Science Advances
AAAS

advances.sciencemag.org/cgi/content/full/6/9/eaax0586/DC1

Supplementary Materials for

Surveillance data confirm multiyear predictions of rotavirus dynamics in New York City

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Published 26 February 2020, *Sci. Adv.* **6**, eaax0586 (2020)
DOI: 10.1126/sciadv.aax0586

The PDF file includes:

Supplementary Materials and Methods

Rotavirus transmission model details

The differential equations describing the rotavirus transmission model are as follows

$$\frac{dM_a}{dt} = B(t) - \omega_M M_a - \mu_a M_a + (1 - \nu_{1,a}(t))\mu_{a-1} M_{a-1}$$

$$\frac{dS_{0,a}}{dt} = \omega_M M_a - \lambda_a(t) S_{0,a} - \mu_a S_{0,a} + (1 - \nu_{1,a}(t))\mu_{a-1} S_{0,a-1}$$

$$\frac{dI_{1,a}}{dt} = \lambda_a(t) S_{0,a} - \gamma_1 I_{1,a} - \mu_a I_{1,a}$$

$$\frac{dR_{1,a}}{dt} = \gamma_1 I_{1,a} - \omega_1 R_{1,a} - \mu_a R_{1,a} + \nu_{2,a}(t)\mu_{a-1}(M_{a-1} + S_{0,a-1}) + (1 - \nu_{2,a}(t))\mu_{a-1} R_{1,a-1}$$

$$\frac{dS_{1,a}}{dt} = \omega_1 R_{1,a} - \sigma_1 \lambda_a(t) S_{1,a} - \mu_a S_{1,a} + (1 - \nu_{2,a}(t))\mu_{a-1} S_{1,a-1}$$

$$\frac{dI_{2,a}}{dt} = \sigma_1 \lambda_a(t) S_{1,a} - \gamma_2 I_{2,a} - \mu_a I_{2,a} + \mu_{a-1} I_{2,a-1}$$

$$\frac{dR_{2,a}}{dt} = \gamma_2 I_{2,a} - \omega_1 R_{2,a} - \mu_a R_{2,a} + \mu_{a-1} R_{2,a-1} + \nu_{2,a}(t)\mu_{a-1}(R_{1,a-1} + S_{1,a-1})$$

$$\frac{dS_{2,a}}{dt} = \omega_1 R_{2,a} + \omega_2 R_{A,a} - \sigma_2 \lambda_a(t) S_{2,a} - \mu_a S_{2,a} + \mu_{a-1} S_{2,a-1}$$

$$\frac{dI_{A,a}}{dt} = \sigma_2 \lambda_a(t) S_{2,a} - \gamma_2 I_{A,a} - \mu_a I_{A,a} + \mu_{a-1} I_{A,a-1}$$

$$\frac{dR_{A,a}}{dt} = \gamma_2 I_{A,a} - \omega_2 R_{A,a} - \mu_a R_{A,a} + \mu_{a-1} R_{A,a-1}$$

where μ_a is the rate of aging out of age group a, and $\nu_{1,a}(t)$ and $\nu_{2,a}(t)$ are the proportion of individuals of age a who received and responded to the first and second dose of rotavirus

vaccine, respectively, at time t (=0 for all $a \neq 2$). All other model parameters are described in the main text and listed in Table S2. Fixed parameter estimates were based on a seminal birth cohort study by Velázquez et al (*25*). Other studies have suggested that there is a short-lived period of immunity following infection (*41–43*), while household transmission studies and viral shedding data highlighted the important role of children as sources of infection (*44*, *45*).

The force of infection is given by: $\lambda(t) = \beta(t)(I_1(t) + \rho_2 I_2(t) + \rho_A I_A(t))$, where $\beta(t)$ is the seasonally-varying transmission parameter. Seasonality in the rate of transmission is modeled using a simple sinusoidal function, such that $\beta(t) = \beta_0(1 + b\cos(2\pi(t - \phi)))$, where β_0 is the baseline transmission rate, b is the amplitude of seasonality, and ϕ is the seasonal offset parameter. We assumed homogeneous mixing, such that all individuals are equally likely to contact one another, but that children <1 year of age, 1-year olds, and 2-year olds were at increased risk of acquiring rotavirus (c_0, c_1, and c_2, respectively), after exploring other mixing assumptions (*9*). We assumed that only a proportion h of moderate-to-severe RVGE cases (D) were hospitalized when fitting our model to the age-specific hospitalization data. The reporting fraction h and the transmission parameters (β_0, a, ϕ, c_0, c_1, c_2) were previously estimated by maximum likelihood (Table S2) (*9*), assuming that the observed number of hospitalization among individuals of age a in month t was Poisson-distributed with mean equal to the model-predicted incidence $hD_{a,t}$, where $D_{a,t}$ is the number of incident cases in age group a: $D_{a,t} = d_1\lambda_a(t)S_{0,a}(t) + d_2\lambda_a(t)S_{1,a}(t)$.

