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Individual-based modeling of potential poliovirus transmission in connected religious communities in North America with low uptake of vaccination

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Abstract

Background: Pockets of undervaccinated individuals continue to raise concerns about their potential to sustain epidemic transmission of vaccine preventable diseases. Prior importations of live polioviruses (LPVs) into Amish communities in North America led to their recognition as a potential and identifiable linked network of undervaccinated individuals.

Methods: We developed an individual-based model to explore the potential transmission of a LPV throughout the North American Amish population.

Results: Our model demonstrates the expected limited impact associated with the historical importations, which occurred in the context of a high level of population immunity attributable to historical exposure to LPVs (wild and vaccine). We show that some conditions could potentially lead to wider circulation and paralytic cases in Amish communities if an importation occurred in or after 2013. The impact will depend on the uncertain historical immunity of members of the community to polioviruses.

Conclusions: Heterogeneity in immunization coverage represents a risk factor for potential outbreaks of polio if a live virus introduction occurs, although overall high population immunity suggests that transmission would remain relatively limited. Efforts to prevent spread between Amish church districts with any feasible measures may offer the best opportunity to contain an outbreak and limit its size.

Keywords

polio; immunization; individual based model; disease outbreaks; under vaccinated

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Conflicts of Interest
None

INTRODUCTION

Although the United States eliminated indigenous wild polioviruses (WPVs) decades ago,[1] various sources of possible reintroduction of live polioviruses (LPVs) remain.[2] Specifically, WPVs from countries that sustain their transmission,[3] circulating vaccine-derived polioviruses (cVDPVs) imported from countries that use oral poliovirus vaccine (OPV),[4] and (un)intentional introductions from laboratories or vaccine production sites present small but real risks.[2] Prior importations of LPVs into Amish communities in North America led to their recognition as a potential and identifiable linked network of undervaccinated individuals.[4, 5]

Dynamic models offer insights about possible outbreaks[6–8] and they can account for heterogeneity in the population.[8–10] For polio immunization overall, heterogeneity represents a complex and important consideration in the United States, because even with very high rates of coverage some people remain undervaccinated and they may cluster.[11] Individual-based (IB) models use individual level data (e.g., age, sex, health status), and an assumed network structure to characterize interactions between all individuals in the population.[12] Specification of the network structure depends on the nature of transmission of the pathogen and the specific population(s) considered. Many published large-scale IB models assume that individuals mix homogeneously at particular places or events.[13–15] IB models may also use a bipartite graph to track movements of people to specific locations based on individual activity schedules derived from census data, surveys, or other data sources.[8] IB models stochastically capture contacts between individuals at mixing site locations, which leads to a self-organizing and dynamic network based on movements. Some IB models also use data from a geographical information system to specify the network.[16, 17] Rahmandad et al. explored potential network structures for poliovirus transmission models and concluded that assumptions made about network structures and mixing significantly influence the results.[18] Following up on a prior study[11] and using insights from an expert review and synthesis of the literature[19, 20] and model calibration process, [21] we developed an IB model to explore the potential for transmission of LPVs in a study population based on our characterization of the North American Amish. We do not specify the type of LPV that would be introduced, although an introduction of WPV type 1 or a cVDPV of any serotype would represent the most likely potential candidates in the context of current global poliovirus epidemiology[22–24]

METHODS

Developing an IB model for the study population requires characterization of the network structure as well as individual attributes and activities. Current estimates suggest that approximately 276,000 Amish people[25] live in approximately 2,000 church districts (i.e., districts) distributed across 30 U.S. states and Ontario, Canada (Figure 1).[25] Districts include approximately 30 families with approximately 135 people on average who attend church services together every other Sunday at a home in the district, send their children to the same school, and interact closely as a community. A large proportion of Amish districts further cluster in strongly interconnected settlements, the largest of which consists of 246 districts as of 2013,[25] although some districts remain much more isolated. The Amish

share some common values, but they also differ to some degree in the level of conservatism (characterized as low [blue triangle], medium [green dot], and high [red square] in Figure 1), (Kraybill D.B., personal communication) with individuals from like-minded districts somewhat clustered geographically and preferentially interacting (e.g., by visiting similar church services in other districts on the Sundays between their own district church services). Households, sometimes consisting of multiple related families, serve as the core structure within the study population, with approximately 20–35 households in each Amish district. [25–28] As districts begin to grow much beyond the average size, their members will decide to split into two districts so as to not become too large according to tradition. Thus, while the number of families varies in each individual district, the distribution remains relatively consistent over time and growth of the population leads to increasing numbers of districts.

Demographic events

The model involves five basic demographic events carried out at the beginning of the simulated day (on days they occur): birth, aging, marriage, death, and district splitting (see Appendix).

Birth: The model gives individuals a specified birthday (either randomly selected at initialization or determined during the simulation) and individuals increase in age on their birthday. Births occur at fixed intervals within families, until the family reaches the target number of children selected at the time of a couple's union.

