Evidence on the virulence, transmission and impact of B.1.617.2 (Delta) among children: update 1

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Introduction

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

The SARS-CoV-2 **variant of concern** (VOC) B.1.617.2 known as Delta by the World Health Organization (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[123].

Delta has been reported to have higher transmissibility than the Alpha VOC and original variant in the general population[456789]. Delta has outcompeted other variants including Alpha in several countries and is the dominant variant at >99% of sequenced VOC cases in Canada since September 5, 2021[101112]. 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[13141516]. A risk profile of the evidence on Delta is available upon request at ocsoevidence-bcscdonneesprobantes@phac-aspc.gc.ca. Vaccination has been shown to protect against serious outcomes of COVID-19 and Canada has one of the highest vaccination coverage rates and currently 81% (October 8, 2021) of the population ≥12 years of age has received two doses of vaccine[1017]. However, COVID-19 vaccines are not yet authorized by Health Canada for those <12 years old.

As of October 2021, children are now more than a month into their school year and Canada is in the fourth wave of the pandemic[1819]. Delta is the dominant variant across Canada and the proportion of Delta has remained around >99% of VOC cases with sequencing data reported across the country. Recent models predict that COVID-19 case counts have slowed and in many parts of Canada they appear to be decreasing[19]. Evidence is 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 0-18 years old including the impact of public health interventions on the spread of Delta among children. This report presents evidence up to October 8, 2021.

What's new

This update identified 16 new studies since September 15, 2021, on the virulence, transmission and impact of Delta among children. This included 1 cluster-randomized control trial, 1 surveillance data analysis, 1 ecologic study, 6 outbreak investigations, and 7 predictive models. The new studies did not include virulence data but rather there were:

- Additional outbreak data on transmission among children and lack of transmission when public health measures (PHMs) (e.g., masking, cohorting, screening and quarantine) were implemented.
- One ecological study examined the impact of when mask use was mandated or not in schools.
- Predictive models that explored the impact of mask mandates as well as other PHMs in schools and/or the community on COVID-19 cases attributable to schools being open both within school populations and in the community.
- Predictive models that examined the impact of extending vaccination to younger children on number of predicted cases, hospitalizations and deaths in a community.

Key points

This review includes 23 studies pertaining to the virulence, transmission and impact of Delta among children with the majority focused on the impact of public health measures (Table 1, Table 2, and Table 3). Of these, one UK cluster-randomized control trial (RCT) in secondary schools, April–June 2021, examined the impact of PHMs, four general population surveillance studies (three US and one UK) focused on Delta cases in children between June and August 2021 when children were not in school. One US ecological study evaluated the impact of masks August–September 2021, and seven outbreak investigations (six US, one France) reported on transmission events and the prevention of transmission events May-August 2021. Six predictive models (four US, one Austria, and one Germany) evaluated Delta transmission in schools or the impact of opening schools on community transmission and the impact of public health measures and four predictive models (US, Australia, UK, and China) reported on the impact of vaccinating children. The level of evidence on all parts of this review is considered low as most outcomes are reported in one or two studies, thus we caution the readers that this review reports preliminary evidence and the conclusions, and strength of them, may change as more studies and evidence become available.

Virulence

Highlights from the current literature include:

- Current evidence suggests that Delta is not more virulent in children than the original variant or Alpha. Two surveillance studies in the US 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][21][22].

Transmissibility

Highlights from the current literature include:

- Without vaccinations and other public health measures such as physical distancing, cohorting and masking, Delta has high transmissibility in children.
- There were high attack rates across seven outbreak investigations when PHMs were not implemented: an attack rate of 50% in an elementary classroom[23]; the odds of a school outbreak was 3.5 times more likely in schools with no mask requirement[24]; an attack rate of 20% in a gymnastics facility[25]; camp outbreaks with an attack rate of 26% with no PHMs[26], 0.08% cases in a camp with multiple PHMs[27]; and a 31-fold increase in infections in camps during Delta circulation compared to the original variant[28]. In a household outbreak, six siblings were infected by their 13 year old sibling (75% attack rate)[29].
- High viral load (identified by low cycle threshold (Ct <20) value, where Ct is a proxy for viral load) in 18.3% of children, both symptomatic (30%) and asymptomatic (70%) was reported at community testing sites in California, where 20% of vaccinated adults also had Ct<20 at the time of testing[30].
- The RCT study and three predictive models showed that infection rate of cases in schools closely follow those case rates of the community and that transmission in schools will not drive Delta transmission in the community[31][32][33][34]. A UK predictive model suggests with high vaccination coverage in adults that the peak infections in fall 2021 may be identified in schools before other settings[35].
- Delta was estimated to result in nearly 10 times the cases attributable to being in school compared to Alpha in a model when keeping all other parameters constant[34].

Impact of public health measures

Vaccination

Highlights from the current literature include:

- In the US, vaccinated adolescents (12-17 years old) 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 and US states with the lowest vaccination coverage had higher adolescent emergency department visits (3.4x) and hospitalizations (3.7x) compared to US states with the highest vaccination coverage[20].
- Several models from the UK, US, Australia and China look at the increases in infections, hospitalizations and deaths after school re-opening in fall 2021 and the potential impact of vaccination coverage in different child age groups (16+, 12+ and 5+, 3+ and all ages). Predictions show increasing reductions (10-90%) with increasing vaccine eligibility in more pediatric age groups[35363738].
- Both in the community and in schools, most models showed that very high vaccination coverage of the population is needed (>80%) before other PHMs (e.g., mask policies, quarantine policies, social distancing, cohorting in schools) added no additional benefit[34353738].

Impact of public health measures on school transmission

Quarantine policies

Highlights from the current literature include:

- An RCT in England secondary schools and colleges found no difference in infections or COVID-19 related days absent between 10 day self isolation for contacts vs. a rapid antigen test for 7 days where those who test negative remain in school[31]. A model predicted the test to stay protocol would result in slightly more cases than quarantine[32].
- Whole class quarantine for 10 days following discovery of a case had the same impact on total number of cases and deaths (~50%) in the community attributable to school opening as a high stringency PHM scenario with masking, cohorting and increased ventilation in schools in a UK modelling study[35].

Masking in schools

Highlights from the current literature include:

- An ecologic study reported that pediatric case rates in counties with school mask requirements experienced 18.53 cases per 100,000 per day lower than counties without school mask requirements[39].
- A US predictive model estimated the peak hospitalization level could exceed January 2021 (when Alpha was dominant) if kindergarten to grade 12 (K-12) were opened without mask policies[40]. If schools had hybrid learning or there was high mask-efficacy, there were fewer excess deaths (7%) and a 71% reduction in peak excess hospitalizations

in the general population attributable to school opening. Overall the number of excess cases were reduced by 23-35% with masks and by an additional 11-13% with hybrid learning[40].

Combinations of public health measures in schools

Highlights from the current literature include:

- Five predictive models examined the potential reduction in Delta cases attributable to in-school transmission in elementary schools, middle schools, and high schools that implemented different combinations of PHMs (masking, testing, cohorting, and improved room ventilation) with different levels of vaccination coverage. In different models vaccination coverage ranged from 30-85% in the eligible population (e.g., children ≥12 years, teachers and community). Baseline scenarios with no public health measures estimate a high level of Delta infections among susceptible children in all school environments (e.g., 75%), and excess infections, hospitalizations and deaths in the community[3340]. The trade-offs between different risk reduction strategies are highlighted below:

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

Highlights from the current literature include:

- 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[33]. 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[33].
- Higher vaccination coverage within the school population was associated with fewer cases and less additional impact from PHMs in the school population. 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[34].
- With universal mask use and school vaccination coverage of 70% of the eligible population, the excess symptomatic infections attributable to school reopening was far less in high schools with only 0.4% excess infections compared to elementary and middle schools with 2.0%, and 3.0% excess infections within the school population, respectively[34].
- Using remote learning as the baseline scenario, universal screening (testing twice a week) was estimated to have averted 57% of excess cases compared to no additional PHMs in both elementary and middle schools[32]. Active testing was shown to be a necessary component of an Austrian model to get $R_o \leq 1$ in all school types[41].

