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Evidence summary of potential for children to contribute to transmission of SARS-CoV-2

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Key points

- In total, seven studies were identified; five investigated intra-familial and close contact transmission, one examined transmission of SARS-CoV-2 in schools and one was a mathematical modelling study estimating age-specific transmissibility of SARS-CoV-2.
- Three of the five studies on intra-familial and close contact transmission reported child-to-adult or child-to-family member transmission, although at very low rates.
- The report on transmission of SARS-CoV-2 in schools examined the spread of SARS-CoV-2 from 18 confirmed cases (nine students and nine staff) to 863 close contacts (735 students and 128 staff) in 15 different schools. All individuals had an opportunity to transmit SARS-CoV-2 (the virus that causes COVID-19) to others in their schools.
 - No teacher or staff member contracted COVID-19 from any of the initial school cases.
 - One child from a primary school and one child from a high school may have contracted COVID-19 from the initial cases at their schools.
- The mathematical modelling study, estimating age-specific transmissibility of COVID-19, concluded that COVID-19 had high transmissibility among adults aged 25 years or older, but low transmissibility among children or people younger than 14 years.
- From the small number of studies identified, it appears that children are not, to date, substantially contributing to the household transmission of SARS-CoV-2. From one study, SARS-CoV-2 transmission in children in schools is also very low, however the evidence remains limited.

Introduction

The Health Information and Quality Authority (HIQA) has developed a series of 'Evidence Summaries' to assist the Clinical Expert Advisory Group (EAG) in supporting the National Public Health Emergency Team (NPHE) in their response to COVID-19. These summaries are based on specific research questions. This evidence summary was developed to address the following research question:

What evidence is available to indicate that children spread SARS-CoV-2?

The processes as outlined in HIQA's protocol were followed (available at www.hiqa.ie). This summary was published in April 2020 and has been updated to reflect newly available evidence until 1 May 2020.

Results

A total of three studies were included from the original search and an additional four studies have been added based on this update, giving a total of seven studies overall considered relevant for inclusion (Table 1). These comprised five primary studies (five case series), one secondary analysis of data and one modelling study. Of the five primary studies, four studies focused on intra-familial and close contact transmission,⁽¹⁻⁴⁾ and one was a report on transmission of SARS-CoV-2 in schools.⁽⁵⁾ The secondary analysis of data focused on household transmission clusters from published literature and publicly available data.⁽⁶⁾ The mathematical modelling study estimated age-specific transmissibility of SARS-CoV-2.⁽⁷⁾ Four studies were from China,^(1-3, 7) one report was from Australia,⁽⁵⁾ one in the French Alps,⁽⁴⁾ and the secondary data analysis paper included data from China, Singapore, South Korea, Japan, and Iran.⁽⁶⁾ Sample sizes ranged from 10 to 695.

Intra-familial and close contact transmission

Five studies (four primary and one secondary analysis) examined intra-familial and close contact transmission. Of the four primary studies, one was a case series of patients admitted to children's hospitals in China (n=10),⁽¹⁾ one was a case series describing the epidemiological and clinical characteristics of 74 children with COVID-19 admitted to two hospitals,⁽³⁾ one was a cluster of COVID-19 cases in the French Alps,⁽⁴⁾ and one was an analysis of local health commissions' public disclosures in China (n=419 index patients, 595 household secondary infections).⁽²⁾

The case series by Cai et al.⁽¹⁾ confirmed transmission of SARS-CoV-2 from one of the 10 included children to two family members. This transmission was from a three month old infant to both parents, who developed symptomatic COVID-19 seven days after looking after the infant.⁽¹⁾ A case report of this infant confirms that, at the time of diagnosis, both parents had negative SARS-CoV-2 PCR results. Seven days after

the child's hospitalisation, the father developed fever and fatigue, while the mother was asymptomatic; both parents showed signs of pneumonia on chest CT scan and had positive SARS-CoV-2 PCR results.⁽⁸⁾ The secondary analysis of data study reported 31 SARS-CoV-2 household transmission clusters, of which 9.7% (3/31) were identified as having a paediatric index case.⁽⁶⁾ The original papers for two of these cases could not be retrieved during this current review update, while the third case was of the infant described above in the case series by Cai et al..⁽¹⁾ The authors conducted an analysis of the data assuming that asymptomatic children are being mistakenly overlooked as the index case in familial clusters. Using this approach (assuming asymptomatic children as the index case), 21% (6/28) of family clusters would have a paediatric index case.⁽⁶⁾

A case series describing the epidemiological and clinical characteristics of 74 children with COVID-19 admitted to two hospitals in China reported no evidence that the virus was transmitted from these 74 children to others, although there is limited reporting of how this information was ascertained in the manuscript.⁽³⁾ Exposure data was available for 68 of the 74 patients with 65 (96%) of these cases being household contacts of adults whose symptoms developed earlier.

