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Overview of COVID-19 In Children and Young Persons

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Outline

- Background
- Objective – Epidemiological analysis of the role children/adolescents play in the COVID-19 pandemic
  - Severity of symptoms of children/adolescents
  - Risk of children/adolescents acquiring SARS-CoV-2
  - Risk of children/adolescents transmitting SARS-CoV-2
- Availability of data
- Results
  - Before the emergence of Variants of Concern (VOCs)
  - Since the emergence of Variants of Concern (VOCs)
- Conclusion

Background – Disease burden for children and adolescents

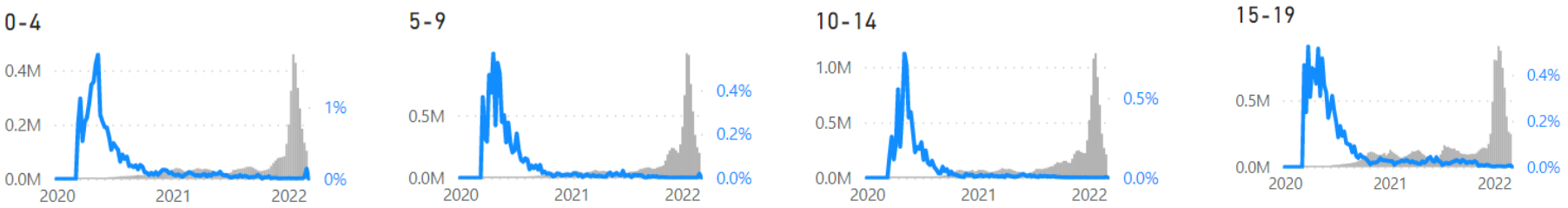
Age group	Number of reported cases	Proportion of all cases
< 5 years	5,299,783	2.5%
5 - 14 years	23,205,414	10.8%
15 - 24 years	31,422,378	14.6%

Total global cases (confirmed and probable) reported to the WHO, all ages: 215,446,888

Age group	Number of deaths	Proportion of reported deaths
< 5 years	2,348	0.1%
5 - 14 years	1,668	0.07%
15 - 24 years	8,454	0.36%

Total global deaths (confirmed and probable) reported to the WHO, all ages: 2,376,780

Cases (confirmed and probable) **and** Case Fatality Ratio (CFR)



