5-2016

Modeling Consequences of Reduced Vaccination Levels on the Spread of Measles

Guillermo Ortiz

Bridgewater State University

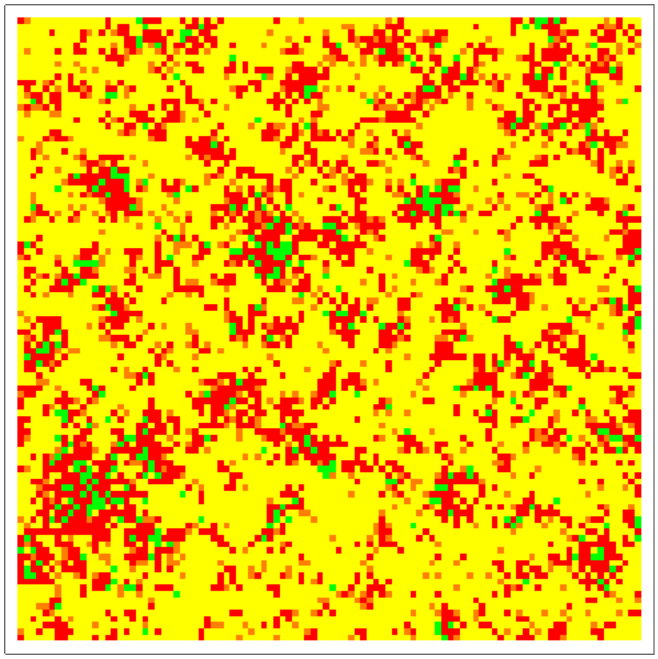
Senior Honors Thesis

Modeling Consequences of Reduced Vaccination Levels on the Spread of Measles

Guillermo Ortiz

Mentors

Dr. Irina Seceleanu and Dr. Kevin Rion



Contents

1 Introduction

In this thesis we propose a mathematical model for the spread of measles in a closed population. In section 1 we offer a motivation for the project, describe the measles virus as well as its history in the US, and provide a brief summary of three epidemiological models from the literature. In section 2.1 we introduce some probabilistic tools used in our model. Section 2.2.1 outlines our stochastic model used for the spread of measles in a population, which is refined in section 2.2.2 to include health interventions from the CDC. We conclude the thesis by presenting in section 3 the results of the simulations of the stochastic model developed and discussing the effects of a decrease in vaccination coverage on the spread of measles in the population.

1.1 Motivation

The cover of the March 2015 issue of the National Geographic magazine lists vaccination, along with climate change and evolution, as one of the dominant topics in the national debate for which scientific facts are met with skepticism by a significant proportion of the US population (Achenbach, 2015). The ever increasing number of measles outbreaks in the US has been linked to a recent anti-vaccine movement which gained momentum after the publication in 1998 of a study erroneously connecting the measles vaccine to autism. The journal later retracted the article and countless scientific studies have since discredited this theory (Farrington, Miller, & Taylor, 2001), but despite strong evidence for the safety and efficacy of the vaccine an increasing proportion of the population are choosing not to vaccinate their children. The most recent measles outbreak, originating at Disneyland in California, resulted in 114 cases across several states, of which almost 70 percent were among people unvaccinated due to personal beliefs (CDC, 2015b). While contagious diseases, such as measles, have a high prevalence among unvaccinated individuals, they also present a threat to those that have been immunized as vaccines are not 100 percent efficient. For example, the Measles, Mumps, Rubella vaccine has a 95 percent efficacy rate at preventing

the disease (Atkinson, 2012), and so while vaccinated members of the population have a lower risk of contracting the disease some are nevertheless at risk. Given this recent, highly concerning trend of parents choosing not to vaccinate their children, we propose to construct a mathematical model simulating the spread of measles in the US and study the consequences of increased levels of unvaccinated individuals in the population.

Among contagious diseases, measles is one of the most infectious viral diseases known with more than 90 percent secondary infection rate in susceptible individuals. In particular, an unvaccinated individual has a 90 percent chance of contracting the disease, while a vaccinated individual has only a 5 percent chance of becoming infected. The mean incubation period from exposure to the measles virus to the onset of the symptoms is 8 days and the mean duration of the infectious period is 7 days. According to the CDC, the vaccination levels needed to ensure herd immunity against measles in developed countries is 93-95 percent.

Historically, before the development of the measles vaccine, approximately 500,000-700,000 cases of measles were reported annually, however the actual occurrence is estimated to have reached over 3 million annually (Atkinson, 2012). After the development of the vaccine in 1963 the incidence of measles dropped and reached a historic low with fewer than 1500 cases reported in 1983 (Atkinson, 2012).

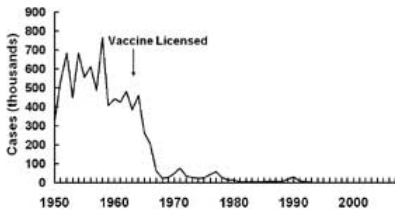


FIGURE 1. Measles cases per year between 1950 and 2000's.

However, despite significant gains in raising the vaccination rate in the US population, between 1989 and 1991 more than 56,000 cases were reported.

This measles resurgence was primarily caused by low vaccination coverage among low-income communities and 90 percent of all fatal cases were among individuals with no history of vaccination (Atkinson, 2012). In response, the Vaccine for Children program was created in 1993 and led to the elimination of measles in the US in the early 2000s (CDC, 2014b).

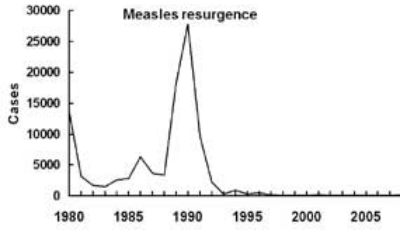


FIGURE 2. Measles resurgence between 1989 and 1991.

After achieving a 2003 high of a 93 percent vaccination rate in the US, recent years have brought a slow decline in the percentage of children vaccinated for measles (CDC, 2014a). Despite the relatively low incidence of infections in the US, the risk of outbreaks remains because the virus is frequently reintroduced from abroad, as measles is still endemic in many countries. Measles could therefore become reestablished if vaccine coverage levels continue to drop significantly (CDC, 2015a).

The increase in frequency and size of the measles outbreaks over the past 7 years has been the result of the spread of the disease in communities with groups of unvaccinated people (CDC, 2015b). Parents who choose not to vaccinate their children tend to live in communities together and form pockets of unvaccinated people, where the virus can take hold and easily spread among people with no immunity to the virus.

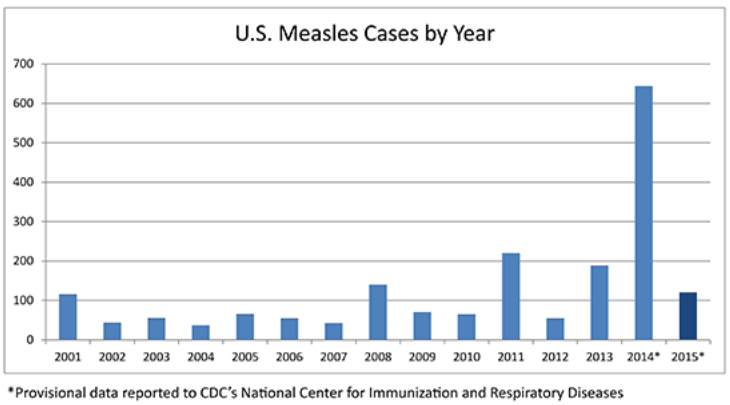


FIGURE 3. Number of measles cases from 2001 to 2015.

The year 2014 had a record number of outbreaks, namely 23 which accounted for approximately 650 infected people (see figure 3). The outbreak with the highest number of cases (383 cases) occurred among primarily unvaccinated Amish communities. Even more

concerning is the trend among upper middle-class families in several wealthy counties across the US refusing to vaccinate their children for personal beliefs (Healy & Paulson, 2015). For example, figure 4 shows several counties in California with lower than 80 percent vaccination coverage.

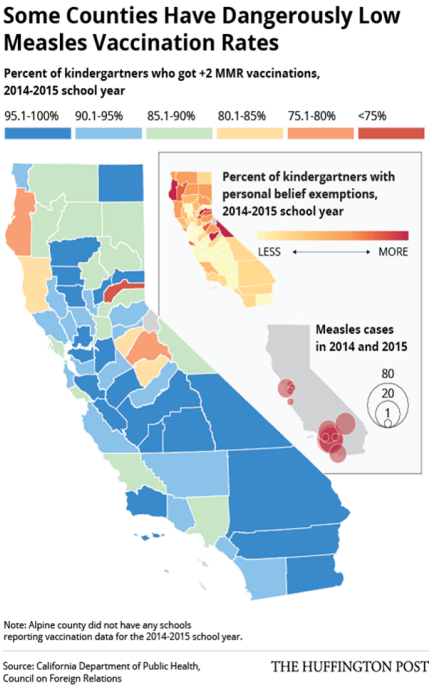


FIGURE 4. Vaccination coverage in California per county.

