COVID-19 - research evidence summaries

Research & Evidence team
Here we provide a summary of key current evidence regarding COVID-19 in children and young people.

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This summary is based on published and pre-print studies identified in our rapid review. As evidence is rapidly emerging the content of this page will be reviewed and updated regularly, the search strategy and inclusion criteria used to identify papers can be downloaded below.

This summary was last updated on 25 May 2020.

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Note: Some included studies, indicated in the reference list [*], provide preliminary findings that have not yet been certified by peer review; these findings should be treated with due caution.
Epidemiology

Can children and young people suffer from COVID-19 disease?

COVID-19 disease has been reported in children and young people of all ages, including shortly after birth.\textsuperscript{1 2 3} There have been far fewer confirmed cases of COVID-19 disease in children than adults (children consistently make up <2% of total case numbers in reports).\textsuperscript{4 5 6 7 8 9 10}

We cannot be certain how many children in the community have been infected by SARS-CoV-2 in the absence of widespread, high quality sero surveillance studies, but it seems increasingly likely that there are comparatively few children infected by SARS-CoV-2 and thus suffering from COVID-19 disease in the community.\textsuperscript{4 11 12 13}

Does COVID-19 affect children and young people in the same way as adults?

Infection with SARS-CoV-2 appears to take a milder course in children than in adults: most infected children present with mild symptoms or are asymptomatic,\textsuperscript{1 4 8 14 15 16 17 18} and very few develop severe or life threatening disease.\textsuperscript{9 19 20 21} In the absence of widespread community or serological testing, it is uncertain what the proportion with sub-clinical symptoms is.

Deaths in children due to COVID-19 have been extremely rare: mortality seems to be consistent at around 0.01% (similar to the incidence seen every year with seasonal influenza).\textsuperscript{14 19}

Transmission

Are children as likely as adults to acquire COVID-19?

Emerging evidence suggests that children may be less likely to acquire the disease.\textsuperscript{4 11 12 22 23 24 25 26 27 28 29} This is supported in countries that have undertaken widespread community testing, where significantly lower case numbers in children than adults have been found.\textsuperscript{4 12}

Can children transmit the virus?

The importance of children in transmitting the virus is difficult to establish, in particular given the number of asymptomatic cases,\textsuperscript{30} but there is some evidence that their role in transmitting the virus is fairly limited. Precise details regarding paediatric transmission cannot be confirmed without widespread sero surveillance, but trends are emerging. Studies of multiple family clusters have revealed children were unlikely to be the index case, in Guangzhou, China and internationally.\textsuperscript{28 31 32 33 34} A SARS-CoV-2 positive child in a cluster in the French Alps did not transmit the virus to anyone else, despite exposure to more than 100 people.\textsuperscript{35}
There is some evidence of asymptomatic transmission, but also a signal that symptomatic patients present a higher risk of transmitting the virus than those who do not develop symptoms.

A recent systematic review and metanalysis of the available data on susceptibility and transmission in children and adolescents, available as a preprint through medRxiv, suggests that overall transmission rates in children are lower than those in adults, but there is considerable heterogeneity in the data. In the Netherlands, separate data from primary care and household studies suggests SARS-CoV-2 is mainly spread between adults and from adult family members to children.

This is a rapidly developing area and current published finding may be out of date. We will update this as soon as further information becomes available.

What is the duration of viral shedding in nasopharyngeal or throat swabs?

The duration of viral shedding (in naso-pharyngeal or throat swabs) has been reported in children to range from 6-22 days (median 12 days).

Can children transmit the virus through their stool?

Several studies have now shown that SARS-CoV-2 can be detected by PCR in the stool of affected infants for several weeks after symptoms have resolved; faecal swabs have been found to be positive for a longer duration than nasal swabs with stool shedding reported to be more than 30 days. This has raised the possibility of faecal-oral transmission. Research from Germany did not identify any live, culturable virus in stool despite viral RNA being detectable, suggesting this represents viral debris rather than active virus. Subsequent reports, however, indicate that there has been infectious virus in stool identified, but how much and how infectious is not yet clear as it is not quantified. This would suggest that faecal-oral transmission theoretically is possible but we would need more evidence to really know the ramifications of this. Hand hygiene remains essential. Further studies are needed.

Clinical features and investigations

What are the symptoms of COVID-19 disease?

Disease presentation can range from no symptoms (asymptomatic) to severe pneumonia requiring ITU admission. The absence of widespread community or serological testing, it is uncertain what proportion are asymptomatic. When there are clinical features, they are non-specific and similar to other viral respiratory infections. The most common presenting features, present in more than 50% of cases are cough and fever; upper respiratory tract symptoms (such as sore throat and rhinorrhea) occur in 30-40% of patients; diarrhoea and vomiting present in approximately 9-10% of cases. There are reports of infants presenting with fever but no respiratory symptoms.