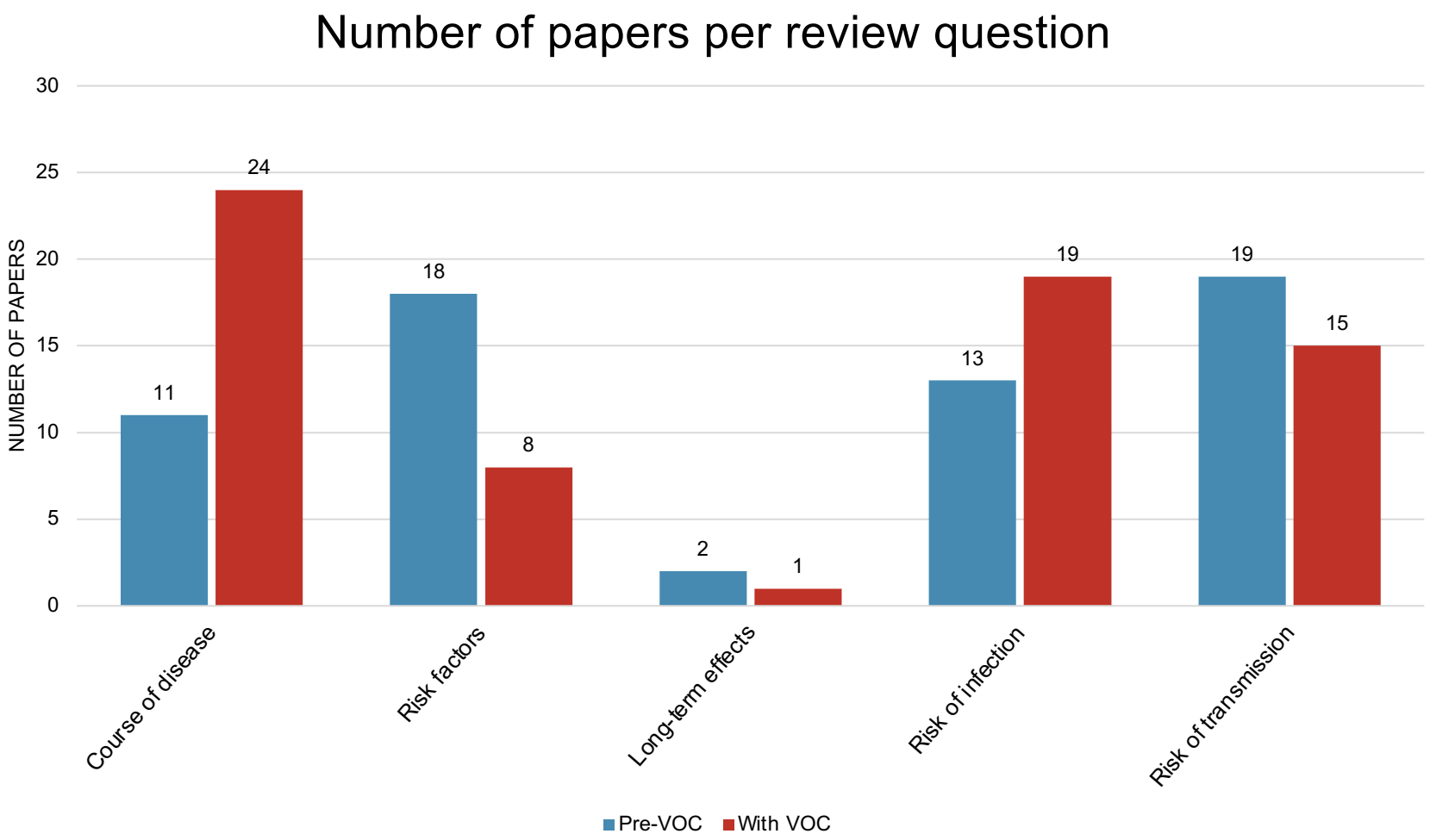
(30 December 2019 – 21 February 2022; 184 countries)

Objective

Epidemiological analysis of the role children (≤10 years of age) and adolescents (10-20 years of age) play in this pandemic

1. Severity of symptoms of children/adolescents
   a. Course of SARS-CoV-2 disease
   b. Risk factors for severe SARS-CoV-2 disease
   c. Long-term effects of SARS-CoV-2 disease
2. Risk of children/adolescents acquiring SARS-CoV-2
3. Risk of children/adolescents transmitting SARS-CoV-2

Availability of data



Results – Severity of symptoms I

Before emergence of variants of concern	Since emergence of variants of concern (Alpha, Beta, Gamma, Delta, Omicron)
– Mostly mild course of disease – 26-44% of children persistently asymptomatic[1-4]	– Mostly mild course of disease[14-20] – **Delta:** slightly higher symptom burden than Alpha[20] – **Delta, Gamma:** more hospitalizations/ICU admissions for school children than Alpha/non-VOC[21-23] – **Omicron:** less severe outcomes compared to Delta, but increased hospitalization (due to high case numbers)[18,24-26]

CAVE: Vaccines might reduce disease severity → difficult to distinguish between VOC and effect of vaccines

Results – Severity of symptoms II

Before emergence of variants of concern	Since emergence of variants of concern (Alpha, Beta, Gamma, Delta, Omicron)
Risk factors for severe disease (incl. PIMS-TS/MIS-C): – Age: unclear[5-8] – Preconditions (e.g. cancer, immunosuppression): no [9-11]	**Risk factors for severe disease (incl. PIMS-TS/MIS-C):** – Unclear
Risk for developing Long-COVID: – Development of long-term effects possible, but mostly rare (1.8-4%) [12-13]	**Risk for developing Long-COVID:** – **Alpha and Delta:** Long term effects reported, but mostly rare (1.7-2.1%)[20]

