SUPPLEMENT: SARS-CoV-2 testing strategies to contain school-associated transmission: model-based analysis of impact and cost of diagnostic testing, screening, and surveillance

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Model Structure

We assumed an SEIR model of COVID-19 transmission, using a previously published model (1). Briefly, when individuals interacted with an agent (i.e. person) infected with SARS-CoV-2, transmission risk was proportional to duration and intensity of exposure. The model drew stochastic outcomes assuming an average incubation period of three days prior to the onset of infectiousness, two days of pre-symptomatic transmission if symptoms develop (2,3), total infectious time of five days (4–7), and overdispersion of infectivity in adolescents and adults (4,8) (Table 1). We assumed that adults with fully asymptomatic disease transmit COVID-19 at half the rate of those with any symptoms (9). Based on data from household contact tracing studies, we further specified that, in absence of vaccination, children under 10 were half as susceptible and half as infectious as symptomatic adolescents and adults (10–14). Beyond interactions with infectious agents within the simulation, students, staff, and their families had a probability of becoming infected through other community interactions equivalent to community per capita daily incidence assuming a 33% case detection rate. In vaccinated individuals, this risk was reduced by 80%; among unvaccinated adults, we upweighted community risk such that adults overall matched the community rate on average.

In scenarios without "test to stay", symptom-driven COVID diagnostic testing still occurred outside of the school environment: individuals with COVID-19 who developed clinically-recognizable symptoms were assumed to self-isolate from out-of-household contacts (including staying home from school) and to obtain testing in the community. Results became available 24 hours after the first appearance of symptoms, at which point classrooms were notified and quarantined for 10 days. Symptom-driven community-based testing, and self-isolation of symptomatic individuals who had not been tested since symptom onset, were assumed to occur regardless of in-school screening practices.

For in-school testing, we assumed (a) specimens (e.g., anterior nasal swabs) were collected from each student and teacher, and (b) aliquots from up to eight specimens obtained in a single classroom were combined for pooled PCR testing, with negligible loss of sensitivity to detect active infection (15,16) When a pooled specimen yielded a positive result, all individual specimens that had been included in the pool were immediately tested separately using PCR to identify the positive individual(s).

Model Parameterization and Calibration

Model parameterization is discussed at length in the Supplement of (1). Briefly, we first identified household attack rates (including differential susceptibility and infectiousness of young children) (17–19). We first adjusted these for the length of time spent in school and reduced infectiousness of asymptomatic individuals (9) to estimate attack rates with no or minimal mitigation. We then further adjusted them for a range of mitigation strategies. To partially validate our model, we compared our estimates of in-school attack rate and in-school R_t to those from empirical studies. We estimated in-school R_t with high mitigation and classroom quarantine and "bubbles" to be 0.2 for elementary schools and 0.64 in high schools, consistent with estimates from schools during 2020-2021 (e.g., (20)). Our estimates also reflect the wide range of attack rates across mitigation levels identified both in data directly from schools (21–23) and from household/population-level estimates (24,25), as well as the association between community incidence level and transmission risk (26).

We assumed that the delta variant is twice as transmissible than the wild type variant (27,28) and that this multiplicative increase is constant across levels of mitigation. The latter assumption is uncertain and requires further empirical evaluation in different contexts; for example, while it may be realistic with cloth masks, early anecdotal evidence from health care settings suggests that high filtration masks (e.g. N95, KN95) may protect nearly as well against the delta variant as they do against wild type. We also assumed that the delta variant has 80% vaccine efficacy, a decrease compared to the wild type (29,30). Some emerging estimates of vaccine efficacy are lower, potentially suggesting a conservative estimate of the value of screening.

For our base case, we assume high mitigation with the delta variant (R_t of approximately 0.4 in elementary schools and 1.2 in middle schools) to reflect the population of schools most likely to implement testing and likely ordering of interventions (e.g., testing will likely only be implemented in schools that have already implemented masking). We also present results with moderate mitigation, doubling the attack rate of the base case, to display the impact of testing in the context of reduced mitigation interventions in schools.

Surveillance Thresholds

Within a small school community, it is challenging to set an optimal threshold for triggering further investigation when conducting surveillance. We expect some COVID-19 cases to enter a school from the community *even if no transmission occurs within the school community*, and ideally the threshold for triggering additional testing should take this into account. However, when testing only a small fraction of the school (10-20%), the expected number of asymptomatic cases detected per testing episode, assuming no in-school transmission, is generally close to 0. In the paper, we chose a 1-case trigger threshold for 3 reasons:

1. At low-to-moderate community notification rates (1-25 cases per 100,000/day), no surveillance scenario with a threshold above 1 could detect even large outbreaks of at least 10 in-school transmissions with any regularity: the maximum probability of detection (i.e., maximum sensitivity) was 35% for a 2-case threshold at 25 cases per 100,000/day. By contrast, a 1-case threshold had a detection probability of 30-75% across 1-25 cases per 100,000/day, while maintaining low rates of false positive triggers.
2. In our model, there was generally at least some in-school transmission at high levels of community incidence, making threshold selection less of a concern, since false positives would be rare under any threshold. (For the same reason, surveillance testing as a method of detecting outbreaks is less useful at these levels, although a benefit remains if community case detection is low, which makes schools less likely to be aware of local incidence risks.)
3. If, in practice, a school calibrated the expected number of cases and associated threshold to the *observed* community incidence rate, this would be a significant underestimate (and for most community incidence levels we evaluated would be near 0). (However, it is not straightforward to correct for case detection, as there is no public, consistently-collected data source in the United States for estimating case detection rate, and most school leaders with whom we spoke would not be comfortable making such an estimate.[1])

Nevertheless, schools (or school districts more broadly) should adapt surveillance thresholds to meet their needs and level of caution. Our model is a st example over a single month for a single school. A

[1] The common approach of comparing percent positivity from in-school testing to population testing is inappropriate, as community testing encompasses primarily exposed symptomatic individuals with a much higher probability of infection than randomly selected individuals.

longer-term strategy might include dynamic switching back to surveillance as well as stricter trigger thresholds when community incidence is high or when surveying large districts.

