

Evaluation of SARS-CoV-2 clearance period in patients with COVID-19: a systematic review and meta-analysis

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Abstract

Background: There is insufficient consensus on the viral shedding period in each background of patients with coronavirus disease 2019 (COVID-19).

Methods: We conducted a comprehensive systematic review and meta-analysis according to the PRISMA guidelines. PubMed and Web of Science were searched for original studies reporting the viral shedding period in patients with COVID-19. A random effects model was used to calculate the mean number of days from the onset. Subanalysis was performed focusing on age, sex, severity, locality, and treatment.

Results Of 55 studies identified, 12 met the selection criteria. The viral shedding period tended to be longer in sputum (19.03 days) than in nasopharynx (14.58 days). The viral shedding period in nasopharynx tended to be longer in severe patients (23.65 days) than in nonsevere patients (12.67 days). It also tended to be longer in patients treated with steroid (21.24 days) than in patients treated without steroid (12.20 days). This period tended to be longer in Asia (16.07 days) than in Europe (12.57 days). Age, sex, and anti-viral drugs did not affect the viral shedding period.

Conclusions Severity, steroid usage, and locality may affect the viral shedding period.

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 was first reported in China in December 2019, after which it spread to the world and became a pandemic [1]. In Wuhan, China, the basic reproduction number of SARS-CoV-2 decreased from 2.35 to 1.05 due to movement restrictions [2]. Although every country has also taken infection control measures such as lockdown, the number of patients with COVID-19 is increasing worldwide. Furthermore, there is concern regarding a re-epidemic caused by unlocking the lockdown [3], therefore, it is important to know how long of a period we should take infection control measures against COVID-19.

A possible cause for the high transmissibility of SARS-CoV-2 is the unintentional spread of the virus from asymptomatic patients with COVID-19. In fact, a seroprevalence study reported that the prevalence of antibodies to SARS-CoV-2 was 4.65% in Los Angeles County on April, 2020 [4], suggesting that there are far more asymptomatic patients than symptomatic patients. Therefore, even when there is no symptom, those who are suspected to be in close contact with patients with COVID-19 may be recommended to stay home for a certain time. Although the quarantine period is generally set at around 14 days at present [5], there is insufficient consensus regarding the number of days required for isolation. In addition, nosocomial infection has become an extremely serious issue due to the high efficiency of virus transmission [6]. It is also not clear till when the body fluids such as blood, sputum, and nasal discharge, and the excrements from patients with COVID-19 remain infectious. Additionally, besides infection control, it is economically important to define the strict protection period for conservation of medical resources such as masks, gowns, aprons, gloves, and face shields. To solve these problems, the detailed information about the viral shedding period in patients with COVID-19 could be very helpful.

Nasal mucus and sputum are used as samples for reverse transcription polymerase chain reaction (RT-PCR) test in several medical institutions not only for diagnosis but also to confirm the elimination of SARS-CoV-2 from the

patient. Some observational studies have reported that a period of approximately 2 weeks after the onset was required for the SARS-CoV-2 to be disappeared from the patients [7, 8]. Surprisingly, it has also been reported that SARS-CoV-2 was re-detected after the RT-PCR test result had become negative [9]. Currently, there is insufficient consensus on the number of days till the virus disappears from the patients with COVID-19 due to the small sample size in each report and the limited information regarding the impact of regional differences. Although some reports have focused on different samples such as sputum, blood, and stool, it is not clear how long SARS-CoV-2 continues to be detected in each sample. Moreover, it remains unknown whether the virus shedding period in patients with COVID-19 is affected by each background such as age, sex, severity, locality, and treatment. Regarding the severity of COVID-19, it has been indicated that COVID-19 is more likely to become severe in the elderly subjects [10], suggesting that the ability to produce neutralizing antibodies could be related to age. However, there is a limitation of reports focusing on whether there is a difference in the viral shedding period depending on age.

We have conducted a systematic review of studies reporting the viral load in patients with COVID-19 over time and determined the viral shedding period from various samples. We also examined the number of days from the appearance of symptoms to the disappearance of the virus by meta-analysis and evaluated the viral shedding period focusing on sample differences (nasal mucus, sputum, blood, and stool), age, sex, severity, locality and treatment.

Results

Study characteristics

We identified 52 studies on PubMed, and seven studies on Web of Science. Of these, four were excluded due to duplication. 26 studies were removed as they did not meet the inclusion criteria based on the title and/or abstract. Furthermore, 17 studies were removed based on the exclusion criteria. Finally, 12 studies that met the selection criteria were included in this meta-analysis (Fig. 1) [7, 8, 11-20].

The characteristics of the studies included in this meta-analysis are summarized in Table 1. The total score of the study quality assessment tools (Quality Assessment Tool for Case Series Studies) from the NHLBI was in the range of 7 to 9 in each study (Supplementary Table 1). The funnel plots in the studies reported the viral shedding period of SARS-CoV-2 in the nasopharyngeal swabs suggested the presence of bias or systemic heterogeneity (Supplementary Fig. 1).

Duration of viral shedding on respiratory samples and the difference between the duration of fever and that of viral shedding.

In terms of respiratory samples including nasopharyngeal swabs and sputum, a total of 223 patients were analyzed [7, 8, 11-14, 16-20], and the duration from the onset of symptoms to the disappearance of viral shedding was found to be 16.06 days (95% CIs 13.31–18.80 days) (Fig. 2a). In terms of nasopharyngeal swabs, 108 patients were analyzed [7, 11-14, 16-20], and the duration from the symptom onset to the disappearance of viral shedding was 14.58 days (95% CIs 12.02–17.15 days) (Fig. 2b). We compared the duration from the onset of symptoms to the disappearance of fever and that from the onset of symptoms to the disappearance of viral shedding [7, 11-13, 17, 19]. We observed that viral shedding continued for 6.73 days (95% CIs 3.24–10.21 days, $p < 0.01$) after the disappearance of fever (Fig. 2c).

