

Characterization of the impacts of heterogeneity in high-risk populations for infectious disease transmission: Modeling polio and measles in the North American Amish

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Abstract

Even in otherwise well-immunized populations like the United States, heterogeneity in immunization can lead to clusters of under-immunized individuals who may sustain transmission of imported vaccine-preventable diseases like polio and measles. Special populations that refuse or miss immunization opportunities consequently represent groups of potential concern for public health authorities. Prior outbreaks of polio and measles in Anabaptist communities, including the North American Amish, led to their identification as high-risk individuals. We developed an individual-based model that characterizes the network and dynamics of mixing among the Amish and applied the model to characterize transmission of introductions of polio or measles viruses. The results of the models demonstrate the wide range of potential outcomes that could have occurred retrospectively or may occur prospectively. Our results suggest that improved characterization of historical vaccination among the Amish would improve public health efforts to manage their risks and the risks they may pose to the broader US population, and we discuss several challenges associated with interpretation and presentation of IB model results for public health decision makers.

Introduction

Integrated models that include system dynamics (SD) components continue to play an important role in high-level policy discussions related to polio globally and nationally.⁽¹⁾ More than a decade of experience using both differential equation-based (DEB) and individual-based (IB) models for polio reveals that DEB models offer value for large scale (i.e., national and global policy questions), while IB models offer value with respect to potentially improved characterization of the heterogeneity in mixing that can impact viral transmission for special population. By allowing different assumptions than homogeneous mixing within populations commonly used by DEB models, IB models can improve understanding of special populations so long as modelers can make evidence-based assumptions about the behaviors and interactions of individuals in those populations. Given the additional complexity included in their formulation and their inherent stochasticity, modelers run many iterations of the IB model to get a sense of the overall population dynamics. The results of many stochastic realizations and visualization of the variability then necessitate making choices for interpretation (e.g., mean behavior, a worst-case realization, etc.).

Public health officials recognized the North American Amish as a network of relatively high-risk communities due to outbreaks of vaccine-preventable diseases like measles,⁽²⁾ polio,^(3,4) and rubella.^(5,6) A prior IB model for poliovirus transmission demonstrated the wide range of dynamic transmission behaviors possible with different theoretical population network and mixing assumptions, and noted the challenges associated with appropriately characterizing

mixing within large (i.e., national, global) populations.⁽⁷⁾ Numbering in the hundreds of thousands in the United States, the North American Amish live in a geographically spread, but well-connected network of communities in relative isolation from the US general population, with individuals who share similar behaviors living in districts of relatively similar sizes. A 2014 study developed a geographical map of the North American Amish population and specifically characterized the mixing assumptions based on available evidence and judgment to explore the probability and spatial-temporal dynamics of potential poliovirus outbreaks following a poliovirus importation.⁽⁸⁾ The model included detailed development of the assumptions about the population and mixing structures based on the available evidence and retrospective analysis of a 1993 importation into an isolated North American Amish community.⁽⁸⁾

In 2014, concern about measles in the U.S. increased significantly when the U.S. reported its highest number of measles cases in the last 20 years, with a large outbreak in Amish communities in Ohio accounting for many of the cases.⁽⁹⁾ This motivated us to adapt the published poliovirus IB model of the North American Amish⁽⁸⁾ to characterize measles transmission and to explore measles outbreaks in the North American Amish.⁽¹⁰⁾ The following section briefly describes the methods we used to model measles in the North American Amish (henceforward “Amish”) and the following sections present our results and discussion of insights.

