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Coronavirus Pandemic

Estimation of Incubation Period and Serial Interval for SARS-CoV-2 in Jiangxi, China, and an Updated Meta-Analysis

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Abstract
Introduction: This paper aims to estimate the incubation period and serial intervals for SARS-CoV-2 based on confirmed cases in Jiangxi Province of China and meta-analysis method.
Methodology: Distributions of incubation period and serial interval of Jiangxi epidemic data were fitted by "fitdistrplus" package of R software, and the meta-analysis was conducted by "meta" package of R software.
Results: Based on the epidemic data of Jiangxi, we found the median days of incubation period and serial interval were 5.9 days [IQR: 3.8 – 8.6] and 5.7 days [IQR: 3.6 – 8.3], respectively. The median days of the infectivity period at pre-symptomatic was 1.7 days [IQR: 1.1 – 2.4]. The meta-analysis based on 64 papers showed the pooled means of the incubation period and serial interval were 6.25 days (95% CrI: 5.75 – 6.75) and 5.15 days (95% CrI: 4.73 – 5.57), respectively.
Conclusions: Our results contribute to a better understanding of COVID-19 and provide useful parameters for modelling the dynamics of disease transmission. The serial interval is shorter than the incubation period, which indicates that the patients are infectious at pre-symptomatic period, and isolation of detected cases alone is likely to be difficult to halt the spread of SARS-CoV-2.

Key words: COVID-19; SARS-CoV-2; incubation period; serial interval; meta-analysis.

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Introduction
At the end of 2019 a cluster of unknown aetiology pneumonia cases emerged in Wuhan City, Hubei Province, China [1]. A few days later, Chinese scientists confirmed the pathogen of this outbreak was a novel coronavirus. In February 2020, the World Health Organization (WHO) named the disease as coronavirus disease-2019 (COVID-19) [2], and renamed the etiological agent as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [3]. Coronaviruses are enveloped positive-stranded RNA viruses, belonging to the family *Coronaviridae*. Analysis of full-genome sequencing and phylogenic shows that SARS-CoV-2 is a beta-coronavirus that belongs to the same subgenus as SARS virus but in different evolutionary branches. Previous studies indicated that fever, cough, dyspnea, and myalgia or fatigue were the most common signs and symptoms presented in SARS-CoV-2 infected patients [4-6]. Droplets, close contact and aerosol are three routes for SARS-CoV-2 transmission, especially the first two routes are mainly responsible for this COVID-19 pandemic [7]. Incubation period, serial interval, infectivity period of SARS-CoV-2 are critical attributes for disease forecasting, informing public health interventions, and are also important indicators for evaluating the ability of virus transmission. Although several individual studies had estimated those essential epidemiological parameters, the results were not conclusive [8]. The aim of this study was to clarify the incubation period and serial interval for SARS-CoV-2 for helping to deepen the understanding of the disease. In order to achieve this research purpose, we designed this study based on the epidemic data of Jiangxi province, China. Most of the patients were constantly exposed to infections, and we could not identify the precise time of infections. So, this paper used processing ideas of deleted data to estimate their incubation period and serial intervals, which were different to other studies. Meantime, we conducted a meta-analysis to quantitatively calculate the pooled mean incubation period and serial interval from several

studies, and carried out sensitivity analysis to assess the stability of our meta-analysis results.

Methodology

Epidemic data sources of Jiangxi province

Individual information of all the confirmed cases in Jiangxi province, including demographic information (age, gender, address etc.), dates of symptom onset, clinical severity and disease outcome, was obtained from the China Information System for Disease Control and Prevention (CISDCP) [9]. The medical experience, initial symptoms of COVID-19, exposure history, travel history and epidemiological linkage were obtained from the individual epidemiological investigation report (The database structure listed in Supplementary Table 1).

Definitions

Cases with a biological specimen, including respiratory specimen, stool specimen, tested positive by Real-time Reverse Transcription Polymerase Chain-reaction (real time RT-PCR) assay for SARS-CoV-2 were diagnosed as confirmed cases. The definition of clinical severity is described in the next paragraph. The serial interval was defined as the time between disease symptom onset of a case and that of its infector. The incubation period was defined as the time interval between date of symptom onset and date of exposure.

Clinical severity

Diagnostic criteria of clinical severity was fulfilled with the "novel coronavirus pneumonia diagnosis and treatment guidelines (7^{th} edition)" published by National Health Commission of People's Republic of China [1]. Briefly, 1) Mild: the clinical symptoms were mild, and no pneumonia manifests on images; 2) Moderate: with fever and respiratory tract symptoms, pneumonia is visible on images; 3) Severe: shortness of breath, or low oxygen saturation, or $Pa0_2$ / $Fi0_2 \leq 300$ mmHg; 4); Critical: Respiratory failure occurs and requires mechanical ventilation, shock occurs, combined with other organ failures requires ICU monitoring treatment.

Literature search strategy for systematic review

The Medline, PubMed, Embase, Web of Science, Google, medRxiv, bioRxiv, and Chinese databases of Wangfang, CNKI and Vip were searched (the last search was updated on 10 August 2020) using the search terms "COVID-19" or "SARS-COV-2" or "2019 NCOV", and "serial interval" or "incubation period". All searches were retrieved and their bibliographies were checked for other relevant publications. Review articles, and bibliographies of relevant identified studies were researched. Only published studies with full-text articles were included.

Data extraction

All the information was extracted and entered into a structured database by three public health physicians with a masters degree or above (Z.T, Z.Z, and X.G), and cross-checked.

Statistical analysis

Including incubation period, serial interval, and infectivity period before symptoms onset were fitted by "Weibull", "gamma", and "lognormal" parametric distributions, and selected the best fit. According to the minimum Akaike information criterion (AIC) and Bayesian Information Criterion (BIC), one thousand bootstrap simulations estimated confidence intervals (CrI) and interquartile range (IQR) for distributions. For cases with multiple exposures, we also considered the time lag between the time of first and last exposure as censored data. The statistical analysis of this part was carried out using "fitdistrplus" package of R software [10]. We used "meta" package of R software to estimate the pooled means of incubation period and serial interval, and assessed the publication bias as well as the sensitivity analysis. Due to some studies using median and IQR value for reporting the average incubation period and serial interval, this paper adopted the Wan`s mathematical method to estimate the mean value and standard deviation from the sample size, median, range and/or interquartile range [11]. For all statistical analyses were conducted in R version 3.6.

Ethics Approval

This study was a part of an emergency research with the aim to control the outbreak of COVID-19. Data collection and analysis of cases were determined by the Health Commission of the Jiangxi province, and approved by the Ethics Committee of Jiangxi Centre for Disease Prevention and Control (Approval number: Jiangxi Centre for Disease Prevention Ethics Approval #2020-01).

