

## COVID-19 in children: A systematic review and meta-analysis

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### ABSTRACT

The aim of this work is to identify the clinical features of pediatric COVID-19 and to relate them with laboratory findings on potential markers of poorer outcomes, such as evidence of organ dysfunction and of superimposed bacterial infection. We performed a systematic literature review with meta-analysis using the data bases Pubmed, Scopus, SciELO, Cochrane Library, Web of Science, EMBASE and Google Scholar. Only pediatric cases with COVID-19 confirmed by rRT-PCR were selected. Demographical and clinical characteristics, laboratory and imaging features, complications, exposure setting, and outcomes were evaluated. After screening, 90 articles were selected for full-text assessment, 42 being included for qualitative and quantitative analyses. Additionally, 31 case reports were included and analyzed separately. For 4210 patients, fever (48.6%, 95% CI: 43.5-53.7%) and cough (44.2%, 95% CI: 39.1-49.3%) were the most prevalent clinical features. 29.7% (95% CI: 23.3-35.5%) of the children did not report any symptom. 66.4% (95% CI: 60.2-72.1%) of children had abnormal radiologic findings. Among the patients, 5.1% (95% CI: 2.7-9.3%) required intensive care unit and 27.5% (95% CI: 19.0-38.1%) presented secondary infections.

The pediatric cases of COVID-19 are generally asymptomatic, with fever and cough, however, being the most frequently observed symptoms. The radiologic images often show ground glass opacities. The overall laboratory biomarkers show a scenario of inflammation. Children presented high co-infection rate, particularly with *Mycoplasma*.

**KEYWORDS:** COVID-19, children, clinical and laboratorial findings, meta-analysis.

### ABBREVIATIONS

ACE2	-	angiotensin converting enzyme II
ALT	-	alanine transaminase
ARDS	-	acute respiratory distress syndrome
AST	-	aspartate transaminase
CDC	-	Centers for Disease Control
CI	-	confidence interval
CK-MB/CK	-	creatinine kinase
COVID-19	-	coronavirus disease 2019
CRP	-	C-reactive protein
DIC	-	disseminated intravascular coagulation
ESR	-	erythrocyte sedimentation rate
GGO	-	Ground glasses opacities
ICU	-	intensive care unit
IHE	-	Institute of Health Economics
LDH	-	lactate dehydrogenase

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MIS-C	- multisystem inflammatory syndrome in children
MODS	- multi-organ dysfunction syndrome
NA	- not available
NOS	- Newcastle-Ottawa Scale
PCT	- procalcitonin
PRISMA	- Preferred Reported Items for Systematic Reviews and Meta-Analysis
rRT-PCR	- real-time reverse transcriptase polymerase chain reaction
RSV	- respiratory syncytial virus
SARS-CoV-2	- severe acute respiratory syndrome coronavirus 2
SD	- standard deviation
SE	- standard error

## 1. INTRODUCTION

The coronavirus disease 2019 (COVID-19) emerged in Wuhan, China, in late 2019 and has rapidly spread throughout the world. By July the 2<sup>nd</sup>, the number of confirmed cases in 220 countries reached 62,662,181 [1]. All data indicate that the elderly (>70 years) and those with previous pathologies such as respiratory problems, diabetes, or hypertension are the population at higher risk. Research indicates that children and teens are as likely to be infected as any other age group and may play a major role in community-based viral transmission [2]. The evidence to date suggests that children and young adults are less likely to develop serious illness [3]. However, some pediatric cases may progress to severe disease, and initial atypical presentations may delay the diagnosis of COVID-19, leading to unfavorable outcomes [2].

Recently, health officials are advising clinicians about a rare but serious inflammatory condition seen in children and linked to COVID-19 [4]. The Centers for Disease Control and Prevention (CDC) is calling the condition multisystem inflammatory syndrome in children (MIS-C) and is urging clinicians to report suspected cases so that officials can learn more [4].

Within this context and in order to contribute to a better understanding of the effects of COVID-19 on children, and also to assist authorities and health professionals in developing recommendations for diagnosis and treatment, we aimed to perform a systematic review, complying with the Preferred

Reported Items for Systematic Reviews and Meta-Analysis (PRISMA) statement, followed by meta-analysis of results of published pediatric COVID-19 studies. Thus, our study aims to identify the clinical features of children with COVID-19 and to relate them to laboratory findings on potential markers of poorer outcomes, such as evidence of organ dysfunction and evidence of superimposed bacterial infection.

## 2. METHODS

### 2.1. Search strategy, study selection and eligibility criteria

The search was conducted for published or unpublished (pre-print or even pre-proof accepted) studies in several electronic databases (Pubmed, Scopus, SciELO, Cochrane Library, Web of Science, EMBASE and Google Scholar) using the terms (COVID-19 OR Coronavirus OR “Coronavirus” OR Coronaviruses OR 2019-nCoV OR SARS-CoV OR MERS-CoV) AND (children OR pediatric OR pediatrics). Following the PRISMA statement [5, 6], titles and abstracts of records retrieved were screened and the full texts of those considered relevant were analyzed. Two authors independently performed the literature search, with disagreements resolved by consensus with a third author. To be included in this work, articles must report cases with demographical, clinical, laboratory and image features of real-time reverse transcriptase polymerase chain reaction (rRT-PCR)-confirmed COVID-19 infection in children. For assessing epidemiologic, clinical, laboratorial, and imaging characteristics eligible study designs were case series, cross-sectional studies, case reports and cohort studies. Article language limit was not set, and we included publications from January 1, 2020 until April 19, 2020. Review articles, opinion articles and letters not presenting original data were excluded.

### 2.2. Data extraction and synthesis

Two authors independently assessed and extracted the data. Information was collected on the type of publication, the publishing institution, country, date of publication, the number of reported cases, age, gender, comorbidities, exposure setting, clinical

features, laboratory findings, imaging findings (chest X-ray or chest CT), complications, and cases at intensive care unit (ICU) and outcomes were filled independently by two investigators. A third researcher checked the article list and data extraction to ensure that there were no duplicate articles or duplicate information of the same patient and resolved discrepancies about study inclusion.

### 2.3. Risk of bias assessment

The quality of each included study was assessed using the Institute of Health Economics (IHE) quality appraisal checklist for case series [7], the critical appraisal tool AXIS for cross-sectional studies [8] and the Newcastle-Ottawa Scale (NOS) for cohort studies [9]. Following the recommendation of IHE we decided to remove from the checklist the items that are not applicable to this work. We considered ten criteria (items 1, 2, 3, 4, 5, 6, 7, 10, 12 and 19). The results were summarized by the scoring method; for the “Yes” items, the score was 1, and for the “No” items, the score was 0. The higher the total score, the lower the risk of bias. The Newcastle-Ottawa Scale takes into consideration the selection, comparability, and ascertainment of outcome. The studies with scores  $\geq 7$  were defined as high quality. The AXIS tool assesses the quality of bias according to 20 criteria that focuses mainly on the presented methods and results. Each criterion is answered by “Yes”, “No” or “Do not know”. As this tool does not provide a numerical scale for assessing the quality of the study, a degree of subjective assessment was required. The studies were classified as High, Moderate or Low quality. The studies’ classification was independently assigned by two authors and discrepancies in assessment were resolved through discussions between the authors or by consultation with a third investigator.

### 2.4. Outcomes

We defined comorbidities, clinical features, radiologic and laboratory findings, exposure setting and complications as the main outcomes.

### 2.5. Meta-analysis

Data statistical analysis was performed using Comprehensive Meta-Analysis software (Version 2.0). The forest plots were generated to illustrate

the prevalence and the weight prevalence estimates along with the 95% confidence interval (CI), using the random effects model. The I-squared statistic ( $I^2$ ) was used as a measure of inconsistency across the findings of the studies. Two different analyses were used to assess the potential impact of publication bias on the meta-analysis. One analysis is a funnel plot in which the logit of event rate was plotted against their corresponding standard error (SE). In the absence of publication bias, the studies will be symmetrically distributed about the weighted event rate. Since its interpretation is largely subjective, Egger’s regression test was also performed.

## 3. RESULTS

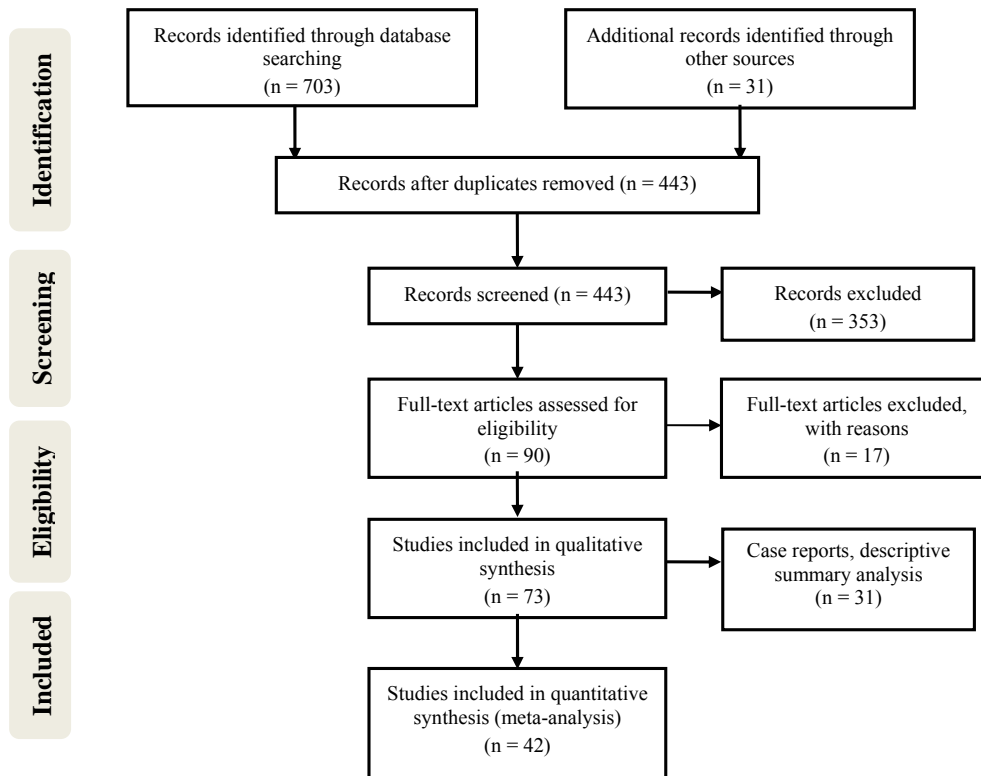
### 3.1. Included studies and characteristics

Complying with the PRISMA statement, the initial search identified 734 articles with potential to be included in this meta-analysis. Figure 1 shows the progression details of the database search regarding the epidemiological, clinical, laboratorial, and imaging features of children diagnosed with COVID-19. After all the steps, 73 studies (4240 patients) were considered suitable for performing qualitative analysis, 42 of them (4188 patients) for quantitative analyses and 31 case reports for descriptive analysis. Among the reasons to exclude studies were lack of information on molecular diagnosis and lack of results in terms of the outcomes of interest. The list of studies included in this work and their main characteristics are summarized in Table 1 and Table 2. All of them were published between January 1, and April 19, 2020.

The demographical characteristics and comorbidities of the study subjects are presented in Table 2. The clinical characteristics of the subjects are summarized in Table 3. The summary of the laboratory and radiologic findings are shown in Tables 4 and 5, respectively. The complications, secondary infections, exposure setting, and outcomes are presented in Tables 6, 7, 8 and 9, respectively.

### 3.2. Risk of publication bias

In the present meta-analysis, the 43 eligible studies were evaluated, independently, by two investigators according to the most adequate critical appraisal tool. The results found in the assessment of the risk of publication bias are summarized in Table 1.



**Figure 1.** PRISMA flow-diagram of database search, study selection and articles included in the systematic review with meta-analysis.

**Table 1.** Main characteristics of the included studies in this systematic review with meta-analysis.

Author	Journal	Date (DD/MM)	Country	Study type	N	Quality score	Reference
Ma, H. <i>et al.</i>	Chinese Journal of Radiology	10/02	China	Case series	22	6	[29]
Wei, M. <i>et al.</i>	JAMA	14/02	China	Case series	9	7	[30]
Kai, F. <i>et al.</i>	Zhonghua Er Ke Za Zhi	16/02	China	Case series	15	7	[31]
Wang, X. F. <i>et al.</i>	Zhonghua Er Ke Za Zhi	17/02	China	Cross-sectional	34	Moderate/High	[32]
Liu, M. <i>et al.</i>	J. Comput. Assist. Tomogr.	25/02	China	Case series	5	6	[33]
Xia, W. <i>et al.</i>	Pediatr. Pulmonol.	26/02	China	Case series	20	6	[34]
Zhou, Y. <i>et al.</i>	CJCP	27/02	China	Case series	9	7	[35]
Cai, J. <i>et al.</i>	Clin. Infect. Dis.	28/02	China	Case series	10	6	[36]
Wang, D. <i>et al.</i>	Zhonghua Er Ke Za Zhi	02/03	China	Cross-sectional	31	Moderate	[37]
Chen, C. <i>et al.</i>	Lancet Child Adolesc Health	03/03	China	Cross-sectional	31	High	[38]
Yao-Ling, M. <i>et al.</i>	CJCP	03/03	China	Cross-sectional	115	Moderate/High	[39]
Hu, Z. <i>et al.</i>	Sci. China Life Sci.	04/03	China	Case series	6	8	[40]
Tang, A. <i>et al.</i>	Medrxiv	10/03	China	Case series	26	6	[41]

Table 1 continued...

Li, W. <i>et al.</i>	Pediatr. Radiol.	11/03	China	Case series	5	6	[42]
Xu, Y. <i>et al.</i>	Nat. Med.	13/03	China	Case series	10	6	[43]
Zhang, X. <i>et al.</i>	Journal of Shandong University (health sciences)	17/03	China	Case series	10	6	[44]
Lu, X. <i>et al.</i>	NEJM	18/03	China	Cross-sectional	171	Moderate	[45]
Yu, H. <i>et al.</i>	Medrxiv	18/03	China	Cross-sectional	82	Low/Moderate	[46]
Sun, D. <i>et al.</i>	World J. Pediatr.	19/03	China	Case series	8	6	[47]
Wu, Q. <i>et al.</i>	Medrxiv	23/03	China	Cross-sectional	74	High	[19]
Zheng, F. <i>et al.</i>	Curr. Med. Sci.	24/03	China	Case series	25	8	[48]
Qiu, H. <i>et al.</i>	Lancet Infect. Dis.	25/03	China	Cohort study	36	8	[49]
Su, L. <i>et al.</i>	Emerg Microbes Infect.	25/03	China	Case series	9	7	[50]
Chen, M. <i>et al.</i>	Research Square	27/03	China	Case series	10	7	[51]
Liu, W. <i>et al.</i>	NEJM		China	Case series	6	8	[52]
Wang, Y. <i>et al.</i>	Lancet Infect. Dis.	02/04	China	Cross-sectional	74	High	[53]
Tan, Y. P. <i>et al.</i>	J. Clin. Virol.	03/04	China	Case series	10	8	[54]
Chen, A. <i>et al.</i>	Radiol Cardiothorac Imaging	06/04	China	Case series	14	9	[55]
Han, Y-n. <i>et al.</i>	J. Med. Virol.	06/04	China	Case series	7	7	[56]
Bo, L. <i>et al.</i>	Indian Pediatr.	07/04	China	Cross-sectional	134	Moderate	[57]
Tagarro, A. <i>et al.</i>	JAMA Pediatr	08/04	Spain	Cross-sectional	41	High	[58]
Zhu, L. <i>et al.</i>	Pediatr. Pulmonol.	08/04	China	Case series	10	8	[59]
Hua, C-H. <i>et al.</i>	Lancet Infect. Dis.	09/04	China	Cross-sectional	43	High	[60]
Qiu, L. <i>et al.</i>	Lancet	09/04	China	Case series	25	9	[17]
Xie, M. <i>et al.</i>	Lancet	09/04	China	Case series	9	8	[61]
CDC COVID-19 Response Team <i>et al.</i>	Morbidity and Mortality Weekly Report	10/04	United States of America	-	2572	-	[62]
Chen, J. <i>et al.</i>	Genes & Diseases	14/04	China	Case series	12	9	[63]
Ma, H. <i>et al.</i>	Lancet Infect. Dis.	14/04	China	Cross-sectional	50	High	[64]
Du, W. <i>et al.</i>	Infection	16/04	China	Case series	14	9	[65]
Xia, W. <i>et al.</i>	Front. Pediatr.	16/04	China	Cross-sectional	114	High	[66]
Liu, S. <i>et al.</i>	Lancet Infect. Dis.	23/04	China	Cross-sectional	248	High	[67]
Xu, H. <i>et al.</i>	Ann. Transl. Med.	24/04	China	Cross-sectional	32	High	[68]

Most of the studies were classified as high quality. It is important to note, however, that the assessment of quality of studies is a subjective task because it is based on the personal judgments of the review authors.

**3.3. Meta-analysis results**

The meta-analysis results are summarized in Table 10 and in the forest plots (Supplementary Figure 1).

**3.3.1. Demographical characteristics and comorbidities**

The mean age of patients among the included studies was 6.5 years (95% CI: 4.2-8.9 years), 46.7% (95% CI: 43.5-49.9%) of the children being female. 10.0% (95% CI: 5.9-16.4%) of the patients presented comorbidities, with 7.6% (95% CI: 3.2-17.0%) of cases reporting congenital heart disease, 1.2%

Table 2. Demographical characteristics and comorbidities of the study subjects.

Author	Date (DD/MM)	N	Mean age (years)	SD	Median age (range)	Gender (female) N (%)	Comorbidities N (%)				Reference
							Number of comorbidities	Cancer	Congenital heart diseases	Asthma	
Ma, H. <i>et al.</i>	10/02	22	-	-	-	10 (45.5)	0	-	-	-	[29]
Wei, M. <i>et al.</i>	14/02	9	0.6	0.3	0.6 (0.2-0.8)	7 (77.8)	-	-	-	-	[30]
Kai, F. <i>et al.</i>	16/02	15	7.9	2.9	7.0 (4.0-14.0)	10 (66.7)	-	-	-	-	[31]
Wang, X. F. <i>et al.</i>	17/02	34	7.6	3.0	-	20 (58.8)	-	-	-	-	[32]
Liu, M. <i>et al.</i>	25/02	5	-	-	5.2 (0.6-13.0)	1 (20.0)	-	-	-	-	[33]
Xia, W. <i>et al.</i>	26/02	20	-	-	2.1 (0.0-14.6)	7 (35.0)	7 (35.0)	2 (10.0)	-	5 (25.0)	[34]
Zhou, Y. <i>et al.</i>	27/02	9	1.6	-	1.0 (0.5-3.0)	5 (55.6)	-	-	-	-	[35]
Cai, J. <i>et al.</i>	28/02	10	6.2	3.8	9.5 (0.3-11.0)	6 (60.0)	0	-	-	-	[36]
Wang, D. <i>et al.</i>	02/03	31	-	-	(0.5-17.0)	16 (51.6)	-	-	-	-	[37]
Chen, C. <i>et al.</i>	03/03	31	-	4.4	6.8 (1.5-17.0)	18 (58.1)	-	-	-	-	[38]
Yao-Ling, M. <i>et al.</i>	03/03	115	-	-	(0.1-15.0)	42 (36.5)	3 (2.6)	1 (0.9)	-	2 (1.7)	[39]
Hu, Z. <i>et al.</i>	04/03	6	9.7	-	9.0 (5.0-15.0)	3 (50.0)	-	-	-	-	[40]
Tang, A. <i>et al.</i>	10/03	26	6.9	0.7	(1.0-13.0)	9 (34.6)	-	-	-	-	[41]
Li, W. <i>et al.</i>	11/03	5	3.1	-	3.0 (0.8-6.0)	1 (20.0)	-	-	-	-	[42]
Xu, Y. <i>et al.</i>	13/03	10	7.5	5.9	6.6 (0.2-15.7)	4 (40.0)	-	-	-	-	[43]
Zhang, X. <i>et al.</i>	17/03	10	-	-	4.0	7 (70.0)	-	-	-	-	[44]
Lu, X. <i>et al.</i>	18/03	171	-	-	6.7 (0.0-15.0)	67 (39.2)	0	1 (12.5)	-	2 (1.2)	[45]
Yu, H. <i>et al.</i>	18/03	82	-	-	(0.0-16.0)	51 (62.2)	0	1 (0.6)	-	-	[46]
Sun, D. <i>et al.</i>	19/03	8	6.8	6.4	5.0 (0.2-15.0)	2 (25.0)	-	-	-	-	[47]
Wu, Q. <i>et al.</i>	23/03	74	-	-	6.0 (0.1-15.1)	30 (40.5)	0	-	-	-	[19]
Zheng, F. <i>et al.</i>	24/03	25	-	-	3.0 (0.3-14.0)	11 (44.0)	-	-	2 (8.0)	-	[48]
Qiu, H. <i>et al.</i>	25/03	36	8.3	3.5	(1.0-16.0)	13 (36.1)	-	-	-	-	[49]
Su, L. <i>et al.</i>	25/03	9	3.6	2.7	3.6 (0.9-9.0)	6 (66.7)	0	-	-	-	[50]
Chen, M. <i>et al.</i>	27/03	10	-	-	(2.0-15.0)	5 (50.0)	-	-	-	-	[51]
Liu, W. <i>et al.</i>	02/04	6	3.5	-	3.0 (1.0-7.0)	4 (66.7)	-	-	-	-	[52]
Wang, Y. <i>et al.</i>	02/04	74	-	-	5.8 (0.2-15.3)	36 (48.6)	14 (18.9)	-	-	-	[53]
Tan, Y. P. <i>et al.</i>	03/04	10	8.0	-	8.8 (1.1-12.1)	7 (70.0)	-	-	-	-	[54]
Chen, A. <i>et al.</i>	06/04	14	4.7	3.4	7.5 (0.2-10.0)	6 (42.3)	-	-	-	-	[55]



Table 3 continued...

