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

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Abstract

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).

Introduction

On December 2019, the outbreak of coronavirus disease (COVID-19) caused by 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 laboratory-confirmed 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 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].

Timely identification 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 $p \leq 0.05$ was considered to be statistically significant. Median with interquartile 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 I^2 statistics and Q test, the random-effect model was used to compute the pooled results when $I^2 > 50\%$ 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 non-significant 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
Age, 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)	
Occupation				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				0.680
Exposure to Wuhan	7 (16.3)	2 (11.1)	5 (20.0)	
Exposure to confirmed or suspected people	36 (83.7)	16 (88.9)	20 (80.0)	
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)	
Comorbidities	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)	0	2 (8.0)	-
Neurodegenerative disease	2 (4.7)	2 (11.1)	0	-
Asthma	1 (2.3)	1 (5.6)	0	-
Symptoms				
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
Incubation period, median(IQR), d	8.0 (5.0-11.0)	9.0 (5.8–12.0)	7.0 (4.0–11.0)	0.459
Onset of illness to, median(IQR), d				
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
Duration 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
Hospitalization time, median(IQR), d	17.0 (11.0–20.0)	18.0 (10.8–20.0)	17.0 (11.0–21.0)	0.961
Laboratory 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
Platelet count, ×109/L	183 (161–223)	180.0 (163.0–211.5)	201.0 (159.2–240.0)	0.424
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)	<0.001
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				
Bilateral distribution of patchy shadows or ground glass opacity	31 (72.1%)	13 (72.2%)	18 (72.0%)	0.987

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, I^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, I^2 = 97.8%) and 51.5% (95% CI: 0.489-0.541, I^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, I^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, I^2 = 86.7%) and 18.8% (95%CI: 0.149-0.226, I^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, I^2 = 94.0%; 20.5%) were significant higher than younger patients (16.7, 95%CI: 0.134–0.200, I^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).

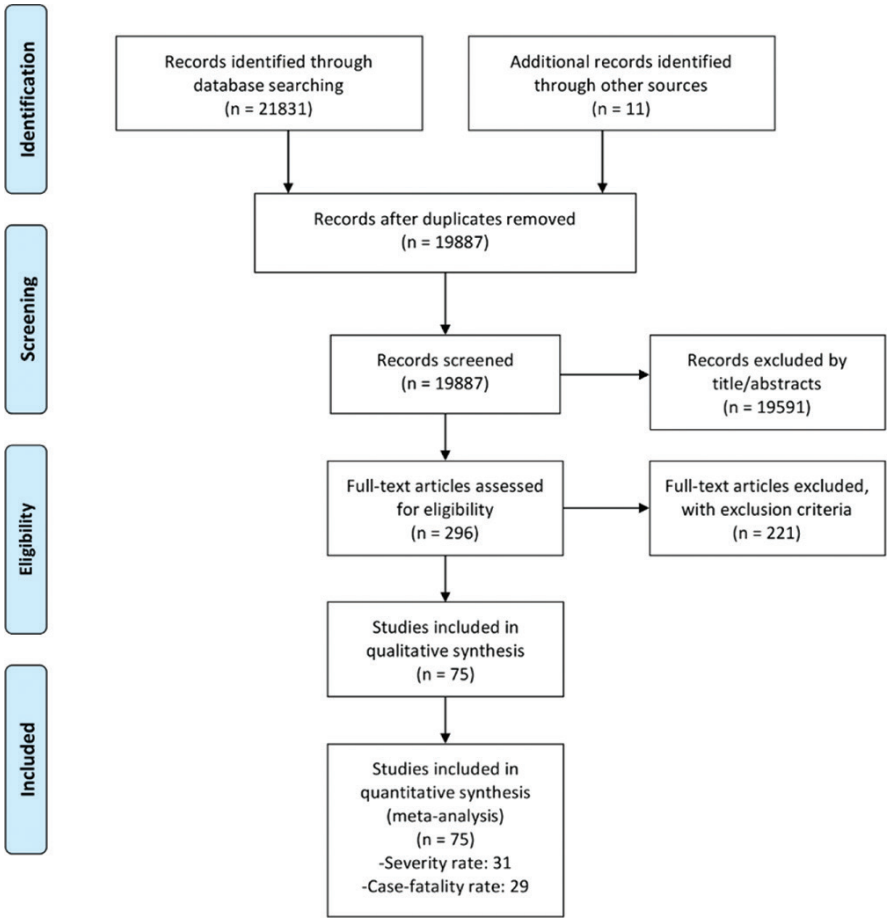


Figure 1: Flowchart of the study selection procedure

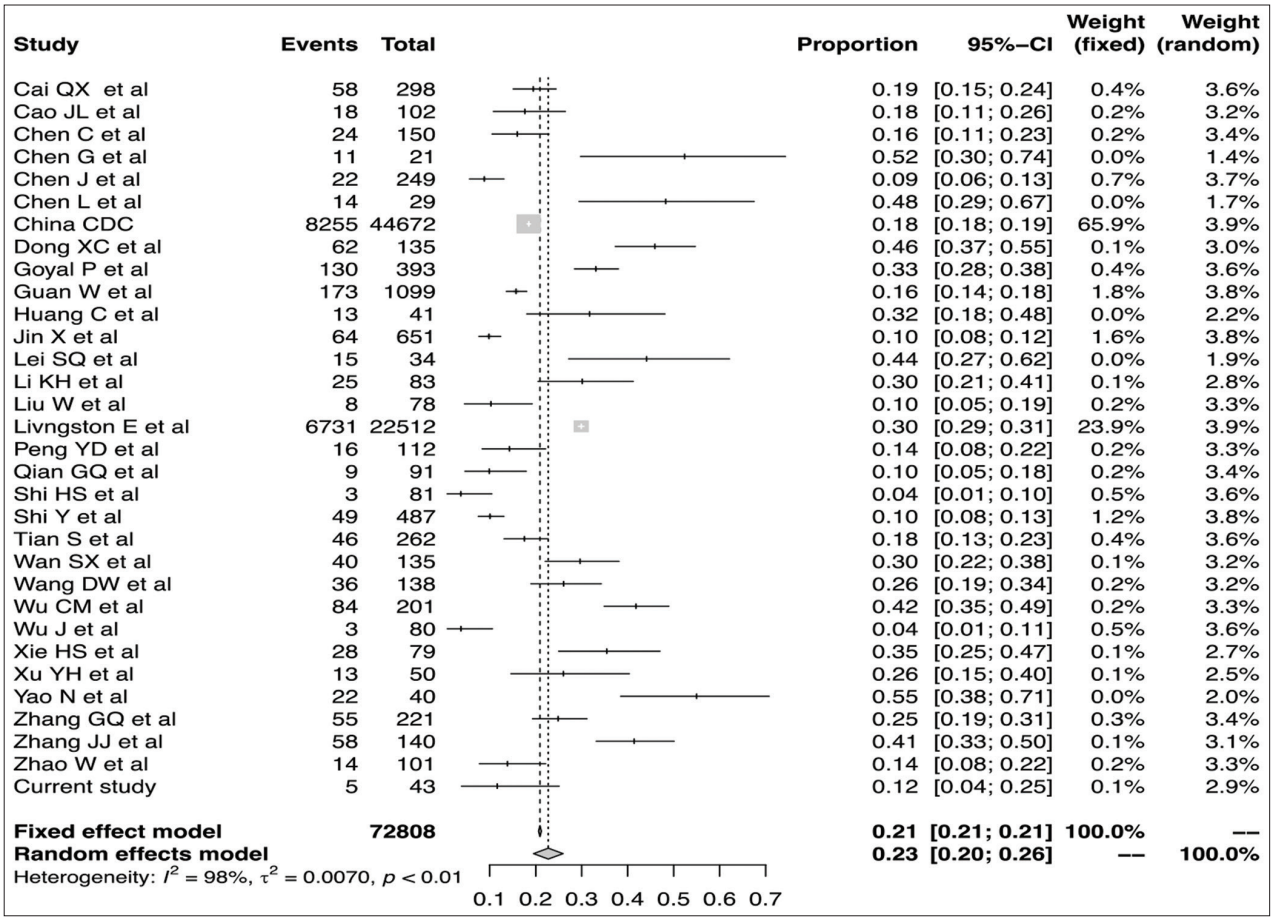


Figure 2: The pooled severity rate of COVID-19 patients

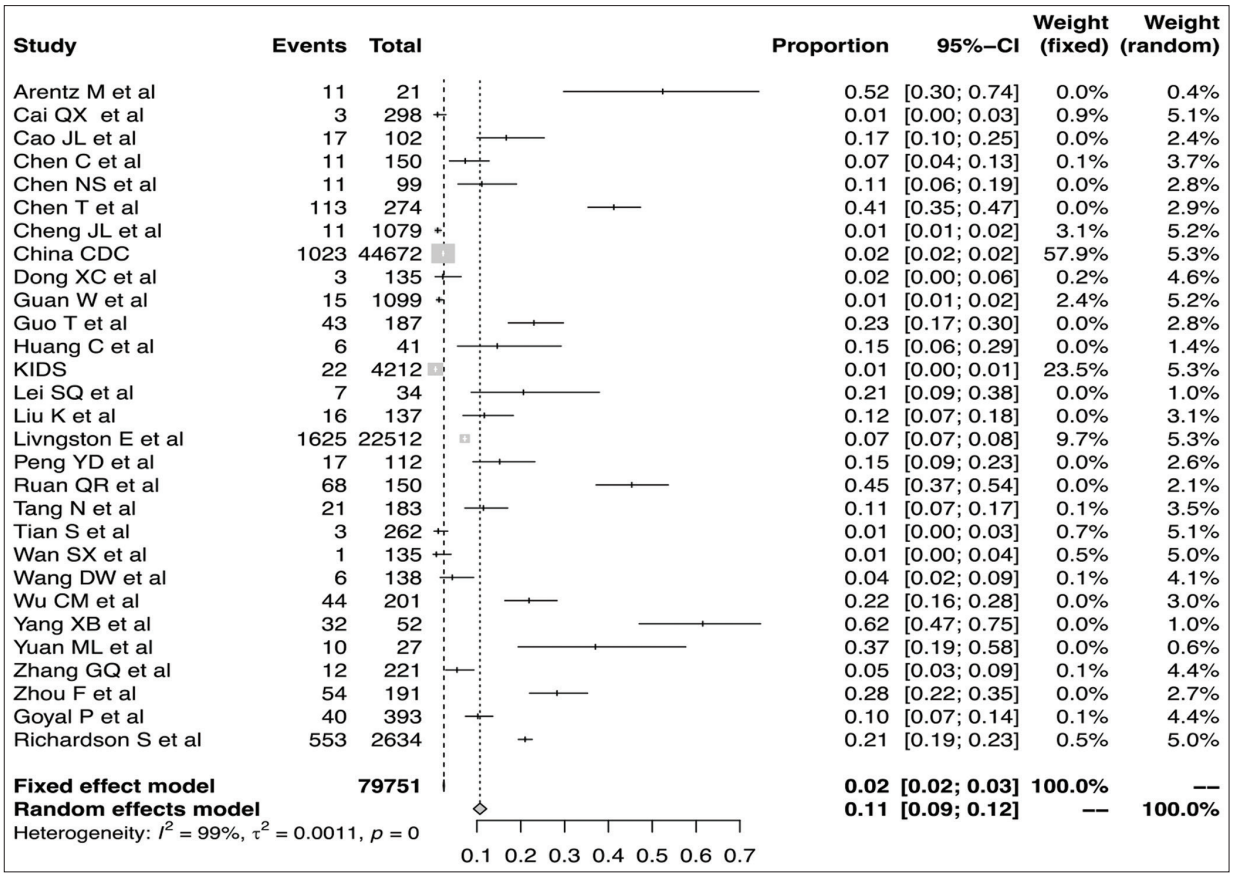
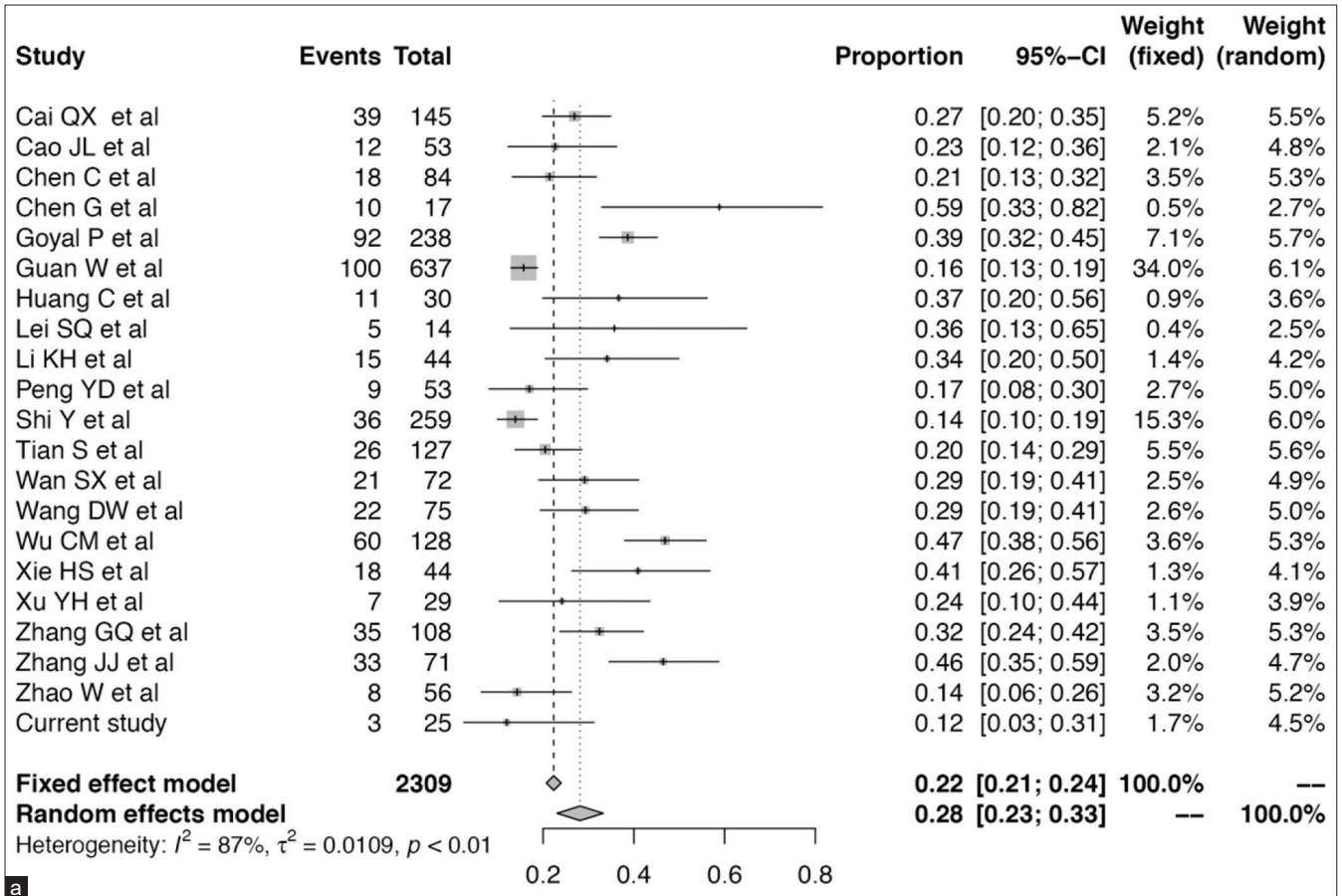


