

COVID-19 disease in children and adolescents

Scientific brief

29 September 2021



Introduction and rationale

SARS-CoV-2 infections among children and adolescents typically cause less severe illness and fewer deaths as compared to adults. While a less severe course of infection is a positive outcome, milder symptoms may have resulted in less testing resulting in fewer identified cases of SARS-CoV-2 infection in children and adolescents. If children and adolescents with mild or no symptoms also transmit the disease, they may also contribute to transmission in the community. Consequently, understanding the symptoms, infectivity and patterns of SARS-CoV-2 transmission in children and adolescents is important for developing, adapting and improving control measures for COVID-19 disease, especially since, vaccination is not currently available or authorized for those under 12 years.

This scientific brief summarizes the current knowledge about SARS-CoV-2 infection acquisition and transmission and COVID-19 disease symptoms in children and adolescents to bring perspective to policy decisions about keeping schools, kindergartens and day care facilities open and insights about intergenerational transmission.

Box 1. WHO uses the following age group designations to describe specific periods in the lives of children, adolescents and young adults:

- First 28 days of life (0-27 days) is the newborn (or neonatal) period
- 1 to 11 months is the postneonatal infant period
- 12 to 59 months (1 to 4 years) refers to young children
- 5 to 9 years refers to older children
- 10 to 14 years refers to young adolescents
- 15 to 19 years refers to older adolescents
- 20 to 24 years refers to young adults

Key questions

This scientific brief combines the work of WHO's Science Division's rapid scoping reviews on COVID-19 in children and adolescents in school settings with a literature review performed by researchers at the Swiss Tropical Public Health Institute (STPHI) and the University of Bern (UBern) in response to a request from the Swiss National COVID-19 Science Task Force (NCF-TF) of the Swiss Federal Office of Public Health. The WHO rapid scoping review addressed the question "What is the best evidence available on SARS-CoV-2 transmission and COVID-19 disease among children and adolescents?". The STPHI/UBern review addressed three key questions about the epidemiology of SARS-CoV-2 infection and COVID-19 in children and adolescents:

1. What are the common symptoms of younger children, school children and adolescents when infected with SARS-CoV-2?
2. Is the risk of children and adolescents becoming infected by SARS-CoV-2 comparable to the risk of adults?
3. Is the probability of transmission of SARS-CoV-2 infection by children and adolescents comparable to that of adults?

Process and methodology

Two, , Rapid scoping reviews¹ were performed by the WHO Science Division to review literature reporting on SARS-CoV-2 infection in children and their role in transmission. Both searches used the Epistemonikos Database via the L-OVE platform <https://iloveevidence.com/> to identify papers published through 15 June 2021. Studies reporting synthesized evidence (including living systematic reviews, systematic reviews with meta-analysis, systematic reviews without meta-analysis, and overviews of reviews) were included. Primary studies and narrative reviews were not considered. However, 12 narrative reviews and 29 primary studies (41 in total) were identified as relevant to the research question. Modelling studies of all types were excluded. The reviews searched the whole COVID-19 evidence base filtering by “school setting” to reveal 1060 potential records. Consulting experts, bibliographies of relevant documents and websites of relevant institutions, particularly, Centers for Disease Control and Prevention (CDC), European Centre for Disease Prevention and Control (ECDC), World Health Organization (WHO), and Public Health England (PHE) resulted in an additional 36 records. The screening of the 1096 unique records (1060 +36) was performed by two reviewers who both confirmed the eligibility of the selected records. Twelve relevant reports based on a synthesis of evidence were identified. These included 7 systematic reviews, 2 living systematic reviews, 1 rapid review, 1 scoping review and 1 technical report describing the frequency of SARS CoV-2 infection and infectiousness to SARS CoV-2 infection in children and adolescents.

An extensive literature review performed by the STPHI/UBern team to inform the Swiss National COVID-19 Task Force (NCS-TF) was based on PubMed and MedRxiv, up to January 21st, 2021 and was updated with papers identified by experts until March 29th, 2021. They screened 2778 studies posted up to January 21st 2021 (peer-reviewed and preprints), of which 31 were deemed relevant to the research questions on COVID-19 symptoms, infectivity and transmissivity in children and adolescents. From a manual search (also including reports and grey literature) they included another 36 articles (23 published reports, 13 not yet published or peer-reviewed or both). Of these 67 articles, 23 were case reports, 19 were cross sectional studies, 8 were cohort studies, 6 were narrative reviews or viewpoints, 10 were systematic reviews and 1 was a modelling study.

