The ecological dynamics of the coronavirus epidemics during transmission from outside sources when $R_0$ is successfully managed below one

Steinar Engen, Huaiyu Tian, Ruifu Yang, Ottar N. Bjørnstad, Jason D. Whittington and Nils Chr. Stenseth

Article citation details
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Review timeline
Original submission: 10 December 2020
1st revised submission: 5 March 2021
2nd revised submission: 18 May 2021
Final acceptance: 28 May 2021

Note: Reports are unedited and appear as submitted by the referee. The review history appears in chronological order.

Review History
RSOS-202234.R0 (Original submission)

Review form: Reviewer 1

Is the manuscript scientifically sound in its present form?
Yes

Are the interpretations and conclusions justified by the results?
Yes

Is the language acceptable?
Yes

Do you have any ethical concerns with this paper?
No

Have you any concerns about statistical analyses in this paper?
No
Recommendation?
Major revision is needed (please make suggestions in comments)

Comments to the Author(s)
This is a really interesting and important paper with crucial results for when we reach the stage when Ro <1 for Covid-19 in most communities. I strongly believe this paper should be published, but I think it would have much stronger impact if details of the technical analyses were moved to an Appendix and the authors focus on describing in more detail the implications of their results.

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Review form: Reviewer 2

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Page 6, lines 30-40: please review this paragraph on the eigenvalues/eigenvectors highlighting the meaning of \( u \) and \( v \) in the description of the epidemic.

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Page 6, line 43: also this part on the stochastic model should be revised to better describe how stochasticity is implemented in the case of the epidemiological model. What are the environmental and the demographic noise in this case?

Page 6, line 51: the notation is not clear. What is \( r \) (or \( rV \))?

Page 7, line 36: these are the variances of what?

Page 7, line 43: ‘the new cases during a day is Poisson distributed’. Please replace ‘is’ with ‘are’. It is not clear how over/under dispersions are considered in the Poisson distribution (which has only one parameter). Are the authors using a negative binomial distribution?

Page 7, eq(1): how does this equation changes for the model without stochasticity? If taking into consideration that the number of susceptible is finite, is this formula representing an upper limit for the extinction? I think that \( n_0 \) at line 52 should be \( N_0 \).

Page 8, lines 8-22: this part is probably the core of the epidemiological model proposed and I suggest to move it before in the methods section and add some more details. For example, it must be clear that columns in the Leslie matrix correspond days after the transmission. The period of infectiousness typically changes among individuals. Does the stochastic model take this aspect into consideration?

Page 8, line 24: are the authors referring to eq. 1? \( D \) does not appear explicitly in this equation, thus I suggest replacing \( \sigma_d \) by its relationship with \( D \) if possible. Since \( D \) is the only factor accounting for the stochasticity, I suggest to better describe its role in the model.

Page 8, line 29 in the legend of fig. 1 there is the variable \( D_m \) that has not been mentioned up to now.

Page 8, lines 39-41: this assumption should be clarified earlier, when presenting the model.

Page 8, lines 48-50: the authors say that they assume that the immigrants have been infected recently. Does this mean that all immigrants are assume to enter the first infectious age? Please add details.

Page 9, line 28: replace ‘has’ with ‘have’

Page 9, eq. (2): from the text I do not understand what this equation represents. From the legend of Fig. 2, I can understand that it is related to the distribution of the total reproductive value, and thus to the distribution of the infected cases at equilibrium. But this is not clear in the text. Moreover, the system at equilibrium should have zero infected since the epidemic should be extinct.

Page 9, line 42: The equilibrium for this system should be the extinction of the epidemic, but I am not sure if this is the equilibrium that is mentioned here. Please clarify. In this case, are the fluctuations due to the immigration process?

