Emerging Evidence on COVID-19

Evidence on the Virulence, Transmission and Impact of B.1.617.2 (Delta) among Children

Introduction

What is the evidence of the virulence, transmission and impact of the Delta variant on children?

The SARS-CoV-2 **variant of concern** (VOC) B.1.617.2 known as Delta by the WHO naming system is currently the predominant variant in many countries (1). VOCs are of concern when compared to the original SARS-CoV-2 variants, as their complement of mutations lead to increased transmissibility, increased virulence (morbidity or mortality), changes in clinical disease presentation, immune evasion, reduced effectiveness of treatments, vaccines and/or public health measures (PHMs) and/or are associated with diagnostic detection failures (1-3).

Delta has been reported to have higher transmissibility than the Alpha VOC and original variant (4-9). Delta has outcompeted other variants including Alpha in several countries and is the dominant variant at 91% of VOC cases in Canada during the week of August 8th, 2021 (10-12). Emerging evidence also reports higher risk of severe outcomes such as hospitalization, ICU admission, and death associated with Delta compared to non-VOCs or Alpha in the general population (13-16). A risk profile of the evidence on Delta is available upon request. Globally, Canada has one of the highest vaccination coverage rates and currently 77.5% (September 15, 2021) of the population ≥12 years of age has received two doses of vaccine (17). However, COVID-19 vaccines are not yet authorized by Health Canada for those <12 years old.

As of September 2021, children have stated the new school year and Canada has entered the fourth wave of the pandemic (18, 19). Delta is the dominant variant across Canada and the number of and proportion of Delta cases is increasing across the country and modelling studies have predicted that the daily number of cases may double in the next month (19). Evidence is just beginning to emerge on the effects of the Delta variant on children. To further inform public health strategies to protect children including in school settings, this evidence brief summarizes what is known on the virulence, transmission and impact of Delta among children aged 0-17 years old including the impact of public health interventions. This report presents evidence up to September 14, 2021.

Key Points

- This review includes seven studies. There were three general population surveillance studies (two USA and one UK) that focused on cases in children between June and August 2021, when Delta was the dominant variant. There was one outbreak investigation at an elementary school among both children and adults in May 2021 and there are three predictive models from the USA on Delta transmission in schools that

examined the impact of public health measures. The level of evidence on all parts of this review is considered low as most outcomes are only underpinned by one or two studies, thus we caution the readers that this evidence is very preliminary and the conclusion may change as more studies become available.

Virulence

- Current evidence suggests that Delta is not more virulent in children than the original variant or Alpha. Two surveillance studies in the USA and one in the UK reported that although the incidence and hospitalization rates have increased, the proportion of COVID-19 cases with severe outcomes (e.g., ICU admission, invasive mechanical ventilation and mortality) has not changed among children during June - August 2021 compared to historical timeframes when Delta was not dominant (20-22).

Transmissibility

- One study described a school outbreak where an unvaccinated teacher was the index case and there was a 50% attack rate in the elementary school classroom despite high adherence of the students to wearing a mask and being seated 6 feet apart, the teacher occasionally removed her mask, this demonstrates the high transmissibility of Delta (23).
- One predictive model reported that school attributable excess transmission would be nearly 10 times lower if Alpha remained the dominant variant (R_0=2.5) compared to Delta as the dominant variant (24).
- Evidence from predictive models and surveillance studies do not suggest that Delta disproportionately affects transmission in children compared to adults. Transmission in school-aged children was expected to be strongly correlated with level of community transmission (25, 26). The models identified that transmission of Delta in schools contributes to the community transmission, but that children will not drive Delta transmission (24).

Impact of Public Health Measures

Vaccination

- A USA surveillance study showed vaccinated adolescents had 10.1 times lower hospitalization rates compared to unvaccinated adolescents during the beginning of a Delta dominated surge in COVID-19 cases (June-July 2021), suggesting that vaccination prevents severe illness (20).
- This study also reported that lower vaccination coverage in the local population was associated with higher emergency department visits (3.4x) and hospitalizations (3.7x) compared to states with the highest vaccination coverage over all adolescent cases (20).

Impact of PHMs (e.g., vaccine coverage, masking, testing, quarantine, cohorting and hybrid learning) on school transmission

- Two predictive models reported that masking and testing of the school population (students and teachers) reduced the number of absent days due to COVID-19 in all school settings (24, 26). One study estimated with no interventions there were 210, 510 and 400 absent days for elementary, middle and high

school, respectively, while days absent were lower at 140, 120 and 76 days with masking and testing (26). The other study reported greater school absences with increased community transmission (24).

- Three predictive models show the potential reduction in Delta cases attributable to school transmission in elementary schools, middle schools and high schools implementing different combinations of masking, testing and cohorting and different levels of vaccination coverage (range 30-70% across models) in the eligible population (e.g., children >12 years, teachers and community).

