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Mathematical Model of Vaccine Noncompliance

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Abstract

Vaccine scares can prevent individuals from complying with a vaccination program. When compliance is high, the critical vaccination proportion is close to being met, and herd immunity occurs, bringing the disease incidence to extremely low levels. Thus, the risk to vaccinate may seem greater than the risk of contracting the disease, inciting vaccine noncompliance. A previous behavior-incidence ordinary differential equation model shows both social learning and feedback contributing to changes in vaccinating behavior, where social learning is the perceived risk of vaccinating and feedback represents new cases of the disease. In our study, we compared several candidate models to more simply illustrate both vaccination coverage and incidence through social learning and feedback. The behavior model uses logistic growth and exponential decay to describe the social learning aspect as well as different functional forms of the disease prevalence to represent feedback. Each candidate model was tested by fitting it to data from the pertussis vaccine scare in England and Wales in the 1970s. Our most parsimonious model shows a superior fit to the vaccine coverage curve during the scare.

1 Introduction

Vaccine noncompliance increased significantly during the pertussis vaccine scare in England and Wales in the 1970s. Large outbreaks of pertussis were caused by the low vaccination coverage. The change in human behavior toward vaccinating is largely subject to beliefs, others' opinions, and awareness of the disease. Additionally, those choosing not to vaccinate may still benefit from others' decisions to vaccinate via herd immunity if a certain proportion of the population (critical vaccination proportion) is vaccinated. Referring to pertussis that has a critical vaccination proportion of 82 percent, vaccination coverage was at approximately 80 percent before the scare, meaning England and Wales were extremely close to reaching that critical proportion. However, vaccination can drive disease prevalence to such low levels that individuals start to believe there is no need to vaccinate, thus causing more outbreaks.

In the case of the 1970s pertussis scare, vaccination coverage dropped drastically to as low as 31 percent, thus causing major outbreaks, as seen in Figure 1. Incidence, the number of new cases of the disease, reached almost 80 thousand. This scare illustrates the impact of the

number of vaccinators on the number of people contracting a disease. Besides the basic SIR model with two parameters, there are numerous variations of the SIR Model to include other factors, including vaccine compliance. The common extensions to the SIR model incorporate birth and death, case importation, and vaccine behavior which include social learning and feedback. One adaptation of the SIR model is the behavior incidence model that seeks to describe vaccinating behavior. In this paper, we compare several candidate models which are updated vaccination SIR models to better describe both vaccination coverage and incidence, specifically during the pertussis vaccine scare [2, 3, 4].

2 Background Model

2.1 Vaccination SIR Model

The basic SIR model consists of two parameters, β, the transmission rate, and γ, where $\frac{1}{\gamma}$ is the average duration of the infection. Figure 2 illustrates the simplest form to model infectious diseases. Here, we focus on a more complex model with additional factors. The compartmental model still consists of three classes: susceptible (S), infectious (I), recovered (R). Also, the movement out of the S class through infection and the movement out of the I class through recovery holds for both the basic and complex SIR model [1].

The updated SIR model, shown in Figure 3, includes additional factors to better describe vaccinating behavior and incidence. A new factor that moves individuals from susceptible to infectious is case importation which is when an individual contracts the disease from a source outside of the population. An example of case importation is the index case, or the first case in a population, that was not present in the population prior. Additionally, birth is an included factor where those individuals who were not vaccinated at birth immediately enter the susceptible class and those who were vaccinated at birth enter the recovered class because they are immune. Lastly, individuals leave the population via death from each of the three classes at a certain rate [1, 3].

2.2 Behavior Incidence Model

The properties of the updated SIR model can be described in Bauch *et al*'s 2012 behavior incidence model. The compartmental characteristics hold for the behavior incidence where the population is divided into three classes: susceptible, infected, and recovered. We assume a closed and constant population, therefore $S + I + R = 1$, where S, I, R are proportions of the population.

