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Reviewer #A

Comment 1: This is a very extensive meta-analysis which is definitely publishable. The mortality statistics are misleading, as these numbers likely reflect hospitalized COVID-19, as in the US, except for above age 70 where mortality may reach over 5%, in younger age groups all comers have well < 1% mortality and only a minority of COVID-19 require hospitalizations. An important thing left out of this most extensive meta-analysis is obesity, which is associated with a poor prognosis generally (Sanchis-Gomar F et al. *Mayo Clinic Proc* 2020; 95: 1445-1453 and Sharma A et al. *MCP* 2020; 95:2040-2042.).

Reply 1: Thank you very much for your comments. Indeed, all patients included in the present meta-analysis were hospitalized COVID-19, and the proportion of severe COVID-19 patients was higher in the present meta-analysis than the previous meta-analysis (49.4% versus 18%), as shown in the **Discussion**. Therefore, our data may reflect the mortality of hospitalized COVID-19 patients. According to your comments, we have changed “mortality” as “in-hospital mortality” in the manuscript. They are also highlighted by yellow in the text.

Additionally, obesity is one of the risk factors of poor prognosis of COVID-19 and should not be ignored. According to your comments, we have cited some references and added some words in the **Discussion** section as follows. They are also highlighted in yellow (**Line 382-391, Page 19-20**).

Obesity is common in Western countries with an increasing prevalence of obesity, and associated with poor prognosis of COVID-19 patients (Sanchis-Gomar F et al. and Sharma A et al.). ACE2 is the receptor of SARS-CoV-2 infection target cells, and ACE2 expression level in adipocytes is higher than that in lung tissue. Obese people have more adipose tissue and therefore higher ACE2 levels. Among the obese population, the renin-angiotensin-aldosterone system is overactive, increasing the production of angiotensin II (Sanchis-Gomar F et al.). Elevated angiotensin II levels in COVID-19 patients are related to the severity of lung injury (Liu Y et al.), which will increase the risk of death. Additionally, it has been confirmed that obesity increases the risk of cardiovascular disease and its mortality (Pranata, R et al.).

Reviewer #B

Comment 1: This manuscript is currently outdated (includes studies through May 26,2020. Also, many of the studies included in this meta-analysis were "published in press (i.e. available online ahead of print" or "pre-printed". It is necessary to comment not on just "pooled mortality", but to clarify (e.g. in tables, etc) which studies were inpatient mortality vs all-cause mortality vs COVID-related mortality).

Reply 1: So far, COVID-19 is still spreading around the world, and the knowledge on COVID-19 is being constantly and rapidly updated. Accordingly, the number of studies related to COVID-19 is growing at an alarming rate. Therefore, it is challenging to comprehensively search all COVID-19-related studies within a period of time. We have to acknowledge that our meta-analysis seems to be slightly outdated.

Notably, our study was conducted during the early outbreak of COVID-19 when effective vaccines and antiviral drugs were lacking at that time. Therefore, it can be more representative of severity of COVID-19 patients treated at that time. We have improved our title by adding some words “during the early outbreak of COVID-19”. They are also highlighted by yellow (**Line 1, page 1**).

“available online ahead of print” means that the article has been accepted but not yet printed, and can only be obtained online. “preprinted” means that the article was not peer-reviewed and accepted but was stored on the preprinted website.

Since all patients included in this meta-analysis were hospitalized COVID-19 patients, all included studies observed inpatient mortality. According to your comments, we have also changed the “mortality” as “in-hospital mortality” in the manuscript. They are also highlighted by yellow in the text.

Comment 2: Line 97- "What is rapid dissemination?" Do the authors mean "increased transmissibility"?

Reply 2: “rapid dissemination” refers to the situation where the virus has been rapidly transmitted. We have changed “dissemination” as “transmission”. They are also highlighted by yellow. They are also highlighted by yellow in the text (**Line 122, page 7**).

Comment 3: Line 105-107 - not a complete sentence.