Results

Estimations from confirmed COVID-19 cases in Jiangxi province

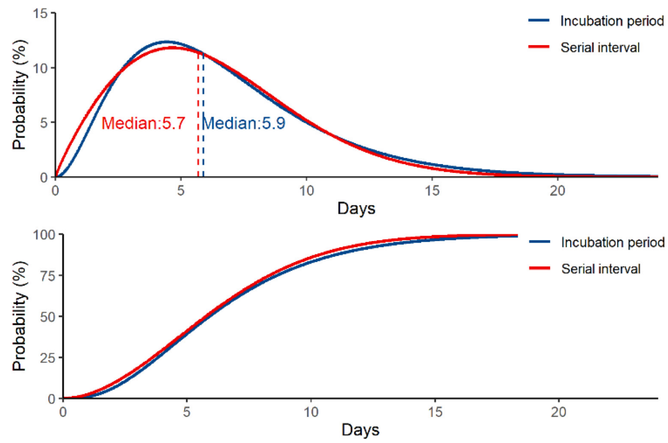
Demography characteristics of confirmed COVID-19 cases in Jiangxi province

The median age of the 930 patients was 43 years old [IQR: 33 – 53] in Jiangxi Province. Most patients were moderate (68%, 635), followed by mild (18%, 165), severe (10%, 97) and critical (4%, 33). The five most common symptoms were fever (66%), cough (42%), fatigue (16%), head discomfort (14%) and throat discomfort (11%). Meanwhile, the occurrent rates of those initial symptoms were not all significantly different in mild, moderate, severe and critical groups (Table 1). The demographic and clinical information of patients included in estimation analysis of the incubation period and serial interval was shown in Supplementary Table 2.

Estimation of incubation period and serial interval from confirmed COVID-19 cases in Jiangxi province

Three hundred and fifty-three confirmed cases with clear exposure time and date of illness onset were included in the incubation period analysis. We found that the incubation period was well approximated by a gamma distribution from our data (Table 2 and Supplementary Figure 1). The median incubation period was 5.9 [IQR: 3.8 – 8.6] days with 95th percentile of 13.3 days (Figure 1). Two hundred and eighty-four pairs of infectees and infectors with clear dates of illness onset were included in the serial interval estimations. We found the serial interval distribution of those 284 pairs was well approximated by a Weibull distribution from our data (Table 2 and Supplementary Figure 2). The median serial interval was 5.7 [IQR: 3.6 - 8.3] days (Figure 1).

Figure 1. Distributions of the incubation period and serial interval.



A) Probability distributions of the incubation period and the serial interval; B) Cumulative probability distributions of the incubation period and the serial interval.

Table 1. Demography and clinical characteristics of laboratory-confirmed COVID-19 cases in Jiangxi province, China by epidemic period.

Characteristics	Levels	Laboratory-confirmed COVID-19 cases in Jiangxi province (930)					p value
		TOTAL (100%, 930)	**Mild (18%, 165)**	**Moderate (68%, 635)**	**Severe (10%, 97)**	**Critical (4%, 33)**	
Age	All (Median, IQR)	43.00 [33.00, 53.00]	42.00 [29.00, 52.00]	42.00 [33.00, 50.00]	48.00 [40.00, 61.00]	66.00 [55.00, 73.00]	< 0.001
	Infants (< 1 y, %)	3 (0.32)	1 (0.61)	2 (0.31)	0 (0.00)	0 (0.00)	< 0.001
	Preschoolers (1-5 ys, %)	9 (0.96)	3 (1.82)	6 (0.94)	0 (0.00)	0 (0.00)	
	School-age children (6-12 ys, %)	4 (0.43)	3 (1.82)	1 (0.16)	0 (0.00)	0 (0.00)	
	Teenagers (13-17 ys, %)	14 (1.50)	6 (3.64)	8 (1.26)	0 (0.00)	0 (0.00)	
	Young adults (18-44 ys, %)	509 (54.44)	86 (52.12)	371 (58.43)	41 (42.27)	7 (21.21)	
	Middle-aged adults (45-59 ys, %)	262 (28.02)	49 (29.70)	175 (27.56)	31 (31.96)	6 (18.18)	
	Young seniors (60-74 ys, %)	108 (11.55)	14 (8.48)	63 (9.92)	18 (18.56)	13 (39.39)	
	Elderly seniors (75 ys, %)	26 (2.78)	3 (1.82)	9 (1.42)	7 (7.22)	7 (21.21)	
Gender	Male (%)	490 (52.69)	86 (52.12)	321 (50.55)	60 (61.86)	23 (69.70)	0.039
Initial symptom	**General symptoms**						
	Fever (%) #	580 (66.59)	97 (65.54)	391 (65.28)	71 (76.34)	21 (67.74)	0.209
	Cough (%) &	369 (42.37)	62 (41.89)	256 (42.74)	39 (41.94)	12 (38.71)	0.974
	Fatigue (%)	141 (16.19)	23 (15.54)	98 (16.36)	14 (15.05)	6 (19.35)	0.945
	Chills (%)	88 (10.10)	9 (6.08)	66 (11.02)	8 (8.60)	5 (16.13)	0.199
	Myalgia (%)	71 (8.15)	14 (9.46)	51 (8.51)	6 (6.45)	0 (0.00)	0.314
	Respiratory symptoms						
	Throat discomfort (%) $	93 (10.68)	14 (9.46)	51 (8.51)	6 (6.45)	0 (0.00)	0.245
	Runny nose (%)	38 (4.36)	6 (4.05)	29 (4.84)	2 (2.15)	1 (3.23)	0.671
	Chest tightness (%)	46 (5.28)	12 (8.11)	28 (4.67)	4 (4.30)	2 (6.45)	0.381
	Shortness of breath (%)	14 (1.61)	4 (2.70)	8 (1.34)	1 (1.08)	1 (3.23)	0.555
	Other symptoms						
	Head discomfort (%) *	119 (13.66)	20 (13.51)	80 (13.36)	18 (19.35)	1 (3.23)	0.141
	Abdomen discomfort (%) ^	30 (3.44)	3 (2.03)	21 (3.51)	6 (6.45)	0 (0.00)	0.209

#: fever including axillary temperature ≥ 37.3 °C; &: Cough including dry cough or phlegm producing cough; $: Throat discomfort including pharyngodynia or pharyngeal itching; *: Head discomfort including Headache or dizzy; ^ Abdomen discomfort including abdominal pain or diarrhea.

Based on 14 clusters with 21 infectees and 14 infectors in Jiangxi epidemic (Supplementary Figure 3), we found a Lognormal distribution well approximated the distribution of infectivity period before symptom onset. The median day was 1.7 days [IQR: 1.1 – 2.4] (Table 2 and Figure 2). This finding indicated that the patients might have been exposed to infection within 1 to 2 days before symptoms onset.

Estimation of the incubation period and serial interval by meta-analysis

Characteristics of papers included in this study

Based on the retrieval strategy of this study, we found a total of 71 relevant studies had reported the average (mean or median) incubation period or/and serial interval of SARS-COV-2 (Figure 3), and most were conducted in Chinese (71%) (Supplementary Table 3).

Quantitative data synthesis on the estimation of the incubation period and serial interval

Among those 71 papers, 64 papers which had reported average estimations with the CrI or IQR, and then were further included in the meta-analysis. As Table 3 shown, the pooled mean incubation period of 42 papers with 13,272 cases was 6.25 days (95% CrI: 5.75 – 6.75). The hierarchical analysis conducted by average indicators (mean and median), the pooled mean incubation periods were 6.14 days (95% CrI: 5.583 – 6.705) and 6.35 days (95% CrI: 5.63 – 7.07) respectively. The mean incubation period estimated in a location outside of China [5.00 days (95% CrI: 3.71 – 6.28)] was slightly shorter than in China of 6.56 days (95% CrI: 6.09 – 7.03). The pooled mean serial interval based on 34 papers with 3,366 infector-infectee pairs was 5.15 days (95% CrI: 4.73 – 5.57), and it has not

Figure 2. Distributions of the infectious period before symptom onset.

