; 0.12]
Omitting Cai QX et al		<u> </u>	0.11	[0.10; 0.13]
Omitting Cao JL et al		-	0.11	
Omitting Chen C et al			0.11	[0.09; 0.12]
Omitting Chen NS et al		÷	0.11	[0.09; 0.12]
Omitting Chen T et al			0.10	[0.08; 0.11]
Omitting Cheng JL et al			0.11	[0.10; 0.13]
Omitting China CDC			0.13	[0.11; 0.15]
Omitting Dong XC et al			0.11	[0.10; 0.13]
Omitting Guan W et al		÷	0.11	[0.10; 0.13]
Omitting Guo T et al			0.10	[0.09; 0.12]
Omitting Huang C et al			0.11	[0.09; 0.12]
Omitting KIDS		÷	0.12	[0.10; 0.14]
Omitting Lei SQ et al		┉╇╼┿╼┿╼┿╼┿╼┿╼┿╼┿╼┿╼┿╼┿╼┿╼┿╼┿╼┿╼┿╼┿╼	0.11	[0.09; 0.12]
Omitting Liu K et al		-	0.11	[0.09; 0.12]
Omitting Livngston E et al			0.10	[0.09; 0.12]
Omitting Peng YD et al		- 1 -	0.11	[0.09; 0.12]
Omitting Ruan QR et al			0.10	[0.08; 0.11]
Omitting Tang N et al			0.11	[0.09; 0.12]
Omitting Tian S et al			0.11	
Omitting Wan SX et al			0.11	[0.10; 0.13]
Omitting Wang DW et al			0.11	[0.09; 0.12]
Omitting Wu CM et al			0.10	[0.09; 0.12]
Omitting Yang XB et al			0.10	[0.09; 0.12]
Omitting Yuan ML et al			0.11	[0.09; 0.12]
Omitting Zhang GQ et al			0.11	
Omitting Zhou F et al			0.10	[0.09; 0.12]
Omitting Goyal P et al		-	0.11	[0.09; 0.12]
Omitting Richardson S et al		-	0.10	[0.08; 0.11]
Random effects model			0.11	[0.09; 0.12]
	-0.1-0.05 0	0.05 0.1		

Figure S3: Sensitivity analysis of pooled fatality rate in COVID-19

Study			Proportion	95%-CI
Omitting Cai QX et al			0.28	[0.23; 0.34]
Omitting Cao JL et al				[0.23; 0.34]
Omitting Chen C et al		· · ·		[0.23; 0.34]
Omitting Chen G et al				[0.22; 0.32]
Omitting Goyal P et al				[0.22; 0.32]
Omitting Guan W et al				[0.24; 0.34]
Omitting Huang C et al				[0.23; 0.33]
Omitting Lei SQ et al				[0.23; 0.33]
Omitting Li KH et al				[0.23; 0.33]
Omitting Peng YD et al				[0.23; 0.34]
Omitting Shi Y et al				[0.24; 0.34]
Omitting Tian S et al				[0.23; 0.34]
Omitting Wan SX et al				[0.23; 0.33]
Omitting Wang DW et al				[0.23; 0.33]
Omitting Wu CM et al				[0.22; 0.32]
Omitting Xie HS et al				[0.22; 0.33]
Omitting Xu YH et al				[0.23; 0.34]
Omitting Zhang GQ et al				[0.23; 0.33]
Omitting Zhang JJ et al				[0.22; 0.32]
Omitting Zhao W et al				[0.24; 0.34]
Omitting Current study				[0.24; 0.34]
]		· · · · · ·		
Random effects model			0.28	[0.23; 0.33]
	-0.3-0.2-0.1	0 0.1 0.2 0.3		

Figure S4: Sensitivity analysis of pooled severe rate of male in COVID-19

Study						Proportion	95%-CI
Omitting Cai QX et al						0.19	[0.15; 0.24]
Omitting Cao JL et al					<u> </u>	0.19	[0.15; 0.23]
Omitting Chen C et al						0.19	[0.15; 0.24]
Omitting Chen G et al						0.19	[0.15; 0.23]
Omitting Goyal P et al						0.18	[0.14; 0.22]
Omitting Guan W et al						0.19	[0.15; 0.24]
Omitting Huang C et al					<u> </u>	0.19	[0.15; 0.23]
Omitting Lei SQ et al						0.18	[0.14; 0.22]
Omitting Li KH et al					<u> </u>	0.18	[0.15; 0.22]
Omitting Peng YD et al					<u> </u>	0.19	[0.15; 0.23]
Omitting Shi Y et al					- +	0.19	[0.16; 0.23]
Omitting Tian S et al						0.19	[0.15; 0.23]
Omitting Wan SX et al						0.18	[0.14; 0.22]
Omitting Wang DW et al					<u> </u>	0.19	[0.15; 0.23]
Omitting Wu CM et al							[0.14; 0.22]
Omitting Xie HS et al						0.18	[0.14; 0.22]
Omitting Xu YH et al					<u> </u>	0.18	[0.15; 0.22]
Omitting Zhang GQ et al						0.19	[0.15; 0.23]
Omitting Zhang JJ et al						0.18	[0.14; 0.21]
Omitting Zhao W et al					<u> </u>	0.19	[0.15; 0.23]
Omitting Current study						0.19	[0.15; 0.23]
Random effects model		- 1			$ \rightarrow$	0.19	[0.15; 0.23]
	-0.2	-0.1	0	0.1	0.2		

