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Original Investigation | **Infectious Diseases**

Model-Estimated Association Between Simulated US Elementary School–Related SARS-CoV-2 Transmission, Mitigation Interventions, and Vaccine Coverage Across Local Incidence Levels

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Abstract

IMPORTANCE With recent surges in COVID-19 incidence and vaccine authorization for children aged 5 to 11 years, elementary schools face decisions about requirements for masking and other mitigation measures. These decisions require explicit determination of community objectives (eg, acceptable risk level for in-school SARS-CoV-2 transmission) and quantitative estimates of the consequences of changing mitigation measures.

OBJECTIVE To estimate the association between adding or removing in-school mitigation measures (eg, masks) and COVID-19 outcomes within an elementary school community at varying student vaccination and local incidence rates.

DESIGN, SETTING, AND PARTICIPANTS This decision analytic model used an agent-based model to simulate SARS-CoV-2 transmission within a school community, with a simulated population of students, teachers and staff, and their household members (ie, immediate school community). Transmission was evaluated for a range of observed local COVID-19 incidence (0-50 cases per 100 000 residents per day, assuming 33% of all infections detected). The population used in the model reflected the mean size of a US elementary school, including 638 students and 60 educators and staff members in 6 grades with 5 classes per grade.

EXPOSURES Variant infectiousness (representing wild-type virus, Alpha variant, and Delta variant), mitigation effectiveness (0%-100% reduction in the in-school secondary attack rate, representing increasingly intensive combinations of mitigations including masking and ventilation), and student vaccination levels were varied.

MAIN OUTCOMES AND MEASURES The main outcomes were (1) probability of at least 1 in-school transmission per month and (2) mean increase in total infections per month among the immediate school community associated with a reduction in mitigation; multiple decision thresholds were estimated for objectives associated with each outcome. Sensitivity analyses on adult vaccination uptake, vaccination effectiveness, and testing approaches (for selected scenarios) were conducted.

RESULTS With student vaccination coverage of 70% or less and moderate assumptions about mitigation effectiveness (eg, masking), mitigation could only be reduced when local case incidence was 14 or fewer cases per 100 000 residents per day to keep the mean additional cases associated with reducing mitigation to 5 or fewer cases per month. To keep the probability of any in-school transmission to less than 50% per month, the local case incidence would have to be 4 or fewer cases per 100 000 residents per day.

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Key Points

Question How is COVID-19 incidence in elementary school communities associated with in-school mitigation (eg, masks), vaccination, and local incidence, and when should decision-makers add or remove mitigation measures?

Findings In this decision analytic model with a simulated population of 638 students and 60 educators and staff in an elementary school, school community incidence decreased with mitigation and vaccination and increased with local incidence. Thresholds for changing mitigation measures depended on the objective (eg, minimizing likelihood of any in-school transmission vs maintaining cases within acceptable limits).

Meaning These findings suggest that appropriate increases and decreases for in-school mitigation depend on policy makers' goals; responsive plans, in which mitigation is deployed based on local COVID-19 incidence and vaccine uptake, may be appropriate.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Abstract (continued)

CONCLUSIONS AND RELEVANCE In this study, in-school mitigation measures (eg, masks) and student vaccinations were associated with substantial reductions in transmissions and infections, but the level of reduction varied across local incidence. These findings underscore the potential role for responsive plans that deploy mitigation strategies based on local COVID-19 incidence, vaccine uptake, and explicit consideration of community objectives.

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Introduction

To balance the educational and social and emotional benefits of in-person education with concerns about SARS-CoV-2 transmission in school settings, the US Centers for Disease Control and Prevention (CDC) recommends using a layered mitigation approach in kindergarten to 12th grade (K-12) schools. Some components of this approach include vaccination for all eligible students and educators and staff, improved ventilation, and indoor masking regardless of vaccination status.[1] Individual states and school districts make local decisions about whether and how to incorporate these recommendations, and requirements for indoor masking have particularly generated debate.[2] In communities with high vaccination rates and low COVID-19 incidence, or where masking is less widely accepted, many schools are considering removing masks and other elements of mitigation.[3,4]

While multiple studies indicate that masks are effective at mitigating the transmission of upper respiratory viruses,[5-10] they are generally viewed as a temporary measure.[11,12] Masks are physiologically safe, but there are limited data on the impact of mask-wearing on learning and social and emotional development, especially for younger children, students with special learning needs, and English language learners.[9,13] With the availability of vaccines for all US residents aged 5 years and older, many public health experts have called for “off-ramps” and “on-ramps” that use available public health data to inform decisions about when to remove or reinstate masking and other mitigation measures.[11,12,14,15]

Establishing these off-ramps and on-ramps requires decision-makers to be explicit about the objectives they seek to achieve, which in turn necessitates a quantitative estimate of the epidemiologic consequences of adding or removing mitigation. We used a previously published simulation model of SARS-CoV-2 transmission within an elementary school community to generate estimates across a range of potential assumptions about intervention effectiveness, student vaccine coverage, and observed local COVID-19 incidence.[16] We evaluated decision thresholds for multiple objectives to support decision-makers across different contexts.

Methods

Modeled Population and Model Structure

We simulated an elementary school with 638 students in 30 separate classes and 60 educators and staff. Household members included 2 adults in each student household (with sibling students grouped in the same household) and 1 additional adult in each educator and staff household. The study adheres to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) reporting guidelines[17] and was designated not human participant research by the Mass General Brigham institutional review board.

The model simulates infection dynamics within the immediate school community (students, educators and staff, and family members) and tracks infections over 30 days. At school, students, educators, and staff interact: within classrooms, during so-called specials classes (eg, related arts), and through random contacts. Outside of school, students and educator and staff interact with household members and other families (simulating social interactions or shared childcare). SARS-CoV-2 is introduced to the immediate school community at a rate proportional to the observed incidence rate for the wider local community (after accounting for an assumed case ascertainment rate).

Transmissions from infected people are modeled as a function of the age (student vs adult) of the infected individual and contact, vaccination status of the contact, and duration and location of exposure, with the latent and infectious periods drawn from distributions with means of 3.5 and 5 days, respectively.[18-23] In-school mitigation measures are simulated as a relative risk reduction on in-school transmission risk. Symptomatic students, educators, and staff with a clinical (vs subclinical) infection are offered diagnostic testing; for selected scenarios, we included weekly polymerase chain reaction screening offered to all students, educators, and staff. People identified with SARS-CoV-2 isolate for 7 days, and in-school contacts quarantine for 7 days. (We assumed all members of a classroom are in-school contacts). Additional details on the model structure are in eMethods 1 in the Supplement and the article by Bilinski et al.[16]

Input Parameters

Selected input parameters are listed in the **Table**, eMethods 1 and eMethods 2 in the Supplement.[16,18-50] Bilinski et al[16] describe other model input.

Infectiousness and Hospitalization Risk

We assumed full-day symptomatic adult-to-adult in-school "secondary attack rates" (SARs) of 2%, 3.5%, and 7% per day for the wild-type virus, Alpha variant, and Delta variant, respectively (eMethods 1 in the Supplement). The full-day SAR is defined as the proportion of susceptible adults exposed to a symptomatic adult index case who acquire SARS-CoV-2 infection per day of contact in the absence of mitigation. Wild-type and Alpha variants are included to provide results against which schools can compare observed data from the 2020 to 2021 academic year. We assumed that elementary students were half as infectious as adults in schools and equally infectious in household settings.[16,32]

Using infection fatality rate and in-hospital mortality rates provided by the CDC for use in COVID-19 models and relative hospitalization rates in different age groups, we assumed hospitalization risks among unvaccinated students and adults (aged 18 to 49 years) with COVID-19 of 0.1% and 2.4%, respectively, and a negligible risk among vaccinated individuals younger than 49 years (eMethods 1 in the Supplement).[42-44]

Vaccine Uptake and Effectiveness

In the base case, we assumed 70% uptake of 2-dose vaccination among adults (including educators, staff, and household members), reflecting US national data,[45] along with 4 potential scenarios of student vaccine uptake (0%, 25%, 50%, and 70%). In sensitivity analyses, we examine 50% adult vaccine uptake and a scenario in which both adults and students have 90% uptake. Given recent observational data on waning vaccine effectiveness, we assumed a base case of 70% vaccine effectiveness,[46-50] along with sensitivity analyses at 90%, 50%, and 25% effectiveness (eMethods 1 in the Supplement).

Mitigation Effectiveness

In the absence of data on the independent impact of individual mitigation measures on transmission, we estimated wide ranges for the effectiveness of 3 packages of interventions: simple ventilation and handwashing (group A; 20%-40% effective); group A plus universal masking (group B; 60%-80% effective); and full implementation of CDC-recommended measures[1] from 2020 to 2021 (eg, group 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) (group C; 90%-100% effective). Group A effectiveness was based on the results of available airflow and air quality studies[51,52]; group

Table. Selected Input Parameters for Agent-Based Dynamic Transmission Model of 30-Day SARS-CoV-2 Outcomes in Elementary Schools

Parameter	Values	Source
Full day in-school symptomatic adult-to-adult secondary attack rate (unmitigated)		
Wild-type	2.0%	Bilinski et al,[16] 2021; Doyle et al,[24] 2021[a]
Alpha	3.5%	Davies et al,[25] 2021[a]
Delta	7.0%	Singanayagam et al,[26] 2021; Dougherty et al,[27] 2021; National Centre for Immunisation Research and Surveillance,[28] 2021[a]
Attack rate multipliers by location and duration of contact (relative to full day in-school contact)		
At-home contacts	2[b]	Assumption based on documented increased attack rates in the home (Thompson et al,[29] 2021) and increased time in close proximity
Brief contacts at school (random and specials classes)	0.125[b]	Assumed to last 1 period out of an 8-period day, with infection risk proportional to time
Brief contacts at school (staff-staff contacts)	0.25[b]	Assumed to last 1 period out of an 8-period day, but with higher risk from closer proximity (eg, break room)
Contacts between households (eg, childcare)	1	Assumption; in-school mitigation measures are not applied to these contacts
Infectiousness (relative to symptomatic adults)		
Student (in-school and asymptomatic at-home)	0.5[b]	Literature review and calibration from Bilinski et al,[16] 2021
Asymptomatic adult	0.5[b]	Byambasuren et al,[30] 2020; He et al,[31] 2020
Student (symptomatic at-home)	1	Paul et al,[32] 2021
Overdispersion multiplier (for adults)	Lognormal distribution (0.84, 0.3)/0.84[b]	Kerr et al,[22] 2020; Endo et al,[33] 2020
Susceptibility (relative to adults)		
Student	0.5[b]	Literature review and calibration from Bilinski et al,[16] 2021
Length of latent and incubation periods and infection (days)		
Time from exposure to infectious (latent period)	Maximum of gamma distribution (5.8, 0.95) minus normal distribution (2, 0.4); 1[b]	Lauer et al,[18] 2020; He et al,[19] 2020; Li et al,[20] 2020; Gatto et al,[21] 2020
Time from exposure to symptoms (if symptoms occur) (incubation period)	Gamma distribution (5.8, 0.95)[b]	Lauer et al,[18] 2020; Li et al,[20] 2020
Duration of infectious period	Lognormal distribution (5, 2)[b]	Li et al,[20] 2020; Kerr et al,[22] 2020; He et al,[19] 2020; Firth et al,[23] 2020[c]
Probability clinical/symptomatic infection		
Probability of asymptomatic infection		
Student	0.4[b]	Fontanet et al,[34] 2021; Stein-Zamir et al,[35] 2020
Adult	0.2[b]	Byambasuren et al,[30] 2020
Probability of subclinical infection, including asymptomatic		
Student	0.8[b]	Han et al,[36] 2021
Adult	0.4[b]	Upper bound of estimate from Byambasuren et al,[30] 2020
Polymerase chain reaction test characteristics		
Sensitivity (during infectious period)	0.9 (asymptomatic testing); 1 (symptomatic testing)[b]	Atkeson et al,[37] 2021; Larremore et al,[38] 2021; Cevik et al,[39] 2021; Wyllie et al,[40] 2020; Kojima et al,[41] 2021
Test turnaround time, d	1[b]	Assumption

(continued)

Table. Selected Input Parameters for Agent-Based Dynamic Transmission Model of 30-Day SARS-CoV-2 Outcomes in Elementary Schools (continued)

Parameter	Values	Source
Weekly screening parameters		
Testing uptake (fraction of school screened each week)	90%[b]	Assumption
Testing day	Monday[b]	Assumption
Hospitalization risk after SARS-CoV-2 infection		
Student (unvaccinated)	0.1%	US Centers for Disease Control and Prevention,[42] 2021; Delahoy et al,[43] 2021[a]
Adult (unvaccinated)	2.4%	US Centers for Disease Control and Prevention,[42] 2021[a]
All (vaccinated)	0%	Rosenberg et al,[44] 2021[a]
Vaccine uptake		
Student	0%, 25%, 50%, and 70% (base case); 90% (sensitivity analysis)	Assumption
Adult	70% (base case); 50% and 90% (sensitivity analysis)	US Centers for Disease Control and Prevention,[45] 2021
Vaccine effectiveness		
All individuals	70% reduction in infection risk (base case); 25%, 50%, and 90% (sensitivity analysis)	Rosenberg et al,[46] 2021; Keehner et al,[47] 2021; Fowlkes et al,[48] 2021; Puranik et al,[49] 2021; Zeng et al,[50] 2021[a]
Risk of exposure in wider local community		
Observed local incidence rate	0-50 cases per 100 000 residents per d	Assumption
Actual incidence of infections within immediate school community sourced from wider local community	3 × observed local incidence rate	Assumption

[a] eMethods 1 in the Supplement includes an explanation of how these parameters were derived from the listed sources.