Duration of viral shedding on various samples

We analyzed the viral shedding period in each type of sample. In terms of sputum, 19 patients were analyzed [7, 18, 19], and the duration from the symptom onset to the disappearance of viral shedding was 19.03 days (95% CIs 8.70–29.36 days) (Fig. 3a). However, the analysis of studies [7, 18, 19], that reported a direct comparison between nasopharyngeal swab and sputum samples revealed that there was no difference in the viral shedding period (Fig. 3b). Among 126 patients with positive in respiratory samples, 72 patients (57.1%) showed positive results in the RT-PCR test of stool samples. The viral shedding period showed no significant difference between nasopharyngeal swabs and stool samples (Fig. 3c). We could not perform a meta-analysis of the viral shedding period in blood samples due to limited reports. We found one report of ten patients in which the viral shedding period was 16.8 days in blood [15].

Duration of viral shedding focused on age, sex, and severity of COVID-19

In terms of nasopharyngeal swabs, we analyzed the viral shedding period in the non-elderly (aged <60 years) and elderly (aged >60 years) patients using data from nasopharyngeal swabs. A total of 15 patients aged <60 years and 47 patients aged >60 years of age were analyzed [11, 16, 20], and there was no significant difference in the viral shedding period between the two groups of patients (Fig. 4a). In addition, we analyzed the viral shedding period in males and female patients. A total of 29 male patients and 33 female patients were analyzed [11, 14, 16], and there was no significant difference in the viral shedding period between the two groups of patients (Fig. 4b). We also analyzed the viral shedding period in patients with different severity of COVID-19 using data from nasopharyngeal swabs. A total of 16 patients with critically severe COVID-19 were analyzed [12, 18], and the duration from the onset of symptoms to the disappearance of viral shedding was found to be 23.65 days (95% CIs 17.24–30.07 days) (Fig. 4c). In contrast, 23 patients with not critically severe COVID-19 were analyzed [14, 17, 19, 20], and the duration from the symptom onset to the disappearance of viral shedding was 12.67 days (95% CIs 9.19–16.15 days) (Fig. 4d).

Duration of viral shedding on nasopharyngeal swab in Asia and Europe

The viral shedding period was analyzed using data from studies conducted in Asia or Europe. In Asia, 79 patients were analyzed [11, 12, 14, 18-20], and the duration from the onset of symptoms to the disappearance of viral shedding was found to be 16.07 days (95% CIs 12.32–19.83 days) (Fig. 5a). However, in Europe, 29 patients were analyzed [7, 13, 16, 17], and the duration from the onset of symptoms to the disappearance of viral shedding was 12.57 days (95% CIs 8.95–16.19 days) (Fig. 5b).

Duration of viral shedding focused on treatments

In terms of nasopharyngeal swabs, we analyzed the viral shedding period in the patients treated with steroid and those treated without steroid. A total of 12 patients treated with steroid were analyzed [11, 12], and the duration from the onset of symptoms to the disappearance of viral shedding was found to be 21.24 days (95% CIs 10.04–32.44 days) (Fig. 6a). In this group, five patients were critically severe, and seven patients were unknown. In contrast, 64 patients treated without steroid were analyzed [11, 13, 14, 16, 19], and the duration from the onset of symptoms to the disappearance of viral shedding was found to be 12.20 days (95% CIs 9.77–14.63 days) (Fig. 6b). In this group, two patients were critically severe, seven patients were severe, six patients were common, one patient was mild, and 48 patients were unknown severity. In terms of nasopharyngeal swabs, we analyzed

the viral shedding period in the patients treated with steroid and those treated without lopinavir. A total of 41 patients treated with steroid were analyzed [11, 12, 14, 19], and the duration from the onset of symptoms to the disappearance of viral shedding was found to be 17.35 days (95% CIs 13.07–21.62 days)(Fig. 6c). In this group, four patients were critically severe, eight patients were severe, three patients were common, and 26 patients were unknown. In contrast, 33 patients treated without steroid were analyzed [11, 13, 16], and the duration from the onset of symptoms to the disappearance of viral shedding was found to be 10.38 days (95% CIs 8.26–12.50 days) (Fig. 6d). In this group, two patients were critically severe, two patients were common, and 29 patients were unknown severity.

Discussion

There has been insufficient information about the clearance period of SARS-CoV-2 from patients with COVID-19 due to the small sample size in each report and the limited information regarding the impact of regional differences. The present investigation revealed that an average of 14.58 days from the onset was required for viral clearance from the nasopharynx, and the longest period of viral shedding was 36 days [12]. Comparison between the duration of fever, one of the typical symptoms of COVID-19, and that of viral shedding revealed that an average of 6.73 days after the disappearance of fever was required for viral clearance. In 33 (20.4%) of 162 patients, the results of RT-PCR retest turned positive from negative during the observational period. Although the results of RT-PCR test in the majority of patients turned negative in the subsequent RT-PCR retest, in some patients, they did not soon turn negative [18]. The present study also showed that the viral shedding period varied significantly from case to case. Hence, it is necessary to collect more detailed information about more specific cases such as a superspreader [21].

In our analysis, the viral shedding period from sputum or stool was not different from nasopharyngeal swabs by direct comparison. Due to the limited number of reports, it was difficult to perform a more detailed evaluation. Recent reports have described that the viral shedding period from sputum tended to be longer than that from nasopharyngeal swabs. In the meta-analysis of 4243 cases, it was observed that virus excretion from stool was continued even after the virus had disappeared from respiratory samples in the 70.3% of patients [22]. Furthermore, the positive rate of the virus was high in patient with digestive symptoms such as diarrhea. It is also possible that several cases without digestive symptoms were included in our analysis. The RT-PCR test for SARS-CoV-2 in blood samples showed positive results in 43 (34.1%) of 126 patients with COVID-19 diagnosed using RT-PCR test of respiratory samples. In our analysis, we could not make a direct comparison of viral shedding period between blood and nasopharyngeal swabs due to the limited number of studies reporting these data in the same patients. The detection of virus in blood may be associated with severity [23]. In our selected studies, all patients with virus detected in blood were severe or critically severe.