Fig S1. Model diagram

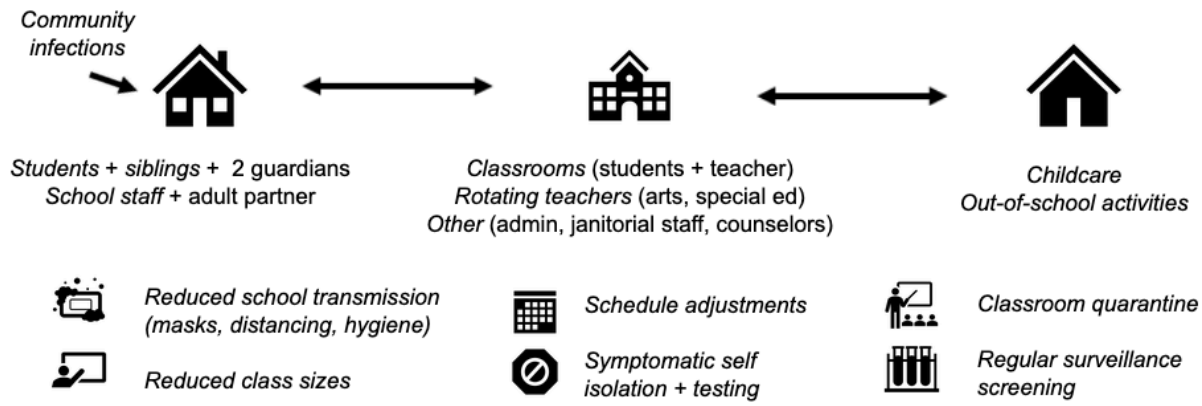

Fig S2. Surveillance characteristics. Color indicates the percentage of the school screened weekly (from unvaccinated individuals) under surveillance, while the line type indicates the transmission level. The left panels depict the probability of triggering screening. The middle panels depict the probability of in-school transmission, conditional on triggering screening (“true positives”). The right panels depict the probability of fewer than 3 in-school transmissions given no screening trigger (“true negatives”).

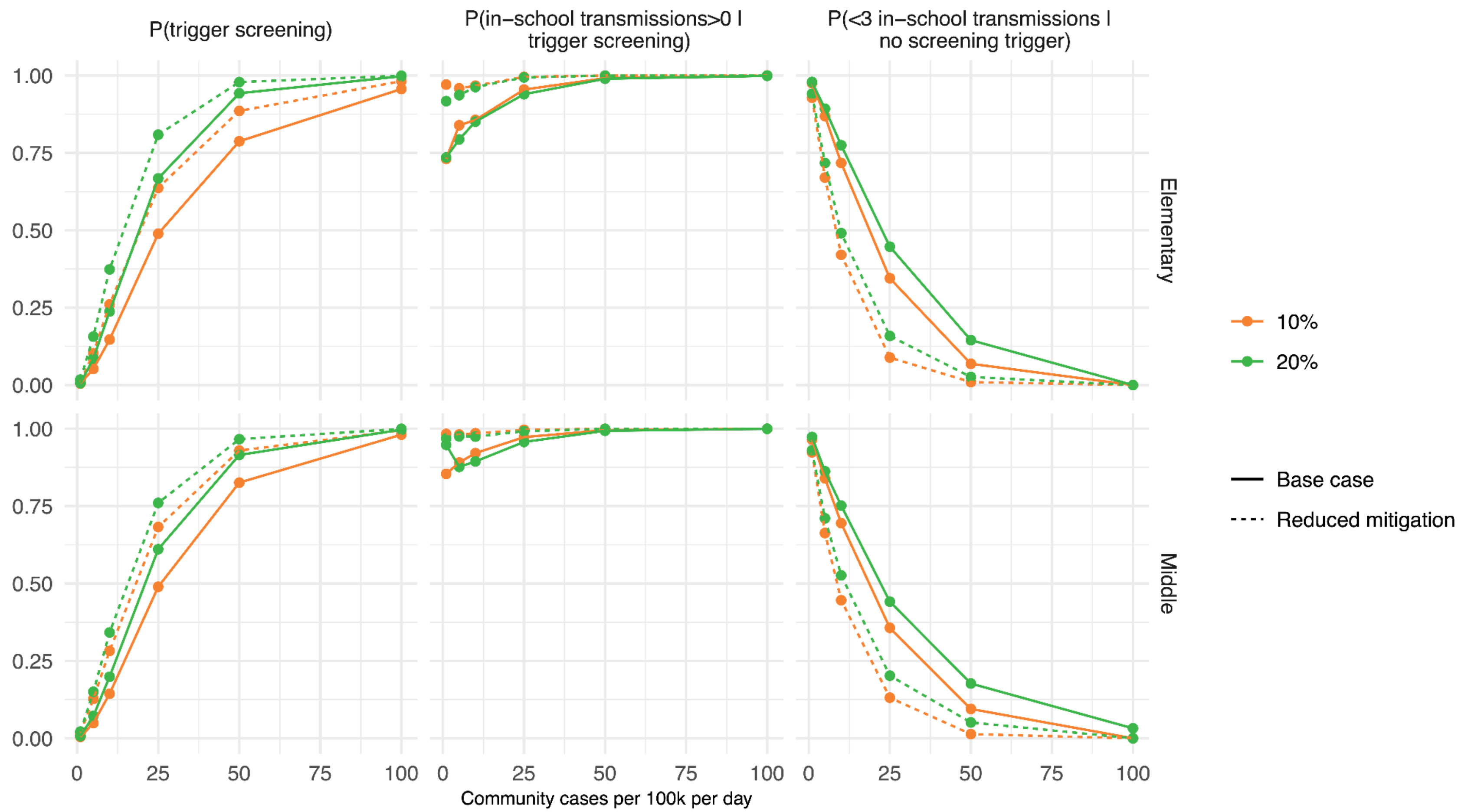

Fig S3. Testing costs, as dollars per student per month, in an elementary school. When exposed students quarantine at home, costs plateau at higher levels of incidence as classroom quarantines cause screening days to be missed; potential costs of community-based testing by exposed students or their contacts are not modeled. For a "test to stay" strategy that provides in-school rapid testing to symptomatic students and exposed contacts, testing costs increase as incidence rises.

