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Title: The role of children (0-18 years of age) in the transmission of SARS-CoV-2: rapid review	
<p>Questions:</p> <ol style="list-style-type: none"> 1. Can children get infected by SARS-CoV-2 and do they present with similar symptoms as adults? 2. Do children more commonly present with asymptomatic than with symptomatic disease? 3. Is there an age-dependent risk of severe disease progression? 4. Can children transmit SARS-CoV-2 and to what extent is this transmission driving the pandemic? 5. Is the risk of children getting infected by SARS-CoV-2 comparable to the risk of adults? 6. Are school closures (i) creche (Kita)/kindergarden to 9th year of schooling (compulsory school) and/or (ii) high schools, universities, higher education institutions an effective way of slowing the pandemic? 	
<p>Summary:</p> <ol style="list-style-type: none"> 1. Children get infected by SARS-CoV-2, but usually develop milder symptoms than adults. 2. While there are asymptomatic pediatric SARS-CoV-2 cases, a majority of pediatric patients develops symptomatic disease. 3. To date there are only limited data and thus only inconclusive evidence that <1 year olds might have a higher risk of severe disease progression. 4. There is only limited evidence as to what extent children transmit SARS-CoV-2. Their role in transmission remains largely open. However, all the available evidence shows that children are not the main drivers of this pandemic. 5. There are several studies showing that children are possibly less prone to getting infected by SARS-CoV-2. 6. School closures can be an effective way of transmission control if a pandemic is driven by children. Whether school closures have a substantial effect on limiting transmission of SARS-CoV-2 remains unclear, but as children seem to not be driving the SARS-CoV-2 pandemic, school closures are probably only of little effect slowing this pandemic. 	

Main text: The role of children and adolescents in the transmission of SARS-CoV-2 remains uncertain impacting policy decision especially concerning opening schools, kindergardens or day care facilities and intergenerational contacts in general. While SARS-CoV-2 disproportionally affects the elderly (>65 years old), who have a higher risk of severe disease progression, children and adolescents seem to usually develop mild and less severe symptoms (Ludvigsson et al. (2020); Morand et al. (2020)). There are several case reports describing potential infection of children by adults, while some studies also claim evidence for transmission of SARS-CoV-2 by children (Cao et al. (2020) and Cai et al. (2020)). Analyzing the original sources (Cai et al. (2020) in Chinese) however does not confirm this potential evidence with for example Cao et al. (2020) stating that the “accumulated cases from adult and pediatric populations strongly supports [sic] the transmission dynamics of pediatric patients” by interpreting, at best, indirect evidence only.

Understanding the pediatric transmission factor and children’s contribution to the pandemic progression is important for adapting and improving the control measures.

We conducted a rapid systematic review by searching Pubmed and medRxiv up to 1 May 2020. We screened 239 studies of which 14 were eligible. Doing manual search we found another 30 articles (18 published, 12 not yet published or peer-reviewed or both), which we also analyzed. Of these 44 articles 27 were case reports, 6 were cross sectional studies, 1 was a cohort study, 7 were reviews or viewpoints and 3 were modelling studies (see also Annex with tables on search and qualification of studies).

Question 1. Can children get infected by SARS-CoV-2 and do they present with similar symptoms as adults?

Pediatric SARS-CoV-2 cases were described from the early beginnings of the pandemic (Liu et al. (2020)). Compared to adults however children usually only develop mild symptoms of the disease (Ludvigsson et al. (2020); Morand et al. (2020); Lu et al. (2020); Dong et al. (2020)) which might lead to false low case numbers as most countries only test or (at the beginning of the pandemic) tested the more severely sick or people at risk for severe disease (e.g. Italy, Switzerland, China).

The reasons for this comparably mild disease progression are not yet completely understood, but possible explanations include (Dong et al. (2020)):

- Reduced maturity and lower function of the ACE2 receptor (which is necessary for SARS-CoV-2 to infect cells) in children than in adults
- Children often experiencing respiratory infections (e.g. respiratory syncytial virus) in winter and thus possibly having higher levels of antibodies and potential crossreactivity against the virus than adults
- Children potentially displaying a different immune response to pathogens (compared to adults) as their immune system is still developing
- Children having less developed immunity hence also less immunopathology

Question 2. Do children more commonly present with asymptomatic than with symptomatic disease?

As children present with a milder disease version and are thus not the main focus of medical interventions, there is comparably little data about pediatric disease progression and the available data might therefore not represent the whole spectrum. Data from Italy for example show that children only make up for 1.2% of all cases, which could be an underreported low number that just shows that children present with a milder disease and do thus not get tested as often (Livingston et al. (2020)).

The percentage of asymptomatic children is described in several publications, all relatively small in size ($30 < n < 172$), as 15-39% (e.g. Lu et al. (2020); Qiu et al. (2020); Chen et al. (2020) (unpublished)). However, it appears that primarily treated or hospitalized patients were analyzed in China, thus potentially skewing the data as children not fitting the testing criteria at that point might not have been included.

A larger China-wide case series performed by Dong et al. (2020) analyzing suspected and confirmed pediatric SARS-CoV-2 cases indicates that only 1.9-6.5% of these cases are completely asymptomatic, with the highest rate of asymptomatic patients in the 11-15 year age bracket and the lowest rate in the <1 year olds. As 2/3 of the study population is not laboratory confirmed but just suspected due to clinical symptoms, blood counts indicative of a viral infection or suspicious chest imaging results, this data could be distorted by other respiratory viruses. Nevertheless, when just analyzing the confirmed cases only 12.9% of these are completely asymptomatic, while a majority displays mild (43.1%) or moderate (40.9%) symptoms.