The two reviews (WHO and STPHI/University of Bern) captured different types of papers. The WHO review focuses on synthesized evidence and the STPHI/University of Bern review includes a broader range of study types. A total of 77 individual studies (12 systematic reviews from WHO and 67 studies from STPHI/University of Bern; minus 2 overlapping studies) informs this scientific brief.

All studies describe the age distribution of study participants in different ways. Age groups in reports often overlap or are reported for a wide range of ages. These inconsistencies make it impossible to summarize the findings using consistent age groups or to adapt the results according to a school stage.

Research evidence

Overall there are proportionally fewer cases of and deaths from COVID-19 disease for children and adolescents than for adults. Of age-disaggregated cases reported to WHO from 30 December 2019 to 13 September 2021², children under-5 represented 1.8% (1 695 265) of global cases and 0.1% (1 721) of global deaths. Older children and younger adolescents (5 to 14 years) were 6.3 % (6 020 084) of global cases and 0.1% (1 245) of global deaths while older adolescents and young adults (15 to 24 years) were 14.5% (13 647 211) of global cases and 0.4% (6 436) of global deaths.

¹ one to 20 January 2021 and a second to 15 June 2021

² [WHO Coronavirus \(COVID-19\) Dashboard](#) | [WHO Coronavirus \(COVID-19\) Dashboard With Vaccination Data](#); last accessed 13 September 2021.

What are the common symptoms of younger children, school children and adolescents when infected with SARS-CoV-2?

Younger children, school children and adolescents usually have fewer and milder symptoms of SARS-CoV-2 than adults and are less likely than adults to experience severe COVID-19 (1-9). The biological mechanisms for the age-related differences in severity are still under investigation but hypotheses include differences in the functioning and maturity of immune systems in young children compared with adults (6).

Some reports from early in the pandemic suggested that there might be an age-dependent risk of severe disease with slightly more severe or critical disease in infants <1 year relative to other paediatric patients (6) (10). However, the studies had methodological limitations that limit their generalizability. Several reviews, describing 32 different cases of neonatal SARS-CoV-2 infection in total, show neonates mostly presenting with mild disease (11-15). These findings are supported by small additional retrospective studies (16-17) and a prospective national cohort study using surveillance data from the UK (18), describing mild SARS-CoV-2 disease progression in neonates. Most reports of neonatal SARS-CoV-2 are case reports or small case series. Multi-centre hospital-based studies, with more complete data and consistent case definitions, have been conducted more recently. A prospective multicentre observational cohort study from 260 hospitals in the UK, following 651 children and young adults (225/651 <1 year old) between 17 January and 3 July 2020, found that the risk of admission to intensive care was associated with age <1 month (odds ratio: 3.21, 95% CI: 1.36-7.66) and age 10-14 years (odds ratio: 3.23, 95% CI: 1.55-6.99), compared with 15-19 year olds (19).

There is not yet conclusive evidence that young age is a particular risk factor for severe disease within the child and adolescent age-range, owing in part to methodological limitations in the cited studies. There are also multiple small studies from around the world describing mild SARS-CoV-2 disease progression, often without hospitalization, even in children with severe underlying health conditions such as cancer and immunosuppression (20-26).

Severe disease and long COVID-19 in children

Children and adolescents can experience prolonged clinical symptoms (known as post COVID condition, or post-acute sequelae of SARS-CoV-2 infection), but the frequency and characteristics of these conditions are still under investigation (27). Due to limited follow up and the absence of studies with control groups, the frequency, characteristics and prognosis of prolonged symptoms following SARS-CoV-2 infection remain uncertain.

Additionally, a hyperinflammatory syndrome, called paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in Europe and multisystem inflammatory syndrome in children (MIS-C) in the USA, can complicate recovery from COVID-19 (28-31).

The severity of disease caused by new variants of SARS-CoV-2 in children and adolescents, in comparison with previous lineages, remains under investigation.

Asymptomatic disease

Initially, some studies reported that more children were presenting with asymptomatic disease than adults, raising the possibility that children could be unknowingly spreading disease in populations (32-33). However, reviews of these studies identified a number of factors limiting the generalization of these study results to the global population (all ages), not the least of which was that confirmation of COVID-19 infection was not available for some of the study subjects. Although there is some evidence that older children have higher rates of asymptomatic disease than infants (< 1 year), the majority of children present with symptomatic disease and do not appear to be silent spreaders of infection (35).

Is the risk of children and adolescents becoming infected by SARS-CoV-2 comparable to the risk of adults? Does the probability of infection differ between age groups?

The risk of becoming infected with SARS-CoV-2 is a combination of susceptibility (host biological factors), environmental factors associated with exposure type (work, shopping, schools etc.) and exposure intensity (level of

community transmission and of preventive measures). It is difficult to separate the influence of these factors on the risk of children and adults becoming infected with SARS-CoV-2. Because of this, the interpretation of studies reporting on levels of infection by age depends not only on study methodology but also on the details provided about the context within which the study was done.