The behavior incidence model is an adaptation of the SIR model with new parameters (see Equation 1). The added equation represents the rate in change of x, the proportion of the population that are vaccinators. The parameters β (the transmission rate) and $\frac{1}{\gamma}$ (average duration of the infection) hold from the basic SIR model. New parameters are introduced in the behavior incidence model, where μ is the birth and death rate, ϵ is the vaccine efficacy, and τ is the case importation rate. The perceived risk of vaccinating is described in $\omega(t)$,

which is time dependent and not a constant parameter. The equations for the behavior incidence model are:

$$\frac{dS}{dt} = \mu(1 - \epsilon x) - \mu S - \beta SI - \tau S \tag{1a}$$
$$\frac{dI}{dt} = \mu I + \beta SI - \gamma I + \tau S \tag{1b}$$
$$\frac{dx}{dt} = \kappa x(1 - x)(-\omega(t) + I) \tag{1c}$$

The behavior incidence model includes both social learning and feedback in the equation describing the proportion of the population that are vaccinators. Social learning is the concept that the behavior of one individual is affected by the behavior of the surrounding individuals, i.e. peer pressure, peer opinions, whereas feedback is when a surge in the number of new cases of a disease impacts the behavior of a single individual. The function $\omega(t)$ seeks to model the social learning aspect of vaccination behavior through a set of five risk evolution curves shown in Figure 4. There is no single function $\omega(t)$, instead Bauch guessed at how perceived risk evolves over time.

The first curve shows an instantaneous increase in risk and a gradual linear decrease, whereas the last curve shows a linear increase to a plateau in the value of risk that eventually linearly decreases. Bauch *et al* concluded the last risk evolution curve most accurately described perceived risk because it is the most complex. The behavior incidence model was found to fit relatively well to both the vaccine coverage and incidence data from the 1970s pertussis scare [3].

3 Candidate Models

Our new candidate models are variations of the vaccination SIR model and they seek to better describe vaccinating behavior. The flowchart from Figure 3 describes these candidate models as well, however, the proportion of the population that are vaccinators, x, is modeled in a different form than the behavior incidence model. The social learning aspect of this model is represented through logistic growth and exponential decay. Before a vaccine scare happens, the proportion of the population that are vaccinators will increase and follow the logistic growth behavior. At the time the vaccine scare starts, t_{scare}, the proportion of the population that are vaccinators will decrease because of the perceived risk of vaccinating. Therefore, during a vaccine scare, exponential decay can describe vaccinating behavior.

Additionally, at the time the scare ends, t_{recover}, the proportion x will increase again following logistic growth. In essence, social learning is portrayed by a switch between logistic growth and exponential decay, depending on if the vaccine scare is occurring. Referring to the logistic growth aspect of this equation, the new parameter, $p_{\max}$, is a threshold parameter on x that can be viewed as the carrying capacity of the proportion of the population that

are vaccinators. Also, the additional new parameters k_1, k_2, and k_3 are all fitted parameters of the new candidate models.

3.1 Model 1

In our first candidate model (Equation 2), we seek to describe both vaccination coverage and incidence through only social learning and no feedback. The equations for the resulting Model 1 are:

$$\frac{dS}{dt} = \mu(1 - \epsilon x) - \mu S - \beta SI - \tau S \tag{2a}$$

$$\frac{dI}{dt} = \mu I + \beta SI - \gamma I + \tau S \tag{2b}$$

$$\frac{dx}{dt} = \begin{cases} k_1 x \left(1 - \frac{x}{p_{\max}}\right) & t \in [0, t_{\text{scare}}] \\ -k_2 x, & t \in [t_{\text{scare}}, t_{\text{recover}}] \\ k_3 x \left(1 - \frac{x}{p_{\max}}\right) & t \in [t_{\text{recover}}, t_{\text{end}}] \end{cases} \tag{2c}$$

The same assumptions and parameters hold from the basic SIR model and the vaccination SIR model. Since Model 1 only includes social learning, the model rate of change of x is solely dependent on t and not dependent on I. There are a total of 13 parameters in Model 1 that also include the initial values, S_0 and I_0.