This is supported by a review by Choi et al. (2020), which shows that only a minority of the infected children is asymptomatic (0-12%), while a majority has at least symptoms of an upper respiratory tract infection (20-65%) or a mild pneumonia (26-80%). Lu et al. (2020) also show that a majority of pediatric patients presents with the symptoms of an upper respiratory tract infection (19.3%) or pneumonia (64.9%).

A study by Lavezzo et al. (2020) (unpublished) in Vo', Italy, showed a comparably higher number of asymptomatic patients (43.2%) for the whole population. As there were no cases of children <10 years old and only 1.0-1.2% in the 11-20 year age bracket, adults seem to present with asymptomatic disease more often than children. While there are also studies showing a lower percentage of asymptomatic adult patients (Zhu et al. (2020)a), children do not appear to be silent virus spreaders as a majority of them still presents with symptomatic disease.

Question 3. Is there an age-dependent risk of severe disease progression?

While most children are usually only mildly sick (Ludvigsson et al. (2020); Morand et al. (2020); Lu et al. (2020)), <1 year olds seem to have a higher rate of severe or critical disease (10.6% for <1 year olds vs. 7.3% for 1-5 year olds) (Dong et al. (2020)). As mentioned in the discussion of Question 2, this study could have been distorted by other respiratory viruses as 2/3 of patients are only suspected and not laboratory confirmed. It seems however to be supported by a CDC report highlighting that the worse disease progression in children occurs in <1 year olds, as these patients "accounted for the

highest percentage (15-62%) of hospitalization among pediatric patients” (CDC COVID-19 Prevention Team (2020)).¹ Due to the fact that more detailed data about children’s hospitalization status are missing (only known in 29% of all pediatric cases) this data may be distorted.

However despite there only being case reports or studies with low patient numbers, the risk for neonates to develop severe disease seems to be low. A retrospective single-centre study by Yu et al. (2020)a describes 7 newborns with SARS-CoV-2 positive mothers. While 4 infants were not tested for SARS-CoV-2 due to unknown reasons, 3 infants were tested of whom 1 tested positive after 36 hours. This infant only had mild shortness of breath, mild signs of pulmonary infection in pulmonary imaging and was apart from this not symptomatic but healthy, as were the other 6. This is supported by another retrospective study by Zhang et al. (2020)b describing 4 SARS-CoV-2 positive neonates, who only displayed mild symptoms and did not need intensive medical care.

A case report by Nathan et al. (2020) describes 5 SARS-CoV-2 positive infants “with poorly tolerated and isolated fever” and neurological symptoms, who recovered quickly and could be discharged in between 1-3 days after admission. This could indicate that even if an infant develops severe SARS-CoV-2 they seem to tolerate and recover from it much better and much faster than adults.

In addition, preliminary results from the Dutch National Institute for Public Health and the Environment (RIVM) suggest that underlying health conditions of children do not seem to increase the risk of severe disease “*with the possible exception of children with severe obesity and or diabetes*”.

The suggestion that even profound underlying health conditions are not risk factors for severe SARS-CoV-2 disease is supported by a report by Balduzzi et al. (2020) describing the mild SARS-CoV-2 disease progression of 5 pediatric cancer patients in Lombardia, Italy. They also mentioned that until now no deaths or severe SARS-CoV-2 disease progressions are reported for pediatric cancer patients in the whole of Italy.

In summary, there is only inconclusive data about a possible age dependent risk for severe disease progression in children. Underlying health conditions however seem to not pose an increased risk.

Question 4. Can children transmit SARS-CoV-2 and to what extent is this transmission driving the pandemic?

¹ Jones et al. (2020)b report the first case of an infant presenting with classic Kawasaki disease, who also tested positive for SARS-CoV-2. In addition, NHS England (based on a single cluster in South East England described by Riphagen et al. (2020)) reported a small increase in critically ill children presenting with “features of toxic shock syndrome and atypical Kawasaki disease with blood parameters consistent with severe COVID-19 in children”. It needs to be highlighted that while only some of these patients tested positive for COVID-19, Kawasaki syndrome usually presents after a viral infection. It needs to be mentioned that this phenomenon has not yet been studied and no causality with COVID-19 has been established so far. (“PICS Statement Regarding Novel Presentation of Multi-System Inflammatory Disease.” Paediatric Intensive Care Society, April 27, 2020. <https://picsociety.uk/wp-content/uploads/2020/04/PICS-statement-re-novel-KD-C19-presentation-v2-27042020.pdf>.)

There is no conclusive evidence as to what extent children can transmit SARS-CoV-2. While some case studies claim that children play a role in the transmission dynamics, the underlying evidence of these studies, as mentioned at the beginning, is either indirect or questionable. For example, Cao et al. (2020) and Cai et al. (2020) report “*what is probably the first evidence indicating children as a source of adult infection*”. This however can not be confirmed when checking the report’s original source (in Chinese). Cao et al. (2020) also state that the “*accumulated cases from adult and pediatric populations strongly supports [sic] the transmission dynamics of pediatric patients*” namely the potential spread within schools as a connector among community nuclei (e.g. families) by analyzing only indirect evidence of the epidemic in China. In contrast, analysis of all available data from family clusters indicate that children were infected by adults first and not by children, who transported the infection into the family from the outside or from schools (Qian et al. (2020); Danis et al. (2020); Qiu et al. (2020); Li et al. (2020)b; Su et al. (2020)).