Figure 3: The pooled case-fatality rate of COVID-19 patients



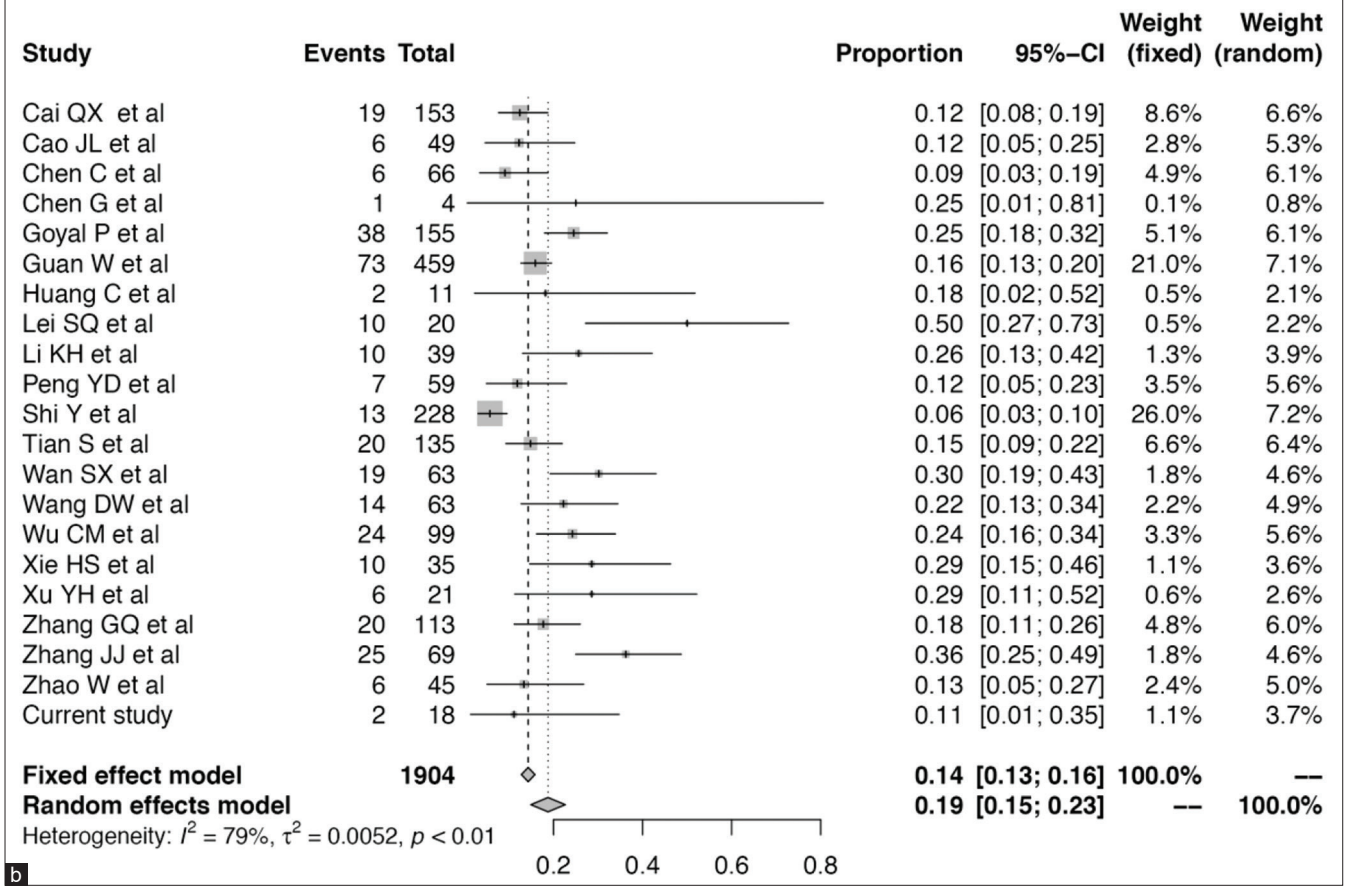


Figure 4: The pooled severity rate in Male (a) and Female (b) of COVID-19 patients

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 *et al.* [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 *et al.* [23]	Jan–Feb,2020	Wuhan, China	59 (SD 16)	150 (84/66)	24 (18/6)	11	9
Chen *et al.* [24]	Dec,2019–Jan 27,2020	Wuhan, China	56 (IQR 50–65)	21 (17/4)	11 (10/1)	–	8
Chen *et al.* [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 *et al.* [16]	Jan 1–Jan 20,2020	Wuhan, China	55.5 (SD 13.1)	99 (67/32)	–	11	9
Chen *et al.* [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	Chongqing, 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 *et al.*. [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)	49 (36/13)	–	6
Tang *et al.*. [38]	Jan 1–Feb 3,2020	Wuhan, China	54.1 (SD 16.2)	183 (98/85)	–	21 (16/5)	7
Tian *et al.*. [39]	Jan 20–Feb 10.2020	Beijing, China	47.5 (1–94)	262 (127/135)	46 (26/20)	3	7
Wan *et al.* [40]	Jan 23–Feb 8,2020	Chongqing, China	47 (IQR 36–55)	135 (72/63)	40 (21/19)	1	8
Wang *et al.*. [41]	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	51 (IQR 43–60)	201 (128/99)	84 (60/24)	44	9
Wu *et al.*. [42]	Jan 22–Feb 14,2020	Jiangsu, China	46.1 (SD 15.42)	80 (39/41)	3	–	9
Xie *et al.*. [43]	Feb 2–Feb 23,2020	Wuhan, China	60 (IQR48–66)	79 (44/35)	28 (18/10)	–	8
Xu *et al.*. [44]	Jan–Feb,2020	Beijing, China	43.9 (SD 16.8)	50 (29/21)	13 (7/6)	–	7
Yang *et al.*. [45]	Dec,2019–Jan 26,2020	Wuhan, China	59.7 (SD 13.3)	52 (35/17)	–	32 (21/11)	9
Yao *et al.*. [46]	Jan 12–Feb 21,2020	Shaanxi, China	53.87 (SD 15.84)	40 (25/15)	22	–	7
Yuan *et al.*. [47]	Jan 1–Jan 25,2020	Wuhan, China	60 (IQR 47–69)	27 (12/15)	–	10 (4/6)	7
Zhang *et al.*. [18]	Jan 2–Feb 10,2020	Wuhan, China	55 (IQR 39–66.5)	221 (108/113)	55 (35/20)	9 (7/2)	9
Zhang *et al.*. [48]	Jan 16–Feb 3,2020	Wuhan, China	57 (IR 25–87)	140 (71/69)	58 (33/25)	–	8
Zhao *et al.*. [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	Heterogeneity		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 y	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 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

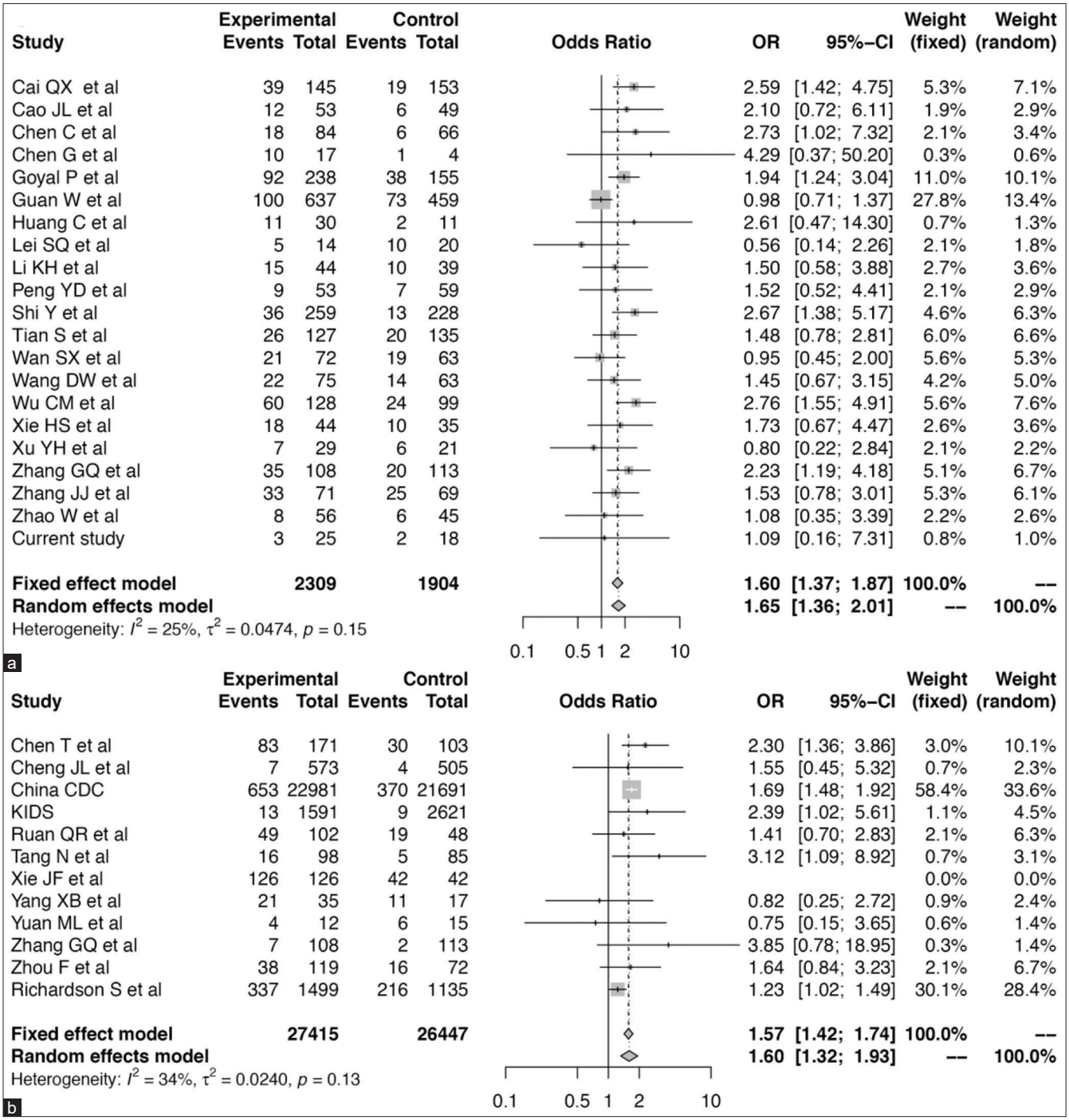


Figure 5: Risk of Severity (a) and Mortality (b) between male and female in COVID-19