[b] Baseline parameter from Bilinski, et al.[16]

[c] This value was set to match the generation time implied by observed estimates of the serial interval and presymptomatic transmission, without assuming waning infectiousness.

B effectiveness was based on both clinical as well as droplet and/or aerosol studies evaluating masking effectiveness[5-10] and a study evaluating the combination of masking and ventilation in a controlled environment[53]; and group C effectiveness was based on observed risk of in-school transmission (0%-3% over the full infectious period) in schools implementing a full suite of mitigation measures in 2020 to 2021 (eMethods 2 in the Supplement).[54-56] The estimates for A and B are based on limited available data and remain highly uncertain; approximate ranges are used to understand the potential consequences of moving between mitigation approaches, and schools may define their specific values within each range based on local degree of implementation.

Simulated Scenarios

The base case included scenarios reflecting wild-type virus, Alpha variant, and Delta variant, different student vaccination coverage (0%, 25%, 50%, and 70% coverage), and 70% adult vaccination uptake. For each variant, we ran the model across a range of observed local incidence levels (0-50 cases per 100 000 residents per day, assumed 33% of cases observed) and in-school mitigation effectiveness (0%-100% reduction to in-school attack rate). To present smoothed results across these continuous ranges and manage the relatively high degree of model stochasticity from discrete model output, we constructed a regression-based meta-model from the raw model output to estimate the outcomes of interest (eMethods 3 in the Supplement).[57] We conducted the sensitivity analyses discussed previously only on the Delta variant scenarios, as these are most relevant for current decision-making.

Outcomes and Decision Thresholds

We evaluated 2 primary outcomes over a 30-day period: (1) probability of any in-school SARS-CoV-2 transmission at each level of mitigation effectiveness and (2) mean increase in total infections among students, educators, staff, and their household members (ie, the immediate school community) associated with moving from more to less intensive mitigation measures (eg, unmasking). For the second outcome, we projected the increase in cases associated with each of 3 discrete changes in mitigation effectiveness, reflecting possible values of the difference between the A and B mitigation scenarios described previously, ie, a change from 60% to 40% mitigation effectiveness (between inner bounds of the respective effectiveness estimates); from 70% to 30% effectiveness (between midpoints); and from 80% to 20% effectiveness (between outer bounds). We identified the observed local incidence thresholds at which policy makers might add or remove mitigation interventions for objectives tied to these outcomes: (1) keeping the monthly probability of in-school transmission less than 25%, 50%, or 75% or (2) keeping the number of cases added to the immediate school community by removing mitigation fewer than 3, 5, or 10 cases per month.

In addition to these primary outcomes, we also evaluated the approximate number of additional hospitalizations that would result from shifting from more to less intensive mitigation by applying the approximate hospitalization risks in the Table to the second primary outcome. We then calculated local incidence thresholds for the objectives of keeping additional hospitalizations less than 1, 3, or 5 hospitalizations per 100 000 individuals in the immediate school community per month.

Statistical Analysis

The model and all analyses were implemented in R version 4.0.2 (R Project for Statistical Computing),[58] and the replication code is publicly available.[59] Rather than conducting traditional statistical tests, which are not appropriate for this type of model-based analysis, we assessed the variability in the outcomes using the sensitivity analyses described previously.

Results

Over 30 days in the simulated elementary school, all outcomes (probability of at least 1 in-school SARS-CoV-2 transmission and the additional cases and hospitalizations associated with decreased mitigation) were substantially higher with the Delta variant and with increased local incidence and lower with increased mitigation effectiveness and higher student vaccination uptake (**Figure 1** and **Figure 2**; eFigure 1 in the Supplement). The local incidence decision thresholds associated with meeting different objectives based on these outcomes (eg, keeping risk of in-school transmission <50%) varied across the different scenarios (**Figure 3**).

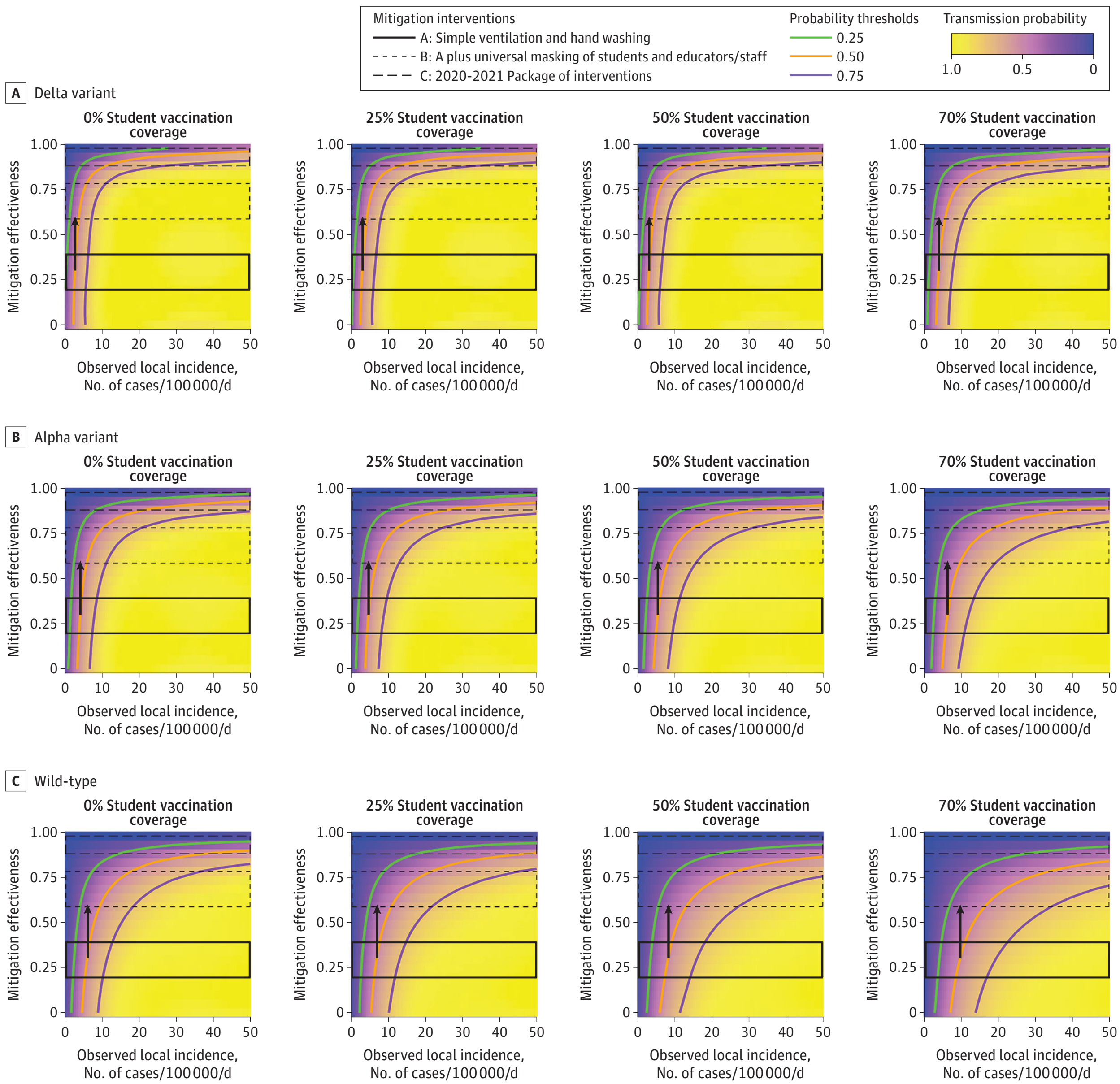
Probability of In-School Transmission

With the Delta variant and 0% student vaccination, if removing masks (or other mitigation measures) was associated with a decrease in mitigation effectiveness to 30% (mitigation group A midpoint), decision-makers who seek to keep the monthly probability of in-school transmission less than 50% could remove masks at or below an observed local incidence of approximately 2 cases per 100 000 residents per day (Figure 1A). With student vaccination rates of 25%, 50%, or 70%, this threshold changed minimally to 3 to 4 cases per 100 000 residents per day (Figure 1A). Thresholds for keeping transmission probability less than 25% and less than 75% are presented in Figure 3 (for the Delta scenario) and in the Supplement for Alpha and wild-type scenarios (eTable 1 and eTable 2 in the Supplement).

Additional Cases Associated With Mitigation Effectiveness Reduction

With the Delta variant and 0% student vaccination, if unmasking (or removing other mitigation measures) is associated with a decrease in mitigation effectiveness from 70% (group B midpoint) to 30% (group A midpoint), decision-makers who seek to keep the number of additional infections associated with removing mitigation (eg, masks) fewer than 5 per month in the immediate school community could remove masks at or below a local incidence of approximately 5 cases per 100 000 residents per day (Figure 2A). With student vaccination rates of 25%, 50%, or 70%, this threshold changed to 7, 10, or 14 cases per 100 000 residents per day, respectively (Figure 2A). If the consequences of removing masks were smaller (eg, a 60% to 40% decreases in effectiveness), these thresholds would be higher (10-32 cases per 100 000 residents per day) (Figure 2). Thresholds for keeping additional cases less than 3 or 10 infections per month are presented in Figure 3 (for the Delta scenario) and in the Supplement for the Alpha and wild-type scenarios (eTable 1 and eTable 2 in the Supplement).

Figure 1. Model-Estimated Probability of at Least 1 In-School SARS-CoV-2 Transmission Over 30 Days in a Simulated Elementary School Setting