  Elementary school (4-11 years) / middle school (12-13 years) / high school (14-18 years):

  - Without testing and masking (Delta R_0=4.0), more than 75% of susceptible (e.g., unvaccinated or not previously infected) students will get infected within three months. With masks (R_0=2.0), the proportion infected drops to 50%/35%/24% and routine testing further reduces infections to 22%/16%/13% for elementary/middle/high schools respectively (26).
  - The models show that higher vaccination coverage within the school population was associated with fewer cases and lower impact of PHMs. However, only in high schools where all students were eligible for vaccination and vaccination coverage exceeded 90% was the impact of other PHMs found to be negligible (24).
  - With universal mask use and school vaccination coverage of 70%, the excess symptomatic infections attributable to school reopening was far less than in high schools with only 0.4% excess infections compared to elementary and middle schools with 2.0%, and 3.0% excess infections, respectively (24).
  - One model showed with Delta, a "test to stay" approach where students with known exposures were allowed to stay in school with daily testing instead of quarantine resulted in slightly more transmission in all school levels (25).
    - Using remote learning as the baseline scenario, universal screening averted 57% of excess cases compared to no additional PHMs in both elementary and middle schools (25)
  - One model showed with Delta circulating, increasing vaccination coverage among eligible individuals in school (e.g., students >12 years, teachers and staff), there would be a decrease in school-attributable transmission in all schools (24). However, the proportion of COVID-19 cases in <12 years may increase, resulting in more cases in elementary schools compared to high schools, as immunity due to infection or vaccination coverage ≥12 years increases because the younger group has a larger proportion of susceptible individuals.
  - A hybrid schedule of in person learning where there is ≥60% remote instruction where students are not in school, could prevent much of the excess transmission by reducing the number and duration of contacts for both elementary and middle school (25).
  - Modelling Delta transmission, the strictest combination of interventions tested (masks + cohorts, 70% vaccine coverage), would result in excess infection among 1.7% of elementary students compared to 6.6% with vaccine coverage only and could achieve a target of <5 excess infections per 1,000 students or teachers (lowest risk target) in middle schools (24).

Overview of the Evidence

Seven studies pertaining to the virulence, transmission and impact of Delta in children were included in this review. Three surveillance studies reported on Delta transmission and virulence among children. One outbreak investigation on Delta transmission in an elementary school. Three predictive models assessing impact of Delta and combinations of public health measures (e.g., masking, testing, cohorting and vaccinations) on transmission in children.

A formal risk of bias assessment was not conducted. The observational studies included surveillance data obtained from large national databases that analyzed data pertaining to children. Due to the nature of surveillance data, the evidence is at high risk of bias as the sample may not be representative of the population and may have insufficient detail to answer the research question. In addition, these studies are subject to missing information, selection bias and confounding factors.

The quantitative predictive models in this review do not identify actual outcomes of strategies that have been tested, but rather present a range of plausible outcomes based on theoretical scenarios. Their results are useful to compare different options as part of a decision-making process, however the results need to be interpreted with caution as the models will vary based on the assumptions, input values and region-specific parameters used.

A key knowledge gap in this research is the lack of high-quality studies reporting evidence on the transmission and virulence of Delta in children compared to the original SARS-CoV-2 variant or other VOCs. A comparison against other VOCs and the original variant is needed to contextualize and understand the difference in the impact of Delta on transmission and severity among children and in adults vs. children, including in school settings.

Overall, the level of evidence of the risk of the Delta variant among children is low and there are knowledge gaps in the existing literature base. Given the small number of studies, the results of further research could potentially change the conclusions of this review.

CONTENTS

VIRULENCE OF DELTA AMONG CHILDREN

- Two surveillance studies in the USA and one from the UK reported cases and hospitalization rates increased in children and adolescents age 0-17 years coinciding with Delta becoming the dominant variant in May-August 2021 (Table 1) (20-22).
    - There was no difference in ICU admission, invasive mechanical ventilation and mortality between March 1, 2020, and June 19, 2021 (before Delta was dominant) and June 20–July 31, 2021 (after Delta was dominant) indicating the proportion of cases that lead to severe outcomes in children 0-17 years has not changed in the USA (20).
    - The USA papers describe increased incidence rates and hospitalization rates in children given the current epidemiological situation of increasing COVID-19 cases.
        - Incidence rates in the USA between August 14–27, 2021 have increased among children and adolescents aged 0–4, 5–11, and 12–17 years: 16.2, 28.5, and 32.7 per 100,000 persons compared to 1.7, 1.9 and 2.9 in June 2021, respectively (21). In the UK cases 5-12 years old increased from 0.35% to 1.05% test positivity and 13-17 years cases increased from 0.16% to 1.33% (22).
        - Hospitalization rates in the USA increased to 1.4 per 100,000 children (0-17 years) in the population the week of August 14, 2021 compared to 0.3 per 100,000 during the week of June 26, 2021, representing a 4.7-fold increase. The increase is similar to the increase in peak hospitalization rate in January, 2021 of 1.5 per 100,000 children. The highest increase in hospitalizations occurred in children 0-4 years with 1.9 per 100,000 compared to 0.2 per 100,000, representing a 10-fold increase (20).
    - The percent of emergency department visits and the rate per 100,000 of hospitalizations in August 2021 when Delta was the dominant variant in the quartile of states with the lowest vaccination coverage was 3.4 times and 3.7 times that in the quartile of states with the highest vaccination coverage, respectively (20).

TRANSMISSION OF DELTA AMONG CHILDREN

One outbreak investigation, two surveillance studies, and a predictive model provide some evidence for Delta's increased transmissibility in children. Compared to Alpha, a predictive model reported that school attributable excess transmission would be nearly 10 times higher for Delta (24).

