

## Best Evidence Topic Report

“Zin en onzin van contact met gezonde kinderen vermijden om virus transmissie te voorkomen?”

|                            |   |
|----------------------------|---|
| Title                      | Sense and nonsense of avoiding contact with healthy children to prevent virus transmission?   |
| Report by                  | Eline Vingerhoets en Valerie Wauteraerts, studenten geneeskunde   |
| Search checked by          | Dr. Marc Van Nuland, ACHG KU Leuven   |
| Clinical scenario          | <p>The pandemic of COVID-19 affects many households. Governments make strict policies to prevent the further spread of the novel coronavirus. Schools are closed and working from home is recommended. A woman goes to her general practitioner to ask advice. Her child, who is now at home, had contact with a classmate who tested positive for coronavirus.</p> <p>Her husband, who works now at home, belongs to the risk population because of decreased immunity. The woman wants to know if her asymptomatic child should be isolated from her husband, the grandparents and/or herself. Does it make sense to avoid contact with healthy children to prevent virus transmission?</p> |
| Answerable question (PICO) | Does it make sense to [avoid contact] (Intervention) with [healthy children] (Population) to [prevent virus transmission] (Outcome)?  |
| Search terms               | <p><b>Medline:</b><br/>         (SARS-CoV-2 OR COVID-19 OR coronavirus OR 2019-nCoV) AND (child* OR pediatr* OR boy OR girl) AND (asymptomatic OR transmis* OR epidemiolog* OR contag*)</p> <p><b>Mesh Terms:</b></p> <ul style="list-style-type: none"> <li>- "COVID-19" [Supplementary Concept] AND "Disease Transmission, Infectious"[Mesh] AND ("Child"[Mesh] OR "Child, Preschool"[Mesh])</li> <li>- "COVID-19" [Supplementary Concept] AND ("Child"[Mesh] OR "Child, Preschool"[Mesh])</li> </ul>   |

|  |  |
|--|--|
|  | <p><b>Embase:</b><br/>(SARS-CoV-2 OR COVID-19 OR coronavirus OR 2019-nCoV) AND (child* OR pediatr* OR boy OR girl) AND (asymptomatic OR transmis* OR epidemiolog*) AND (2019:py OR 2020:py)</p> <p><b>Cochrane:</b><br/>Free search term: COVID-19</p>   |
| Search date                                  | March 18, 2020   |
| Search outcome (number of hits)              | <p><b>Medline:</b><br/>719 hits of which 706 irrelevant and 6 were excluded based on language (Chinese)</p> <p>Mesh termen: 11 hits, all of them were excluded based on language (Chinese)</p> <p><b>Embase:</b><br/>114 hits of which 106 irrelevant and 6 were excluded based on language (Chinese) or the full text was not available</p> <p><b>Cochrane:</b> 2 special collections on Coronavirus (COVID-19)</p> <p>Exclusion criteria were articles not corresponding to the search query (e.g. vertical transmission) and articles in a language other than English.</p> |
| Relevant papers (number of final inclusions) | <p><b>Medline:</b> 7 relevant papers</p> <p><b>Embase:</b> 2 (also found in Medline (Pubmed)) relevant papers</p> <p><b>Cochrane:</b> 1 relevant paper</p>   |

| <b>Evidence table</b>  |                                      |  |                                       |  |  |  |
|--|--------------------------------------|--|---------------------------------------|--|--|--|
| <b>Title</b>   | <b>Author, date, country</b>         | <b>Patient group</b>   | <b>Study type (level of evidence)</b> | <b>Outcomes</b>  | <b>Key results</b>   | <b>Study weaknesses</b>  |
| Cochrane special collection on coronavirus (COVID-19): infection control and prevention measures, section physical interventions to interrupt or reduce the spread of respiratory viruses <sup>1</sup> | Jefferson T. et al., July 6, 2011    | People of all ages   | Cochrane Systematic Review            | Effectiveness of physical interventions in the spread of respiratory viruses | The four highest quality cluster-randomised trials indicate most effect on preventing respiratory virus spread with hygienic measures, such as handwashing, especially around younger children. Benefit from reduced transmission from children to household members is broadly supported also in other study designs where the potential for confounding is greater. Multiple case-control studies suggested implementing transmission barriers, isolation and hygienic measures are effective at preventing respiratory virus epidemics. | Not specific about the transmission of COVID-19  |
| Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China <sup>2</sup>   | Wang Y. et al, March 17, 2020, China | 55 asymptomatic patients (aged 2 - 69 years old) were tested positive for the SARS-CoV-2 after their family member's diagnoses of COVID-19 | Observational study                   | Clinical characteristics   | Of the 55 patients, 14 turned out to be mild cases, 39 developed ordinary symptoms and 2 were severe COVID-19 cases during hospitalization. A two years old boy was diagnosed as ordinary COVID-19 after testing for three times within two weeks.   | Retrospective analysis<br><br>Potential selection bias: enrolled cases were identified from systematic screening of the family members of patients positive for COVID-19 |
| Novel  | Wei M.                               | 9 hospitalized   | Observational                         | Transmission   | This study showed that infants can be infected by  | Small sample size  |

