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Host genetic diversity limits parasite success beyond agricultural systems: a meta-analysis

Alice K. E. Ekroth, Charlotte Rafaluk-Mohr and Kayla C. King

Article citation details
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Original submission:	6 June 2019
1st revised submission:	2 August 2019
2nd revised submission:	21 August 2019
Final acceptance:	27 August 2019

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

Review History

RSPB-2019-1331.R0 (Original submission)

Review form: Reviewer 1

Recommendation
Major revision is needed (please make suggestions in comments)

Scientific importance: Is the manuscript an original and important contribution to its field?
Good

General interest: Is the paper of sufficient general interest?
Good

Quality of the paper: Is the overall quality of the paper suitable?
Marginal

Is the length of the paper justified?
Yes

Should the paper be seen by a specialist statistical reviewer?
No

Do you have any concerns about statistical analyses in this paper? If so, please specify them explicitly in your report.
Yes

It is a condition of publication that authors make their supporting data, code and materials available - either as supplementary material or hosted in an external repository. Please rate, if applicable, the supporting data on the following criteria.

Is it accessible?
No

Is it clear?
No

Is it adequate?
No

Do you have any ethical concerns with this paper?
No

Comments to the Author
GENERAL COMMENTS TO THE AUTHORS:
The authors address an important and timely research question, i.e. they ask whether there is broad evidence for the monoculture effect – an increased success of parasites in proliferating in host populations with higher genetic diversity – outside of agricultural systems. The author used a meta-analytical approach for addressing their research question, collating information from 22 different studies. While I found this a very timely study and interesting manuscript, I think some revision of the manuscript is necessary to make the analysis fully understandable and reproducible.
1) Some more details regarding the moderator variables would be helpful: the source of information (e.g. for host range) was unclear for some, and I also found terminology confusing (e.g. parasite load – viral load). In fact, I think use of terminology such as "parasite functional groups" (lines 35, 167, 234; most likely referring to macro- and microparasites as can be learnt from the legend of figure 2) in combination with terms such as "parasite load" (line 119) and "viral load" (120) showcases that there might be some inconsistencies in the definition of variables, which makes it impossible to fully appreciate any results from the analyses.
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Please find specific comments below. Hopefully, some suggestions are useful to the authors.

SPECIFIC COMMENTS:
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Lines 119-120 Please check: the terms "parasite load", "viral concentrations" and "viral load" appear to all refer to the same thing. Moreover, what does 'parasites' distinguish from viruses (i.e. are macroparasites and bacteria etc included all in the group of parasites)? Why is there a measurement of "parasite virulence" and not an equivalent of "viral virulence"? Are measures of pathogen load (I use this term here as an equivalent for "parasite load", "viral concentrations" and "viral load") given for all of the 22 studies included in your meta-analysis? For me, the lack of understanding what went exactly into the analysis means that the current methods description does not necessarily allow to reproduce your study and a thorough revision of the description of variables is in my opinion necessary.
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Line 223 Please check: “strength of the direction of the effect size” appears to be somewhat confusing terminology, for most test statistics, one may expect an effect size/magnitude of effect and a direction of effect, which are two different aspects?
Line 230 Consider to reword “We found that host reproduction was not a factor that significantly…” to make clear that you did not find such effect in your analysis rather than providing any evidence of a true independence of the variables.
Line 231 Perhaps “strength of effect size” can be reworded to make clear which effect not moderated by host reproduction?
Line 231-233 The sentence “A study by Altermatt & Ebert (2008) followed parasite infection…” reads as a method description rather than results? This sentence was also unclear to me, since I was not able to understand how a single study can be meaningfully be used as a ‘separate variable’ in a meta-analytical model.
Line 231-233 I do not understand the terminology “strength of the direction of the effect size”? Please check.
Line 229-244 Perhaps consider to present all significant effects first and then report those moderator variables for which no impact on the monoculture effect were found with your particular data set?
Line 250 Since “approaches” are not appropriately defined in your methods (see comment line 172), I found it impossible to acknowledge the key results highlighted in this sentence.
Line 250 I assume “environments” refer to laboratory and field-based studies? If so, perhaps mention this here and avoid the generic term ‘environment’(which could be misinterpreted in terms of different abiotic or biotic natural environments).
Line 251 The sentence “revealed under the majority of the biological variables we tested” is in my opinion highly misleading and should be deleted (unless the authors provide a strong reason why not): if there is variation in a response variable and such variation is tested against a broad set biological predictor variables, the number of predictor variables does not say anything about how broadly inference can be made. In this particular study, the authors did not find much evidence of host traits affecting the monoculture effects and they were not able to test for different abiotic or biotic environments such as different climates or biogeographical regions or habitats etc.
Line 255 The lack of an effect in an analytical model and a finite data set does not allow conclusion on the independence of variables? Can you exclude any possible effect of sample size and bias?
Line 264 Is it “pathogen’s host specificity” rather than “pathogen specificity”?

Review form: Reviewer 2

Recommendation
Major revision is needed (please make suggestions in comments)

Scientific importance: Is the manuscript an original and important contribution to its field?
Good

General interest: Is the paper of sufficient general interest?
Good

Quality of the paper: Is the overall quality of the paper suitable?
Acceptable

Is the length of the paper justified?
Yes

Should the paper be seen by a specialist statistical reviewer?
No

Do you have any concerns about statistical analyses in this paper? If so, please specify them explicitly in your report.
Yes

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Is it accessible?
N/A

Is it clear?
N/A

Is it adequate?
N/A

Do you have any ethical concerns with this paper?
No

Comments to the Author
This manuscript is a meta-analysis that focuses on the monoculture effect – that is, whether host populations with low genetic diversity are at greater risk of infectious disease outbreaks. This is something that has been demonstrated in agricultural systems. This manuscript is an important extension asking whether this effect also holds in non-agricultural systems, using a meta-analysis to address this question. The topic is interesting, but I have several questions/comments related to the work that was done and the manuscript.

1. The authors pitch the abstract in dramatic terms – "Human activities are greatly reducing the genetic diversity of species worldwide". That's a strong statement but, understandably given that it's in the abstract, there are no references to support it. In the main text, the statement is more measured: "Threats to genetic diversity are on the rise. Habitat alterations, pollution, and global temperature changes, as well as the restriction of species geographical ranges may lead to higher

chances of genetic drift and reduced population genetic diversity (7).” Reference 7 is a manuscript on a single species of damselfly, so doesn’t seem especially appropriate here (especially since one of their main conclusions is “Our results suggest that, although a marginal significant decrease in the allelic richness was found in the edge populations, genetic diversity has been preserved during the range expansion of this species.”)

At face value, this statement seems obvious – surely we’ve lost lots of local diversity, right? But studies of local biodiversity at the species level have found that, excluding areas converted to concrete or agriculture, there actually isn’t much evidence for overall losses in species-level biodiversity at the local level (see Vellend et al. 2017 Ecology, McGill et al. 2015 TREE). So, I encourage the authors to really explore what we know about changes in biodiversity at the population level and to use that to frame their study.

(Note: this comment applies in the discussion, too)

2. Some of the methods for the literature review are unclear or need to be better specified. Specifically:
a. Why are there only approximate numbers for the top part of the flow chart?
b. Table 2 is presented as showing the studies that were excluded from the analysis, but this is only the studies excluded at the full text screening step.
c. Lines 113-115 & Figure S1: Did the search require all of these terms? Or were subsets of them used?
d. One paper that is relevant that wasn’t included is the Strauss et al. 2017 Proc B paper, which found that more diverse populations had *higher* densities of infected hosts. It’s possible it came out after the authors selected their studies.

3. One part of the analysis focuses on whether parasites are specialists or generalists. How was this determined? No information is given about this, even though it seems like this might have been challenging to do in some cases. In addition to giving information on how this was determined, the assignment that was given (specialist vs. generalist) should be added to Table 1.

4. Lines 216ff: The authors point to the funnel plot as indicating that there is no publication bias, since the majority of points fall within the plot. However, the plot (Figure S2) is not very funnel shaped – it actually seems like the funnel shape is flipped from what is typical for funnel plots for meta-analyses (Figure S2 shows greater spread at the top than the bottom). What does that indicate about the datasets included in the study?

5. For the analysis of host reproduction: what would be found if the Altermatt & Ebert study was excluded from the analysis? Based on figure 2A, it seems like there is a (potentially significant, based on 95% CIs) larger effect size for asexual hosts than sexual ones.

6. Lines 258ff: What is the basis of the statement on lines 260-262 that the monoculture effect is “equally prevalent”? Do you mean that it was found in highly specialized interactions, broad spectrum interactions at the genotypic level, and those that cross host-species boundaries? Or do it actually refer to prevalence (rather than simply whether it happens at least once)? If the latter, that needs to be explained better. If the former, the wording needs to change. For this paragraph (and comment 3 above), it would help to give more explanation of how these different groups were defined.

Additional (more specific) comments:
1. Line 96: I’d suggest adding something to the effect of “and in non-agricultural systems” at the end of this sentence.
2. Lines 103-104: This sentence (which indicates that a parasite’s ability to have a high abundance

in its host is related to host mortality) conflicts somewhat with the argument in the previous paragraph.
3. Lines 222-225: I had to read this sentence a few times to understand it. I think the second half would be clearer if it said something like "where field studies (r = 0.2801) had larger effect sizes than lab studies (r = 0.1077).
4. Lines 235-237: it would help to add a little explanation for the reader – it takes some effort on the part of the reader to move from "microparasites showed a strong, positive impact" to the biologically interesting effect that this indicates.
5. Line 290: For this paragraph, it seems more important that a monoculture effect was found in the field, than the one that was found for the field was stronger than the lab.