Kai, F. <i>et al.</i>	16/02	15	0	8 (53.3)	5 (33.3)	1 (6.7)	-	1 (6.7)	-	-	-	-	-	-	-	-	-	-	-	[31]			
Wang, X. F. <i>et al.</i>	17/02	34	0	3 (8.8)	17 (50.0)	13 (38.2)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[32]		
Liu, M. <i>et al.</i>	25/02	5	0	3 (60.0)	2 (40.0)	2 (40.0)	-	-	-	-	-	-	-	-	-	-	-	-	1 (20.0)	-	[33]		
Xia, W. <i>et al.</i>	26/02	20	0	-	12 (60.0)	13 (65.0)	-	3 (15.0)	-	2 (10.0)	-	-	-	-	-	-	-	-	3 (15.0)	-	[34]		
Zhou, Y. <i>et al.</i>	27/02	9	0	5 (55.6)	4 (44.4)	2 (22.2)	-	1 (11.1)	-	0	-	-	-	-	-	-	-	-	0	-	[35]		
Cai, J. <i>et al.</i>	28/02	10	0	0	8 (80.0)	6 (60.0)	4 (40.0)	2 (20.0)	3 (30.0)	0	-	-	-	-	-	-	-	-	0	-	[36]		
Wang, D. <i>et al.</i>	02/03	31	0	4 (12.9)	20 (64.5)	14 (45.2)	2 (6.5)	-	2 (6.5)	0	-	-	-	-	-	-	-	-	3 (9.7)	-	[37]		
Chen, C. <i>et al.</i>	03/03	31	0	12 (38.7)	14 (45.2)	13 (41.9)	2 (6.5)	2 (6.5)	3 (9.7)	-	1 (3.2)	-	-	-	-	-	-	-	-	-	[38]		
Yao-Ling, M. <i>et al.</i>	03/03	115	0	61 (53.0)	29 (25.2)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[39]		
Hu, Z. <i>et al.</i>	04/03	6	0	5 (83.3)	1 (16.7)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[40]		
Tang, A. <i>et al.</i>	10/03	26	0	9 (35.0)	11 (42.0)	12 (46.0)	-	2 (8.0)	-	-	-	-	-	-	-	-	-	-	2 (8.0)	-	[41]		
Li, W. <i>et al.</i>	11/03	5	0	4 (80.0)	1 (20.0)	1 (20.0)	1 (20.0)	1 (20.0)	-	-	1 (20.0)	-	-	-	-	-	-	-	-	-	[42]		
Xu, Y. <i>et al.</i>	13/03	10	0	1 (10.0)	7 (70.0)	5 (50.0)	-	2 (20.0)	-	0	-	-	-	-	-	-	-	-	3 (30.0)	-	[43]		
Zhang, X. <i>et al.</i>	17/03	10	0	5 (50.0)	4 (40.0)	1 (10.0)	-	1 (10.0)	-	-	-	-	-	-	-	-	-	-	-	-	[44]		
Lu, X. <i>et al.</i>	18/03	171	0	39 (22.8)	71 (41.5)	83 (48.5)	79 (46.2)	13 (7.6)	9 (5.3)	49 (28.7)	-	-	-	-	-	-	-	-	11 (6.4)	15 (8.8)	[45]		
Yu, H. <i>et al.</i>	18/03	82	0	8 (9.8)	58 (70.7)	51 (62.2)	-	-	-	2 (2.4)	-	-	-	-	-	-	-	-	7 (8.5)	-	[46]		
Sun, D. <i>et al.</i>	19/03	8	0	0	6 (75.0)	6 (75.0)	-	-	-	8 (100.0)	-	-	-	-	-	-	-	-	1 (12.5)	4 (50.0)	3 (37.5)	1 (12.5)	[47]
Wu, Q. <i>et al.</i>	23/03	74	0	30 (40.5)	20 (27.0)	24 (32.4)	0	-	-	2 (2.7)	2 (2.7)	2 (2.7)	2 (2.7)	2 (2.7)	2 (2.7)	2 (2.7)	2 (2.7)	2 (2.7)	3 (4.1)	3 (4.1)	3 (4.1)	5 (6.8)	[19]
Zheng, F. <i>et al.</i>	24/03	25	-	-	13 (52.0)	11 (44.0)	-	-	-	2 (8.0)	2 (8.0)	2 (8.0)	2 (8.0)	2 (8.0)	2 (8.0)	2 (8.0)	2 (8.0)	2 (8.0)	4 (16.0)	3 (12.0)	-	-	[48]
Su, L. <i>et al.</i>	25/03	9	0	6 (67.0)	2 (22.0)	1 (11.0)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[50]
Qiu, H. <i>et al.</i>	25/03	36	0	10 (27.8)	13 (36.1)	7 (19.4)	1 (2.8)	-	-	1 (2.8)	-	-	-	-	-	-	-	-	3 (8.3)	2 (5.6)	-	-	[49]
Chen, M. <i>et al.</i>	27/03	10	0	4 (40.0)	4 (40.0)	5 (50.0)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[51]
Liu, W. <i>et al.</i>	02/04	6	0	0	6 (100.0)	6 (100.0)	-	-	-	-	-	-	-	-	-	-	-	-	-	4 (67.0)	-	-	[52]
Wang, Y. <i>et al.</i>	02/04	74	0	18 (24.3)	35 (47.3)	41 (55.4)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[53]
Tan, Y. P. <i>et al.</i>	03/04	10	0	3 (30.0)	4 (40.0)	3 (30.0)	-	-	-	-	-	-	-	-	-	-	-	-	-	2 (20.0)	-	-	[54]
Chen, A. <i>et al.</i>	06/04	14	0	1 (7.1)	6 (42.9)	6 (42.9)	-	2 (14.3)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[55]
Han, Y-n <i>et al.</i>	06/04	7	0	0	5 (71.4)	5 (71.4)	1 (14.3)	-	-	3 (42.9)	-	-	-	-	-	-	-	-	-	4 (57.1)	-	-	[56]



Table 3 continued...

Bo, L. <i>et al.</i>	07/04	22	0	2 (9.1)	14 (63.6)	13 (59.1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[57]	
Zhu, L. <i>et al.</i>	08/04	10	0	4 (40.0)	4 (40.0)	3 (30.0)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	[59]	
Hua, C-H <i>et al.</i>	09/04	43	0	10 (23.3)	21 (48.8)	12 (27.9)	-	7 (16.3)	-	1 (2.3)	-	1 (2.3)	2 (4.7)	3 (7.0)	3 (7.0)	-	-	-	-	-	-	-	[60]	
Qiu, L. <i>et al.</i>	09/04	25	0	0	21 (84.0)	17 (68.0)	2 (8.0)	4 (16.0)	-	0	16 (64.0)	0	4 (16.0)	6 (24.0)	0	0	-	-	-	-	-	-	[17]	
Xie, M. <i>et al.</i>	09/04	9	0	7 (77.8)	1 (11.1)	1 (11.1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[61]	
CDC COVID-19 Response Team <i>et al.</i>	10/04	257	2281	1 (0.3)	163 (56.0)	158 (54.3)	71 (24.4)	21 (7.2)	-	39 (13.4)	-	81 (27.8)	48 (16.5)	37 (12.7)	-	66 (22.7)	-	-	-	-	-	-	-	[62]
Chen, J. <i>et al.</i>	14/04	12	0	2 (16.7)	7 (58.3)	9 (75.0)	2 (16.7)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[63]	
Mia, H. <i>et al.</i>	14/04	50	0	6 (12.0)	32 (64.0)	22 (44.0)	1 (2.0)	8 (16.0)	-	-	-	-	2 (4.0)	3 (6.0)	2 (4.0)	2 (4.0)	2 (4.0)	2 (4.0)	2 (4.0)	2 (4.0)	2 (4.0)	2 (4.0)	[64]	
Xia, W. <i>et al.</i>	16/04	114	0	23 (20.2)	62 (54.4)	61 (53.5)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[66]	
Du, W. <i>et al.</i>	16/04	14	0	8 (57.1)	5 (35.7)	3 (21.4)	1 (7.1)	-	-	0	1 (7.1)	1 (7.1)	0	0	0	2 (14.3)	0	0	0	0	0	0	[65]	
Liu, S. <i>et al.</i>	23/04	248	0	92 (37.1)	93 (37.5)	84 (33.9)	3 (1.2)	-	-	4 (1.6)	79 (31.9)	1 (0.4)	6 (2.4)	6 (2.4)	4 (1.6)	4 (1.6)	4 (1.6)	4 (1.6)	4 (1.6)	4 (1.6)	4 (1.6)	4 (1.6)	[67]	
Xu, H. <i>et al.</i>	24/04	32	0	0	14 (43.8)	18 (56.3)	3 (9.4)	5 (15.6)	3 (9.4)	-	-	2 (6.3)	-	-	-	2 (6.3)	-	-	-	-	-	-	[68]	

NA - Not available.

Table 4. Summary of the laboratory findings.

Author	Date (DD/MM)	N	NA	Laboratory findings N (%)													Reference						
				Leukocytosis	Leukopenia	Lymphocytosis	Lymphopenia	Neutrophilia	Neutropenia	High hemoglobin	Low hemoglobin	High platelets	Low platelets	High creatinine	High CK-MB	High LDH		High ALT	High AST	High ESR	High CRP	High PCT	High D-dimer
Kai, F. <i>et al.</i>	16/02	15	0	0	8 (53.3)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[31]
Wang, X. F. <i>et al.</i>	17/02	34	0	5 (14.7)	0	0	1 (2.9)	-	-	-	-	-	-	-	-	-	-	5 (14.7)	1 (2.9)	-	-	-	[32]



Table 4 continued...

Qiu, H. <i>et al.</i>	25/03	36	0	7 (19.4)	0	0	0	11(30.6)	-	-	-	-	-	-	-	0	11 (30.6)	-	2 (5.6)	3 (8.3)	0	1 (2.8)	6 (16.7)	3 (8.3)	[49]
Su, L. <i>et al.</i>	25/03	9	0	1 (11.1)	1 (11.1)	-	-	-	-	-	-	-	-	-	-	6 (66.7)	6 (66.7)	-	6 (66.7)	6 (66.7)	-	-	-	-	[50]
Chen, M. <i>et al.</i>	27/03	10	0	-	4 (40.0)	8 (80.0)	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (10.0)	0	-	[51]
Liu, W. <i>et al.</i>	02/04	6	0	0	4 (66.7)	0	6 (100.0)	3 (50.0)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[52]
Wang, Y. <i>et al.</i>	02/04	74	0	7 (9.5)	4 (5.4)	25 (33.8)	-	6 (8.1)	5 (6.8)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[53]
Tan, Y. P. <i>et al.</i>	03/04	10	0	1 (10.0)	0	1 (10.0)	0	-	-	-	-	-	-	-	-	-	3 (30.0)	1 (10.0)	0	3 (30.0)	-	1 (10.0)	-	-	[54]
Chen, A. <i>et al.</i>	06/04	14	0	1 (7.1)	4 (28.6)	0	3 (21.4)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3 (21.4)	-	-	[55]
Han, Y-n. <i>et al.</i>	06/04	7	0	2 (28.6)	0	0	7 (100.0)	1 (14.3)	0 (0)	-	-	-	1 (14.3)	0 (0)	3 (42.9)	2 (28.6)	4 (57.1)	2 (28.6)	1 (14.3)	3 (42.9)	3 (42.9)	2 (28.6)	3 (42.9)	2 (28.6)	[56]
Zhu, L. <i>et al.</i>	08/04	10	0	-	4 (40.0)	0	0	-	-	-	-	-	-	-	-	-	-	-	2 (20.0)	-	-	0	0	-	[59]
Hua, C-H. <i>et al.</i>	09/04	43	0	-	5 (11.6)	-	3 (7.0)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[60]
Qiu, L. <i>et al.</i>	09/04	25	0	4 (16.0)	0	5 (31.3)	0	3 (12.0)	0 (0)	-	-	3 (12.0)	1 (4.0)	0 (0)	24 (96.0)	4 (16.0)	17 (68.0)	8 (32.0)	4 (16.0)	17 (68.0)	8 (32.0)	17 (68.0)	0	8 (32.0)	[17]
Xie, M. <i>et al.</i>	09/04	9	0	-	-	-	-	1 (11.1)	-	-	-	1 (11.1)	1 (11.1)	-	-	-	-	-	-	-	-	3 (33.3)	-	-	[61]
Chen, J. <i>et al.</i>	14/04	12	0	-	-	0	2 (16.7)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	[63]
Ma, H. <i>et al.</i>	14/04	50	0	-	-	-	-	10 (20.0)	6 (12.0)	2 (4.0)	7 (14.0)	-	-	-	-	-	-	-	-	-	-	-	-	-	[64]
Du, W. <i>et al.</i>	16/04	14	0	-	4 (28.6)	-	1 (7.1)	-	-	-	2 (14.3)	-	-	-	7 (50)	1 (7.1)	1 (7.1)	-	1 (7.1)	1 (7.1)	-	1 (7.1)	5 (35.7)	-	[65]

Table 4 continued...

Xu, H. <i>et al.</i>	24/04	32	0	2 (6.3)	1 (3.1)	<sup>9</sup> (28.1)	2 (6.3)	<sup>8</sup> (25.0)	0	-	-	-	-	11 (34.4)	<sup>6</sup> (18.9)	1 (3.1)	-	3 (9.4)	-	<sup>6</sup> (18.8)	[68]
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NA - Not available; CK-MB - creatine kinase; LDH - lactate dehydrogenase; ALT - alanine transaminase; AST - aspartate transaminase; ESR - erythrocyte sedimentation rate; CRP - C-reactive protein; PCT - procalcitonin.

Table 5. Summary of the radiologic findings.

Author	Date (DD/MM)	N	NA	Radiologic findings N (%)										Reference	
				Normal	Anormal	Unilateral	Bilateral	GGO	Fine mesh shadows	Consolidation	Pleural effusion				
Kai, F. <i>et al.</i>	16/02	15	0	6 (40.0)	9 (60.0)	-	-	-	-	7 (46.7)	2 (13.3)	-	-	0	[31]
Wang, X. F. <i>et al.</i>	17/02	34	0	0	34 (100.0)	0	34 (100)	-	-	34 (100)	-	-	-	-	[32]
Liu, M. <i>et al.</i>	25/02	5	0	1 (20.0)	4 (80.0)	3 (60.0)	1 (20.0)	4 (80.0)	0	4 (80.0)	0	1 (20.0)	0	[33]	
Xia, W. <i>et al.</i>	26/02	20	0	4 (20.0)	16 (80.0)	6 (30.0)	10 (50.0)	12 (60.0)	4 (20.0)	10 (50.0)	10 (50.0)	0	-	[34]	
Zhou, Y. <i>et al.</i>	27/02	9	0	1 (11.1)	8 (88.9)	-	-	7 (77.8)	7 (77.8)	3 (33.3)	1 (11.1)	-	-	[35]	
Cai, J. <i>et al.</i>	28/02	10	6	0	4 (100.0)	4 (100.0)	0	4 (100.0)	-	-	-	-	-	[36]	
Wang, D. <i>et al.</i>	02/03	31	1	16 (53.3)	14 (46.7)	-	-	9 (30.0)	-	-	-	-	0	[37]	
Chen, C. <i>et al.</i>	03/03	31	0	19 (61.3)	12 (38.7)	8 (25.8)	4 (12.9)	-	-	-	-	-	-	[38]	
Yao-Ling, M. <i>et al.</i>	03/03	115	0	27 (23.5)	88 (76.5)	-	-	-	-	-	-	-	-	[39]	
Hu, Z. <i>et al.</i>	04/03	6	0	3 (50.0)	3 (50.0)	-	-	3 (50.0)	-	-	-	-	-	[40]	
Tang, A. <i>et al.</i>	10/03	26	0	8 (30.8)	18 (69.2)	11 (42.3)	7 (26.9)	-	-	-	-	-	-	[41]	
Li, W. <i>et al.</i>	11/03	5	0	2 (40.0)	3 (60.0)	3 (60.0)	0	3 (60.0)	-	-	-	-	-	[42]	
Xu, Y. <i>et al.</i>	13/03	10	0	1 (10.0)	9 (90.0)	-	-	5 (50.0)	-	-	-	-	-	[43]	
Zhang, X. <i>et al.</i>	17/03	10	0	1 (10.0)	9 (90.0)	-	-	-	-	-	-	-	-	[44]	
Lu, X. <i>et al.</i>	18/03	171	0	-	-	-	-	56 (32.7)	53 (31.0)	-	-	-	-	[45]	
Yu, H. <i>et al.</i>	18/03	82	0	2 (2.4)	-	38 (46.3)	30 (36.6)	18 (22.0)	-	-	3 (3.7)	1 (1.2)	-	[46]	
Sun, D. <i>et al.</i>	19/03	8	0	0	8 (100.0)	2 (25.0)	6 (75.0)	6 (75.0)	7 (87.5)	-	-	-	1 (12.5)	[47]	
Wu, Q. <i>et al.</i>	23/03	74	0	37 (50.0)	37 (50.0)	21 (28.4)	16 (21.6)	9 (12.2)	-	-	-	-	-	[19]	
Zheng, F. <i>et al.</i>	24/03	25	1	8 (33.3)	16 (66.7)	5 (31.3)	6 (37.5)	-	-	-	-	-	-	[48]	
Qiu, H. <i>et al.</i>	25/03	36	0	17 (47.2)	19 (52.7)	-	-	19 (52.7)	-	-	-	-	-	[49]	
Su, L. <i>et al.</i>	25/03	9	0	5 (55.6)	4 (44.4)	1 (11.1)	-	1 (11.1)	-	-	-	-	-	[50]	

Table 5 continued...

Chen, M. <i>et al.</i>	27/03	10	0	2 (20.0)	8 (80.0)	6 (60.0)	2 (20.0)	3 (30.0)	5 (50.0)	1 (10.0)	-	[51]
Liu, W. <i>et al.</i>	02/04	6	1	1 (20.0)	4 (80.0)	0	4 (80.0)	1 (20.0)	3 (60.0)	-	-	[52]
Wang, Y. <i>et al.</i>	02/04	74	0	34 (45.9)	40 (54.1)	26 (35.1)	14 (18.1)	26 (35.1)	-	14 (18.9)	-	[53]
Tan, Y. P. <i>et al.</i>	03/04	10	0	5 (50.0)	5 (50.0)	-	-	4 (40.0)	1 (10.0)	-	-	[54]
Chen, A. <i>et al.</i>	06/04	14	0	7 (50.0)	7 (50.0)	3 (21.4)	4 (28.6)	4 (28.6)	0	1 (7.1)	0	[55]
Han, Y-n. <i>et al.</i>	06/04	7	0	2 (28.6)	5 (71.4)	-	-	-	-	-	-	[56]
Bo, L. <i>et al.</i>	07/04	22	0	2 (9.1)	20 (90.9)	5 (22.7)	15 (68.2)	13 (59.1)	-	15 (68.2)	-	[57]
Zhu, L. <i>et al.</i>	08/04	10	0	5 (50.0)	5 (50.0)	3 (30.0)	2 (20.0)	-	-	-	-	[59]
Hua, C-H. <i>et al.</i>	09/04	43	7	7 (19.4)	29 (80.6)	16 (44.4)	4 (11.1)	9 (25.0)	-	-	-	[60]
Qiu, L. <i>et al.</i>	09/04	25	0	3 (12.0)	22 (88.0)	11 (44.0)	11 (44.0)	1 (4.0)	22 (88.0)	-	-	[17]
Xie, M. <i>et al.</i>	09/04	9	0	6 (66.7)	3 (33.3)	-	-	-	-	-	-	[61]
Ma, H. <i>et al.</i>	14/04	50	0	7 (14.0)	43 (86.0)	-	-	29 (58.0)	25 (50.0)	-	1 (2.0)	[64]
Chen, J. <i>et al.</i>	14/04	12	0	2 (16.7)	10 (83.3)	-	-	-	-	-	-	[63]
Du, W. <i>et al.</i>	16/04	14	0	3 (21.4)	11 (78.6)	5 (35.7)	6 (42.9)	-	-	-	-	[65]
Xia, W. <i>et al.</i>	16/04	114	0	32 (28.1)	82 (71.9)	46 (20.4)	36 (31.6)	46 (40.4)	46 (40.4)	-	-	[66]
Xu, H. <i>et al.</i>	24/04	32	0	6 (18.8)	19 (59.4)	8 (25.0)	3 (9.4)	8 (25.0)	-	-	-	[68]

NA - Not available; GGO - Ground glass opacities.

Table 6. Complications.

Author	Date (DD/MM)	N	Complications N (%)								Reference	
			Acute respiratory distress syndrome	Acute cardiac injury	Acute kidney injury	Secondary infection	Septic shock	DIC or coagulopathy	MODS	Others		
Xia, W. <i>et al.</i>	26/02	20	-	-	-	8 (40.0)	-	-	-	-	-	[34]
Wang, D. <i>et al.</i>	02/03	31	-	-	-	-	-	-	-	-	1 (3.2)	[37]
Yao-Ling, M. <i>et al.</i>	03/03	115	-	-	-	7 (15.6)	-	-	-	-	-	[39]
Lu, X. <i>et al.</i>	18/03	171	-	-	-	-	-	-	-	1 (0.6)	-	[45]
Yu, H. <i>et al.</i>	18/03	82	1 (1.2)	1 (1.2)	-	27 (32.9)	2 (2.44)	2 (2.44)	-	2 (2.44)	1 (1.2)	[46]
Sun, D. <i>et al.</i>	19/03	8	-	1 (12.5)	1 (12.5)	-	2 (25.0)	2 (25.0)	2 (25.0)	2 (25.0)	3 (37.5)	[47]

Table 6 continued...

Wu, Q. <i>et al.</i>	23/03	74	-	-	-	-	19 (25.7)	-	-	-	-	-	-	-	-	[19]
Zheng, F. <i>et al.</i>	24/03	25	2 (8.0)	-	-	-	5 (20.0)	-	-	-	-	-	-	-	-	[48]
Chen, M. <i>et al.</i>	27/03	10	-	-	-	-	-	-	-	-	-	-	-	1 (10.0)	-	[51]
Wang, Y. <i>et al.</i>	02/04	74	-	-	-	-	31 (41.9)	-	-	-	-	-	-	-	-	[53]
Tan, Y. P. <i>et al.</i>	03/04	10	-	-	-	-	4 (40.0)	-	-	-	-	-	-	-	-	[54]
Tagarro, A. <i>et al.</i>	08/04	41	-	-	-	-	-	2 (4.9)	-	-	-	-	-	-	-	[58]
Qiu, L. <i>et al.</i>	09/04	25	-	10 (40.0)	-	-	18 (72.0)	1 (4.0)	4 (16.0)	-	-	-	-	19 (76.0)	-	[17]
Ma, H. <i>et al.</i>	14/04	50	-	5 (10.0)	1 (2.0)	-	6 (12.0)	-	-	-	1 (2.0)	-	-	3 (6.0)	-	[64]
Xia, W. <i>et al.</i>	16/04	114	-	-	-	-	34 (29.8)	-	-	-	-	-	-	-	-	[66]
Liu, S. <i>et al.</i>	23/04	248	-	-	-	-	25 (10.1)	-	-	-	-	-	-	-	-	[67]

DIC- Disseminated intravascular coagulation; MODS - Multi-organ dysfunction syndrome.

Table 7. Secondary infections.

