Coronavirus disease (COVID-19) in pregnancy: A living systematic review on clinical manifestations, risk factors, maternal and perinatal outcomes

Editor’s comments

1. We were interested in this topic and of course the matter of covid in pregnancy is of great clinical importance. With regard to the request for a living systematic review, we will make a decision when we see the revised paper and decide whether to proceed. Our procedures for living systematic reviews allow for no more than 3 updates per year, separate open access fees to cover the costs of the update. Updates are published under the original doi so they are not considered separate publications in Pubmed.

   Since the submission of our manuscript (search until 12th May 2020; 34 cohort studies; 2426 women), we have now included 52 more studies in our revised manuscript. This reflects the volume of publications in this area and reinforces the need for the living systematic review. We agree with the frequency of suggested updates. Since completion of this round of analysis, we have identified further 9 studies with 10,284 pregnant women (2,268 pregnant women with COVID-19; search until 7th of July 2020).

2. Several editors remarked that they did not find the estimates of clinical symptom prevalence (Figure 2) and maternal and perinatal outcome prevalence (Figure 3) to be very informative because a) they are just prevalence estimates; b) they are not relative to patients without COVID; and c) there is a large amount of heterogeneity.

   Since our initial submission, we now have more comparative data on
   - clinical manifestations and outcomes in pregnant vs non-pregnant women with COVID-19 (8 studies; 95,247 women)
   - risk factors for severe COVID-19 including intensive care admission and invasive ventilation in pregnant women (16 studies; 2,437 women)
   - Pregnancy related outcomes between pregnant women with and without COVID-19 (8 studies; 91,862 women)

   Following the comments from the Editors and peer reviewers, we have focussed on the comparative analyses, which mostly have low heterogeneity. We have addressed the high heterogeneity in prevalence estimates where possible through subgroup and sensitivity analysis. As the number of studies continue to increase, we expect to see an improvement in the precision of our estimates with subsequent rounds. With our weekly search updates and regular analysis in the living systematic review, we are well placed to rapidly include this information when they become available. If our paper is accepted, if required we will be able to incorporate the latest version of the analysis with further data.

3. In contrast, while we found the relative risk estimates (Table) very interesting, these are based (primarily) on 1-2 studies and have very wide confidence intervals, with lots of uncertainty. It's possible that in 6 months the studies used to population the Table will increase in number and the results will be more reliable, but at this time we were not sure what we learn (except that, from Figure 3, risk is appears low).

   The relative estimates in this current version have reasonable precision, particularly for comparative data on symptoms, risk factors and COVID-related outcomes. We agree with the Editors that in six months, there will be more data, with increased precision in the estimates. However, we consider it appropriate to publish our work at this time point for the following reasons
   - The estimates for prevalence vary with the method of screening (universal, symptom-based), and helps to quantify the expected rates of COVID-19 in pregnancy and plan screening strategies
   - Pregnant women with COVID-19 appear to manifest symptoms less frequently than non-pregnant, and clinicians will need to be aware of this finding
   - Pregnant women may potentially be at increased risk of severity of COVID-19 than non-pregnant reproductive aged women
   - Key maternal risk factors for severe COVID-19 are emerging – age, comorbidity, body mass index. Also no evidence so far to suggest third trimester or parity predisposes to increased risk
   - The living systematic review framework allows us to seamlessly update our findings
4. We think you should consider excluding case reports and case series. Even now, most of the included studies are small retrospective cohorts of fewer than 100 patients, many of which are from China (where there have been concerns about patients being included in multiple case series).

In our previously submitted version, case reports and case series were only included to report on mother-to-child transmission. All other questions were addressed using cohort studies. We defined cohort studies as those studies that sampled participants based on exposure, followed-up over time, and ascertained the outcomes (Dekker et al 2012). We also only included studies with at least 10 participants. We have now excluded case reports and case series in our revised version.