Age has been reported as one of the risk factors for the severity of COVID-19 [10]. Additionally, the peak viral load in saliva exhibited a positive correlation with age in a previous report [24]. However, in our analysis, no difference was found in the viral shedding period from nasopharyngeal swabs between patients aged <60 years and those aged >60 years. In this analysis, the severity of COVID-19 was not considered. The elderly group might have included several nonsevere patients with COVID-19. This result indicated that age, itself, may not influence on the viral shedding period. One study reported that activity of daily living was associated with prognosis in older

patients with COVID-19 [25]. If all the elderly patients are not always at high risk of prolonged viral clearance or worsening of COVID-19, it may be better to identify higher risk populations among them, and more careful prevention strategies for COVID-19 may only be applied to these population.

Males tend to have higher severity and mortality in COVID-19 than female [26]. Although the exact cause of high mortality and severity in male has not been clarified, previous research using mouse model of viral pneumonia suggested that estrogen might suppress excessive immune responses to virus infection in lung [27]. In our analysis, there was no difference in the viral shedding period between male and female. In previous reports, it is controversial whether there is difference in the viral shedding period between male and female [28]. It is necessary to evaluate in detail what type of male patients with COVID-19 are high-risk population for extension of viral clearance.

We observed a possibly longer time period for virus disappearance from the respiratory samples of patients with severe COVID-19 than that in patients with nonsevere COVID-19. It was possible that the viral load of SARS-CoV-2 was high in patients with critically severe COVID-19 [29]. Moreover, the reduction of viral load correlated with seroconversion in SARS [30] and seroconversion was delayed in patients with severe COVID-19 [31]. Viral load or viral clearance rate may be associated with the severity of COVID-19. Regarding patients with critically severe COVID-19, medical staff must treat them as having high risk of SARS-CoV-2 transmission, for example using tracheal intubation and sputum aspiration. Therefore, it may be necessary to implement infection control measures more carefully and for longer duration for patients with critically severe COVID-19 than for patients with nonsevere COVID-19.

We observed that the viral shedding period in Europe tended to be shorter than that in Asia, although it was impossible to compare the data directly due to lack of studies on the viral shedding period in both Europe and Asia. It had been speculated that the viral shedding period in Europe tends to be longer than that in Asia, as the mortality rate of COVID-19 was reported to be higher in Europe than in Asia [32]. It is possible that the severity of patients with COVID-19 in Asia might have been considered to be high in the present analysis. Further studies on the viral shedding period focusing on locality or race are required in the near future.

Our analysis showed that the viral shedding period increased in patients treated with steroid, which was consistent with previous studies [33, 34]. Since there were no clear difference in severity or patient background between patients with steroid and that without steroid in our analysis, it was suggested that glucocorticoid itself associated with the delay of virus clearance. Recently, a randomized trial revealed that the use of dexamethasone 6 mg per day for up to 10 days reduced 28-day mortality among patients treated with respiratory support [35]. Since the persistent use of glucocorticoid may result in worse clinical outcomes including secondary bacterial infection and mortality [36], the duration of glucocorticoid use should be as short as possible. There are not enough reports on whether anti-viral drugs shorten the viral shedding period. Consistent with previous reports [37], no apparent reduction in viral shedding period was observed in the lopinavir-treated group in our analysis. Although there was a bias in the patient background such as the severity or percentage of steroid usage, no apparent reduction in viral shedding period was also observed in other anti-viral treatment.

There were several limitations in our study. First, the small number of cases included in each report was a limitation to the analysis. Second, regional and racial differences were evaluated in only two areas, Europe and Asia. Moreover, only Italy and Germany were included in Europe, and only China and Korea were included in Asia.

Third, the observation period was insufficient for evaluating the viral shedding period in each report. The number of days to achieve viral clearance may have been underestimated. Fourth, the heterogeneity was high. Sensitivity analysis could not be performed because of the small number of patients. Fifth, all reports included in our analysis were case series that were of low evidence level. Sixth, in the analysis of the effects of steroids on the viral shedding period, the effects of other drugs could not be ruled out. Seventh, positive result of RT-PCR test does not always indicate the existence of infectious virus. Finally, we did not completely rule out the possibility of publication bias based on the funnel plot whose results did not generate a symmetrical pattern.

In conclusions, our research summarized recent information on viral shedding period. The period of virus excretion from the nasopharynx was 14.58 days from the onset of COVID-19 and up to 36 days, and viral shedding continued for 6.73 days after the disappearance of fever. The virus shedding period may be extended depending on the sample difference (nasal mucus and sputum) and the background (severity, steroid usage, and locality) of the patients with COVID-19.

Methods

Search strategy

We searched for articles documenting the viral shedding period of SARS-CoV-2 in patients with COVID-19 on two websites (PubMed and Web of Science) using the search terms [(COVID-19) AND (viral load)], with no language restriction. The searches were performed two times to identify articles published until April 28, 2020, and final searches were performed on April 28, 2020. This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [38]. This study is registered with PROSPERO (CRD42020193268).

Article selection process

The inclusion criteria are available on the Internet, which included studies of human subjects, original articles (not reviews or case reports), title or abstract consisting of the terms “COVID-19” and “viral load”, and linkage from the search site to the full text (PDF or website) of the article. Studies that did not provide raw data on the mean and standard deviation (SD) of the viral shedding period were excluded. We excluded case reports that reported 1 or 2 cases in our analysis since they were difficult to calculate the average value and standard deviation properly. Redundancies between the PubMed and Web of Science were eliminated, i.e., individual studies were counted only once in this analysis.

Quality assessment

Two authors (Y.O. and T.M.) independently assessed and selected all references. In case of inconsistent results, a third author (A.K.) provided an opinion to resolve the issue. The quality of selected studies was evaluated according to the study quality assessment tools (Quality Assessment Tool for Case Series Studies) from the National Heart, Lung, and Blood Institute (NHLBI) [39]. The evidence level was evaluated based on Oxford Centre for Evidence-Based Medicine 2011 [40]. Asymmetry of a funnel plot was used to assess publication bias.

Data extraction

Data were extracted from all studies included in this analysis (author, year of publication, country where the study was conducted, study design, number of patients, age, percentage of females, severity, treatment, comorbidity, and specimen) and entered in Table 1. Severity was classified according to the clinical classification of the COVID-19 released by the National Health Commission of China [41]. To elucidate the viral shedding period, the average number of days when SARS-CoV-2 disappeared after the onset of symptoms and its SD were extracted. Patients whose result of RT-PCR for SARS-CoV-2 did not turn negative during the observation period were excluded from this analysis. In patients in whom SARS-CoV-2 was re-detected despite being undetected once, the period when the virus was completely undetected was extracted. Asymptomatic patients were excluded from the analysis. When raw data were unavailable, the values were calculated manually using information available in the published graphs and tables.