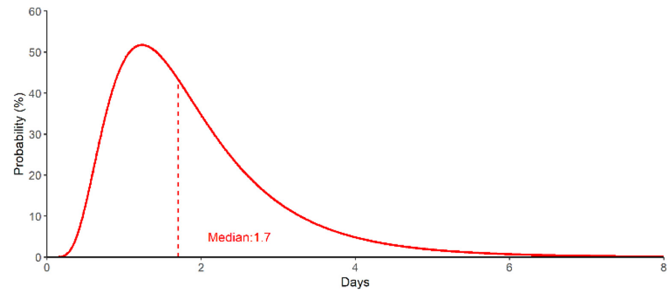


Figure 3. A flow diagram of the study selection process.

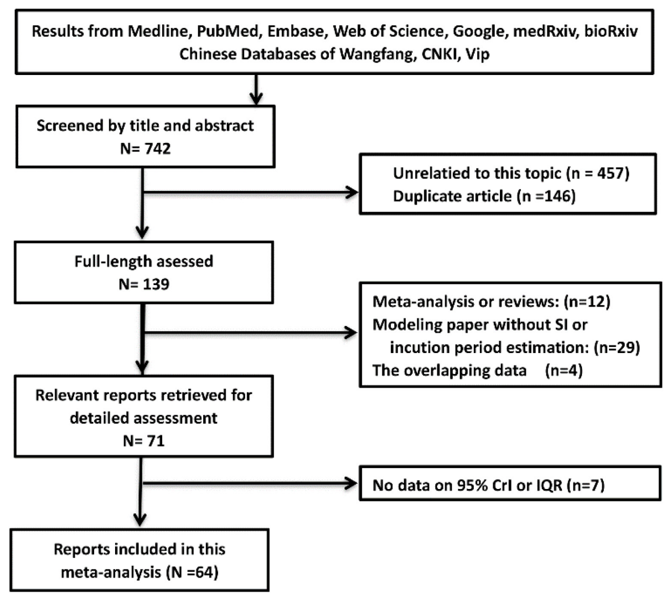


Table 2. Comparison of the three distributions of incubation period, serial interval and infectious period (boot = 1000).

Distributions	Mean ± SD	Median [IQR]	Parameters	AIC	BIC
Incubation period (days)					
Gamma	6.6 ± 3.8	5.9 [3.8, 8.6]	Shape = 3.04, Rate = 0.46	1213.98	1221.71
Weibull	6.8 ± 3.7	6.1 [3.7, 8.9]	Shape = 1.82, Scale = 7.51	1217.80	1225.54
Lognormal	5.5 ± 4.6	5.4 [3.6, 8.4]	Meanlog = 1.70, Sdlog = 0.62	1239.62	1247.35
Serial interval (days)					
Gamma	6.2 ± 3.6	5.5 [3.5, 8.1]	Shape = 2.85, Rate = 0.46	1286.49	1293.79
Weibull	6.2 ± 3.7	5.7 [3.6, 8.3]	Shape = 1.88, Scale = 6.99	1280.40	1287.70
Lognormal	6.4 ± 4.8	5.1 [3.2, 8.0]	Meanlog = 1.63, Sdlog = 0.67	1321.76	1329.06
Infectious period before illness onset (days)					
Gamma	1.9 ± 1.1	1.8 [1.2, 2.5]	Shape = 3.32, Rate = 1.71	56.25	58.34
Weibull	2.0 ± 1.1	1.8 [1.1, 2.7]	Shape = 1.79, Scale = 2.20	58.70	60.78
Lognormal	1.8 ± 1.0	1.7 [1.1, 2.4]	Meanlog = 0.50, Sdlog = 0.54	53.50	55.89

We used maximum likelihood estimation to find the optimal parameters for gamma, lognormal, and Weibull distributions fitted to the data. The fits of the three distributions were compared using Akaike information criterion (AIC) and Bayesian Information Criterion (BIC).

been modified in any subgroup stratified by average indicator or location. Forest plots of the pooled estimation of the mean incubation period and serial interval were shown in Supplementary Figures 3 - 7. Every single study involved in the meta-analysis was omitted after every test to investigate the influence of the individual dataset on the pooled means. The corresponding pooled means were relatively stable, indicating that our results were statistically robust (Supplementary Figure 8). Begg's and Egger's test were performed to assess the publication bias of the literature, and no publication bias was found (Table 3).

Discussion

Based on the epidemic data of Jiangxi and the meta-analysis of 42 papers, we found that the average incubation period was 5.9 days [IQR: 3.8 – 8.6] and 6.25 days (95% CrI: 5.75 – 6.75), respectively. This finding indicated that the incubation period of around 6 days for SARS-COV-2 is more extensive than that for SARS (4.0 days) [12] and MERS (5.0 days) [13]. This study showed 95% of cases would show symptoms within 13.3 days, which was consistent with other previous studies [14, 15], supporting that the currently used 2-weeks quarantine period in many countries is reasonable. Based on the epidemic data of Jiangxi and the meta-analysis of 34 papers, the estimation of the average serial interval was 5.7 days [IQR: 3.6 – 8.3] and 5.15 days (95% CrI: 4.73 – 5.57), respectively. Our findings showed that the serial interval was shorter than the incubation period, suggesting that the patients with SARS-CoV-2 might be infectious at the pre-symptomatic period [16, 17]. This finding is consistent with the clinical observations that a substantial portion of transmission may occur before symptoms onset [18]. Recently, we found the evidence of the infectivity period before symptom onset in 14 clusters of Jiangxi epidemic was 1.7 days [IQR: 1.1 – 2.4], which was shorter than Lauren`s studies [19]. His report showed the infection might occur on average around 2.6 days before symptoms onset of the infector (Tianjin, Singapore). Other studies also confirmed the pattern of transmission during the incubation period existed in clusters [20-22]. Pre-symptomatic transmission brought a challenge for prevention and control for COVID-19 epidemic, comprehensive tracking, and timely isolation of close contacts is one of the key measures to control the source of infection. We had plotted all the estimated average incubation period and serial interval with 95% CrI or IQR of those 71 published researches retrieved in this meta-analysis (Supplementary Figure 9). The average incubation period of 49 researches (including this paper) ranged from 2.87 to 10.90 days (Supplementary Figure 9 A). Nearly half of the researches reported the average incubation period was between 5 days to 7 days (Supplementary Figure 9 C), and 37.3% reported it was longer than 7 days. The average serial interval of 34 researches (including this paper) ranged from 1.90 to 7.60 days (Supplementary Figure 9 B). Nearly 71% of researches reported the average serial interval was less than six days (Supplementary Figure 9 D). More details of those 71 studies were summarized in Supplementary Table 3. The pooled mean incubation period calculated in this paper is more prolonged than Malahat`s meta-analysis (5.68 days) [23] and Zhang (5.35 days) [24]. The reason for this inconsistency may be due to the incomprehensiveness of literature inclusion in those two papers. In our meta-analysis, we had retrieved 41 papers with the incubation period reported, and 37.3% of papers revealed that the average incubation period was more than 7 days. The researched papers included in Zhang's meta-analysis were only 11 and Malahat's meta-analysis were only 19. Additionally, the papers

Table 3. Summary about meta-analysis on estimation of incubation period and serial interval.

