

eCommons@AKU

Woman and Child Health

Division of Woman and Child Health

7-17-2021

Risk of infection and transmission of SARS-CoV-2 among children and adolescents in households, communities and educational settings: A systematic review and meta-analysis

Omar Irfan

Jiang Li

Kun Tang

Zhicheng Wang

Zulfiqar Ahmed Bhutta

Follow this and additional works at: https://ecommons.aku.edu/pakistan_fhs_mc_women_childhealth_wc Part of the Infectious Disease Commons, Maternal and Child Health Commons, Pediatrics Commons, Virus Diseases Commons, and the Women's Health Commons © 2021 The Author(s) JoGH © 2021 ISoGH Cite as: Irfan O, Li, J, Tang K, Wang Z, Bhutta ZA. Risk of infection and transmission of SARS-CoV-2 among children and adolescents in households, communities and educational settings: A systematic review and meta-analysis. J Glob Health 2021;11:05013.

journal of

Risk of infection and transmission of SARS-CoV-2 among children and adolescents in households, communities and educational settings: A systematic review and meta-analysis

Omar Irfan^{1*}, Jiang Li^{1*}, Kun Tang^{1,2}, Zhicheng Wang², Zulfiqar A Bhutta^{1,3}

¹Centre for Global Child Health, The Hospital for Sick Children, Toronto, Canada ²Vanke School of Public Health, Tsinghua University, Beijing, China ³Institute for Global Health & Development, the Aga Khan University, Karachi, Pakistan *Joint first authors.

Correspondence to:

Zulfiqar A Bhutta Professor & Co-Director, Centre for Global Child Health Hospital for Sick Children 686 Bay Avenue Toronto, ON, M5G 0A4 Canada **Background** There is uncertainty with respect to SARS-CoV-2 transmission in children (0-19 years) with controversy on effectiveness of school-closures in controlling the pandemic. It is of equal importance to evaluate the risk of transmission in children who are often asymptomatic or mildly symptomatic carriers that may incidentally transmit SARS-CoV-2 in different settings. We conducted this review to assess transmission and risks for SARS-CoV-2 in children (by age-groups or grades) in community and educational-settings compared to adults.

Methods Data for the review were retrieved from PubMed, EMBASE, Cochrane Library, WHO COVID-19 Database, China National Knowledge Infrastructure (CNKI) Database, WanFang Database, Latin American and Caribbean Health Sciences Literature (LILACS), Google Scholar, and preprints from medRixv and bioRixv) covering a timeline from December 1, 2019 to April 1, 2021. Population-screening, contact-tracing and cohort studies reporting prevalence and transmission of SARS-CoV-2 in children were included. Data were extracted according to PRISMA guidelines. Meta-analyses were performed using Review Manager 5.3.

Results Ninety studies were included. Compared to adults, children showed comparable national (risk ratio (RR)=0.87, 95% confidence interval (CI)=0.71-1.060 and subnational (RR=0.81, 95% CI=0.66-1.01) prevalence in population-screening studies, and lower odds of infection in community/household contact-tracing studies (odds ratio (OR)=0.62, 95% CI=0.46-0.84). On disaggregation, adolescents observed comparable risk (OR=1.22, 95% CI=0.74-2.04) with adults. In educational-settings, children attending daycare/preschools (OR=0.53, 95% CI=0.38-0.72) were observed to be at lower-risk when compared to adults, with odds of infection among primary (OR=0.85, 95% CI=0.55-1.31) and high-schoolers (OR=1.30, 95% CI=0.71-2.38) comparable to adults. Overall, children and adolescents had lower odds of infection in educational-settings compared to community and household clusters.

Conclusions Children (<10 years) showed lower susceptibility to COVID-19 compared to adults, whereas adolescents in communities and high-schoolers had comparable risk. Risks of infection among children in educational-settings was lower than in communities. Evidence from school-based studies demonstrate it is largely safe for children (<10 years) to be at schools, however older children (10-19 years) might facilitate transmission. Despite this evidence, studies focusing on the effectiveness of mitigation measures in educational settings are urgently needed to support both public health and educational policy-making for school reopening.

As of 5 April 2021, there have been 131.0 million confirmed COVID-19 cases and nearly 2.8 million confirmed deaths globally [1]. The response in countries worldwide has gone from an initial stage of strict lockdowns and business closures to variable periods of relaxation with social distancing, use of face masks and hand hygiene, and now vaccination roll outs for adults. During this period, daycare centers, schools and educational institutions were closed initially and then reopened RESEARCH THEME 1: COVID-19 PANDEMIC

School closures are understandable. Children play an important role in the transmission of some respiratory infectious diseases and may suffer from more severe outcomes than adults, such as influenza [2,3], rendering school closures an effective public health policy in reducing the spread and influence of these diseases. This is especially true in novel pandemics where pharmaceutical interventions, such as vaccines, are not immediately available and delaying disease spread is a priority [3-6]. However, children and adolescents under 19 years of age comprise a small proportion of total reported COVID-19 cases (1%-10%) [7-9]. This group has been reported to present with a milder clinical course compared to adults infected with SARS-CoV-2, with more favorable outcomes in general [7,9-11].

To date, there is much controversy concerning the benefits of the ongoing and future closure of schools and other educational institutions in controlling the COVID-19 pandemic, as limited data on transmission of COVID-19 in educational settings is available [12-16]. It is of equal importance to evaluate the risk of susceptibility and transmission in children who are often asymptomatic or mildly symptomatic carriers, that may incidentally transmit SARS-CoV-2 in both educational and community settings, especially with the third wave of COVID-19 and newer variants spreading in many Countries crippling the health care system and economy.

We undertook a systematic review of the infection and transmission rates and risks of SARS-CoV-2 in children and adolescents in household, community and educational settings since the beginning of the pandemic, to help in understanding policy responses for safe school reopening for children of various ages.

METHODS

This systematic review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines.

In this review, we focused on the following review objectives:

- 1-What is the overall risk of infection in children and adolescents compared to adults (>19 years) from population screening and contact-tracing studies?
- 2-What are the odds of being an infected contact in children and adolescents compared to adults (>19 years) in educational settings?
- 3-What is the risk of infection for children and adolescents in educational settings in comparison to that in communities?

Literature search

To investigate the risk of SARS-CoV-2 infection and transmission in children and adolescents and their potential contribution to transmission in various settings, we searched for national and subnational prevalence studies, and contact-tracing studies (CTS) from community/household clusters and educational settings.

Data for the review were retrieved from PubMed, EMBASE, Cochrane Library, WHO COVID-19 Database, China National Knowledge Infrastructure (CNKI) Database, WanFang Database, Latin American and Caribbean Health Sciences Literature (LILACS), Google Scholar, and "Living Evidence of COVID-19" (a database updated daily with published articles from PubMed and EMBASE and preprints from medRixv and bioRixv) covering a timeline from December 1, 2019 to April 1, 2021. Preprints from ChinaXiv (http://www.chinaxiv. org/home.htm) were also searched. Complementary searches were conducted by manually searching the national public health websites, and the John Hopkins Humanitarian Health Resource. The reference lists of all retrieved articles were examined as well. There was no language restriction applied for the search. The search terms applied for each research question and the specific search strategies for PubMed and other databases are provided in Table S1 in the **Online Supplementary Document**.

