Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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The influence of corticosteroid on patients with COVID-19 infection: A meta-analysis

Dear Editor,

Coronavirus disease 2019 (COVID-19) has rapidly spread globally in just two more months. This emerging outbreak caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has already affected a large number of people from over 100 countries in the world [1].

Currently, there is not any specific effective vaccine or anti-viral treatment for COVID-19. The pathological feature of severe COVID-19 pneumonia is an inflammation response of alveolar damage and mucinous exudate [2]. Lung injury is related to the immune responses triggered by human coronaviruses that lead to the proliferation/activation of immune cells to release excessive and uncontrolled release pro-inflammatory cytokines [3]. Therefore, it is crucial to strengthen the treatment to suppress the proinflammatory response and control cytokine storm at this stage.

Corticosteroids are commonly given to treat severe acute respiratory infections of viral aetiology due to their anti-inflammatory effect. However, at present, there is no document from randomized clinical trials to support corticosteroids treatment for COVID-19. Although, intravenous corticosteroids were commonly used in patients with severe SARS or MERS pneumonia, their efficacy and their use to treat COVID-19 infection remain controversial [4]. Although an earlier meta-analysis evaluated the influence of corticosteroids on patients with coronavirus infection, with just two studies with COVID-19 patients included, their meta-analysis mainly evaluated the role of corticosteroids in severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle Eastern respiratory syndrome (MERS)-CoV and did not investigate the effect of corticosteroids on mortality in COVID-19 patients. With an increased number of COVID-19 literature now published, it has enabled a more robust and profound analysis of current data which is urgently needed by the international medical and scientific communities. Therefore, we aim to perform this meta-analysis to identify the roles of corticosteroids in patients with or without severe COVID-19.

An electronic search was performed in Pubmed, Embase, Cochrane library, and China National Knowledge Infrastructure (CNKI), using the keywords “steroid” or “corticosteroid” or “cortisol” or “prednisolone” or “prednisone” or “glucocorticoid” or “hydrocortisone” or “dexamethasone” or “methylprednisolone” AND “novel coronavirus” or “2019-nCoV” or “COVID-19” or “SARS-CoV-2” between 2019 and present time (i.e., up to May 7th, 2020) and without language restrictions. The inclusion criteria for studies were as follows: (1) studies comparing the use of corticosteroids between severe and non-severe COVID-19 patients; (2) patients must be diagnosed with COVID-19 infection and (3) Abstracts, case reports, review articles, editorials or letters were excluded. The title, abstract and full text of all documents identified according to these search criteria were assessed independently by two reviewers (Y.W. and G.A.). A meta-analysis was then carried out for calculating the individual and pooled risk ratios (RR) with their relative 95% confidence interval (95% CI), using RevMan 5.3 (Cochrane Collaboration). Heterogeneity among studies was evaluated using Cochran's Q test and the I^2 statistic, with an I^2 less than 25%, 25% to 50%, and greater than 50% corresponding to low, moderate, and high heterogeneity, respectively. $P < .05$ was considered statistically significant.

A total of 466 studies were originally identified based on our search criteria, 411 of which were excluded after title, abstract or full text reading since they were review articles, editorial materials or letters, and did not report the use of corticosteroid in patients with or without severe COVID-19. Thus, 16 studies were finally included in our meta-analysis [5-20]. The study population ranged from 30 to 1099. The details of each included study are shown in Table 1. The pooled RR of these studies is presented in Fig. 1. Although the heterogeneity was considerably high (i.e., I^2, 88%; $P < 0.00001$), severe patients were found to be more likely to require corticosteroids therapy (RR = 2.11, 95%CI = 1.53–2.92, $P < 0.00001$). In addition, no statistically difference was found between survivors and non-survivors regarding the use of corticosteroids (RR = 1.38, 95%CI = 0.87–2.18, $P = .17$) (Fig. 2).

During COVID-19 infection, both the innate and adaptive immune reaction are needed to clear virus adequately and should be appropriately controlled to minimize immunopathological destruction. Corticosteroids are crucial to delay the progress of the pneumonia by inhibiting effect on inflammatory factors, but the most common complication resulted from corticosteroids is secondary infection. Here, due to the lack of sufficient data in the included studies, we can't further perform a subgroup analysis of different types and doses of corticosteroids used in COVID-19 patients and time from illness onset to corticosteroids treatment. However, our brief meta-analysis indicates that patients in critical conditions are more likely to receive corticosteroids. Moreover, there are no differences in mortality among COVID-19 pneumonia patients with or without corticosteroids treatment. More studies are needed to elucidate how and when to use corticosteroids should be used in severe COVID-19 patients.

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Declaration of Competing Interest

None of the authors have conflicts of interest to declare.

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Table 1
General characteristics of the patients enrolled.