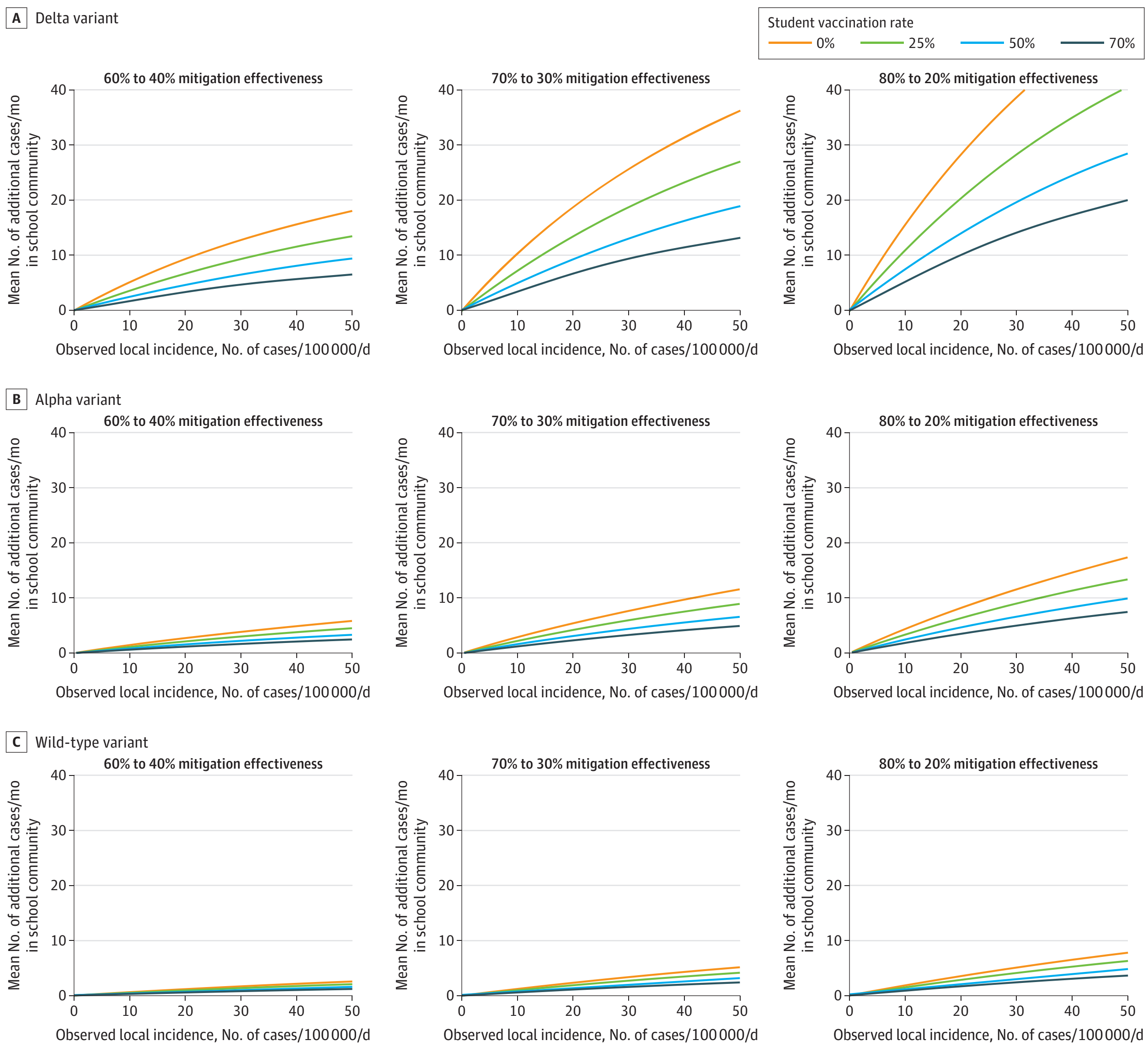


Panels reflect decreasingly transmissible variants from top to bottom and increasing student vaccination coverage from left to right. Bands of mitigation effectiveness reflect approximate assumptions for the A, B, and C mitigation intervention scenarios described in the Methods section. The contour lines represent thresholds for different probability levels; probabilities are lower than the threshold above the contour line and higher below it. The arrow indicates the local COVID-19 incidence rate at which a school might opt to move to the next more intensive mitigation strategy at a baseline of 30% effectiveness, if the objective is to maintain a probability of the 1 in-school transmission per month at less than 50%. Adult vaccination coverage is assumed to be 70% in all scenarios.

Additional Hospitalizations Associated With Mitigation Effectiveness Reduction

The rate of additional hospitalizations associated with decreases in mitigation effectiveness mirrored the additional cases and had a similar association with local incidence and student vaccination coverage (eFigure 1 in the Supplement). The local incidence thresholds required to keep the number of additional hospitalizations from mitigation reductions less than 1 per 100 000 individuals in the immediate school community per month were 21 or fewer cases per 100 000 residents per day across a range of student vaccination and mitigation effectiveness values, except with 90% vaccination for both students and adults (Figure 3). The thresholds were higher for an objective of keeping additional hospitalizations fewer than 5 per 100 000 individuals in the immediate school

Figure 2. Model-Estimated Mean Number of Additional Cases Over 30 Days in the Immediate School Community Associated With Reductions in Mitigation Effectiveness in the Simulated Elementary School Setting



Panels reflect decreasingly transmissible variants from top to bottom, and larger differences in effectiveness between intensive and less intensive mitigation measures from left to right. The changes in mitigation effectiveness reflect the midpoints or bounds of the A and B mitigation scenarios presented in Figure 1: 60% to 40% mitigation effectiveness (smaller effectiveness decrease); 70% to 30% effectiveness (moderate effectiveness decrease); and 80% to 20% effectiveness (larger effectiveness decrease). Adult vaccination coverage is assumed to be 70% in all scenarios.

community per month, although still 29 or fewer cases per 100 000 residents per day for the larger changes in mitigation effectiveness (eg, 70% to 30%) with a student vaccination rate of 25% or less.

Sensitivity Analyses

When adding weekly screening of students, educators, and staff in the Delta variant scenarios, the additional cases associated with changes in mitigation effectiveness decreased substantially (**Figure 4**A). Assuming a decrease in mitigation effectiveness from 70% to 30%, a 50% student vaccination rate, and a goal of fewer than 5 additional cases per month in the immediate school community, decision-makers could remove mitigation at or below a local incidence of approximately 21 cases per 100 000 residents per day when weekly screening is implemented, compared with 10 cases per 100 000 residents per day with only diagnostic testing (Figure 4A, eTable 4 in the Supplement). Similarly, the probability of at least 1 in-school transmission per month decreases with the implementation of weekly screening, although the changes in decision thresholds are less stark (eFigure 3 and eTable 4 in the Supplement). The 50% and 25% vaccine effectiveness analyses (Figure 4B; eFigure 4, eFigure 5, eTable 5, and eTable 6 in the Supplement) showed increased transmission and smaller changes in the decision thresholds across student vaccination coverage compared with the 70% and 90% effectiveness analyses (Figure 1, Figure 2, Figure 3, and Figure 4; eFigure 6 and eTable 7 in the Supplement). Higher vaccination coverage in both adults and students substantially increased the local incidence thresholds (Figure 3), while lower adult vaccine coverage (ie, 50%) only moderately changed model-estimated decision thresholds, aside from the additional hospitalization objectives. The hospitalization results were sensitive to the adult vaccination rate given that unvaccinated hospitalization risk is highest in adults and we assumed complete vaccine protection against hospitalization (a conservative assumption regarding the consequences of unmasking) (eFigure 2 and eTable 3 in the Supplement).

Figure 3. Observed Local Incidence Decision Thresholds for the Delta Variant Baseline Scenario

Outcome		Probability of ≥1 in-school transmission per mo, with baseline mitigation effectiveness of:								
		40%			30%			20%		
Decision objective		To keep probability of ≥1 in-school transmission less than:								
		25%	50%	75%	25%	50%	75%	25%	50%	75%
		Baseline mitigation can only achieve objective at or below observed local incidence of:[a]								
Student vaccine coverage	0%	<1	3	6	<1	2	6	<1	2	5
	25%	1	3	7	<1	3	6	<1	3	6
	50%	1	4	7	1	3	7	1	3	6
	70%	1	4	8	1	4	7	1	3	7
	90%[b]	2	5	10	2	5	9	1	4	8
Outcome		Mean additional cases per mo associated with change in mitigation effectiveness:[c]								
		60% to 40%			70% to 30%			80% to 20%		
Decision objective		To keep mean additional cases below:								
		3	5	10	3	5	10	3	5	10
		Mitigation can only be reduced at or below observed local incidence of:								
Student vaccine coverage	0%	6	10	22	3	5	10	2	3	6
	25%	8	14	33	4	7	14	3	4	9
	50%	12	22	>50	6	10	22	4	6	14
	70%	18	32	>50	9	14	32	6	9	20
	90%[b]	34	>50	>50	15	27	>50	10	17	40
Outcome		Mean additional hospitalizations per 100 000 per mo associated with change in mitigation effectiveness:[c]								
		60% to 40%			70% to 30%			80% to 20%		
Decision objective		To keep mean additional hospitalizations below:								
		1	3	5	1	3	5	1	3	5
		Mitigation can only be reduced at or below observed local incidence of:								
Student vaccine coverage	0%	7	25	>50	3	11	20	2	7	12
	25%	10	37	>50	4	16	29	3	10	18
	50%	14	>50	>50	7	22	45	5	14	25
	70%	21	>50	>50	10	33	>50	6	21	38
	90%[b]	>50	>50	>50	>50	>50	>50	32	>50	>50

Units of observed local incidence thresholds are cases per 100 000 residents per day. It was assumed that 33% of all actual cases are observed.

[a] If observed local incidence is above these thresholds, additional mitigation measures beyond baseline will be needed to achieve each objective (eg, keep probability of at least 1 in-school transmission per month below 50%).

[b] The Delta baseline scenario presented in this table reflects 70% adult vaccination coverage, 70% vaccine effectiveness, and no weekly screening, except for the 90% student vaccination rows, which reflect 90% adult vaccination coverage (since it is assumed adult coverage will always be at least as high as student coverage).

[c] Only includes estimated mean additional cases and hospitalizations in the immediate school community (students, teachers, staff, and household members). The potential for additional cases in the wider community stemming from in-school transmission was not modeled.

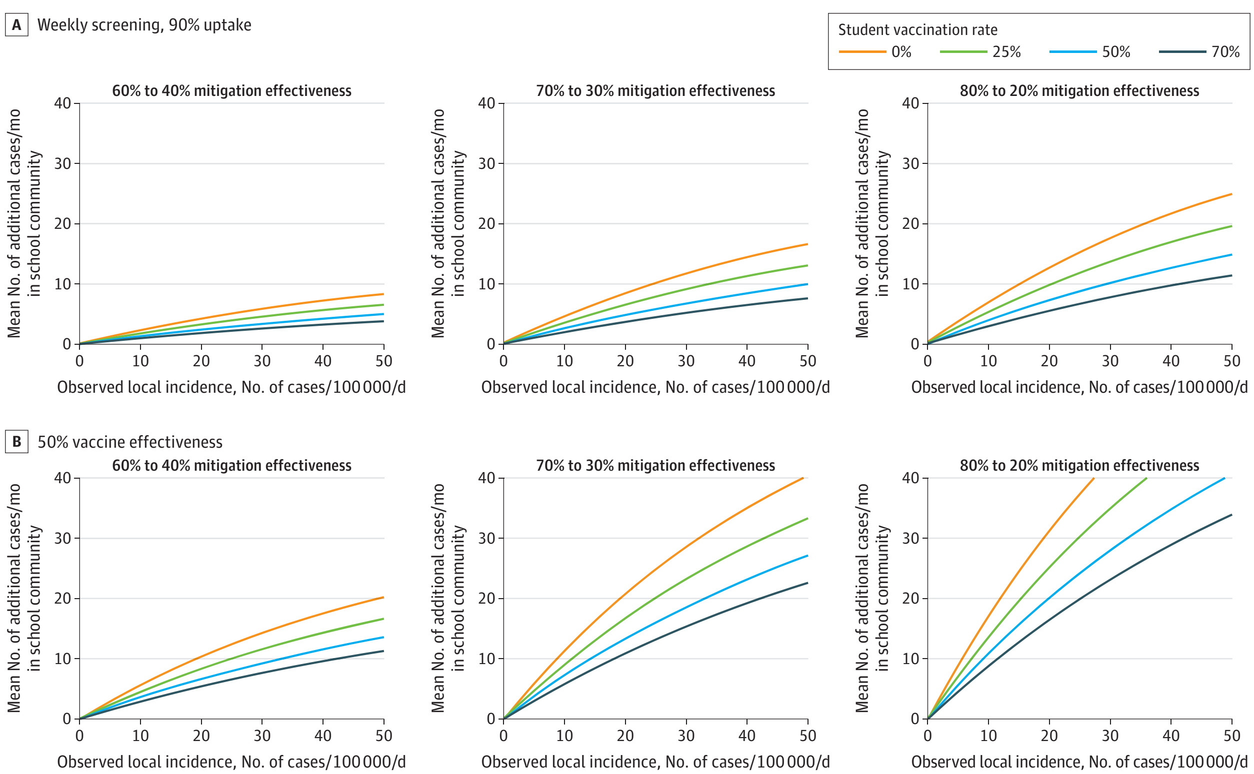
Discussion

We used a previously published agent-based dynamic transmission model to examine the association between vaccine uptake and effectiveness, in-school mitigation measures including masking, observed local COVID-19 incidence, and SARS-CoV-2 transmissions in an elementary school community. In order to inform ongoing decisions about masking and other measures in schools, we identified thresholds of observed local COVID-19 incidence at which decision-makers might choose to increase or decrease mitigation measures, depending on their objectives. There were 4 key findings.

First, the local incidence thresholds for adding or removing mitigation (on-ramps and off-ramps) depend on the objective that the school community seeks to achieve. When the objective is to minimize the probability of any in-school transmission, thresholds are much lower than when the objective is to keep the number of additional cases less than a given level (Figure 3). This result is intuitive, but the model provides a sense of the magnitude of this difference. Additionally, many incidence thresholds identified in this analysis are low relative to historic and current COVID-19 incidence in many districts across the United States, suggesting that even with high rates of vaccination, depending on their goals, communities may continue to find value in measures such as masking and ventilation until incidence decreases.