Delta is highly transmissible in a school setting. An outbreak investigation in an elementary school in the USA May 2021 describes an unvaccinated teacher who taught until 2 days post symptom onset. There was a 50% attack rate in the classroom despite high adherence by the students to wearing a mask and being seated 6 feet apart (23). The teacher occasionally took off her mask, and the positive case pattern in the classroom and epidemiological investigation was consistent with the teacher as the source of exposure (23).

Evidence from predictive models and surveillance studies do not suggest that Delta disproportionately affects transmission in children. Transmission in school-aged children was expected to be strongly correlated with level of community transmission (25, 26). The models identified that transmission of Delta in schools contributes to the community transmission, but that children and school settings will not drive Delta transmission (24).

IMPACT OF PUBLIC HEALTH MEASURES

One USA surveillance study and three predictive models parameterized to mimic different areas in the USA are included in this section. The surveillance data highlights that vaccinated adolescents had a 10.1 times lower risk of hospitalization compared to unvaccinated adolescents from June 20-July 31, 2021, when Delta was becoming dominant (20). There was no further analysis of potential differences in vaccine protection by variants that caused infection.

Overall, the predictive models indicate that PHMs including vaccination coverage in students, teachers, staff and the community reduced the transmission of Delta among school-aged children. The models identified that transmission of Delta in school contributes to the transmission of infection but was not driving Delta transmission.

The three predictive models examine the scenario where Delta is dominant, with the general assumption that Delta is more transmissible and thus has a higher R_0 (range 4.0-5.0) compared to previous variants or VOCs. Scenarios include different levels of vaccination coverage (30-70%) and non-pharmaceutical interventions (NPIs) (e.g., masking, testing and cohorting) for comparison. Outputs are presented by type of school (i.e., elementary, middle and high school) to account for varying levels of vaccination coverage, size of schools and mixing patterns of staff and students in these schools.

<u>COVID-19 cases attributable to school transmission in elementary, middle and high schools:</u>

Elementary Schools:

Elementary schools generally include children 4-11 years old, thus none of the children are eligible for vaccination in these settings. Key findings on elementary schools from the predictive models are listed below:

- The baseline scenario of 30-50% immunity (from infection or vaccination) and no NPIs estimated more than 75% of susceptible students will get infected within three months (26). The addition of masks dropped the proportion infected to 50% and testing further reduces infections to 22% (26).
- Compared to fully remote instruction, 5-day in-person attendance with no in-school testing (90% of teachers and staff were vaccinated with 80% vaccine effectiveness) was associated with a 40% projected increase (excess cases attributable to school transmission) in infections among students at a community case rate of 10 cases/100k/day and a 38% increase at 50 community cases/100k/day (25).

  - In a community with 10 cases/100k/day, weekly screening averted 57% of excess incidence (cases attributable to school transmission) relative to remote learning (25).
  - If students with known exposures were allowed to stay in school with daily testing (the "test to stay" strategy), slightly more transmission occurred compared to isolation of exposed cases (quarantine) (25). With "test to stay" compared to quarantine and 10 community notifications/100k/day, weekly screening prevented 46% rather than 57% of excess transmission, and weekly surveillance of 20% of a random sample of unvaccinated students and teachers prevented 17% rather than 25% (25).
- A 70% vaccination coverage without additional NPIs resulted in 6.6% excess symptomatic cases in elementary schools across a 128-day semester, compared to 15% with 60% vaccination coverage and 18% with 50% vaccination coverage (24).
  - With universal mask use, community and school vaccination coverage of 70%, will result in 2.0% excess symptomatic cases (24).
  - With increasing vaccination coverage from 50% to 70%, there is a 24% decline in school-attributable transmission, suggesting that adult to child transmission represents an important source of school-attributable illness (24).
  - Increasing vaccination coverage of teachers from 70% to 90% reduced the estimated excess rate of infection from 6.6 to 3.9 symptomatic cases per 100 elementary students across the four-month semester, representing a reduction of 41% (24). This suggests that increasing vaccination coverage among elementary school teachers can reduce infection among their students (24).
  - The strictest combination of interventions tested (masks + cohorts, 70% vaccine coverage), would result in excess infection among 1.7% of elementary students assuming they are equally as susceptible as older children and 0.4% of elementary students assuming students are half as susceptible as older children compared to 6.6% with only 70% vaccination coverage in >12 years (24).

Middle Schools:

Middle schools generally include children 11-13 years old, thus some of the children are eligible for vaccination in these settings. Key findings on middle schools from the predictive models are listed below:

- The baseline scenario of no NPIs and with 30% of middle school children vaccinated, estimated more than 75% of susceptible students will get infected within three months (26). The addition of masks dropped the proportion infected to 35% and testing further reduces infections to 16% (26).
- Compared to fully remote instruction, a 5-day middle school attendance (assuming 90% of teachers and staff were vaccinated with 80% vaccine effectiveness, and 50% of middle school students were vaccinated, and quarantine of known close contacts) increased incidence (excess cases attributable to school transmission) by 72% at a community case rate of 10 cases/100k/day and by 60% at 50 community case/100k/day (25).
  - In a community with 10 cases/100k/day, universal weekly screening averted 57% of excess incidence (cases attributable to school transmission) relative to remote learning and weekly surveillance of 20%

of a random sample of unvaccinated students and teachers prevented averted 34% of the excess transmission associated with school attendance (25).