Table 1: how are these estimates of \( R_t \) obtained? Is it reasonable to assume the same model parameters for all countries, where different policies were imposed? Please mention the source of the data used and add details about the data? The estimation of \( R_t \) is a difficult task when referring to one country, thus it is very difficult to understand how reliable are these estimates for
multiple countries. Please note that in the main text the authors speak about R0, but in the table there is Rt.
Page 10, line 15: what is R_eff?
Page 12, line 15-16: what are variables D_x and E? these details would be interesting if better explained. Probably this part should go in the methods

Decision letter (RSOS-202234.R0)

We hope you are keeping well at this difficult and unusual time. We continue to value your support of the journal in these challenging circumstances. If Royal Society Open Science can assist you at all, please don’t hesitate to let us know at the email address below.

Dear Dr Whittington

The Editors assigned to your paper RSOS-202234 "The ecological dynamics of the Corona epidemics during transmission from outside sources when R0 is successfully managed below one" have now received comments from reviewers and would like you to revise the paper in accordance with the reviewer comments and any comments from the Editors. Please note this decision does not guarantee eventual acceptance.

We invite you to respond to the comments supplied below and revise your manuscript. Below the referees’ and Editors’ comments (where applicable) we provide additional requirements. Final acceptance of your manuscript is dependent on these requirements being met. We provide guidance below to help you prepare your revision.

We do not generally allow multiple rounds of revision so we urge you to make every effort to fully address all of the comments at this stage. If deemed necessary by the Editors, your manuscript will be sent back to one or more of the original reviewers for assessment. If the original reviewers are not available, we may invite new reviewers.

Please submit your revised manuscript and required files (see below) no later than 21 days from today’s (ie 11-Feb-2021) date. Note: the ScholarOne system will ‘lock’ if submission of the revision is attempted 21 or more days after the deadline. If you do not think you will be able to meet this deadline please contact the editorial office immediately.

Please note article processing charges apply to papers accepted for publication in Royal Society Open Science (https://royalsocietypublishing.org/rsos/charges). Charges will also apply to papers transferred to the journal from other Royal Society Publishing journals, as well as papers submitted as part of our collaboration with the Royal Society of Chemistry (https://royalsocietypublishing.org/rsos/chemistry). Fee waivers are available but must be requested when you submit your revision (https://royalsocietypublishing.org/rsos/waivers).

Thank you for submitting your manuscript to Royal Society Open Science and we look forward to receiving your revision. If you have any questions at all, please do not hesitate to get in touch.

Kind regards,
Anita Kristiansen
Editorial Coordinator
Royal Society Open Science
openscience@royalsociety.org
on behalf of Professor Enrico Bertuzzo (Associate Editor) and Pete Smith (Subject Editor)
openscience@royalsociety.org

Associate Editor Comments to Author (Professor Enrico Bertuzzo):
Comments to the Author:
I apologized for the long time it took to finalize the first round of reviews, but it has been rather challenging to secure reviewers during the holiday break. At any rate, the manuscript has now been reviewed by two experts in the field. They both find that the methods developed are interesting and original, but that a major revision would be needed to properly present the material. I share their opinion. In particular, the authors should keep in mind the general audience RSOS is aimed at when revising their manuscript. For instance, a graphical illustration of a Leslie matrix would be helpful to accompany the description in page 7. The reviewers offer detailed suggestions for the revision that I am confident the authors will consider.

Reviewer comments to Author:
Reviewer: 1
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Your revised paper should include the changes requested by the referees and Editors of your manuscript. You should provide two versions of this manuscript and both versions must be provided in an editable format:
- one version identifying all the changes that have been made (for instance, in coloured highlight, in bold text, or tracked changes);
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Please ensure that any equations included in the paper are editable text and not embedded images.

Please ensure that you include an acknowledgements' section before your reference list/bibliography. This should acknowledge anyone who assisted with your work, but does not qualify as an author per the guidelines at https://royalsociety.org/journals/ethics-policies/openness/.

While not essential, it will speed up the preparation of your manuscript proof if accepted if you format your references/bibliography in Vancouver style (please see https://royalsociety.org/journals/authors/author-guidelines/#formatting). You should include DOIs for as many of the references as possible.