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

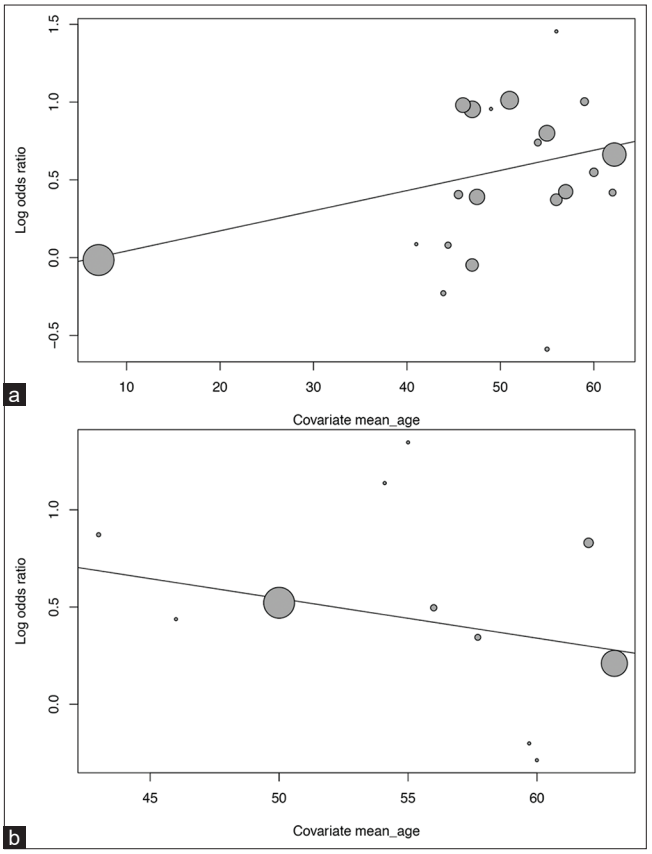


Figure 6: Meta-regression of age and log odds of Sex and Severity (a) or Mortality (b) in COVID-19

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 non-infectious 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 meta-analysis 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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References

1. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, *et al.* A familial cluster of pneumonia associated with the 2019 novel Coronavirus indicating person-to-person transmission: A study of a family cluster. Lancet. 2020;395(10223):514-23. https://doi.org/10.1016/s0140-6736(20)30154-9
PMid:31986261
2. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, *et al.* Clinical

characteristics of Coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708-20.
PMid:32109013

3. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, *et al.* Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: A descriptive study. Lancet Infect Dis. 2020;20(4):425-34. https://doi.org/10.1016/s1473-3099(20)30086-4
PMid:32105637
4. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, *et al.* Genomic characterisation and epidemiology of 2019 novel Coronavirus: Implications for virus origins and receptor binding. Lancet. 2020;395(10224):565-74.
PMid:32007145
5. World Health Organization. Coronavirus Disease 2019 (COVID-19) Situation Report No. 75. Geneva: World Health Organization; 2020. Available from: https://apps.who.int/iris/handle/10665/331688.
6. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, *et al.* Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized With COVID-19 in the New York city area. JAMA. 2020;323(20):2052-9. https://doi.org/10.1001/jama.2020.6775
PMid:32320003
7. Cheng JL, Huang C, Zhang GJ, Liu DW, Li P, Lu CY, *et al.* Epidemiological characteristics of novel Coronavirus pneumonia in Henan. Zhonghua Jie He He Hu Xi Za Zhi. 2020;43(4):327-31.
PMid:32118390
8. Epidemiology Working Group for NCIP Epidemic Response, Chinese Center for Disease Control and Prevention. The epidemiological characteristics of an outbreak of 2019 novel Coronavirus diseases (COVID-19) in China. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(2):145-51.
PMid:32064853
9. Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. JAMA. 2020;323(14):1335. https://doi.org/10.1001/jama.2020.4344
PMid:32181795
10. Korean Society of Infectious Diseases, Korean Society of Pediatric Infectious Diseases, Korean Society of Epidemiology, Korean Society for Antimicrobial Therapy, Korean Society for Healthcare-associated Infection Control and Prevention, Korea Centers for Disease Control and Prevention. Report on the epidemiological features of Coronavirus disease 2019 (COVID-19) outbreak in the republic of Korea from January 19 to March 2, 2020. J Korean Med Sci. 2020;35(10):e112. https://doi.org/10.3346/jkms.2020.35.e112
PMid:32174069
11. Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, *et al.* Gender differences in patients With COVID-19: Focus on severity and mortality. Front Public Health. 2020;8:152. https://doi.org/10.1101/2020.02.23.20026864
PMid:32411652
12. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet. 2020;395(10229):1054-62. https://doi.org/10.1016/s0140-6736(20)30566-3
PMid:32171076
13. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, *et al.* Risk factors associated with acute respiratory distress syndrome and death in patients with Coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020;180(7):934-43. https://doi.org/10.1001/jamainternmed.2020.0994
PMid:32167524
14. Cai Q, Huang D, Ou P, Yu H, Zhu Z, Xia Z, *et al.* COVID-19 in a designated infectious diseases hospital outside Hubei Province, China. Allergy. 2020;75(7):1742-52. https://doi.org/10.1111/all.14309
PMid:32239761
15. Chen J, Qi T, Liu L, Ling Y, Qian Z, Li T, *et al.* Clinical progression of patients with COVID-19 in Shanghai, China. J Infect. 2020;80(5):e1-6.
PMid:32171869
16. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, *et al.* Epidemiological and clinical characteristics of 99 cases of 2019 novel Coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet. 2020;395(10223):507-13. https://doi.org/10.1016/s0140-6736(20)30211-7
PMid:32007143
17. Shi Y, Yu X, Zhao H, Wang H, Zhao R, Sheng J. Host susceptibility to severe COVID-19 and establishment of a host risk score: Findings of 487 cases outside Wuhan. Crit Care. 2020;24(1):108. https://doi.org/10.1186/s13054-020-2833-7
PMid:32188484
18. Zhang G, Hu C, Luo L, Fang F, Chen Y, Li J, *et al.* Clinical features and short-term outcomes of 221 patients with COVID-19 in Wuhan, China. J Clin Virol. 2020;127:104364. https://doi.org/10.1016/j.jcv.2020.104364
PMid:32311650
19. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* Clinical features of patients infected with 2019 novel Coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506. https://doi.org/10.1016/s0140-6736(20)30183-5
PMid:31986264
20. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, *et al.* Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1. https://doi.org/10.1186/2046-4053-4-1
PMid:25554246
21. Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, *et al.* Characteristics and outcomes of 21 critically Ill patients With COVID-19 in Washington state. JAMA. 2020;323(16):1612-4. https://doi.org/10.1001/jama.2020.4326
PMid:32191259
22. Cao J, Hu X, Cheng W, Yu L, Tu WJ, Liu Q. Clinical features and short-term outcomes of 18 patients with Corona virus disease 2019 in intensive care unit. Intensive Care Med. 2020;46(5):851-3. https://doi.org/10.1007/s00134-020-05987-7
PMid:32123993
23. Chen C, Chen C, Yan JT, Zhou N, Zhao JP, Wang DW. Analysis of myocardial injury in patients with COVID-19 and association between concomitant cardiovascular diseases and severity of COVID-19. Zhonghua Xin Xue Guan Bing Za Zhi. 2020;48(7):567-71.
PMid:32141280
24. Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, *et al.* Clinical and immunological features of severe and moderate Coronavirus disease 2019. J Clin Invest. 2020;130(5):2620-9.
PMid:32217835
25. Chen L, Liu HG, Liu W, Liu J, Liu K, Shang J, *et al.* Analysis of clinical features of 29 patients with 2019 novel Coronavirus pneumonia. Zhonghua Jie He He Hu Xi Za Zhi. 2020;43(1):E005.
PMid:32164089
26. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, *et al.* Clinical characteristics of 113 deceased patients with Coronavirus disease 2019: Retrospective study. BMJ. 2020;368:m1091. https://doi.org/10.1136/bmj.m1091
PMid:32217556
27. Dong XC, Li JM, Bai JY, Liu ZQ, Zhou PH, Gao L, *et al.*

Epidemiological characteristics of confirmed COVID-19 cases in Tianjin. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(5):638-41. PMid:32164400

28. Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, *et al.* Clinical characteristics of COVID-19 in New York city. N Engl J Med. 2020;382(24):2372-4. PMid:32302078
29. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, *et al.* Cardiovascular implications of fatal outcomes of patients with Coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020;5(7):811-8. https://doi.org/10.1001/jamacardio.2020.1017 PMid:32219356
30. Jin X, Lian JS, Hu JH, Gao J, Zheng L, Zhang YM, *et al.* Epidemiological, clinical and virological characteristics of 74 cases of Coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. Gut. 2020;69(6):1002-9. PMid:32213556
31. Lei S, Jiang F, Su W, Chen C, Chen J, Mei W, *et al.* Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. E Clin Med. 2020;21:100331. https://doi.org/10.1016/j.eclinm.2020.100331 PMid:32292899
32. Li K, Wu J, Wu F, Guo D, Chen L, Fang Z, *et al.* The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. Invest Radiol. 2020;55(6):327-31. https://doi.org/10.1097/rli.0000000000000672 PMid:32118615
33. Liu K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, *et al.* Clinical characteristics of novel Coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J (Engl). 2020;133(9):1025-31. https://doi.org/10.1097/cm9.0000000000000744 PMid:32044814
34. Liu W, Tao ZW, Wang L, Yuan ML, Liu K, Zhou L, *et al.* Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel Coronavirus disease. Chin Med J (Engl). 2020;133(9):1032-8. https://doi.org/10.1097/cm9.0000000000000775 PMid:32118640
35. Peng YD, Meng K, Guan HQ, Leng L, Zhu RR, Wang BY, *et al.* Clinical characteristics and outcomes of 112 cardiovascular disease patients infected by 2019-nCoV. Zhonghua Xin Xue Guan Bing Za Zhi. 2020;48(6):450-5. PMid:32120458
36. Qian GQ, Yang NB, Ding F, Ma AH, Wang ZY, Shen YF, *et al.* Epidemiologic and clinical characteristics of 91 hospitalized patients with COVID-19 in Zhejiang, China: A retrospective, multi-centre case series. QJM. 2020;113(7):474-81. https://doi.org/10.1093/qjmed/hcaa089 PMid:32181807
37. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(5):846-8. https://doi.org/10.1007/s00134-020-05991-x PMid:32125452
38. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel Coronavirus pneumonia. J Thromb Haemost. 2020;18(4):844-7. https://doi.org/10.1111/jth.14768 PMid:32073213
39. Tian S, Hu N, Lou J, Chen K, Kang X, Xiang Z, *et al.* Characteristics of COVID-19 infection in Beijing. J Infect. 2020;80(4):401-6. PMid:32112886
40. Wan S, Xiang Y, Fang W, Zheng Y, Li B, Hu Y, *et al.* Clinical features and treatment of COVID-19 patients in Northeast Chongqing. J Med Virol. 2020;92(7):797-806. https://doi.org/10.1002/jmv.25783 PMid:32198776
41. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al.* Clinical characteristics of 138 hospitalized patients with 2019 novel Coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9. https://doi.org/10.1001/jama.2020.1585 PMid:32031570
42. Wu J, Liu J, Zhao X, Liu C, Wang W, Wang D, *et al.* Clinical characteristics of imported cases of Coronavirus disease 2019 (COVID-19) in Jiangsu Province: A multicenter descriptive study. Clin Infect Dis. 2020;71(15):706-12. https://doi.org/10.1093/cid/ciaa199 PMid:32109279
43. Xie H, Zhao J, Lian N, Lin S, Xie Q, Zhuo H. Clinical characteristics of non-ICU hospitalized patients with Coronavirus disease 2019 and liver injury: A retrospective study. Liver Int. 2020;40(6):1321-6. https://doi.org/10.1111/liv.14449 PMid:32239591
44. Xu YH, Dong JH, An WM, Lv XY, Yin XP, Zhang JZ, *et al.* Clinical and computed tomographic imaging features of novel Coronavirus pneumonia caused by SARS-CoV-2. J Infect. 2020;80(4):394-400. https://doi.org/10.1016/j.jinf.2020.02.017 PMid:32109443
45. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, *et al.* Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475-81. https://doi.org/10.1016/s2213-2600(20)30079-5 PMid:32105632
46. Yao N, Wang SN, Lian JQ, Sun YT, Zhang GF, Kang WZ, *et al.* Clinical characteristics and influencing factors of patients with novel Coronavirus pneumonia combined with liver injury in Shaanxi region. Zhonghua Gan Zang Bing Za Zhi. 2020;28(3):234-9. PMid:32153170
47. Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel Coronavirus in Wuhan, China. PLoS One. 2020;15(3):e0230548. https://doi.org/10.1371/journal.pone.0230548 PMid:32191764
48. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, *et al.* Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020;75(7):1730-41. https://doi.org/10.1111/all.14238 PMid:32077115
49. Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation between chest CT findings and clinical conditions of Coronavirus disease (COVID-19) pneumonia: A multicenter study. AJR Am J Roentgenol. 2020;214(5):1072-7. https://doi.org/10.2214/ajr.20.22976 PMid:32125873
50. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, *et al.* Early transmission dynamics in Wuhan, China, of novel Coronavirus-infected pneumonia. N Engl J Med. 2020;382(13):1199-207. PMid:31995857
51. Lam CW, Chan MH, Wong CK. Severe acute respiratory syndrome: Clinical and laboratory manifestations. Clin Biochem Rev. 2004;25(2):121-32. PMid:18458712
52. Cai G. Bulk and Single-Cell Transcriptomics Identify Tobacco-Use Disparity in Lung Gene Expression of ACE2, the Receptor of 2019-nCov, MedRxiv; 2020. https://doi.

org/10.1101/2020.02.05.20020107

53. Jaillon S, Berthenet K, Garlanda C. Sexual dimorphism in innate immunity. Clin Rev Allergy Immunol. 2019;56(3):308-21. https://doi.org/10.1007/s12016-017-8648-x
PMid:28963611

54. Patel SK, Velkoska E, Burrell LM. Emerging markers in cardiovascular disease: Where does angiotensin-converting enzyme 2 fit in? Clin Exp Pharmacol Physiol. 2013;40(8):551-9. https://doi.org/10.1111/1440-1681.12069
PMid:23432153

55. Cai H. Sex difference and smoking predisposition in patients with COVID-19. Lancet Respir Med. 2020;8(4):e20. https://doi.org/10.1016/s2213-2600(20)30117-x
PMid:32171067

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	Total	M/F	Severity	Mortality	Quality
Arentz *et al*. [1]	February 20-March 5, 2020	USA	70 (IR 43-92)	21	11/10	21	11	8
Bernheim *et al*. [2]	January 18-February 2, 2020	China	45.3 (SD 15.6)	121	61/60	-	-	9
Cai *et al*. [3]	January 11-February 6, 2020	Shenzhen, China	47 (IQR 33–61)	298	145/153	58	3	8
Cao *et al*. [4]	January 3-February 1, 2020	Wuhan, China	54 (37–67)	102	53/49	18	17	6
Chang *et al*. [5]	January 16-January 29, 2020	Beijing, China	34 (IQR 34–48)	13	10/3	-	-	7
Chen *et al*. [6]	January-February, 2020	Wuhan, China	59(SD 16)	150	84/66	24	11	9
Chen *et al*. [7]	December 2019-January 27, 2020	Wuhan, China	56 (IQR 50–65)	21	17/4	11	-	8
Chen *et al*. [8]	January 20-February 6, 2020	Shanghai, China	51 (IQR 36–64)	249	126/123	22	-	9
Chen *et al*. [9]	January 14-January 29, 2020	Wuhan, China	56 (IR 26–79)	29	21/8	14	-	8
Chen *et al*. [10]	January 1-January 20, 2020	Wuhan, China	55.5 (SD 13.1)	99	67/32	-	11	9
Chen *et al*. [11]	January 13-February 12, 2020	Wuhan, China	62 (IQR 44–77)	274	171/103	-	113	9
Chen *et al*. [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
China CDC [14]	February 11, 2020	China	30–69	44672	22981/21691	8255	1023	8
Chuang *et al*. [15]	January 18-January 27, 2020	China	51 (SD 14)	21	13/8	-	-	7
Australia [16]	January 13, 2020	Australia	43 (IR 8–66)	15	9/6	-	-	5
NERC [17]	February 14, 2020	Korea	42.6 (IR 20–73)	28	15/13	-	-	6
Dong *et al*. [18]	January 7-February 24, 2020	Tianjin, China	48.6 (SD 16.8)	135	72/63	62	3	8
Easom *et al*. [19]	January 29-February 24, 2020	UK	42.5 (IR 0.5–76)	68	32/36	-	-	9
Goyal *et al*. [20]	Mar 3-Mar 27, 2020	USA	62.2 (IQR 48.6–73.7)	393	238/155	130	40	7
Grasselli *et al*. [21]	February 20-March 18, 2020	Italy	63 (IQR 56–70)	1591	1304/287	1591	405/1581	9
Guan *et al*. [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
Huang *et al*. [24]	December 16, 2019-January 2, 2020	Wuhan, China	49 (41–58)	41	30/11	13	6	9
Huang *et al*. [25]	December 21, 2019-January 28, 2020	Wuhan, China	56.24 (SD 17.14)	34	14/20	-	-	7
Jin *et al*. [26]	January 17-February 8, 2020	Zhejiang, China	45	651	331/320	64	-	8
KSID [27]	January 19-March 2, 2020	Korea	20–50	4212	1591/2621	-	22	8
Lei *et al*. [28]	January 1-February 5, 2020	Wuhan, China	55 (IQR 43–63)	34	14/20	15	7	9
Li *et al*. [29]	January-February, 2020	Chongqing, China	45.5 (SD 12.3)	83	44/39	25	-	7
Li *et al*. [30]	December-January 22, 2020	Wuhan, China	59(IR 15–89)	425	240/185	-	-	9
Li *et al*. [31]	December 28-February 10, 2020	Southwest, China	47 (SD 15)	131	63/68	-	-	8
Liu *et al*. [32]	December 30, 2019-January 24, 2020	Hubei, China	55 (SD 16)	137	61/76	-	16	8
Liu *et al*. [33]	December 30-January 15, 2020	Wuhan, China	38 (IQR 33–57)	78	39/39	8	-	9
Livngston *et al*. [34]	March 15, 2020	Italy	64	22512	13462/9050	9	1625	3
Mizumoto *et al*. [35]	February 5-February 20, 2020	Japan	-	634	321/313	-	-	8
Pan *et al*. [36]	January 12-February 6, 2020	Wuhan, China	40(SD 9)	21	6/15	-	-	8
Pan *et al*. [37]	December 30-January 31, 2020	Wuhan, China	44.9 (SD 15.2)	63	33/30	-	-	7
Peng *et al*. [38]	January 20-February 15, 2020	Wuhan, China	62 (IQR 55–67)	112	53/59	16	17	8
Qian *et al*. [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 *et al*. [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
Su *et al*. [46]	January 13-January 31, 2020	Taiwan, China	56.6	10	7/3	-	-	5
Sun *et al*. [47]	January 26-February 16, 2020	Singapore	42 (IQR 34–54)	54	29/25	-	-	8
Tang *et al*. [48]	January 1-February 3, 2020	Wuhan, China	54.1 (SD 16.2)	183	98/85	-	21	7
Tian *et al*. [49]	January 20-February 10, 2020	Beijing, China	47.5 (1–94)	262	127/135	46	3	7
Wan *et al*. [50]	January 23-February 8, 2020	Chongqing, China	47 (IQR 36–55)	135	72/63	40	1	8
Wang *et al*. [51]	January 1-January 28, 2020	Wuhan, China	56 (42–68)	138	75/63	36	6	9
Wang *et al*. [52]	January 16-February 17, 2020	Wuhan, China	45 (SD 14)	90	33/57	-	-	7
Wu *et al*. [53]	December 25, 2019-January 26, 2020	Wuhan, China	51 (IQR 43–60)	201	128/99	84	44	9
Wu *et al*. [54]	January-February, 2020	Chongqing, China	44 (SD 11)	80	42/38	-	-	8
Wu *et al*. [55]	January 22-February 14, 2020	Jiangsu, China	46.1 (SD 15.42)	80	39/41	3	-	9
Wu *et al*. [56]	February 9-February 15, 2020	Hubei, China	68 (IQR 53–67)	38	25/13	-	-	9
Xie *et al*. [57]	February 2-February 23, 2020	Wuhan, China	60 (IQR48–66)	79	44/35	28	-	8
Xie *et al*. [58]	January 21-January 30, 2020	Wuhan, China	70 (IQR 64–78)	168	126/42	-	168	5
Xu *et al*. [59]	January 23-February 4, 2020	Guangdong, China	50 (IR 18–86)	90	39/51	-	-	7
Xu *et al*. [60]	January 10-January 26, 2020	Zhejiang, China	41 (IQR 32–52)	62	36/27	-	-	8
Xu *et al*. [61]	January-February, 2020	Beijing, China	43.9 (SD 16.8)	50	29/21	13	-	7
Yang *et al*. [62]	January 17-February 10, 2020	Zhejiang, China	45.11 (SD 13.35)	149	81/68	-	-	7
Yang *et al*. [63]	December 2019-January 26, 2020	Wuhan, China	59.7 (SD 13.3)	52	35/17	52	32	9
Yao *et al*. [64]	January 12-February 21, 2020	Shaanxi, China	53.87 (SD 15.84)	40	25/15	22	-	7
Young *et al*. [65]	January 23-February 3, 2020	Singapore	47 (IR 31–73)	18	9/9	-	-	8
Yuan *et al*. [66]	January 1-January 25, 2020	Wuhan, China	60 (IQR 47–69)	27	12/15	-	10	7
Zha *et al*. [67]	January 24-February 24, 2020	Wuhan, China	39 (IQR 32–54)	31	20/11	-	-	8
Zhang *et al*. [68]	January 2-February 10, 2020	Wuhan, China	55 (IQR 39–66.5)	221	108/113	55	12	9
Zhang *et al*. [69]	January 16-February 3, 2020	Wuhan, China	57 (IR 25–87)	140	71/69	58	-	8
Zhang *et al*. [70]	January 13-February 26, 2020	Wuhan, China	65 (IQR 56–70)	28	17/11	-	-	8
Zhang *et al*. [71]	January 18-February 3, 2020	Beijing, China	36 (IR 15–49)	9	5/4	-	-	6
Zhang *et al*. [72]	January 17-February 8, 2020	Zhejiang, China	45.4	645	328/317	-	-	8
Zhao *et al*. [73]	-	Hunan, China	44.4 (SD 12.3)	101	56/45	14	-	7
Zhou *et al*. [74]	December 29, 2019-January 31, 2020	Wuhan, China	56 (IQR 46–67)	191	119/72	-	54	9
Zhou *et al*. [75]	January 16-January 30, 2020	Wuhan, China	52.8 (SD 12.2)	62	39/23	-	-	8
Current study	January 20-February 14, 2020	Changchun, China	41 (IQR 33–52)	43	25/18	5	-	8