Review form: Reviewer 3

Recommendation
Accept with minor revision (please list in comments)

Scientific importance: Is the manuscript an original and important contribution to its field?
Excellent

General interest: Is the paper of sufficient general interest?
Excellent

Quality of the paper: Is the overall quality of the paper suitable?
Excellent

Is the length of the paper justified?
Yes

Should the paper be seen by a specialist statistical reviewer?
No

Do you have any concerns about statistical analyses in this paper? If so, please specify them explicitly in your report.
No

It is a condition of publication that authors make their supporting data, code and materials available - either as supplementary material or hosted in an external repository. Please rate, if applicable, the supporting data on the following criteria.

> **Is it accessible?**
> N/A
>
> **Is it clear?**
> N/A
>
> **Is it adequate?**
> N/A

Do you have any ethical concerns with this paper?
No

Comments to the Author
This is a highly interesting and clear study that demonstrates how reduced genetic diversity in host populations renders them more vulnerable to disease. This phenomenon is best understood from agricultural scenarios and it is actually quite surprising that it has not been addressed before in natural systems in a systematic manner. Given that genetic diversity is declining alongside biodiversity, this could have severe implications for risks of disease, yet this is the first systematic quantification of that risk.

Overall, I found the manuscript well written and clear, and the analyses suitable, and the conclusions warranted based on the results. I also appreciate that the study spans across different host-pathogen systems to really show how generalizable this finding is. I would expect the study to be well cited, I certainly would have wanted to cite this results on multiple occasions. I have some suggestions that could further improve the clarity of the work, but these are such that they could be easily achieved in a revision.

I realize that space may be limiting but I would find it greatly helpful if the authors would clarify HOW the monoculture effect is expected to function in the Introduction. While this may seem straightforward, there may be different aspects to consider. For example, for an already established pathogen, identical hosts may indeed promote between-host transmission, but such homogeneity may filter out non-compatible strains. Greater transmission may be achieved with greater strain diversity. Hence, it is not always obvious that low genetic diversity would be most conductive to transmission. Highly relevant to this is the infection genetics of the interaction (gene-for-gene, matching allele, specialist-generalist at the within species level), which deserves some discussion in the introduction.

Related to the above, I wondered whether it would not have been possible to estimate the effect of infection genetics? For some of these interactions such data is should be available.

Given that host genetic diversity is such a key measurement in the study, I would have wanted to see more information on how it was extracted from the studies, and what the measurements actually are. Is it only genetic diversity or also resistance phenotypes obtained through inoculations? Measured using neutral markers? Measured at relevant resistance/immunity loci? What do low and high genetic diversity mean in practice?

The term 'monoculture effect' was used in manuscript to refer to the effect of lower genetic diversity. This may create some confusion with those familiar with agricultural terminology where there are true – and vast – monocultures. I would recommend the authors to use genetic diversity instead.

Related to the point above (and given that many interested in wild life disease may not have any ideas about agricultural setting), a more general title framed around low genetic diversity and disease risk might work better than the current title.

Minor comments
Sentence starting on 77- does not read well, perhaps missing a word?

Line 85 – by disease impact do you mean virulence?

Decision letter (RSPB-2019-1331.R0)

24-Jun-2019

Dear Miss Ekroth:

I am writing to inform you that your manuscript RSPB-2019-1331 entitled "Diversity and disease: evidence for the monoculture effect beyond agricultural systems" has, in its current form, been rejected for publication in Proceedings B.

This action has been taken on the advice of referees, who have recommended that substantial revisions are necessary. With this in mind we would be happy to consider a resubmission, provided the comments of the referees are fully addressed. However please note that this is not a provisional acceptance.

The resubmission will be treated as a new manuscript. However, we will approach the same reviewers if they are available and it is deemed appropriate to do so by the Editor. Please note that resubmissions must be submitted within six months of the date of this email. In exceptional circumstances, extensions may be possible if agreed with the Editorial Office. Manuscripts submitted after this date will be automatically rejected.

Please find below the comments made by the referees, not including confidential reports to the Editor, which I hope you will find useful. If you do choose to resubmit your manuscript, please upload the following:

1) A ‘response to referees’ document including details of how you have responded to the comments, and the adjustments you have made.
2) A clean copy of the manuscript and one with 'tracked changes' indicating your 'response to referees' comments document.
3) Line numbers in your main document.

To upload a resubmitted manuscript, log into http://mc.manuscriptcentral.com/prsb and enter your Author Centre, where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Resubmission." Please be sure to indicate in your cover letter that it is a resubmission, and supply the previous reference number.

Sincerely,

Professor Gary Carvalho
mailto: proceedingsb@royalsociety.org

Comments to Author:
Thank you for submitting your manuscript to PRSB, for consideration as an evidence synthesis article. I now have reports from 3 experts in the field, and I have also read the manuscript myself.

Collectively, I am pleased to say that there is a consensus, that you tackle a clear, distinctive and timely issue, that complements well, our existing understanding of such considerations within agricultural systems. In the main, the manuscript is clear, with an informative range of literature included. However, as you will see from the comments below, there are many issues identified, that would further strengthen and clarify your manuscript, particularly in the context of an evidence synthesis article. Please do remember at the outset, and the criteria are available on the PRSB website, that our evidence synthesis articles, are intended to reach a defined, though necessarily broad readership, a component of which may comprise non-specialists. In such circumstances, it is therefore vital that there is clarity, accessibility and consistency in the methodology employed, the inferences drawn, and of course, with sufficient robustness, to contribute to the respective evidence base in a representative manner.

I would therefore ask you to consider the comments below, providing a full response, and I encourage you to submit a new manuscript. Foremost among the issues, including some of my own, I summarise here. First of all, you will see that there are issues relating to clarity and accessibility of the methodology employed, especially some components of the meta-analysis. Specifically, your use of the funnel plot, requires additional consideration, and I would also ask you, whether it is possible to increase the robustness and independence of your inferences, by considering any additional such test? I agree fundamentally, that some statements require tempering, especially those statements, reporting a lack of effects. There is also a need to more broadly exercise clarity and consistency in the terminology employed, especially to avoid confusion, and to promote accessibility to non-specialists. Some statements, as identified by the referees, do not have full referencing. Always ensure that statements made, including those in the abstract, are consistent with the tone and emphasis within the manuscript, and that they are also very clear. For example, you start out in the abstract by emphasising the impact that humans have had on genetic diversity. Different people will have different ideas of what is included within "genetic diversity", and as you are really focusing on within species diversity, then that needs to be made explicit: the impact of humans, on biodiversity more generally, including species richness and diversity, will have different drivers and impacts, and it is important, here to clarify the biological level you are referring to. As one of the referees points out, please exercise consistency and balance in statements made. One of the referees, illustrates this point, by an overstatement relating to work on a single species of damselfly. While still on the abstract, you do of course refer to the "monoculture effect", and I would suggest just including a few words to clarify specifically, for the benefit of non-specialists, what that actually is. There are additional issues relating to methodology, such as how the host genetic diversity has been estimated from published studies?

An additional factor, as identified by the referees is to ensure as with all high quality scientific publications, that there is appropriate balance in how you survey and synthesise the literature, and how you arrive at recommendations and inferences. Clearly, this is even more important within an evidence synthesis article, and therefore, reporting data to the contrary of your own findings, such as Vellend et al.,. 2017, and McGill et al., 2015 (see referee report + any others?). Additional information is required concerning how the parasites are classified into specialists and generalists. I also agree that the title requires revision: it is vitally important at the outset, that the readership knows the biological level on which you are focusing, and therefore do include the word "genetic", as in genetic diversity.

Further details on the resubmission process are provided below. Please do ensure that you provide a full and annotated response to the various issues raised, with a rough indication of how and where, changes are made in the manuscript. While the course I cannot guarantee their availability, I will do my best, in the interests of consistency and efficiency, to approach the original 3 reviewers. While you will see there are some substantive matters requiring additional work, I very much hope that you will be motivated to consider a full resubmission, and I have confidence that an appropriate response, would likely increase not only the quality, but also the accessibility and likely impact of your evidence synthesis article. As with all peer-review processes, however, please note that the invitation for resubmission, does not necessarily guarantee publication, and this will of course depend upon the nature of your response, and ongoing opinions of our identified referees. Please do note, that it would be highly unusual for PRSB to allow a further round of Major revision, and therefore a clear and constructive approach to resubmission would be highly beneficial.

Reviewer(s)' Comments to Author:

Referee: 1

Comments to the Author(s)
GENERAL COMMENTS TO THE AUTHORS:
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Line 211 Suggst to also mention the number of unique host-parasite species associations reported in the 22 studies.
Line 211 Perhaps consider to delete "to answer the research question and"? You found 22 studies to match inclusion criteria but they were not selected in terms of analytical power etc.