- The "test to stay" strategy increased transmission slightly compared to the remote-only baseline (e.g., a 72% increase with quarantine to an 82% increase with test-to-stay at 10 community notifications/100k/day) (25).
- A hybrid schedule of in person learning with ≥60% remote instruction, could prevent much of the excess transmission by reducing the number and duration of contacts for both elementary and middle school (25).

- Under a 70% vaccination coverage with out additional NPIs, there will be 8.8% excess symptomatic cases in middle schools across a 128-day semester, compared to 11% with 60% vaccination coverage and 13% with 50% vaccination coverage (24).
  - With universal mask use, community and school vaccination coverage of 70%, an estimated 3.0% excess symptomatic infection attributable school transmission is predicted
  - Achieving lower risk tolerances, such as <5 excess infections per 1,000 students or teachers, required high vaccination (70%), a cohort approach.
  - Given 45% vaccine effectiveness (VE), masking all middle school students would avert symptomatic infection for 3.9% of students compared to masking only unvaccinated students and teachers. At 85% VE and above, there was little difference in school-attributable transmission.

High Schools:

High schools generally include children 14-17 years old, thus the children are eligible for vaccination in this settings. Key findings on high schools from the predictive models are listed below:

- The baseline scenario (Delta R_0= 4.0) of no NPIs and assuming 40% of middle school children were vaccinated, estimated more than 75% of susceptible students will get infected within three months (26).
- In high schools the addition of masks dropped the proportion infected to 24% and testing further reduces infections to 13% (26).
- With greater transmissibility, Delta R_0=5.0, 88% of susceptible students can be infected without public health measures and with masking this would be reduced to 41% (26).

- With a 70% vaccination coverage without additional NPIs, there will be 4.4% excess symptomatic cases in elementary schools across a 128-day semester, compared to 7.2% with 60% vaccination coverage and 10% with 50% vaccination coverage (24).
  - With universal mask use, community and school vaccination coverage of 70%, the excess symptomatic infection attributable to school transmission is 0.4% in high schools.
  - At 70% coverage without additional NPIs, an excess of 4.0 (89% HPDI: 0, 7.1) symptomatic cases per 100 students is estimated across the 128-day semester, and at 95% vaccination coverage an excess of 0.2 (89% HPDI: -0.2, 0.6) cases per 100 students was estimated. High school students could achieve a

transmission tolerance of fewer than 10 excess cases per 1,000 population without NPIs if vaccination coverage is >90% (24).

- Given 45% VE, masking all high school students would avert symptomatic infection for an additional 6.1% of students compared to masking only unvaccinated students and teachers. At 85% VE and above, there was little difference in school-attributable transmission (24).

School absences in elementary, middle and high schools:

- Two predictive models reported that PHMs (e.g., masking and testing) reduced the number of COVID-19 absent days in elementary and middle school students (24, 26).
  - One study estimated 210, 510, 400 absent days for the school without any intervention and with masking and testing, absent days were lower at 140, 120, 76 days for elementary, middle and high school, respectively (26).
  - Another study reported that with weekly screening, there was an average of 0.6 quarantine/isolation days per elementary school student per month at 10 community notifications/100k/day and 2.6 quarantine/isolation days per elementary school student per month at 50 community notifications/100k/day (24).
  - In middle school students, quarantine of only unvaccinated students offsets the higher transmission, resulting in slightly fewer isolation or quarantine days per student than in elementary schools. A "test to stay" strategy resulted in far fewer days spent in isolation or quarantine, averaging <0.2 days per student per month, even at the highest modeled rates of community transmission and paired with maximal case detection through weekly screening (24).

Comparison of impact of transmission in schools of Delta compared to Alpha:

- One predictive model ran scenarios for Alpha (R_0=2.5) and reported that school attributable excess transmission would be substantially lower if Alpha remained the dominant variant (24).
  - At 70% community vaccination coverage and with universal masking, school attributable excess transmission would be nearly ten times lower for Alpha than Delta. This scenario estimates fewer than 25% probability of an in-school transmission per month (24).
  - Comparisons of the risk to the student population:
    - Estimated at 1 excess case per high school with Alpha compared to an excess of 4 cases with Delta.
    - In middle schools, it is estimated that there was 4 excess cases per school with Alpha compared to 13 cases with Delta.
    - In elementary schools, there was an excess of 1-5 cases per school with Alpha compared to 8 excess cases with Delta.
    - If the vaccination coverage exceeded 75%, high schools could achieve <1 excess cases in 1,000 students) without any additional NPIs with Alpha.

EVIDENCE TABLE

Table 1: Evidence on the virulence, transmission and impact of Delta in Children (n=7)

