Did Patients With COVID-19 Receive Timely Treatment in the Early Epidemic? A Systematic Review and Meta-analysis

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Abstract

Background: COVID-19 showed a significant difference in case fatality rate between different regions at the early stage of the epidemic. In addition to the well-known factors such as age structure, detection efficiency, and race, there was also a possibility that medical resource shortage caused the increase of the case fatality rate in some regions.

Methods: Medline, Cochrane Library, Embase, Web of Science, CBM, CNKI, and Wan fang of identified articles were searched through 29 June 2020. Cohort studies and case series with duration information on COVID-19 patients were included. Two independent reviewers extracted the data using a standardized data collection form and assessed the risk of bias. Data were synthesized through description and analysis methods including a meta-analysis.

Results: A total of 109 articles were retrieved. The time interval from onset to the first medical visit of COVID-19 patients in China was 3.38±1.55 days (corresponding intervals in Hubei province, non-Hubei provinces, Wuhan, Hubei provinces without Wuhan were 4.22±1.13 days, 3.10±1.57 days, 4.20±0.97 days, and 4.34±1.72 days, respectively). The time interval from onset to the hospitalization of COVID-19 patients in China was 8.35±6.83 days (same corresponding intervals were 12.94±7.43 days, 4.17±1.45 days, 14.86±7.12 days, and 5.36±1.19 days, respectively), and when it was outside China, this interval was 5.27±1.19 days.

Conclusion: In the early stage of the COVID-19 epidemic, patients with COVID-19 did not receive timely treatment, resulting in a higher case fatality rate in Hubei province, partly due to the relatively insufficient and unequal medical resources. This research suggested that additional deaths caused by the out-of-control epidemic can be avoided if prevention and control work is carried out at the early stage of the epidemic.

PROSPERO registration number CRD42020195606.

Background

In December 2019, the COVID-19 epidemic broke out in Wuhan, China, and rapidly spread around the world.[1–3] By the end of 2020, the total number of confirmed cases worldwide had exceeded 80.64 million, and the death toll had exceeded 1.76 million.[4] Currently, no specific medicine for the treatment of COVID-19 has been found globally.[5, 6] The WHO recommended that the treatment of COVID-19 should be mainly based on supportive treatment, including oxygen therapy for severe patients and those at risk of serious diseases, and more advanced respiratory support for critically ill patients.[7] Timely hospitalization is a significant factor in prognosis and the risk of disease and death, especially patients with underlying diseases or the elderly.[8–10] The timely treatment mainly depends on whether the medical resources in the area where patients live are sufficient, meanwhile, to a certain extent, it also depends on the patient's willingness to pay a medical visit.[11, 12] Through the collection and analysis of articles, this research

compared the time intervals from onset to first medical visit and onset to the hospitalization of COVID-19 patients in different regions and assessed the supply and demand status of medical resources, to provide an evidence-based reference for authorities to guide people's health-related behaviors during epidemics, to stem the spread of the disease, reduce health care burden and death rate.

Methods

Search strategy

This research was implemented following rapid review and PRISMA guidelines. This rapid review was registered in PROSPERO on June 29, 2020, with the protocol of CRD42020195606. Articles publishing before June 29, 2020, that reported medical information of COVID-19 patients were included in this research, the following databases were comprehensively searched, including the Cochrane Library, MEDLINE (via PubMed), EMBASE, Web of Science, CBM (China Biology Medicine disc), CNKI (China National Knowledge Infrastructure), and Wan fang database. The following search formulas were used in this research, including (“COVID 19” OR “COVID-19” OR “SARS-CoV-2” OR “2019 novel coronavirus” OR “2019-nCoV” OR “2019-CoV” OR “coronavirus disease 2019” OR “coronavirus disease-19” OR “Novel coronavirus” OR “2019-novel coronavirus”) AND (“symptom onset” OR “illness onset” OR “first symptom” OR “onset of illness”) AND (“admission” OR “hospitalization”) AND (“see a doctor” OR “first medical visit” OR “first medical care” OR “visit hospital”). Besides, World Health Organization (WHO), Chinese Center for Disease Control and Prevention (CCDC), National Health Commission of the People’s Republic of China, USA National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov), International Standard Randomized Controlled Trial Number (ISRCTN) registry, Google Scholar, the preprint servers medRxiv (https://www.medrxiv.org/) and bioRxiv (https://www.biorxiv.org/), and Social Science Research Network (SSRN, https://www.ssrn.com/index.cfm/en/) were also included as retrieval sources. The retrieval strategy for this research was reviewed by information experts.

Inclusion and exclusion criteria

Case series and cohort studies that reported the medical visit time of COVID-19 patients were included. Abstracts, case reports, letters, news, guidelines, comments, and articles that were unable to obtain all relevant data or full texts were excluded. There were no restrictions on language or publication status.

Article screening

After deleting duplicates in all the retrieved articles, two reviewers (P Du and Q Shi) used EndNote to independently screen these articles in two steps. The first step was to filter the title and summary using predefined criteria. The second step was to review the articles that were likely to meet the requirements by reading the full text and determine whether they will be finally included. The reasons for the exclusion of all unqualified articles were recorded, PRISMA flowcharts were used to record the process of article screening, and screening objections were resolved through discussion or consultation with a third reviewer (X Luo).

