Parental Decisions Unfold in Layers during a Vaccine Scare: Insights from Measles Vaccine Uptake Data

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Abstract
Unlike any other situation, vaccine scares pose a serious challenge to individuals making vaccination decisions, especially for childhood diseases. The scare causes a multi-fold increase in the perceived vaccine risk until it far outweighs the perceived infection risk, at which point some parents stop vaccinating. More parents adopt this behaviour in the beginning and it becomes increasingly acceptable to avoid the vaccine. Although individuals switch back to accepting vaccination when outbreaks occur or vaccine fears recede, vaccine uptake often resurges more slowly than it dropped in the first place. Thus, vaccination decisions evolve in a very different (nonlinear) fashion in the beginning and in the end of a scare. Here, we used measles vaccine coverage data from England and Wales from 1995-2009 to study this phenomenon. We fitted a differential equation model based on evolutionary game theory to the data. The model describes the vaccinating decisions of individuals as they depend on the perceived risks of the vaccine, where the risk evolves throughout the vaccine scare. Individuals can adopt a strategy of non-vaccinator, timely vaccinator, or delay vaccinator (someone who waits a few years to vaccinate). The model with a delayer strategy explains the vaccine coverage data better than the same model without a delayer strategy, as measured by an information criterion. The fitted model also illustrates how the abundance of the three strategy types unfolds in qualitatively different ways throughout the vaccine scare.

INTRODUCTION
The impact of public perceptions and collective behaviour regarding vaccination decisions is increasingly explored in the study of infectious disease modelling [1-6]. Studies suggest that individual attitudes toward vaccination are highly dependent on the perceived risk of acquiring a serious disease [7]. When disease risk is low, a small risk of adverse events from the vaccine become relatively important and that leads to vaccine coverage lower than what is required to control transmission. When disease risk is too high, on the other hand, vaccine coverage may increase above that required to guarantee population protection. These effects have been examined by combining mathematical or network models of disease transmission with game theory or other behavioural modelling frameworks, where the influence of certain types of vaccinating behaviour on the stability and equilibria of epidemic models is analysed [3,8-15]. However, less effort has been taken to understand vaccine scares. Although vaccine scares appear to exemplify the similar “free-rider problem”, little is known about the mechanisms governing how vaccine coverage evolves in the beginning and in the end of a scare. A recent study on vaccine scare by the authors points out that social learning and feedback from disease incidence can explain the vaccine coverage data during a scare, better than competing explanations that ignore social learning and/or feedback mechanisms [16].

In this manuscript, we attempt to address this question using data from the measles-mumps-rubella (MMR) vaccine scare in the United Kingdom (UK) [17]: MMR vaccine uptake in the UK started to decline after a faulty study linking MMR vaccine to inflammatory bowel disease published in 1995 [18] and to autism in 1998 [19]. In a decade, vaccine coverage went well below the target vaccine coverage of 95%. Despite the confidence of researchers and health professionals in the safety of the vaccine, the uptake of MMR vaccine recovered only very slowly [20, 21] (Figure 1). Moreover, some parents, instead of avoiding the vaccine altogether, opted to delay vaccination until their child was a few years older, an age at which they felt the vaccine was no longer dangerous.

We use an evolutionary game theoretical model including delay strategies from a paper by same authors [10] and show that...
the model including a delay strategy can better explain the decline
and resurgence observed in the data of vaccine coverage during the
MMR vaccine scare than the same model without a delay strategy.
Fitting the ‘delay model’ to data also shows how vaccination
decisions unfold in different ways according to timely, delayed and
no vaccination strategies throughout the scare.

MODEL AND METHODS

We use a model with a delay strategy from Bhattacharyya and
Bauch (2010) [10], where the decision to adopt a strategy is based
on a social learning process described by the imitation dynamic of
evolutionary game theory. An individual parent samples other
parents in the population at a constant rate. If the sampled parent
is playing a different strategy and is receiving a higher payoff (i.e.
their child’s health is perceived to be better), the individual switches
to that strategy with a probability proportional to the expected gain
in payoff. In our model, we have three strategies: individuals do
choose to vaccinate as soon as the vaccine schedule permits ('timely
vaccinator'), or they can delay vaccination until the age when the
vaccine is supposedly less dangerous ('delay strategy'), or they can
not vaccinate at all ('non-vaccinator'). The payoff gain of strategies
depends on the difference between the penalty for being vaccinated
and the penalty for risking infection, which depends on the current
disease prevalence and perceived cost of vaccination.