Reply 3: According to your comments, we have improved the language expression in the **Lines 135-138**. They are highlighted by yellow in the text (**Lines 133-136, Page 7**).

male, pre-existing comorbidities, elevated inflammatory markers, and complications (i.e., acute respiratory distress syndrome [ARDS], acute cardiac injury, acute kidney injury and sepsis) were associated with an increased risk of death.

Comment 4: Line 108 - Manuscript, unfortunately, is outdated. There are effective vaccines at this time.

Reply 4: We agree with your comments. In the **Introduction** section, we have added the sentences as follows. They are highlighted by yellow in the main text (**Line 138, Page 7**).

In the early stages of COVID-19 outbreak, because effective vaccines and antiviral drugs for SARS-CoV-2 are lacking, the management of critically ill patients is often challenging.

Comment 5: Line 126 - What is "coronary pneumonia"?

Reply 5: "coronary pneumonia" refers to Coronavirus Disease 2019 (COVID-19). In the early stages of COVID-19 outbreak, this disease has not been officially named. Some early studies used "new coronary pneumonia" or "neo-coronary pneumonia" to mean COVID-19. In order to search the literature more comprehensively, our search terms included "coronary pneumonia".

Comment 6: Line 130 - Again, manuscript is outdated since it only includes data through late May 26.

Reply 6: This comment is similar to the **Comment 1**. Indeed, the major objective of our study is to evaluate the in-hospital mortality of COVID-19 patients during the early COVID-19 outbreak and explore risk factors of death at that time, and the last search was performed on May 26, 2020. It can be representative of reflecting the overall severity of COVID-19 patients at that time. Additionally, it had to be acknowledged that it is challenging to comprehensively search all COVID-19 related studies in the context of dramatic increase of COVID-19 related studies. Therefore, large-scale prospective studies should be necessary in future to explore the mortality and risk factors of death in COVID-19 patients.

Comment 7: Line 179. - A substantial number of these studies are in either "published in press (i.e. available online ahead of print" and "preprinted" Also, what is the difference between the two.

Reply 7: This comment is similar to the **Comment 1**. “available online ahead of print” means that the article has been accepted but not yet printed, and can only be obtained online. “preprinted” means that the article was not peer-reviewed and accepted but was stored on the preprinted website.

Comment 8: Line 288 - It is not appropriate to compare mortality between China and New York State (a single US state).

Reply 8: According to your comments, we have added some words in the **Line 372**. They are highlighted by yellow in the text (**Line 371, page 19**). Such data are extracted from a previous meta-analysis paper.

It seems to be the lowest in China (3.1%) and **the highest in the United Kingdom (20.8%) and** New York State (20.99%).

Comment 9: Line 297-198. Is this true? If so, please provide references.

Reply 9: The interventions taken by countries are different, such as the use of efficacious face masks and case isolation. According to your comments, we have added a reference in the **Line 392** (Hradsky O). They are highlighted by yellow in the text (**Line 392, Page 20**).

Comment 10: Line 321. Is this true? If so, please provide references.

Reply 10: As shown in the **Discussion**, male may be deficient of estrogen and more susceptible to SARS-CoV-2 infection. According to your comments, we have added a reference in the **Line 425** (Vahidy FS.). They are highlighted by yellow in the text (**Line 425, Page 21**).

Comment 11: Figure 2A - Table 2A - This table title does not include a proper title. Should at least be labelled as patients with Severe COVID illness.

Reply 11: According to your comments, we have revised the title of Figure 2 and changed “severe patients” as “severe COVID-19 patients”.

Comment 12: Table 1 - "America' is not a country. "Spanish" is not a country. The column labelled longest follow-up period would be easier to read if it actually included exact days or weeks (rather than "until x date"

Reply 12: Thank you very much for your comments. According to your comments, we have changed “America” and “Spanish” as “United States” and “Spain”, respectively. We have also changed the longest follow-up period as the exact days in the **Table 1**. They are highlighted by yellow in the **Table 1**.