Data extraction

Data were extracted independently by two reviewers (P Du and Q Shi) using a standardized data collection form, and all objections were resolved through discussion or consultation with a third reviewer (X Luo). The third reviewer was responsible for checking the consistency and accuracy of the data. Data extraction includes the following three aspects: 1) Basic information (title, author, country, date of publication, research type), 2) Patient information (number, gender, age, disease type, sample size, grouping variables), 3) Result information (the interval from first symptom onset to the first medical visit, the interval from the first symptoms onset to the first hospitalization, clinical outcome).

Data analysis

The 1st time interval was defined as the interval from the first symptom onset to the first medical visit of COVID-19 patients, and the 2nd time interval was defined as the interval from the first symptoms onset to the first hospitalization of COVID-19 patients. Exposure history was defined as COVID-19 patients with a history of travel to the source of the outbreak or a history of exposure to confirmed cases. The duration of viral shedding was defined as the number of days from the onset of the symptoms until the successive negative detection of SARS-CoV-2 RNA. In the retrieval articles, the statistics of the 1st and 2nd time intervals were described by mean ± standard deviation or median (interquartile range), while some research only provided point estimates, maximum and minimum values. This research used an estimation method proposed by Luo[13] and Wan[14] et al. to unify the time intervals of all research as mean ± standard deviation, and the sample size weighting method was used to calculate the weighted mean of each time interval sample. Linear or nonlinear regression was used to fit the trend of time interval of patients in different periods. The patients were divided into two groups according to the severity of the disease: common patients (mild and moderate cases) and severe patients (severe and critical cases) in the meta-analysis. Heterogeneity was defined as $P < 0.05$ and $I^2 > 50\%$.[15] Mean difference (MD) with 95% confidence intervals (CI) was used as the effect size. Sensitivity analysis was conducted by comparing the difference between the fixed-effect model and the random effect model. Two-sided P values < 0.05 were considered statistically significant. All statistical analysis was implemented on RStudio (Version 1.2.5033).

Assessment of risk of bias

Two reviewers (P Du and Q Shi) independently assessed the risk of bias for each research, resolved objections by discussion, and consulted a third reviewer (X Luo) if necessary. Appropriate assessment tools were selected to assess the risk of bias according to research types in the article: The Newcastle-Ottawa scale which consists of 8 parts, with each part using a star rating, should be used for the cohort study.[16] The more the stars, the lower the risk of bias. Furthermore, for a case series study, methodological assessment tools recommended by the National Institute for Excellence in Health and Care (NICE) should be used.[17] The risk of bias was assessed against 8 criteria, and the results were summarized using a scoring method with 1 point for “Yes” and 0 point for “No”. The higher the scores, the lower the risk of bias.

Quality of evidence assessment

Two reviewers (P Du and Q Shi) used GRADE guidelines[18, 19] to independently assessed the quality of evidence and used GRADEpro to create a form, in which the results of each research included in the meta-analysis were classified for evidence quality. The overall quality was downgraded based on 5 factors (risk of bias, inconsistency, imprecision, indirectness, and publication bias) and upgraded based on 3 factors (large effect size, dose-effect relationship, and negative bias). The overall quality of evidence was classified as high, medium, low, or very low, reflecting the trust degree that the effect estimates were accurate.

Results

Article research results

After a systematic retrieval, 2, 435 articles were retrieved for the first time. After deleting duplicates, 109 articles were finally included in the evaluation through screening titles, abstracts, and full texts, including 103 case series and 6 cohort studies, and the patient information of 101 articles (92.7%) was collected before April 2020. The processes of article retrieval and screening were shown in Fig. 1. A total of 18, 777 patients were included in this research, including 8, 405 females (44.8%), 9,671 males (51.5%), and 701 patients (3.7%) with unknown gender. China contributed 100 (91.7%) articles, 38 (34.9%) of which were from Hubei province (the most affected province in China). The remaining 9 (8.3%) articles were from abroad shown in Supplement I (2 articles from Singapore,[2, 20] 2 articles from Korea,[21, 22] 2 articles from Germany[23], 2 article from the United States[24, 126], 1 article from Japan[24] and 1 article from French[125]).

This research intended to assess whether the patient had received treatment in time by collecting the 1st and 2nd time intervals. Among the included 109 articles, 30 articles only reported the 1st time interval, 73 articles only reported the 2nd time interval, and 6 articles reported both time intervals. The included articles' assessment of the risk of bias was provided in Supplement II (Tables S1-S2).

Time interval from onset to the first medical visit

Figure 2 showed the 1st time interval in 36 articles, of which 10 articles (27.8%) were from Hubei Province and 26 articles (72.2%) were from non-Hubei provinces. The 1st time interval was not mentioned in the included articles outside China. The 1st time interval was mostly concentrated in about 5 days, the minimum time interval was 0 (median) days (an article from Shenyang, China[49], 65.38% (17 out of 26) of COVID-19 patients paid a medical visit on the day of onset), the maximum time interval was 7.52 (mean) days (an article from Hubei Province researching on severe patients[106]). In terms of the 1st time interval, no significant difference was found between patients from Hubei province and non-Hubei provinces.