While several reviews highlight the possibility that children could play a prominent role in virus transmission as they mostly only display mild symptoms (Kelvin and Halperin (2020); CDC COVID-19 Prevention Team (2020)), there is no direct evidence that children can transmit SARS-CoV-2 and “no transmission of the SARS-CoV-2 virus from children to adults has been described to date” (Morand et al. (2020)), thus indicating that pediatric infections do not drive the pandemic.

A retrospective study by Jones et al. (2020)a (not yet peer-reviewed) claims to show no significant differences in viral loads between age groups, including children and adolescents. This would suggest that children are potentially equally infectious as adults.² The study however is not conclusive. First, Jones et al. (2020)a did not specify the specimen from which the viral RNA was isolated. As Zou et al. (2020), Yu et al. (2020)b and Wang et al. (2020) showed, Ct values, which were used to calculate the viral loads of different specimens, are not comparable. Second, Jones et al. (2020)a compared 49 children (0-10 years of age) and 78 adolescents (11-20 years of age) with 3585 adults, finding no significant difference in viral loads. A reanalysis by independent biostatisticians suggests that there is moderate evidence for increasing viral load with increasing age. Due to small sample sizes in the younger age groups, and thus limited power of the statistical tests, a definitive conclusion on whether viral load does or does not increase with age appears difficult to reach based on these data.

A cohort study by Fontanet et al. (2020) (not yet peer-reviewed) appears to show a SARS-CoV-2 cluster in a school in Oise, northern France with a higher infection attack rate (IAR) for adolescents (15-17 years old) than for adults (≥ 18 years old). To assess the cluster and calculate attack rates they used their own, not externally validated antibody tests. Having a closer look at the data shows that Fontanet et al. (2020) must have included other children and adolescents (probably siblings) in the student population. Thus, an analysis of attack rate generated for this mixed groups of students and (probably) siblings (most likely not enrolled at the school as they would otherwise not have counted as contacts of the respective students) cannot support a conclusion that transmission started and spread at the school. Additionally, the 2 index cases were not laboratory confirmed

² A small study by L’Huillier et al. (2020) (not yet peer-reviewed) analyzed the viral load of 23 symptomatic infants, children and teenagers, but no adults. The infants, children and teenagers showed viral loads comparable to those of adults in other studies in other locations. Virus isolation, as a marker for infectiousness, however was only successful in 12 of these 23 cases with the small sample size limiting the power of the study.

but appear to have been only clinically diagnosed with SARS-CoV-2 related symptoms after having been in contact with a laboratory confirmed case. As (i) they could thus also have had another non-SARS-CoV-2 infection and (ii) as there is no further information about their status (e.g. student, teacher, school staff) or with whom they interacted more closely (e.g. class mates, sport groups), the SARS-CoV-2 -cluster at the school might not have been caused by them. These limitations do not allow to add further evidence to the role of children in SARS-CoV-2 transmission.

There is however evidence that children might not be as infectious as adults when infected with SARS-CoV-2. Danis et al. (2020) describe a pediatric patient who was infected while on holidays in France and despite him being symptomatic did not infect even close contacts while visiting three schools when coming back to the UK. It is not further discussed in the paper why this child visited three schools. Further support comes from a not yet peer-reviewed study by Zhu et al. (2020)^b which analyzes SARS-CoV-2 household clusters world-wide and could show that only 9.7% of the clusters were started by a pediatric index case. Even if accounting for asymptomatic index cases or traveling to a high risk area (which is more likely to be undertaken by an adult) this changed to 21% respectively 9% of all cases.

Preliminary results from a report of the RIVM (Dutch National Institute for Public Health and the Environment) also indicate that children might be less infectious as data from contact tracing showed children and adolescents (0-19 years old) not infecting others (Fig. 1). As RIVM only tested symptomatic patients and focused on testing high-risk patients, the number of tested children is low, which in turn limits the power of the study.

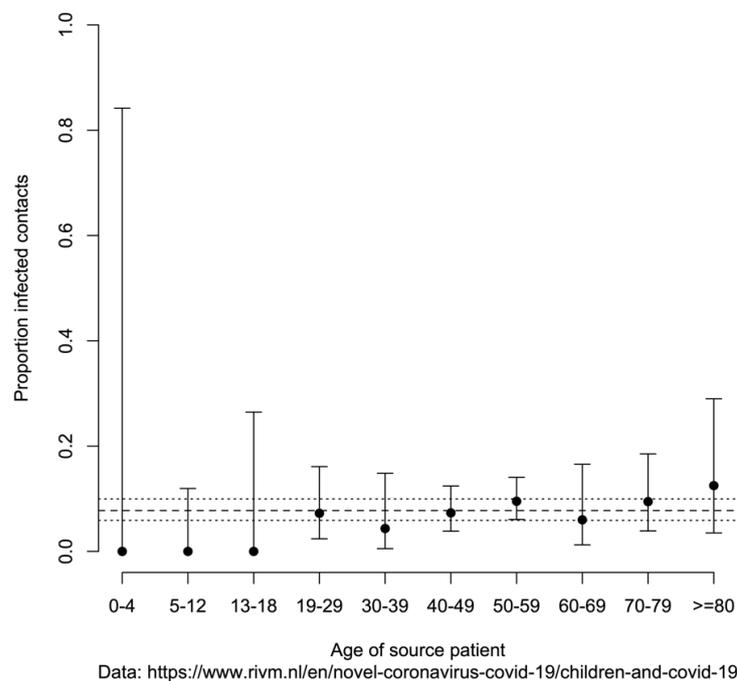


Figure 1: Proportion of infected contacts according to the age of the index patient. Horizontal lines indicate the average proportion of infected contacts (dashed line) and the 95% confidence interval (dotted lines). Bars indicate 95% confidence intervals for each age group. Data: <https://www.rivm.nl/en/novel-coronavirus-covid-19/children-and-covid-19>.

