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Disease persistence in epidemiological models: The interplay between vaccination and migration

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ABSTRACT

We consider the interplay of vaccination and migration rates on disease persistence in epidemiological systems. We show that short-term and long-term migration can inhibit disease persistence. As a result, we show how migration changes how vaccination rates should be chosen to maintain herd immunity. In a system of coupled SIR models, we analyze how disease eradication depends explicitly on vaccine distribution and migration connectivity. The analysis suggests potentially novel vaccination policies that underscore the importance of optimal placement of finite resources.

1. Introduction

Countries are increasingly connected by travel and economics. Due to economic disparities and political turmoil, extreme heterogeneity exists in childhood vaccination coverage across the two sides of multiple national boundaries. It has been suggested that the immunization coverage of neighboring countries or those countries well connected by travel can or should be used when crafting national level immunization policy. In the case of hepatitis B, Gay and Edmunds [1] argue that it would be four times more cost effective for the United Kingdom to sponsor a vaccination program in Bangladesh than to introduce its own universal program. When indigenous wild poliovirus was eradicated in all but four endemic countries in 2005: India, Nigeria, Pakistan and Afghanistan, it was exported from northern Nigeria and northern India and subsequently caused >50 outbreaks and paralyzed >1500 children in previously polio-free countries across Asia and Africa [2]. And in 2007, the WHO estimated that there were 197,000 measles deaths, despite the 82% worldwide vaccination coverage. In countries where measles has been largely eliminated, cases imported from other countries remain an important source of infection [3]. It is clear that a country needs to be concerned with the vaccination rate of a neighboring country as well as its own.

On another scale, vaccination policies must also take into consideration the subpopulation dynamics within a country. Wilson et al. [4] models linked urban and rural epidemics of HIV and discusses how to optimize a limited treatment supply to minimize new infections. Cummings et al. [5] uses data to identify a distinct pattern in the periodicity of measles outbreaks in Cameroon before the widespread vaccination efforts of the Measles Initiative. The southern part of Cameroon experienced a significant measles epidemic approximately every three years. In contrast, the three northern provinces contend with annual measles epidemics. In 2000 and 2001, these cyclic outbreaks coincided, exacerbating the situation and causing a much more severe epidemic [5].

Noting that a small contribution of infections from one population to another could drive a new type of epidemic that would not normally occur, we study how migration between populations could change dynamics and respective herd immunity levels in metapopulation models. We analyze a model of a disease imported between subpopulations of a region by short-term and long-term migration with limited vaccination coverage. Our initial study is based on the analysis of a system of canonical SIR compartmental models. The system allows the rigorous proof of the qualitative affects migration has on herd immunity. The model can be enhanced to include more compartments or seasonal forcing, but most of these systems will require numerical exploration of trends in spatial synchrony and bifurcation analysis, which will be explored in future papers. In this article, we revisit the fundamental ways migration is modeled in metapopulation models and how it fundamentally affects herd immunity.

Migration is often treated as a phenomenological input to maintain incidence in a population that might experience local fade-out

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[6]. Long-term migration has been analyzed by Liebovitch and Schwartz [7], with a thorough derivation of the linear flux term coupling the patches. This approach also agrees with the classes of models proposed by Sattenspiel and Dietz [8] and Lloyd and Jansen [9]. Keeling and Rohani [10] investigated the spatial coupling of dynamics exhibited in models using multiple formulations of migration including mass-action coupling and linear flux terms. However, they did not explore the impact of coupling in the presence of vaccination needed to maintain disease free states. Additional analysis of mixed long-term and short-term migration in transport-related disease spread can be found in [11–13]. These papers derive the global asymptotic stability of the disease free state for a new disease. Because there is no vaccination, the papers conclude that it is essential to strengthen restrictions of passenger travel as soon as the infectious diseases appear.

Our paper considers how migration directly affects the vaccination levels needed for herd immunity against a known disease and how that would impact optimum usage of limited vaccination supplies. We investigate the dynamics of models that include mass-action coupling, an assumption that assumes mixing occurs at fast time scales, and linear migration, which is more consistent with mixing occurring at long time scales. The organization of this paper is as follows: We introduce a coupled compartmental model in Section2 and perform stability analysis of the disease free state as a function of the migration and vaccination rates. We also consider normal forms of the bifurcations created by the short-term and long-term migration dynamics. Section 3 describes how vaccination rates should be adjusted with respect to short-term and long-term migration levels to preserve herd immunity. Section 4 has a summary of our observations and conclusions.

2. The model

We start with the classic Susceptible, Infected, Recovered (SIR) model. Let S, I, and R denote the number of people in each of the disease classes for a population of size N. Let the parameters $\beta > 0$ denote the contact rate, $\mu > 0$ denote the birth/death rate, and $\kappa > 0$ denote the recovery rate. The vaccination rate, $0 \leqslant v \leqslant 1$, represents the removal of a percentage of the incoming newborn population to recovered. The standard form for this system is

$$\begin{aligned}\frac{dS}{dt} &= (1-v)\mu N - \frac{\beta SI}{N} - \mu S,\\ \frac{dI}{dt} &= \frac{\beta SI}{N} - \kappa I - \mu I,\\ \frac{dR}{dt} &= v\mu N + \kappa I - \mu R.\end{aligned} \tag{1}$$

The death rates in the classes balance the births so that the population size $N > 0$ is constant. For a detailed analysis of the single patch formulation of this system, see Hethcote [14].