The full model
captures disease and social dynamics in two age classes 1 and 2, and
is described by:

\[
\frac{dS}{dt} = \alpha S \left( 1 - \frac{S}{N} \right) - \mu S - S \left( \beta \frac{I}{N} + \beta \frac{I}{N} \right) - aS,
\]

\[
\frac{dI}{dt} = S \left( \beta \frac{I}{N} + \beta \frac{I}{N} \right) - \mu I - aI - \gamma I,
\]

\[
\frac{dS}{dt} = a(1-x)S - S \left( \beta \frac{I}{N} + \beta \frac{I}{N} \right) - aS - \gamma S,
\]

\[
\frac{dI}{dt} = S \left( \beta \frac{I}{N} + \beta \frac{I}{N} \right) + aI - \mu I - \gamma I,
\]

\[
\frac{dx}{dt} = \delta x \left( 1 - \frac{x}{x} \right) \left( P - P \right) + x \left( 1 - \frac{x}{x} \right) \left( P - P \right),
\]

and the perceived payoff for all three vaccination class are

\[
P_1 = r_1 v_1, \]

\[
P_2 = r_2 v_2 \left( 1 - \frac{a}{\theta + 1} \right), \]

\[
P_3 = r_3 v_3 \left( 1 - \frac{a}{\theta + 1} \right) + \frac{a}{\theta + 1} v_3.
\]

We assume that the vaccine penalty $r_1$ evolves over time. The
penalty $r_1$ is constant at a low level before the scare starts
in the year 1995, at which point it instantaneously increases to a
higher value, and then is followed by an exponential decay to align
the pre-scare level. Although we have assumed an exponential curve
to describe how scare declines over time, it is not known how the risk
perception actually evolved, and we do not have a mechanistic model
for how it evolved during that time period.

Parameter estimation and model selection methodology

We use parameter estimation and model selection methodology
to determine the most parsimonious model describing the England
and Wales MMR vaccine uptake data during the time period 1995-
2009 (Figure 1). We implemented a least-square technique using
trust-region reflective algorithm in Matlab R2013b, and computed the
maximum likelihood estimator $\theta$ by $\pi^{-1 / 2}$, where
$RSS_m$ is the residual sum squares of the fit between data and model
output $x$. We simulated the model for 100 years at lower vaccination
rate to discard transients and calibrate the pre-scare vaccine uptake
from data. We then start with pre-scare level vaccine uptake, and
simulate the model with a modified risk evolution curve and fit next
15 years of model output $x$ (population density of timely vaccinators)
to vaccine uptake data from 1995-2009.

We evaluated the parsimony of the two models: delay model
and no-delay model. In contrast to delay model, the no-delay model
constitutes two strategies, namely vaccinator or non-vaccinator. We
used the Akaike Information Criterion (AIC) to evaluate the most
parsimonious model between the two:
AIC = −2ln(M) + 2l, \hspace{1cm} (3)

Where \( l \) is the number of parameters in the model to be estimated, and \( M \) is the maximized value of the likelihood function for the estimated model. Information criteria have a strong rooting in information theory, and favour models that explain the data as well as possible with as few parameters as possible [22]. The model with the most negative AIC score is the most parsimonious model, suggesting that it is more likely to be capturing crucial determinants of the observed dynamics.

RESULTS

We begin the parameter estimation by fitting the delay model (i.e., model with delay strategy) to the MMR vaccine scare data. The delay model has interesting dynamical features including stable and oscillatory dynamics at different values of the imitation sampling rate \( \delta \) and the perceived vaccine risks at the two age classes \( (r^1, r^2) \). In fitting the model to the data, we assume the perceived risk \( r^1 \) (say, pre-\( r^1 \)) of timely vaccination is relatively low before the scare, and at the beginning of the scare it instantly increases to a higher level (say, post-\( r^1 \)) and then decreases exponentially at certain rate to asymptotically align with the pre-scare level. We estimate the parameters \( \delta \), pre- and post-\( r^1, r^2 \), perceived probability infection \( \alpha \) and exponential decay rate. Other demographic and disease parameters such as transmission rate and recovery rate are assumed to be the same baseline values in the paper Bhattacharyya and Bauch (2010) [10]. For model selection we also fit a no-delay model assuming only two complementary strategies vaccination and no-vaccination and estimate similar parameters like \( \delta \), pre- and post-\( r^1, r^2 \), \( \alpha \), and exponential decay rate.