While there are reports describing asymptomatic or presymptomatic patients being infectious, further studies specifically targeting the infectiousness of children are missing.

Question 5. Is the risk of children getting infected by SARS-CoV-2 comparable to the risk of adults?

There is evidence that children do not get infected by SARS-CoV-2 as easily as adults. Li et al. (2020)^b present a case where a family member infected all of his close relatives except a child (aged 7 years), who stayed asymptomatic and was tested negative for SARS-CoV-2. A retrospective cohort study by Bi et al. (2020), analyzing 1286 close contacts of 391 index cases, however showed that the secondary attack rate for children <10 years was similar to adults (7.4% vs. 6.6%). Close contacts were defined as people who lived, traveled, had a meal, or socially interacted (no closer definition) with an index patient. A cohort study by Li et al. (2020)^a on the other hand, analyzing 392 household contacts of 105 index patients, calculated a much lower secondary attack rate (SAR) for children than for adults (4% vs. 17.1%), meaning that their risk of getting infected was lower than for adults. It is particularly interesting that the risk for smaller children (aged 0-5 years) was lower than for older children (aged 6-17 years) (SAR: 2.3% vs. 5.4%, respectively).

The hypothesis that children are less prone to infection by SARS-CoV-2 is supported by Jing et al. (2020) (not yet peer-reviewed), who analyzed 195 clusters from the epidemic in China and found that the probability of infection among children (<20 years old) was 0.26 times the probability of infection among the elderly (>60 years old). While this is a substantial reduction in probability, it must also be considered that the number of contacts among children – especially in schools – is considerably higher than among the elderly (e.g., Ferguson et al (2020) assumed the per-capita contacts within schools to be double those elsewhere), partially offsetting their reduced probability of infection. Mizumoto et al. (2020) (not yet peer-reviewed) also showed that the attack rate in household acquired cases was much lower for children (3.8%(females) - 7.2%(males)) than for adults aged 50-59 years (AR 21.9% (females) - 22.2%(males)). This was confirmed by Zhang et al. (2020)^a who analyzing the susceptibility of infection of close contacts reported a lower risk of infection for children (0-14 years old) compared to people older than 15 years of age.

A population-based study in Iceland by Gudbjartsson et al. (2020) also demonstrated that children (<10 years old) were infected with SARS-CoV-2 less often than individuals >10 years old. This was the case not only for the general population but also for higher-risk individuals (symptomatic, returning travelers from high-risk areas or contacts of infected people). In Vo', Italy, only 0.5-1.2% of the cases were 11-20 years of age and there were no cases in the 0-10 year age bracket, despite some children living together with confirmed adult cases (Lavezzo et al. (2020)) (not yet peer-reviewed).

Local cases in Switzerland (not yet published) seem to confirm these suspicions. In a creche in Riehen 77 children were exposed to a SARS-CoV-2 positive caretaker and while 14 of those children got sick in the second week of quarantine, none of them tested positive for SARS-CoV-2. In another example of a creche a SARS-CoV-2 positive care taker had contact with 10 children and 10 adults of whom none got sick. In schools in Basel City, no transmission was ever observed even if there were teacher index cases.

This is supported by a report of the National Centre for Immunisation Research and Surveillance (NCIRS) in New South Wales, Australia, where 18 initial cases (9 students and 9 teachers) in 15 different schools (primary and high schools) had close contact to 735 fellow students and 128 staff. None of the 128 staff contracted SARS-CoV-2 and the 2 initial cases (1 student and 1 staff) only infected 2 fellow students. Australia did not close schools but advised children to receive online learning at home, which resulted in fewer children physically attending the schools. This reduced attendance could in turn have influenced the results of the study. However despite the limitations of the report there does not seem to be a major risk of infection in schools and kindergardens.

It should be noted that Lazzerini et al. (2020) have observed that some parents are delaying potentially life saving treatments for their children fearing SARS-CoV-2 infections leading to severe disease and deaths. As children mostly present with mild disease, seem to be less prone to infection while potentially being less infectious when infected, there seems to be a higher risk of the perceived danger of SARS-CoV-2 and the consequent delay in life-saving treatment than the virus's actual danger to children.

Question 6. Are school closures (i) creche (Kita)/kindergarden to 9th year of schooling (compulsory school) and/or (ii) high schools, universities, higher education instutitons an effective way of slowing the pandemic?

In a modeling study that was not peer-reviewed, but frequently cited, Ferguson et al (2020) compare different non-pharmaceutical interventions finding that school closures alone would reduce total deaths by 2-4% and peak ICU bed demand by 14-21%. However, their modeling results apply for a high reproductive number R_0 of 2.2 and 2.4 and suggest that for a lower reproductive number of 1.0 or 0.6 (as is currently the case in Switzerland) school closure alone could reduce total deaths by 16-20%³.

Zhang et al. (2020) claim in another mathematical model that "social distancing alone, as implemented in China during the outbreak, is sufficient to control" SARS-CoV-2 with proactive school closures as part of other control measures potentially only further delaying the pandemic by reducing peak incidence by 40-60%. They showed that school closures alone could not stop the pandemic. They do however not explain what social distancing measures were analyzed and were using mixing patterns during school holidays and during regular weekdays excluding school contacts for their model. This limits the significance of the study as children do still socialize in these settings compared to the setting of social distancing.