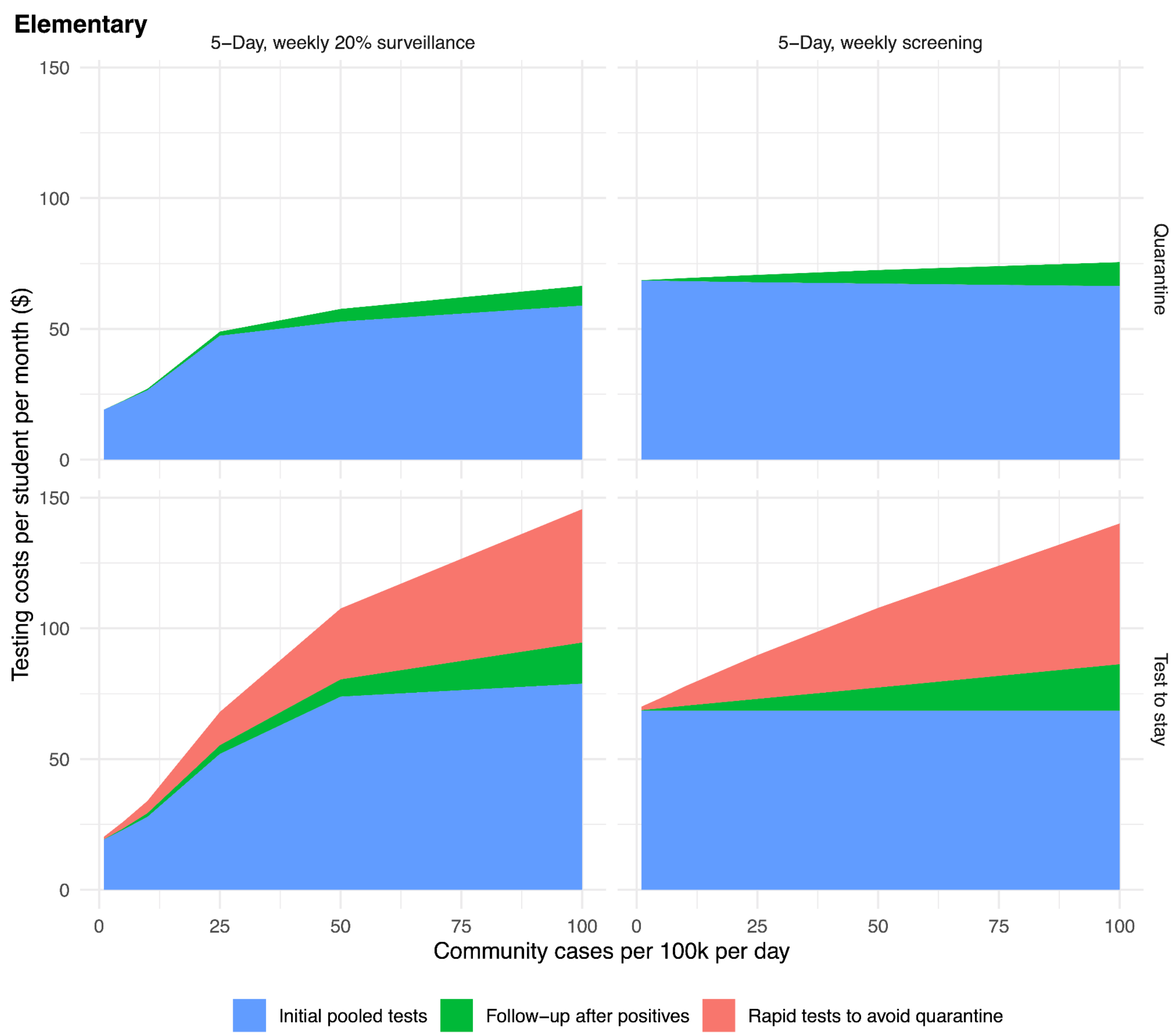

Fig S4. Testing costs, as dollars per student per month, in a middle school. When exposed students quarantine at home, costs plateau at higher levels of incidence as classroom quarantines cause screening days to be missed; potential costs of community-based testing by exposed students or their contacts are not modeled. For a “test to stay” strategy that provides in-school rapid testing to symptomatic students and exposed contacts, testing costs increase as incidence rises.

