PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	A rapid review of available evidence on the serial interval and generation time of COVID-19
AUTHORS	Griffin, John; Casey, Miriam; Collins, Aine; Hunt, Kevin; McEvoy, David; Byrne, Andrew; McAloon, Conor; Barber, Ann; Lane, Elizabeth; More, SImon

VERSION 1 – REVIEW

REVIEWER	Eric Lau University of Hong Kong, Hong Kong
REVIEW RETURNED	21-Jul-2020

GENERAL COMMENTS	The study reviewed the latest evidence on serial intervals and generation time. The authors provided detailed discussion of the source of bias and methodological issues which is valuable. Comments to the author 1. Abstract, please clarify why 19 studies were evaluated in detail, out of 27. 2. Given that a systematic review of COVID-19 epidemiology, including serial intervals (Park et al. J Clin Med 2020), reviewed data up to late February. As pandemic evolved quickly, the authors may consider updating the review. 3. Please update the references if some of the preprints have been published. 4. Abstract and Conclusion. It is unclear why Cereda et al. was highlighted as most relevant to European countries. Another study by Lavezzo et al. also analyzed data in Italy. Furthermore, did the author expect difference in Europe vs other places? 5. Materials and Methods. “Some of the papers contained parameter estimates derived only from original data without the fitting of statistical distributions. As these papers were considered to be less useful for model development than papers containing distribution-derived estimates, they were also omitted from further consideration.” However, Table 1 did not present the fitted statistical distributions so it’s unclear why these papers were excluded. 6. Table 1. Ref 18. It’s unusual that the 95% CI for the mean and median did not overlap at all, given a relatively small sample size. 7. Discussion, generation times can be estimated (Table 1), though it cannot be directly estimated or observed. 8. Conclusion, please explain in the discussion why the bias can be minimized from using early cases. Minor comments 9. Table 1, please clarify upfront that the first estimates were serial intervals. 10. Discussion, range of estimates obtained, typo ‘contracts’

	11. Discussion, typo ‘the(y) set that last date’

REVIEWER	Tim Russell Centre for the Mathematical Modelling of Infectious Diseases, London School of Hygiene and Tropical Medicine
REVIEW RETURNED	05-Aug-2020

GENERAL COMMENTS	The authors review estimates for the serial interval and generation time of COVID-19. They do so within a systematic review framework, combining search terms with Boolean operators to isolate the relevant papers. They describe in detail which studies are deemed appropriate and which are not. The results of all included distributions are presented in the form of a single large box plot. The study is well conceived, well written and on an important topic. Therefore I believe with just some minor changes, it is of publishable standard. I especially believe the discussion is of great value, given the level of detail about the limitations and potential issues of the papers reviewed, that it goes in to. Major comments: There are bound to be more up to date estimates now. Therefore, the review should be updated before publication. Minor Comments: The single box-plot nicely summarises the results and is probably the simplest way of presenting the results. However, the authors make a point of only including the studies which report a distribution for either the serial interval or generation time. Therefore, I believe (perhaps as a supplementary plot), it would be a nice addition to show the distributions for all estimated SIs and GTs, perhaps in a ridge plot style figure. There is a missing space at the start of the "Funding" subsection Its really just a matter of style, but I thought the first paragraph of the discussion was a bit too vague, mentioning mainly the importance of preprints. Perhaps the point would have resonated more with some comparison between number of preprints and number of published articles, or something similar. Although, I am very aware this is just a minor point, and I don't think it necessarily needs to be addressed. Re-reading and rewording the paragraph could strengthen the discussion though I believe I like the long list of bullet points outlining potential issues with the papers included in the review. I believe analyses like this are of great importance, as they help to improve the quality of future papers

VERSION 1 – AUTHOR RESPONSE

Reviewers' Comments to Author:

Reviewer: 1
Reviewer Name: Eric Lau
Institution and Country: University of Hong Kong, Hong Kong Please state any competing interests or

state ‘None declared’: None declared

The study reviewed the latest evidence on serial intervals and generation time. The authors provided detailed discussion of the source of bias and methodological issues which is valuable.

