

Emerging Evidence on COVID-19

Evidence Brief on Age-Dependent Transmission

Introduction

What is the evidence for age-dependent transmission of SARS-CoV-2?

It is important to establish whether there are differences in the potential to transmit SARS-CoV-2 among children of different age groups (preschool 0-4 years old, primary school 5-11 years old, intermediate 12-13 years old and high school 14-19 years old) compared to adults. This evidence brief is an update to the June 22, 2020 version and includes COVID-19 literature up to July 20, 2020 that measures age-dependent transmission or estimates transmission scenarios among children of different age groups such as in school.

Key Points

- Empirical evidence suggests that a low proportion of SARS-CoV-2 cases occur in children <19 years old. Of the cases in children, a large proportion may be asymptomatic, but they are still capable of transmitting the virus (Table 1).
- Few contact tracing or outbreak studies have reported children <19 years old as the index case (Table 1). However, there are instances where an infected child has passed SARS-CoV-2 to an adult or another child. Most studies conclude that children have not been the main drivers of transmission of SARS-CoV-2 to date.
- One study estimated the relative infectivity of children to adults to be 85% (65-110%). However, few children were the index case in the household outbreaks investigated, which resulted in the study being underpowered (Dattner et al., 2020). In a systematic review, pooled odds ratio of being an infected contact in children compared with adults for all contact tracing studies was reported as 0.44 (0.29, 0.69) (Viner et al., 2020).
- Viral load in symptomatic children was shown to be the same as adults in three studies of symptomatic COVID-19 cases (Table 2).
- Six publications use mathematical models to investigate the impact of relaxing intervention measures by targeting different age groups on the epidemic (Table 1).
 - Re-opening schools: the most recent model examines the risk of opening schools in a low transmission vs. high community transmission scenario, indicating opening schools in low transmission scenarios along side other public health interventions did not result in a large spike in cases. Two other mathematical models demonstrate that allowing younger children (pre-school and primary school aged) to return to school would have the smaller impact on the basic reproduction number (R_0), whereas the return of secondary school grades will have

the greatest impact (Di Domenico, Pullano, Sabbatini, Boëlle, & Colizza, 2020; Keeling et al., 2020).

- Of the three models that analyzed lifting interventions by age groups, results suggest that relaxing measures by age group could reduce the impact of COVID-19. Specifically, releasing younger individuals (0-19) from strict lockdown can lead to lower overall fatality rates compared to the simultaneous release of all individuals after a lockdown (Castilho, Gondim, & Marchesin, 2020; Zhao & Feng, 2020).

Overview of the Evidence

The evidence for age-dependent transmission of SARS-CoV-2 has been directly and indirectly explored in a number of predictive models. These models are based on scenarios and are parameterized using observational data from the outbreak; caution should be exercised in using these findings, as the extent to which the results can be generalized to the local context is variable.

Empirical evidence from surveillance, estimates of transmission and descriptions of transmission clusters or outbreaks are obtained from data collected during retrospective outbreak investigations, which have a moderate to high risk of bias. Many studies identified in this brief are in preprint format and have not completed a peer-review process. There is some evidence that may allow estimation of transmission rates among child age groups compared to adults, this evidence is accumulating rapidly and there is a high probability that estimates or conclusions will change as additional evidence becomes available.

CONTENTS

EVIDENCE OF AGE-DEPENDANT TRANSMISSION AND TRANSMISSION POTENTIAL	3
THE IMPACT OF RELAXING INTERVENTION MEASURES BY TARGETING DIFFERENT AGE GROUPS	16
OTHER EVIDENCE SYNTHESIS PRODUCTS CONDUCTED TO LOOK AT TRANSMISSION AMONG DIFFERENT AGE GROUPS.....	19

EVIDENCE OF AGE-DEPENDANT TRANSMISSION AND TRANSMISSION POTENTIAL

The age distribution of COVID-19 cases has shown strong age dependence with fewer cases documented in children, and few transmission events attributed to transmission from an infected child. In this updated review, several studies were added from cluster investigations and school community investigations conducted in countries in Asia, Europe, Australasia, North America and South America that add a significant update to this review.

It is hypothesized that the apparent age-dependence we see in epidemiological data may have several contributing factors including that children may be less susceptible to infection and/or are less prone to showing clinical symptoms when infected. Several studies in Table 1 provide evidence that a significantly lower proportion of children are infected with SARS-CoV-2 compared to adult populations, that children are less susceptible to SARS-CoV-2 infection than adults and that they may be less likely to have symptoms. This susceptibility appears to increase between 10 and 20 years old. Models like the one by Davies et al. show the impact of different rates of transmission by age and the impact of assumptions around how readily asymptomatic or paucisymptomatic transmission occurs (Davies et al., 2020).

Contact tracing studies in Table 1, such as the results from South Korea, agree that children are infrequently identified as the index case or a contact in cluster investigations. However, a unique finding of this study was that the few 10-19 year old index cases had a high rate of transmission (18.6%) compared to their household contacts (Park et al., 2020). Speculation around this increase in transmission includes that children in this age group are taller, and can contaminate more shared air with adults and that they may be less likely to adhere to optimal personal hygiene behaviors. Across other studies a child <18 years old is rarely implicated as the index case in a family or non-household cluster (Table 1).

