SUPPLEMENT: “When do elementary students need masks in school? Model-estimated risk of in-school SARS-CoV-2 transmission and related infections among household members before and after student vaccination”

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Table S1. Selected input parameters for agent-based dynamic transmission model of 30-day SARS-CoV-2 outcomes in elementary schools

	Values	Source
Adult-to-adult daily attack rate*		
Wild type	2.0%	See below
Alpha	3.5%	See below
Delta	7.0%	See below
Infectiousness (relative to symptomatic adults)		
Student	0.5	Baseline model parameter from Bilinski et al.[1]
Asymptomatic adult	0.5	
Susceptibility (relative to adults)		
Student	0.5	Baseline model parameter from Bilinski et al.[1]
Infectious period		
All Individuals	Lognormal (5,2)	Baseline model parameter from Bilinski et al.[1]
Hospitalization risk after SARS-CoV-2 infection**		
Student	0.29% (for 0% vaccine uptake) 0.26% (for 50% vaccine uptake)	See below
Adult	1.93%	See below
Vaccine uptake		
Student	0% and 50%	Assumption
Adult	70%	Assumption
Vaccine Effectiveness		
All Individuals	90% reduction in infection risk	CDC[2]
Risk of Community Exposure		
Student	3 times observed community incidence rate	Assumption
Adults	3 times observed community incidence, divided by fraction of population susceptible***	Assumption
Mitigation effectiveness****		
A: Simple ventilation and handwashing	20-40%	See below
B: A, plus universal masking of elementary students and educators/staff	70-80%	See below
C: “2020-2021 package of interventions”	90-100%	See below

* Adult-to-adult daily attack rate: Based on calibration analyses described in previous work (Bilinski et al.[1]), the adult-to-adult wild-type variant attack rate was assumed to be 2% per day. This is also consistent with data from school settings with minimal mitigation; a lower-bound estimate from CDC data suggest a total in-school attack rate of 11%,[3] corresponding to a daily attack rate near 2% (assuming a constant daily attack rate over a 5 day infectiousness period). The transmissibility of the alpha variant is estimated at 59% higher than wild type in the US,[4] so we assumed a daily attack rate of 3.5%. The delta attack rate has been estimated at 60% higher than that for the alpha variant in a setting with high vaccine uptake,[5] and a case study of a recent outbreak in a largely unvaccinated population reported an overall household delta attack rate of 53%,[6] corresponding to a daily attack rate of approximately 7% per school day (again assuming a 5 day infectiousness period and an in-school attack rate approximately half the household attack rate). In order to reflect the baseline attack rate, the estimate from the largely unvaccinated population was used. The student-to-student daily attack rate was assumed to be one-quarter of the adult-to-adult rate to reflect the assumption that students are both 50% less infectious and 50% less susceptible to infection.

** Hospitalization risk following SARS-CoV-2 infection: The hospitalization risk among unvaccinated patients with SARS-CoV-2 was assumed to be the overall infection fatality rate divided by the mortality rate among hospitalized patients, using estimates provided by the CDC for use in COVID-19 models[7]; the 0-17 year old age group (20/million IFR; 0.7% hospitalized mortality rate) was used for the student estimate and the 18-49 year old age group (500/million IFR; 2.1% hospitalized mortality rate) was used for the adult estimate. The overall hospitalization risk among both unvaccinated and vaccinated patients was calculated using the vaccine coverage scenarios implemented in the model and assuming that the risk of infection in vaccinated individuals was 90% lower than the risk in unvaccinated individuals. Adult values applied to educators/staff and to adult household members of both students and educators/staff. The 2% hospitalization rate used for adults is similar to inputs in other models, such as the low estimate used by Lemaitre et al.[8]

*** Risk of community exposure was inflated by the fraction of population susceptible (i.e., unvaccinated and potential breakthrough cases), so that actual case rate among adults matches the assumed community incidence rate.

**** Mitigation measures:

A: Simple ventilation and handwashing: open windows if present, portable air filters, maintain existing HVAC systems, and regular handwashing. Vouriot et al.[9] estimate that seasonal changes in ventilation increase secondary infections by 30-40% in fall and 80-90% in winter relative to summer, but note there is wide variation based on classroom activities. If an intervention replicates summer-levels of ventilation, this would correspond to a 23-29% reduction in the attack rate in the fall and a 44-47% reduction in the winter. Burridge et al.[10] also present a wide range of studies on ventilation and surface cleaning, some of which show good ventilation (i.e., opening windows) could reduce the risk of infections by about half in an office setting (which is often less active than a classroom). Data from airflow studies estimate reduction in exposure to aerosols of 65% with portable HEPA filters.[11] Combining these data, we estimated a range of 20-40% risk reduction (since most classrooms will not have access to portable air cleaners).

B: Intervention in A, plus universal masking: a policy of masking all students and educators/staff, accounting for the impact of imperfect adherence and technique. The IHME COVID-19 Forecasting Team conducted a meta-analysis that estimated using non-medical masks was associated with a 43% or 35% reduction in respiratory virus infection risk.[12] Additively combining these risk reductions with the risk reductions in the group A interventions generated the assumed range of 70-80% effectiveness for this group of interventions. It should be noted that, though, that there is large uncertainty in this effect, and the effectiveness will likely depend on the specific context of mask use. For example, some non-school case studies suggest reductions in infection risk of 70-

79% with masking.[13] Data from studies of simulated respiratory particles demonstrate fitted filtration efficiency values (proportion of particles kept behind a mask) of 50-79% with cloth masks.[14,15]

C: Combination interventions as implemented in many settings in the 2020-2021 school year: Includes B, plus physical distancing of 3-6 feet when masked and >6 when unmasked, daily cleaning of surfaces, restrictions on shared items, and cohorting of students.[16] This is the assumed maximum mitigation effect. CDC reports very effective in-school mitigation when the full package of interventions are implemented,[14] including those from Falk et al.[17] and Zimmerman et al.[18] Many studies reported total in-school secondary attack rates of 0.5-1.0% with implementation of this package of interventions; this corresponds to a 93% reduction on the unmitigated wild-type SAR.

While clinical data are available for C, data about the effectiveness of A and B were derived from limited data cited above, as well as expert opinion, and should be used only as approximations to estimate the impact of individual mitigation interventions.

Model code and additional information on the methods used are available at: https://github.com/abilinski/BackToSchool2/tree/master/3 - Scripts/Paper 3 (code) and https://github.com/abilinski/BackToSchool2/tree/master/5 - Drafts/Paper 3 (methods description).

Methods

To generate Figures 1 and 2, we generated 550,000 paired samples of observed community incidence and mitigation effectiveness using Latin hypercube sampling to draw from a joint independent uniform distribution with limits of 0 to 60 case notifications/100k/day and 0 to 100% mitigation. For each scenario in each paired sample, we ran the model presented in Bilinski et al.[1] using the model code available at https://github.com/abilinski/BackToSchool2/tree/master/3 - Scripts/Paper 3, varying the following parameters: (1) baseline daily adult-to-adult secondary attack rates of 2% (reflecting the wild-type virus), 3.5% (alpha variant), and 7% (delta variant); (2) child vaccination coverage of 0% and 50%; (3) adult vaccination coverage of 50% and 70%; and (4) remote and in-school instruction. We assumed reduced transmission and susceptibility for children and for asymptomatic adults (Table S1). To calculate in-school transmissions presented in Figure 1, we analyzed only model runs for in-person instruction and calculated the number of transmissions occurring in the school building (classrooms, staff rooms, and random interactions). To calculate average additional infections among the immediate school community during in-school instruction relative to remote instruction, for each paired sample, we subtracted the total number of infections during remote instruction from the number of total infections during in-school instruction.

To generate smoothed heatmaps and associated contour line estimates, we fit regressions to the raw model output for each outcome and associated scenario (e.g., more than one in-school transmission in the wild-type, 0% child vaccine, 70% adult vaccine scenario) as a function of observed community incidence and mitigation effectiveness. We tested five specifications: linear, quadratic, cubic, and quartic polynomials, as well as linear regression with a log transformation on each predictor:

- Linear specification: $Outcome = \beta_0 + \beta_1 Incidence + \beta_2 Mitigation + \beta_3 Incidence * Mitigation$
- Quadratic specification: $Outcome = \sum_{k=0}^{2}\sum_{l=0}^{2}\beta_{k,l} Incidence^k * Mitigation^l$
- Cubic specification: $Outcome = \sum_{k=0}^{3}\sum_{l=0}^{3}\beta_{k,l} Incidence^k * Mitigation^l$
- Quartic specification: $Outcome = \sum_{k=0}^{4}\sum_{l=0}^{4}\beta_{k,l} Incidence^k * Mitigation^l$
- Log specification: $Outcome = \beta_0 + \beta_1 \ln Incidence + \beta_2 \ln Mitigation + \beta_3 \ln Incidence * \ln Mitigation$

For each scenario, we selected the regression which minimized the root mean-squared prediction error in a hold-out test set containing 55,000 (10%) of the samples.

To assess how well the smoothing functions fit the expected value of the model output, we calculated the R^2 between binned averages of the model-generated outcomes in an out-of-sample test set and the average outcome predicted by the selected smoothing function across the range of community incidence and mitigation values. We evaluated the fit for two different bin sizes: “large” bins, with a bin width of 5 for community incidence and 0.1 for mitigation effectiveness, and “small” bins with a bin width of 1 for community incidence and 0.1 for mitigation effectiveness (Table S2). While noise persists in the additional infections outcome for scenarios with lower infection rates (wild type and alpha) due to a larger relative impact of model stochasticity (which is more pronounced in the small bins), these do not impact the substantive conclusions presented in the letter. For additional context on the smoothing process, we present empirical and smoothed bin estimates (for both bin sizes) for the additional infections outcome in Figures S5-S8; raw binned heatmaps are presented in Figures S9-S16. Figures S5-

S8 show that despite stochasticity, the smoothing functions used for the heatmaps (Figures 1-2, S1-S2) do not deviate from the raw model output in a way that impacts letter conclusions.

