Web Material

Impact of Public Health Responses During a Measles Outbreak in an Amish Community in Ohio: Modeling the Dynamics of Transmission

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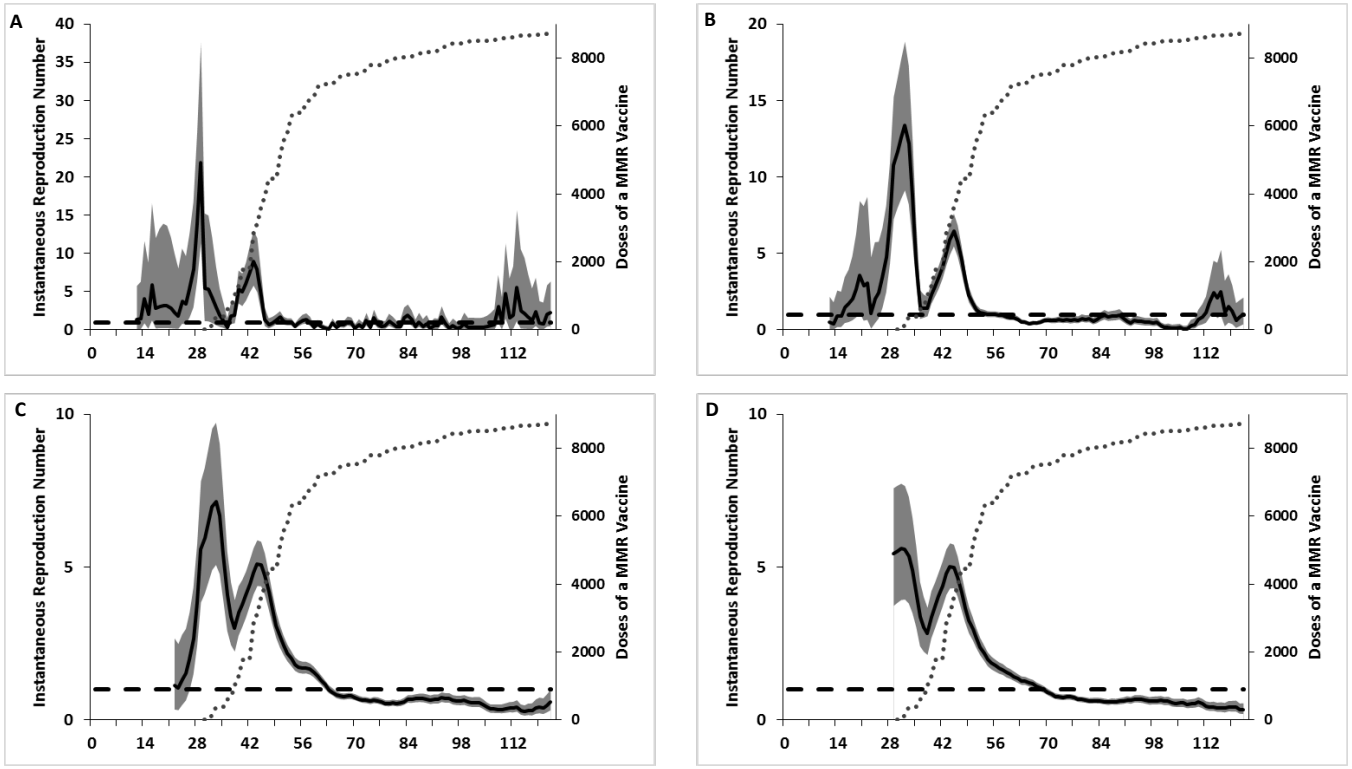
Web Appendix

