Evidence Summary

COVID-19 Supplement on School Re-Opening (1 of 3): Clinical Features and Transmission in Children

K2P Evidence summaries use global research evidence to provide insight on public health priority topics that are ambiguous and have important uncertainty. This document informs policymakers and other stakeholders by synthesizing the best available evidence and presenting its relevance to local contexts. Evidence summaries do not provide recommendations but rather articulate evidence in a clear, objective and factual manner.

Evidence Summary

+ Included

Synthesis of evidence on a priority question or topic

Local context

× Not Included

Does not provide **recommendations**

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K2P Evidence Summary

COVID-19 Supplement on School Re-Opening (1 of 3): Clinical Features and Transmission in Children

Knowledge to Policy Center K2P

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Key Messages

Key Messages

As schools plan for re-opening, understanding the role children play in the coronavirus infectious disease 2019 (COVID-19) pandemic is critical. This evidence summary provides an overview of the clinical features and transmission of COVID-19 in children based on the latest research evidence.

Clinical Features

- While COVID-19 affects all age-groups in children, children are affected less severely than adults with a considerably lower burden of morbidity and mortality compared to adults
- Majority of infected children present with mild to moderate symptoms or are asymptomatic (i.e. go undetected)
- Very few children become critically ill. Children with co-morbidities appear more likely to suffer from complications.
- Some children may develop multisystem inflammatory syndrome (MIS-C) with severe illness
- Death in children due to COVID-19 is rare

Susceptibility of children to infection with SARS-CoV-2

- Currently available evidence suggests that children may be less susceptible to infection with SARS-CoV-2 compared to adults
- While the reason why COVID-19 seems to affect children less often and less severely than adults is not yet fully understood, emerging evidence suggests that the expression of SARS-CoV-2 receptor ACE2 protein is lower in younger children and starts to increase in later childhood

SARS-CoV-2 Viral load and shedding in children

Emerging data on SARS-CoV-2 viral load and shedding suggests the following:

- Infected children of all ages (including mildly symptomatic and asymptomatic) can carry high SARS-CoV-2 viral loads
- Infected children may have viral loads similar to (or slightly higher than) adults, indicating that children shed SARS-CoV-2 RNA (whether viable or not) in a similar manner to adults
- SARS-CoV-2 RNA has been identified in the stools (i.e. fecal samples) of children and seems to be present in the stools for a longer time than in the respiratory tract (upper airways) of children
- Presence of SARS-CoV-2 RNA in children's respiratory or gastrointestinal specimens does not necessarily equate to infectiousness as viral load is a proxy measurement of infectivity (the latter which also depends on the viability of the virus)

- Clinical significance of viral shedding, particularly through gastrointestinal tract, remains unclear, highlighting the need for further investigation

Role of children in transmission

- Transmission of SARS-CoV-2 from children occurs; however, currently available evidence suggests that transmission mainly takes place between adult peers and from adult family members to children
- Household transmission studies showed that children were much less likely to be the index case (however, many of the studies involved testing symptomatic household contacts and may have missed asymptomatic infections)
- Data on COVID-19 in schools is scarce, especially that many schools have been closed in response to the pandemic; in settings where schools remained open or using data prior to closures, there is little evidence of significant outbreaks or major transmission into community
- Existing data, so far, suggests that children are not the primary drivers of SARS-CoV-2 transmission or outbreaks in school settings
- While few significant outbreaks of COVID-19 have been reported, they may be difficult to detect because many infected children do not develop symptoms. Outbreaks involving staff-to-staff transmission were most common, while transmission between staff and students were less common and student-to-student transmission were least common
- Most of the studies investigating school settings emphasized the importance of low community transmission and the application of physical distancing, hygiene and other measures to restrict the spread of the virus in schools
- Improved understanding of pre-symptomatic and asymptomatic infection is needed to determine the extent to which children play a role in onward transmission of COVID-19

Implications

- There are still important uncertainties about spread of SARS-CoV-2 in children.
- From the currently available evidence, it appears that children, to date, are not substantially contributing to the household or school transmission of SARS-CoV-2. However, given that transmission dynamics change and are affected by other interventions, the current evidence base will evolve as countries continue to lift certain restrictions (initially implemented with lockdown). In many of the countries included in this document, those restrictions were still in place when educational activities resumed in schools.
- Reopening of schools in Fall 2020, alongside easing of other restrictions highlights the need to exercise vigilance (by governments, schools, communities, households) and closely monitor, measure and assess changes in the number of COVID-19 cases, to prompt immediate action according to the most updated evidence.

الرسائل الرئيسية

بينما تتحضر المدارس لإعادة فتح أبوابها، من المهم فهم الدور الذي يلعبه الأطفال في جائحة كوفيد-19. يقدم ملخص الأدلة هذا نظرة عامة على الخصائص السريرية لكوفيد-19 وسبل انتقاله لدى الأطفال بناءً على أحدث الأدلة العلمية.