Table S2. Test sample R^2 for heatmap smoothing functions. Estimates of R^2 were made on an out-of-sample test set.

Outcome	Adult Vaccination	Child Vaccination	Variant	R^2 with Binned Model Output	
				Large Bins	Small Bins
Probability of at least one in-school transmission	70%	0%	Delta Variant	0.99	0.97
			Alpha Variant	>0.99	0.98
			Wild-type	>0.99	0.98
		50%	Delta Variant	>0.99	0.98
			Alpha Variant	>0.99	0.98
			Wild-type	0.99	0.97
	50%	0%	Delta Variant	0.99	0.97
			Alpha Variant	0.99	0.98
			Wild-type	>0.99	0.99
		50%	Delta Variant	0.99	0.98
			Alpha Variant	>0.99	0.98
			Wild-type	>0.99	0.98
Additional cases in school community	70%	0%	Delta Variant	>0.99	0.98
			Alpha Variant	0.98	0.92
			Wild-type	0.94	0.74
		50%	Delta Variant	0.98	0.91
			Alpha Variant	0.92	0.64
			Wild-type	0.71	0.29
	50%	0%	Delta Variant	>0.99	0.99
			Alpha Variant	0.99	0.93
			Wild-type	0.95	0.79
		50%	Delta Variant	0.98	0.92
			Alpha Variant	0.92	0.69
			Wild-type	0.72	0.34

Supplemental Figures

Figure S1. **Model-predicted probability of at least one in-school SARS-CoV-2 transmission over 30 days in a simulated elementary school setting, with 50% ADULT VACCINATION COVERAGE.** This figure replicates Figure 1, with 50% adult vaccination coverage in contrast to 70%. Note that the observed community incidence cutoff for the 50% transmission threshold in the delta variant scenario with a 0% child vaccination rate is about 4/100,000/day. Also note that the model does not directly account for the effect of adult vaccination levels on observed community incidence – a community with lower vaccination rates is likely to be at a higher community incidence (i.e., to the right on the x-axis) and vice versa.

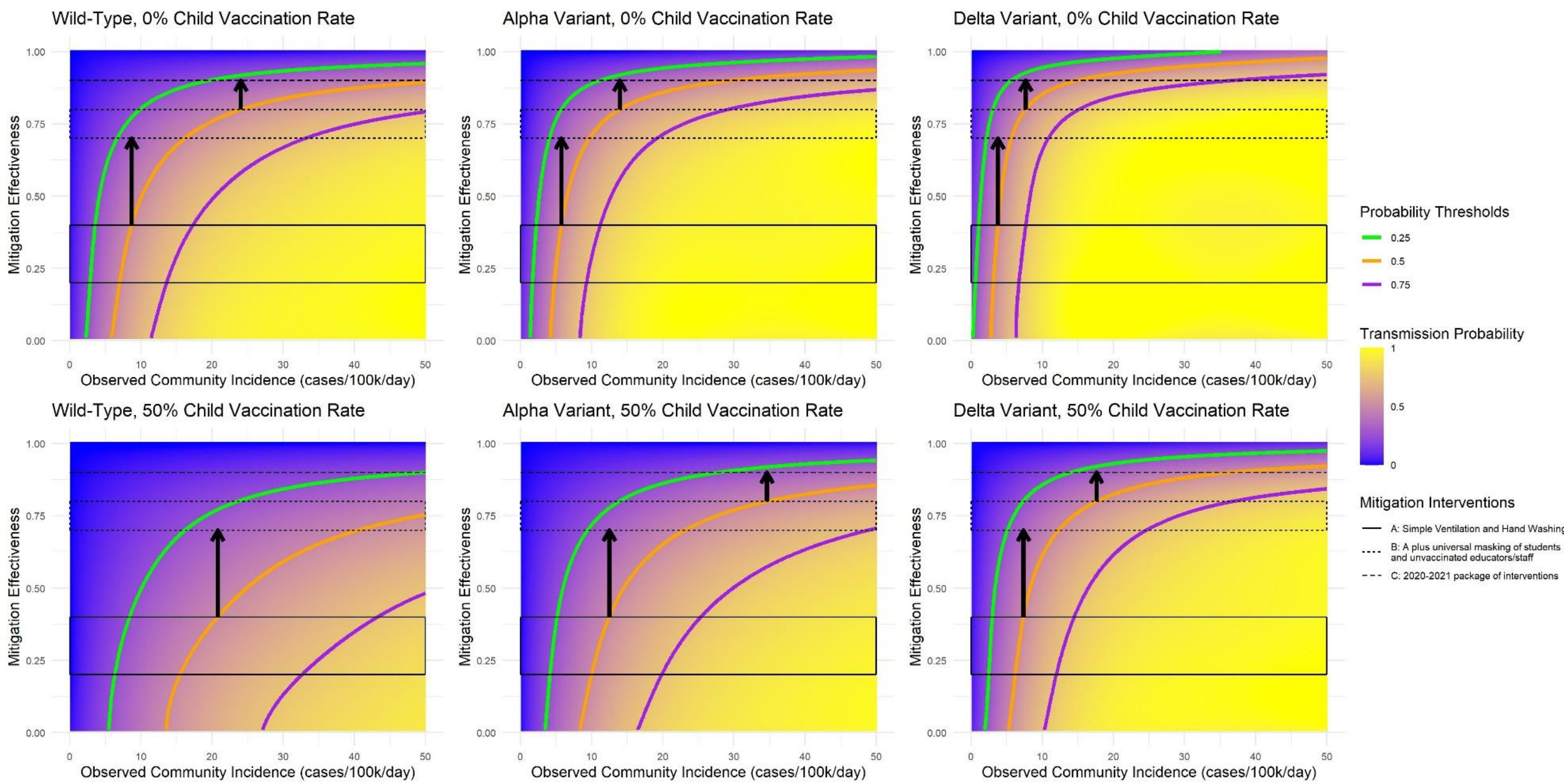


Figure S2. Model-predicted average number of additional cases over 30 days in the immediate school community (students, educators/staff, and their household members) during in-person instruction compared to remote instruction in the simulated elementary school setting, with 50% ADULT VACCINATION COVERAGE. This figure replicates Figure 2, with 50% adult vaccination coverage in contrast to 70%. Note that the observed community incidence cutoffs for the 5 and 10 additional cases thresholds in the delta variant scenario with a 0% child vaccination rate are about 15/100,000/day and 7/100,000/day, respectively. Also note that the model does not directly account for the effect of adult vaccination levels on observed community incidence – a community with lower vaccination rates is likely to be at a higher community incidence (i.e., to the right on the x-axis) and vice versa.

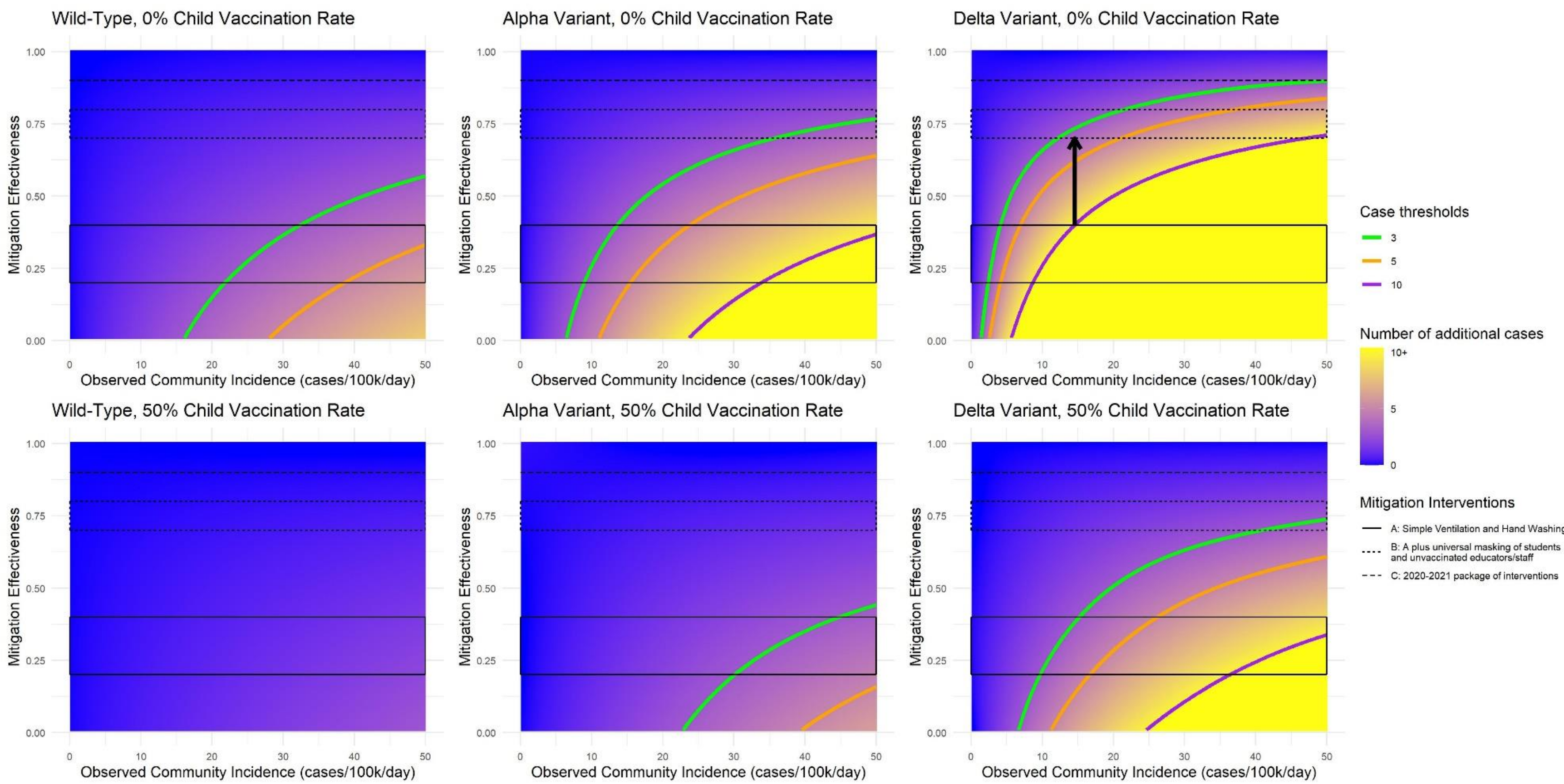


Figure S3. Average increase in hospitalizations among parents, teachers, staff, and adult family members per 100k, relative to remote instruction, with 70% adult vaccination.