Results – Risk of child/adolescent infection

Before emergence of variants of concern	Since emergence of variants of concern (Alpha, Beta, Gamma, Delta, Omicron)
– Lower case numbers and lower seroprevalence especially for younger children compared to adults[27,34-36] – Risk of infection for younger children about 50% lower than for adults[28-30] – Secondary attack rate increases with age[31-33]	– Higher prevalence during Alpha and Delta waves compared to older adults[37,38] – **Alpha, Delta:** Risk of infection for (younger) children lower than for adults[39-42]

CAVE: Adult vaccination status is often not reported
Relative risks of infection depend on community transmission and strength of preventive measures in different age groups

Results – Risk of child/adolescent transmission

Before emergence of variants of concern	Since emergence of variants of concern (Alpha, Beta, Gamma, Delta, Omicron)
– SARS-CoV-2 viral load increases with age [43,44] – Transmission and cluster development possible[45-47] – Limited transmission in schools or households with fewer secondary cases from pediatric index cases than from adults [29,48-50] – Risk of transmission dependent on community transmission [49]	– SARS-CoV-2 viral load potentially comparable [51,52] – Transmission and cluster possible[53,54] – **Alpha:** secondary attack rate from children comparable to adults [42,53,55]

CAVE: Adult vaccination status is often not reported
Relative risks of infection depend on community transmission and strength of preventive measures in different age groups

Conclusion

- Severity of disease in children/adolescents
  - Mostly mild disease
  - Long-term effects occur (but most likely rare)
- Child/adolescent susceptibility to and transmission of SARS-CoV-2
  - Potentially age-dependent (lower risk for younger children)
  - Age-related differences dependent on further factors
    - Community transmission
    - Exposure differences in age groups
    - Non-pharmaceutical measures
- Limitations of available data (external validity etc.)
  - Poor reporting of age
  - Poor reporting of epidemiological context and preventive measures in place

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Thank you for your attention

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References (I)

References
1. Buitrago-Garcia D, Egli-Gany D, Counotte MJ, Hossmann S, Imeri H, Ipekci AM, et al. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis. PLoS Med. 2020;17(9):e1003346.
2. Richard A, Wisniak A, Perez-Saez J, Garrison-Desany H, Petrovic D, Piumatti G, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies, risk factors for infection and associated symptoms in Geneva, Switzerland: a population-based study. medRxiv. 2020.
3. Ulyte A, Radtke T, Abela IA, Haile SR, Blankenberger J, Jung R, et al. Variation in SARS-CoV-2 seroprevalence across districts, schools and classes: baseline measurements from a cohort of primary and secondary school children in Switzerland. BMJ Open. 2021;11(7):e047483.
4. Ulyte A, Radtke T, Abela IA, Haile SR, Berger C, Huber M, et al. Clustering and longitudinal change in SARS-CoV-2 seroprevalence in school children in the canton of Zurich, Switzerland: prospective cohort study of 55 schools. BMJ. 2021;372:n616.
5. Sheth S, Shah N, Bhandari V. Outcomes in COVID-19 Positive Neonates and Possibility of Viral Vertical Transmission: A Narrative Review. Am J Perinatol. 2020;37(12):1208-16.
6. Kyle MH, Glassman ME, Khan A, Fernandez CR, Hanft E, Emeruwa UN, et al. A review of newborn outcomes during the COVID-19 pandemic. Semin Perinatol. 2020;44(7):151286.
7. Gale C, Quigley MA, Placzek A, Knight M, Ladhani S, Draper ES, et al. Characteristics and outcomes of neonatal SARS-CoV-2 infection in the UK: a prospective national cohort study using active surveillance. Lancet Child Adolesc Health. 2021;5(2):113-21.
8. Swann OV, Holden KA, Turtle L, Pollock L, Fairfield CJ, Drake TM, et al. Clinical characteristics of children and young people admitted to hospital with covid-19 in United Kingdom: prospective multicentre observational cohort study. BMJ. 2020;370:m3249.
9. Boulad F, Kamboj M, Bouvier N, Mauguen A, Kung AL. COVID-19 in Children With Cancer in New York City. JAMA Oncol. 2020;6(9):1459-60.