Methods

Similar to the IB model of poliovirus transmission in the Amish,⁽⁸⁾ we used NetLogoTM as the modeling platform for the measles model and the same geographical mapping to approximately map the locations of the Amish districts.^(8, 11) We refer the reader for details about the population and network assumptions to the prior publications.^(8, 10) Briefly, the model begins by mapping the locations of districts during the year the model starts, based on approximate addresses known for these districts and accounting for growth in the number of Amish districts that occurred over time. For each district, the model then populates the households and assigns attributes to the individuals. The model specifically considers the levels of religious conservatism based on the judgment of an Amish expert,^(8, 10) who classified the Amish districts known to exist in 2008 as high, medium, and low conservatism representing the least to most acceptance of modern technology (including vaccines and other medical technologies), and assigns these at the district level. The model assumes mixing associated with activities involving multiple districts preferentially leads to contacts between individuals from districts with similar levels of conservatism. The model matches overall distributions of age, sex, and household size and compositions for the Amish.⁽⁸⁾ On each simulated day, the model assigns activity schedules appropriate to each individual based on sex and age, and evaluates the need to replace some of the scheduled daily activities stochastically with less common individual or group activities (e.g., weddings), as appropriate based on probabilities of these relatively less frequent events. For each individual, the model tracks key events, including birth, death, aging, and marriage, and for districts the model tracks the process of districts splitting as they grow to a population size that exceeds the typical district size in the state.⁽⁸⁾ We assume that families mix in their households, and that children can mix with other children at school and/or at one of three fixed play areas per district. We also assume that convening events lead individuals to mix as part of the specific

activities. Generally, we assume homogeneous mixing of individuals engaged in the same activity in the same location, although we apply activity-appropriate age or sex restrictions in some instances.⁽⁸⁾ The model tracks the entire simulated Amish population for stochastic events that may lead to contact with individuals in infected districts, and for districts containing or visited by infectious people the model tracks activities in 30-minute time steps for every day of the simulation period. At each time step, a change in individual activities leads to the appropriate end of current contacts, possible change of location and temporary formation of new contacts, with interactions between contacts representing potential opportunities for infected individuals to transmit virus to susceptible individuals. We assume probabilities of transmission that consider the nature of the contact as close (i.e., more intense) or community (with lower transmission probability) based on the nature of the activities and account for observed seasonality in transmission.⁽⁸⁾

To model measles, we made appropriate adjustments in model input values that account for the different latency, infectiousness, and other factors.⁽¹⁰⁾ We modeled two known measles outbreaks that occurred in the Amish: one in 1988 following measles introductions into local Amish communities from the general population in Pennsylvania, which led to 130 reported cases among the Amish in Lebanon County⁽²⁾ and an unknown total number of cases in the US associated with this outbreak, and the 2014 outbreak that followed the return of four Amish missionaries from the Philippines to Knox County, Ohio, which led to 382 reported cases.^(9, 12)

For this analysis, we focus on characterization of the variability in the model results of the different outbreaks considered and their potential interpretation by public health authorities. We look across the models for polio and measles, and compare the information provided by performing multiple iterations of the models to develop distributions of the results. We also report the results of the estimated incidence and the cumulative number of infections as a function of time.

Results

Figure 1 shows the distribution of the cumulative number of infections between importation and die-out of transmission based on 1,000 iterations for the (a) 1993 poliovirus importation into an isolated community, (b) the 1988 Pennsylvania measles outbreak, and (c) the 2014 Ohio measles outbreak. We assume a case-to-infection ratio of 1 for measles, but recognize that not all measles cases get reported to the public health system. For the 1993 polio outbreak, the true number of infections remains unknown, because most poliovirus infections occur asymptotically, with paralysis occurring in an estimated 1 per 1000 wild poliovirus serotype 3 infections.^(8, 13) The low number of model infections appears consistent with the lack of any observed cases, and the variability in the estimated number of infections remains of no practical consequence. In contrast, the 1988 Pennsylvania measles outbreak led to 130 reported measles cases among the Amish in Lebanon County,⁽²⁾ with 542 cases reported for Pennsylvania in 1988 overall⁽¹⁴⁾ and other cases reported in Amish communities in 4 other states affected by this outbreak with the total size of the interstate outbreak unknown. Figure 1b suggests a wide range, with a mean of 588 modeled infections. For the 2014 Ohio outbreak, the state reported 382 measles infections in the Amish, and Figure 1c shows a distribution that includes some iterations

that yield approximately 382 infections, but many other iterations with less or more modeled infections.

Figures 2a and 2b show the incidence and cumulative infections as a function of time for 200 iterations of the 1988 Pennsylvania outbreak model. Each iteration creates a path, and collectively the cumulative results show considerable spread, consistent with the distribution shown in Figure 1b. These figures display the results visually in such a way that the variability in the different iterations appears as a large mass. Figures 2c and 2d show similar results for the 2014 Ohio measles outbreak.