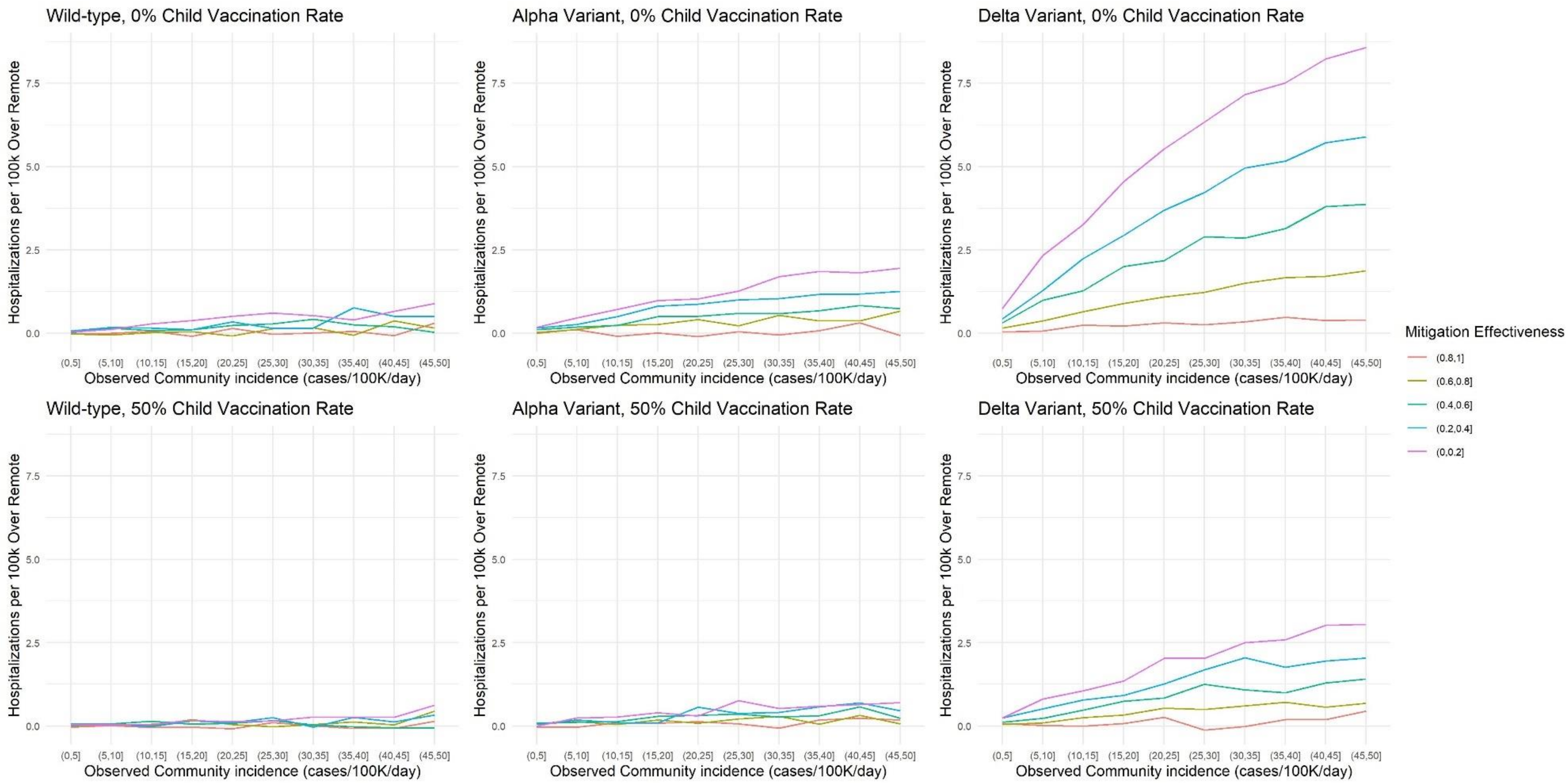


Figure S4. Average increase in hospitalizations among parents, teachers, staff, and adult family members per 100k, relative to remote instruction, with 50% adult vaccination

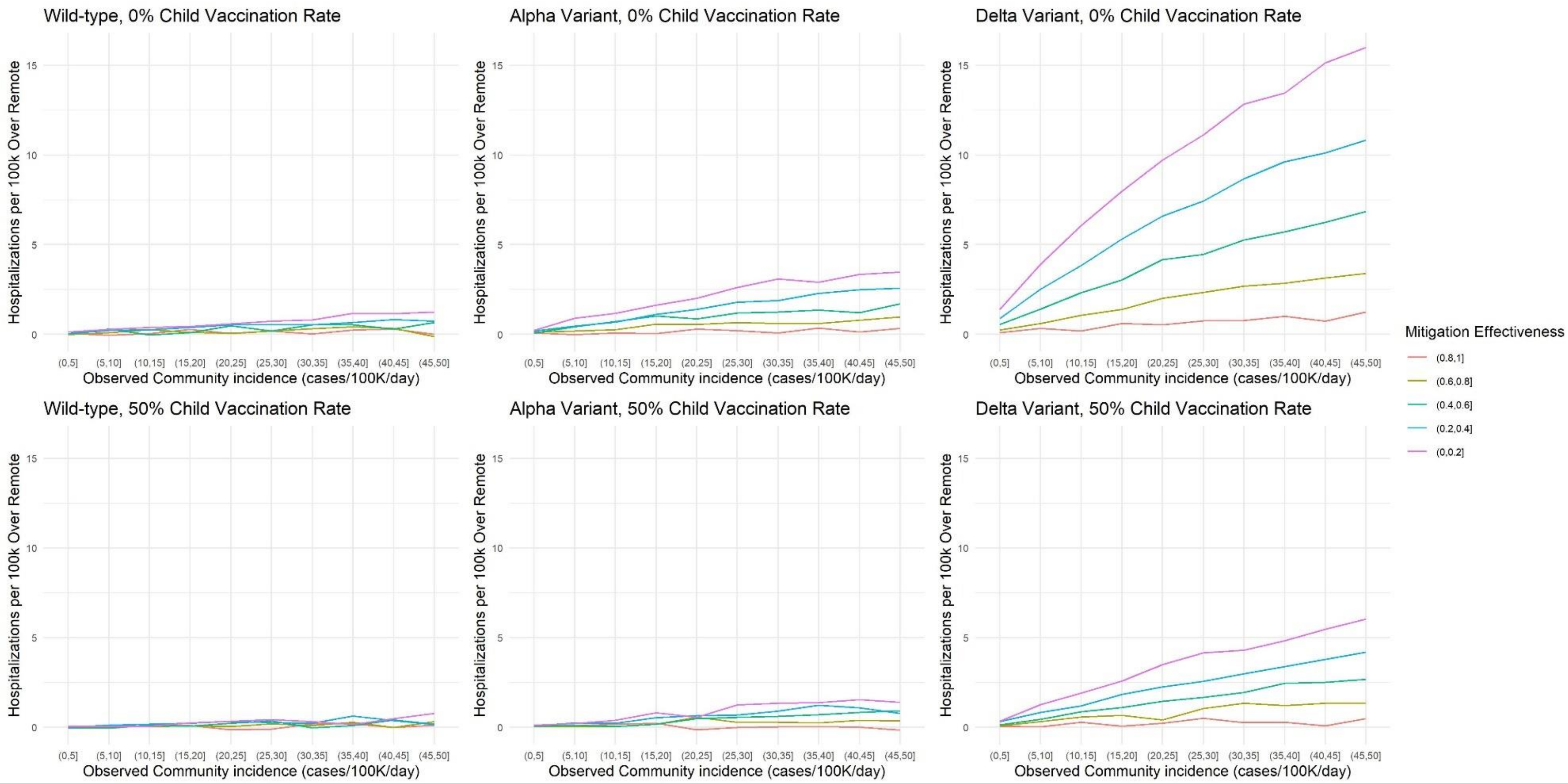


Figure S5. Model-predicted average number of additional cases over 30 days in the immediate school community (students, educators/staff, and their household members) during in-person instruction compared to remote instruction in the simulated elementary school setting, with 70% ADULT VACCINATION COVERAGE. This figure includes both the raw binned averages of the model output for large bins and the smoothed estimates for each bin (calculated at the midpoint).