To quantify the consequences of the choice among vaccine skeptics to opt out of immunization programs and thus raise awareness about the importance of vaccination, our project will create a mathematical model simulating the spread of measles in the US assuming different levels of immunization in the population. Our project can help better explain the effects that the individual choice not to get vaccinated can have on the entire US population, and thus raise awareness for the importance of vaccination and the shared responsibility for reducing outbreaks through individual immunization. Our mathematical model will also be helpful in better understanding the effects that public health policies can have on the spread of measles once an epidemic occurs.

1.2 Literature Review

Before we outline our mathematical model for the spread of measles, we first give a brief outline of some epidemiological models in the literature that provided us with a starting point for our approach.

The first model that we discuss is due to Greenwood (1931) and is one of the earliest foundational epidemiological models. In his model Greenwood used two possible states for individuals to be in during the epidemic,–Susceptible and Infected–and modeled the spread of the disease in the population based on the interactions between individuals in these two states. If $I(t)$ is the number of newly infected individuals from time t to time $t+1$, and $X(t)$ is the number of susceptible individuals at time t, then at the next time unit the number of infected people is $X(t+1) = X(t) + I(t)$. Let p denote the chance that the contact between two individuals is sufficient to produce a new infection. Greenwood used the Binomial distribution with success probability p to model the chance of j individuals remaining infected at time $t+1$ out of the i susceptible individuals at time t, that is $\mathbb{P}(X(t+1) = j | X(t) = i) = \binom{i}{j} p^{i-j}(1-p)^j$ if $i \geq j$ and 0 if $i < j$. These transition probabilities can then be summarized in a matrix $A_{r\times r}$, where r is the initial number of susceptible individuals in the population. Then $a_{ij} = \mathbb{P}(X(t+1) = j | X(t) = i)$ and $(X(t))_{t\in\mathbb{N}}$ for $1 \leq i, j \leq r$ is a Markov chain.

The importance of Greenwood's model resides in the fact that it is the first stochastic model introduced for studying the spread of a disease in a closed population and its main ideas serve as the basis for current models in epidemiology. However, due to the time in which Greenwood's model was created, its major drawback is that it does not take into account varying immunity levels in the population. As vaccination coverage is the main concern of our research, Greenwood's model cannot illuminate the benefits of immunization.

Before discussing another stochastic model which more closely resembles the direction that we took in our own project, let us take a moment to explore a different type of model in the field of epidemiology. A deterministic model is one in which no randomness is allowed and

the outcome of the system is simply a function of the initial conditions. In their deterministic SIR model, Smith and Moore used functions to describe the Hong Kong flu in New York City in the 1960's (Smith & Moore, 2004). They employed three states–Susceptible, Infected, Recovered; however, instead of using probability distributions to determine the transition from one state to the next, they used rates of change with respect to time. While the functions $S(t)$, $I(t)$, and $R(t)$ kept track of the number of individuals in each state, their derivatives $\frac{dS}{dt}$, $\frac{dI}{dt}$, and $\frac{dR}{dt}$ accounted for the number of individuals entering or leaving each state. We did not employ a deterministic model as infectious diseases generally spread in a stochastic fashion.

We now introduce the last major literature source that influenced our model significantly. Continuing the work of Greenwood, the model created by Yaesoubi and Cohen features three states – Susceptible, Infected, and Recovered – and involves the use of probability distributions to determine how individuals transition from one state to the next (Yaesoubi & Cohen, 2011). In their article the authors make reference to Greenwood's model as a foundational source for their work. In particular, they make use of a discrete-time Markov chain with two dynamic driving events, $I(t)$ and $R(t)$, for their transition probabilities. Here, $I(t)$ represents the probability of a susceptible individual transitioning to the infected state and $R(t)$ that of an infected individual transitioning to the recovered state. The authors ran simulations for the influenza virus, and compared their results to the evolution of an outbreak that occurred in an English boarding school during the late 1970's. Their model employs Binomial distributions for the transition probabilities as well as lays a detailed foundation for how to account in the model for the specific parameters of an infectious disease. Our stochastic model outlined in section 2.2 uses Yaesoubi-Cohen's model as a starting point with several areas of improvement. Most notably, the authors did not account in their model for the exposed state in which individuals carry the disease but are not yet infectious (incubation period) as well as for public health interactions from the CDC once a measles outbreak is reported.

1.3 Description of Research Question

As an increasing number of individuals in our society have embraced a mistrust of scientific research and the false claims endorsed by various public figures and celebrities about side effects of vaccination, skepticism about the safety of vaccination has emerged as a public health concern. As a result, this recent anti-vaccine movement has led to a resurgence of measles cases in the US with more and more parents choosing not to vaccinate their children. To better understand the effects that this recent reduction of vaccination levels in certain counties in the US can have on the spread of measles in the entire US population, we created a stochastic model simulating the spread of measles in a closed population with the goal of studying the long-term consequences of decreased vaccination levels on the number and duration of measles outbreaks. We employed a non-homogeneous Markov model with four states - Susceptible, Exposed, Infected, and Recovered, in which the transition probabilities of the dynamic driving events from one state to the next are determined by a variety of distributional assumptions. We used our model to simulate the dynamics of the spread of measles using different resistivity levels in the population, and thus were able to illustrate the influence pockets of unvaccinated people have on the incidence of the disease. Furthermore, our model incorporates public health intervention factors in response to a measles outbreak such as quarantining and immunizing individuals, and thus can be used to inform health policies for preventing and controlling the spread of measles in the US.

2. The Stochastic Model

In this section we explain in detail the components that make up our stochastic model for the spread of measles in a population. We begin by defining the mathematical tools in our model employed from the field of probability theory. We then outline the reasoning behind the modeling assumptions and the choices underlying the equations for the driving events in our model. Finally, we modify our stochastic model to account for public health intervention factors and describe the new equations for the driving events.

2.1 A Review of Probability Theory

In this section we introduce some basic concepts from probability theory in order to outline the concepts underlying the random variables employed in the model. To do this, we first present a few definitions.

Definition 2.1. *A **random experiment** is a procedure with a well-defined set of possible outcomes that can be repeated as often as we like.*
*A **sample outcome** is any potential outcome from an experiment. The collection of all sample outcomes of an experiment is referred to as the **sample space** of the experiment.*

In general, we denote a sample outcome by the lowercase letter s and a sample space with the uppercase letter S. If a sample outcome belongs to a sample space we say that s is in S which we denote as $s \in S$. Rolling a die, flipping a coin, and drawing a card from a standard deck are all examples of random experiments. For example, in the random experiment of rolling a standard die we obtain the sample space $S = \{1, 2, 3, 4, 5, 6\}$ and when flipping a coin the sample space is $S = \{H, T\}$ where H and T denote the coin showed heads and tails, respectively. We can also refer to a *realization* of an experiment as an outcome that has been observed. For example, if we roll a die and it lands on 6, then we say that the realization of the experiment of rolling a die was 6.

Definition 2.2. *An **algebra** $\mathcal{A}$ associated with the sample space S is a non-empty collection of subsets of S closed under the operations of intersection, union, and complement.*

Once an algebra is chosen, its elements are our events.

Definition 2.3. *An **event** is any collection of sample outcomes of an experiment that is in the associated algebra $\mathcal{A}$.*

We denote events with a subscripted or unsubscripted letter A.
We now focus on assigning probabilities to events and describing probability distributions. We begin by introducing the probability function and Kolgomorov's Axioms.

Definition 2.4. *For a sample space S, with associated algebra $\mathcal{A}$, $\mathbb{P} : \mathcal{A} \to [0,1]$ is a* ***probability function*** *if and only if:*

(i) $0 \leq \mathbb{P}(A) \leq 1$, $\forall A \in \mathcal{A}$

(ii) $\mathbb{P}(S) = 1$

(iii) *For any sequence of events $A_1, A_2, \ldots \in \mathcal{A}$ with $A_j \cap A_k = \varnothing$ when $j \neq k$,*

$$\mathbb{P}\left(\bigcup_{n=1}^{\infty} A_n\right) = \sum_{n=1}^{\infty} \mathbb{P}(A_n)$$

Then, $\mathbb{P}$ is a function that assigns to each event A a number $\mathbb{P}(A)$ between 0 and 1 and we refer to $\mathbb{P}(A)$ as the probability of the event A.