The search results from various databases were uploaded into Covidence Systematic Review Software (Veritas Health Innovation 2016, Melbourne, Australia) for screening.

Inclusion and exclusion criteria

We included population screening studies investigating the age-specific prevalence of SARS-CoV-2 infections, contact-tracing and cohort studies reporting the incidence and attack rate (number of infections secondary to a suspected close contact) of children (0-9 years) and adolescents (10-19 years old) compared to adults, case

series presenting direct evidence of COVID-19 cases transmitted by SARS-CoV-2 positive children compared to adults, and data from national public health websites and official government reports, when available. We excluded review articles, opinions, viewpoints and communication letters (if not presenting data on number of infections or attack rate of SARS-CoV-2) and modeling studies were also excluded. Studies that did not report the number of infections or attack rate of SARS-CoV-2, and studies with possible duplications of cases (eg, overlapping time periods within the same institutions/cities/countries) were also excluded.

Study screening

Two review authors independently reviewed each title and abstract from the search results. Upon obtaining the full text, two reviewers independently screened the full text and decided whether to include or exclude the study, in accordance with the criteria specified previously. Any disagreements were resolved by independent review by a third author.

Data extraction

The following data were extracted from each study using standardized data abstraction forms: authors, country, study type, study period and its relationship with the epidemic curve in the country/area and school closure/ reopen status, study setting (household, community, daycare, primary or secondary school; other mitigation measures if any), case definition (index case, primary case, secondary case), testing methods, contact-tracing methods, sampling method, number of infected children and/or adults (specified whether or not student-contacting staff) and total number of students and staff in the educational setting (or reported attack rate).

Meta-analysis and qualitative synthesis

For each dichotomous outcome, the weighted mean prevalence and 95% confidence interval (CI) was calculated. The meta-analyses were performed using Review Manager 5.3 adopting the random-effects models. Pooled risk ratios (RR) between children and adults were presented in both national and subnational prevalence studies with disaggregation into active infection and past infection indicated by PCR testing and antibodies seroprevalence, respectively. The pooled odds ratios (OR) of children being infected in households were presented and disaggregated by children (<10 years) and adolescent (10-19 years), and school operational status (open/partially open or closed) in the region/Country. The odds of contracting infection in children compared to adults in schools and daycare centers were also analyzed. Total number of children and adolescents tested and diagnosed with COVID-19 were computed separately for communities and educational settings to calculate the odds ratio (OR) of risk of infection in educational settings compared to community settings. Statistical heterogeneity across studies was evaluated by calculating the I² statistic. I² values equal to or above 50% were considered as "significant" heterogeneity in this study. Additionally, the χ^2 test for heterogeneity was performed and the forest plot was visually inspected to assess the degree of overlap between the CIs of included studies. The characteristics, biases, and results of the included studies were summarized narratively. For studies included but not eligible for meta-analysis due to a lack of sufficient data, we also qualitatively synthesized the results to present a full picture.

Assessment of methodological quality and risk of bias

Two independent reviewers assessed each included study for methodological quality. A quality assessment tool was adopted from the National Heart, Lung, and Brain Institute (NHLBI) and Research Triangle Institute International [17] for observational studies, where are as the quality of prevalence studies was assessed using a critical appraisal checklist for prevalence studies [18]. Study quality was scored on basis of clear study objectives, case definition, consecutive inclusion of cases, sample sizes, comparability of included patients, measurement of outcomes, length of follow-up, and appropriately defined statistical methods and results. However, studies were not excluded based on study quality. Studies with score 6-8 were considered to be good quality, 4-5 considered fair quality and <4 considered poor quality.

RESULTS

The systemic literature search yielded 3700 results during the search dates. Of these, 117 studies were examined in full text and 90 were included in the final analysis after addition of 3 studies from other resources (Figure 1). The characteristics of included studies were summarized in Table S2 in the **Online Supplementary Document**. Thirty studies were excluded because they either presented overlapping data, provided little age-dis-

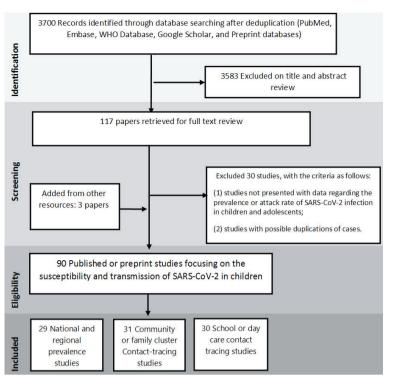


Figure 1. PRISMA flow diagram of study selection process.

aggregated data for children, or were commentaries, editorials or reviews with no empirical data.

The overall risk of SARS-Cov-2 infection among children and adolescents in comparison to adults

To investigate the overall risk of SARS-Cov-2 infection among children and adolescents, we included 60 studies, of which 29 were population-screening studies [19-47] and 31 were CTS [48-78].

The prevalence of COVID-19 in children and adolescents (<20 years of age) were reported in 11 national and 18 subnational surveillance studies. Among them, six were from low- and middle-income countries (LMICs). Compared to adult populations, a comparable risk of SARS-CoV-2 infection was observed in children and adolescents in both national (RR=0.87, 95% CI=0.71-1.06) and subnational (RR=0.81, 95% CI=0.66-1.01) surveillance studies, as shown in Figure 2 and Figure 3. When disaggregated by testing methods (ie, RT-PCR vs serological test), children and adolescents showed a similar lower risk of past infection from seroprevalence data in national (RR=0.77, 95%

CI = 0.62-0.96) studies but insignificant effect in subnational studies (RR = 0.80, 95% CI = 0.59-1.08). The risk of active infection was lower compared to adults but insignificant in both national studies (RR=0.98, 95% CI=0.69-1.38) and subnational surveillance studies at point estimate level (RR=0.77, 95% CI=0.48-1.22).