Part of the articles made statistics of COVID-19 patients' 1st time interval in groups according to the severity of the disease, exposure history, time around Wuhan's cordon sanitaire, etc. Firstly, 6 articles grouped patients according to the severity of the disease, and the results showed that the longer the 1st

time interval, the worse the patient's health condition. However, a research of Wuhan showed that the 1st time interval in severe patients (7.52 days) was longer than that in common patients (5.35 days), whereas the 1st time interval of critically ill patients was shorter (4.8 days).[106] Secondly, an article from Shenyang grouped patients according to whether they had an exposure history, and the result showed that patients without an exposure history (4 days) had a longer 1st time interval compared with those who had one (0 days).[49] Thirdly, an article from Hunan province indicated that the 1st time interval of patients after January 23 (cordon sanitaire day of Wuhan) (1 day) was shorter than that before January 23 (3 days).[28]

Time interval from onset to hospitalization

Figure 3 showed the 2nd time interval in 70 articles, of which 31 (44.3%) articles were from Hubei Province (27 articles from Wuhan), and 39 (55.7%) articles were from non-Hubei provinces. The 2nd time interval was 1(median) day to 25.9 (mean) days among the 70 articles, the minimum value appeared in an article from non-Hubei provinces[84] and the maximum value appeared in an article from Wuhan that researched 55 COVID-19 patients' delayed treatment cases.[37] The 2nd time interval of Hubei COVID-19 patients was 3 days to 25.9 days, and it was 1 day to 8.5 days for non-Hubei COVID-19 patients. In general, COVID-19 patients in Hubei province had a longer 2nd time interval than those in non-Hubei provinces. Equally, an included article showed the same research result (5.7 days in Hubei province and 4.5 days in non-Hubei provinces) after compared the 2nd time interval in 647 patients from Hubei province and 943 patients from non-Hubei provinces.[85]

Part of the articles made statistics of COVID-19 patients' 2nd time interval in groups according to clinical outcome, the severity of the disease, and the duration of viral shedding. There were 4 articles from Hubei province dividing COVID-19 patients into two groups (cure and death) according to clinical outcome. Two of them indicated that the 2nd time interval of the cured group was shorter than that of the dead group clearly[79, 86] (3 days/5 Days and 7 days/10 days in the 2 articles respectively). Additionally, 8 articles grouped patients according to the severity of the disease, and the results showed that the longer the 2nd time interval, the worse the patients' health condition. Moreover, 3 articles grouped patients by the duration of viral shedding[74, 94, 96], and the results showed that the longer the 2nd time interval, the longer the duration of viral shedding.

Figure 4 summarized the 2nd time interval in 9 articles outside China, ranging from 3.5 days to 8 days. An article from South Korea divided COVID-19 patients into two groups according to whether they were admitted to the ICU, and results showed that the 2nd time interval of the patients admitted to the ICU (4.7 days) was shorter than the patients did not admit to the ICU (8.2 days).[22] A German article divided COVID-19 patients into two groups according to whether they had ARDS, and the results showed that the 2nd time interval of ARDS patients (7 days) was longer than common patients (3 days).[23]

Estimation of the 1st time interval and the 2nd time interval

Figure 5A indicated the daily number of newly confirmed COVID-19 cases in Wuhan, Hubei province without Wuhan and non-Hubei provinces from January 20, 2020 to March 10, 2020. As shown in the

figure, most of the new cases confirmed in the early and middle of February. In Fig. 5B and 5C, this research took the median follow-up time point as the horizontal axis, and the 1st and 2nd time intervals were taken as the vertical axis to draw scatter plots. There was a decreasing trend for the 1st time interval in Wuhan, and no obvious trend in non-Hubei provinces or Hubei province without Wuhan. Figure 5C showed that the 2nd time interval of COVID-19 patients had a relatively obvious trend of gradual increase since February in Wuhan. Non-Hubei provinces had a trend of decrease, and no obvious trend was observed in Hubei province without Wuhan because only 4 articles were included.

Through research, the 1st time interval of COVID-19 patients in China was approximately 3.38 ± 1.55 days, with a median of 2.60(2.35, 4.70) days. In Hubei province, it was 4.22 ± 1.13 days, with a median of 4.35 days(3.46, 4.84). In non-Hubei provinces, it was 3.10 ± 1.57 days, with a median of 2.48(2.31, 4.50) days. In Hubei province without Wuhan, it was 4.34 ± 1.72 days, with a median of 3.79(2.57, 5.35) days. In Wuhan, it was 4.20 ± 0.97 days, with a median of 4.35(3.46, 4.84). There was no estimation of patients' the 1st time interval outside China due to a lack of relevant data.

The 2nd time interval of COVID-19 patients was approximately 8.35 ± 6.83 days, with a median of 5.39 (3.35, 10.54) days. In Hubei province, it was 12.94 ± 7.43 days, with a median of 10.81 (6.90, 24.65) days. In non-Hubei provinces, it was 4.17 ± 1.45 days, with a median of 4.35 (3.20, 4.65) days. In Hubei province without Wuhan, it was 5.36 ± 1.19 days, with a median of 5.7 (5.70, 6.00) days. In Wuhan, it was 14.86 ± 7.12 days, with a median of 11.00 (9.35, 24.65) days. Outside China, it was 5.27 ± 1.19 days, with a median of 4.65 (4.65, 5.00) days.

Meta-analysis of the time interval of common patients and severe patients

Six articles from China (1 article[106] from Hubei province and 5 articles[28, 31, 36, 90, 108] from non-Hubei provinces) had reported the 1st time interval according to the severity of disease of COVID-19 patients. the meta-analysis results showed that compared with common patients, the 1st time interval of severe patients was longer [MD=-1.25, 95%CI (-1.71, -0.80), $P < 0.01$, $I^2 = 0\%$] (Fig. 6).