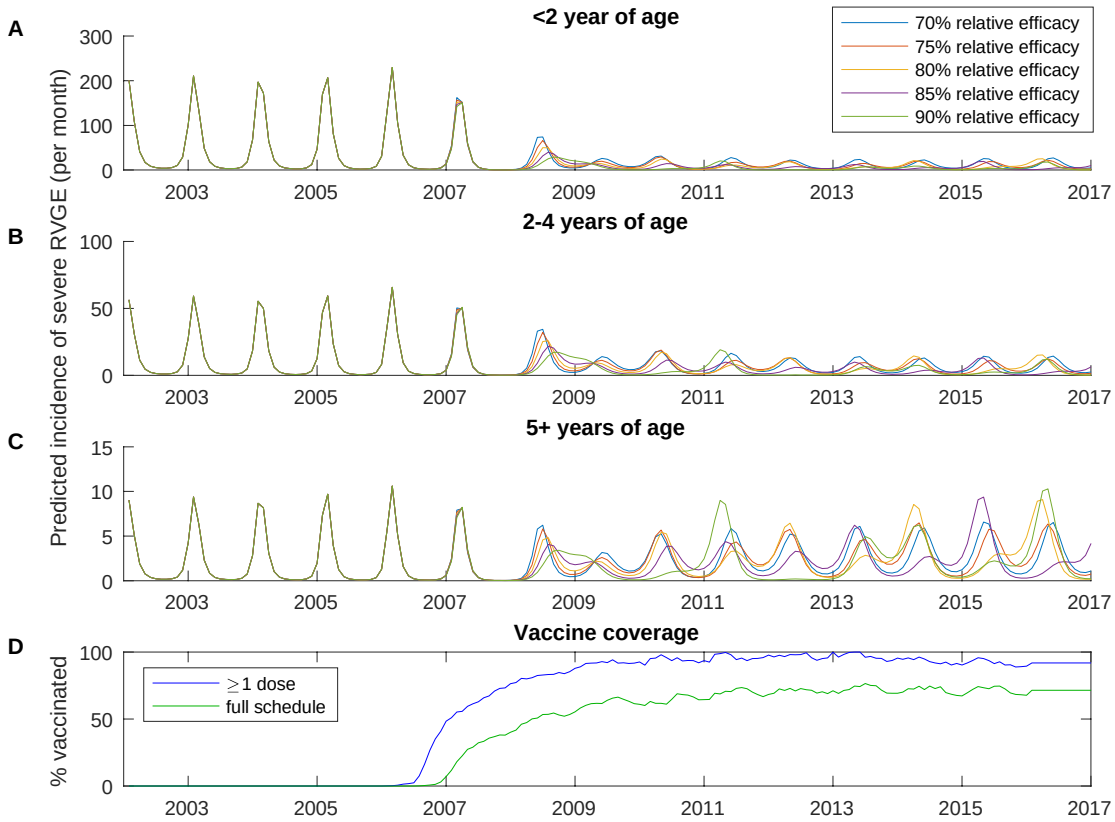

Fig. S1. Predicted incidence of severe RVGE in New York, 2002–2016, for different values of the relative efficacy of the first vaccine dose. Dynamic model predictions are based on a previously described mathematical model fit to monthly hospitalization data from New York State (1993-2004), which was simulated to predict the impact of vaccination through 2016. Model predictions for the weekly incidence of moderate-to-severe rotavirus-associated gastroenteritis in children (**A**) <2 years old, (**B**) 2-4 years old, and (**C**) ≥5 years old are plotted. (**D**) Vaccine coverage used in the model are based on estimates of coverage with at least one dose (blue) and the full series (green) from the Citywide Immunization Registry. We assumed a relative efficacy of an incomplete vaccine course ranging from 70-90%.