	Child	iren	٨d	ults		Risk Ratio	Risk Ratio
Study or Subgroup	Events		Events		Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.1.1 Infection positivity		0.0000				,	
Gudbiartsson 2020	0	848	100	12232	0.5%	0.07 [0.00, 1.15]	←
ICMR COVID Study group	4718	129135	35466	892383	13.7%	0.92 [0.89, 0.95]	
Office for National Statistics 2020	18	5977	96	29824	7.3%	0.94 [0.57, 1.55]	
Public health agency of Sweden 2020	3	485	17	2086	2.2%	0.76 [0.22, 2.58]	
Riley 2021	417	25122	2023	180835	13.2%	1.48 [1.34, 1.65]	
Yousaf 2020	14	69	33	126	6.7%	0.77 [0.45, 1.35]	
Subtotal (95% CI)		161636		1117486	43.6%	0.98 [0.69, 1.38]	
Total events	5170		37735				
Heterogeneity: Tau ² = 0.10; Chi ² = 78.59	, df = 5 (P	< 0.0000	1); I ² = 94	%			
Test for overall effect: Z = 0.12 (P = 0.90))						
1.1.2 Seroprevalence							
Canada COVID-19 report August CBS	30	3581	245	34156	9.2%	1.17 [0.80, 1.70]	
Hallal 2020	46	3399	303	21597	10.3%	0.96 [0.71, 1.31]	
Murhekar 2021	271	3021	2864	26061	13.1%	0.82 [0.72, 0.92]	
Netherlands PIENTER corona 2020	116	21300	70	7000	10.5%	0.54 [0.41, 0.73]	
Pollan 2020	388	11422	2712	49653	13.2%	0.62 [0.56, 0.69]	-
Subtotal (95% CI)		42723		138467	56.4%	0.77 [0.62, 0.96]	◆
Total events	851		6194				
Heterogeneity: Tau ² = 0.05; Chi ² = 25.07		< 0.0001); I ² = 849	6			
Test for overall effect: Z = 2.37 (P = 0.02))						
							•
Total (95% CI)		204359		1255953	100.0%	0.87 [0.71, 1.06]	
Total events	6021		43929				
Heterogeneity: Tau ² = 0.07; Chi ² = 155.8	•	(P < 0.00	001); I² =	94%			0.2 0.5 1 2 5
Test for overall effect: Z = 1.41 (P = 0.16)							Favours children Favours adults
Test for subgroup differences: Chi ² = 1.3	35. df = 1	(P = 0.24)	, I ² = 26.0	%			

Figure 2. Pooled risk ratio of SARS-Cov-2 infection in children vs adults in national surveillance, disaggregated by infection positivity and seroprevalence.

Thirty-one studies undertook contact-tracing in community, household and family clusters, of which, 12 were from LMICs. The pooled odds of secondary attack in children and adolescents was significantly lower than that in adults (OR=0.62, 95% CI=0.46-0.84), with high heterogeneity (I^2 =0.91) (Figure 4, Panel A). When further disaggregated by the schools' operational status (ie, school closure vs school fully or partially open) during the study period, both children and adolescents were found to have lower risk of infection than did adults when

	Chil	dren	Adu	ilts		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
2.1.1 Infection positvity							
Bignami 2021	25304	1320140		4879790	12.0%	0.78 (0.77, 0.79)	
Lavezzo 2020	3	467	70	2345	2.7%	0.22 [0.07, 0.68]	·
Menachemi 2020	29	77	231	821	9.6%	1.34 [0.98, 1.82]	
Streeck 2020	5	55	132	857	4.1%	0.59 [0.25, 1.38]	
Subtotal (95% CI)		1320739		4883813	28.4%	0.77 [0.48, 1.22]	
Total events	25341		120928				
Heterogeneity: Tau ² = 0.15; C			= 0.0006); l² = 83%			
Test for overall effect: Z = 1.13	2 (P = 0.2)	6)					
2.1.2 Seroprevelence							
Bendavid 2020	9	621	40	2709	5.1%	0.98 [0.48, 2.01]	
Biggs 2020	0	48	19	648	0.6%	0.34 [0.02, 5.54]	·
Bogogiannidou 2020	0	490	5	1585	0.5%	0.29 [0.02, 5.30]	·
Gidding 2020	2	670	17	2561	1.8%	0.45 [0.10, 1.94]	
Gonzalez 2021 (1)	220	583	236	768	11.3%	1.23 [1.06, 1.43]	
Nawa 2020	0	98	3	644	0.5%	0.93 [0.05, 17.88]	← →
Pagani 2020	52	475	866	3668	10.1%	0.46 [0.36, 0.60]	
Public Health Ontario 2020	11	1378	86	7524	5.9%	0.70 [0.37, 1.30]	
Shakiba 2020	24	134	97	417	8.4%	0.77 [0.51, 1.15]	
Smith 2021	15	555	21	503	5.7%	0.65 [0.34, 1.24]	
Stringhini 2020	33	455	186	2311	9.0%	0.90 [0.63, 1.29]	
Sutton 2020	0	29	9	877	0.5%	1.54 [0.09, 25.85]	·
Weis 2020	1	58	51	562	1.1%	0.19 [0.03, 1.35]	•
Wiens 2021	196	740	215	1100	11.1%	1.36 [1.14, 1.61]	
Subtotal (95% CI)		6334		25877	71.6%	0.80 [0.59, 1.08]	-
Total events	563		1851				
Heterogeneity: Tau ² = 0.16; C	hi² = 65.9	4, df = 13 (P < 0.000	01); l² = 80'	%		
Test for overall effect: Z = 1.4	6 (P = 0.1-	4)					
Total (95% CI)		1327073		4909690	100.0%	0.81 [0.66, 1.01]	•
Total events	25904		122779				
Heterogeneity: Tau ² = 0.10; C	hi ² = 114.	22, df = 17	(P < 0.00	001); l ² = 8:	5%		
Test for overall effect: Z = 1.9	0 (P = 0.0)	3)	202				Favours children Favours adults
Test for subgroup differences	s: Chi ² = 0	.02, df = 1 ((P = 0.88)	, I² = 0%			r avours children Favours adults
Footnotes		a					

(1) children population was 0-15 years old

Figure 3. Pooled risk ratio of SARS-Cov-2 infection in children vs adults in subnational surveillance, sub-grouped into infection positivity and seroprevalence.

schools were fully or partially open (OR=0.52, 95% CI=0.33-0.83), but no significant effect during school closures (OR=0.72, 95% CI=0.46-1.14).

In a subgroup analysis of CTS (based on 18 out of the 31 studies) in which age-disaggregation was possible, we found that the pooled OR for SARS-CoV-2 infection among children compared to adults was 0.57 (95% CI=0.37-0.87), suggesting a significantly lower risk of secondary attack in this population at the community and household level. However, a comparable risk of secondary attack was observed among adolescents (OR=1.22, 95% CI=0.74-2.04) (Figure 4, Panel B).

Infection and transmission of COVID-19 among children and adolescents in educational settings compared to adult teachers and staff

Thirty studies conducted in educational settings were included [12-15,57,79-103], among which six studies were cross-sectional studies and the remaining 24 were contact-tracing or cohort studies. Upon checking the availability of sufficient data for comparison of children vs adults, 24 studies were included in the meta-analysis.

The pooled estimate of the included studies suggested that children and adolescents appeared to have a lower though statistically insignificant risk of secondary attack in school settings when compared to adults (OR=0.84, 95% CI=0.62-1.14) (Figure 5). Subgroup analysis also suggested significant lower odds of infection among children attending daycare centers/preschools (OR=0.53, 95% CI=0.38-0.72), but insignificant effect in primary schools (OR=0.85, 95% CI=0.55-1.31) compared to the adult staff. However, high-school students had comparable risk of infection to adults (OR=1.30, 95% CI=0.71-2.38).