Comments to the author
1. Abstract, please clarify why 19 studies were evaluated in detail, out of 27.

The wording of this part of the abstract has been modified to make it clearer why studies were evaluated in detail.

2. Given that a systematic review of COVID-19 epidemiology, including serial intervals (Park et al. J Clin Med 2020), reviewed data up to late February. As pandemic evolved quickly, the authors may consider updating the review.

The review has been updated. In the paper that we originally submitted to BMJ, there were only 8 published papers available. The updated review now contains 40 published papers. Because of the very limited number of published papers available at the time of the original review, we also included pre-prints. In the intervening period, some of these pre-prints have now been published and additional papers have been published. In light of this, we have only included published papers in the updated review.

3. Please update the references if some of the preprints have been published.

This has been done.

4. Abstract and Conclusion. It is unclear why Cereda et al. was highlighted as most relevant to European countries. Another study by Lavezzo et al. also analyzed data in Italy. Furthermore, did the author expect difference in Europe vs other places?

The study by Cereda et al. was highlighted because we believed that it was more relevant to Ireland than non-European based studies. We preferred this paper to the Lavezzo paper because we had concerns about certain aspects of the Lavezzo pre-print paper, namely that there was a lack of clarity on how the number of infector-infectee pairs was obtained and the fact that the researchers reported an increase in the serial interval over time. This finding is contrary to what would be expected when mitigation measures are implemented and was in contrast to the findings of other studies included in the review. In the pre-print, Lavezzo et al. did not provide any explanation as to why this increase might have occurred. The Lavezzo paper has now been published. The number of infector-infectee pairs is still somewhat unclear and the authors now report a decrease in the serial interval over time. The Cereda et al. paper has not been published and is not included in the current review. Overall, we have decided not to recommend a specific value of the serial interval in the updated review but to emphasise the need for individual countries/geographical area to obtain estimates of the serial interval/generation time from data obtained locally.

5. Materials and Methods. “Some of the papers contained parameter estimates derived only from original data without the fitting of statistical distributions. As these papers were considered to be less useful for model development than papers containing distribution-derived estimates, they were also omitted from further consideration.” However, Table 1 did not present the fitted statistical distributions so it’s unclear why these papers were excluded.

Based on the comments of Reviewer 1 and Reviewer 2, we have now included the papers that were not based on statistical distributions and we have included them in two ridge plot (Supplementary

figures 1and 2) in the supplementary information as recommended by Reviewer 2.

6. Table 1. Ref 18. It's unusual that the 95% CI for the mean and median did not overlap at all, given a relatively small sample size.

In the updated version of the review, this paper is now numbered 34. We agree that the difference between the mean and median values is hard to understand. The raw serial interval values on which the parameters are based can be extracted from Figure 2 of the paper. The parameter estimates in the paper, particularly the median value, do not seem to be consistent with these data points. We contacted the authors of this paper with a view to getting clarification on the estimates in their paper but we did not receive a reply. We have inserted the following sentence in the discussion our review to draw attention to this point

"However these estimates, particularly the estimate of the median, do not seem to be consistent with the individual serial interval values that can be extracted from Figure 2 of the paper."

The raw data that we extracted from the paper are plotted in supplementary figure 2.

7. Discussion, generation times can be estimated (Table 1), though it cannot be directly estimated or observed.

We have modified the text to deal with this point as follows:
"Most of the estimates were for serial interval rather than generation time because infection times are difficult to measure and are generally not available. Consequently, data on generation times are rarely available. Instead, typically, the onset of symptoms is observed."