Statistics

A meta-analysis was performed to estimate the viral shedding period in patients with COVID-19. Clinical data were analyzed and the outcomes were expressed as mean number of days from the onset of symptoms and 95% confidence intervals (CIs). For all outcomes, the mean differences were calculated using the random effects model (DerSimonian and Laird method). I^2 values of 25%, 50%, and 75% were defined as low, moderate, and high, respectively [42]. All analyses were conducted using R version 4.0.0 (R project for Statistical Computing) and EZR version 1.42 [43].

Data Availability Statement

We declare that we publish all data.

Declarations

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Author contributions statement

Y.O. and T.M. designed the study, did the literature search. Y.O. and T.M. independently acquired data, screened records, extracted data, assessed risk of bias, and did statistical analyses. All authors wrote and revised the manuscript.

Additional information

The authors declare no conflict of interest.

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Table

Table 1. Background of patients with COVID-19.

Author Year Country	EL ^A (study design)	Number of patients	Age (year) [median, (min, max)]	Female (%)	Severity (Number of patients)	Treatment (Number of patients)	Comorbidity (Number of patients)	Specimen
Xu T et al. [11] 2020 China	4 (Case series)	51	43 (7, 80)	51.0	NA	Lopinavir (28) Interferon (19) Glucocorticoid (8) Umifenovir (17) Thymosin (15) Budesonide/Terbutaline (1) Ribavirin (1)	Hypertension (4) Diabetes (3) Chronic kidney disease (1) Chronic obstructive pulmonary disease (1) Chronic hepatitis C (1)	Swab
Shen C et al. [12] 2020 China	4 (Case series)	5	60s (30s, 70s)	40	Critically severe (5)	Methylprednisolone (5) Lopinavir/ritonavir (4) Favipiravir (2) Interferon (4) Umifenovir (1) Darunavir (1) Convalescent plasma (5)	Hypertension (1) Mitral insufficiency (1)	Swab
Wölfel R et al.[7] 2020 Germany	4 (Case series)	9	NA	NA	NA	NA	Hypothyroidism (1) Chronic obstructive pulmonary disease (1) Hypercholesterinemia (1)	Swab Sputum Stool Urine Blood
Lescure FX et al. [13] 2020 France	4 (Case series)	5	46 (30, 80)	40	Common (2) Critically severe (3)	Remdesivir(3)	Gout (1) Hypertension (1) Thyroid cancer (1)	Swab Blood Urine Stool Conjunctiva Pleural fluid Swab
Liu F et al.[14] 2020 China	4 (Case series)	10	42.5 (30, 62)	60	Common (1) Severe (6) Critically severe (3)	Lopinavir (10) Interferon (9) Glucocorticoid (3) Umifenovir (3)	Hypertension (1) Cardiovascular disease (1) Chronic liver disease (1)	Swab
Duan K et al. [15] 2020 China	4 (Case series)	10	52.5 (34, 78)	40	Critically severe (10)	Ribavirin (3) Remdesivir (1) Oseltamivir (1) Peramivir (1) Umifenovir (9) Interferon (2) Glucocorticoid (6) Convalescent plasma (10)	Hypertension (3) Cardiovascular and cerebrovascular diseases (1)	Serum
Gautret P et al. [16] 2020 France	4 (Case series)	36	47 (10, 87)	58.3	NA	Hydroxychloroquine (20) Azithromycin (6)	NA	Swab
Danis K et al. [17] 2020 France	4 (Case series)	6	NA	NA	Mild (1) Common (5)	None	NA	Swab Sputum
Zheng S et al.[8] 2020	4 (Case series)	96	55 [44.3-64.8] ^B	40	Mild or Common (22)	Glucocorticoids (78) Antivirals (96) ^C	Diabetes mellitus Heart disease Chronic lung disease	Respiratory samples Stool

China					Severe (44) Critically severe (30)		Renal failure Liver disease HIV infection Cancer	Serum Urine
Huang Y et al. [18] 2020 China	4 (Case series)	16	59.5 (26, 79)	18.8	Critically severe (16)	NA	Diabetes (6) Chronic cardiac disease (10) Chronic pulmonary disease (5) Chronic neurologic disease (2) Any malignancy (1) Liver disease (2)	Swab Sputum Conjunctiva Serum Plasma Urine Gastric fluid Stool
Kim ES et al. [19] 2020 Korea	4 (Case series)	28	40 (20, 73)	46.4	Mild (6) Common (16) Severe (6)	lopinavir/ritonavir (19)	Diabetes (2) Asthma (1) Liver disease (1) Malignancy (1) Obesity (5)	Swab Sputum
Zou L et al. [20] 2020 China	4 (Case series)	18	59 (26, 78)	50	Mild (2) Common (13) Critically severe (3)	NA	NA	Swab

^AEL, Evidence Level was evaluated based on Oxford Centre for Evidence-Based Medicine 2011[40]

^Bmedian [interquartile range]

^Cantiviral treatment comprises interferon α inhalation, lopinavir-ritonavir combination, umifenovir, favipiravir, and darunavir-cobicistat combination.