We now introduce three important concepts necessary for our discussion of probability distributions. First, we need to introduce the concept of conditional probability.

Definition 2.5. *Given two events A_1 and A_2 for which A_2 has a non-zero probability, we call $\mathbb{P}(A_2|A_1)$ the* ***conditional probability*** *of A_2 occurring given that A_1 has occurred. We define this as follows: $\mathbb{P}(A_2|A_1) = \dfrac{\mathbb{P}(A_2 \cap A_1)}{\mathbb{P}(A_1)}$.*

Definition 2.6. *We say that two events A_1 and A_2, are* ***stochastically independent*** *with respect to $\mathbb{P}$ if $\mathbb{P}(A_1 \cap A_2) = \mathbb{P}(A_1) \cdot \mathbb{P}(A_2)$.*

We remark that when A_1 and A_2 have non-zero probabilities, A_1 and A_2 are independent if and only if the occurrence of A_1 does not affect the probability that A_2 occurs, that is, $\mathbb{P}(A_2|A_1) = \mathbb{P}(A_2)$.

Definition 2.7. *A* ***random variable*** *from a sample space S, denoted $X : S \to \mathbb{R}$, is a function that maps the outcomes of S to a real number and has the property that for all $a < b$ in $\mathbb{R}$, $(a < X < b) := \{s \in S; X(s) \in (a,b)\}$ is in $\mathcal{A}$.*

The advantage of using a random variable is that it often reduces the sample space of the experiment into a more manageable set. For example, consider the experiment of rolling two standard dice. The sample space for the event consists of the 36 pairings of the individual dice (x, y) where $x, y \in \{1, 2, 3, 4, 5, 6\}$. Now, let X be the random variable that denotes

the sum of the faces after rolling the two dice. Then the possible values for X are the real numbers 2,3,...,12. Hence, we reduced our sample space to only 11 possible outcomes.
Now that we have the basics of the concepts we need to introduce the probability distributions used in the model, we begin by explaining the fundamentals of the Binomial distribution.
In order to discuss the idea of a binomial distribution we first introduce the idea of a Bernoulli trial.

Definition 2.8. *A Bernoulli trial is an experiment which has only two possible outcomes, success or failure, with the probability of success being p.*

In notation, we write $\mathbb{P}(success) = \mathbb{P}(X = 1) = p$ and $\mathbb{P}(failure) = \mathbb{P}(X = 0) = 1 - p$.
A binomial experiment denoted $Binomial(n, p)$, then is obtained by performing a specified number n of independent Bernoulli trials, each with a success probability of p. The outcome X of the binomial experiment is the number of successes observed during the n trials. To determine the probability of obtaining k successes in n trials, that is $\mathbb{P}(X = k)$, the idea is to count the number of ways that we can get k successes in n trials, and then multiply by the probability of getting k successes (p^k) and $n - k$ failures ($(1 - p)^{n-k}$).
In general, a binomial distribution meets the following conditions:

(i) Perform n independent Bernoulli trials each with probability p of success.

(ii) The random variable X counts the number of successes in n trials.

(iii) The probability of k successes in n trials is given by the formula

$$\mathbb{P}(X = k) = \binom{n}{k} p^k (1 - p)^{n-k}$$

In summary, the outcomes of an experiment in which n independent Bernoulli trials are performed where each trial has probability p of success are binomially distributed. We denote that X follows a binomial distribution with n trials and probability p of success by $X \sim Binomial(n, p)$.
Moreover, it is important to note that what is defined as a success depends on the observer's interest. To explain this behavior, consider a competition between two individuals in which

the participants pick a side of a fair coin which then gets flipped five times with the winner being decided by who's side is observed the most. This scenario will yield a binomial distribution since each flip of the coin can be regarded as identical Bernoulli trials, however what is defined as success differs by player. If we have Player 1 as the observer, having chosen "Heads" as his means to victory, then success will be defined as observing the coin landing heads up and we will count how many successes occur in the five trials.

Another probability distribution that is of interest to us is the exponential distribution, which is used to model waiting times. For example, the exponential distribution can be used to find the probability of waiting for a train at a particular train station knowing that on average one train arrives every 5 minutes. In general what we are interested in finding is the probability of having to wait as long as a particular time t and thus we concern ourselves with finding the probability of waiting t or less units of time. Moreover, a fundamental parameter of interest in an exponential experiment is the average waiting time which is usually denoted as $\frac{1}{\lambda}$, where λ is the average number of arrivals per time unit. We then say that a random variable X follows an exponential distribution if:

$$\mathbb{P}(X \leq t) = \int_0^t \lambda e^{-\lambda t} dt, t \in [0, \infty)$$

and write $X \sim Exponential(\lambda)$.

On the example with the waiting times of trains, if we are interested in finding the probability of having to wait at most 20 minutes to see the first train arrive given that on average a train arrives every 5 minutes we proceed as follows:

$$\mathbb{P}(X \leq 20) = \int_0^{20} \frac{1}{5} e^{-\frac{t}{5}} dt = 0.981684$$

and thus $\mathbb{P}(X \leq 20) = 0.981684$.

2.2 The SEIR Model

Now that we have laid out the probabilistic terminology, we turn to describing the components of our model for the spread of measles in a closed population. We have chosen to

model this using stochastic processes, which incorporate randomness and assign probabilities to transitions between states of the system. This is in contrast to a deterministic model, for which the evolution of the system is a function of the initial conditions. The goal of our stochastic model is to simulate the spread of measles in a closed population to study the consequences of reduced vaccination coverage on the number and duration of measles outbreaks. We employed what is called a SEIR model which has four states: **S**usceptible, **E**xposed, **I**nfectious, and **R**ecovered. These are the four states an individual can be in during a measles outbreak. At first an individual in the population is susceptible (S) to acquiring the disease. Then upon being exposed to the disease we say that the individual is in the exposed state (E), which means the individual has contracted the disease but it is not infectious and cannot spread it. After the incubation period has ended, on average lasting 8 days for measles, the individual becomes infectious (I) and can spread the virus throughout the duration of the infectious period. For measles the period lasts on average 7 days, and afterwards the individual transitions to the recovered state (R).

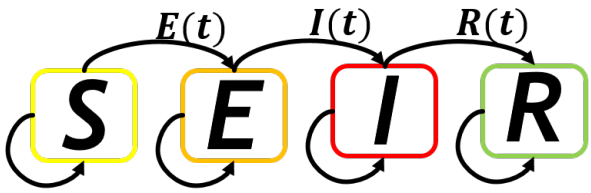


FIGURE 5. Diagram of how individuals transition through the different states S, E, I, R.

After an individual finishes the cycle and reaches the recovered state, the individual is no longer able to contract the virus as successful recovery grants life-long immunity to the measles virus. It is important to note that an individual in the susceptible state may or may not be vaccinated. Consequently, the chance of Transitioning from susceptible to exposed varies. For a vaccinated individual the probability of contracting the disease upon contact with the virus is five percent, while an unvaccinated individual has a probability of ninety percent (Atkinson, 2012).

2.2.1 Dynamic Driving Events

In this section we introduce the dynamic driving events that describe the transitions of individuals from one state to the next. Since we are using a stochastic model, we will start by defining the random variables that are involved in our model. We let $X_S(t)$ represent the number of individuals in the susceptible state at time t. Similarly, we let $X_E(t)$, $X_I(t)$, and $X_R(t)$ represent the number of individuals in the exposed, infected, and recovered states at time t, respectively. These random variables enable us to keep track of the number of people in each state at all times t and thus will help us explain the evolution of the distribution of the states over time. We assume in our model that the population is closed, and so if N denotes the population size, then the equation $X_S(t) + X_E(t) + X_I(t) + X_R(t) = N$ for all times t.

We now focus on explaining how the distribution of the $SEIR$ states changes over time. We do this by associating the changes to dynamic driving events. This attention to the individual transitions is used in deriving the distributions of the dynamic driving events which are represented by the random variables $E(t)$, $I(t)$, and $R(t)$ and symbolize the number of newly exposed, infected, and recovered individuals at during the time from t to $t+1$. Since an individual in state S can either get exposed or not at time t (similarly an individual in state E can either become infectious or not and an individual in state I can either recover or not) we model these random variables using the Binomial distribution where success is defined as transitioning to the next state.