Similarly, there were seven investigations within school communities. Even though cases were identified in the school, most were not attributed to transmission at school and instead were attributed to transmission from a family member at home. Two of the school investigations from Chile and France reported very high seroprevalence after school closures (Fontanet, Tondeur et al., 2020; Torres et al., 2020). The study in France was in one of the epicenters of an outbreak, and was thought to have been going on for approximately 3 weeks before the school closed. The results were high seroprevalence across all age groups in this investigation (Fontanet, Tondeur et al., 2020). The study from a school community in Santiago Chile indicated that there was high prevalence among the preschool teachers and parents due to meetings that had taken place in the first few weeks of schools opening (Torres et al., 2020).

Table 1: Twenty-three studies that inform age-dependent factors of COVID-19 transmission including predictive models (n=2), contact tracing studies (n=10), school/daycare studies of transmission (n=7), synthesis research on age related transmission (n=4)

Reference	Title	Study Description	Key Outcomes
Predictive Models of age-dependent transmission			
(Davies et al., 2020)	Age-dependent effects in the transmission and control of COVID-19 epidemics	Dynamic transmission models were fit to a range of available data on the age distribution of reported cases, and 2 studies that looked for infections among close contacts, to estimate the age-specific susceptibility to SARS-CoV-2 infection and the age-specific fraction of infections that develop full clinical symptoms of COVID-19. Data from China, Italy, Japan, Singapore, Canada and South Korea was used. The model examined epidemiological evidence to better understand whether children have lower susceptibility to infection, lower propensity to show clinical symptoms or both. The model accounting for both fit the data best.	<ul style="list-style-type: none"> • Susceptibility to SARS-CoV-2 infection in <20 yo is approximately half that of adults aged over 20 years. Relative susceptibility to infection was 0.40 (0.25-0.57) in 0-9 yo vs. 0.88 (0.70-0.99) in 60-69 yo. • Clinical symptoms manifest in 21% (95% credible interval: 12–31%) of infections in 10-19 yo, rising to 69% (57–82%) of infections in >70 yo. • Results were consistent across countries and intervention contexts. • These results show that interventions targeting schoolchildren may be less effective than for other respiratory infections. • Age-structure of a population is important for estimating the burden of SARS-CoV-2. • A comparison of COVID-19 vs. influenza in 3 cities with different age structures indicates that school closures delay the COVID-19 peak 1-6 days and decreased it by 10-19% vs. 10-89 days and 17-35% for influenza.
(Lau, Grenfell, Nelson, & Lopman, 2020)	Characterizing super-spreading events and age-specific infectivity of COVID-19 transmission in Georgia, USA	Individual-level spatiotemporal mechanistic framework to statistically integrate case data with geo-location data and aggregate mobility data, enabling a more granular understanding of the transmission dynamics of COVID-19. Data: March 1- May 3, the analysis included the 5 most infected counties with n=9559 COVID-19 cases with demographic information.	<ul style="list-style-type: none"> • They did not look at children as a separate age group because there were not enough observations. Younger children seem to be less susceptible to SARS-CoV-2. • We estimate that the infected children and adults <60 yo may be 2.38 [1.30, 3.51] times more transmissible than infected elderly (>=60 yo), and the former may be the main driver of super-spreading.

Surveillance / Contact Tracing Data			
(Park et al., 2020) <i>new</i>	Contact tracing during Coronavirus Disease outbreak, South Korea, 2020	<p>Summary of S. Korea’s retrospective cluster investigations from Jan 20- Mar 27 59073 contacts of 5706 COVID-19 cases were traced. RT-PCR was used to determine COVID-19 status. They did not test asymptomatic contacts and had different thresholds for testing household vs. non-household contacts.</p> <p>Age category: # index/# contacts traced</p> <p>0–9: 29 (0.5%)/ 237 (0.4%) 10–19: 124 (2.2%)/ 457 (0.8%) 20–29: 1695 (29.7%)/ 15810 (26.8%) 30–39: 668 (11.7%)/ 8,636 (14.6%) 40–49: 807 (14.1%)/ 9709 (16.4%) 50–59: 1107 (19.4%)/ 11353 (19.2%) 60–69: 736 (12.9%)/ 8490 (14.4%) 70–79: 338 (5.9%)/ 2,389 (4.0%) >80: 202 (3.5%) / 1992 (3.4%)</p> <ul style="list-style-type: none"> Index and contracts in the 20-29 year group and the 50-59 year group represented the largest age categories identified as the index case and traced for COVID-19 infection. <p>In this study, the index case was the first case to be identified in time since they could not confirm who transmitted to whom.</p>	<ul style="list-style-type: none"> Overall: <ul style="list-style-type: none"> 11.8% (95% CI 11.2%–12.4%) of household contacts were infected 1.9% (95% CI 1.8%–2.0%) of non-household contacts were infected. Index case age category: positive/N (% , 95% CI) in household contacts. <ul style="list-style-type: none"> 0–9: 3/57 (5.3%, 1.3–13.7) 10–19: 43/231 (18.6%, 14.0–24.0) 20–29: 138/12393 (1.1%, 0.9–1.3) 30–39: 70/7,407 (0.9%, 0.7–1.2) 40–49: 206/1749 (11.8%, 10.3–13.4) 50–59: 300/2045 (14.7%, 13.2–16.3) 60–69: 177/1039 (17.0%, 14.8–19.4) 70–79: 86/477 (18.0%, 14.8–21.7) ≥80: 50/348 (14.4%, 11.0–18.4) <ul style="list-style-type: none"> Note transmission from a 10-19 year old index case to household contacts was significantly higher than other younger age groups. Index case age category: positive/N (% , 95% CI) in non-household contacts. <ul style="list-style-type: none"> 0–9: 2/180 (1.1%, 0.2–3.6) 10–19: 2/226 (0.9%, 0.1–2.9) 20–29: 138/12393 (1.1%, 0.9–1.3) 30–39: 70/7,407 (0.9%, 0.7–1.2) 40–49: 161/7960 (2.0%, 1.7–2.3) 50–59: 166/9308 (1.8%, 1.5–2.1) 60–69: 215/7451 (2.9%, 2.5–3.3) 70–79: 92/1912 (4.8%, 3.9–5.8) ≥80: 75/1,644 (4.6%, 3.6–5.7) 0.9%, 369/42788 confirmed COVID-19 cases in the Netherlands have been 0-18 yo.
(Van Der Hoek et al., 2020)	[De rol van kinderen in de transmissie van	Data from the Dutch surveillance system Osiris was analysed up to May 11, 2020.	