Aging: Aging leads to changes in death rates and daily activity schedules. For example, the activity schedules for young children remain completely tied to their mothers' schedules up to the age of 5 years, after which they start their own more independent activity schedules. Amish adolescents reaching the age of 16 years enter "rumspringa" (literally: running around), a period of exposure to the non-Amish ways of life at the end of which they make a choice to either adopt the Amish way of life or to leave the Amish community completely. [29] Based on an average retention rate of 85%, [25] we assume that 15% of the people turning 16 years old will leave the study population and thus exit the modeled population. We ignore the very small number of non-Amish individuals who choose to join the Amish population each year. The model does not characterize contacts with the general population, which we assume maintains high levels of population immunity. [10]

Marriage: Marriage occurs whenever a man reaches his age of marriage, which we sample from a distribution, and he marries a woman of comparable age (0–2 years younger) preferably living in a nearby district and never living further away than 50 km. Whenever two people get married they start living together in a new household in one of their home districts, or move into the groom's homestead in the case of marriage of the youngest son.

Death: We use death rates consistent with demographic data of a comparable US demography. If a person dies and leaves only one person behind in his or her household, the survivor joins another (randomly selected) household in the district instead of living alone. [27] When a mother with any children under the age of 5 years dies, the model links the schedules of these children to another adult woman in the household or district.

District splitting: Whenever birth or marriage leads to a district size of at least the split size, which we varied by state based primarily on the estimated average district size we estimated for each state, the district splits.[25] The model selects a new location in the US or Canada for the new district in the same settlement as the original location with a probability of 75%, based on historic changes,[25] or at a new location at a random distance (max 1500 km) and direction from the source district with arable land and low urbanization. We checked the creation of new districts over time against historic data. After the creation of a new district, the model randomly selects remaining households in the district to move to the new location, until approximately half of the people move.

Activities by age and gender

Characterization of activities by age and gender presents a challenge because of limited data. [25, 27–31] Amish people typically work close to home and remain relatively isolated from the non-Amish population, except for the men who may work in outside factories or other settings.[26] We assume that most adolescent and adult men work as farmers (50%), while the remainder operate small trade businesses (25%) or work outside the district in a factory or other setting (25%). We assume that adolescent and adult women and all seniors work in their homes, which may include home stores for goods they produce (e.g., baked goods, quilts), and that young children stay with their mothers throughout the day, except for when they sleep. Finally, older children attend school and help with farming (boys) or household chores (girls).

Susceptibility and infectiousness

Because Amish people rarely travel far and their daily activities vary relatively little, we characterize most of their contacts as local and consistent with a daily activity schedule that includes a somewhat limited number of activities. Some less common activities also occur, including barn raisings, family events, and visits to friends or family in other districts. Once per year, the model schedules all weddings that may occur in the upcoming year with different probabilities for each month. Each district includes one bishop and two ministers at all times.[27, 28] The appendix provides our assumptions about all activities in the model.

We assume that due to reasonable hygienic conditions, polioviruses spread primarily via oropharyngeal transmission.[19, 20, 32] The model tracks infectious people as viruses move through the population, which includes 7 immunity states for individuals with different susceptibility and infectiousness characteristics. Table 1 summarizes the different assumptions about susceptibility and infectiousness for these seven states, with higher susceptibility to infection and infectiousness to others if infected for historic compared to recent immunity states. The model assigns those individuals never vaccinated or exposed to any live poliovirus to the *fully susceptible* state. We assume that a fraction of people born since 2000 received 3 or more successful doses of inactivated poliovirus vaccine (IPV), and thus enters the *recent IPV vaccination* state. After a stochastic waning period (see Table 1), IPV recipients enter the *historic IPV vaccination* state. Following recovery from a first infection with a LPV, fully susceptible people enter the *1 recent LPV infection* state and then after a stochastic waning duration they enter the *1 historic LPV infection* state. Previously-infected individuals can become re-infected, at which point they enter the *2 or more recent*

LPV infections state and wane to a *2 or more historic LPV infections* state. IPV recipients also enter the *2 or more recent LPV infections* state when infected. We assume that only fully susceptible individuals can experience paralytic poliomyelitis after infection (i.e., a case).[11, 19, 20] Once infected, people continue their normal activity patterns (consistent with the high proportion of infections that remain asymptomatic).[33]

The model takes into account that senior Amish people likely benefit from historic immunity because of exposure to WPVs prior to 1955[11] or from prior efforts to vaccinate their communities using OPV. Some Amish people born between 1955 and 2000 probably experienced LPV infections either from exposure to WPVs or direct or indirect exposure to OPV, which can spread from vaccine recipients to unvaccinated contacts.[11, 34] Given significant uncertainty about the fraction of the population with historic immunity, the model considers a historic immunity fraction (HIF) of 50% ('low') and 95% ('high') for people born between 1955 and 2000 (we assume historic LPV exposure for all individuals born prior to 1955).[11] In 2000, the United States switched to exclusive use of IPV and widespread circulation of LPVs stopped.[11] Although it remains unclear how many Amish people born since 2000 received IPV, most Amish people appear to receive some vaccination and the coverage rate likely correlates with the local level of conservatism and access to immunization.[31, 35, 36] In the absence of good data, we estimated lower and upper bounds for the IPV coverage rate in districts with low, medium, and high levels of conservatism. Because coverage rates may vary between districts as well as within districts, the coverage rates listed in Table 1 represent both the fraction of districts of each level of conservatism in which any person receives vaccination (i.e. a probability per district) and the fraction of newborns vaccinated in those districts. These assumptions allow for local clustering of vaccination practices. The square of the values in Table 1 thus provides an estimate of the overall coverage rate over all districts of a certain level of conservatism. The two possible HIF settings (low and high) combine with the two possible IPV settings (low and high) to generate four possible sets of immunity assumptions.