We have put in place a robust approach to eliminate duplications (page 8, para 2) : reviewed the characteristics of mother and babies, as well as the setting of the study to determine if the cases were reported elsewhere; excluded the smaller study if there was suspicion of overlap, and only included studies if they reported different outcomes; contacted the authors of primary studies when there was uncertainty about duplicate data; reviewed the timeline of data collection. When there was no overlap in the variables studied such as risk factor or outcome, we included both studies on the same population.

5. We wonder whether the low rates seen here simply reflect the lower risk of women in their younger reproductive years, and that women with major predisposing conditions tend not to get pregnant as often as healthy women? We don't have a meaningful and generalizable comparison group.

We now have more comparative data with non-pregnant reproductive aged women in this revised version and have reported on the risk factors for severe COVID-19.

6. Despite the low quality of the evidence available at present, we think this paper has potential because you could put together a framework for adding studies to a review in a situation where it is likely that new evidence will be coming along at a fast enough pace to see change in a matter of months or a few years.

Our living systematic review has been developed to address the issues of rapid publications of large volume data, which requires seamless updating. We agree with the Editors that our framework will allow rapid update as new evidence emerges. Within less than two months, between our initial submission and revised version, there has been a significant increase in evidence.

7. One of our clinical editors commented that the information patients and doctors want centers around the questions listed below, and wondered whether it might make sense to construct the review so it can answer these questions as evidence becomes available:

With the availability of comparative data, we are now able to provide the findings for the above questions. There are certain questions such as physical distancing in pregnancy and monitoring for which no data are currently available but is part of our ongoing search. We have structured our review so that these questions are addressed in the methods, results and discussion.

a. Am I more likely as a pregnant woman to contract covid?
   Our Fig 2 provides rates of COVID-19 in pregnancy identified using various sampling strategies. While comparative data are available to assess if pregnancy is a risk factor for severe COVID-19 (Table 2), there are very few data to assess if pregnancy is a risk factor for COVID-19.

b. How will I spot it? ie Does my presentation differ from those who are not pregnant?
   Figure 4 compares clinical manifestations of COVID-19 in pregnant vs non-pregnant women, and we have provided the rates of various COVID-19 manifestations in Fig 3. Appendix 6b reports on comparative characteristics of pregnant and non-pregnant women with COVID-19.

c. How likely am I to need hospital admission?
   We have now provided data on the odds of admission to intensive care or requiring invasive ventilation in pregnant vs non-pregnant women with COVID-19 (Table 1). We have refrained from reporting on hospital admissions, as studies did not provide details on whether pregnant women were admitted for COVID-19, and we were unable to disentangle admissions for labour and delivery from COVID-19.

d. If I am admitted or have severe disease how likely am I/my child to have bad outcomes?
Table 2 provides risk factors for severe disease in pregnant women with COVID-19, but due to above issues related to poor reporting of reasons for admissions to the hospital, the above question could not be answered.

e. Will I pass it to my child? (And if so does that really matter?)

The mother to child transmission was mainly reported in case reports and case series and have now been excluded as requested. We are able to reinstate the results if the Editors request it.

f. Finally I'd like to see results by trimester.

We have assessed trimester as a risk factor for COVID related or pregnancy related complications and to-date, not found an association with any outcomes. Most articles did not report trimester specific data, and we have highlighted this as a research priority. But we are in a position to incorporate this information into our living systematic review and update our results, once these become available.

g. Should pregnant women be advised to be more physically distant than other people? Do they need special monitoring if they are suspected of infection? Does their baby?

We have now reported the findings on association between history of COVID-19 positivity in support person and risk of the disease in the mother, and also in comparison with non-pregnant women with COVID-19 (Appendix 6).

8. Other things to include are data (supplementary material) on the actual included studies (forest plots or tables). Right now we only have summary measures for most of the signs and symptoms and outcomes and not information at the study base level which we need to verify the level of heterogeneity.

The study-level estimates are now provided in Fig 2, 4, 5 and in Appendix 9.

9. Please clarify how you pooled the proportion data. Typical approaches use some form of transformation to account for being close to the extremes of the parameter space (see: https://doi.org/10.1186/2049-3258-72-39) for reference.