3.2 Model 2

Furthermore, our second candidate (Equation 3) is a variation of Model 1 that includes both social learning and feedback. A form of I, the infected individuals is introduced in the equation representing the rate of change of vaccinators. The equations that derive S, I, R, and x in Model 2 are:

$$\frac{dS}{dt} = \mu(1 - \epsilon x) - \mu S - \beta SI - \tau S \tag{3a}$$

$$\frac{dI}{dt} = \mu I + \beta SI - \gamma I + \tau S \tag{3b}$$

$$\frac{dx}{dt} = \begin{cases} k_1 x \left(1 - \frac{x}{p_{\max}}\right) \left(\frac{I}{a+I}\right) & t \in [0, t_{\text{scare}}] \\ -k_2 x \left(1 - \frac{I}{a+I}\right), & t \in [t_{\text{scare}}, t_{\text{recover}}] \\ k_3 x \left(1 - \frac{x}{p_{\max}}\right) \left(\frac{I}{a+I}\right) & t \in [t_{\text{recover}}, t_{\text{end}}] \end{cases} \tag{3c}$$

Model 2 includes both social learning and feedback, therefore the rate of change of x is dependent on both t and I, unlike Model 1. The new term including I is a variation of the Holling Type II functional response which tries to better model vaccinating behavior [**?**] (*Dawes citation not working*). A new parameter a is introduced, creating a total of 14 parameters in Model 2 that also includes the initial conditions, S_0 and I_0.

4 Fitting Method

4.1 Model Selection

In order to compare and analyze our two candidate models, we fit the models to the 1970s pertussis vaccine scare data. Using a built-in Matlab minimization routine `fminsearch`, our models were fit to the data. Each model was separately fit to both vaccination coverage and incidence, resulting in two sets of best fit parameters for each model. We evaluated the parsimony of each model to find the model with the least amount of parameters and an accurate fit. Akaike Information Criterion correction score (AIC_c) was calculated to numerically compare the models using Equation 4, where the most parsimonious model has the lowest AIC_c score. The correction rescales the score to account for a small data set. The parameters to find the score include k, the number of parameters, L, the likelihood function, and n, the sample size. The formulas for AIC and AIC_c are as follows:

$$AIC = 2k - 2\ln(L) \tag{4a}$$

$$AIC_c = AIC + \frac{2k(k+1)}{n-k-1} \tag{4b}$$

Furthermore, a shotgun method was used to explore parameter space more fully. Each parameter was given a realistic range of nominal values and at each iteration, an initial value vector was randomized to be used in the minimization routine. We set the number of iterations to a certain value, where more iterations meant a more in depth search of parameter values. The AIC_c score was then calculated to compare Model 1 and 2.

4.2 Subset Selection

Additionally, a method called subset selection was implemented to test all possible combinations of fitted parameters in the models. Parameters either have *a priori* information about their nominal value or not. For the parameters in the $\frac{dx}{dt}$ equation of both models, k_1, k_2, k_3, t_{scare}, and t_{recover}, we do not have *a priori* information about their value so we always fit those parameters in the minimization routine. However, we know enough about the nominal value of the other parameters which allows us to either fit those parameters or give them a nominal value in the fitting method. Table 1 shows the nominal values of those parameters we have *a priori* information.

Subset selection was implemented for both models to find the sets of best fit parameters for both coverage and incidence. For each subset, the AIC_c was calculated to use as a comparison between all the possible parameter subsets. In Model 2, the additional parameter a was always a fitted parameter, as it was present in $\frac{dx}{dt}$. Figure 5 shows an example parameter subset of Model 1 that has a total of 13 parameters.

5 Results

We analyzed each model against both vaccine coverage and incidence with the most parsimonious parameter subset, as explained in the subset selection process. The results of each model can be found in Figure 6.