الخصائص السريرية

- ← بينما يطال كوفيد-19 جميع الفئات العمرية لدى الأطفال، الا أن تأثُّر الأطفال بهذا الوباء يأتي أقل حدة من البالغين، مع نسبة إصابة ووفيات منخفضة مقارنة بالبالغين
- ← يُظهر معظم الأطفال المصابين بكوفيد-19، أعراض خفيفة إلى متوسطة، أو بدون أعراض حتى (أي لا يتم تشخيصهم)
- ← عدد قليل من الأطفال تكون إصابتهم بكوفيد-19 خطيرة. حيث يظهر أن الأطفال الذين يعانون من أمراض أخرى، أكثر عرضة للمضاعفات
- ← قد يصاب الأطفال الذين يعانون من كوفيد-19 بمتلازمة الالتهاب متعدد الأجهزة (MIS-C) بشكل حاد
- ← من النادر وفاة طفل بسبب كوفيد-19

تعرض الأطفال للإصابة بفيروس كورونا المستجد

- ← تشير الأدلة والبراهين العلمية المتاحة إلى أن الأطفال أقل عرضة للإصابة بفيروس كورونا المستجد مقارنة بالأشخاص البالغين
- ← في حين أن سبب تأثير كوفيد-19 الخفيف وقليل الخطورة على الأطفال، مقارنةً بالبالغين، لا يزال غير مفهوم بشكل كامل بعد، تشير الأدلة العلمية المستجدة إلى أن بروتين ACE2، وهو مستقبِل لفيروس كورونا المستجد، موجود بنسب أقل لدى الأطفال الأصغر سنًا ويزداد في مراحل الطفولة اللاحقة

الحمل الفيروسي لكوفيد-19 وإفرازه

تشير البيانات العلمية المستجدة عن نسبة وجود الفيروس في الجسم وإفرازه إلى ما يلي:

- ← يمكن للأطفال من جميع الأعمار حمل نسب عالية من فيروس كوفيد-19 في أجسامهم
- ← قد يكون لدى الأطفال المصابين، حمل فيروسي لكوفيد-19 مماثل للحمل الفيروسي لدى البالغين (أو بنسب أعلى قليلاً)، ما يشير الى أن الأطفال يطلقون الحمض النووي الريبي الفيروسي (RNA) (سواء كان قابلاً للحياة أم لا) بطريقة مماثلة للبالغين
- ← تم تحديد الحمض النووي الريبي (RNA) لفيروس كورونا في براز الأطفال ويبدو أنه يستقر في البراز لفترة أطول من مدة وجوده في الجهاز التنفسي للأطفال
- ← إن وجود الحمض النووي الريبي (RNA) لفيروس كورونا في عينات الجهاز التنفسي أو الجهاز الهضمي للأطفال لا يعني العدوى لأن نسب الحمل الفيروسي ليست مقياساً لإمكانية نشر أو نقل الفيروس (حيث ترتبط نسب الحمل الفيروسي بحيوية الفيروس).

الحمل الفيروسي يعني كمية الفيروس في عينة اختبار مأخوذة من المريض. بالنسبة لـ كوفيد-19، هذا يعني عدد الجينومات الفيروسية التي تم الكشف عنها في مسحة البلعوم الأنفي من المريض، أي في فحص الـ PCR. أما إفراز الفيروس فهي عملية إطلاق الفيروس من جسم الشخص المصاب (ممكن عبر النفس، السعال، العطس،البراز، وغيرها...)

- التفسير السريري لعملية إفراز فيروس كورونا (إطلاق الفيروس من الجسم)، خاصة عبر الجهاز الهضمي، لا يزال غير واضح، ما يظهر الحاجة إلى المزيد من البحوث

دور الأطفال في عملية انتقال العدوى

- يمكن للأطفال أن ينقلوا فيروس كورونا المستجد، ومع ذلك، تشير الأدلة والبراهين العلمية الموجودة حاليًا إلى أن انتقال العدوى يحدث بشكل أساسي بين أفراد بالغين، ومن أفراد أسرة بالغين إلى الأطفال
- أظهرت دراسات حول انتقال العدوى في المنازل، أن الأطفال نادرًا ما يكونون هم الحالة الأولى أو الأساسية (على الرغم من أن العديد من الدراسات تضمنت اختبار أفراد العائلة في المنزل التي تظهر عليهم الأعراض، وبالتالي، ربما فاتها الأفراد الذين لا تظهر عليهم أعراض)
- لا بد من الإشارة الى أن الأدلة العلمية الخاصة بكوفيد-19 في المدارس قليلة، خصوصاً وأن العديد من المدارس قد أغلقت أبوابها استجابةً للوباء؛ أما في الأماكن التي ظلت فيها المدارس مفتوحة (أو من البيانات المتوفرة قبل إغلاق المدارس) ، فالأدلة التي تشير الى حدوث حالات تفشي كبيرة او نقل العدوى الى المجتمع قليلة
- تشير البيانات المتاحة حالياً إلى أن الأطفال ليسوا المحركين الأساسيين لانتقال أو تفشي فيروس كورونا المستجد في المدارس.
- في حين تم الإبلاغ عن عدد قليل من حالات تفشي كوفيد-19 بين الأطفال، إلا أنها تحدث (وقد يكون من الصعب تشخيصها بسبب النقص النسبي في الأعراض بين الأطفال المصابين). كانت حالات التفشي بين الموظفين هي الأكثر شيوعًا، بينما كان انتقال العدوى بين الموظفين والطلاب أقل شيوعًا، أما إنتقال العدوى من طالب إلى طالب، فكان الأقل شيوعًا.
- أكدت معظم الدراسات التي تبحث في البيئات المدرسية على أهمية انخفاض الانتقال المجتمعي للوباء والالتزام بتدابير التباعد الإجتماعي والنظافة وغيرها للحد من تفشي فيروس كورونا
- لا بد من تطوير فهم المدارس للحالات في مرحلة ما قبل الأعراض (pre-symptomatic) والحالات التي لا تظهر أعراض (asymptomatic) لتحديد إلى أي مدى يلعب الأطفال دورًا في عملية انتشار فيروس كوفيد-19