We pooled individual study estimates using the Freeman-Tukey Transformation random effects meta-analysis as recommended and have now added this information to the methods section (page 10, para 2).

10. Our statistician felt this was comprehensive at the moment, but that some of the methods might require adjusting as further evidence is collected (he agreed that case reports might be excluded).

We agree and acknowledge that as further evidence is published, we will adjust our analysis as required. Please see our response to comment 4 on excluding case reports.

11. Our patient editors would like you to include information about why patients or members of the public were not included. This should go in the methods section. For example, were they unavailable due to COVID restrictions, was there no funding available, was the data or software not open access? How might you involve them in future?

Due to the short time period and COVID disruptions, we initially did not involve patients or members of the public at inception.

Since then, we have involved members of Katie’s Team, a dedicated Patient and Public Involvement Group focusing on Women’s Health, who have provided their comments on the conduct of the living systematic review and its findings. We will continue to engage with them in subsequent updates. This includes obtaining their input on what concerns they may have regarding pregnancy and COVID-19. Prof Thangaratinam is on the Steering Committee of Katie’s Team and have worked closely with them on many projects, including co-authoring publications.
Reviewer #1 comments

12. I commend the authors for being able to pull together such an important “living review” and for the strong collaboration. The methods are robust and the authors are clearly aware of the critical limitations of previous work. This research is an important contribution to the literature and especially timely given the need for synthesis as huge amounts of research, of varying quality, are produced daily. My comments are mostly minor.

We thank the reviewer for this comment.

13. In the abstract and the methods, the authors state that they searched the various databases from inception to May 12th, 2020. Given that the first known cases of COVID-19 were reported in December 2019, it seems that the search period could be narrowed considerably (from December to May 12th, 2020).

We agree with the reviewer and we have restricted our search from December 2019 and updated so in the methods section. This however does not impact on our search results.

14. I agree with the authors’ careful interpretation of the higher rates of preterm birth observed in the review. The following statement, however, needs some elaboration/explanation. “It is essential to compare disease severity to that of age-matched non-pregnant women with COVID-19. The relatively high rates of preterm birth and caesarean section in pregnant women with COVID-19 is likely iatrogenic with urgent delivery required due to deteriorating maternal condition, often resulting in fetal distress, than a direct effect of SARS-CoV-2 infection.” The first part of the statement about the need for age-matched comparisons is important. Chronic conditions and advancing age are both risk factors for COVID-19, preterm birth, and C-section. I think the discussion could be improved by adding more about the need for improved consideration of confounders in these studies, including chronic conditions and their risk factors: obesity, diabetes, hypertension. The second part of the sentence regarding iatrogenic causes of maternal deterioration requires some justification. I am uncertain how the data presented in this article support iatrogenic causes for the higher rates of preterm birth or C-section. Some additional explanation for this conclusion is needed.

We have now evaluated the association between various maternal risk factors and adverse outcomes in pregnant women with COVID-19. These have been addressed in the discussion section in comparison to the known risk factors in general population (page 19, para 2), and the relevance of our findings on maternal comorbidity and COVID-19 to clinical practice as follows

‘Mothers with pre-existing comorbidities will need to be considered as a high-risk group for COVID-19, along with those with obesity and high maternal age. Clinicians will need to balance the need for regular multidisciplinary antenatal care to manage women with pre-existing comorbidities against unnecessary exposure to the virus, through virtual clinic appointments where possible.’ (page 20, para 2).

We have now provided estimates on rates of overall preterm birth and spontaneous preterm birth. Our discussion section now includes potential reasons for increased preterm birth as follows

‘We observed an increase in rates of preterm birth in pregnant women with COVID-19 than those without the disease. These could be medically indicated preterm births, as the overall rates of spontaneous preterm births in pregnant women with COVID-19 was broadly similar to the rates observed in the pre-pandemic period.’ (page 19, para 2).