Line 223 Please check: "strength of the direction of the effect size" appears to be somewhat confusing terminology, for most test statistics, one may expect an effect size/magnitude of effect and a direction of effect, which are two different aspects?
Line 230 Consider to reword "We found that host reproduction was not a factor that significantly…" to make clear that you did not find such effect in your analysis rather than providing any evidence of a true independence of the variables.
Line 231 Perhaps "strength of effect size" can be reworded to make clear which effect not moderated by host reproduction?
Line 231-233 The sentence "A study by Altermatt & Ebert (2008) followed parasite infection…" reads as a method description rather than results? This sentence was also unclear to me, since I was not able to understand how a single study can be meaningfully be used as a 'separate variable' in a meta-analytical model.
Line 231-233 I do not understand the terminology "strength of the direction of the effect size"? Please check.
Line 229-244 Perhaps consider to present all significant effects first and then report those moderator variables for which no impact on the monoculture effect were found with your particular data set?
Line 250 Since "approaches" are not appropriately defined in your methods (see comment line 172), I found it impossible to acknowledge the key results highlighted in this sentence.
Line 250 I assume "environments" refer to laboratory and field-based studies? If so, perhaps mention this here and avoid the generic term 'environment'(which could be misinterpreted in terms of different abiotic or biotic natural environments).
Line 251 The sentence "revealed under the majority of the biological variables we tested" is in my opinion highly misleading and should be deleted (unless the authors provide a strong reason why not): if there is variation in a response variable and such variation is tested against a broad set biological predictor variables, the number of predictor variables does not say anything about how broadly inference can be made. In this particular study, the authors did not find much evidence of host traits affecting the monoculture effects and they were not able to test for different abiotic or biotic environments such as different climates or biogeographical regions or habitats etc.
Line 255 The lack of an effect in an analytical model and a finite data set does not allow conclusion on the independence of variables? Can you exclude any possible effect of sample size and bias?
Line 264 Is it "pathogen's host specificity" rather than "pathogen specificity"?

Referee: 2

Comments to the Author(s)
This manuscript is a meta-analysis that focuses on the monoculture effect – that is, whether host populations with low genetic diversity are at greater risk of infectious disease outbreaks. This is something that has been demonstrated in agricultural systems. This manuscript is an important extension asking whether this effect also holds in non-agricultural systems, using a meta-analysis to address this question. The topic is interesting, but I have several questions/comments related to the work that was done and the manuscript.

1. The authors pitch the abstract in dramatic terms – "Human activities are greatly reducing the genetic diversity of species worldwide". That's a strong statement but, understandably given that it's in the abstract, there are no references to support it. In the main text, the statement is more measured: "Threats to genetic diversity are on the rise. Habitat alterations, pollution, and global temperature changes, as well as the restriction of species geographical ranges may lead to higher chances of genetic drift and reduced population genetic diversity (7)." Reference 7 is a manuscript on a single species of damselfly, so doesn't seem especially appropriate here

(especially since one of their main conclusions is "Our results suggest that, although a marginal significant decrease in the allelic richness was found in the edge populations, genetic diversity has been preserved during the range expansion of this species.")

At face value, this statement seems obvious – surely we've lost lots of local diversity, right? But studies of local biodiversity at the species level have found that, excluding areas converted to concrete or agriculture, there actually isn't much evidence for overall losses in species-level biodiversity at the local level (see Vellend et al. 2017 Ecology, McGill et al. 2015 TREE). So, I encourage the authors to really explore what we know about changes in biodiversity at the population level and to use that to frame their study.

(Note: this comment applies in the discussion, too)

2. Some of the methods for the literature review are unclear or need to be better specified. Specifically:
a. Why are there only approximate numbers for the top part of the flow chart?
b. Table 2 is presented as showing the studies that were excluded from the analysis, but this is only the studies excluded at the full text screening step.
c. Lines 113-115 & Figure S1: Did the search require all of these terms? Or were subsets of them used?
d. One paper that is relevant that wasn't included is the Strauss et al. 2017 Proc B paper, which found that more diverse populations had *higher* densities of infected hosts. It's possible it came out after the authors selected their studies.

3. One part of the analysis focuses on whether parasites are specialists or generalists. How was this determined? No information is given about this, even though it seems like this might have been challenging to do in some cases. In addition to giving information on how this was determined, the assignment that was given (specialist vs. generalist) should be added to Table 1.

4. Lines 216ff: The authors point to the funnel plot as indicating that there is no publication bias, since the majority of points fall within the plot. However, the plot (Figure S2) is not very funnel shaped – it actually seems like the funnel shape is flipped from what is typical for funnel plots for meta-analyses (Figure S2 shows greater spread at the top than the bottom). What does that indicate about the datasets included in the study?

5. For the analysis of host reproduction: what would be found if the Altermatt & Ebert study was excluded from the analysis? Based on figure 2A, it seems like there is a (potentially significant, based on 95% CIs) larger effect size for asexual hosts than sexual ones.

6. Lines 258ff: What is the basis of the statement on lines 260-262 that the monoculture effect is "equally prevalent"? Do you mean that it was found in highly specialized interactions, broad spectrum interactions at the genotypic level, and those that cross host-species boundaries? Or do it actually refer to prevalence (rather than simply whether it happens at least once)? If the latter, that needs to be explained better. If the former, the wording needs to change. For this paragraph (and comment 3 above), it would help to give more explanation of how these different groups were defined.

Additional (more specific) comments:
1. Line 96: I'd suggest adding something to the effect of "and in non-agricultural systems" at the end of this sentence.
2. Lines 103-104: This sentence (which indicates that a parasite's ability to have a high abundance in its host is related to host mortality) conflicts somewhat with the argument in the previous paragraph.

3. Lines 222-225: I had to read this sentence a few times to understand it. I think the second half would be clearer if it said something like "where field studies (r = 0.2801) had larger effect sizes than lab studies (r = 0.1077).
4. Lines 235-237: it would help to add a little explanation for the reader – it takes some effort on the part of the reader to move from "microparasites showed a strong, positive impact" to the biologically interesting effect that this indicates.
5. Line 290: For this paragraph, it seems more important that a monoculture effect was found in the field, than the one that was found for the field was stronger than the lab.

Referee: 3

Comments to the Author(s)
This is a highly interesting and clear study that demonstrates how reduced genetic diversity in host populations renders them more vulnerable to disease. This phenomenon is best understood from agricultural scenarios and it is actually quite surprising that it has not been addressed before in natural systems in a systematic manner. Given that genetic diversity is declining alongside biodiversity, this could have severe implications for risks of disease, yet this is the first systematic quantification of that risk.

Overall, I found the manuscript well written and clear, and the analyses suitable, and the conclusions warranted based on the results. I also appreciate that the study spans across different host-pathogen systems to really show how generalizable this finding is. I would expect the study to be well cited, I certainly would have wanted to cite this results on multiple occasions. I have some suggestions that could further improve the clarity of the work, but these are such that they could be easily achieved in a revision.

I realize that space may be limiting but I would find it greatly helpful if the authors would clarify HOW the monoculture effect is expected to function in the Introduction. While this may seem straightforward, there may be different aspects to consider. For example, for an already established pathogen, identical hosts may indeed promote between-host transmission, but such homogeneity may filter out non-compatible strains. Greater transmission may be achieved with greater strain diversity. Hence, it is not always obvious that low genetic diversity would be most conductive to transmission. Highly relevant to this is the infection genetics of the interaction (gene-for-gene, matching allele, specialist-generalist at the within species level), which deserves some discussion in the introduction.

Related to the above, I wondered whether it would not have been possible to estimate the effect of infection genetics? For some of these interactions such data is should be available.

Given that host genetic diversity is such a key measurement in the study, I would have wanted to see more information on how it was extracted from the studies, and what the measurements actually are. Is it only genetic diversity or also resistance phenotypes obtained through inoculations? Measured using neutral markers? Measured at relevant resistance/immunity loci? What do low and high genetic diversity mean in practice?

The term 'monoculture effect' was used in manuscript to refer to the effect of lower genetic diversity. This may create some confusion with those familiar with agricultural terminology where there are true – and vast – monocultures. I would recommend the authors to use genetic diversity instead.

Related to the point above (and given that many interested in wild life disease may not have any ideas about agricultural setting), a more general title framed around low genetic diversity and disease risk might work better than the current title.

Minor comments
Sentence starting on 77- does not read well, perhaps missing a word?

Line 85 – by disease impact do you mean virulence?

Author's Response to Decision Letter for (RSPB-2019-1331.R0)

See Appendix A.

RSPB-2019-1811.R0

Review form: Reviewer 1

Recommendation
Accept with minor revision (please list in comments)

Scientific importance: Is the manuscript an original and important contribution to its field?
Good

General interest: Is the paper of sufficient general interest?
Excellent

Quality of the paper: Is the overall quality of the paper suitable?
Good

Is the length of the paper justified?
Yes

Should the paper be seen by a specialist statistical reviewer?
No

Do you have any concerns about statistical analyses in this paper? If so, please specify them explicitly in your report.
No

It is a condition of publication that authors make their supporting data, code and materials available - either as supplementary material or hosted in an external repository. Please rate, if applicable, the supporting data on the following criteria.

> **Is it accessible?**
> No

Is it clear?
No

Is it adequate?
No

Do you have any ethical concerns with this paper?
Yes

Comments to the Author

The authors have thoroughly revised their manuscript and improved the study. I have only some specific comments to add that can be addressed in a short revision.
The authors are encouraged to publish the data set and R code of analysis rather than referring to literature from which data were extracted in order to facilitate data accessibility by peers; I was not able to find the relevant data in the supplements or a link to an external repository in the current manuscript version.