We now examine the dynamic driving events in the order in which they are used in the model beginning with $E(t)$.

First, we focus on the distribution of the process of randomly selecting one susceptible individual and recording a 1 if the person becomes exposed during the time interval from t to $t + 1$, and 0 if the person remains in the susceptible state. This is a two valued process, so it has a $Bernoulli(q(t))$ distribution for some number $q(t) \in [0, 1]$.

Once we find the value of $q(t)$, it follows that the number $E(t)$ of susceptible individuals

that become exposed is $Binomial(X_S(t), q(t))$ distributed.

To find this $q(t)$, we introduce an auxiliary variable Y which is 1 if the person becomes exposed during the interval, and is zero otherwise. In this case, $q(t) = \mathbb{P}(Y = 1)$.

The event $(Y = 1)$ that we select an individual that transitioned to the exposed state during this time interval depends on the persons vaccination state ($V = 1$ for vaccinated, $V = 0$ if not), and the number of encounters with infectious individuals. This number of encounters with infectious individuals depends in turn on the number of encounters the person has with other individuals in the population, and the proportion of that population that is infectious. Let U be the number of encounters our randomly selected susceptible individual has with others in the population, and W be the number of infectious encounters.

Our modeling assumptions are that:

i. $U \sim Poisson(\lambda)$, where λ is the mean number of contacts individuals have per unit of time.

ii. $W|U = n \sim Binomial(n, \beta(t))$, where $\beta(t)$ is the proportion $\dfrac{X_I}{N}$ of the population that is infectious.

iii. $Y|W = j \sim Bernoulli(1 - (1 - p)^j)$, where $1 - (1 - p)^j$ is the chance of contracting the disease at least once in j encounters with infectious individuals.

Here, the notation $W|U = n \sim Binomial(n, \beta(t))$ is short hand for the assertion that the conditional distribution of W given that $U = n$ is $Binomial(n, \beta(t))$; and in like fashion, $Y|W = j \sim Bernoulli(1 - (1 - p)^j)$ is a shorthand for the claim that the conditional distribution of Y given that $W = j$ is $Bernoulli(1 - (1 - p)^j)$. Also, implicit in this is the assumption that Y depends on U only through W so that for all n and j, $\mathbb{P}(Y = 1|U = n, W = j) = \mathbb{P}(Y = 1|W = j)$.

To find the value of p in (iii), we call on the law of total probability in finding the probability of the event A that the person we select transitions to the exposed state upon encountering an infectious person. Using ν as the proportion of the population that is vaccinated, we set the chance $\mathbb{P}(V = 1)$ that we select a vaccinated person at ν, and the chance $\mathbb{P}(V = 0)$ that we select an unvaccinated person at (1-ν). Then since there are 5%, and 90% chances

respectively for vaccinated and unvaccinated persons to transition from the susceptible to the exposed state upon encountering an infectious person, we have that $\mathbb{P}(A|V=1)=0.05$ and $\mathbb{P}(A|V=0)=0.90$. This leads to

$$\begin{aligned} p &= \mathbb{P}(A) \\ &= \mathbb{P}(A|V=1)\mathbb{P}(V=1)+\mathbb{P}(A|V=0)\mathbb{P}(V=0) \\ &= 0.05\cdot\nu+0.90(1-\nu). \end{aligned} \tag{1}$$

Now to find q(t), we appeal to the law of total probability once again.

$$\begin{aligned} q(t) &= \mathbb{P}(Y=1) \\ &= \mathbb{P}((Y=1)(W\in\mathbb{N}_0)(U\in\mathbb{N}_0)) \\ &= \sum_{n=0}^{\infty}\sum_{j=0}^{n}\mathbb{P}((Y=1)(W=j)(U=n)) \\ &= \sum_{n=0}^{\infty}\sum_{j=0}^{n}\mathbb{P}((Y=1)|(W=j))\mathbb{P}(W=j|U=n)\mathbb{P}((U=n)) \\ &= \sum_{n=0}^{\infty}\sum_{j=0}^{n}(1-(1-p)^j)\binom{n}{j}\beta(t)^j(1-\beta(t))^{n-j}e^{-\lambda}\frac{\lambda^n}{n!} \end{aligned} \tag{2}$$

So,

$$\begin{aligned} q(t) &= \sum_{n=0}^{\infty}\sum_{j=0}^{n}\frac{e^{-\lambda}\lambda^n}{n!}\binom{n}{j}\beta(t)^j(1-\beta(t))^{n-j}(1-(1-p)^j) \\ &= \sum_{n=0}^{\infty}\frac{e^{-\lambda}\lambda^n}{n!}\sum_{j=0}^{n}\binom{n}{j}\beta(t)^j(1-\beta(t))^{n-j}(1-(1-p)^j) \\ &= \sum_{n=0}^{\infty}\frac{e^{-\lambda}\lambda^n}{n!}\left(\sum_{j=0}^{n}\binom{n}{j}\beta(t)^j(1-\beta(t))^{n-j}-\sum_{j=0}^{n}\binom{n}{j}\beta(t)^j(1-\beta(t))^{n-j}(1-p)^j\right) \\ &= \sum_{n=0}^{\infty}\frac{e^{-\lambda}\lambda^n}{n!}\left((\beta(t)+1-\beta(t))^n-\sum_{j=0}^{n}\binom{n}{j}(\beta(t)(1-p))^j(1-\beta(t))^{n-j}\right) \end{aligned}$$

$$
\begin{aligned}
q(t) &= \sum_{n=0}^{\infty} \frac{e^{-\lambda}\lambda^n}{n!} - \sum_{n=0}^{\infty} \frac{e^{-\lambda}\lambda^n}{n!} \left((\beta(t)(1-p) + 1 - \beta(t))^n\right) \\
&= 1 - \sum_{n=0}^{\infty} \frac{e^{-\lambda}\lambda^n}{n!} \left((\beta(t)(1-p) + 1 - \beta(t))^n\right) \\
&= 1 - e^{-\lambda} \sum_{n=0}^{\infty} \frac{(\lambda(1-\beta(t)p))^n}{n!} \\
&= 1 - e^{-\lambda} e^{\lambda - \lambda\beta(t)p}.
\end{aligned} \tag{3}
$$

Therefore we obtain the simplified expression for the probability that an individual transitions from susceptible to exposed during the interval of time from t to $t+1$ is

$$q(t) = 1 - e^{-\lambda\beta(t)p}. \tag{4}$$

We formally introduce the probability mass function of $E(t)$ by expressing the probability that $E(t)$ takes on a value k between 0 and $X_S(t)$ as

$$\mathbb{P}(E(t) = k) = \binom{X_S(t)}{k} q(t)^k (1 - q(t))^{X_S(t)-k}. \tag{5}$$

Once an individual becomes exposed to the disease, they are now in state E and have a chance of transitioning to the infected state. So we now turn our attention to the random variable $I(t)$, which accounts for the number of individuals transitioning from the exposed state to the infected state at time t. Similarly to $E(t)$, our random variable $I(t)$ also follows a binomial distribution with probability α) that keeps track of the number of the $X_E(t)$ exposed individuals that transition to the infected state. Here, α is the chance of transitioning from exposed to infectious in the time interval from t to $t+1$. We find $\alpha(t)$ by modeling the random duration U of the incubation period by an exponential distribution with mean duration ϕ which is 8 days for measles. Again we introduce the probability mass function of $I(t)$ at time t by expressing the probability that $I(t)$ takes on a value i between 0 and $X_E(t)$ as

$$\mathbb{P}(I(t) = i) = \binom{X_E(t)}{i} \alpha^i (1 - \alpha)^{X_E(t)-i}. \tag{6}$$

So now after having introduced both $E(t)$ and $I(t)$ we turn our attention to the last random variable $R(t)$, which keeps track of the number of individuals transitioning from the infected state to the recovered state at time t. Once more this random variable follows a binomial distribution with probability $\rho(t)$ that keeps track of the number of the $X_I(t)$ infectious individuals that transition to the recovered state. Here, $\rho(t)$ is the chance of transitioning from infectious to recovered in the time interval from t to $t+1$. We find $\rho(t)$ by modeling the random duration Y of the infectious period by an exponential distribution with mean duration μ which is 7 days for measles. Finally, we introduce the probability mass function of $R(t)$ by expressing the probability that $R(t)$ takes on a value r between 0 and $X_I(t)$ as

$$\mathbb{P}(R(t)=r)=\binom{X_I(t)}{r}\rho(t)^r(1-\rho(t))^{X_I(t)-r}. \tag{7}$$

We now have all the necessary information regarding the transition probabilities to discuss how these transitions work. Recalling that we are dealing with a closed population, where $X_S(t)+X_E(t)+X_I(t)+X_R(t)=N$ holds true at all times t. Moreover, the previous equation must also hold true at time $t+1$ which leads us to the so-called dynamic driving constraints describing the transitions of individuals between the four states from time t to time $t+1$:

$$\begin{aligned}
X_S(t+1) &= X_S(t)-E(t)\\
X_E(t+1) &= X_E(t)+E(t)-I(t)\\
X_I(t+1) &= X_I(t)+I(t)-R(t)\\
X_R(t+1) &= X_R(t)+R(t).
\end{aligned}$$