الإنعكاسات

- لا تزال الشكوك قائمة حول مدى انتشار فيروس كورونا لدى الأطفال.
- بناءً على الأدلة العلمية الموجودة حاليًا، يبدو أن الأطفال، حتى الآن، لا يساهمون بشكل كبير في انتشار فيروس كورونا المستجد في المنزل أو المدرسة. ومع ذلك، نظرًا لتغيّر ديناميكيات نقل العدوى وانتشارها، مع تغيّر الإجراءات والتدخّلات، فإن قاعدة الأدلة العلمية الحالية ستتطور مع استمرار البلدان في رفع بعض القيود (التي تم تنفيذها مبدئيًا مع الإغلاق). في العديد من البلدان المذكورة في هذه الوثيقة، كانت هذه القيود لا تزال سارية عند استئناف الأنشطة التعليمية في المدارس.
- إعادة فتح المدارس في خريف 2020، بالتوازي مع تخفيف قيود أخرى، يسلط الضوء على الحاجة إلى توخي الحذر (من قبل الحكومات والمدارس والمجتمعات والعائلات) والمراقبة عن كثب وقياس وتقييم التغييرات في عدد حالات كوفيد-19، لاتخاذ إجراءات فورية وفقًا لأحدث الأدلة العلمية.

Content

Preamble

Worldwide, governments have temporarily closed educational institutions as part of broader efforts to control the spread of SARS-Cov-2. According to the United Nations Educational, Science and Cultural Organization (UNESCO), 193 countries had implemented country-wide school closures by April 1st 2020, affecting around 1.6 billion learners worldwide (more than 90% of the global student population) (8).

As governments look beyond containment to reopening economies and easing lockdown measures, the topic of school re-opening has taken center-stage.

This K2P Evidence Summary provides an overview of the clinical features and transmission of COVID-19 in children based on the latest research evidence, which can assist policy makers, public health officials and the public in better understanding the role of children in COVID-19 transmission given its policy implications in relation to reopening schools. It constitutes the first product (out of three) within the Supplement on School Reopening launched as part of the K2P COVID-19 Series.

Search Strategy

We ran the following search on PubMed (last updated September 7, 2020):

(coronavirus[TIAB] OR COVID-19[TIAB] OR SARS-COV-2[TIAB]) AND (school[TIAB] OR schools[TIAB] OR nursery[TIAB] OR nurseries[TIAB]). The search yielded 509 citations.

(viral load*[TIAB] OR viral shed*[TIAB]) AND (COVID-19 OR COVID19 OR SARS-COV-2[TIAB]) AND (children[TIAB]). The search yielded 34 citations.

We also searched Health Systems Evidence, Social Systems Evidence, and Google Scholar using variations of the terms “COVID-19” and “children”.

Overall, we identified 40 relevant studies. These included 15 systematic reviews, 1 rapid review, 1 scoping review, 1 literature review, 18 single studies and 4 reports.

Background to Evidence Summary

A K2P Evidence Summary uses global research evidence to provide insight on public health priority topics that are ambiguous and have important uncertainty. This short document informs policymakers and other stakeholders by synthesizing the best available evidence and presenting its relevance to local contexts.

Evidence summaries do not provide recommendations but rather articulate evidence in a clear, objective and factual manner.

The preparation of this K2P Evidence Summary involved the following steps:

1) *Identifying and selecting a relevant topic according to K2P criteria.*
2) *Appraising and synthesizing relevant research evidence about the problem.*
3) *Drafting the Evidence Summary in such a way as to present global and local research evidence concisely and in an accessible language.*
4) *Undergoing merit review.*
5) *Finalizing the Evidence Summary based on the input of merit reviewers.*
6) *Submitting finalized Evidence Summary for translation into Arabic, validating the translation and Dissemination*

Clinical Features and Transmission of COVID-19 in Children

This section provides an overview of the clinical features and transmission of COVID-19 in children. Such information is critical to inform any decisions related to school re-opening/closure during COVID-19 pandemic.

Clinical Features

Evidence from eight systematic reviews revealed the following key clinical features related to COVID-19 (1, 2, 9-14):

- COVID-19 affects all age-groups in children
- Children are affected less severely than adults with a considerably lower burden of morbidity and mortality compared to adults.
- Most infected children present with mild to moderate symptoms or are asymptomatic.
- Very few children become critically ill (with some evidence suggesting a higher incidence of severe illness among children under the age of one).
- Some children may develop multisystem inflammatory syndrome (MIS-C) with severe illness
- Death in children due to COVID-19 can occur, but it is rare
- Children with co-morbidities appear more likely to suffer from complications
- COVID-19 symptoms in children are non-specific and most commonly include cough and fever
- Laboratory and radiological investigations may be normal or mildly altered

Children currently comprise less than 5% of total COVID-19 cases worldwide (1, 2)

Nonetheless, the true incidence of COVID-19 infection in children is not known due to lack of widespread testing and the prioritization of testing for adults and those with severe illness (5).