STUDY	METHODS	KEY OUTCOMES
Surveillance Data analysis (n=3)		
Riley (2021) (22) *Preprint* Surveillance data analysis UK Jun-Jul 2021	REal-time Assessment of Community Transmission-1 (REACT-1) study conducted throat and nose swabs from a representative sample of people in England aged 5 years and older. Test positivity is calculated. Round 13 commenced on 24 June 2021 and swabs were collected up to and including 5 July 2021 (round 13 interim). The results from round 13 interim and complete results for round 12, in which swabs were collected from 20 May to 7 June 2021, were compared to measure the rate of change of the epidemic in England and identifying key drivers of that change (growth or decline).	UK surveillance data reported Delta infections by age group between round 12 (May 20-Jun 7) and 13 (Jun 24-Jul 5) when the proportion of Delta cases rose from ~60% to ~90%. • Analysis by age revealed substantial increases in infections between round 13 and round 12 in all age groups under 75 years, especially in younger age groups. • Weighted prevalence in school-aged children 13 to 17 years increased eight-fold from round 12, with prevalence of infections (test positivity) in 13 to 17 year olds at 1.33% (95% CI 0.97%, 1.82%) in round 13 compared to 0.16% (95% CI 0.08%, 0.31%) in round 12. • Weighted prevalence in children 5 to 12 years increased three-fold, with prevalence of infections in 5 to 12 year old at 1.05% (95%CI 0.71%, 1.56%) in round 13 compared to 0.35% (95%CI 0.23%, 0.54%) in round 12. • In round 13, the prevalence of infections in adults 25 to 75 years were lower (between 0.63% and 0.13%) compared to children 5 to 12 years (1.05%) and 13 to 17 years (1.33%). Overall, prevalence in adults also decreased with increasing age groups.
Delahoy (2021) (20) Surveillance data analysis USA Mar 2020–Aug 2021	This analysis uses Coronavirus Disease 2019–Associated Hospitalization Surveillance Network (COVID-NET) data to describe COVID-19–associated hospitalizations among U.S. children and adolescents aged 0–17 years during March 1, 2020–August 14, 2021.	• During the week ending August 14, 2021, the weekly COVID-19–associated hospitalization rate among children and adolescents was five times higher (from 0.3/100,000 to 1.4/100,000) than the week ending June 26, 2021. The most apparent increase occurred among children aged 0–4 years (from 0.2/100,000 to 1.9/100,000, during the same period), representing nearly a ten times increase. • During June 20–July 31, 2021, among 68 adolescents hospitalized with COVID-19 with ascertained vaccination status, the hospitalization rate among unvaccinated

		adolescents was 0.8 per 100,000 person-weeks (95% CI = 0.6–0.9), compared with 0.1 (95% CI = 0.0–0.1) in fully vaccinated adolescents (rate ratio = 10.1; 95% CI = 3.7–27.9). • Among 3,116 hospitalized children and adolescents with COVID-19 between March 1, 2020, and June 19, 2021, 827 (26.5%) were admitted to an ICU, 190 (6.1%) required invasive mechanical ventilation, and 21 (0.7%) died. Among 164 hospitalized children and adolescents with COVID-19 during June 20–July 31, 2021, 38 (23.2%) were admitted to an ICU, 16 (9.8%) required invasive mechanical ventilation, and three (1.8%) died. The differences in the indicators of severe disease between the two periods were not statistically significant.
Siegel (2021) (21) Surveillance data analysis USA Aug 2020–Aug 2021	This analysis uses daily COVID-19 case data were obtained from CDC's case-based surveillance system and daily emergency department (ED) visits were obtained from the National Syndromic Surveillance Program Surveillance to analyze COVID-19–associated hospitalizations among U.S. children and adolescents aged 0–17 years between August 2020–August 2021.	• Incidence in August 2021 among children and adolescents aged 0–4, 5–11, and 12–17 years reached 16.2, 28.5, and 32.7 per 100,000 persons compared to 1.7, 1.9 and 2.9 in June 2021, respectively. • The percent of COVID-19 emergency department visits in August 2021 in the quartile of states with the lowest vaccination coverage was 3.4 times that in the quartile of states with the highest vaccination coverage. • The rate (per 100,000 persons) of COVID-19 admissions in August 2021 in the quartile of states with the lowest vaccination coverage was 3.7 times that in the quartile of states with the highest vaccination coverage. • The percentage of hospitalizations resulting in an ICU admission ranged from 10% to 25% during August 2020–June 2021 compared to 20% and 18% in July and August 2021, respectively. • The percentage of hospitalizations resulting in invasive mechanical ventilation ranged from 0% to 3% and was highest in October 2020 compared to 2% and <1 % in July and August 2021, respectively.

		• Among 63 patients aged 0–17 years admitted to an ICU in July and August 2021, 17 (27%) were aged 0–4 years, 17 (27%) were 5–11 years, and 29 (46%) were 12–17 years.
Outbreak Investigation on Transmission (n=1)		
Lam-Hine (2021) (23) Outbreak investigation USA May- Jun 2021	This is an outbreak investigation of 27 Delta variant cases that occurred in Marin County, California following an exposure to an unvaccinated teacher in an elementary school during May-June 2021. Approximately 72% of eligible individuals in the city where the school was located were vaccinated. Whole genome sequencing (WGS) of all 18 available specimens identified the Delta variant. The specimen from the teacher was unavailable for WGS, and it not known whether the teacher was infected with Delta	• At an elementary school in California, an unvaccinated teacher (who occasionally removed their mask in the classroom) became infected with Delta and worked for two days after symptom onset. The attack rate in the classroom was 50%, 80% (8/10) for students in the two rows seated closest to the teacher's desk and was 28% (4/14) in the three back rows (Fisher's exact test; p = 0.036). The students' adherence to mask wearing was considered high and desks were 6ft apart. • During May 24–June 1, six of 18 students in a separate grade at the school also became infected. They may be unrelated. • Eight additional cases were also identified in parents and siblings of students in these two grades. Among these additional cases, three were in persons fully vaccinated.
Predictive Models on Transmission and Impact of PHMs (n=3)		
Zhang (2021) (26) *Preprint* Predictive model USA Aug 2021*	Model: Susceptible-Infected-Recovered (SIR) model. Outcomes: • Number of new infections during 1 semester (107 days) among K-12 population under different assumptions (e.g. mask usage, routine testing, and levels of incoming protection). • School absences Assumptions: • Baseline R_0 of 4 to account for the increased infectivity of Delta. • Assumes 0.5% of incoming students are infected and one case enters the school per week (e.g., infected outside school).	Baseline scenario: • With a baseline R_0 of 4.0 and no testing or masking more than 75% of susceptible students get infected within three months in all settings. Elementary school: • With masks (R_0=2.0), the proportion infected drops to 50%. Testing half the masked population ("testing") further drops infections to 22%. • In the sensitivity analysis, a baseline R_0 of 5.0 results in 95% infected without mitigation and 70% with masking. Middle school: • With masks (R_0=2.0), the proportion infected drops to 35%. Testing half the masked population ("testing") further drops infections to 16%.