Author	Date (DD/MM)	N	NA	Secondary infections N (%)										Reference		
				Respiratory virus	Cytomegalovirus	Epstein-Barr virus	Influenza virus	Parainfluenza	Coxsackie	Adenovirus	Mycoplasma	Other bacteria				
Xia, W. <i>et al.</i>	26/02	20	0	1 (5.0)	1 (5.0)	-	3 (15.0)	-	-	-	-	-	4 (20.0)	-	-	[34]
Yao-Ling, M. <i>et al.</i>	03/03	115	70	-	-	-	-	2 (4.4)	-	-	1 (2.2)	4 (8.9)	-	-	-	[39]
Yu, H. <i>et al.</i>	18/03	82	0	3 (8.8)	2 (2.4)	2 (2.4)	1 (1.2)	-	-	-	1 (1.2)	17 (42.5)	1 (1.2)	-	-	[46]
Wu, Q. <i>et al.</i>	23/03	74	40	3 (8.8)	3 (8.8)	3 (8.8)	1 (3.0)	-	-	-	-	16 (40.0)	-	-	-	[19]
Zheng, F. <i>et al.</i>	24/03	25	0	-	-	-	2 (8.0)	-	-	-	-	3 (12.0)	1 (4.0)	-	-	[48]
Wang, Y. <i>et al.</i>	02/04	74	0	-	1 (1.4)	2 (2.7)	0	-	-	-	-	28 (37.8)	-	-	-	[53]
Tan, Y. P. <i>et al.</i>	03/04	10	0	0	-	-	0	-	-	-	0	3 (30.0)	1 (10.0)	-	-	[54]
Tagarro, A. <i>et al.</i>	08/04	41	0	-	-	-	2 (4.9)	-	-	-	-	-	-	-	-	[58]
Qiu, L. <i>et al.</i> *	09/04	25	0	2 (8.0)	-	3 (12.0)	9 (36.0)	1 (4.0)	3 (12.0)	2 (8.0)	9 (36.0)	1 (4.0)	-	-	-	[17]
Ma, H. <i>et al.</i>	14/04	50	0	1 (2.0)	-	-	-	-	-	-	-	5 (10.0)	-	-	-	[64]
Xia, W. <i>et al.</i>	16/04	114	0	-	-	-	-	-	-	-	-	29 (25.4)	-	-	-	[66]
Liu, S. <i>et al.</i>	23/04	248	0	0	-	-	1 (0.4)	-	-	-	0	24 (9.7)	-	-	-	[67]

NA - not available. \*There are children with more than one secondary infection.

**Table 8.** Exposure setting.

Author	Date (DD/MM)	N	NA	Exposure setting N (%)				Reference
				Household	Epidemic area	Contact with index case directly	Others	
Ma, H. <i>et al.</i>	10/02	22	5	-	-	17 (100.0)	-	[29]
Wei, M. <i>et al.</i>	14/02	9	0	9 (100.0)	7 (77.8)	9 (100.0)	-	[30]
Kai, F. <i>et al.</i>	16/02	15	0	-	3 (20.0)	12 (80.0)	-	[31]
Xia, W. <i>et al.</i>	26/02	20	0	13 (65.0)	-	13 (65.0)	7 (35.0)	[34]
Zhou, Y. <i>et al.</i>	27/02	9	0	9 (100.0)	3 (33.3)	9 (100.0)	-	[35]
Cai, J. <i>et al.</i>	28/02	10	0	7 (70.0)	2 (20.0)	8 (80.0)	1 (10.0)	[36]
Wang, D. <i>et al.</i>	02/03	31	0	28 (90.3)	9 (29.0)	21 (67.7)	-	[37]
Chen, C. <i>et al.</i>	03/03	31	0	29 (93.5)	0	-	1 (3.2)	[38]
Yao-Ling, M. <i>et al.</i>	03/03	115	0	105 (91.3)	115 (100.0)	-	-	[39]
Hu, Z. <i>et al.</i>	04/03	6	0	-	3 (50.0)	6 (100.0)	-	[40]
Li, W. <i>et al.</i>	11/03	5	0	4 (80.0)	1 (20.0)	-	-	[42]
Xu, Y. <i>et al.</i>	13/03	10	0	7 (70.0)	7 (70.0)	4 (40.0)	-	[43]
Zhang, X. <i>et al.</i>	17/03	10	0	10 (100.0)	-	-	-	[44]
Lu, X. <i>et al.</i>	18/03	171	0	154 (90.1)	-	133 (77.8)	15 (8.8)	[45]
Yu, H. <i>et al.</i>	18/03	82	0	-	82 (100.0)	-	-	[46]
Sun, D. <i>et al.</i>	19/03	8	0	5 (62.5)	8 (100.0)	5 (62.5)	-	[47]
Wu, Q. <i>et al.</i>	23/03	74	6	65 (95.6)	-	-	3 (4.1)	[19]
Zheng, F. <i>et al.</i>	24/03	25	4	16 (76.2)	5 (23.8)	16 (76.2)	-	[48]
Qiu, H. <i>et al.</i>	25/03	36	0	32 (88.9)	12 (33.3)	32 (88.9)	-	[49]
Su, L. <i>et al.</i>	25/03	9	0	9 (100.0)	6 (66.7)	9 (100.0)	2 (22.2)	[50]
Chen, M. <i>et al.</i>	27/03	10	0	6 (60.0)	3 (30.0)	6 (60.0)	1 (10.0)	[51]
Liu, W. <i>et al.</i>	02/04	6	0	-	5 (83.3)	-	1 (16.7)	[52]
Wang, Y. <i>et al.</i>	02/04	74	0	74 (100.0)	-	74 (100.0)	-	[53]
Wang, X. F. <i>et al.</i>	12/02	34	0	28 (82.4)	26 (76.5)	-	-	[32]
Tan, Y. P. <i>et al.</i>	03/04	10	0	10 (100.0)	4 (10.0)	10 (100.0)	-	[54]
Chen, A. <i>et al.</i>	06/04	14	-	-	10 (71.4)	4 (28.6)	-	[55]
Han, Y.-n. <i>et al.</i>	06/04	7	0	-	-	7 (100.0)	-	[56]
Tagarro, A. <i>et al.</i>	08/04	41	0	-	-	16 (39.0)	25 (61.0)	[58]
Zhu, L. <i>et al.</i>	08/04	10	0	7 (70.0)	3 (30.0)	7 (70.0)	-	[59]
Hua, C-H. <i>et al.</i>	09/04	43	0	40 (93.0)	20 (46.5)	-	3 (7.0)	[60]
Qiu, L. <i>et al.</i>	09/04	25	0	3 (12.0)	2 (8.0)	-	20 (80.0)	[17]
Xie, M. <i>et al.</i>	09/04	9	0	8 (88.9)	9 (100.0)	-	-	[61]
CDC COVID-19 Response Team <i>et al.</i>	10/04	2572	2388	-	16 (8.7)	168 (91.3)	-	[62]
Chen, J. <i>et al.</i>	14/04	12	0	-	4 (33.3)	8 (67.7)	-	[63]
Ma, H. <i>et al.</i>	14/04	50	0	40 (80.0)	1 (2.0)	-	9 (18.0)	[64]

Table 8 continued...

Du, W. <i>et al.</i>	16/04	14	0	14 (100.0)	0	-	-	[65]
Liu, S. <i>et al.</i>	23/04	248	0	-	240 (97.2)	-	8 (2.8)	[67]
Xu, H. <i>et al.</i>	24/04	32	0	29 (90.6)	12 (37.5)	-	-	[68]

NA - not available.

Table 9. Outcomes.

Author	Date (DD/MM)	N	NA	Outcomes N (%)				Reference
				Hospitalization	ICU	Mean hospitalization (range) days	Discharge	
Ma, H. <i>et al.</i>	10/02	22	0	17 (77.3)	-	-	5 (22.7)	[29]
Wei, M. <i>et al.</i>	14/02	9	0	9 (100.0)	0	-	-	[30]
Kai, F. <i>et al.</i>	16/02	15	0	15 (100.0)	-	12.0 (7.0-17.0)	5 (33.3)	[31]
Xie, M. <i>et al.</i>	09/04	9	0	9 (100.0)	-	11.6 (6.0-18.0)	9 (100.0)	[61]
Liu, M. <i>et al.</i>	25/02	5	0	5 (100.0)	-	9.8 (4.0-14.0)	5 (100.0)	[33]
Xia, W. <i>et al.</i>	26/02	20	0	20 (100.0)	-	12.9 (8.0-20.0)	18 (90.0)	[34]
Zhou, Y. <i>et al.</i>	27/02	9	0	9 (100.0)	0	-	-	[35]
Cai, J. <i>et al.</i>	28/02	10	0	10 (100.0)	-	-	10 (100.0)	[36]
Wang, D. <i>et al.</i>	02/03	31	0	31 (100.0)	-	-	24 (77.4)	[37]
Chen, C. <i>et al.</i>	03/03	31	0	31 (100.0)	-	-	23 (74.2)	[38]
Yao-Ling, M. <i>et al.</i>	03/03	115	0	115 (100.0)	2 (1.7)	-	-	[39]
Hu, Z. <i>et al.</i>	04/03	6	0	6 (100.0)	0	6.0 (5.0-7.0)	3 (50.0)	[40]
Tang, A. <i>et al.</i>	10/03	26	0	26 (100.0)	-	13.6	17 (65.4)	[41]
Li, W. <i>et al.</i>	11/03	5	0	5 (100.0)	-	13.0 (12.0-14.0)	3 (60.0)	[42]
Xu, Y. <i>et al.</i>	13/03	10	0	10 (100.0)	0	-	4 (40.0)	[43]
Zhang, X. <i>et al.</i>	17/03	10	0	10 (100.0)	-	-	-	[44]
Lu, X. <i>et al.</i>	18/03	171	0	171 (100.0)	3 (1.8)	-	149 (87.1)	[45]
Yu, H. <i>et al.</i>	18/03	82	0	82 (100.0)	8 (9.8)	11.2	60 (73.2)	[46]
Sun, D. <i>et al.</i>	19/03	8	0	8 (100.0)	8 (100.0)	18.2 (12.0-24.0)	5 (62.5)	[47]
Wu, Q. <i>et al.</i>	23/03	74	0	74 (100.0)	-	-	74 (100.0)	[19]
Zheng, F. <i>et al.</i>	24/03	25	0	25 (100.0)	2 (8.0)	-	1 (4.0)	[48]
Qiu, H. <i>et al.</i>	25/03	36	0	36 (100.0)	-	14.0	36 (100.0)	[49]
Su, L. <i>et al.</i>	25/03	9	0	9 (100.0)	0	-	9 (100.0)	[50]
Chen, M. <i>et al.</i>	27/03	10	0	10 (100.0)	0	18.0 (7.0-26.0)	10 (100.0)	[51]
Liu, W. <i>et al.</i>	02/04	6	0	6 (100.0)	1 (16.7)	7.5 (5.0-13.0)	6 (100.0)	[52]
Wang, Y. <i>et al.</i>	02/04	74	0	74 (100.0)	1 (1.4)	10.0	66 (89.2)	[53]
Wang, X. F. <i>et al.</i>	17/02	34	0	34 (100.0)	-	-	34 (100.0)	[32]
Tan, Y. P. <i>et al.</i>	03/04	10	0	10 (100.0)	-	17.2 (11.0-25.0)	10 (100.0)	[54]
Han, Y-n. <i>et al.</i>	06/04	7	0	7 (100.0)	-	-	7 (100.0)	[56]
Bo, L. <i>et al.</i>	07/04	22	0	22 (100.0)	-	-	-	[57]



Table 9 continued...

Tagarro, A. <i>et al.</i>	08/04	41	0	25 (60.0)	4 (9.7)	--	-	[58]
Zhu, L. <i>et al.</i>	08/04	10	0	10 (100.0)	-	-	7 (70.0)	[59]
Hua, C-H. <i>et al.</i>	09/04	43	0	43 (100.0)	-	20.2 (3.0-32.0)	43 (100.0)	[60]
Qiu, L. <i>et al.</i>	09/04	25	0	25 (100.0)	0	14.9 (8.0-25.0)	25 (100.0)	[17]
CDC COVID-19 Response Team <i>et al.</i>	10/04	2572	1827	147 (19.7)	15 (2.0)	-	-	[62]
Chen, J. <i>et al.</i>	14/04	12	0	12 (100.0)	-	-	-	[63]
Ma, H. <i>et al.</i>	14/04	50	0	50 (100.0)	-	11.8 (8.2-13.8)	38 (76.0)	[64]
Du, W. <i>et al.</i>	16/04	14	0	14 (100.0)	-	-	-	[65]
Xia, W. <i>et al.</i>	16/04	114	0	114 (100.0)	-	-	114 (100.0)	[66]
Liu, S. <i>et al.</i>	23/04	248	0	248 (100.0)	-	-	-	[67]
Xu, H. <i>et al.</i>	24/04	32	0	32 (100.0)	0	-	32 (100.0)	[68]

NA - Not available; ICU - intensive care unit.

Table 10. Meta-analysis results (see also the respective forest plots in Supplementary Figure 1).

Variables	Number of studies	Mean/Prevalence	95% CI	n	Q	I <sup>2</sup>	tau <sup>2</sup>	P-value
Age	14	6.5	4.2-8.9	292	1968.2	99.34	16.6	<0.001
Gender (Female)	42	46.7	43.5-49.9	3984	64.0	35.96	0.04	0.012
<b>Comorbidities</b>								
Any comorbidity	15	10.0	5.9-16.4	1042	63.21	77.9	0.76	<0.001
Congenital heart diseases	3	7.6	3.2-17.0	70	0.612	0	0	0.736
Cancer	4	1.2	0.5-3.3	393	2.08	0	0	0.556
Asthma	2	10.3	5.3-19.0	370	1.23	18.62	0.12	0.268
<b>Clinical features</b>								
No symptoms/None	36	29.7	23.3-35.5	1389	137.2	74.5	0.45	<0.001
Fever	41	48.6	43.5-53.7	1754	123.1	67.5	0.22	<0.001
Cough	39	44.2	39.1-49.3	1633	107.1	64.5	0.20	<0.001
Pharyngitis or sore throat	16	9.6	5.1-17.3	1047	113.2	86.8	1.28	<0.001
Rhinorrhea	16	10.6	8.5-13.1	756	13.2	0	0	0.585
Nasal congestion	7	8.5	5.3-13.3	315	7.39	18.8	0.09	0.286
Tachypnea or dyspnea	18	7.2	3.8-13.3	1114	92.1	81.5	1.24	<0.001
Expectoration	8	19.3	10.1-33.9	480	37.2	81.2	0.74	<0.001
Headache or dizziness	13	6.7	3.1-14.0	855	59.46	79.8	1.53	<0.001
Nausea/abdominal pain or vomiting	18	10.1	6.5-15.3	1106	56.4	69.9	0.60	<0.001
Diarrhea	20	12.1	8.4-17.1	1137	51.9	63.4	0.43	<0.001
Anorexia	5	2.7	1.4-4.9	411	2.0	0	0	0.736
Fatigue or myalgia	18	7.7	4.7-12.4	1092	61.3	72.3	0.72	<0.001

Table 10 continued...

Clustering of the symptoms								
1	21	32.0	26.6-37.9	328	21.3	6.28	0.02	0.371
≥2	21	35.6	25.6-47.1	328	52.8	62.1	0.64	<0.001
Radiologic findings								
Anormal	35	66.4	60.2-72.1	930	87.0	60.9	0.31	<0.001
Unilateral	23	34.2	29.3-39.3	693	32.2	31.6	0.08	0.074
Bilateral	22	30.5	23.1-39.2	684	71.3	70.5	0.48	<0.001
GGO	27	39.0	31.7-46.7	925	90.8	71.4	0.40	<0.001
Fine mesh shadows	13	41.4	29.1-54.8	457	48.1	79.0	0.53	<0.001
Consolidation	8	22.4	9.7-43.8	236	40.9	82.9	1.55	<0.001
Pleural effusion	8	3.9	1.7-8.4	214	5.14	0	0	0.643
Laboratory findings								
Leukocytosis	22	14.5	10.7-19.3	673	37.9	44.6	0.25	0.013
Leukopenia	30	16.8	11.3-24.3	799	103.5	72.0	0.99	<0.001
Neutrophilia	11	17.1	10.0-27.7	399	36.2	72.5	0.58	<0.001
Neutropenia	11	14.5	7.1-27.3	399	44.1	77.3	1.18	<0.001
Lymphocytosis	26	25.5	17.3-35.9	725	117.3	78.7	0.97	<0.001
Lymphopenia	26	13.8	9.1-20.3	698	68.9	63.7	0.71	<0.001
Low hemoglobin	6	11.1	5.6-20.6	205	9.79	48.9	0.40	0.081
High hemoglobin	5	20.7	15.0-27.8	158	1.6	0	0	0.809
High platelets	7	11.5	7.5-17.2	197	4.87	0	0	0.521
Low platelets	6	4.9	1.8-12.7	205	8.3	39.8	0.63	0.14
High CRP	21	21.0	14.4-29.5	188	58.4	65.7	0.63	<0.001
High PCT	14	19.7	9.6-36.1	367	70.5	81.6	1.78	<0.001
High ESR	9	27.9	17.9-40.7	203	18.0	55.5	0.38	0.001
High AST	14	24.5	15.1-37.2	309	43.7	70.2	0.81	<0.001
High ALT	16	15.7	10.7-22.3	317	28.6	47.5	0.32	0.018
High D-dimer	8	19.9	13.1-29.1	143	8.39	16.6	0.09	0.299
High LDH	16	33.9	23.8-45.8	363	49.6	69.8	0.64	<0.001
High Creatinine	7	7.2	3.5-14.1	289	9.8	38.6	0.35	0.135
High CK	7	45.8	31.0-61.4	207	18.4	67.4	0.44	0.005
Exposure setting								
Household	27	83.5	76.8-88.6	884	86.0	69.7	0.74	<0.001
Epidemic area	30	45.1	24.8-67.2	3490	563.5	94.9	5.82	<0.001
Contact with index case	23	75.5	65.8-83.1	743	90.0	75.6	0.79	<0.001
Complications								
Hospitalization	41	96.9	92.3-98.8	2235	471.5	91.5	7.65	<0.001
ICU	17	5.1	2.7-9.3	1377	43.1	62.9	0.89	<0.001
ARDS	2	3.6	0.6-19.8	107	2.4	59.2	1.13	0.118
Secondary infection	11	27.5	19.0-38.1	767	67.3	85.1	0.53	<0.001
- RSV	7	4.3	2.1-8.5	469	7.9	24.0	0.23	0.246
- Cytomegalovirus	4	4.2	1.8-9.2	210	3.7	18.8	0.15	0.296

Table 10 continued...

- Epstein-Barr virus	4	5.6	2.5-12.0	215	5.0	40.6	0.3	0.168
- Influenza virus	9	4.5	1.4-13.2	559	38.5	79.2	2.4	<0.001
- Mycoplasma	11	21.5	14.4-30.8	727	55.2	81.9	0.51	<0.001
- Other bacteria	3	1.3	0.4-4.1	241	0.45	0	0	0.799
Septic chock	4	6.0	2.0-16.5	156	0.07	50.6	0.66	0.108
MODS	4	3.8	0.6-15.0	311	11.3	73.3	2.09	0.01
<b>Outcomes</b>								
Deaths	3	0.4	0.2-1.0	1164	0.38	0	0	0.826

CI - confidence interval; GGO - Ground glass opacities; CRP - C-reactive protein; PCT - procalcitonin; ESR - erythrocyte sedimentation rate; AST - aspartate transaminase; ALT - alanine transaminase; LDH - lactate dehydrogenase; CK - creatine kinase; ICU - intensive care unit; RSV - respiratory syncytial virus; MODS - multi-organ dysfunction syndrome.

**Table 11.** Case reports included in this systematic review.

Author	Journal	Date (DD/MM)	Country	N	Reference
Chan, J. F. W. <i>et al.</i>	Lancet	24/01	China	1	[69]
Cai, J. H. <i>et al.</i>	Zhonghua Er Ke Za Zhi	04/02	China	1	[70]
Deng, H. <i>et al.</i>	Chinese J. Pediatr. Emerg. Med.	07/02	China	2	[71]
Zhang, Y. H. <i>et al.</i>	Zhonghua Er Ke Za Zhi	11/02	China	1	[72]
Chen, F. <i>et al.</i>	Zhonghua Er Ke Za Zhi	11/02	China	1	[73]
Wang, J. <i>et al.</i>	Chin. J. Contemp. Pediatr.	16/02	China	1	[74]
Lingkong, Z. <i>et al.</i>	Zhonghua Er Ke Za Zhi	17/02	China	1	[75]
Le, H. T. <i>et al.</i>	Lancet Child Adolesc Health	23/02	Vietnam	1	[76]
Pan, X. <i>et al.</i>	Lancet Infect. Dis.	24/02	China	1	[77]
Quan, S. <i>et al.</i>	Chinese J. Pediatr. Emerg. Med.	25/02	China	1	[78]
Zhang, G. X. <i>et al.</i>	Chin. J. Contemp. Pediatr.	26/02	China	1	[79]
Kam, K. <i>et al.</i>	Clin. Infect. Dis.	28/02	China	1	[80]
Wang, S. <i>et al.</i>	Clin. Infect. Dis.	12/03	China	1	[81]
Xing, Y. <i>et al.</i>	Medrxiv	13/03	China	3	[82]
Ji, L. N. <i>et al.</i>	World J. Pediatr.	16/03	China	2	[83]
Cui, Y. <i>et al.</i>	J. Infect. Dis.	17/03	China	1	[84]
Li, Y. <i>et al.</i>	Pediatr Pulmonol	18/03	China	2	[85]
He, J. <i>et al.</i>	Lancet Child Adolesc Health	20/03	China	2	[86]
Liu, H. <i>et al.</i>	J. Infect.	21/03	China	4	[87]
Lou, X. X. <i>et al.</i>	J. Paediatr. Child Health	22/03	China	3	[88]
Qian, G. <i>et al.</i>	Clin. Infect. Dis.	23/03	China	1	[89]
Park, J. Y. <i>et al.</i>	J. Korean Med. Sci.	23/03	Korea	1	[90]
Zeng, L. <i>et al.</i>	JAMA Pediatr	26/03	China	3	[91]
Yin, X. <i>et al.</i>	Radiol. Infect. Dis.	27/03	China	1	[92]

Table 11. continued...

Escalera-Antezana, J. <i>et al.</i>	Travel Med. Infect. Dis.	27/03	Bolivia	2	[93]
Zhang, T. <i>et al.</i>	J. Med. Virol.	29/03	China	3	[94]
Rahimzadeh, G. <i>et al.</i>	J. Pediatr. Rev.	01/04	Iran	3	[95]
Canarutto, D. <i>et al.</i>	Pediatr. Pulmonol.	06/04	Italy	1	[96]
Lin, J. <i>et al.</i>	Pediatr. Pulmonol.	06/04	China	1	[97]
Jones, V. C. <i>et al.</i>	Hosp. Pediatr.	07/04	United States of America	1	[22]
Zhang, Z-J. <i>et al.</i>	Eur. Respir. J.	08/04	China	4	[98]

Table 12. Summary of the case report findings.