A more detailed overview of the findings is provided in box 1 below.

Box 1: Clinical Features

Clinical presentation

- Across studies, the majority of infected children showed mild (33-42.5%) or moderate signs of the infection (39.6- 51%) (2, 9).
- Asymptomatic infection ranged from 15% to 27.7% across included studies (2, 9, 12, 14). In one systematic review, the pooled proportion of asymptomatic infection was 40.45% (13).

Clinical symptoms

- The two most common symptoms were **fever** and **cough** (1, 2, 9, 10, 12).
- 6-13% of patients also presented with **gastrointestinal manifestations** (mainly diarrhea and vomiting) (1, 2, 9, 10, 12).
- Dyspnea was more common in infants as compared to the other age groups (2, 10).

Severity of infection

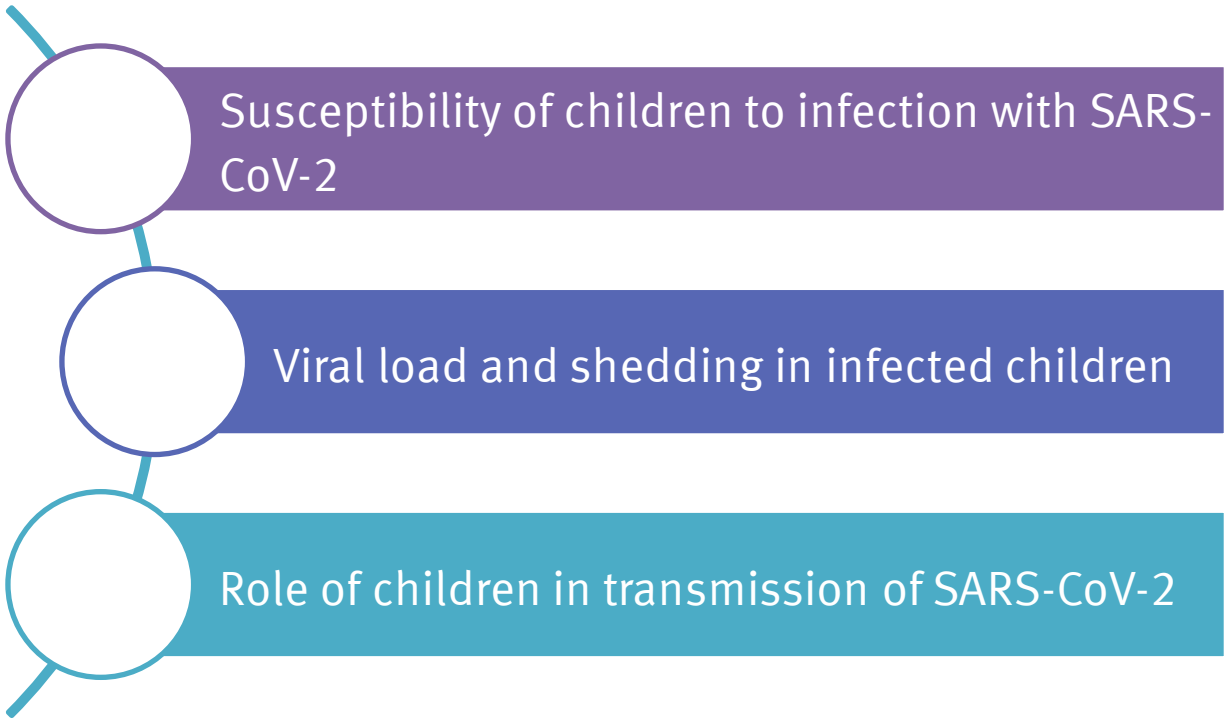
- Percentage of children with severe or critical illness ranged from 2-7% across included studies (1, 2, 9); 2- 3% were admitted to intensive care unit or required mechanical ventilation (2, 12). Among children under one-year old, critical cases accounted for 10.6-14%, indicating higher incidence of severe illness among children under one year old (9) (2). Similar patterns were observed in the study by Ludvigsson et al. where the prevalence of severe and critical disease was 10.6% in children aged <1 at diagnosis, 7.3% (1-5 years), 4.2% (6-10 years), 4.1% (11-15 years) and 3.0% (16-17 years) (15).
- Mortality rate ranged from none to 0.09% across included studies (2, 9, 10, 12).
- 15% of patients (n=17, median age of 9) were identified with multisystem inflammatory syndrome (MIS-C), manifesting with symptoms overlapping with but distinct from Kawasaki disease (10). MIS-C patients had high prevalence of gastrointestinal, dermatologic/mucocutaneous, and cardiovascular symptoms (10, 16). 65% of the MIS-C cases required intensive care because of hypotension (no deaths were reported) (10).

Underlying medical conditions & co-morbidities

- Underlying medical conditions were reported in 35.6% of children (233 out of 655). Imunocompromised children or those with respiratory/cardiac disease comprised the largest subset of COVID-19 children with underlying medical conditions (2, 12). Significant comorbidities were reported in 22% of patients (129 out of 587) with known underlying disease status (2).