We have addressed the caesarean section rates as follows ‘Although over 60% of pregnant women were delivered by caesarean section in the non-comparative studies, we did not find a significant difference in comparative studies of pregnant women with and without COVID-19. The precision of the estimates is expected to improve with the publication of more data in the future.’ (page 19, para 2).

15. While there is an appendix with information about the studies included in the review, more of these details need to be in the main manuscript (both results and discussion). Specifically, it needs to be clearer to the reader that most of the studies had tiny sample sizes (<100). While the authors report in the results where the various studies came from, they omit information about which ones are most influential to the
results. From my reading, only about 7 studies have 100 or more COVID-19 confirmed or suspected individuals in the sample. Thus, while 94 studies were included, a very small number are driving most of the estimates. This is an important limitation of the existing literature base.

The overall sample size, and the size of many of the included studies are higher than those in the previous version. We have now removed case reports and case series and provided details on the contribution of individual studies to the overall estimate, both in the main Figures and Supplementary files where appropriate. This version includes 16 studies with sample sizes of more than 100 women with confirmed or suspected COVID-19. We have acknowledged the small numbers of studies and sample sizes where appropriate in the discussion section.

16. Major comment: More information and discussion is needed about the comparison samples used to obtain the odds ratios for the COVID-19 infected women versus the non-infected women. It seems like only 3 or 4 studies had comparison samples of women without COVID-19. There are limited details about these comparison samples. I am concerned about selection bias in the comparison sample and think that any results presented on these comparisons need to be very, very cautious (including in the abstract). For example, approximately 60% of COVID-19 suspected or diagnosed women had a c-section, based on 2 studies only (where are these? Are these tertiary hospitals, high risk women, etc.). The authors, however, state “there were no differences in rates of c-section between the groups.” First, the confidence interval is enormous and it is hard to draw any conclusion here. Second, the c-section rate in the comparison group is just over 30%. The difference may not be statistically significant, but it is huge (60 versus 30%). More information about the few studies used to calculate these ORs is needed so the reader can better assess potential threats to internal validity (e.g. should we believe these ORs or not?).

We have highlighted the limitations of the studies in our discussion section, and refrained from presenting caesarean section estimates in the abstract in the revised version.

17. For the comparisons between the COVID-19 women and those without the virus, I would prefer more care in the presentation of these results for fear of readers not necessarily recognizing the preliminary “living” nature of the results. If a reader scans the abstract only, he/she may think that there is a higher pre-term birth rate based on systematic review of the literature and not realize the review consisted of only two studies. The abstract, results, and discussion need to be more explicit about how limited the literature base is for these types of comparisons.

Our abstract identifies our study design as a living systematic review. We have now reported the number of studies included in the meta-analysis for all outcomes in the abstract and main manuscript as suggested, and highlighted where appropriate.

Reviewer #2 comments

18. In conclusion, it’s an interesting paper, however, not enough for BMJ. Considering its issues, as described below, I do not recommend to publish in this journal. It may be suitable in another BMJ affiliated journal with a lower impact factor after a revision.

We consider BMJ as the suitable journal for this work for the following reasons

- Traditional systematic review cannot keep pace with the rapid publication of new evidence. A platform that reaches a wide audience is needed to disseminate the findings of a living systematic review to avoid duplication of work, inform health care professionals and policy makers. To our knowledge BMJ is the only high impact generalist journals to offer this platform.
- Our living systematic review addresses all relevant questions to assess the key questions around clinical manifestations, outcomes and risk factors for COVID-19 and associated complications in pregnant and recently pregnant women, which is of interest to the all healthcare professionals
- We have highlighted the significant increase in the numbers of relevant studies between our initial submission and revision, and this number is only expected to increase. By providing a single publication, that is regularly updated, will be the main reference for guideline makers and policy makers, with high citation potential.
19. Methods: Ambiguous exclusion criteria: is it only duplicated patients? Very few studies on high-risk pregnant patients. Follow-up time is also unclear.