The first equation describes the number of susceptible individuals, $X_S(t+1)$, at the next time unit $t+1$ which is given by the number of susceptible individuals, $X_S(t)$, at the current time t minus the newly exposed individuals $E(t)$ which leave state S and transition to state E. The number of exposed individuals, $X_E(t+1)$, at the next time unit $t+1$ is given by the number of exposed individuals, $X_E(t)$, at the current time t plus the newly exposed $E(t)$ minus the newly infected individuals $I(t)$ which leave state E and transition to state I. Similarly, the

number of of infected individuals, $X_I(t+1)$, at the next time unit $t+1$ is given by the number of infected individuals, $X_I(t)$, at the current time t plus the newly infected $I(t)$ minus the newly recovered $R(t)$ which leave state I and transition to state R. Finally, the number of recovered of individuals, $X_R(t+1)$, at the next time unit $t+1$ is given by the number of recovered individuals, $X_R(t)$, at the current time t plus the newly recovered $R(t)$. We note that adding the four equations we get that $X_S(t+1) + X_E(t+1) + X_I(t+1) + X_R(t+1) = X_S(t) + X_E(t) + X_I(t) + X_R(t) = N$, and so the population size is constant for all t.

2.2.2 Public Health Responses

The stochastic model outlined above describes the dynamics of how individuals in a closed population transition between the four states $S \to E \to I \to R$ once the measles virus is detected in the population. However, the model does not take into account any public health interventions or changes in the behavior of individuals as the number of measles cases continues to increase in the population. Because the measles virus is able to spread uninhibited in the $SEIR$ model outlined above, it is not realistic and so in this section we refine our model by taking into account public health interventions such as vaccination campaigns and quarantining of infected individuals. When a measles outbreak is reported, the Center for Disease Control and Prevention immediately reacts in two major ways: (1) the CDC urge individuals who are potentially infected to quarantine themselves, and (2) the CDC also promptly immunizes those in the outbreak area who fail to provide documentation of measles immunization and thus effectively increases the vaccination coverage of the population. These public health interventions are often performed before laboratory confirmation of an outbreak is obtained as the CDC recommends that "control activities should not be delayed for laboratory results on suspected cases" (CDC, 1989). To make our $SEIR$ model more realistic, we incorporated both of these public health responses into the model, a refinement that was not present in any of the reviewed literature.

In order to incorporate the quarantining component of the public health response into the

model, we introduced a new random variable, $Z(t)$, that keeps track of the number of individuals tagged for quarantine who fail to comply. This new random variable changes the model substantially by allowing only a small minority of infected individuals who choose not to comply with the quarantine to continue to spread the disease. The rest of the infected individuals have only one time unit since they become infected to spread the disease before they elect to go into quarantine. Since at each time t individuals will either comply to quarantine or fail to comply, we modeled $Z(t)$ as a Binomially distributed random variable choosing from the pool of currently infected individuals, $X_I(t)$, with a fixed probability of success that is set at the start of the model. If we let d be the probability that an individual tagged for quarantine fails to comply to quarantining, then the probability mass function of $Z(t)$ at time t is expressed by the probability that $Z(t)$ takes on a value z between 0 and $X_I(t)$ as

$$\mathbb{P}(Z(t) = z) = \binom{X_I(t)}{z} d^z (1-d)^{X_I(t)-z}. \tag{8}$$

As a consequence of introducing voluntary quarantining, the infected state $X_I(t)$ is now split into two subgroups: those infected individuals who do not comply to quarantine and keep infecting others for one time unit, $X_I(t)$, and those infected individuals who comply to the quarantine and thus stop infecting others, $X_{I^*}(t)$. Since we now have two groups of infected individuals, $X_I(t)$ and $X_{I^*}(t)$, we must account for the driving event $R(t)$ keeping track of the individuals that transition from state I to state R separately, and thus we obtain two random variables $R_1(t)$ and $R_2(t)$ that sum up to the original random variable $R(t) = R_1(t) + R_2(t)$. We introduce the probability mass functions of $R_1(t)$ and $R_2(t)$ by expressing the probability that $R_1(t)$ takes on a value r_1 and that $R_2(t)$ takes on a value r_2 where r_1 is between 0 and $X_I(t)$ and r_2 is between 0 and $X_{I^*}(t)$ as

$$\mathbb{P}(R_1(t) = r_1) = \binom{X_I(t)}{r_1} \rho(t)^{r_1} (1-\rho(t))^{X_I(t)-r_1} \tag{9}$$

and

$$\mathbb{P}(R_2(t) = r_2) = \binom{X_{I^*}(t)}{r_2} \rho(t)^{r_2} (1 - \rho(t))^{X_{I^*}(t) - r_2}. \tag{10}$$

As a result of the split among the infected individuals, the aforementioned dynamic driving constraints change as follows:

$$X_S(t+1) = X_S(t) - E(t) \tag{11}$$

$$X_E(t+1) = X_E(t) + E(t) - I(t)$$

$$X_I(t+1) = I(t) + Z(t) - R_1(t)$$

$$X_{I^*}(t+1) = X_I(t) - Z(t) - R_2(t)$$

$$X_R(t+1) = X_R(t) + R_1(t) + R_2(t).$$

The obvious change in this new set of equations is that the number of individuals, $X_I(t)$, that will be able to infect others at the next time unit is given by the newly infected, $I(t)$, plus the infected individuals who do not comply to quarantine, $Z(t)$, minus the individuals who recover from this group, $R_1(t)$. Also, those who do comply to the quarantine remain isolated in state I^* until they become recovered, and so the number of infected individuals who do not spread the disease at the next time unit, $X_{I^*}(t)$, is given by those who are currently infected, $X_I(t)$, minus those who refuse to go into quarantine, $Z(t)$, minus those who recover from this group, $R_2(t)$.

The second component of the CDC's public health intervention is the vaccination campaign once the occurrence is detected in the population. We modeled these vaccination campaigns by adjusting the vaccination fixed parameter v, indicating the proportion of vaccinated individuals in the population, to a function, $V(t)$, that increases over time. The function $V(t)$ denotes the proportion of the population that is vaccinated at time t, given that at each time unit the CDC vaccinates $\omega \cdot 100$ percent of the unvaccinated individuals. Since

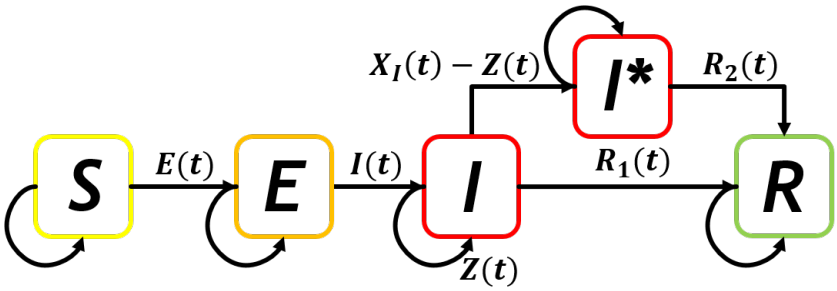


FIGURE 6. Diagram of how individuals transition through the different states S, E, I, I^*, R after accounting for quarantining.

we are dealing with a closed population the proportion of vaccinated individuals in the population can only increase over time as vaccination are performed and can never exceed 1. Then the proportion of vaccinated individuals at the next time unit, $V(t+1)$, is given by the proportion of the currently vaccinated, $V(t)$, plus the proportion of the currently unvaccinated individuals, $(1 - V(t))$, who become immunized, namely $\omega \cdot (1 - V(t))$. In notation we have:

$$V(t+1) = V(t) + (1 - V(t))\omega, \tag{12}$$

where ω is a constant giving the proportion of the unvaccinated individuals that get vaccinated by the CDC at each time unit.