	→ Pooled proportion of co-infection ranged from 5.6% to 10.14% (12, 13), of which Mycoplasma pneumonia and influenza virus were the most common pathogens (13). → Children with underlying conditions may be at greater risk of infection or more severe disease (11).
Lab and imaging findings	→ Most common laboratory findings were normal white blood cell followed by elevated creatine kinase MB (CK-MB) and lymphopenia (2, 9). → Frequent imaging features were normal images and ground-glass opacity (9, 10). → Asymptomatic COVID-19 patients could have abnormal laboratory and radiational manifestations (14)

Transmission of COVID-19 in Children



Susceptibility of children to infection with SARS-CoV-2

Currently available evidence suggests that children may be less susceptible to infection with SARS-CoV-2 compared to adults (17-19).

A summary of the key findings is provided below:

- A preprint systematic review of 32 studies (18 contact-tracing and 14 population-screening) looking at susceptibility to SARS-CoV-2 infection amongst children and adolescents compared with adults found preliminary evidence that children, particularly those below age 12-14 years, have lower susceptibility to SARS-CoV-2, with a 43% lower odds of being an infected contact (though the heterogeneity was high). The majority of studies were consistent with lower seroprevalence in children compared with adults. Data specifically on adolescents are sparse, but consistent with susceptibility and seroprevalence in adolescents more similar to adults. The review provides no information on the infectivity of children (17)
- Another systematic review identified six studies estimating the proportion of children infected; data from population-based studies in South Korea, Italy, California, Netherlands and Iceland, and a hospital-based study in the UK suggest children may be less likely to be infected (20)

- A review of the literature on the effect of age on transmission of SARS-CoV-2 infection found evidence indicating lower susceptibility to infection for children aged under 10 years compared to adults given the same exposure, and elevated susceptibility to infection in adults aged over 60 years compared to younger/middle aged adults (18)
- A recent modelling analysis from China, Italy, Japan, Singapore, Canada and South Korea estimated that individuals under the age of 20 were approximately half as susceptible to SARS-CoV-2 infections as adults over 20 years (19).

The reason why COVID-19 seems to affect children less often and less severely than adults is not yet fully understood. While this could be partially explained by the relatively fewer opportunities for children to expose themselves to people beyond family members and school mates and the asymptomatic or too mildly infection which may go unnoticed (20), there is emerging evidence suggesting that the expression of SARS-CoV-2 receptor ACE2 protein is lower in young children and starts to increase in later childhood (2, 21, 22). In a recently published study, children under the age of 10 had significantly lower ACE2 expression (P=0.004) compared to other age groups (23). Additional studies are required to expose the mechanistic basis of differential clinical manifestations among various patient populations.

SARS-CoV-2 viral load and shedding in infected children

Emerging data on SARS-CoV-2 viral load and shedding in children suggests the following (23-29):

- Infected children of all ages (including mildly symptomatic and asymptomatic) can carry high SARS-CoV-2 viral load
- Infected children may have viral load similar to (or slightly higher than) adults, indicating that children shed viral RNA (whether viable or not) in a similar manner to adults
- SARS-CoV-2 RNA has been identified in the stools of children and seems to be present in the stools for a longer time than in the respiratory tract of children
- Presence of SARS-CoV-2 RNA in children's respiratory or gastrointestinal specimens does not directly equate to infectiousness as viral load is a proxy measurement of infectivity and, thus, may not necessarily translate to transmissibility.
- Clinical significance SARS-CoV-2 viral shedding, particularly via the gastrointestinal tract remains unclear, highlighting the need for further investigation

Viral load refers to the quantity (or titre) of virus in a volume of fluid at a given time.

Viral shedding occurs when a virus replicates inside the body and is released into the environment.

While the detection of viral RNA by PCR does not directly indicate infectivity (given the exact load of viable virus is unknown and will depend on the specimen from which the virus is identified), the detection of viral RNA and the measure of viral load are potentially useful markers for infectiousness, as well as for assessing disease severity and prognosis (3, 4).

A more detailed overview of the findings is provided below:

Presenting results from the largest pediatric COVID-19 biospecimen repository to date, Yonker et al. concluded that while a low expression of ACE2 (i.e. angiotensin converting enzyme 2 receptor for SARS-COV-2) in children under the age of 10 probably corresponds to reduced infection rates, children of all ages, once infected, can carry high SARS-CoV-2 viral load, with the highest viral load observed in the first 2 days of symptoms; yet children displayed relatively mild or no symptoms. There was no age correlation with viral load among younger and older children (23). Findings from Hans et al. suggest that both mildly symptomatic and asymptomatic children have high levels of viral RNA in the nose and sputum early during infection (with symptomatic children having higher initial RNA load in nasopharyngeal swab specimens than asymptomatic children), but that these levels decline drastically within 1-2 weeks (24).

Three studies compared findings between children and adults, either directly or indirectly. L'Huillier et al. reported similar viral load in symptomatic children and symptomatic adults, but failed to compare the children and adults statistically (28). Jones et al. (30) analyzed 3,303 COVID-19 patient sputum samples in Germany and found that viral load of at least 250,000 copies were present in 29% of patients aged 0-6 years old (n=38), 37.3% of those aged 0-19 (n=150), and 51.4% of those aged 20 and above (n=3153) (30). While the authors concluded that infected people in all age groups can carry viral load likely to represent infectivity, a secondary re-analysis of these data by another author suggest there is moderate, but not overwhelming evidence for increasing viral load with increasing age based on a test for trend (26). In contrast, Heald-Sargent et al. found equivalent or more viral nucleic acid in the upper respiratory tract of children under the age of five with mild to moderate COVID-19 compared with older children (5-17 years) and adults (18-65 years) (25).