Eight articles from China (2 articles[33, 57] from Hubei province and 6 articles[28, 36, 41, 76, 77, 99] from non-Hubei provinces) had reported the 2nd time interval according to the severity of disease of COVID-19 patients. One of the 8 articles[33] showed that the 2nd time interval for severe patients and common patients in Wuhan were 6 and 5 days, respectively, however, it was excluded from the meta-analysis since it only provided a point estimate. The meta-analysis results showed that compared with common patients, the 2nd time interval of severe patients was longer [MD=-1.92, 95%CI (-2.55, -1.30), $P < 0.01$, $I^2 = 0\%$] (Fig. 7).

Sensitivity analysis and quality of evidence

By comparing the difference between the fixed-effect model and the random effect model, the results of the sensitivity analysis showed that MD values and 95%CI results were close either in the 1st time interval

or in the 2nd time interval, which indicated that the meta-analysis in this research was stable. The details of the sensitivity analysis can be found in Table 1.

Table 1
Sensitivity-analysis of the time interval of common patients and severe patients.

Research Factors	Fixed effect model MD(95%CI)	Random effect model MD(95%CI)
Duration from symptom onset to first medical visit	-1.25(-1.71, -0.80)	-1.25(-1.71, -0.80)
Duration from symptom onset to admission	-1.92(-2.55, -1.30)	-1.92(-2.55, -1.30)

The qualities of the evidence included in the articles were very low according to the GRADE quality assessment. Details were provided in Supplement III.

Discussion

COVID-19 was a highly infectious emerging disease that had caused a global pandemic.[127] The rapid development of the epidemic had exposed the deficiencies in epidemic prevention and control, public health systems, and health care systems of various countries. In some areas, the unequal allocation of medical resources directly led to the delay of patient medical visits and treatment.[128]

The results of this research showed that the 1st time interval of COVID-19 patients in China was 0 days to 7.52 days, with an estimated value of 3.38 ± 1.55 days, and it was 4.22 ± 1.13 days in Hubei Province and 3.10 ± 1.57 days in non-Hubei provinces. Overseas articles did not involve the time data. The 1st time interval was approximately 1 day longer for COVID-19 patients in Hubei than in non-Hubei areas, whereas the time interval between Wuhan and the rest of Hubei province was relatively similar. This indicated that people in Hubei province had poorer access to health care than other provinces during the outbreak, which had further contributed to the spread of COVID-19 there.

The lack of public awareness of COVID-19 at the beginning of the epidemic, coupled with the fact that most SARS-CoV-2 infected individuals have mild symptoms and the early clinical manifestations of the disease are difficult to distinguish from the common cold, might lead infected individuals to ignore the initial mild symptoms and not pay a timely medical visit. As shown in Fig. 5B, the cordon sanitaire policies implemented from January 23 in Wuhan had strengthened people's attention to COVID-19, and the 1st time interval had been significantly shortened after these cordon sanitaire policies.[28] Therefore, timely disclosure of the outbreak and strong preventive and control measures can help raise the awareness of the public.

At the end of January, China implemented the highest level of public health emergency response policies, including quarantine and medical observation for people with an exposure history, case tracing, and

screening of close contacts. An article from Shenyang showed that the 1st time interval of patients with an exposure history was shorter than that of those without an exposure history, which was related to these policies.[49] Nevertheless, the outbreak of COVID-19 caused a certain degree of social panic, and some suspected patients were afraid of paying a medical visit and handled by themselves through home isolation, which was also a reason leading to the delay of patients' medical visits and treatment.[129, 130] Therefore, during the critical period of epidemic prevention and control, national and local authorities should disclose information in an understandable, timely, transparent and coordinated manner to reduce public panic.[131] At the same time, the authorities should strengthen epidemiological investigation, health education, public awareness of medical visits, to urge the patients to pay a medical visit in time.

The 2nd time interval of COVID-19 patients in China was 1 day to 15 days, with an estimated value of 8.35 ± 6.83 days, and it was 12.94 ± 7.43 days in Hubei Province, and 4.17 ± 1.45 days in non-Hubei provinces. The 2nd time interval outside China was 3 days to 8 days, with an estimated value of 4.89 ± 0.89 days. If the regional disparities in the 2nd time interval of COVID-19 patients between China and outside China might be influenced by lifestyle, health systems, and patient treatment,[23] then the more obvious differences among multiple regions in China were more likely due to the variances in the supply and demand status of medical resources. The mean of the 2nd time interval in Hubei provinces was obviously longer and the standard deviation was strongly bigger than those non-Hubei provinces of China may indicate that Hubei Province had not only the longest 2nd time interval but also a huge difference in system composition compared with other regions. Figure 5B showed that there was a slight difference in the 1st time interval of patients between Wuhan and non-Hubei provinces, while Fig. 5C showed that the 2nd time interval of patients in Wuhan was significantly longer than that in non-Hubei provinces, and the trend of increasing over time in Fig. 5C could be considered consequently caused by medical overwhelmed in Wuhan with the rapid accumulation of cases.[77, 78] Therefore, the length of the 2nd time interval, to some extent, reflected the inadequacy of medical resources in Wuhan during the health emergency. However, as a provincial capital city, the number of tertiary hospitals in Wuhan ranked ahead in China,[132] and the proportion of medical staffs (10.19 health technical personnel per thousand, 3.69 licensed physicians per thousand, 5.07 registered nurses per thousand) were much higher than national average level, in which corresponding numbers were 7.26, 2.77 and 3.18.[132, 133] If the outbreak is out of control at the initial stage, the shortage of medical resources in a specific period cannot be avoided even in an area with relatively sufficient self-resource reserves and supplements mobilized from other areas.