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-- A copy of your point-by-point response to referees and Editors. This will expedite the
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include a suitable title and informative caption. An example of appropriate titling and captioning
may be found at https://figshare.com/articles/Table_S2_from_Is_there_a_trade-off_between_peak_performance_and_performance_breadth_across_temperatures_for_aerobic_scope_in_teleost_fishes_/3843624.

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completed, these will be noted by red message boxes.

Author's Response to Decision Letter for (RSOS-202234.R0)

See Appendix A.

RSOS-202234.R1 (Revision)

Review form: Reviewer 2

Is the manuscript scientifically sound in its present form?
Yes

Are the interpretations and conclusions justified by the results?
Yes

Is the language acceptable?
Yes
Do you have any ethical concerns with this paper?
No

Have you any concerns about statistical analyses in this paper?
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Recommendation?
Accept with minor revision (please list in comments)

Comments to the Author(s)
The authors replied in detail to all my comments. I find that the manuscript has been improved, the method section is now quite clear and easy to read. I only have few additional minor comments.

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Please find in the following other minor comments.

Line 119-122: articles are missing

Line 122: please clarify the sentence ‘survivals up to age when there are no longer transmission are 1’.

Line 128: if I understand correctly, each column of the Leslie matrix corresponds to a time step, which in this model is a day. I think it is better to specify this here. Thus the rates are daily rates, correct?

Line 131: please specify ‘The number of transmitters’

Line 135: why the sum of the components of the stable age distribution is one? In the previous line the authors stated that the population grows approximately exponentially! I guess there should be a multiplication by a scalar (which depends on time) in front of the eigenvector u. Please clarify.

Line 164: please define n0.

Line 177: Here the focus is the stationary distribution of V. However, I still have to completely understand what it represents from an epidemiological point of view. In lines 146-152 I find the definition of V, but I do not see why for immigration our focus is this stationary distribution.

Line 430: ‘total reproductive’. Probably missing ‘number’

Line 595, Fig1, legend: In panel 1 of figure 1 there is not a log-scale. Please correct the legend and revise also line 248
Decision letter (RSOS-202234.R1)

We hope you are keeping well at this difficult and unusual time. We continue to value your support of the journal in these challenging circumstances. If Royal Society Open Science can assist you at all, please don’t hesitate to let us know at the email address below.

Dear Dr Whittington

On behalf of the Editors, we are pleased to inform you that your Manuscript RSOS-202234.R1 "The ecological dynamics of the Corona epidemics during transmission from outside sources when R0 is successfully managed below one" has been accepted for publication in Royal Society Open Science subject to minor revision in accordance with the referees' reports. Please find the referees' comments along with any feedback from the Editors below my signature.

We invite you to respond to the comments and revise your manuscript. Below the referees’ and Editors’ comments (where applicable) we provide additional requirements. Final acceptance of your manuscript is dependent on these requirements being met. We provide guidance below to help you prepare your revision.

Please submit your revised manuscript and required files (see below) no later than 7 days from today's (ie 06-May-2021) date. Note: the ScholarOne system will ‘lock’ if submission of the revision is attempted 7 or more days after the deadline. If you do not think you will be able to meet this deadline please contact the editorial office immediately.

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Thank you for submitting your manuscript to Royal Society Open Science and we look forward to receiving your revision. If you have any questions at all, please do not hesitate to get in touch.

Kind regards,
Anita Kristiansen
Editorial Coordinator

Royal Society Open Science
openscience@royalsociety.org

on behalf of Professor Enrico Bertuzzo (Associate Editor) and Pete Smith (Subject Editor)
openscience@royalsociety.org

Associate Editor Comments to Author (Professor Enrico Bertuzzo):
Comments to the Author:
The manuscript has been reviewed by the two original reviewers and both are satisfied with the revision (one review report is not included because the reviewers simply replied by mail with a positive feedback). The first reviewers points to some minor corrections that I am confident the authors can implement while preparing the final files.
Reviewer comments to Author:
Reviewer: 2

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Please find in the following other minor comments.

Line 119-122: articles are missing

Line 122: please clarify the sentence ‘survivals up to age when there are no longer transmission are 1’.