Risk of contracting SARS-CoV-2 infection among children and adolescents in schools compared to community settings

Using the existing evidence from both community-based studies and studies conducted in educational settings, we further calculated the pooled odds ratios for contracting infection among children and adolescent in educational settings vs communities and household-clusters. When total number of children and adolescents tested and diagnosed with COVID-19 in the two settings were compared, children observed lower odds of

Figure 4a. Study or Subgroup	Childr Events		Adu Events		Weight	Odds Ratio M-H, Random, 95% CI	Odds Ratio M-H, Random, 95% Cl
3.3.1 During school closure						0.0440.10.10	
Chaw 2020	12	430	39	1317	4.4%	0.94 [0.49, 1.81]	
Dattner 2020 Supta 2020	441 6	1738 6	432 7	978 116	5.4% 0.9%	0.43 [0.36, 0.51] 189.80 [9.74, 3699.75]	
liang 2020	1	1	7	11	0.3%	1.80 [0.06, 54.33]	
Kim 2020	1	78	, o	170	0.7%	6.60 [0.27, 163.84]	
Kong 2020	5	5	11	11	0.1 /0	Not estimable	
.i 2020	4	100	60	292	3.3%	0.16 [0.06, 0.46]	
.iu 2020	93	1867	421	9713	5.4%	1.16 [0.92, 1.46]	+
uo 2020	14	357	113	3053	4.6%	1.06 [0.60, 1.87]	
Park 2020	50	694	2119	58379	5.3%	2.06 [1.54, 2.76]	
osfay-Barbe 2020	0	4	47	57	0.8%	0.02 [0.00, 0.49]	<u>←</u>
Qifang Bi 2020	17	233	67	811	4.7%	0.87 [0.50, 1.52]	
Schwartz 2020	3	5	8	11	1.4%	0.56 [0.06, 5.22]	
Vang Y 2020	13	36	64	92	3.9%	0.25 [0.11, 0.56]	
Vang Z 2020	2	10	130	179	2.2%	0.09 [0.02, 0.46]	
(hang (3) 2020	2	46	10	323	2.2%	1.42 [0.30, 6.71]	
Zhang 2020	47	756 6366	606	6437 81950	5.2% 51.0%	0.64 [0.47, 0.87]	
Subtotal (95% CI)	711	0300		01950	51.0%	0.72 [0.46, 1.14]	
Fotal events Heterogeneity: Tau² = 0.51; Chi² = 149.87, df = 15 (P · Fest for overall effect: Z = 1.41 (P = 0.16)); I² = 90	4141)%				
3.3.2 During schools open/partially open							
	22	70		40	2.20	0 52 10 40 4 57	
Atherstone 2021	32	79	9 21	16	3.2%	0.53 [0.18, 1.57]	
Cheng 2020 James 2020	1	281 8	21 33	2286 37	1.6% 1.7%	0.39 [0.05, 2.87] 0.04 [0.01, 0.27]	←
Korea Centers for Disease Control and Prevention	2	8 155	33 12	2201	1.7%	1.18 [0.15, 9.17]	
aws 2020	19	68	36	120	4.4%	0.90 [0.47, 1.75]	
_aws 2020 _axminarayan 2020	428	6075	2800	42556	5.5%	1.08 [0.97, 1.20]	+
.opez 2020	420	123	2000	42550	4.0%	0.49 [0.22, 1.05]	
Aaltezou 2020	30	43	38	66	3.9%	1.70 [0.75, 3.84]	+
Aetlay 2021	210	4672	1599	13245	5.5%	0.34 [0.30, 0.40]	-
Aizumoto 2020	10	175	284	2321	4.4%	0.43 [0.23, 0.83]	
Rosenberg 2020	42	156	88	182	4.9%	0.39 [0.25, 0.62]	
Russell 2020	6	39	613	3672	3.8%	0.91 [0.38, 2.17]	
Somekh 2020	15	58	21	36	3.7%	0.25 [0.10, 0.60]	
an der Hoek 2020	0	43	55	666	0.9%	0.13 [0.01, 2.09]	·
Subtotal (95% CI)		11975		67496	49.0%	0.52 [0.33, 0.83]	•
Fotal events	809		5627				
Heterogeneity: Tau ² = 0.53; Chi ² = 187.41, df = 13 (P ·	< 0.00001); I ² = 93	3%				
Fest for overall effect: Z = 2.73 (P = 0.006)							
Total (95% CI)		18341		149446	100.0%	0.62 [0.46, 0.84]	•
Fotal events	1520		9768				Ť
Heterogeneity: Tau ² = 0.42; Chi ² = 337.35, df = 29 (P): I ² = 91					
Test for overall effect: Z = 3.13 (P = 0.002)	0.00001	/	~				0.01 0.1 1 10 100
	0.22\ 18-	0.0%					Favours children Favours adults
Test for subgroup differences: Chi ² = 0.96, df = 1 (P =	0.33), 1-=	: 0%					
et a sta							
Figure 4b.				27			
	Child		Adu			Odds Ratio	Odds Ratio
Study or Subgroup			Events		Weight	Odds Ratio M-H, Random, 95% Cl	Odds Ratio M-H, Random, 95% Cl
3.2.1 Children	Events	Total	Events	Total		M-H, Random, 95% Cl	
3.2.1 Children Atherstone 2021	Events 5	Total 8	Events 9	Total 16	2.3%	M-H, Random, 95% Cl 1.30 [0.23, 7.38]	
3.2.1 Children Alherstone 2021 Chaw 2020	Events 5 4	Total 8 267	Events 9 39	Total 16 1317	2.3% 3.9%	M-H, Random, 95% Cl 1.30 [0.23, 7.38] 0.50 [0.18, 1.41]	
3.2.1 Children therstone 2021 Chaw 2020 Dattner 2020	Events 5 4 149	Total 8 267 891	9 39 432	Total 16 1317 978	2.3% 3.9% 6.0%	M-H, Random, 95% Cl 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32]	
3.2.1 Children Nherstone 2021 Chaw 2020 Jattner 2020 Jiang 2020	5 4 149 1	Total 8 267 891 1	9 39 432 7	Total 16 1317 978 11	2.3% 3.9%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33]	
.2.1 Children therstone 2021 hhaw 2020 Jattner 2020 iang 2020 cong 2020	Events 5 4 149 1 4	Total 8 267 891 1 4	9 39 432 7 5	Total 16 1317 978 11 5	2.3% 3.9% 6.0% 0.9%	M-H, Random, 95% Cl 1.30 (0.23, 7.38) 0.50 (0.18, 1.41) 0.25 (0.20, 0.32) 1.80 (0.06, 54.33) Not estimable	
3.2.1 Children therstone 2021 Shaw 2020 Dattner 2020 Iang 2020 Kong 2020 Kong 2020	Events 5 4 149 1 4 0	Total 8 267 891 1 4 88	9 39 432 7 5 12	Total 16 1317 978 11 5 2201	2.3% 3.9% 6.0% 0.9% 1.2%	M-H, Random, 95% Cl 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85]	
5.2.1 Children therstone 2021 Chaw 2020 Jattner 2020 liang 2020 Gong 2020 Gorea Centers for Disease Control and Prevention Jaws 2020	Events 5 4 149 1 4 0 9	Total 8 267 891 1 4 88 44	Events 9 39 432 7 5 12 18	Total 16 1317 978 11 5 2201 60	2.3% 3.9% 6.0% 0.9% 1.2% 4.2%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50]	