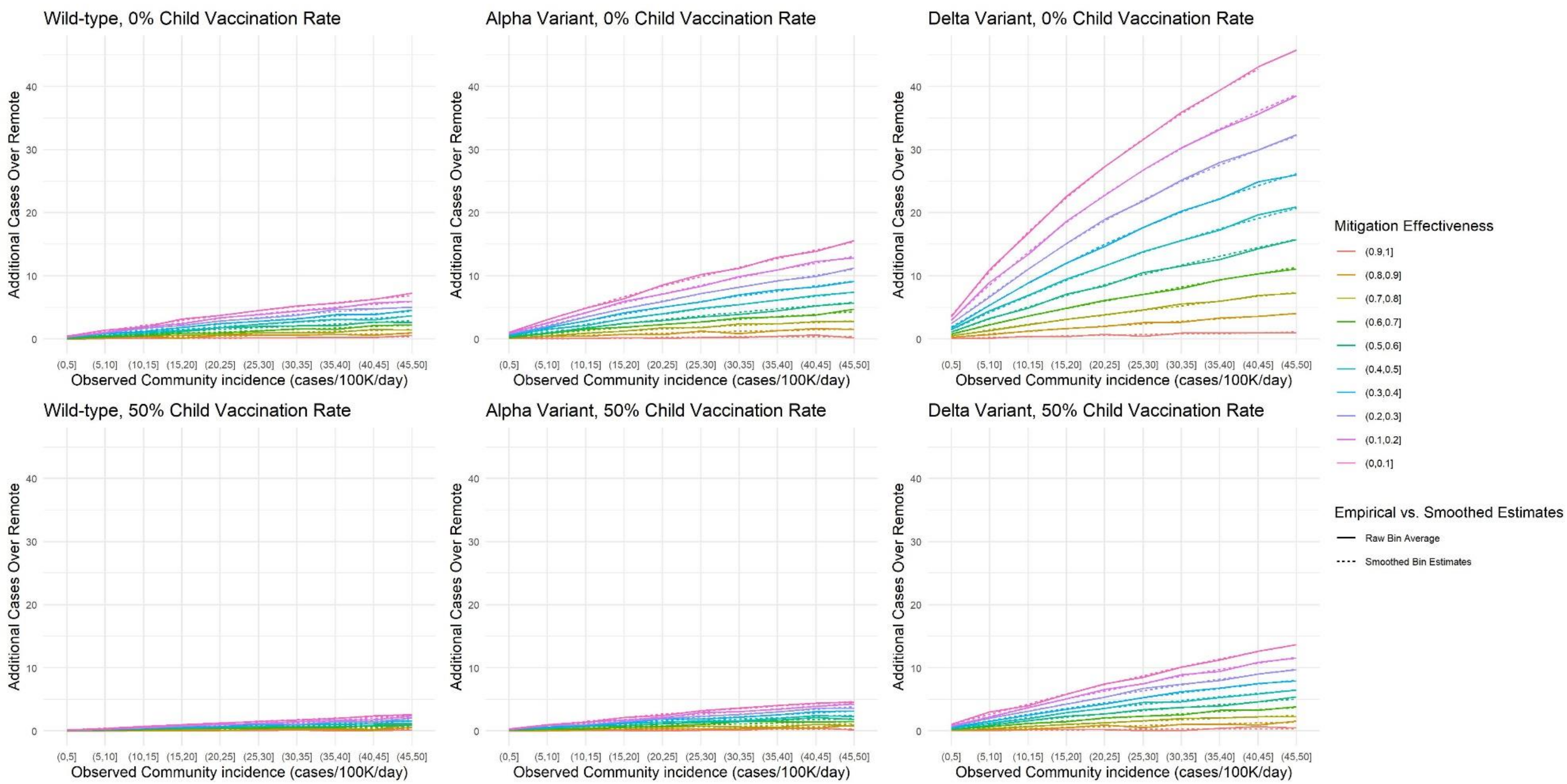


Figure S6. Model-predicted average number of additional cases over 30 days in the immediate school community (students, educators/staff, and their household members) during in-person instruction compared to remote instruction in the simulated elementary school setting, with 70% ADULT VACCINATION COVERAGE. This figure includes both the raw binned averages of the model output small bins and the smoothed estimates for each bin (calculated at the midpoint).

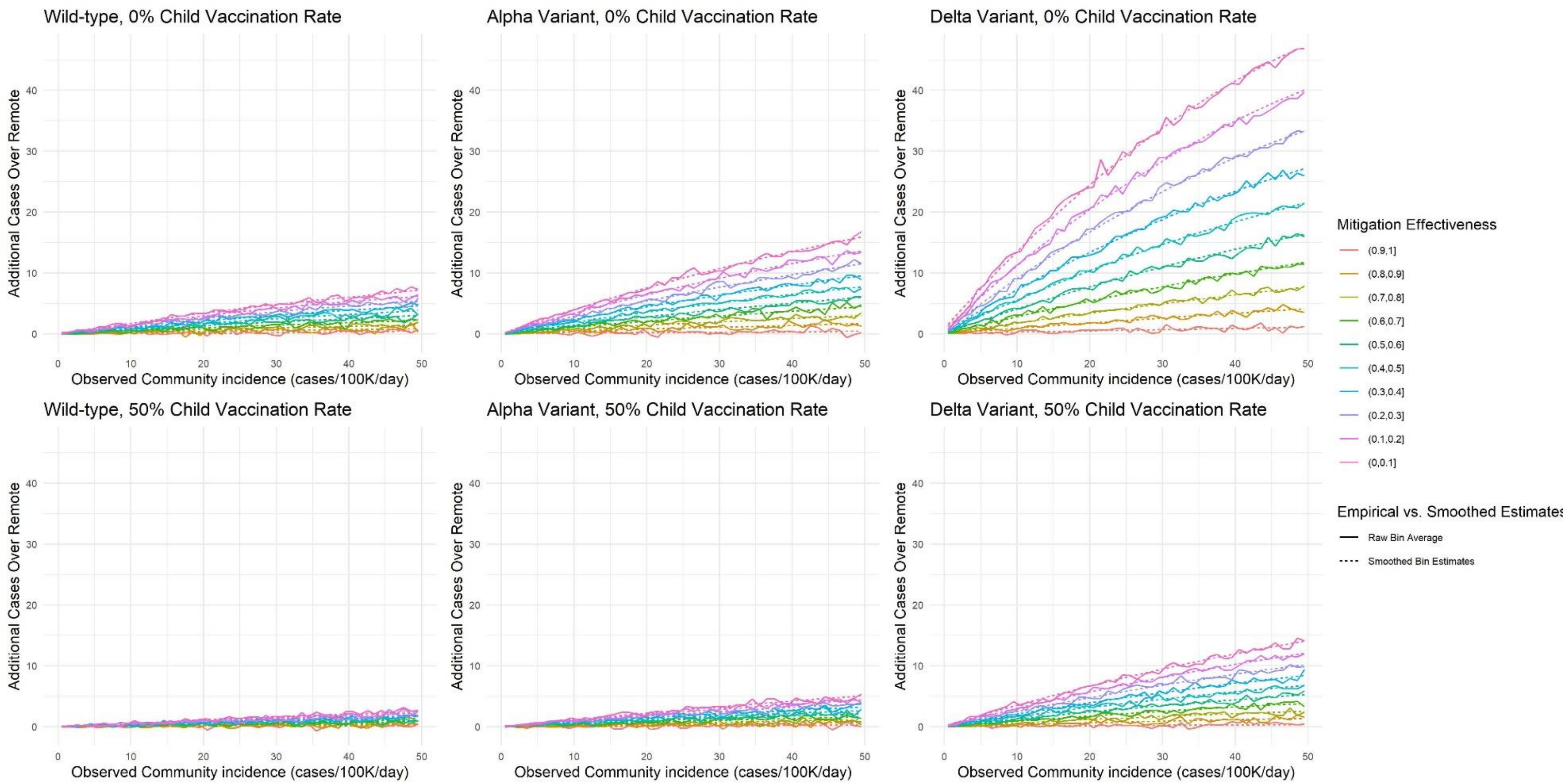


Figure S7. Model-predicted average number of additional cases over 30 days in the immediate school community (students, educators/staff, and their household members) during in-person instruction compared to remote instruction in the simulated elementary school setting, with 50% ADULT VACCINATION COVERAGE. This figure includes both the raw binned averages of the model output for large bins and the smoothed estimates for each bin (calculated at the midpoint).