Second, these on-ramps and off-ramps are highly dependent on the effectiveness of each type of mitigation, which can vary across contexts and individual school settings. We evaluated a wide range of effectiveness: 20% to 40% risk reduction for simple ventilation and handwashing, 60% to 80% for ventilation and handwashing plus universal indoor masking, and 90% to 100% for the full multilayered mitigation packages often used in 2020 to 2021. Data on these measures are limited,

Figure 4. Weekly Screening and Vaccine Effectiveness Sensitivity Analyses for the Mean Number of Additional Cases Over 30 Days in the Immediate School Community Associated With Reductions in Mitigation Effectiveness in the Simulated Elementary School Setting



A, This scenario is for the Delta variant, with weekly in-school screening (90% uptake) and 70% vaccine effectiveness. B, This scenario is for the Delta variant, with 50% vaccine effectiveness and only diagnostic testing. Adult vaccination coverage is assumed to be 70% in both scenarios. Panels reflect larger differences in effectiveness between intensive and less intensive mitigation measures from left to right.

and these ranges are uncertain; schools may be able to assess where they fall within these ranges based on adherence to past mitigation measures and the resources available. Screening of asymptomatic students, educators, and staff may be another tool to support more permissive off-ramps when unmasking is strongly desired. Weekly screening decreased the additional modeled cases associated with mitigation relaxation compared with only diagnostic testing (Figure 4A), approximately doubling the local incidence thresholds for removing other mitigation measures (eTable 4 in the Supplement), but schools need to weigh the cost of screening against these benefits. Weekly screening after unmasking may also provide valuable information about the consequences of this change in an individual school.

Third, student vaccination coverage was associated with a very substantial shift in incidence-based thresholds; less intensive in-school mitigation measures are needed to maintain lower transmission as student vaccination rates increase (Figure 3). The incidence-based thresholds were also sensitive to vaccine effectiveness. The higher modeled values (eg, 90%) may more accurately reflect recent vaccination for children (before waning vaccine effectiveness occurs)[60] and/or booster vaccinations for adults[61] with the Delta variant, and the lower values (eg, 25% and 50%) may reflect values in the future, with further waning or new variants, including Omicron (eTables 5-7 in the Supplement).[62] Importantly, substantial racial and economic disparities are quickly emerging in elementary student vaccination rates, mirroring these disparities in adults.[63,64] These results demonstrate that efforts to ensure equitable access to accurate information, trustworthy messengers, and convenient vaccination sites will be critical to ensuring equitable application or relaxation of mitigation measures in schools.

Fourth, many policy makers have suggested that the objective of COVID-19 policies should be reducing hospitalizations and deaths, rather than numbers of infections or reported cases, noting that widespread availability of vaccination will reduce morbidity and mortality when infections occur.[44,65] Although our approach to estimating hospitalization rates is approximate, it provides insight into the order of magnitude of potential hospitalizations resulting from different levels of mitigation effectiveness. To achieve even a fairly permissive objective of avoiding 5 additional hospitalizations per 100 000 individuals per month, some scenarios permit unmasking only at incidence thresholds below 30 observed cases per 100 000 residents per day (if removing mitigation is associated with moderate or large decreases in effectiveness, with low student vaccination uptake). In scenarios with high student vaccination rates or smaller incremental mitigation effectiveness, unmasking could achieve this goal at high levels of local incidence (ie, >45 cases per 100 000 per day).

Limitations

These results should be interpreted in the context of model limitations. First, several key data inputs were highly uncertain, including the effectiveness of individual mitigation interventions, proportions of all SARS-CoV-2 infections that are observed and reported, and hospitalization risks. To account for this uncertainty, we presented results across a range of mitigation effectiveness assumptions; incidence-based thresholds can be adjusted to reflect different proportions detected through simple multiplication (eg, to convert base-case assumption of 33% detection to 50% detection, incidence thresholds can be multiplied by 1.5); and the hospitalization rate objectives (eg, keep additional hospitalizations below 5 per 100 000 individuals per month) can be multiplied by similar conversion factors. COVID-19 incidence data at the most local level available (eg, school or city or town), including data from high-uptake asymptomatic screening, could provide the best information to inform the connection between observed and actual case counts. Additionally, this analysis focused on students, educators, staff, and their household members; additional downstream effects in the nonschool community are not captured (eg, infections from students to family outside the immediate household), which is especially relevant for the hospitalization rate results, because downstream infections in older individuals are more likely to result in hospitalizations compared with those in the relatively younger immediate school community.

Conclusions

In this modeling study of a simulated elementary school and the risks of in-school SARS-CoV-2 transmission, we found that the risks of transmission and resulting infections among students, educators, staff, and their household members are high when a highly infectious variant predominates and students are unvaccinated. Mitigation measures or vaccinations for students substantially reduced these modeled risks. Appropriate on-ramps and off-ramps for in-school mitigation depend on the objectives that policy makers seek to achieve. These findings provide a framework for responsive plans in which mitigation is deployed based on local COVID-19 incidence and vaccine uptake. For evidence-based COVID-19 policy, school policy makers must define clear goals and select thresholds to add or remove mitigation measures based on these goals.

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SUPPLEMENT.

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eMethods 2. Sources for Mitigation Ranges
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Supplemental Online Content

Giardina J, Bilinski A, Fitzpatrick MC, et al. Model-estimated association between simulated US elementary school–related SARS-CoV-2 transmission, mitigation interventions, and vaccine coverage across local incidence levels. *JAMA Netw Open.* 2022;5(2):e2147827. doi:10.1001/jamanetworkopen.2021.47827

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods 1. Model Structure and Parameterization

Basic Transmission Model and Course of Infection
The model used in this study, adapted from the model described by Bilinski, et al.[1], is an agent-based implementation of an SEIR model. Susceptible individuals who are exposed to an infectious individual have a daily probability of becoming infected determined by the daily attack rate, the location and length of the contact, the relative infectiousness of the infected contact (determined both by age and the potential for overdispersion among adults), and the relative susceptibility of the susceptible individual, as detailed in Table 1 in the main text – the probability of infection from a contact is the product of these terms. Following infection, an individual goes through an latent period determined by the distributions listed in Table 1. Following the latent period, an individual is infectious for a duration drawn from a lognormal distribution (as described in Table 1), and can either be asymptomatic or symptomatic, and clinical or subclinical (all asymptomatic individuals are subclinical, but not vice versa). Symptoms and clinical presentation of disease, if they appear, occur after infectiousness begins, with the length of time between exposure and presentation drawn from a gamma distribution (as described in Table 1). Following the infectious period, an individual cannot be reinfected.

Population
The simulated elementary school had 638 students across 6 grades, with 5 classes per grade. There is one teacher for each classroom and 30 additional staff members in the school, for a total of 60 teachers/staff. This synthetic population was developed by Bilinski, et al.[1], based on data from Wheaton[2] and National Center for Education Statistics[3], and is meant to reflect the average size of elementary schools in the US (weighted by the proportion of total elementary school students in the US attending each school) and the number and distribution of siblings within a school. Each student household includes two adults, with siblings assigned to the same household, and each teacher/staff household is assumed to have one additional adult.

Preventative Interventions

Vaccines
Individuals in the school community are randomly vaccinated according to the coverage rates in Table 1. Vaccinated individuals have a probability of being protected against infection equal to the vaccine efficacy; individuals are either fully protected or not protected at all through the course of the entire modeled period.

In-School Mitigation Interventions
The mitigation effectiveness described in the main text is applied as a multiplier to the full day in-school symptomatic adult-to-adult secondary attack rate listed in Table 1. For example, 40% mitigation effectiveness applied to the delta variant attack rate of 7% results in an actual attack rate of 4.2% (7%*(100% - 40%)). This mitigation is only applied to in-school contacts and is not applied to home or childcare contacts.

Isolation and Quarantine
Infected students and teachers/staff who present clinical symptoms are immediately isolated for 7 days and given a PCR test (with 100% sensitivity for symptomatic individuals). Once an individual has a positive result, all unvaccinated individuals in classrooms who had contact with that individual are quarantined for 7 days. (In order to reflect actual practices within schools, if an individual has a positive test result within three days of a classroom coming out of quarantine, that classroom is not re-quarantined.)

Weekly Screening
For the sensitivity analysis including weekly screening, all individuals at school (i.e., students and teachers/staff) are offered PCR tests every Monday. We assume that there is 90% uptake of the tests each week (randomly selected from the eligible population), and that the PCR tests have 90% sensitivity for asymptomatic individuals and a one-day turnaround time. Following the receipt of a positive test result, the infected individual and their classroom contacts are isolated and quarantined using the procedure described above.

Classroom and Schedule Structure
Students are randomly sorted into classrooms (within grades) and attend school 5 days a week (unless the student is isolated or classrooms are quarantined). In addition to interacting with students in their primary classroom, each day some classroom cohorts also attend "specials" classes (e.g., related arts) with a different teacher. On days when a student does not attend school (because it is a weekend), the student's household randomly interacts with another household with two parents present (from across the two households) to reflect shared childcare.

Seeded Infections

The individuals in the school community are seeded daily with infections sourced from the wider local community. The daily probability that an individual not protected by a vaccine (see above) acquires an infection from the wider local community is equal to the actual local incidence rate (ie, the observed local incidence rate divided by the assumed percentage of cases that are observed) divided by the proportion of the population that is not protected by the vaccine (this normalization by the fraction of the susceptible population ensures that the rate of infection introductions into the school is equal to the actual local incidence rate). Since children currently make up a significant fraction of cases in the wider community,[4] children and adults were assumed to have equal local incidence rates. Also, note that it is assumed that this daily probability of infections sourced from the wider local community includes secondary infections from cases within a household that were directly sourced from the wider community. This means that, if a parent acquires a local community-sourced infection, the model does not allow them to pass it to their child (on the other hand, any school-sourced infections can be transmitted within a household). This assumption is made to ensure the rate of infections introduced to a school is not inflated beyond the actual local incidence rate, and that the model is focused on simulating the dynamics of school-related infections.

Secondary Attack Rates

We used previously reported findings to derive full day symptomatic adult-to-adult in-school secondary attack rates (SARs), defined as the proportion of susceptible adults exposed to a symptomatic adult index case who acquire SARS-CoV-2 infection per full school day of contact in the absence of mitigation, for wild-type virus, alpha variant, and delta variant. As in previous work, the adult-to-adult wild-type variant attack rate was 2%/day,[1] consistent with 2020-21 data from schools with minimal mitigation; a lower-bound estimate suggests a total in-school attack rate of 11%,[5] corresponding to a daily attack near 2% (assuming a constant daily attack rate over a 5-day infectious period). The transmissibility of the alpha variant is estimated at 59% higher than wild-type in the US,[6] so we assumed an attack rate of 3.5%/day.

To estimate the daily attack rate for the delta variant, we identified estimates for the overall household attack rates among unvaccinated populations since we apply the effects of vaccination within our model. The estimates for overall household attack rates included 38% in a UK-based study on symptomatic index cases,[7] 53% in a case study of an outbreak associated with an Oklahoma gymnastics facility,[8] and 71% in a government report from Australia on infections in homes where the index case was infected at school.[9] The estimate from the UK study was strictly for unvaccinated contacts, while the estimates from the Oklahoma and Australia studies were from populations with relatively low vaccination rates. We used the middle 53% estimate for the overall household attack in our model, which corresponds to a 14% daily household attack rate assuming a 5-day infectious period. Assuming that the daily household attack rate is double the in-school rate, to reflect a higher degree of contact within the home, and a 5-day infectious period, this estimate corresponds with about a 7%/day in-school attack rate.

This also aligns with a previous school modeling study, which assumed a twofold increase in transmissibility of delta compared to the alpha variant,[10] which would also suggest a 7%/day attack rate for delta compared to 3.5%/day for alpha. A case study of an elementary school outbreak estimated an overall classroom attack rate of about 50% from a single unvaccinated teacher,[11] which reflects a daily attack rate of about 13%, significantly higher than 7%/day. This is potentially a case of overdispersion in infectiousness, however, which is reflected in our model by applying a multiplier to individual infectiousness drawn from a lognormal distribution (see Table 1).[12,13] Within the model, we also apply reductions in the attack rate for asymptomatic adults (half as infectious),[14] children at school (half as infectious and half as susceptible),[1] and children at home (half as infectious if asymptomatic and half as susceptible).[1] We assumed symptomatic students were equally infectious as adults within the household setting to reflect recent evidence that younger children are potentially at least as infectious as older children in that setting, possibly because of increased contacts between younger children and their caregivers.[15]

Hospitalization risk

In order to parameterize the hospitalization risk among unvaccinated patients with SARS-CoV-2, we used estimates of the overall infection fatality rate (IFR) and the mortality rate among hospitalized patients, provided by the CDC for use in COVID-19 models.[16] If it is assumed that all patients who die are hospitalized prior to death, dividing the IFR by the mortality rate among hospitalized patients will recover the probability that an individual who has SARS-CoV-2 will be hospitalized (assuming, of course, that the IFR and hospitalized mortality rate are correctly estimated). The CDC parameter set provided estimates across four age groups: 0-17 years old, 18-49 years old, 50-64 years old, and 65+ years old. We used the parameters from the 18-49 years old age group for the unvaccinated adults in the model since parents of elementary school aged children are likely to fall into this age group, although some caregivers and teachers/staff could fall into higher age ranges. This age group had an IFR of 500/million and a 2.1% chance of death among hospitalized patients, leading to an estimated hospitalization risk of 2.4% among all unvaccinated adults.