The duration of viral shedding from the respiratory tract (upper airway) of children was up to 24 days from symptom onset (with a mean of 11.1 days). This is shorter than the reported durations of adult patients (longest observed duration was 60 days, with a mean of 20 days) (29).

While COVID-19 is thought to predominantly be transmitted by respiratory droplets, emerging evidence suggests that fecal-oral transmission is possible (24, 29, 31, 32). In addition to shedding SARS-CoV-2 RNA through the respiratory tracts, children infected with SARS-CoV-2 shed the virus through gastrointestinal tracts, as indicated by the identification of SARS-CoV-2 RNA in the stools of children (29, 31, 33). Of the 42 children who underwent testing with stool PCR, rectal swab or anal swab (across included studies), 86% returned a positive result (29). The mean duration of viral shedding via the gastrointestinal tract was 23.6 days from symptom onset; in 89% of cases, viral shedding via the gastrointestinal tract continued after nasopharyngeal or throat swabs became negative, for as long as 4 weeks (29). SARS-CoV-2 shedding seems to be present in feces for a longer time than in the respiratory tract of children (32). As well as suggesting the possibility of faecal-oral transmission of SARS-CoV-2, the presence of SARS-CoV-2 RNA in the stool may mean that wastewater can be used as a surveillance method for community spread (34).

Presence of SARS-CoV-2 RNA in a patient's respiratory or gastrointestinal specimens does not directly equate to infectiousness of that individual (as the exact load of viable virus is unknown) (3, 35). Viral load is a proxy measurement of infectivity and, thus, may not necessarily translate to transmissibility (35). Studies assessing the relationship between viral load and infectivity are critical to understand the role children play in transmission. Additionally, the clinical significance of SARS-CoV-2 viral shedding, particularly through the gastrointestinal tract, remains unclear, highlighting the need for further investigation to characterize the pattern and clinical

significance of viral shedding, including whether longer viral shedding times in stools in children pose a higher risk of transmission(20).

Role of children in transmission of COVID-19

To enable better understanding of children's role in transmitting COVID-19, transmission dynamics must be examined in representative populations using a combination of study designs including rigorous epidemiological studies and laboratory studies while taking into consideration the social and socio-economic contexts (36).

Improved understanding of pre-symptomatic and asymptomatic infection is needed to determine the extent to which children play a role in onward transmission of COVID-19 to their peers and to adults in both school and community settings (3).

Acknowledging the limited information, findings from four systematic reviews (2 preprints) and two rapid reviews gave no indications that children played an important role in COVID-19 transmission to date (15, 17, 20, 36, 37). The majority of reviews presented their results narratively. Key findings are summarized below (see table in Annex 1 for details):

- Transmission from children does occur in household and educational settings; however, existing evidence suggests that transmission mainly takes place between adult peers and from adult family members to children
- Transmission of COVID-19 among children or from children to adults appears to be less common
- Household transmission studies showed that children have not played a substantive role in household transmission of SARS-CoV-2 and were much less likely to be the index case (though many of the studies involved testing symptomatic household contacts and thus, may have missed asymptomatic infections)
- Data on COVID-19 in schools are scarce, especially that many schools have been closed in response to the pandemic; in settings where schools remained open or using data prior to closures, there is little evidence of significant outbreaks or major transmission into community
- Existing data so far suggests that children are not the primary drivers of SARS-CoV-2 transmission or outbreaks in school settings

These findings align with more recent (albeit limited) data from several EU countries, Australia and England that have resumed educational activities in schools (see Box 2). Preliminary data suggests low levels of COVID-19 transmission in school

settings whereby children were not the primary drivers of SARS-CoV-2 transmission. Very few significant outbreaks of COVID-19 have been reported: outbreaks involving staff-to-staff transmission were most common, while transmission between staff and students were less common and student-to-student transmissions were least common. Outbreaks may be difficult to detect due to the fact that many infected children do not develop symptoms (and school outbreaks tend to rely on detecting symptomatic cases). As schools worldwide gradually re-open (alongside easing of other restrictions), more large-scale data with longer durations will become available, providing more robust evidence on the transmission dynamics of COVID-19 in children and within school settings and the broader community.

It is worth noting that community transmission was low when many of the countries reported in this document resumed educational activities, with adequate controls and protections in place to restrict the spread of the virus in school settings. Additionally, certain restrictions (initially implemented with lockdown) were still enforced when educational activities resumed in schools.

While none of the studies compared secondary/high schools to primary school, a pre-print literature review on COVID-19 transmission in children suggested the presence of stronger spread of SARS-CoV-2 in secondary/high schools (e.g. Germany, France), with more limited spread in primary schools. However, some countries with large class sizes in primary schools (e.g. Chile) still reported sizeable outbreaks in some of those schools, though the transmission routes to both staff and students were unclear (18). A retrospective cohort study focusing on primary schools exposed to COVID-19 in February and March 2020 in a city north of Paris identified only three separate symptomatic infected students in three different elementary schools with no secondary cases in students, teachers and non-teaching staff of the corresponding schools in the 14 days following these initial cases. These results differed from another study performed by the same author in the high school of the same city, where the rate of seroprevalence for anti-SARS-CoV-2 was 38% among highs school students, 43% among teaching staffs, and 59% among non-teaching staff who participated in the investigation (38, 39). The possible changes in transmission among older students, as suggested above warrants further assessment.