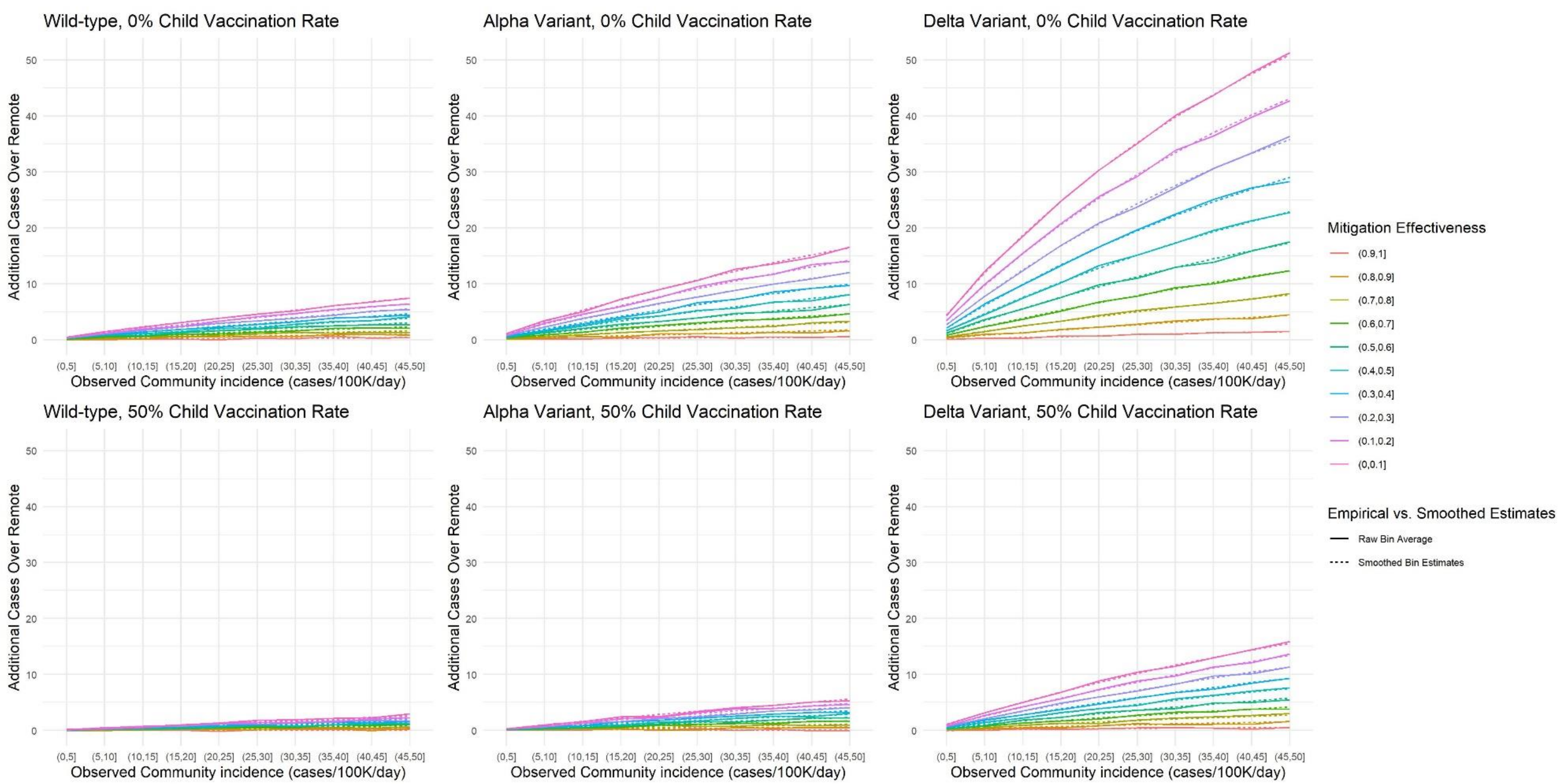


Figure S8. Model-predicted average number of additional cases over 30 days in the immediate school community (students, educators/staff, and their household members) during in-person instruction compared to remote instruction in the simulated elementary school setting, with 50% ADULT VACCINATION COVERAGE. This figure includes both the raw binned averages of the model output for small bins and the smoothed estimates for each bin (calculated at the midpoint).

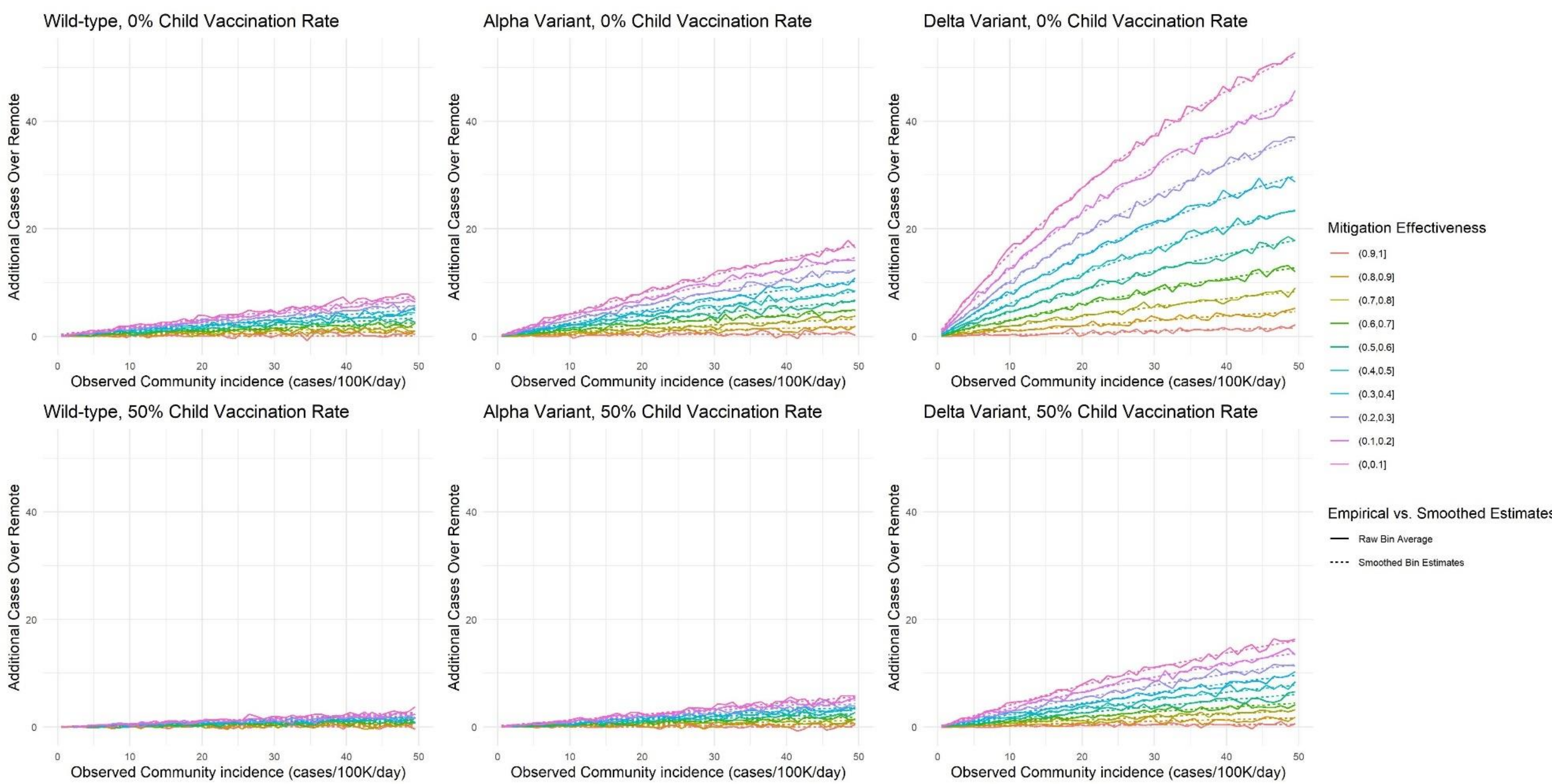


Figure S9. **Model-predicted probability of at least one in-school SARS-CoV-2 transmission over 30 days in a simulated elementary school setting, with 70% ADULT VACCINATION COVERAGE.** This figure is a raw binned heatmap for large bins corresponding to Figure 1.

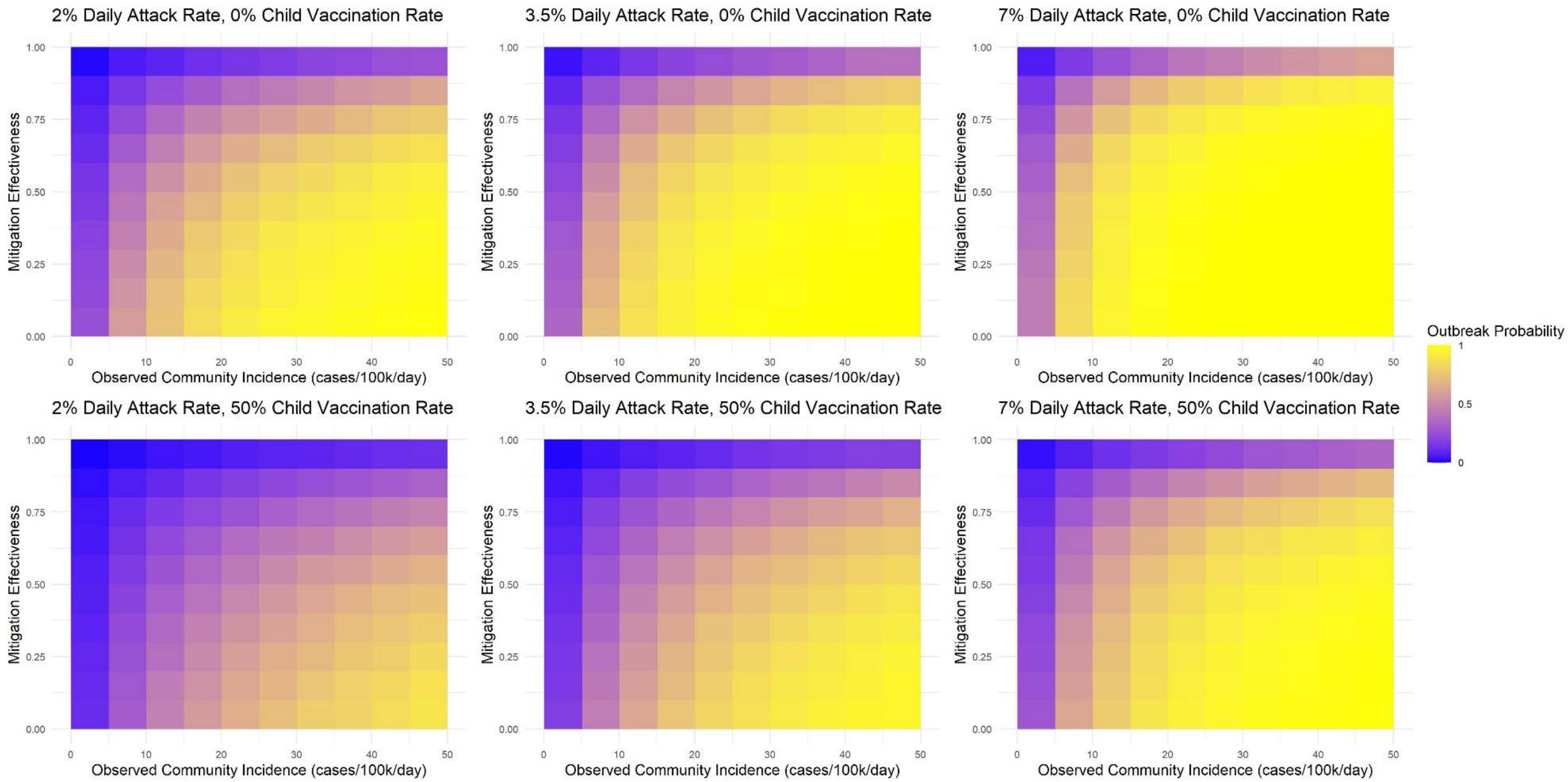


Figure S10. **Model-predicted probability of at least one in-school SARS-CoV-2 transmission over 30 days in a simulated elementary school setting, with 70% ADULT VACCINATION COVERAGE.** This figure is a raw binned heatmap for small bins corresponding to Figure 1.