The 0-17 years old age group had a 20/million IFR and 0.7% hospitalized mortality rate, resulting in an estimated 0.29% hospitalization risk for each infection in this age group. For the elementary student group, however, this estimate could not be directly applied in the model, since older children (e.g., 12-17 years old) in general have an observed increased risk of hospitalization.[17] Instead, given that preliminary seroprevalence estimates from the CDC show roughly equivalent cumulative incidence of SARS-CoV-2 infection between the 5-11 and 12-17 years old age groups,[18] and that a COVID-NET study indicated cumulative incidence of hospitalization among the 5-11 year old group was about 38% of the cumulative incidence of the 12-17 year old group,[17] we multiplied the 0.29% hospitalization risk estimate by 38% to arrive at our final estimate of a 0.1% hospitalization risk of all unvaccinated students in the model.

Finally, we assumed that all vaccinated individuals had a negligible risk of hospitalization, since recent data has shown high vaccine effectiveness against hospitalization for ages <49.[19] Also, note that the 2% hospitalization rate used for adults is similar to inputs in other models, such as the low estimate used by Lemaitre, et al.[20] Still, this parameter should be considered to be highly uncertain and only used to provide a sense of the order of magnitude of hospitalizations resulting from cases in the immediate school community. The estimate of the number of hospitalizations from this parameter will probably be biased downward because (1) it does not consider wider community level effects of cases within the immediate school community (e.g., spread from students to elderly relatives) and (2) it assumes no hospitalization risk from breakthrough cases, which is not reflected in the available data, especially for older age groups – while vaccination greatly reduces the risk of hospitalization, it does not completely eliminate it.[19]

Vaccine Effectiveness

Although initial clinical trials in adults demonstrated vaccine efficacy >90%,[21,22] this likely wanes over time; observational data from the US during months when the delta variant predominated suggest vaccine effectiveness of 42-76%, in addition to a meta-analytic estimate of 72%.[23-27] In the base case, we modeled vaccine effectiveness of 70% in preventing all infections among students, educators/staff, and household members. We also conducted sensitivity analyses with 90%, 50%, and 25% effectiveness. The higher values (e.g., 90%) may more accurately reflect the impact of very recent vaccination for children (before waning vaccine effectiveness occurs)[28] and/or booster vaccinations for adults,[29] and the lower values (25%, 50%) may reflect values in the future, with further waning or new variants, including omicron.[30]

eMethods 2. Sources for Mitigation Ranges

***A**: Simple ventilation and handwashing (open windows if present, portable air filters, maintain existing HVAC systems, and regular handwashing): 20-40% assumed effectiveness*

Vouriot, et al.[31] 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.[32] 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.[33] Combining these data, we estimated a range of 20-40% risk reduction (since most classrooms will not have access to portable air cleaners).

***B**: Interventions in A, plus universal masking (a policy of masking all students and educators/staff): 60-80% assumed effectiveness*

There are few studies on the specific combination of masking and ventilation/handwashing that do not consider other interventions as well. Considering data from studies of masks alone, a meta-analysis estimated that using non-medical masks was, depending on the model used, associated with a 43% or 35% reduction in respiratory virus infection risk.[34] A recent study from Abaluck, et al.[35] found that a cluster randomized intervention in Bangladesh to promote the use of masks increased mask use by 29% and was associated with a 9.3% percentage point decrease in COVID-19 seroprevalence. The authors note that the effect of universal masking would likely be several times higher; they report a simple instrumental variable analysis in the supplementary material that estimates a 32% reduction in seroprevalence from universal masking, which is in line with the meta-analysis estimates on the reduction in infection risk from masking alone. Similarly, a meta-analysis on mask effectiveness across studies focusing on SARS-CoV-1, MERS, and SARS-CoV-2 by Chu, et al.[36] found a 44% reduction in risk for masks used in the community. There is substantial uncertainty in this estimate, with many studies reporting higher risk reductions.[37] Additionally, data from studies of simulated respiratory particles demonstrate fitted filtration efficiency values (proportion of particles kept behind a mask) of up to about 80% with consumer grade masks.[38,39] An experimental and mathematical modeling study on aerosol dynamics from Rothamer, et al.[40] estimated that a non-medical procedure mask with a baseline effectiveness of 29% had an effectiveness of 62-77% when combined with different levels of ventilation, with this combined effectiveness increasing for masks with better baseline effectiveness. This is also consistent with the meta-analysis from Chu, et al.[36] on masking in a healthcare setting (likely to be accompanied by ventilation; 70% reduction in risk) and a range of case studies suggesting masking effectiveness can reach as high as 70-79% in non-school settings, including in some households in China and during an outbreak on a US Navy ship.[37] We anticipated that the combined effectiveness of both masking and ventilation/handwashing (B) would be between the effectiveness estimates for mitigation groups A and C, and based on the data above, we assumed that masking and ventilation/handwashing was approximately 60-80% effective.

***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):[41] 90-100% assumed effectiveness*

This is the assumed maximum mitigation effect. CDC reports very effective in-school mitigation when the full package of interventions are implemented,[42] including those from Falk, et al.[43] and Zimmerman, et al.[44] 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.

eMethods 3. Meta-Modeling Methods

The raw model output is highly stochastic and can only be evaluated at discrete parameter values, so to generate the presented smoothed heatmaps and associated contour lines, line graphs, and decision cutoffs across a continuous range of local incidence and mitigation effectiveness, we fit regressions for each outcome and associated scenario (e.g., at least one in-school transmission in the wild-type, 0% child vaccine, 70% adult vaccine scenario) as a function of observed local incidence and mitigation. This is essentially an application of regression meta-modeling, which is described by Jalal, et al.[45] as a way to summarize model results.

For each scenario (described in the main text), we ran 100 replicates of the base model for each combination of observed local incidence from 0 to 60 cases/100k/day (incremented by 1) and mitigation effectiveness from 0 to 100% (incremented by 1%) using the model code available at https://github.com/abilinski/BackToSchool2. (We only present 0 to 50 case notifications/100k/day in the study results to avoid boundary issues that can arise when fitting the regressions to stochastic output.)

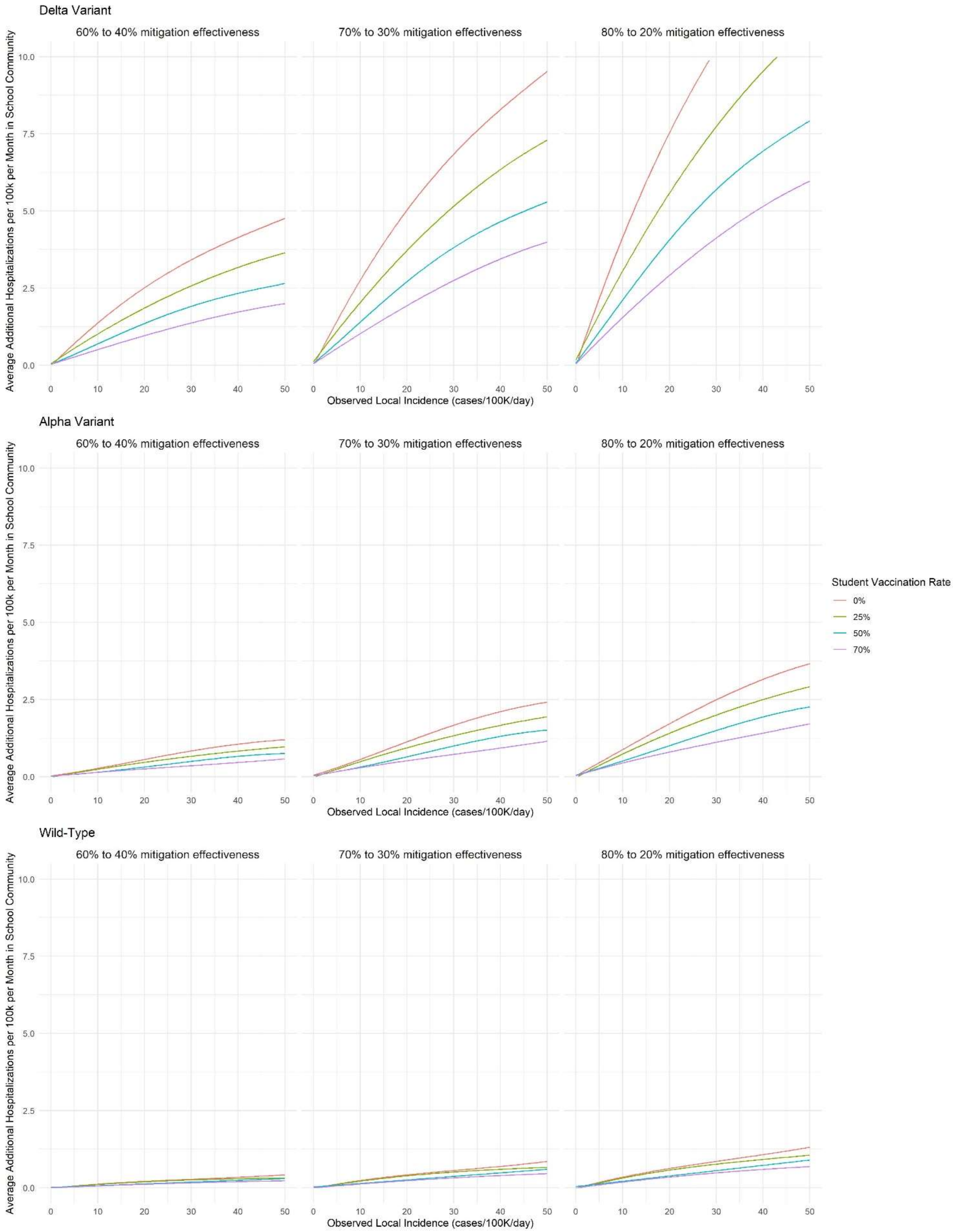
For each outcome of interest (i.e., more than one in-school transmission, total number of cases, total number of hospitalizations), the dependent variable of the regression was the mean of 90 replicates in a training sample at each combination of incidence and mitigation. (Note that for the additional cases and hospitalization metrics, we fit the regression to the overall number of cases and hospitalizations in the immediate school community, and then subtracted the fitted regression across the different mitigation levels to generate the estimated average additional cases/hospitalizations from moving between each mitigation level.) 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: $Outcome = \beta_0 + \beta_1 \ln Incidence + \beta_2 \ln Mitigation + \beta_3 \ln Incidence * \ln Mitigation$