The delay model fits the data very well, explaining approximately 77% of the variability in the data (Figure 2a). It can also capture the steady decline and gradual upsurge in pre- and post-scare vaccine uptake data. This decline in timely vaccination uptake results in a disease outbreak (Figure 2c), and increase in delayed vaccination. The estimated parameter values are given in (Table 1). There is a 40% increase in perceived vaccine risk and so, a proportion of population adopts a delaying strategy during the scare. As timely vaccination coverage rebounds, the delaying vaccination start declining to the previous level.

![Figure 2](image)

Figure 2 Fitting of delay model to the measles vaccine scare data: (a) timely vaccine uptake (black line) from model fitting to data (red circles), (b) delayed vaccine uptake, and (c) prevalence.

In comparison, the no-delay model provides a much poorer fit to the data (Figure 3a). It cannot capture the decline and surge in the data, even with a greater estimated perceived vaccine risk during the scare (Table 1). By comparing the fits of the delay and no-delay model, we can see the effects of adding a delaying strategy to the dynamics of vaccination game. Enough vaccine exemption increases disease transmission in population and results in a huge outbreak that feeds back to the individual decision-making process to change vaccination coverage. Adding a delaying strategy to the game reduces the intensity of the feedback by minimizing the outbreak size (compare Figure 2c and Figure 3b). This increases the potential of the delay model to explain the steady decline of vaccine uptake and thus improves the model fit to data. The same is also reflected in AIC values of the two fits (Table 1).

Examining population densities of all three strategies over the entire period of vaccine scare shows how decisions evolve and unfold from timely vaccination to delaying vaccination or no vaccination throughout the scare. As seen in (Figure 4a), there are always some vaccine exemptions with a bigger proportion of population choose delaying vaccination than declining vaccination altogether. However, as the scare spreads and perceived vaccination risk spikes up, both delaying and no vaccination increases in the beginning, but with greater rate of no-vaccination than delaying vaccination (1995-2005). Thus, more individuals choose no vaccination than delaying vaccination as the scare persists. However, the disease outbreak due to vaccine exemption changes individual decisions and they switch back to vaccination (Figure 4b). Here, in this phase of rebound of vaccine uptake (2005-2007), the dynamics are different than earlier. Obviously, a maximum proportion choose timely vaccination, so both delaying and no vaccination strategies decrease over time; but unlike before, fewer parents choose delaying vaccination than no vaccination. So, a majority of population decides on timely vaccination, a few choose non-vaccination, and a minimum still choose delaying vaccination. Thus dynamics of vaccination game are different in the decline and resurgence of vaccine uptake during a scare.

DISCUSSION

In modern times, information spreads very rapidly due to mass media channels, newspapers, and web-based social networking. This leads to considerable uncertainty and heterogeneity in public
Table 1: Parameter estimation from delay and no-delay model.

<table>
<thead>
<tr>
<th>Fitted parameters and statistics</th>
<th>Delay model</th>
<th>No-delay model</th>
</tr>
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<tbody>
<tr>
<td>Imitation rate ($\delta$)</td>
<td>45.029</td>
<td>45.031</td>
</tr>
<tr>
<td>Pre-scare vaccine risk ($r_{pv}$)</td>
<td>0.0031</td>
<td>0.00001</td>
</tr>
<tr>
<td>Post-scare vaccine risk ($r_{p}$)</td>
<td>0.0128</td>
<td>0.0569</td>
</tr>
<tr>
<td>Vaccine risk at age class 2 ($r_v$)</td>
<td>0.0025</td>
<td>-</td>
</tr>
<tr>
<td>Perceived probability of infection ($\alpha$)</td>
<td>0.522</td>
<td>0.1583</td>
</tr>
<tr>
<td>Exponential decay rate</td>
<td>0.09</td>
<td>0.2526</td>
</tr>
<tr>
<td>Goodness-of-fit</td>
<td>0.7685</td>
<td>0.5339</td>
</tr>
<tr>
<td>AIC</td>
<td>-67.19</td>
<td>-64.45</td>
</tr>
</tbody>
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![Figure 3](image3.png) Fitting of no-delay model to the data: (a) vaccine uptake (black line) fitted to data (red circles), (b) prevalence.