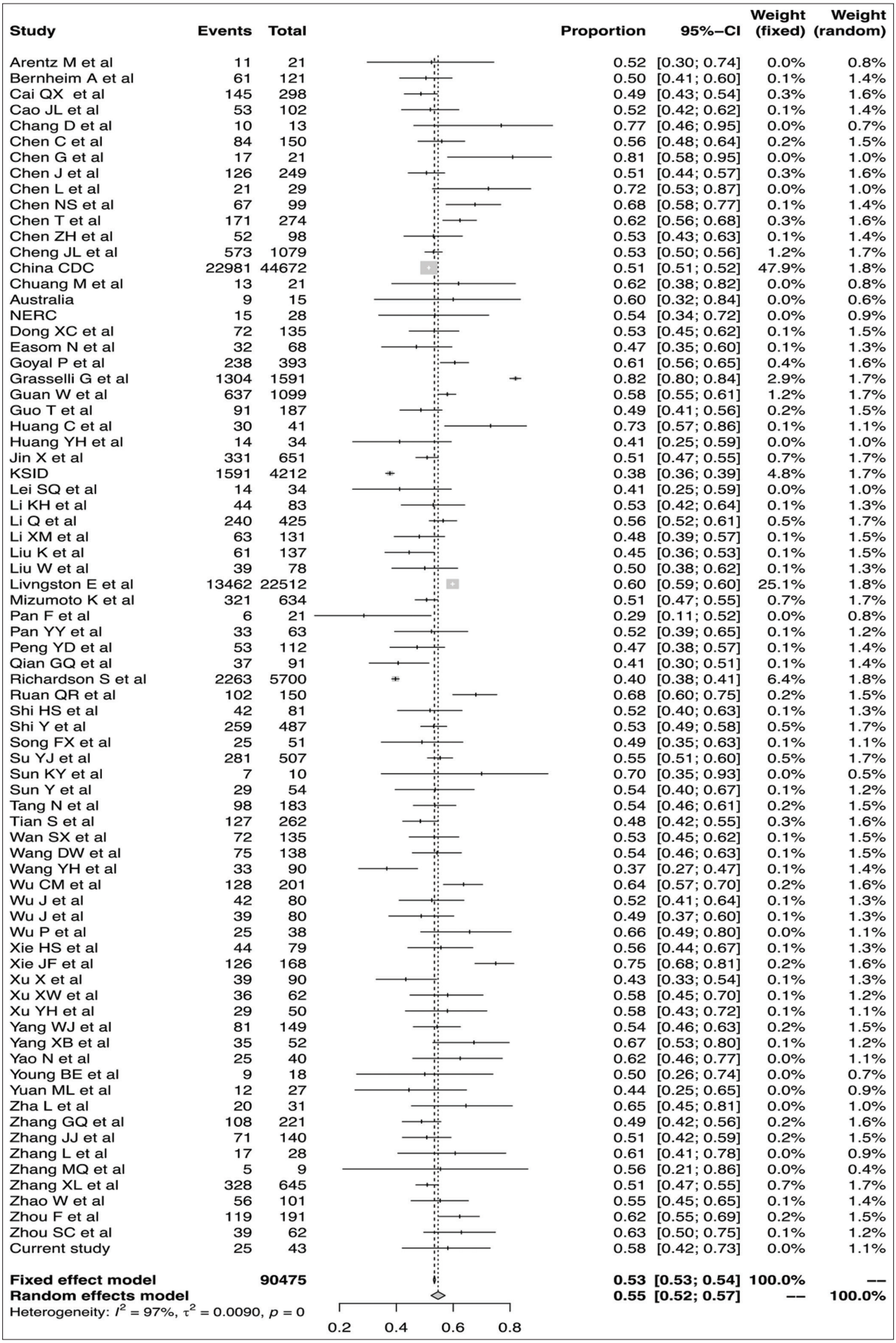

Figure S1: The pooled morbidity of male with COVID-19

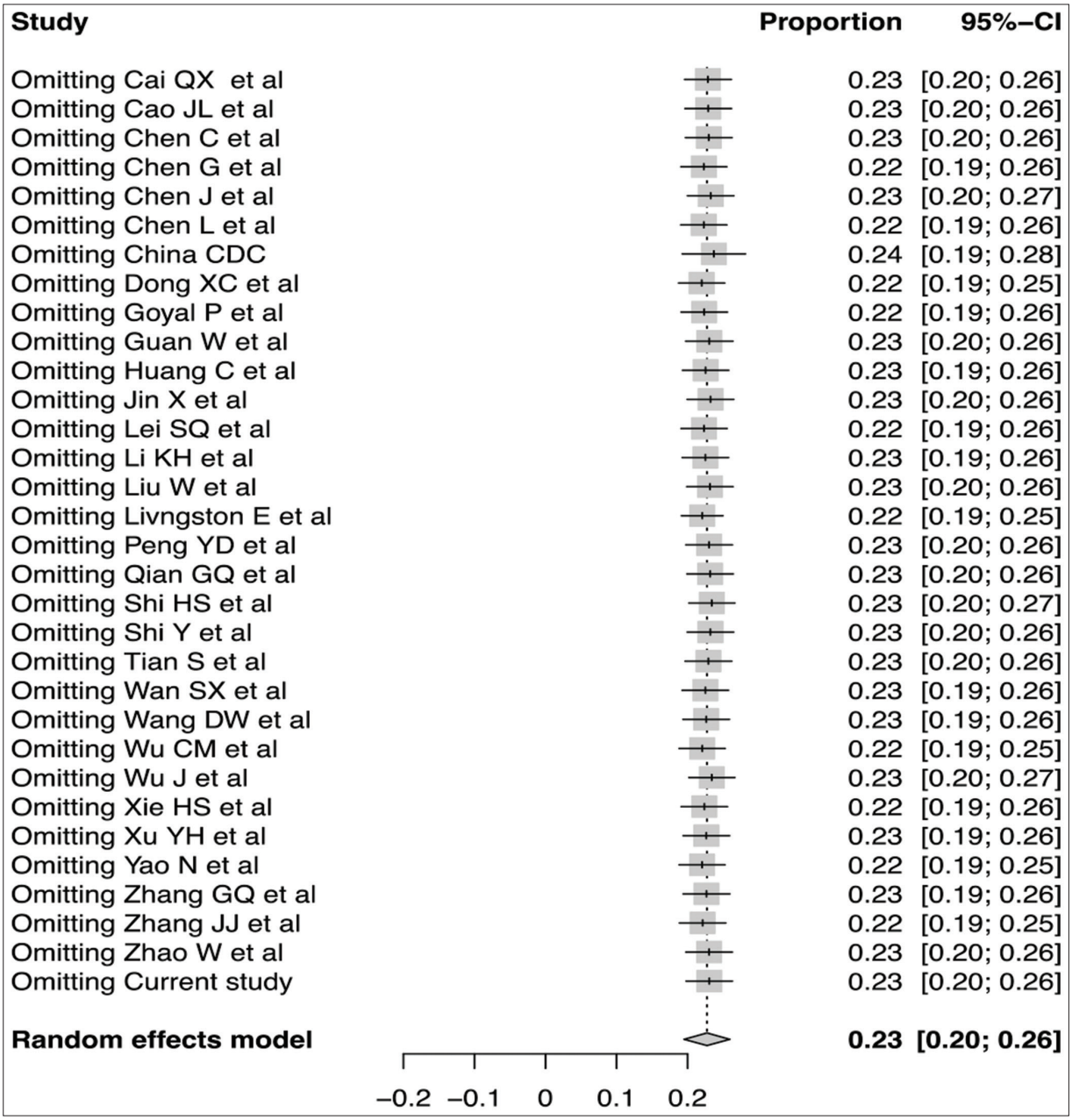

Figure S2: Sensitivity analysis of pooled severe rate in COVID-19

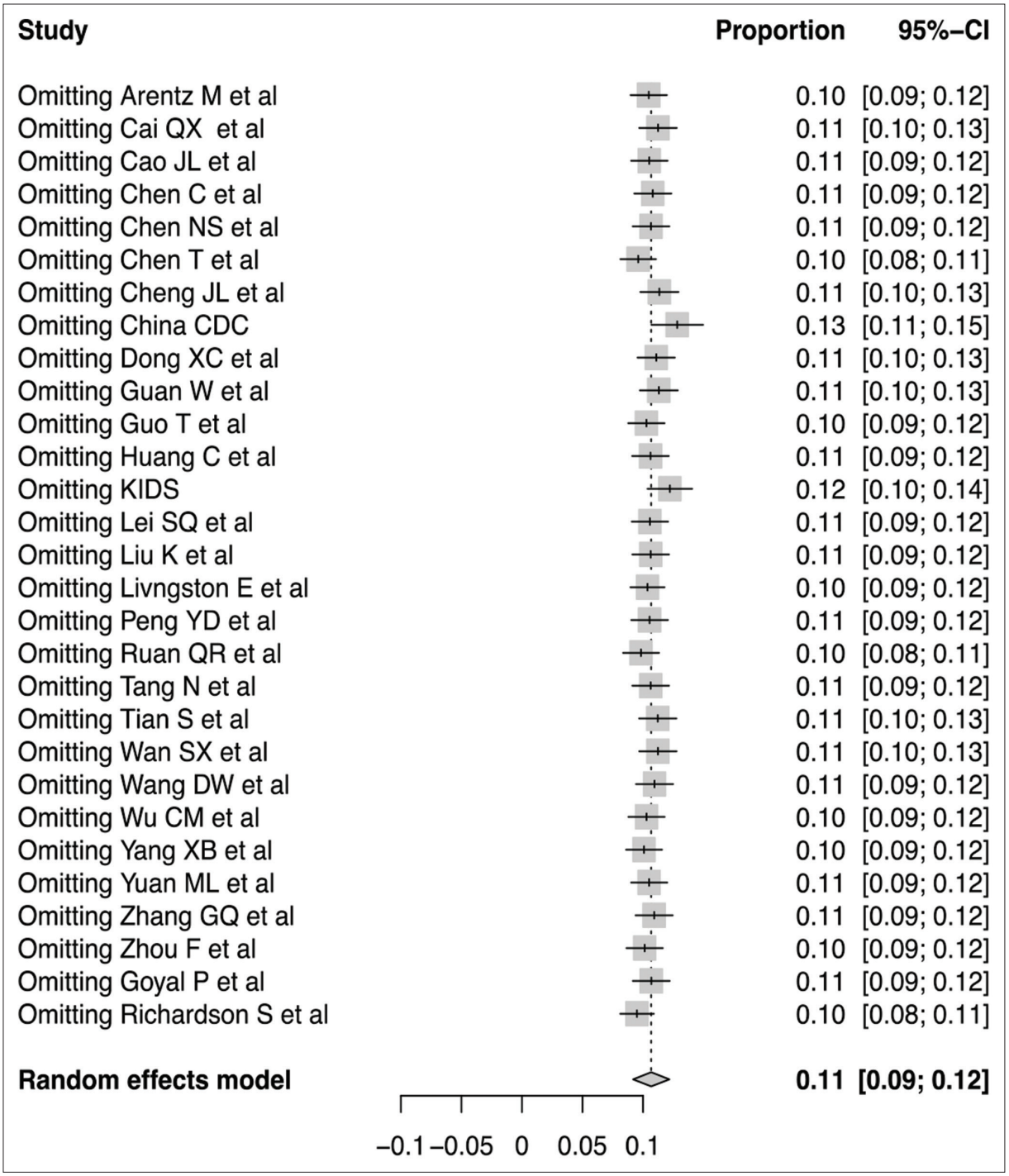

Figure S3: Sensitivity analysis of pooled fatality rate in COVID-19

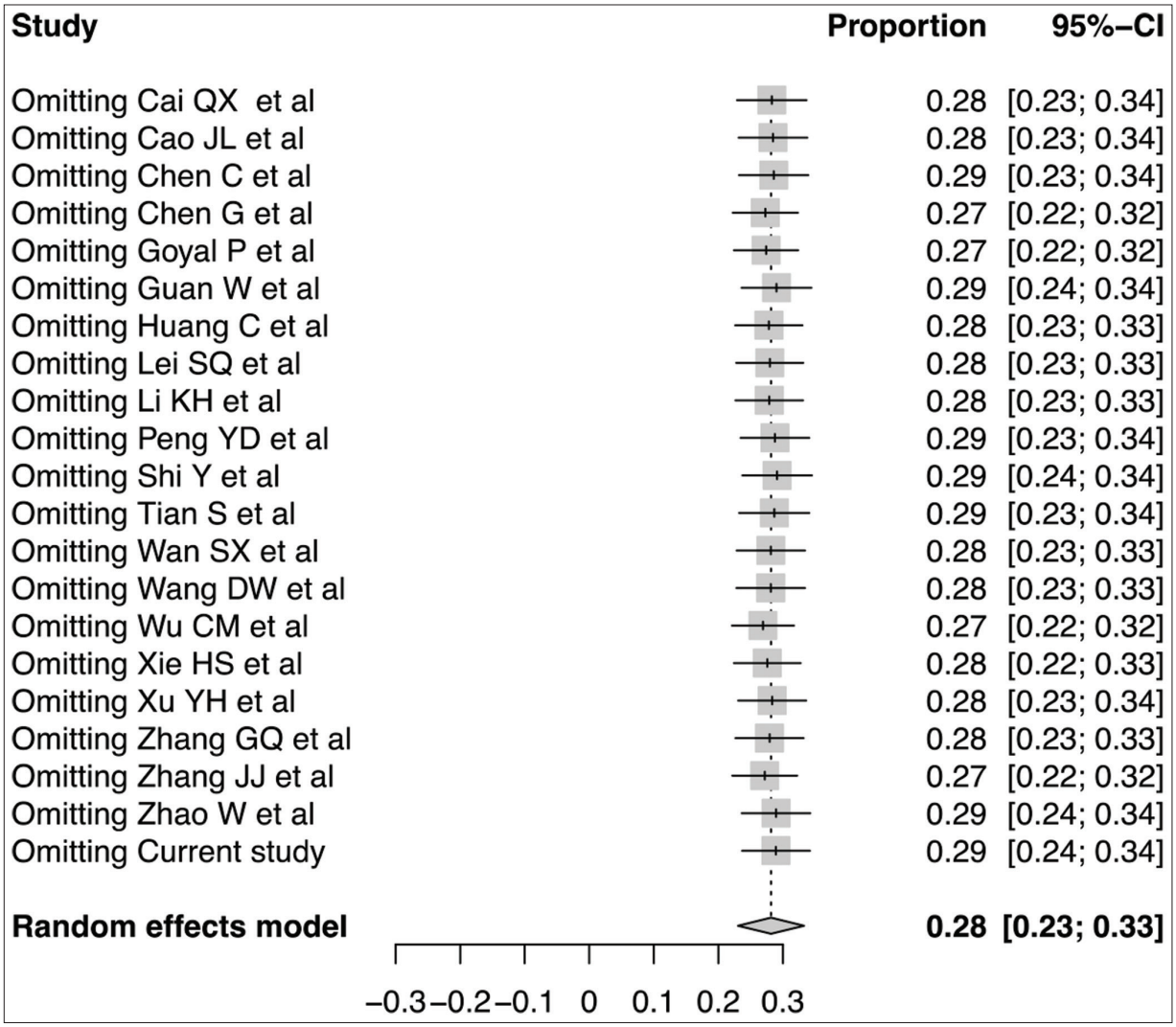