The analysis of public disclosures data⁽²⁾ based on 419 index patients and their 595 household secondary infections, reported no cases of infection by an index patient 15 years of age or younger. Data presented suggests that three of the index patients were aged less than 18 years and were linked with three secondary cases; however, there are some concerns over the accuracy in the presentation of these data.

Danis et al.⁽⁴⁾ investigated a cluster of COVID-19 cases in the French Alps, linked to one single adult index case. Eleven contacts of this index case tested positive for SARS-CoV-2 (RT-PCR of upper or lower respiratory sample), of which one was a nine year old child, co-infected with other respiratory viruses (picornavirus and influenza A). While symptomatic, the child visited three schools (duration of visit was not reported) and attended one ski class. Overall, 172 contacts were identified of which 112 were school contacts. Of these, 169 individuals were contacted, 70 (41%) had respiratory symptoms during the investigation and a total of 73 were tested with one additional case of COVID-19 identified.

School-based transmission

A report released on 26 April from New South Wales (NSW), Australia examined transmission of SARS-CoV-2 in NSW schools.⁽⁵⁾ It examined the spread of SARS-CoV-2 from 18 confirmed cases (nine students and nine staff) from 15 schools, to 863 close contacts (735 students and 128 staff) in these schools. A close contact was defined as a person who had been in face-to-face contact for at least 15 minutes or in the same room for two hours with a case while infectious. Close contacts of cases

were usually either students or teachers who shared the same class or classes or extracurricular activities as the case or in their close circle of friends. All of these 18 cases are reported to have had an opportunity to transmit SARS-CoV-2 to others in their schools. The report's preliminary findings were that only two students may have contracted SARS-CoV-2 from the initial 18 cases. One secondary case (diagnosed based on the presence of antibodies) was presumed to have been infected following close contact with a student case in a high school. The other secondary case (nose/throat swab positive) was presumed to have been infected by a staff member (teacher), who was a positive case, in a primary school. A full peer-reviewed report is being prepared for publication.

Transmission modelling

In a mathematical modelling study estimating age-specific transmissibility of SARS-CoV-2, Zhao et al.⁽⁷⁾ concluded that SARS-CoV-2 had high transmissibility among adults aged 25 years or older, but low transmissibility among children or people younger than 14 years. The model fit was compared to data from 29 cases (10 of whom had exposure to the Huanan seafood market); this is a very small sample to check the fit of a model. Furthermore, those with exposure to the seafood market may not be representative of transmission patterns more generally.

Study quality

The five primary studies were of low to moderate quality for their design, as there was a lack of detail as to how cases were selected, what the criteria for testing contacts was, what testing was undertaken and how consistently testing was conducted across all contacts.⁽¹⁻⁵⁾ Two studies had small sample sizes^(1, 4) and three studies had not undergone peer review at the time of writing.^(2, 3, 5) Two studies used existing public data,^(2, 6) meaning there is potential for double counting of cases across studies. The secondary analysis of data focused on household transmission clusters from published literature and publicly available data was also a preprint.⁽⁶⁾ The modelling study by Zhao et al.⁽⁷⁾ had a very small sample to check the fit of a model and the sample from the seafood market may not be representative of transmission patterns more generally. This paper was also a pre-print, from a non peer-reviewed journal.