Figures

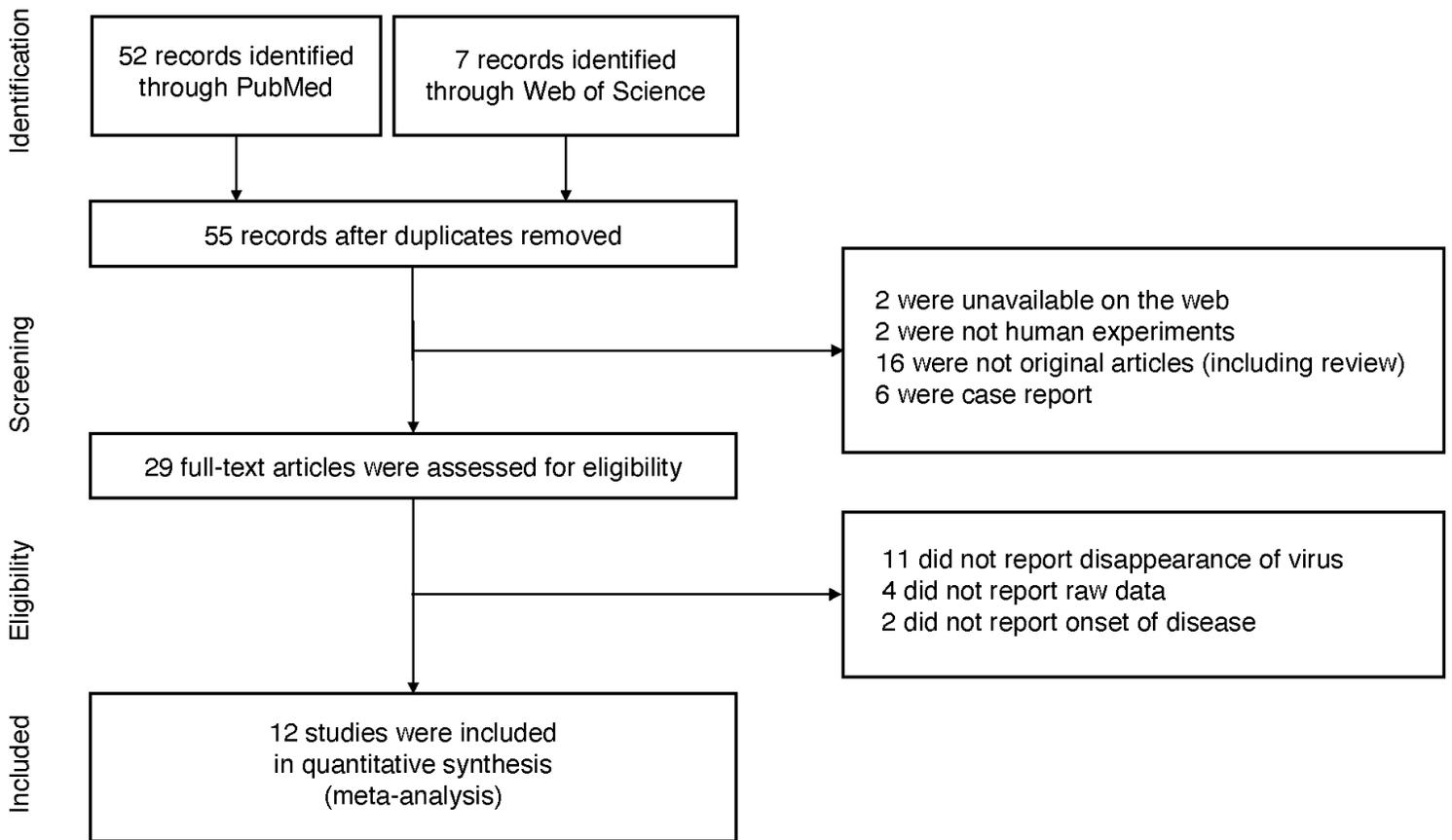


Figure 1

PRISMA flow diagram.