Figure S4: Sensitivity analysis of pooled severe rate of male in COVID-19

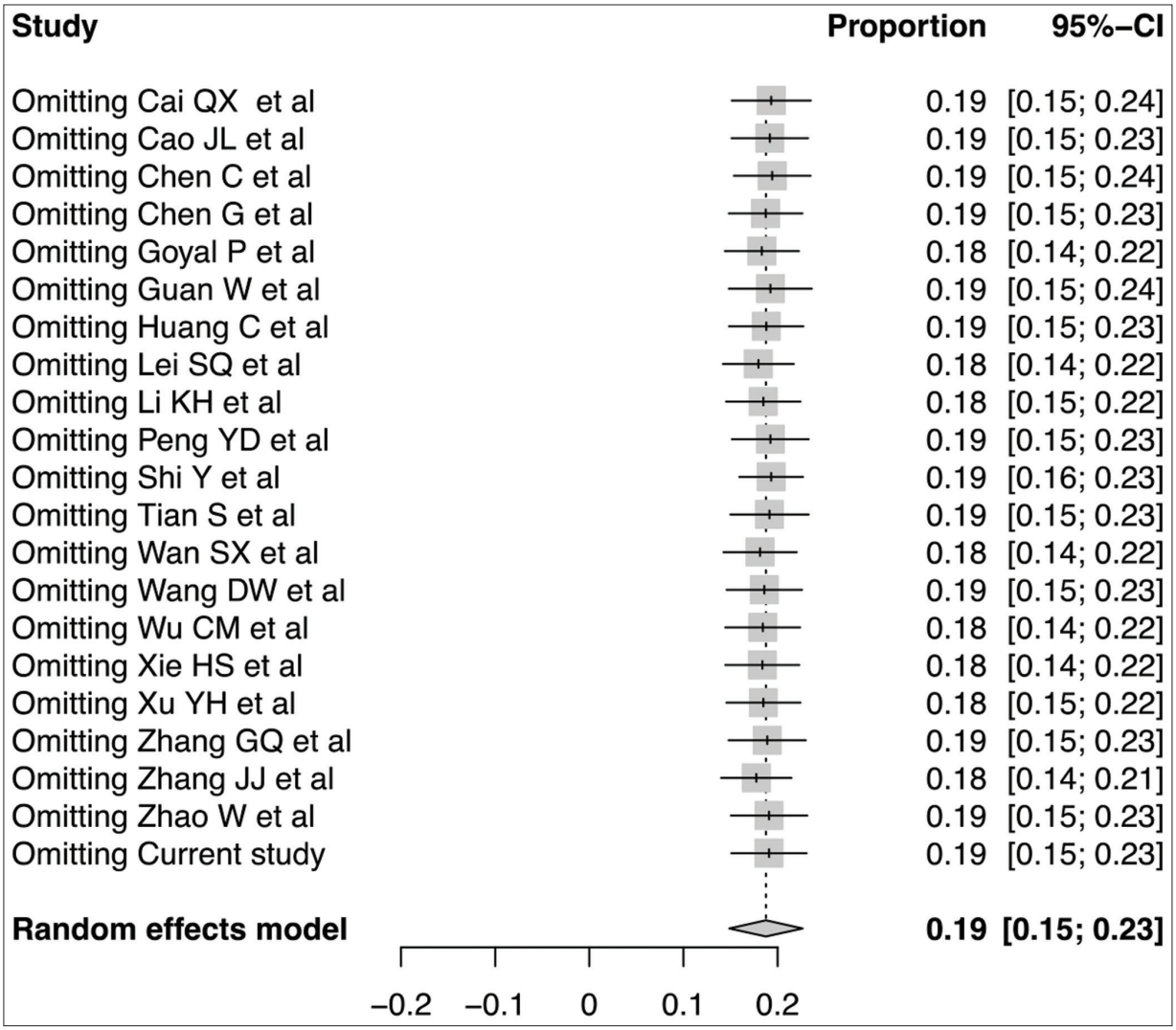

Figure S5: Sensitivity analysis plot of pooled severe rate of female in COVID-19

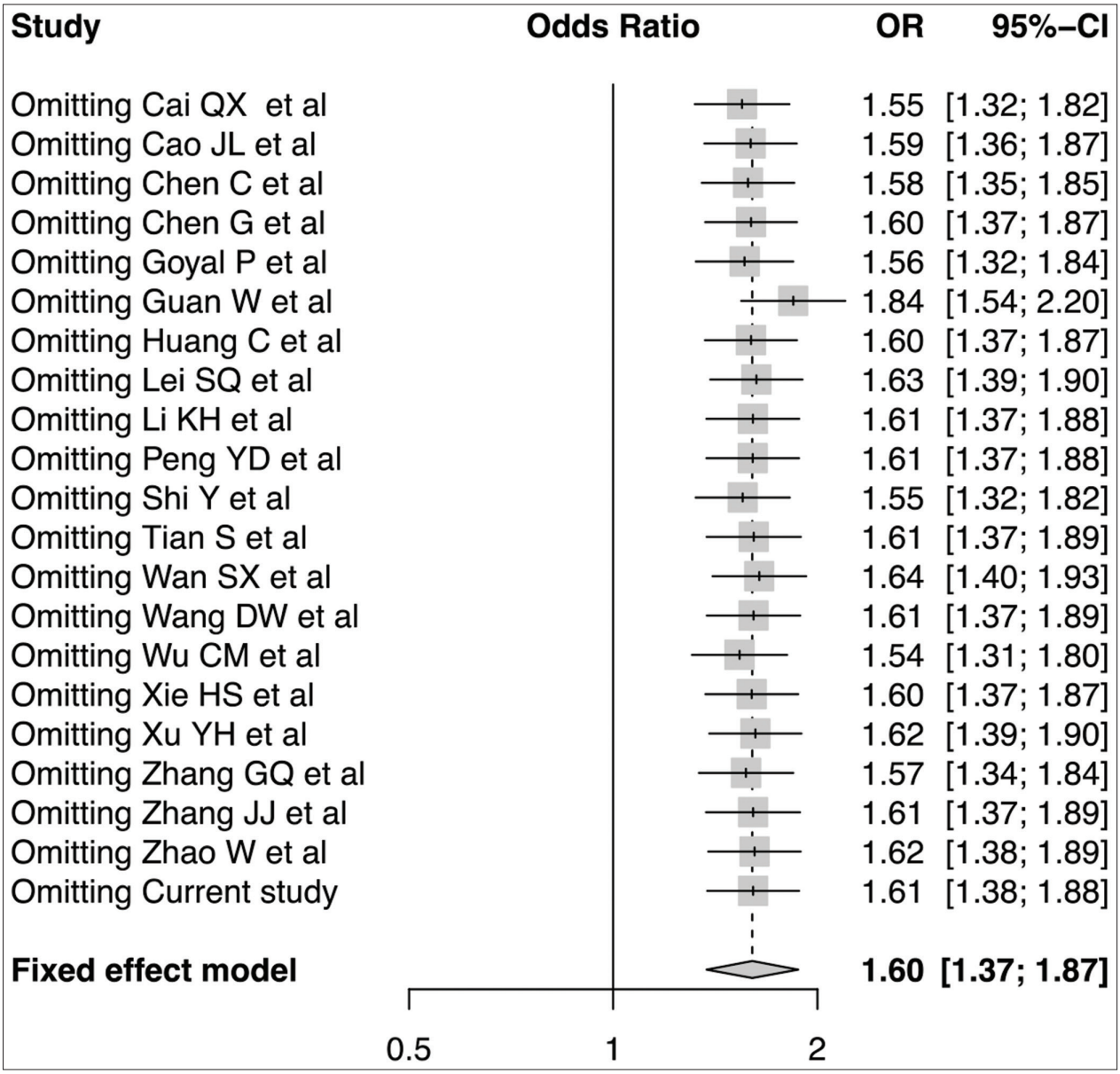

Figure S6: Sensitivity analysis plot of pooled risky between sex and severity in COVID-19

