

Response to Reviews: rsif-2022-0123.R1

Dr. Holt,

Thank you for the opportunity to submit a final revision of our manuscript, "Anticipating infectious disease re-emergence and elimination: a test of early warning signals using empirically based models," for publication in the *Journal of the Royal Society Interface*. Three of the four referee's stated they were satisfied with our revision and our responses to their review comments. Referee 1 is concerned we did not completely address their comments from the initial review. We have taken steps, where reasonable, to address those comments in this final version. All line numbers reference the revised manuscript, unless otherwise noted. Our responses are in blue text (in the PDF version of this letter), as are additions in the manuscript itself. We have included the original critique by Referee 1, with our initial responses in red text (in the PDF version of this letter).

Sincerely,
Andrew Tredennick, on behalf of all coauthors

Referee: 1

Comments to the Author for R1 (revised version)

The revision of the paper does not take into account many of my comments on the previous submission. I still do not think that supplement is necessary, and the results are not sufficiently interesting from the point of data analysis. Some acronyms are not defined.

Based on our responses to Referee 1's original critique, all comments were addressed in the manuscript except for one. Specifically:

- Referee 1 noted that population size in Niger has increased substantially from 2000 to 2020, and asked how this is reflected in the recent paper. We noted in our response that the increase in population is unlikely to invalidate our findings. However, we have now included three new sentences in the Discussion section: "Another potential limitation is that the population of Niger has increased substantially since the end of the time series' we analyzed in 2005. This presents a limitation to our work because we cannot definitively say whether our results are robust to such large changes in population size. However, our analysis across cities with different population sizes suggests that EWS would remain a viable tool. Elimination may be easier to detect, as demonstrated by our result that EWS performed better in larger cities." (lines 312-316)

- We respectfully disagree with the reviewer that the supplementary material is unnecessary. The supplement serves as a resource for especially interested readers, but it contains information that is not necessary to understand or evaluate the manuscript. It also contains several large figures that are best suited for a supplement rather than journal pages.
- We have gone through the manuscript and defined all acronyms.

For your reference, we also include the reviewer's comments following our initial submission together with our responses:

The paper by Tredennick et al "Anticipating infectious disease re-emergence and elimination: a test of early warning signals using empirically based models" attempts to analyze a bulk of early warning signal statistics in modeled measles data and in 11 years of weekly incidence real data (1995-2005).

The paper is organized as the main text and a supplement with detailed analysis. I can understand such a layout when there is a strong main message to publicize with less relevant technical information in a supplement. However, in this paper the main message is mild (some EWS work, others don't, in a particular dataset in a particular country), more interesting information is in the data analysis in the supplement, but there, too, it could be presented in more detail and with added figures. Moreover, in the supplement, the authors repeat analytical information from the main text, which is unnecessary.

I think the paper should be revised and prepared as a regular long article with detailed explanation of Methods, Data, Results in a clear concise layout (not split between two parts with repetitions).

Thank you for this feedback. We note that the original manuscript was presented as a regular article with Introduction, Materials and methods, Results, and Discussion sections. We have left the structure intact, but have moved almost all methods and results from the supplement to the main text. For example, lines 82-106, 158-165, 194-218, and tables 1-3 in the methods and table 4 in the results are entirely new in the revised manuscript. In particular, we have completely rewritten the presentation of the model to avoid repetitions.

It would be useful to include at least one detailed multi-panel figure with all EWS indicators plotted for comparison. The authors can present the best and the worst cases and discuss them accordingly.

We think the referee is suggesting that we plot each EWS over time. This is certainly possible, but requires specifying a moving window width. Because our focus is testing EWS without the added complexity of defining the moving window width, we have opted to not include this figure.

Indeed, as mentioned in the preamble to the Editor, we have removed the limited moving window analysis entirely. We have already included an analogous figure for just the two time periods in the supplementary information (figure S6 and S7).

As I understand it, the scope of the magazine assumes a submission with medical impact. However, the authors themselves admit that application of this approach in real time may be impossible to “operationalise”. Why then did they choose the Interface magazine for their submission?

JRSI seeks scholarly work at the interface of, in our case, the physical and biological sciences. The application of statistical physics concepts to infectious disease dynamics falls within this remit.

As the paper presents results in its current form, it applies known techniques to a historic dataset with general assumptions on the studied phenomenon (measles outbreaks). The novelty of the current manuscript is minor, in my opinion. It would better fit a magazine like PLoSOne or the like.

We respectfully disagree. This is the first paper, to our knowledge, that tests early warning signals using empirically based models where: 1) the dynamics represent a real dataset and 2) the transcritical bifurcation point can still be known exactly. Other tests of early warning signals for disease emergence and elimination have been applied to simulated/theoretically modeled time series absent of data or to data series themselves, with no underlying model. This work fills an important gap between theory and application. It also fits well with *JRSI*’s scope.

The paper considers the data back in the 1990s. The population of Nigeria increased from 122 million in 2000 to 206 million in 2020 (roughly speaking, it doubled in 20 years). How is this reflected in the submitted paper? How would the authors’ approach address the recent outbreak in 2019? See [Jean Baptiste et al 2021], <https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-021-10436-1>

In principle, a model could be developed provided there are accurate data to estimate likely introductions to account for immigration rates beyond the high birth rates already included in our model. In general, however, the conclusions we have drawn are not especially hampered by data limitation and another outbreak (2019) is not anticipated to invalidate any findings. We set out to test EWS in a mode-data fusion framework using a well known data set (1995-2005). We are excited to consider other data sets in the future, but inclusion of the 2019 outbreak is beyond the scope of this manuscript.

Minor comments

In the supplement, in Fig. S3 top panel, it would be sufficient to show 15 years or so, as it is better to align time scales for comparison of the panels.

Done (now figure S4).

Some statements in the paper are either dubious or unclear: “natural gradient of extra-demographic stochasticity” (gradient is a specific term in natural sciences, and extra-demographic is not defined); “demographic stochasticity due to differences in population size” (can this be stated about cities that all have several million populations?)

We have revised the first statement (line 82) and tempered the second statement (line 84).

Typos in lines 105, 307.

Fixed.

Referee: 2

Comments to the Author

The authors have made substantial efforts to address the comments of all reviewers. I appreciate their efforts. As I already made clear in my first review, my concerns were less technical but more on the novelty and suitability to the journal. Those (obviously my subjective) views, however, remain unchanged. I encourage authors to publish their codes, so that readers can reproduce their results and apply them for their own work.

No comments to address. The code will be archived on Zotero.

Referee: 3

Comments to the Author

The authors have responded to my previous comments to my satisfaction.

No comments to address.

Referee: 4

Comments to the Author

My comments were addressed.

No comments to address.