Discussion

Paediatric SARS-CoV-2 accounts for a small percentage of patients. In a large national epidemiological study from Iceland (where 6% of the population underwent SARS-CoV-2 qRT-PCR testing), children under 10 years of age had a lower incidence of SARS-CoV-2 infection than adolescents or adults.⁽¹¹⁾ This would suggest that children are less susceptible to SARS-CoV-2 infection. However it is also noted that paediatric SARS-CoV-2 is often milder than that in adults and a large proportion

are likely to be asymptomatic.^(9, 10) Given initial test capacity constraints, there has been an international trend towards restricting or prioritising RT-PCR testing to designated groups such as healthcare workers and or those with a greater disease burden. As a function of this, fewer cases are diagnosed in children leading to a higher relative underreporting. A recent mathematical model study argued that the most plausible explanation for low case rates in children was age-specific severity, (that is, children are more likely to be asymptomatic and experience milder symptoms) rather than being less susceptible to acquiring the infection.⁽¹²⁾

The WHO-China Joint Mission noted that infected children tended to be identified by contact tracing and that interviewees could not recall episodes of transmission from a child to an adult.⁽¹³⁾ The emerging evidence in the included studies has highlighted child to adult or family member transmission has the potential to occur, although at extremely low rates. It is difficult to ascertain from the broader literature who exactly was the index patient. The case series of 74 children with COVID-19 reported no evidence that the virus was transmitted from children to others. However, the studies focused on intra-familial and close contact transmission suggested transmission from children to other family members could occur.

In the case of the three month old, described in the case series⁽¹⁾ included in this current review, it is feasible that the virus could have been transmitted from the parents to the infant as it was undetermined whether the incubation period was shorter in the infant than in the parents. In their secondary analysis of existing data, Zhu et al.⁽⁶⁾ reported that assuming asymptomatic children were the index case in all familial clusters would still produce a situation where children only accounted for a limited percentage of household cluster transmissions. Preliminary results from unpublished data from 54 households (123 adults and 116 children) from the Dutch National Institute for Public Health and the Environment also highlights that there is no indication that children younger than 12 years were the first to be infected within the family.⁽¹⁴⁾

Preliminary analysis of data on the spread of SARS-CoV-2 within NSW schools has demonstrated a low transmission rate. From 18 cases, there were only two confirmed transmissions out of 863 close contacts with only one case presumed to be transmitted by a child. A recent rapid systematic review on school closure during coronavirus outbreaks (including COVID-19) found limited and conflicting information.⁽¹⁵⁾ The authors cite recent modelling studies of COVID-19 which predict that school closures alone would prevent 2% to 4% of deaths, much less than other social distancing interventions.⁽¹⁵⁾

The mathematical modelling study also concluded that COVID-19 has low transmissibility among children or people younger than 14 years. Some studies of

familial transmission which describe presumed contact and transmission have not been included here. For example, in an analysis of open access databases, Henry et al.⁽¹⁶⁾ reported that 35% (29 patients) of children and adolescents across 14 countries were noted to have an infected family member. However, they did not specifically report transmission from child to adult. Liao et al.⁽¹⁷⁾ reported three cases where asymptomatic adolescents and young adults (aged 10 to 35 years) infected family members; however, it is unclear what age these patients were, so they have not been included in this review. The majority of included studies have looked at familial transmission in known cases and it is often unclear in the literature who the index patient is. Only one study has examined transmission of SARS-CoV-2 in schools. Reliable, large scale data on spread from symptomatic and asymptomatic children is lacking.

Conclusion

There is currently limited information on the contribution of children to the transmission of SARS-CoV-2. Very few definitive cases of virus transmission from children have been published to date. From the small number of published studies identified, it appears that children are not, to date, substantially contributing to the household transmission of SARS-CoV-2. From one study, SARS-CoV-2 transmission in children in schools is also very low.

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Table 1 Characteristics of included studies