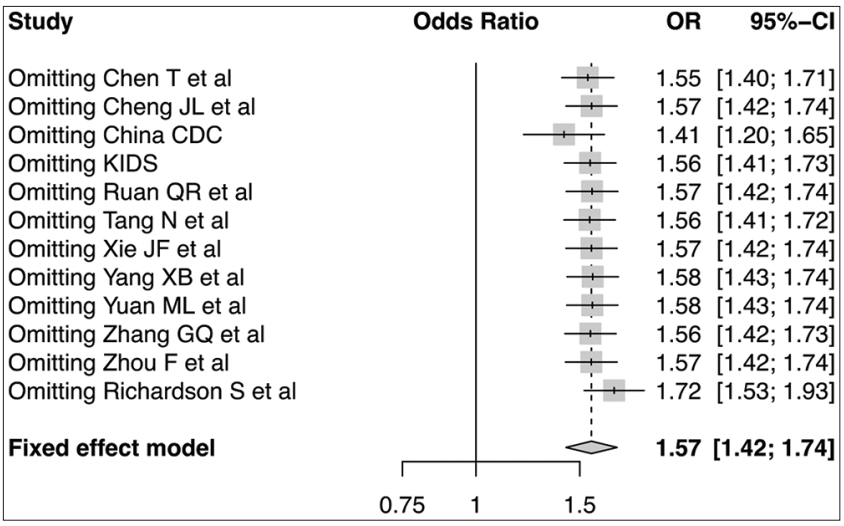

Figure S7: Sensitivity analysis plot of pooled risky between sex and mortality in COVID-19

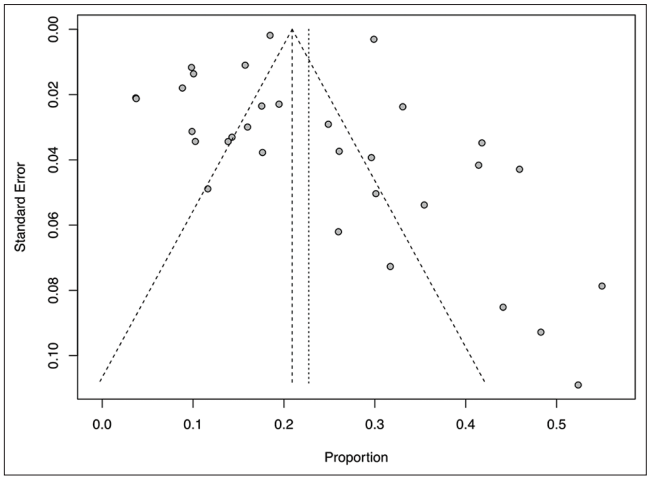

Figure S8: Funnel plot of pooled severe rate in COVID-19

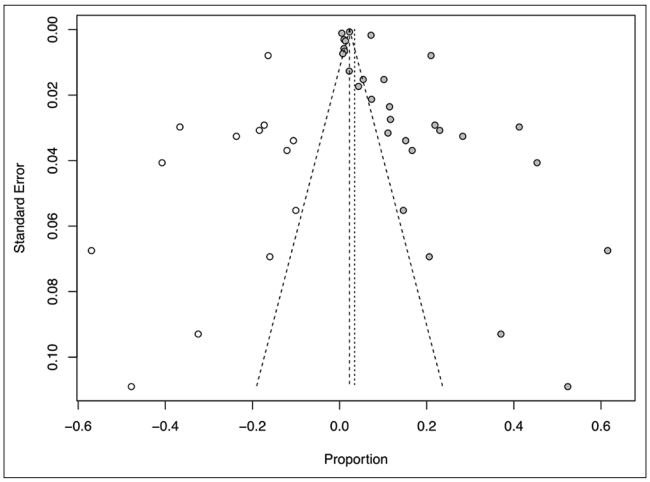

Figure S9: Funnel plot of pooled fatality rate in COVID-19 (trim-fill method)

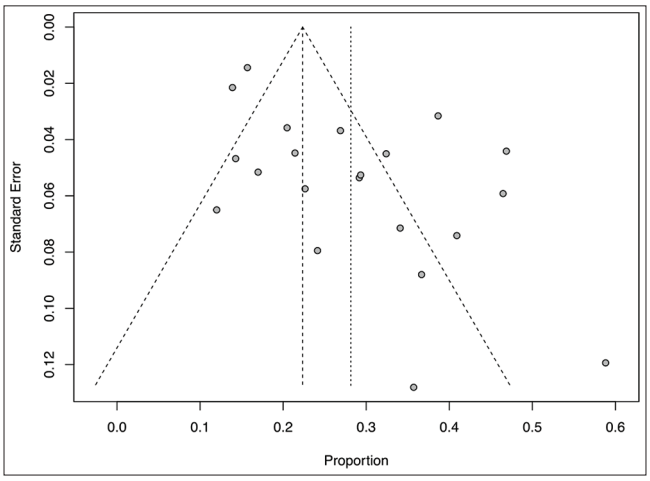

Figure S10: Funnel plot of pooled severe rate of male in COVID-19

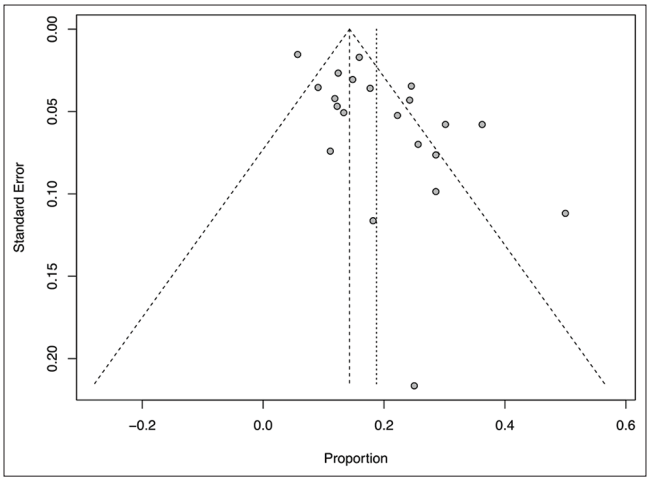

Figure S11: Funnel plot of pooled severe rate of female in COVID-19

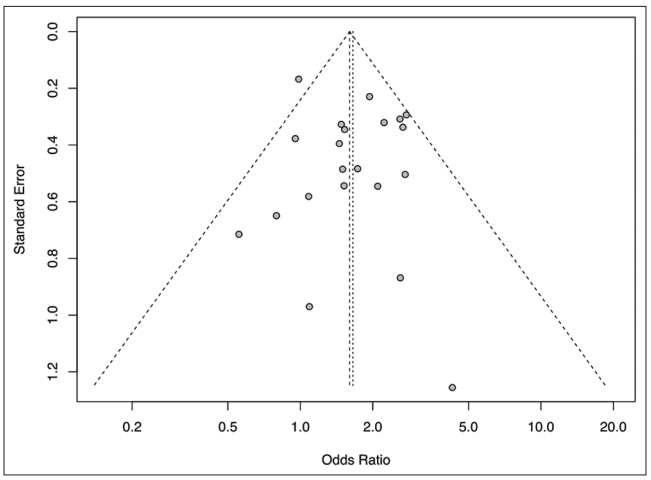

Figure S12: Funnel plot of pooled risky between sex and severity in COVID-19

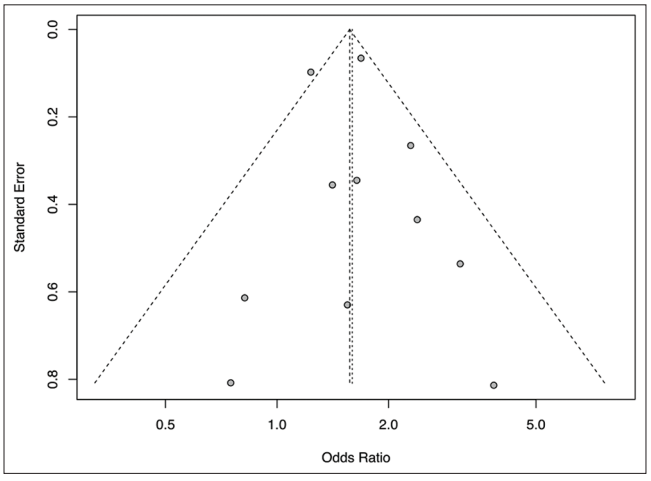

Figure S13: Funnel plot of pooled risky between sex and mortality in COVID-19

References

1. Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, *et al*. Characteristics and outcomes of 21 critically Ill patients with COVID-19 in Washington state. JAMA. 2020;323(16):1612-4. https://doi.org/10.1001/jama.2020.4326
   PMid:32191259
2. Bernheim A, Mei X, Huang M, Yang Y, Fayad ZA, Zhang N, *et al*. Chest CT findings in coronavirus disease-19 (COVID-19): Relationship to duration of infection. Radiology. 2020;295:200463. https://doi.org/10.1148/radiol.2020200463
3. Cai Q, Huang D, Ou P, Yu H, Zhu Z, Xia Z, *et al*. COVID-19 in a designated infectious diseases hospital outside Hubei Province, China. Allergy. 2020;75(7):1742-52.
   PMid:32239761
4. Cao J, Hu X, Cheng W, Yu L, Tu WJ, Liu Q. Clinical features and short-term outcomes of 18 patients with corona virus disease 2019 in intensive care unit. Intensive Care Med. 2020;46(5):851-3. https://doi.org/10.1007/s00134-020-06037-y
   PMid:32123993
5. Chang D, Lin M, Wei L, Xie L, Zhu G, Cruz CS, *et al*. Epidemiologic and clinical characteristics of novel coronavirus infections involving 13 patients outside Wuhan, China. JAMA. 2020;323(11):1092-3. https://doi.org/10.1001/jama.2020.1623
   PMid:32031568
6. Chen C, Chen C, Yan JT, Zhou N, Zhao JP, Wang DW. Analysis of myocardial injury in patients with COVID-19 and association between concomitant cardiovascular diseases and severity of COVID-19. Zhonghua Xin Xue Guan Bing Za Zhi. 2020;48(7):567-71.
   PMid:32141280
7. Chen G, Wu D, Guo W, Huang D, Wang H, Wang T, *et al*. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Investig. 2020;130(5):2620-9.
   PMid:32217835
8. Chen J, Qi T, Liu L, Ling Y, Qian Z, Li T, *et al*. Clinical progression of patients with COVID-19 in Shanghai, China. J Infect. 2020;80(5):e1-6.
   PMid:32171869
9. Chen L, Liu HG, Liu W, Liu J, Liu K, Shang J, *et al*. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. Zhonghua Jie He He Hu Xi Za Zhi. 2020;43:E005.
   PMid:32026671
10. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, *et al*. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet. 2020;395(10223):507-13. https://doi.org/10.1016/s0140-6736(20)30211-7
    PMid:32007143
11. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, *et al*. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: Retrospective study. BMJ. 2020;368:m1091.
    PMid:32217556
12. Chen Z, Fan H, Cai J, Li Y, Wu B, Hou Y, *et al*. High-resolution computed tomography manifestations of COVID-19 infections in patients of different ages. Eur J Radiol. 2020;126:108972. https://doi.org/10.1016/j.ejrad.2020.108972
    PMid:32240913
13. Cheng JL, Huang C, Zhang GJ, Liu DW, Li P, Lu CY, *et al*. Epidemiological characteristics of novel coronavirus pneumonia in Henan. Zhonghua Jie He He Hu Xi Za Zhi. 2020;43(4):327-31.
    PMid:32118390
14. Team. NCPERE. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(2):145-51.
    PMid:32064853
15. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, *et al*. CT imaging features of 2019 novel coronavirus (2019-nCoV). Radiology. 2020;295(1):202-7.
16. COVID-19 National Incident Room Surveillance Team. COVID-19, Australia: Epidemiology report 3. Reporting week ending 19:00 AEDT 15 February 2020. Commun Dis Intell. 2018;2020:44. https://doi.org/10.33321/cdi.2020.44.15
    PMid:32074480
17. COVID-19 National Emergency Response Center EaCMT, Korea Centers for Disease Control and Prevention. Early epidemiological and clinical characteristics of 28 cases of coronavirus disease in South Korea. Osong Public Health Res Perspect. 2020;11(1):8-14. https://doi.org/10.24171/j.phrp.2020.11.1.03
    PMid:32149037
18. Dong XC, Li JM, Bai JY, Liu ZQ, Zhou PH, Gao L, *et al*. Epidemiological characteristics of confirmed COVID-19 cases in Tianjin. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(5):638-42.
    PMid:32164400
19. Easom N, Moss P, Barlow G, Samson A, Taynton T, Adams K, *et al*. Sixty-eight consecutive patients assessed for COVID-19 infection: Experience from a UK Regional infectious diseases unit. Influenza Other Respir Viruses. 2020;14(4):374-9. https://doi.org/10.1111/irv.12739
    PMid:32223012
20. Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, *et al*. Clinical characteristics of Covid-19 in New York City. N Engl J Med. 2020;382(24):2372-4.
    PMid:32302078
21. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, *et al*. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020;323(16):1574-81. https://doi.org/10.1001/jama.2020.5394
    PMid:32250385
22. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, *et al*. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708-20.
23. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, *et al*. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020;5(7):811-8.
    PMid:32219356
24. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.
25. Huang Y, Tu M, Wang S, Chen S, Zhou W, Chen D, *et al*. Clinical characteristics of laboratory confirmed positive cases of SARS-CoV-2 infection in Wuhan, China: A retrospective single center analysis. Travel Med Infect Dis. 2020;2020:101606. https://doi.org/10.1016/j.tmaid.2020.101606
    PMid:32114074
26. Jin X, Lian JS, Hu JH, Gao J, Zheng L, Zhang YM, *et al*. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. Gut. 2020;69(6):1002-9.
    PMid:32213556
27. Korean Society of Infectious DKSoPI, Diseases Korean Society of, Epidemiology Korean Society for Antimicrobial, Therapy Korean Society for Healthcare-associated Infection, Control Prevention, Korea Centers for Disease, Control Prevention. Report on the epidemiological features of coronavirus disease 2019 (COVID-19) outbreak in the republic of Korea from January