The probability of transmission through assumed contact patterns

Contacts between infectious and susceptible individuals may lead to poliovirus transmission. For each contact between an infectious individual and a susceptible individual, the model evaluates the probability of transmission as the product of the basic transmission probability associated with the time of year (much higher in summer than in winter), a multiplier if the activity involves close contact (instead of the less intense community contact), the relative infectiousness at the time of contact, and the relative susceptibility of the susceptible individual, depending on the immunity type of the infected and infectible individuals involved (Table 1). The assumed contact patterns, seasonality, and probabilities of transmission for close and community contact by activity and events produce an effective average basic reproductive number (R_0) in the same range as prior analyses.[11, 32] The actual serotype of the LPV introduced would impact the R_0 of the virus. The input values we used in the model approximate good hygiene conditions for serotype 1. We compared our transmission dynamics to R_0 by testing random introductions into a fully-susceptible model population (i.e., no recent or historic immunity at all) by running 200 iterations for four fixed introduction days.

We constructed the model using NetLogo™.[37] The model process begins by mapping the approximate location of districts, assigning levels of conservatism, and populating each district by iteratively adding households until the district reaches its total size. Each district contains a school and three fixed play areas, which serve as mixing sites for children. For each household, the model creates a composition with aggregate demographic statistics (age distribution, family size distribution) that correspond to those reported in the literature.[30, 31] Based on age and gender, the model then begins a simulation run by assigning appropriate daily activity schedules for each time step to each individual and it stochastically replaces prescheduled daily activities with less common individual or group activities according to assumed frequencies for those events. Individuals in the model go to an activity-appropriate location (e.g. a household or a school) and contact other people at the same location performing similar activities. We used a time step of 30 minutes in the model to balance computational demands with the need to capture the granularity of simulated activities. During every time step in the model, after assigning and executing new activities for all people, the model generates temporary contact links between people at the same location after consideration of age or gender restrictions appropriate for the type of activity. We assume that people preferentially contact those from districts with similar conservatism (i.e., inter-district activities/events preferentially involve people from districts with similar conservatism) while people at the same location mix homogeneously.

We explored the model behavior with respect to the 1993 introduction of type 3 WPV into an isolated and unvaccinated non-Amish but similar religious community in Alberta, Canada[4] with low vaccine uptake by introducing a WPV into an isolated district in Montana (no Amish districts exist in Alberta) and running 1000 iterations using low immunity assumptions and the estimated overall Amish population size and distribution from 1993.[25] We also ran 1,000 iterations based on the current aggregate Amish population for each of the four possible sets of immunity assumptions (HIF low/high, IPV coverage low/high) using randomly selected individuals as the first infection in randomly selected districts on randomly selected days of the year. We allow iterations to continue until all infectious individuals recover from their infections (i.e., no infectious individuals remain). Finally, we also ran a series of 12×100 iterations of the model to explore the impact of the LPV introduction timing by using a single date in each month for the introduction. For this experiment we used the lowest immunity settings and introduced the virus into a simulated district located in the middle of the large Holmes settlement in Ohio.

RESULTS

Our simulation of the 1993 Canadian LPV introduction, which we approximated by introducing a LPV with a relatively high R_0 and paralysis-to-infection ratio for a WPV3 virus into a Amish district in Montana, did not result in any cases or inter-district transmission in any of the 1000 iterations, although the virus reached approximately half of the 135 district residents in approximately 50% of all runs (see Appendix A6). This result appears consistent with the actual Canadian experience of transmission observed within the community of introduction with limited circulation and no reported infections outside of the community.[4]

Table 2 summarizes key results for the different levels of assumed immunity (i.e., HIF and IPV). Overall, it takes an average of approximately 80–100 days from the time of introduction until the first case appears (if 3 or more appear), with higher values for higher IPV use, and 110–140 days on average until the second case (if any cases occur). These results provide some indication of the ability of increased use of IPV to lead to a delay of the detection of cases and transmission in a population (i.e., for HIF low compare IPV high to IPV low), while higher levels of population immunity and sufficient levels of IPV can prevent transmission (i.e., for HIF high compare IPV high to IPV low). Table 2 reveals that the duration and intensity of poliovirus circulation within the population depend on the immunity assumptions, but we anticipate relatively low transmission overall. At the lowest immunity settings, a poliovirus infection introduced into the study population leads to infection at some point during the simulation in 2% of the study population on average (i.e., approximately 5,000 people) reaching 3% of the districts (i.e. approximately 60 districts, mostly clustered in settlements), and resulting in 13 paralytic cases on average, with up to almost 200 cases in some iterations. Figure 2 (top left) shows that on the lowest immunity settings, approximately 75% of the simulations reach less than 2% of the population before the virus dies out, and poliovirus transmission would most likely not reach more than 10% of the study population, with only 38 of 1,000 runs in which the infection reaches between 12 and 24% of the study population. Figure 2 (top right) also shows estimated cases on the lowest immunity settings ranging between 0 and 200, with approximately 70% of the iterations ending up with fewer than 10 cases. At higher immunity settings, the fraction of people infected seldom exceeds 2% and the number of cases rarely exceeds 10 (Table 2, Figure 2).