Lines 37-38 Please check the order of "parasite's host range, host reproduction, parasite diversity, virulence, and the method by which parasite success was recorded" – list host traits, parasites traits and then bias such as "host reproduction, parasite's host range, parasite diversity, virulence, and the method by which parasite success was recorded".
Lines 51-52 The last sentence of the abstract needs to be rewritten; the current beginning of the sentence "Consequently, this phenomenon could become increasingly common" does not link to the previous sentence
Line 68 Replace "higher chances of genetic drift" with "increased genetic drift" or euqivalent?
Line 89 Replace "parasite infection" with "parasite success"?
Line 114 Suggest to reword "parasite infection": it is not clear if you refer to something like parasite prevalence or parasite spread or any measure of the parasite success.
Line 118 I think this sentence can be clarified: "host survival might be less informative because the interplay of virulence, force of infection and the timing of infection determined the overall spread of pathogens in host populations (Wells et al 2017)" (Wells, K., Hamede, R., Kerlin, D.H., Storfer, A., Hohenlohe, P.A., Jones, M.E. & McCallum, H.I. (2017) Infection of the fittest: devil facial tumour disease has greatest effect on individuals with highest reproductive output. Ecology Letters, 20, 770–778).
Line 156 and Line 170 Replace "parasite infection measure" with "parasite success measure"?
Line 197 You may replace "many parasite species (>1 Species)" with "> 1 parasite species" or "multiple parasite species"?
Line 230 Would be helpful to mention what kind of test statistics 'r' and 'z' refer to.
Line 231 If 'Q' refers to Cochran's Q-test, perhaps add this information here?
Line 238 Perhaps mention here that excluding the study by Altermatt & Ebert (2008) means excluding the Daphnia study?
Line 240-242 Please check: the statement "If the parasites were macroparasites (r = - 0.0091), no effect of host genetic diversity was revealed in the study, but the success of microparasites (r = 0.2207) was limited by high host population genetic diversity." Suggest that you run separate models for these two parasite groups rather than including the micro-macro-parasite categorization as a moderator variable in a single model? If so, this should be mentioned in the methods; otherwise it would be helpful to explain to what kind of test statistics 'r' refers to (explain in line 230 where first mentioned) to avoid any confusion?
Lines 254-255 Suggest to delete "populations, given that their susceptibility is not influenced by a parasite's host range" (the link to host specificity is in my opinion rather unclear, especially as EIDs can emerge after spillover events from different host species or due to changing population conditions).

Line 258-259 The sentence "However, we show that low host genetic diversity does not appear to be associated with a parasite's host range." Needs to be rewritten for two reasons: first, I think you explore the effects of host rang on parasite success in populations with low versus high genetic diversity? Second, I don't think you 'show' the absence of an effect but rather you did not found any evidence of such effect. I would expect a more appropriate statement to read as "However, we found no evidence that a parasite's host range affected its success in host populations with low versus high genetic diversity"?
Lines 284-285 Host diversity/host range and should not only depend on "new individuals" but rather regional species pools, which may change with shifting species distribution and invasive species, for example. There is increasing recognition that host specificity changes in variable environments (e.g. Wells, K. & Clark, N.J. (2019) Host specificity in variable environments. Trends in Parasitology, 6, 452-465). Suggest to explicitly mention here 'species' and changing ecological opportunities in addition to "new individuals".

Review form: Reviewer 2

Recommendation
Accept as is

Scientific importance: Is the manuscript an original and important contribution to its field?
Excellent

General interest: Is the paper of sufficient general interest?
Excellent

Quality of the paper: Is the overall quality of the paper suitable?
Good

Is the length of the paper justified?
Yes

Should the paper be seen by a specialist statistical reviewer?
No

Do you have any concerns about statistical analyses in this paper? If so, please specify them explicitly in your report.
No

It is a condition of publication that authors make their supporting data, code and materials available - either as supplementary material or hosted in an external repository. Please rate, if applicable, the supporting data on the following criteria.

Is it accessible?
N/A

Is it clear?
N/A

Is it adequate?
N/A

Do you have any ethical concerns with this paper?
No

Comments to the Author
I think the authors have done a good job overall of addressing the topics raised in the first round of review. I have just one minor correction: Supplementary Figure 1 still lists 22 studies, not 23, so I think it wasn't updated.

Decision letter (RSPB-2019-1811.R0)

12-Aug-2019

Dear Miss Ekroth:

Your manuscript has now been peer reviewed and the reviews have been assessed by an Associate Editor. The reviewers' comments (not including confidential comments to the Editor) and the comments from the Associate Editor are included at the end of this email for your reference. As you will see, the reviewers and the Editors have raised some concerns with your manuscript and we would like to invite you to revise your manuscript to address them.

We do not 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 Associate Editor, 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 note that we cannot guarantee eventual acceptance of your manuscript at this stage.

To submit your revision please log into http://mc.manuscriptcentral.com/prsb and enter your Author Centre, where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions", click on "Create a Revision". Your manuscript number has been appended to denote a revision.

When submitting your revision please upload a file under "Response to Referees" in the "File Upload" section. This should document, point by point, how you have responded to the reviewers' and Editors' comments, and the adjustments you have made to the manuscript. We require a copy of the manuscript with revisions made since the previous version marked as 'tracked changes' to be included in the 'response to referees' document.

Your main manuscript should be submitted as a text file (doc, txt, rtf or tex), not a PDF. Your figures should be submitted as separate files and not included within the main manuscript file.

When revising your manuscript you should also ensure that it adheres to our editorial policies (https://royalsociety.org/journals/ethics-policies/). You should pay particular attention to the following:

Research ethics:
If your study contains research on humans please ensure that you detail in the methods section whether you obtained ethical approval from your local research ethics committee and gained informed consent to participate from each of the participants.

Use of animals and field studies:

If your study uses animals please include details in the methods section of any approval and licences given to carry out the study and include full details of how animal welfare standards were ensured. Field studies should be conducted in accordance with local legislation; please include details of the appropriate permission and licences that you obtained to carry out the field work.

Data accessibility and data citation:
It is a condition of publication that you make available the data and research materials supporting the results in the article. Datasets should be deposited in an appropriate publicly available repository and details of the associated accession number, link or DOI to the datasets must be included in the Data Accessibility section of the article (https://royalsociety.org/journals/ethics-policies/data-sharing-mining/). Reference(s) to datasets should also be included in the reference list of the article with DOIs (where available).

In order to ensure effective and robust dissemination and appropriate credit to authors the dataset(s) used should also be fully cited and listed in the references.

If you wish to submit your data to Dryad (http://datadryad.org/) and have not already done so you can submit your data via this link http://datadryad.org/submit?journalID=RSPB&manu=(Document not available), which will take you to your unique entry in the Dryad repository.

If you have already submitted your data to dryad you can make any necessary revisions to your dataset by following the above link.

For more information please see our open data policy http://royalsocietypublishing.org/data-sharing.

Electronic supplementary material:
All supplementary materials accompanying an accepted article will be treated as in their final form. They will be published alongside the paper on the journal website and posted on the online figshare repository. Files on figshare will be made available approximately one week before the accompanying article so that the supplementary material can be attributed a unique DOI. Please try to submit all supplementary material as a single file.

Online supplementary material will also carry the title and description provided during submission, so please ensure these are accurate and informative. Note that the Royal Society will not edit or typeset supplementary material and it will be hosted as provided. Please ensure that the supplementary material includes the paper details (authors, title, journal name, article DOI). Your article DOI will be 10.1098/rspb.[paper ID in form xxxx.xxxx e.g. 10.1098/rspb.2016.0049].

Please submit a copy of your revised paper within three weeks. If we do not hear from you within this time your manuscript will be rejected. If you are unable to meet this deadline please let us know as soon as possible, as we may be able to grant a short extension.

Thank you for submitting your manuscript to Proceedings B; we look forward to receiving your revision. If you have any questions at all, please do not hesitate to get in touch.

Best wishes,
Dr The Proceedings B Team
mailto: proceedingsb@royalsociety.org

Associate Editor Board Member
Comments to Author:
Thank you for the resubmitted MS. Please do address the remaining suggestions by Referee #1, and especially the request to promote accessibility of your data set and R code. As before, please include your response letter indicating how you have responded.

Reviewer(s)' Comments to Author:

Referee: 1

Comments to the Author(s).
The authors have thoroughly revised their manuscript and improved the study. I have only some specific comments to add that can be addressed in a short revision.
The authors are encouraged to publish the data set and R code of analysis rather than referring to literature from which data were extracted in order to facilitate data accessibility by peers; I was not able to find the relevant data in the supplements or a link to an external repository in the current manuscript version.

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EIDs can emerge after spillover events from different host species or due to changing population conditions).
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Lines 284-285 Host diversity/host range and should not only depend on “new individuals” but rather regional species pools, which may change with shifting species distribution and invasive species, for example. There is increasing recognition that host specificity changes in variable environments (e.g. Wells, K. & Clark, N.J. (2019) Host specificity in variable environments. Trends in Parasitology, 6, 452-465). Suggest to explicitly mention here ‘species’ and changing ecological opportunities in addition to “new individuals”.

Referee: 2

Comments to the Author(s).
I think the authors have done a good job overall of addressing the topics raised in the first round of review. I have just one minor correction: Supplementary Figure 1 still lists 22 studies, not 23, so I think it wasn’t updated.

Author's Response to Decision Letter for (RSPB-2019-1811.R0)

See Appendix B.

Decision letter (RSPB-2019-1811.R1)

27-Aug-2019

Dear Miss Ekroth

I am pleased to inform you that your manuscript entitled "Host genetic diversity limits parasite success beyond agricultural systems: a meta-analysis" has been accepted for publication in Proceedings B.

You can expect to receive a proof of your article from our Production office in due course, please check your spam filter if you do not receive it. PLEASE NOTE: you will be given the exact page length of your paper which may be different from the estimation from Editorial and you may be asked to reduce your paper if it goes over the 10 page limit.

If you are likely to be away from e-mail contact please let us know. Due to rapid publication and an extremely tight schedule, if comments are not received, we may publish the paper as it stands.

If you have any queries regarding the production of your final article or the publication date please contact procb_proofs@royalsociety.org

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Electronic supplementary material:
All supplementary materials accompanying an accepted article will be treated as in their final form. They will be published alongside the paper on the journal website and posted on the online figshare repository. Files on figshare will be made available approximately one week before the accompanying article so that the supplementary material can be attributed a unique DOI.

Thank you for your fine contribution. On behalf of the Editors of the Proceedings B, we look forward to your continued contributions to the Journal.