Differences in immune responses may play a role in influencing the severity of symptoms.

Please see ‘Can SARS-CoV-2 trigger a Kawasaki like syndrome’ below for further...
information about the symptoms of the hyper-inflammatory response syndrome.

Are there any signs that could help differentiate COVID-19 from other childhood respiratory viral infections?

There appears to be little in the way of clinical signs in children to differentiate COVID-19 from other childhood respiratory virus infections. There have not been any firm descriptions of wheeze with COVID-19 in the literature so far. There are some cases indicating possible (not proven) association with skin manifestations in patients with suspected or confirmed COVID-19 (but please note, this case series does not describe the age of patients so includes adults), which may persist for some time once other symptoms have resolved and include acral areas of erythema oedema with some vesicles or pustules, other vesicular eruptions, urticarial lesions, other maculopapular lesions, livedo or necrosis. Dermatological exanthem, papularmacular and chilblain like lesions associated with COVID-19 have also been reported in children.

Can SARS-CoV-2 trigger a Kawasaki like syndrome?

An emerging phenomenon of a hyperinflammatory response syndrome, resembling Kawasaki shock, is reported in a case study describing a six month old who was treated for Kawasaki’s and then subsequently was found to test positive for SARS-CoV-2. A case series from London described eight children who presented with a hyperinflammatory syndrome similar to 'Kawasaki shock', four of whom had known family exposure to COVID-19. Studies from Italy and France have also described similar cases of a hyperinflammatory syndrome with some evidence of previous COVID-19 infection, as well as in the US.

Symptoms reported include abdominal pain, vomiting and diarrhoea, with persistent high-grade fever and frequently progress to shock with cardiac involvement. Children tend to have high inflammatory markers, myocarditis, macular popular rashes and non-suppurative conjunctivitis. Respiratory involvement does not seem to be present. Investigations are underway to ascertain a link and mechanism of disease.

Further information can be found on the management of children presenting like this. The document details information on how to include cases you might be managing into research studies, such as the DIAMONDS study.

How long after being exposed to SARS-CoV-2 does a child develop symptoms?

The assumed incubation period (time from exposure to index case to developing symptoms) varies in different studies: it has been reported to be between 2- 10 days, with median (and mode) of 7 days vs. 24h – 28d vs. mean of 10 days (IQR 7.75 – 25.25).

Can a child be asymptomatic but still have COVID-19?

Yes, there are reports of asymptomatic cases with positive laboratory confirmed COVID-19. In the absence of widespread community or serological testing, it is uncertain what proportion of children do not have any symptoms or have sub-clinical symptoms. Testing of 120 asymptomatic cancer patients in a US cancer centre revealed 2.5% to be positive (vs. 14.7% of their care givers).
What are blood and imaging tests of children with COVID-19 likely to show?

Laboratory findings are non-specific, and often normal. They may include slightly elevated inflammatory markers including c-reactive protein, and raised liver transaminases. Lymphocytopenia is seen, but more children appear to have raised or normal lymphocyte counts.

Radiological investigations in infected children are also often normal. However, findings may include features consistent with pneumonia such as ground glass opacities or consolidation (commonly bilateral, but with less peripheral predominance than is reportedly found in adults) and CT changes have been found in asymptomatic positive children.

There are several cases of reported co-infection of SARS-CoV-2 and other respiratory viruses, which illustrates that the identification of another respiratory pathogen should not preclude SARS-CoV-2 testing in children.

If a swab is negative for COVID-19 infection is it possible that a child has COVID-19 infection?

We know that virtually no test is perfectly sensitive (correctly picks up all people with the disease) or specific (correctly picks up all people who don’t have the disease) and the same is true for COVID-19. The test that is used to confirm whether someone has COVID-19 infection or not uses swabs from the back of the nose and throat. These are used to look for COVID-19 genetic material in the cells that have been picked up, using a technique called reverse transcriptase polymerase chain reaction (RT-PCR). It is possible to still have COVID-19 infection even if the RT-PCR does not detect COVID-19 genetic material, particularly very early or very late in the disease. We don’t yet know exactly how sensitive or specific the RT-PCR test is at detecting COVID-19 but if there is a high clinical suspicion of infection if a second swab improves the sensitivity. RT-PCR does not tell you if a child has been infected with COVID-19 in the past.

Blood tests are being developed to detect whether someone has or has had COVID-19 infection. These have not yet been validated and are not currently in use in the UK. Once they come into general use they will give more information about the sensitivity and specificity of the swabs and how many people have had COVID-19 infection already.