As expected the introduction of both the quarantining and vaccination campaigns considerably reduced the number of infections. In the following section we present the results of simulations using different parameters in our model that help us to better understand the importance of vaccination by comparing the outcome of the dynamic systems of two populations with different starting vaccination levels.

3 Results

Now that we have discussed the theoretical foundations and the various components of our stochastic model, we will shift our attention to running simulations using a computer program consisting of two major components. The first component of the program is called the Disease

Tracker and keeps track of the number of individuals in each state as well as the number of individuals transitioning between states at each unit of time t, and then generates a graph displaying $X_S(t)$, $X_E(t)$, $X_I(t)$, and $X_R(t)$ over time. The second component of the program is called the Spatial Tracker and visually displays the geographic spread of the disease in the population over the course of time. After we discuss in detail the two components of the program, we present the results of the simulations using different parameters for the model, and highlight how changes in these parameters affect the outcomes of this dynamic system.

3.1 Disease Tracker

The first component of the program is called the Disease Tracker and determines the number of individuals in each state $S - E - I - I^* - R$ at all times t. The program employs the probability distributions for the dynamic driving events $E(t)$, $I(t)$, and $R(t)$ as described in section 2.2 to determine the number of individuals in each state given by $X_S(t)$, $X_E(t)$, $X_I(t)$, $X_{I^*}(t)$, and $X_R(t)$. The program stores the values of X_S, X_E, X_I, X_{I^*}, and X_R for each unit of time and then visually displays the results. Moreover, the program has a series of parameters that can be adjusted such as N–the fixed number of individuals in the population, v–the proportion of vaccinated individuals in the population, τ–the number of infectious individuals at time $t = 1$, and n–the number of iterations (here representing days) for the program. Furthermore, the program also has a series of parameters that are fixed related to the measles virus such as $\phi = 7$ days, the mean duration of the incubation period for measles, and $\mu = 8$, the mean duration of infection for measles. The program was developed using the software Mathematica.

The program begins by creating an $n \times 10$ array, M, with n rows representing the number of days elapsed in the simulation (program initialized at time $t = 1$), and with 10 columns that record the values of $X_S(t)$, $X_E(t)$, $X_I(t)$, $X_I^*(t)$, $X_R(t)$, $E(t)$, $I(t)$, $R_1(t)$, $R_2(t)$, and $Z(t)$ for all iterations t with $1 \leq t \leq n$. At time $t = 1$, we have that $X_I(1) = \tau$ and $X_S(1) = N - \tau$ and all other variables are zero. The dynamic driving events ($E(t)$, $I(t)$, $R_1(t)$, $R_2(t)$, and $Z(t)$) are generated using the $RandomVariate$ command in Mathematica for the Binomial

Distribution. The program iteratively generates the values of $X_S(t)$, $X_E(t)$, $X_I(t)$, $X_I^*(t)$, $X_R(t)$, $E(t)$, $I(t)$, $R_1(t)$, $R_2(t)$, and $Z(t)$using equations $1-11$ in section 2.2, for $1 \leq t \leq n$. The program then plots a graph that represents the values over time in the columns of matrix M that contain the values of $X_S(t)$, $X_E(t)$, $X_I(t)$, and $X_R(t)$.

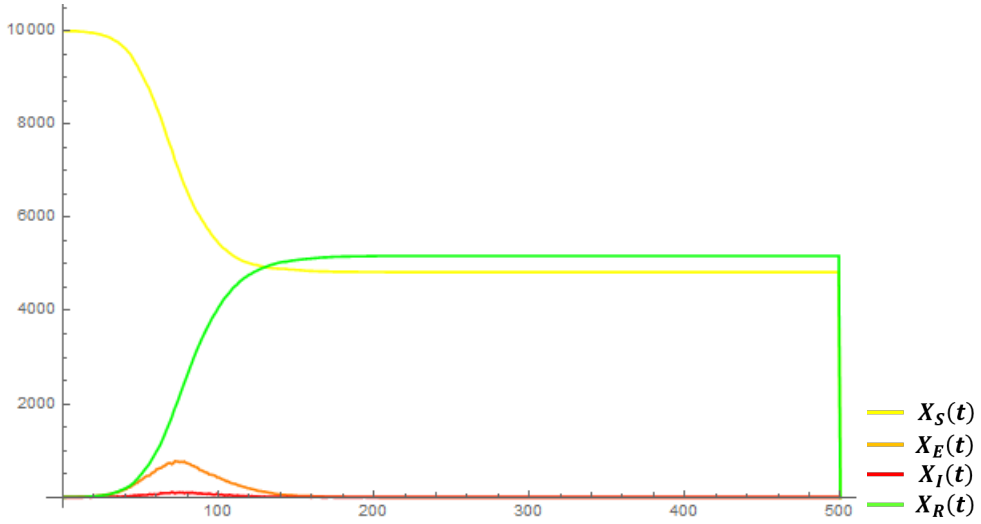


FIGURE 7. Sample result from Disease Tracker graph.

In the graph we can observe the number of susceptible susceptibles $X_S(t)$ in yellow, the number exposed $X_E(t)$ in orange, the number of infected $X_I(t)$ in red, and the number of recovered $X_R(t)$ in green for all times t from 1 to n =500. The graph serves the purpose of visually displaying the spread of the disease by tracking the number of individuals in states $SEIR$ across time, the duration of the outbreak, the end behavior of the system, and the time at which the outbreak peaked. The information recorded in array M and the visual display of the number of individuals in each state enables us to compare the outcomes of the system for different vaccination rates in the population. In particular, we ran simulations using the same parameters for the model but varying the vaccination rates in the population ($v = 90\%$ and $v = 75\%$ respectively). The results of these simulations are presented in section 3.3.

3.2 Spatial Tracker

The second component of our program, called the Spatial Tracker, creates a color coded grid in which each cell represents an individual in the population and the color of the cell corresponds to the state in which the individual is: yellow for state S, orange for state E, red for state I, and green for state R. This program serves as a visual aid displaying how the disease spreads over time in a community. The Spatial Tracker program calls upon the Disease Tracker component of the program to obtain the number of individuals in each of the states $S - E - I - R$, at time t and then color-codes each cell in the grid according to their corresponding state. The program begins by randomly selecting τ members of the population as the infected individuals at time $t = 1$ and then uses a probability model that weighs in proximity to an infected individual to select those individuals who will then become exposed at the next unit of time. The reasoning behind using proximity to the infected as a factor that influences who gets exposed at time t is that individuals in a population will interact more often with those who are closer to them and thus their chances of exposure, and therefore infection, are elevated. However, as we are simulating small communities, we adopted the assumption that the mixing in the population is homogeneous and thus individuals in the population that are not in the proximity of infected people can also be exposed, however with a reduced probability.

The program works by creating a matrix A in which each (i, j) position corresponds to an individual in the population. The entries a_{ij} in the matrix correspond to the states at which individual (i, j) is at time t. The values of the matrix A change over time and range from 0 to 3. A susceptible individual is represented in the matrix A by the value 0, exposed by 1, infected by 2, and recovered by 3. Each individual in the population begins in the susceptible state except the τ individuals that are randomly selected to be infected at time $t = 1$. The program then calls upon the Disease Tracker to gather information about the number of individuals in each state at the next time unit. To select which individuals become exposed at the next iteration $t + 1$, the program makes it more likely for an individual to be exposed

if it is located in the vicinity of an infected individual at time t. If an infected individual is located at position (i, j), these so-called neighbors located in the $(i \pm 1, j \pm 1)$ positions have a higher probability of transitioning to state E (provided they are susceptible) than susceptible individuals that are not neighbors. Based on this probability model, the program chooses $E(t)$ individuals that become exposed at time $t+1$. Concurrently, at each time unit, the Spatial Tracker program calls on the Disease Tracker to randomly selected $I(t)$ individuals in state E to transition to state I, and $R(t)$ individuals in state I to transition to state R. As the individuals transition from one state to the next from time t to time $t+1$, the entries in the matrix A are increased by 1 unit, and their corresponding color-coding in the grid (0–Yellow–S; 1–Orange–E; 2–Red–I; 3–Green–R) are updated.