- Higher vaccination coverage among eligible individuals in school (e.g., students ≥12 years, teachers and staff) was associated with a decrease in school-attributable transmission in all schools[34]. In elementary and middle schools, a hybrid schedule of in-person learning where ≥60% of the time students receive remote instruction and are not in school, could prevent much of the excess transmission by reducing the number and duration of contacts[32].
- The strictest combination of interventions tested (masks, cohorting and 70% vaccination coverage), would result in the largest reduction in excess infections. For example, strict PHMs would result in excess infections among 1.7% of elementary students compared to 6.6% with 70% vaccination coverage only[34]. Lower risk tolerances of <5 excess infections per 1,000 students or teachers could be achieved in middle schools with cohorting and a 70% vaccination coverage[34].

Overview of the evidence

Twenty-three studies pertaining to the virulence, transmission and impact of Delta in children were identified and included in this review. Virulence studies included observational studies of surveillance data from mainly large national databases. Studies reporting transmissibility were from outbreak investigations and predictive modelling studies. Studies reporting PHMs including the impact of vaccinations were mainly predictive models with some evidence obtained from a cluster-RCT and an ecologic study.

A formal risk of bias assessment was not conducted. One RCT was identified, although generally considered the 'gold-standard', they are not always feasible and the evidence may not be representative of real-world settings, thus limiting the generalizability of the findings.

The observational studies included surveillance and ecological studies obtained from large national databases with 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 or infants 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. Real-world studies that assess the impact of different PHMs, including vaccination coverage in school and community settings on transmission, virulence, and impact of the Delta variant in children, are also needed.

Overall, the level and quality of evidence on the Delta variant and children is low and there are knowledge gaps in the existing literature base. As more studies and evidence emerge, the conclusions and/or strength of the findings of this review is likely to change.

Virulence of Delta among children

Two surveillance studies in the US 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[20][21][22] Table 1.

- 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 US[20].
- The US papers describe increased incidence rates and hospitalization rates in children given the current epidemiological situation of increasing COVID-19 cases.
    - Incidence rates in the US 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]. In August 2021 approximately 50% of adolescents (12-17 years) in the US were vaccinated, whereas the UK has just approved 1 dose for 12-15 year olds in October 2021.
    - Hospitalization rates in the US 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].

Transmission of Delta among children

Seven outbreak investigations Table 2, three surveillance studies Table 1, and three predictive models Table 3 provide some evidence for Delta's increased transmissibility in children. However, cases in children have been shown to be linearly correlated with community case rates, suggesting increased transmissibility across all age groups for Delta, however no age specific

differences have been reported[313233]. 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 in the community[34]. With high vaccination coverage (80%) in adults, it is possible that surveillance data moving forward may detect peaks of community infection first in schools and then other settings due to the large proportion of the school population (i.e., children <12 years of age) remaining ineligible for vaccination at the present time[35]. Compared to Alpha the increased transmissibility of Delta is estimated to result in 10 times the school attributable excess cases[34].

High viral load and incidence of asymptomatic cases in children was reported in a surveillance study where 18.3% of children under 12 years of age had Ct (cycle threshold value used as a proxy for viral load) values of <20 (suggesting high viral load), and 70% of these children were asymptomatic at the time of testing[30]. There was no comparator group to evaluate whether there was a change from previous variants in circulation.

Delta outbreak investigations in different settings

There were two studies that reported high transmissibility of Delta in school settings. The first was an outbreak investigation in an elementary school in the US May 2021 that 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]. The second is an analysis of all school associated COVID-19 outbreaks during the first 3-6 weeks of school in the US for K-12 schools between July-August 2021 that reported outbreak risk was 3.5 times higher in schools with no mask requirement than in those with a mask requirement implemented at the time school started[24].

There were three camp related outbreak studies, two of which reported on multiple camps during summer 2021. One study reported on the successful prevention of outbreaks at nine overnight camps due to implemented PHMs which included testing (before and during camp), masking, and physical distancing, as well as vaccination of staff and campers aged 12+. Six cases in campers ages 8-14 years and three in staff were reported among 7,173 persons attending these camps and no secondary transmission was identified during camp[27]. In an evaluation of outbreaks at summer camps in Louisiana when there was a thirty-one-fold increase in confirmed camp-associated cases statewide (June-July 2021 vs. June–July 2020)[28], the mean outbreak size was 11.5 cases (range: 2–59 cases) among the 28 camps with outbreaks and PHM strategies ranged from none to some preventative measures (e.g., masking indoors, vaccination of staff)[28]. A single outbreak at a 5-day overnight church camp had an attack rate of 26% where there was

no requirement for proof of vaccination or masking and none of the campers were symptomatic at the beginning of the camp[26].

Another outbreak occurred in a gymnastics facility resulting in 47 linked-cases and an overall attack rate of 20% in the gymnastics facility (staff and gymnasts) and a household attack rate of 20%[25]. Within a household cluster the index case (a 13 year old) spread Delta to six unvaccinated siblings (100%) and not to their vaccinated parents[29].

Taken together the outbreak investigations show that Delta can result in a high attack rate, particularly when PHMs are not employed.

Impact of public health measures

One UK cluster-randomized controlled trial, one US surveillance study, one ecologic study and seven predictive models parameterized to mimic different areas in the US, Austria, and Germany are included in this section. The surveillance study and one predictive model evaluated hospitalizations and deaths attributable to transmission in schools. Six predictive models, one RCT, and an ecologic study examined transmission in school settings, and one model examined transmission while children were on summer vacation. Two modelling studies and one RCT reported school absences as an outcome. One predictive model compared the impact of transmission of Delta versus Alpha in a school setting.

Impact of vaccinating children

There are few data points on the protective effect of extending vaccination to children and youths against Delta, one study analysed surveillance data from the US recently highlighted that vaccinated adolescents had a 10.1 times lower risk of hospitalization compared to unvaccinated adolescents from June 20-July 31, 2021[20]. In the same analysis, 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]. Suggesting both direct and indirect protection from vaccine coverage in the whole population. There was no further analysis of potential differences in vaccine protection by variants that caused infection.

Four predictive models (one each in the US, UK, Australia, and China) that were parameterized to assess different levels of vaccination coverage in children are included in this section, Table 3 Overall, the predictive models indicate that extending vaccination coverage to younger children reduces pediatric and general population cases, hospitalizations and deaths. Most models look at different scenarios of vaccine coverage and other PHMs (e.g., masking, social distancing and

vary the stringency of other PHMs) to explore how well different combinations control the number of COVID-19 cases.