Indictors	Stratification	N. of Papers	Estimations		Homogeneity		Publication Bias	
			Mean	95% CrI	I^2	P value]	p for Begg' test	p for Egger' test
Incubation period	All	42	6.248	5.745 - 6.750	99%	< 0.01	0.484	0.891
	Average (median)	22	6.351	5.631 - 7.070	99%	< 0.01	0.498	0.754
	Average (mean)	20	6.144	5.583 - 6.705	91%	< 0.01	0.364	0.569
	Location (China)	33	6.558	6.087 - 7.030	98%	< 0.01	0.621	0.724
	Location (outside of China)	9	4.998	3.710 - 6.276	95%	< 0.01	0.864	0.935
Serial interval	All	34	5.150	4.730 - 5.569	86%	< 0.01	0.694	0.612
	Average (median)	3	5.199	3.566 - 6.832	90%	< 0.01	0.354	0.145
	Average (mean)	31	5.150	4.710 - 5.589	86%	< 0.01	0.487	0.458
	Location (China)	23	5.014	4.734 - 5.294	92%	< 0.01	0.548	0.489
	Location (outside of China)	11	5.158	5.005 -5.311	81%	< 0.01	0.697	0.749

with the average incubation period of more than 7 days were only accounted for 10% and 15% in their meta-analysis, which may lead to underestimation of the incubation period estimations.

Conclusions

Our results contribute to a better understanding of COVID-19 and provide useful parameters for modelling the dynamics of disease transmission. The serial interval is shorter than the incubation period, which indicates the patients are infectious at pre-symptomatic period. The current practice of the two-week quarantine period in many regions is reasonable. Considering that there are still approximately 5% of cases with incubation periods of more than 13 days, it is necessary to maintain social distance and wear a mask for a certain period after the quarantine period.

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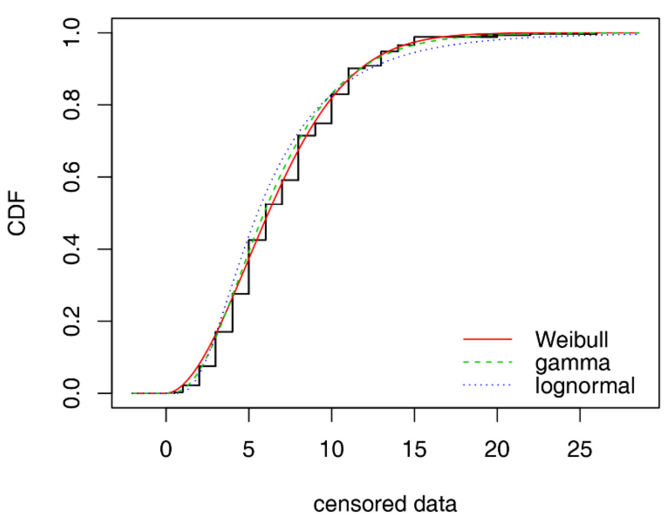
Conflict of interests: No conflict of interests is declared.

Annex – Supplementary Items

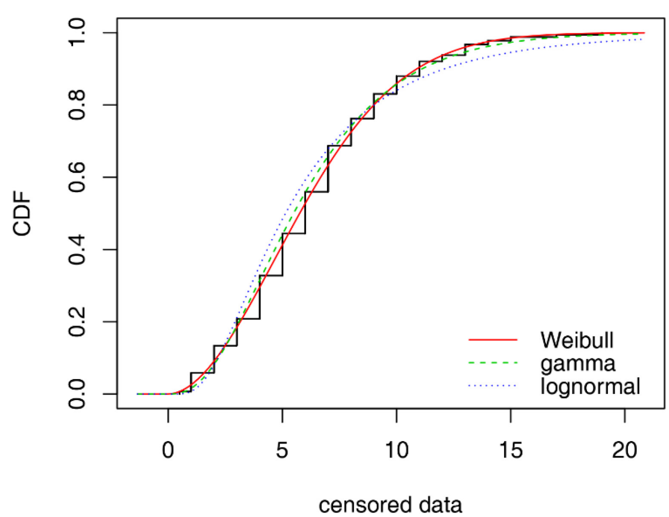
Supplementary Table 1. The standardized form used for data extraction in this study.

Information	Data source
Demography information	
Age	CISDCP and epidemiological investigation reports
Gender	CISDCP and epidemiological investigation reports
City of case detection	CISDCP
Date of case confirmed	CISDCP
Date of case quarantined	Epidemiological investigation reports
City of case onset	Epidemiological investigation reports
Medical experience	
Hospital name of case first visit	Epidemiological investigation reports
Date of first healthcare consultation	Epidemiological investigation reports
Date of hospitalization	CISDCP
Initial symptoms of case	Epidemiological investigation reports
Date of symptoms onset	Epidemiological investigation reports
Disease outcome	CISDCP
Disease severity	CISDCP
Exposure history and epidemiological linkage	
Dates of first exposure	Epidemiological investigation reports
Dates of last exposure	Epidemiological investigation reports
Type of exposure each time	Epidemiological investigation reports
Index infector of each exposure	Epidemiological investigation reports
Intergenerational relationship with the indicated case	Epidemiological investigation reports
Travel history to Hubei within 14 days before symptoms onset	
Residence in or visit	Epidemiological investigation reports
Date of arrival in Jiangxi	Epidemiological investigation reports

Supplementary Figure 1. Comparison of Empirical and theoretical cumulative density function of the incubation period.



Supplementary Figure 2. Comparison of Empirical and theoretical cumulative density function of the serial interval.



Supplementary Table 2. Demographic and clinical information of patients included in estimation analysis of the incubation period and serial interval.

Characteristics	Levels	TOTAL 930 (100%)	Patients included in incubation period analysis 353 (38%)	P value	Patients included in serial interval analysis 284 (31%)	P value
Age	All (Median, IQR)	43.00 [33.00, 53.00]	45.00 [35.00, 55.00]	0.114	45.00 [33.75, 57.00]	0.099
	Infants (< 1 y, %)	3 (0.32)	2 (0.57)	0.749	2 (0.70)	0.409
	Preschoolers (1-5 ys, %)	9 (0.96)	1 (0.28)		2 (0.70)	
	School-age children (6-12 ys, %)	4 (0.43)	2 (0.57)		2 (0.70)	
	Teenagers (13-17 ys, %)	14 (1.50)	4 (1.13)		4 (1.41)	
	Young adults (18-44 ys, %)	509 (54.44)	180 (50.99)		144 (50.70)	
	Middle-aged adults (45-59 ys, %)	262 (28.02)	104 (29.46)		80 (28.17)	
	Young seniors (60-74 ys, %)	108 (11.55)	47 (13.31)		40 (14.08)	
	Elderly seniors (75 ys, %)	26 (2.78)	13 (3.68)		10 (3.52)	
Gender	Male (%)	490 (52.69)	175 (49.58)	0.350	130 (45.77)	0.049
Initial symptom	**General symptoms**					
	Fever (%) #	580 (66.59)	204 (60.71)	0.064	164 (60.97)	0.105
	Cough (%) &	369 (42.37)	139 (41.37)	0.803	111 (41.26)	0.803
	Fatigue (%)	141 (16.19)	49 (14.58)	0.550	39 (14.50)	0.569
	Chills (%)	88 (10.10)	32 (9.52)	0.846	23 (8.55)	0.526
	Myalgia (%)	71 (8.15)	29 (8.63)	0.877	19 (7.06)	0.653
	Respiratory symptoms					
	Throat discomfort (%) $	93 (10.68)	42 (12.50)	0.425	31 (11.52)	0.781
	Runny nose (%)	38 (4.36)	13 (3.87)	0.824	13 (4.83)	0.875
	Chest tightness (%)	46 (5.28)	15 (4.46)	0.664	10 (3.72)	0.381
	Shortness of breath (%)	14 (1.61)	6 (1.79)	1.000	4 (1.49)	1.000
	Other symptoms					
	Head discomfort (%) *	119 (13.66)	42 (12.50)	0.661	32 (11.90)	0. 519
	Abdomen discomfort (%) ^	30 (3.44)	12 (3.57)	1.000	8 (2.97)	0.856
Clinical severity	Mild (%)	165 (17.74)	73 (20.68)	0.180	60 (21.13)	0.225
	Moderate (%)	635 (68.28)	245 (69.41)		196 (69.01)	
	Severe (%)	97 (10.43)	28 (7.93)		22 (7.75)	
	Critical (%)	33 (3.55)	7 (1.98)		6 (2.11)	