<p><i>new</i></p>	<p>SARS-CoV-2] in Dutch</p>	<p>This is preliminary data and the study is on going. Family cluster investigations were prospective enrolment at first confirmed case between March 23 and April 16. N=54 families Note: schools were closed during this study period.</p>	<ul style="list-style-type: none"> ○ 0-3 yo, 74 cases ○ 4-11 yo, 38 cases ○ 12-18 yo, 257 cases • There was no difference between Ct values of children or adults. • Results of a transmission pair analysis indicated 21 cases of parent to child transmission and 2 cases of child-to-child transmission within a household. • None of the 43 contacts of 10 COVID-19 cases under 18 yo developed infections compared to adults where secondary transmission was 8.3%. • In the family investigations, children were less likely to report symptoms in the last 14 days (67%) vs. adults (91%) or have specific respiratory symptoms (25% vs. 78%) • Seroconversion at 2-3 weeks post initial investigation: <ul style="list-style-type: none"> ○ 1-5 yo, 21% (3/14) ○ 6-11 yo, 13% (4/31) ○ 12-17 yo, 32% (12/38) ○ 18-45 yo, 31% (11/35) ○ >45 yo, 43% (13/30) • The study concluded that children can become infected, but they do not appear to contribute as much to transmission as adults.
<p>(Sun et al., 2020) <i>new</i></p>	<p>Children infected with SARS-CoV-2 from family clusters</p>	<p>Analysis of 74 children admitted to a Wuhan hospital Jan 28- Mar3. Cases were confirmed by RT-PCR.</p>	<ul style="list-style-type: none"> • In all pediatric cases at least one adult family member was infected before the children in the household.
<p>(Somekh et al., 2020) <i>new</i></p>	<p>The role of children in the dynamics of intra family Coronavirus 2019 spread in densely populated area</p>	<p>Bnei Brak, Israel, which is one of the most crowded cities in the world and the city with the highest rates of children per family in Israel.</p>	<ul style="list-style-type: none"> • 13 family clusters were investigated. <ul style="list-style-type: none"> ○ 12/13 index cases were adults exposed at the synagogue, holiday feast, work or unknown in 50%. ○ 1/13 was 14.5 yo that was exposed at Yeshiva.

		<p>Children 0–19 years of age comprise 50% of the 200,000 population. The average number of children in a family is 4.57. In each family cluster all members were tested by RT-PCR</p>	<ul style="list-style-type: none"> • RT-PCR positive cases within these clusters included [relative risk of being positive compared to >18yo] <ul style="list-style-type: none"> ○ >18 yo: 58.3%, 21/36 ○ 5-17 yo: 32.5%, 13/40 [0.61, 95%CI 0.39–0.96, p=0.037] ○ 0-4 yo: 11.8%, 2/18 [0.47, 95%CI 0.30–0.71, p<0.002] • The study concludes they could not show a dominant role for children in transmission of SARS-CoV-2 even in a densely populated city with a high proportion of children.
<p>(Dattner et al., 2020) <i>new</i></p>	<p>The role of children in the spread of COVID-19: Using household data from Bnei Brak, Israel, to estimate the relative susceptibility and infectivity of children</p>	<p>Data from Bnei Brak up to May 2 was used for analysis. Epidemiological cluster investigations of 637 households were included. Estimates were generated from a stochastic dynamic model.</p>	<ul style="list-style-type: none"> • Most index cases were adults. • Adults had a higher risk of being infected than children (44% vs. 25%). • Children under 1 yo had a higher risk of being infected compared to those aged 1-4 yo. • Their model estimates that children may have a lower infectivity compared to adults. Relative infectivity 85% (65-110%). Few child index cases meant this estimate is underpowered.
<p>(Lavezzo et al., 2020) <i>preprint</i></p>	<p>Suppression of COVID-19 outbreak in the municipality of Vo, Italy</p>	<p>Two population surveys were conducted to collect nasopharyngeal swabs from 2,812 and 2,343 in the municipality of Vo, Italy.</p>	<ul style="list-style-type: none"> • No infections were detected in either survey in 234 tested children ranging from 0-10 yo, despite 13 of them living in the same household as infected people. Based on household secondary infection rate positive children were expected.
<p>(Zhang et al., 2020)</p>	<p>Changes in contact patterns shape the dynamics of the COVID-19 outbreak in China</p>	<p>Contact surveys were conducted in two cities: Wuhan and Shanghai. The surveys were conducted from Feb 1 to Feb 10. The dataset included 1245 contacts in Wuhan and 1296 in Shanghai.</p>	<ul style="list-style-type: none"> • Susceptibility to SARS-CoV-2 infection increased with age. Young individuals (aged 0-14 yo) had a lower risk of infection than individuals aged 15-64 yo {OR = 0.34 [95% confidence interval (CI): 0.24 to 0.49], p < 0.0001}.