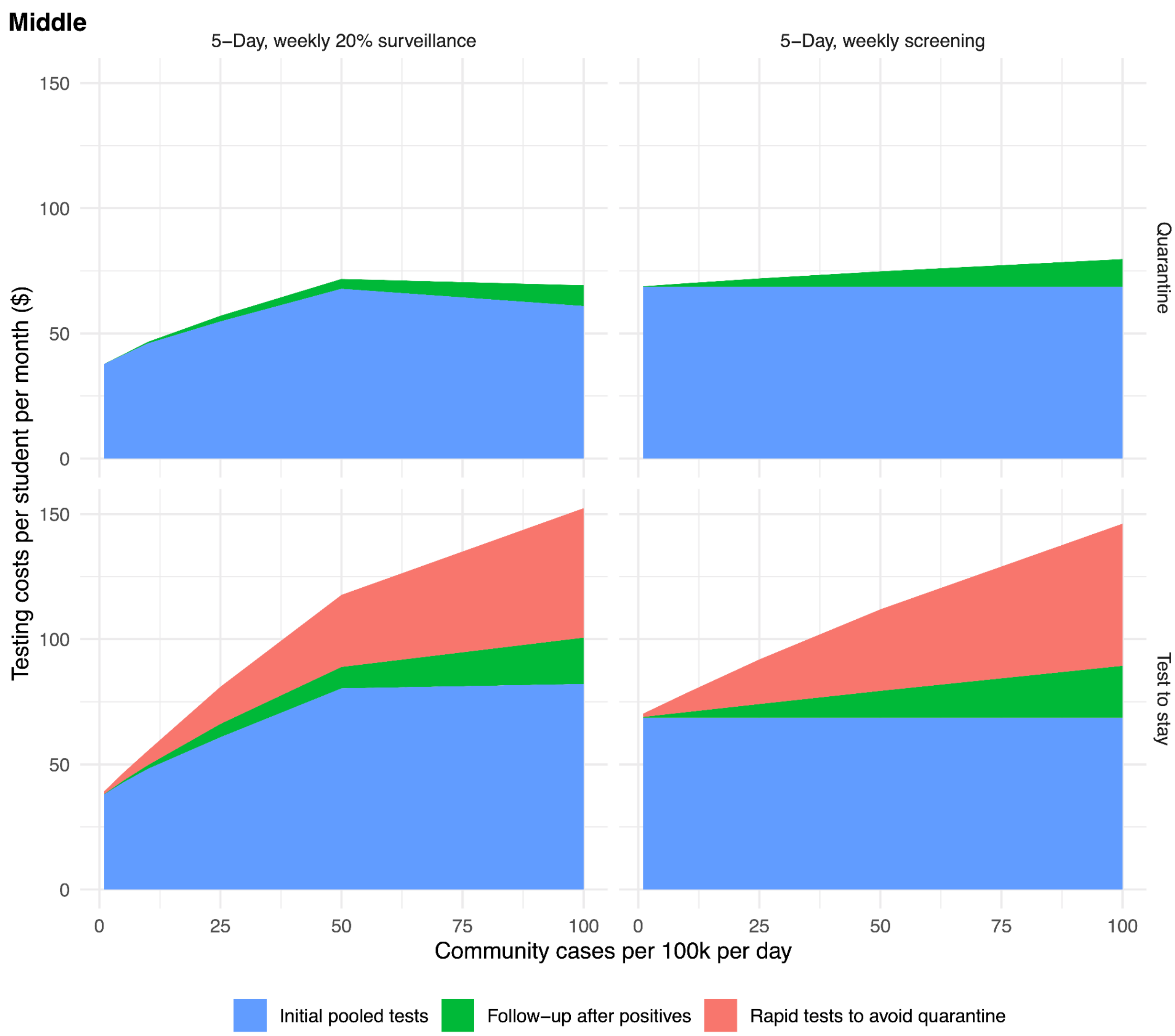

Fig S5. Childcare or parent productivity costs (elementary school). Planned costs reflect scheduled days of remote learning, and unplanned costs reflect days spent in isolation or quarantine. Rows reflect two different approaches to managing exposed contacts (quarantine for 10 days at home, top row; or staying at school with a week of daily rapid tests, bottom row). “Test to stay” is not modeled for Hybrid and Remote schedules.

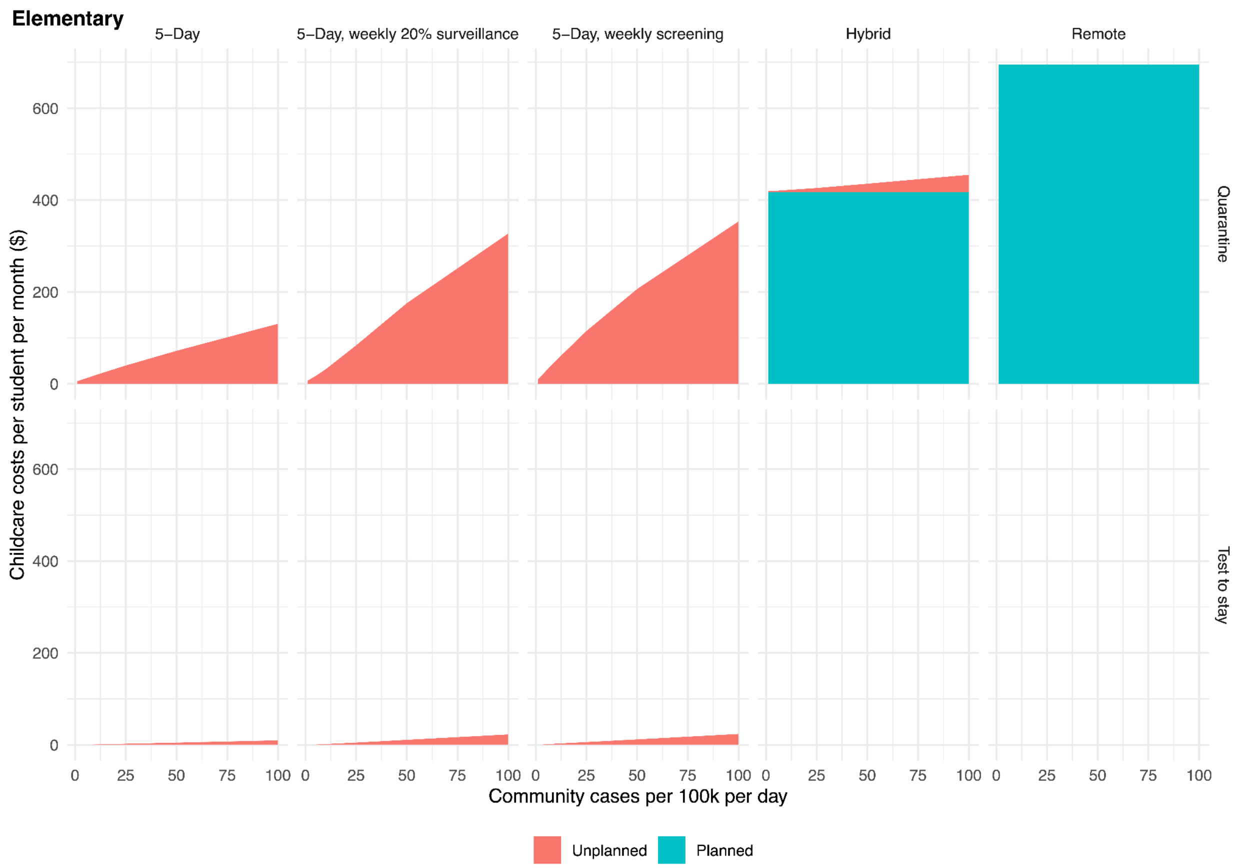

Fig S6. Childcare or parent productivity costs (middle school). We assume that for a combination of health and logistical reasons, full classrooms quarantine after exposure. If only unvaccinated students were asked to quarantine, then costs of 5-Day + Quarantine scenarios would be reduced.

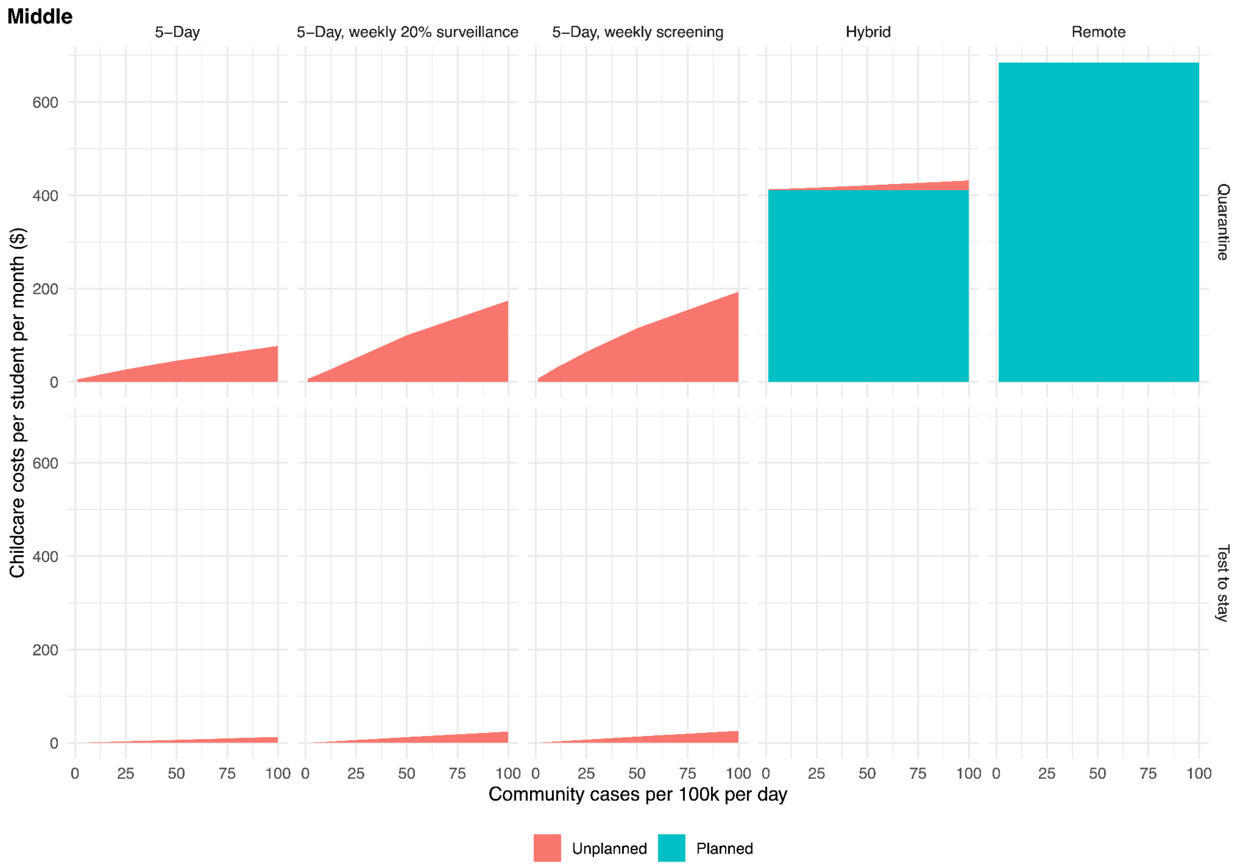

Fig S7. Costs associated with rapid antigen screening tests (weekly tests at $12 per test + $8 per sample collection, PCR confirmation of positive results with same one-day turnaround, 0.5% false positive rapid tests, no change in sensitivity for acute infection) compared to the costs of schedule-based mitigation and of full-time in-person attendance without asymptomatic screening.

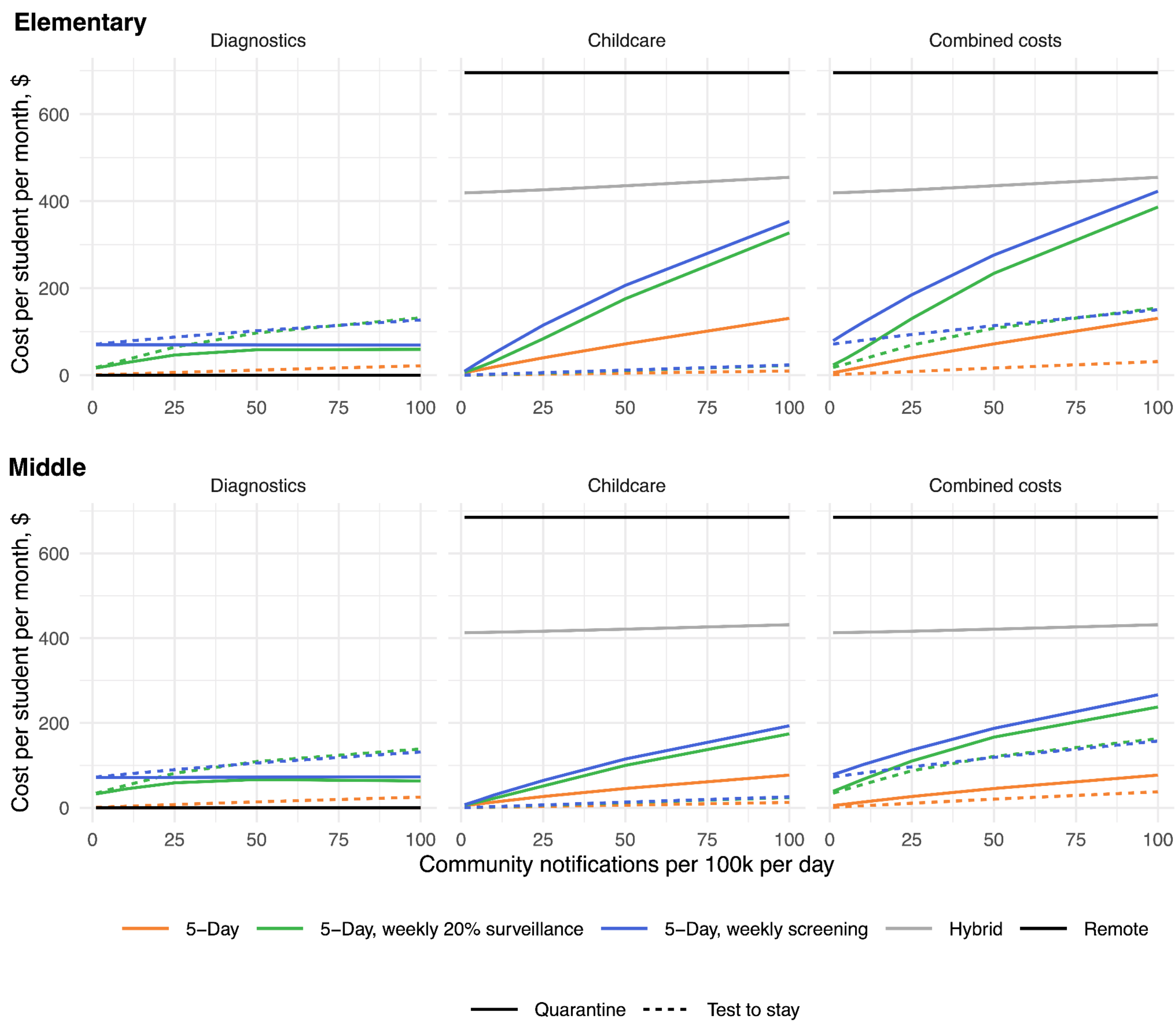

Fig S8. Cost-effectiveness of rapid screening (cost per infection directly averted among students and staff), comparing weekly screening to full-time attendance without screening, under the same rapid screening assumptions as in Figure S7. For testing costs (orange), we show the strategy of weekly screening in which exposed contacts quarantine at home (solid line), which dominates the "test to stay" strategy. By "dominates", we mean that if optimizing over test costs only, it is strictly higher value to quarantine contacts, rather than implement test-to-stay. Likewise, for combined costs of testing plus childcare (blue), we show the strategy of weekly screening with exposed contacts undergoing daily rapid tests to stay at school (dashed line), which dominates at-home quarantine.

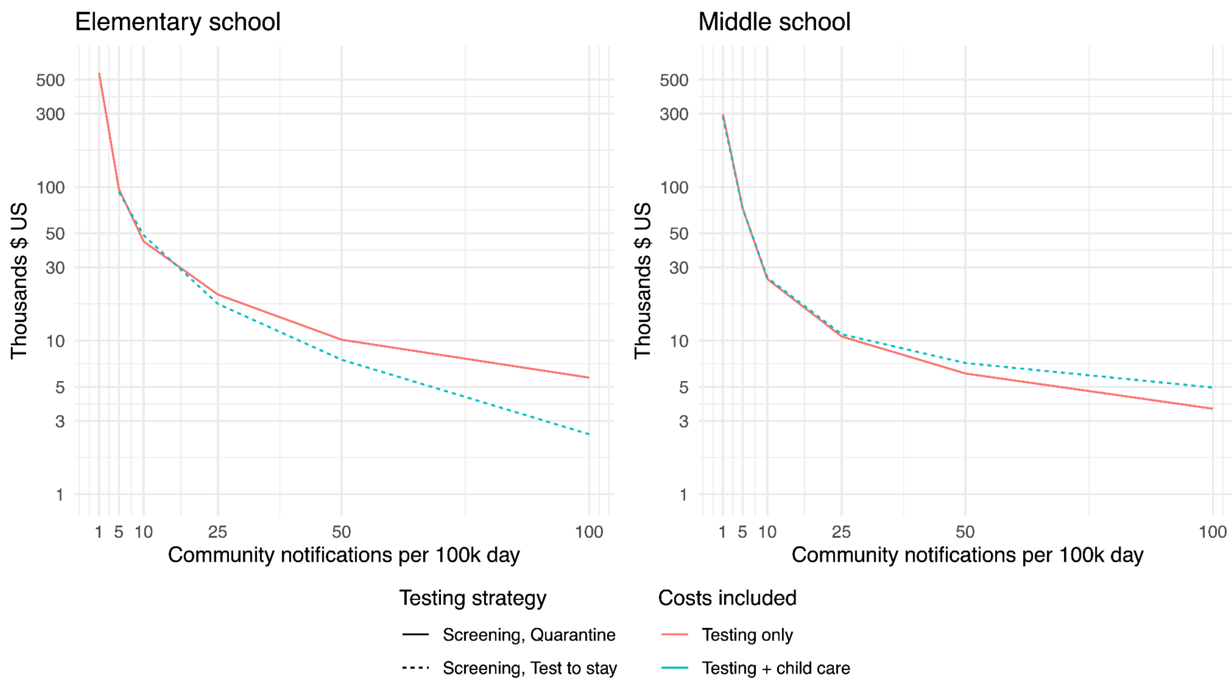

Fig S9. Cost-effectiveness of weekly screening (cost per infection directly averted among students and staff), comparing screening to full-time attendance without screening, assuming a two-fold increase in transmission rate over the base case (due to increased variant transmissibility or reduced in-school mitigation). For testing costs (orange), we show the strategy of weekly screening in which exposed contacts quarantine at home (solid line), which dominates the "test to stay" strategy. By "dominates", we mean that if optimizing over test costs only, it is strictly higher value to quarantine contacts, rather than implement test-to-stay. Likewise, for combined costs of testing plus childcare (blue), we show the strategy of weekly screening with exposed contacts undergoing daily rapid tests to stay at school (dashed line), which dominates at-home quarantine.

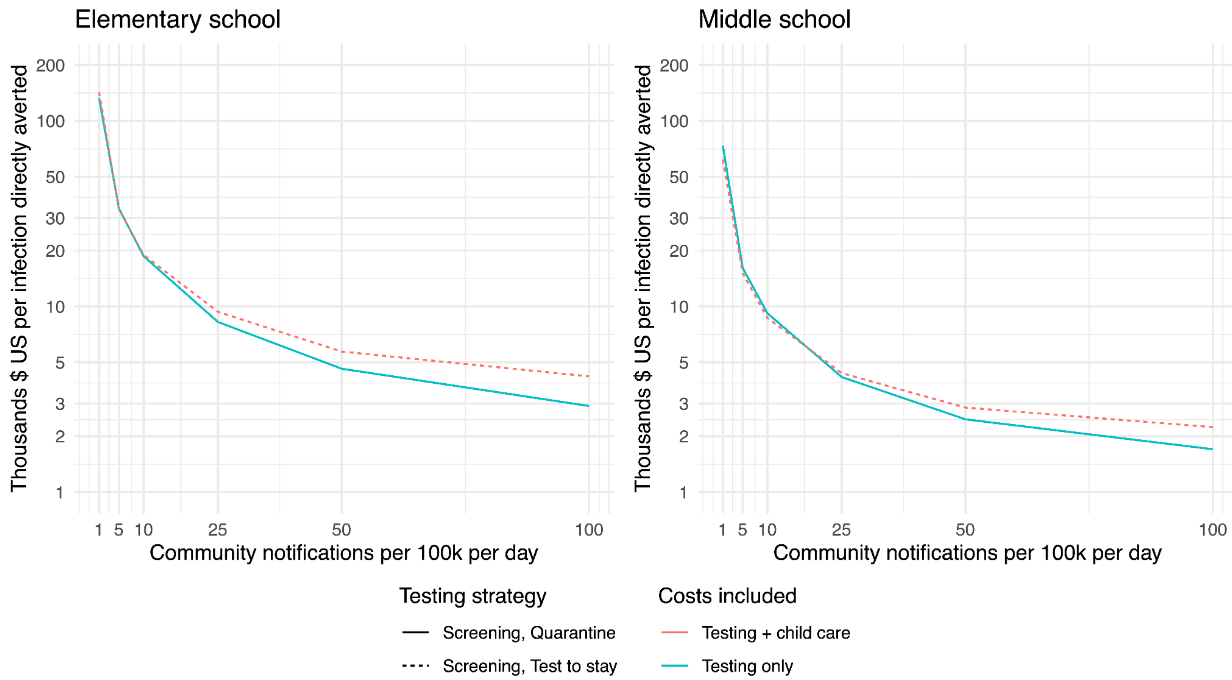

Fig S10. One-way sensitivity analyses, transmission effects of weekly screening. The outcome is the absolute difference in incidence (infections of students or teachers per school per month) between 5-day attendance with and without weekly screening, in an elementary (A) and middle school (B). The dotted horizontal line indicates the outcome when all parameters are at their base values (values indicated in gray text in the row where that parameter is varied).

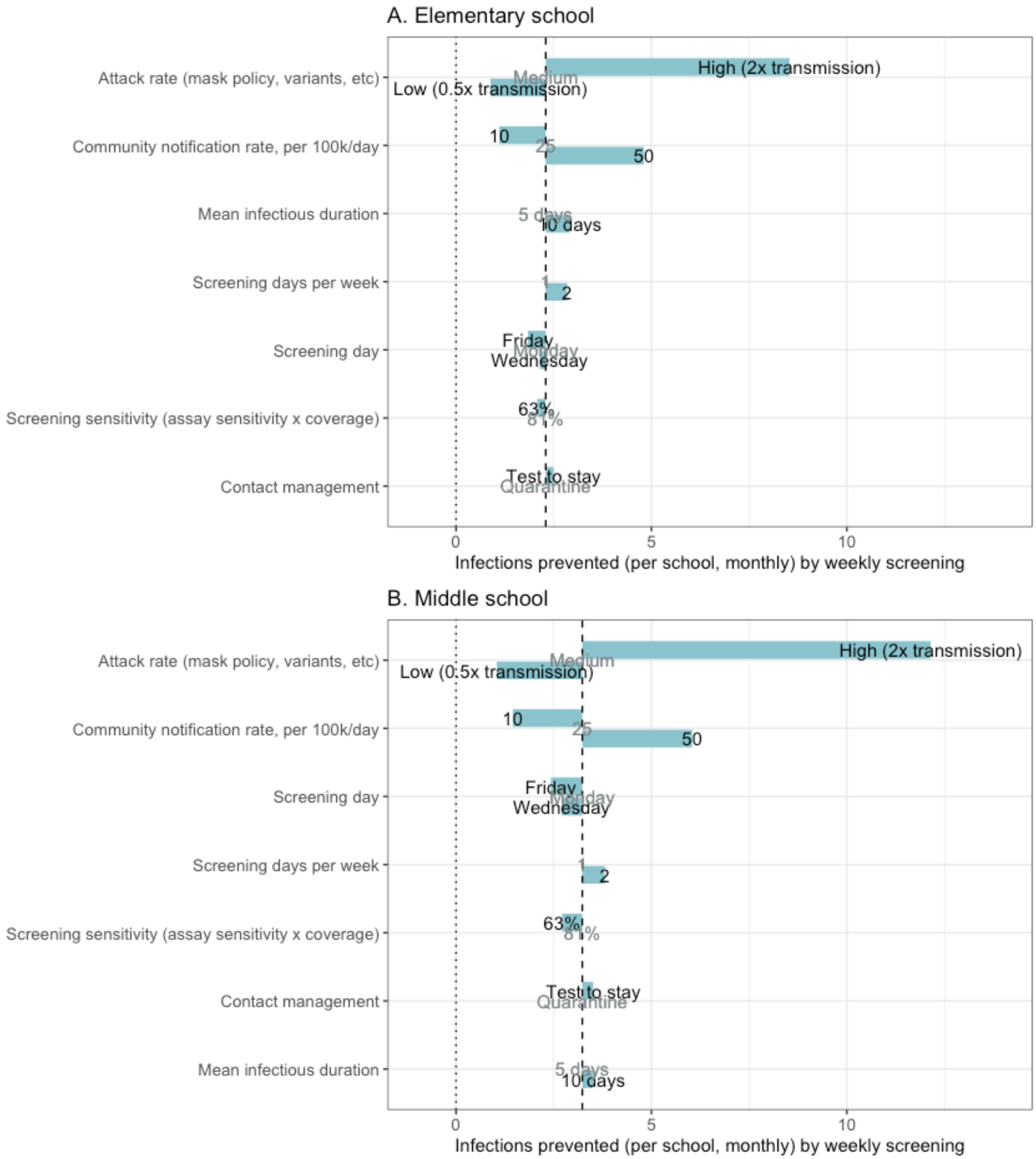

Table S1. Comparison of transmission, case-detection, operational, and cost outcomes between different schedules and screening frequencies

	Infected (proportion of school per month)	Difference in proportion of school infected, per month vs full-time without screening	Proportion of incremental infections prevented (of difference between 5-day no screening and Remote)	Proportion of cases detected	In-person attendance (proportion of school days)	Testing costs ($ per student per month)	Testing + child care costs ($ per student per month)
Elementary school, community notification rate 10/100k/day							
5-Day, no screening, quarantine	0.01	0	0	0.23	0.989	0	19.03
5-Day, no screening, test-to-stay	0.01	0.0002	-0.06	0.23	0.999	3.47	4.36
5-Day, weekly 10% surveillance, quarantine	0.009	-0.0005	0.19	0.31	0.985	18.93	44.94
5-Day, weekly 10% surveillance, test-to-stay	0.01	-0.0002	0.06	0.35	0.999	24.25	25.56
5-Day, weekly 20% surveillance, quarantine	0.009	-0.0007	0.25	0.39	0.981	27.09	58.97
5-Day, weekly 20% surveillance, test-to-stay	0.009	-0.0005	0.17	0.44	0.999	33.98	35.59
5-Day, 1x/week screening, quarantine	0.008	-0.0016	0.57	0.66	0.97	69.42	120.26

5-Day, 1x/week screening, test-to-stay	0.009	-0.0013	0.46	0.73	0.999	77.81	80.25
5-Day, 2x/week screening, quarantine	0.008	-0.0019	0.69	0.77	0.968	124.19	178.24
5-Day, 2x/week weekly screening, test-to-stay	0.008	-0.0017	0.61	0.88	0.998	134.03	136.86
Hybrid	0.007	-0.0025	0.92	0.23	0.397	0	421.76
Remote	0.007	-0.0028	1	0	0	0	695.32
Elementary school, community notification rate 50/100k/day							
5-Day, no screening, quarantine	0.046	0	0	0.22	0.957	0	71.99
5-Day, no screening, test-to-stay	0.047	0.0013	-0.1	0.25	0.997	14.73	19.41
5-Day, weekly 10% surveillance, quarantine	0.042	-0.0034	0.28	0.45	0.912	46.65	194.49
5-Day, weekly 10% surveillance, test-to-stay	0.043	-0.0026	0.21	0.55	0.994	80.29	89.69
5-Day, weekly 20% surveillance, quarantine	0.041	-0.0054	0.44	0.54	0.896	57.65	233.33
5-Day, weekly 20% surveillance, test-to-stay	0.042	-0.0038	0.32	0.66	0.994	107.6	118.43
5-Day, 1x/week screening, quarantine	0.039	-0.0069	0.57	0.63	0.877	72.52	278.98

5-Day, 1x/week screening, test-to-stay	0.04	-0.0056	0.46	0.74	0.993	107.84	119.56
5-Day, 2x/week screening, quarantine	0.038	-0.0084	0.69	0.73	0.87	126.85	345.93
5-Day, 2x/week weekly screening, test-to-stay	0.039	-0.0064	0.53	0.89	0.992	169.93	183.79
Hybrid	0.036	-0.0099	0.81	0.22	0.389	0	435.62
Remote	0.034	-0.0121	1	0	0	0	695.32
Middle school, community notification rate 10/100k/day							
5-Day, no screening, quarantine	0.012	0	0	0.23	0.992	0	13.48
5-Day, no screening, test-to-stay	0.013	0.0006	-0.12	0.26	0.999	46.62	68.93
5-Day, weekly 10% surveillance, quarantine	0.011	-0.0013	0.27	0.34	0.989	4.47	5.76
5-Day, weekly 10% surveillance, test-to-stay	0.011	-0.0008	0.16	0.42	0.999	55.46	57.6
5-Day, weekly 20% surveillance, quarantine	0.011	-0.0017	0.34	0.43	0.987	23.84	42.07
5-Day, weekly 20% surveillance, test-to-stay	0.011	-0.0015	0.3	0.52	0.999	31.24	33.09
5-Day, 1x/week screening, quarantine	0.009	-0.0028	0.57	0.64	0.982	70.06	100.16

5-Day, 1x/week screening, test-to-stay	0.01	-0.0027	0.54	0.74	0.998	78.57	81.31
5-Day, 2x/week screening, quarantine	0.009	-0.0035	0.7	0.77	0.982	125.35	155.67
5-Day, 2x/week weekly screening, test-to-stay	0.009	-0.0031	0.62	0.9	0.998	135.35	138.51
Hybrid	0.008	-0.0044	0.89	0.22	0.398	0	413.93
Remote	0.007	-0.005	1	0	0	0	684.79
Middle school, community notification rate 50/100k/day							
5-Day, no screening, quarantine	0.055	0	0	0.22	0.973	0	45.46
5-Day, no screening, test-to-stay	0.058	0.0023	-0.11	0.28	0.996	71.78	171.71
5-Day, weekly 10% surveillance, quarantine	0.049	-0.0062	0.31	0.44	0.947	18.18	24.48
5-Day, weekly 10% surveillance, test-to-stay	0.051	-0.0049	0.24	0.59	0.993	117.73	129.93
5-Day, weekly 20% surveillance, quarantine	0.047	-0.0089	0.44	0.51	0.94	52.13	139.47
5-Day, weekly 20% surveillance, test-to-stay	0.048	-0.0073	0.36	0.66	0.993	92.72	104.17
5-Day, 1x/week screening, quarantine	0.044	-0.0118	0.58	0.63	0.931	74.8	189.83

5-Day, 1x/week screening, test-to-stay	0.045	-0.0103	0.5	0.76	0.992	111.96	125.28
5-Day, 2x/week screening, quarantine	0.041	-0.0148	0.73	0.75	0.929	131.25	248.46
5-Day, 2x/week weekly screening, test-to-stay	0.043	-0.0123	0.6	0.9	0.991	173.31	188.37
Hybrid	0.037	-0.0183	0.9	0.23	0.394	0	421.16
Remote	0.035	-0.0204	1	0	0	0	684.79

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