Discussion

The variability in the results leads to important challenges for policy makers interested in using the results. Each iteration shows just one possible realization given the set of inputs, and this helps to convey the importance of real stochasticity in actual events. In this case, we see that one unfortunate transmission event in an iteration into a high-density area or event (e.g., resulting from an occasional family visit for a wedding or other large gathering) may increase the number of individuals who become infected by an order of magnitude compared to a similar run without that specific event. Similarly, the location of time and district of the initial virus introduction significantly affect the expected size of the outbreak.⁽⁸⁾ For retrospective modeling, this allows for potential exploration of paths that might have occurred and better understanding of events that drive the total cases and kinetics of outbreaks. Prospectively, the model allows for consideration of events that could lead to better or worse outcomes occurring by chance and better understanding of the effects of response designs in different possible realization paths.

Policy makers seeking to use the results for management may find it difficult to evaluate and characterize the baseline in simple terms when presented with distributions of results, particularly for retrospective analyses. On top of this, implementing policies may change different metrics of interest, for example, policy makers may want to reduce the expected number of total cases or focus on reducing the behavior in the tail. In practical terms, modelers can only show a small number of figures to report outputs, and this creates the need for effective communication between the modeler and the policy makers. In IB models, the effects of policy may play out on the micro level, which may provide more insights about how the implementation of policies may play out in practice, but it may make communication of the benefits of actions more difficult as well, because the curves in Figure 2 with and without policy interventions would most likely overlap.

In addition to the stochastic effects that play out in IB models, which lead for variable results, uncertainty may also represent an important consideration. Specifically, in the models for transmission of polio and measles in the North American Amish we only partially consider uncertainties related to historical immunity, transmission probabilities, seasonality, and the frequencies of inter-district interactions. IB models typically require many more assumptions than deterministic SD models, and often insufficient data exist to support all numerical input assumptions. This implies a need to vary more uncertain inputs than typical deterministic models, with some challenges associated with controlling any observed input uncertainty effect for pure stochastic variations, which places more demands on effective communication to policy

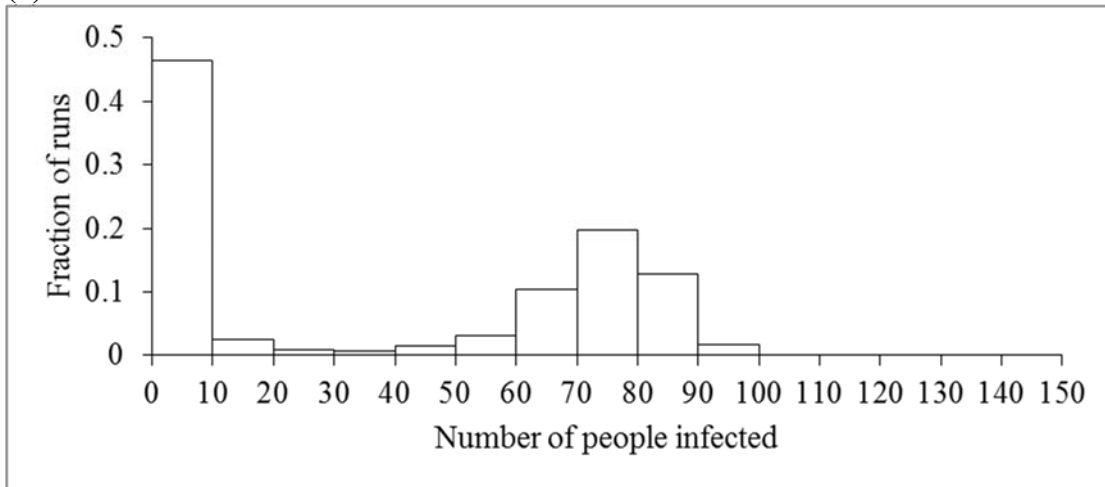
makers. Both deterministic SD models and IB models come with different benefits and limitations, and the nature of the policy questions should drive the choice of the most appropriate modeling approach.