Our exclusion criteria states that we have included cohorts with a minimum of 10 participants, and duplicates. Rather than excluding high-risk women, we have undertaken sensitivity analysis to determine if the findings are influenced by the characteristics of the included women. We have now provided more information in the methods section on the inclusion and exclusion criteria for articles in the review (page 9, para 1).

20. Results - answer the research question? Credible? Well presented?: the paper needs some rewording (ie babies to neonates or infant, depending on child-age). Presentation of results could be improved.

We have now used the term neonates consistently. We have revised presentation of results.

21. Interpretation and conclusions: based on the analysis, concerning pregnancy-related maternal outcomes the rates of preterm birth increased 3-fold (15%) and preterm premature rupture of membranes (PPROM) was 5%, which are significant results to focus on clinical decision making and policies. Should pregnant women be considered a high-risk group? especially in the 3rd trimester. Please clarify.

The risk estimates provided in table 2 compares risk of preterm birth in pregnant women with and without COVID-19. We advise caution in the interpretation of the findings due to the small numbers of studies with comparative data.

22. There’s also no data on first trimester abortions related to COVID-19 causes. If asymptomatic or slightly symptomatic, many women are not being tested. Is there an impact? Any results?

We are limited by the data that is available from published studies and have recommended that more robust studies with maternal data by trimester of exposure is required to determine the effects of COVID-19 on early pregnancy outcomes such as miscarriage.

23. As for perinatal outcomes, 43% (95% CI 8 – 87%, I2=100%) of newborns were admitted to the neonatal unit. Of those admitted to the NICU, only 19% were breast fed, this is a big impact for the mother-child contact and attachment. If they were not contaminated, any speculations are of why there where not breast fed?

We have made considerable changes to our manuscript following feedback from the reviewers and editorial team and now no longer include mother to child transmission data which were provided mainly as case reports.

24. What about the impact of obesity? Was BMI a factor considered?

Our revised manuscript now includes risk factors predisposing pregnant women to COVID-19 and related complications. Pregnant women with high body mass index were at increased risk of COVID-19 and severe COVID-19 (Fig 5).

25. Abstract/summary/key messages/What this paper adds: there are many limitations in the study. A long delay between symptoms initiation and randomization (which could have an influence on the time to recovery, a parameter that was not analyzed statistically). Is there a difference in the category distribution? with more severe patients in the placebo group, was there a substantial difference?

The above comments do not relate to our review as there are no randomised trials in our work

26. A primary conclusion that is disputable (including the speculation that pre-term birth is due to iatrogenic causes may be not justified). The absence of evidence is not the evidence of absence, therefore cautions are needed and required until we know more.

Please see our response to Comment 14.

27. What's the effect on mortality?

We have now compared the rates of mortality in pregnant vs non-pregnant reproductive aged women with COVID-19 (Table 1).
28. **What was the main COVID treatment, do we need to give an expansive drug to shorten the time to recovery?**
   We did not assess the effects of any treatment in our submitted review.

29. **We need to know more:**
   - statistical analysis in the treatment and therapy used
   We did not assess the effects of any treatment in our submitted review.

30. **What are the distribution between the trimesters. Does the outcome change if only 2nd and 3rd trimester considered?**
   Please see our response to Comment 7f.

31. **What are the proportion of worsening categories in each group?**
   We are not certain about what categories or groups are referred to by the reviewer.

**Reviewer #3 comments**

*Thanks for send me this manuscript for reviewing, I've been studied it very carefully. It was very interesting and very well designed. I think it is appropriate to publish it after some minor revisions as below:*

32. **Please mention the critical appraisal tool and add a subheading as quality assessment**
   We thank the reviewer for their comments. We have provided the details of the quality assessment tool in the methods section (page 10, para 1), and have provided the findings under the results section subheading of our quality assessment ‘Quality of the included studies’ (page 12, para 2).