Box 2: COVID-19 Transmission in selected countries where schools have resumed

EU countries: An investigation of COVID-19 infections identified in the school settings of selected EU countries (led by the European Center for Disease and Control), found evidence suggesting that child-to-child transmission in schools is uncommon, and not the primary cause of COVID-19 infection in children. Additionally, children were not the primary drivers of SARS-CoV-2 transmission to adults in the school setting. While very few significant outbreaks of COVID-19 have been reported, they do occur, and may be difficult to detect due to the relative lack of symptoms in infected children (and school outbreaks tend to rely on detecting symptomatic cases). Authors concluded that in the presence of properly implemented physical distancing, hygiene and other measures, schools are unlikely to be "more effective propagating environments than other occupational or leisure settings with similar densities of people" (3).

New South Wales, Australia: A national contact tracing study in all schools and early childhood education and care services (ECEC) between April and July 2020 identified 6 confirmed cases of COVID-19 (4 students and 2 staff) from 6 schools (3 primary schools, 2 high schools and 1 ECEC service). There was no evidence of secondary transmission in any of the 6 educational settings despite the identification of 521 close contacts (62 adults and 459 students/children) (6). Similar low transmission rates were reported in a prospective cohort study conducted in Australian educational settings during January-March 2020; reported transmission rates were as follows: child to child (0.3%); child to staff (1.0%); staff to child (1.5%) and staff-staff (4.4%) (7). It is worth noting that community circulation of SARS-CoV-2 was extremely low in New South Wales, and thus schools remained open throughout the period (29 April to 3 July). Authors concluded that with community awareness, implementation of hygiene and mitigation strategies, staying at home when symptomatic, early testing and contact tracing, transmission can continue to be limited in these settings.

England, UK: A prospective national surveillance by Public Health England identified a low risk of COVID-19 infections or outbreaks among staff and students in educational settings during the first month of schools re-opening after easing of COVID-19 lockdown. From 01 to 30 June 2020, the number of children attending any educational setting increased from 475,000 to 1,646,000. During the same period, 170 reports of COVID-19-related events in educational settings were received by Public Health England: 67 single confirmed cases, 4 co-primary cases and 30 COVID-19 outbreaks, with a strong correlation between number of outbreaks and regional COVID-19 incidence (0.51 outbreaks for each SARS-CoV-2 infection per 100,000 in the community; p=0.001). The probable transmission direction for the 30 confirmed outbreaks was: staff-to-staff (n=15), staff-to-student (n=7), student-to-staff (n=6) and student-to-student (n=2). Most school children with COVID-19 infection were identified as part of contact tracing after their parent was diagnosed with COVID-19. (Ismail et al 2020). It is worth noting that educational settings in England opened when COVID-19 incidence was low[1] and only in regions with low community transmission and with strong infection control and social distancing measures in place (in addition to school attendance not being mandatory). Additionally, the majority of schools that initially opened were preschools and primary schools, thus results are not likely to be generalizable to secondary schools.

Implications

There are still important uncertainties about the spread of SARS-CoV-2 in children including the infectiousness of asymptomatic children, probability of fecal-oral transmission, relationship between viral load and transmission, possible changes in transmission among older children, and role of children in reinfection.

From the currently available evidence, it appears that children, to date, are not substantially contributing to the household or school transmission of SARS-CoV-2. However, given that transmission dynamics change (40) and are affected by other interventions, the current evidence base will evolve as countries continue to lift certain restrictions (initially implemented during lockdown). In many of the countries reported in this document, those restrictions were still in place when educational activities resumed in schools.

Reopening of schools in Fall 2020, alongside easing of other restrictions highlights the need to exercise vigilance (by governments, schools, communities, households) and closely monitor, measure and assess changes in the number of COVID-19 cases, to prompt immediate action according to the most updated evidence.

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Annexes

Annexes

Annex 1: Key findings from evidence syntheses on role of children in transmission of COVID-19

Author's last Name and year	Study Parameters	Findings (including statistical data)
Viner et al., 2020	**Study design:** Pre-print systematic review and meta-analysis **Scope:** Population transmissions including schools and household. **Date last searched:** 28 July 2020 **Number of studies:** 37 **Age of children:** Children and young people (‹20 years). **Countries:** 23 middle and high-income countries in East Asia and Europe	**Population Transmission:** Weak evidence suggests that children and young people play a less important role in SARS-CoV-2 transmission at the population level. **Schools transmission:** Three school contact tracing studies found minimal transmission by child or teacher index cases. Other national CTS undertaken in schools in the Republic of Ireland and Singapore before schools closed identified very few secondary cases resulting from infected children attending school. **Household transmission:** A national South Korean study, found that secondary attack rate from children to household members was extremely low
Ludviggson et al., 2020	**Study design:** Systematic literature review **Scope:** Household and school transmission **Date last searched:** 12 May 2020 **Number of studies:** 47 **Age of children:** N/A **Countries:** N/A	**Household transmission:** Household transmission studies show that children were rarely the index case and other case studies suggested that children with COVID-19 infrequently caused outbreaks. Viral load: Data on viral load were scarce, but those indicated that children may have had lower levels than adults. However, it is highly likely that children can transmit the SARS-COV-2 virus, which causes COVID-19, and even asymptomatic children can have viral load. **School transmission:** Real-world evidence points towards a limited spread of COVID-19 between children and from children. One nine-year-old boy attended three schools while symptomatic with COVID-19, but none of his 112 school contacts contracted the disease. The Australian National Centre for Immunization Research in New South