Author Country Study design	Population setting Patient demographics Clinical characteristics	Primary outcome results
<p>Cai⁽¹⁾</p> <p>China (Shanghai)</p> <p>Case Series</p> <p>DOI: 10.1093/cid/ciaa198</p>	<p>Population setting: 10 patients admitted to a Children’s Hospital for screening based on presenting with acute fever and/or respiratory symptoms AND an epidemiological link to an adult case/exposure to an epidemic area.</p> <p>Demographics: <i>Age:</i> 3-131 months (mean: 74 months) <i>Gender:</i> Male n = 4, female n = 6</p> <p>Clinical characteristics: <i>Presentation:</i> Fever n=8 (80%); cough n=6 (60%); sore throat n=4 (40%); stuffy nose n=3 (30%); sneezing and rhinorrhoea n=2 (20%). RNA positive within 4-48 hours after symptom onset. RNA (nasopharyngeal/throat swabs) undetectable within 6-22 days (mean: 12 days) after illness onset. RNA (faecal samples) positive 3-13 days after illness onset in five patients, and within 18-30 days after illness onset. All patients discharged when they recovered with two consecutive RNA (respiratory samples) tested negative.</p>	<p>Confirmed transmission Transmission from infected child to adult contacts: N=2 3-month-old infant whose two parents developed symptomatic COVID-19 seven days after looking after the infant. Source of infant infection not reported. Infant had positive nasopharyngeal swabs for 8 days.</p> <p>Number of secondary symptomatic cases including the child and his/her family members who were exposed to a common index case and developed symptoms: 1 to 4 (mean: 2.43).</p> <p>Mean time to transmission/symptoms onset Not reported. Parents developed symptomatic COVID-19 seven days after looking after the infant.</p>
<p>Danis⁽⁴⁾</p> <p>France</p> <p>Case Series (cluster)</p> <p>DOI: 10.1093/cid/ciaa424</p>	<p>Population setting: 1 adult index case (laboratory-confirmed), 11 secondary cases and 1 tertiary case. 1 paediatric case secondary case (laboratory-confirmed) and 112 school contacts. In total, there was 172 contacts (112 school-based) and 73 had RT-PCR tests.</p> <p>Demographics (paediatric case): <i>Age:</i> 9 years <i>Gender:</i> Male</p> <p>Clinical characteristics (paediatric case): <i>Presentation:</i> symptomatic (unspecified)</p>	<p>Confirmed transmission Transmission from infected child: N=0</p> <p>Mean time to transmission/symptoms onset Not applicable</p> <p>Other relevant findings Possible transmission of other viruses (picornavirus) by paediatric case: 3/10 (30%) of contacts</p>

<p>National Centre for Immunisation Research and Surveillance (NCIRS)⁽⁵⁾</p> <p>Epidemiological study</p> <p>Australia (New South Wales)</p> <p>URL: http://ncirs.org.au/sites/default/files/2020-04/NCIRS%20NSW%20Schools%20COVID_Summary_FINAL%20public_26%20April%202020.pdf</p>	<p>Population setting: 18 COVID-19 cases (9 students, 9 staff) and 863 (735 students, 128 staff) close contacts from 15 schools (10 high schools, 5 primary schools).</p> <p><i>High schools</i> 12 index cases (8 students, 4 staff) with 695 close contacts (598 students, 97 staff).</p> <p><i>Primary schools</i> 6 index cases (1 student, 5 staff) with 168 close contacts (137 students, 31 staff).</p> <p>Demographics: <i>Age:</i> Not reported <i>Gender:</i> Not reported</p> <p>Clinical characteristics: Not reported</p>	<p>Confirmed transmission Number of secondary cases in students: N=2 Presumed student to student transmission: N= 1 (high school), secondary case diagnosed based on presence of antibodies. Presumed teacher to student transmission: N= 1 (primary school), secondary case diagnosed as nose/throat swab positive. Presumed student to teacher transmission: N= 0</p> <p>Mean time to transmission/symptoms onset Not reported</p>
<p>Wu⁽³⁾</p> <p>China</p> <p>Case series</p> <p>DOI: 10.1101/2020.03.19.20027078</p>	<p>Population setting: 74 paediatric laboratory-confirmed SARS-CoV-2 cases admitted in Qingdao Women's and Children's Hospital and Wuhan Children's Hospital</p> <p>Demographics: <i>Age:</i> ≤ 3 months: 7 (9.5%) 3 to 6 months: 4 (5.4%) 6 months to 1 year: 5 (6.76%) 1 to 3 years: 12 (16.2%) 3 to 10 years: 31 (41.9%) >10 years: 15 (20.3%) <i>Gender:</i> Male n = 44 (59.5%), female n = 30 (40.5%)</p> <p>Clinical characteristics: <i>Presentation:</i> Cough n=24 (32.4%); fever n=20 (27%); fatigue n=5 (6.8%); Chest congestion n=4 (5.4%); anorexia n=3 (4%); diarrhoea</p>	<p>Confirmed transmission Transmission from infected child to contacts: N=0</p> <p>Mean time to transmission/symptoms onset Not applicable</p>