Multiple population-based SARS-CoV-2 seroprevalence and viral shedding studies have investigated whether children and adolescents are infected at the same rate as adults, but the results have been mixed (34). Three systematic reviews concluded that overall children aged <10 years were less susceptible than older children and adults, although seroprevalence in adolescents appears similar to adults (36-38). It should be noted that the studies reported on were conducted during times of strict social distancing when children and adults may have had different levels of exposure to the virus, i.e. children home from schools but adults at work or food shopping.

In some serologic studies, children were less likely to have detectable antibodies than adolescents or adults. However, these studies have limitations – including serologic tests that were not optimized for use in children and low overall community transmission at the time of the study – that make the results difficult to interpret (58-61). In Iceland, a seroprevalence study, published 11 June 2020, found that no children <10 years of age had evidence of infection (39). It should be noted, however, that this was early in the course of the pandemic, very few children were tested, and seroprevalence was low in this study among all age groups.

Two studies in Switzerland found that seroprevalence among children aged 5-9 years was slightly lower than adolescents and adults (40-41). However, many of the children had an indeterminate IgG antibody test result, and the percentage of indeterminate results was much higher among those aged 5-9 years than in all other age groups. A study in India identified the highest probability of transmission, given exposure, within in case-contact pairs of similar age. Transmission risk was higher in children aged 0-14 and among adults aged 65 years and older, perhaps reflecting intergenerational social and physical interactions in India (42).

One in-depth investigation of immune responses in three children who were infected by others showed that all demonstrated IgA antibody responses in saliva, but two did not develop IgG antibodies and never shed any virus detectable by RT-PCR. Evidence about infection in children should be interpreted with view to the possibility that children may be infected but these infections may go undetected because they do not shed virus or seroconvert (43).

In a study in which all household members were exposed to an infected person, children 5–17 years of age were about 61% and children 0–4 years were 47% less likely to have positive PCR results compared with those older than 18 years of age (44). Household studies with narrower age groups (45-46) found that secondary attack rates for younger children (0-4 and 0-5 respectively) were lower than for school aged children and adolescents. The detailed relationship between age and susceptibility to infection requires further investigation. More detailed epidemiological information about the factors influencing susceptibility of children and adolescents to the new SARS-CoV-2 variants is urgently needed.

Is the probability of transmission of SARS-CoV-2 infection by children and adolescents comparable to that of adults?

Children and adolescents can infect others with SARS-CoV-2. COVID-19 outbreaks have been identified in secondary schools, summer camps and day care centres, particularly when neither physical distancing nor masks were used to reduce risk (47-50). There is some evidence, however, that children may be less infectious, as measured by secondary attack rates, than adolescents and adults (51).

The largest school cluster in Israel was reported from a high school in Jerusalem ten days after the reopening of schools on 13 May 2020 (47). Testing of the complete school community revealed that 153 students and 25 staff members were infected with SARS-CoV-2 during the outbreak; and that the attack rate (the percentage of an at-risk population that contracts a disease during a specified time interval) in these groups was 13.2% and 16.6% respectively. At a sleepover camp in the United States, 76% of 344 campers and staff who were tested had positive tests for SARS-CoV-2 infection by RT-PCR (48). Reviews of transmission in schools have suggested low overall transmission to and from children, particularly in the context of low overall transmission in the community (51-53). The experience from schools that first opened in United Kingdom of Great Britain and Northern Ireland, shows that

outbreaks among pupils were uncommon in the context of few students attending school and low overall community transmission (54). A cross-sectional study of schools in Berlin found that 8 out of 24 classes had at least one student infected (55). No large outbreaks were detected, however, and the risk of infection was associated with inconsistent mask use. Another study from Germany also found low risk of transmission in schools and day care centres (56).

Infectious SARS-CoV-2 has been cultured in children as young as 7 days (57). Studies assessing viral RNA shedding levels by age report mixed results based on use of different testing systems (58-60). However, the type of specimen from which viral RNA is isolated makes a difference to the threshold values for RT-PCR cycles used to determine viral load which may account for some of the reported variation by age (61,63), although statistical analysis of the same data found that viral load did indeed increase with age (62). Children and adolescents who become infected with SARS-CoV-2 shed virus in their respiratory tract and sometimes in their faeces (64-69). Amongst diagnosed individuals tested at the same time point after symptom onset, SARS-CoV-2 viral RNA shedding in the respiratory track appears similar in children, adolescents and adults (70,73).