Study	Setting	Sample size	Severe patients			Non-severe patients		
			n, (%)	Age, (years)[a]	Male, (%)	*n*, (%)	Age, (years)[a]	Male, (%)
Huang CL et al. [5]	China	41	13 (31.7%)	49.0 (41.0–61.0)	11 (85.0%)	28 (68.3%)	49.0 (41.0–57.5)	19 (68.0%)
Guang W et al. [6]	China	1099	173 (15.7%)	52.0 (40.0–65.0)	100 (57.8%)	926 (84.3%)	45.0 (34.0–57.0)	537 (58.0%)
Zhang W et al. [7]	China	65	9 (13.8%)	81.2 ± 8.3	3 (33.3%)	56 (86.2%)	48.2 ± 16.6	26 (46.4%)
Yuan Q et al. [8]	China	223	31 (13.9%)	56.4 ± 12.4	18 (58.1%)	192 (86.1%)	44.9 ± 16.0	87 (45.3%)
Qu R et al. [9]	China	30	3 (10.0%)	60 ± 5.29	NR	27 (90.0%)	49.44 ± 14.86	NR
Wan SX et al. [10]	China	135	40 (29.6%)	56.0 (52.0–73.0)	21 (52.5%)	95 (70.4%)	44.0 (33.0–49.0)	52 (54.7%)
Li XC et al. [11]	China	548	269 (49.1%)	65.0 (54.0–72.0)	153 (56.9%)	279 (50.9%)	56.0 (44.0–66.0)	126 (45.2%)
Xu J et al. [12]	China	155	30 (19.4%)	50.97 ± 13.55	20 (66.7%)	125 (80.6%)	39.84 ± 15.09	67 (53.6%)
Liu W et al. [13]	China	78	11 (14.1%)	66.0 (51.0–70.0)	7 (63.6%)	67 (85.9%)	37.0 (32.0–41.0)	32 (47.8%)
Ruan QR et al. [14]	China	150	68 (45.3%)	67.0 (15.0–81.0)	49 (72.0%)	82 (54.7%)	50.0 (44.0–81.0)	53 (65.0%)
Wang ZL et al. [15]	China	69	14 (20.3%)	70.5 (62.0–77.0)	7 (50.0%)	55 (79.7%)	37.0 (32.0–51.0)	25 (45.0%)
Wu CM et al. [16]	China	201	84 (41.8%)	58.5 (50.0–69.0)	60 (71.4%)	117 (58.2%)	48.0 (40.0–54.0)	68 (58.1%)
Yang XB et al. [17]	China	52	32 (61.5%)	64.6 (11.2)	21 (66.0%)	20 (38.5%)	51.9 (12.9)	14 (70.0%)
Zhou F et al. [18]	China	191	54 (28.3%)	69.0 (63.0–76.0)	38 (70.0%)	137 (71.7%)	52.0 (45.0–58.0)	81 (59.0%)
Cao JL et al. [19]	China	102	17 (16.7%)	72.0 (63.0–81.0)	13 (76.5%)	85 (83.3%)	53.0 (47.0–66.0)	40 (47.1%)
Wang DW et al. [20]	China	138	36 (26.1%)	66.0 (57.0–78.0)	22 (61.1%)	102 (73.9%)	51.0 (37.0–62.0)	53 (52.0%)

[a] Age data presented as median (IQR) or mean (SD); NR, not reported.

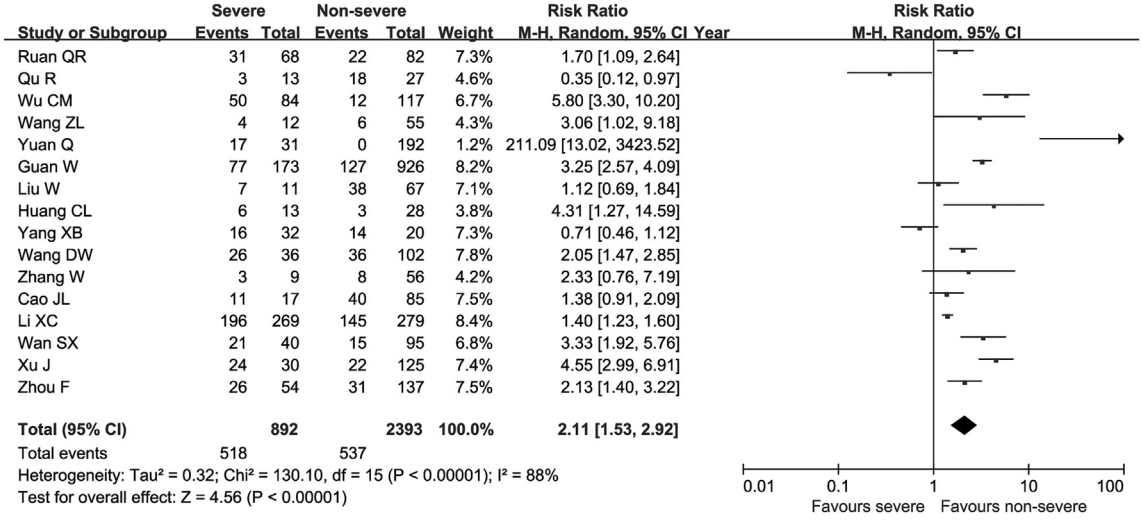

Fig. 1. The use of corticosteroids in severe and non-severe patients.

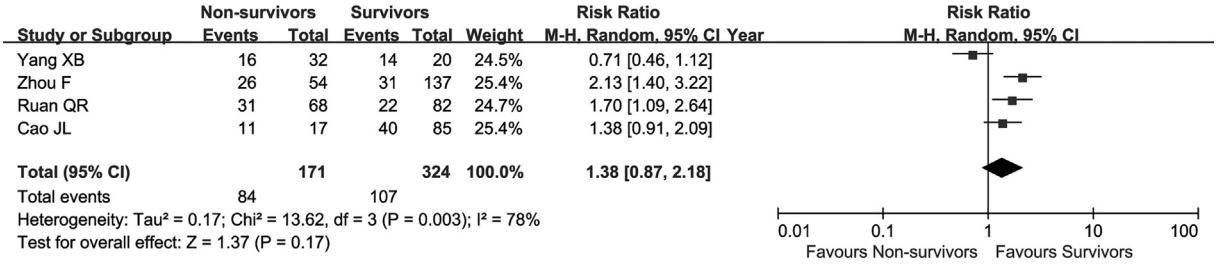

Fig. 2. Effect of corticosteroids on mortality.

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