**Reviewer #4 comments**

33. In their manuscript, Dr. Allotey et al. report their initial findings from a living systematic review on COVID-19 in pregnancy. In this report, the authors identified 94 cohort studies and case series that met their inclusion criteria. The outcomes of interest were grouped into maternal outcomes related to COVID, pregnancy outcomes, and neonatal outcomes. The number of studies and patients with data for each outcome varied dramatically. The authors included all women who tested positive for COVID, regardless of their indication for testing. Their conclusions are that pregnant women may be less likely to exhibit symptoms than the non-pregnant population and that few are admitted to the ICU.

   The number of case reports on COVID-19 in pregnancy is increasing rapidly as more people around the world are affected with the disease. This work attempts to collate and present data from multiple reports of COVID-19 in pregnancy through a living systematic review, which they describe would be updated monthly. This type of resource would be helpful to patients, clinicians, and policymakers.

   We thank the reviewer for acknowledging the importance of our living systematic review.

34. The authors included of all women with COVID-19, regardless of the indications for being tested. There likely is a significant publication bias introduced from early studies when testing was very limited, where only the sickest women or those with typical symptoms were tested. Until testing becomes more wide spread and more studies with universal screening are published, the true associations between COVID-19 and pregnancy outcomes will not be fully understood. The authors do perform sensitivity analyses by individual symptom status, but these results are not discussed in the manuscript. The authors may consider discussing the following notes and highlighting the results from their sensitivity analyses in the main text:
   a. **Why were studies where the indications for testing were unknown grouped with the symptomatic group? Was this appropriate?**
      We have now analysed the symptomatic and not known groups separately in the revised version.
   b. **Did the authors examine what percent of women reported any symptoms (not just stratified by individual symptoms)?**
Fig 4 shows that overall, the rate of presenting with any symptom in pregnant vs non-pregnant women was lower but not statistically significant.

c. Was testing indication considered/weighted in the pooled estimates?

We carried out a subgroup analysis by testing indication and reported in Appendix 7 and 8. We reported in the text of the manuscript that the rates or manifestation and outcomes were similar when the analysis were restricted to the indications for testing.

d. Once more studies are published, the authors should consider further delineating studies by testing indications for more meaningful interpretations of the outcome data

We agree with the reviewer and will incorporate this in future sensitivity analysis. For now, we have provided details of studies and testing strategy in our main Fig and Tables.

35. In their attempts to be comprehensive and increase their sample size, the authors included studies published from many countries. The review, as submitted, is predominantly weighted by studies from China. I think this approach is appropriate for understanding disease characteristics and severity among pregnant women. However, it is major source of heterogeneity when considering pregnancy and neonatal outcomes. The baseline characteristics of pregnant women, how/where they receive care, and their pregnancy outcomes vary dramatically by country (and even within some countries). Thus, most of the pregnancy and perinatal outcomes, including cesarean delivery, preterm birth, stillbirth, NICU admission, are impossible to interpret without having a comparison to a non-COVID-19 pregnant population from the same institution/country (much of the pregnancy and neonatal outcome data presented in Figure 3). Table 1, while not stratified by country, does present the available cohort data, including odds ratios, which are more meaningful. However, at this time, there are only 1 or 2 studies, making the results not generalizable (and not enough to warrant a systematic review). The authors do acknowledge these issues as a limitations, though I am not certain having more pooled cohort studies from very different populations will provide meaningful insights into the effects of COVID-19 on pregnancy outcomes. This may be best studied on a local or national level.

Since the submission of our initial manuscript, we have had more reports from the USA, which have overtaken the number of studies from China. Our report on the prevalence of COVID-19 has also been presented with information on the country of origin, and we have carried out subgroup analysis by country income status (high income vs low-middle income). We have also provided details of studies and testing strategy in our main Fig and Tables to aid interpretation.

Reviewer #5 comments

36. The authors present a living systematic review on clinical manifestations, maternal and perinatal outcomes of COVID19 in pregnancy. The research questions are scientifically sound, and the analyses were well conducted. In addition, literature selection criteria and information management strategies as well as sensitivity analyses contribute to gain more evidence robustness in comparison to other publications.

