Linking early warning signals to the temporal epidemiology of measles in Nigerien cities

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Abstract

Forecasting the trajectory of infectious disease outbreaks over time is a fundamental challenge facing society.

Introduction

Theory shows that epidemic transitions can be anticipated by trends in the statistical properties of disease time series (AERO papers). The existence of statistical trends in the data that precede critical transitions, so-called 'early warning signals' (EWS), imply that we may be able to anticipate disease emergence and outbreaks. The end goal is a model-independent detection system, where statistical properties of disease surveilence data can trigger warnings of impending outbreaks without the need to fit mechanistic models of disease transmission (Han and Drake 2017).

However, there is currently a gap between the theoretical work, which has relied on knowing the underlying disease dynamics, and the eventual goal of applying EWS in real-world situations where the underlying disease dynamics may be unknown. Theoretical development of EWS has focused on anticipating when the population becomes supercritical, when $\mathscr{R}_0 > 1$, after which an outbreak is inevitable, perhaps with some bifurcation delay (Dibble et al. 2016). Knowing the value of $\mathscr{R}_0$ through time makes it possible to test the accuracy of EWS that are estimated from state variables alone. Empirical application of EWS does not require knowing the value of $\mathscr{R}_0$ through time, meaning that "tests" require making assumptions about when critical transitions occur. Whether EWS track and/or anticipate underlying dynamics of real disease time series remains unknown, and is a critical knowledge gap that must be filled before EWS can confidently be deployed.

To fill this gap we will fit a mechanistic model to incidence data of measles in Niger to estimate the temporal epidemiology of the disease, yielding the very same parameters that are known in data-free modeling studies. In particular, we are interested in the correlation between EWS and the time-varying repreoductive ratio, known as the effective reprodutive ratio ($\mathscr{R}_E$). If EWS and $\mathscr{R}_E$ are significantly and positively correlated, then we have empirical evidence that EWS are applicable in real-world settings. If EWS and $\mathscr{R}_E$ are negatively correlated or not significantly posivitely correlated, then we have evidence that EWS may not be applicable in certain settings.

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Materials and Methods

Data

We used weekly measles case report data from four Nigerien cities, collected over an 11 year period (1995-2005) (Figure 1). These data are ideal for stress testing EWS because each city has different population sizes, has different dynamics in terms of size of outbreaks and length of inter-epidemic periods, and each time series has different amounts of "noise" (though, the difference in variability is probably just reflective of population size differences). The data come from [*somewhere/someone*], and used here with permission from [*somewhere/someone*].

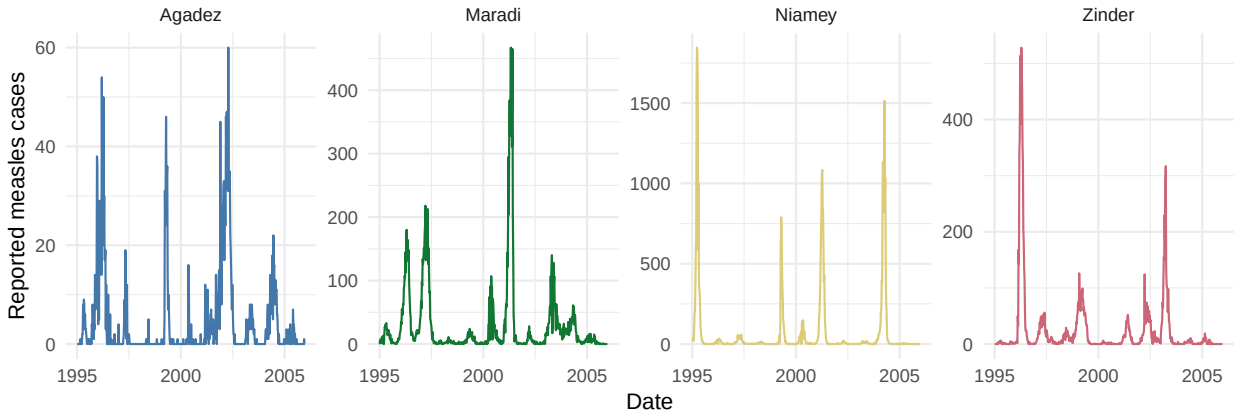

Figure 1: Time series of weekly measles case reports from four cities in Niger.

Stochastic *SI* model

The model is a continuous time *SI* model with limited demography, specified as a set of stochastic differential equations:

$$dS = \mu_t N_t dt - \lambda_t S_t dt + dU_t \quad (1)$$

$$dI = \psi_t dt + \lambda_t S_t dt - \gamma I_t dt + dV_t \quad (2)$$

where μ_t is birth rate at time t, γ is the time-invariant recovery rate, ψ_t is rate of imported infections, λ_t is the time-varying force of infectionm, and U_t and V_t are noise terms. We do not include a death process in the model because we expect death rates from the susceptible and infectious classes to be minimal relative to births and we are not interested in the recovered class since we know total population size. Excluding deaths means we can avoid making further assumptions about demographic rates – we are already making assumptions about birth rates (e.g., the rate is the same across cities, but with city-specific population size). We model stochasticity in births and imported infections by drawing time-specific values from Poisson distributions. Transitions in the model are shown in Table 1. We model λ_t as a function of a seasonal tranmission rate subject to additional environmental variability through time:

$$\lambda_t = \frac{\beta_t I_t}{N_t}, \tag{3}$$

$$\beta_t = \beta \left(1 + \sum_{i=1}^{6} q_i \xi_{i_t} \right) \Gamma_t, \tag{4}$$

where β_t is the rate of transmission at time t, β is the mean transmission rate, ψ accounts for measles infections from external sources that are not part of the local dynamics, and the term $\sum_{i=1}^{6} q_i \xi_{i_t}$ is a B-spline to model seasonality in transmission. The B-spline bases (ξ_{i_t}) are periodic with a 1 year period. The transmission rate (β_t) is also subject to stochastic process noise at each time step, Γ_t, which we model as a gamma-distributed white (temporally uncorrelated) noise with mean 1 and variance σ^2 (Bretó and Ionides 2011). In this model, the effective reproductive ratio at time t is: $\mathscr{R}_{E(t)} = \beta_t / \gamma$.

We assume observed case reports ($\mathbf{y}$) are drawn from a Poisson distribution subject to a constant reporting fraction (ρ),

$$y_t \sim \text{Poisson}\left(\rho I_t\right). \tag{5}$$

Table 1: Transitions in the SI model. We show the determinstic transmission rate for clarity, but our model uses the stochastic tranmission rate.

Transition	$(\Delta S, \Delta I)$	Propensity
birth	$(1,0)$	$N_t \mu$
imported infections	$(0,1)$	ψ_t
transmission (deterministic)	$(-1,1)$	$SI\beta_t / N_t$
transmission (stochastic)	$(-k,k)$	$\frac{S}{k} \sum_{j=0}^{k} \binom{k}{j} (-1)^{k-j+1} \tau_{\text{f}}^{-1} \ln(1 + (\beta_t I / N_t)) \tau_{\text{f}} (S-j)$
recovery	$(0,-1)$	$I\gamma$