Figure 3 shows the fraction of simulations in which each of the 2,007 districts became infected and shows that the relatively dense and central settlements in the states of Ohio and Pennsylvania become infected most often (up to 5% or 6% of all runs at the lowest level of assumed immunity), while the more remote settlements (e.g., Montana, Missouri) rarely become infected. This suggests that the proximity to and connectedness with other districts represent important determinants of the outbreak kinetics. The random selection of the source district implies low probability of introduction into relatively more isolated areas. Figure 4 further shows a clear correlation between district density in the area of the source district and the resulting outbreak size, although we see some exceptions to this generalization.

The time of introduction also represents an important factor because of the impact of the assumed seasonality in the transmission probability and the activity schedule, which both impact R_0 . Figure 5 shows the results of the 12×100 runs with different starting months (with all else equal) and confirms that winter introductions typically result in much less transmission, although the virus may still survive through the winter and spread during the next summer. The individually plotted results in Figure 5 show substantial variation in the results due to the stochastic nature of contacts that transmit the virus.

DISCUSSION

Our results provide important insights about the dynamics of a potential LPV introduction into the North American Amish population. The level of historic immunity and acceptance of IPV represent important sources of uncertainty, which we varied in our analyses. Unlike the general US population, which continues to benefit from high levels of population immunity overall due to high rates of childhood immunization, many young Amish people may remain fully susceptible to polioviruses, and we anticipate that these individuals interact preferentially with one another (i.e., cluster socially). The number of expected cases depends on the time and place of the virus introduction. For example, introduction into dense communities will result in continued transmission and much higher case counts on average than an introduction into relatively more remote settlements. Introduction during spring or summer will generally lead to more transmission and more cases as seasonal effects increase the force of viral transmission.

The IB model yields numerous potential realizations of possible futures that collectively provide information about the overall types of behavior that we might expect, but each individual run differs and this suggests an important role of stochastic events in determining the exact transmission path that follows an introduction in a highly heterogeneous population. While transmission within a district may occur after an LPV introduction, stochastic contacts between distant friends or family can significantly influence the course of the overall outbreak. Large community gatherings such as weddings represent potentially large sources of inter-district transmission, which accelerate viral spread during the spring and may prolong a poliovirus outbreak into the late fall. Given the relative isolation of Amish communities from any clusters of under-vaccinated individuals in the general population, we do not anticipate that a poliovirus outbreak in the Amish communities might immediately spill over into the general population or vice versa. However, in either case, efforts to detect the outbreak and prevent its spread would represent a high priority. Although preventing spread within a district after virus detection may represent a challenge given the speed of transmission within a district, efforts to prevent spread between districts with any feasible measures may offer the best opportunity to contain an outbreak and limit its size.

We highlight several important limitations of our approach. First, our model relies on a large number of assumptions and the estimates depend on the quality of the data and the model inputs used. With regard to the activity patterns, we believe the basic activity schedules probably reasonably represent typical patterns, but we remain highly uncertain about the occasional inter-district movements, which determine the large scale transmission patterns. Specifically, the frequency, size, and time of weddings as well as the composition of their guests (i.e., from nearby vs. distant districts) substantially affect the timing, duration, and size of outbreaks. In addition, significant uncertainty exists about how polioviruses transmit in populations, and our estimates depend on highly uncertain values. We characterized the transmission probabilities based on estimated R_0 values in historic poliovirus outbreaks appropriate for North America,[11, 21, 32] but we remain uncertain about whether these differ for the Amish. The two most important parameters we identified include the basic transmission probability throughout the year and the modifiers for activities with close or

community contact, especially the activities that involve inter-district contact. In addition, the model assumes that all individuals go through the same relative infectiousness curve once infected. Our use of an average for all individuals rather than including variability between individuals may affect the behavior of the model (i.e., it inhibits some individuals from becoming relatively much better or worse individual spreaders), but we do not anticipate that this leads to any major impacts, and data to support an alternative characterization remain limited.[19] The model allows for a relatively high amount of preferential contact based on distance, mindset, gender, and age. However, we do not keep track of extended family and friendship structures within the study population (i.e., we only track the core family), which may reduce the extent of repeated mixing with individuals outside of the home district somewhat compared to reality (i.e., the model stochastically selects the destination for each distant visit from within a certain range and districts with a certain mindset).