19 to March 2, 2020. J Korean Med Sci. 2020;35(10):e112. https://doi.org/10.3346/jkms.2020.35.e112
PMid:32174069

28. Lei S, Jiang F, Su W, Chen C, Chen J, Mei W, *et al*. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. EClinicalMedicine. 2020;21:100331. https://doi.org/10.1016/j.eclinm.2020.100363
PMid:32292899
29. Li K, Wu J, Wu F, Guo D, Chen L, Fang Z, *et al*. The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. Investig Radiol. 2020;55(6):327-31. https://doi.org/10.1097/rli.0000000000000672
PMid:32118615
30. Li Q, Guan X, Wu P. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020;382:1199-207.
31. Li X, Zeng W, Li X, Chen H, Shi L, Li X, *et al*. CT imaging changes of corona virus disease 2019(COVID-19): a multi-center study in Southwest China. J Transl Med. 2020;18(1):154. https://doi.org/10.1186/s12967-020-02324-w
PMid:32252784
32. Liu K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, *et al*. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J (Engl). 2020;133(9):1025-31.
PMid:32044814
33. Liu W, Tao ZW, Lei W, Yuan ML, Liu K, Zhou L, *et al*. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Chin Med J (Engl). 2020;133(9):1032-8.
PMid:32118640
34. Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. JAMA. 2020;323(14):1335. https://doi.org/10.1001/jama.2020.4344
PMid:32181795
35. Mizumoto K, Kagaya K, Zarebski A, Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Eurosurveillance. 2020;25(10):2000180. https://doi.org/10.2807/1560-7917.es.2020.25.10.2000180
PMid:32183930
36. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, *et al*. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. Radiology. 2020;295(3):715721.
PMid:32053470
37. Pan Y, Guan H, Zhou S, Wang Y, Li Q, Zhu T, *et al*. Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): A study of 63 patients in Wuhan, China. Eur Radiol. 2020;30(6):3306-9. https://doi.org/10.1007/s00330-020-06731-x
PMid:32055945
38. Peng YD, Meng K, Guan HQ, Leng L, Zhu RR, Wang BY, *et al*. Clinical characteristics and outcomes of 112 cardiovascular disease patients infected by 2019-nCoV. Zhonghua Xin Xue Guan Bing Za Zhi. 2020;48(6):450-5.
PMid:32120458
39. Qian GQ, Yang NB, Ding F, Ma AH, Wang ZY, Shen YF, *et al*. Epidemiologic and Clinical Characteristics of 91 Hospitalized Patients with COVID-19 in Zhejiang, China: A retrospective, multi-centre case series. QJM. 2020;113(7):474-81.
PMid:32181807
40. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, *et al*. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA. 2020;323(20):2052-9. https://doi.org/10.3410/f.737797860.793574198
PMid:32320003
41. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(5):846-8. https://doi.org/10.1007/s00134-020-06028-z
PMid:32125452
42. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, *et al*. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: A descriptive study. Lancet Infect Dis. 2020;20(4):425-34.
43. Shi Y, Yu X, Zhao H, Wang H, Zhao R, Sheng J. Host susceptibility to severe COVID-19 and establishment of a host risk score: Findings of 487 cases outside Wuhan. Crit Care. 2020;24(1):108. https://doi.org/10.1186/s13054-020-2833-7
PMid:32188484
44. Song F, Shi N, Shan F, Zhang Z, Shen J, Lu H, *et al*. Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. Radiology. 2020;295(1):210-7. https://doi.org/10.1148/radiol.2020200274
PMid:32027573
45. Sun K, Chen J, Viboud C. Early epidemiological analysis of the coronavirus disease 2019 outbreak based on crowdsourced data: A population-level observational study. Lancet Digital Health. 2020;2(4):e201-8. https://doi.org/10.1016/s2589-7500(20)30026-1
46. Su YJ, Lai YC. Comparison of clinical characteristics of coronavirus disease (COVID-19) and severe acute respiratory syndrome (SARS) as experienced in Taiwan. Travel Med Infect Dis. 2020;2020:101625. https://doi.org/10.1016/j.tmaid.2020.101625
PMid:32184131
47. Sun Y, Koh V, Marimuthu K, Ng OT, Young B, Vasoo S, *et al*. Epidemiological and clinical predictors of COVID-19. Clin Infect Dis. 2020;71:786-92.
PMid:32211755
48. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18(4):844-7. https://doi.org/10.1111/jth.14768
PMid:32073213
49. Tian S, Hu N, Lou J, Chen K, Kang X, Xiang Z, *et al*. Characteristics of COVID-19 infection in Beijing. J Infect. 2020;80(4):401-6.
PMid:32112886
50. Wan S, Xiang Y, Fang W, Zheng Y, Li B, Hu Y, *et al*. Clinical features and treatment of COVID-19 patients in Northeast Chongqing. J Med virol. 2020;92(7):797-806.
51. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al*. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9. https://doi.org/10.1001/jama.2020.1585
PMid:32031570
52. Wang Y, Dong C, Hu Y, Li C, Ren Q, Zhang X, *et al*. Temporal changes of CT findings in 90 patients with COVID-19 pneumonia: A longitudinal study. Radiology. 2020;296(2):E55-64.
PMid:32191587
53. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, *et al*. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020;180(7):934-43. https://doi.org/10.1001/jamainternmed.2020.0994
PMid:32167524

54. Wu J, Wu X, Zeng W, Guo D, Fang Z, Chen L, *et al*. Chest CT findings in patients with coronavirus disease 2019 and its relationship with clinical features. Investig Radiol. 2020;55(5):257-61. https://doi.org/10.1097/rli.0000000000000670
PMid:32091414

55. Wu J, Liu J, Zhao X, Liu C, Wang W, Wang D, *et al*. Clinical characteristics of imported cases of COVID-19 in Jiangsu Province: A multicenter descriptive study. Clin Infect Dis. 2020;71:706-12. https://doi.org/10.1093/cid/ciaa199

56. Wu P, Duan F, Luo C, Liu Q, Qu X, Liang L, *et al*. Characteristics of ocular findings of patients with coronavirus disease 2019 (COVID-19) in Hubei Province, China. JAMA Ophthalmol. 2020;138(5):575-8. https://doi.org/10.1001/jamaophthalmol.2020.1291
PMid:32232433

57. Xie H, Zhao J, Lian N, Lin S, Xie Q, Zhuo H, *et al*. Clinical characteristics of non-ICU hospitalized patients with coronavirus disease 2019 and liver injury: A retrospective study. Liver Int. 2020;40(6):1321-6. https://doi.org/10.1111/liv.14449
PMid:32239591

58. Xie J, Tong Z, Guan X, Du B, Qiu H. Clinical characteristics of patients who died of coronavirus disease 2019 in China. JAMA Network Open. 2020;3(4):e205619. https://doi.org/10.1001/jamanetworkopen.2020.5619]
PMid:32275319

59. Xu X, Yu C, Qu J, Zhang L, Jiang S, Huang D, *et al*. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2. Eur J Nucl Med Mol Imaging. 2020;47(5):1275-80.
PMid:32107577

60. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, *et al*. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: Retrospective case series. BMJ. 2020;368:m606. https://doi.org/10.1136/bmj.m792
PMid:32075786

61. Xu Y, Dong J, An W, Lv XY, Yin XP, Zhang JZ, *et al*. Clinical and computed tomographic imaging features of novel coronavirus pneumonia caused by SARS-CoV-2. J Infect. 2020;80(4):394-400. https://doi.org/10.1016/j.jinf.2020.02.017
PMid:32109443

62. Yang W, Cao Q, Qin L, Wang X, Cheng Z, Pan A, *et al*. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): A multi-center study in Wenzhou city, Zhejiang, China. J Infect. 2020;80(4):388-93. https://doi.org/10.1016/j.jinf.2020.02.016
PMid:32112884

63. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, *et al*. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475-81. https://doi.org/10.1016/s2213-2600(20)30079-5

64. Yao N, Wang SN, Lian JQ, Sun YT, Zhang GF, Kang WZ, *et al*. Clinical characteristics and influencing factors of patients with novel coronavirus pneumonia combined with liver injury in Shaanxi region. Zhonghua Gan Zang Bing Za Zhi. 2020;28(3):234-9.
PMid:32153170

65. Young BE, Ong SW, Kalimuddin S, Low JG, Tan SY, Loh J, *et al*. Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. JAMA. 2020;323(15):1488-94.
PMid:32125362

66. Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. PLoS One. 2020;15(3):e0230548. https://doi.org/10.1371/journal.pone.0230548
PMid:32191764

67. Zha L, Li S, Pan L, Tefsen B, Li Y, French N, *et al*. Corticosteroid treatment of patients with coronavirus disease 2019 (COVID-19). Med J Aust. 2020;212(9):416-20.
PMid:32266987

68. Zhang G, Hu C, Luo L, Fang F, Chen Y, Li J, *et al*. Clinical features and short-term outcomes of 221 patients with COVID-19 in Wuhan, China. J Clin Virol. 2020;127:104364. https://doi.org/10.1016/j.jcv.2020.104364
PMid:32311650

69. Zhang J, Dong X, Cao Y, Yuan YD, Yang YB, Yan YQ, *et al*. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020;75(7):1730-41.

70. Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, *et al*. Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China. Ann Oncol. 2020;31(7):894-901.
PMid:32224151

71. Zhang MQ, Wang XH, Chen YL, Zhao KL, Cai YQ, An CL, *et al*. Clinical features of 2019 novel coronavirus pneumonia in the early stage from a fever clinic in Beijing. Zhonghua Jie He He Hu Xi Za Zhi. 2020;43:E013. https://doi.org/10.1016/j.ijid.2020.03.040
PMid:32061066

72. Zhang X, Cai H, Hu J, Lian J, Gu J, Zhang S, *et al*. Epidemiological, clinical characteristics of cases of SARS-CoV-2 infection with abnormal imaging findings. Int J Infect Dis. 2020;94:81-7.
PMid:32205284

73. Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: A multicenter study. Am J Roentgenol. 2020;214(5):1072-7. https://doi.org/10.2214/ajr.20.22976
PMid:32125873

74. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet. 2020;395(10229):1054-62. https://doi.org/10.3410/f.737524760.793572688
PMid:32171076

75. Zhou S, Wang Y, Zhu T, Xia L. CT features of coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. Am J Roentgenol. 2020;214(6):1287-94.
PMid:32134681