<p>(Mizumoto, Omori, & Nishiura, 2020) <i>preprint</i></p>	<p>Age specificity of cases and attack rate of novel coronavirus disease (COVID-19)</p>	<p>Summarized Japan's cases up to March 7. 313 domestically acquired cases from 2496 close contacts that were investigated.</p>	<ul style="list-style-type: none"> The attack rate was low among children (male 7.2%, female 3.0%) compared to adults which peaked in the 50-59 age group (22.23%, 21.9%). As these were all exposed or symptomatic-suspected COVID-19 samples, it appears that the risk of disease given exposure is low among children.
<p>(Bi et al., 2020)</p>	<p>Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study</p>	<p>Summary of case data from Jan 14 to Feb 12, 2020, the Shenzhen Center for Disease Control and Prevention. There were 391 SARS-CoV-2 cases and 1286 close contacts identified through symptomatic surveillance and contact tracing.</p>	<ul style="list-style-type: none"> Transmission from a child to adult was not documented. The authors conclude that children had a similar risk of infection as adults. However, there are few observations and large uncertainty in the data for the child age categories. Contact-based (exposed) testing results by age: 0-9= 14.9%, 10-19= 5.7%, 20-59= 10.3-17.2%. Symptom-based testing results by age: 0-9 & 10-19= 2.1%, 20-59=7.9-24.3%.
<p>(Danis et al., 2020)</p>	<p>Cluster of Coronavirus Disease 2019 (COVID-19) in the French Alps, February 2020</p>	<p>Ski Chalet outbreak in the French Alps February 2020. The index case spread SARS-CoV-2 to 11 people at the chalet during a 4 day stay.</p>	<ul style="list-style-type: none"> A pediatric case in this outbreak visited 3 different schools while symptomatic and no secondary cases were caused by this case.
<p>School and Daycare Investigations</p>			
<p>(Yung et al., 2020) <i>new</i></p>	<p>Novel coronavirus 2019 transmission risk in educational settings</p>	<p>Case reports of cases that attended daycare and secondary school from contact tracing studies in February and March in Singapore. Schools were not closed in Singapore, but they cancelled extracurricular activities, staggered breaks, and cohorted children. A strict cleaning protocol was also implemented. Daycares with a positive case closed for 14 days.</p>	<ul style="list-style-type: none"> 3 incidents are reported: <ul style="list-style-type: none"> A 12 year old and a 5 year old were identified through contact tracing of an adult case they had contact with. None of the 8 symptomatic contacts at the secondary school or 34 in the preschool tested SARS-CoV-2 positive by RT-PCR. The 3rd cluster was an adult staff member at a preschool. Up to 16 staff members were infected. 77 children (8 symptomatic) all tested negative.

			The 23% of children not swabbed did not develop symptoms.
(National Centre for Immunisation Research and Surveillance, 2020) <i>new</i>	COVID-19 in schools – the experience in NSW	In New south Wales between March and Mid-April 9 students and 9 staff from 15 different schools were diagnosed with SARS-CoV-2 infection. 735 students and 128 staff were close contacts.	<ul style="list-style-type: none"> • 2 children were potential secondary cases. • Most of the cases and observations were from high schools (12 cases/ 695 contacts). 235 contacts received RT-PCR tests and 75 received serology tests 30 days post exposure. One serology test was positive. • 1/263 close contact (53 tested) was identified from all the close contacts of 6 cases across 5 primary schools.
(Heavey, Casey, Kelly, Kelly, & McDarby, 2020) <i>new</i>	No evidence of secondary transmission of COVID-19 from children attending school in Ireland, 2020	The retrospective epidemiological investigations here targeted any case that had attended schools as a student or employee prior to school closures (Mar 12) in Ireland. Only symptomatic contacts were tested.	<ul style="list-style-type: none"> • 3 adults and 3 children had 1155 contacts between school, sports, music (woodwind instruments) and choir practice. • Only 1 transmission event was detected, this occurred outside of school between 2 infected adults and a susceptible adult.
(Armann et al., 2020) <i>new</i>	Anti-SARS-CoV-2 IgG antibodies in adolescent students and their teachers in Saxony, Germany (SchoolCoviDD19): very low seroprevalence and transmission rates	Seroprevalence survey conducted in eastern Saxony Germany among 13 secondary schools (grade 8-11) May 25- June 30, 2020. Anti-SARS-CoV-2 IgG were assessed using 3 assays starting with Diasorin Liaison, Abbott Diagnostics and Euroimmun to confirm results. 1538 students and 507 teachers participated in this study. The community PCR confirmed prevalence was 0.15% (based on surveillance data).	<ul style="list-style-type: none"> • Overall seroprevalence was 0.6% <ul style="list-style-type: none"> ○ Students 0.7%, 12/1538 (5 had confirmed COVID-19 and 22 had family members with confirmed COVID-19) ○ Teachers 0.2%, 1/507 (2 had family members with confirmed COVID-19) • No clusters of cases were identified even from schools with COVID-19 cases prior to lockdown (March 13). • This paper concludes that students and teachers do not seem to play a crucial role in driving SARS-CoV-2.
(Fontanet et al., 2020) <i>new</i>	SARS-CoV-2 infection in primary schools in northern France	Retrospective cohort in France. Serological tests and questionnaire data were collected April 28-30 to measure exposure among	<ul style="list-style-type: none"> • Infection attack rate (IAR), no difference between groups (P = 0.29) <ul style="list-style-type: none"> ○ Students (primary school 6-11 yo) 45/510 (8.8%) ○ Teachers 3/42 (7.1%)