5.2.1 Children therstone 2021 Shaw 2020 Dattner 2020 tiang 2020 Song 2020 Sorea Centers for Disease Control and Prevention .aws 2020 .awmianarayan 2020	Events 5 4 149 1 4 0 9 40	Total 8 267 891 1 4 88 44 1072	Events 9 39 432 7 5 12 18 2800	Total 16 1317 978 11 5 2201 60 42556	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.8%	M-H, Random, 95% CI 1,30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76]	
3.2.1 Children Wherstone 2021 Chaw 2020 Dattner 2020 Gather 2020 Gorga 2020 Gorea Centers for Disease Control and Prevention .aws 2020 .awminarayan 2020 Li 2020	Events 5 4 149 1 4 0 9 40 60	Total 8 267 891 1 4 88 44 1072 1048	Events 9 39 432 7 5 12 18 2800 421	Total 16 1317 978 11 5 2201 60 42556 9713	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.8% 5.9%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.3] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77]	
3.2.1 Children therstone 2021 Chaw 2020 Jattner 2020 Jattner 2020 Korga 2020 Korea Centers for Disease Control and Prevention Laws 2020 .awminarayan 2020 .ju 2020 .opez 2020	Events 5 4 149 1 4 0 9 40 60 13	Total 8 267 891 1 4 88 44 1072 1048 123	Events 9 39 432 7 5 12 18 2800 421 18 18	Total 16 1317 978 11 5 2201 60 42556 9713 92	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.8% 5.9% 4.6%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05]	
5.2.1 Children therstone 2021 Chaw 2020 Dattner 2020 Sorg 2020 Kong 2020 Korea Centers for Disease Control and Prevention .aws 2020 .awrinarayan 2020 .ju 2020 .opez 2020	Events 5 4 149 1 4 0 9 40 60	Total 8 267 891 1 4 88 44 1072 1048	Events 9 39 432 7 5 12 18 2800 421	Total 16 1317 978 11 5 2201 60 42556 9713	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.8% 5.8% 4.6% 4.3%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.3] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77]	
5.2.1 Children therstone 2021 Shaw 2020 Dattner 2020 Song 2020 Korea Centers for Disease Control and Prevention .aws 2020 .axminarayan 2020 ju 2020 Opez 2020 Park 2020 Jiang Bi 2020	Events 5 4 149 1 4 0 9 40 60 60 113 5 11	Total 8 267 891 1 4 88 44 1072 1048 123 237 148	9 39 432 7 5 12 18 2800 421 18 2119 67	Total 16 1317 978 11 5 2201 60 42556 9713 92 58379 811	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.8% 5.9% 4.6% 4.3% 5.0%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.57 [0.24, 1.39] 0.87 [0.24, 1.39] 0.88 [0.46, 1.73]	
5.2.1 Children therstone 2021 Shaw 2020 Sattner 2020 Sorra Centers for Disease Control and Prevention .aws 2020 .awrinarayan 2020 .ui 2020 .opez 2020 Sarki 2020 Sarki 2020 Sosenberg 2020 Sosenberg 2020	Events 5 4 149 1 4 0 9 40 600 610 5 11 5	Total 8 267 891 1 4 88 44 1072 1048 123 237 148 25	Events 9 39 432 7 5 12 18 2800 421 18 2119 67 88	Total 16 1317 978 11 5 2201 60 42556 9713 92 58379 811 182	2.3% 3.9% 6.0% 0.9% 4.2% 5.8% 5.8% 4.6% 4.3% 5.0% 3.9%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74]	
5.2.1 Children therstone 2021 Shaw 2020 Dattner 2020 Song 2020 Gorea Centers for Disease Control and Prevention .aws 2020 .awminarayan 2020 .ju 2020 .opez 2020 Park 2020 Diffang Bi 2020 Rosenberg 2020 Russell 2020	Events 5 4 149 1 4 0 9 40 60 13 5 111 5 1	Total 8 267 891 1 4 88 4 1072 1048 123 237 148 25 16	Events 9 39 432 7 5 12 18 2800 421 18 2119 67 88 613	Total 16 1317 978 11 5 2201 60 42556 9713 92 58379 811 182 3672	2.3% 3.9% 6.0% 0.9% 4.2% 5.8% 4.3% 4.3% 5.0% 3.9% 1.9%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.33] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52]	M.H, Random, 95% Cl
5.2.1 Children therstone 2021 Shaw 2020 Dattner 2020 Song 2020 Korea Centers for Disease Control and Prevention .aws 2020 .awminarayan 2020 Ju 2020 Park 2020 Park 2020 Jiang Bi 2020 Rosenberg 2020 Russell 2020 an der Hoek 2020	Events 5 4 149 1 4 0 9 400 600 133 5 11 5 11 5 1 1 0	Total 8 267 891 1 4 88 44 1072 1048 123 237 148 25 16 31	Events 9 39 432 7 5 12 18 2800 421 18 2119 67 88 613 55	Total 16 1317 978 111 5 2201 60 42556 9713 92 58379 811 1822 3672 866	2.3% 3.9% 6.0% 0.9% 4.2% 5.8% 4.6% 4.3% 5.9% 3.9% 3.9% 1.2%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.57 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.52]	M.H, Random, 95% Cl
5.21 Children therstone 2021 haw 2020 Dattner 2020 Song 2020 Song 2020 Song 2020 Sorea Centers for Disease Control and Prevention .aws 2020 .aws 2020 .aws 2020 Park 2020 Park 2020 Park 2020 Sosenberg 2020 Sosenberg 2020 Russell 2020 an der Hoek 2020 Chang 2020	Events 5 4 149 1 4 0 9 40 60 13 5 111 5 1	Total 8 267 891 1 4 88 44 1072 1048 123 237 148 255 16 31 756	Events 9 39 432 7 5 12 18 2800 421 18 2119 67 88 613	Total 16 1317 978 11 5 2201 60 42556 9713 92 58379 811 182 3672 666 6437	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.8% 4.8% 4.8% 4.3% 5.0% 3.9% 1.2% 5.8%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.71 [0.01, 2.90] 0.64 [0.47, 0.87]	M-H, Random, 95% Cl
5.2.1 Children therstone 2021 Shaw 2020 Dattner 2020 Song 2020 Gorea Centers for Disease Control and Prevention .aws 2020 .awminarayan 2020 .ju 2020 .opez 2020 Park 2020 Difang Bi 2020 Rosenberg 2020 Russell 2020 an der Hoek 2020 Fung 2020 Subtotal (95% CI)	Events 5 4 149 1 4 0 9 40 60 60 13 5 11 1 5 1 1 5 47	Total 8 267 891 1 4 88 44 1072 1048 123 237 148 25 16 31	g 39 432 7 5 12 18 2800 421 18 2119 67 88 613 55 606	Total 16 1317 978 111 5 2201 60 42556 9713 92 58379 811 1822 3672 866	2.3% 3.9% 6.0% 0.9% 4.2% 5.8% 4.6% 4.3% 5.9% 3.9% 3.9% 1.2%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.57 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.52]	M-H, Random, 95% Cl