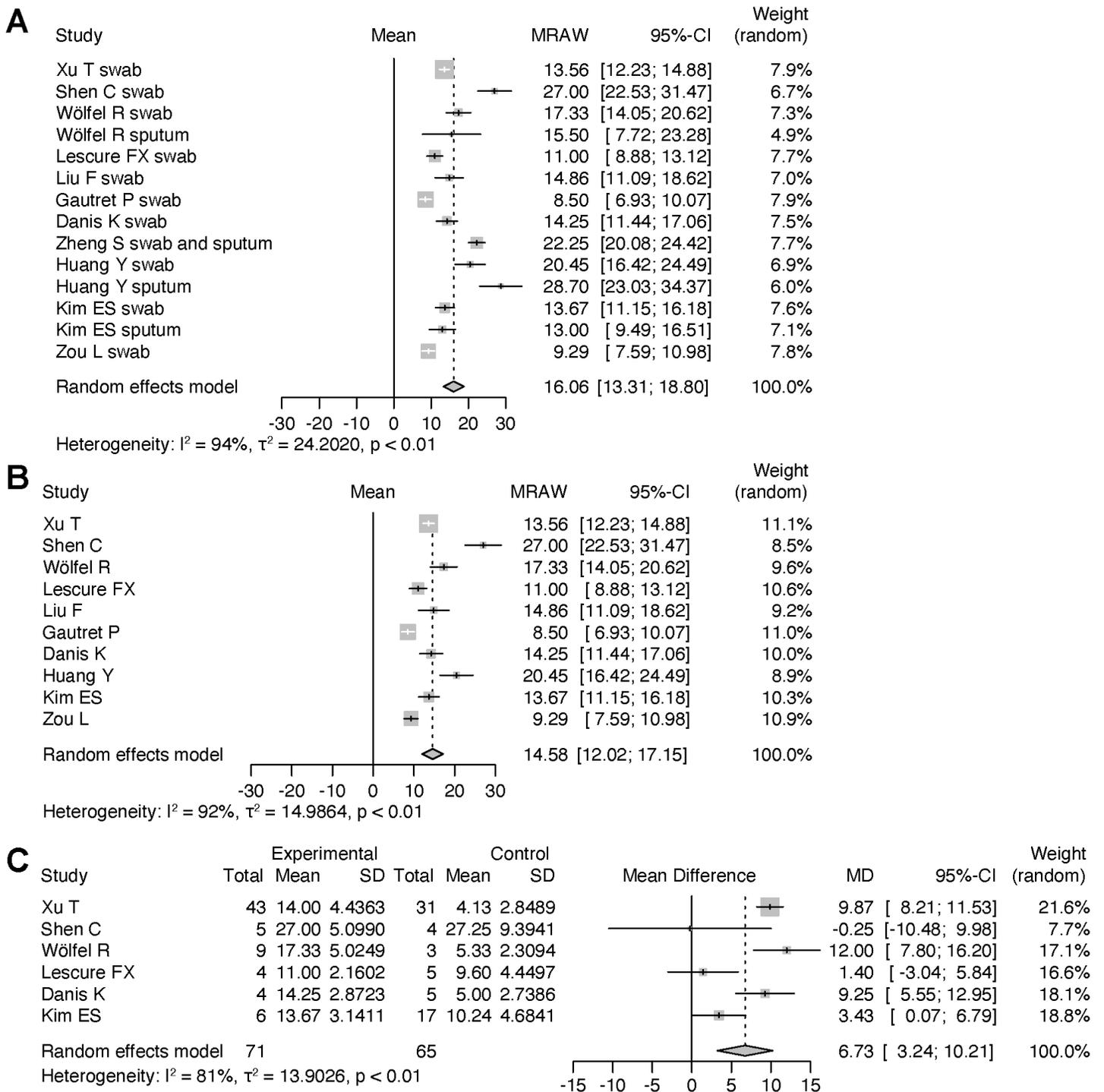


Figure 2

Forrest plot: meta-analysis of the viral shedding period in respiratory samples and the difference from the duration of fever. The viral shedding period in respiratory samples (A) and nasopharyngeal swabs (B) was calculated using the random effects model. The difference between the duration of fever and that of viral shedding in swabs was calculated using the random effects model (C). MRAW: the raw data of mean. 95%-CI: 95% confidence interval. SD: standard deviation. MD: mean difference.

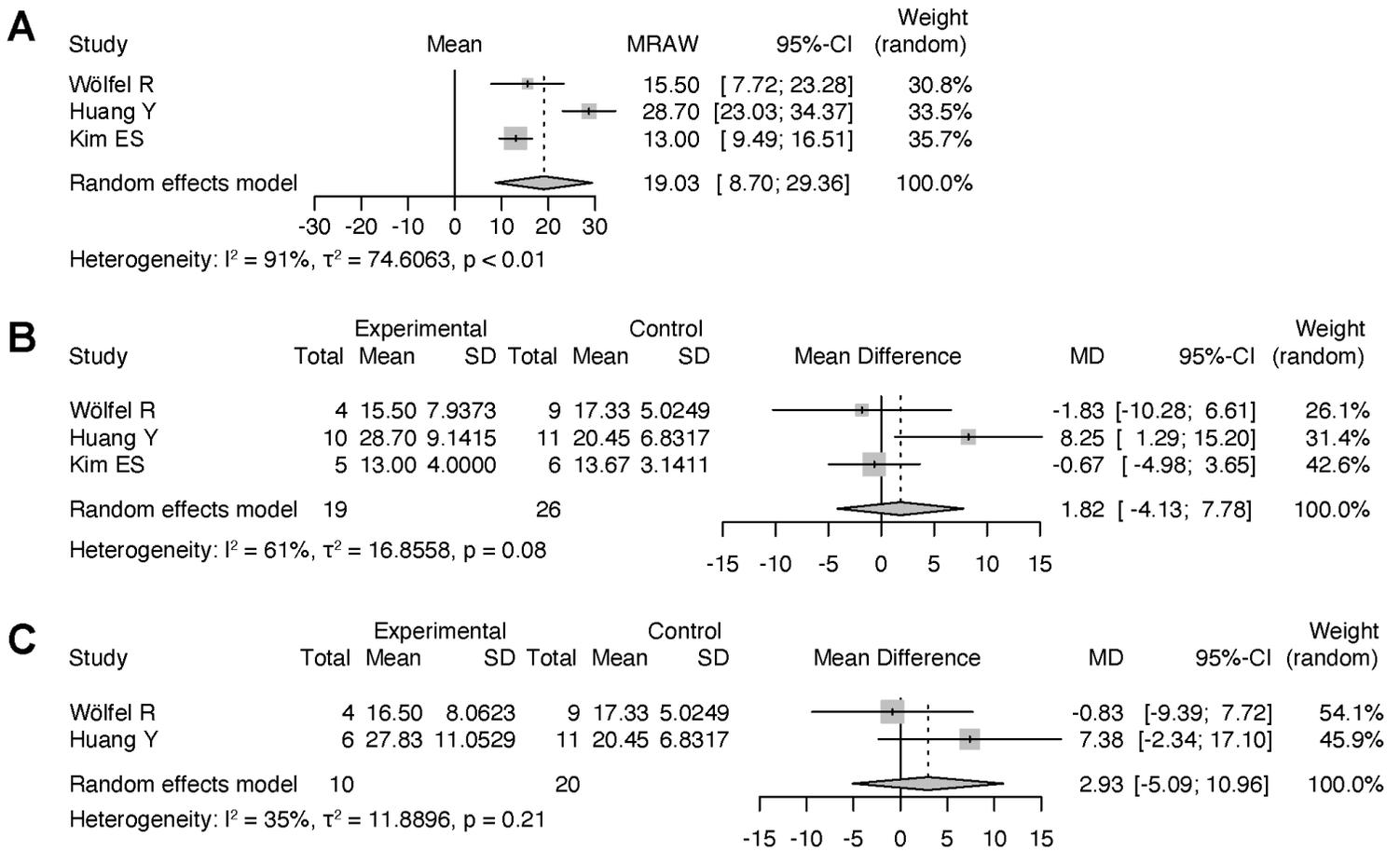


Figure 3

Forrest plot: meta-analysis of the viral shedding period in various samples. The viral shedding period in sputum (A) was calculated using the random effects model. The difference in the viral shedding period between nasopharyngeal swabs and sputum was calculated using the random effects model (B). The difference in the viral shedding period between nasopharyngeal swabs and stool was calculated using the random effects model (C). MRAW: the raw data of mean. 95%-CI: 95% confidence interval.