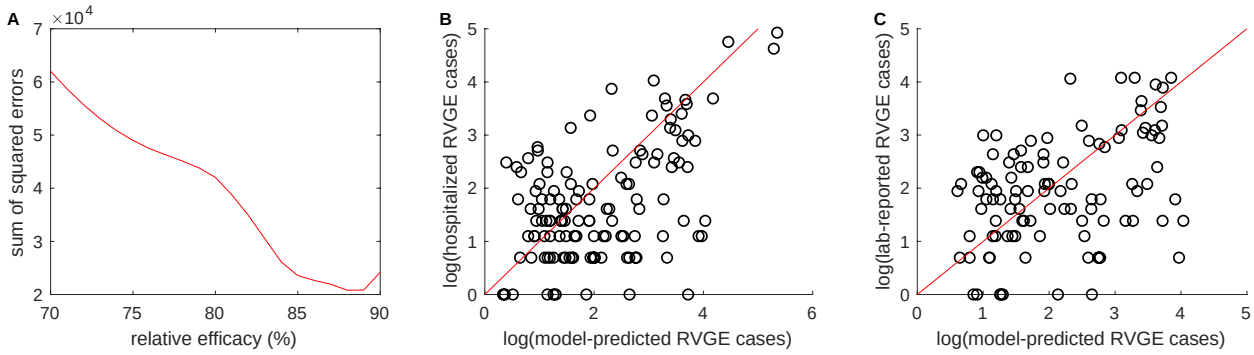

Fig. S2. Fit of model to laboratory-reported rotavirus cases for different values of the relative efficacy of one vaccine dose. (**A**) The sum of the squared difference between the model-predicted number of RVGE cases per month and the observed number of hospitalized and laboratory-confirmed cases from January 2008 through December 2016 for values of the relative efficacy of one vaccine dose between 70-90%. The sum of squared errors is minimized with a relative efficacy of 88%. (**B**) Scatter plot of the log of the number of model-predicted RVGE cases per month versus the log of the observed monthly number of rotavirus-coded hospitalizations. (**C**) Scatter plot of the log of the number of model-predicted RVGE cases per month versus the log of the observed monthly number of laboratory-reported RVGE cases. The red line in (B) and (C) represents a perfect 1:1 correspondence.

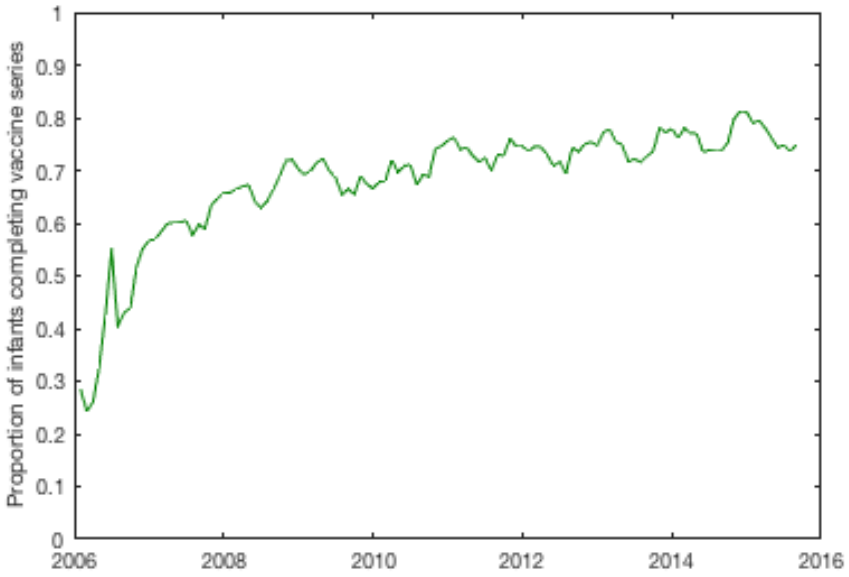

Fig. S3. Proportion of infants completing a full rotavirus vaccine series. The proportion of infants who completed the rotavirus vaccine series (at least 3 doses of RotaTeq, at least 2 doses of Rotarix, or at least 3 doses of a combination of the two vaccines) was calculated by dividing the proportion of infants receiving at least 1 dose by the proportion of infants receiving the full vaccine course at a lag of 4 months.