![Figure 4](image4.png) (a) Dynamics of all three vaccine classes (timely: black, delayed: brown, no-vaccination: green), and (b) disease prevalence from fitting the delay model to the data. Details explanations are given in the text.

opinions, and potentially rapid temporal evolution, thus modelling individual behaviour and predicting its impact on disease outbreaks has great importance in public health policies. The whole-cell pertussis and MMR scare in UK [17], and the Yellow fever scare in Brazil [23] exemplify scenarios where public opinion and/or public reaction have an impact on the outcome of a vaccination campaign, and the difficulty in dealing with scare events. On many occasions, individuals do the exact opposite of what is recommended by public health authorities due to their mistrust of such authorities (although in the case of the whole-cell pertussis vaccine scare, the data on vaccine risk were not so clearly questionable). So, individual vaccinating decisions evolve in a sub-optimal and irrational manner, especially during a scare. This has significant impact on the success of disease containment strategies. Moreover, as access to vaccines expands, the primary barrier to ensuring high vaccine uptake becomes individual choice instead of access. These examples show why modelling vaccinating behaviour needs more attention than ever before, if we are to improve control of vaccine-preventable infectious diseases.

A recent work by same authors shows that social learning and feedbacks from disease incidence may be crucial governing mechanisms of the population response to a vaccine scare, in addition to changes in subjective vaccine risk perception [16]. Here, in the present piece of work, we use an evolutionary game theory based model including a delayer strategy, in addition to timely and no vaccination strategies, to analyze the vaccine uptake data from the MMR scare (1995-2009) in UK. Using a model selection approach, we show that the model with delayer strategies is more parsimonious than the model without delayer strategies, with respect to describing the MMR scare data. The delay model also explains how individual decisions to vaccinate are distributed over three strategies--timely, delayer and non-vaccinator--in the beginning and in the end of the scare. So, the message from our current work is that delayer strategies played a very important role in behaviour-prevalence dynamics during the scare. In Reference [16], the authors attributed the poor fit of their model to the MMR data to the absence of stochasticity or spatial heterogeneity. However, the present results show that a third option must be considered: that delayer strategies contributed to the observed pattern of the vaccine scare. This is consistent with anecdotal evidence that, during the MMR vaccine scare, many parents believed that the vaccine was safe only after the age at which autism typically first presents in a child, and thus they delayed vaccination until the child was 3-4 years old, instead of avoiding vaccination altogether.

One of our crucial model assumptions is that perceived vaccine risk instantly spikes high from a pre-scare level and then declines exponentially during a vaccine scare to align with the pre-scare level. While we do not know of any specific mechanistic model of how individuals risk perception evolves in reality during a pediatric vaccine scare, it might be worthwhile to experiment with a wide range of possible functional forms. Different functional forms require differing numbers of parameters, thus enable the explanatory power of the behavioural model to be tested against a broad range of potential competing candidates, as opposed to a single candidate. Also, different risk evolution curves reflect variability in public health efforts to restore faith in a safe and efficacious vaccine, and are represented as the eventual decline in perceived vaccine risk and thus its role in the resurgence in the vaccine uptake.

In the 21st century, when the world is frequently facing complex emerging and re-emerging infectious diseases, even a small adverse effect from any public health recommendation may be transformed to a huge scare because of rapid spread of information. Thus, behaviour-prevalence modelling is essential to understand such real world situations where individual choice is a significant driver of the system, such as vaccine scares. While there has been a reasonable advancement in theoretical development of such models, there are only few studies that overlap with empirical data [16,24-28], especially with vaccine scare data, where vaccine coverage drops remarkably after years of steady behaviour. With a few exceptions, the integration of empirical and theoretical approaches is occurring more slowly than purely theoretical developments. However, this rapid theoretical development must be accompanied by a closer integration of these models with empirical data. These will not only help in understanding how public opinions evolve during the scare, but also help to inform policy strategies to containment an epidemic.
REFERENCES