Of the 107 articles included, 6 articles compared the 1st time interval, and 8 articles compared the 2nd time interval in COVID-19 patients with various disease severities. The results showed that both time intervals were longer in patients with severe disease than in patients with mild disease and common patients. Meta-analysis comparing the length of the 2nd time interval between common patients and severe patients revealed that delayed hospitalization may be an influential factor in the exacerbation of the patient's condition. Although one research from Wuhan reported a shorter the 1st time interval in critically ill patients than in the common patients, this may be related to the fact that the average age of critically ill patients (69yrs old) is higher than that of the common patients (43yrs old),[106] and numerous

researches have confirmed the strong correlation between age and severity of disease in patients with COVID-19.[6] Some research indicated that delayed treatment would also affect virus shedding time,[74] resulting in a higher risk of infection among close contacts, easy spread, and the occurrence of cluster outbreaks, which was not conducive to the national epidemic prevention and control.

Advantages and limitations

This research analyzed whether COVID-19 patients receive treatment in time by summarizing the 1st and 2nd time intervals from the 109 articles. In terms of advantages, our research demonstrated the supply and demand status of medical resources in the early stage of the epidemic by comparing the differences in the 1st time interval and the 2nd time interval of patients in different regions and with various disease severities, to analyze whether there is an increase in case fatality rate caused by insufficient medical resources and provide a reference for national or regional medical resource allocation, personnel scheduling, and prevention and control policy decisions.

The research had several limitations. Firstly, only seven articles outside China were included in this research, which may have caused some bias. Secondly, the estimation of time intervals may affect the accuracy of the research results due to the sample size weighting method and the conversion method of median to estimate the mean, as well as missing data in some articles.

Conclusion

It was found that the 1st time interval was similar between Hubei and non-Hubei patients, but the 2nd time interval of Hubei was much longer than that of non-Hubei patients. The 2nd time interval of COVID-19 patients outside China was close to that of non-Hubei provinces. Both the 1st and 2nd intervals were longer in severe patients than in common patients. This phenomenon supported that there was a medical overwhelmed resource and patients with COVID-19 did not receive timely treatment in Hubei province at the beginning of the epidemic, and this could explain why the case fatality rate in Hubei province was much higher than that in other parts of China at the beginning of the outbreak. Besides detection efficiency, the relative lack of medical resources was another important reason that was ignored.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data analyzed for this study are included in the supplementary II.

Competing interests

The authors have no conflicts of interest to declare.

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Authors' contributions

PD, SY and XF conceptualised the study. PD, YC, XL and QS designed the search strategy and ran the searches. PD, XL, QS, ML, JW and XS screened abstracts and full text and extracted data that were double-checked by each other or YC. SY, XF, PD, and TL did the data analysis and participated in data interpretation. XM, TY, QS, DP and WC assessed the risk of bias for each research and the quality of evidence. WC, XF, SY and PD prepared the first draft of the manuscript. All authors reviewed results or reviewed and contributed to the manuscript.