CONCLUSIONS

Studies to assess the level of historic immunity and current immunization practices in Amish communities would significantly reduce the uncertainty around our estimates of possible numbers of cases. Although we believe our model captures the essential sources of inter-district transmission, additional quantitative insights into inter-district contact patterns among the Amish would also significantly improve the accuracy of our model, particularly regarding the preferential mixing aspects and the distribution of travel distances. Efforts to better map the levels of immunity in different Amish communities and connectedness between them may help to support any future efforts required to develop appropriate response strategies in the event of a possible future poliovirus introduction in these communities. The continued threat of LPV introduction leads to preparedness efforts, including recommendations for a United States IPV stockpile.[38] Even a single case of polio detected in the US, including in the Amish, would likely trigger an aggressive outbreak response. Efforts to remain prepared for outbreak response and plan a stockpile should consider the role of populations like the Amish and other sources of heterogeneity.[39]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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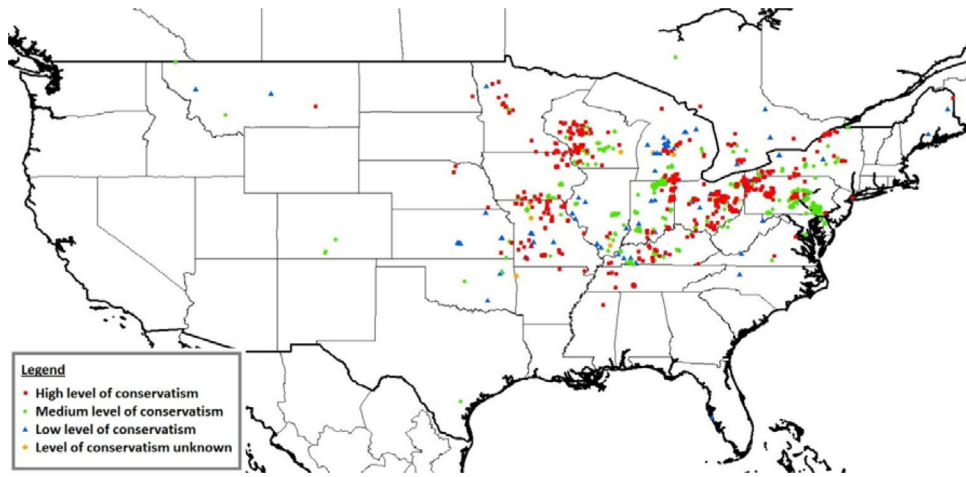


Figure 1: Geographic distribution of North American Amish districts in 2008 and assumed characterization of level of conservatism.
(Kraybill D.B., personal communication)