|   |                                      |  |                     |                                 |  |  |
|---|--------------------------------------|--|---------------------|---------------------------------|--|--|
| coronavirus infection in hospitalized infants under 1 year of age in China <sup>3</sup>   | et al, February 14, 2020, China      | infants (aged 1 - 11 months) diagnosed with COVID-19 infection between December 8, 2019, and February 6, 2020, in China  | study               | dynamics                        | <p>COVID-19. The earlier stage of the COVID-19 epidemic primarily involved adults older than 15 years.</p> <p>Because infants younger than 1 year cannot wear masks, they require specific protective measures. Adult caretakers should wear masks, wash hands before close contact with infants, and sterilize the infants' toys and tableware regularly.</p> <p>Family clustering occurred for all infected infants.</p> | <p>Potential selection bias: inclusion only of infants who were hospitalized, and lack of inclusion of asymptomatic patients.</p> <p>Retrospective study design</p>                          |
| Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China <sup>4</sup> | Hu Z. et al., March 3, 2020, China   | 24 asymptomatic patients, aged 5 to 95 years old (5/24 aged < 15 years old), who were close contacts of COVID-19 patients in Nanjing                             | Observational study | Clinical characteristics        | <p>Only five cases developed typical symptoms during hospitalization.</p> <p>17 patients showed typical or atypical findings on chest CT-scan. Seven patients had normal images and no symptoms during hospitalization. These seven patients were younger.</p> <p>Young cases (&lt;15 years old) were prone to be asymptomatic even during hospitalization and to have a normal CT image.</p>                              | <p>Small sample size</p> <p>Retrospective analysis</p> <p>Potential selection bias: possibility of missing (other) carriers when only screening from close contacts of positive patients</p> |
|   |                                      |  |                     | Transmission dynamics           | <p>An asymptomatic COVID-19 carrier transmitted the virus to his cohabiting family members, and 1 of the infected individuals developed severe COVID-19 pneumonia and was admitted to ICU.</p>   |  |
| Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China <sup>5</sup>                    | Dong Y. et al, March 16, 2020, China | 2143 pediatric patients (<18 years old) with COVID-19 were reported to the Chinese Center for Disease Control and Prevention from January 16 to February 8, 2020 | Case series         | Epidemiological characteristics | <p>No statistically significant difference in the number of pediatric patients between boys and girls.</p> <p>Children at all ages were susceptible to COVID-19. However, young children, particularly infants, were vulnerable to 2019-nCoV infection.</p>  | <p>Retrospective analysis</p> <p>No clinical features of children's COVID-19 assessed</p>  |
|   |                                      |  |                     | Clinical characteristics        | <p>Compared with the adults' cases, the severity of children's COVID-19 cases was milder, and the case fatality rate was much lower.</p>   |  |
|   |                                      |  |                     | Transmission dynamics           | <p>Most of the children were exposed to family members and/or other children with COVID-19 which clearly indicates person-to-person transmission.</p>  |  |

|   |  |   |  |                          |   |  |
|---|--|---|--|--------------------------|---|--|
| A case series of children with 2019 novel coronavirus infection: clinical and epidemiological features <sup>6</sup> | Cai J. et al, February 28, 2020, China | Between 19 January and 3 February, 2020, ten children with confirmed 2019-nCoV infection were admitted to the hospital in Shanghai, Hainan, Hefei and Qingdao | Case series                                | Clinical characteristics | Children with COVID-19 usually presented with mild respiratory infections, as compared with adult cases.  | Small sample size<br>Case series<br>Retrospective analysis |
|   |  |   |  | Transmission dynamics    | This study highly support the evidence of human-to-human transmission of COVID-19. The mean incubation period was 6.5 days. This is longer compared to adult cases in who 5.2 days was observed.<br>The mean number of secondary symptomatic cases in household exposure setting was 2.43.<br>Virus shedding in respiratory (mean 12 days) and stool (2 weeks - one month) specimens is long in children with a mild COVID-19 infection.<br>Most of pediatric cases occurring outside of Wuhan were secondary cases after exposure to adult cases through household contact or travel contact. However, transmission from the infected child to adult contacts is possible. The major pattern of transmission was intrafamily transmission. |  |
| A well infant with coronavirus disease 2019 (COVID-19) with high viral load <sup>7</sup>                            | Kam K., February 28, 2020              | A 6-month old boy whose parents tested positive for COVID-19  | Case report                                | Clinical characteristics | The child was tested positive with a nasopharyngeal swab on day one of admission. He was found to be viremic with detection of SARS-CoV-2 in his blood sample on day two. Besides from a single transient temperature of 38,5° C during this viremic phase, he had no clinical signs or symptoms during hospitalization. Samples from the nasopharynx continue to remain positive up to day 16 of admission. The infant had also a positive stool sample on day 9 of admission.   | Case report of only one patient<br>Retrospective analysis  |
| SARS-CoV-2 infection in children: Transmission dynamics and clinical characteristics <sup>8</sup>                   | Cao Q. et al, February 26, 2020, China | Accumulated and daily new case numbers of children in China outside Hubei province between January 20 and February 10, 2020                                   | Perspective (opinion based on 14 articles) | Transmission dynamics    | Infection can occur by respiratory droplets containing the virus (respiratory route) or by contact with contaminated objects. Airborne or aerosol transmission can occur similar to previous SARS outbreak.<br><br>In the emerging stage person-to-person transmission in the community occurs almost exclusively among adults. Afterwards, intrafamilial transmission occurs, especially transmission to the elderly and children. So aggregative onset is an important feature in pediatric cases. Children at that stage can further become the main spreader of   | No statistical analysis<br>Opinion based                   |