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Figures

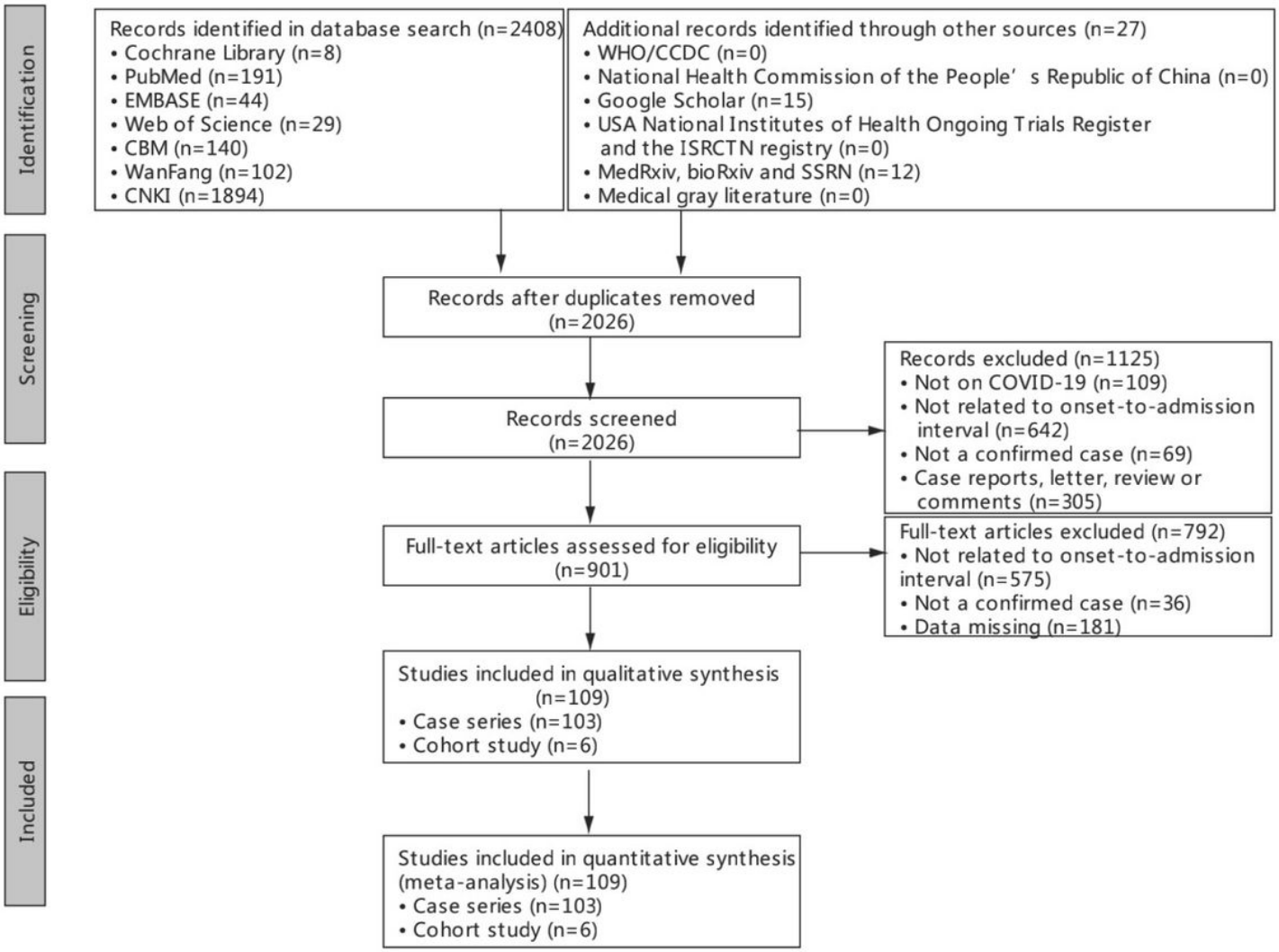

Figure 1

The processes of article retrieval and screening.

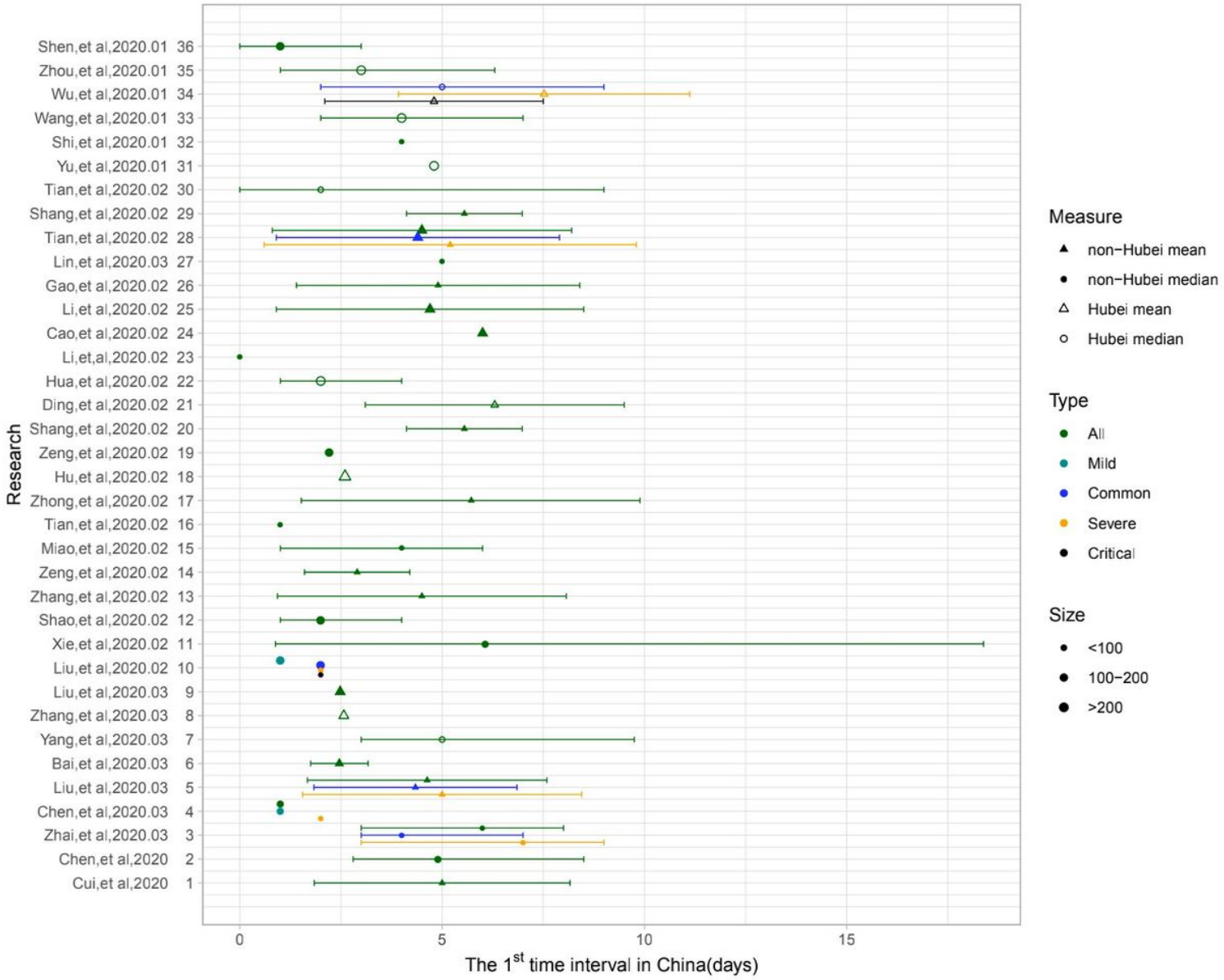

Figure 2

The distribution of the 1st time interval of COVID-19 patients in China. The articles are sorted by the follow-up time end date, with the most recent at the top. Hollow points and solid points represented articles from Hubei province and non-Hubei provinces respectively. The mean was represented by a triangle and the median was represented by a circle. The length of a line segment was determined by the standard deviation of the interval and the interquartile spacing, and the point estimate had no corresponding line segment. Patients with different severity of disease were shown in different colors. The sample size was represented by the size of the points.