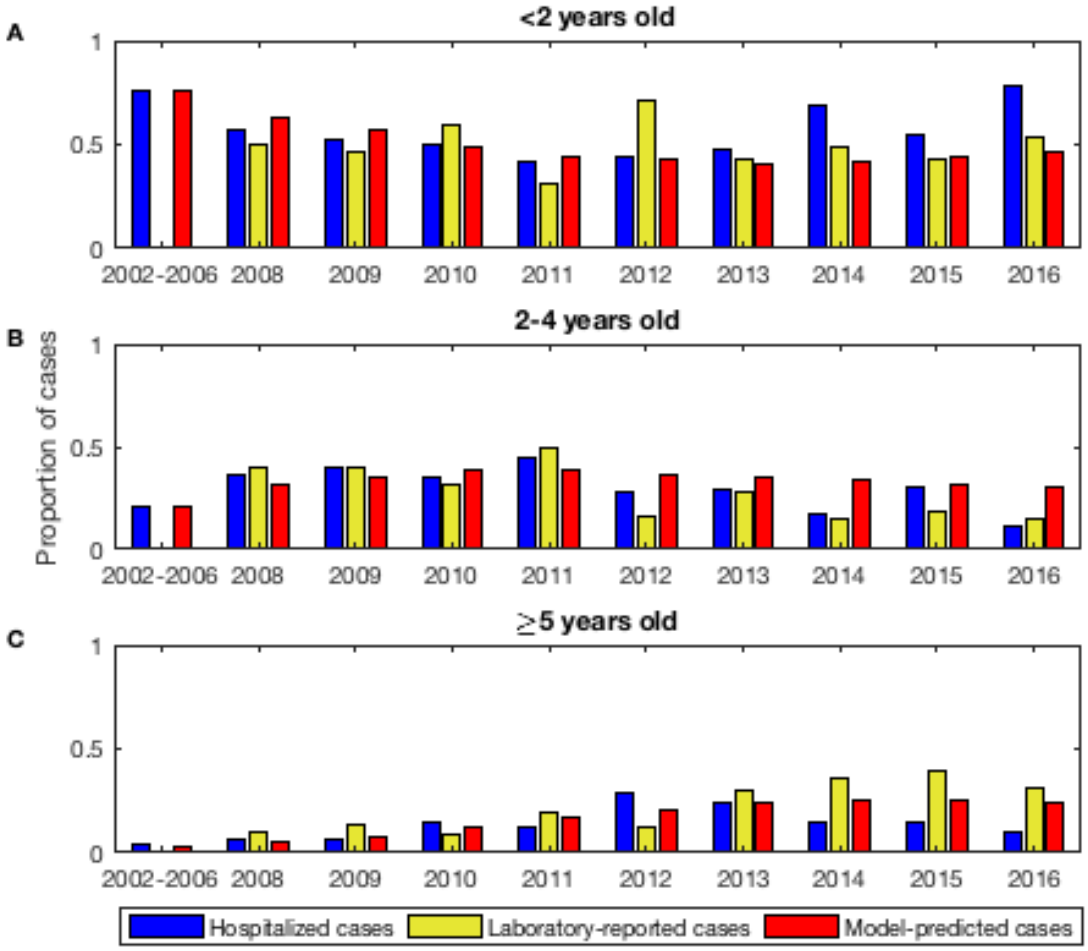

Fig. S4. Age distribution of rotavirus-coded hospitalizations, laboratory-reported cases, and model-predicted RVGE cases. The proportion of cases in each of three age groups (<2 years old, 2-4 years old, or ≥5 years old) is plotted by rotavirus season (July-June) for the pre-vaccination period (July 2002-June 2006) and for each post-vaccination season. The year listed corresponds to the second half of the rotavirus season (e.g. 2008 corresponds to the July 2007-June 2008 rotavirus season).

Table S1. Rotavirus-coded hospitalizations and laboratory-reported cases in New York City, 2002–2016. The number and percent of rotavirus principal or other diagnosis inpatient admissions by residents to New York City hospitals are shown by age group for ICD-9CM code '008.61' and ICD-10CM code 'A08.0' during each rotavirus season, from January 2002 through June 2016. The number and percent of confirmed rotavirus cases reported by New York City laboratories are shown by age group for February 2008 through June 2016. Rotavirus periods cover the 12 months July through June, with the exception of 2008 which was incomplete. The 2008 season included hospitalizations from July 2007 through June 2008, but laboratory reported cases only for February through June 2008, since laboratory rotavirus case data were only available after rotavirus became a reportable disease in January 2008 in New York City.