5.2.1 Children therstone 2021 Shaw 2020 Dattner 2020 Song 2020 Korea Centers for Disease Control and Prevention .aws 2020 .awminarayan 2020 Ju 2020 Park 202	Events 5 4 149 1 4 0 9 40 60 133 5 11 5 11 5 1 1 0 47 354	Total 8 267 891 4 88 44 1072 1048 123 237 148 25 16 31 756 4759	Events 9 39 432 7 5 12 18 2800 421 18 2119 67 88 613 55 6006 7309	Total 16 1317 978 11 5 2201 60 42556 9713 92 58379 811 182 3672 666 6437	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.8% 4.8% 4.8% 4.3% 5.0% 3.9% 1.2% 5.8%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.71 [0.01, 2.90] 0.64 [0.47, 0.87]	M-H, Random, 95% Cl
k.2.1 Children therstone 2021 haw 2020 Dattner 2020 Song 2020 Gorga Centers for Disease Control and Prevention .aws 2020 .aws 2020 .aws 2020 Park 2020 Par	Events 5 4 149 1 4 0 9 40 60 133 5 11 5 11 5 1 1 0 47 354	Total 8 267 891 4 88 44 1072 1048 123 237 148 25 16 31 756 4759	Events 9 39 432 7 5 12 18 2800 421 18 2119 67 88 613 55 6006 7309	Total 16 1317 978 11 5 2201 60 42556 9713 92 58379 811 182 3672 666 6437	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.8% 4.8% 4.8% 4.3% 5.0% 3.9% 1.2% 5.8%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.71 [0.01, 2.90] 0.64 [0.47, 0.87]	M-H, Random, 95% Cl
3.2.1 Children therstone 2021 Chaw 2020 Dattner 2020 Dattner 2020 Gong 2020 Gorea Centers for Disease Control and Prevention Laws 2020 Laws 2020 Dattiner Strong 2020 Park 2020	Events 5 4 149 1 4 0 9 40 60 133 5 11 5 11 5 1 1 0 47 354	Total 8 267 891 4 88 44 1072 1048 123 237 148 25 16 31 756 4759	Events 9 39 432 7 5 12 18 2800 421 18 2119 67 88 613 55 6006 7309	Total 16 1317 978 11 5 2201 60 42556 9713 92 58379 811 182 3672 666 6437	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.8% 4.8% 4.8% 4.3% 5.0% 3.9% 1.2% 5.8%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.71 [0.01, 2.90] 0.64 [0.47, 0.87]	M-H, Random, 95% Cl
3.2.1 Children Wherstone 2021 Chaw 2020 Dattner 2020 Gather 2020 Gorga 2020 Gorea Centers for Disease Control and Prevention .aws 2020 .awminarayan 2020 Li 2020	Events 5 4 149 1 4 0 9 40 60 133 5 11 5 11 5 1 1 0 47 354	Total 8 267 891 4 88 44 1072 1048 123 237 148 25 16 31 756 4759	Events 9 39 432 7 5 12 18 2800 421 18 2119 67 88 613 55 6006 7309	Total 16 1317 978 11 5 2201 60 42556 9713 92 58379 811 182 3672 666 6437	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.8% 4.8% 4.8% 4.3% 5.0% 3.9% 1.2% 5.8%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.71 [0.01, 2.90] 0.64 [0.47, 0.87]	M-H, Random, 95% Cl
5.2.1 Children therstone 2021 haw 2020 pattner 2020 itang 2020 Gorga 2020 Gorea Centers for Disease Control and Prevention .aws 2020 .aws 2020 .aws 2020 .aws 2020 .ark 2020 .a	Events 5 4 149 1 4 0 9 40 60 133 5 11 5 11 5 1 1 0 47 354	Total 8 267 891 4 88 44 1072 1048 123 237 148 25 16 31 756 4759	Events 9 39 432 7 5 12 18 2800 421 18 2119 67 88 613 55 6006 7309	Total 16 1317 978 11 5 2201 60 42556 9713 92 58379 811 182 3672 666 6437	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.8% 4.8% 4.8% 4.3% 5.0% 3.9% 1.2% 5.8%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.71 [0.01, 2.90] 0.64 [0.47, 0.87]	M.H, Random, 95% Cl
k.2.1 Children therstone 2021 Draw 2020 Dattner 2020 Song 2020 Korea Centers for Disease Control and Prevention .aws 2020 .awminarayan 2020 .iu 2020 Order 2020 Park 2	Events 5 4 149 1 4 0 9 40 60 13 5 11 1 5 11 0 47 354 0.00001)	Total 8 267 891 1 4 88 44 1072 1048 123 237 148 25 16 31 756 4759 ; I ² = 85	Events 9 39 39 432 7 5 12 18 2800 421 18 2119 67 88 613 55 606 7309 %	Total 16 1317 978 11 5 2201 60 42556 9713 92 58379 811 182 3672 666 6437 127096	2.3% 3.9% 6.0% 9.9% 4.2% 5.8% 5.8% 5.9% 4.3% 5.0% 3.9% 1.2% 5.8% 5.8% 5.8%	M-H, Random, 95% CI 1,30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.07, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87]	M.H, Random, 95% Cl
 b.2.1 Children b.2.1 Children therstone 2021 braw 2020 pattner 2020 cong 2020 corea Centers for Disease Control and Prevention aws 2020 awrayan 2020 copez 2020 ark 2020 cosenberg 2020<td>Events 5 4 149 1 4 0 9 40 60 60 13 5 1 11 5 1 1 0 47 354 0.00001)</td><td>Total 8 267 891 1 4 1072 1048 1072 1048 237 148 25 16 31 756 4759 71</td><td>Events 9 39 39 432 7 5 12 18 2800 421 18 2119 67 613 55 606 7309 % 9</td><td>Total 16 1317 978 2201 5201 60 42556 9713 92 58379 811 182 3672 666 6437 127096</td><td>2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 5.8% 4.8% 4.3% 5.0% 3.9% 1.2% 5.8% 56.9%</td><td>M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.48 [0.16, 1.43]</td><td>M.H, Random, 95% Cl</td>	Events 5 4 149 1 4 0 9 40 60 60 13 5 1 11 5 1 1 0 47 354 0.00001)	Total 8 267 891 1 4 1072 1048 1072 1048 237 148 25 16 31 756 4759 71	Events 9 39 39 432 7 5 12 18 2800 421 18 2119 67 613 55 606 7309 % 9	Total 16 1317 978 2201 5201 60 42556 9713 92 58379 811 182 3672 666 6437 127096	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 5.8% 4.8% 4.3% 5.0% 3.9% 1.2% 5.8% 56.9%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.48 [0.16, 1.43]	M.H, Random, 95% Cl