The relationship between age, viral load and transmission across the full symptom spectrum of SARS-CoV-2 infection has not been comprehensively investigated because people with no, or mild symptoms are seldom tested systematically. The relative transmissibility of SARS-CoV-2 at different ages remains uncertain, largely because of the challenges involved in disentangling the influences of biological, host and environmental factors (71, 72-77). More studies about the role of testing at all school levels and well-designed prospective longitudinal studies that can address questions about SARS-CoV-2 transmission at school and at the household level are needed. Also missing is detailed epidemiological information about the factors influencing transmissibility of the new SARS-CoV-2 variants in children and adolescents.

Limitations

Many early studies reported on clinically apparent cases in healthcare settings with limited diagnostic testing. Studies carried out in hospital settings in different geographical locations were hard to compare because they differ in the reasons and criteria for hospitalization of children and adolescents with COVID-19. Some countries focused on monitoring clinical progress, others on isolation of cases and still others on admitting only the sickest children. All these studies made important observations, but some may have underestimated the proportion of children amongst all COVID-19 cases because the milder symptoms resulted in under-detection of infection (72, 76-77).

Over time, it has become possible to design, conduct and analyse studies to reduce some of the biases in selection and measurement. Even so, the context in which a study is conducted (level of community transmission, control measures in place) limits the generalizability of the findings. Differences between studies that attempt to address the same research question about SARS-CoV-2 in children and adolescents may result both from differences in the circumstances under which studies were done as well as in study methodology.

A final limitation of this scientific brief is the lack of information on the effect of new variants of COVID-19 on children and adolescents. There is not yet enough information about how these variants may change patterns of disease, infectivity and transmission in newborns, children, adolescents, young adults and older adults.

Future studies among children and adolescents, both in the general population and in outbreak settings, should report findings with sufficient detail by age and sex to allow for comparisons in risk between newborns, postneonatal infants, young children, older children, adolescents, young adults and older adults. In addition, the context of the study, within which the interventions are performed or where other conditions which drive social mixing patterns differ, should be clearly articulated to assist with interpretation of study findings.

Conclusions

Children and adolescents are susceptible to SARS-CoV-2 infection and may transmit the virus to others. The risk of transmission to and from children depends on the level of community transmission, the measures implemented to control the virus and also biological factors related to the virus itself (i.e. the type of variant circulating). Younger

children may be less susceptible than older children and adolescents but the precise role of children and adolescents in the overall transmission requires further investigation.

In general, children infected with SARS-CoV-2 can present with milder symptoms of COVID-19 disease although the new variants of SARS CoV-2, including the Delta variant, require more investigation to determine if this remains the case. Appropriate preventive measures, including physical distancing, cleaning your hands, coughing into a bent elbow or a tissue, adequate ventilation in indoor settings, and masks (for older children-see guidance below), should be consistently implemented in schools for all ages, especially since children under the age of 12 years are not yet eligible for vaccination in most contexts.

Links to other WHO guidance and reports on COVID-19 and children and adolescents

Advice on the use of masks for children in the community in the context of COVID-19 - Guidance document (21 August 2020) available at

https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC_Masks-Children-2020.1

Breastfeeding and COVID-19 – Scientific brief (23 June 2020), available at

<https://www.who.int/publications/i/item/10665332639>, IRIS Link:

https://apps.who.int/iris/bitstream/handle/10665/332639/WHO-2019-nCoV-Sci_Brief-Breastfeeding-2020.1-eng.pdf

Estimating mortality from COVID-19 disease- Scientific brief, available at

<https://www.who.int/publications/i/item/WHO-2019-nCoV-Sci-Brief-Mortality-2020.1>

Severe disease and Multi-symptom COVID-19 Syndrome

<https://www.who.int/publications/i/item/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19>

Q & As on breastfeeding

<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/q-a-on-covid-19-and-breastfeeding>

Q & As on schools and COVID-19

<https://www.who.int/news-room/q-a-detail/q-a-schools-and-covid-19>

Q & As on addressing violence women and children COVID

https://www.who.int/publications/i/item/WHO-2019-nCoV-Violence_actions-2020.1

COVID-19 Resource pages from WHO

https://www.who.int/maternal_child_adolescent/links/covid-19-mncah-resources-care-for-young-children/en/

https://www.who.int/maternal_child_adolescent/links/covid-19-mncah-resources-for-pregnancy-childbirth-postnatalcare/en/

Acknowledgements

We thank Margarethe Wiedenmann (Swiss Tropical Public Health Institute), Nicola Low and Myrofora Goutaki (University of Bern) for sharing their review and subsequent policy brief for the Swiss National COVID-19 Task Force for this scientific brief.

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