Predictors of severity

How many days into the illness is a child likely to be sickest?

We do not currently have sufficient evidence to draw any conclusions on this.

Are there any factors that increase the risk of the child being severely affected, e.g. passive smoking?

We do not currently have sufficient evidence to draw any conclusions on this.

Are there haematological or radiological findings which predict disease severity?
At risk groups

Are there any groups that are at higher risk of developing severe COVID-19 illness?

Data on COVID-19 and children with underlying medical conditions is sparse. Immunosuppression does not appear to significantly increase the risk of severe disease. Contact tracing on a dialysis unit who had contact with a member of staff who tested positive found three children to be positive, but only one had symptoms. A case report of a child with cystic fibrosis who contracted COVID-19 from his grandfather, identified though contact tracing, also remained asymptomatic. There is a case report of COVID-19 pneumonia triggering acute chest syndrome in an adolescent with known sickle cell disease on daily hydroxyurea. On screening patients and caregivers with cancer in one of the largest paediatric cancer centres in the US, 20 of 178 paediatric patients tested positive. Only one (5%) required hospitalisation for symptoms of COVID-19, with none requiring critical care.

Comorbidities identified among adults as increasing the risk of severe COVID-19 may not apply to children. CDC data from the USA reports that a high proportion of cases needing admission had at least one co-morbidity (most commonly respiratory). Further data from Italy and the US also finds that children with co-morbidities are over represented in those admitted to hospital, though most were reported to have mild illness. Notably there is no apparent difference in severity according to age in the Italian data, whereas CDC data noted increased hospitalisation in infants (under one year of age) and Dong et al noted higher rates of severe or critical illness infants under one year of age.

The RCPCH have provided guidance for the need for shielding in certain groups. This guidance continues to be reviewed as new evidence emerges.

What are the characteristics of children admitted to PICU?

Severe illness is far less frequent in children than adults, but it is still significant in a very small number of children and young people.

Data on PICU admissions in Italy showed a higher proportion of those admitted to ITU had a co-morbidity (3 out of 4 children needing ICU admission in this case series). In a cross sectional study of 46 North American PICUs, 48 children were admitted to 14 PICUs, with a median age of 13 (4.2 to 16.6). Most presented with respiratory symptoms but there were other presentations, such as with vaso-occlusive crisis (sickle cell) and diabetic ketoacidosis. A total of 40 children (83%) had at least one pre-existing underlying medical condition. The most common comorbidity was medically complex, defined as children who had a long-term dependence on technological support (including tracheostomy) associated with developmental delay and/or genetic abnormalities. Of those, 20% (aged six years or older) had obesity, 38% required invasive ventilation. Extra corporeal membrane oxygenation was required for one patient (2%). Two children died, so the overall ICU mortality rate was <5% (vs. published mortalities of 50-62% in adults admitted to ICU). For those who had been discharged at the time of publication of the paper, the median (range) length of PICU stay was five days (three to nine days) and the mean hospital length of stay
seven days (four to thirteen days).

In summary, studies from PICU admissions in US and Italy have found that those with comorbidities are over represented, most commonly respiratory or complex neurodisability – groups which are otherwise at increased risk of complications from all respiratory viruses. It is not clear if the SARS-CoV-2 infection was causal, contributary or incidental to the ICU admission. The rates of complications from SARS-CoV-2 infection do not appear disproportionate to those from other respiratory viruses from this early data.

**Neonatal**

**Are neonates at increased risk of severe disease?**

Many case reports/series have been published looking at the outcomes of pregnant mothers with COVID-19 and their newborn babies. Mothers and their babies in general appear to do well and neonates without comorbidities do not appear to be at an increased risk of severe disease.91 92 93

**Can COVID-19 increase the risk of pre-term birth, if the mother acquires it in the late second or third trimester?**

There is a small increase in the rates of preterm birth.94 however, the statistical significance of this is unclear.95

One case series has described 10 infants delivered prematurely by COVID-19 positive mothers, via emergency caesarean section, who had a more difficult neonatal course, including one death with disseminated intravascular coagulation.96 All of these infants tested negative for SARS-CoV-2, and the reason for their premature delivery is unclear from the report.

**Can the virus be transmitted vertically?**

As yet, cord blood, amniotic fluid and placental swabs of COVID-19 positive mothers persistently tests negative for SARS-CoV-2 and the vast majority of newborns have not acquired COVID-19 themselves or had adverse outcomes.82 83 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 There are a few cases of infants delivered to COVID-19 positive mothers, who have elevated SARS-CoV-2 IgM after birth, which may indicate intrauterine transmission but this is not clear because these babies tested negative on swab PCR and false positives with IgM are not uncommon.113 114 There have also been cases of newborns and very young infants testing positive shortly after birth (including several94 at or before 12 hours of age)2 92 115 however they have not suffered any known significant complications of the disease and mostly required minimal respiratory support.