		<p>primary school families and staff from February/March 2020. Before school closures Feb 14 there were 3 infected students.</p>	<ul style="list-style-type: none"> ○ Non-teaching staff 1/28 (3.6%) ○ Parents 76/641 (11.9%) ○ Relatives 14/119 (11.8%) ● Familial clustering of cases was documented by the high proportion of antibodies among parents (61.0% versus 6.9%; $P < 0.0001$) and relatives (44.4% versus 9.1%; $P = 0.002$) of infected pupils. ● Asymptomatic cases were reported in 41.4% of children and 9.9% of adults. Only 2 adults were hospitalized in this study group.
<p>(Torres et al., 2020) <i>new</i></p>	<p>SARS-CoV-2 antibody prevalence in blood in a large school community subject to a COVID-19 outbreak: a cross-sectional study</p>	<p>Santiago Chile outbreak March 12 (10 days after schools opened). 52 cases from a large school community (K-12, N=2950) were identified. The school was closed and the community was quarantined. Seroprevalence survey was conducted May 4-19 of all students and staff. Test used: The Novel Coronavirus (2019-nCoV) IgG/IgM Test Kit (Colloidal gold) from Genrui Biotech Inc, China, High school students had a significantly lower seropositivity ($p=0.01$) than other students. Among seropositive cases 40% (95%CI: 30-50%) of students and 18% (95%CI: 8-34%) of staff reported no symptoms.</p>	<ul style="list-style-type: none"> ● N=1009 students, 235 staff were included in the study <ul style="list-style-type: none"> ○ Preschool 12.3% (95%CI 7.8-18.6), N=147 ○ Elementary 10.8% (7.81-14.7), 286 ○ Middle School 11.9% (8.81-15.9), 295 ○ High School 5.7% (3.6-8.9), 281 ○ Teachers 20.6% (14.7-27.6), 165 ○ Support Staff 7.1% (2.4-15.9), 70 ● Students had a higher seropositivity than staff $p=0.003$. ● The primary school had higher seropositive staff and analysis of contact rates indicated children with more contacts were more likely to be seropositive. ● Sources with the greatest likelihood of possible contagion in students were: a home caregiver (OR: 27.9), a household relative (OR: 5.4), a classmate (OR: 3.2), and teacher (OR: 2.2) <p>This study attributes the age distribution to preschool parent-teacher meetings.</p>
<p>(Fontanet, Tondeur et al., 2020) <i>preprint, new</i></p>	<p>Cluster of COVID-19 in northern France: a retrospective</p>	<p>After 2 cases from a high school were identified in Oise France, part of the epicenter, a retrospective seroepidemiology study was conducted March 30- April 4th to</p>	<ul style="list-style-type: none"> ● 452/661 participants reported symptoms. ● 10 participants were hospitalized (9 were SARS-CoV-2 seropositive) and there were no deaths. <p>Serology Results:</p> <ul style="list-style-type: none"> ● 171/661 had antibodies

	<p>closed cohort study</p>	<p>investigate the pupils, teaches and non-teaching staff serology levels. Response rate was 37%, this low level of participation may reflect a bias in the sample. They also sampled a nearby blood bank for comparison.</p>	<ul style="list-style-type: none"> • IAR of 25.9% (95%CI; 22.6-29.4) <ul style="list-style-type: none"> ○ Pupils = 38.3% ○ Teachers = 43.4% ○ Non-teaching staff = 59.3% ○ Parents = 11.4% ○ Siblings = 10.2% • IFR 0% (one-sided 97.5% CI:0 - 2.1). • Hospitalization rate 5.3% (95%CI: 2.4 –9.8). • The blood donor samples had seropositive rates of (3.0%, 95%CI = 1.1- 6.4). • Based on the epidemiological information there appears to have been an outbreak at this high school from the last week of January to mid-February when schools closed.
<p>Synthesis Research</p>			
<p>(Li et al., 2020)</p>	<p>The role of children in transmission of SARS-CoV-2: a rapid review</p>	<p>Rapid Review (search date Apr30): Evidence for four categories: 1) studies reporting documented cases of SARS-CoV-2 transmission by infected children; 2) studies presenting indirect evidence on the potential of SARS-CoV-2 transmission by (both symptomatic and asymptomatic) children; 3) studies reporting cluster outbreaks of COVID-19 in schools; and, 4) studies estimating the proportions of children infected by SARS-CoV-2.</p>	<ul style="list-style-type: none"> • 16 studies included • Conclusions: <ul style="list-style-type: none"> ○ Case series and outbreak reports detailing transmission in children are few. Those studies which are available demonstrate that transmission by children is possible but do not quantify the likelihood of transmission in children compared to adults. ○ There is little evidence on transmission dynamics in school settings. Given the current paucity of data, further investigation and close monitoring will be essential where schools have re-opened and in settings where schools have remained open. ○ Children are infected, but perhaps less frequently than adults.