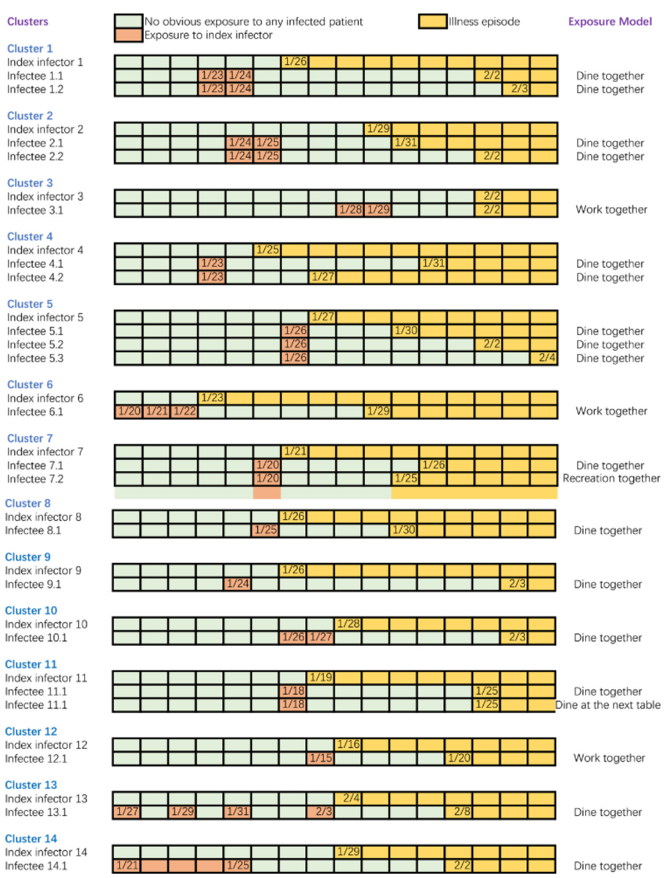
Supplementary Table 3. Summary of papers included in this Systematic review.

Author	Onset Period	Location	Reported IP (days) #		Reported SI (days) #		Included in meta-analysis
			N	Estimation	N	Estimation	
Ally BiZhu Jiang [1]	As of 2020/2/15	China (age > 65y)	22	10.90 [8.90, 13.50]			YES
		China (age < 65y)	110	7.00 [5.90, 8.10]			YES
Carlos A. Prete[2]	2020/2/15 - 2020/3/19	Brazil			65	2.97±3.29	YES
Cereda [3]	2020/1/14 - 2020/3/8	Italy			90	6.60 (0.70,19.00)	YES
Chenkai Zhao[4]	2020/1/16 - 2020/2/17	China	136	6.60 [4.0, 11.0]			YES
Chong You[5]	As of 2020/3/31	China	169	7.00 [4.50, 10.0]	198	4.60±5.55	YES
Chunzen Hua[6]	As of 2020/2/29	China	42	9.10 (7.98, 10.21)			YES
Dechuan Kong[7]	As of 2020/1/27	China	88	6.00 [3.5, 9.5]			YES
Enrico Lavezzo[8]	Not mentioned	Italy			120	7.20 (5.90, 9.60)	YES
F. Najafi[9]	2020/2/22 - 2020/3/29	Iran			21	5.71±3.89	YES
Guoqing Qian[10]	As of 2020/2/11	China	88	6.00 [3.0, 8.0]			YES
Haiyan Yang[11]	As of 2020/2/20	China	284	Median: 7.00			NO
Hansol Lee[12]	As of 2020/3/1	South Korea	47	3.00 (0.60, 8.20)			YES
HaoYuan Cheng [13]	2020/1/15 - 2020/2/26	Taiwan			12	7.00 (3.70, 13.20)	YES
Hiroshi Nishiura[14]	Not mentioned	Japan			28	4.00 [3.10, 4.90]	YES
Hyunjin Son [15]	2020/2/26 - 2020/3/24	Korea			28	5.54 (4.08, 7.01)	YES
Jantien A Backer [16]	As of 2020/1/29	China	88	6.40 (5.60, 7.70)			YES
Jiaqiang Liao [17]	2020/1/25 - 2020/2/18	China			12	1.90 (0.37, 6.16)	YES
Jiaye Liu[18]	As of 2020/2/25	China	58	5.00 [3.00, 8.00]			YES
Jing Jia [19]	As of 2020/2/23	China	44	Median: 6.4			NO
Jing Qin [19]	As of 2020/2/12	China	1211	8.62 (8.02, 9.28)			YES
Joseph T. Wu [20]	As of 2020/2/28	China			43	7.00 (5.80, 8.10)	YES
Juan Chen [21]	As of 2020/2/11	China	12	Median: 8.0			NO
Juanjuan Zhang [22]	2019/12/14-2020/2/17	China	49	5.20 (1.80, 12.40)	35	5.10 (1.30, 11.60)	YES
June Young Chun [23]	As of 2020/3/31	South Korea	72	2.87 [2.33, 3.50]			YES
Kai Wang [24]	As of 2020/2/27	China			27	5.90 (3.90, 9.60)	YES
Kaike Ping [25]	As of 2020/2/16	China	93	8.06 [6.89, 9.36]			YES
Ke Men [26]	As of 2020/2/5	China	59	5.84 (5.09, 6.59)			YES
Keisuke Ejima [27]	Not mentioned	Singapore, China, Germany, France, and Korea	31	5.23 [3.29, 8.22]			YES
Kin On Kwok[28]	2020/1/18 - 2020/2/8	China	26	4.58 (3.35, 5.85)			YES
Lauren C. Tindale [29]	2020/1/19 - 2020/2/26	Singapore	93	5.99 (4.97, 7.14)	57	4.0 (2.73, 5.57)	YES
		China	135	8.68 (7.72, 9.70)	73	5.0 (3.82, 6.12)	YES
Lijun Sun [30]	2020/1/20 - 2020/2/15	China	55	7.50 (5.00, 11.80)			YES
Liling CHAW [31]	2020/3/5-2020/4/5	Brunei			35	4.26 (2.84, 5.67)	YES
Lin Yang [32]	2020/1/20 - 2020/2/29	China	178	5.40 (4.80, 6.00)	152	4.60 (3.70, 5.50)	YES
Long V. Bui [33]	Not mentioned	Vietnam	19	6.40 (4.89, 8.50)			YES
Menghui Li [34]	2020/1/21 - 2020/2/29	China			337	5.80 (5.38, 6.24)	YES
Merle M Böhmer [35]	As of 2020/2/19	Germany	12	4.00 (2.00, 4.30)			YES
Moran Ki [36]	As of 2020/2/10	South Korea	15	Mean: 3.9	16	Mean: 6.60	NO
Natalie M. Linton [37]	As of 2020/1/31	China	52	5.00 (4.20, 6.00)			YES
Pei Wang [38]	Not mentioned	China	483	7.00 [4.00, 11.00]			YES
Pham Quang Thai [39]	As of 2020/3/1	Vietnam			33	3.24 (1.38, 5.10)	YES
Qianqian Song [40]	As of 2020/1/21	China	90	5.01 (4.31, 5.69)			YES
Qifang Bi [41]	2020/1/14 - 2020/2/12	China			48	6.30 (5.20, 7.60)	YES
Qinxue Shen [42]	2020/1/30- 2020/2/26	China	6	Median: 7.50			NO
Qun Li [43]	As of 2020/1/22	China	10	5.20 (4.10, 7.00)	10	7.5 (5.30, 19.00)	YES
Rachael Pung [44]	As of 2020/2/15	Singapore	36	4.00 [3.00, 6.00]			YES
Sheikh Taslim Ali [45]	2020/1/9- 2020/2/13	China	677	5.10 (4.70, 5.50)			YES
Shi Zhao [46]	As of 2020/2/15	China			21	4.40 (2.90, 6.70)	YES
Sijia Tian [47]	As of 2020/2/10	China	203	Median: 6.70			NO
Sofia K. Mettler [48]	2020/1/20 - 2020/4/7	South Korea			76	3.58 (2.62, 4.53)	YES
SR Patrikar [49]	Not mentioned	India	196	6.93 (6.11, 7.75)			YES
Stephen A. Lauer [50]	As of 2020/1/31	China	181	5.10 [4.50, 5.80]			YES