Choice of time window

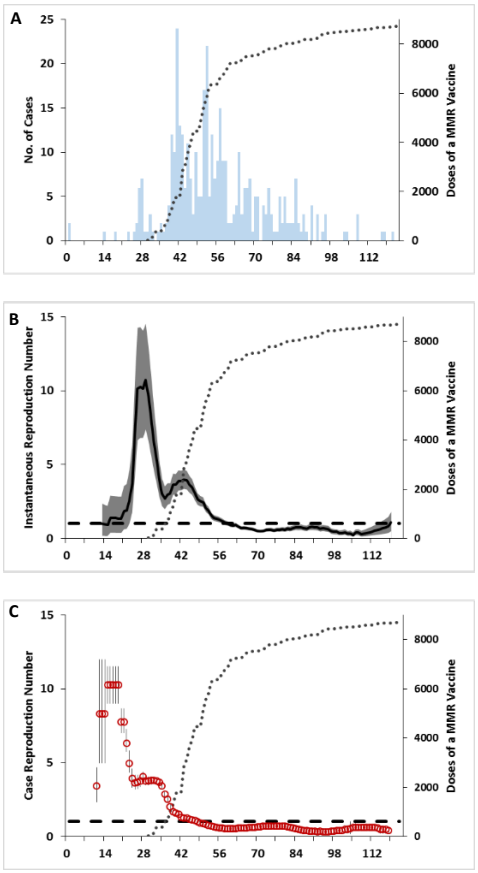
We evaluated the use of different time window widths to estimate R_t (Web Figure 1). As previously described (1), use of larger window sizes led to less variable and more precise R_t estimates, and to delays in the time needed for R_t to fall below 1. In these analyses, reductions in transmissibility coincided with containment measures irrespective of the choice of time window, and estimates remained at or near unity as control measures continued. Thus, selection of a 2-week window seemed appropriate for this evaluation.



Web Figure 1. Daily estimates of the instantaneous reproduction number R_t over sliding A) 1-day, B) 7-day, C) 21-day, and D) 28-day windows; the black line shows the median estimate, the shaded gray areas the 90% confidence intervals, and the horizontal dashed line the threshold value $R_t = 1$. Note that the scale of the axes differ. Superimposed in all figures is the cumulative number of daily doses of MMR vaccine given at local health department vaccination clinics during the outbreak.

Use of daily counts of onset of symptoms to estimate *R*

In our data set, the day of rash onset variable was more populated than the day of symptom onset variable, so rash onset dates were used to construct an epidemic curve and to infer a temporal pattern of *R*. Previous applications of this procedure, however, have used incidence data by day of symptom onset, as for many diseases including measles, infectiousness starts around the time of symptom onset (1–3). Below we present daily estimates of the instantaneous and case reproduction numbers derived from an epidemic curve based on days of illness onset. We show qualitatively similar patterns in transmissibility compared to that seen when using rash onsets, as well as reductions in transmissibility as containment measures start to get under way (Web Figure 2).



Web Figure 2. A) The daily epidemiologic curve; the daily total numbers of confirmed outbreak-associated measles case-patients in Ohio in 2014 according to day of illness onset are shown (N = 383); for 48 measles case-patients, the date of illness onset could not be determined, and the date of rash onset minus 2 days (the median number of days between illness onset and rash for all other cases) is shown. B) Daily estimates of the instantaneous reproduction number R_t over sliding 14-day windows; the black line shows the median estimate, the shaded gray areas the 90% confidence intervals, and the horizontal dashed line indicates the threshold value R_t = 1; C) Daily estimates of the case reproduction number (R_c) over sliding 14-day windows; the reds circle shows the mean estimate, the bars represent the 90% confidence intervals, and the horizontal dashed line indicates the threshold value R_c = 1. Superimposed in all figures is the cumulative number of daily doses of MMR vaccine given at local health department vaccination clinics during the outbreak.

Evaluation of a range of measles vaccine effectiveness at baseline

Similar results were obtained from models for a range of vaccine effectiveness at baseline (84.8% and 97.0%) (Web Table 1).