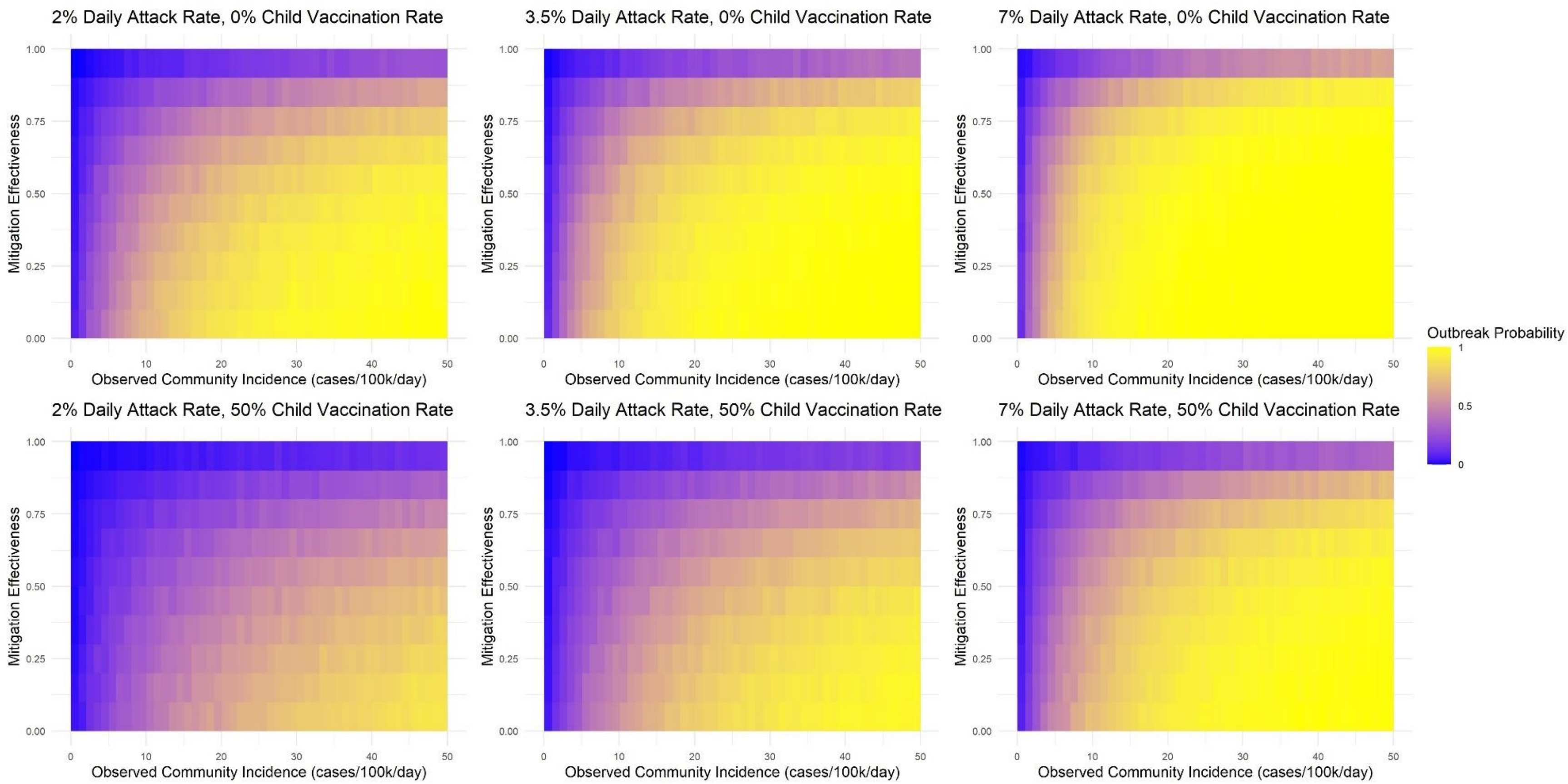


Figure S11. **Model-predicted probability of at least one in-school SARS-CoV-2 transmission over 30 days in a simulated elementary school setting, with 50% ADULT VACCINATION COVERAGE.** This figure is a raw binned heatmap for large bins corresponding to Figure S1.

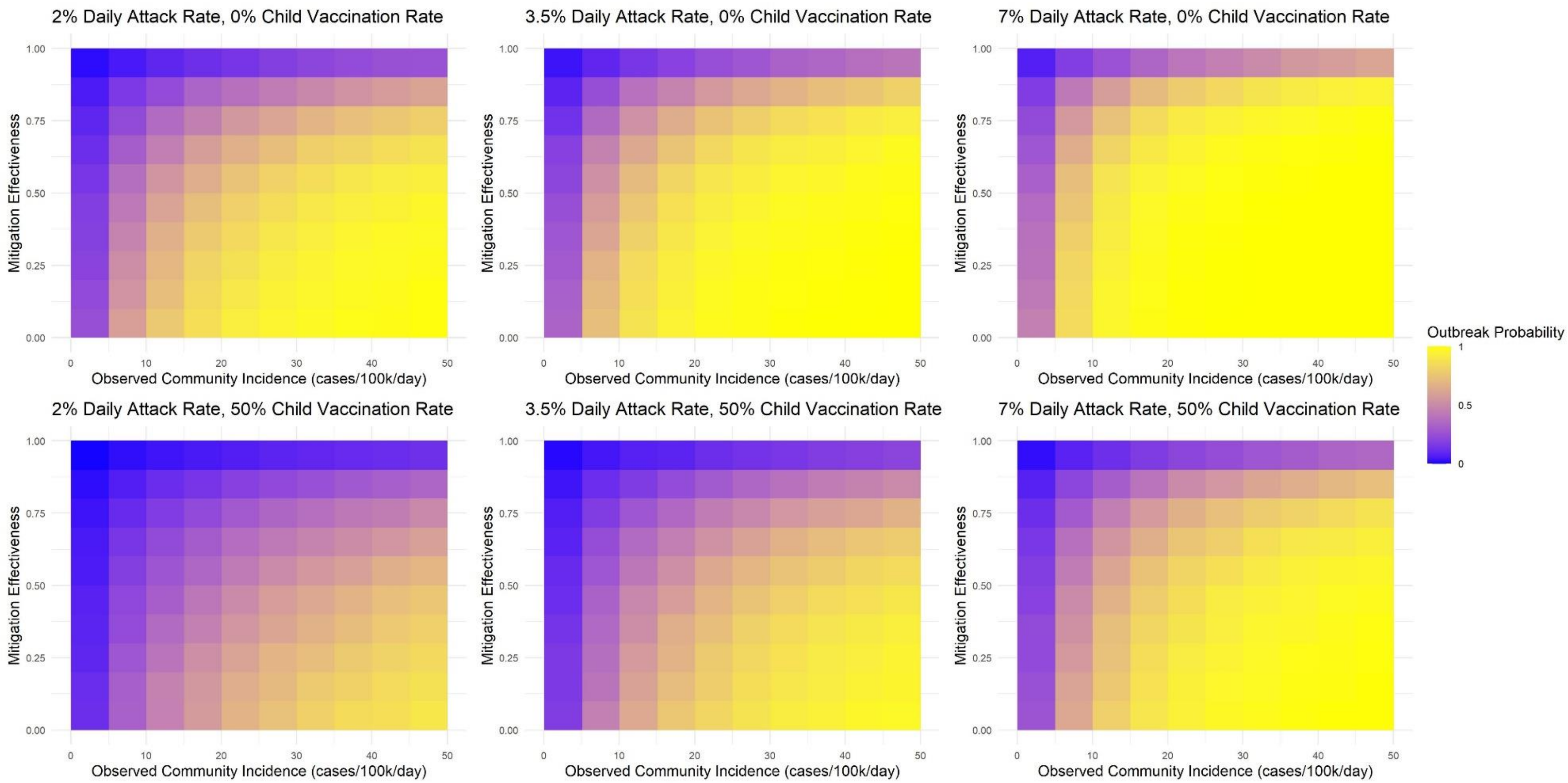


Figure S12. **Model-predicted probability of at least one in-school SARS-CoV-2 transmission over 30 days in a simulated elementary school setting, with 50% ADULT VACCINATION COVERAGE.** This figure is a raw binned heatmap for small bins corresponding to Figure S1.

