

## SUPPLEMENTARY INFORMATION

## Supplementary Notes: The dynamics of measles in sub-Saharan Africa

Authors: Matthew J. Ferrari, Rebecca F. Grais, Nita Bharti, Andrew J. K. Conlan, Ottar N. Bjørnstad, Lara J. Wolfson, Philippe J. Guerrin, Ali Djibo, Bryan T. Grenfell

## Contents

1. Appendix A: Critical community size for Niamey.
2. Appendix B: Outbreak Detection.
3. Appendix C: Metapopulation model.
4. Appendix D: Sensitivity of metapopulation model to changes in reactive vaccination strategies.
5. Appendix E: Impacts of SIA vaccination.
6. Appendix F: Fitting the TSIR model.

## Appendix A: Critical community size for Niamey.

The critical community size (CCS), the population size necessary for long-term local persistence, for measles has been classically estimated at between 300-500 thousand<sup>1,2</sup>. We investigated the critical community size for Niamey by simulating realizations of the stochastic TSIR model with the estimated seasonality for Niamey and a low rate of stochastic immigration (10 infectious immigrants per year) as in Grenfell et al.<sup>3</sup>. We assumed the current birthrate for Niger (50.73 births per 1000 per year), discounted by a 70% vaccination rate. We simulated measles time series for 100 years, after a 100-year burn-in to account for transient dynamics. We then calculated the proportion of years with 0 fadeouts (2 consecutive bi-weeks with 0 cases) for communities ranging from 10 000 to 5 million. For comparison we also show the relationship between fadeouts and community size using the same model structure but with weaker seasonality consistent with that estimated for pre-vaccination London<sup>2</sup>. The strong seasonality in Niamey results in a CCS that is much greater than we would expect based on the classic assumptions for the industrialized world (Fig. S1)<sup>1,2</sup>. While the same model with London-type seasonality show very few fadeouts above 300-500 thousand, Niamey still shows significant fadeouts at populations of 5-10 million, which suggests that the long-term dynamics will continue to be highly erratic even as the city grows.

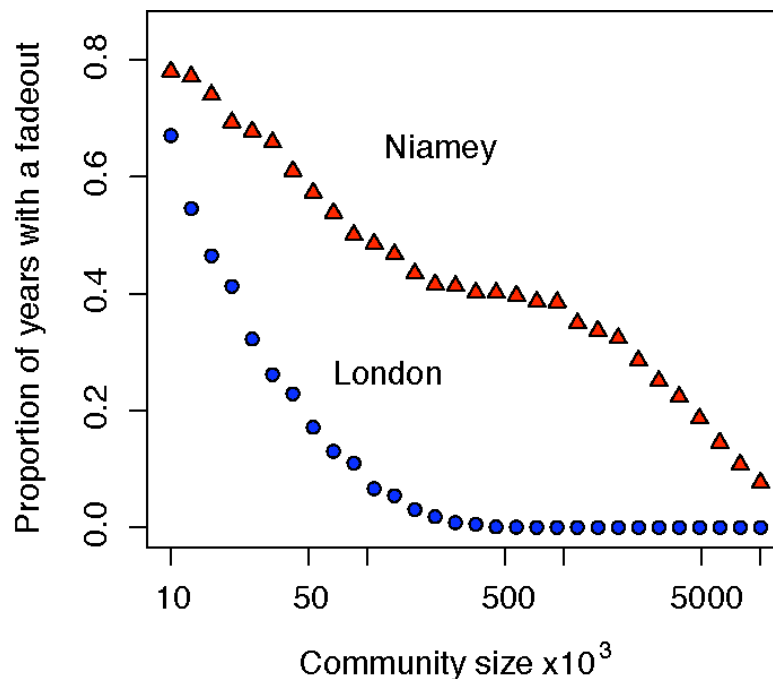


Figure S1. Critical community size for Niamey and pre-vaccination London. The y-axis indicates the proportion of years (out of 24) for which measles goes locally extinct (defined as 2 biweeks with 0 reporting). Red triangles give the mean proportion for 100 stochastic realizations of the TSIR model with the estimated Niamey seasonality and the observed Niamey birthrate with 70% vaccine coverage. The blue circles show the same for the pre-vaccination London seasonality with the observed birthrate.

## Appendix B: Outbreak Detection

A key question in the face of erratic dynamics is how to optimize the decision to commit limited resources to ORV in a timely manner. The strong seasonality in Niamey works in our favour here, since surveillance may be enhanced when outbreaks are more likely. During the last 20 years, large outbreaks have tended to begin early relative to the seasonal fluctuation in transmission rate: 7 of 10 outbreaks of >2500 cases occurred when there were >10 cases reported in October, at the onset of the dry season (Fig. S2 vertical line). The seasonal nature of measles outbreaks in Niamey, and Niger as a whole, is familiar to regional public health workers and our quantitative analysis allows us to formalize this to develop a decision-rule for public health planning. For example, a possible action threshold for early response, which minimizes the likelihood of false positives, could be to initiate an ORV if the number of cases in October exceeds 10 (an ‘October Rule’) given the current level of vaccine coverage.

The 3 large outbreaks in Niamey that do not fit the ‘October rule’ followed years with <200 reported cases (Fig.S2 horizontal line). While the number of susceptibles is not directly observable, it relates inversely to the number of cases in the previous year<sup>4</sup>. Thus epidemic surveillance should be heightened both during the early dry season, when large outbreaks are likely to start, and if more than 1 year has passed since a major epidemic<sup>5</sup>. An action threshold could be a part of a larger vaccination and response program to minimize morbidity and mortality. If, following periods of low incidence, there is an indication of a potential outbreak, it may be necessary to consider vaccination even if the threshold level has not been met.