Variables (N=52)	Events/N (%) or mean
Age	4.66 ± 452
Sex (Female)	19/52 (36.5)
<b>Comorbidities</b>	
Any comorbidity	0
<b>Clinical features</b>	
No symptoms/None	5/51 (9.8)
Fever	35/51 (68.6)
Cough	19/51 (37.3)
Pharyngitis or sore throat	4/51 (7.8)
Rhinorrhea	7/51 (13.7)
Nasal congestion	5/51 (7.8)
Tachypnea or dyspnea	8/51 (15.7)
Expectoration	2/51 (3.9)
Headache or dizziness	3/51 (5.9)
Nausea/abdominal pain or vomiting	7/51 (13.7)
Diarrhea	7/51 (13.7)
Anorexia	5/51 (7.8)
Fatigue or myalgia	6/51 (11.8)
Lethargy	4/51 (7.8)
<b>Clustering of the symptoms</b>	
0	5/45 (11.1)
1	12/45 (26.7)
≥ 2	28/45 (62.2)
<b>Radiologic findings</b>	
Normal	15/47 (31.9)
Anormal	32/47 (68.1)
Unilateral	7/11 (63.6)
Bilateral	4/11 (36.4)
GGO	11/22 (50.0)
Fine mesh shadows	6/22 (27.3)
Consolidation	7/22 (31.8)
Pleural effusion	1/22 (4.5)
<b>Laboratory findings</b>	
Leukocytosis	9/36 (25.0)

Table 12 continued...

Leukopenia	4/36 (11.1)
Lymphocytosis	14/30 (46.7)
Lymphopenia	4/30 (13.3)
Neutrophilia	5/21 (23.8)
Neutropenia	10/21 (47.6)
High hemoglobin	0
Low hemoglobin	7/21 (33.3)
High platelets	5/23 (21.7)
Low platelets	1/23 (4.3)
High CRP	15/34 (44.1)
High PCT	9/17 (52.9)
High ESR	6/10 (60.0)
High AST	4/17 (23.5)
High ALT	2/16 (12.5)
High D-dimer	1/8 (12.5)
High LDH	3/10 (30.0)
High Creatinine	1/10 (10.0)
<b>Exposure setting</b>	
Household	41/49 (83.7)
Epidemic area	24/49 (49.0)
Contact with index case	35/49 (71.4)
<b>Complications</b>	
Acute respiratory distress syndrome	2/5 (40.0)
Acute cardiac injury	1/5 (20.0)
Acute kidney injury	1/5 (20.0)
Acute liver injury	1/5 (20.0)
Secondary infection	3/5 (60.0)
- RSV	1/3 (33.3)
- Influenza virus	1/3 (33.3)
- Other bacteria	1/3 (33.3)
Septic chock	1/5 (20.0)

Table 12 continued...

Outcomes	
Hospitalization	49/51 (96.1)
ICU	4/51 (7.8)
Discharge	24/51 (47.1)
Deaths	0

GGO - Ground glass opacities; CRP - C-reactive protein; PCT - procalcitonin; ESR - erythrocyte sedimentation rate; AST - aspartate transaminase; ALT - alanine transaminase; LDH - lactate dehydrogenase; RSV - respiratory syncytial virus; ICU - intensive care unit.

(95% CI: 0.5-3.3%) diagnosed with cancer and 10.3% (95% CI: 5.3-19.0%) presented asthma (Table 10, Supplementary Figure 1).

### 3.3.2. Clinical features and clustering of the symptoms

Regarding the clinical features, the most commonly found among children were fever (48.6%, 95% CI: 43.5-53.7%), cough (44.2%, 95% CI: 39.1-49.3%) and expectoration (19.3%, 95% CI: 10.1-33.9%). It is important to note that 29.7% (95% CI: 23.3-35.5%) of the children did not report any symptom. Some gastrointestinal claims, namely nausea, abdominal pain or vomiting and diarrhea were also reported, among others (Table 10, Supplementary Figure 1).

In 35.6% (95% CI: 25.6-47.1%) of the cases, children stated 2 or more symptoms and in 32.0% (95% CI: 25.6-47.1%) only one symptom was identified (Table 10, Supplementary Figure 1).

### 3.3.3. Radiologic findings

The radiologic images of 66.4% (95% CI: 60.2-72.1%) of the children were considered abnormal, with 34.2% (95% CI: 29.3-39.3%) of the cases being unilateral pneumonia, and in 30.5% (95% CI: 23.1-39.2%) of the cases the infection compromises the two lungs. Furthermore, fine mesh shadows and ground glass opacities (GGO) were found in 41.4% (95%CI: 29.1-54.8%) and in 39.0% (95% CI: 31.7-46.7%) of the cases, respectively. Other radiologic findings like consolidation and pleural effusion were also reported (Table 10, Supplementary Figure 1).

### 3.3.4. Laboratory findings

Regarding the laboratory findings, high C-reactive protein (CRP) (21.0%, 95% CI: 14.4-29.5%), high

procalcitonin (PCT) (19.7%, 95% CI: 9.6-36.1%), high erythrocyte sedimentation rate (ESR) (27.9%, 95% CI: 17.9-40.7%), high aspartate transaminase (AST) (24.5%, 95% CI: 15.1-37.2%), high alanine transaminase (ALT) (15.7%, 95% CI: 10.7-22.3%), high D-dimer (19.9%, 95% CI: 13.1-29.1%), high lactate dehydrogenase (LDH) (33.9%, 95% CI: 23.8-45.8%) and high creatine kinase (CK) (45.8%, 95% CI: 31.0-61.4%) were the most prevalent results. Lymphocytosis (25.5%, 95% CI: 17.3-35.9%) and high hemoglobin (20.7%, 95% CI: 15.0-27.8%) were also found, among other laboratory findings (Table 10, Supplementary Figure 1).

### 3.3.5. Exposure setting

Most of the children contacted with the new coronavirus in their household environment (83.5%, 95% CI: 76.8-88.6%), or by contact with an index case (75.5%, 95% CI: 65.8-83.1%). 45.1% (95% CI: 24.8-67.2%) of the children became infected after being present in an epidemic area (Table 10, Supplementary Figure 1).

### 3.3.6. Complications and outcomes

Among the children, 96.9% (95% CI: 92.3-98.8%) required hospitalization, and 5.1% (95% CI: 2.7-9.3%) needed intensive care unit (ICU) assistance. Secondary infections caused by other virus (respiratory syncytial virus (RSV), cytomegalovirus, Epstein-Barr virus, influenza virus) or even by bacteria were reported for 27.5% (95% CI: 19.0-38.1%) of the cases. An important finding was that 21.5% (95% CI: 14.4-30.8%) of the children presented secondary infection caused by *Mycoplasma* (Table 10, Supplementary Figure 1). Death only occurred for 0.4% (95% CI: 0.2-1.0%) of the cases (Table 10, Supplementary Figure 1).

### 3.4. Publication bias

Publication bias was assessed with a funnel plot of standard error by logit event, with no evidence of bias (Supplementary Figure 2). Additionally, the Egger's regression test (P-value = 0.1522) suggested that there was no notable evidence of publication of bias.

### 3.5. Case reports

We found 31 case report articles (Table 11), summarizing 52 cases of COVID-19. The mean age was  $4.66 \pm 4.52$  years, 36.5% of children being female. The most common clinical features were fever (68.6%) and cough (37.3%). A case report included in this study described the case of a

6-month-old infant diagnosed with Kawasaki disease and COVID-19. In addition to the symptoms reported in Table 12, the child also developed a maculopapular rash, limbic-sparing conjunctivitis, prominent tongue papilla and swelling of the hands and lower extremities. Regarding the radiologic images, 68.1% of patients had abnormal findings, GGO being the most common finding (50.0%). Lymphocytosis (46.7%), neutropenia (47.6%), high CRP (44.1%), high PCT (52.9%) and high ESR (60.0%) were the most common laboratory findings. Among the complications, 40.0% presented acute respiratory distress syndrome (ARDS) and 60.0% secondary infections. Most of the cases described in these case reports were hospitalized (96.1%) and 7.8% needed ICU assistance.

#### 4. DISCUSSION

The World Health Organization declared the COVID-19 as a pandemic health emergency [10]. Person-to-person transmission of the new coronavirus occurs primarily through close contact with an infected person, mainly *via* respiratory droplets and after touching contaminated objects [10].

In the early stages of the outbreak, COVID-19 was predominantly more prevalent among adults with more than 15-years-old, and the proportion of confirmed cases among children was relatively small [11, 12]. Angiotensin converting enzyme II (ACE2) is known to be the cell receptor for SARS-CoV-2 and it is speculated that children were less sensitive to this new coronavirus since the maturity and function (binding ability) of ACE2 in children may be lower than in adults [13]. The first COVID-19 pediatric case was reported on January 20, 2020, in a 10-year-old boy from Shenzhen, China, whose family had visited Wuhan. Since then, however, more regions have launched coronavirus detection campaigns and, since younger children cannot wear masks and have not taken other special preventive and control measures, the number of cases of infection in children has increased significantly, especially in younger age groups [11, 12]. Limited data are available on the prevalence of COVID-19 in pediatric populations because children were rarely tested for the virus in the earlier phase of the outbreak [11, 12]. The epidemic characteristics of COVID-19 in children are not yet clear, which poses a serious challenge to pediatric medical workers [14].

This systematic review with meta-analysis summarizes the current available information regarding the pediatric COVID-19. Although some meta-analyses dealing with COVID-19 in children were previously performed [15, 16] the present meta-analysis includes more studies and consequently a large number of children, which increases the statistical power of the results now obtained, allowing for a better understanding of the clinical features, radiologic and laboratory findings, and potential complications of the pediatric cases of COVID-19.

Our results indicate that, in general, children infected with SARS-CoV-2 were asymptomatic or present only mild symptoms like sore throat and nasal congestion, or even minor gastrointestinal symptoms like nausea or diarrhea. It is suggested that prior infections and frequent immunizations with routine vaccines (like BCG) may contribute to better immunity against SARS-CoV-2 infection in very young children [17]. Symptomatic infection with the new coronavirus is not common in children, which may be also due to higher respiratory reserve, fewer underlying diseases, and more effective innate immune response in this group [18]. Relatively stronger humoral responses in children may also contribute to this phenomenon. Innate immunity can react more rapidly in response to pathogen invasion than adaptive immunity [19]. Otherwise, the symptoms more frequently described in COVID-19-positive children were fever and cough. Furthermore, at radiologic level, GGO and fine mesh shadows were often noticed, and at laboratory level, lymphocytosis and leukopenia were observed. These general conclusions are in agreement with the previous meta-analysis of pediatric COVID-19 [15, 16]. There are no significant differences in these general results when compared with the meta-analysis findings of SARS-CoV-2 infected adults [20, 21].

Recently, a potential link between COVID-19 infection and the development of Kawasaki disease in children has been hypothesized [22, 23]. Kawasaki disease is an acute pediatric multisystem vasculitis, primarily affecting individuals between the ages of 6 months and 5-year-old and is the primary cause of acquired heart disease within the pediatric population of industrialized nations [22, 23]. The cause of Kawasaki disease remains unknown, despite several decades of investigation, but some evidence suggests that an infection can trigger the rise of the disease [22, 23].

Our results have shown that, generally, children infected with SARS-CoV-2 presented thrombocytosis that may indicate the development of coronary artery disease [24], high ESR that is associated with acute inflammation [24], high CRP that can predict cardiac sequelae [24], and liver function tests showing evidence of hepatic inflammation [24] (high AST and ALT), which all together are common biochemical features found in patients with Kawasaki disease [24]. Moreover, our results demonstrated that the infected children also presented high levels of CK that may be an indication of damage in CK-rich tissue (such as in rhabdomyolysis, myocardial infarction, myositis and myocarditis) [24], high levels of D-dimer that are related with deep venous thrombosis, pulmonary embolism or disseminated intravascular coagulation [24], high PCT that may be a signal of systemic inflammatory syndrome and sepsis in children [25], and high LDH levels that indicates tissue damage caused by infections [24]. These results are consistent with Kawasaki disease physiopathology. In a broader approach, the set of these altered biomarkers related with thromboembolic disease and inflammation condition, together with persistent fever, are consistent with MIS-C that are now being described as appearing in some children diagnosed with COVID-19.

Other important finding of our work was the prevalence of secondary infections in children, mainly caused by *Mycoplasma*. *Mycoplasma pneumoniae* is a common childhood pathogen in older children. Since the co-infection rate was elevated in children, it is plausible to think that SARS-CoV-2 co-infection with *Mycoplasma* may prolong the time from onset to becoming virus-negative [17]. Accumulating evidence shows that microbial co-infection increases the risk of disease severity in humans and there have been very few studies about SARS-CoV-2 co-infection with other pathogens [26, 27]. Co-infection may significantly inhibit the immune system of host, increasing the intolerance to the antibacterial therapy, and may be detrimental to the prognosis of the disease [26, 27]. These results suggest that more attention should be given to SARS-CoV-2 infected children who also have co-infection with other respiratory pathogens. The high co-infection rate observed in children highlights the importance of SARS-CoV-2

screening, especially during the peak season for colds, influenza, and other respiratory illnesses [26, 27].

Other authors have previously suggested that an approach that relies on certifying potential markers of poorer outcomes, such as evidence of organ dysfunction and of superimposed bacterial infection should be assessed in children in an earlier stage of SARS-CoV-2 infection [28]. As all the works, the present meta-analysis presents some limitations, namely, the degree of heterogeneity (P-value < 0.05) that indicates some inconsistency across the included studies. Furthermore, almost all the included studies were performed in China. It would be better to include studies with a broad geographic distribution to get a more comprehensive understanding of pediatric cases of COVID-19. Due to the rapid emergence of COVID-19-related publications, the results of this meta-analysis may be outdated relatively soon.

## 5. CONCLUSIONS

This work showed that pediatric cases of COVID-19 are generally asymptomatic with fever and cough being the symptoms most frequently observed. The radiologic images often show GGO and fine mesh shadows, indicating lung damages. The overall laboratory biomarkers show a scenario of inflammation consistent with MIS-C, which can be related with some cases of Kawasaki disease being diagnosed in post-SARS-CoV-2 infected children. The high co-infection rate, particularly with *Mycoplasma*, may be a factor that worsens the clinical condition of infected children.

## ACKNOWLEDGMENTS

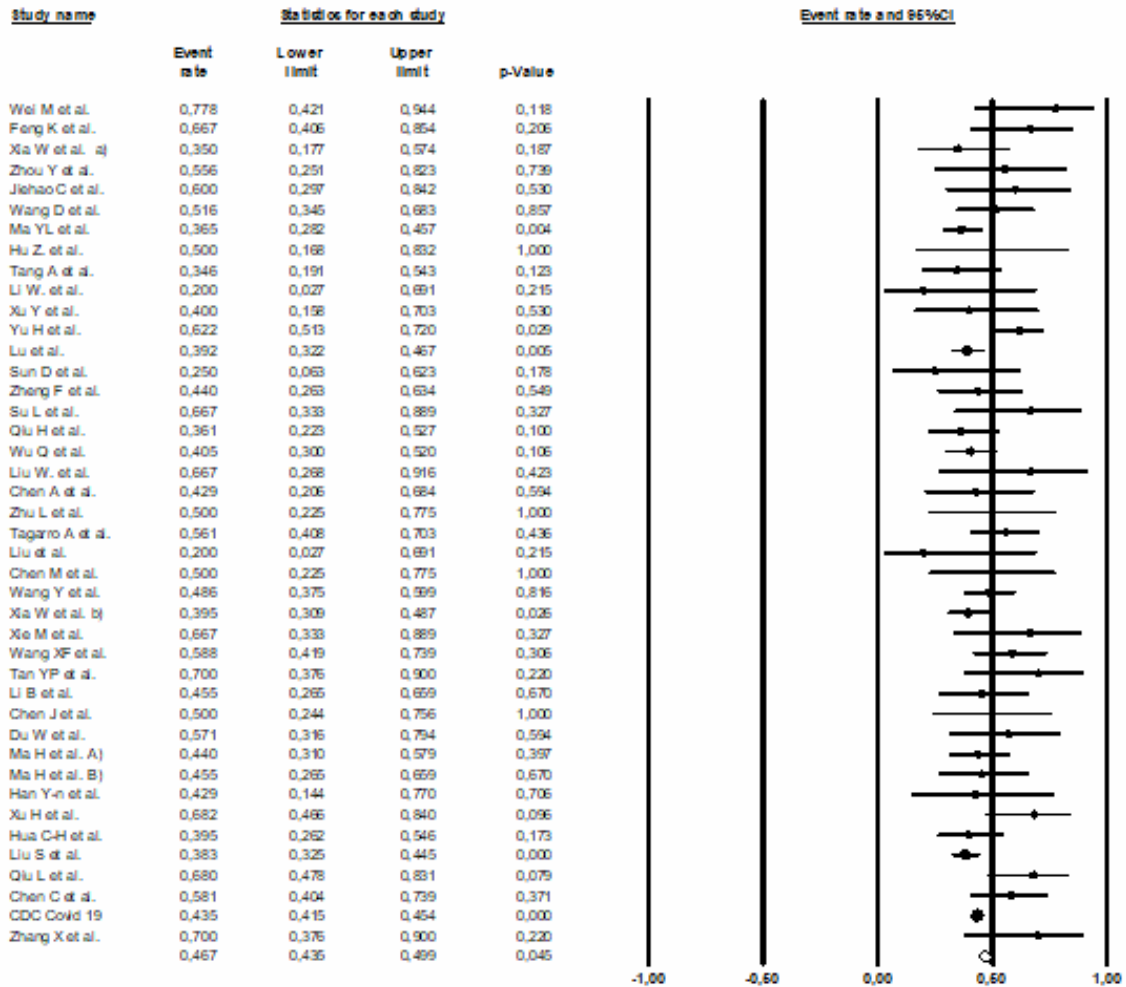
Ângelo Luís acknowledges the contract of Scientific Employment in the scientific area of Microbiology financed by Fundação para a Ciência e a Tecnologia (FCT). Authors would also like to thank “Operação Centro-01-0145-FEDER-000019-C4-Centro de Competências em Cloud Computing”, co-financed by the CENTRO 2020, FEDER funds (Project POCI-01-0145-FEDER-007491) and Fundação para a Ciência e a Tecnologia (UIDB/00709/2020).

## CONFLICT OF INTEREST STATEMENT

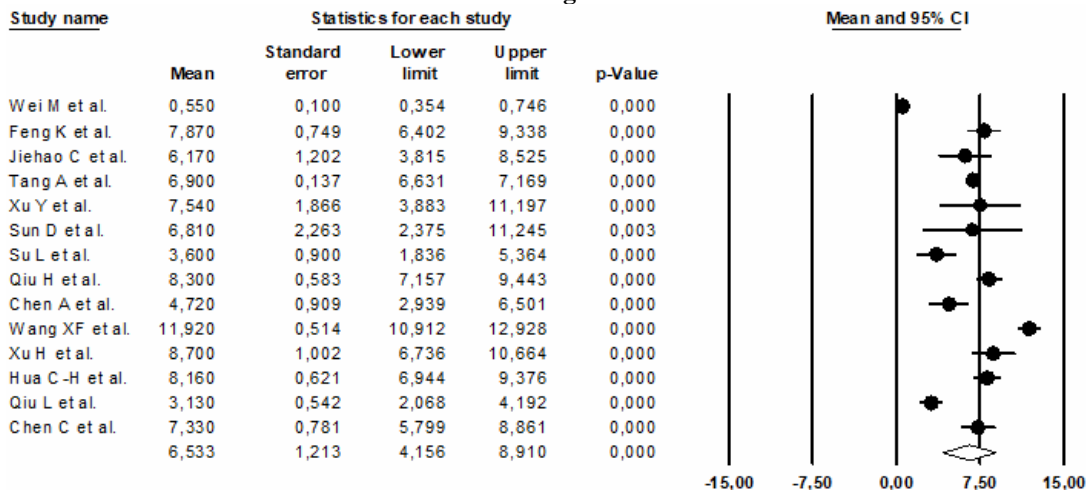
The authors have no conflicts of interest relevant to this article to disclose. The authors have no financial relationships relevant to this article to disclose.

Demographical characteristics

Female



Age



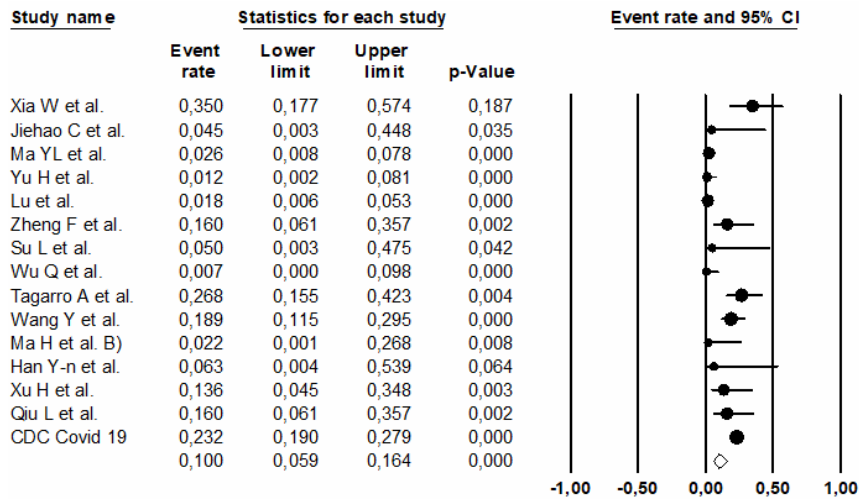
Supplementary Figure 1



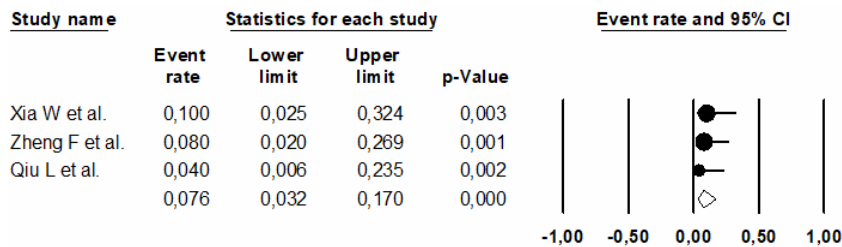
Supplementary Figure 1 continued...