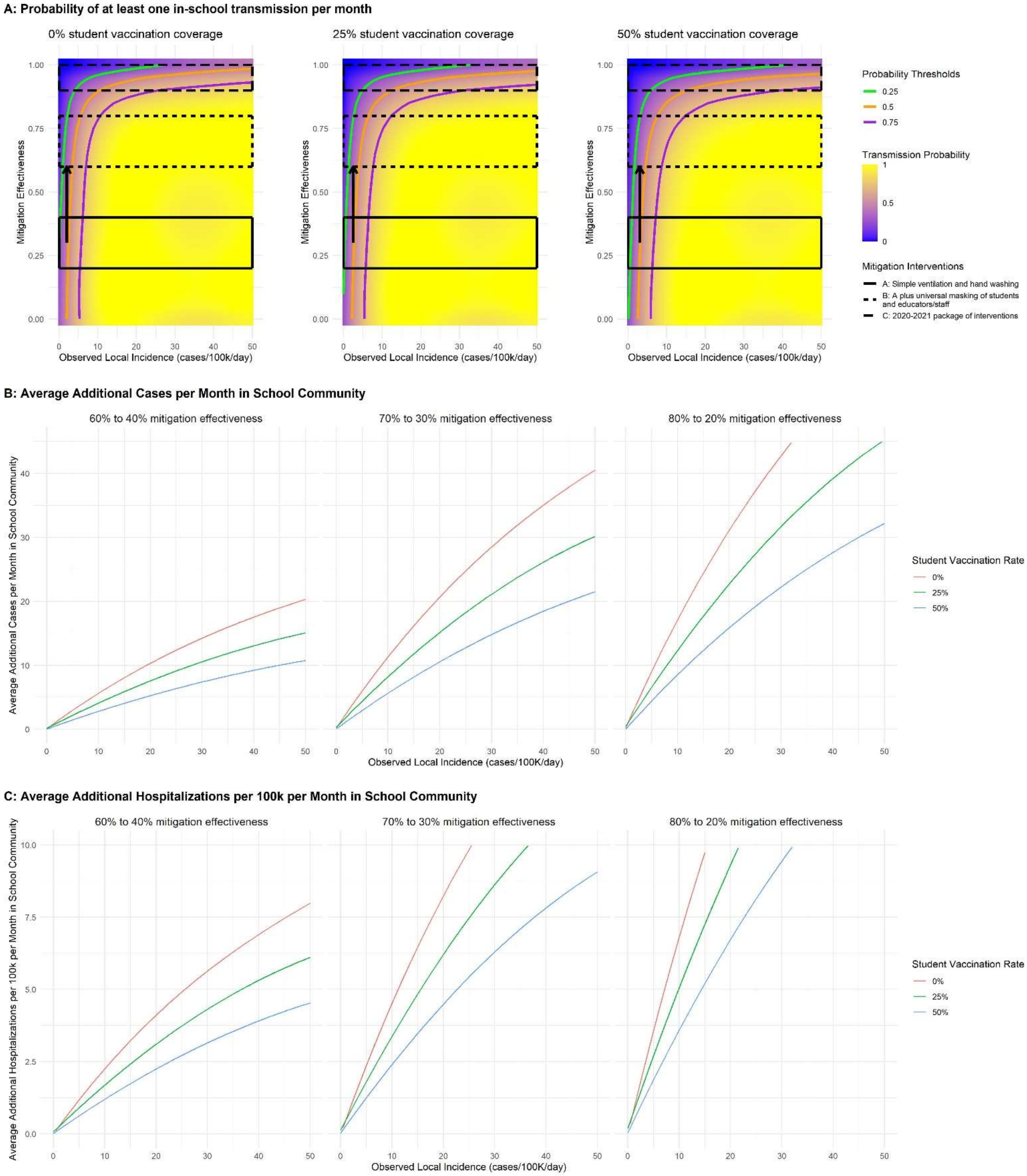
For each combination of outcome measure and scenario, we selected the regression which minimized the root mean-squared prediction error in a hold-out test set containing 10 replicates (10%) at each combination of incidence and mitigation.

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 the hold-out test set and the average outcome predicted by the selected meta-model at the midpoint of the local incidence and mitigation values for each bin. We evaluated the fit for two different bin sizes: “large” bins, with a bin width of 5 for local incidence and 0.1 for mitigation effectiveness, and “small” bins with a bin width of 1 for local incidence and 0.1 for mitigation effectiveness. The lowest R^2 was 0.95 for the small bins and 0.98 for the large bins, indicating that the smoothing procedure to generate the figures accurately reflects the average model output within these bin sizes over the different scenarios analyzed.

eFigure 1. Model-Estimated Average Number of Additional Hospitalizations per 100 000 Individuals Over 30 Days in the Immediate School Community Associated With Reductions in Mitigation Effectiveness in the Simulated Elementary School Setting (With 70% Adult Vaccination, 70% Vaccine Effectiveness, and No Weekly Screening)



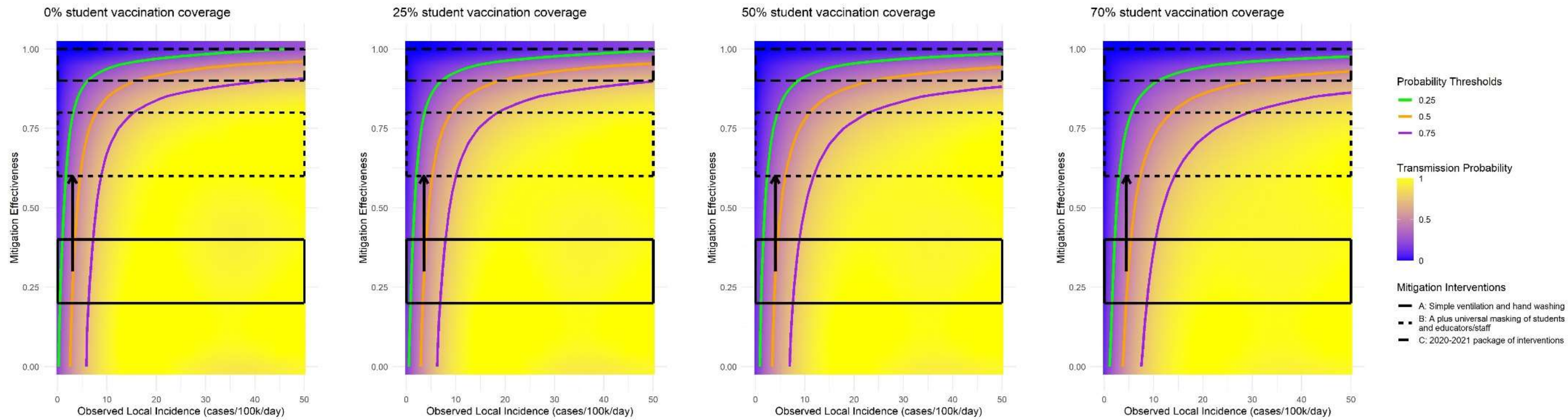
eFigure 2. Sensitivity Analysis for 50% Adult Vaccination Rate (With Delta Variant, 70% Vaccine Effectiveness, and No Weekly Screening)



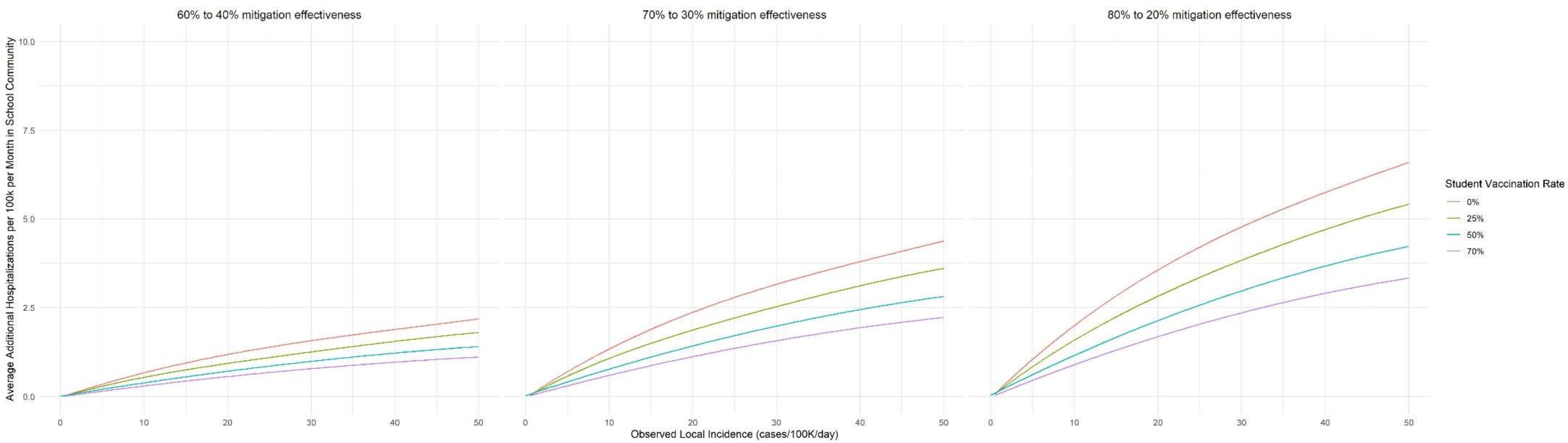
The row panels display the three outcomes analyzed in the study: (A) probability of at least one in-school transmission over 30 days; (B) model-estimated average number of additional cases over 30 days in the immediate school community associated with reductions in mitigation effectiveness; (C) model-estimated average number of additional hospitalizations per 100,000 individuals over 30 days in the immediate school community associated with reductions in mitigation effectiveness. The arrows in panel A indicate the local COVID-19 incidence rate at which a school might opt to move to the next more intensive mitigation strategy at a baseline 30% effectiveness, if the objective is to maintain the probability of at least one in-school transmission per month below 50%. 70% student vaccination coverage was not analyzed here because we assumed adult coverage would also be greater than student coverage.

eFigure 3. Sensitivity Analysis for Weekly Screening (With Delta Variant, 70% Adult Vaccination Rate, and 70% Vaccine Effectiveness)

