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Samit Bhattacharyya & Chris Bauch

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Mathematical models of the interplay between individual vaccinating decisions and disease dynamics

A need for closer integration of models and data

Samit Bhattacharyya[1] and Chris T. Bauch[2]

[1]Departments of Mathematics and Biology; School of Medicine; University of Utah; Salt Lake City, UT USA; [2]Department of Mathematics and Statistics; University of Guelph; Guelph, ON Canada

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Correspondence to: Samit Bhattacharyya and Chris T. Bauch; Email: samit@math.utah.edu and cbauch@uoguelph.ca

In non-mandatory vaccination policies, individual choice can be a major driver of vaccine uptake. Choice thereby influences whether public health targets can be achieved. Individual vaccinating decisions can be influenced by perceptions of vaccine risks or infection risks. There is also the potential for non-vaccinators to strategically "free-ride" on herd immunity provided by vaccinators. This strategic interaction between individuals generates a social dilemma—a conflict between self-interest and what is best for the group as a whole. Game theory and related mathematical approaches that couple mechanistic models of vaccinating decisions with mechanistic models of disease spread can capture this social dilemma and address relevant questions. The past decade has seen significant growth in the theoretical literature developing and analyzing such models. Here, we argue that using these models to address specific public health challenges will require more work that integrates information from empirical studies into the development and validation of such models, as well as more collaboration between mathematical modelers, psychologists, economists and public health experts.

Distorted perception of vaccine risks and infection risks can lead to failure to achieve public health vaccine coverage targets. Nowhere is this better exemplified than in "vaccine scares," such as the whole cell pertussis vaccine scare during the 1970s and Measles-Mumps-Rubella (MMR) vaccination during the late 1990s in Great Britain, both of which saw significant declines in vaccine coverage despite lack of good evidence for vaccine risks.[1] This is also exemplified by seasonal influenza vaccination, which is non-mandatory in most of the countries including the US and Canada:[2] despite influenza vaccine's excellent safety record, vaccine coverage in many populations remains sub-optimal.[3] Sub-optimal coverage also occurs among health care workers (HCWs). For example, Gharbieh et al. studied influenza vaccination rates among HCWs in three Middle East countries [United Arab Emirates (UAE), Kuwait and Oman], and found suboptimal rates for various reasons including doubts about vaccine efficacy, lack of information about the importance of immunization, and concerns about vaccine side effects. A low perceived risk of becoming infected, whether justified by historically low infection rates or not, can contribute as much as inflated perception of vaccine risk does: studies identify perceived lack of infection risk as a factor in non-uptake of influenza vaccine.[3]

The dependence of vaccine decision-making on perceived disease burden in population suggests a feedback loop whereby individual vaccinating decisions influence disease transmission through vaccinating activities, and the level of disease prevalence in turn influences how many individuals choose to seek vaccination (**Fig. 1**). More specifically, the phenomenon of "herd immunity" or "indirect protection," whereby unvaccinated individuals experience a reduced risk of

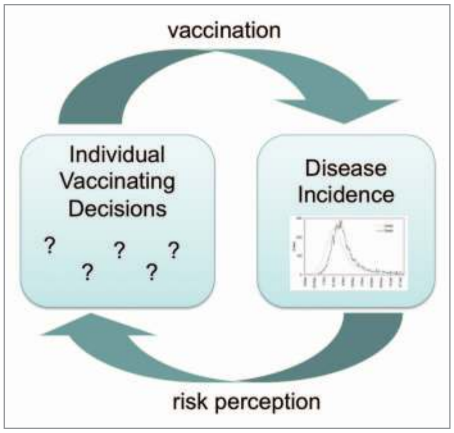

Figure 1. Interacting feedbacks arising from vaccinating behavior and disease incidence.

infection due to others having vaccinated, can create an enduring social dilemma: non-vaccinators who benefit from herd immunity provided by vaccinators are essentially "free-riding," as well as impeding disease elimination goals.[5]

This social dilemma describes a game theoretical (strategic) interaction, where the "payoffs" (costs/benefits) of a "strategy" (action) depend upon what strategies are adopted by others in the population. Game theory provides a useful tool to analyze and predict such strategic interactions[6] and has been applied to the social dilemma of voluntary vaccination.[7-9] In deciding whether to vaccinate themselves or their children, individuals weigh up the cost and risk related to vaccines vs. the benefit of reducing the risk of infection, which can depend implicitly on others' vaccinating decisions—through the level of disease prevalence observed by the individual—or explicitly—through knowledge of how many others choose a 'vaccinate' strategy.