(Ludvigsson, 2020a)	Children are unlikely to be the main drivers of the COVID-19 pandemic: a systematic review	Systematic review up to May 12, (no protocol, data extraction or quality assessment = low quality). The authors screened 600 papers to identify key papers for the review.	<ul style="list-style-type: none"> • Children make up a small percentage of cases across studies. • Children tend to have milder disease. • Children are rarely the index case in household transmission events. • Even asymptomatic children have viral loads, but opening daycares and schools is unlikely to have an impact on the bigger picture of mortality.
(Viner et al., 2020) <i>preprint</i>	Susceptibility to and transmission of COVID-19 amongst children and adolescents compared with adults: a systematic review and meta-analysis	Rapid systematic review up to May 16. Includes 18 studies on contact tracing and population screening. The analysis dichotomized age at <20 yo.	<ul style="list-style-type: none"> • Pooled odds ratio of being an infected contact in children compared with adults for all contact tracing studies was 0.44 (0.29, 0.69). • There was heterogeneity across countries in terms of the proportion of children infected. • There is weak evidence that children and young people play a lesser role in transmission of SARS-CoV-2 at a population level.
(Zhu et al., 2020)	Children are unlikely to have been the primary source of household SARS-CoV-2 infections	A review of the literature up to March 31. They looked for evidence of the role of children in transmission of SARS-CoV-2.	<ul style="list-style-type: none"> • 3/31 clusters investigated had a pediatric index case. This suggests that children are not the primary source of household transmission.

IAR= Infection Attack Rate, IFR= Infection fatality rate, CI= confidence interval.

One of the hypotheses suggested to explain why children seem to transmit SARS-CoV-2 less frequently than adults is that their viral load may be lower. Three studies were included in this review, two used RT-PCR cycle counts to estimate viral load and the third cultured virus from RT-PCR positive samples. All three studies (Table 2) sampled only symptomatic cases, and all agreed that the viral load was not different from adults.

Two case studies (Table 2) of several SARS-CoV-2 infected children failed to detect transmission to their caregivers, with the possible exception of an infant who may or may not have been the index case in her family.

Studies measuring the proportion of SARS-CoV-2 infection in children have consistently reported lower infection prevalence compared to adults regardless of whether the sampling frame is targeted at potentially exposed, high risk populations or targeted at the general population (Desmet et al., 2020; Gudbjartsson et al., 2020; Johansen et al., 2020; Ludvigsson, 2020b)

Table 2: Nine studies that describe viral load (n=3) and proportion of SARS-CoV-2 by age group or SARS-CoV-2 case studies (n=2) of transmission and synthesis of research (n=1) on children

Reference	Title	Study Description	Key Outcomes
Viral Load in Samples from Symptomatic Cases of Different Age Groups			
(Baggio et al., 2020) <i>preprint, new</i>	SARS-CoV-2 viral load in the upper respiratory tract of children and adults with early acute COVID-19	Switzerland, single center cross-sectional study of viral load among children and adults tested within 5 days of symptom onset by RT-PCR. Data collected March 10-May 26. N=405	<ul style="list-style-type: none"> • Viral load in log10 RNA copies/mL, <ul style="list-style-type: none"> ○ Child (0-11 yo): 6.13 ± 2.02 (range 3.06-9.21) ○ Adolescent (12-19 yo): 5.85 ± 2.32 (range 2.36-9.42) ○ Young adult (20-45 yo): 5.91 ± 1.88 (range 2.37-9.39) ○ Adult (>45 yo): 6.33 ± 2.05 (range 2.49-9.39) • No correlation between viral load and age was found in this study.
(L'Huillier, Torriani, Pigny, Kaiser, & Eckerle, 2020) <i>new</i>	Culture-competent SARS-CoV-2 in nasopharynx of symptomatic neonates, children, and adolescents	Switzerland, case series of 23 children. They cultured SARS-CoV-2 from the upper respiratory tract samples between Jan 25- Mar 31. 23/638 patients <16 years were SARS-CoV-2 positive. Samples were collected a median of 2 days post symptom onset.	<ul style="list-style-type: none"> • 12/23 children had virus that could be cultured. <ul style="list-style-type: none"> ○ Median viral RNA load (VRL) at diagnosis was 3.0×10^6 copies/mL ○ Mean VRL 4.4×10^8 [IQR 6.9×10^3–4.4×10^8] copies/mL ○ Peak VRL 5.3×10^9 copies/mL • The data show that viral load at diagnosis is comparable to that of adults, and that symptomatic children of all ages shed infectious virus in early acute illness.

<p>(Jones et al., 2020)</p>	<p>An analysis of SARS-CoV-2 viral load by patient age</p>	<p>Jan 1 to Apr 26 virology laboratories at Charité, Berlin screened 59,831 patients for COVID-19 infection, 3,712 (6.2%) with a positive real-time RT-PCR result. School groups: kindergarten (ages 0-6), grade school (ages 7-11), high school (ages 12-19), university (ages 20-25), adult (26-45 years), and mature (age over 45).</p>	<ul style="list-style-type: none"> • Although there were fewer children tested than adults, the proportion positive: <ul style="list-style-type: none"> ○ By 10 year blocks, <ul style="list-style-type: none"> ▪ 1-10 yo=2.25% ▪ 11-20 yo=3.9% ▪ adult age groups 4.96-6.25% ▪ elderly 7.8-10.69% ○ By school group, <ul style="list-style-type: none"> ▪ kindergarten =2.10% ▪ grade school =2.57% ▪ high school 4.13% ▪ university 5.82% ▪ adults 5.27% ▪ mature adults 7.56% • Viral load was reported to be not significantly different across age groups by the author. • The viral load was back translated to: 43k 1-10 yo, 63k 11-20 yo, 183k 21-30 yo, 164k 31-40 yo. P=0.008 by kurkal-wallis test.
<p>Case studies</p>			
<p>(Wongsawat et al., 2020)</p>	<p>Risk of novel coronavirus 2019 transmission from children to caregivers: a case series</p>	<p>This study reports on 3 cases in children in Thailand. The children were exposed by an infected family member.</p>	<ul style="list-style-type: none"> • Caregivers of the mildly sick children did not develop an infection to SARS-CoV-2.
<p>(Cai et al., 2020)</p>	<p>A case series of children with 2019 novel coronavirus infection: clinical and epidemiological features</p>	<p>Case series of pediatric cases. N=10 describes the clinical course of each case. One case may have transmitted to her parents, although it is plausible that she had a shorter incubation period.</p>	<ul style="list-style-type: none"> • A 3 month old infant that became ill with COVID-19 prior to her parents. They were from Wuhan and exposure of the infant is unknown.