References (II)

References
10. Hrusak O, Kalina T, Wolf J, Balduzzi A, Provenzi M, Rizzari C, et al. Flash survey on severe acute respiratory syndrome coronavirus-2 infections in paediatric patients on anticancer treatment. Eur J Cancer. 2020;132:11-6.
11. Minotti C, Tirelli F, Barbieri E, Giaquinto C, Dona D. How is immunosuppressive status affecting children and adults in SARS-CoV-2 infection? A systematic review. J Infect. 2020;81(1):e61-e6.
12. Radtke T, Ulyte A, Puhan MA, Kriemler S. Long-term Symptoms After SARS-CoV-2 Infection in Children and Adolescents. JAMA. 2021.
13. Molteni E, Sudre CH, Canas LS, Bhopal SS, Hughes RC, Antonelli M, et al. Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2. Lancet Child Adolesc Health. 2021
14. Lam-Hine T, McCurdy SA, Santora L, Duncan L, Corbett-Detig R, Kapusinszky B, et al. Outbreak Associated with SARS-CoV-2 B.1.617.2 (Delta) Variant in an Elementary School - Marin County, California, May-June 2021. MMWR Morb Mortal Wkly Rep. 2021;70(35):1214-9.
15. Ulyte A, Radtke T, Abela IA, Haile SR, Ammann P, Berger C, et al. Evolution of SARS-CoV-2 seroprevalence and clusters in school children from June 2020 to April 2021 reflect community transmission: prospective cohort study Ciao Corona. MedRxiv. 2021.
16. Ryu BH, Hong SI, Lim SJ, Cho Y, Hong KW, Bae IG, et al. Features of COVID-19 Among Children and Adolescents Without Risk Factors Before and After the Delta Variant Outbreak in South Korea. Pediatr Infect Dis J. 2022;41(1):e34-e5.
17. Butt AA, Dargham SR, Chemaitelly H, Al Khal A, Tang P, Hasan MR, et al. Severity of Illness in Persons Infected With the SARS-CoV-2 Delta Variant vs Beta Variant in Qatar. JAMA Intern Med. 2022;182(2):197-205.

References (III)

References
18. Wang L, Berger NA, Kaelber DC, Davis PB, Volkow ND, Xu R. COVID infection severity in children under 5 years old before and after Omicron emergence in the US. medRxiv. 2022.
19. Meyer M, Holfter A, Ruebsteck E, Gruell H, Dewald F, Koerner RW, et al. The alpha variant (B.1.1.7) of sars-cov-2 in children: First experience from 3544 nucleic acid amplification tests in a cohort of children in germany. Viruses. 2021;13(8).
20. Molteni E, Sudre CH, Canas LS, Bhopal SS, Hughes RC, Chen L, et al. Illness characteristics of COVID-19 in children infected with the SARS-CoV-2 Delta variant. MedRxiv. 2021.
21. Çelebi MY, Kıymet E, Böncüoğlu E, Şahinkaya Ş, Cem E, Düzgöl M, et al. Evaluation of childhood hospitalization rates and degree of severity of SARS-CoV-2 variants including of the B.1.1.7 (Alpha), B.1.315/P.1 (Beta/Gamma), and B.1.617.2 (Delta). J Med Virol. 2022.
22. Oliveira EA, Simoes ESAC, Oliveira MCL, Colosimo EA, Mak RH, Vasconcelos MA, et al. Comparison of the First and Second Waves of the Coronavirus Disease 2019 (COVID-19) Pandemic in Children and Adolescents in a Middle-Income Country: Clinical Impact Associated with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Gamma Lineage. J Pediatr. 2022.
23. Shoji K, Akiyama T, Tsuzuki S, Matsunaga N, Asai Y, Suzuki S, et al. Comparison of the clinical characteristics and outcomes of COVID-19 in children before and after the emergence of Delta variant of concern in Japan. J Infect Chemother. 2022.
24. Iuliano AD, Brunkard JM, Boehmer TK, Peterson E, Adjei S, Binder AM, et al. Trends in Disease Severity and Health Care Utilization During the Early Omicron Variant Period Compared with Previous SARS-CoV-2 High Transmission Periods - United States, December 2020-January 2022. MMWR Morb Mortal Wkly Rep. 2022;71(4):146-52.
25. Cloete J, Kruger A, Masha M, du Plessis NM, Mawela D, Tshukudu M, et al. Rapid rise in paediatric COVID-19 hospitalisations during the early stages of the Omicron wave, Tshwane District, South Africa. MedRxiv. 2021;13:S27-S8.