**Can the virus be transmitted or through breast milk?**

Most reports of breast milk from COVID-19 positive mothers have found that the breastmilk has tested negative for COVID-19 so it would not appear that the virus can be transmitted through breast milk.3 83 93 109 116 117

There is now a report of viral RNA being found in breast milk in a neonate who subsequently tested positive for COVID-19. It is not clear if this represents live virus, or if the infant
acquired the infection from breast milk.118 WHO continues to recommend breastfeeding with appropriate precautions for COVID-19 positive mothers.

Does having COVID-19 in pregnancy cause any long-term problems for the baby?

We do not currently have sufficient evidence to draw conclusions on this.

**Therapeutics**

**What treatments are available for children with COVID-19?**

For those without severe disease, which will be most children, supportive management (ensuring oxygenation, hydration and nutrition) is appropriate. For more information, please see the RCPCH guidance on the clinical management of children admitted to hospital with suspected COVID-19.

**What studies are enrolling children currently to therapeutic trials?**

For those who develop more severe or critical illness (RCPCH treatment criteria), please consider enrolment in the RECOVERY trial. This study is open at many sites including district general hospitals, and from 11 May will be including children down to those just born.

If you are considering entering a child to RECOVERY, we suggest you check with your Regional Infectious Disease team and watch the relevant video(s) and view the FAQs on the study website. Please note that there are separate training videos in respect to children and infants of less than 29 days of age. If you are still uncertain about eligibility, there is the possibility for you to contact an 'on-call' member of the study team to discuss further, but please only do this if you are particularly uncertain.

If you think entry into RECOVERY is indicated, it can take place in the hospital where the child is admitted - you don't have to wait for them to be transferred to a regional centre.

**Is it safe to give ibuprofen to a child who has tested positive for COVID-19 or is highly likely to be positive?**

There is currently insufficient evidence to establish a link between use of ibuprofen, or other nonsteroidal anti-inflammatory drugs (NSAIDs), and contracting or worsening of COVID-19. Whilst an early report suggested ibuprofen was associated with poorer outcomes, subsequent work has not supported this. The RCPCH has made a statement about the use of ibuprofen in suspected/confirmed COVID-19. *It remains a very powerful, safe and effective medicine for reducing fever in infants, children and young people and adults.*

**Is there an effective vaccine?**

Vaccines will hopefully provide protection against future outbreaks of COVID-19, though these are still early in the drug development pipeline and unlikely to be available this year.

**Prognosis**
What is the prognosis of a child who has had COVID-19?

The short-term prognosis in those who recover appears to be good with both infants\textsuperscript{119} and children largely appearing to make a full recovery.\textsuperscript{21 120}

Are there any long-term complications (in specific groups) such as reduced exercise tolerance, developmental delay, or worsening of cardiac function?

We do not currently have sufficient evidence to draw any conclusions on this.

Delayed access to care

Is there any evidence that delayed access to or provision of care, as a result of the COVID-19 pandemic, is causing children harm?

An Italian case series reports children identified whose parents reported avoiding accessing hospital due to concerns over SARS-CoV-2 infection.\textsuperscript{121} There is significant morbidity and mortality reported. Further evidence is required to ascertain the true presence and extent of this problem, which is a major concern around the world currently, across all age groups.

Summary

COVID-19 does not appear to be as severe in children than in adults: children are often asymptomatic or have a mild course. There is evidence of critical illness and death, but it is rare. There is also some evidence that children may be less likely to acquire the infection. The role of children in transmission, once they have acquired the infection, is unclear, although there is no clear evidence that they are any more infectious than adults. Symptoms are non-specific and most commonly cough and fever. Laboratory and radiological investigations may be normal or mildly altered. There is some evidence of infection in newborns which could indicate vertical transmission, but it is not clear if this is intrauterine or perinatal. Early evidence suggests both infected mothers and newborns are not particularly more severely affected than other groups. Early evidence suggests no significant increased risk for children with immunosuppression, but further data is needed. Children with respiratory and complex neurodisability appear more likely to suffer complications and need hospital +/- PICU admission, but not obviously more than would be expected from infection with other respiratory viruses.

Next steps

We will continue to collate and summarise the evidence around COVID-19 and children and young people as it emerges, in partnership with The Don’t Forget the Bubbles team. A comprehensive summary of all the papers identified on COVID-19 and children published to date is hosted by Don’t Forget the Bubbles.

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