**Comorbidities**

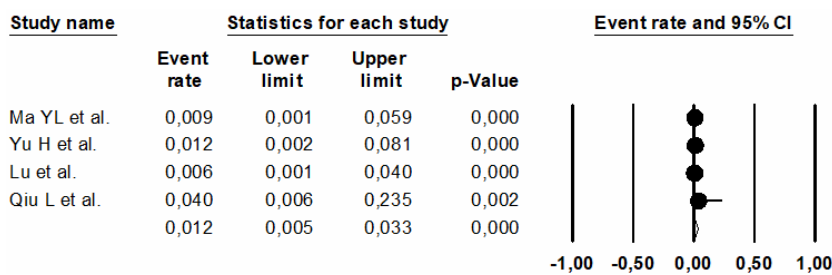
**Any**



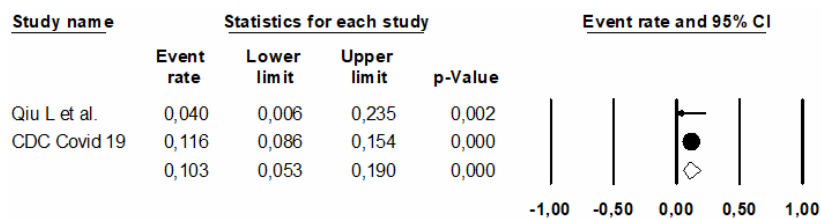
**Congenital Heart Diseases**



**Cancer**



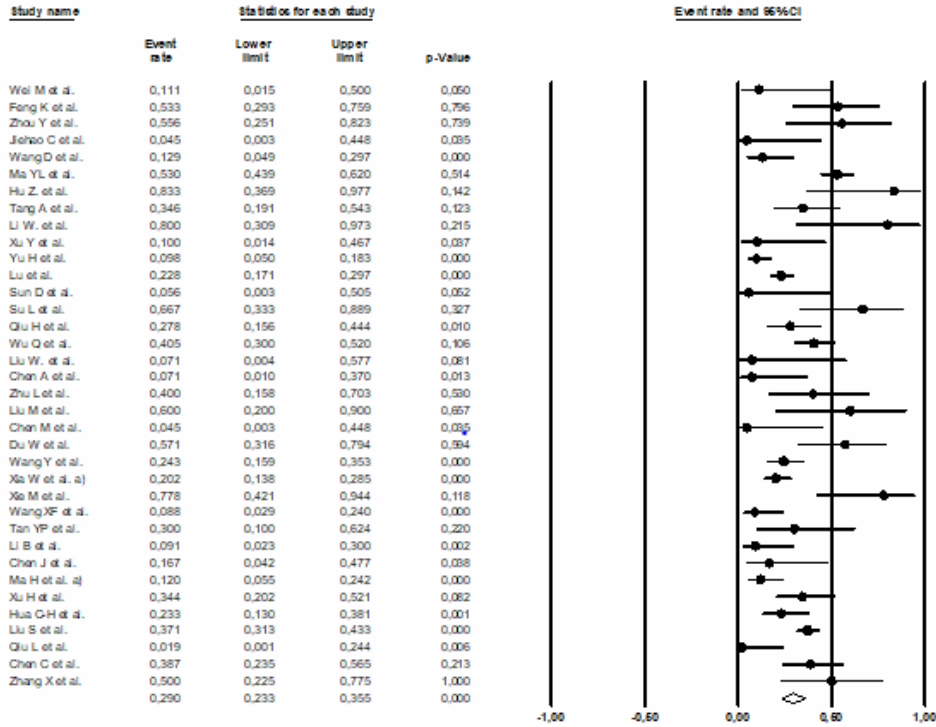
**Asthma**



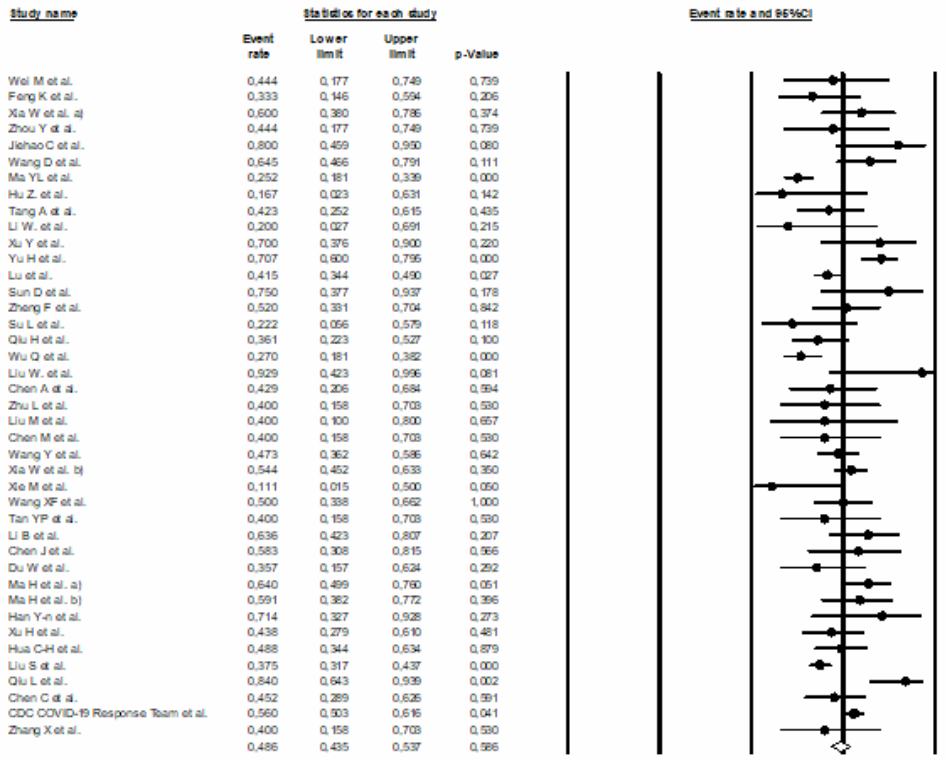
Supplementary Figure I continued...

Clinical features

Asymptomatic

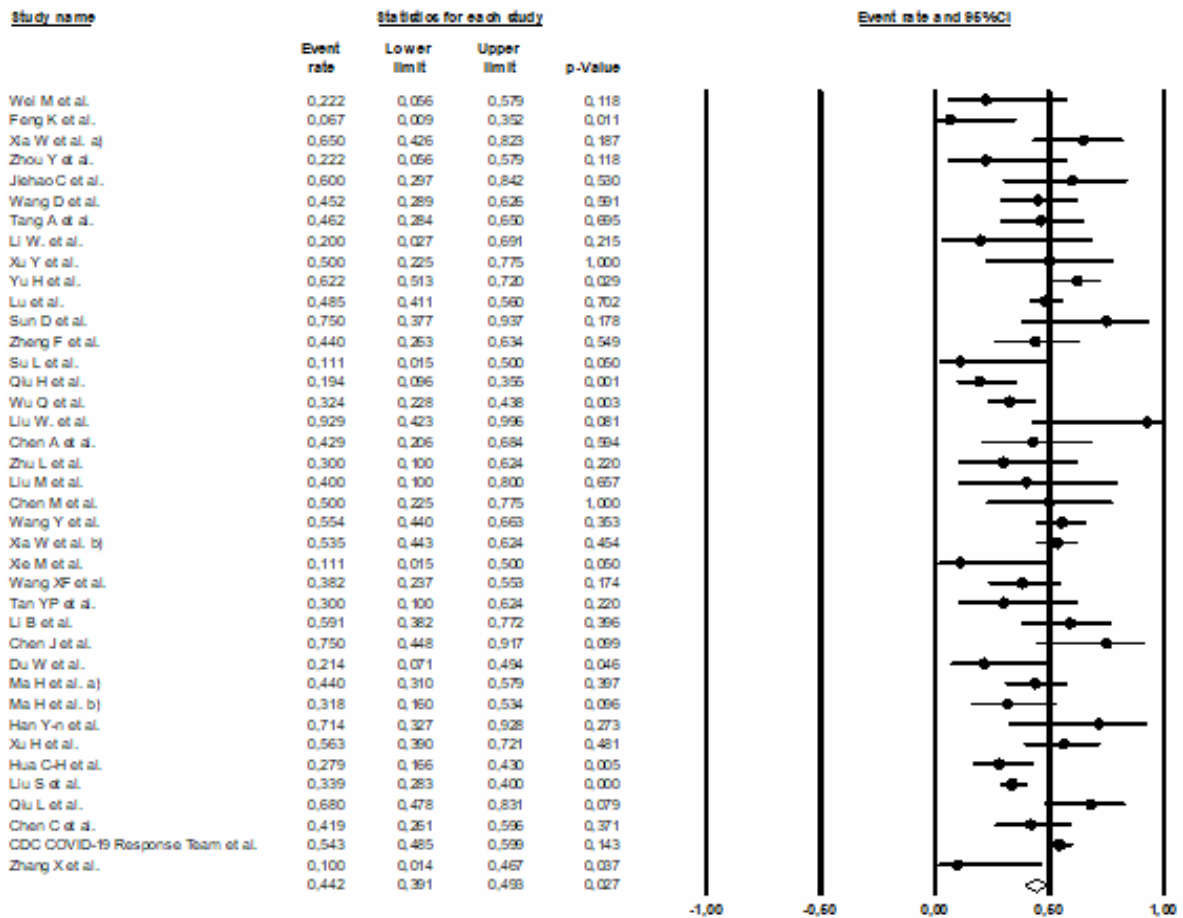


Fever

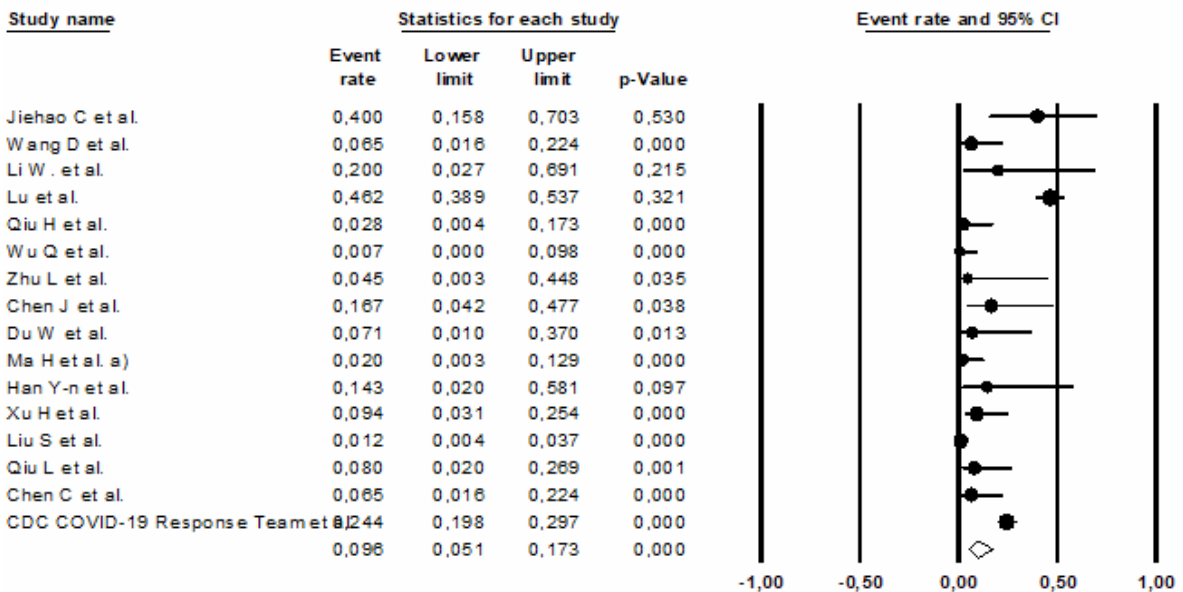


Supplementary Figure 1 continued...

**Cough**

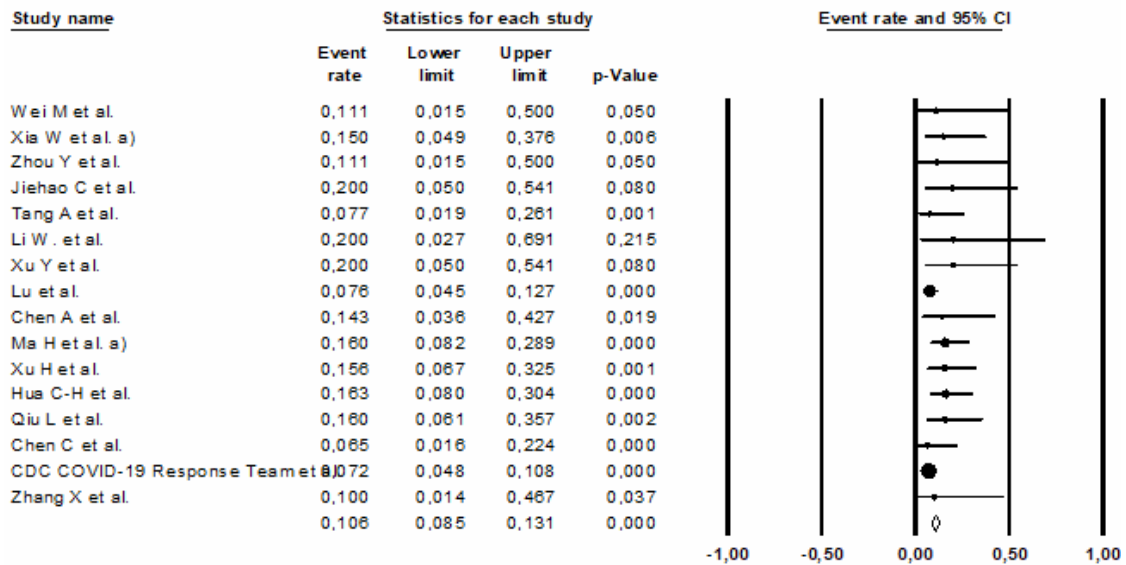


**Pharyngitis or sore throat**

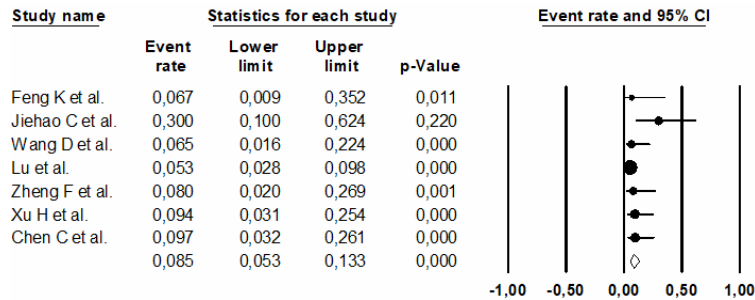


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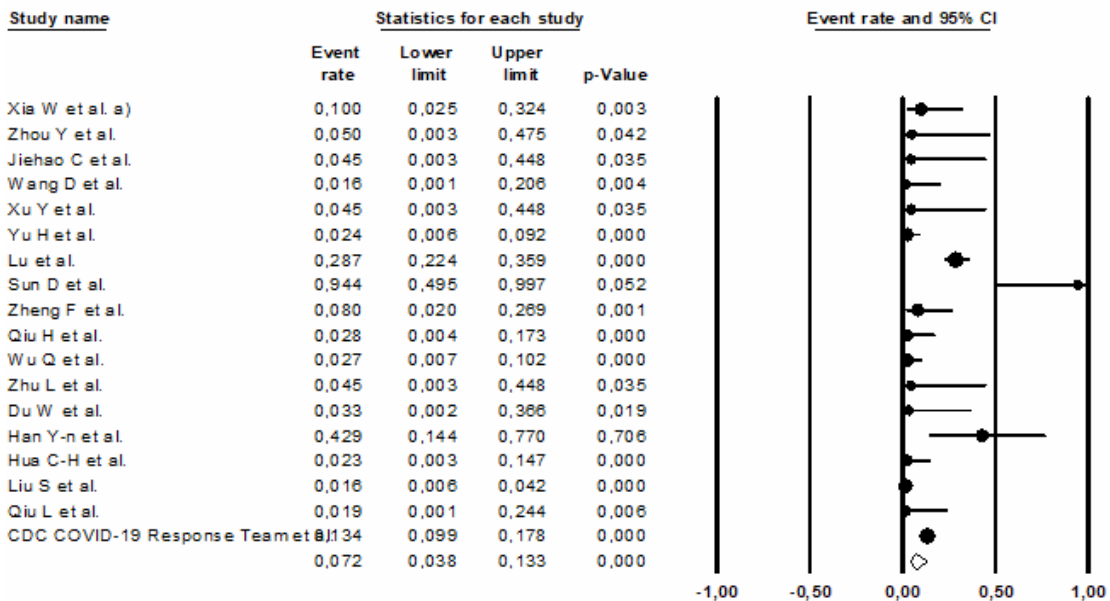
**Rhinorrhoea**



**Nasal congestion**

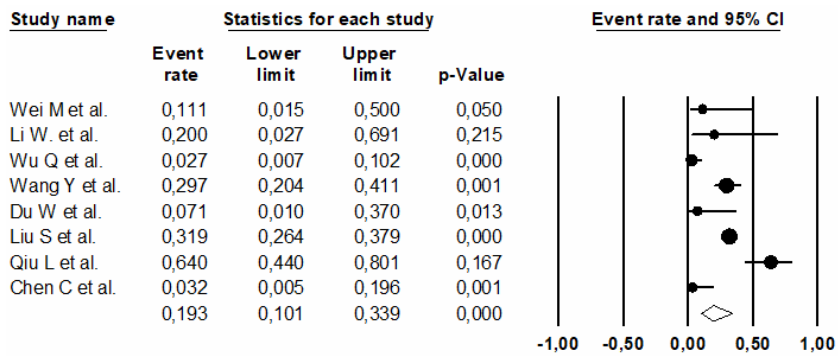


**Tachypnea or dyspnea**

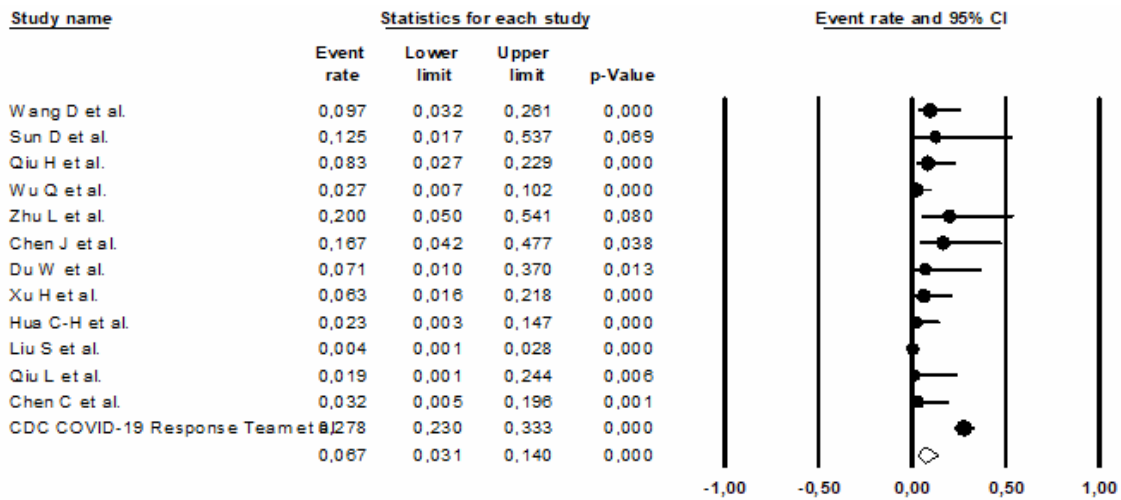


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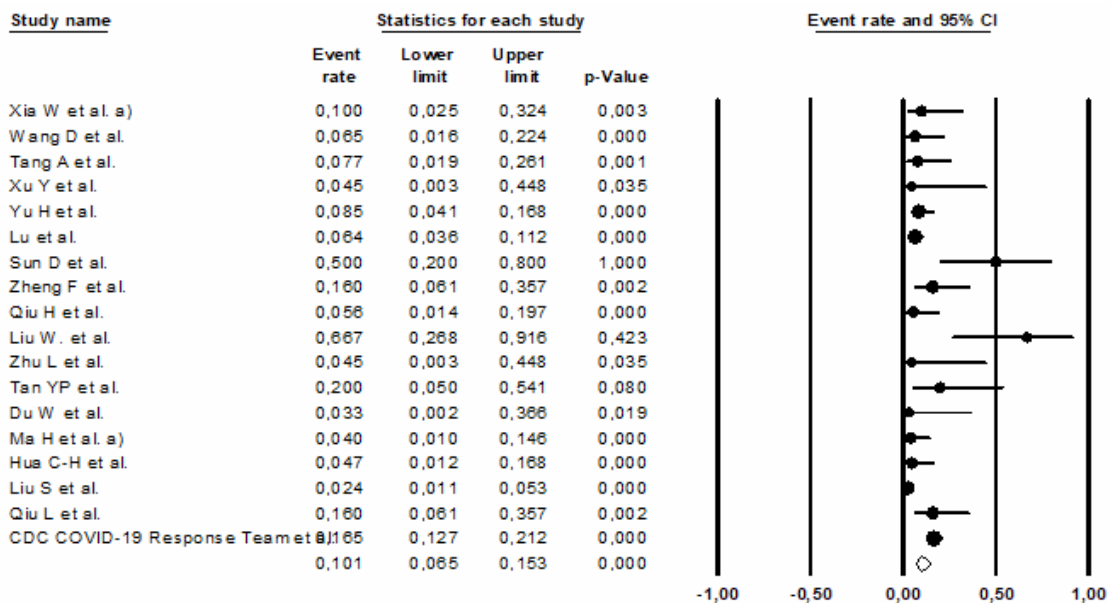
**Expectoration**