References (IV)

References
26. Marks KJ, Whitaker M, Anglin O, Milucky J, Patel K, Pham H, et al. Hospitalizations of Children and Adolescents with Laboratory-Confirmed COVID-19 - COVID-NET, 14 States, July 2021-January 2022. MMWR Morb Mortal Wkly Rep. 2022;71(7):271-8.
27. Children's Task and Finish Group. Children's Task and Finish Group: update to 4th Nov 2020 paper on children, schools and transmission. 2020.
28. Viner RM, Mytton OT, Bonell C, Melendez-Torres GJ, Ward J, Hudson L, et al. Susceptibility to SARS-CoV-2 Infection Among Children and Adolescents Compared With Adults: A Systematic Review and Meta-analysis. JAMA Pediatr. 2021;175(2):143-56.
29. Zhu Y, Bloxham CJ, Hulme KD, Sinclair JE, Tong ZWM, Steele LE, et al. A meta-analysis on the role of children in SARS-CoV-2 in household transmission clusters. Clin Infect Dis. 2020.
30. Madewell ZJ, Yang Y, Longini IM, Jr., Halloran ME, Dean NE. Household Transmission of SARS-CoV-2: A Systematic Review and Meta-analysis. JAMA Netw Open. 2020;3(12):e2031756.
31. Li W, Zhang B, Lu J, Liu S, Chang Z, Peng C, et al. Characteristics of Household Transmission of COVID-19. Clin Infect Dis. 2020;71(8):1943-6.
32. Yung CF, Kam KQ, Chong CY, Nadua KD, Li J, Tan NWH, et al. Household Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 from Adults to Children. J Pediatr. 2020;225:249-51.
33. Somekh E, Gleyzer A, Heller E, Lopian M, Kashani-Ligumski L, Czeiger S, et al. The Role of Children in the Dynamics of Intra Family Coronavirus 2019 Spread in Densely Populated Area. Pediatr Infect Dis J. 2020;39(8):e202-e4.
34. Pollan M, Perez-Gomez B, Pastor-Barriuso R, Oteo J, Hernan MA, Perez-Olmeda M, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. Lancet. 2020;396(10250):535-44.
35. Stringhini S, Wisniak A, Piumatti G, Azman AS, Lauer SA, Baysson H, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study. Lancet. 2020;396(10247):313-9.

References (V)

References
36. Stringhini S, Zaballa ME, Perez-Saez J, Pullen N, de Mestral C, Picazio A, et al. Seroprevalence of anti-SARS-CoV-2 antibodies after the second pandemic peak. Lancet Infect Dis. 2021.
37. Riley S, Eales O, Haw D, Wang H, Walters CE, Ainslie KEC, et al. REACT-1 round 13 interim report: acceleration of SARS-CoV-2 Delta epidemic in the community in England during late June and early July 2021. MedRxiv. 2021.
38. Riley S, Walters CE, Wang H, Eales O, Haw D, Ainslie KEC, et al. REACT-1 round 9 final report: Continued but slowing decline of prevalence of SARS-CoV-2 during national lockdown in England in February 2021. MedRxiv. 2021.
39. Abu-Raddad LJ, Chemaitelly H, Ayoub HH, Coyle P, Malek JA, Ahmed AA, et al. Introduction and expansion of the SARS-CoV-2 B.1.1.7 variant and reinfections in Qatar: A nationally representative cohort study. PLoS Med. 2021;18(12):e1003879.
40. Roberts RJ, Brooker A, Lakshman R. Outbreak of SARS-CoV-2 in a Children's Nursery in the United Kingdom. Pediatr Infect Dis J. 2021.
41. Clifford S, Waight P, Hackman J, Hue S, Gower CM, Kirsebom FC, et al. Effectiveness of BNT162b2 and ChAdOx1 against SARS-CoV-2 household transmission - a prospective cohort study in England. MedRxiv. 2021.
42. Loss J, Wurm J, Varnaccia G, Schienkiewitz A, Iwanowski H, Loer AK, et al. Transmission of SARS-CoV-2 among children and staff in German daycare centers: results from the COALA study. MedRxiv. 2021.
43. Bellon M, Baggio S, Bausch FJ, Spechbach H, Salamun J, Genecand C, et al. SARS-CoV-2 viral load kinetics in symptomatic children, adolescents and adults. Clin Infect Dis. 2021.
44. Euser S, Aronson S, Manders I, Van Lelyveld S, Herpers B, Sinnige J. SARS-CoV-2 viral load distribution reveals that viral loads increase with age: a retrospective cross-sectional cohort study. medRxiv. 2021.
45. Szablewski CM, Chang KT, Brown MM, Chu VT, Yousaf AR, Anyalechi N, et al. SARS-CoV-2 Transmission and Infection Among Attendees of an Overnight Camp - Georgia, June 2020. MMWR Morb Mortal Wkly Rep. 2020;69(31):1023-5.