In the US, with 85% vaccination coverage of 12+ year olds, school opening with no other PHMs is estimated to lead to a 2-fold increase in pediatric hospitalizations[38]. Reducing contacts in schools by 25% or 50% through masking, ventilation and distancing is expected to decrease the overall median cumulative hospitalizations in 0-19 year olds by 8% and 23%, respectively[38]. Extending vaccination eligibility to children aged 5-11 years regardless of level of physical contacts, reduces hospitalizations in 0-19 year olds by ~50% compared to no vaccination[38]. Early vaccination in 5-11 year olds and reaching a 90% overall vaccination coverage in 12+ year olds, 60% of remaining hospitalizations will be averted and the need of extra mitigation measures may be avoided[38]. Delaying COVID-19 vaccination among children by 3 months, vaccination occurs January 2022 instead of October 2021, will void most of the benefits measured over the school year[38].

- A UK model estimated a 5-fold increase in cases with school reopening despite 80% vaccination coverage among adults. Extending vaccination coverage (80%) to 16+ years/ 12+ years / all ages reduces the total number of infections by 10%/ 40% / >90% and deaths by ~ 1000 / 5000 / nullifies impact of opening schools[35].
- An Australian model which assessed the impact of extending vaccination coverage to 5+ year olds from 15+ year olds report using a Pfizer or Mixed vaccination program leads to fewer infections when R_{eff} is high (R_{eff} 5-7)[36]. Vaccine coverage >85% including those 5+ years is needed to achieve herd immunity for a R_{eff} of 5 (Delta scenario), where a R_{eff} of 7 (more transmissible than Delta scenario) will not achieve herd immunity regardless of the program[36].
- A modelling study from China reported high attack rates given low efficacy of vaccines (54% VE, vaccine not stated) despite good vaccine coverage in individuals 3+ years[37]. Extending vaccinations to 3-17 year olds achieved the highest reduction in infections (55%-57%)[37]. High vaccine effectiveness (VE) and high coverage (e.g., 90% VE and >93% coverage) or moderate to strict PHMs with lower vaccine effectiveness and coverage are needed to reach vaccine-induced herd immunity[37]. A 90% reduction in infections is possible with a "US-like" scenario (VE of 79% and natural immunity of 22%) by vaccinating individuals 3+ years[37].

Lifting community public health measures and vaccination coverage

A German modelling study assessed the impact of COVID-19 by age group (including children) and showed that lifting PHMs (e.g., masking) too early with insufficient vaccination coverage results in high community case incidence and the highest incidences are in the unvaccinated 0-14 year old age groups[42]. The longer PHMs are maintained as vaccination coverage increases,

the lower the incidence of community infections including in the unvaccinated children (0-14 years)[42].

Impact of public health measures on K-12 schools

There were few empirical studies on the impact of PHMs with Delta in circulation. One study reported schools in the US with mask requirements had 18.53 cases per 100,000 per day lower than the average change for counties without school mask requirements ($p<0.001$), which was significant in an ecological analysis after controlling for covariates ($p<0.001$)[39].

The remaining studies were predictive models that indicate PHMs including vaccination coverage in students, teachers, staff and the community reduced the transmission of Delta among school-aged children and the burden of COVID-19 cases, hospitalizations and deaths in the community. The models identified that transmission of Delta in school contributes to the transmission of infection, but does not drive Delta transmission in the community.

As each model is parameterized a little differently and considers different PHMs, vaccination coverage and outcomes, it is difficult to directly compare across models. Each of the seven 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 4.0-6.0) compared to previous variants or VOCs. Scenarios include different levels of vaccination coverage (30-85%) and PHMs (e.g., masking, testing, quarantine policies 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 or for all K-12 schools. The summary below highlights outcomes related to the number of infections, however some models also report on school absences, hospitalizations and deaths, these are detailed in Table 3. Overall, a reduction in the number of cases was correlated with a decrease in all other outcomes.

Elementary schools

Elementary schools generally include children 4 up to 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 PHMs estimated more than 75% of susceptible students will get infected within three months[33]. The addition of masks dropped the proportion infected to 50% and testing further reduces infections to 22%[33].
- 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[32].

- In a community with 10 cases/100k/day, weekly screening averted 57% of excess incidence (cases attributable to school transmission) relative to remote learning[32].
- 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)[32]. 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%[32].

- A 70% vaccination coverage without additional PHMs 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[34].
  - With universal mask use, community and school vaccination coverage of 70%, will result in 2.0% excess symptomatic cases[34].
  - 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[34].
  - 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%[34]. This suggests that increasing vaccination coverage among elementary school teachers can reduce infection among their students[34].
  - 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[34].
- In a modelling study in Austria with 80% vaccination coverage in teachers and 60% in family members reduced the cases in different school types. For elementary schools R_o could be reduced to <1 with a combination of PHMs (room ventilation, cohorting, mask policies) or testing twice per week or a combination of both[41].

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 PHMs and with 30% of middle school children vaccinated, estimated more than 75% of susceptible students will get infected within three months[33]. The addition of masks dropped the proportion infected to 35% and testing further reduces infections to 16%[33].
- 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 cases/100k/day[32].
    - 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[32].
    - 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)[32].
    - 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[32].
- Under a 70% vaccination coverage without additional PHMs, there were 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[34].
    - 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%) and a cohort approach[34].
    - Given 45% vaccine effectiveness, 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[34].

High schools

High schools generally include children 14-17 years old, although some studies included students 11-18 years, thus most children are eligible for vaccination in this settings.

A UK cluster-randomized controlled trial in secondary schools in children 11-18 years reported that there was no difference in symptomatic PCR-confirmed infection between self-isolation of school-based COVID-19 contacts for 10 days and voluntary daily lateral flow (LFD) device testing (aIRR 0.94, p=0.61) or days absent[31].

Key findings on high schools from the predictive models are listed below:

- The baseline scenario (Delta R_0= 4.0) of no PHMs and assuming 40% of high school children were vaccinated, estimated more than 75% of susceptible students will get infected within three months[33]. The addition of masks dropped the proportion infected to 24% and testing further reduces infections to 13%[33].
- 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%[33].
- With a 70% vaccination coverage without additional PHMs, 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[34].
    - With universal mask use, community and school vaccination coverage of 70%, the excess symptomatic infection attributable to school transmission is reduced to 0.4% in high schools[34].
    - At 70% coverage without additional PHMs, 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 PHMs if vaccination coverage is >90%[34].
    - 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[34].
- In a modelling study from Austria, 80% vaccination coverage in teachers, 60% in family members, and 50% in eligible students reduced the cases in different school types. The largest impact was in secondary schools given they are eligible for vaccination. Other PHMs were still needed, but control of Delta spread could be achieved with fewer or less stringent other PHMs (active testing, room ventilation, cohorting, or mask policies)[41].

K-12 schools

These schools include students from kindergarten to grade 12 which includes children from 5 to 18 years old, some of which are eligible for vaccination.

A model of re-opening schools in the US with 75% vaccination coverage and no masks, reported the excess infections in the general population due to school opening could be reduced by 23%-36% with masks and an additional 11-13% reduction with hybrid learning[40].

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 with a 70% community vaccination coverage, universal masking and vaccine effectiveness of 85%, school attributable excess transmission would be nearly ten times lower (<1 infection per school) for Alpha than Delta. This scenario estimates fewer than 25% probability of an in-school transmission per month[34].

At a 70% community vaccination coverage with no additional PHMs, there was a higher number of infections (between 1-5 cases per school) for Alpha but it was still lower than for Delta (4-13 cases per school).

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)
- Daycare terms: (Delta or B.1.617) and (daycare or ECEC)
- Children terms: (Delta or B.1.617) and (children or adolescent or youth or pediatric) and/or (transmission or severity)
- Age terms: (Delta or B.1.617) and (age or years)

This review contains research published up to October 8, 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 October 8, 2021.