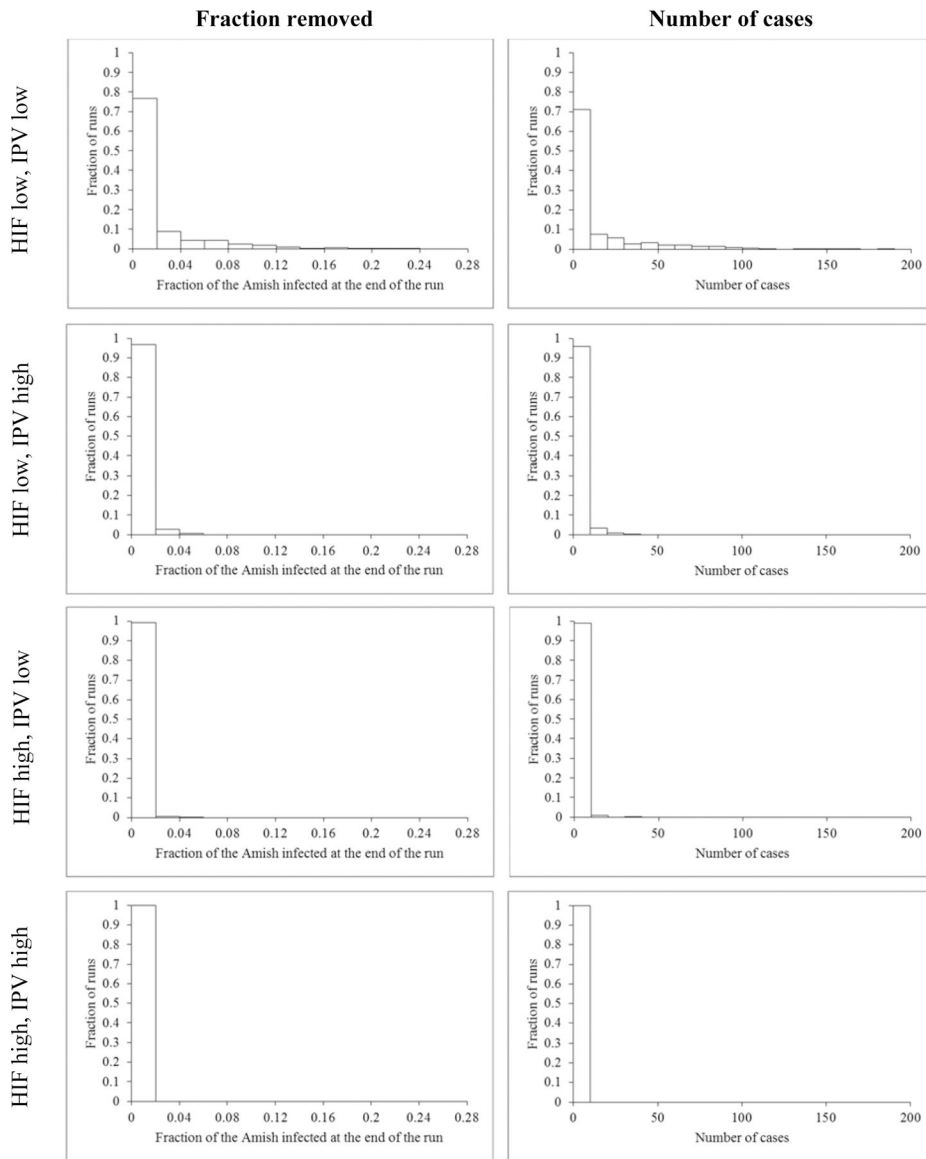
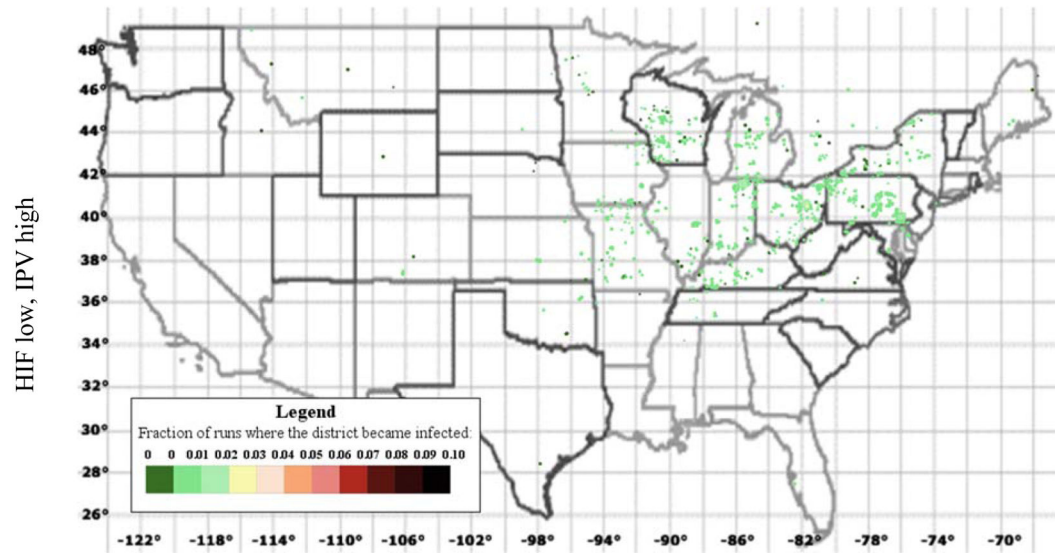
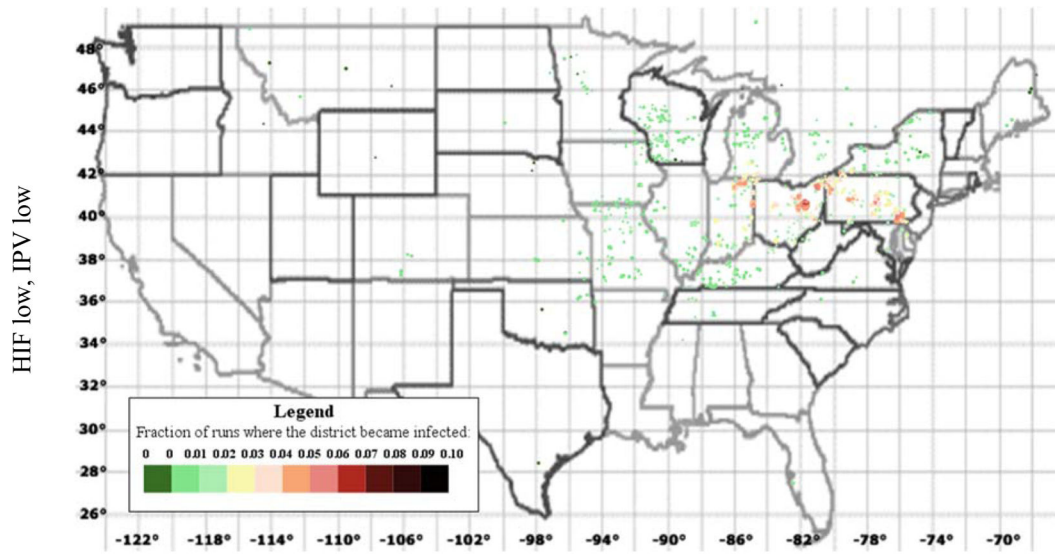


Figure 2: Histograms of the total fraction of people infected and paralytic cases per iteration for each HIF and IPV setting