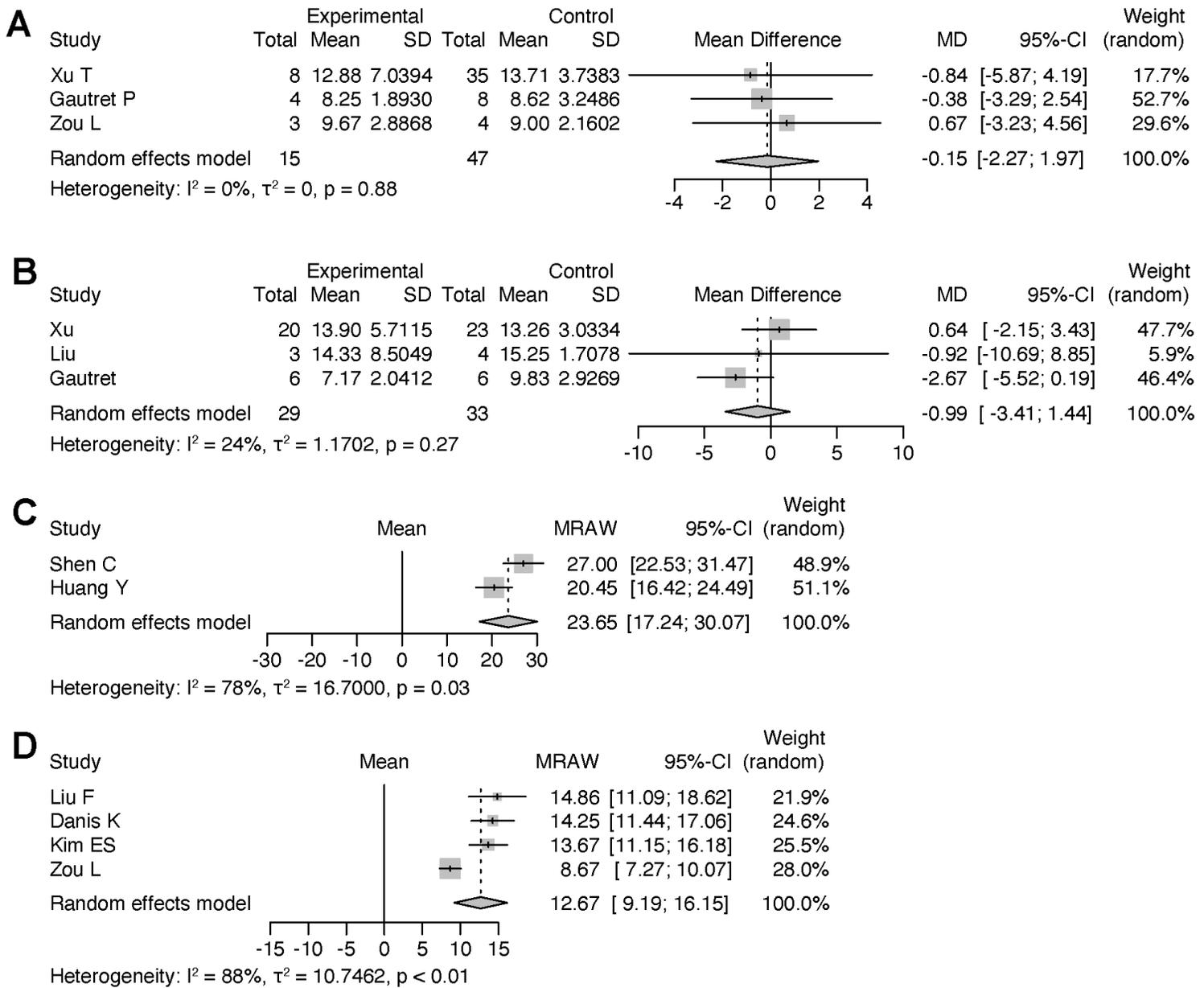


Figure 4

Forrest plot: meta-analysis of the viral shedding period in various patient background. The difference in the viral shedding period between the elderly and the non-elderly was calculated using the random effects model (A). The difference of viral shedding between male and female patients was calculated using the random effects model (B). The viral shedding period in critically severe patients (C) or not critically severe patients (D) was calculated using the random effects model. 95%-CI: 95% confidence interval. SD: standard deviation. MD: mean difference.