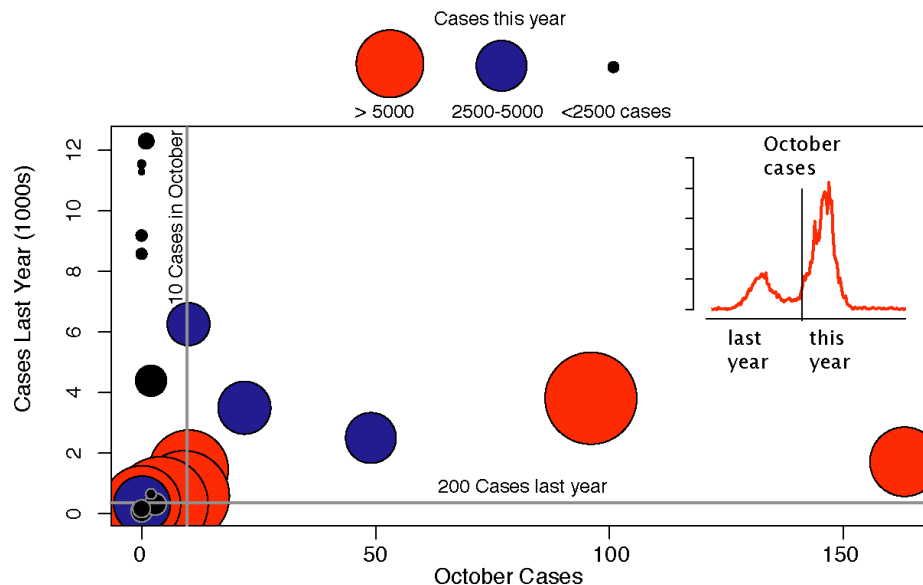


Figure S2. Monitoring for measles outbreak response

A) The number of measles cases in Niamey in the current year as a function of the number of cases in the previous year (y-axis) and the number of cases in October of the

current year (x-axis). The size and color of circles indicate outbreak size. Grey lines give the proposed thresholds for initiating a supplemental vaccination programme.

Recent interesting work by Stone et al.<sup>6</sup> has shown a relationship between the timing of epidemic peak and epidemic magnitude for moderately forced acute SIR dynamics. Based on their results we have examined the relationship between epidemic magnitude and epidemic peak for the Niamey measles time series from 1986-2005 (Fig. S3A and B) and for measles reports at the Arrondissement scale for 2001-2004 (Fig S3C) (2005 was left out as it followed an SIA). In both cases there is no clear negative relationship between the timing of the outbreak peak and the outbreak magnitude, contrary to the findings of Stone et al. The estimated seasonality in Niamey is much stronger than the forcing used in the Stone et al. simulations. Many of the outbreaks in Niger tend to be “curtailed”<sup>6</sup> by the decline in seasonal transmission rate prior to the exhaustion of the susceptible population. The result is that the timing of outbreak peaks in Niger tends to be strongly synchronous over a range of epidemic magnitudes (Fig. S3). As a result, peak timing has limited power to predict future outbreaks. Stone et al.’s work does, however, illustrate the potential of dynamical methods for measuring susceptibility during control programmes when the gold standard of longitudinal serology (e.g.<sup>7</sup>) is not available.

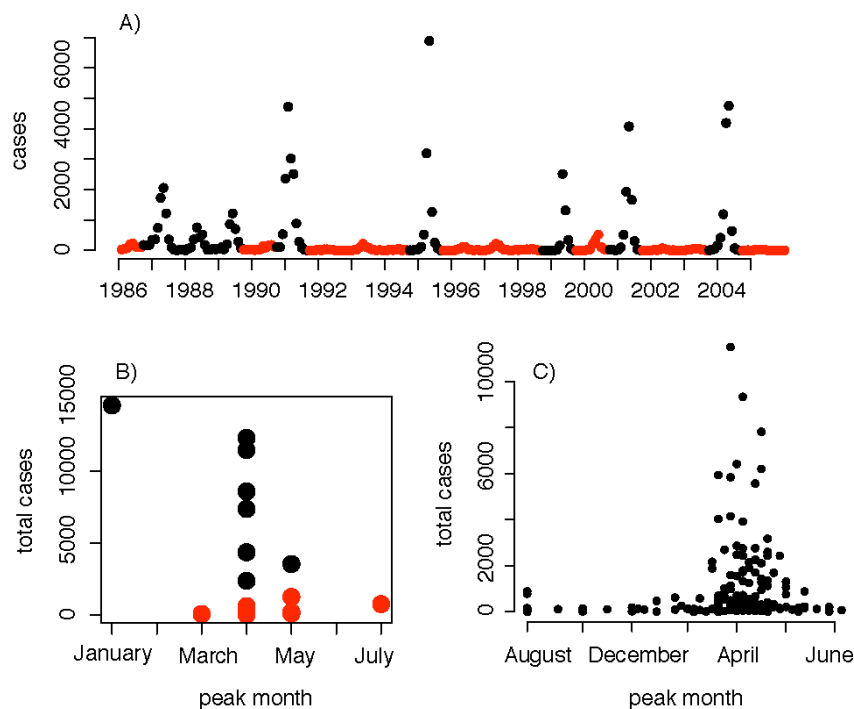


Figure S3. Relationship between the timing of epidemic peak and the epidemic size. A) The Niamey measles time series from 1986-2005, with small outbreaks and “skips” highlighted in red. B) The total measles epidemic size per year plotted against the month of the peak in cases for the Niamey time series from 1986-2005. Red indicates small outbreaks and “skips” as in A. Compare to Figure 1B,D in Stone et al. C) The total measles epidemic size per year plotted against the month of the peak in cases for 39 Arrondissements in Niger from 2001-2004.

