Author	Onset Period	Location	Reported IP (days) #		Reported SI (days) #		Included in meta-analysis
			N	Estimation	N	Estimation	
Steven Sanche [51]	As of 2020/1/30	China	24	4.20 [3.50, 5.10]			YES
Valentina Viego [52]	2020/3/20 - 2020/5/8	Argentina	15	7.90 (4.60, 11.10)	17	6.80 (4.00, 9.60)	YES
W. Guan [53]	As of 2020/1/29	China	291	4.00 [2.00, 7.00]			YES
Wei Qin [54]	2020/1/12 - 2020/2/21	China			42	6.50 [4.80, 8.20]	YES
Wei Xia [55]	As of 2020/2/26	China	124	4.90 [4.40, 5.40]	50	4.10±3.30	YES
Xi He [56]	2019/12/18 - 2020/3/5	China			77	5.80 (4.80, 6.60)	YES
Xiao Yu [57]	As of 2020/2/19	China	132	7.80 [5.00, 8.20]			YES
Xiaoke Xu [58]	2020/1/15 - 2020/2/29	China			34	5.00 (4.40, 5.50)	YES
Xiaoli Wang [59]	As of 2020/4/12	China	219	6.30 (6.00, 6.60)	76	7.60 [3.30, 11.00]	YES
Xiaorong Wang [60]	As of 2020/2/12	China	35	4.50 (3.00, 6.40)	9	5.2 (3.80, 6.80)	YES
Xiaoying Xia [61]	As of 2020/2/10	China	10	7.00 (5.39, 8.61)			YES
Xingqiang Pan [62]	As of 2020/2/20	China	18	6.00 (5.20, 6.91)			YES
Xiuquan Nie [63]	As of 2020/2/8	China	2907	5.00 [2.00, 8.00]			YES
Xue Jiang [64]	As of 2020/2/5	China	2015	Median: 7			NO
Ye Shen [65]	Mid-Jan to early Feb	China	539	7.00 [4.00, 12.00]			YES
Yousef M Alsofayan [66]	As of 2020/3/1	Saudi Arabia	309	Median: 6			NO
Yuhao Deng [67]	As of 2020/3/31	China	198	8.50 (7.22, 9.15)			YES
Zhanwei Du [68]	2020/1/21 - 2020/2/8	China			468	3.96 (3.53, 4.39)	YES
Zhanwei Du [69]	2020/1/20 - 2020/2/19	China			264	5.29 (4.72, 5.86)	YES
Zuopeng Xiao [70]	As of 2020/2/21	China	2555	8.98 [7.98, 9.90]			YES

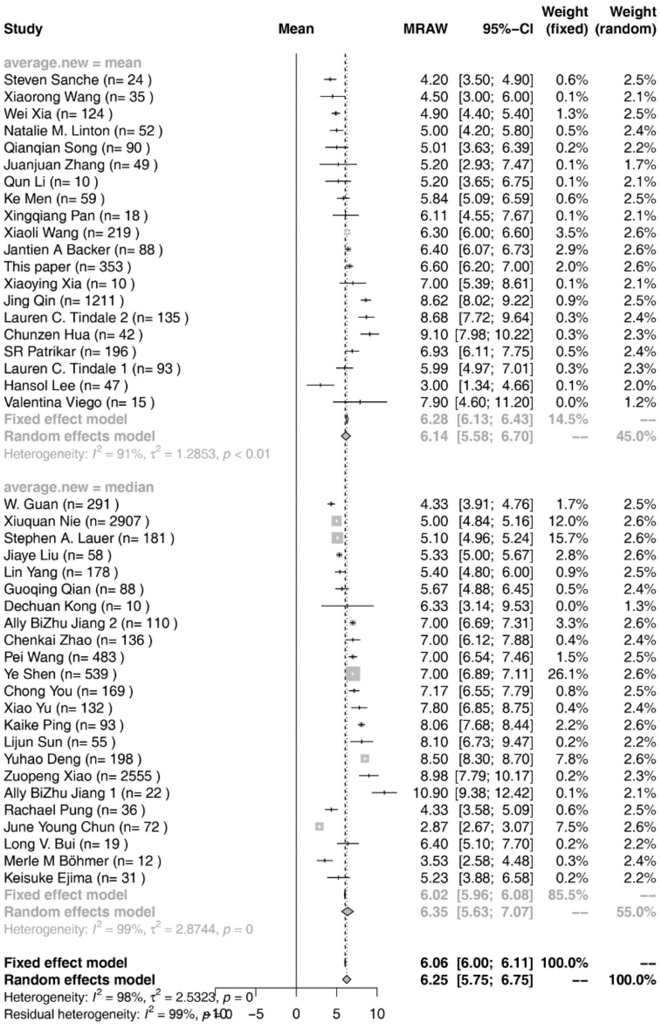
IP: Incubation period; SI: serial interval; average estimation was expressed as median [IQR] or mean (95%CrI) or mean ± SD.

Supplementary Figure 3. Estimation of the infectivity period before illness onset from 14 clusters in Jiangxi COVID-19 epidemic.