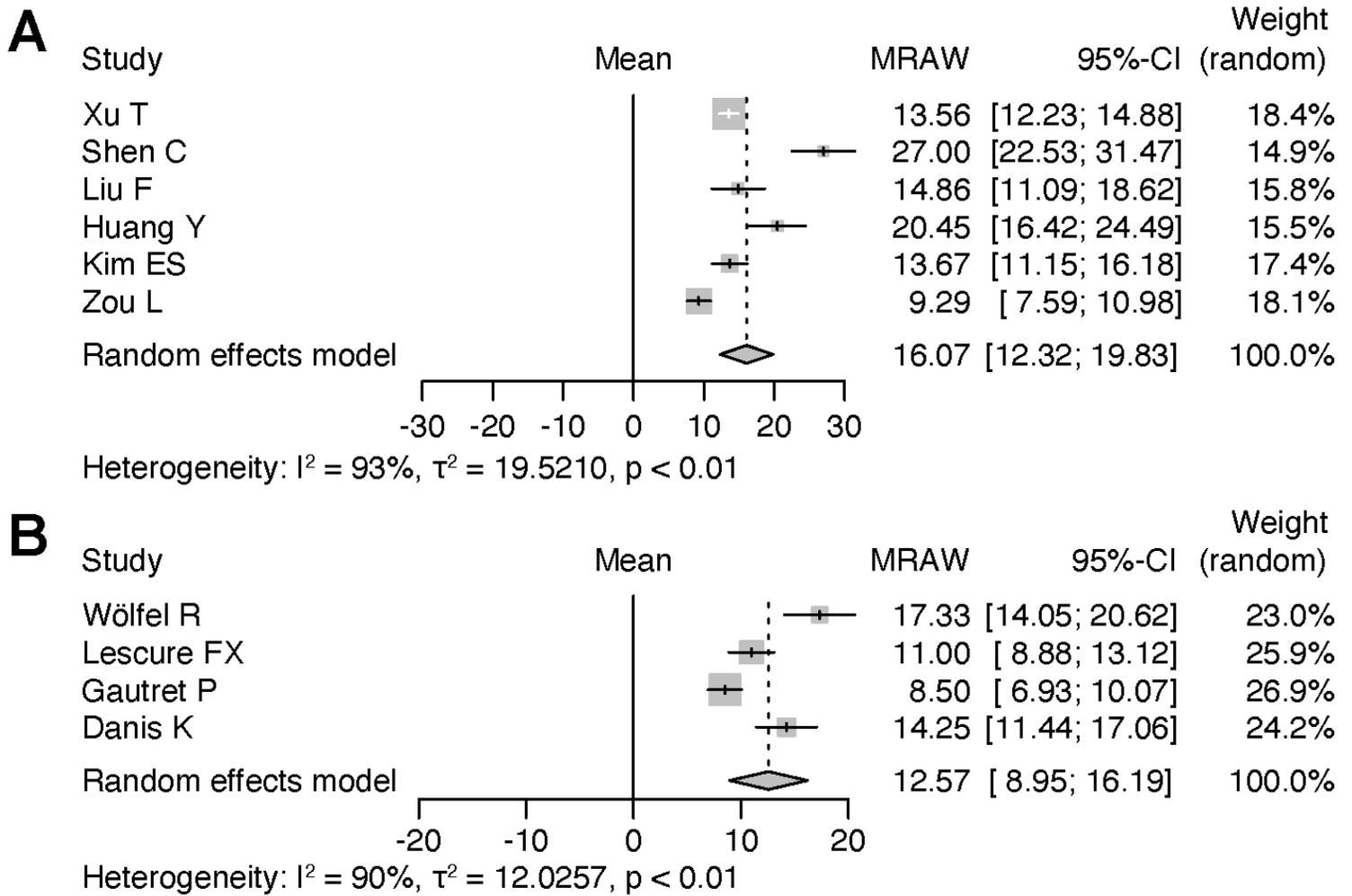


Figure 5

Forrest plot: meta-analysis of the viral shedding period in nasopharyngeal swabs in Asia or Europe. The viral shedding period in nasopharyngeal swabs in Asia (A) or in Europe (B) was calculated using the random effects model. MRAW: the raw data of mean. 95%-CI: 95% confidence interval.

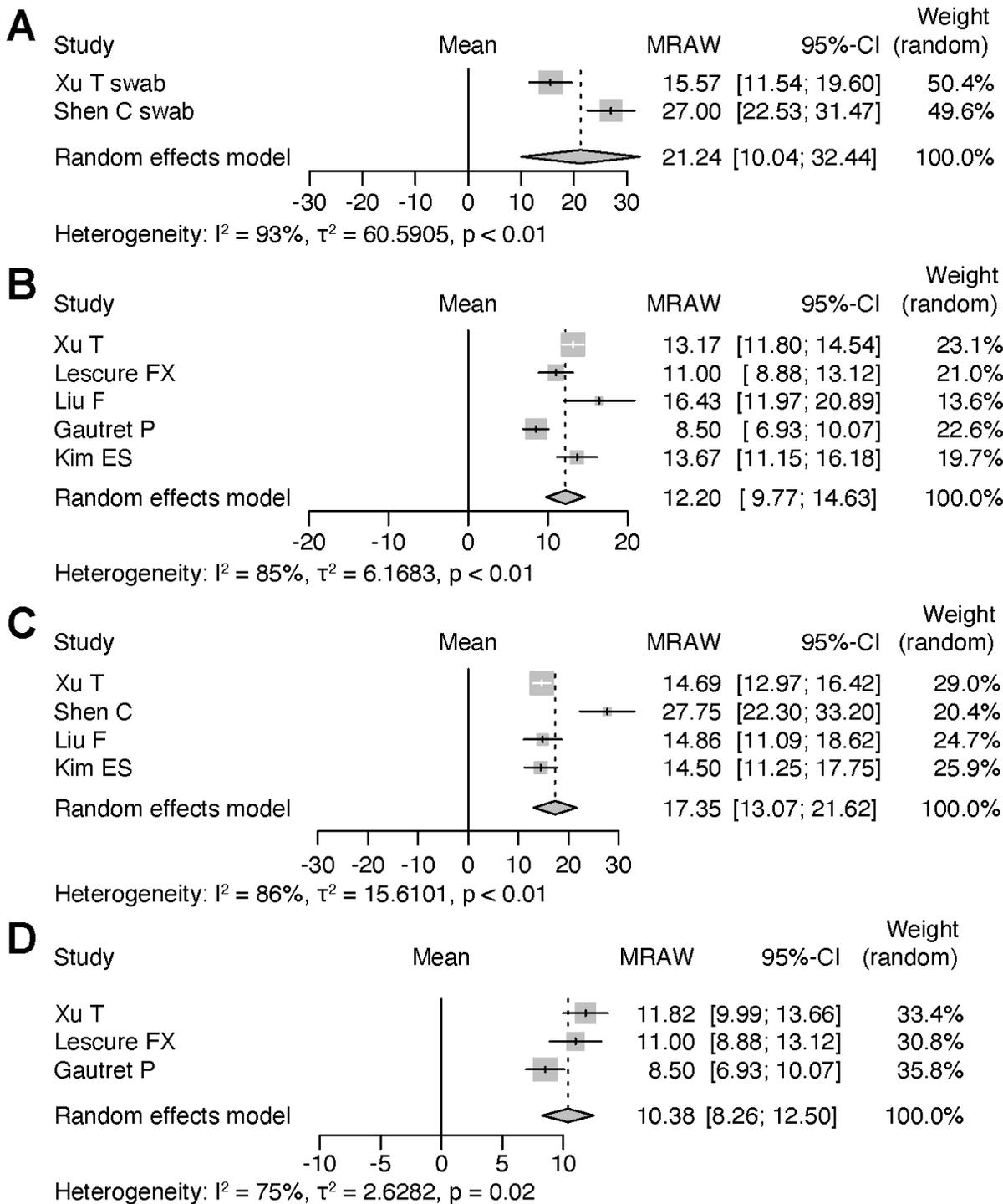


Figure 6

Forrest plot: meta-analysis of the viral shedding period in patients treated with or without steroid. The viral shedding period in patients treated with steroid (A), or without steroid (B) was calculated using the random effects model. The viral shedding period in patients treated with lopinavir (C), or without lopinavir (D) was calculated using the random effects model. 95%-CI: 95% confidence interval. SD: standard deviation. MD: mean difference.

Supplementary Files

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