Line 128: if I understand correctly, each column of the Leslie matrix corresponds to a time step, which in this model is a day. I think it is better to specify this here. Thus the rates are daily rates, correct?

Line 131: please specify ‘The number of transmitters’

Line 135: why the sum of the components of the stable age distribution is one? In the previous line the authors stated that the population grows approximately exponentially! I guess there should be a multiplication by a scalar (which depends on time) in front of the eigenvector u. Please clarify.

Line 164: please define n0.

Line 177: Here the focus is the stationary distribution of V. However, I still have to completely understand what it represents from an epidemiological point of view. In lines 146-152 I find the definition of V, but I do not see why for immigration our focus is this stationary distribution.

Line 430: ‘total reproductive’. Probably missing ‘number’

Line 595, Fig1, legend: In panel 1 of figure 1 there is not a log-scale. Please correct the legend and revise also line 248

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Your revised paper should include the changes requested by the referees and Editors of your manuscript. You should provide two versions of this manuscript and both versions must be provided in an editable format:
one version identifying all the changes that have been made (for instance, in coloured highlight, in bold text, or tracked changes);
a 'clean' version of the new manuscript that incorporates the changes made, but does not highlight them. This version will be used for typesetting.

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  2) A 'clean' version of the new manuscript that incorporates the changes made, but does not highlight them.
-- An individual file of each figure (EPS or print-quality PDF preferred [either format should be produced directly from original creation package], or original software format).
-- An editable file of each table (.doc, .docx, .xls, .xlsx, or .csv).
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Author’s Response to Decision Letter for (RSOS-202234.R1)

See Appendix B.

Decision letter (RSOS-202234.R2)

We hope you are keeping well at this difficult and unusual time. We continue to value your support of the journal in these challenging circumstances. If Royal Society Open Science can assist you at all, please don't hesitate to let us know at the email address below.

Dear Dr Whittington,

I am pleased to inform you that your manuscript entitled "The ecological dynamics of the coronavirus epidemics during transmission from outside sources when R0 is successfully managed below one" is now accepted for publication in Royal Society Open Science.

If you have not already done so, please remember to make any data sets or code libraries 'live' prior to publication, and update any links as needed when you receive a proof to check - for instance, from a private 'for review' URL to a publicly accessible 'for publication' URL. It is good practice to also add data sets, code and other digital materials to your reference list.
COVID-19 rapid publication process:

We are taking steps to expedite the publication of research relevant to the pandemic. If you wish, you can opt to have your paper published as soon as it is ready, rather than waiting for it to be published the scheduled Wednesday.

This means your paper will not be included in the weekly media round-up which the Society sends to journalists ahead of publication. However, it will still appear in the COVID-19 Publishing Collection which journalists will be directed to each week (https://royalsocietypublishing.org/topic/special-collections/novel-coronavirus-outbreak).

If you wish to have your paper considered for immediate publication, or to discuss further, please notify openscience_proofs@royalsociety.org and press@royalsociety.org when you respond to this email.

You can expect to receive a proof of your article in the near future. Please contact the editorial office (opencience@royalsociety.org) and the production office (opencience_proofs@royalsociety.org) to let us know if you are likely to be away from e-mail contact -- if you are going to be away, please nominate a co-author (if available) to manage the proofing process, and ensure they are copied into your email to the journal. Due to rapid publication and an extremely tight schedule, if comments are not received, your paper may experience a delay in publication.

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On behalf of the Editors of Royal Society Open Science, thank you for your support of the journal and we look forward to your continued contributions to Royal Society Open Science.

Best regards,

Lianne Parkhouse
Editorial Coordinator
Royal Society Open Science
openscience@royalsociety.org

on behalf of Professor Enrico Bertuzzo (Associate Editor) and Pete Smith (Subject Editor)
openscience@royalsociety.org

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Appendix A

Dear Professor Enrico Bertuzzo (Associate Editor), Pete Smith (Subject Editor) and Anita Kristiansen, Editorial Coordinator,

Manuscript ID RSOS-202234

Thank you very much for your feedback of February 11 this year on our submission RSOS-202234. We are pleased that you invited us to submit a revision. We have carefully attended to all comments provide by the reviewers - all of which contributed to sharpen and improve the previous version of our submission. Here we detail how we have addressed the reviewers’ comments and suggestions.