With the parsimony analysis, Model 1 was found to be the more parsimonious model for both vaccination coverage and incidence. Our hypothesis was that adding feedback to the model would improve the accuracy of the fit to the data. However, contrary to our hypothesis, feedback weakened the accuracy of fit for Model 2. As seen in the coverage plot of Model 2 for coverage, the model does not fit to the lowest data points of the vaccine scare, whereas Model 1 more accurately approaches that low coverage percentage.

Referring to the incidence data, both models failed to describe the beginning behavior of the vaccine scare, specifically the small outbreak in 1974. However, both models succeed in creating the following larger outbreaks of pertussis during that time period. Our prediction was not correct with these two models, as Model 1 had a lower AIC_c score for both data sets. Table 2 shows the the AIC_c score and best fit parameter sets for each model against the coverage and incidence data.

Not all parameters were fit, as seen in the varying sizes of the parameter sets, which was a result of the subset selection process. The nominal values can be realistically interpreted for each parameter. A specific observation is that k_3 is greater than k_1 in all parameter sets. Furthermore, the models fit vaccination coverage more accurately than they fit incidence, simply by the visuals. However, Model 1 described the behavior during the pertussis vaccine scare better overall.

6 Conclusions and Future Directions

6.1 Concluding Remarks

The results show that Model 1 was the more parsimonious model for both vaccination coverage and incidence. In particular, the goodness of fit for Model 1 suggests vaccination coverage may be independent of incidence because Model 1 only included social learning, not feedback. Additionally, alternating between logistic growth and exponential decay at times of a vaccine scare can accurately describe the social learning behavior of vaccinators vs non-vaccinators. The switch between the start of the scare and the end of the scare helps

to better model this behavior.

We also see in each set of best fit parameters that k_3, logistic growth parameter after the scare, is consistently greater than k_1, logistic growth parameter before the score. This finding suggests the proportion of the population that are vaccinators increases faster post-scare than it does pre-scare. Lastly, feedback could improve model performance, however it likely should take a different form than in Model 2.

6.2 Future Directions

There are many remaining directions for this research to explore. While these models can accurately describe vaccination coverage and incidence when fit separately to the data, we want to be able to fit each model simultaneously to the data sets. In order to do so, the vaccination coverage and incidence data needs to be normalized to create only one set of best fit parameters per model from the simultaneous fit. Also, both our two candidate models and Bauch *et al*'s behavior-incidence model are dependent on time, therefore, future work can determine if an autonomous model could better describe vaccinating behavior. Such work can be executed by further altering the social learning aspect of Model 1 and Model 2.

Similar to the variation of the Holling Type II functional response in Model 2, other candidate models based on the Holling type functional responses could be created and tested to try to better model vaccinating behavior. This would provide variations in describing the behavior of feedback. Furthermore, referring to the parameters of the $\frac{dx}{dt}$ equation of both models, t_{scare} and t_{recover} were always fit. By looking at the data and graphs, the nominal value of those times could be approximated, thus allowing us to either fit them or give them a nominal value in the subset selection process. Overall, we want to compare our model candidates to Bauch *et al*'s behavior-incidence model using the same minimization routine in order to see the difference in fit to the vaccination coverage and incidence data of the 1970s pertussis vaccine scare.

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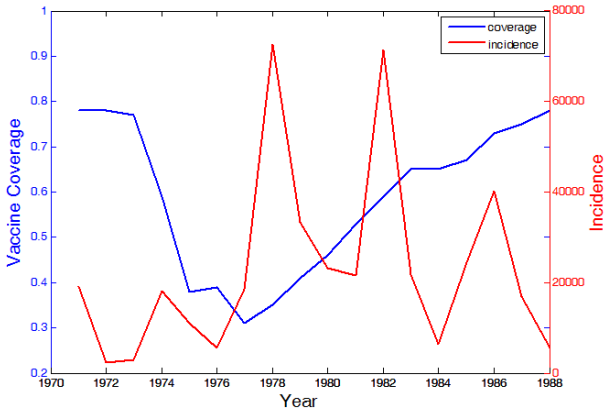

Figure 1: Vaccine coverage (blue curve) and incidence (red curve) from the pertussis vaccine scare in England and Wales from 1971 to 1988.