	• Considers three levels of incoming protection through infection or vaccine-acquired immunity of low= 30% for elementary schools, mid= 40% for middle schools, or high= 50% for high schools. Levels of protection were based on CDC reports that 30% of students in the middle school age-range are vaccinated, 40% of students in the high-school age-range are vaccinated, and prior infection among all primary-school children is approximately 10%. • Universal mask usage decreases infectivity by 50%. • A scenario analysis also considered an R_0 of 5.0. • Weekly testing may occur among 50% of the student population, where positive tests prompt quarantine until recovery, with compliance contingent on symptom status.	• In the sensitivity analysis, a baseline R_0 of 5.0 results in 93% infected without mitigation and 57% with masking. High school: • With masks (R_0=2.0), the proportion infected drops to 24%. Testing half the masked population ("testing") further drops infections 13%. • In the sensitivity analysis, a baseline R_0 of 5.0 results in 88% infected without mitigation and 41% with masking. School absence: • Assuming a conservative total of 10 days of school absence per 5 new infections, there will be an estimated 210, 510, 400 absent days from school without any intervention for the low, mid and high situations and with masking and testing days absent were lower at 140, 120, 76 respectively.
Bilinski (2021) (25) *Preprint* Predictive model USA Aug 2021*	Model: ▪ Validated agent-based network model. The model incorporates interactions between individuals in school, household, and out-of-school childcare settings, as well as infections introduced exogenously through other community interactions. Scenario without testing: ▪ The study modeled three scenarios without school-based testing: 1. Five-day in-person attendance (the base case, and also the schedule assumed for all testing scenarios), 2. A hybrid model in which half of each class attends school on Monday and Tuesday and the other half on Thursday and Friday (a strategy used in 2020-21) and	Infections by varying public health measures: Elementary: • Compared to fully remote instruction, 5-day in-person attendance with no in-school testing was associated with a 40% projected increase in COVID incidence among students (mean 1.9 additional infections per school per month) at a community notification rate of 10/100k/day and a 38% increase (8 additional infections per school per month) at 50 community notifications/100k/day. • If students with known exposures were allowed to stay in school with daily testing (the "test to stay" strategy), slightly more transmission occurred (e.g., a 43% increase over the remote-instruction baseline, at 10 community notifications/100k/day). • In a community with 10 notifications/100k/day, weekly screening averted 57% of excess incidence relative to

	3. Fully remote learning (a proxy for anticipated infection risk unrelated to in-person education). Scenario with diagnostic testing: ▪ The study includes ○ diagnostic testing ("test to stay" policies that take the place of isolation for symptomatic students or quarantine for exposed classrooms); ○ screening (routinely testing asymptomatic students and teachers to identify infections and contain transmission); ○ surveillance (weekly testing a random sample of 10-20% of the school population from unvaccinated individuals to signaling undetected transmission and trigger additional investigation or interventions). Outcomes: • Projected 30-day cumulative incidence of SARS-CoV-2 infection • Proportion of cases detected • Proportion of planned and unplanned days out of school Assumptions: • Delta variant is dominant and is approximately twice as transmissible as the original variant. • Elementary school students are half as susceptible and half as infectious as adults and that middle school students have similar susceptibility and infectiousness as adults. • Middle students were more susceptible and more infectious, in-person attendance had greater potential to increase transmission, although 50% student vaccination kept it partially in check	remote learning in both the elementary and the middle school. • With "test to stay" instead of quarantine and 10 community notifications/100k/day, weekly screening prevented 46% rather than 57% of excess transmission, and weekly 20% surveillance prevented 17% rather than 25%. Middle school: • Compared to remote instruction, 5-day middle school attendance (with quarantine of known close contacts) increased incidence by 72% (3 added infections per school per month) at a community notification rate of 10/100k/day and by 60% (10 added infections per school per month) at 50 community notifications/100k/day. • In a community with 10 notifications/100k/day, universal weekly screening averted 57% of excess incidence relative to remote learning. In a community with 10 notifications/100k/day, weekly 20% surveillance averted 34% of the excess transmission associated with school attendance. • The "test to stay" strategy increased transmission slightly compared to the remote-only baseline (e.g. a 72% increase with quarantine to an 82% increase with test-to-stay at 10 community notifications/100k/day). • A "test to stay" strategy after case detection slightly diminished the transmission benefits of screening or surveillance. Elementary and Middle school: • A hybrid schedule of in person learning where there is ≥60% remote instruction, could prevent much of the excess transmission by reducing the number and duration of contacts for both elementary and middle school. School absences: Elementary school: • With weekly screening, there was an average of 0.6 quarantine/isolation days per student per month at 10 community