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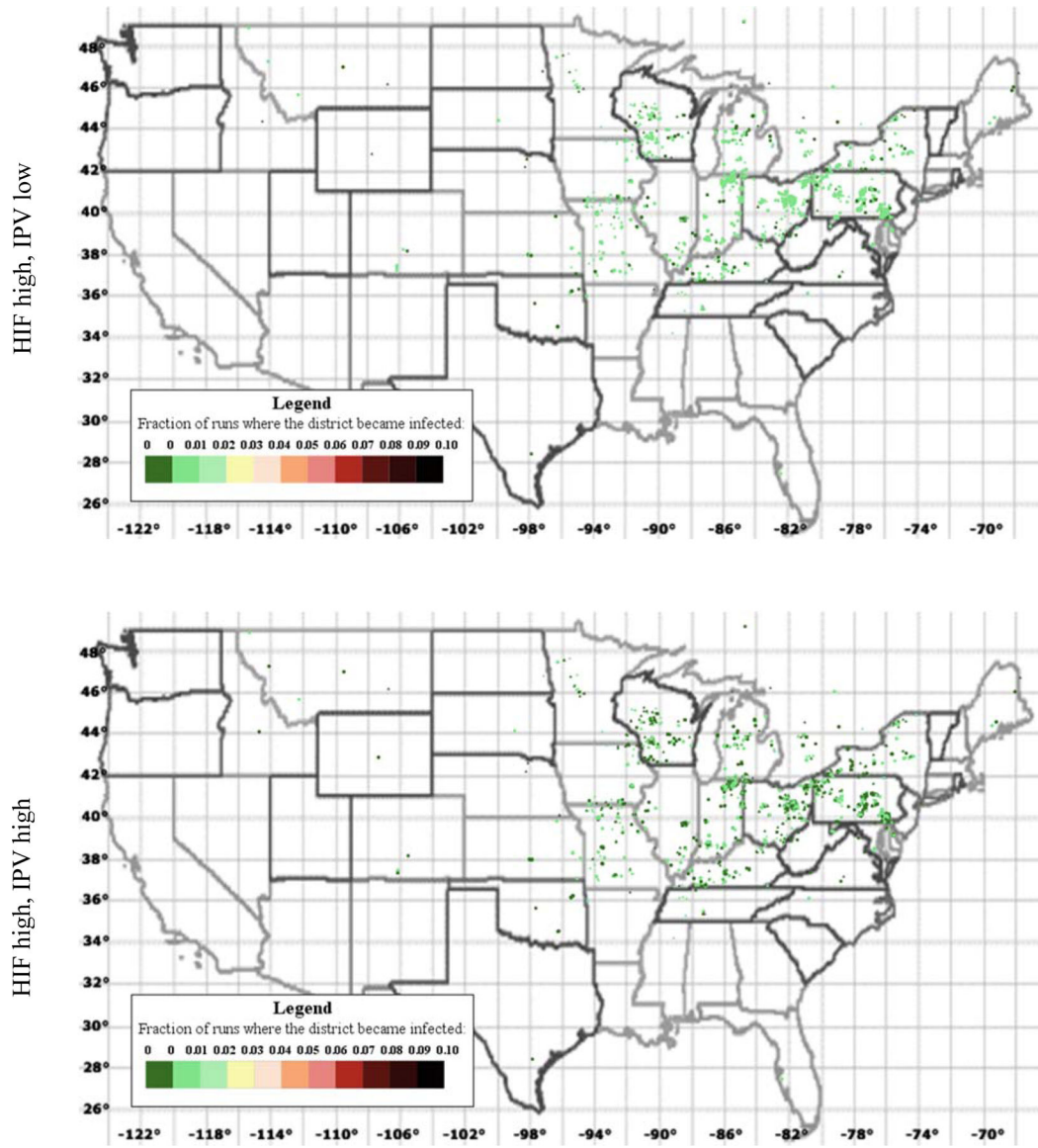


Figure 3:
Fraction of runs in which each district became infected using a map with linear scaling (i.e. stretched such that latitudes and longitudes conform to a perpendicular grid)

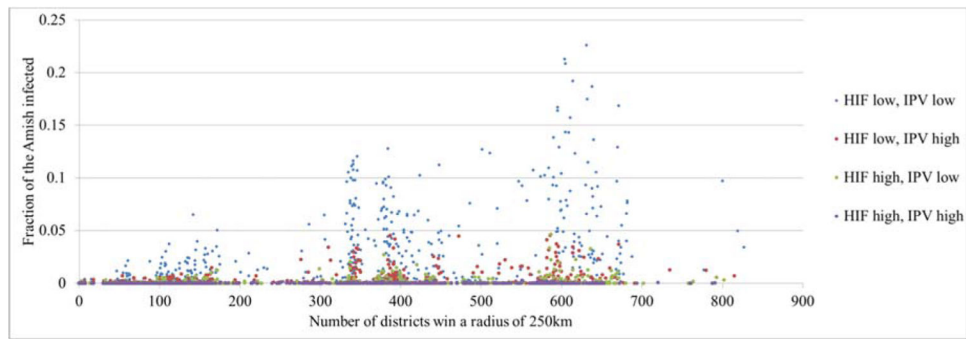


Figure 4: Relationship between district density, as measured by the number of Amish districts within 250 km of the point of virus introduction, and the total fraction of the Amish infected for all simulation runs in the main experiment

