PCI response to reviewers, Round 3

Editor comments: The reviewers all think that the manuscript has improved but they raise several concerns, with which I agree.

First, there seem to be at least typoes in some equations. As stressed by one of the reviewers, since these are delay-differential equations, notations are paramount so please double (triple) check the mathematical notations.
It seems to us that a main issue was that part of our analysis was only in the Mathematica notebook. We agree that these details belong in the appendices and have included them in the updated manuscript. We have also replaced variables that were a source of confusion. We hope that the updated appendices will satisfy the reviewers.
Second, I agree with another reviewer that the manuscript would probably benefit from a tuning down of the novelty claims (e.g. no model has shown that, or there is no trade-off) to instead better describe the originality of the model, i.e. adding seasonality for an obligate-killer parasite.
We agree that the manuscript is improved by toning down some of the language. The manuscript is now more precise in its description of the generality of our findings.
These are only minor revisions but I believe they are necessary, especially for the accuracy of the notations and formulations.

Reviewer #1: The authors made minor changes to the manuscript, primarily by adding a helpful discussion comparing their study to past obligate killer models.
Sorry for the confusion, we made 2 uploads after receiving comments from reviewers on our original draft. The main difference between the first and second upload was the added discussion of obligate killer parasites. The majority of changes to the original submission are in both the uploads. We have made additional changes to the current submission.

Unfortunately, however, my main concern from the previous round remains unaddressed. As I previously stated, I disagree with the assertion made by the authors that they investigate virulence evolution "in the absence of any explicit mechanistic trade-off," (L37). In my view, this claim is grossly overstated. The fact that the parasite needs to kill the host to complete transmission is a form of trade-off – not unlike the classic virulence-transmission trade-off.
We agree that a trade-off emerges from multiple constraints on the parasite. One constraint is that the life cycle of these parasites require that they kill their host before the end of the season to release progeny but not release progeny too early or risk high environmental decay. We discuss how these conflicting constraints lead to the evolution of intermediate virulence starting on line 177. However, the obligate-killer constraint alone has not resulted in the evolution of an intermediate virulence strategy in prior investigations. The obligate-killer constraint is discussed in more depth in the paragraph starting on line 185.
In the current model, the trade-off leading to the evolution of intermediate virulence emerges not as a consequence of an assumed fixed relationship between virulence and transmission as is assumed in most models of virulence evolution. Instead, intermediate virulence evolution emerges from the within-season population dynamics driven by host phenology and is therefore liable to be variable and responsive to environmental variables. This does generate a trade-off between inter-season transmission and virulence in the broadest sense, but the trade-off is not one that is assumed within the model framework. We have change the language throughout the text to clarify these points.
I recommended the authors refrain from generalising the manuscript as a model "in the absence of traditional mechanistic trade-offs" (in abstract).
We agree with the reviewer that there were sentences in the previous drafts that needed to

be toned down to appropriately acknowledge that our model is specific to certain disease systems. We have altered all statements that we thought could be interpreted as over generalizations.

I notice that neither "obligator killer" or "parasitoid" appears in the title or abstract. I believe that the readers will benefit from more explicit reframing as a system specific model.
We agree with the reviewer that our model and results are specific to disease systems with obligate host killer parasites and have added "obligate-killer" to the title and abstract.
Reviewer #2: I enjoyed reading this manuscript last time, and it still seems very interesting and well conducted to me. The authors have engaged with my comments constructively. I just have one remaining comment, which is that the function g is still stated to be a probability density function in the text, which I still think can't be the correct definition (as you state in your response and the 2nd half of that sentence, I think it is just a rate). Otherwise I think you've done a great job.
Thank you for clarifying, we agree with you and have changed this sentence. We also thank you for your thoughtful and constructive comments as they have greatly improved this manuscript.

Reviewer #3: The authors addressed all my comments but those concerning the mathematical rigor one would expect from such a theoretical paper.

Specifically, concerning item 4.9 of the "Response to reviewers", the authors only fixed some "typos" while I was requesting much more rigor and detail in the appendices. For instance, in the current version of the preprint, $v_2(t)$ is expressed for $\tau < t < t_l$ (implying $\tau < t_l$), while τ can clearly be greater than t_l (see e.g. Fig. 1). I realize that my previous review suggested the authors to make this correction although what I meant is that v_2 should be defined from $t = \tau$ (as opposed to $t = 0$).
We apologize that we did not correctly interpret the reviewers comments in the last draft. We thought we addressed the reviewer's comment by defining v_2 from $t = \tau$.

There is still an issue with the handling of the delay.
Thank you for clarifying what needs to be included in the appendices. We added a more detailed description of our original analysis to the appendices. This should convince the reviewer that the delay has been handled correctly.