Only Report on Proportion of Children Infected with SARS-CoV-2			
(Gudbjartsson et al., 2020)	Spread of SARS-CoV-2 in the Icelandic population	This study describes the results of two sampling techniques in Iceland. 1) symptom/contact history and 2) population screening.	<ul style="list-style-type: none"> Targeted testing of children: (<10 years) 38/564 positive (6.7%) vs. older ages 1183/8635 (13.7%). There was a gradual increase in the proportion that tested positive between 10 and 20 years. The population screening group detected 0/848 children positive vs. 100/12232 (0.8% 95%CI 0.7-1.0) in older ages groups, this is despite the school remaining open in Iceland. Children in Iceland had lower positive tests compared to other age groups despite not closing their schools.
(Johansen et al., 2020)	Infection prevention guidelines and considerations for paediatric risk groups when reopening primary schools during COVID-19 pandemic, Norway, April 2020	Summary of a risk assessment and IPC guidelines developed by the Norwegian Institute for Public Health. Data up to May 11	<ul style="list-style-type: none"> 8135 COVID-19 cases in Norway <ul style="list-style-type: none"> 0-5 yo 0.9%, n=72 6-13 yo 2.0%, n=162 14-19 yo 4.2%, n=341 >19 yo 93%, n=7560 The rest of the document includes guidelines for school re-opening.
(Desmet et al., 2020)	No SARS-CoV-2 carriage observed in children attending daycare centers during the first weeks of the epidemic in Belgium	An on-going study in Belgium of nasopharyngeal carriage in daycare children was on-going at the start of the epidemic. From March 2-12 samples collected across 8 daycare centers were tested for SARS-CoV-2.	<ul style="list-style-type: none"> 0/84 positive samples from children age 6 months to 30 months. There was no evidence of SARS-CoV-2 transmission at these daycare facilities.
Synthesis Research			

(Ludvigsson, 2020b)	Systematic review of COVID-19 in children show milder cases and a better prognosis than adults	A systematic review of COVID-19 in children including evidence (45 papers) up to March 18.	<ul style="list-style-type: none"> The proportion of cases that were <19 yo was small across countries. In China 2% (n=44672 cases) were 0-19 yo. Italian reported 1.2% (n=22 512 cases) were children. This is consistent with SARS where 6.9% of cases were children and none died (Caselli & AricÃ², 2020).
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THE IMPACT OF RELAXING INTERVENTION MEASURES BY TARGETING DIFFERENT AGE GROUPS

Six publications use mathematical models to investigate the impact of relaxing intervention measures by targeting different age groups on the epidemic (Table 1). In the context of re-opening schools, two mathematical models demonstrate that allowing younger children (pre-school and primary school aged) to return to school would have the smaller impact on R, whereas the return of secondary school grades will have the greatest impact (Di Domenico et al., 2020; Keeling et al., 2020). A more recent model examines several European countries and estimates that countries with low transmission and high intensity interventions for controlling the epidemic can fully reopen schools, however if community transmission is high, then care should be taken to re-open schools slowly (Stage, Shingleton, Ghosh, & et al., 2020).

Of the three models that analyzed lifting interventions by age groups, results suggest that relaxing measures by age group could reduce the impact of COVID-19. Specifically, releasing younger individuals (0-19) from strict lockdown would result in lower overall fatality rates compared to the simultaneous release of all individuals after a lockdown (Castilho et al., 2020; Zhao & Feng, 2020).

Table 3: Six publications that investigate the impact of relaxing intervention measures by targeting different age groups on the epidemic.

Reference	Publication Title	Study Description	Key Outcomes
Returning to School			
(Stage et al., 2020)	Shut and re-open: the role of schools in the spread of COVID-19 in Europe	Investigates the effect of school closure and subsequent reopening on the transmission of COVID-19, by considering Denmark, Norway, Sweden, and German states as case studies.	<ul style="list-style-type: none"> The effect of school closure on growth rate of the epidemic has a noticeable reduction in the growth rate approximately 9 days after implementation. Large-scale reopening of schools while controlling or suppressing the epidemic appears feasible in