In contrast, Davies et al. (2020) showed in another mathematical model (also not yet peer-reviewed) that school closures only have a limited effect in transmission and control of the pandemic in countries like Italy or the United Kingdom if children are as susceptible to infection as adults (independently of the transmission rate of asymptomatic patients). The effect is higher in countries with a higher proportion of children (like Zimbabwe).

Viner et al. (2020) saw no impact of school closures on transmission control during the SARS coronavirus epidemic. As school closures would only work if there is a high attack

³ This estimate is not contained in the paper by Ferguson et al, but obtained through a simple linear extrapolation of the reproductive number.

rate in children and if they have a high rate of transmitting the virus in schools (no evidence for previous coronavirus outbreaks) and due to the immense socio-economic cost of closing schools, Viner et al. (2020) propose a more gradual approach similar to Taiwan where schools are closed locally in case of an outbreak at school.

As universities and institutions of higher education are frequented by adults, who play a bigger role in driving the pandemic and as higher education is usually easier to do remotely and with less social disruption, closing universities and institutions of higher education seems to be more reasonable. There is however no evidence supporting this as data are missing.

Conclusions:

1. Evidence of the ability of children to either transmit the SARS-CoV-2 virus or not to transmit the SARS-CoV-2 virus is currently very sparse. While it appears that children are not the main drivers of this epidemic, their role in transmission remains open.

Thus,

2. We currently cannot provide strong conclusions on whether children can or cannot transmit the SARS-CoV-2 virus,
and we caution that
3. Absence of evidence is not evidence of absence: it cannot be assumed that children do not transmit the virus.

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Recommendations from the Task Force:

The absence of conclusive evidence for the role of children in transmission, together with the importance of developing policies for schools and other children-related activities on rapid timescales, **creates a situation of “decision under uncertainty”**. **It remains scientifically incorrect at this point in time to assume that “children do not transmit”**. Instead, **in the face of this uncertainty, we consider the adoption of a precautionary principle to be the appropriate stance**, *i.e.* we must accept the possibility that children may transmit the virus and adopt measures to minimize the consequences of this transmission. The use of the precautionary principle in this specific situation is also advocated by prominent organizations like the US Centers for Disease Control and Prevention which states that “social distancing and everyday preventive behaviors remain important for all age groups” (CDC COVID-19 Prevention Team (2020)). The Germany Academy of Sciences (Leopoldina) takes the precautionary stance that children can transmit the virus, and based on this stance elaborates a number of conditions and measures for school re-openings (Leopoldina 2020).

The question of whether and when to open schools under conditions of uncertainty is a conflict of values. All children have a right to free and *adequate* basic education that

is available to all children (Art. 19 and 62 of the Constitution). Pre-primary and primary education in distance learning is not sustainable and negatively affects the equality of chances. The longer the epidemic is expected to last, the more important it becomes to enable the right to education to be implemented without waiting for complete safety to return. In order to decrease the moral cost of schools re-opening, measures aimed at diminishing transmission within schools will need to be implemented. Accommodations for high-risk students, students living with high risk family members, and high-risk school staff will also need to be devised, and may include the continuation of distance learning in some cases. All approaches that are adopted should ensure equal access for disabled and low-income students.

Suggested policy measures for schools

Maintaining the usually recommended social distancing (> 2 m distance among individuals) in schools is challenging or nearly impossible, both due to the often-constrained spaces available and to the difficulty of children respecting social distances, particularly over extended periods of time. Therefore, school re-opening should be accompanied by substantial measures to minimize transmission and these measures should be clearly communicated to both school personnel and parents. Constant monitoring of transmission in schools and by children in particular should be the basis for subsequently relaxing these measures progressively.

Basic measures include:

- Children with symptoms stay at home
- Children take the most direct way from home to school and back
- Children and teachers avoid use of public transportation where possible, carry masks when using it
- Parents minimize time spent on school premises and strictly adhere to hygiene and social distancing rules if at school

Additional social-distancing measures should be strongly considered. A non-exhaustive list of measures to be considered but tailored to the specific school settings (infrastructure and resources) includes:

- Limit the number of children per class in schools (e.g. max 15)
- Limit the number of children per room in creches (Kitas) (e.g. max 5)
- Reduce the number of hours of school per day or the number of days of school per week, focusing only on core subjects (e.g. main language, mathematics, natural sciences)
- Prevent mixing among classes during recess, for example by staggering the time of recess by grade or defining separate recess areas
- Cancel high-contact activities (e.g. team sports)
- Stagger lunch hours or allow children to go home for lunch, including day schools
- Close or minimize participation of children in after-school settings (e.g. 'Hort')
- Continue home-schooling for an additional time period for higher grades like high schools, universities and higher education settings, i.e., reopen only creches (Kitas), kindergardens, primary schools and middle schools (the nine compulsory years).

These measures should at all times be supplemented with **strict hygiene measures** with frequent hand washing mandated by the schools, complemented by

- compulsory equipping of schools with hand-disinfection stations,
- no physical contact among children,
- no handshaking with teachers,
- avoidance of close assemblages in school procedures (e.g. “Morgenkreis”),
- more frequent cleaning of school toilets.

Open points for further discussion:

The absence of conclusive evidence for the role of children in transmission further highlights the urgency of obtaining robust data on this matter. This is recognized both nationally and internationally (e.g., Kelvin et al. (2020); Lu et al. (2020); Fineberg (2020)). Robustly determining the absence of a role of children in transmission will allow full school reopening, render social distancing measures in children less severe, and exclude that schools will negatively affect the reproductive number of the epidemic.