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

Acknowledgments

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

Knowledge mobilized by the Office of the Chief Science Officer: ocsoevidence-bcscdonneesprobantes@phac-aspc.gc.ca

Evidence tables

Table 1. Evidence on the virulence of Delta in children (n=4)

Study	Method	Key outcomes
Surveillance data analysis (n=4)		
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 US 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 (0-11 years old) and adolescents (12 - 17 years old) 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 US 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.
Archarya (2021)[30] Preprint	Surveillance data from free symptomatic and asymptomatic community PCR testing sites in San Francisco at Unidos en Salud and UC Davis, California during a	• 359/869 samples were positive, 75% from unvaccinated individuals (children and adults). No difference in Ct between vaccinated and unvaccinated or symptomatic and

new Surveillance data analysis US Jun- Aug 2021	two-month period from June 17 to August 31, 2021 (n=869 samples) when Delta was dominant. Ct values were calculated and compared. Lower Ct values equate to higher viral loads and increased likelihood of being infectious.	asymptomatic (children and adults combined). Similar Ct values were found across age groups, genders and vaccine types. • Ct values in some children under 12 who are not yet eligible for vaccination were low. 18.3% (20/109) of children under 12 years of age had Ct-values <20, of which 14 (70%) were asymptomatic at the time of testing. This was similar to 20% of vaccinated individuals had Ct<20.

Table 2. Evidence on the transmission of Delta in children (n=7)

Study	Method	Key outcomes
Outbreak investigations on transmission (n=7)		
Lam-Hine (2021)[23] Outbreak investigation US 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 is 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.
Nathan (2021)[29] **new** Outbreak investigation France Aug 2021*	This is an outbreak investigation in six siblings infected with the Delta variant that occurred in a family setting. The parents were both fully vaccinated with BNT162b2 (Pfizer).	• The index case was reported to be the second child (13 years old) of a family of 6 siblings who presented with fever and asthenia over 4 days. • Both parents were fully vaccinated with BNT162b2 (Pfizer) one month before, and remained negative. • The eldest child (15 years old) was overweight and a history of epilepsy and required hospitalization after seven days of high fever and cough. The child was confirmed to be infected with the Delta variant. • The youngest four children (7 year old twins, and two year old twins) were found to be positive for SARS-CoV-2 infection, and experienced mild symptoms (i.e., fever, asthenia, runny nose, and diarrhea).
Dougherty (2021)[25] **new** Outbreak investigation US Apr – May 2021	This is an outbreak investigation in a gymnastics facility in Oklahoma, USA that occurred during April 15 to May 3, 2021. There were 47 cases linked to the gymnastics facility, including household contacts. Forty (85%) persons in the outbreak were unvaccinated.	• Forty-seven COVID-19 cases, including 21 laboratory-confirmed Delta variant and 26 epidemiologically linked cases, were associated with a gymnastics facility index case on April 15. • The index gymnastics facility identified 23 gymnasts, 3 staff, and their 21 household contacts. The median patient age was 14 years (range = 5–58 years). • The overall gymnastics facility (gymnasts and staff) and household attack rates were 20% (26/133) and 53% (42/80), respectively.

		• Among gymnasts, the attack rate was 19% (23/122). Of these, females had an attack rate of 20% (13/64) and males had an attack rate of 17% (10/58).
Matthias (2021)[26] **new** Outbreak investigation USA Jun 2021	COVID-19 outbreaks at two events sponsored by the same organization. This is an outbreak investigation in a 5-day overnight church camp for 14-18 year olds (n=335 campers and staff) and a 2 day men's conference (n=530 attendees and staff). No proof of COVID-19 vaccination or SARS-CoV-2 pretesting or testing on arrival, or masks were required. An overnight church camp housed campers in large, shared boarding facilities of approximately 100 campers each, dined in a cafeteria together, participated in indoor and outdoor small group activities in which campers were with the same persons during program events, and participated in activities with all campers during all 5 days. Several camp staff also attended a men's conference June 18-19 at a different location than the camp.	• On June 16, day 4 of a 5-day camp the first camper became ill and departed. They had a positive PCR test and the campers and staff were requested to quarantine and test. • Among the 87 persons with camp-associated cases (attack rate (AR) =26%), none reported symptom onset before the camp started on June 13. • Among samples sequenced from specimens from 31 infected persons (15 from camp-associated cases, eight from conference-associated cases, and eight from secondary cases), the B.1.617.2 (Delta) variant was identified in 27 (87%), the B.1.1.7 (Alpha) variant was identified in three (10%); and the P.1 (Gamma) variant was identified in one (3%).
Braun (2021)[27] **new** Outbreak investigation US Jun-Aug 2021	This study investigates multicomponent prevention strategies for outbreaks at an overnight camp in the US. The camps implemented multiple prevention strategies including vaccination, frequent testing, cohorting, masking, physical distancing, and hand hygiene	• No transmission was detected at the camps as a result of testing for SARS-CoV-2, masking, hygiene, social distancing, isolation, and quarantine policies in a population with high vaccination coverage (65% overall). • There were 7,173 persons attending nine camps and vaccine coverage was 65%.

	during June–August 2021. All camps requested that staff members and campers adhere to masking and physical distancing when interacting with persons outside their immediate family for 10–14 days before arrival at camp. Vaccination coverage was 93% among eligible persons aged ≥12 years. Campers across all nine camps were required to submit at least one negative SARS-CoV-2 RT-PCR test result from a test performed within 72 hours before the start of camp, regardless of vaccination status.	• 6 confirmed (RT-PCR) SARS-CoV-2 infections were identified during screening and 3 additional symptomatic cases were identified, yielding a total of nine cases (0.1%) in 4 camps identified across the camp population during the 2021 season. • Of these nine, three were in vaccinated staff all identified before camp started and not attributed to camp related exposures. • Six were in unvaccinated campers aged 8–14 years. Two were identified during pre-arrival screening, one was symptomatic and the others were identified during the first 8 days of camp. • Campers from camps with confirmed cases were either sent home or isolated according to local health department guidance.
Jehn (2021)[24] **new** Outbreak investigation US Jul-Aug 2021	This is a summary of outbreak investigations to assess school mask policies in K-12 Schools in Maricopa and Pima Counties, which account for >75% of Arizona's population. Schools resumed in-person learning for the 2021–22 academic year during late July through early August 2021. Schools that were included had a no mask requirement, early mask requirement that was in place when school began, or a late mask requirement that was implemented any time after school began. A school-associated outbreak was defined as the occurrence of two	• During July 15–August 31, 2021, 191 school-associated outbreaks occurred, 16 (8.4%) in schools with early mask requirements, 62 (32.5%) in schools with late mask requirements, and 113 (59.2%) in schools without a mask requirement. • After adjusting for potential described confounders, the odds of a school-associated COVID-19 outbreak in schools without a mask requirement were 3.5 times higher than those in schools with an early mask requirement (aOR = 3.5; 95% CI = 1.8–6.9).

	or more laboratory-confirmed COVID-19 cases among students or staff members at the school within a 14-day period and at least 7 calendar days after school started. Logistic regression analyses adjusted for school county, enrollment size, grade levels present, Title I status, and 7-day COVID-19 case rate in the school's zip code during the week school commenced.	
Tonzel (2021)[28] **new** Outbreak investigation US Jun-Jul 2021	This is an outbreak investigation in Louisiana youth summer camps. Delta variant became predominant during June–July 2021. This period also coincided with apparent underutilization of preventive measures such as vaccination, masking, and physical distancing.	• The mean outbreak size was 11.5 cases (range = 2–59 cases); the mean outbreak size of day camps was 9.3 cases (range = 2–21 cases) and overnight camps was 13.6 cases (range = 2–59 cases). • There was a thirty-one-fold increase in confirmed camp-associated cases statewide compared with June–July 2020. • Among the 321 camp-associated cases identified, the median age was 12 years (range = 5–54 years) and 274 (85.4%) cases occurred among campers (range = 5–18 years) and two camper cases (0.7%) were fully vaccinated against COVID-19. • Among the camps with outbreaks 1/28 (3.6%) required indoor masking for staff members and campers, 7/28 (25.0%) reported unmasked interactions among cohorts of campers, 1/28 (3.6%) mandated vaccination for all staff members and contractors, and 28/28 camps reported some form of cohorting of campers.
*Publication date is used to estimate when the study was conducted.		