Sincerely,

Professor Gary Carvalho
Evidence Synthesis Editor, Proceedings B
mailto: proceedingsb@royalsociety.org

Comments to Author:
Thank you for the additional responses and amendments to the collective referee comments. I am now happy with the manuscript, and thank you for responding so constructively, during the peer-review process. We look forward to seeing publication of your manuscript, as an Evidence Synthesis article, in PRSB.

Appendix A

Response to referees

Manuscript: RSPB-2019-1331
Title: Diversity and disease: evidence for the monoculture effect beyond agricultural systems

Dear Prof. Carvalho,

Thank you both to you and the three reviewers whose comments have greatly improved the quality and ease of understanding of our manuscript. We have now revised the manuscript in line with the comments. Please find reviewer comments with our responses below.

Comments to Author:
Thank you for submitting your manuscript to PRSB, for consideration as an evidence synthesis article. I now have reports from 3 experts in the field, and I have also read the manuscript myself.

Collectively, I am pleased to say that there is a consensus, that you tackle a clear, distinctive and timely issue, that complements well, our existing understanding of such considerations within agricultural systems. In the main, the manuscript is clear, with an informative range of literature included. However, as you will see from the comments below, there are many issues identified, that would further strengthen and clarify your manuscript, particularly in the context of an evidence synthesis article. Please do remember at the outset, and the criteria are available on the PRSB website, that our evidence synthesis articles, are intended to reach a defined, though necessarily broad readership, a component of which may comprise non-specialists. In such circumstances, it is therefore vital that there is clarity, accessibility and consistency in the methodology employed, the inferences drawn, and of course, with sufficient robustness, to contribute to the respective evidence base in a representative manner.

I would therefore ask you to consider the comments below, providing a full response, and I encourage you to submit a new manuscript. Foremost among the issues, including some of my own, I summarise here. First of all, you will see that there are issues relating to clarity and accessibility of the methodology employed, especially some components of the meta-analysis. Specifically, your use of the funnel plot, requires additional consideration, and I would also ask you, whether it is possible to increase the robustness and independence of your inferences, by considering any additional such test? I agree fundamentally, that some statements require tempering, especially those statements, reporting a lack of effects. There is also a need to more broadly exercise clarity and consistency in the terminology employed, especially to avoid confusion, and to promote accessibility to non-specialists. Some statements, as identified by the referees, do not have full referencing. Always ensure that statements made, including those in the abstract, are consistent with the tone and emphasis within the manuscript, and that they are also very clear. For example, you start out in the abstract by emphasising the impact that humans have had on genetic diversity. Different people will have different ideas of what is included within "genetic diversity", and as you are really focusing on within species diversity, then that needs to be made explicit: the impact of humans, on biodiversity more generally, including species richness and diversity, will have different drivers and impacts, and it is important, here to clarify the biological level you are referring to. As one of the referees points out, please exercise consistency and balance in statements made. One of the referees, illustrates this point, by an overstatement relating to work on a single species of damselfly. While still on the abstract, you do of course refer to the "monoculture effect", and I would suggest just including a few words to clarify specifically, for the benefit of non-specialists, what that actually is. There are additional issues relating to methodology, such as how the host genetic diversity has been estimated from published studies?

An additional factor, as identified by the referees is to ensure as with all high quality scientific publications, that there is appropriate balance in how you survey and synthesise the literature, and how you arrive at recommendations and inferences. Clearly, this is even more important within an evidence synthesis article, and therefore, reporting data to the contrary of your own findings, such as Vellend et al.,. 2017, and McGill et al., 2015 (see referee report + any others?). Additional information is required concerning how the parasites are classified into specialists and generalists. I also agree that the title requires revision: it is vitally important at the outset, that the readership knows the biological level on which you are focusing, and therefore do include the word "genetic", as in genetic diversity.

Further details on the resubmission process are provided below. Please do ensure that you provide a full and annotated response to the various issues raised, with a rough indication of how and where, changes are made in the manuscript. While the course I cannot guarantee their availability, I will do my best, in the interests of consistency and efficiency, to approach the original 3 reviewers. While you will see there are some substantive matters requiring additional work, I very much hope that you will be motivated to consider a full resubmission, and I have confidence that an appropriate response, would likely increase not only the quality, but also the accessibility and likely impact of your evidence synthesis article. As with all peer-review processes, however, please note that the invitation for resubmission, does not necessarily guarantee publication, and this will of course depend upon the nature of your response, and ongoing opinions of our identified referees. Please do note, that it would be highly unusual for PRSB to allow a further round of Major revision, and therefore a clear and constructive approach to resubmission would be highly beneficial.

We thank the editor for these comments and have addressed them as follows:

We understand that the shape of our funnel plot is unusual. The typical shape of a funnel plot derives from the expectation that studies with smaller sample sizes have a greater degree of error. In this meta-analysis, however, the studies with small sample sizes were all experimental studies carried out in controlled laboratory environments, whereas the studies with large sample sizes were predominantly field studies, subjected to much higher levels of noise and environmental stochasticity. It is most likely due to this that in our analysis studies with large sample sizes had higher errors than those with small sample sizes. We have colourised the points on the funnel plot by field vs. lab study setting to highlight this difference (new Supp Figure 2). In spite of the unusual shape of the funnel, the plot is very symmetrical; as asymmetry would indicate publication bias, we take the good symmetry of the plot coupled with our explanation for the unusual pattern of error distributions to be indicative of no publication bias. To support this conclusion, Rosenberg's fail-safe N, which we calculated, gave us a very large number (>600) of studies to be added to our analysis for the effect to become non-significant. Thus, there is no evidence of publication bias in our meta-analysis. A more detailed description of the funnel plot has been added into the results section (new line: 219-227).

We have now clarified the statements used in our manuscript and added corresponding references. In particular, the damselfly paper has been removed and replaced with two papers illustrating the effect human activities could have on within-species population genetic diversity. We have also included a sentence in our introduction that references the two papers (Vellend et al 2017, and McGill et al 2015) suggested by reviewer 2.

We understand that there is some controversy to the terminology used, such as the definition of specialist vs generalist which we have now changed it to 1 host species vs >1 host species. In addition, we have added information to table 1 (host diversity measure and host range) to clarify how we extracted measures of host diversity from the studies collected in our manuscript. A table has also been added to the supplementary information that contains our definitions of the moderator variables used.

The statement on human impact on genetic diversity has now been removed from the abstract. We have also made sure that the abstract focuses on within-species population diversity to avoid confusion with biodiversity or species diversity in general.

Please see responses to specific reviewer comments below.

Referee: 1

The authors address an important and timely research question, i.e. they ask whether there is broad evidence for the monoculture effect – an increased success of parasites in proliferating in host populations with higher genetic diversity – outside of agricultural systems. The author used a meta-analytical approach for addressing their research question, collating information from 22 different studies. While I found this a very timely study and interesting manuscript, I think some revision of the manuscript is necessary to make the analysis fully understandable and reproducible.

1) Some more details regarding the moderator variables would be helpful: the source of information (e.g. for host range) was unclear for some, and I also found terminology confusing (e.g. parasite load – viral load). In fact, I think use of terminology such as “parasite functional groups” (lines 35, 167, 234; most likely referring to macro- and microparasites as can be learnt from the legend of figure 2) in combination with terms such as “parasite load” (line 119) and “viral load” (120) showcases that there might be some inconsistencies in the definition of variables, which makes it impossible to fully appreciate any results from the analyses.

We have now included a table in the supplement (Supp. Table 1) that contains the variable and definition to help clarify the terminology that we use in addition to adding information to the text.

As the information for host range was often extracted from a paper other than the study paper, we included a column in Table 1 under the category host range to clarify our source of information.

2) Some methods description made it difficult to follow the analytical approach and result

(e.g. symbol ‘r’ used for “correlation coefficient” and “effect size” while it is not fully clear if these terminologies are used for the same analysis or not).

Yes, these terminologies are used for the same analysis. The correlation coefficient r can be used as a measure of effect size (Field & Gillett 2010, Rosenthal & DiMatteo 2001). r for two samples with means and standard deviations is the same as a t statistic. Whether the effect size is positive or negative indicates the direction and the number indicates the magnitude, as with other meta-analysis methods such as Cohen’s d. We hope our method section now reads clearer.

3) I found the authors put too much emphasis on the ‘independence’ of the monoculture effect (e.g. lines 34, 259) from the studied moderator variables. It is unclear it the lack of effects is true independence or an effect of the finite data set; more generally, any lack of an effect in an analytical model does not allow strong conclusions about a natural process? Please find specific comments below. Hopefully, some suggestions are useful to the authors.

We have removed the use of the word “independence” from both the abstract and discussion. The sentence in the discussion now reads as “However, we show that low host genetic diversity does not appear to be associated with a parasite’s host range.” (new line: 258-259)

SPECIFIC COMMENTS:

Line 1 Replace “Diversity” with “Genetic diversity” or equivalent in title? It is otherwise not clear if your study addresses genetic diversity within population or biological species diversity).

We have changed the title to “Low genetic diversity increases parasite success beyond agricultural systems: a meta-analysis” instead.

Line 31 Perhaps revise the term “biological conditions”? This term is difficult to understand and it is unclear if you address host species traits, pathogen traits, environmental filters or anything else.

We no longer mention “biological conditions” in the abstract, but have changed this terminology to “biological traits” throughout our paper as we wished to use a word that encompasses all the biological moderator variables tested in this analysis (new line: 105, 186).

Line 34 I think some rewording of “The effect was independent…” is necessary: lack of effects in an analytical model cannot necessarily be interpreted as independence since sampling bias and limited variation in a finite data set can explain a lack of effect as much as any underlying biological process?