Rotavirus Coded-Hospitalizations and Laboratory-Reported Cases Before (2002-2006) and After (2008-2016) Rotavirus Vaccine Introduction										
Age (years)	**2002-2006 average**	**2008***	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**
Rotavirus-Coded Hospitalizations, Count (Percent of Total)										
<2y	407 (76.3%)	82 (56.9%)	90 (52.9%)	42 (50.0%)	52 (41.9%)	27 (43.5%)	51 (47.2%)	28 (68.3%)	44 (55.0%)	33 (78.6%)
2-4y	107 (20.0%)	52 (36.1%)	68 (40.0%)	30 (35.7%)	56 (45.2%)	17 (27.4%)	31 (28.7%)	7 (17.1%)	24 (30.0%)	5 (11.9%)
≥5y	20 (3.7%)	10 (6.9%)	12 (7.1%)	12 (14.3%)	16 (12.9%)	18 (29.0%)	26 (24.1%)	6 (14.6%)	12 (15.0%)	4 (9.5%)
All ages	534	144	170	84	124	62	108	41	80	42
Laboratory-Reported Rotavirus Cases, Count (Percent of Total)										
<2y	-	50 (50.5%)	111 (46.3%)	32 (59.3%)	20 (31.7%)	22 (71.0%)	66 (42.6%)	40 (49.4%)	93 (42.7%)	67 (54.0%)
2-4y	-	39 (39.4%)	96 (40.0%)	17 (31.5%)	31 (49.2%)	5 (16.1%)	43 (27.7%)	12 (14.8%)	40 (18.3%)	19 (15.3%)
≥5y	-	10 (10.1%)	33 (13.8%)	5 (9.3%)	12 (19.0%)	4 (12.9%)	46 (29.7%)	29 (35.8%)	85 (39.0%)	38 (30.6%)
All ages	-	99	240	54	63	31	155	81	218	124
Model-Predicted Rotavirus Cases, Count (Percent of Total)										
<2y	569.9 (75.4%)	49.4 (62.5%)	222.3 (56.9%)	30.8 (48.3%)	109.4 (44.3%)	11.7 (43.1%)	71.9 (40.7%)	21.8 (41.2%)	88.6 (43.6%)	23.9 (45.9%)
2-4y	160.1 (21.2%)	25.2 (31.9%)	139.0 (35.6%)	24.8 (38.9%)	95.6 (38.7%)	10.0 (36.9%)	62.1 (35.2%)	17.8 (33.7%)	63.3 (31.2%)	15.7 (30.1%)
≥5y	25.7 (3.4%)	4.5 (5.7%)	29.5 (7.6%)	8.2 (12.9%)	42.0 (17.0%)	5.5 (20.1%)	42.7 (24.2%)	13.2 (25.1%)	51.2 (25.2%)	12.5 (24.1%)
All ages	755.7	79.1	390.8	63.8	247.0	27.2	176.7	52.7	203.1	52.2

Table S2. Fixed and estimated parameter values.

Fixed parameters	***Variable***	***Value***	***Source***
Birth rate	$B(t)$	0.0120 to 0.0165 $year^{-1}$	(*46*)
Duration maternal immunity	$1/\omega_M$	3 months	(*47*)
Duration of infectiousness			
First infection	$1/\gamma_1$	1 week	(*48*)
Subsequent infections	$1/\gamma_2$	0.5 week	(*49*–*51*)
Duration of temporary immunity			
Following first and second infection	$1/\omega_1$	9 months	(*42*, *43*)
Following subsequent infections	$1/\omega_2$	12 months	(*41*, *50*)
Relative risk of reinfection			
Following first infection	σ_1	0.62	(*25*)
Following second infection	σ_2	0.35	(*25*)
Relative infectiousness			
Second infection	ρ_2	0.5	(*44*, *45*), Assumption
Subsequent infections	ρ_A	0.1	(*44*, *45*), Assumption
Proportion of individuals with moderate-to-severe RVGE			
First infection	d_1	0.13	(*25*)
Second infection	d_2	0.03	(*25*)
Estimated parameters	***Variable***	***Maximum-likelihood estimate***	
Baseline transmission rate (per person per month)	β_0	1.49×10^{-5}	(*9*)
Reporting fraction (mean)	h	0.037	
Amplitude of seasonality in transmission	b	0.049	
Phase shift of seasonal transmission	ϕ	0.678	
Relative risk of infection for <1 year olds	c_0	1.57	
Relative risk of infection for 1-year olds	c_1	2.08	
Relative risk of infection for 2-year olds	c_2	1.50	