Table 3. Evidence on the impact of public health measures including vaccination on Delta in children (n=12)

Study	Methods	Key outcomes
Randomized control trial (n=1)		
Young (2021)[31] **new** RCT UK Apr- Jun 2021	An open-label, cluster-randomised, controlled trial in secondary schools (11-18 years) and further education colleges in England. Schools were randomly assigned (1:1) to self-isolation of school-based COVID-19 contacts for 10 days (control) or to voluntary daily lateral flow device (LFD) testing for 7 days with LFD-negative contacts remaining at school (intervention). Outcomes: The co-primary outcomes, across all students and staff, were: 1. The number COVID-19-related school absences among those otherwise eligible to be in school. 2. The extent of in-school SARS-CoV-2 transmission with the Delta variant predominantly in circulation. Analysis: Results were adjusted for randomisation strata groups and participant type (student vs staff) and accounted for repeated measurements from the same school over time. Infection incidence models were also adjusted for community SARS-CoV-2 case counts at the lower tier local authority level in the previous week.	Infections: • The rate of infections in students was similar: 61.7 per 100 000 per week in the control group and 63.4 per 100 000 per week in the intervention group. No difference between study groups in symptomatic PCR-confirmed infection (aIRR 0.94, 95%CI 0.73–1.20, p=0.61). • Infection rates in students were approximately linearly related to community case rates, plateauing as community incidence increased. • Infection were lower in staff than students across both groups (aIRR 0.75 (95% CI 0.61–0.92); p=0.0060). School absences: • Students had 55 718 (1.80%) COVID-19-related absences during 3 092 515 person-school-days in the control group, and 48 609 (1.47%) during 3 305 403 person-school-days in the intervention group. The adjusted incidence rate ratio aIRR for COVID-19-related absence in the intervention group was 0.80 (95%CI 0.53–1.21; p=0.29). • Staff were less likely to be absent for COVID-19-related reasons than students across both groups (aIRR 0.39, 95%CI 0.31–0.48, p<0.0001). • There was no evidence of an impact on all-cause absence rates (intention-to-treat aIRR 0·97, 95%CI 0·82–1·16, p=0·77), with non-COVID-

		19-related reasons responsible for most absences.
Ecologic studies (n=1)		
Budzyn (2021)[39] **new** Ecologic study US Jul – Sep 2021	This ecologic study assessed impact of masking in schools on incidence of infection among K-12 students across the US using data from July –September 4, 2021. Counties with 1) a valid school start date, and MCH Strategic Data included a known school mask requirement for at least one district; 2) in districts with known school mask requirements, a uniform mask requirement for all students or no students; and 3) at least 3 weeks with 7 full days of case data since the start of the 2021–22 school year were included. County-specific pediatric COVID-19 rates (number of cases per 100,000 population aged <18 years) from CDC's COVID Data Tracker were tabulated and aggregated by school start week. A multiple linear regression was constructed that adjusted for age, race and ethnicity, pediatric COVID-19 vaccination rate, COVID-19 community transmission, population density, social vulnerability index score, COVID-19 community vulnerability index score, percentage uninsured, and percentage living in poverty.	• Counties without school mask requirements experienced larger increases in pediatric COVID-19 case rates after the start of school compared with counties that had school mask requirements ($p<0.001$). • The average change from week −1 (1–7 days before the start of school) to week 1 (7–13 days after the start of school) for counties with school mask requirements (16.32 cases per 100,000 children and adolescents aged <18 years per day) was 18.53 cases per 100,000 per day lower than the average change for counties without school mask requirements (34.85 per 100,000 per day) ($p<0.001$). • Pediatric COVID-19 case rates during the weeks before (weeks −3, −2, and −1) and after (weeks 0, 1, and 2) the start of school indicate that counties without school mask requirements experienced larger increases than those with school mask requirements ($p<0.05$). • After controlling for covariates, school mask requirements remained associated with lower daily case rates of pediatric COVID-19 ($p<0.001$).
Predictive models on transmission and impact of public health measures (n=6)		
Lasser (2021)[41] Preprint **new**	Cluster Analysis: Austrian data up to December 22, 2020 on 616	• The no mitigation scenario R_o was 2.6 (SD2.1) elementary/ 3.2 (SD 2.4) middle/ 3.6 (SD 2.7) secondary

Predictive Model Austria Sep 2021*	clusters was included to calibrate the model. Model: An agent-based epidemiological model on school transmission. Outcomes: Quantify the impact of PHMs in schools such as room ventilation, reduction of class size, wearing of masks during lessons, vaccinations, and school entry testing by SARS-CoV-2 antigen test across different school types for student-source cases and teacher-source cases. Vaccine scenarios: • 80% of teachers, 60% of family members are vaccinated and 0% or 50% of the student population is vaccinated, depending on the school type. Assumptions: • Delta variant is dominant. • A cluster is at least two cases of SARS-CoV-2 infection, which were epidemiologically linked. • Transmission risk for school contacts were 70% [66%; 74%] (2.5 and 97.5 percentile) lower than household contacts. • Age dependant transmission increases with age: Children are 0.5% [0%; 2.25%] less likely to transmit an infection per year they are <18 years. • Average school sizes of 152, 144, and 674 students for	schools. Clusters with teachers as the source were larger R_o 4.4 (SD 2.9) elementary/ 8.1 (SD 4.5) middle/ 9.8 (SD 6.1) in secondary schools. • Among elementary schools up to 63% of cases had no onward transmission. Infections with varying PHMs and no vaccination coverage scenarios: • Screening to actively find cases (twice per week) with antigen tests was the most effective PHM. This alone could reduce R_o <1 in elementary schools. • In most scenarios more than one PHM was needed to get R_o below one. Combining room ventilation, reduced class sizes and mask policies only reduced R_o <1 in elementary schools. ○ Room ventilation had the largest reduction in cluster size (64%) and was the second impact on cases. ○ Reduction in class sizes resulted in reduced cluster sizes. ○ Wearing a mask had a large reduction in cases and on cluster sizes. • Overall a combination of preventative testing and other PHMs was needed to drop R_o <1. With vaccine coverage of 80% in teachers/60% in household adults reduces the number of cases and vaccination in 50% of eligible students further reduces the number of cases, making it easier to control spread with other PHMs.