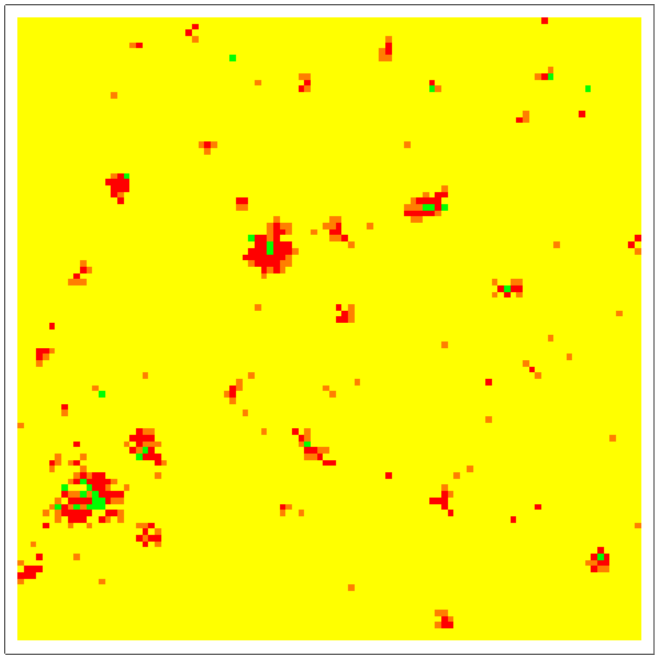


FIGURE 8. Sample result from Spatial Tracker program.

This enables us to visualize the geographic spread of the disease and understand what public health policies to put in place. Given that there is a $\frac{1}{500}$ chance of dying from measles, at the end of the n iterations, the program determines the amount of deceased people by selecting from the number of individuals which are still infected with a probability of $\frac{1}{500}$, and then relabels these individuals' cells as deceased by turning that cell black. The Spatial

Tracker program then uses the *Manipulate* command in Mathematica to create an animation of the color-coded grid from $t = 1$ to $t = n$ days.

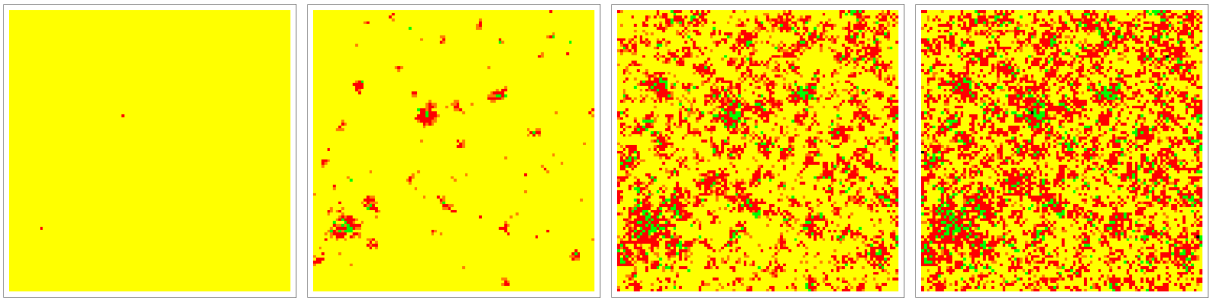


FIGURE 9. Geographic spread of the disease from $t = 1$ to $t = 100$.

3.3 Simulations

We now present the results obtained from the simulations of our stochastic model using the Disease Tracker and Spatial Tracker programs. We first outline the results of the initial $SEIR$ model that did not account for the public health interventions of the CDC as outlined in section 2.2.2. In this first set of results, we showcase two simulations for closed populations with $N = 10000$ individuals where the first simulation has a fixed vaccination coverage of 90 percent (under herd immunity and close to national average) and the second population has a vaccination coverage of 75 percent (exhibited by several counties in the US). The graphs generated by the Disease Tracker program go from $t = 1$ to $t = 200$ days.

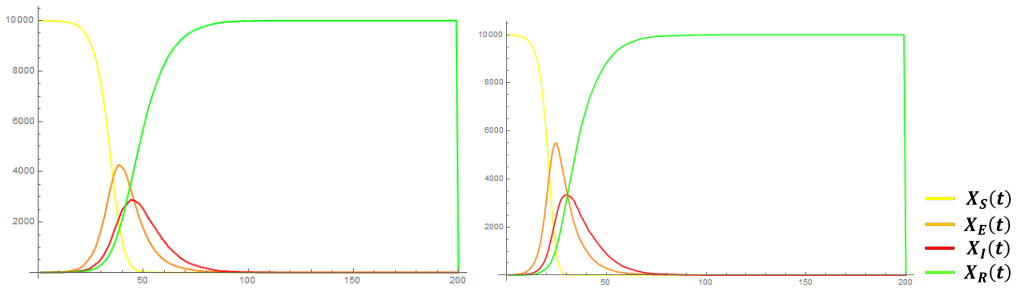


FIGURE 10. Graph depicting $X_S(t)$, $X_E(t)$, $X_I(t)$, and $X_R(t)$ from $t = 1$ to $t = 200$ for population 1 (left) at 90 percent coverage and population 2 (right) at 75 percent coverage.

We note that since neither of these simulations accounted for the CDC's public health intervention, both populations eventually became completely infected. This is represented by the fact that eventually all individuals in the population reached the recovered state (R). Next we show the results for both simulations using 90% and 75% vaccination levels of the Spatial Tracker program. Since the population has 10,000 individuals, the Spatial Tracker creates a grid of dimensions 100×100 in which each (i, j) cell represents an individual. Each cell in the grid is color-coded (yellow for state S, orange for state E, red for state I, green for state R) corresponding to the state that the individual is at time t. The figures 11 and 12 below represent the results of the simulations for the population with 90% vaccination coverage, and the 75% vaccination level, respectively, at time $t = 1$, $t = 20$, $t = 40$, and $t = 60$ days. These time-lapse images help us visualize the geographic spread of the disease in the population over time.

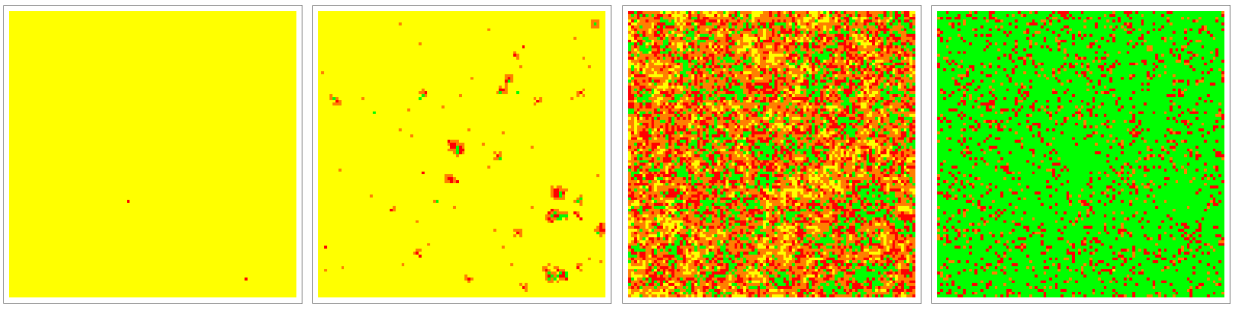


FIGURE 11. Time lapse of the progression of the disease in population with 90 percent vaccination coverage from $t = 1$ to $t = 60$.

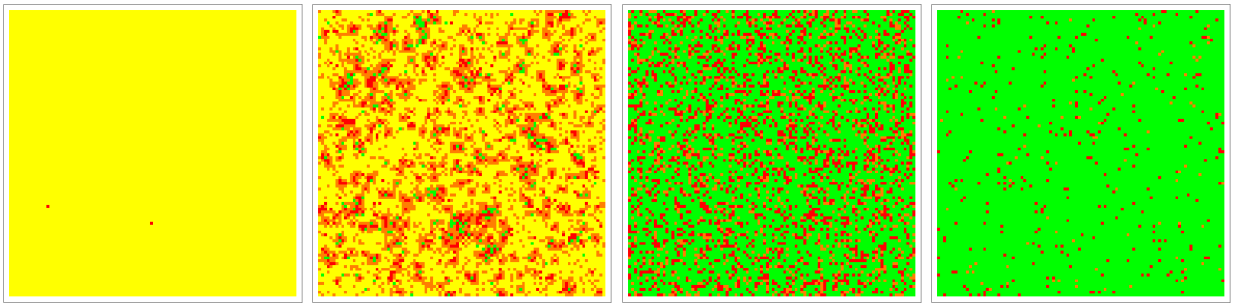


FIGURE 12. Time lapse of the progression of the disease in population with 75 percent vaccination coverage from $t = 1$ to $t = 60$.

As shown by their respective graphs, each population at time $t = 60$ is almost entirely green with some red cells, meaning that almost every individual is in the recovered state (R) and that the few remaining infected individuals will also transition to state R on average after 8 days. As highlighted before, these simulations do not account for any public health interventions or any changes in behavior of the individuals in the population as the disease spreads. Therefore, these simulations are not realistic as they allow the virus to spread uninhibited.