References (VI)

References
46. Pray IW, Gibbons-Burgener SN, Rosenberg AZ, Cole D, Borenstein S, Bateman A, et al. COVID-19 Outbreak at an Overnight Summer School Retreat - Wisconsin, July-August 2020. MMWR Morb Mortal Wkly Rep. 2020;69(43):1600-4.
47. Stein-Zamir C, Abramson N, Shoob H, Libal E, Bitan M, Cardash T, et al. A large COVID-19 outbreak in a high school 10 days after schools' reopening, Israel, May 2020. Euro Surveill. 2020;25(29).
48. Boast A, Munro A, Goldstein H. An evidence summary of Paediatric COVID-19 literature. Don't Forget the Bubbles. 2020.
49. Ismail SA, Saliba V, Lopez Bernal J, Ramsay ME, Ladhani SN. SARS-CoV-2 infection and transmission in educational settings: a prospective, cross-sectional analysis of infection clusters and outbreaks in England. Lancet Infect Dis. 2021;21(3):344-53.
50. Gold JAW, Gettings JR, Kimball A, Franklin R, Rivera G, Morris E, et al. Clusters of SARS-CoV-2 Infection Among Elementary School Educators and Students in One School District - Georgia, December 2020-January 2021. MMWR Morb Mortal Wkly Rep. 2021;70(8):289-92.
51. Hwang H, Lim JS, Song SA, Achangwa C, Sim W, Kim G, et al. Transmission dynamics of the Delta variant of SARS-CoV-2 infections in South Korea. J Infect Dis. 2021
52. Julin CH, Robertson AH, Hungnes O, Tunheim G, Bekkevold T, Laake I, et al. Household Transmission of SARS-CoV-2: A Prospective Longitudinal Study Showing Higher Viral Load and Increased Transmissibility of the Alpha Variant Compared to Previous Strains. Microorganisms. 2021;9(11).
53. Loenenbach A, Markus I, Lehfeld AS, An der Heiden M, Haas W, Kiegele M, et al. SARS-CoV-2 variant B.1.1.7 susceptibility and infectiousness of children and adults deduced from investigations of childcare centre outbreaks, Germany, 2021. Euro Surveill. 2021;26(21).
54. Buchan SA, Tibebu S, Daneman N, Whelan M, Vanniyasingam T, Murti M, et al. Increased household secondary attacks rates with Variant of Concern SARS-CoV-2 index cases. Clin Infect Dis. 2021.
55. Lyngse FP, Molbak K, Skov RL, Christiansen LE, Mortensen LH, Albertsen M, et al. Increased transmissibility of SARS-CoV-2 lineage B.1.1.7 by age and viral load. Nat Commun. 2021;12(1):7251.

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Appendix

Methods

- Rapid literature reviews
- Databases:
  - PubMed and MedRxiv
  - PubMed and COAP living evidence database
- Time frame for systematic search:
  - 1 January 2020 – 21 January 2021 (supplemented by non-systematic search until 29 March 2021)
  - 1 January 2020 – 31 January 2021 (to be extended until March 2022)
- Include a broad array of studies
  (both peer-reviewed and published and non-peer-reviewed)