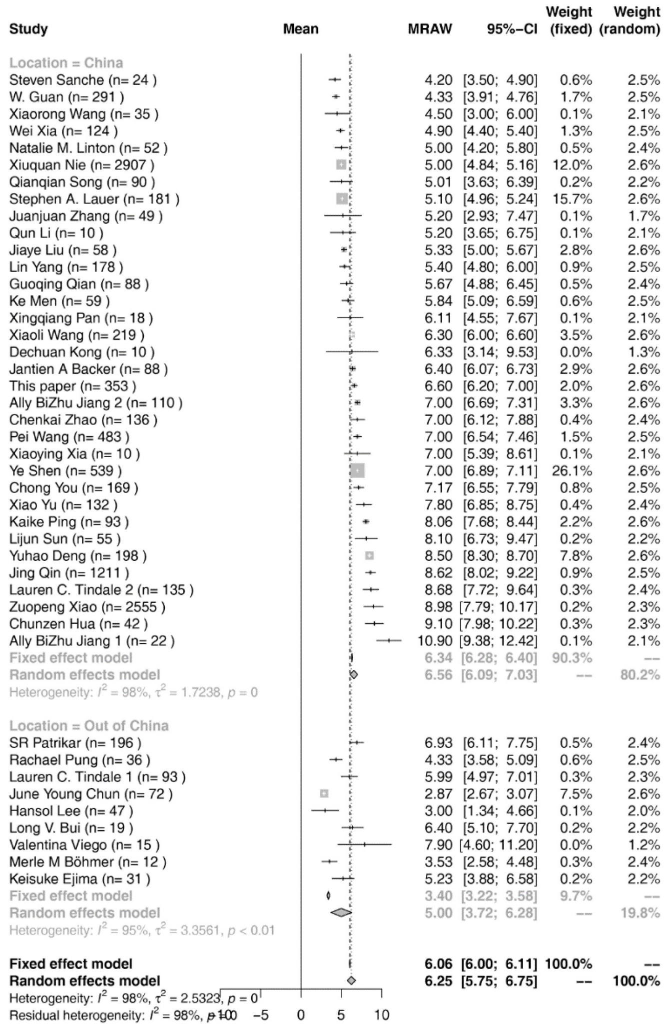


The time lag between the dates of symptom onset of index infectors and the dates of secondary cases exposed to corresponding index infectors within clusters. The model of cluster included dine together, work together and reaction together. Numbers in the boxes represent the date of symptom onset or exposure date to corresponding index infectors.

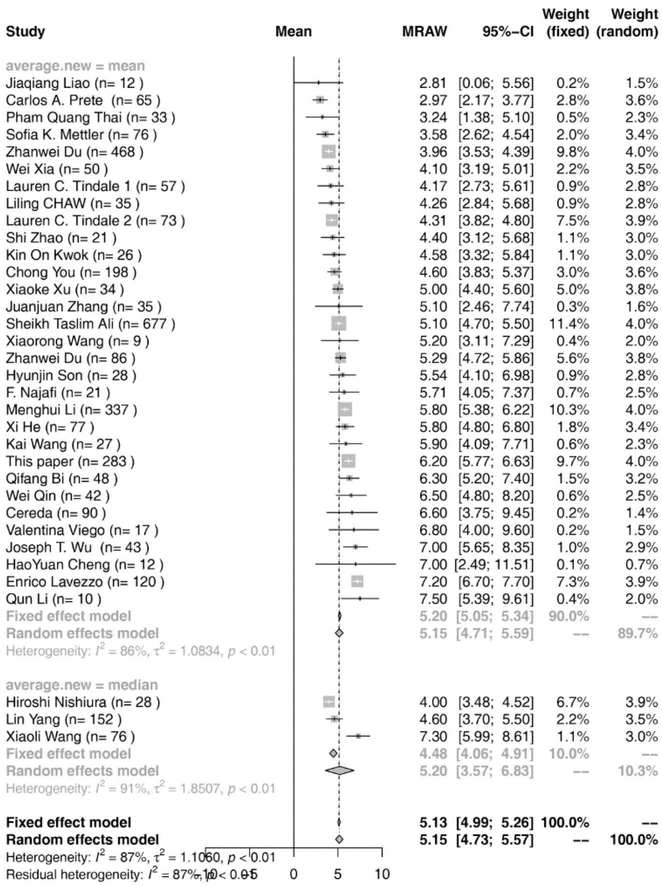
Supplementary Figure 4. Forest plot of pooled estimation of the average incubation period (Stratified by average indicators of researches used).



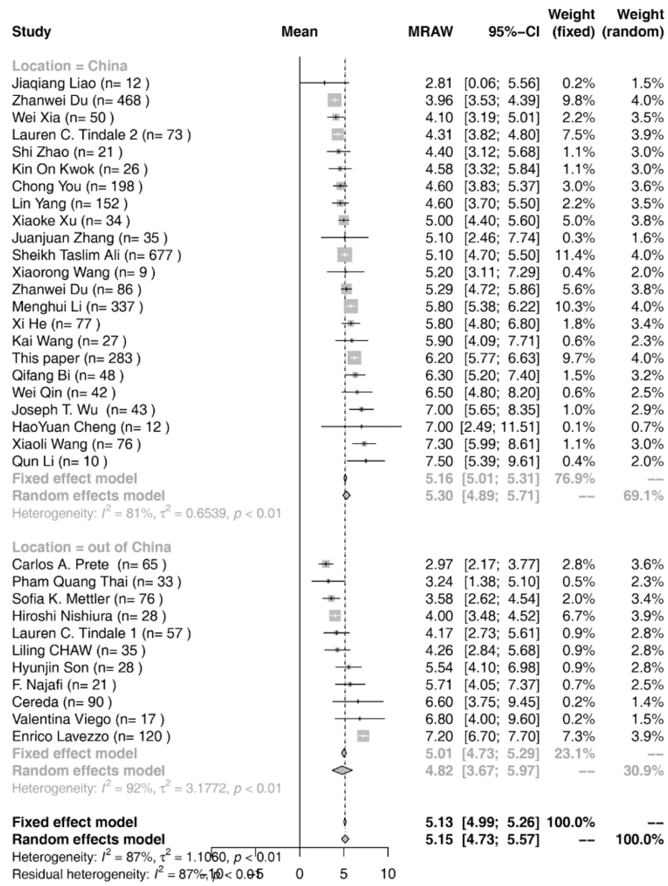
Supplementary Figure 5. Forest plot of pooled estimation of the average incubation period (Stratified by location of researches carried out).