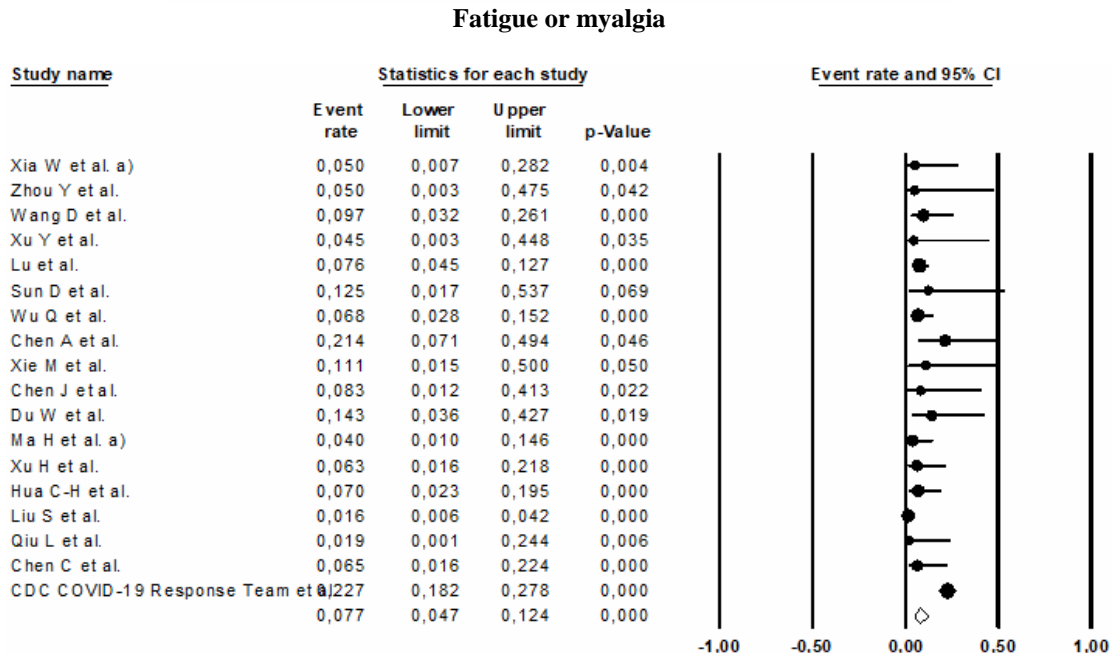
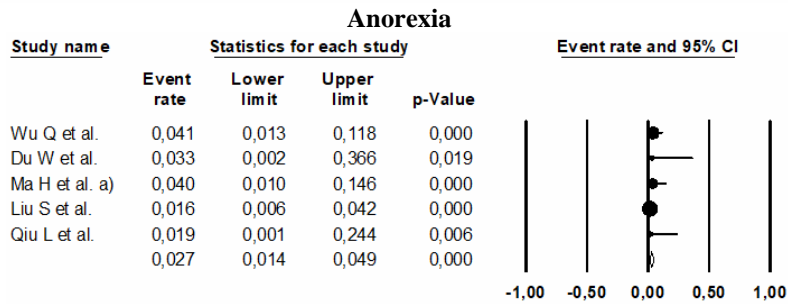
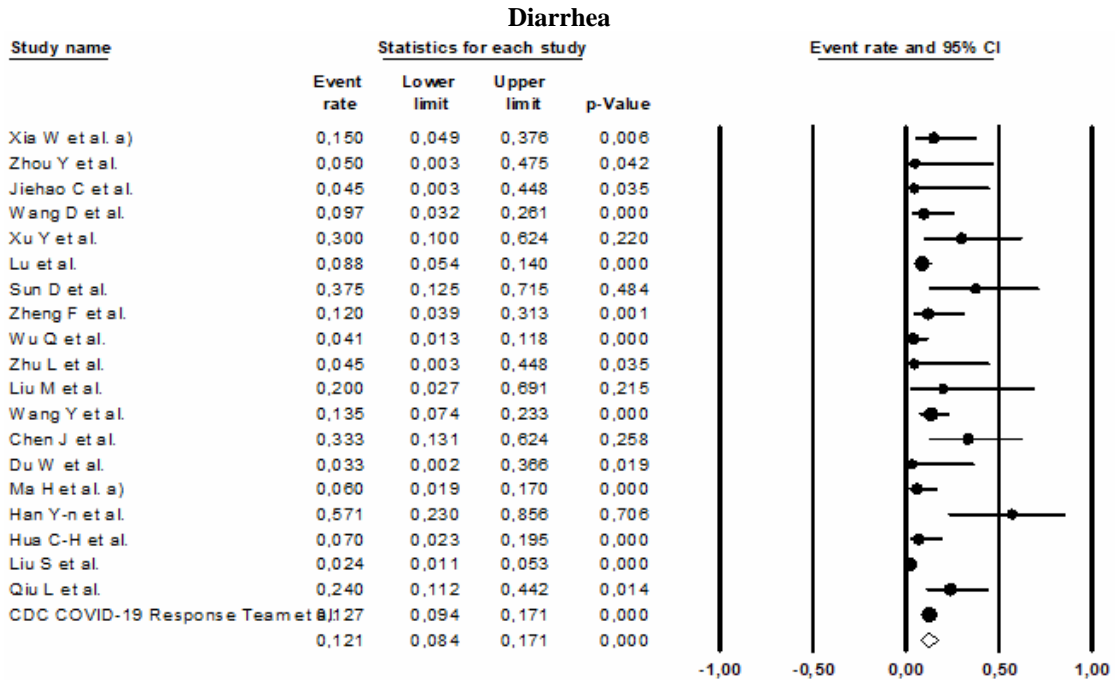
**Headache or dizziness**



**Nausea/abdominal pain or vomiting**

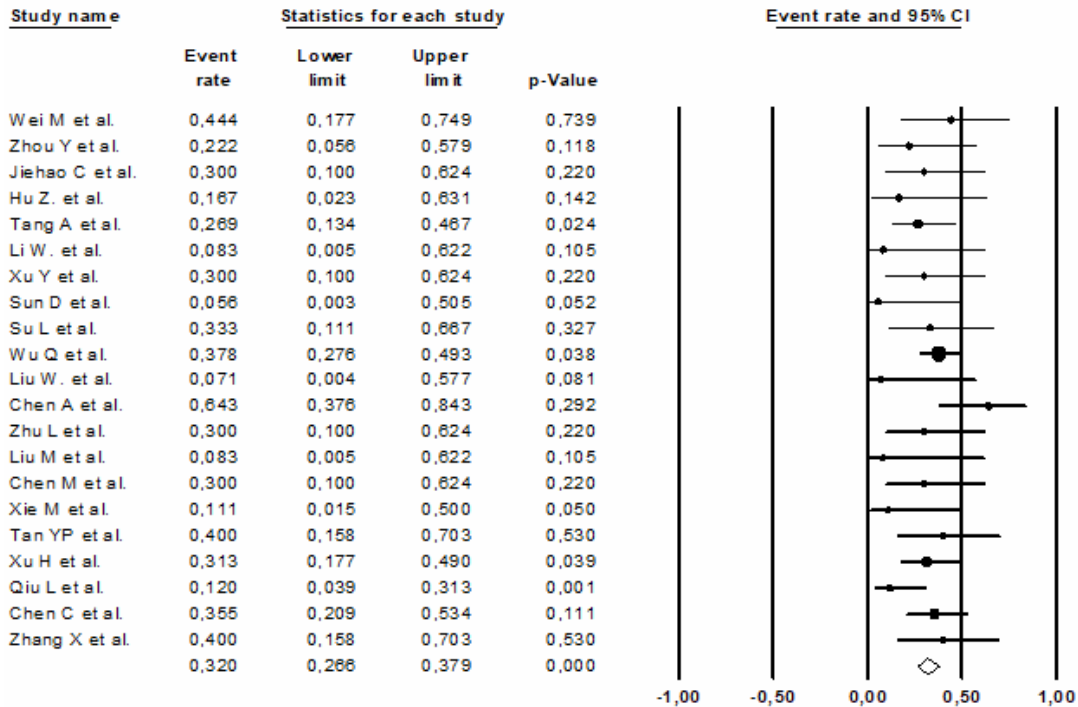


Supplementary Figure 1 continued...

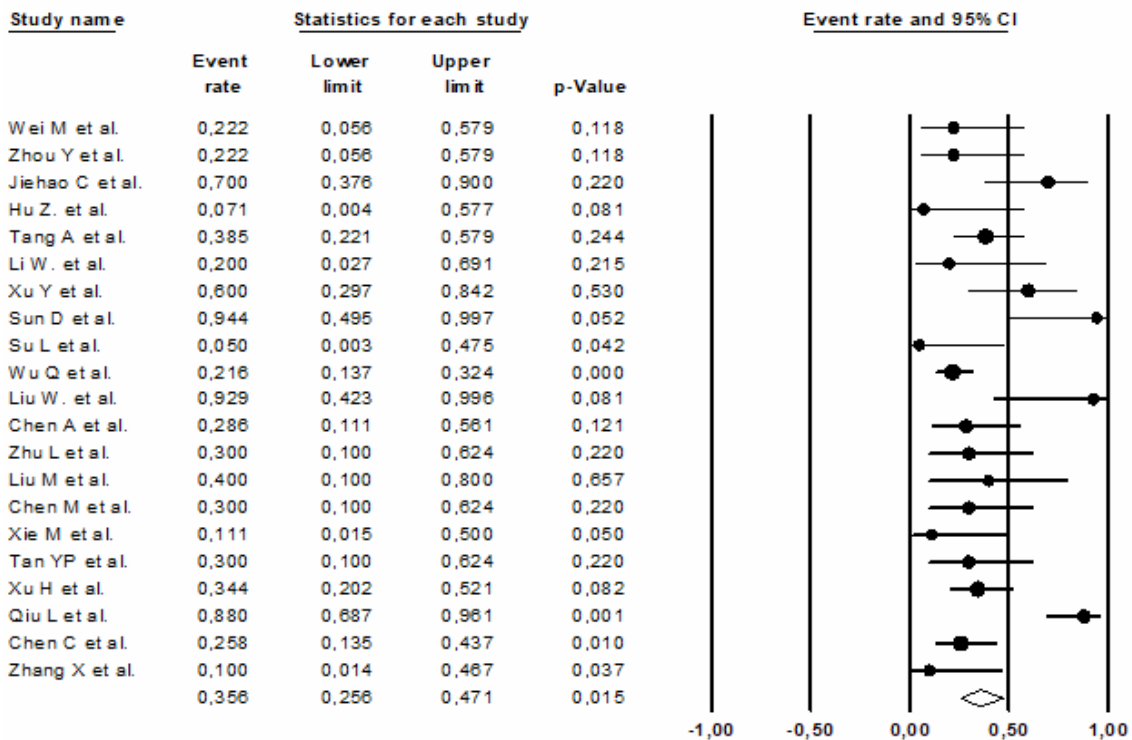


Supplementary Figure 1 continued...

1 symptom



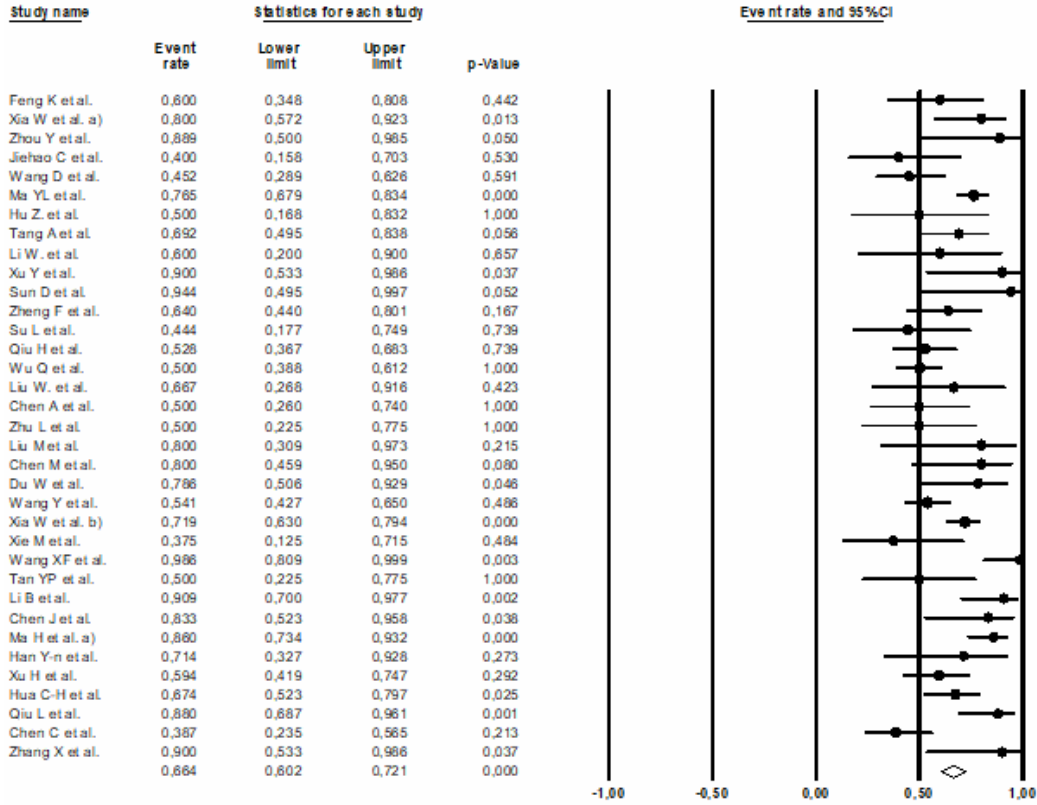
2 symptoms



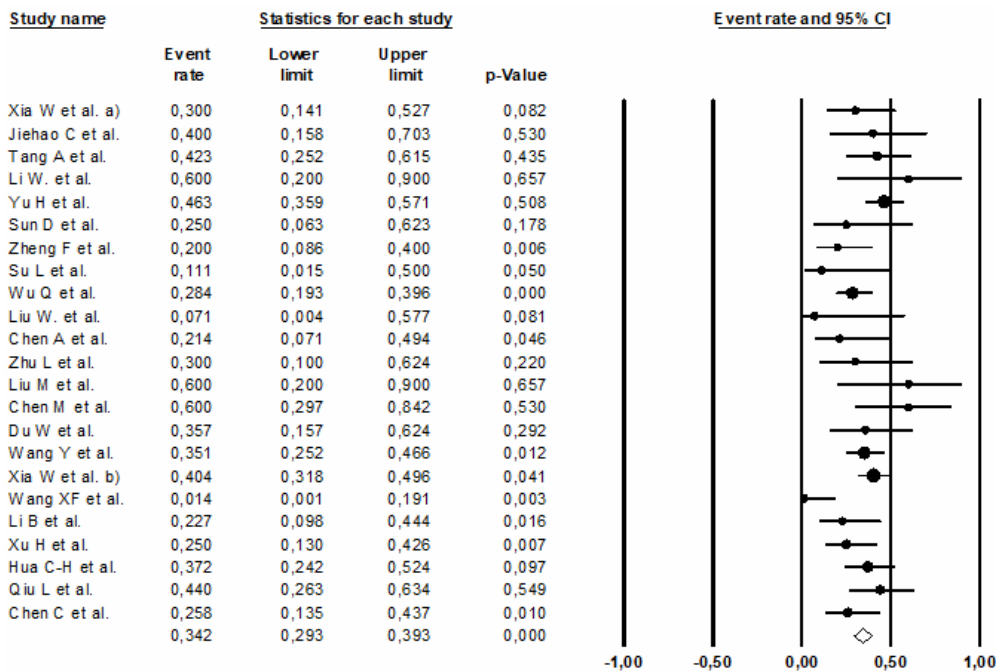
Supplementary Figure I continued...

**Radiological findings**

**Anormal**

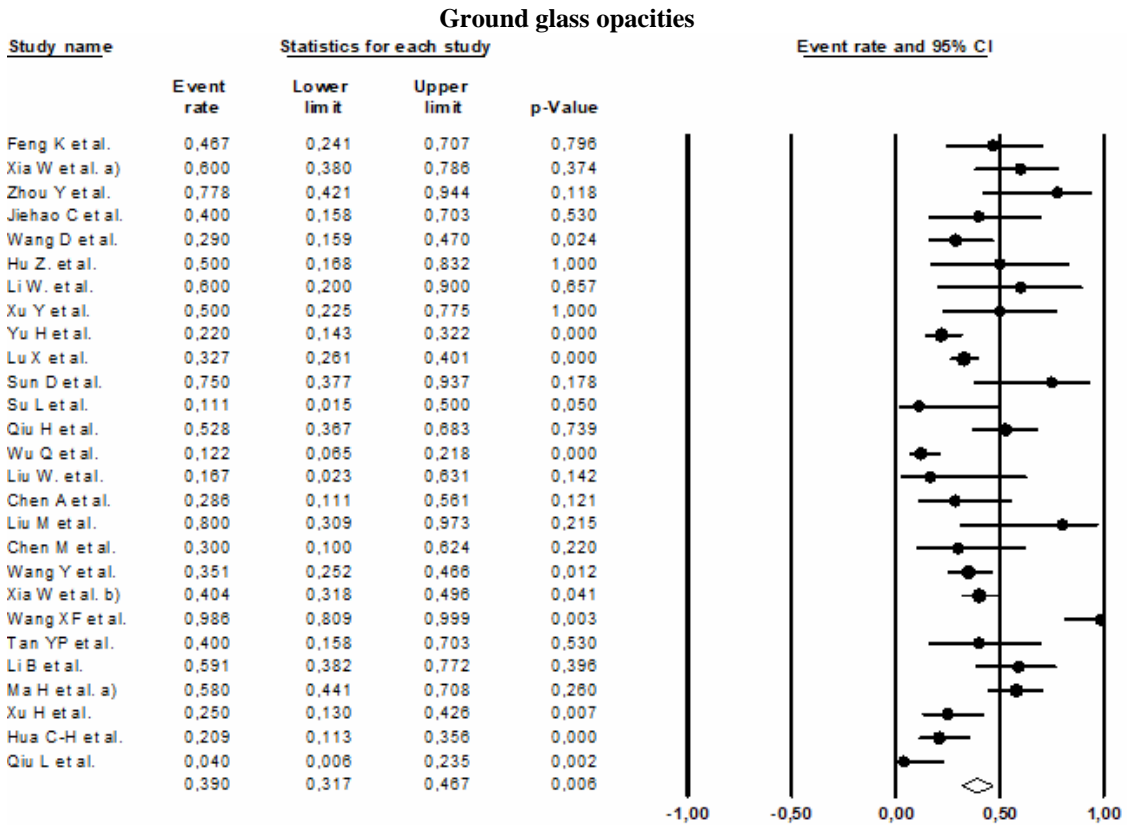
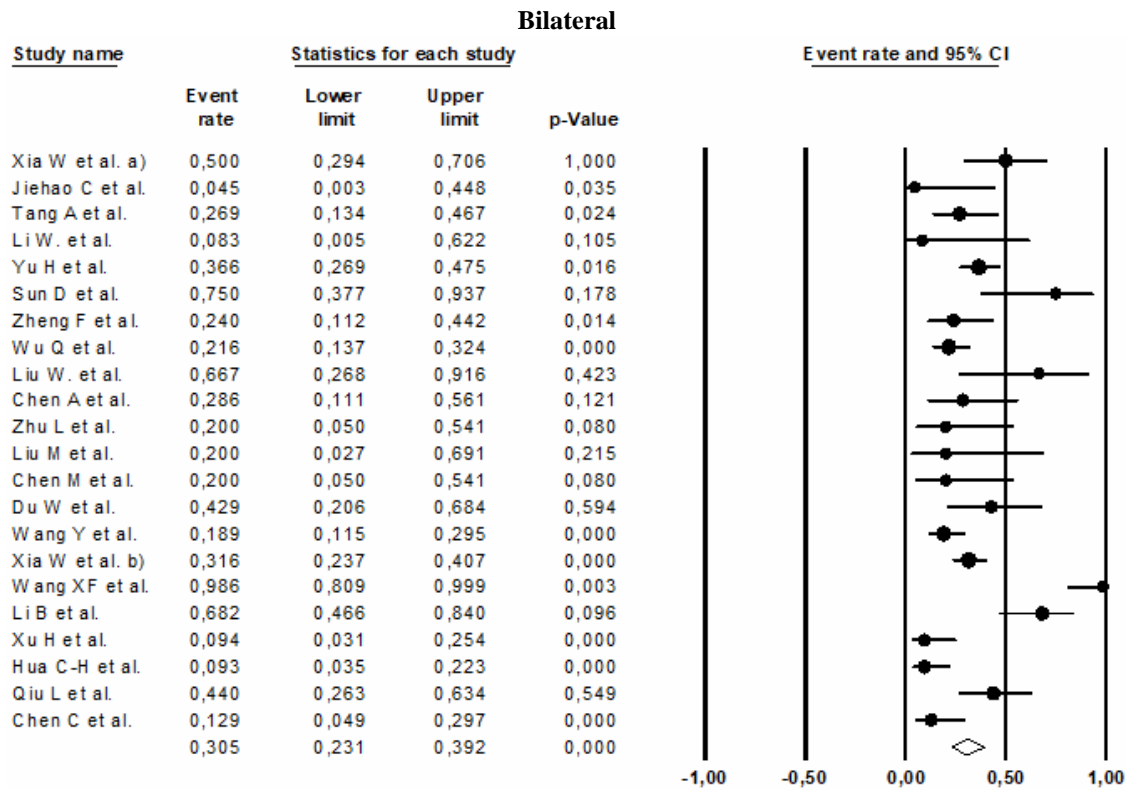


**Unilateral**

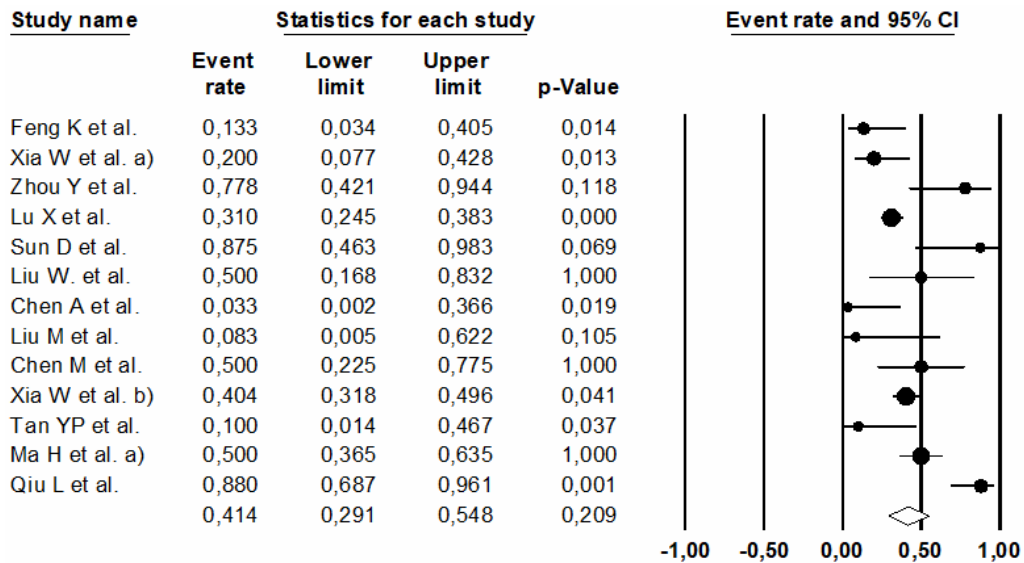
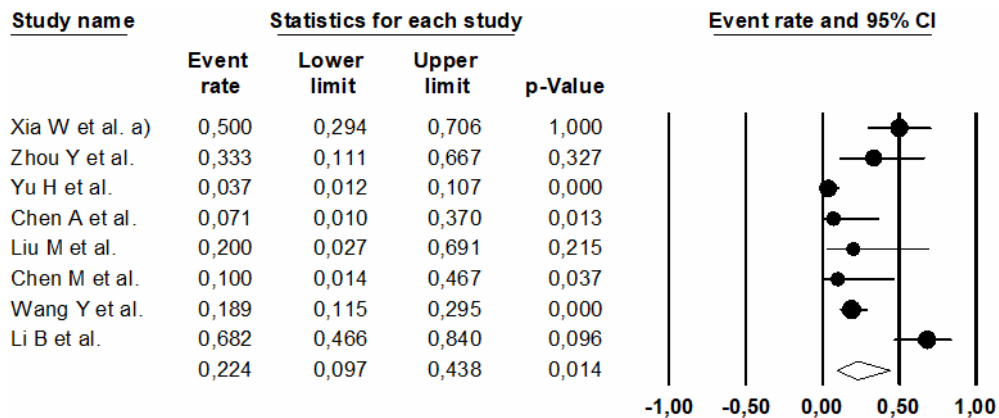
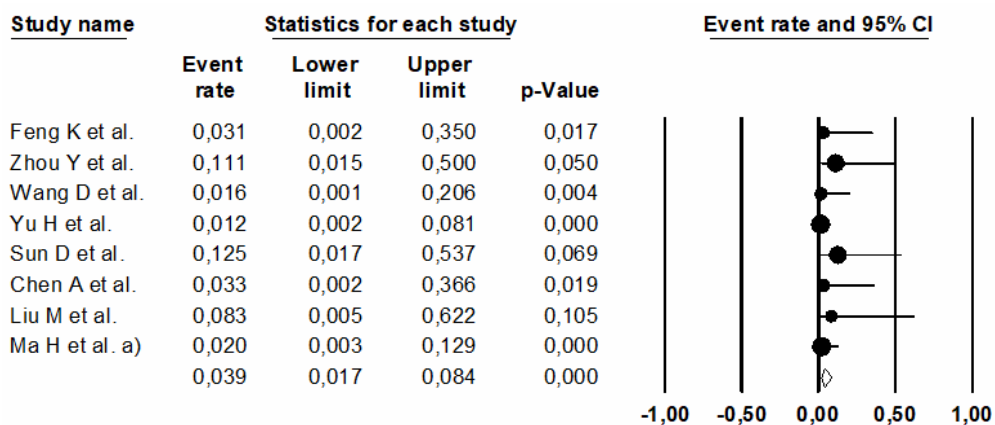




Supplementary Figure I continued...