	• Schools adopted high mitigation (i.e., masking, ventilation, and distancing) • 90% of teachers and staff and 50% of middle school students were vaccinated with an 80% efficacious vaccine.	notifications/100k/day and 2.6 quarantine/isolation days per student per month at 50 community notifications/100k/day. Middle school: • Quarantine of only unvaccinated students more than offsets the higher transmission, resulting in slightly fewer isolation or quarantine days per student than in the elementary school. • A "test to stay" strategy resulted <0.2 isolation and quarantine days per student per month, even at the highest modeled rates of community transmission and paired with maximal case detection through weekly screening.
Head (2021) (24) *Preprint* Predictive model USA Aug 2021	Model: A discrete-time, age-structured, individual-based stochastic model was used to simulate transmission of Delta among a synthetic population, representative of Bay Area cities. Outcomes: • Increase in total number of symptomatic infections in students and teachers/staff resulting over a 128-day semester in a 380 person elementary school, 420 person middle school, 620 person high school from in-school instruction compared to remote instruction • Scenarios evaluate various non-pharmaceutical interventions (NPIs) (mask use, cohorts, and weekly testing of students/teachers) implemented in schools, various community-wide vaccination coverages (50%, 60%, 70%), and student (≥ 12 years) and teacher/staff vaccination coverages (50% - 95%). • Quantitatively assessed the added benefit of universal masking over masking among unvaccinated	Elementary schools: Infections with no additional NPIs: • 70% community vaccination coverage and without additional NPIs there are 25 (6.6%) excess symptomatic cases per 380-person elementary school across a 128-day semester, with 60% vaccination coverage there are 57 (15%) cases and with a 50% vaccination coverage there are 69 (18.2%) cases. Infections with varying NPIs: • In scenarios where the vaccine coverage was lower e.g., 50% in general population or elementary schools where children <12 years were not vaccinated, NPIs had the largest impact on reducing excess symptomatic infections attributable to school transmission. • Under the Bay Area reopening plan (universal mask use, community and school vaccination coverage of 70%), the estimated excess symptomatic infection attributable to school transmission was 8 cases (2%) in elementary schools. • As simulated community vaccination coverage of the eligible population (12+ years) increased from 50% to 60% to 70%, the percent of elementary school children with a school-attributable symptomatic illness fell

	students and teachers, across varying levels of vaccine effectiveness (45%, 65%, 85%), and compared results between Delta and Alpha variant circulation. • Highest estimated hospitalization rates among students of all grade levels when no NPIs were modelled. • The second primary outcome was the minimum set of interventions to keep excess infections under a predetermined risk tolerance (<5 to <50 cases/1000 school population). Assumptions/Parameters: • Community contact rates were ascertained from a vaccinated household survey of Bay Area families with children, February to April, 2021. • R_0 as 4.6, based on an average of R_0 for the Alpha (R_0 = 2.5 and proportion = 16%) and Delta variant (R_0 = 5.0 and proportion = 84%). • Universal masking, effectiveness for reducing both inward and outward transmission is 15% for elementary school students, 25% for middle school students, 35% for high school students, and 50% for teachers and staff. • The scenario of masking plus weekly testing of all students and teachers, in which we assumed a test with 85% sensitivity was administered every 7 days with 1 day to get results back. • Children under 10 years of age are considered equally as susceptible to SARS-CoV-2 as older children and adults when compared with half as susceptible. • Higher probability of hospitalization among individuals aged 10 to 20 years compared to individuals under 10 years.	from 8.7% to 7.8% to 6.6%, representing a 24% decline in school-attributable transmission. • Increasing the vaccination coverage of the eligible teachers from 70% to 95% reduced the estimated excess rate of infection from 6.6 (89%HPDI: 0, 11.5) to 3.9 (89%HPDI: -0.2, 9.2) symptomatic cases per 100 elementary students across the four-month semester, representing a reduction of 41%. • Where community vaccine coverage was 50% and no additional NPIs were taken, an excess incidence of 8.7 cases (89% HPDI: 2.9, 13.2) per 100 elementary students was estimated. With masks, an excess incidence of 3.1 cases (89% HPDI: 0, 5.9) per 100 elementary school students was estimated. • At 70% vaccine coverage, NPIs of masking and cohorts reduced the excess student cases from 57 to 7 in a 380 student school. • Achieving lower risk tolerances, such as <5 excess infections per 1,000 students or teachers, required a cohort approach in elementary and middle school populations. The strictest combination of interventions tested (masks + cohorts, 70% vaccine coverage), would result in excess infection among 1.7% (89% HPDI: -0.2, 4.2) of elementary students assuming equal susceptibility to older children and 0.4% (89% HPDI: -0.2, 1) of elementary students assuming they are half as susceptible. Hospitalizations: • The highest hospitalization rate simulated in elementary schools was 1.3 hospitalizations per one million students, under 50% vaccination coverage and no additional precautions, assuming elementary children are equally susceptible to infection as older children and adults. Middle School Infections with no additional NPIs:

	• The Bay area reopening scenario was70% community vaccination coverage with vaccine at 85% effectiveness and universal masking.	• A 70% community vaccination coverage and without additional NPIs, there are 37 (8.8%) excess symptomatic cases per 420-person middle school across a 128-day semester, with 60% vaccination coverage there are 45 (10.7%) cases and with a 50% vaccination coverage there are 53 (12.6%) cases. Infections with varying NPIs: • Under the Bay Area reopening plan (universal mask use, community and school vaccination coverage of 70%), the estimated excess symptomatic infection attributable to school reopening among 3.0% of middle school students (13 cases per school). • Where community vaccine coverage was 50% and no additional NPIs were taken, an excess incidence of 12.5 cases (89%HPDI: 8.8, 16.6) per 100 elementary students was estimated. With masks, an excess incidence of 5.6 cases (89%HPDI: 0, 10.4) per 100 middle school students was estimated. • Achieving lower risk tolerances, such as <5 excess infections per 1,000 students or teachers, required a cohort approach in middle school populations. • Given 45% vaccine effectiveness (VE), masking all middle school students would avert symptomatic infection for 3.9% of students compared to masking only unvaccinated students and teachers. At 85% VE and above, there was little difference in school-attributable transmission between masking unvaccinated persons versus masking all persons. Hospitalizations: • The maximum hospitalization rate simulated was 4.8 hospitalizations per one million middle school students over the 128-day semester, under 50% vaccination coverage and no additional precautions. Simulated interventions combining masks and cohorts yielded hospitalization rates for the four-month semester under 3 per 10 million

		students, regardless of assumptions about susceptibility. High school Infections with no additional NPIs: • With a 70% community vaccination coverage and without additional NPIs, there are 27 (4.4%) excess symptomatic cases per 620-person high school across a 128-day semester, with 60% vaccination coverage there are 45 (7.3%) cases and with a 50% vaccination coverage there are 65 (10.5%) cases. Infections with varying NPIs: • Under the Bay Area reopening plan (universal mask use, community and school vaccination coverage of 70%), the estimated excess symptomatic infection attributable to school reopening among 0.4% of high school students (3 cases per school). • Where community vaccine coverage was 50% and no additional NPIs were taken, an excess incidence of 9.6 per 100 students in high schools (89% HPDI: 6.5, 13.2) was estimated. With masks an excess incidence of 2.0 (89% HPDI: -0.2, 4.4) cases per 100 high school students was estimated. • Among high school students and teachers/staff, estimated a median of zero excess infections when within-school vaccine coverages exceeded 90%. • At 70% coverage of the eligible school population, an excess of 4.0 (89% HPDI: 0, 7.1) symptomatic cases per 100 students across the 128-day semester, and at 95% coverage an excess of 0.2 (89% HPDI: -0.2, 0.6) cases per 100 students was estimated. • Masking all high school students would avert symptomatic infection for 6.1% of students compared to masking only unvaccinated students and teachers. At 85% VE and above, there was little difference in school-attributable transmission between masking

		unvaccinated persons versus masking all persons. Impact of transmission of Delta versus Alpha: • If the Alpha variant had remained the dominant variant (R0 = 2.5) with the Bay area reopening plan, school attributable excess transmission would be nearly ten times lower (<1 infection per school) than under circulation of the Delta variant. • Under a 70% community vaccination coverage and no additional NPIs the most lenient risk tolerance of <50 additional cases per 1,000 students was achievable. Under this scenario, risk to the student population was estimated at 1 excess case per high school with Alpha compared to an excess of 4 cases with Delta. In middle schools, it is estimated that there is a, 4 excess cases per school with Alpha compared to 13 cases with Delta. In elementary schools, there was an excess of 1-5 cases per school with Alpha compared to 8 excess cases with Delta. If the vaccination coverage exceeded 75%, high schools could achieve <1 excess cases in 1,000 student) without any additional NPIs with Alpha. Hospitalizations • If the Alpha variant had remained dominant, hospitalizations among students do not occur.

*= publication date is used to estimate when the study was conducted. 89%HPDI= 89th percentile highest probability density interval (HPDI), considered more stable than 95%.

Methods:

A daily scan of the literature (published and pre-published) is conducted by the Emerging Science Group, PHAC. The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley. The daily summary and full scan results are maintained in a refworks database and an excel list that can be searched. One of the foci is to identify studies as variants of concern or under investigation. Studies identified under this foci were further characterized in our VOC/VOI database. Targeted keyword searching was conducted within these repositories to identify relevant citations on COVID-19 and SARS-CoV-2.

Search terms used included:

SCHOOL TERMS: (Delta or B.1.617) AND school AND/OR (transmission or severity)

CHILDREN TERMS: (Delta or B.1.617) AND (children or adolescent or youth or pediatric) AND/OR (transmission or severity)

This review contains research published up to September 14, 2021.

Grey Literature

A grey literature search was conducted to compliment the database search. The grey literature search focused on targeted governmental agencies. A detailed list of websites searched is available upon request. The grey literature search was conducted September 7-10. 2021.

Each potentially relevant reference was examined to confirm it had relevant data and relevant data was extracted into the review.

Peer-review

This document underwent peer-review by a subject matter expert, and editorial and science to policy review by the Office of the Chief Science Officer.

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