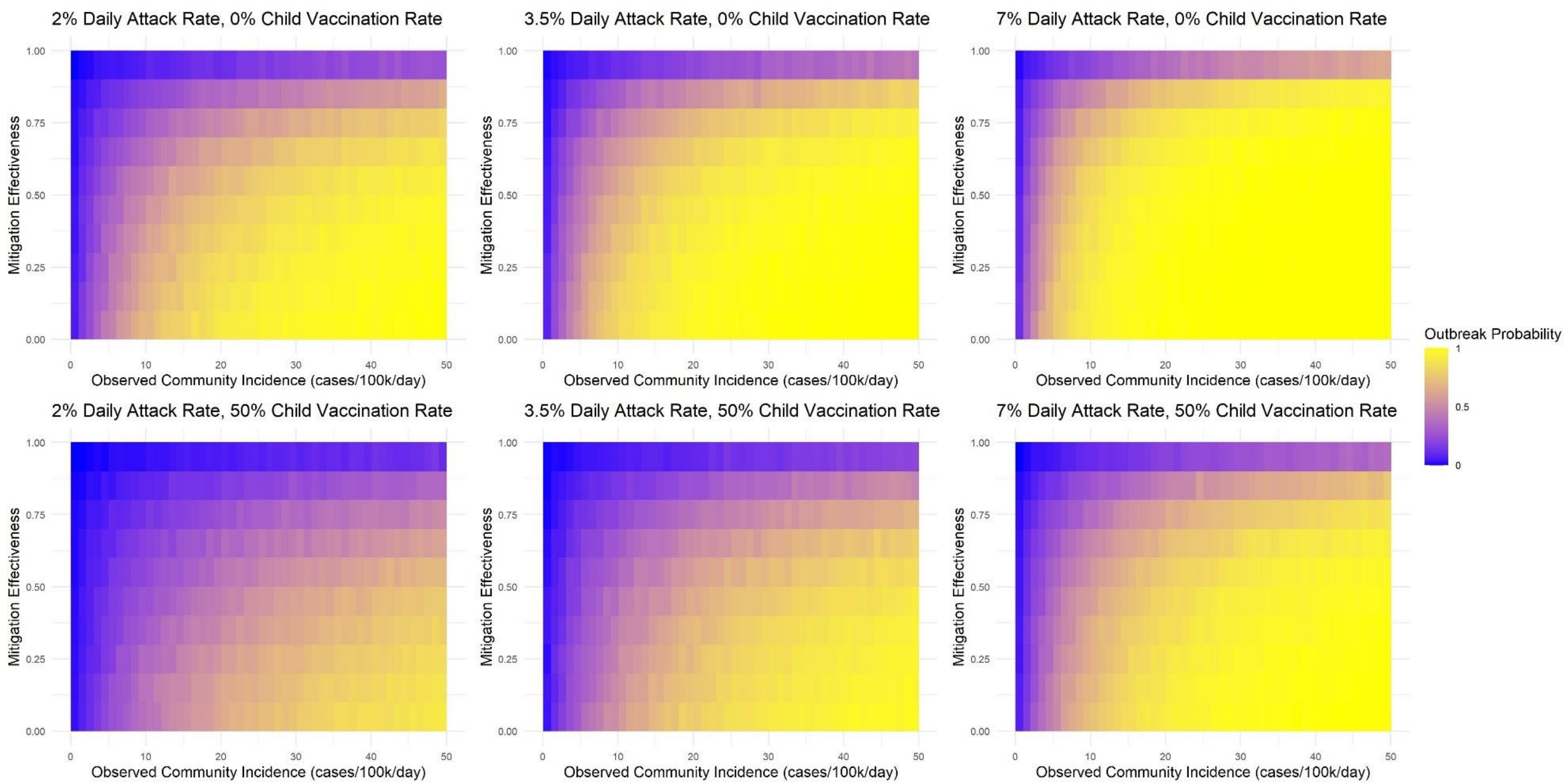


Figure S13. Model-predicted average number of additional cases over 30 days in the immediate school community (students, educators/staff, and their household members) during in-person instruction compared to remote instruction in the simulated elementary school setting, with 70% ADULT VACCINATION COVERAGE. This figure is a raw binned heatmap for large bins corresponding to Figure 2.

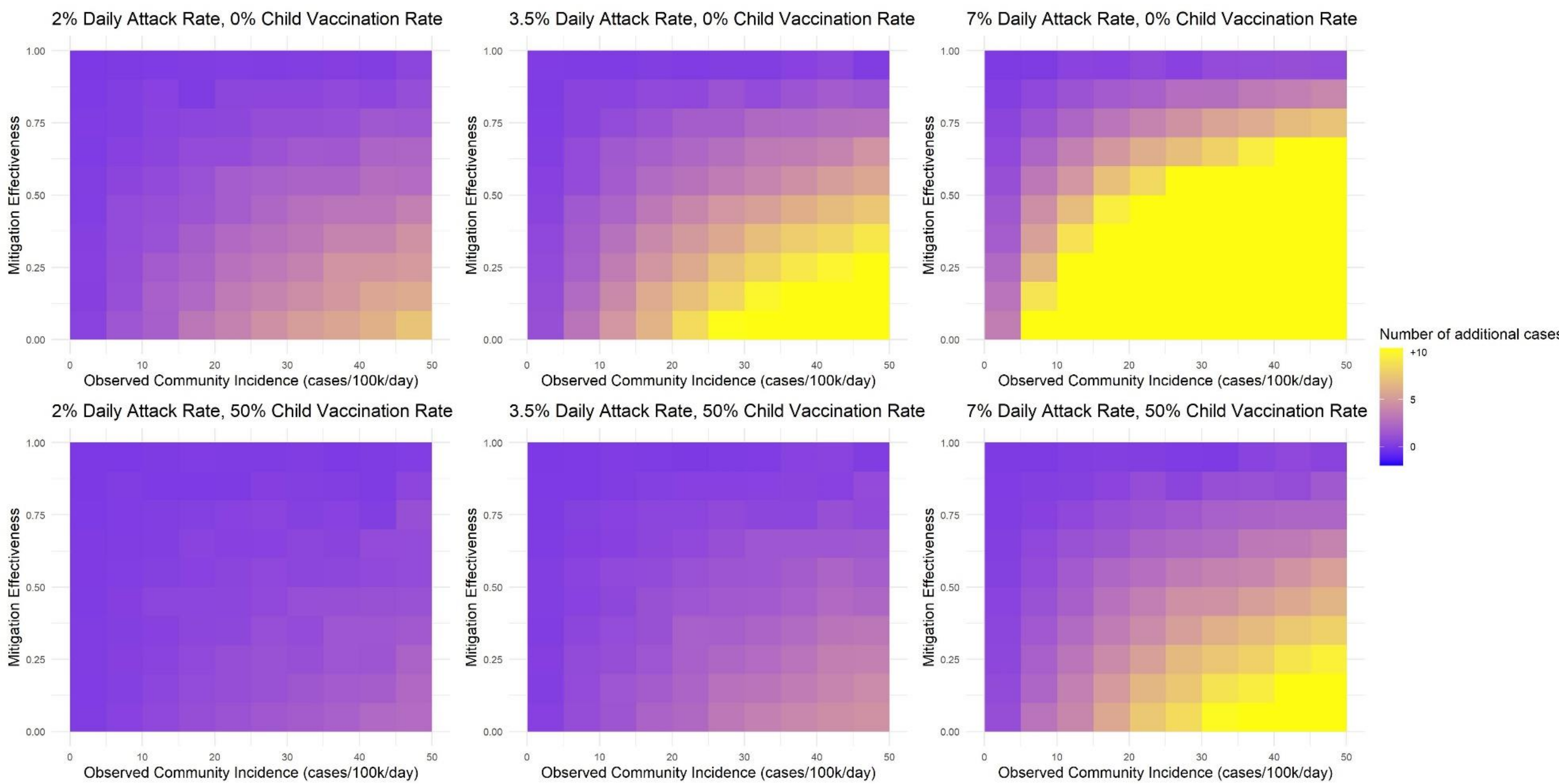


Figure S14. Model-predicted average number of additional cases over 30 days in the immediate school community (students, educators/staff, and their household members) during in-person instruction compared to remote instruction in the simulated elementary school setting, with 70% ADULT VACCINATION COVERAGE. This figure is a raw binned heatmap for the small bins corresponding to Figure 2.