Author's last Name and year	Study Parameters	Findings (including statistical data)
		Wales described nine high-school students and nine staff with confirmed COVID-19. These 18 individuals had contact with 735 students and 128 staff and only two children may have contracted COVID-10 from these initial school cases, but no staff contracted COVID-19
Madewell et al., 2020	**Study design:** Pre-print systematic review and meta-analysis **Scope:** Household secondary transmissions **Date last searched:** July 29, 2020 **Number of studies:** 40 **Age of children:** N/A **Countries:** China, South Korea, USA, Spain, Australia, Brazil, Brunei, Germany, India, Israel Italy, Singapore, Taiwan, and UK.	**Household transmission:** Data suggests that children have not played a substantive role in household transmission of SARS-CoV-2 and most studies reported significantly lower household secondary attack rate of SARS-CoV-2 from children contacts than adult contacts (16% versus 31 %, respectively). One limitation is that many of the included studies involved testing symptomatic household contacts, which likely missed asymptomatic infections, although secondary attack rate estimates were similar across studies testing all contacts and only symptomatic contacts.
Li et al., 2020	**Study design:** Rapid review **Scope:** Population-based and school-based and household transmission **Date last searched:** 30 April 2020 **Number of studies:** 16 **Age of children:** 0-18 years **Countries:** Iceland, Italy, South Korea, Netherlands, California and the UK.	**School transmission:** There is limited evidence detailing transmission of SARS-CoV-2 from children especially in school settings. Two studies reported a cluster outbreak of COVID-19 in schools and one case report described a pediatric case that attended school but did not transmit the disease to any other pupils or staff despite a large number of contacts in different classes. **Household transmission**: One study reported a 3-month-old whose both parents developed symptomatic COVID-19 seven days after caring for the infant. **Household and school transmission:** One retrospective study followed up 661 pupils and staff in a French high school affected by an outbreak of COVID-19 and found that 40.9% of pupils and staff became infected by school contacts. For household contacts, 10.9% of parents and siblings of infected pupils were also infected.

Author's last Name and year	Study Parameters	Findings (including statistical data)
		However, almost all the students in the study were aged 15-17 years, and appeared to have similar disease characteristics to young adults. Rate of infection reported might be not applicable to younger children.
Rajmil, 2020	**Study design:** Rapid scoping review **Scope:** School and family transmission **Date last searched:** 28 May 2020 **Number of studies:** 14 **Age of children:** N/A **Countries:** China, Taiwan, Korea, Vietnam, Australia, Geneva, the Netherlands, Ireland and Spain	**School transmission:** Studies analyzing school contacts found an extremely low level of COVID-19 transmission at school and suggested that school closures may be less effective in COVID-19 as compared to influenza outbreaks. In Ireland, no secondary school cases were detected after analyzing 125–475 contacts of 3 detected cases in students (10–15 years old) before school closures. **Household transmission**: Although no complete data were available, 75–100% of COVID-19 cases reported in the included studies were from family transmission, and the percentage of asymptomatic children varied from 15% to 60%. **Sero-prevalence**: Preliminary results of study of COVID-19 IgG prevalence carried out in Spain at the general population level indicate that children ‹15 years have a lower prevalence of IgG antibodies than adults Author highlighted current lack of reliable, valid and comparable data on epidemiological surveillance, on the diagnostic tests, and the scarce knowledge on mechanism of transmission and prognostic
Merckx et al., 2020	**Study design:** Systematic review **Scope:** Households, schools, daycares, and clinical settings **Date last searched:** 25 June, 2020 **Number of studies:** 18 **Age of children:** ≤20 years	**Household transmission:** Children were rarely index case and rarely caused secondary cases which was different from influenza. Children had lower relative infectivity **School transmission:** In settings where schools remained open or using data prior to closures, there is little evidence of outbreaks or major transmission into the community. In Australian

Author's last Name and year	Study Parameters	Findings (including statistical data)
	Countries: China, Singapore, South Korea, Japan, Iran, Switzerland, Israel, Australia, France, Ireland, Sweden, USA, Germany, Denmark, Norway, Canada and Italy.	schools, two children contracted COVID-19 after exposure to 9 infected students and 9 infected staff among 735 students and 128 staff. An outbreak in a French high-school is described among 15–17 year olds, with limited cases among sibling contacts. An Irish study describes exposure to an infected child in primary school, two in high school and 3 infected adults, and yet follow-up and testing detected no cases. **Community**: No increased transmission from school-reopening amidst low community transmission, nor from partial return of younger groups amidst higher transmission. No increased staff cases, but increased student cases on return, especially older students (Germany) **Sero-prevalence:** In 455 children ages 5-19 in Geneva, 6% were sero-positivity versus 8.5% in adults. In Spain, 2.9% of children aged 5-9 were seropositive versus 5.2% overall; lower in younger children

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