	elementary, middle, and secondary schools. • Masks reduce transmission risks by 50% and 30% if the transmitting and contracting agents wear a mask, respectively.	
Mele (2021)[40] Preprint **new** Predictive Model US Sep 2021*	Model: • A stochastic agent-based Susceptible-Exposed-Infected-Recovered (SEIR) simulation model of community transmission. Outcomes: additional community infections hospitalizations, deaths due to school opening. Scenarios: 1. School masking (100% compliance) or without (0% compliance) with schools fully open or hybrid (rotating half joining remotely). 2. Mask efficacy (50% or 70% reduction in transmission and susceptibility) to capture quality and fit. Assumptions: • Each scenario begins July 1, 2021. • Delta variant is 93% dominant. • R_0 increases to 4.47 when Delta is 93% of the observed cases at the end of July. • Working adults wear masks (50% effective) at rates of 50%, 40%, or 30% for urban, suburban, and rural census-tracts, respectively. • Vaccines are 50% and 88% effective, for one dose and two doses, respectively.	Infections by varying public health measures: Baseline scenario: • When schools are open with no masks the highest number of new infections occur in all age groups, with 80% excess infections (occurring post-school opening) than the best scenarios studied. Masking or hybrid learning scenarios: • When students wear masks that are 50%/70% effective there is a 23%/36% reduction in excess infections in the general population. • Hybrid schooling provides an additional 11-13% reduction in excess cases. Hospitalizations and deaths: Baseline scenarios: • When schools are open without masking, the peak estimated hospitalization level exceeds the peak observed in January 2021, with over 18,000 new deaths occurring within 6 months of schools opening. • With no school-masking, approximately 6%, 46%, and 48% of hospitalizations occur in children, adults, and 65+, respectively. Masking and hybrid learning scenarios: • If schools are hybrid or there is high mask-efficacy, there are fewer deaths and a reduction in peak hospitalization of 71%.

	• Children and adults have the same uptake patterns and vaccine coverage reaches 75%.	• With schools fully open, a 20% increase in school mask-efficacy leads to a 7% and 29% reduction in cumulative deaths and peak hospitalizations.
Koslow (2021)[42] Preprint **new** Predictive Model Germany Jul 2021*	Model: • A Susceptible-Infected-Recovered (SIR)-type model that accounts for age-dependence and includes realistic contact patterns between age groups was used to assess community transmission. Outcomes: • Incidence in infections. • Simulations begin on 6 June 2021 and runs for 90 days. Scenarios: 1. Lifting of the regional PHMs on the first of July, without wearing masks and no testing of commuters. 2. Dismiss all regional PHMs on the first of July, but masks will continue to be worn and commuters are regularly tested once a week for the virus. 3. Postpones the relaxation of all regional PHMs to the first of August to allow for increased vaccination coverage and then immediately also lifts wearing of masks as well as testing of commuters. 4. Late opening of the first of August and keep the mask mandate and test commuters once per week.	Baseline scenario: lifting all PHMs in July with no masking or testing: • For Delta-40%, the incidences in all age groups continuously rise. Despite the school holidays the 5-14 year olds are affected the most (68.6/100 000 population). The 0-4 year olds are hit less due to a reduced infection risk (29.9/ 100 000). • For Delta-60%, the 0-4 year olds and 5-14 year olds have median incidences of 155.9/ 100 000 and 375/ 100 000, respectively. In older adults the infections rise up to 150/ 100 000 in 15-59 year olds and 45-76/ 100 000 in those that are prioritized for vaccination (60+years). Lifting all PHMs in July with the exception of masks: • For Delta-40%, 0.7/ 100 000 in 0-4 year olds and 1.6/ 100 000 and 5-14 year olds. The 75th percentiles are relatively large. • For Delta-60%, 2.1/ 100 000 for 0-14 years and 5/ 100 000 for 5-15 years. The 75% percentile for 5-14 year olds are hit hardest with incidences of up to 300/ 100 000 compared to ~100/ 100 000 in adults 15-59 years. Delay in opening to August and lifting masking and testing: • For Delta-40%, 0.8/ 100 000 in 0-4 year olds and 1.7/ 100 000 in 5-14 year olds.

	Assumptions: • Delta is 40-60% more infectious than Alpha. • Delta was 50% of the variants on day 40 and over 80% on day 44 of the simulation. • Wearing masks equates to a 20% to 40% reduction in contacts in the categories school, work and other. • Fully vaccinated people after three weeks to those who gained immunity by recovering from COVID-19 (100% immune). • Partially vaccinated individuals have reduced protection that takes effect 3 weeks afters the first dose.	• For Delta-60%, 2.7/ 100 000 in 0-4 year olds and 5.6/ 100 000 in 5-14 year olds. The 75%-percentile was highest for 5-14 year olds. Delay in opening to August and keeping masks and testing: • For Delta-40%, 0.5/ 100 000 for 0-4 year olds and 1.2/ 100 000 for 5-14 year olds. • For Delta-60%, 1.1/ 100 000 for 0-4 year olds and 2.6/ 100 000 for 5-14 year olds.
Zhang (2021)[33] Preprint Predictive model US Aug 2021*	Model: Susceptible-Infected-Recovered (SIR) model of in-school transmission 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 Scenarios: • 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	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%. • In the sensitivity analysis, a baseline R_0 of 5.0 results in 93% infected

	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%. • A scenario analysis also considered an R_0 of 5.0. 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). • Universal mask usage decreases infectivity by 50%. • Weekly testing may occur among 50% of the student population, where positive tests prompt quarantine until recovery, with compliance contingent on symptom status.	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)[32] Preprint Predictive model US Aug 2021*	Model: ▪ Validated agent-based network model of in-school transmission. 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. Outcomes:	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-19 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

	• Projected 30-day cumulative incidence of SARS-CoV-2 infection • Proportion of cases detected • Proportion of planned and unplanned days out of school 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 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	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 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

	population from unvaccinated individuals to signaling undetected transmission and trigger additional investigation or interventions). 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 • 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.	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. School absences: Elementary school: • With weekly screening, there was an average of 0.6 quarantine/isolation days per student per month at 10 community 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 maximal case detection through weekly screening.

Head (2021)[34] Preprint Predictive model US Aug 2021*	Model: A discrete-time, age-structured, individual-based stochastic model of school cases was used to simulate transmission of Delta among a synthetic population, representative of Bay Area cities. Outcomes: • 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 • Hospitalization rates among students of all grade levels. • The minimum set of interventions to keep excess infections under a predetermined risk tolerance (<5 to <50 cases/1000 school population). Scenarios: • Scenarios evaluate various public health measures (PHMs: 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	Elementary schools: Infections with no additional PHMs: • A 70% community vaccination coverage and without additional PHMs there are 25 (6.6%) excess symptomatic cases per 380-person elementary school across a 128-day semester. Infections with varying PHMs: • A 70% vaccination coverage with universal mask use and VE of 85%, the excess symptomatic infection attributable to school transmission was 8 cases (2%) in elementary schools. • As community vaccination coverage of the eligible population (12+ years) increased from 50% to 70%, school-attributable symptomatic illness fell from 8.7% 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, representing a reduction of 41%. • At 70% vaccine coverage, 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

	unvaccinated students and teachers, across varying levels of vaccine effectiveness (45%, 65%, 85%), and compared results between Delta and Alpha variant circulation. 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	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. Hospitalizations: • Under a 50% vaccination coverage and no PHMs, the maximum hospitalization rate was 1.3 hospitalizations per one million and 3 per 10 million with masks and cohorts. Middle School Infections with no additional PHMs: • A 70% community vaccination coverage and without additional PHMs, there are 37 (8.8%) excess symptomatic cases per 420-person middle school across a 128-day semester. Infections with varying PHMs: • At 70% vaccine coverage with universal mask use and VE of 85%, the estimated excess symptomatic infection attributable to school reopening among 3.0% of middle school students (13 cases per school). • 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.