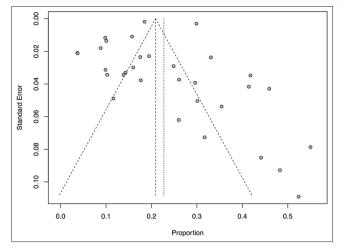
Figure S5: Sensitivity analysis plot of pooled severe rate of female in COVID-19

Study	Odds Ratio		OR	95%–CI
Omitting Cai QX et al Omitting Cao JL et al Omitting Chen C et al Omitting Chen G et al Omitting Goyal P et al Omitting Guan W et al Omitting Huang C et al Omitting Lei SQ et al Omitting Lei SQ et al Omitting Peng YD et al Omitting Peng YD et al Omitting Tian S et al Omitting Wan SX et al Omitting Wang DW et al Omitting Wu CM et al Omitting Xu YH et al Omitting Zhang GQ et al Omitting Zhang JJ et al Omitting Zhao W et al Omitting Zhao W et al Omitting Current study			1.59 1.58 1.60 1.56 1.84 1.60 1.63 1.61 1.61 1.61 1.61 1.64 1.61 1.64 1.61 1.62 1.62 1.61 1.62 1.61	[1.32; 1.82] [1.36; 1.87] [1.35; 1.85] [1.37; 1.87] [1.32; 1.84] [1.54; 2.20] [1.37; 1.87] [1.39; 1.90] [1.37; 1.88] [1.37; 1.88] [1.37; 1.89] [1.37; 1.89] [1.37; 1.89] [1.31; 1.80] [1.37; 1.87] [1.39; 1.90] [1.34; 1.84] [1.37; 1.89] [1.38; 1.89] [1.38; 1.88] [1.38; 1.88]
	0.5 1	1 2		

Figure S6: Sensitivity analysis plot of pooled risky between sex and severity in COVID-19

Study	Odds	Ratio	OR	95%-CI
Omitting Chen T et al			1.55	[1.40; 1.71]
Omitting Cheng JL et al			1.57	[1.42; 1.74]
Omitting China CDC			1.41	[1.20; 1.65]
Omitting KIDS		-	1.56	[1.41; 1.73]
Omitting Ruan QR et al			1.57	[1.42; 1.74]
Omitting Tang N et al			1.56	[1.41; 1.72]
Omitting Xie JF et al			1.57	[1.42; 1.74]
Omitting Yang XB et al			1.58	[1.43; 1.74]
Omitting Yuan ML et al		<u> </u>	1.58	[1.43; 1.74]
Omitting Zhang GQ et al			1.56	[1.42; 1.73]
Omitting Zhou F et al			1.57	[1.42; 1.74]
Omitting Richardson S et al			- 1.72	[1.53; 1.93]
Fixed effect model	Γ		1.57	[1.42; 1.74]
	0.75	1 1.5		

Figure S7: Sensitivity analysis plot of pooled risky between sex and mortality in COVID-19





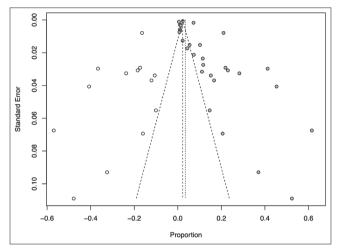


Figure S9: Funnel plot of pooled fatality rate in COVID-19 (trim-fill method)

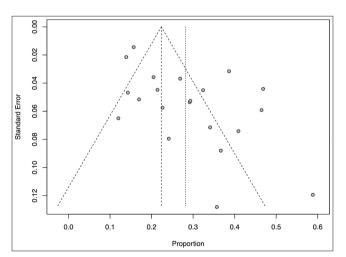


Figure S10: Funnel plot of pooled severe rate of male in COVID-19

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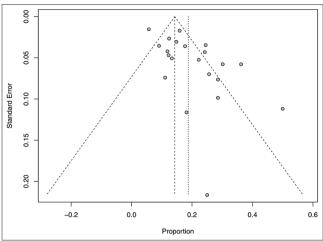


Figure S11: Funnel plot of pooled severe rate of female in COVID-19

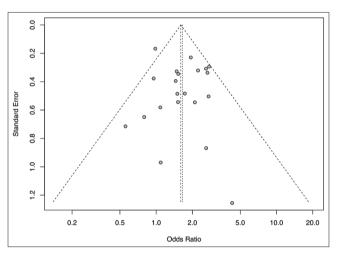


Figure S12: Funnel plot of pooled risky between sex and severity in COVID-19

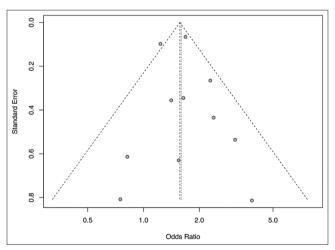


Figure S13: Funnel plot of pooled risky between sex and mortality in COVID-19

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