We now consider two coupled subpopulations where the disease dynamics of each population are described by the SIR model. Let S_k, I_k, and R_k denote the number of people in each of the disease classes, $\mu_k > 0$ denote the birth/death rates, and v_k denote the vaccination rates of subpopulations N_k for $k = 1, 2$. To model long-term movement (linear mixing), let $c_1 \geqslant 0$ denote the rate of migration from population two to population one and vice versa for the rate $c_2 \geqslant 0$. To model short-term movement (mass action mixing), let $0 \leqslant c_3 \leqslant 1$ be a scaling of the number of infectives from one population who move into the other population for a short time and mix with the susceptibles to produce additional infections. Because β is proportional to the average number of contacts a person can make per unit time, we distribute the contacts for the susceptibles between the infected people by mass action within and outside the population by using the prefactors c_3 and $(1 - c_3)$ respectively as in Keeling and Rohani [10]. The coupled two population model is as follows:

$$\begin{aligned}\frac{dS_1}{dt} &= (1-v_1)\mu_1 N_1 - \frac{(1-c_3)\beta S_1 I_1}{N_1} - \frac{c_3\beta S_1 I_2}{N_1} - \mu_1 S_1 + c_1 S_2 - c_2 S_1,\\ \frac{dI_1}{dt} &= \frac{(1-c_3)\beta S_1 I_1}{N_1} + \frac{c_3\beta S_1 I_2}{N_1} - \kappa I_1 - \mu_1 I_1 + c_1 I_2 - c_2 I_1,\\ \frac{dR_1}{dt} &= v_1\mu_1 N_1 + \kappa I_1 - \mu_1 R_1 + c_1 R_2 - c_2 R_1,\\ \frac{dS_2}{dt} &= (1-v_2)\mu_2 N_2 - \frac{(1-c_3)\beta S_2 I_2}{N_2} - \frac{c_3\beta S_2 I_1}{N_2} - \mu_2 S_2 + c_2 S_1 - c_1 S_2,\\ \frac{dI_2}{dt} &= \frac{(1-c_3)\beta S_2 I_2}{N_2} + \frac{c_3\beta S_2 I_1}{N_2} - \kappa I_2 - \mu_2 I_2 + c_2 I_1 - c_1 I_2,\\ \frac{dR_2}{dt} &= v_2\mu_2 N_2 + \kappa I_2 - \mu_2 R_2 + c_2 R_1 - c_1 R_2.\end{aligned} \tag{2}$$

We keep the number of people in the subpopulations constant by letting $\rho = N_2/N_1$ and setting the constraint $c_2 = c_1\rho$. This system is overdetermined by the subpopulation constraints, $S_k + I_k + R_k = N_k$ for $k = 1, 2$, and therefore the analysis omits the variables R_k for $k = 1, 2$.

Motivated by the distinct subpopulation dynamics of Cameroon described in Cummings et al. [5], numerical simulations will use parameters based on Cameroon demographics. The values are listed in Table 1. The subpopulation sizes are totals for the northern and southern regions based on data in [5]. The birth/death rates are averages over the northern and southern regions based on data in [5]. The recovery rate is a parameter that is derived from the biological characteristics of measles. The contact rate was estimated using the average age of incident measles cases over the period 1998–2006 from passive surveillance data [5]. The specific results here are fairly insensitive to changes to β. An SIR model is used here without the exposed class but we expect the inclusion of an exposed class would not substantively change our qualitative results.

Table 1
Parameter values for model based on Cameroon data.

Parameter	Value	Unit	Description
N_1	4,451,000	people	Northern subpopulation size
N_2	10,212,000	people	Southern subpopulation size
ρ	2.2943	None	Ratio of N_2/N_1
β	700	year^{-1}	Contact rate
κ	100	year^{-1}	Measles recovery rate
μ_1	.0428	year^{-1}	Birth and death rate for N_1
μ_2	.0329	year^{-1}	Birth and death rate for N_2

2.1. General system analysis

We start with a general analysis of the system to determine the conditions necessary for the populations to be disease free.

Proposition 1. *System (2) has a disease free equilibrium (DFE) and is given by*

$$(S_1, I_1, S_2, I_2) = (N_1\hat{S}_1, 0, N_2\hat{S}_2, 0), \tag{3}$$

for

$$\hat{S}_1 = \frac{(1-v_1)(\mu_1 c_1 + \mu_1\mu_2) + (1-v_2)\mu_2 c_1\rho}{\mu_1 c_1 + \mu_1\mu_2 + \mu_2 c_1\rho}, \tag{4}$$

$$\hat{S}_2 = \frac{(1-v_1)\mu_1 c_1 + (1-v_2)(\mu_1\mu_2 + \mu_2 c_1\rho)}{\mu_1 c_1 + \mu_1\mu_2 + \mu_2 c_1\rho}. \tag{5}$$