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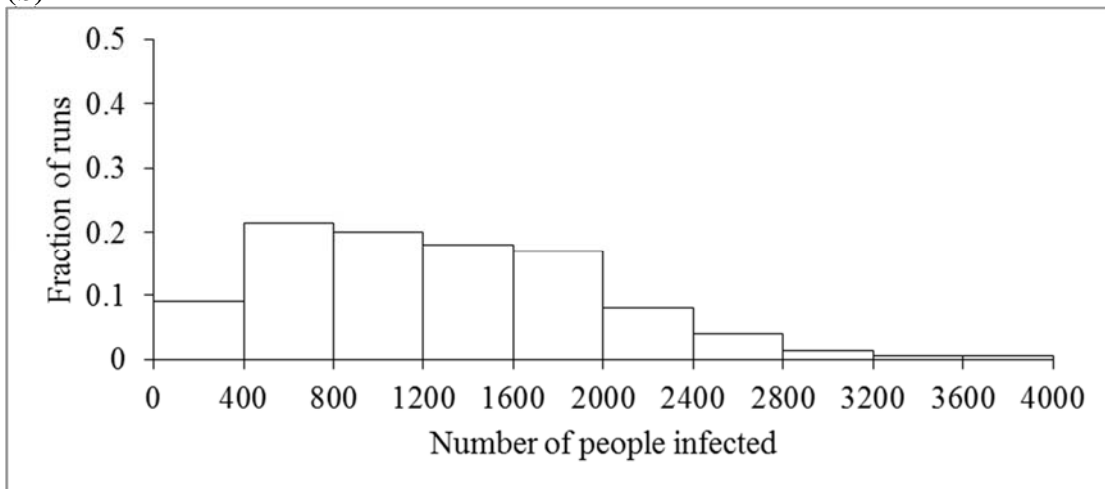
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Figure 1. Distribution of the cumulative numbers of infections for 1,000 iterations of the model for (a) 1993 poliovirus serotype 3 introduction into an isolated Northwestern Amish community, (b) 1988 Pennsylvania measles outbreak, and (c) 2014 Ohio measles outbreak

(a)



(b)



(c)