	years compared to individuals under 10 years. • The Bay area reopening scenario was 70% community vaccination coverage with vaccine at 85% effectiveness and universal masking.	Hospitalizations: • Under 50% vaccination coverage the maximum hospitalization rate was 4.8 hospitalizations per million (no PHMs) and 3 per 10 million (with masks and cohorts) over the 128-day semester. High school Infections with no additional PHMs: • With a 70% community vaccination coverage and without additional PHMs, there are 27 (4.4%) excess symptomatic cases per 620-person high school across a 128-day semester. Infections with varying PHMs: • At 70% vaccine coverage, universal mask use and 85% VE, the excess symptomatic infection attributable to school reopening among 0.4% of high school students (3 cases per school). • 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. • At 90% vaccine coverage within schools, there is a median of zero excess infections. • At 45% VE, 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. Impact of transmission of Delta versus Alpha:

		• An Alpha scenario (R0 = 2.5) with 70% vaccine coverage and 85% VE, 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 PHMs 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 1-5 excess case per school with Alpha compared to an excess of 4-13 cases with Delta. • If the vaccination coverage exceeded 75%, high schools could achieve <1 excess cases in 1,000 student) without any additional PHMs with Alpha. Hospitalizations • If the Alpha variant had remained dominant, hospitalizations among students do not occur.
Predictive models on vaccination coverage in children (n=4)		
Bracis (2021)[38] Preprint **new** Predictive Model US Oct 2021*	Model: Adapted a previously developed deterministic compartment model. All simulations included in this analysis started on June 1st, 2021. Scenarios: Analysis is focused on the impact of vaccination programs dynamics in King County based on: 1. Extending vaccination to children aged 5-11 with different starting dates	Hospitalizations: Base-case scenario: • With 85% vaccination coverage of 12+ year-olds estimates unregulated school opening results in 2-fold increase in pediatric hospitalizations from 163 (median, IQR 95-226) if schools remained closed to 325 (median, IQR 264-400) if physical contacts at schools are fully restored (100% PPI) for the entire school year. Different proportions of physical interaction (PPI):

	(October 2021 and January 2022). 2. Different proportions of physical interactions (PPI) at schools restored varying from completely closed to fully opened. 3. Improving the overall vaccination coverage among eligible population. Outcomes: • Assessed the impact of different vaccination programs by comparing: ○ The cumulative hospitalizations (overall, by vaccination status and by age group). ○ The peak numbers of hospitalizations. ○ The proportion of simulations requiring additional mitigation measures and the proportion of time under additional restrictions (SD max) calculated over the school year (Sept 2021 – June 2022). Scenarios: • Assessed the impact of early vaccination of children aged 5-11 compared to scenarios in which only individuals ages 12 and over are vaccinated. • Analyzed the expected benefits of offering vaccination to children age 5-12 starting on Oct.1, 2021 relative to:	• Reducing contacts in schools by 25% PPI or 50% PPI through masking, ventilation and distancing is expected to decrease the overall median hospitalizations in 0-19 year olds by 8% and 23%, respectively. Extending vaccination to 5-11 year olds and changing PPIs: • Extending vaccination eligibility to children aged 5-11 years (85% vaccine coverage), and reducing contacts by 25% PPI prevents 756 fewer hospitalizations and ~50% fewer hospitalizations in the youngest age group compared to no vaccination. • Significantly more hospitalizations in 0-19 year olds are prevented if physical contacts in schools are fully restored (100% PPI) or in-person schooling is managed with some mitigation measures (75% PPI). Delaying vaccination: • Delaying childhood vaccination by 3 months will void most of the benefits measured over the school year including reductions in total, pediatric hospitalizations. Increasing vaccination coverage: • Early vaccination in 5-11 year olds and reaching a 90% overall vaccination coverage in 12+ year olds, 60% of remaining hospitalizations will be averted and the need for extra mitigation measures may be avoided. Length of time of social distancing: • Unregulated school opening will require additional time under maximum social distancing imposed for 26% (median, IQR 23-28) of the

	1. Delaying this access by another 3 months. 2. Continuing to vaccinate individuals 12 years and older only. Assumptions: • Approximately 80% of the infections on June 1, 2021 were with the Alpha variant while the remaining 20% are with Delta variant. • 85% of the currently eligible population (12 years and older) is vaccinated, implies that 72.9% of the total population is vaccinated with approximately 33% of the unvaccinated population being children of school age.	school year to manage outbreaks compared to 62% for scenarios with schools closed. • Delaying childhood vaccination by 3 months will void most of the benefits measured over the school year including days requiring maximal social distancing.
McBryde (2021)[36] **new** Predictive Model Australia Sep 2021*	Model: A mathematical model which incorporates age-specific mixing, infectiousness, susceptibility and severity to assess the final size of the epidemic under different public health intervention scenarios in Australia. Outcomes: This study takes into account vaccination and additional mitigation measures to assess: • Final infected population • Cumulative hospitalizations • Deaths • Years of life lost following an epidemic wave Scenarios: • The study considers three vaccine program possibilities. ○ 1. All vaccinations being Pfizer	Transmission: • For all effective reproduction numbers (Reff) and vaccination programs, prioritizing transmitters (<55 year-olds) leads to fewer (or, at worst, an equal number of) infections. • Extending vaccination to 5+ year olds (from 15+) improves outcomes for infections using a Pfizer or Mixed vaccination program if Reff is high (Reff 5-7). • If Reff is 5, (Delta scenario) herd immunity can be achieved only if the minimum vaccination age is extended down to 5+ years. • If Reff=7, (worse than Delta scenario) there is no program or strategy that achieves herd immunity. • If Reff=3, (Alpha scenario) herd immunity can be achieved at 60% coverage using a Pfizer or Mixed

	○ 2. All vaccinations being AstraZeneca ○ 3. Mixed: Pfizer for <60 years of age and AstraZeneca for >=60s (Current ATAGI policy). • Age cutoffs for vaccine eligibility: ○ 1. 15+ years ○ 2. 5+ years • Age-specific coverage strategies including all of the population over the age cut-off: ○ 1. The vulnerable first strategy: Vaccinate the older, more vulnerable population (55+ year-olds) first, followed by <55 year-olds. ○ 2. The transmitters first strategy: Vaccinate the more sociable (<55 year-olds) first followed by the older. ○ 3. The untargeted strategy: Even distribution of vaccine across all eligible age groups. • Uptake proportion: ○ Considers different uptake proportions, indicative of the maximum vaccine acceptance of the target groups. Assumptions: • Pre-vaccination R_0 of 5 for Delta • Main analysis assumes a maximum uptake of 90% across all eligible age groups.	program and transmitter strategy (<55 year olds)). • AstraZeneca does not achieve herd immunity under any model assumptions. • If the effective reproduction ratio could be constrained to below 2.7, through non-vaccination means, then herd immunity is achievable using AstraZeneca, Pfizer or mixed programs. • If the Reff is as high as five, at least 85% of the population including children (5-16 year olds) would need be vaccinated to achieve herd immunity using a "Mixed" program approach (vaccinating over 60s with AstraZeneca and under 60s with Pfizer). Years of life lost, hospitalizations, and deaths: • Lowering the age of vaccine eligibility to include 5 year-olds typically worsens the outcome for YLL for a given coverage until adult coverage is saturated. At this point, vaccinating those aged 5-15 years reduces YLL. • In all cases the Pfizer and Mixed vaccination programs outperform the AstraZeneca only program for hospitalizations, deaths, and YLL.