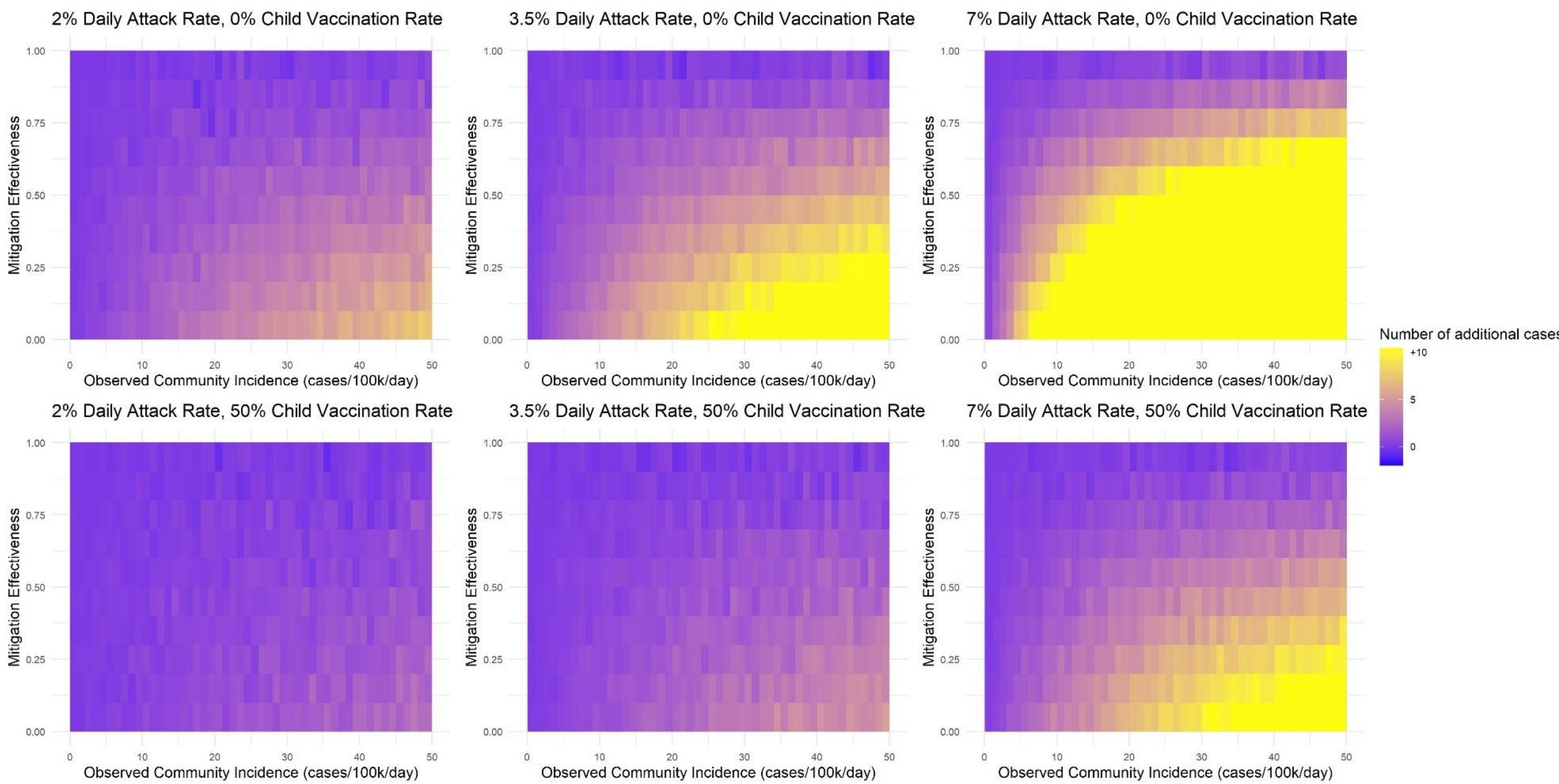


Figure S15. Model-predicted average number of additional cases over 30 days in the immediate school community (students, educators/staff, and their household members) during in-person instruction compared to remote instruction in the simulated elementary school setting, with 50% ADULT VACCINATION COVERAGE. This figure is a raw binned heatmap for the large bins corresponding to Figure S2.

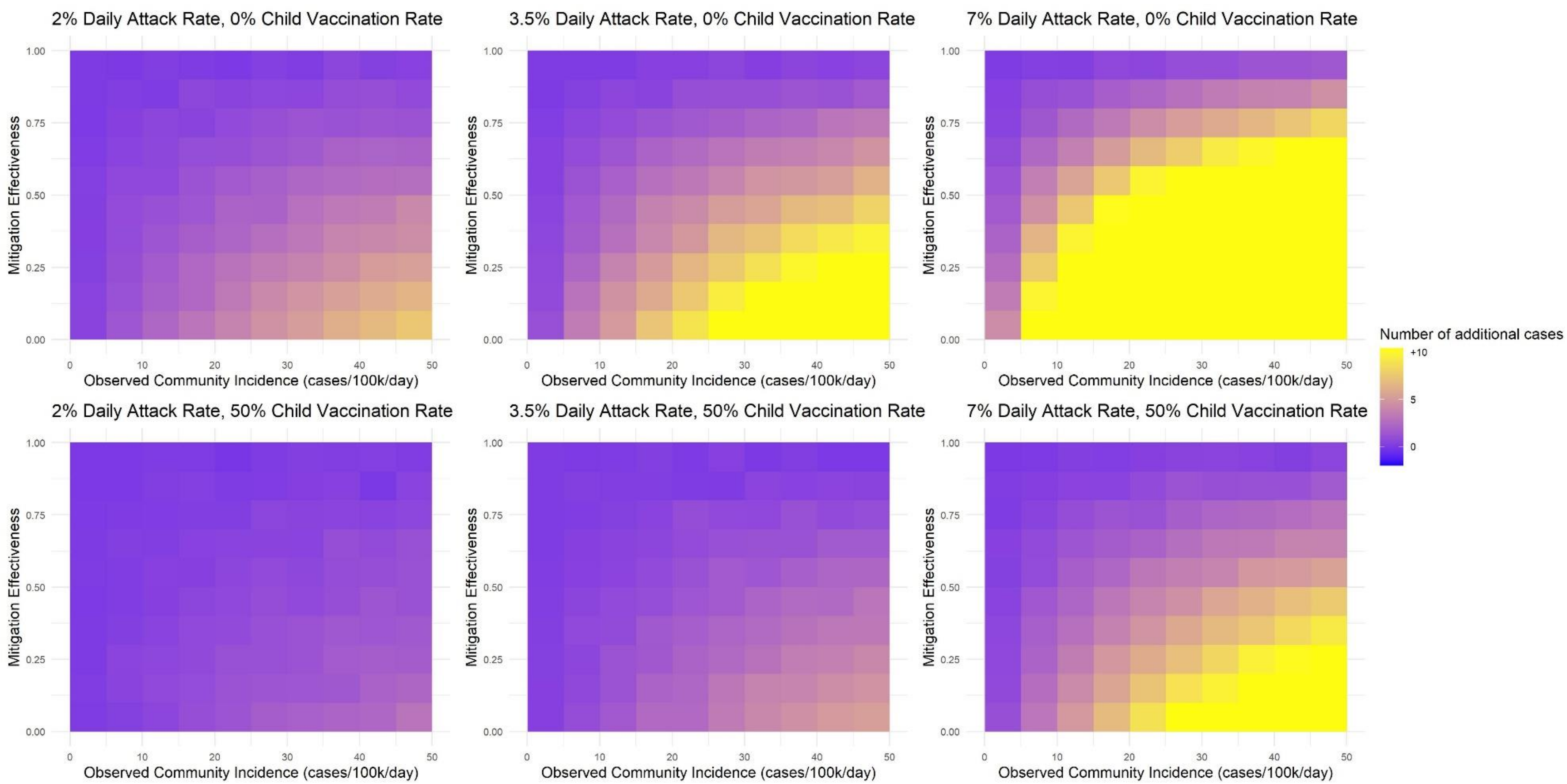
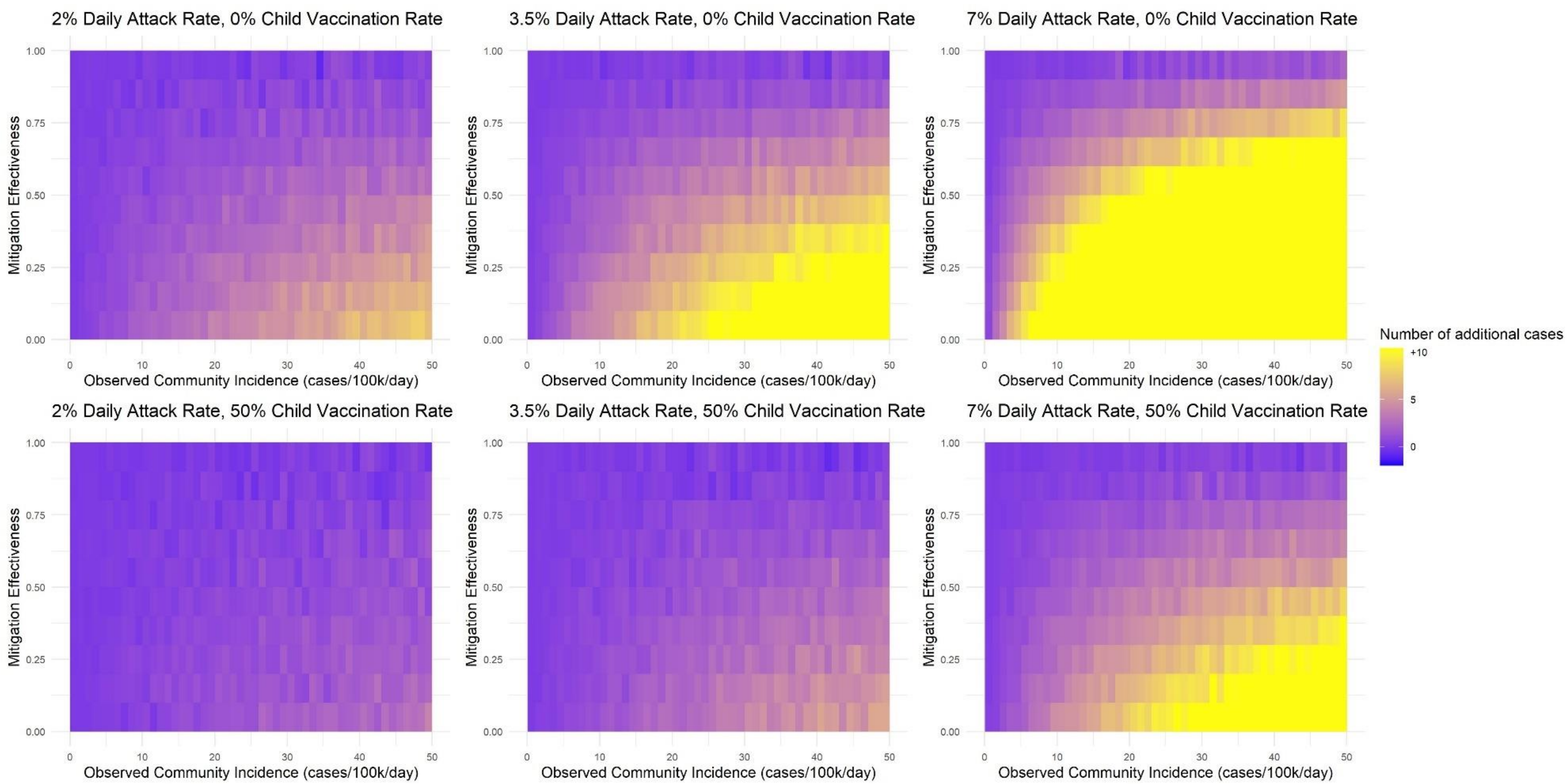


Figure S16. Model-predicted average number of additional cases over 30 days in the immediate school community (students, educators/staff, and their household members) during in-person instruction compared to remote instruction in the simulated elementary school setting, with 50% ADULT VACCINATION COVERAGE. This figure is a raw binned heatmap for small bins corresponding to Figure S2.



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