k.2.1 Children therstone 2021 Daw 2020 Dattner 2020 Song 2020 (orea Centers for Disease Control and Prevention .aws 2020 .awminarayan 2020 .ju 2020 .ju 2020 Park 202	Events 5 4 149 4 0 9 40 60 13 5 11 5 11 0 47 354 0.00001) 27 8	Total 8 267 891 1 4 4 88 84 44 1072 1048 25 16 31 756 4759 ; F = 85 71 163	Events 9 39 432 7 5 12 18 2800 421 18 2119 67 88 613 55 606 7309 % 9 39 39	Total 16 1317 978 111 5 2201 60 42556 9713 92 58379 811 182 3672 866 6437 127096 16 1317	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.9% 4.6% 4.3% 5.9% 5.0% 5.8% 5.8% 5.8% 5.8% 5.8%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.67 [0.37, 0.87] 0.57 [0.37, 0.87] 0.48 [0.16, 1.43] 1.69 [0.78, 3.68]	M.H, Random, 95% Cl
k.2.1 Children therstone 2021 Draw 2020 Dattner 2020 Song 2020 Korea Centers for Disease Control and Prevention .aws 2020 .awminarayan 2020 .iu 2020 .opez 2020 Park 2	Events 5 4 149 1 4 4 0 9 40 60 13 5 11 5 5 1 1 0 47 354 0.00001) 277 8 291	Total 8 8 267 891 1 4 4 88 84 44 1072 1048 47 25 16 31 756 4759 (] = 85 71 163 846	Events 9 39 432 7 5 12 18 2800 421 18 2119 67 88 613 56 606 7309 % 9 9 9 939 432	Total 166 1317 978 2201 600 42556 9713 922 58379 811 1822 3672 666 6437 127096 166 1317 978	2.3% 3.9% 6.0% 0.9% 4.2% 5.8% 4.6% 4.3% 5.9% 1.9% 1.9% 5.8% 56.9% 3.7% 4.6% 4.6%	M-H, Random, 95% CI 1,30 [0.23, 7.38] 0,50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.24, 1.63] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.16, 1.43] 1.69 [0.78, 3.68] 0.66 [0.55, 0.80]	M.H, Random, 95% Cl
 b.2.1 Children b.2.1 Children therstone 2021 braw 2020 pattner 2020 liang 2020 corea Centers for Disease Control and Prevention aws 2020 awrinarayan 2020 ui 2020 opez 2020 ark 2020 Diffang Bi 2020 Russell 2020 an der Hoek 2020 brand 2020 Subtotal (95% CI) folal events feterogeneity: Tau² = 0.42; Chi² = 95.45, df = 14 (P Test for overall effect: Z = 2.60 (P = 0.009) b.2.2 Adolescents therstone 2021 braw 2020 pattner 2020 clim 2020 	Events 5 4 149 1 4 0 9 40 600 133 5 11 11 5 11 0 47 354 5 0.00001) 27 8 291 1	Total 8 8 267 891 1 4 88 44 1072 88 1048 1048 123 237 148 25 161 3756 4759 ; *= 85 71 163 846 78 756 757 756 757 756 757 756 757 756 757 757	Events 9 39 339 432 7 7 5 12 12 12 12 12 12 12 12 12 12 12 12 12 12 12 12 12 12 12 13 8 613 55 606 7309 39 39 432 0	Total 16 1317 978 11 5 2201 60 42556 971 92 58379 811 182 3672 666 6437 127096 16 1317 978 16 1317 127096	2.3% 3.9% 6.0% 0.9% 4.2% 5.8% 4.6% 4.3% 5.9% 1.9% 1.9% 5.8% 56.9% 3.7% 4.6% 4.6%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.48 [0.16, 1.43] 1.69 [0.78, 3.68] 0.66 [0.55, 0.80] 6.60 [0.27, 163,84]	M.H, Random, 95% Cl
 b.2.1 Children b.2.1 Children therstone 2021 braw 2020 Dattner 2020 cong 2020 corea Centers for Disease Control and Prevention a.aws 2020 a.awrinarayan 2020 b.2.2 2020 ark 2020 babbotal (95% CI) Total events fest for overall effect: Z = 2.60 (P = 0.009) b.2.2 Adolescents therstone 2021 baw 2020 battner 2020 chaw 2020 corea Centers for Disease Control and Prevention 	Events 5 4 149 4 0 9 40 60 13 5 11 5 11 0 47 354 0.00001) 277 8 291 1 1	Total 8 267 891 1 4 88 4072 1048 1021 1048 1232 237 148 25 163 31 756 375 71 163 846 78 1 1	Events 9 39 39 432 5 12 12 12 12 12 2800 421 1 15 2119 67 7309 % 9 9 39 432 0 0 6 6	Total 16 1317 978 111 5 2201 60 42556 9713 92 58379 811 182 3672 666 6437 127096 16 1317 978 1317 978 170 160 127096 160 1317 187 197 187 197 187 197 197 197 197 197 197 197 19	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 4.3% 5.9% 4.3% 5.0% 3.9% 56.9% 3.7% 4.6% 6.0% 0.9%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.07, 10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.16, 1.43] 1.69 [0.78, 3.68] 0.66 [0.57, 18.84] Not estimable	M.H, Random, 95% Cl
k.2.1 Children therstone 2021 Dattner 2020 Dattner 2020 Song 2020 (orea Centers for Disease Control and Prevention .aws 2020 .awminarayan 2020 .ju 2020 .ju 2020 Park 2020 Dattner Josepher 2020 Wassell 2020 Rosenberg 2020 Wassell 2020 an der Hoek 2020 Chang 2020 Subtotal (95% CI) Total events Heterogeneity: Tau ^a = 0.42; Chi ^a = 95.45, df = 14 (P < Fest for overall effect: $Z = 2.60$ (P = 0.009) k.2.2 Adolescents	Events 5 4 149 1 4 4 0 9 40 60 60 13 5 11 5 1 1 0 47 354 5 0.00001) 77 8 291 1 1 1 1	Total 8 267 891 1 4 88 1072 1048 1072 1048 123 237 14 25 16 31 756 31 756 31 756 31 756 31 766 31 756 34 71 163 846 78 67 67	Events 9 39 432 7 5 12 12 12 12 12 12 12 12 12 12 12 12 12	Total 166 1317 978 2201 600 42556 9713 922 58379 811 1822 3672 666 6437 127096 166 1317 978 170 62201	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 5.9% 4.6% 1.2% 5.8% 5.8% 5.8% 5.6.9% 3.7% 4.6% 0.9% 1.9%	M-H, Random, 95% CI 1,30 [0.23, 7.38] 0,50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.16, 1.43] 1.69 [0.78, 3.68] 0.66 [0.55, 0.80] 6.60 [0.27, 163, 84] Not estimable 2.76 [0.35, 21.57]	M.H, Random, 95% Cl