	<p>(n=3 (4%); dyspnoea n=2 (2.7%); headache n=2 (2.7%), expectoration, n= 2 (2.7%)</p> <p><i>Severity of infection:</i> severe pneumonia n=1; asymptomatic infection n= 20; mild pneumonia n= 29; acute upper respiratory tract infection n= 24</p> <p>RNA positive after symptom onset: Median 2 days (range, 1-6)</p> <p>RNA (faecal samples) positive: 10/74 (13.51%)</p> <p>Viral RNA remained positive in stools of 8 convalescent patients after respiratory specimens were negative, for a median of 11 days (range 5 to 23)</p>	
<p>Xu⁽²⁾</p> <p>China</p> <p>Epidemiological study</p> <p>DOI: 10.1101/2020.03.02.20029868</p>	<p>Population: 419 index patients and their 595 household secondary infections.</p> <p>Index patient: first case patient and the only person who returned home from Wuhan/other cities in Hubei Province in the household.</p> <p>Secondary cases: patients who had no known exposure to virus sources outside of the family.</p> <p>Setting: Local Health Commissions' public disclosures</p> <p>Demographics: Not reported</p> <p>Clinical characteristics: Not reported</p>	<p>Confirmed transmission</p> <p>No case infected by index patient (first case patient) 15 years of age or younger was reported.</p> <p>3 index patients were aged <18 years and infected 3 secondary cases, one aged 0-17 years, one 18-49 years and one 65+</p> <p>Mean time to transmission/symptoms onset</p> <p>No data on child transmission specified.</p> <p>In the full data set, the time between the onset of symptoms in a case patient and the onset of symptoms in the household contacts infected by that patient, was 5.9 days.</p>
<p>Zhao⁽⁷⁾</p> <p>China (Wuhan City)</p> <p>Mathematical model</p> <p>DOI: 10.1101/2020.03.05.20031849</p>	<p>Population data: 29 COVID-19 cases, 10 with history of exposure to Huanan seafood market, 19 without exposure</p> <p>Model parameters data sources</p> <ul style="list-style-type: none"> • Age group proportions, birth rate and death rate - Wuhan Statistical Yearbook • Other parameters – literature 	<p>Model with four-age-groups:</p> <p>Highest transmissibility occurred between the age groups 15 – 44 years and 45 – 64 years, among those ≥ 65 years, or from 45 – 64 years to ≥ 65 years.</p> <p>Lowest transmissibility occurred from age group 0-14 years to 15 – 44 years, or from 45 – 64 years to ≤14 years.</p> <p>Model with five-age-groups:</p> <p>Highest transmissibility occurred between age group 25 – 59 years and ≥ 60 years, or among 25 – 59 years.</p>

		<p>Lowest transmissibility occurred from age group 15 – 24 years to 25 – 59 years, or from age group 0-5 years to 6-14 years, or, to 15-24 years.</p>
<p>Zhu⁽⁶⁾</p> <p>Five countries (China, Singapore, South Korea, Japan, and Iran)</p> <p>Secondary data analysis of published data</p> <p>DOI: 10.1101/2020.03.26.20044826</p>	<p>Population: 31 household transmission clusters</p> <p>Setting: review of published literature and datasets between December 2019 and March 2020</p> <p>Demographics of included children: <i>Mean age (n = 103):</i> 5.35 (± 4.65) <i>Gender (n = 105):</i> 56.19% female</p> <p>Clinical characteristics: <i>Presentation (n=81):</i> Fever 77%; cough 59%; rhinorrhoea 17%; tachypnoea 12%; nausea/vomiting 12%; sore throat 12%; chills 11%; retraction 11%; diarrhoea 6%; fatigue/myalgia/weakness 2% <i>Severity of infection (n = 102):</i> Asymptomatic 19%; Mild - Moderate 69%; Severe 12%</p>	<p>Confirmed transmission Cluster with paediatric index case: 3/31 (9.7%)* Number of secondary cases: 5 Cluster with paediatric index case, assuming that asymptomatic children are being mistakenly overlooked as the index case in familial clusters: 6/28 (21%)</p> <p>Mean time to transmission/symptoms onset Not reported</p> <p>* Note: One case included here is also included in the case series by Cai et al.⁽¹⁾</p>

**Published by the Health Information and Quality Authority
(HIQA).**

For further information please contact:

Health Information and Quality Authority

George's Court

George's Lane

Smithfield

Dublin 7

D07 E98Y

+353 (0)1 8147400

info@hiqa.ie

www.hiqa.ie

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