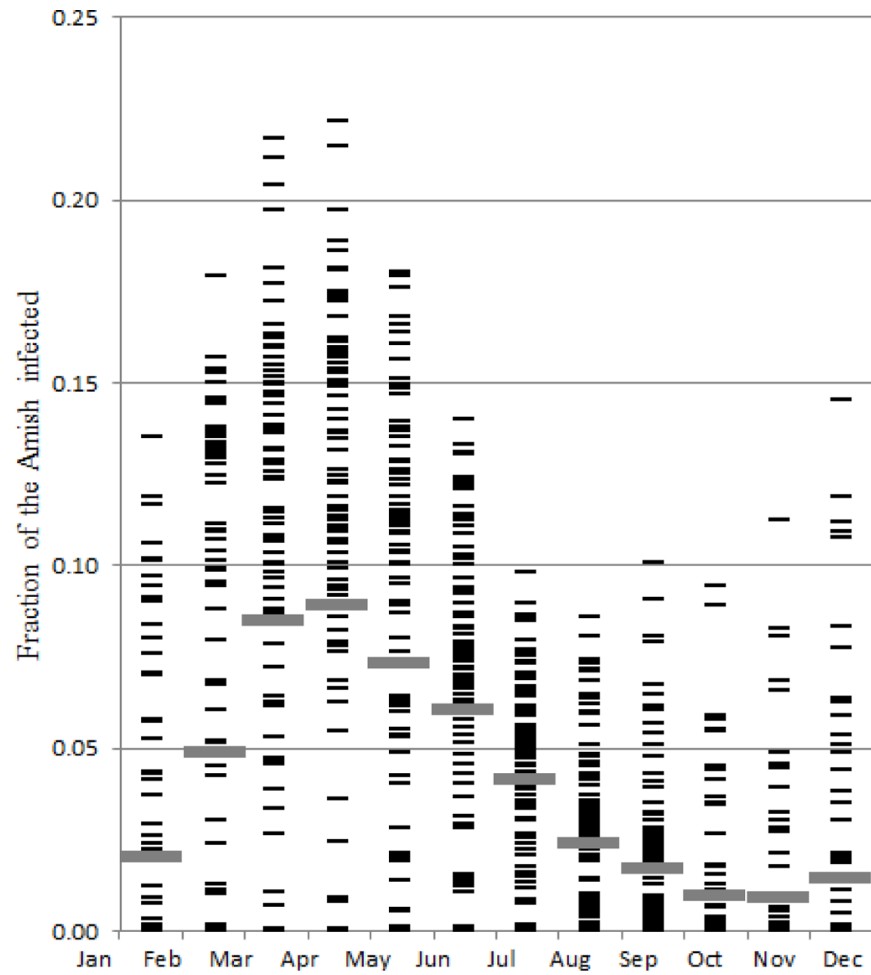


Figure 5: Relationship between month of introduction into a central district in Holmes County and the fraction of the North American Amish population infected assuming low HIF and low current IPV coverage (average and distribution over the 100 runs). The small black lines indicate results of individual runs, while the bigger grey lines represent the average for each month.

Table 1:

Values and sources for key model inputs related to poliovirus transmission

Model Input [symbol] ^{Source}	Value	
Relative susceptibility for the five immunity types[32]		
Fully susceptible	1	
1 recent LPV infection	0.42	
2 or more recent LPV infection	0.21	
1 historic LPV infection	0.8	
2 or more historic LPV infections	0.7	
Recent IPV vaccination (3 or more successful doses)	0.72	
Historic IPV vaccination (3 or more successful doses)	1	
Paralysis to infection ratio (if fully susceptible)[21]	0.005	
Relative infectiousness curves for the five immunity types[11]	Varies by immunity state and time (see Appendix A4)	
Probability distribution waning (i.e., the time between acquiring recent immunity and moving to historic immunity)[11]	Gamma distribution resulting from a 5-stage process with a total duration of 4 years (see Appendix A4)	
Seasonality in transmission probability per 30 minutes of activity [p_t] ^{a,b}		
– Constant during winter (Dec 15 - Mar 15)	0.004	
– Sinusoidal during the rest of the year	Amplitude 0.0028 Peak 0.0096 on July 31	
Multiplier for community contact compared to close contact [m]	0.1	
IPV coverage rates since 2000 (see text)	Lower bound	Upper bound
– High level of conservatism	0.3	0.7
– Medium level of conservatism	0.4	0.8
– Low level of conservatism	0.5	0.9

^aWe assume constant p_t during the winter, with a sine function for the rest of the year: $p_t = 0.0068 + 0.0028 * \sin(((t-143) / 276) * 2\pi)$, with t the numbered day of the year

^bCalibrated to yield R0 values consistent with prior work[32]

Table 2:

Key results for the main experiment for two different levels of assumed historic immunity and two levels of current vaccine acceptance

		HIF low, IPV low	HIF low, IPV high	HIF high, IPV low	HIF high, IPV high
Fraction of runs with no cases		0.513	0.734	0.826	0.975
Fraction of runs with >2 cases		0.374	0.14	0.062	0
Days to first case in runs with >2 cases		78	99	82	N/A
Days to second case in runs with > 2 cases		112	131	118	N/A
Days third case in runs with >2 cases		134	157	151	N/A
Number of cases	Min	0	0	0	0
	Mean	13	1	1	0
	Max	188	31	35	2
Fraction of the Amish infected	Min	<0.00	<0.00	<0.00	<0.00
	Mean	0.02	<0.00	<0.00	<0.00
	Max	0.23	0.05	0.05	<0.00
Fraction of districts infected	Min	0.00	0.00	0.00	0.00
	Mean	0.03	0.01	0.00	0.00
	Max	0.38	0.12	0.13	0.02
Duration of circulation (days)	Min	0	0	0	0
	Mean	87	142	35	57
	Max	720	861	393	588
Fraction of runs with >1% infected		0.30	0.07	0.03	0.00
Fraction of runs with >10% infected		0.12	0.00	0.00	0.00
Fraction of runs with >20% infected		0.04	0.00	0.00	0.00
Fraction of runs with >50% infected		0.00	0.00	0.00	0.00
Fraction of runs that last 1 year		0.64	0.85	0.94	1.00
Fraction of runs that last 2 years		0.97	1.00	1.00	1.00
Fraction of runs that last 3 years		1.00	1.00	1.00	1.00