Web Table 1. Model Predictions of Measles Outbreak Sizes and Durations in an Amish Community in Ohio in 2014, With and Without the Vaccination Campaign[a], Based on Two Initial Levels (Lower and Upper Bounds) of MMR Coverage Prior to Initiation of Containment Efforts, and a Range of MMR Vaccine Effectiveness at Baseline[b]

Vaccine Effectiveness[b]	Assumed MMR Coverage[c]	No. of Measles Case-Patients[d]				Duration of Outbreak (days)[d]				Absolute Reduction	
		Vaccination Campaign Included									
		No		Yes		No		Yes			
		No.	90% CI	No.	90% CI	Duration	90% CI	Duration	90% CI	No.	Duration
84.8%	14% (lower)	19,346	19,317, 19,373	9,796	9,490, 10,079	215	198, 242	256	211, 321	9,550	-41
	68% (upper)	10,263	10,235, 10,282	1,301	168, 2,128	200	179, 224	168	138, 231	8,962	32
97.0%	14% (lower)	18,800	18,767, 18,823	9,247	8,939, 9,525	213	193, 239	257	213, 318	9,553	-44
	68% (upper)	7,596	7,613, 7,573	519	88, 1,193	194	174, 218	123	103, 135	7,077	71

[a] County health department clinics offering vaccination were held from day 30 to day 123 of the outbreak; first doses of MMR were delivered to 8,726 unvaccinated individuals.
[b] Based on a median vaccine effectiveness of 92.5% (IQR, 84.8%-97.0%) when vaccine was received ≥12 months (4).
[c] ≥1-dose MMR coverage.
[d] Values are the medians and 90% confidence intervals (CI) generated from 500 model simulations.

Evaluation of the effect of vaccination assuming an effectiveness of 90.5% for campaign doses

In these models, we assumed a vaccine effectiveness of 90.5% for campaign doses, based on the effectiveness of the vaccine as post-exposure prophylaxis (5), and incorporated this in the model by obtaining the product of the cases vaccinated per day and 0.905. Similar results were obtained from these models compared to our base model (Web Table 2).

Web Table 2. Model Predictions of Measles Outbreak Sizes and Durations in an Amish Community in Ohio in 2014, With and Without the Vaccination Campaign[a], Based on Two Initial Levels (Lower and Upper Bounds) of MMR Coverage Prior to Initiation of Containment Efforts, and Assuming a Vaccine Effectiveness of Campaign Doses of 90.5%

Assumed MMR Coverage[b]	No. of Measles Case-Patients				Duration of Outbreak (days)				Absolute Reduction	
	Vaccination Campaign Included									
	No		Yes		No		Yes			
	No.	90% CI	No.	90% CI	Duration	90% CI	Duration	90% CI	No.	Duration
14% (lower)	18,976	18,949, 19,006	10,438	10,196, 10,698	213	191, 232	248	209, 301	8,538	-35
68% (upper)	8,470	8,455, 8,492	952	217, 1602	198	178, 221	144	115, 161	7,518	54

[a] County health department clinics offering vaccination were held from day 30 to day 123 of the outbreak; first doses of MMR were delivered to 8,726 unvaccinated individuals; assuming a vaccine effectiveness of 90.5% (5), doses were effectively given to 7,897 individuals.

[b] ≥1-dose MMR coverage.

[c] Values are the medians and 90% confidence intervals (CI) generated from 500 model simulations.

Evaluation of delays in vaccine protection (immunologic response) and outbreak response

We evaluated the effect of a possible delay in vaccine protection (time for an immune response to develop), by delaying the vaccination campaign by 1 week (i.e., by adding 7 days to the day of vaccine receipt). Similarly, we studied the effect of the promptness in the public health response by advancing or delaying the vaccination campaign by 1 week. Assuming an initial vaccination coverage of 45%, every 7-day delay in initiating the vaccination campaign was associated with an approximate 500 additional cases by the end of the epidemic (Web Table 3). Delays in implementing immunization activities also led to shorter outbreak durations, presumably from high measles transmissibility and a rapid depletion of susceptible persons due to infection.

Web Table 3. Model Predictions of the Impact of Earlier or Delayed Initiation of the Vaccination Campaign on the Size and Duration of the Measles Outbreak in an Amish Community in Ohio in 2014, Assuming an MMR Coverage of 45% Prior to Initiation of Containment Efforts[b]

Timing of Initiation of the Vaccination Campaign	No. of Measles Case-Patients[c]	90% CI	Duration of Outbreak (days)[c]	90% CI
1 week earlier	2,890	2332, 3432	296	201, 439
Observed[a]	3,353	2,551, 4,003	247	183, 370
1 week later	3,829	2,785, 4,627	206	160, 320

[a] County health department clinics offering vaccination were held from day 30 to day 123 of the outbreak; first doses of MMR were delivered to 8,726 unvaccinated individuals.
[b] ≥1-dose MMR coverage.
[c] Values are the medians and 90% confidence intervals (CI) generated from 500 model simulations.