We have made two major changes in the manuscript. First, there is now a new appendix in which the basic Leslie matrix theory is given, with precise definitions of the matrix elements, the dominant eigenvalue and the left and right eigenvectors. We also include the basic stochastic theory used in the model, and explain how the diffusion approximation can be defined. The main text is then changed accordingly with just a short presentation of the model referring to the appendix.

Second, much new research has been done since we wrote our manuscript, in particular estimation of transmission rates at times after infection. Originally we used a very simple model here with constant rates in an interval \( t_1 \) to \( t_2 \), and did some sensitivity analysis varying these parameters. Now it is known that the rates follow a curve approximately proportional to a gamma distribution. We now use estimates of this from Du et al. (2020), as proposed by reviewer 2, which is a gamma with scape parameter 1.87 and mean 6.6. We keep this form in all our graphs, multiplying all transmission rates with the relevant factor to obtain different values of \( R_0 \). Accordingly, all our figures have been updated, and we have simplified a little since sensitivity analysis on the transmission rates are no longer required. The effect of the
new transmission rates is that they change a little the relation between the dominant eigenvalue $\lambda$ and $R_0$, and make the first age classes having larger reproductive values.

Specific comments and suggestions from the reviewers:

Reviewer 1:

We have moved most of the Leslie matrix theory into a new Appendix A with two parts, deterministic and stochastic theory. Accordingly, much of the technicalities have been removed from the main text.

We are using the parameter $R_0$, but point out that when $R_E$ gets smaller than $R_0$ when a fraction of the population is immune, our results apply by simply replacing $R_0$ by $R_E$.

Reviewer 1 asks for more discussion of time to extinction when $R_{eff}$ is close to 1. We have dealt with this by now using $R_0$ as large as 0.9 as reference value in the sensitivity analysis in the graphs shown in Fig.2. Accordingly, the horizontal axes now goes all the way up to 1000 days in all three graphs. Further, in the upper panel we include new lines for $R_0 = 0.95$ and 0.98.

As proposed by the reviewer we have added a comment on new more transmissible strains that will make it harder to reduce $R_0$.

Reviewer 2:

The general comment by reviewer 2 is taken care of by removing the Leslie theory to an appendix (as proposed by reviewer 1), also adding some more explanation here, as well as now using new realistic estimates of the transmission rates for the corona virus. We added a new paragraph in the beginning of the model section. We also shortened the model section using less mathematical symbols and moved the main part to an appendix. The notation is
standard in Leslie matrix theory and should be no problem.

1) More detailed explanations of the relations between the ecological and epidemiological model are given in a new section at the beginning of the modeling, explaining in particular how rates of transmission come into the model, replacing birth rates in ecology.

2) We agree that immunity of a fraction of the population no longer make $R_0$ the relevant parameter. However, changes in immunity is slow compared to the rather short period a person can transmit the decease. Accordingly, we point out that our analysis is valid also when $R_{eff} < R_0$ simply by reinterpreting $R_0$ or simply replace it by $R_{eff}$.

3) We have now adjusted the transmission rates so they are proportional to the gamma distribution estimated by Du et al. (2020), making our results more realistic.

4) relevant anymore. The table has been taken out.

Page 3, line 27: We have removed the NPI abbreviation which is not required.

Page 3, line 27: NPI has been removed.

Page 3, line 29: The sentence has been corrected.

Page 4, line 18: a reference to availability of vaccines has been added.

Page 4, line 27: This section has been updated.

Page 4, line 46-48: This paper addresses immigration of infections into a population, but does not attempt to evaluate the effectiveness of specific quarantine measures. An effective quarantine would be represented in our theoretical approach as a decrease in $R_E$. 