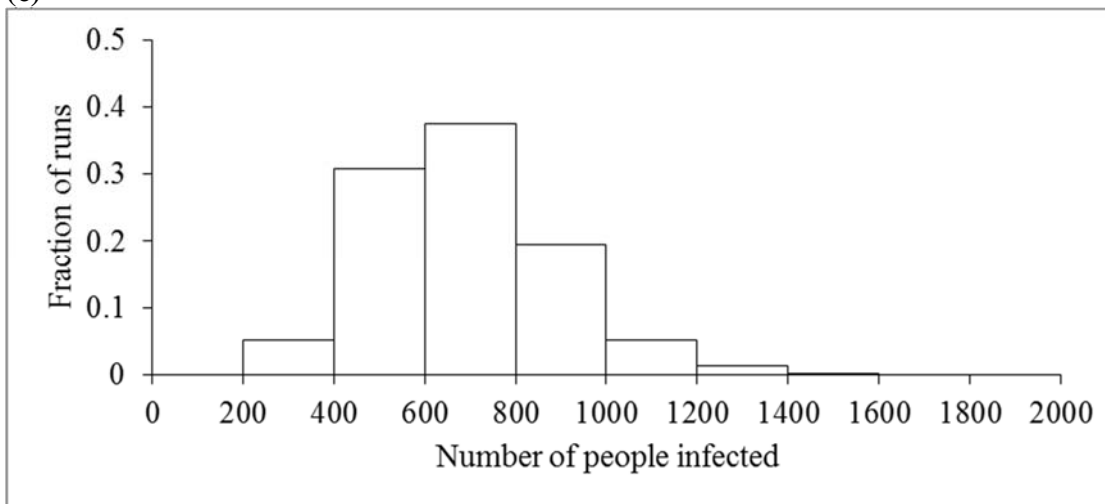
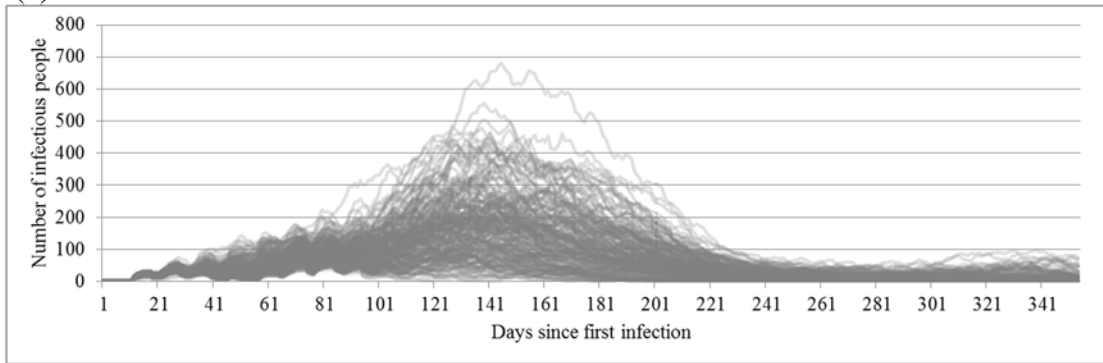
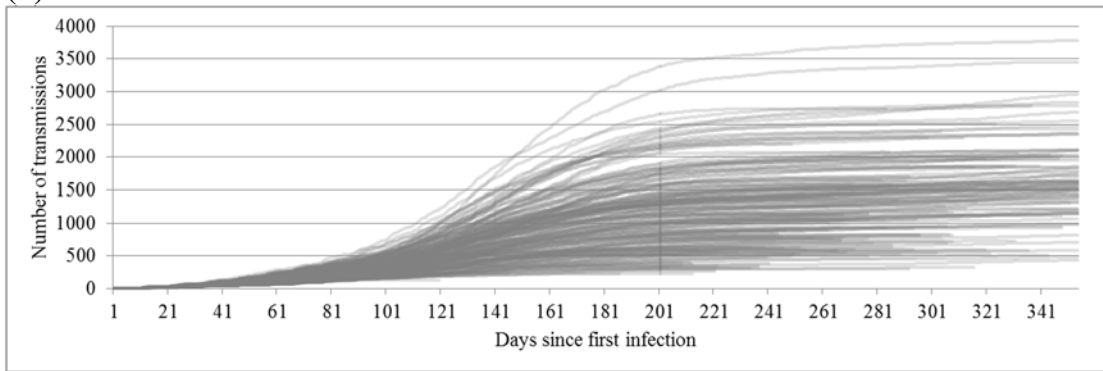


Figure 2. Visualization of 200 iterations of the (a) infectious people and (b) cumulative infections as a function of time for the 1988 Pennsylvania measles outbreak and (c) infectious people and (d) cumulative infections for the 2014 Ohio measles outbreak.

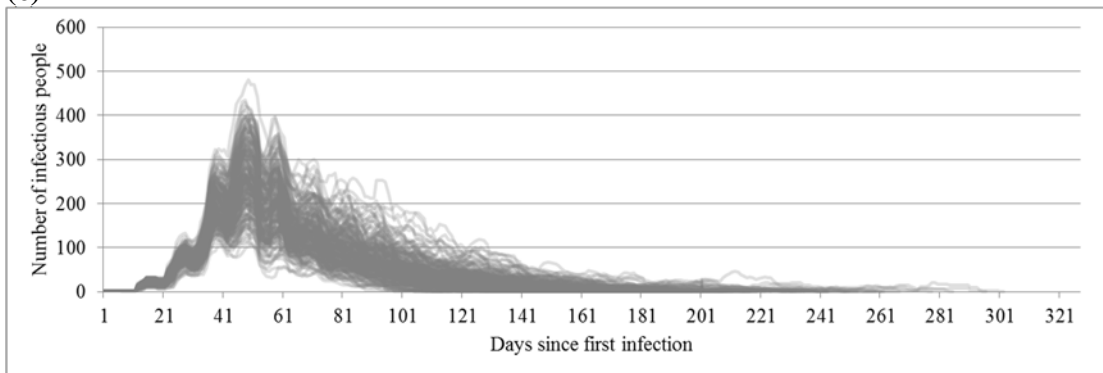
(a)



(b)



(c)



(d)