A: Probability of at least one in-school transmission per month

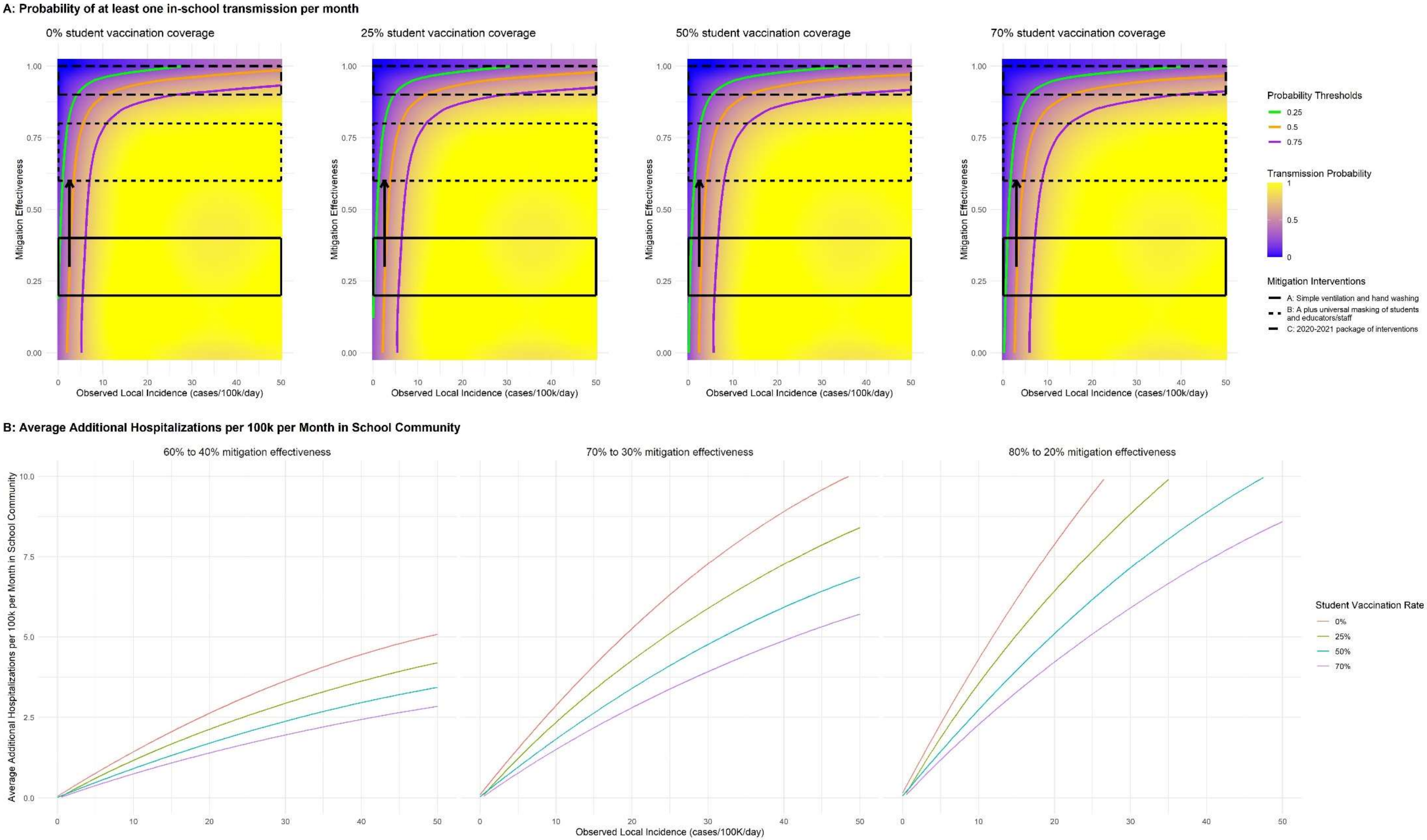


B: Average Additional Hospitalizations per 100k per Month in School Community



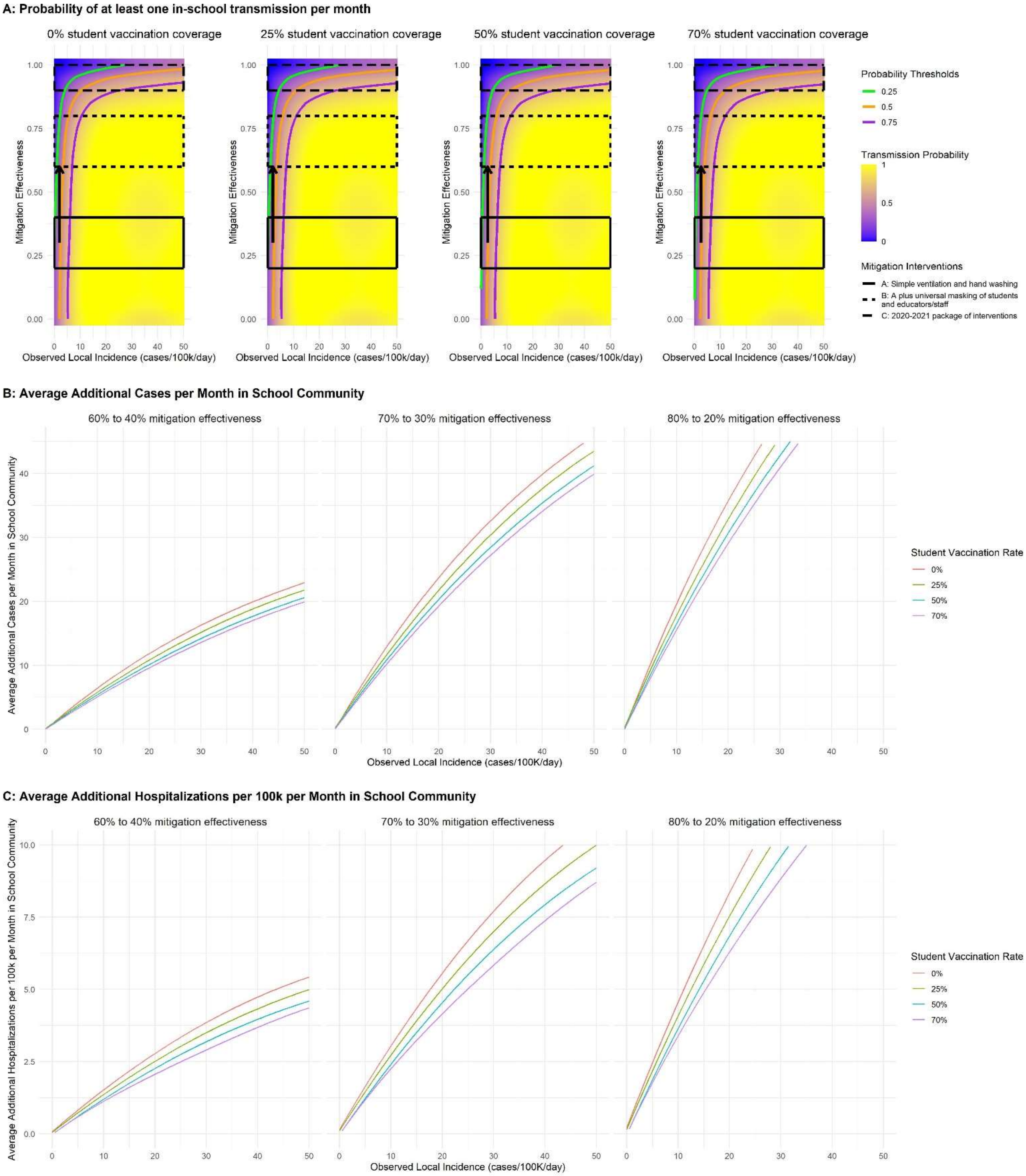
The row panels display two of the outcomes analyzed in the study: (A) probability of at least one in-school transmission over 30 days; (B) model-estimated average number of additional hospitalizations per 100,000 individuals over 30 days in the immediate school community associated with reductions in mitigation effectiveness. The arrows in panel A indicate the local COVID-19 incidence rate at which a school might opt to move to the next more intensive mitigation strategy at a baseline 30% effectiveness, if the objective is to maintain the probability of at least one in-school transmission per month below 50%. The third outcome (model-estimated average number of additional cases over 30 days in the immediate school community associated with reductions in mitigation effectiveness) is shown in Figure 4A, in the main text.

eFigure 4. Sensitivity Analysis for 50% Vaccine Effectiveness (With Delta Variant, 70% Adult Vaccination Rate, and No Weekly Screening)



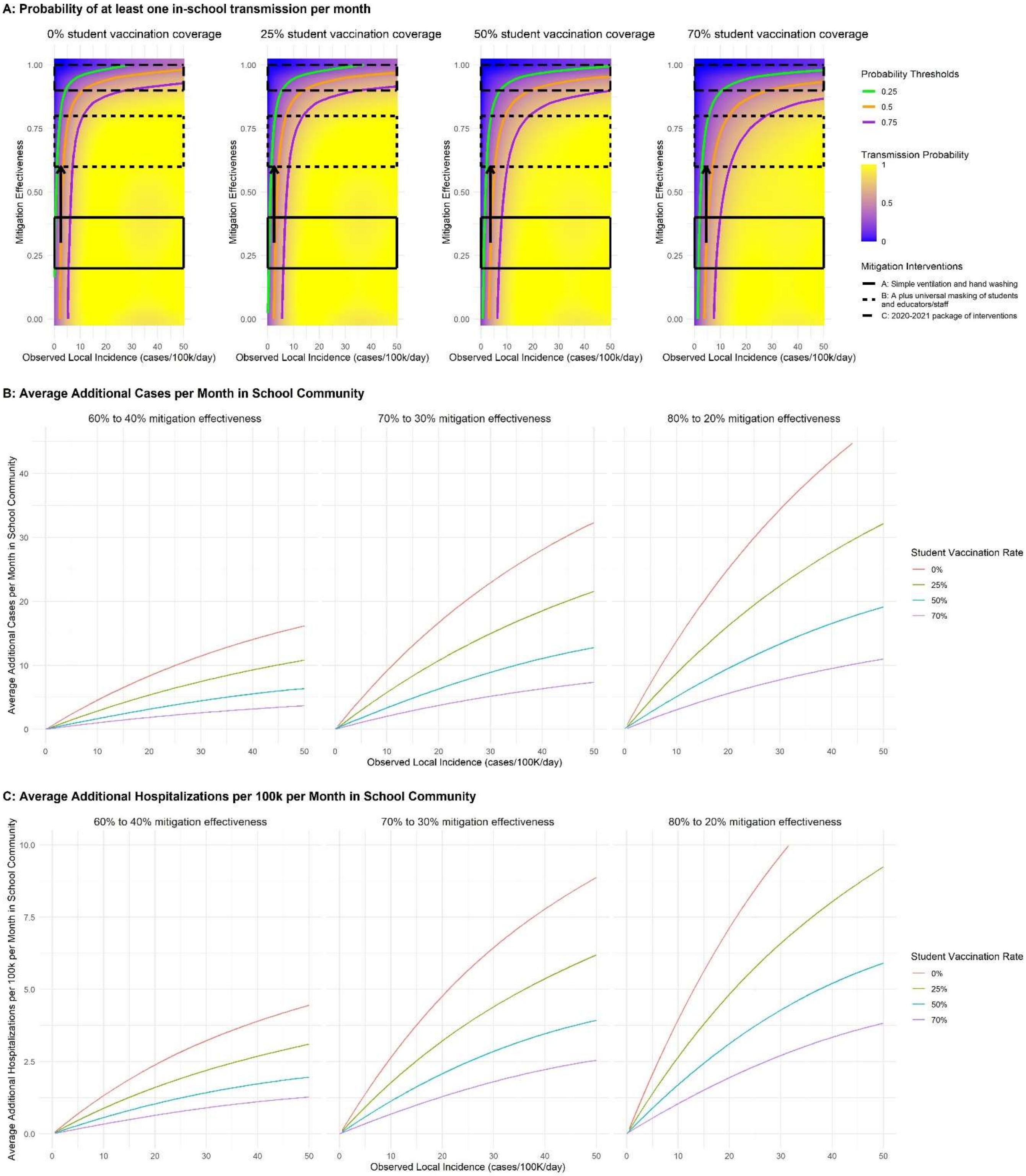
The row panels display two of the outcomes analyzed in the study: (A) probability of at least one in-school transmission over 30 days; (B) model-estimated average number of additional hospitalizations per 100,000 individuals over 30 days in the immediate school community associated with reductions in mitigation effectiveness. The arrows in panel A indicate the local COVID-19 incidence rate at which a school might opt to move to the next more intensive mitigation strategy at a baseline 30% effectiveness, if the objective is to maintain the probability of at least one in-school transmission per month below 50%. The third outcome (model-estimated average number of additional cases over 30 days in the immediate school community associated with reductions in mitigation effectiveness) is shown in Figure 4B, in the main text. Note that the hospitalization outcome assumes perfect vaccine protection against hospitalization, even with decreased protection against infection.

eFigure 5. Sensitivity Analysis for 25% Vaccine Effectiveness (With Delta Variant, 70% Adult Vaccination Rate, and No Weekly Screening)



The row panels display the three outcomes analyzed in the study: (A) probability of at least one in-school transmission over 30 days; (B) model-estimated average number of additional cases over 30 days in the immediate school community associated with reductions in mitigation effectiveness; (C) model-estimated average number of additional hospitalizations per 100,000 individuals over 30 days in the immediate school community associated with reductions in mitigation effectiveness. The arrows in panel A indicate the local COVID-19 incidence rate at which a school might opt to move to the next more intensive mitigation strategy at a baseline 30% effectiveness, if the objective is to maintain the probability of at least one in-school transmission per month below 50%. Note that the hospitalization outcome assumes perfect vaccine protection against hospitalization, even with decreased protection against infection.

eFigure 6. Sensitivity Analysis for 90% Vaccine Effectiveness (With Delta Variant, 70% Adult Vaccination Rate, and No Weekly Screening)



The row panels display the three outcomes analyzed in the study: (A) probability of at least one in-school transmission over 30 days; (B) model-estimated average number of additional cases over 30 days in the immediate school community associated with reductions in mitigation effectiveness; (C) model-estimated average number of additional hospitalizations per 100,000 individuals over 30 days in the immediate school community associated with reductions in mitigation effectiveness. The arrows in panel A indicate the local COVID-19 incidence rate at which a school might opt to move to the next more intensive mitigation strategy at a baseline 30% effectiveness, if the objective is to maintain the probability of at least one in-school transmission per month below 50%.

eTable 1. Observed Local Incidence Decision Thresholds (in Cases per 100 000 Residents per Day) for the Alpha Variant Baseline Scenario

Outcome		Probability of at least 1 in-school transmission per month, with baseline mitigation effectiveness of:								
		40%			30%			20%		
Decision Objective		*To keep probability of at least 1 in-school transmission below:*								
		25%	50%	75%	25%	50%	75%	25%	50%	75%
		Baseline mitigation can only achieve objective at or below observed local incidence of:[a]								
Student Vaccine Coverage	0%	1	4	8	1	4	8	1	4	7
	25%	2	5	9	2	4	9	1	4	8
	50%	2	6	11	2	5	10	2	5	9
	70%	3	7	13	2	6	12	2	6	11
Outcome		Average additional cases per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep average additional cases below:*								
		3 cases	5 cases	10 cases	3 cases	5 cases	10 cases	3 cases	5 cases	10 cases
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	23	42	>50	10	18	42	7	12	25
	25%	30	>50	>50	14	24	>50	9	15	34
	50%	44	>50	>50	19	35	>50	12	22	>50
	70%	>50	>50	>50	27	>50	>50	17	30	>50
Outcome		Average additional hospitalizations per 100,000 per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep average additional hospitalizations per 100k below:*								
		1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	37	>50	>50	18	>50	>50	11	37	>50
	25%	>50	>50	>50	21	>50	>50	14	>50	>50
	50%	>50	>50	>50	30	>50	>50	20	>50	>50
	70%	>50	>50	>50	43	>50	>50	26	>50	>50

The alpha baseline scenario presented in this table reflects 70% adult vaccination coverage, 70% vaccine effectiveness, and no weekly screening. Units of observed local incidence thresholds are cases/100,000/day. It is assumed that 1/3 of all actual cases are observed.

[a]If observed local incidence is above these thresholds, additional mitigation measures beyond baseline will be needed to achieve each objective (e.g., keep probability of at least 1 in-school transmission per month below 50%).