|  |  |  |  |                          |  |  |
|--|--|--|--|--------------------------|--|--|
|  |  |  |  |                          | SARS-CoV-2 because their infection is usually mild.  |  |
|  |  |  |  | Clinical characteristics | <p>Infected children may be asymptomatic or have fever, dry cough and fatigue; some patients experience gastrointestinal symptoms, including abdominal discomfort, nausea, vomiting, abdominal pain and diarrhea.</p> <p>Most infected children have mild clinical manifestations and usually have a good prognosis. Usually they recover within 1–2 weeks after the onset of the disease.</p> |  |

### **Main results:**

Multiple studies provide evidence about the human-to-human transmission of COVID-19. The virus transmission occurs through respiratory droplets and contact with contaminated objects. Positive stool samples suggest that indirect transmission might also be possible via feces. The most seen pattern of transmission was intrafamily transmission. Children of all ages are susceptible for COVID-19 infection and younger children, particularly infants (<1y), are most vulnerable. Infected children are often asymptomatic or have a mild disease course with symptoms as fever, mild cough or sore throat. One case even describes a high viral load with a viremia in a 6-month old boy with a single temperature increase to 38,5°C. The case fatality rate in children is much lower as compared with adults. Children might have a longer incubation time compared to adults with a mean of 6,5 days. Prolonged virus shedding is observed in respiratory tract and feces at the convalescent stage. As a consequence of their mild and unnoticed coronavirus infection, children can become the main spreader of the virus. Hygienic measures in children are very effective in preventing the spread of respiratory viruses.

### **Risks of bias:**

Most of the included studies have a low grade of evidence. In our research we were confronted with bias due to small sample sizes and retrospective study designs. Most studies originate from the first epidemic region in China and may have a selection bias. The recent onset of this new disease and therefore scarce data about this topic, is the main reason for these bias.

### **Clinical bottom line:**

Even healthy children may play an important role in the transmission of COVID-19 because they could be asymptomatic or have only mild symptoms of infection. Due to these mild course of the disease and the prolonged viral shedding, children can easily spread the virus without people knowing it. Persons in close contact with these healthy children, especially risk populations, should be aware of this. We advise them to

avoid unnecessary contact with children. Adult caretakers should wash hands before and after close contact with infants and sterilize their toys and tableware regularly.

## References

1. Jefferson T, Del Mar CB, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, van Driel ML, Nair S, Jones MA, Thorning S, Conly JM. Physical interventions to interrupt or reduce the spread of respiratory viruses. *Cochrane Database of Systematic Reviews* 2011, Issue 7.  
Part of: Bero, L., Lasserson, T., Opiyo, N., Featherstone, R. & Mehta, M. (2020). Coronavirus (COVID-19): infection control and prevention measures. *Cochrane Library*
2. Wang, Y., Liu, Y., Liu, L., Wang, X., Luo, N. & Ling, L. (2020). Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China. *The Journal of Infectious Diseases*
3. Wei, M., Yuan, J., Liu, Y., Fu, T., Yu, X., & Zhang, Z. J. (2020). Novel coronavirus infection in hospitalized infants under 1 year of age in China. *Jama*.
4. Hu, Z., Song, C., Xu, C., Jin, G., Chen, Y., Xu, X., ... & Wang, J. (2020). Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. *Science China Life Sciences*, 1-6.
5. Dong, Y., Mo, X., Hu, Y., Qi, X., Jiang, F., Jiang, Z., & Tong, S. (2020). Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China. *Pediatrics*.
6. Cai, J., Xu, J., Lin, D., Xu, L., Qu, Z., Zhang, Y., ... & Xia, A. (2020). A Case Series of children with 2019 novel coronavirus infection: clinical and epidemiological features. *Clinical Infectious Diseases*.
7. Kam, K. Q., Yung, C. F., Cui, L., Lin Tzer Pin, R., Mak, T. M., Maiwald, M., ... & Thoon, K. C. (2020). A well infant with coronavirus disease 2019 (COVID-19) with high viral load. *Clinical Infectious Diseases*.
8. Cao, Q., Chen, Y. C., Chen, C. L., & Chiu, C. H. (2020). SARS-CoV-2 infection in children: Transmission dynamics and clinical characteristics. *Journal of the Formosan Medical Association= Taiwan yi zhi*.