We have now changed this phrasing to read “Our study also suggests that host genetic diversity is overall a robust defence against infection regardless of a parasite’s host range, host reproduction, parasite diversity, virulence, and the method by which parasite success was recorded. ” (new line: 36-38)

Line 36 I think it is impossible for readers to understand “empirical environment” from reading the abstract alone. I assume you refer to field versus laboratory studies?

We have changed this to “study setting (field or lab-based environment)” (new line: 35).

Line 83 Perhaps mention that Nosema sp. is microsporidian?

This has now been added to the manuscript.

Line 84 Perhaps mention that Crithidia sp. is trypanosomelid?

This has now been added to the manuscript.

Line 101 Perhaps consider to change order for “meta-analysis model and Pearson’s", in order to follow the same order of the two approaches in introduction, methods and results?

Thank you for spotting this. We have now changed the order where it now reads as: “ We searched the published literature for all publicly available data sources and compared the effects of low and high host genetic diversity on parasite success using Pearson’s correlation coefficient effect size *r* (with positive values indicating an effect of low host genetic diversity on parasite success) with a nested random mixed effects meta-analysis model. “ (new line: 101-105)

Line 103 Replace “diversity” with “genetic diversity”?

We have done this.

Line 103 You define ‘parasite success’, which is used as a variable in your meta-analytical models here at the end of the introductions rather than in the methods. I think this definition needs some revision and perhaps some more details (in the methods). If ‘parasite success’ is a vector of measures for each study, it is important to clarify o how different measures (i.e. infection load, prevalence etc.) where standardized? Also, I found the description “ability to have a high abundance in the host populations” somewhat vague. To reproduce your study, a more detailed description would be necessary (in the methods), which I couldn’t find in the manuscript?

We have revised our definition of parasite success and have moved this to the method section. The sentence now reads as “We define ‘parasite success’ as any measure of a parasite’s ability to proliferate within a host population reported in a given study. As parasite presence within a host population is measured differently across studies, the following terms were included as measurements of parasite success; parasite load, parasite virulence, parasite abundance, host mortality rate, viral concentrations, viral load, infection rate, and infection intensity.”(new line: 119-124)

Line 112 The date/ time window of your literature search should be provided.

This has now been provided and changed to the following “In July 2019, the literature was searched using keyword searches on Web of Knowledge, Google Scholar and PubMed, with the terms ‘host genetic diversity’,……” (new line: 113)

Lines 119-120 Please check: the terms “parasite load”, “viral concentrations” and “viral load” appear to all refer to the same thing. Moreover, what does ‘parasites’ distinguish from viruses (i.e. are macroparasites and bacteria etc included all in the group of parasites)? Why is there a measurement of “parasite virulence” and not an equivalent of “viral virulence”? Are measures of pathogen load (I use this term here as an equivalent for “parasite load”, “viral concentrations” and “viral load”) given for all of the 22 studies included in your meta-analysis? For me, the lack of understanding what went exactly into the analysis means that the current methods description does not necessarily allow to reproduce your study and a thorough revision of the description of variables is in my opinion necessary.

These are measurement terms reported by authors of the studies included in this meta-analysis. As measurements of disease impact/parasite spread/parasite prevalence are not uniform across literature, we combined them under the term “parasite success”. This is a standard method used in meta-analyses. To clarify, we now include a full description of moderator variable terminology can now be found in Supp. Table 1.

Line 121 Please check: is there a difference between “reference lists” and “paper citations” or can “along with paper citations” be deleted?

We have now deleted “along with paper citations”.

Line 129 Replace “diversity” with “genetic diversity”?

This has now been done.

Line 150 Please check: “Field & Gillet (2010)” is not in the reference list? Also, would be possible to describe the methods here in brief?

Thank you for spotting this. We have now added this citation to the reference list. As a result, the reference numbers have changed throughout the manuscript. How we calculated r depended on the data extracted from the papers (found in Table 1) where the methods are different for mean values and t-values (please see Field and Gillet 2010 for details). Writing out each calculation would take up a disproportionate amount of space in the manuscript, so we only included the raw data and a reference for the methods in the manuscript.

Line 150 Confusing to read about “direct comparison between two continuous variables” in a sentence after you write about a correlation test. Please check.

We have now clarified our choice of the use of r (new line: 154-161)

Line 151 Sorry but I do not understand how the ‘two continuous variables’ of “low vs high host population diversity were generated from a suite of studies that each report a parasite effect in two different populations of relatively low and high genetic diversity. This needs in my opinion clarification; perhaps on of the variables fed into the correlation tests was ‘parasite success’?

See above.

Line 152 Confusing that the symbol “r” is used for a Pearson’s correlation coefficient“ in line 149 and now described as an “effect size”. Not sure if you refer to the same analysis or not, suggest to revise.

See above.

Lines 150-157 These statements was unclear to me: I do not understand how low vs high host population diversity was used as “two continuous variables” – aren’t these two different treatments used to calculate a single vector of observed effect sizes used in the meta-analytical model? Also, you mentioned that effect size r was calculated from different measures such as reported statistics, raw data received from authors, or t-values and df. How were all these data standardized for a sound measure of effect size r?

We apologise for the misunderstanding of this section of the methods. We think this comes from the explanation used for r which we have now clarified (r is a standardisation of these measures).

Line 161 If you “collected several effect sizes per study” this seems to be a source of strong pseudo-replication that needs justification. Why not simply focusing on a single or average effect size per study?

We control for the possible pseudo-replication by using a nested random effects model (rma.mv function in the package metafor).

Line 166 What does “empirical environment” mean? Is this categorical moderator variables of different habitat types? Presumably, this a binary moderator of field versus laboratory environment as mentioned in line 173? Perhaps defining this moderator when first mentioned helps to better understand your analysis?

We have changed “empirical environment” throughout the manuscript to “study setting” to clarify that we are comparing field or lab-based environment studies. We have also added a table of variable definitions in the supplement (Supp. Table 1).

Lines 166-170 I found some of the moderator variables insufficiently defined to reproduce the study. For example, what are “parasite functional groups” (line 167) and how many different functional groups were included in this variable? I am not able to understand which aspect is covered in the variable “initial parasite diversity” (line 167) – it is unclear to me is this is a measure of the number of parasite species/ a measure of parasite diversity recorded to be associated with the surveyed host populations or overall list of parasite species known to be associated with the host species etc. More generally, the source of information for moderator variable is unclear; which source was used to estimate “host range (line 167), for example?

We have now added a table in the supplement to clarify how we define our moderator variables (Sepp. Table 1).

Line 172 I do not understand what aspects are covered with the terms “empirical contexts or approach”. How is approach defined in your particular study?

This has now been changed in the text “We tested for an effect of both study setting (field or lab-based environments) and parasite infection measure on the relationship between host genetic diversity and parasite success. For the latter, we separated measures into three groups based on those used in studies included in the meta-analysis: parasite prevalence, parasite load, and host mortality (Supp. Table 1).” (new line: 176-180).

Line 211 Suggest to also mention the number of unique host-parasite species associations reported in the 22 studies.

This information has been added to new line 214.

Line 211 Perhaps consider to delete "to answer the research question and"? You found 22 studies to match inclusion criteria but they were not selected in terms of analytical power etc.

This sentence was now been revised to "We found 23 papers containing data that followed the inclusion criteria."

Line 223 Please check: "strength of the direction of the effect size" appears to be somewhat confusing terminology, for most test statistics, one may expect an effect size/magnitude of effect and a direction of effect, which are two different aspects?

We have changed the terminology of the results section and hope it now reads clearer.

Line 230 Consider to reword "We found that host reproduction was not a factor that significantly…" to make clear that you did not find such effect in your analysis rather than providing any evidence of a true independence of the variables.

This has been changed to read "We found no evidence of an effect of host reproduction on the direction or magnitude of the effect size (Q = 4.0711, d.f. = 2, p = 0.1306, Fig. 2A), even when we excluded the study by Altermatt & Ebert (2008) (Q = 0.9147, d.f. = 1, p = 0.3389)." (new line: 236-238).

Line 231 Perhaps "strength of effect size" can be reworded to make clear which effect not moderated by host reproduction?

This has been changed to the above.

Line 231-233 The sentence "A study by Altermatt & Ebert (2008) followed parasite infection…" reads as a method description rather than results? This sentence was also unclear to me, since I was not able to understand how a single study can be meaningfully be used as a 'separate variable' in a meta-analytical model.

We have moved and altered this sentence to the methods section. The reason we placed the study by Altermatt & Ebert (2008) as a separate variable for the moderator analysis of host reproduction, was due to the host species (*Daphnia magna*) undergoing both asexual and sexual reproduction within the experiment, which we explain "However, one study was placed under a separate reproduction group as the host (*Daphnia magna*) had undergone both sexual and asexual reproduction." (new line: 189-190)

Line 231-233 I do not understand the terminology "strength of the direction of the effect size"? Please check.

This terminology has now been removed from the manuscript.

Line 229-244 Perhaps consider to present all significant effects first and then report those moderator variables for which no impact on the monoculture effect were found with your particular data set?

We thank the reviewer for this suggestion. We have decided to keep our original ordering of the results as we want the grouping of the moderator variable to follow the same structure as the methods section. This grouping also allows us to separate variables based on study setting and measurements of biological traits.

Line 250 Since "approaches" are not appropriately defined in your methods (see comment line 172), I found it impossible to acknowledge the key results highlighted in this sentence.

We have changed the wording to study measures. We hope this is clearer.

Line 250 I assume "environments" refer to laboratory and field-based studies? If so, perhaps mention this here and avoid the generic term 'environment'(which could be misinterpreted in terms of different abiotic or biotic natural environments).