Modeled outcomes using an infectious period of 5 days

Models including the vaccination campaign using an infectious period of 5 days show somewhat larger final outbreak sizes, and thus the number of cases averted is smaller (although not considerably different), presumably because the disease is going through the population at a faster rate (the estimates also had shorter outbreak durations). When comparing the expected (as predicted by the model) and the observed number of cases, prior to the initiation of control measures, using this shorter period led to a an overestimation of the number of cases compared to what was observed early during the outbreak, which may be the result of the assumption of homogenous mixing. Both our base model and this model show that the number of cases averted by vaccination efforts is significant, and highlight the potential importance of other control measures and of social behavior. These results are presented in Web Table 4.

Web Table 4. Model Predictions of Measles Outbreak Sizes and Durations in an Amish Community in Ohio in 2014, With and Without the Vaccination Campaign[a], Based on Two Initial Levels (Lower and Upper Bounds) of MMR Coverage Prior to Initiation of Containment Efforts, and Using a Period of Infectiousness of 5 Days

Assumed MMR Coverage[b]	No. of Measles Case-Patients				Duration of Outbreak (days)				Absolute Reduction	
	Vaccination Campaign Included									
	No		Yes		No		Yes			
	No.	90% CI	No.	90% CI	Duration	90% CI	Duration	90% CI	No.	Duration
14% (lower)	18,975	18,939, 19,001	10,332	9,415, 10,920	179	150, 200	169	141, 229	8,643	10
68% (upper)	8,471	8,449, 8,488	1,947	191, 3,332	161	137, 186	123	109, 135	6,524	38

[a] County health department clinics offering vaccination were held from day 30 to day 123 of the outbreak; first doses of MMR were delivered to 8,726 unvaccinated individuals.

[b] ≥1-dose MMR coverage.

[c] Values are the medians and 90% confidence intervals (CI) generated from 500 model simulations assuming a contagious period of 5 days.

Calculation of doubling time

The period of time required for the number of cases to double, or doubling time T_d, was estimated during the exponential growth phase, in the early stages of this outbreak, using the following formula (6, 7):

$T_d \approx \ln 2(T)/\ln[N_1/N_0]$,

where N_1 and N_0 are the number of cases at times t_1 and t_0, respectively, and T is the time interval between t_1 and t_0. Based on the observed epidemic curve, there were 2 cases by day 13 and 96 cases by day 42 of the outbreak. Substituting these numbers into the equation yields a doubling time T_d of 5.2 days.

Differential equation representation of model structure

General structure of the model using differential equations; the model was a direct stochastic implementation of this differential equation model. The equations describe the rate of change in the number of susceptible (S), pre-infectious (E), infectious (I), immune (R) individuals at time *t*. β is the rate at which two specific individuals come into effective contact, σ is the rate at which pre-infectious individuals become infectious; and γ is the rate at which infectious individuals recover or become immune, per unit time. θ is the rate at which unvaccinated individuals are removed from the susceptible and added to the recovered category through vaccination; we had detailed data on the uptake of vaccination during the campaign (i.e., dates of vaccine administration), so individuals from the susceptible class were moved to the recovered/immune class based on the day of measles vaccine receipt. Unlike other model structures (8, 9), the model does not have a vaccine compartment, e.g., to keep track of vaccine recipients who were not successfully immunized through vaccination.

$$\frac{dS(t)}{dt} = -\beta I(t)S(t) - \theta(t)S(t)$$

$$\frac{dE(t)}{dt} = \beta I(t)S(t) - \sigma E(t)$$

$$\frac{dI(t)}{dt} = \sigma E(t) - \gamma I(t)$$

$$\frac{dR(t)}{dt} = \gamma I(t) + \theta(t)S(t)$$

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