Regarding interpretation of their findings, I would suggest the authors to discuss about the following:

Since typical symptoms were less frequent in pregnant women than in the general population and admission rate to ICU was lower than in other studies, should we imply that pregnant women have a milder clinical presentation than non-pregnant?

We have now included additional studies, which show that fewer pregnant women reported typical COVID-19 symptoms such as fever and myalgia. There was increased risk of ICU admission in pregnant women with COVID-19. We have covered this in our discussion as follows

‘But in our review, fewer pregnant and recently pregnant women with COVID-19 manifested these symptoms than non-pregnant population, indicating possible high rates of asymptomatic presentation in this population. This is very likely due to the strategy of universal screening for COVID-19 in pregnancy, and the low thresholds for testing than in non-pregnancy’ (page 18, para 2)
37. Would selection bias be a possible explanation to those findings? For instance, are pregnant women more likely to be tested than non-pregnant and therefore mild cases are overrepresented? Is the likelihood of being tested related to the increased awareness of pregnant women to health harms, including COVID-19?

   Please see response to comment 36.

38. As compared to other populations, the proportion of severe cases among pregnant women was lower (5% vs 5%-17%). However, as compared to individuals aged 22-44, it was higher (5% vs 2%-4.2%). So, should we still consider pregnant women as a high-risk group in clinical practice settings?

   Comparative analysis is indicative of increased risk of intensive care unit admissions in pregnant women with COVID vs non-pregnant reproductive aged women (Table 1), indicating the potential need to consider pregnancy as a high-risk group.

39. What would be the quantitative impact (on results) of excluding suspected cases from the analyses? How do authors plan to address these exclusions in the future updates of this living systematic review?

   We carried out sensitivity analysis restricting to only confirmed diagnosis only and the findings were similar. Appendix 7 and 8.

Minor

40. Abstract: I would mention that prediction intervals were also estimated.

   We have not provided this due to limitations in word count.

41. Page 13: Line 43. Not sure why 84% pneumonia. From Fig. 3, it seems like it was 40%.

   The revised estimate of pneumonia in Fig 3 is now 49%.

Reviewer #6 comments

42. The reviewer’s understanding of this paper is that the key questions being addressed are whether pregnant women are a high risk group within a population affected by COVID-19; the likelihood of the baby having COVID-19 transferred to them and what needs to be learnt in order to manage the care of mother and baby. These are clearly questions important to patients and/or carers.

   We agree with the reviewer.

43. Should the issue of ethnicity of the mother be included or highlighted more in light of this being an issue emerging more generally in data being collected on susceptibility to and outcomes from contracting COVID-19.

   To-date, we have not identified ethnicity as a risk factor, but data are limited, and we have identified this as a research gap. We will continue to evaluate and report in our updated review.

44. It would be useful to have it explained clearly whether the outcomes being considered in this LSR can be reassessed, changed and/or expanded in the future to potentially include parameters of importance to patients and/or carers following consultation with patients and/or carers.

   We agree with the reviewer. Our systematic review is designed as a living systematic review and is well placed to include measures of importance as identified by patients/carers and the wider research community. As new studies emerge, we may need to revise our living protocol to incorporate previously missed outcomes. But we expect this to be unlikely as our protocol captures all potentially relevant outcomes.

45. Expand the details on how the LSR will change (or not change) as time moves on and more and different data are available from studies on COVID-19 and pregnancy and childbirth.

   We thank the reviewer for their comments. We have added more information in the methods section (page 7, para 3)
46. This study could report on the ease or difficulty of including patient/carer involvement data because of the nature of current studies and whether studies, in the future, on this topic should more proactively involve patients/carers.

Please see our response to Comment 11.

47. Other topics
Since the submission of the initial version, a substantial number of studies have been included in our living systematic review. This meant involvement of more researchers to manage the volume of new studies, and in the writing of the manuscript. Elena Stallings along with John Allotey are now joint authors as they have both contributed equally to this version of the manuscript.