We have change "environments" to "study settings (lab or field)" to avoid confusion with abiotic factors.

Line 251 The sentence "revealed under the majority of the biological variables we tested" is in my opinion highly misleading and should be deleted (unless the authors provide a strong reason why not): if there is variation in a response variable and such variation is tested against a broad set biological predictor variables, the number of predictor variables does not say anything about how broadly inference can be made. In this particular study, the authors did not find much evidence of host traits affecting the monoculture effects and they were not able to test for different abiotic or biotic environments such as different climates or biogeographical regions or habitats etc.

This sentence has been deleted.

Line 255 The lack of an effect in an analytical model and a finite data set does not allow conclusion on the independence of variables? Can you exclude any possible effect of sample size and bias?

We understand that the word "dependent" in this sentence was too strong a term and have now changed the wording.

Line 264 Is it "pathogen's host specificity" rather than "pathogen specificity"?

We have changed "pathogen specificity" to "a pathogen's host specificity". (new line: 263)

<u>Referee: 2</u>

This manuscript is a meta-analysis that focuses on the monoculture effect – that is, whether host populations with low genetic diversity are at greater risk of infectious disease outbreaks. This is something that has been demonstrated in agricultural systems. This manuscript is an important extension asking whether this effect also holds in non-agricultural systems, using a meta-analysis to address this question. The topic is interesting, but I have several questions/comments related to the work that was done and the manuscript.

1. The authors pitch the abstract in dramatic terms – “Human activities are greatly reducing the genetic diversity of species worldwide”. That’s a strong statement but, understandably given that it’s in the abstract, there are no references to support it. In the main text, the statement is more measured: “Threats to genetic diversity are on the rise. Habitat alterations, pollution, and global temperature changes, as well as the restriction of species geographical ranges may lead to higher chances of genetic drift and reduced population genetic diversity (7).” Reference 7 is a manuscript on a single species of damselfly, so doesn’t seem especially appropriate here (especially since one of their main conclusions is “Our results suggest that, although a marginal significant decrease in the allelic richness was found in the edge populations, genetic diversity has been preserved during the range expansion of this species.”)

We have modified this statement in the abstract. We have also removed the damselfly reference and added two new references (Altizer et al 2003, Pauls et al 2013) to support the statement in the introduction. (new line: 70)

At face value, this statement seems obvious – surely we’ve lost lots of local diversity, right? But studies of local biodiversity at the species level have found that, excluding areas converted to concrete or agriculture, there actually isn’t much evidence for overall losses in species-level biodiversity at the local level (see Vellend et al. 2017 Ecology, McGill et al. 2015 TREE). So, I encourage the authors to really explore what we know about changes in biodiversity at the population level and to use that to frame their study.

(Note: this comment applies in the discussion, too)

Given our meta-analysis examines the impact of within-species population genetic diversity on infection, we would like for this level of diversity to remain the focus of our paper. Nonetheless, we thank the reviewer for suggesting we include reference to species biodiversity and its relevance here. We have now included a sentence in the introduction which highlights that species biodiversity is not always impacted by human activity (new line: 69-70). Moreover, in the discussion we refer to Civitello et al. 2015 who found that biodiversity can reduce infectious disease similar to our findings.

2. Some of the methods for the literature review are unclear or need to be better specified. Specifically:

a. Why are there only approximate numbers for the top part of the flow chart?

Approximate numbers are often given for PRISMA flow charts where other papers have reported the initial literature search in the same manner (Caro et al. 2016 Nat. Comms., Pike et al. 2019 Proc B).

b. Table 2 is presented as showing the studies that were excluded from the analysis, but this is only the studies excluded at the full text screening step.

This is a standard approach used in meta-analyses. As we found over 1000 studies in our initial screening of the literature search, it would be impossible to list all the reasons as to why papers were excluded. The table legend now reads as “Studies excluded from meta-analysis at full text screen stage” to highlight that we only include reasons for exclusion at the full text screen stage.

c. Lines 113-115 & Figure S1: Did the search require all of these terms? Or were subsets of them used?

These were used in subsets, for example “host genetic diversity” and “disease spread”, or “low and high genetic diversity” and “parasite prevalence”, and so on. We have added details of this aspect of the search in the manuscript. (new line: 113-116)

d. One paper that is relevant that wasn’t included is the Strauss et al. 2017 Proc B paper, which found that more diverse populations had *higher* densities of infected hosts. It’s possible it came out after the authors selected their studies.

Thank you for pointing this out. We have now included this study in our meta-analysis.

3. One part of the analysis focuses on whether parasites are specialists or generalists. How was this determined? No information is given about this, even though it seems like this might have been challenging to do in some cases. In addition to giving information on how this was determined, the assignment that was given (specialist vs. generalist) should be added to Table 1.

We have now changed the terminology to host range (parasite able to infect 1 host species or parasite able to infect >1 host species) clarify this. We have also included this information into table 1.

4. Lines 216ff: The authors point to the funnel plot as indicating that there is no publication bias, since the majority of points fall within the plot. However, the plot (Figure S2) is not very funnel shaped – it actually seems like the funnel shape is flipped from what is typical for funnel plots for meta-analyses (Figure S2 shows greater spread at the top than the bottom). What does that indicate about the datasets included in the study?

The flipped shape of the funnel plot is due to how standard error was measured and is not uncommon (please see Sterne & Egger 2001 Journal of clinical epidemiology). Our study contained many studies with small population sizes. These were mainly experimental studies which are less likely to have less error as they are controlled studies. To highlight this, we have colourized the points on the funnel plot. As there is no asymmetry in our funnel plot, this indicates that there is no publication bias.

5. For the analysis of host reproduction: what would be found if the Altermatt & Ebert study was excluded from the analysis? Based on figure 2A, it seems like there is a (potentially significant, based on 95% CIs) larger effect size for asexual hosts than sexual ones.

This is an interesting point. We decided to compare asexual and sexual host reproduction without the *Daphnia* paper. When we excluded the study by Altermatt & Ebert, we still found no significant effect of host reproduction the direction of the effect size (Q = 0.7433, d.f. = 1, p = 0.3886). We have included this result in our manuscript as “We found no evidence of an effect of host reproduction on the direction or magnitude of the effect size (Q = 4.0711, d.f. = 2, p = 0.1306, Fig. 2A), even when we excluded the study by Altermatt & Ebert (2008) (Q = 0.9147, d.f. = 1, p = 0.3389) (new line: 236-238)

6. Lines 258ff: What is the basis of the statement on lines 260-262 that the monoculture effect is “equally prevalent”? Do you mean that it was found in highly specialized interactions, broad spectrum interactions at the genotypic level, and those that cross host-species boundaries? Or do it actually refer to prevalence (rather than simply whether it happens at least once)? If the latter, that needs to be explained better. If the former, the wording needs to change. For this paragraph (and comment 3 above), it would help to give more explanation of how these different groups were defined.

We have removed this statement and also added a column to table 1 under the title “host range”. We have also added a supplement table (Supp. Table 1) with the definitions of all the moderator variables used in our study.

Additional (more specific) comments:

1. Line 96: I’d suggest adding something to the effect of “and in non-agricultural systems” at the end of this sentence.

We have added this recommendation to our manuscript.

2. Lines 103-104: This sentence (which indicates that a parasite’s ability to have a high abundance in its host is related to host mortality) conflicts somewhat with the argument in the previous paragraph.

We understand the confusion of this sentence and have modified and moved it to the method section. Hopefully this reads clearer: “We define ‘parasite success’ as any measure of a parasite’s ability to proliferate within a host population reported in a given study.” (new line: 119-121)

3. Lines 222-225: I had to read this sentence a few times to understand it. I think the second half would be clearer if it said something like “where field studies (r = 0.2801) had larger effect sizes than lab studies (r = 0.1077).

This sentence has now been changed to the following “We found that the effect size is influenced by study setting (Q = 9.2111, d.f. = 1, p = 0.0024, Fig. 1B), where the magnitude of the effect size is significantly greater for field studies (r = 0.2801) in comparison to lab studies (r = 0.0922). “ (new line: 230-233)

4. Lines 235-237: it would help to add a little explanation for the reader – it takes some effort on the part of the reader to move from “microparasites showed a strong, positive impact” to the biologically interesting effect that this indicates.

Thanks for the suggestion. We decided to leave it as a factual representation of the results in this section but we do discuss it more in the discussion.

5. Line 290: For this paragraph, it seems more important that a monoculture effect was found in the field, than the one that was found for the field was stronger than the lab.

We have now changed the wording to reflect this interesting finding.

Referee: 3

This is a highly interesting and clear study that demonstrates how reduced genetic diversity in host populations renders them more vulnerable to disease. This phenomenon is best understood from agricultural scenarios and it is actually quite surprising that it has not been addressed before in natural systems in a systematic manner. Given that genetic diversity is declining alongside biodiversity, this could have severe implications for risks of disease, yet this is the first systematic quantification of that risk.

Overall, I found the manuscript well written and clear, and the analyses suitable, and the conclusions warranted based on the results. I also appreciate that the study spans across different host-pathogen systems to really show how generalizable this finding is. I would expect the study to be well cited, I certainly would have wanted to cite this results on multiple occasions. I have some suggestions that could further improve the clarity of the work, but these are such that they could be easily achieved in a revision.

I realize that space may be limiting but I would find it greatly helpful if the authors would clarify HOW the monoculture effect is expected to function in the Introduction. While this may seem straightforward, there may be different aspects to consider. For example, for an already established pathogen, identical hosts may indeed promote between-host transmission, but such homogeneity may filter out non-compatible strains. Greater transmission may be achieved with greater strain diversity. Hence, it is not always obvious that low genetic diversity would be most conductive to transmission.