We thus urge that the re-opening of schools be accompanied by a real-time, rapid research protocol. This should involve repeat PCR and antibody testing among a sample of schoolchildren, teachers and other adult school employees to ascertain the presence of infection and the rate of acquisition of new infection among the children, and the monitoring of infection among the adults in closest contact with large groups of children. This approach can provide an early indication of spread of infection among and from schoolchildren.

References

Balduzzi, Adriana, Erica Brivio, Attilio Rovelli, Carmelo Rizzari, Serena Gasperini, Maria Luisa Melzi, Valentino Conter, and Andrea Biondi. “Lessons after the Early Management of the COVID-19 Outbreak in a Pediatric Transplant and Hemato-Oncology Center Embedded within a COVID-19 Dedicated Hospital in Lombardia, Italy. Estote Parati.” Bone Marrow Transplantation, April 20, 2020. <https://doi.org/10.1038/s41409-020-0895-4>.

Bi, Qifang, Yongsheng Wu, Shujiang Mei, Chenfei Ye, Xuan Zou, Zhen Zhang, Xiaojian Liu, et al. “Epidemiology and Transmission of COVID-19 in 391 Cases and 1286 of Their Close Contacts in Shenzhen, China: a Retrospective Cohort Study.” The Lancet Infectious Diseases, April 27, 2020. [https://doi.org/10.1016/s1473-3099\(20\)30287-5](https://doi.org/10.1016/s1473-3099(20)30287-5).

Cai JH, Wang XS, Ge YL, Xia AM, Chang HL, Tian H, et al., First case of 2019 novel coronavirus infection in children in Shanghai. Zhonghua Er Ke Za Zhi, 2020, 58: E002 [Article in Chinese]

Cao, Qing, Yi-Ching Chen, Chyi-Liang Chen, and Cheng-Hsun Chiu. “SARS-CoV-2 Infection in Children: Transmission Dynamics and Clinical Characteristics.” Journal of the Formosan Medical Association 119, no. 3 (2020): 670–73. <https://doi.org/10.1016/j.jfma.2020.02.009>.

Center for Disease Control and Prevention, COVID-19 Response Team, Coronavirus disease 2019 in children, Morbidity and Mortality Weekly Report, 2020, 69, 422-426 (April 10, 2020)

Chen, Chuming, Mengli Cao, Ling Peng, Xiaoyan Guo, Fangji Yang, Weibo Wu, Li Chen, Yang Yang, Yingxia Liu, and Fuxiang Wang. “Coronavirus Disease-19 Among Children

<p>Outside Wuhan, China.” SSRN Electronic Journal (Preprints with The Lancet), 2020. https://doi.org/10.2139/ssrn.3546071.</p>
<p>Choi, Soo-Han, Han Wool Kim, Ji-Man Kang, Dong Hyun Kim, and Eun Young Cho. “Epidemiology and Clinical Features of Coronavirus Disease 2019 in Children.” <i>Clinical and Experimental Pediatrics</i> 63, no. 4 (2020): 125–32. https://doi.org/10.3345/cep.2020.00535.</p>
<p>“Children and COVID-19.” RIVM (National Institute for Public Health and the Environment). Accessed April 29, 2020. https://www.rivm.nl/en/novel-coronavirus-covid-19/children-and-covid-19.</p>
<p>Danis, Kostas, Olivier Epaulard, Thomas Bénét, Alexandre Gaymard, Séphora Campoy, Elisabeth Bothelo-Nevers, Maude Bouscambert-Duchamp, et al. “Cluster of Coronavirus Disease 2019 (Covid-19) in the French Alps, 2020.” <i>Clinical Infectious Diseases</i>, 2020. https://doi.org/10.1093/cid/ciaa424.</p>
<p>Davies, Nicholas G, Petra Klepac, Yang Liu, Kiesha Prem, Mark Jit, and Rosalind M Eggo. “Age-Dependent Effects in the Transmission and Control of COVID-19 Epidemics.” <i>MedRxiv Preprint</i>, 2020. https://doi.org/10.1101/2020.03.24.20043018.</p>
<p>Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, Tong S, <i>Epidemiology of COVID-19 Among Children in China, Pediatrics</i>, 2020, 145: e20200702.</p>
<p>Ferguson NM et al., Report 9: Impact of non-pharmaceutila interventions (NPIs) to reduce COVID-10 mortality and healthcare demand, Imperial College COVID-19 Response Team, 16 March 2020</p>
<p>Fineberg, Harvey, personal communication, 17 Apr 2020 (Dr. Fineberg is a US physician and a Harvard Professor, a former Dean of Harvard’s Public Health School, a former President of US National Academy of Medicine, and the Chair of the Standing Committee requested by the White House in response to COVID-19; https://en.wikipedia.org/wiki/Harvey_V._Fineberg</p>
<p>Fontanet, Arnaud, Laura Tondeur, Yoann Madec, Rebecca Grant, Camille Besombes, Nathalie Jolly, Sandrine Fernandes Pellerin, et al. “Cluster of COVID-19 in Northern France: A Retrospective Closed Cohort Study.” <i>MedRxiv Preprint</i>, 2020. https://doi.org/10.1101/2020.04.18.20071134.</p>
<p>Gudbjartsson, D.F., A. Helgason, H. Jonsson, O.T. Magnusson, P. Melsted, G.L. Norddahl, J. Saemundsdottir, et al. “Spread of SARS-CoV-2 in the Icelandic Population.” <i>The New England Journal of Medicine</i>, April 14, 2020. https://doi.org/10.1056/NEJMoa2006100.</p>
<p>Jing Q-L et al., Household Secondary Attack Rate of COVID-19 and Associated Determinants, <i>medRxiv preprint</i>, 2020, https://doi.org/10.1101/2020.04.11.20056010.</p>
<p>Jones, Terry C., Barbara Mühlemann, Talitha Veith, Marta Zuchowski, Jörg Hofmann, Angela Stein, Anke Edelmann, Victor Max Corman, and Christian Drosten. “An Analysis of SARS-CoV-2 Viral Load by Patient Age.”(a) Accessed April 30, 2020. https://zoonosen.charite.de/fileadmin/user_upload/microsites/m_cc05/virologie-ccm/dateien_upload/Weitere_Dateien/analysis-of-SARS-CoV-2-viral-load-by-patient-age.pdf.</p>
<p>Jones, Veena G., Marcos Mills, Dominique Suarez, Catherine A. Hogan, Debra Yeh, J. Bradley Segal, Elizabeth L. Nguyen, Shiraz Maskatia, Roshni Mathew, and Gabrielle R Barsh. “COVID-19 and Kawasaki Disease: Novel Virus and Novel Case.” <i>Hospital Pediatrics (Pre-Publication Release)</i>, 2020b. https://doi.org/10.1542/hpeds.2020-0123.</p>