Figure 3

The distribution of the 2nd time interval of COVID-19 patients in China. The description was the same as Figure 2 except for the 2nd time interval.

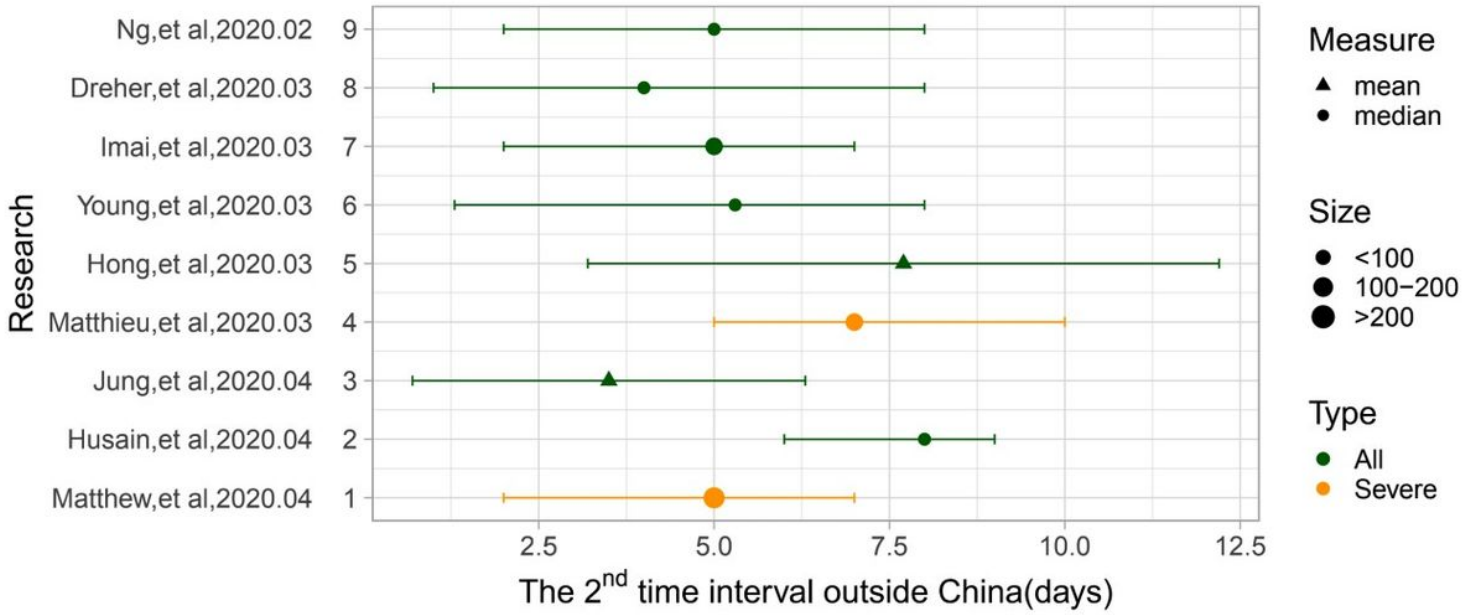

Figure 4

The distribution of the 2nd time interval of COVID-19 patients outside China. The articles are sorted by the follow-up time end date, with the most recent at the top. Hollow points and solid points represented articles from Hubei province and non-Hubei provinces. The mean was represented by a triangle and the median was represented by a circle. The length of a line segment was determined by the standard deviation of the interval and the interquartile spacing. The sample size was represented by the size of the points.