	• Younger age group (0-19 years) were less susceptible.	

Cuesta-Lazaro (2021)[35]
Preprint
new
 	
Predictive Model
 	
UK
 	
Sep 2021*
	Model:
	• An individual-based model which uses fine-grained UK geographic and demographic information and a strong focus on the details of policy interventions to describe the spread of infectious diseases.
	Outcomes:
	• Infections and deaths.
	Scenarios:
	• Vaccination of adults only, adding 16-17 years, 12-17 years or all children. (Coverage = 80% in all scenarios.
	• All simulations began from 10th July 2021 and all scenarios were run up to 1st February 2022. Impact of PHMs in the school environment under two scenarios which are variations on the BASELINE:
	  ○ CLASS-QUARANTINE: When a pupil develops symptoms, their whole classrooms stays at home for 10 days.
	  ○ SOCIAL-SCHOOLS: Variations in the intensity of contacts between individuals in schools to mimic the effect of policies such as mask wearing, social distancing and cohorting.
	Assumptions:
	• Delta variant is dominant.
		The most effective interventions are a priori vaccination of children 12+ (at 80% coverage) followed by the largest reductions in school contact intensity (use of cohorting and mask policies).
		
		Number of infections:
		• The vaccination of 16+/ 12+/ all children reduces the total number of infections by about 10%/ 40%/ ~90% compared to having only 80% of adults vaccinated.
		• Given 80% of adults are vaccinated, infections in this model rise in schools before other community settings.
		• Vaccination coverage of only 40% in 12-18 year olds only reduces infections by 30% and has little impact on the deaths.
		
		Number of deaths:
		• With 80% vaccination coverage in adults, deaths in these scenarios were shifted to younger age groups and most occurred in unvaccinated individuals. Simulations suggest that vaccination of 16+/12+ at 80% reduces the total number of deaths by ~ 1000/5000 compared to vaccinating adults only.
		• Vaccinating all children nullifies the impact of opening schools and there is no increase in cases in fall 2021.
		
		PHMS:
		• The best results are achieved by layering PHMs (e.g., combining mask wearing, social distancing, and increased ventilation in classrooms)

	• Some community PHMs are still in place, such as partial mask wearing and the isolation of positive cases. • Vaccination campaigns were completed before the simulations began, which means none of these simulations are intended as forecasts, but rather to assess the relative effects of different interventions.	in schools, with the potential to reduce fatalities by up to 50%. • The CLASS-QUARANTINE scenario, significantly dampens the peak of the daily death curve, and the effect on the cumulative number of deaths is similar to that seen from near maximal contact intensity reduction.
Liu (2021)[37] Preprint **new** Predictive Model China Sep 2021*	Model: Compartmental model of SARS-CoV-2 transmission and vaccination, based 106 on an age-structured stochastic SIR scheme. Outcomes: • Percentage of the population in China that needs to be vaccinated in order to reach herd immunity (Re=1) against Delta. • Comparing vaccination strategies on effective reproduction number at the time the infection is seeded (Re) in China. Scenarios: • Simulated epidemic with 40 infectious individuals and compared the effectiveness of three different vaccination strategies in reducing the number of cumulative infections from Sept 2021 to Sept 2022 for several different scenarios. ○ Baseline scenario: Where an epidemic is triggered by 40 infections on September 1,	Baseline scenario (epidemic on Sept 1, 2021): • Vaccine coverage of the total target population is 86.4%, 93.0%, and 95% when vaccinating 18+ (strategy 1), individuals 3+ are vaccinated since Sept 1, 2021 (strategy 2), and individuals 3+ since Nov 2020 (strategy 3), respectively. • The Re is 4.50 (95%CI: 3.80- 4.98), 4.49 (95%CI: 3.90-4.89), and 3.67 (95%CI: 3.64-3.68) for strategy 1-3, respectively. • The estimated infection attack rates are 47.3% (95%CI: 45.8- 48.6%), 44.0% (95%CI: 42.3-45.9%), and 42.3% (95%CI: 39.5-44.0%) for strategy 1- 3, respectively. • Strategy 2-3, where children 3+ years are vaccinated, achieves the highest reduction in infection attack rates with a 55.3% and 57.0% reduction, respectively. • Overall, vaccine efficacy has the largest impact, followed by the vaccine efficacy of individuals aged 3-17 and 60+ relative to individuals aged 18-59 years. • Delaying the start of the epidemic: • Re remains above the epidemic threshold for all three strategies

	2021 and vaccines have been rolling out in China since November 30, 2020. ○ Scenario 1: Delay of the start of the epidemic (e.g., by keeping strict restriction for international travels) to October – November 2021 to allow the immunity to build up in the population, potentially reaching herd immunity levels. ○ Scenario 2: PHMs during an outbreak scenario. ○ Scenario 3: Delaying the start of the epidemic to October-November 2021 and adopting PHMs. ○ Scenario 4: Herd immunity. Strategies: • Strategy 1: random distribution of vaccines to adults 18+ since Nov 2020. • Strategy 2: same as 1 but individuals 3+ also receive vaccination starting on Sept 1, 2021. • Strategy 3: random distribution of vaccines to individuals 3+ since Nov 2020. Assumptions: • R_0 as 6.0 for Delta. • In each vaccination strategy scenario, about 2% of the population is not eligible to receive the vaccine. • Vaccine effectiveness is assumed at 54.3% against Delta infection and vaccine	even if the epidemic is delayed to November 1, 2021, when the vaccination coverage reaches ~ 97%. • Strategies 2 and 3 lead to a higher reduction of the infection attack rate (less than 4,200 per 10,000 individuals) with respect to the scenario with no intervention. PHMs during an outbreak: • With PHMs, the mean net reproduction number for strategy 1 and 2 can be reduced to below 1 only when R 0 ≤1.3, while for strategy 3, R0 can be up to 1.6. Delaying the start of the epidemic and adopting PHMs: • With an epidemic in October-November 2021 and moderate PHMs (R0 in the range 1.5-2.0), strategy 2 and 3 can succeed in blocking transmission. Strategy 1 requires strict PHMs (R0<1.3) to prevent a major wave. Herd immunity: • A 95% VE, Re decreases below 1.0 for strategy 2 and 3. The estimated herd immunity threshold under these two strategies is 94.0% and 88.1%, respectively. When the adult population is vaccinated (strategy 1) with an R0 2.9, the estimated infection attack rate is relatively low (13.2%). • A VE< 85%, herd immunity is unattainable, even where the vaccine coverage is 100%. • Vaccine-induced herd immunity may only be achievable with higher vaccine effectiveness and high

	immunity duration is life-long and no natural initial immunity. • Children under 15 years of age were estimated to have a lower susceptibility to SARS-CoV-2 infection compared to adults (i.e., individuals aged 15 to 64 years), while individuals 181 aged 65+ years had the highest susceptibility to infection. • PHMs are considered as a combination of case isolation, contact tracing, mask wearing, social distancing, and improved hygiene.	coverage (e.g., VE of 90% and > 93% coverage). • In the presence of PHMs, a lower vaccine efficacy and vaccine coverage percentage is needed to reach herd immunity (e.g., under moderate PHMs if VE is 90% and 80% vaccine coverage). • In a "US-like" scenario where VE=79%, 22% of the population has natural immunity, extending vaccinations to children 3-17 years results in more than 90% reduction of infections.
*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%.		

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