Kelvin AA, Halperin S, COVID-19 in children: the link in the transmission chain, <i>The Lancet</i> , 2020, Published online March 25, 2020, DOI: 10.1016/S1473-3099(20)30236-X
Lavezzo, Enrico, Elisa Franchin, Constanze Ciavarella, Gina Cuomo-Dannenburg, Luisa Barzon, Claudia Del Vecchio, Lucia Rossi, et al. "Suppression of COVID-19 Outbreak in the Municipality of Vo, Italy." <i>MedRxiv Preprint</i> , 2020. https://doi.org/10.1101/2020.04.17.20053157 .
Lazzerini, Marzia, Egidio Barbi, Andrea Apicella, Federico Marchetti, Fabio Cardinale, and Gianluca Trobia. "Delayed Access or Provision of Care in Italy Resulting from Fear of COVID-19." <i>The Lancet Child & Adolescent Health</i> 4, no. 5 (April 9, 2020). https://doi.org/10.1016/s2352-4642(20)30108-5 .
Leopoldina – Nationale Akademie der Wissenschaften, Dritte ad-hoc-Stellungnahme: Coronavirus-Pandemie – Die Krise nachhaltig überwinden, April 13th, 2020
L'Huillier, Arnaud G, Giulia Torriani, Fiona Pigny, Laurent Kaiser, and Isabelle Eckerle. "Shedding of Infectious SARS-CoV-2 in Symptomatic Neonates, Children and Adolescents." <i>MedRxiv Preprint</i> , 2020. https://doi.org/10.1101/2020.04.27.20076778 .
Li, Peng, Ji-Bo Fu, Ke-Feng Li, Yan Chen, Hong-Ling Wang, Lei-Jie Liu, Jie-Nan Liu, et al. "Transmission of COVID-19 in the Terminal Stage of Incubation Period: a Familial Cluster." <i>International Journal of Infectious Diseases</i> , 2020b. https://doi.org/10.1016/j.ijid.2020.03.027 .
Li, Wei, Bo Zhang, Jianhua Lu, Shihua Liu, Zhiqiang Chang, Peng Cao, Xinhua Liu, et al. "The Characteristics of Household Transmission of COVID-19." <i>Clinical Infectious Diseases</i> , 2020a. https://doi.org/10.1093/cid/ciaa450 .
Liu, Weiyong, Qi Zhang, Junbo Chen, Rong Xiang, Huijuan Song, Sainan Shu, Ling Chen, et al. "Detection of Covid-19 in Children in Early January 2020 in Wuhan, China." <i>New England Journal of Medicine</i> 382, no. 14 (February 2020): 1370–71. https://doi.org/10.1056/nejmc2003717 .
Livingston, Edward, and Karen Bucher. "Coronavirus Disease 2019 (COVID-19) in Italy." <i>Jama</i> 323, no. 14 (March 17, 2020): 1335. https://doi.org/10.1001/jama.2020.4344 .
Lu X et al, SARS-CoV-2 Infection in Children, <i>The New England Journal of Medicine</i> , 2020, DOI: 10.1056/NEJMc2005073
Ludvigsson, Jonas F. "Systematic Review of COVID-19 in Children Shows Milder Cases and a Better Prognosis than Adults." <i>Acta Paediatrica</i> , 2020. https://doi.org/10.1111/apa.15270 .
Mizumoto, Kenji, Ryosuke Omori, and Hiroshi Nishiura. "Age Specificity of Cases and Attack Rate of Novel Coronavirus Disease (COVID-19)." <i>MedRxiv Preprint</i> , 2020. https://doi.org/10.1101/2020.03.09.20033142 .
Morand A, Fabre A, Minodier P, Boutin A, Vanel N, Bosdure E, Fournier PE, COVID-19 virus and children: What do we know? <i>Archives de Pédiatrie</i> , 2020, 27: 117-118.
Nathan, Nadia, Blandine Prevost, and Harriet Corvol. "Atypical Presentation of COVID-19 in Young Infants." <i>The Lancet</i> , April 27, 2020. https://doi.org/10.1016/s0140-6736(20)30980-6 .
National Centre for Immunisation Research and Surveillance (NCIRS). "COVID-19 in Schools – the Experience in NSW (Prepared by the National Centre for Immunisation Research and Surveillance (NCIRS))," April 26, 2020.