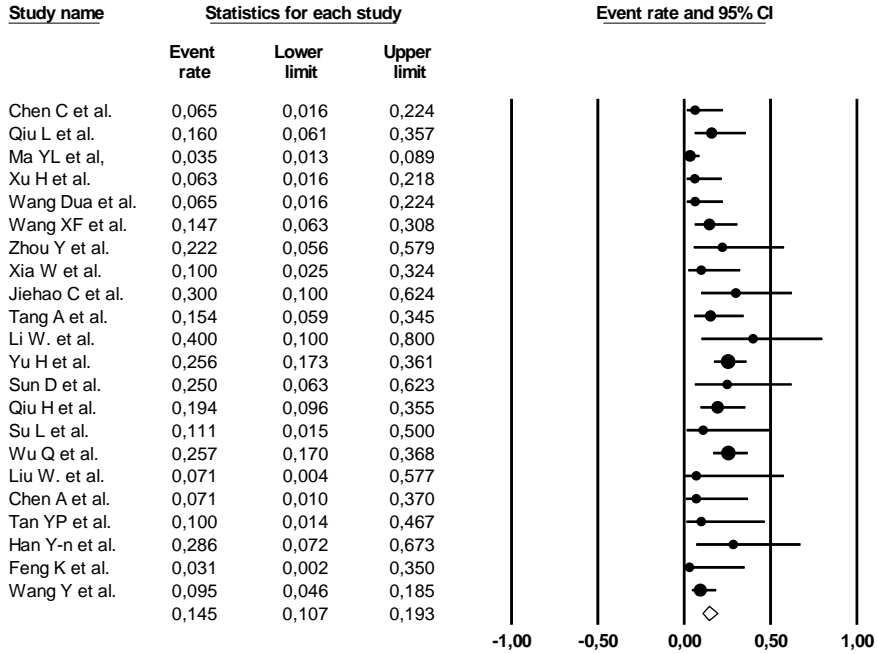
Supplementary Figure I continued...

**Fine mesh shadows****Consolidation****Pleural effusion**

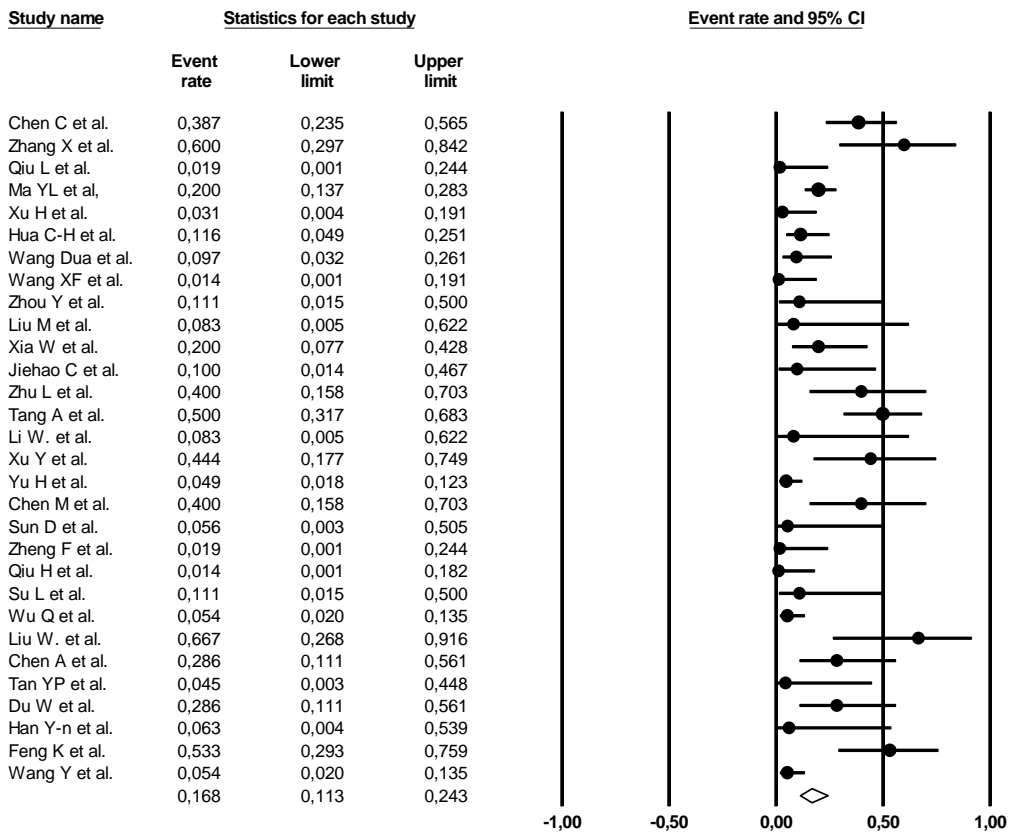
Supplementary Figure I continued...

**Laboratory findings**

**Leukocytosis**

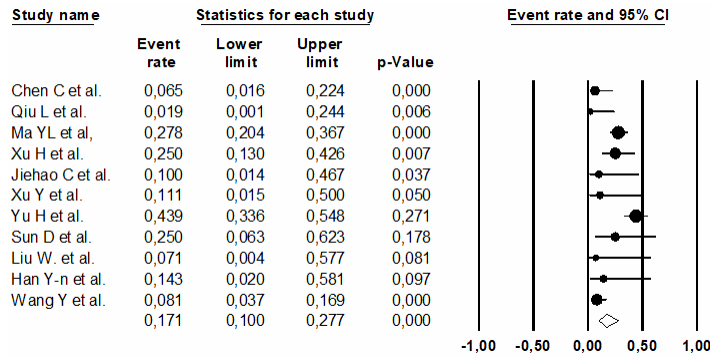


**Leukopenia**

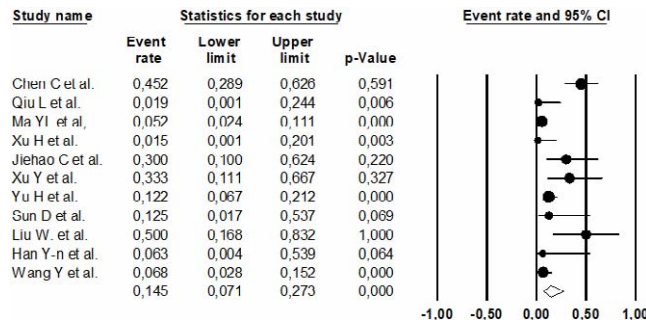


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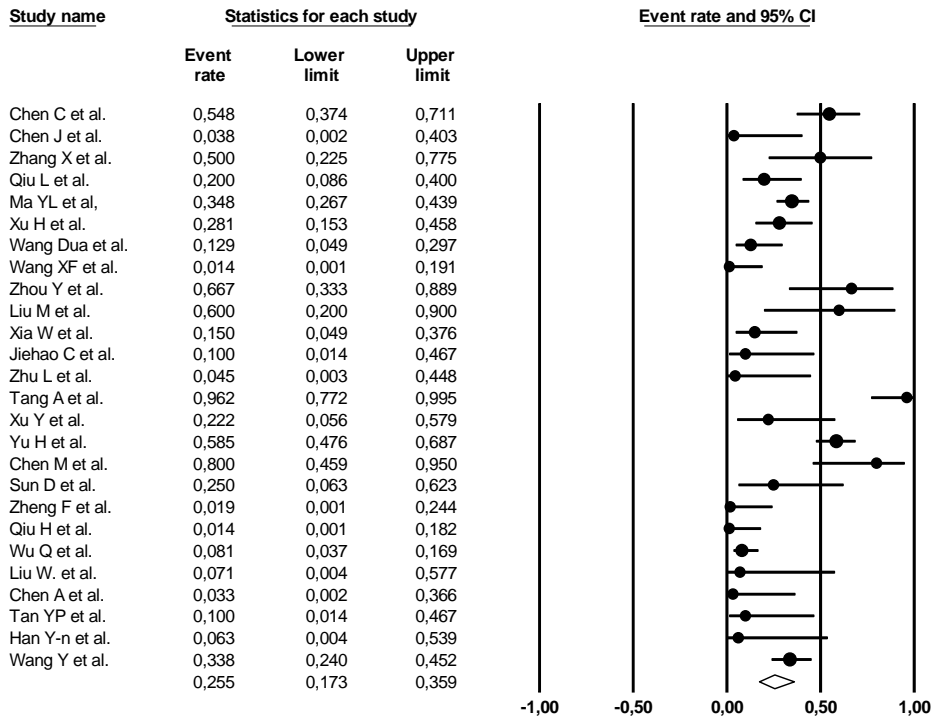
### Neutrophilia



### Neutropenia

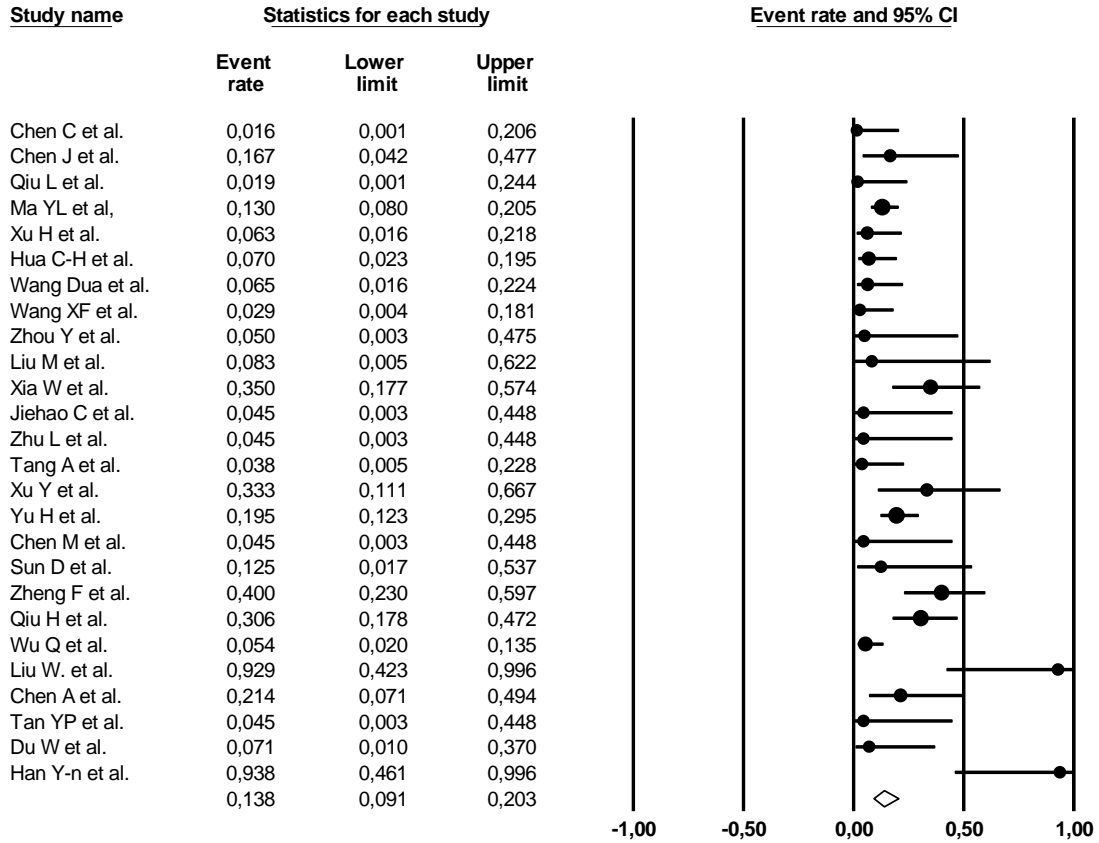


### Lymphocytosis

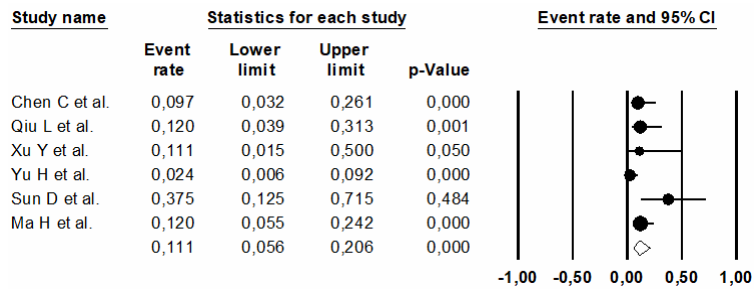


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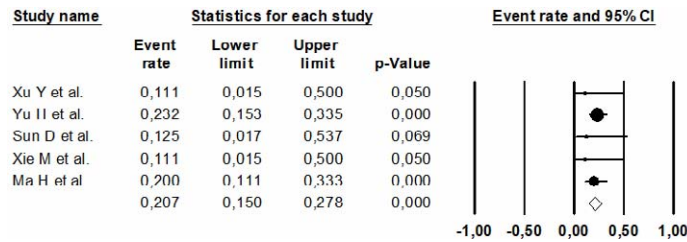
### Lymphopenia



### Low hemoglobin

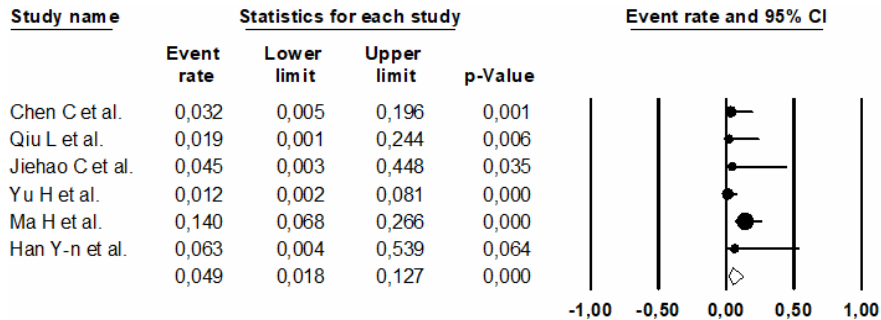


### High hemoglobin

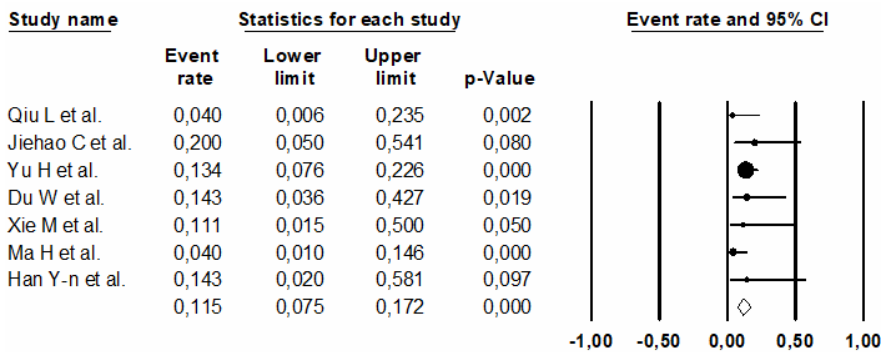


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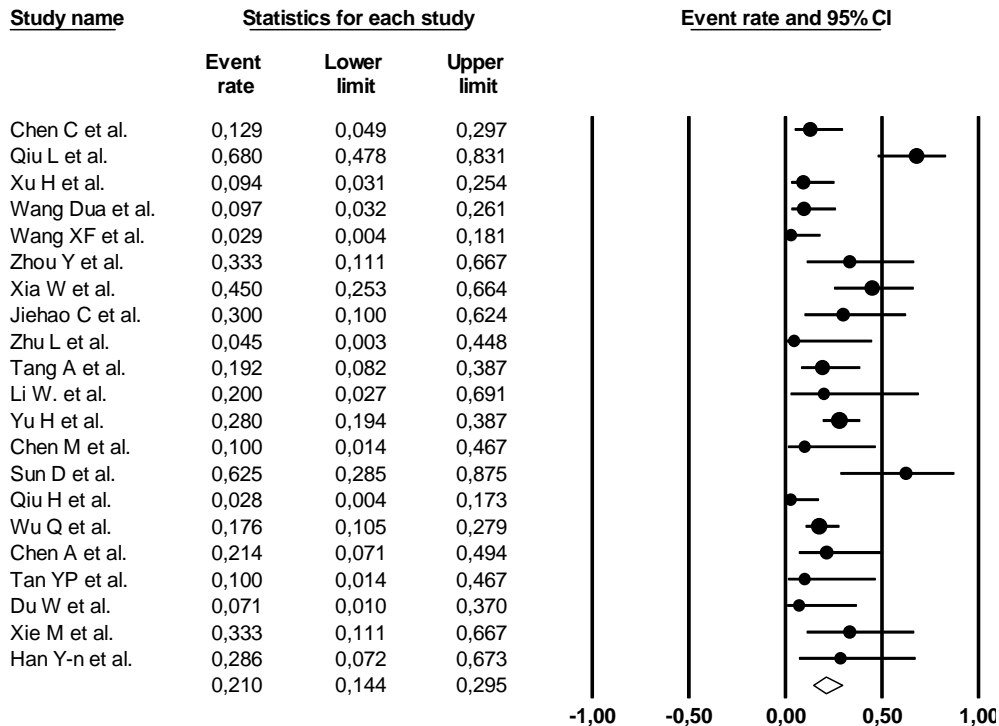
**Low platelets**



**High platelets**

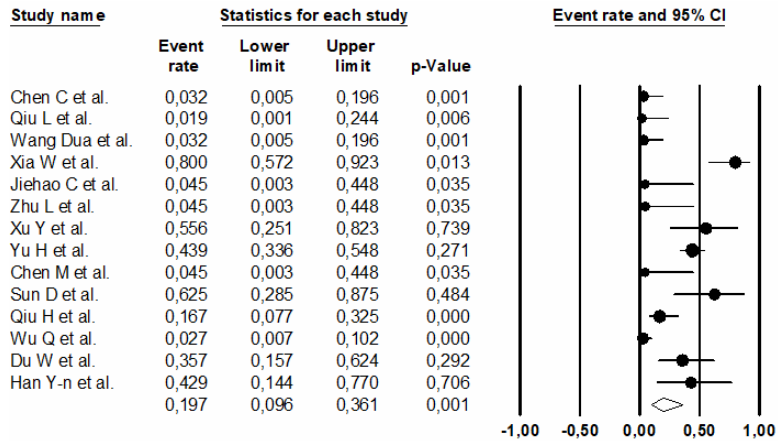


**High CRP**

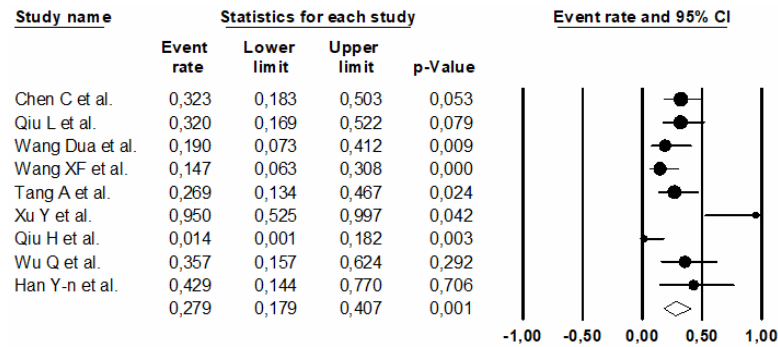


Supplementary Figure I continued...

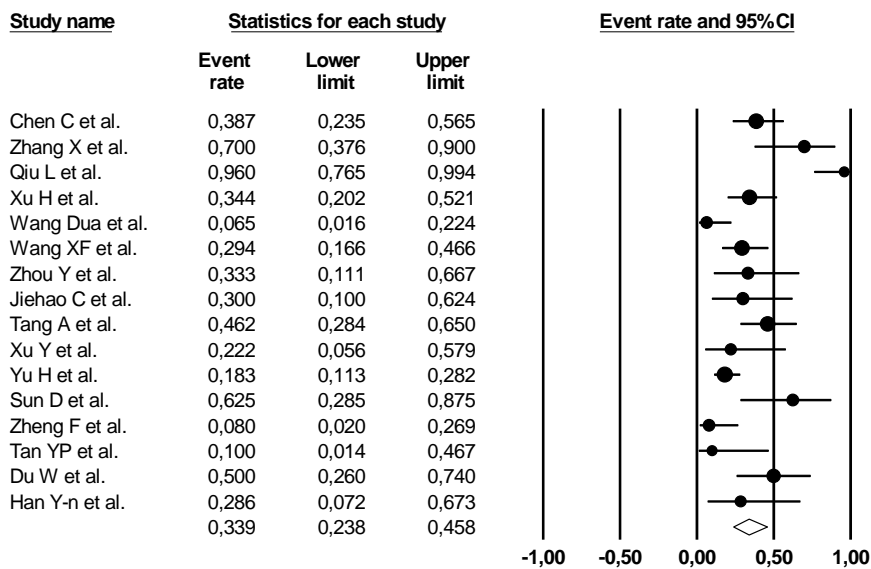
### High PCT



### High ESR

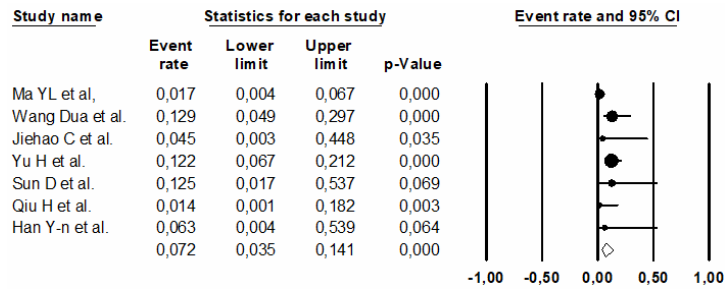


### High LDH

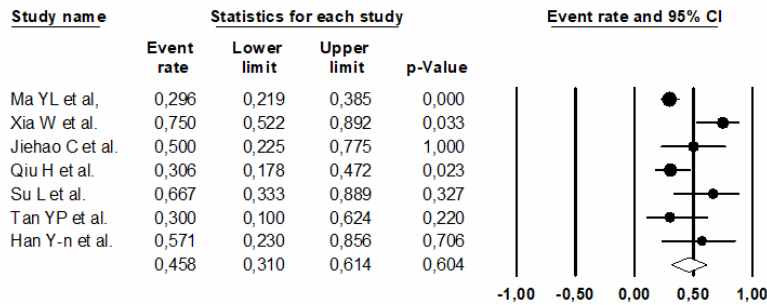


Supplementary Figure 1 continued...