8. Conclusion, please explain in the discussion why the bias can be minimized from using early cases.

We believe that the following text in the discussion deals with this point
"The value of estimating the serial interval, generation time and other key parameters at the start of an epidemic was emphasized by a number of authors. As highlighted by Bi et al. [9], the study of an emerging pathogen at the time of its introduction provides a unique opportunity to characterize its transmission and natural history. In particular, it is possible to make assumptions about when and where cases were likely infected that are more difficult when the pathogen is widespread. Furthermore, during these early phases, uninfected and asymptomatic contacts are often closely tracked, providing critical information on transmission and natural history."

Minor comments
9. Table 1, please clarify upfront that the first estimates were serial intervals.

We have modified Table 1 to reflect this.

10. Discussion, range of estimates obtained, typo 'contracts'

This has been corrected.

11. Discussion, typo 'the(y) set that last date'

This has been corrected.

Reviewer: 2
Reviewer Name: Tim Russell
Institution and Country: Centre for the Mathematical Modelling of Infectious Diseases, London School of Hygiene and Tropical Medicine, UK Please state any competing interests or state 'None declared': None declared

The authors review estimates for the serial interval and generation time of COVID-19. They do so within a systematic review framework, combining search terms with Boolean operators to isolate the relevant papers. They describe in detail which studies are deemed appropriate and which are not. The results of all included distributions are presented in the form of a single large box plot. The study is well conceived, well written and on an important topic. Therefore I believe with just some minor changes, it is of publishable standard. I especially believe the discussion is of great value, given the level of detail about the limitations and potential issues of the papers reviewed, that it goes in to.

Major comments:

There are bound to be more up to date estimates now. Therefore, the review should be updated before publication.

The review has been updated. In the paper that we originally submitted to BMJ, there were only 8 published papers available. The updated review now contains 40 published papers. Because of the very limited number of published papers available at the time of the original review, we also included pre-prints. In the intervening period, some of these pre-prints have now been published and additional papers have been published. In light of this, we have only included published papers in the updated review.

Minor Comments:

The single box-plot nicely summarises the results and is probably the simplest way of presenting the results. However, the authors make a point of only including the studies which report a distribution for either the serial interval or generation time. Therefore, I believe (perhaps as a supplementary plot), it would be a nice addition to show the distributions for all estimated SIs and GTs, perhaps in a ridge plot style figure.

We have now included two ridge plots (Supplementary figures 1and 2) to address this comment. We also provide more detail on the data and parameters that we were able to extract from each paper included in the review. This is summarised in Supplementary table 1.

There is a missing space at the start of the "Funding" subsection

This has now been resolved.

Its really just a matter of style, but I thought the first paragraph of the discussion was a bit too vague, mentioning mainly the importance of preprints. Perhaps the point would have resonated more with some comparison between number of preprints and number of published articles, or something similar. Although, I am very aware this is just a minor point, and I don't think it necessarily needs to be addressed. Re-reading and rewording the paragraph could strengthen the discussion though I believe

This sentence has now been removed, noting a focus solely on published papers (that is, no pre-prints). This brief introduction emphasises the importance of these parameters, the dynamic nature of

available information and the need for caution in interpretation. Each of these points is elaborated further throughout the Discussion.

I like the long list of bullet points outlining potential issues with the papers included in the review. I believe analyses like this are of great importance, as they help to improve the quality of future papers.

VERSION 2 – REVIEW

REVIEWER	Eric Lau University of Hong Kong, China
REVIEW RETURNED	08-Oct-2020

GENERAL COMMENTS	The authors have addressed all my comments satisfactorily, and have done a marvelous job reviewing the recent publications on serial intervals and generation time. The study would provide valuable information on these parameters and consideration on the methodological issues.

REVIEWER	Timothy Russell London School of Hygiene and Tropical Medicine, UK
REVIEW RETURNED	07-Oct-2020

GENERAL COMMENTS	I believe the authors have addressed the comments of both original reviews sufficiently well. The text has been sharpened up where needed, the results completely updated and two ridge plots of all the distributions included have appeared, which are a nice addition. I therefore think the manuscript is now of publishable standard. This is a nice contribution.