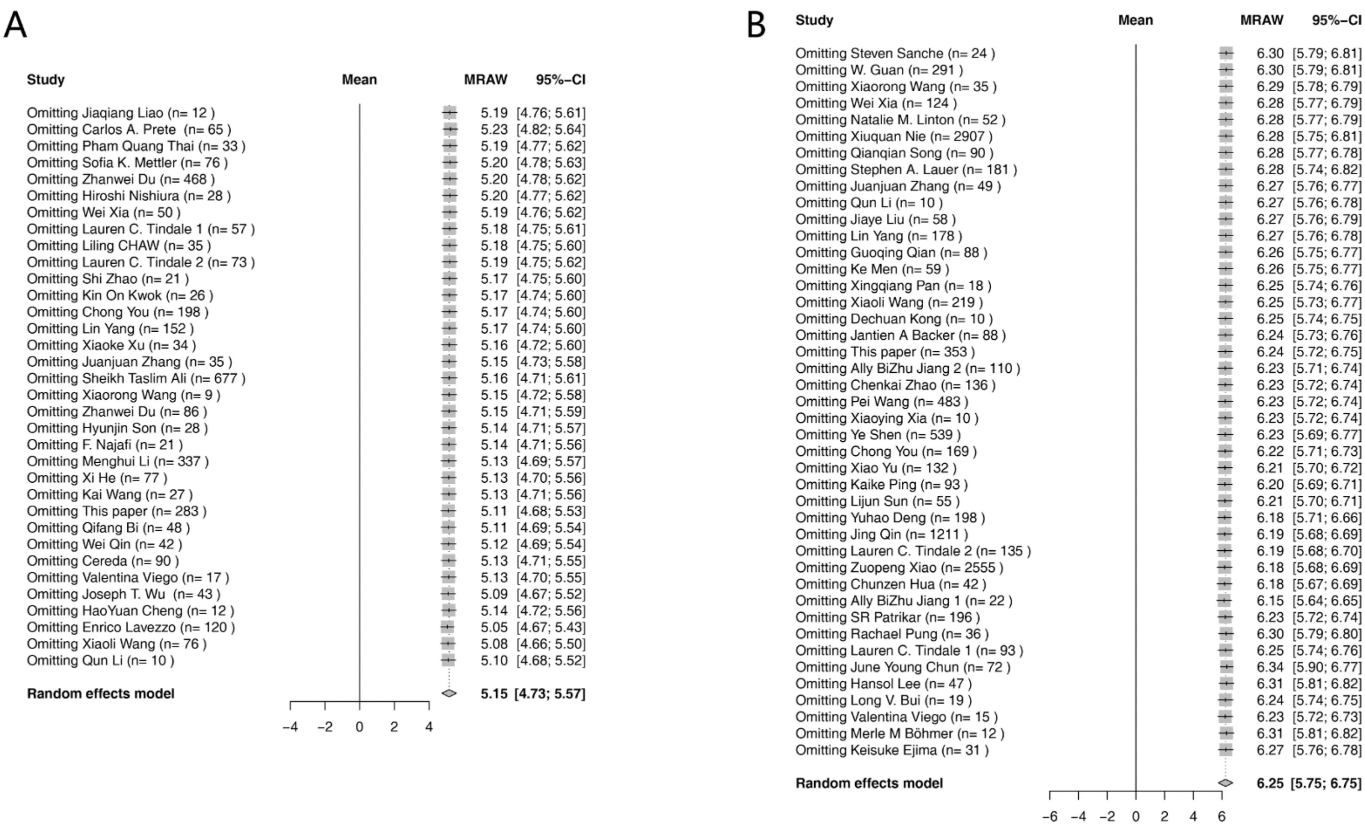
Supplementary Figure 6. Forest plot of pooled estimation of the average serial interval (Stratified by average indicators of researches used).



Supplementary Figure 7. Forest plot of pooled estimation of the average serial interval (Stratified by location of researches carried out).

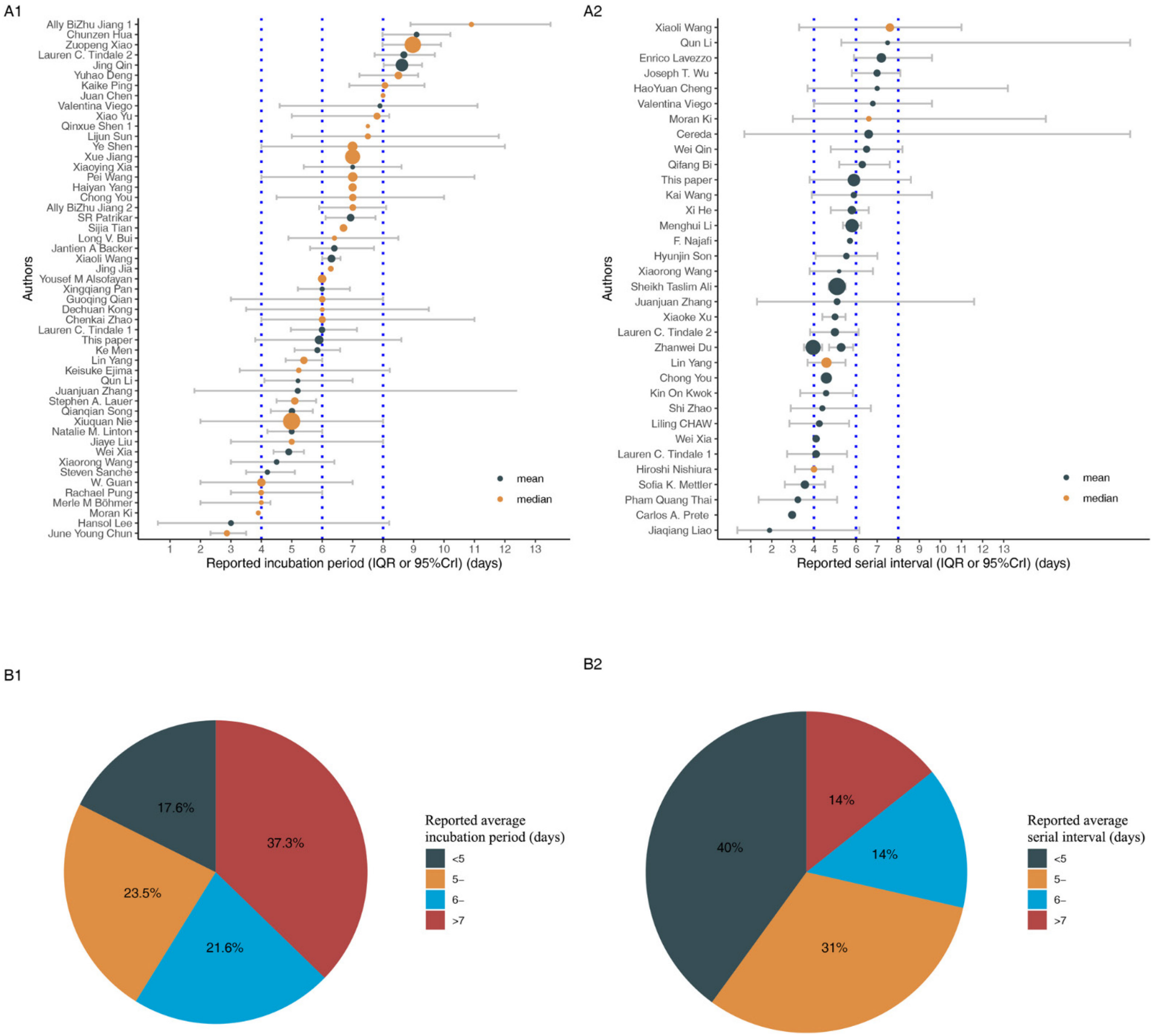


Supplementary Figure 8. Forest plot of influence investigation of the individual dataset on the pooled means.



A) Influence investigation of individual dataset on the pooled serial interval; B) Influence investigation of individual dataset on the pooled incubation period.

Supplementary Figure 9. Average incubation period and serial intervals reported from 71 published researches in this meta-analysis.



A) Reported mean or median incubation period of papers included in this meta-analysis; B) Reported mean or median serial interval of papers included in this meta-analysis; C) constituent ratio of reported average incubation period; D) constituent ratio of reported average serial interval.