Figure 2: This flowchart shows the movement of individuals between the susceptible, infectious, and recovered classes in the basic SIR model.

$\beta = \frac{17}{22} \cdot 365 \quad \text{years}^{-1}$	$\tau = 3.7 \times 10^{-6} \quad \text{years}^{-1}$
$\frac{1}{\gamma} = 22 \quad \text{days}$	$p_{\max} = .78$
$\mu = .02 \quad \text{years}^{-1}$ $\epsilon = 1$	$I_0 = .0001$

Table 1: The nominal values of parameters that have *a priori* information.

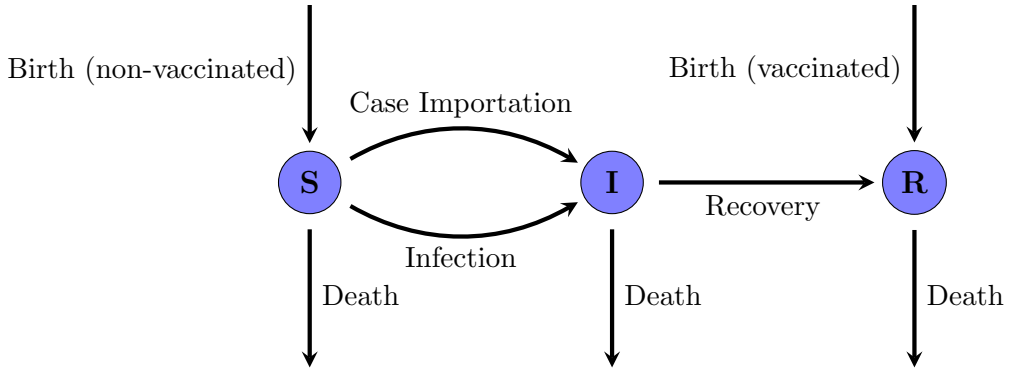

Figure 3: This flowchart shows the movement of individuals between the susceptible, infectious, and recovered classes in our updated SIR model.

Figure 4: The five risk evolution curves illustrate the perceived risk of vaccination over time.

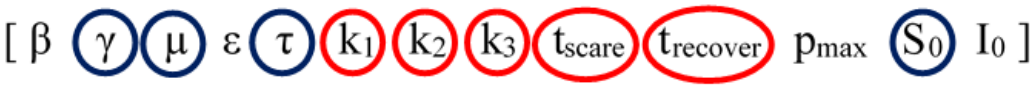

Figure 5: Example of a subset of parameters for Model 1: always fitted parameters (circled in red), parameters fit in this particular subset (circled in blue), and the parameters given a nominal value (not circled).