3
Page 4, line 52-54: The sentence has been rephrased.

Page 5, line 28: it should be clear that it is the time to extinction that follows an inverse Gaussian distribution.

Page 5, line 41: The reference has been added.

Page 6, line 16: We prefer not to introduce an additional symbol for time here. The equation explains what happens in one time step only.

The following comments are taken care of by the removal into the new Appendix A with more explanations, as well as the additional explanation in the introduction. We have now clearly pointed out that our transmission rates should be interpreted as mean values for the age group, thus in general covering effects of for example hospitalization and isolation.

Page 6, line 30-40: now this is done in Appendix A.

Page 6, line 35: Yes, the referee is right, we now use the notation for matrix transposition here.

Page 6, line 43: The explanation of the stochasticity is now better taken care of in the last part of Appendix A.

Page 6, line 51: r and V are both defined precisely.

Page 7, line 36: The concept of individual reproductive values and their variances are now explained better in Appendix A, section on the stochastic model.

Page 7, line 43: One advantage with the diffusion approximation is that it is only based on means and variances. This enables us to express over dispersion with the respect to the Poisson by a single parameter $D$ (variance
to mean ratio). There is no need for considering specific models, such as for example the negative binomial. Its meaning is explained in Appendix A.

Page 7 eq(1): The notation \( N_0 \) is the correct one for the total population size (number of transmitters). The formula expresses probabilities of extinctions before time \( t \). We have added two horizontal lines to Fig.2 at 0.1 and 0.9 so that it is easier to see at which times the probabilities take these values.

Page 8, lines 8-22: taken care of by the new section in the introduction as well as Appendix A.

Page 8, line 24: This part has been changed. We now refer to Fig.2 (based on equation (1)) and the meaning of the parameters should be clear.

Page 8, line 29: All figures are redone, the order is changed and the legends are modified. It should now be ok.

Page 8: We actually know very little about how long the relevant immigrants have been infected. But, no symptoms may indicate that their infection on average was recent. We have in all our illustrations used that the mean reproductive values \( v_m \) of the immigrants are the mean for the first three days. However, our model is general so that \( v_m \) may be replaced by realistic values when such estimates are available.

Page 9, line 28: thanks, corrected.

Page 9, eq(2): we have made it clear that with immigration the process will not go extinct. The stochastic process \( V \) then reaches a stationary distribution, which is what we report by equation (2) illustrated by the lower panel of Fig.3.

Page 9, line 42: no, no extinction occur under constant immigration.
Table 1: has been removed from the manuscript.

page 10, line 15: $R_{eff}$ is now better explained in Appendix A.

page 12, line 15-16: It should be quite clear from an equation given right above that $D_x$ is the over-dispersion in the distribution of $X$ (variance to mean ratio).

Sincerely,

Steinar Engen and Nils Chr. Stenseth on behalf of the authors
Dear Royal Society Open Science Editorial Team,

Manuscript ID RSOS-202234

Thank you for the positive response to our manuscript 'The ecological dynamics of the Corona epidemics during transmission from outside sources when R0 is successfully managed below one.'

We have made the changes proposed by the referee:

The term 'population' is replace by 'number of infectious individuals' where that is appropriate (lines 132, 134, 143, 348, 426, 436, 438)

line 119-122: two articles are added

line 128: We have added the word 'daily' to explain that the time unit is days.

line 131: changed to 'number of infectious individuals'

line 135: This was a misunderstanding. In the population dynamics theory one use the term 'age distribution' for the distribution of individuals among age classes. These are not absolute numbers of individuals in the classes, but the relative frequencies and hence add up to one. This is now clarified.

Line 164: This was a misprint. The small n should be a capital one, which is clearly defined. This has been changed.

Line 177 and lines 146-152: We have added a verbal explanation on how the balance between the reduction due to $R < 1$ and the increase due to immigration leads to a stochastic equilibrium which is what we describe by a stationary distribution.

line 430: missing 'value' is added.
line 595 and legend to Fig.1: We now just use the term ’growth rate $r$’ and remove ’on the log scale’ since it obviously may be misunderstood.