[b]Only includes estimated average additional cases and hospitalizations in the immediate school community (students, teachers/staff, and household members). The potential for additional cases in the wider community stemming from in-school transmission was not modeled.

eTable 2. Observed Local Incidence Decision Thresholds (in Cases per 100 000 Residents per Day) for the Wild-Type Variant Baseline Scenario

Outcome		Probability of at least 1 in-school transmission per month, with baseline mitigation effectiveness of:								
		40%			30%			20%		
Decision Objective		*To keep probability of at least 1 in-school transmission below:*								
		25%	50%	75%	25%	50%	75%	25%	50%	75%
		Baseline mitigation can only achieve objective at or below observed local incidence of:[a]								
Student Vaccine Coverage	0%	3	7	13	2	6	11	2	5	10
	25%	3	7	15	3	7	13	2	6	12
	50%	4	9	18	3	8	16	3	7	14
	70%	5	11	22	4	10	19	4	8	17
Outcome		Average additional cases per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep additional cases below:*								
		3 cases	5 cases	10 cases	3 cases	5 cases	10 cases	3 cases	5 cases	10 cases
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	>50	>50	>50	26	48	>50	17	29	>50
	25%	>50	>50	>50	33	>50	>50	21	38	>50
	50%	>50	>50	>50	47	>50	>50	30	>50	>50
	70%	>50	>50	>50	>50	>50	>50	39	>50	>50
Outcome		Average additional hospitalizations per 100,000 per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep additional hospitalizations per 100k below:*								
		1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	>50	>50	>50	>50	>50	>50	37	>50	>50
	25%	>50	>50	>50	>50	>50	>50	46	>50	>50
	50%	>50	>50	>50	>50	>50	>50	>50	>50	>50
	70%	>50	>50	>50	>50	>50	>50	>50	>50	>50

The wild-type baseline scenario presented in this table reflects 70% adult vaccination coverage, 70% vaccine effectiveness, and no weekly screening. Units of observed local incidence thresholds are cases/100,000/day. It is assumed that 1/3 of all actual cases are observed.

[a]If observed local incidence is above these thresholds, additional mitigation measures beyond baseline will be needed to achieve each objective (e.g., keep probability of at least 1 in-school transmission per month below 50%).

[b]Only includes estimated average additional cases and hospitalizations in the immediate school community (students, teachers/staff, and household members). The potential for additional cases in the wider community stemming from in-school transmission was not modeled.

eTable 3. Observed Local Incidence Decision Thresholds (in Cases per 100 000 Residents per Day) for the 50% Adult Vaccination Rate Sensitivity Analysis

Outcome		Probability of at least 1 in-school transmission per month, with baseline mitigation effectiveness of:								
		40%			30%			20%		
Decision Objective		*To keep probability of at least 1 in-school transmission below:*								
		25%	50%	75%	25%	50%	75%	25%	50%	75%
		Baseline mitigation can only achieve objective at or below observed local incidence of:[a]								
Student Vaccine Coverage	0%	<1	3	6	<1	2	6	<1	2	5
	25%	1	3	6	<1	3	6	<1	2	6
	50%	1	4	7	1	3	7	1	3	6
Outcome		Average additional cases per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep average additional cases below:*								
		3 cases	5 cases	10 cases	3 cases	5 cases	10 cases	3 cases	5 cases	10 cases
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	5	9	19	2	4	9	2	3	6
	25%	7	12	28	3	6	12	2	4	8
	50%	11	19	45	5	9	19	3	6	12
Outcome		Average additional hospitalizations per 100,000 per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep average additional hospitalizations per 100k below:*								
		1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	4	14	26	2	6	11	1	4	7
	25%	6	19	37	3	9	16	2	6	10
	50%	8	28	>50	4	13	23	3	8	14

The sensitivity analysis presented in this table reflects the delta variant, 50% adult vaccination coverage, 70% vaccine effectiveness, and no weekly screening. 70% student vaccination coverage was not analyzed here because we assumed adult coverage would also be greater than student coverage. Units of observed local incidence thresholds are cases/100,000/day. It is assumed that 1/3 of all actual cases are observed.

[a]If observed local incidence is above these thresholds, additional mitigation measures beyond baseline will be needed to achieve each objective (e.g., keep probability of at least 1 in-school transmission per month below 50%).

[b]Only includes estimated average additional cases and hospitalizations in the immediate school community (students, teachers/staff, and household members). The potential for additional cases in the wider community stemming from in-school transmission was not modeled.

eTable 4. Observed Local Incidence Decision Thresholds (in Cases per 100 000 Residents per Day) for the Weekly Screening Sensitivity Analysis

Outcome		Probability of at least 1 in-school transmission per month, with baseline mitigation effectiveness of:								
		40%			30%			20%		
Decision Objective		*To keep probability of at least 1 in-school transmission below:*								
		25%	50%	75%	25%	50%	75%	25%	50%	75%
		Baseline mitigation can only achieve objective at or below observed local incidence of:[a]								
Student Vaccine Coverage	0%	1	4	7	1	3	7	<1	3	6
	25%	1	4	8	1	4	7	1	3	7
	50%	2	5	9	1	4	8	1	4	8
	70%	2	5	10	2	5	9	2	4	9
Outcome		Average additional cases per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep average additional cases below:*								
		3 cases	5 cases	10 cases	3 cases	5 cases	10 cases	3 cases	5 cases	10 cases
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	13	24	>50	6	11	24	4	7	15
	25%	18	34	>50	8	15	34	5	9	20
	50%	26	>50	>50	11	21	>50	7	13	29
	70%	36	>50	>50	16	29	>50	10	18	41
Outcome		Average additional hospitalizations per 100,000 per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep average additional hospitalizations per 100k below:*								
		1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	16	>50	>50	7	28	>50	5	16	32
	25%	22	>50	>50	9	38	>50	6	22	44
	50%	30	>50	>50	13	>50	>50	9	30	>50
	70%	42	>50	>50	18	>50	>50	11	42	>50

The sensitivity analysis presented in this table reflects the delta variant, 70% adult vaccination coverage, 70% vaccine effectiveness, and weekly screening (90% uptake). Units of observed local incidence thresholds are cases/100,000/day. It is assumed that 1/3 of all actual cases are observed.

[a]If observed local incidence is above these thresholds, additional mitigation measures beyond baseline will be needed to achieve each objective (e.g., keep probability of at least 1 in-school transmission per month below 50%).

[b]Only includes estimated average additional cases and hospitalizations in the immediate school community (students, teachers/staff, and household members). The potential for additional cases in the wider community stemming from in-school transmission was not modeled.

eTable 5. Observed Local Incidence Decision Thresholds (in in Cases per 100 000 Residents per Day) for the 50% Vaccine Effectiveness Sensitivity Analysis

Outcome		Probability of at least 1 in-school transmission per month, with baseline mitigation effectiveness of:								
		40%			30%			20%		
Decision Objective		*To keep probability of at least 1 in-school transmission below:*								
		25%	50%	75%	25%	50%	75%	25%	50%	75%
		Baseline mitigation can only achieve objective at or below observed local incidence of:[a]								
Student Vaccine Coverage	0%	<1	3	6	<1	3	6	<1	2	5
	25%	1	3	6	<1	3	6	<1	2	6
	50%	1	3	7	<1	3	6	<1	3	6
	70%	1	4	7	1	3	7	1	3	6
Outcome		Average additional cases per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep average additional cases below:*								
		3 cases	5 cases	10 cases	3 cases	5 cases	10 cases	3 cases	5 cases	10 cases
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	5	9	19	3	4	9	2	3	6
	25%	6	11	25	3	5	11	2	3	7
	50%	8	14	33	4	7	14	3	4	9
	70%	10	18	42	5	9	18	3	5	11
Outcome		Average additional hospitalizations per 100,000 per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep average additional hospitalizations per 100k below:*								
		1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	7	23	49	3	11	19	2	7	12
	25%	8	31	>50	4	13	24	3	8	15
	50%	11	41	>50	5	17	32	3	11	20
	70%	14	>50	>50	6	22	41	4	14	24

The sensitivity analysis presented in this table reflects the delta variant, 70% adult vaccination coverage, 50% vaccine effectiveness, and no weekly screening. Note that the hospitalization outcome assumes perfect vaccine protection against hospitalization, even with decreased protection against infection. Units of observed local incidence thresholds are cases/100,000/day. It is assumed that 1/3 of all actual cases are observed.

[a]If observed local incidence is above these thresholds, additional mitigation measures beyond baseline will be needed to achieve each objective (e.g., keep probability of at least 1 in-school transmission per month below 50%).

[b]Only includes estimated average additional cases and hospitalizations in the immediate school community (students, teachers/staff, and household members). The potential for additional cases in the wider community stemming from in-school transmission was not modeled.

eTable 6. Observed Local Incidence Decision Thresholds (in Cases per 100 000 Residents per Day) for the 25% Vaccine Effectiveness Sensitivity Analysis

Outcome		Probability of at least 1 in-school transmission per month, with baseline mitigation effectiveness of:								
		40%			30%			20%		
Decision Objective		*To keep probability of at least 1 in-school transmission below:*								
		25%	50%	75%	25%	50%	75%	25%	50%	75%
		Baseline mitigation can only achieve objective at or below observed local incidence of:[a]								
Student Vaccine Coverage	0%	<1	3	6	<1	2	6	<1	2	5
	25%	<1	3	6	<1	2	6	<1	2	5
	50%	<1	3	6	<1	3	6	<1	2	6
	70%	1	3	6	<1	3	6	<1	2	6
Outcome		Average additional cases per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep average additional cases below:*								
		3 cases	5 cases	10 cases	3 cases	5 cases	10 cases	3 cases	5 cases	10 cases
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	4	8	16	2	4	8	1	2	5
	25%	5	9	18	2	4	8	1	3	5
	50%	5	9	20	3	4	9	2	3	6
	70%	6	10	21	3	5	10	2	3	6
Outcome		Average additional hospitalizations per 100,000 per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep average additional hospitalizations per 100k below:*								
		1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	6	22	44	3	10	18	2	6	11
	25%	7	25	>50	3	11	20	2	7	13
	50%	8	28	>50	4	13	22	3	8	14
	70%	9	31	>50	4	14	25	3	9	15

The sensitivity analysis presented in this table reflects the delta variant, 70% adult vaccination coverage, 25% vaccine effectiveness, and no weekly screening. Note that the hospitalization outcome assumes perfect vaccine protection against hospitalization, even with decreased protection against infection. Units of observed local incidence thresholds are cases/100,000/day. It is assumed that 1/3 of all actual cases are observed.

[a]If observed local incidence is above these thresholds, additional mitigation measures beyond baseline will be needed to achieve each objective (e.g., keep probability of at least 1 in-school transmission per month below 50%).

[b]Only includes estimated average additional cases and hospitalizations in the immediate school community (students, teachers/staff, and household members). The potential for additional cases in the wider community stemming from in-school transmission was not modeled.

eTable 7. Observed Local Incidence Decision Thresholds (in Cases per 100 000 Residents per Day) for the 90% Vaccine Effectiveness Sensitivity Analysis

Outcome		Probability of at least 1 in-school transmission per month, with baseline mitigation effectiveness of:								
		40%			30%			20%		
Decision Objective		*To keep probability of at least 1 in-school transmission below:*								
		25%	50%	75%	25%	50%	75%	25%	50%	75%
		Baseline mitigation can only achieve objective at or below observed local incidence of:[a]								
Student Vaccine Coverage	0%	<1	3	6	<1	3	6	<1	2	5
	25%	1	3	7	1	3	6	<1	3	6
	50%	1	4	8	1	4	7	1	3	7
	70%	2	5	10	2	5	9	1	4	8
Outcome		Average additional cases per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep average additional cases below:*								
		3 cases	5 cases	10 cases	3 cases	5 cases	10 cases	3 cases	5 cases	10 cases
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	6	11	25	3	5	11	2	3	7
	25%	10	18	44	5	9	18	3	6	12
	50%	19	35	>50	9	15	35	6	10	21
	70%	37	>50	>50	15	29	>50	10	17	43
Outcome		Average additional hospitalizations per 100,000 per month associated with change in mitigation effectiveness:[b]								
		60% to 40%			70 to 30%			80% to 20%		
Decision Objective		*To keep average additional hospitalizations per 100k below:*								
		1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.	1 hosp.	3 hosp.	5 hosp.
		Mitigation can only be reduced at or below observed local incidence of:								
Student Vaccine Coverage	0%	7	27	>50	4	12	21	2	7	13
	25%	11	47	>50	5	18	36	4	11	21
	50%	19	>50	>50	9	32	>50	6	19	38
	70%	34	>50	>50	15	>50	>50	10	34	>50

The sensitivity analysis presented in this table reflects the delta variant, 70% adult vaccination coverage, 90% vaccine effectiveness, and no weekly screening. Units of observed local incidence thresholds are cases/100,000/day. It is assumed that 1/3 of all actual cases are observed.

[a]If observed local incidence is above these thresholds, additional mitigation measures beyond baseline will be needed to achieve each objective (e.g., keep probability of at least 1 in-school transmission per month below 50%).

[b]Only includes estimated average additional cases and hospitalizations in the immediate school community (students, teachers/staff, and household members). The potential for additional cases in the wider community stemming from in-school transmission was not modeled.

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