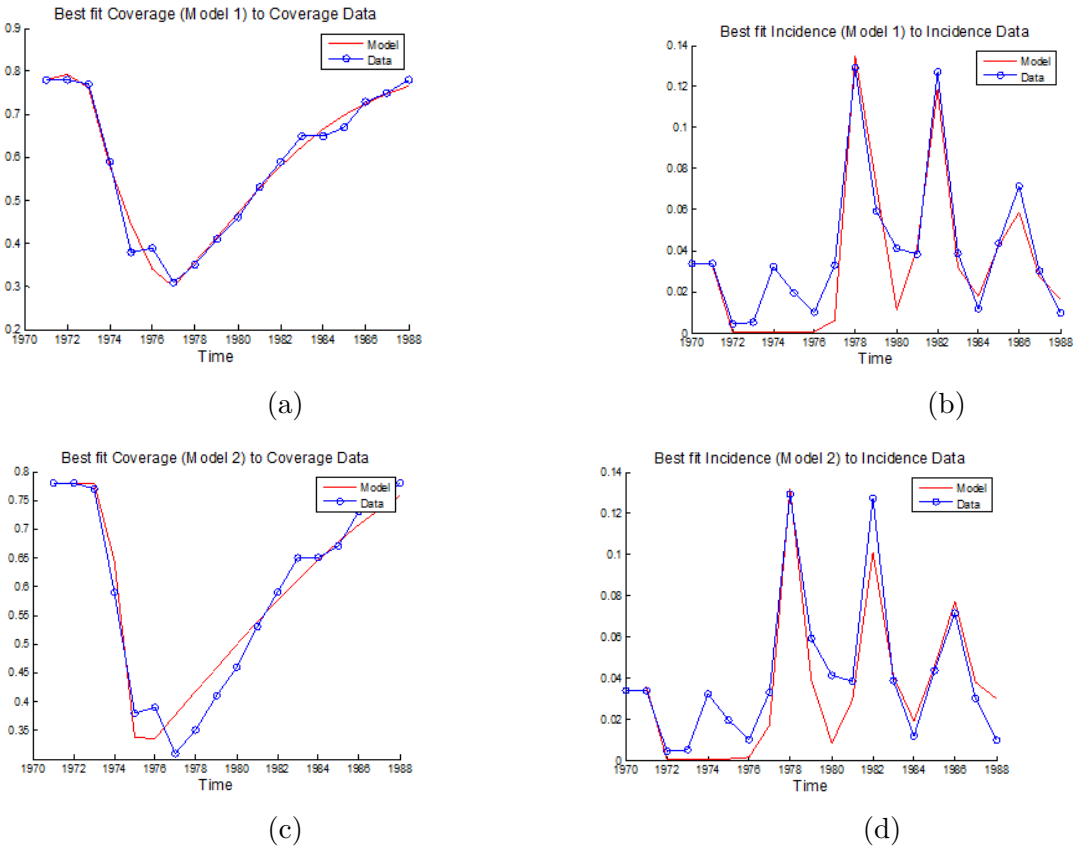

Figure 6: Parsimony analysis of candidate models for pertussis vaccine scare: Model 1 graphs (a,b) and Model 2 graphs (c,d) with the data (blue line) and best model fit (red line)

Model 1 Coverage (a)	Model 1 Incidence (b)	Model 2 Coverage (c)	Model 2 Incidence (d)
$AIC_c \approx -34$	$AIC_c \approx -42$	$AIC_c \approx 202$	$AIC_c \approx -42$
$\gamma = 16.7946$	$\beta = 82.553$	$\beta = 341.7778$	$\beta = 82.553$
$\mu = 0.0143$	$\mu = 0.0592$	$\gamma = 10.8968$	$\mu = 0.0592$
$\epsilon = 0.9959$	$\epsilon = 0.3707$	$\mu = 1.0866$	$\epsilon = 0.3707$
$k_1 = 0.1252$	$k_1 = 0.1671$	$\epsilon = 0.561$	$k_1 = 0.1671$
$k_2 = 0.2837$	$k_2 = 0.2959$	$\tau = 0.0114$	$k_2 = 0.2959$
$k_3 = 0.2679$	$k_3 = 0.2565$	$k_1 = 0.0053$	$k_3 = 0.2565$
$t_{\text{scare}} = 2.9278$	$t_{\text{scare}} = 3.0198$	$k_2 = 1.1404$	$t_{\text{scare}} = 3.0198$
$t_{\text{recover}} = 6.7797$	$t_{\text{recover}} = 12.8933$	$k_3 = 0.7526$	$t_{\text{recover}} = 12.8933$
	$p_{\max} = 0.8268$	$t_{\text{scare}} = 3.714$	$I_0 = 0.0001$
	$I_0 = 0.0001$	$t_{\text{recover}} = 5.1468$	
		$p_{\max} = 0.9977$	
		$a = 0.3811$	
		$S_0 = 0.4702$	
		$I_0 = 0.5246$	

Table 2: The best fit parameters for Model 1 and Model 2 against both vaccination coverage and incidence.