The pace of research applying game theoretical and related approaches to modeling behavior-disease interactions in the context of vaccination is increasing rapidly (see Funk et al.[7] for a review). These "behavior-incidence" models often seek the "Nash equilibrium" level of vaccine coverage, which is the solution of the game: at the Nash equilibrium vaccine coverage, no individual could be better off by unilaterally changing to a different strategy, hence the population is expected to remain at this level of coverage. Many models have found the Nash equilibrium vaccine coverage to be suboptimal due to aforementioned free rider effects.[8,10-12] However, others have explored exceptions to the rule, which may occur when taxes or subsidies are applied[9] or for specific disease features such as when infection severity increases with age.[13] Even when these models are not strictly game theoretical (i.e., seeking to prove that a vaccine coverage level is a Nash equilibrium), they are motivated by the problem of feedback between disease dynamics and vaccinating behavior.

The state-of-the-art of such behavior-prevalence models incorporates increasing realism with respect to both vaccinating behavior and disease dynamics. For example, models have abandoned the classical game theoretical assumption that individuals are purely rational by incorporating a distinction between real vs. perceived risk,[14] allowing risk perception to evolve with vaccine coverage over time,[15] accounting for social learning and imitation processes[15-17] and incorporating the effect of delayed information on disease.[18] On the disease dynamic side, transmission through a network of contacts is being studied,[16,19,20] and features like age structure[15,21] and seasonal forcing[18] are being incorporated into models.

Due to the nonlinear feedback inherent in such systems (**Fig. 1**), these models exhibit patterns of distinct dynamical behavior that can be categorized. For instance, they exhibit "policy resistance," where the response of a system to introduction of a new intervention tends to defeat the intervention.[22,31] In the case of vaccines, the emergence of free-riding non-vaccinators represents the policy resistance. The systems can also exhibit "outcome inelasticity," where a health outcome remains unchanged over a broad range of possible conditions. In the case of voluntary vaccination during a pandemic, it has been predicted that the timing of an epidemic peak will remain unchanged across a broad range of transmission rate, due to behavioral feedbacks.[23] Finally, policy reinforcement is also possible, where the behavioral response actually helps facilitate implementation of a policy. This can occur in game theoretical models of chickenpox vaccination, where the Nash equilibrium vaccine coverage can actually exceed the socially optimal vaccine coverage.[13]

Among other predictions, these models have suggested that a universal influenza vaccine conferring long-lasting immunity could actually increase the frequency of occasional but severe epidemics,[24] that free-riding behavior could emerge surprisingly quickly in a new pediatric vaccine program, even in the first few years,[25] that long cycles in disease prevalence could emerge when self-interested vaccination decisions are based on delayed information,[18] and how imperfect vaccines can aggravate the social dilemma of voluntary vaccination.[26]

The models have also suggested solutions to the social dilemma, such as taxes and subsidies,[9] or offering several years of free vaccines to individuals who pay for one year of vaccination,[27] though it has also been shown that some incentive programs could be detrimental. For example, incentive programs that put the decision to vaccinate a group in the hands of one individual, rather than in all the members of the group, could thereby lead to greater variation (stochasticity) in vaccine uptake over time, which in turn might lead to greater variability in epidemic size and, potentially, more severe epidemics.[27]

These recent enhancements in behavior-prevalence models make possible their application to real-world situations where individual choice is a significant driver of vaccine uptake, such as vaccine scares. Such models may also be useful to national/state level decision-makers for deciding how to optimize budget allocation among various regions or states to elimination or eradication goals.[28,29] On the theoretical side, many of the required developments are already happening. For instance, models are incorporating more sophisticated treatments of disease transmission processes, and also abandoning the convenient but simplistic classical picture of individuals as purely rational optimizers. However, for such models to contribute to public health policy, this rapid theoretical development must be accompanied by a closer integration of these models with empirical data. With a few exceptions,[14,21] this is occurring more slowly than purely theoretical developments. In particular, better information is needed regarding (1) how individuals perceive vaccine and infection risks, especially (a) how these perceptions depend on real vaccine adverse events or infections experienced/observed by individuals and (b) how that varies over time, (2) how these risk perceptions translate into vaccinating behavior, (3) how individual decision-making interacts with influence from the media and medical professionals and (4) how the opinions and actions of other individuals influences an individual's vaccinating behavior, through social influence for example. There is also a need to think about exactly how to the outcomes of modeling studies can be used to inform public health policies regarding vaccine-preventable diseases.

Human behavior is a central and fundamental aspect of public health policies regarding infectious disease interventions.[30] Game theoretical and related approaches that integrate perceptions of risk and mechanisms of disease transmission into health policy models can help us meet public health goals but will also require fruitful collaboration among psychologists, economists, epidemiologists, public health experts, and mathematicians.

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