Qian, Guoqing, Naibin Yang, Ada Hoi Yan Ma, Liping Wang, Guoxiang Li, Xueqin Chen, and Xiaomin Chen. "COVID-19 Transmission Within a Family Cluster by Presymptomatic Carriers in China." *Clinical Infectious Diseases*, 2020. <https://doi.org/10.1093/cid/ciaa316>.

Qiu, Haiyan, Junhua Wu, Liang Hong, Yunling Luo, Qifa Song, and Dong Chen. "Clinical and Epidemiological Features of 36 Children with Coronavirus Disease 2019 (COVID-19) in Zhejiang, China: an Observational Cohort Study." *The Lancet Infectious Diseases*, 2020. [https://doi.org/10.1016/s1473-3099\(20\)30198-5](https://doi.org/10.1016/s1473-3099(20)30198-5).

Riphagen, Shelley, Xabier Gomez, Carmen Gonzalez-Martinez, Nick Wilkinson, and Paraskevi Theocharis. "Hyperinflammatory Shock in Children during COVID-19 Pandemic." *The Lancet*, May 6, 2020. [https://doi.org/10.1016/s0140-6736\(20\)31094-1](https://doi.org/10.1016/s0140-6736(20)31094-1).

Su, Liang, Xiang Ma, Huafeng Yu, Zhaohua Zhang, Pengfei Bian, Yuling Han, Jing Sun, et al. "The Different Clinical Characteristics of Corona Virus Disease Cases between Children and Their Families in China – the Character of Children with COVID-19." *Emerging Microbes & Infections* 9, no. 1 (January 2020): 707–13. <https://doi.org/10.1080/22221751.2020.1744483>.

Viner, Russell M, Simon J Russell, Helen Croker, Jessica Packer, Joseph Ward, Claire Stansfield, Oliver Mytton, Chris Bonell, and Robert Booy. "School Closure and Management Practices during Coronavirus Outbreaks Including COVID-19: a Rapid Systematic Review." *The Lancet Child & Adolescent Health*, 2020. [https://doi.org/10.1016/s2352-4642\(20\)30095-x](https://doi.org/10.1016/s2352-4642(20)30095-x).

Wang, Wenling, Yanli Xu, Ruqin Gao, Roujian Lu, Kai Han, Guizhen Wu, and Wenjie Tan. "Detection of SARS-CoV-2 in Different Types of Clinical Specimens." *Jama*, March 11, 2020. <https://doi.org/10.1001/jama.2020.3786>.

Yu, Nan, Wei Li, Qingling Kang, Zhi Xiong, Shaoshuai Wang, Xingguang Lin, Yanyan Liu, et al. "Clinical Features and Obstetric and Neonatal Outcomes of Pregnant Patients with COVID-19 in Wuhan, China: a Retrospective, Single-Centre, Descriptive Study." *The Lancet Infectious Diseases*, March 24, 2020a. [https://doi.org/10.1016/s1473-3099\(20\)30176-6](https://doi.org/10.1016/s1473-3099(20)30176-6).

Yu, Fengting, Liting Yan, Nan Wang, Siyuan Yang, Linghang Wang, Yunxia Tang, Guiju Gao, et al. "Quantitative Detection and Viral Load Analysis of SARS-CoV-2 in Infected Patients." *Clinical Infectious Diseases*, March 28, 2020b. <https://doi.org/10.1093/cid/ciaa345>.

Zhang, Juanjuan, Maria Litvinova, Yuxia Liang, Yan Wang, Wei Wang, Shanlu Zhao, Qianhui Wu, et al. "Changes in Contact Patterns Shape the Dynamics of the COVID-19 Outbreak in China." *Science*, April 29, 2020a. <https://doi.org/10.1126/science.abb8001>.

Zhang, Zhi-Jiang Xiang, Xue-Jie Xiang Yu, Tao Xiang Fu, Yu Xiang Liu, Yan Xiang Jiang, Bing Xiang Yang, and Yongyi Xiang Bi. "Novel Coronavirus Infection in Newborn Babies Under 28 Days in China." *European Respiratory Journal*, April 8, 2020b, 2000697. <https://doi.org/10.1183/13993003.00697-2020>.

Zhu, Jieyun, Pan Ji, Jielong Pang, Zhimei Zhong, Hongyuan Li, Cuiying He, Jianfeng Zhang, and Chunling Zhao. "Clinical Characteristics of 3,062 COVID-19 Patients: a Meta-Analysis." *Journal of Medical Virology*, 2020a. <https://doi.org/10.1002/jmv.25884>.

Zhu, Yanshan J, Conor D Bloxham, Katina E Hulme, Jane Wei Marcus Sinclair, Zhen E Tong, Lauren C Steele, Ellesandra Yih Noye, et al. "Children Are Unlikely to Have Been the Primary Source of Household SARS-CoV-2 Infections." *MedRxiv Preprint*, 2020b. <https://doi.org/10.1101/2020.03.26.20044826>.

Zou, Lirong, Feng Ruan, Mingxing Huang, Lijun Liang, Huitao Huang, Zhongsi Hong, Jianxiang Yu, et al. "SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected

Patients.” *New England Journal of Medicine* 382, no. 12 (March 19, 2020): 1177–79.
<https://doi.org/10.1056/nejmc2001737>.