### High Creatinine

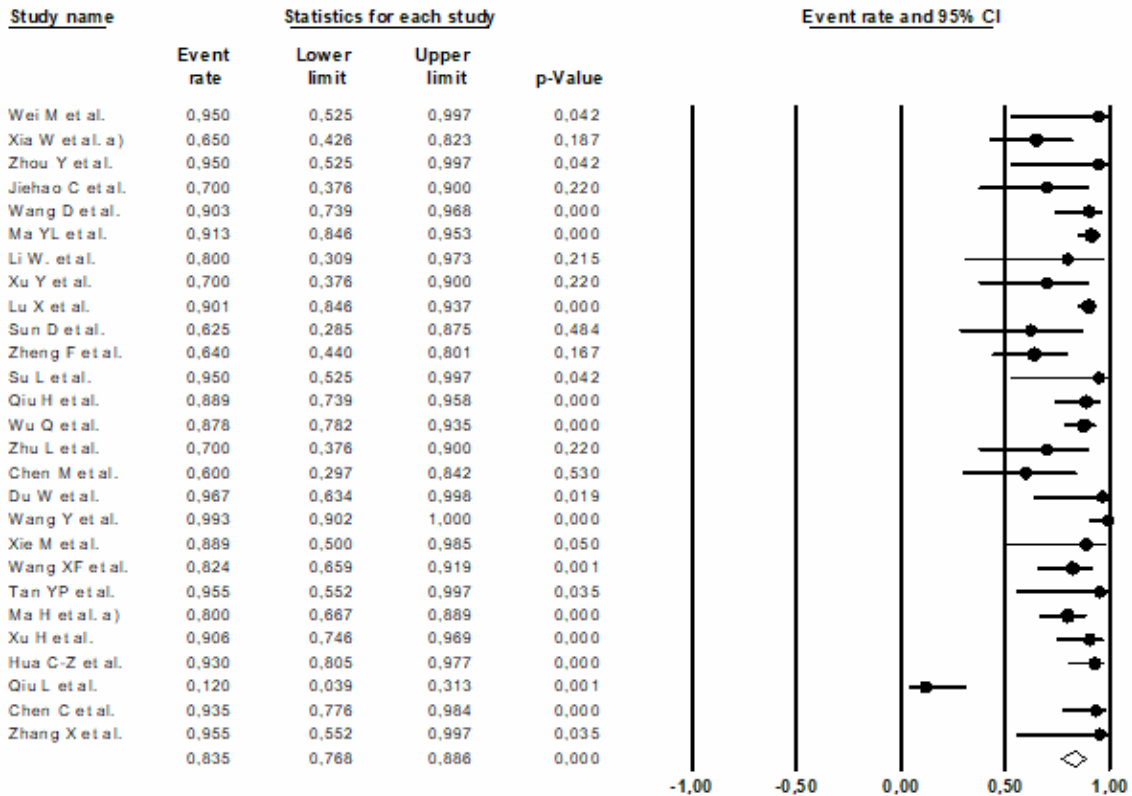


### High CK



### Exposure setting

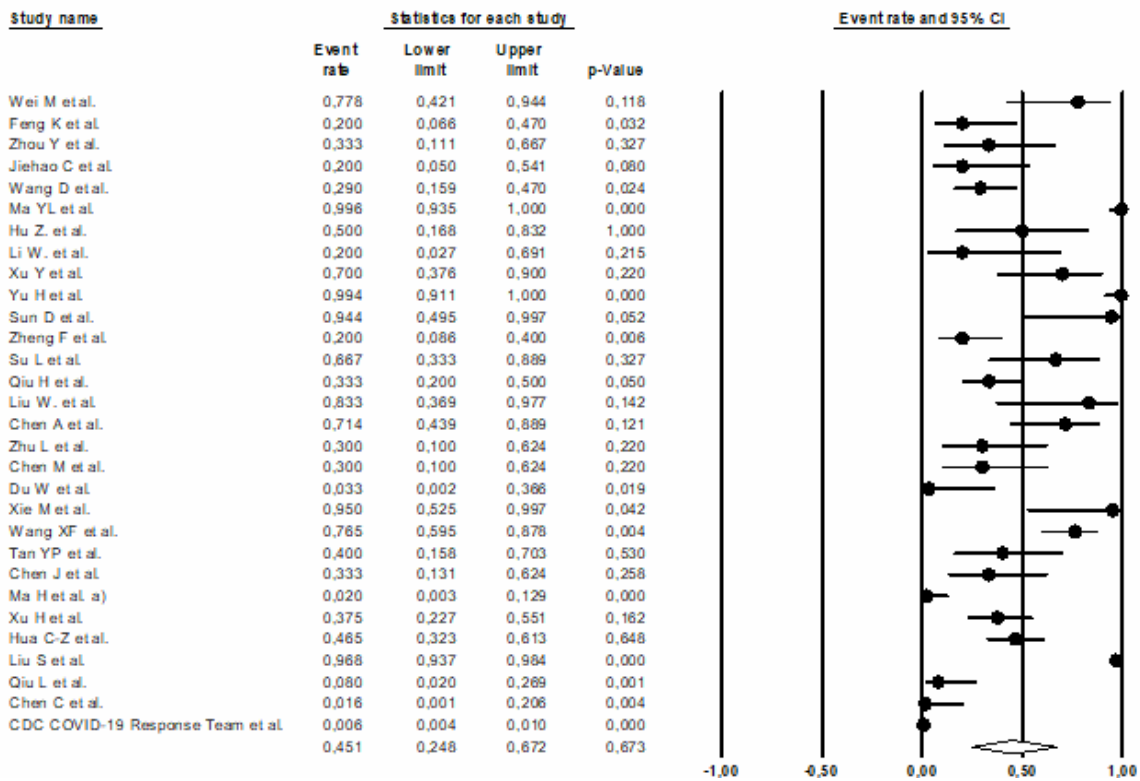
#### Household



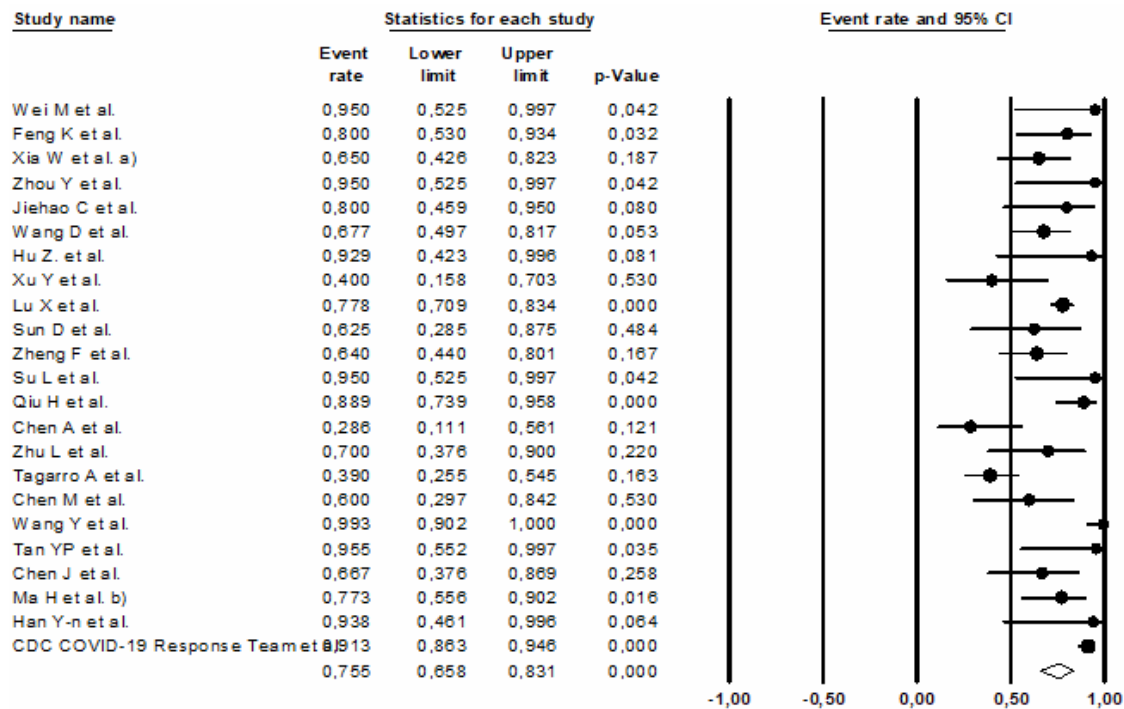


Supplementary Figure 1 continued...

**Epidemic area**



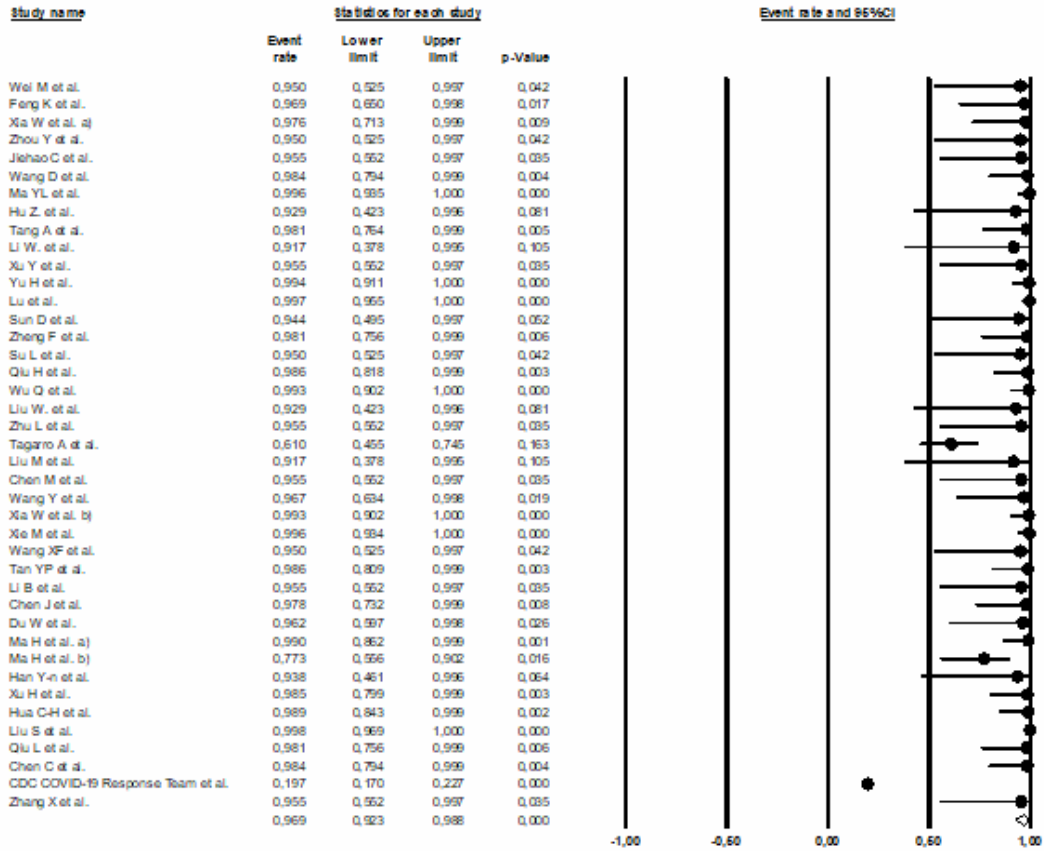
**Contact with index case**



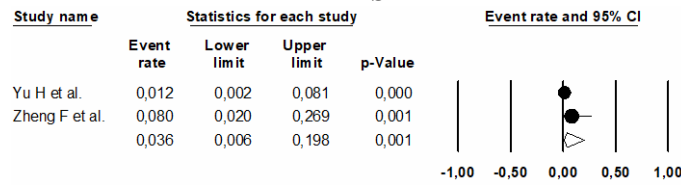
Supplementary Figure 1 continued...

**Complications**

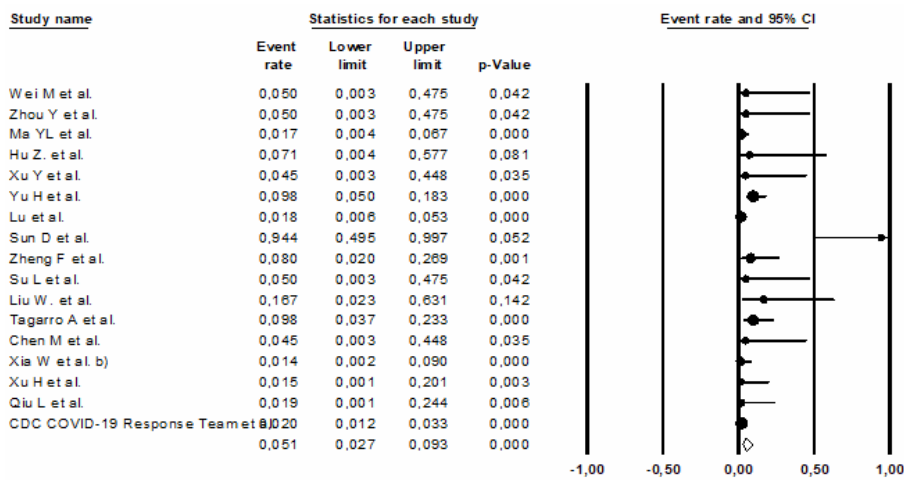
**Hospitalization**



**ARDS**

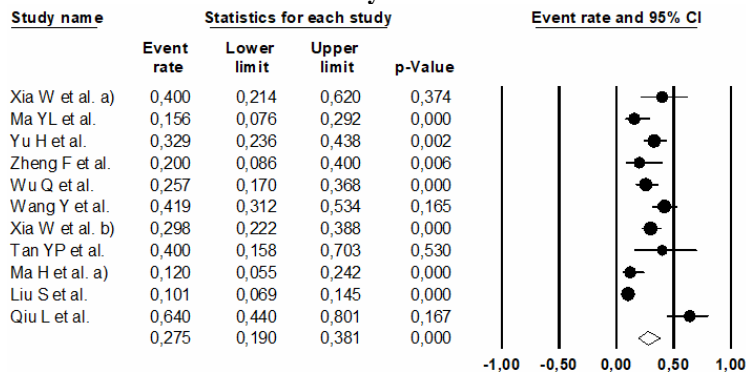


**ICU**

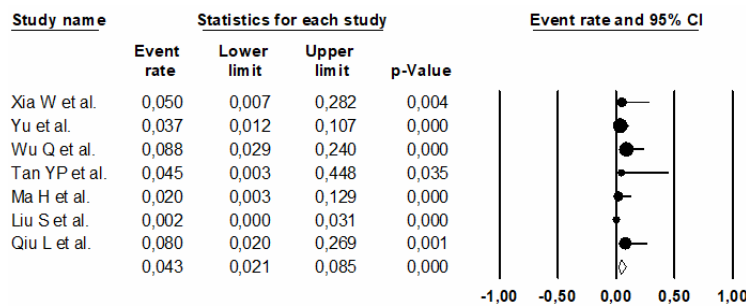


Supplementary Figure I continued...

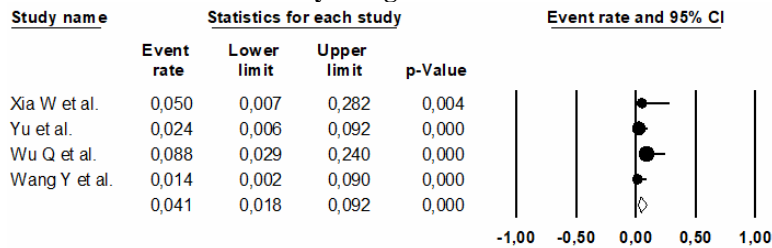
**Secondary infections**



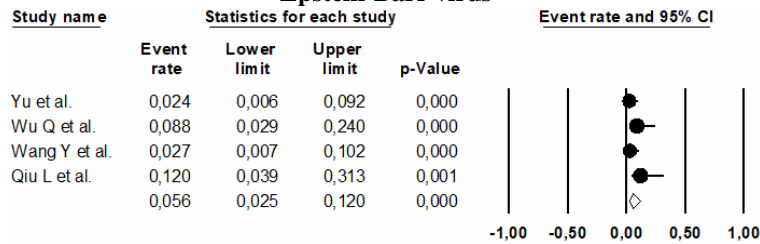
**RSV**



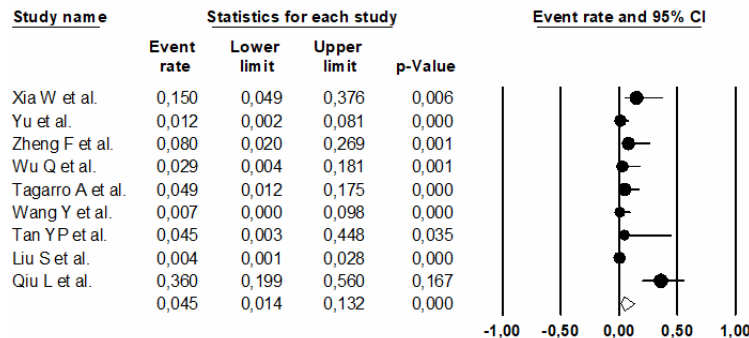
**Cytomegalovirus**



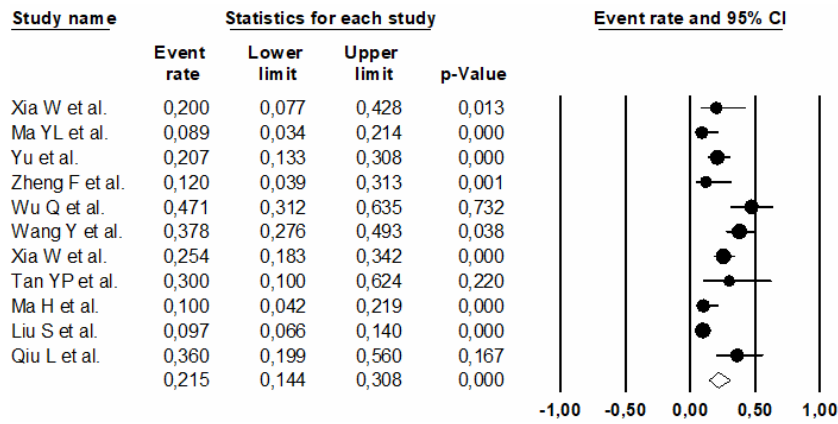
**Epstein-Barr virus**



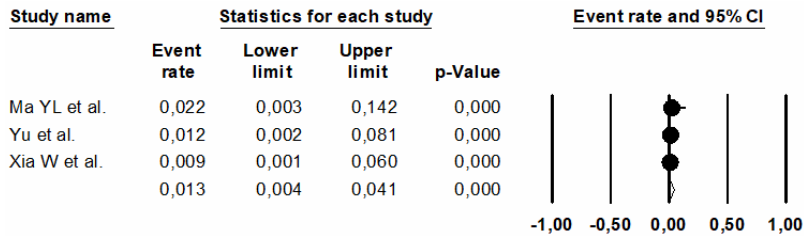
**Influenza virus**



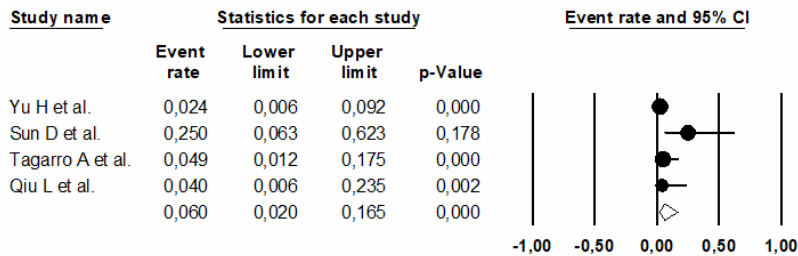
**Mycoplasma**



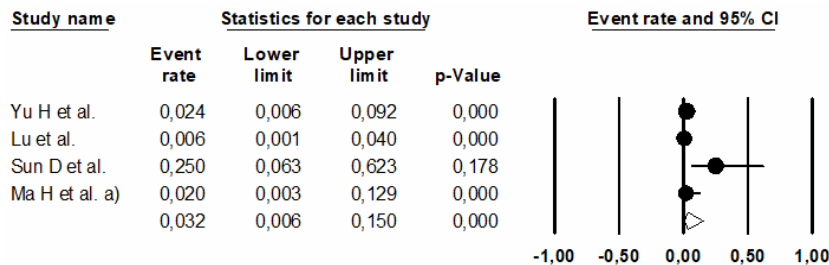
**Other bacteria**



**Septic chock**

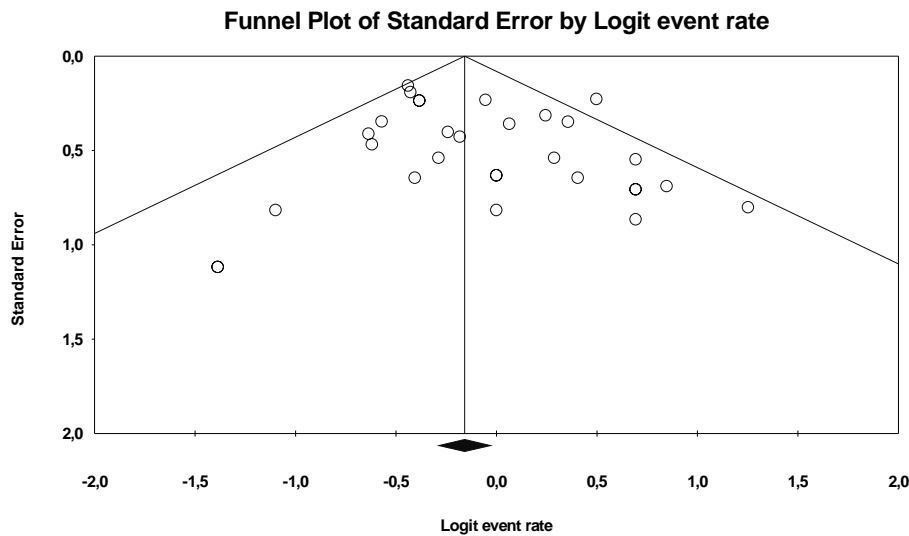


**MODS**



**Supplementary Figure 1:** Forest plots of comparisons of this meta-analysis.

CRP - C-reactive protein; PCT - procalcitonin; ESR - erythrocyte sedimentation rate; AST - aspartate transaminase; ALT - alanine transaminase; LDH - lactate dehydrogenase; CK - creatine kinase; ICU - intensive care unit; ARDS - acute respiratory distress syndrome; RSV - respiratory syncytial virus; MODS - multi-organ dysfunction syndrome.



Supplementary Figure 2: Funnel Plot.

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