We now show the results of the simulations of our stochastic model after incorporating quarantining and the vaccination campaigns of the CDC in our model. Similar to the other simulations, the population size is $N = 10000$ where in simulation 1 the initial vaccination coverage is 90 percent, that is 90 percent of the population is already vaccinated before the CDC's intervention, and for simulation 2 the initial vaccination coverage is 75 percent. In both cases the proportion of individuals in state I who refuse to go into quarantine, the relevant parameter for $Z(t)$, is 10 percent. Both populations presented also have the parameter ω set at 10 percent, meaning that at each time unit the CDC is able to vaccinate 10 percent of the unvaccinated population. For these simulations the graphs generated from the Disease Tracker program range from $t = 1$ to $t = 500$.

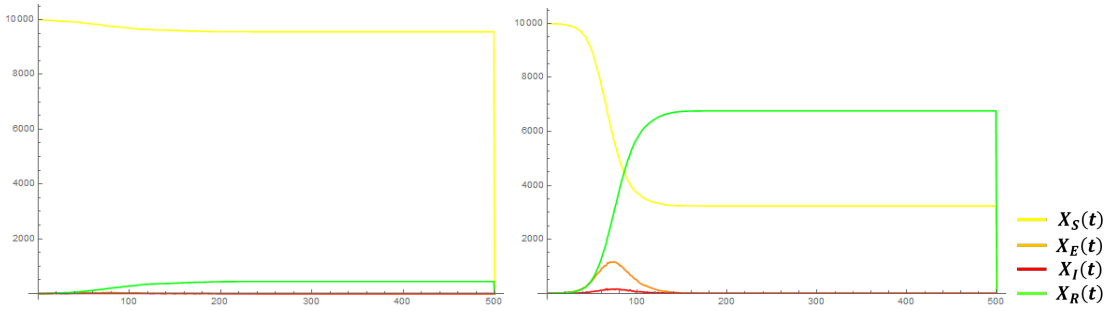


FIGURE 13. Graph depicting $X_S(t)$, $X_E(t)$, $X_I(t)$, and $X_R(t)$ from $t = 1$ to $t = 500$ for population at 90 percent coverage (left) and population at 75 percent coverage (right).

With this new set of results, we can make two main inferences from our model: (1) there is a significant difference that public health intervention have on the spread of the disease,

and (2) there is a substantial difference in the spread of the disease that we can attribute to the difference in vaccination coverage. To better quantify this difference, in the first population with 90% vaccination coverage there were under 500 total infections by time $t = 500$ days, which is less that 5 percent of the population, and in the second population with 75% vaccination coverage there were over 6500 infections, which is over 65 percent of the population.

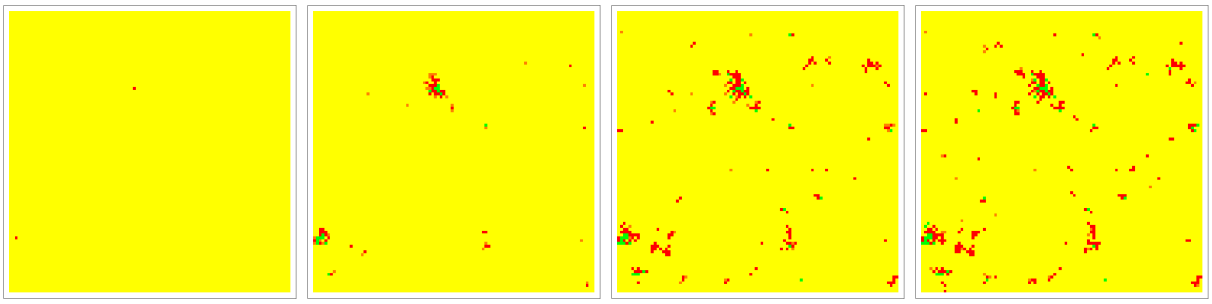


FIGURE 14. Time lapse of the progression of the disease in population with 90 percent vaccination coverage from $t = 1$ to $t = 100$.

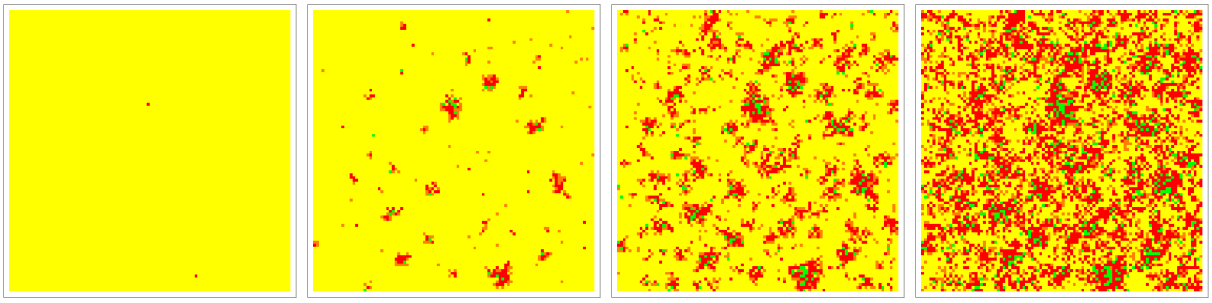


FIGURE 15. Time lapse of the progression of the disease in population with 75 percent vaccination coverage from $t = 1$ to $t = 80$.

The results of the simulations using the Spatial Tracker program reinforce the idea that within our model: there is a significant effect that public health interventions have on the dynamics of the system. Moreover, it highlights that the disease spreads in clusters around an initial infection which underscores the importance of complying with the quarantine recommendations of the CDC. By observing the population in simulation 2 which is at an initial 75 percent vaccination coverage, we can visually emphasize how a community with this reduced vaccination coverage is at high risk of a severe measles outbreak. Furthermore, if a population's vaccination coverage is lower than 75 percent according to our model the

results can be catastrophic. It is also important to note that both populations started with a vaccination coverage that was under herd immunity level (94 percent) explaining why the population for the first simulation, which had a starting vaccination coverage of 90 percent, still had hundreds of measles cases during the simulated outbreak.

4 Conclusions

The simulations for our stochastic model suggest that a reduction in the vaccination rates of a population can significantly impact the number of measles cases and the duration of a measles outbreak. Moreover, since vaccinated individuals still pose a risk of contracting the disease, counties with low vaccination rates in the United States increase the threat of measles outbreaks even for communities with average vaccination rates as they can allow the virus to gain a foothold in a section of the population that can then continue to spread the virus to other communities. As measles is still endemic in various countries around the world, and noting that today's world is highly interconnected, measles can be reintroduced in the US from foreign contact. If the virus is allowed to take hold in these communities with under 80% vaccination coverage we may all be at risk of contracting this disease which was declared eradicated in the year 2000 in the Americas. Ultimately, we argue that the best way to prevent such a scenario would be to raise vaccination coverage for the entire population to reach the herd immunity level of 93-95 percent.

References

Achenbach, J. (2015). The age of disbelief. *National Geographic*, 30-47.

Atkinson, W. (2012). *Epidemiology and prevention of vaccine-preventable diseases* (12th ed.). Center for Disease Control and Prevention.

CDC. (1989). Measles prevention: Recommendations of the immunization practices advisory committee (acip). *Morbidity and Mortality Weekly Report*, *38*, 1-18.

CDC. (2014a). National, state, and local area vaccination coverage among children aged 1935 monthsunited states, 2013. *Morbidity and Mortality Weekly Report*, *63*, 741-748.

CDC. (2014b). Vaccines for children program (vfc).

CDC. (2015a). Frequently asked questions about measles in the u.s.

CDC. (2015b). Measles outbreak california, december 2014-february 2015. *Morbidity and Mortality Weekly Report*, *64*, 153-154.

Farrington, P., Miller, E., & Taylor, B. (2001). Mmr and autism: further evidence against a causal association. *Vaccine*, *19*, 3632-3635.

Greenwood, M. (1931). On the statistical measure of infectiousness. *The Journal of Hygiene*, *31*, 336-351.

Healy, J., & Paulson, M. (2015). Vaccine critics turn defensive over measles. *New York Times*.

Smith, D., & Moore, L. (2004). The sir model for spread of disease - the differential equation model. *Journal of Online Mathematics and its Applications*.

Yaesoubi, R., & Cohen, T. (2011). Generalized markov models of infectious disease spread: A novel framework for developing dynamic health policies. *European Journal of Operational Research*, *215*, 679687.