We hope we have clarified these points on how the monoculture effect is expected to function in the Introduction (new lines: 51-57). We are unclear on how homogeneity can filter out non-compatible strains. Could they please provide a reference on this process?

Highly relevant to this is the infection genetics of the interaction (gene-for-gene, matching allele, specialist-generalist at the within species level), which deserves some discussion in the introduction.

Related to the above, I wondered whether it would not have been possible to estimate the effect of infection genetics? For some of these interactions such data is should be available.

We looked into this in the process of doing the meta-analysis. However, we couldn’t find infection genetics data for almost all of our host-parasite combinations, and thus could not make a meaningful comparison across studies.

Given that host genetic diversity is such a key measurement in the study, I would have wanted to see more information on how it was extracted from the studies, and what the measurements actually are. Is it only genetic diversity or also resistance phenotypes obtained through inoculations? Measured using neutral markers? Measured at relevant resistance/immunity loci? What do low and high genetic diversity mean in practice?

We have added a column entitled “Measure of host diversity” to table 1 to clarify how diversity was measured for the different studies.

The term ‘monoculture effect’ was used in manuscript to refer to the effect of lower genetic diversity. This may create some confusion with those familiar with agricultural terminology where there are true – and vast – monocultures. I would recommend the authors to use genetic diversity instead.

We understand the point of this reviewer and have changed the terminology. We do introduce the monoculture effect in the introduction as we feel this is important, but have thereafter we refer to low genetic diversity or simply genetic diversity as suggested.

Related to the point above (and given that many interested in wild life disease may not have any ideas about agricultural setting), a more general title framed around low genetic diversity and disease risk might work better than the current title.

Title has been changed to “Low genetic diversity increases parasite success beyond agricultural system: a meta-analysis”.

Minor comments
Sentence starting on 77- does not read well, perhaps missing a word?

We have added a word and the sentence no reads as: “Firstly, given that parasite transmission can be determined by host density (2), the relative effects of density versus host genetic diversity need to be elucidated (16)”.

Line 85 – by disease impact do you mean virulence?

We meant population-level disease impact. This has now been clarified in the text: “In other cases, we see an increase in parasite success on the homogenous host populations when multiple parasite species infect (23–26) but not always between one host-parasite species pair (27,28)”. (new line: 86-88)

Thank you for your consideration of the revised version of this manuscript,

Alice Ekroth
Charlotte Rafaluk-Mohr
Kayla King

Appendix B

Response to referees

Manuscript: RSPB-2019-1331
Title: Diversity and disease: evidence for the monoculture effect beyond agricultural systems

Dear Prof. Carvalho,

Thank you both to you and the two reviewers whose additional comments have further improved our manuscript. We have addressed all comments and our responses can be found below.

Referee: 1

Comments to the Author(s).
The authors have thoroughly revised their manuscript and improved the study. I have only some specific comments to add that can be addressed in a short revision.
The authors are encouraged to publish the data set and R code of analysis rather than referring to literature from which data were extracted in order to facilitate data accessibility by peers; I was not able to find the relevant data in the supplements or a link to an external repository in the current manuscript version.

We thank the reviewer for this suggestion and have added a supplementary file containing our R code and data set.

Lines 37-38 Please check the order of "parasite's host range, host reproduction, parasite diversity, virulence, and the method by which parasite success was recorded" – list host traits, parasites traits and then bias such as "host reproduction, parasite's host range, parasite diversity, virulence, and the method by which parasite success was recorded".

We have now changed the order of our moderator variables to match this suggestion. The sentence now reads: "Our study also suggests that host genetic diversity is overall a robust defence against infection regardless of host reproduction, parasite's host range, parasite diversity, virulence, and the method by which parasite success was recorded." (new line: 36-38)

Lines 51-52 The last sentence of the abstract needs to be rewritten; the current beginning of the sentence "Consequently, this phenomenon could become increasingly common" does not link to the previous sentence

Thank you for spotting this. We have now changed the last sentence to the following: "Combined, these results highlight the importance of monitoring declines of host population genetic diversity as shifts in parasite distributions could have devastating effects on at-risk populations in nature." (new line: 39-41)

Line 68 Replace "higher chances of genetic drift" with "increased genetic drift" or euqivalent?

We have changed the wording to "increased genetic drift".

Line 89 Replace "parasite infection" with "parasite success"?

We have changed the wording to "parasite success".

Line 114 Suggest to reword "parasite infection": it is not clear if you refer to something like parasite prevalence or parasite spread or any measure of the parasite success.

As above, we have replaced "parasite infection" with "parasite success".

Line 118 I think this sentence can be clarified: "host survival might be less informative because the interplay of virulence, force of infection and the timing of infection determined the overall spread of pathogens in host populations (Wells et al 2017)" (Wells, K., Hamede, R., Kerlin, D.H., Storfer, A., Hohenlohe, P.A., Jones, M.E. &

McCallum, H.I. (2017) Infection of the fittest: devil facial tumour disease has greatest effect on individuals with highest reproductive output. Ecology Letters, 20, 770–778).

We thank the reviewer for this comment and have added this sentence and the reference to the manuscript, which can now be found on line 93-95.

Line 156 and Line 170 Replace “parasite infection measure” with “parasite success measure”?

We have now changed all instances where we mention “parasite infection measure” to “parasite success measure”.

Line 197 You may replace “many parasite species (>1 Species)” with “> 1 parasite species” or “multiple parasite species”?

We have now changed this to “multiple parasite species (>1 Species)”.

Line 230 Would be helpful to mention what kind of test statistics ‘r’ and ‘z’ refer to.

Thank you for drawing our attention to this. We realised that the use of the test statistic “r” may be causing some confusion as it was mentioned by multiple reviewers. In addition, we have also become aware that other test statistics may be more appropriate for our distribution of sample sizes. To improve our meta-analysis, we have decided to change the effect size measurement to Hedges’s *g*. As you can see from our funnel plot (Supplementary figure 2), a number of studies have very small sample sizes and Hedges’s g takes this into account (Hedges 1981, Borenstein et al 2011). We found that changing to effect size g this did not change the conclusions drawn from our analysis. Indeed, study setting and parasite functional group are still significant, where all other moderator variables are still non-significant. To be completely transparent in the methodology we chose to use in our meta-analysis, we have included the R script and data set as a supplementary file.

Line 231 If ‘Q’ refers to Cochran's Q-test, perhaps add this information here?

This information has now been added.

Line 238 Perhaps mention here that excluding the study by Altermatt & Ebert (2008) means excluding the Daphnia study?

We have added “Daphnia” to the sentence, which now reads: “We found no evidence of an effect of host reproduction on the direction or magnitude of the effect size (Q = 4.0711, d.f. = 2, p = 0.1306, Fig. 2A), even when we excluded the Daphnia study by Altermatt & Ebert (2008) (Q = 0.9147, d.f. = 1, p = 0.3389)”. (new line: 237-239)

Line 240-242 Please check: the statement “If the parasites were macroparasites (r = - 0.0091), no effect of host genetic diversity was revealed in the study, but the success of microparasites (r = 0.2207) was limited by high host population genetic diversity.” Suggest that you run separate models for these two parasite groups rather than including the micro-macro-parasite categorization as a moderator variable in a single model? If so, this should be mentioned in the methods; otherwise it would be helpful to explain to what kind of test statistics ‘r’ refers to (explain in line 230 where first mentioned) to avoid any confusion?

Thank you for spotting this. We did not run two separate models and so have changed the sentence to: “The success of microparasites (g = 0.6277), and not macroparasites (g = - 0.1725) was limited by high host population genetic diversity.” (new line: 241-242) We hope this is clearer.

Lines 254-255 Suggest to delete “populations, given that their susceptibility is not influenced by a parasite’s host range” (the link to host specificity is in my opinion rather unclear, especially as EIDs can emerge after spillover events from different host species or due to changing population conditions).

We have removed the last part of the sentence. The full sentence now reads: “Our findings additionally highlight the potential damage that emerging infectious diseases may have on genetically homogenous host populations.” (new line: 252-254)

Line 258-259 The sentence “However, we show that low host genetic diversity does not appear to be associated with a parasite’s host range.” Needs to be rewritten for two reasons: first, I think you explore the effects of host rang on parasite success in populations with low versus high genetic diversity? Second, I don’t think you ‘show’ the absence of an effect but rather you did not found any evidence of such effect. I would expect a more appropriate statement to read as “However, we found no evidence that a parasite’s host range affected its success in host populations with low versus high genetic diversity”?

We agree with the reviewer and have changed the wording of the sentence to the above suggestion. (new line: 257-258)

Lines 284-285 Host diversity/host range and should not only depend on “new individuals” but rather regional species pools, which may change with shifting species distribution and invasive species, for example. There is increasing recognition that host specificity changes in variable environments (e.g. Wells, K. & Clark, N.J. (2019) Host specificity in variable environments. Trends in Parasitology, 6, 452-465). Suggest to explicitly mention here ‘species’ and changing ecological opportunities in addition to “new individuals”.

We have now changed this sentence, which now reads: “Whilst adding individuals to a population could increase diversity and reduce inbreeding (49), a risk may be that new individuals, new species, and changes in ecological opportunities bring in new parasites to the population (50,51).” (new line: 283-286)

Referee: 2

Comments to the Author(s).
I think the authors have done a good job overall of addressing the topics raised in the first round of review. I have just one minor correction: Supplementary Figure 1 still lists 22 studies, not 23, so I think it wasn’t updated.

Thank you for spotting this. We have now corrected the supplementary information.

Thank you for your consideration of the revised version of this manuscript,

Alice Ekroth
Charlotte Rafaluk-Mohr
Kayla King