In addition, some key steps are missing to convince the reader that the expression of $v_2(t)$ is correct.
We apologize that the steps taken to find $v_2(t)$ were unclear. Briefly, $\frac{dv_1}{dt}$ is linear and once solved can be plugged into $\frac{ds}{dt}$ to solve for $s(t)$. $\frac{dv_2}{dt}$ can then be solved by plugging in the solution for $s(t)$. We hope that the updated appendices will convince the reviewer that this expression is correct.

The notations are confusing (e.g. d, both a parameter and a mathematical notation, and s, both a state variable and a dummy variable).
We thank the reviewer for pointing out that some of our notation was confusing. We have changed d to μ and now use u instead of s as a dummy variable to avoid any repeat notation.
After having struggled with the equations, I reached the conclusion that the authors simply attempted to copy the equations from their Mathematica notebook (more or less carefully, assuming it does the right thing anyway). However, since these are delay differential equations coupled with several discontinuities in time (at times $t = T$ and $t = t_l$), I would have expected the authors to be much more careful in writing their mathematical derivations. If this is properly done in the Mathematica notebook, and if the case $\tau < t_l$ is just shown as an example in appendix, then this should be explicitly stated.
We appreciate the time the reviewer spent trying to check our equations. We should have

provided a more detailed account of our analysis in the appendices rather than only showing them in the Mathematica notebook. We have now clarified our analysis in the appendices.

Moreover, an additional Mathematica notebook in pdf version focusing on these derivations should be provided as supplementary material. (I am not a Mathematica user so I had to use Wolfram player to open the current notebook, in which I noticed that the case $\tau < T - t_l$ is treated separately, but not the case $\tau < t_l$ as far as I could see.)
This is an excellent idea, thank you for suggesting we provide a pdf version of our Mathematica notebook focusing on the analysis for interested readers. This is now available on the Github repository associated with this manuscript.

Then, the criterion for the parasite-free equilibrium to be unstable should be $f'(0) > 1$, with $v_2(T) = f(v_1(0))$. Instead the authors heuristically assume $v_1(0) = 1$ and consider $v_2(T) > 1$ as a stability criterion. However, it is unclear whether this heuristic assumption is mathematically valid. I would have expected a more rigorous derivation in appendix.
We apologize that our analysis was unclear. Despite relatively complex within-season dynamics, our between-season dynamics ($\hat{v} = v_2(T)$) boil down to a one dimensional discrete time dynamic, as there are no carry-over effects for hosts. Therefore, the increase condition for the parasite ($v_2(T) > 1$) must correspond to a greater parasite population at the next census point than the previous one.

The same concerns apply to the derivation of the mutant invasion criterion. Since invasion fitness is expressed relatively implicitly (with integral terms) and numerically computed with Mathematica, wouldn't it be possible to numerically evaluate $f'_m(0)$ with Mathematica instead of making use of a heuristic argument?
It is likely possible to numerically evaluate this expression. However, from past experience, the extreme values in some of the exponential terms can make it difficult for Mathematica's search algorithm to find the value of τ^* that satisfies $f'_m(0) = 0$. We do not see the benefit of evaluating this expression numerically if the heuristic argument is valid.

To sum up, and as already indicated in my previous review, the appendices mostly repeat the text. Their usefulness is therefore limited. I would have expected more detailed and rigorous mathematics in the appendices, or alternatively supplementary Mathematica notebook in pdf version dedicated to explaining the mathematical derivations. To be recommendable, a preprint must be technically sound. I am not yet convinced this is the case.
We thank the reviewer for the time they have spent checking our mathematical analysis. We hope that this current draft now addresses all of their concerns.

Other remarks:

In the para preceding eq. 1: τ is introduced without having been defined.
Thank you for noticing this. We now define τ before it is introduced in the initial conditions.
In the eq. preceding line 74: there is a +- typo in the exponential term.
Thank you for catching the typo. We have corrected it.
Lines 89-90: that sentence does not make sense to me.
Thank you for pointing out that this idea was confusing. The number of new parasites released upon host death is constant regardless of τ when there is no trade-off. Thus the trait that is effectively evolving is the *rate* that the new parasites are assembled in between infection and host death. For example, long τ corresponds to slow assembly of new parasites. We have edited the writing for clarity (line 91).

Line 136: replace high with low.
Thank you for catching that this sentence was not written clearly. We changed the sentence to "increasing variation in host emergence timing favors parasites with higher virulence, but only when variation in host emergence timing is moderate."
Line 220: regarding the consequences for population dynamics, you might consider citing

Hilker, F. M., Sun, T. A., Allen, L. J. S., Hamelin, F. M. (2020). Separate seasons of infection and reproduction can lead to multi-year population cycles. Journal of theoretical biology, 489, 110158.
Thank you, we now cite this paper as evidence that this could be an interesting extension of our framework.

Line 247: you might add "monocyclic plant parasites" and consider citing (again)

Hamelin, F. M., Castel, M., Poggi, S., Andrivon, D., Mailleret, L. (2011). Seasonality and the evolutionary divergence of plant parasites. Ecology, 92(12), 2159-2166.
Thank you, we agree that this is an appropriate citation for this extension.