Reviewer’s report

Title: Interpreting changes in measles genotype: the contribution of chance, migration and vaccine coverage

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Reviewer: piero manfredi

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General

The paper offers an interesting stochastic modelling perspective of an important issue, i.e. the interpretation of measles genotypes data. These data are used to assess the circulation of wild measles virus and therefore are critically important to monitor progresses towards the goal of measles elimination.

I did'nt know papers on the argument so the idea seems novel to me. The paper is well written, and gives a convincing explanation of the phenomenon of increasing diversity of measles virus. The presentation is exemplar of how a rather technical tool (stochastic epidemic modelling) may be made accessible to a wide non-technical audience. Therefore I believe the article is worthy of publication.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

-- p2 As regards the main fact that diversity is negatively associated with transmission, I gave a quick glance – I am not expert of this field - to the cited empirical literature and did find its findings sometimes contadictory. For instance at p3, L6 from top it is not clear to me whether citation [3] really support the authors’ point that a low degree of diversity is associated with high virus circulation (in the summary of [3] it is indeed stated that “endemic co-circulation of several viruses may well be a characteristic of communities with low vaccination rates (see also p. 876).

Fig. 1, The definition of the various Patterns is just “reasonable” or it correspond to some agreed standard?

p3, L7 from top = “some population with high coverage”

p6, L4 from bottom = importation “ratio” is perhaps more correct than rate (by the
usual reason that the denominator is not the “at risk population”). When the authors say “importation rate per city of 0.5 per year, it would be clearer to say “i.e. 0.5 per 500,000 population per year”.

Is there any reference for the chosen range of importation rates?

p7, L8 from bottom = 0.5?

Figs3,4. Though easily understandable, the values of the importation rate are not specified.

Appendix, p2, L1 from top, One can simply state: “by drawing a random number from the Binomial distribution with parameters”

Appendix, p2 L10 from top, The description “..parameters consisting of …”, can be more usefully introduced in the first place it appears i.e. p2, L1 from top.

Table 2. rt not defined.

Discretionary Revisions (which the author can choose to ignore)

-- Role of spatial structure. At beginning it was unclear to me the reason to introduce a spatial structure (no heterogeneity between cities was assumed, neither in coverage nor in transmission), without having considered first an even more basic exercise, i.e. the case a non spatially-structured homogeneously mixing population with importation of infection. Since all spatial parameters are actually equalized this case (with N=106) should resemble much (not fully because of aggregation of stochastic variates) the case e=0.5. For ease of presentation I would suggest the authors to emphasise in their results the basic unstructured case as the departure point, and to declare more explicitly that one of the foci of the analysis is to show the consequences of taking spatial structure into consideration.

-- Presentation of results. It is very concise, it could be usefully expanded a bit.

For instance about the no persistence case, it is right what the author state about the role of city mixing. But in addition the case of the low importation rate (=0.5) case suggests that extinction is almost always the most likely outcome (figure 3), despite a typical “measles R0” (=13), especially in case of reasonable or no cities intermixing (the latter case is understandable since it deals with closed populations with 500,000 inhabitants, not far from the “Bartlett-300,000” measles critical population size). This strong lack of persistence is not very realistic for measles especially as the authors declare they intend to mimic a country. This should at least be discussed.

-- Replicates. Is the number of simulation replicates (n=100) appropriate for reconstructing the underlying multinomial distribution? for instance for importation e=0.5 the fluctuations in frequencies of patterns 3.2 and 4 (the only two likely outcome) for high coverage (80-90) seems to be a consequence of the
insufficient number of replicates. And similarly one would guess that for importation=0.5, \text{Prob}(3.2) should decline as \text{Prob}(4) increases for large coverage, which is unclear from Fig. 2.

-- It would perhaps help the reader to add a few lines to specify the importance of using a stochastic model in this specific case, compared to deterministic models which are much more common in the public health literature (the same problem of strains coexistence in a deterministic setting would lead, given the equalisation of rates, to trivial answers in most cases).

**What next?:** Accept after discretionary revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests