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Interventions in measles outbreaks: the potential reduction in cases associated with school suspension and vaccination interventions

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Introduction

Measles is an extremely contagious disease that has been resurgent in the US and globally in 2019.[1] Over 1200 cases of measles were reported in the US in 2019, the most since 1992.[2] Approximately 10% of these cases have led to hospitalization, 5% of which had complications including pneumonia and encephalitis.[3] Measles can compromise an individual's immune system, potentially causing problems after recovery,[4, 5] and may also lead to death.[6]

Fortunately, immunity to measles is conferred to 97% of people who receive 2 doses of the MMR (measles, mumps, and rubella) vaccine. In the US, the first dose is recommended at 12 months and the second before starting school.[7] As measles is highly infectious, 92%-96% of a homogeneously mixed population should be vaccinated to achieve herd immunity.[8]

Vaccination rates were sufficiently high to eliminate measles in the US (meaning no continuous transmission within the US for at least 12 months) in 2000.[9] Subsequent decreases in vaccination rates in some areas have facilitated measles transmission, putting the US's elimination status in jeopardy.[10] The US marginally retained its elimination status in 2019.[11]

In the US, schoolchildren must either be vaccinated against measles or obtain a vaccine exemption. Requirements for acquiring a vaccine exemption vary by state, however, and 45 of the 50 states allow exemptions for nonmedical reasons as of May 2020.[12]

A small minority of parents refuse vaccinations for their children and seek exemptions for nonmedical reasons, including concerns about the perceived safety of vaccines, a lack of knowledge concerning vaccines, a low perceived susceptibility to measles, and social influences.[13,14] Vaccine hesitancy, defined as the "delay in acceptance or refusal of vaccination despite availability of vaccination services,"[15] is not evenly distributed in the population, leading to geographic clusters of unvaccinated children.[16,17] This clustering potentially would allow measles to spread in a community that has a vaccination rate above the herd-immunity threshold.[18]

Three measles outbreaks in Washington (Clark County) and New York (Rockland County and New York City) states in 2019 infected 71, 312, and 649 people,[19-21] respectively. Local government enacted public health interventions in each area with the aim of limiting the spread of measles. These interventions included suspending unvaccinated students from schools[19,22-24] and mandatory vaccinations.[25] Other interventions included contract tracing,[9,20] free vaccination clinics,[25] and prohibiting unvaccinated minors from entering places of public assembly[23] (the last was rescinded after a court challenge[26]). An overview of public health interventions for measles outbreaks is given by Gastañaduy et al.[27]

Beyond these states, the 2020 COVID-19 pandemic demonstrated the ability and willingness of many governments to limit school attendance to control the spread of an infectious disease (eg, Governor of the State of Texas[28]), albeit with significant concerns.[29,30]

Texas is the most populous American state that allows nonmedical vaccine exemptions. Its vaccine laws have been found to be among the least effective in the US at reducing vaccine exemptions.[31] Nonmedical vaccine exemptions have increased annually in Texas[32] since a law change in 2003 made it easier to opt out of vaccination.[33] Studies have raised concerns about the potential for measles outbreaks in Texas.[32-35]

We simulated measles outbreaks in 6 Metropolitan Statistical Areas (MSAs) of Texas using an agent-based model. The model included the location, enrollment size, and vaccination rates of the schools in each MSA. Public health interventions in which unvaccinated students were either suspended from school, vaccinated, or both were included in the simulations to evaluate how successful different interventions may be in reducing the overall number of measles cases.

Methods

Agent-based model

We forecast the spread of measles under different public health interventions with an agent-based model. The agent-based model was developed using FRED (A Framework for Reconstructing Epidemiological Dynamics).[36] The simulations follow the approach discussed in Sinclair et al[34]; we summarize the key features of the simulation model here, with some updates from the model previously discussed,[34] including the addition of 6 public health intervention scenarios.

We chose 6 MSAs in Texas to simulate measles outbreaks: Austin-Round Rock-Georgetown; Dallas-Fort Worth; Houston-Sugar Land-Baytown; Midland; and Tyler. These MSAs have previously been identified as having a risk of larger measles outbreaks than other areas in Texas.[34,35]

An MSA is a geographically contiguous group of one or more counties with close economic and social ties[37]; these ties (such as commuting) may allow an infectious disease to spread within an MSA more readily than to external areas. Dallas-Fort Worth and Houston-Sugar Land-Baytown are the fourth and fifth largest MSAs in the US, respectively. The member counties of each MSA are periodically updated by the United States Census Bureau; these simulations use the September 2018 boundaries.[38]

FRED uses a synthetic population of the United States based on the 2010 census.[39,40] Each member of the US population is represented by an agent. Each agent is assigned a household location based on the population size of each US census block. The characteristics of each agent are drawn from the distribution of the population's characteristics in each geographic area. This allows the agents in any geographical area to be representative of the real-life population. These characteristics are age, gender, race, household size, and household income.

Agents were assigned to schools or workplaces depending on their age and employment rates. Agents representing school students were assigned to public or private schools, with a probability weighted by their demographic characteristics.[39,40] Each school in the model corresponds to a real-world equivalent, at the same location and with the same age range and student enrollment.[39,40] Agents representing workers were assigned to workplaces based on commuting patterns and the distribution of workplace sizes.

Table 1. Contact distributions

Distribution	Household	Neighborhood	School	Workplace
1	30	33	24.67	12.33
2	23	35.34	27	14.67
3	12	39	30.67	18.33

Transmission

Agents in our model sequentially attended 3 mixing locations each simulated day: their household, school or workplace, and neighborhood (agents representing the unemployed and retired did not attend a school or workplace). Agents could come into contact with one another if they were simultaneously located in the same place. These contacts allowed measles to potentially spread among the population.

The basic reproduction number, R_0, is the average number of new infections that will occur from a single case being introduced to an entirely susceptible population. For measles, R_0, has been found to be approximately 12–18,[41,42] although studies have found outbreaks beyond this range.[43] We calibrated the transmissibility of measles in our model using a simulated entirely susceptible population of Austin-Round Rock-Georgetown. The transmissibility determines the probability that an infectious contact will be made between an infectious and a susceptible agent, if they are co-located in a mixing location (household, school, workplace, and neighborhood).

Previous infectious disease studies have attempted to quantify the relative number of infections that occur in different locations where people interact. We primarily assume that during an outbreak in a hypothetical entirely susceptible population, 30% of transmissions would occur in households, 33% in neighborhoods, and 37% in schools and workplaces; with twice the per-capita transmission rate in schools relative to workplaces[44,45] (we refer to this as “contact distribution 1”).

Relative contact rates calculated by Bayham and Fenichel[46] were also used for further simulations of Austin-Round Rock-Georgetown. The proportion of infections occurring in the household were set to the upper and lower boundaries calculated by Bayham and Fenichel (“contact distribution 2” and “contact distribution 3”), and the remaining transmission proportions were redistributed between neighborhoods, schools, and workplaces (relative to the proportions used by Ferguson et al[45]). The 3 distributions of contact rates are given in Table 1. Changing contact rates can alter the transmissibility of measles in our models. Calibration simulations were run with each contact distribution using 1000 simulations in Austin-Round Rock-Georgetown.

In each simulation, schools are closed on weekends, only agents designated as weekend workers (assumed to be 20% of workers) attended their workplaces on weekends, and neighborhood contact rates were assumed to double on weekends compared to weekdays.

Vaccination rates

Simulations used 2 sets of vaccination rates. The first used the reported 2018 vaccination rates. If vaccination rates continue to fall, we assume that the fall will be concentrated in schools that are undervaccinated in 2018; therefore, the second set decreases vaccination rates by 5% in only the schools that are undervaccinated in 2018, while keeping the others constant. In Texas, 0.2% of students are medically ineligible for vaccination.[47] Assuming a 0.2% uncertainty on this value, we assume any school with a vaccination rate under 99.6% is undervaccinated.

The MMR vaccine is 97% effective at conferring immunity to measles with the recommended 2 doses; a single dose provides immunity to 93% of recipients.[7]

We vaccinated the school-attending agents according to the published vaccination rate[48] of the real-world equivalent to their simulated school. Private-school vaccination rates are published individually in Texas, but public-school rates are only published on the school district level. We assumed that all public schools in a district had the same vaccination rate.

Not all schools and school districts report their vaccination rates, despite this being mandatory.[48] Vaccination rates for these schools and school districts were estimated using the distribution of vaccination rates of nearby schools and districts, with the method discussed in Sinclair et al.[34]

We assume all agents representing people born before 1957 are immune to measles due to prior exposure, in line with Centers for Disease Control and Prevention (CDC) assumptions.[49] Agents in the synthetic population are assigned ages rather than birth dates; we defined agents who are aged 62 or older as those who were born before 1957 (this corresponds to being born before 1957 on January 1, 2019).

94.8% of the rest of the agents (ie, not school-attending or aged 62 or older) were assumed to be vaccinated, using findings from an antibody seroprevalence analysis[50] and an assumed 97% vaccination efficacy. This was also the vaccination rate assumed for the 2.2% of school-aged agents in the model designated as home-schooled.[40]

Measles model

Measles infection was modeled as having 6 stages: an initial incubation period of 11.50 ± 1.23 days (median, dispersion of a lognormal distribution); a 1-day latent phase; a 3-day fever phase; a 4-day rash phase; a 10-day recovery phase; and an indefinite immune phase.[51] Agents in the latent, fever, and rash phases could infect other, susceptible agents. Fifty percent and 95% of agents in the fever phase and rash phase, respectively, confined themselves to their household.

Measles was introduced at the start of each simulation to one school student for whom a vaccine had been refused. We record the total number of measles cases among students for whom a vaccine has been refused for nonmedical reasons (“refusers”) and other members of the population (“bystanders”), comprising those for whom vaccination failed to confer immunity, those who are medically ineligible, and unvaccinated members of the population who do not attend school.

Outbreaks were simulated for 270 days, corresponding to approximately the length of a school year (the daily interactions of students may differ during the summer vacation).

Interventions

In simulations where a measles outbreak occurred (defined as 3 or more cases linked in time and place[3]), we evaluated different public health intervention scenarios targeting unvaccinated school students. Interventions were either triggered in only the schools with at least one measles case (on the first day of a student entering the rash stage) or in all schools across the MSA (on the first day that a third agent in the MSA entered the rash stage). Interventions were not triggered if fewer than 3 cases occurred in the simulation run.

Two types of interventions were simulated: suspension from school and mass vaccination. These follow 2 strategies employed in Washington and New York states' 2018-2019 outbreaks.[19,22,24,25]

For suspensions, all unvaccinated students did not attend school as part of their weekday routines (but continued to interact with other agents in their households and neighborhoods). This comprised both students for whom a vaccine had been refused and medically exempt students. Students were suspended until 21 simulated days passed without any rash cases among agents at their school or in the MSA (for the school-specific and MSA-wide interventions, respectively). Twenty-one days is the upper limit on incubation time for measles, thus reducing the risk of susceptible students returning to school while another student has been exposed to measles but is not yet symptomatic.

Recognizing that policymakers may feel pressured to readmit students to schools without measles cases during an MSA-wide intervention, we also simulated an intervention where all unvaccinated students were initially suspended on the declaration of an outbreak. Students were then readmitted to individual schools after 21 days, or 21 days after the last measles case appeared in their school. Students were suspended again if measles presented in their school.

It may be considered unjust to mandate the suspension of students who are medically exempt from vaccination. Additional simulations in one MSA (Austin-Round Rock-Georgetown) were run in which only refusers were suspended (and not medically exempt students) to provide a comparison of potential outbreak sizes.

The second intervention explored was the vaccination of students for whom a vaccine had previously been refused. Medically exempt students were not vaccinated. In simulations where outbreaks occurred, unvaccinated students took 1–7 days (randomly drawn from a uniform distribution) to receive a vaccination and a further 11–24 days (random, uniform distribution) for the vaccine to succeed or fail.[52] Immunity was conferred to 93% of newly vaccinated agents, matching the efficacy of one dose of the MMR vaccine to confer immunity.[7]

Each intervention was simulated 1000 times in 6 Texas MSAs at 2018 vaccination rates. Further simulations explored a scenario in which the vaccination rate of each school that is undervaccinated in 2018 drops 5%. Simulations with no interventions were also run.

Both intervention types (suspension and vaccination) represent idealized scenarios. In the school suspension scenario, it assumes that measles cases are identified on the first day of the rash stage and that all schools and students are compliant with the suspension. Not all schools were initially compliant with an order to suspend students in the 2018–2019 Rockland County outbreak.[53] We also do not account for any possible increase in out-of-school interactions between suspended students. In the vaccination case, it assumes parents who have previously chosen not to vaccinate their children will do so in the event of an outbreak. While there is some recent evidence of mass vaccine uptake during outbreaks in undervaccinated communities,[3,54,55] it is unlikely that all children will be vaccinated, even if vaccination is mandatory.

The potential benefit of alternative interventions, contact tracing and high vaccination coverage prior to outbreaks, have previously been investigated with an early version of the FRED agent-based model framework.[56]

Statistical Analysis

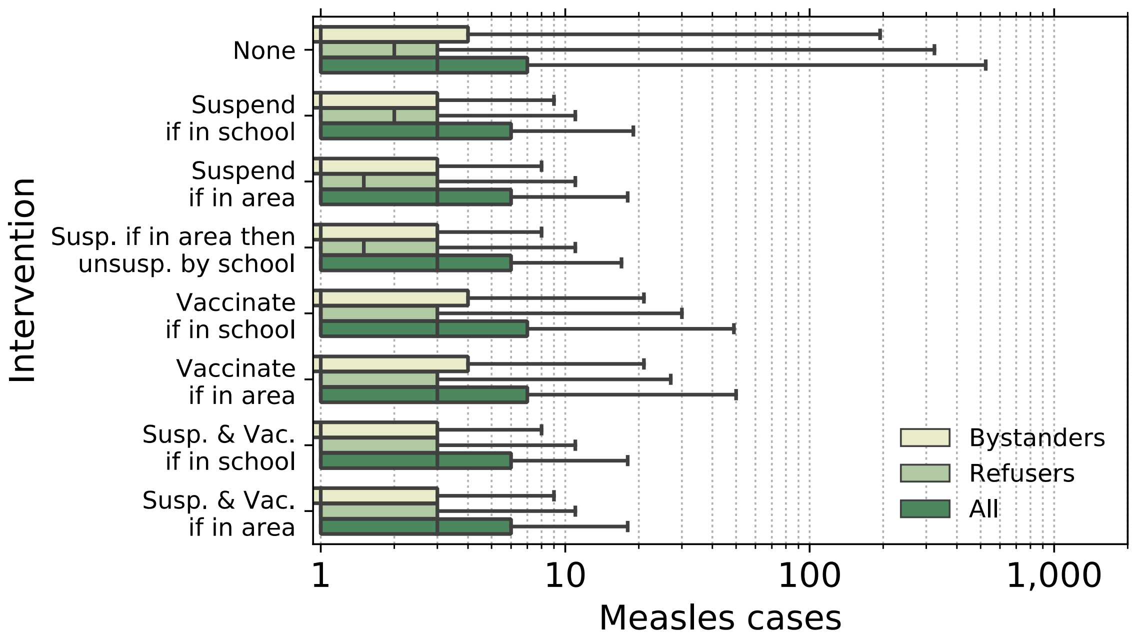
FRED simulations are stochastic: the number of agents infected with measles in each outbreak is dependent on which agent is the primary case. Our simulations randomly select a student for whom a vaccine has been refused to be the primary case. If this student attends a school with many other susceptible students, a large outbreak may ensue. Alternatively, if the primary case occurs in the only unvaccinated student in a school, it is less likely that the primary case will infect many other students, resulting in a smaller number of cases.

As we aim to evaluate the potential benefits of different public health interventions, we focus on the plausible worst-case scenario. We consider the plausible worst-case scenario to be the number of cases at the 95th percentile (ie, 1-in-20 measles introductions) when the simulation results are ordered by the total number of measles cases. Uncertainties on the 95th percentile were evaluated with a nonparametric bootstrap estimate on the simulation results (1000 samples, each of size 1000).

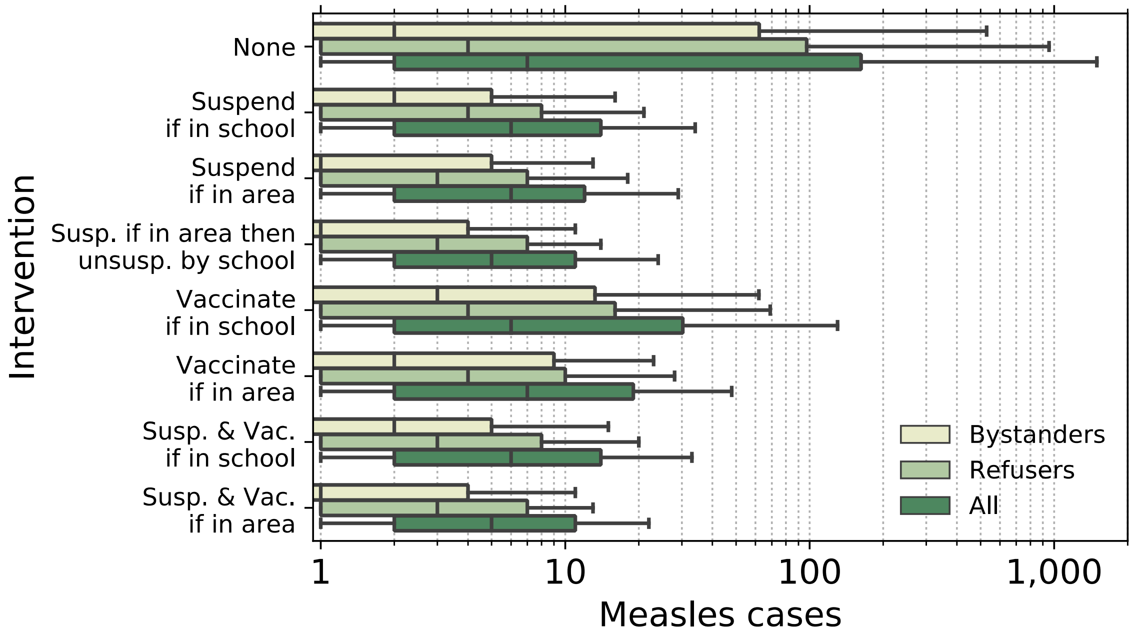
Results

Public health interventions which suspend, vaccinate, or both suspend and vaccinate students from school during measles outbreaks are associated with statistically significant reductions in the potential number of cases (see Figure 1 for forecasts in Austin-Round Rock-Georgetown, and Appendixes 1 and 2 for all 6 MSAs).

Suspending unvaccinated students from school during an outbreak is forecast to be the most effective single intervention, reducing the number of infections in a plausible worst-case scenario by 96.6 (95.5–97.4)% (median, confidence interval). At 2018 vaccination rates, the 95th percentile forecast outbreak sizes are similar regardless of whether the suspension applies only in schools that students with measles attend, to all schools in an MSA, or if the suspension is initially MSA-wide and followed by a staggered readmission in schools without measles. For example, in the Austin-Round Rock-Georgetown MSA, a forecast 527 (466–572) cases if there

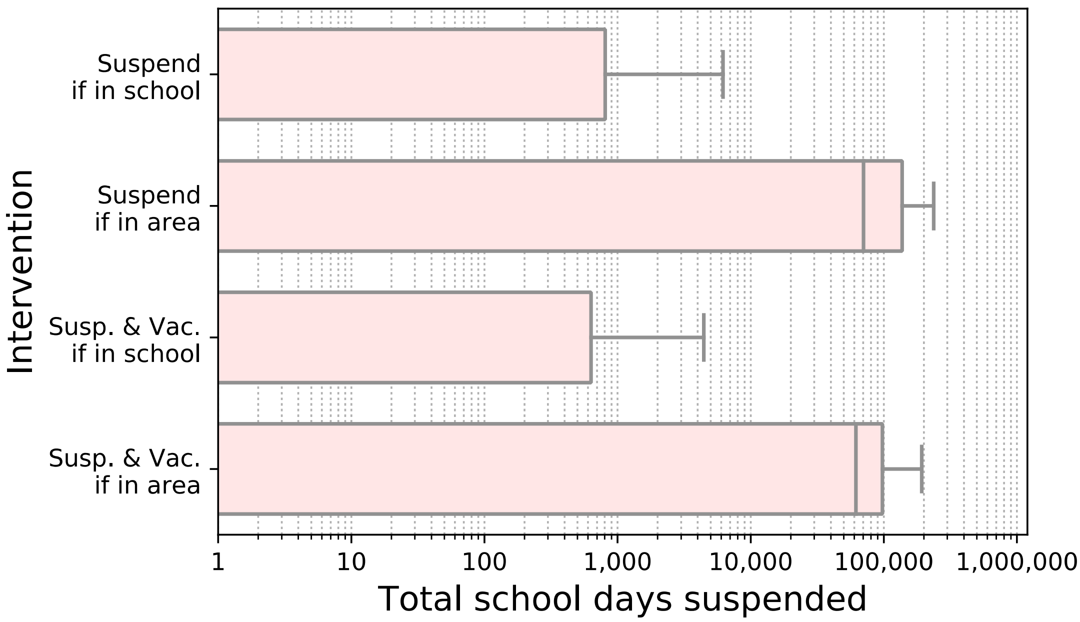


(a) 2018 vaccination rates

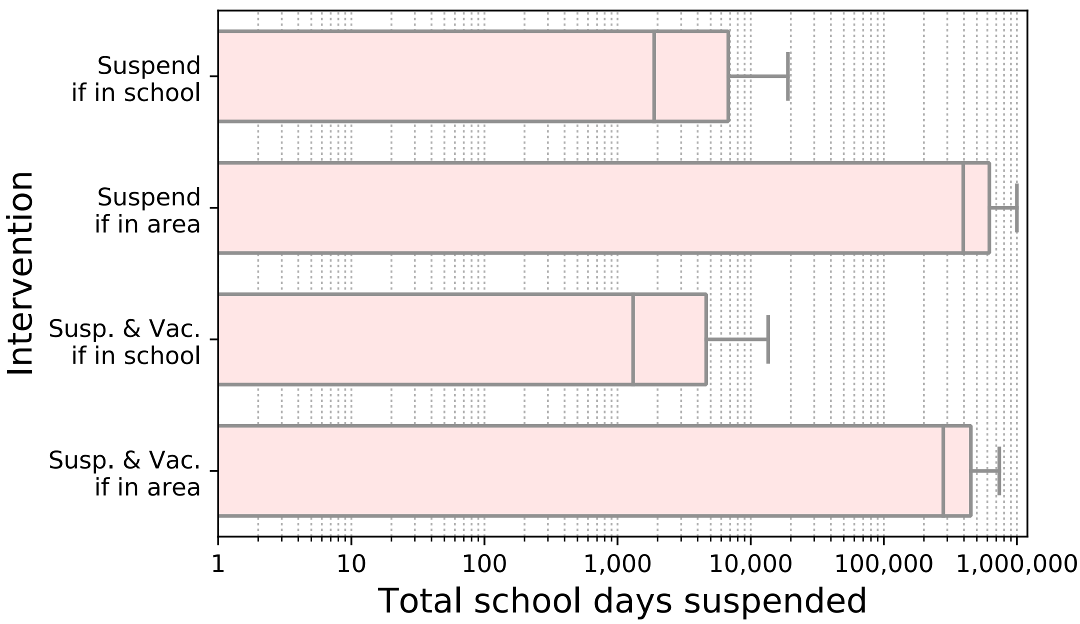


(b) 5% reduction in vaccination rates in 2018 under-vaccinated schools

Figure 1. Forecast number of measles cases with a range of public health interventions. Forecasts use (a) 2018 school vaccination rates, and (b) if vaccination rates drop 5% in schools which, in 2018, are undervaccinated. Interventions comprise suspending and vaccinating unvaccinated students if measles cases are present in their school or metropolitan area. Results are for the Austin-Round Rock-Georgetown metropolitan statistical area (MSA). Bars indicate the median and interquartile range of the number of measles cases from 1000 simulations in each MSA. Whiskers show the 5-95% confidence interval; we assume the upper end to be a plausible worst-case scenario. Cases are forecast for students for whom a vaccine has been refused ("refusers") and the rest of the population ("bystanders") as well as the combined population ("all"). Forecasts for 5 other MSAs are provided in Appendixes 1 and 2.



(a) 2018 vaccination rates



(b) 5% reduction in vaccination rates in 2018 under-vaccinated schools

Figure 2. Forecast number of student-days suspended after measles introductions in the Austin-Round Rock-Georgetown metropolitan statistical area (MSA). Forecasts use (a) 2018 school vaccination rates, and (b) if vaccination rates drop 5% in schools which, in 2018, are undervaccinated. The total number of days each unvaccinated student was suspended from their school was summed for 4 intervention scenarios which mandate student suspensions. Bars indicate the median and interquartile range of the number of measles cases from 1000 simulations in each MSA. Whiskers show the 5-95% confidence interval; we assume the upper end to be a plausible worst-case scenario. Cases are forecast for students for whom a vaccine has been refused ("refusers") and the rest of the population ("bystanders") as well as the combined population ("all"). Forecasts of total student-days suspended for 5 other MSAs are provided in Appendixes 3 and 4.

is no intervention are reduced to 19 (17–21), 18 (16–20), and 17 (15–20) cases with the respective suspensions, at 2018 vaccination rates (Appendix 1).

Suspending unvaccinated students from schools with measles cases reduces (in a plausible worst-case scenario) measles cases by 68%–96% of the cases without an intervention, in the 4 MSAs which have the largest forecast outbreaks. The benefit is reduced in MSAs with smaller forecast outbreaks (dropping to 82% and 55% in Beaumont-Port Arthur and Midland, respectively). Suspension interventions reduce cases by 97%–98% if vaccination rates drop 5% in schools undervaccinated in 2018.

If vaccination rates drop 5%, the MSA-wide suspension intervention is associated with a statistically significant reduction compared to the other suspension interventions in each MSA evaluated (suspending students in schools with measles and suspending students in all schools, followed by a staggered readmission in measles-free schools). For example, in Austin-Round Rock-Georgetown, not intervening could see 1503 (1295–1691) cases, whereas suspending unvaccinated students across the MSA reduces this to 24 (21–26); suspending students only in schools with measles and a staggered readmission of students from an MSA-wide suspension are associated with 34 (31–39) and 29 (27–33) cases, respectively (see Appendix 2).

Vaccinating eligible students is also associated with a reduction in outbreak sizes, albeit less so than suspending students. In half of the MSAs, vaccinating during an outbreak anywhere in the MSA forecasts fewer cases than vaccinating only in schools with measles cases (at 2018 vaccination rates); the outbreak sizes are forecast to be similar in the other half. If vaccination rates drop 5%, the worst-case outbreak sizes in the MSA vaccination intervention drops by 31%–78% compared to the size of the school-only vaccination intervention.

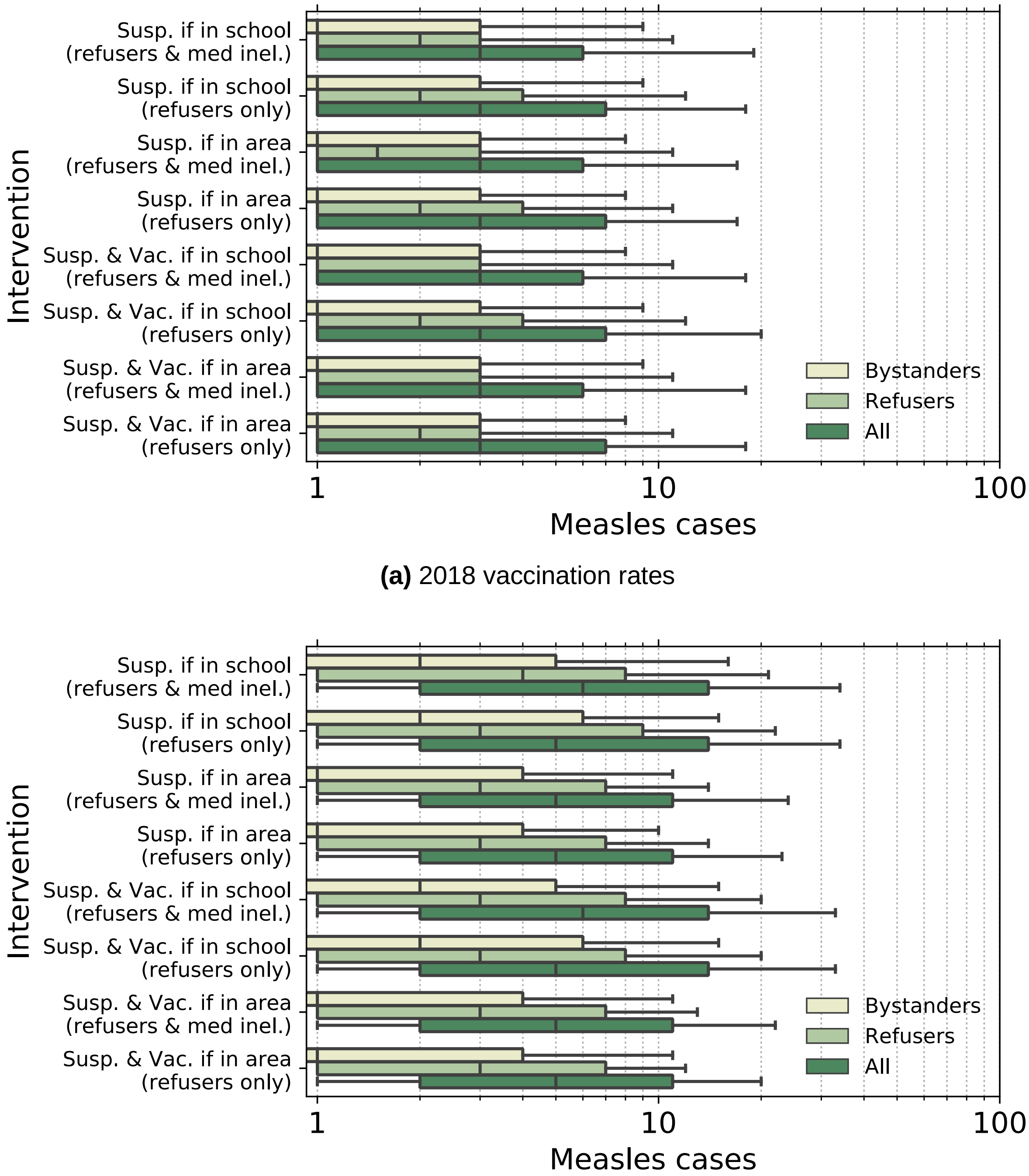
The combined interventions, in which students are both suspended and vaccinated, are not associated with further reductions in the worst-case number of infections at 2018 vaccination rates, compared to only suspending students. The same applies if vaccination rates drop 5%.

The total number of school days missed by suspended students for 4 intervention scenarios are given in Figure 2 for Austin-Round Rock-Georgetown (other MSAs given in Appendixes 3 and 4). At both 2018 and reduced vaccination rates, suspending all unvaccinated students in an MSA leads to approximately 10–100 times more missed school days than targeting schools with measles cases. At 2018 vaccination rates, suspending all unvaccinated students in Houston-Sugar Land-Baytown could result in more than 1.1 million student days lost in school, in a plausible worst-case outbreak. This would be reduced to under 5000 if only schools with measles cases were targeted.

We did not find a statistically significant difference in the potential worst-case outbreak sizes whether medically ineligible students were included in suspension policies or not (at the 2018 or the reduced vaccination rates) (Figure 3 and Appendix 5).

Alternative contact distributions

The distribution of R_0 values for each calibrated set of contact distributions are provided in Table 2. The distributions are generated from the 1000 simulations for



(a) 2018 vaccination rates

(b) 5% reduction in vaccination rates in 2018 under-vaccinated schools

Figure 3. Forecast outbreak sizes comparing applying intervention policies only to "refusers" (students for whom a vaccine has been refused) and to all unvaccinated students (ie, including medically ineligible students). Policies comprise suspending and vaccinating unvaccinated students if measles cases are present in their school or metropolitan area. Forecasts are shown for Austin-Round Rock-Georgetown. Bars indicate the median and interquartile range of the number of measles cases from 1000 simulations in each MSA. Whiskers show the 5%-95% confidence interval; we assume the upper end to be a plausible worst-case scenario. Cases are forecast for students for whom a vaccine has been refused ("refusers") and the rest of the population ("bystanders") as well as the combined population ("all").

each contact distribution. The R_0 values for each of the contact distributions are similar.

At 2018 vaccination rates, contact distribution 3 forecasts fewer cases than contact distribution 1 in the “no intervention” case, with 415 (348–451) and 527 (466–572) cases, respectively (Appendix 6). However, there is no significant difference in the number of cases between any of the contact distributions when interventions are enacted at 2018 or reduced vaccination rates.

Refusers and Bystanders

Across all simulations where 25 or more cases are forecast (including each intervention), 58 (46–70)% (mean, SD) of measles infections occur in children for whom a vaccine has been refused, with 42 (30–54)% occurring in other people (ie, bystanders). For simulations with 3–24 cases, the percentage of infections among refusers was 48 (24–72)% (mean, SD). With contact distribution 2, the forecast fraction of cases in bystanders were 42 (30–54)% (>24 cases) and 46 (23–69)% (3–24 cases), and for contact distribution 3: 37 (26–48)% and 43 (20–66)%, respectively.

Discussion

Our simulations suggest that the public health interventions applied may significantly reduce the potential size of measles outbreaks in 6 Texas metropolitan areas, with a 68%–96% reduction in areas with the largest potential outbreak sizes. If we assume that similar findings would be found across the US, the interventions enacted in Clark County, Rockland County, and New York City during their 2018–2019 outbreaks may have been effective at limiting the spread of measles.

Our results suggest that suspending unvaccinated students from schools is associated with fewer total measles cases than vaccinating susceptible students during an outbreak (however, both are beneficial). This may be due to several causes, but an important factor is likely to be the time delay between deciding to seek a vaccine and gaining immunity. This period, taking 1 to 4 weeks in these simulations, leaves students vulnerable to infection at the beginning of the outbreak. Additionally, the 93% success rate of one dose of the MMR vaccine means 7% of unvaccinated students effectively take no action to lessen their chance of infection.

Suspending students across an MSA appears to have little advantage over suspending students only in schools with measles cases at 2018 vaccination rates; however, a significant benefit is predicted if vaccination rates drop 5% in undervaccinated schools. Alternatively, if vaccination rates drop, initially suspending all unvaccinated students in an MSA, before readmitting students in schools without measles cases, may reduce the total number of measles cases compared to only ever suspending students in schools with measles cases, but less successfully than suspending all unvaccinated students in an MSA.

Table 2. Distribution of R_0 values from 1000 calibration simulations with a completely susceptible population for the 3 contact distributions provided in Table 1

Distribution	Min	Quartile 1	Median	Quartile 3	Max
1	12	12.86	13.30	13.74	15
2	12	12.81	13.25	13.74	16
3	12	12.80	13.32	13.78	15

The advantage of suspending all unvaccinated students in an MSA is that they are not attending a school if someone presents there with measles (except for the cases before an outbreak is declared). If students are only suspended from schools once an enrolled student is identified as having measles, there may have been opportunities for infections. However, these simulations suggest this does not lead to significantly more infections in a plausible worst-case scenario. This may be due to the relatively long incubation time for measles (up to 21 days[3]). Quickly suspending all unvaccinated students in a school limits the opportunity for measles to spread within a school, as only the original infectious student (and any vaccinated students without immunity) will ever potentially attend the school while infectious.

On the other hand, if vaccination rates drop, there is a much larger number of susceptible students in some schools, all of whom have the chance to become infected by the school's initial measles case before anyone is suspended. This might lead to a greater number of measles cases in the community and potentially leads to more infections occurring outside of schools.

Nonmedical vaccine exemptions have increased annually since 2003 in Texas, suggesting that, unless something occurs to change vaccine perceptions, MSA-wide interventions may become optimal in the future. Drops in vaccination rates may be compounded as the fraction of the population born before 1957 (who are all presumed immunized due to prior exposure[49]) decreases with time.

Both suspending and vaccinating unvaccinated students does not yield any significant reduction in cases compared to only suspending unvaccinated students at 2018 vaccination rates, but does if vaccination rates drop. This suggests that stronger interventions be used in areas with lower vaccination rates.

Despite not appearing to further reduce outbreak sizes, vaccinating unvaccinated students who are suspended is nevertheless beneficial to the students and the wider population. Newly vaccinated students are unlikely to be infected in future outbreaks and therefore unlikely to infect anyone else. Newly vaccinated students may also be able to return to schools sooner than waiting out an epidemic at home. It also may be beneficial to vaccinate students if an outbreak occurs anywhere in their MSA, if suspension interventions are only applied in schools where measles cases are recorded (a scenario that has not been investigated here).

Suspending students is likely to be easier to implement than vaccinating students for whom a vaccine has previously been refused: even with a mandatory vaccination order, there were ethical and practical issues with enacting New York City's vaccination policy[25] (a debate that is also playing out in other countries which recently introduced mandatory vaccination laws[57,58]). However, if out-of-school interactions increase among suspended students, then suspending students may not be as effective as predicted. It may be beneficial to encourage those responsible for the suspended students to restrict the students' interactions, especially among their peers, to prevent the potential spread of measles outside of schools.

Interventions targeted at specific schools are also likely to be easier to implement than MSA-wide interventions. It will require fewer resources to check that action has been taken at a subset of the schools than all of the schools. Furthermore, the number of school days lost through suspension is greatly reduced if suspensions are targeted at schools with measles cases, compared to applying them to all schools.

Additionally, MSAs are not a government level of power. Health departments operate on county, state, and national levels (albeit some MSAs are only one county in size). This may cause obstacles to enacting MSA-wide interventions quickly in the event of an outbreak. To preempt potential problems, county or state health departments should ensure they have measles outbreak intervention policies prepared and coordinated across county lines in advance of a measles outbreak.

It is unlikely that any intervention effort will have a 100% compliance rate and accurately identify all measles cases. These forecasts are therefore for idealized scenarios; the potential number of measles cases may be higher in reality.

There was no statistically significant difference found between the potential number of measles cases when all unvaccinated students (ie, refusers and medically ineligible students), or only refusers, were suspended. As no greater risk to the general population was found, it may be equitable to allow these students to attend school during outbreaks during a suspension intervention. However, there would be a risk of infection for these students, and the option for parents/guardians to isolate them, and thus reduce infection risk, should also be considered.

Our model evenly distributes medically ineligible students across schools: if a school had a higher concentration of students, it might be at risk of larger outbreaks. This should be evaluated when deciding if medically ineligible students should stay home from school or not.

The similarities in results between the 3 contact distributions suggest that the benefit of each intervention would be robust across a range of communities that may have different contact distributions.

The 2-dose effectiveness of the MMR vaccine is taken to be 97%, as reported by the Advisory Committee on Immunization Practices[7]; however, studies have found values for the 2-dose effectiveness ranging from 67%–100%.[59-64] If a higher effectiveness was used in our simulations, we would expect the forecast number of cases in each scenario to be reduced, especially among "bystanders" (those whose vaccine failed). We would also expect vaccination interventions to improve more than school suspension interventions. However, given the much smaller number of cases forecast with school suspension interventions, we would still expect these to be advantageous compared to vaccination interventions.

Limitations

There are several limitations to this study. Primarily, all models necessarily simplify the real-life system they are modeling. Agent-based models allow a high level of specificity in the daily actions and behavior of their agents, but some of this behavior must be simplified and generalized. For example, we assume that agents interact with their household members every day, that every student has the same probability of interacting with other students in their age group, and that agents preferably interact with agents who live near them rather than far away. The model does not account for mass-gathering events, such as theme parks and churches, which have been linked to outbreaks,[65,66] nor does it account for potential infections from healthcare-seeking behavior, such as in doctor's offices and hospital waiting rooms. The model does not stratify agents along cultural or religious lines,[54,67,68] instead relying on household locations, school locations, and school type (private or public). Alternative modeling approaches make other assumptions: the classic SIR-type model of epidemiology[69] assumes everyone within a compartment interacts equally with one another at all times, for example. In this model, as with all models, the simplifications must be considered along with the results.

The vaccination rate data published by the Texas Department of State Health Services[48] is limited by law and school responses. Texas law mandates that all schools and districts report the vaccination coverage of their students; however, only 83% responded in the 2017–2018 school year. Data from individual public schools is not published, in part due to privacy concerns,[70] necessitating the use of school-district aggregated data. We assume that geographically close public schools are likely to have a similar vaccination coverage; however, if there are individual public schools with low vaccination rates, our forecasts may underestimate potential outbreak sizes. Legislative bills to allow individual public school data to be published have failed in recent years.[71,72]

We assume that home-schooled students have vaccination rates consistent with the general population, as vaccination rates are not collected for home-schooled students in Texas. As Texas allows unvaccinated children to enroll in schools, there is not a strong motivation for vaccine-hesitant parents to home-school. Home-schooled students represent a small fraction of school students and can be assumed to interact with fewer other students than their school-attending peers, suggesting they do not have a large effect on the spread of infectious diseases.

We would not expect a different home-school vaccination rate to greatly alter the relative benefit of each intervention, as the interventions are only applied to children in schools (although outbreak sizes would change). However, vaccination interventions may be slightly less effective, as more schoolchildren would become infected before developing immunity.

Not all medically exempt students are susceptible to measles: some students are exempt due to prior measles infection. However, medically exempt students make up a very small fraction of the student population and, in places where there have not been large or regular measles outbreaks, it is likely that most medically exempt students are not exempt due to prior infection.

The forecast number of measles cases presented here is slightly different from those in previous work using FRED.[34] These differences are due to a few factors: updates in the counties present in the MSAs (here the September 2018[38] boundaries were used; previously the July 2015 boundaries were used[73]); updates in the FRED code, requiring recalibration of the transmissibility of measles; and different seeds for random-number generators.

Conclusions

Simulations of measles outbreaks in Texas find that 2 types of interventions enacted during outbreaks, suspending unvaccinated students from school and mandatory vaccinations, are associated with reductions in the potential number of measles cases by up to 96%. Suspending students from school is associated with the fewest measles cases. At 2018 vaccination rates, suspending and vaccinating students concurrently has no significant reduction in the potential number of cases compared to only suspending students, provided out-of-school contacts do not increase during the suspension. Further, at 2018 vaccination rates, policies that affect all schools in a metropolitan area have no significant reduction in the number of cases compared to policies which only target schools with measles cases. Only suspending unvaccinated students in schools with measles cases leads to 10–100 factor reduction in total school days suspended by all students, compared to suspending all unvaccinated students in a metropolitan area. However, if vaccination rates drop 5% in schools that were undervaccinated in 2018, area-wide policies are forecast to be more beneficial. These results only evaluate interventions taken during an outbreak; vaccination before an outbreak is the most effective means of reducing outbreak sizes.

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Appendix 1. Forecast number of cases with 2018 vaccination rates. Forecast number of measles cases with different policy interventions are provided. Forecasts use 2018 school vaccination rates in 6 Texas metropolitan statistical areas (MSAs). Forecasts with different interventions are provided. Values are the 95th percentile in cases from 1000 simulations, which we assume to be a plausible worst-case scenario. Confidence interval on the 95th percentile value, calculated using a nonparametric bootstrap estimate, is provided in parentheses.

Intervention	Austin-Round Rock-Georgetown	Beaumont-Port Arthur	Dallas-Fort Worth-Arlington	Houston-Sugar Land-Baytown	Midland	Tyler
None	527 (466-572)	11 (9–11)	477 (462–497)	53 (44–81)	22 (18–25)	146 (141–160)
Suspend unvaccinated students if measles in school	19 (17–21)	9 (8–9)	26 (20–28)	17 (15–20)	12 (11–13)	19 (17–20)
Suspend unvaccinated students if measles in area then unsuspend by case free schools	18 (16–20)	9 (8–9)	24 (20–27)	16 (14–20)	12 (11–13)	18 (17–19)
Suspend unvaccinated students if measles in area	17 (15–20)	8 (8–9)	23 (19–26)	16 (14–18)	12 (11–13)	18 (16–19)
Vaccinate unvaccinated students if measles in school	49 (43–59)	10 (8–12)	75 (67–84)	32 (27–41)	15 (14–17)	42 (36–44)
Vaccinate unvaccinated students if measles in area	50 (43–53)	9 (8–10)	60 (55–71)	24 (20–29)	16 (14–17)	38 (35–42)
Suspend & vaccinate unvaccinated students if measles in school	18 (16–20)	9 (7–9)	22 (20–25)	17 (14–18)	12 (10–13)	19 (16–18)
Suspend & vaccinate unvaccinated students if measles in area	18 (17–20)	8 (8–10)	22 (20–25)	16 (15–19)	12 (10–13)	17 (17–20)

Appendix 2. Forecast number of cases if vaccination rates drop 5% in schools which, in 2018, are undervaccinated**.** Forecast number of measles cases with different policy interventions are provided. Forecasts use a 5% drop from 2018 school vaccination rates in schools which, in 2018, are undervaccinated, for 6 Texas metropolitan statistical areas (MSAs). Forecasts with different interventions are provided. Values are the 95th percentile in cases from 1000 simulations, which we assume to be a plausible worst-case scenario. Confidence interval on the 95th percentile value, calculated using a nonparametric bootstrap estimate, is provided in parentheses.

Intervention	Austin-Round Rock-Georgetown	Beaumont-Port Arthur	Dallas-Fort Worth-Arlington	Houston-Sugar Land-Baytown	Midland	Tyler
None	1503 (1295–1691)	103 (91–126)	1445 (1213–1596)	1634 (1436–1848)	152 (127–165)	337 (306–359)
Suspend unvaccinated students if measles in school	34 (31–39)	21 (19–23)	35 (30–41)	45 (39–52)	22 (21–25)	24 (21–26)
Suspend unvaccinated students if measles in area then unsuspend by case free schools	29 (27–33)	17 (15–19)	32 (28–36)	31 (28–35)	19 (16–20)	22 (20–24)
Suspend unvaccinated students if measles in area	24 (21–26)	15 (14–17)	24 (21–27)	22 (20–24)	16 (15–18)	20 (18–22)
Vaccinate unvaccinated students if measles in school	132 (113–153)	38 (31–40)	157 (115–181)	185 (154–210)	44 (39–49)	61 (54–72)
Vaccinate unvaccinated students if measles in area	49 (43–53)	25 (22–26)	44 (36–50)	41 (38–45)	29 (28–32)	42 (38–49)
Suspend & vaccinate unvaccinated students if measles in school	33 (30–37)	17 (16–20)	34 (31–36)	39 (35–46)	21 (18–24)	23 (21–26)
Suspend & vaccinate unvaccinated students if measles in area	22 (20–24)	14 (13–16)	20 (19–22)	22 (20–23)	15 (14–16)	18 (17–20)

Appendix 3. Forecast number of student-days suspended after measles introductions (1000s). Forecasts use the 2018 school vaccination rates in 6 Texas metropolitan statistical areas (MSAs). The total number of days each unvaccinated student was suspended from their school was summed for 4 intervention scenarios that mandate student suspensions. Values are the 95th percentile in cases from 1000 simulations, which we assume to be a plausible worst-case scenario. Confidence interval on the 95th percentile value, calculated using a nonparametric bootstrap estimate, is provided in parentheses.

Intervention	Austin-Round Rock-Georgetown	Beaumont-Port Arthur	Dallas-Fort Worth-Arlington	Houston-Sugar Land-Baytown	Midland	Tyler
Suspend unvaccinated students if measles in school	6.2 5.7–6.7)	0.9 (0.8–1.1)	9.1 (7.9–10.7)	4.8 (4.0–6.7)	1.0 (0.9–1.0)	4.5 (4.3–4.7)
Suspend unvaccinated students if measles in area	237.7 (225.2–254.4)	19.8 (17.8–20.3)	789.5 (747.6–827.3)	1132.5 (1053.9–1214.8)	6.8 (6.4–7.1)	20.0 (18.8–20.7)
Suspend & vaccinate unvaccinated students if in school	4.5 (4.0–5.1)	0.7 (0.5–0.8)	6.9 (5.9–7.3)	4.0 (3.2–4.5)	0.7 (0.7–0.8)	3.2 (3.1–3.4)
Suspend & vaccinate unvaccinated students if in area	195.9 (184.7–209.5)	12.9 (11.9–13.6)	626.7 (587.4–690.6)	843.8 (762.7–918.2)	5.1 (4.7–5.3)	16.5 (14.80–17.6)

Appendix 4. Forecast number of student-days suspended after measles introductions (1000s). Forecasts use a 5% drop from 2018 school vaccination rates in schools which, in 2018, are undervaccinated for six Texas metropolitan statistical areas (MSAs). The total number of days each unvaccinated student was suspended from their school was summed for 4 intervention scenarios that mandate student suspensions. Values are the 95th percentile in cases from 1000 simulations, which we assume to be a plausible worst-case scenario. Confidence interval on the 95th percentile value, calculated using a nonparametric bootstrap estimate, is provided in parentheses.

Intervention	Austin-Round Rock-Georgetown	Beaumont-Port Arthur	Dallas-Fort Worth-Arlington	Houston-Sugar Land-Baytown	Midland	Tyler
Suspend unvaccinated. students if measles in school	20.0 (17.9–21.7)	7.3 (6.5–8.3)	19.1 (15.9–22.5)	32.0 (26.5–38.2)	8.3 (7.5–9.3)	8.0 (7.2–8.6)
Suspend unvaccinated students if measles in area	1000.0 (915.9–1070.8)	135.8 (123.1–141.2)	4640.1 (4384.7–4898.6)	5101.1 (4808.8–5536.2)	86.2 (81.8–90.2)	62.4 (58.6–65.6)
Suspend & vaccinate unvaccinated students if in school	13.6 (12.4–15.3)	4.7 (4.2–5.3)	13.7 (12.1–15.0)	20.6 (17.8–23.4)	5.5 (5.1–5.8)	5.5 (5.0–6.2)
Suspend & vaccinate unvaccinated students if in area	736.9 (705.5–797.5)	87.8 (83.0–95.6)	3316.0 (3178.5–3481.8)	3752.2 (3574.8–4010.3)	59.8 (56.2–64.3)	46.0 (43.3–48.0)

Appendix 5. Forecast outbreak sizes if interventions are applied only to "refusers" (1000s), compared to when interventions are applied to both refusers and students who are medically ineligible for vaccination. Forecasts given for 2018 vaccination rates, and for a 5% drop from 2018 school vaccination rates in schools which, in 2018, are undervaccinated. Forecasts for different intervention policies in Austin-Round Rock-Georgetown. Values are the 95th percentile in cases from 1000 simulations, which we assume to be a plausible worst-case scenario. Confidence interval on the 95th percentile value is provided in parentheses.

	2018 vaccination rate		2018 vaccination rate -5%	
Intervention	Refusers and medically ineligible	Refusers only	Refusers and medically ineligible	Refusers only
None	527 (466–572)	n/a	1503 (1295–1691)	n/a
Suspend unvaccinated students if measles in school	19 (17–21)	18 (17–18)	34 (31–39)	34 (31–38)
Suspend unvaccinated students if measles in area	17 (15–20)	18 (16–18)	24 (21–26)	23 (22–24)
Suspend & vaccinate unvaccinated students if in school	18 (16–20)	18 (17–18)	33 (30–37)	33 (31–35)
Suspend & vaccinate unvaccinated students if in area	18 (17–20)	21 (18–21)	22 (20–24)	21 (19–22)

Appendix 6. Forecast number of measles cases for 3 different contact distributions. The 3 contact distributions represent different estimates of the mean ratio of contacts made in households, workplaces, schools, and neighborhoods provided in Table 1. Forecasts are given for 2018 vaccination rates, and for a 5% drop from 2018 school vaccination rates in schools which, in 2018, are undervaccinated. Forecasts for different intervention policies in Austin-Round Rock-Georgetown. Vaccination policies only applied to refusers and not medically ineligible students. Values are the 95th percentile in cases from 1000 simulations, which we assume to be a plausible worst-case scenario. Confidence interval on the 95th percentile value is provided in parentheses.

	2018 vaccinate rate			2018 vaccinate rate -5%		
Intervention	Distribution 1	Distribution 2	Distribution 3	Distribution 1	Distribution 2	Distribution 3
None	527 (466–572)	517 (459–584)	415 (348–451)	1503 (1295–1691)	1636 (1472–1851)	1437 (1180–1686)
Suspend unvaccinated students if measles in school	19 (17–21)	21 (19–23)	19 (17–20)	34 (31–39)	34 (32–38)	31 (27–34)
Suspend unvaccinated students if measles in area	18 (16–20)	20 (18–21)	18 (17–20)	24 (21–26)	24 (23–25)	20 (19–22)
Vaccinate unvaccinated students if measles in school	49 (43–59)	62 (55–73)	59 (52–68)	132 (113–153)	163 (145–188)	135 (120–155)
Vaccinate unvaccinated students if measles in area	50 (43–53)	57 (51–62)	56 (46–62)	49 (43–53)	52 (47–59)	55 (50–65)
Suspend & vaccinate unvaccinated students if measles in school	18 (16–20)	21 (16–21)	19 (15–19)	33 (30–37)	36 (30–38)	30 (27–33)
Suspend & vaccinate. unvaccinated students if measles in area	18 (17–20)	19 (18–23)	17 (17–22)	22 (20–24)	20 (19–22)	19 (18–21)