			<p>countries such as Denmark or Norway, where community transmission is generally low.</p> <ul style="list-style-type: none"> • School reopening can contribute to significant increases in the growth rate in countries like Germany, where community transmission is relatively high.
(Keeling et al., 2020) <i>preprint</i>	The impact of school reopening on the spread of COVID-19 in England	Using an SEIR model, eight strategies for reopening primary and secondary schools in England starting on June 1 were analyzed.	<ul style="list-style-type: none"> • The study predicts that reopening schools with half class sizes, or that is focused on younger children is unlikely to push R above 1, although there is noticeable variation between the regions of the country. • Since older children have a greater number of social contacts and therefore a greater potential for transmission, reopening secondary schools results in larger increases in case burden compared to only reopening primary schools. • The more year groups allowed to return to school at one time, the greater the effect on R, with the return of secondary school grades having the greatest impact.
(Di Domenico et al., 2020) <i>preprint</i>	Expected impact of reopening schools after lockdown on COVID-19 epidemic in Île-de-France	This stochastic discrete age-structured epidemic model was used to assess the impact of reopening schools in the Île-de-France region of France after the withdrawal of lockdown scheduled for May 11. Authors explore several scenarios of partial, progressive, or full school reopening combined with moderate social distancing interventions and large-scale tracing, testing, and isolation.	<ul style="list-style-type: none"> • Results indicate that reopening all schools on this date would lead to a 2nd wave similar to the 1st and overwhelm the ICU system. • If just pre-schools and primary schools opened and middle/high schools reopen 1 month later following a progressive protocol, the ICU capacity would not be overwhelmed and would reach at most 72% capacity (95% CI: 55-83%). • There is no difference in the epidemic risk if pre-school and primary schools are reopened promptly or progressively, allowing full attendance for the younger children.

			<ul style="list-style-type: none"> • Full attendance for middle and high school students is not recommended.
Lifting Interventions by Age Group			
(Castilho et al., 2020) <i>preprint</i>	Assessing the efficiency of different control strategies for the Coronavirus (COVID-19) epidemic	This SEIR model was used to explore four different strategies to lift interventions in Brazil. These strategies based on age groups were analyzed using 3 age classes: children (0 to 19), adults (20 to 59), and elderly (60 to 100). The strategies include: 1) splitting the effort equally among the 3 groups, 2) stronger isolation (x2) of the elderly compared to infants/adults, 3) stronger isolation (x2) of infants/adults compared to the elderly, 4) stronger isolation (x2) of adults compared to infants/elderly.	<ul style="list-style-type: none"> • Results indicate that stronger isolation of the elderly compared to children and adults is the best strategy. • All other options result in 7.5% more deaths. • Authors also found that social distancing among adults has the greatest impact on R0.
(Scala, Flori, & Spelta, 2020) <i>preprint</i>	Between geography and demography: key interdependencies and exit mechanisms for COVID-19	This SIOR model analyzed the impact of mobility restrictions and age-based lockdowns in Italy during the outbreak.	<ul style="list-style-type: none"> • The most intensively interacting age-class are the young (0-19) and the old (70+). Mitigation strategies geared towards these two classes can produce a significant impact on diffusion rates in the post-lock down phase.
(Zhao & Feng, 2020) <i>preprint</i>	Staggered release policies for COVID-19 control: costs and benefits of sequentially relaxing restrictions by age	This SEIR model investigated the impact of sequential timing of relaxing restrictions across age groups in reducing health risks from COVID-19.	<ul style="list-style-type: none"> • Results show that releasing the least vulnerable group of a population before other groups will reduce the overall number of deaths. • A properly constructed sequential release of age-defined subgroups (young, middle-aged, old) from strict lockdown can lead to lower overall fatality rates compared to the simultaneous release of all individuals after a lockdown.

			<ul style="list-style-type: none"> • However, the timing of each step of the staggered release is very important. For example, releasing the middle-aged group too soon after releasing the young group would cause a drastic increase in infections and deaths.
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OTHER EVIDENCE SYNTHESIS PRODUCTS CONDUCTED TO LOOK AT TRANSMISSION AMONG DIFFERENT AGE GROUPS.

The synthesis products below were identified during our search. These products are part of the grey literature and inform the topic of transmission of SARS-CoV-2 in select age groups.

Table 3: Synthesis products that are up to date or evergreen and present information on transmission in different age groups.

Reference	Publication Title	Study Description	Key Outcomes
Rapid Review			
<u>NCCMT Rapid Review</u>	Rapid review: what is the specific role of daycares and schools in COVID-19 transmission?	Updated July 9, 2020 1. What is known about the likelihood of transmission of COVID-19 amongst children and adults in daycare and schools and among children to their household members? 2. What is known about likelihood of transmission of COVID-19 by infants, toddlers, and school-aged children to others in other settings?	<ul style="list-style-type: none"> • 23 publications are summarized that show some potential transmission of SARS-CoV-2 among children of different ages. No transmission among young daycare age children was identified. • A potential outbreak in a high school is described, however the results are based on serology 6 weeks after schools closed in an epicenter.
<u>COVID-Explained</u>	COVID-19 and children: our crowd-sourced data	Updated July 8, 2020. Researchers and students at Brown, MIT, Harvard, Mass General and elsewhere crowd sourcing data on COVID-19 in daycares and camps in the USA.	<ul style="list-style-type: none"> • They report 970 daycare settings with 27234 students and a total of 42 cases (0.15%). Among staff infections were 106/9587 (1.01%). • There is also information from camps.

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 literature on the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. The daily summary and full scan results are maintained in a Refworks database and an Excel list that can be searched. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. Search terms used included: age-dependent, children and transmission. This review contains research published up to July 20, 2020. Each potentially relevant reference was examined to confirm it had relevant data and relevant data is extracted into the review.

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