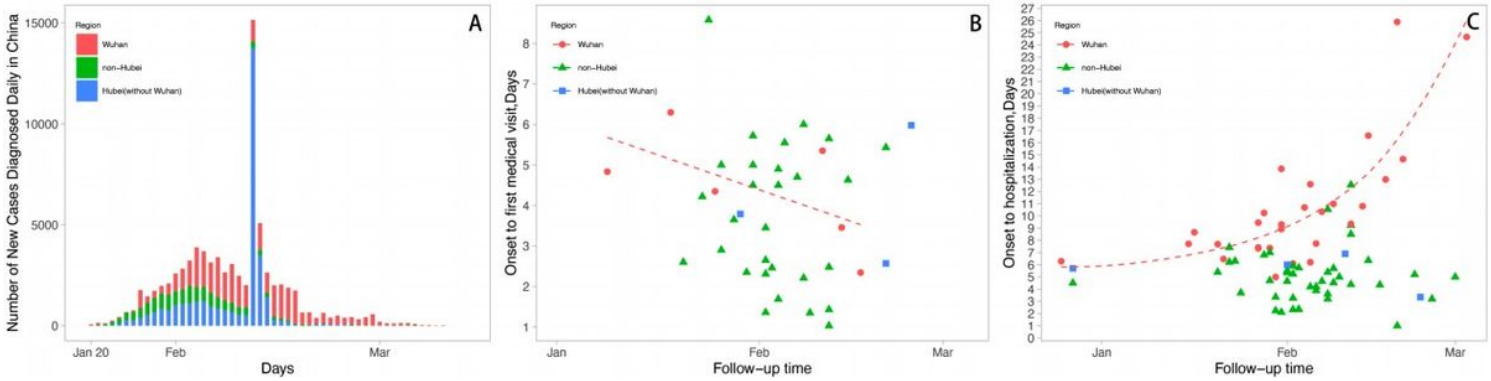

Figure 5

Estimation of the 1st time interval and the 2nd time interval in China. Figure 5A was a stacked histogram of the number of daily new confirmed COVID-19 cases in Wuhan, Hubei Province without Wuhan, and non-Hubei provinces from January 20, 2020 to March 10, 2020. Figure 5B was a scatter plot of the median follow-up time point and the 1st time interval. Figure 5C was a scatter plot of the median follow-up time point and the 2nd time interval.

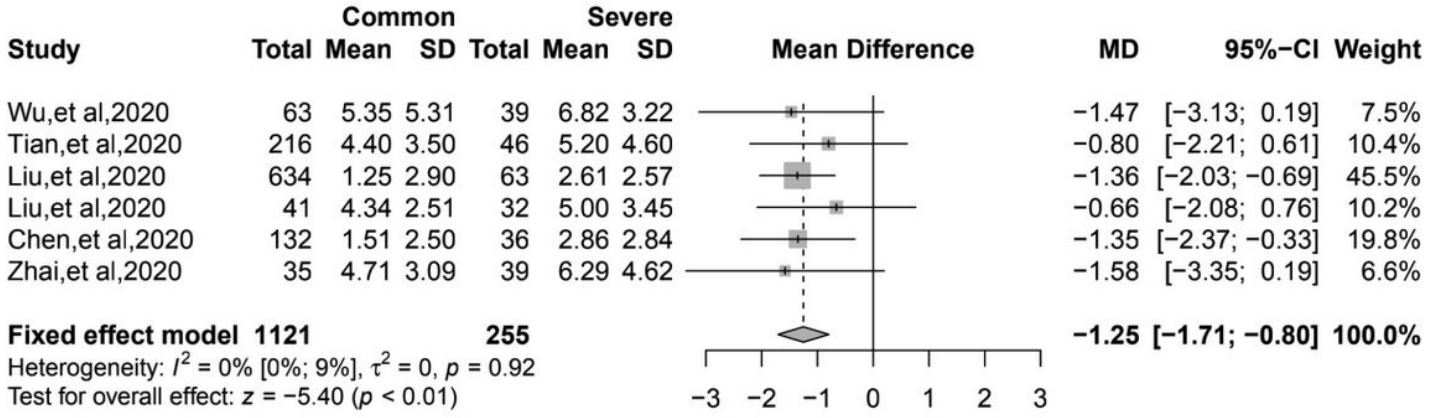

Figure 6

Meta-analysis of the 1st time interval of common and severe patients.

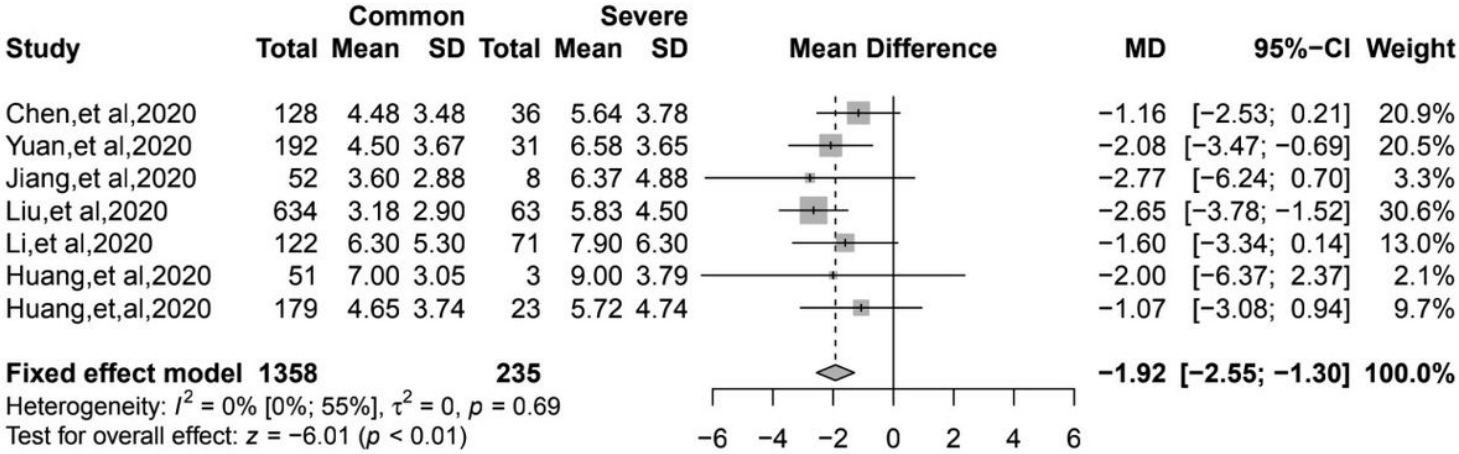

Figure 7

Meta-analysis of the 2nd time interval of common and severe patients.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryI.docx
- SupplementaryII.docx
- SupplementaryIII.docx