Rapid Reviews Infectious Diseases

Review 1: "An Ae-stratified Mathematical Model to Inform Optimal Measles Vaccination Strategies"

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The MIT Press

Published on: Jun 05, 2025

URL: https://rrid.mitpress.mit.edu/pub/18np49mx

RR\ID Evidence Scale rating by reviewer:

- **Potentially informative.** The main claims made are not strongly justified by the methods and data, but may yield some insight. The results and conclusions of the study may resemble those from the hypothetical ideal study, but there is substantial room for doubt. Decision-makers should consider this evidence only with a thorough understanding of its weaknesses, alongside other evidence and theory. Decision-makers should not consider this actionable, unless the weaknesses are clearly understood and there is other theory and evidence to further support it.

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Review: This article examines the issue of protection against measles for infants too young to receive vaccination. The idea is an excellent one, but the execution is somewhat lacking. My major issues concern Figure 1, the mathematical model and the interpretation of PRCCs in Figure 6.

Figure 1 needs to be more informative. It's unclear from the figure itself what the different colours represent. Upon further investigation, I think the authors do the reader a disservice by not distinguishing even further: the first bar should be clearly labelled as infants with maternal immunity, while the second bar should be labelled as infants with non-maternal immunity but not vaccinable. I also take some issue with the labels, as 0–5m, 6–8m etc suggests that individuals who are aged 5–6m are not being considered, when in fact this is not true. The authors should also use the en dash for ranges and relationships throughout, not hyphens (both in the figures and the text).

The model has a serious issue, which is that it is degenerate. While the measles components are fine, the population components are not. Without measles or vaccination, the model would essentially be

$M'+S'=b(M+S)-d(M+S)$

This is a simple one-dimensional model that has three outcomes, all of which are flawed:

1. if $b>d$, the population goes to infinity, which is unrealistic
2. if $b<d$, the population dies out, which is also unrealistic
3. if $b=d$, then these terms are all irrelevant, and the model is in a knife-edge case (which is also unrealistic).

Fundamentally, the birth and death terms must not be of the same order. The easiest option is a constant birth term and a linear death term. However, other options, like linear birth and quadratic death (this is what logistic-growth models possess) are also doable. The authors need to recast their model along these terms and re-run the analysis and simulations.

Finally, the interpretation of the PRCCs in Figure 6 is erroneous. Significance in PRCCs occurs when |PRCC|>0.4, so only the first two parameters are significant (and arguably the last one). The p-value is not relevant for significance in PRCCs. I would like to see the Monte Carlo simulations for the two (or three) most significant parameters. My guess is that the trend for the lowest one will be near-uniform anyway. But this will in fact be a stronger result than having 7 out of 9 parameters be significant; if everything is significant, then nothing is, whereas investigating the two strongest ones will tell us a lot more.

In summary, this is a promising approach, which will yield stronger results when the model is fixed and the interpretation of the graphs is correct.