k.2.1 Children therstone 2021 haw 2020 pattner 2020 pattner 2020 (orea Centers for Disease Control and Prevention .aws 2020 .aws 2020 .ayarxinarayan 2020 .u 2020 .opez 2020 ark 2020 Diffang Bi 2020 Russell 2020 an der Hoek 2020 Subtotal (95% CI) Total events telerogeneity: Tau ² = 0.42; Chi ² = 95.45, df = 14 (P < Test for overall effect: Z = 2.60 (P = 0.009) .2.2 Adolescents therstone 2021 .haw 2020 Dattner 2020 Statuer 2020 South and Souther Sout	Events 5 4 149 149 40 60 13 5 11 15 1 11 5 11 0 47 354 5 0.00001) 27 8 291 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Total 8 267 891 1 4 88 41 1048 1233 237 148 265 31 7566 4759 71 1633 846 78 1 63 84 1 78 1 78 1 78 1 78 1 78 1 78 1 78 1 78 1 78 1 78 1 77 1 1 1 1 1 1 1 1	Events 9 39 39 432 7 5 12 18 2800 421 18 2800 421 18 2119 67 67 55 606 7309 9 39 432 0 6 122 0 6 122 18	Total 166 1317 978 111 5 2201 600 42556 9713 92 58379 811 182 3672 666 6437 127096 166 1317 978 170 6 2001 160 1317 127 127 127 127 127 127 127 1	2.3% 3.9% 6.0% 0.9% 4.2% 5.9% 4.6% 5.9% 4.6% 5.0% 3.9% 1.2% 5.8% 56.9% 3.7% 4.6% 6.0% 0.9%	M-H, Random, 95% Cl 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 10.685] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 17.3] 0.89 [0.46, 17.3] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.48 [0.16, 1.43] 1.69 [0.78, 3.68] 0.66 [0.25, 0.80] 6.60 [0.27, 163.84] Not estimable 2.76 [0.35, 21.57] 1.67 [0.62, 4.45]	M.H, Random, 95% Cl
 b.2.1 Children therstone 2021 braw 2020 Dattner 2020 cong 2020 corea Centers for Disease Control and Prevention a.aws 2020 a.awrinarayan 2020 b.2.2 Adolescents thereogeneity: Tau² = 0.42; Ch² = 95.45, df = 14 (P < fest for overall effect: Z = 2.60 (P = 0.009) b.2.2 Adolescents therestone 2021 chaw 2020 b.2.2 Adolescents therestone 2021 chaw 2020 corea Centers for Disease Control and Prevention a.ws 2020 and er Hoek 2020 thereogeneity: Tau² = 0.42; Ch² = 95.45, df = 14 (P < fest for overall effect: Z = 2.60 (P = 0.009) b.2.2 Adolescents therestone 2021 chaw 2020 corea Centers for Disease Control and Prevention a.ws 2020 a.ws 2020 a.ws 2020 a.ws 2020 a.ws 2020 	Events 5 4 149 1 4 0 9 40 60 13 3 5 11 5 1 1 0 47 354 0.00001) 7 7 8 291 1 1 1 1 1 0 33	Total 8 267 891 1 4 88 44 1072 1048 44 1072 1048 425 16 123 237 148 25 16 4759 (F=85 71 163 846 75 163 846 163 846 756 757 756 757 756 757 757 75	Events 9 39 39 432 5 12 12 18 12 12 2800 421 1 1 2119 67 55 56 556 6566 6566 6 9 9 39 432 0 0 6 12 12 12 12 13 432 12 13	Total 16 1317 978 111 5 2201 60 42556 9713 92 58379 811 182 3672 666 6437 127096 16 1317 978 170 6 2201 06 0 9713 182 192 10 10 10 10 10 10 10 10 10 10	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 4.3% 5.9% 4.3% 5.0% 3.9% 5.6.9% 3.7% 4.6% 6.0% 0.9% 1.9% 4.7%	M-H, Random, 95% Cl 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.07, 41] 0.33 [0.04, 2.52] 0.17 [0.07, 2.90] 0.64 [0.16, 1.43] 1.69 [0.78, 3.68] 0.66 [0.57, 0.80] 6.60 [0.27, 163.84] Not estimable 2.76 [0.35, 21.57] 1.67 [0.62, 4.45] 0.93 [0.66, 1.33]	M.H, Random, 95% Cl
k.2.1 Children therstone 2021 Draw 2020 Dattner 2020 Song 2020 Korea Centers for Disease Control and Prevention .aws 2020 .awminarayan 2020 .iu 2020 .opez 2020 Park 2	Events 5 4 149 1 4 4 0 9 40 60 9 40 60 13 3 5 1 1 5 1 1 0 47 354 5 0.00001) 7 7 8 291 1 1 1 1 1 1 1 33 3 45	Total 8 267 891 1 4 884 4072 1048 237 148 237 148 237 148 237 148 237 148 237 148 237 148 237 143 123 237 148 123 237 148 123 237 148 123 310 71 163 846 78 67 24 819 457	Events 9 39 432 7 5 12 12 12 12 12 12 12 12 12 12 12 12 13 8 2800 421 18 55 606 607 7309 9 9 9 9 9 9 9 9 9 9 30 9 2 30 9 2 2 2 2 10 10 10 10 10 10 10 10 10 10 10 10 10	Total 166 1317 978 2201 600 42556 9713 922 58379 811 1822 3672 666 6437 127096 166 1317 978 170 60 9713 358379	2.3% 3.9% 6.0% 0.9% 1.2% 5.9% 4.6% 5.9% 1.2% 5.8% 5.8% 5.8% 5.8% 5.9% 1.9% 4.6% 0.9% 1.9% 4.0% 5.8%	M-H, Random, 95% CI 1,30 [0.23, 7.38] 0,50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.24, 1.63] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.64 [0.55, 0.80] 6.60 [0.27, 163.84] Not estimable 2.76 [0.35, 21.57] 1.67 [0.62, 4.45] 0.93 [0.65, 13, 36]	M.H, Random, 95% Cl
k.2.1 Children therstone 2021 haw 2020 Dattner 2020 Song 2020 Gorea Centers for Disease Control and Prevention .aws 2020 .aws 2020 .aws 2020 Park 2020 Park 2020 Park 2020 Park 2020 Park 2020 Park 2020 Park 2020 Park 2020 Subtotal (95% cl) Total events Heterogeneity: Tau ^a = 0.42; Chi ^a = 95.45, df = 14 (P < Test for overall effect: Z = 2.60 (P = 0.009) 8.2.2 Adolescents therstone 2021 Chaw 2020 Dattner 2020 Gorea Centers for Disease Control and Prevention .aws 2020 Park 2	Events 5 4 149 40 60 133 5 11 5 11 5 11 0 47 354 5 11 1 5 27 8 291 1 1 1 1 1 1 33 45 6 6	Total 8 267 891 4 88 44 1072 1048 237 148 225 166 31 756 4759 71 163 846 67 71 163 846 78 1 67 24 819 457 85	Events 9 39 39 432 7 5 12 18 2800 421 18 2800 421 18 2119 67 55 606 7309 9 9 39 432 0 6 12 10 12 2119 67	Total 166 1317 978 111 5 2201 606 42556 9713 92 58379 811 182 3672 666 6437 127096 146 1317 978 1370 6 201 6 0 0 0 13 182 3672 6 6 0 13 182 3672 6 6 6 0 13 182 3672 6 6 6 6 13 17 9 182 3672 6 6 6 6 13 17 9 7 8 182 3672 6 6 6 6 6 437 127096 13 127096 13 13 127096 13 13 13 13 127096 13 13 13 13 13 13 13 13 13 13	2.3% 3.9% 6.0% 0.9% 1.2% 4.2% 5.9% 4.6% 5.9% 1.2% 5.8%	M-H, Random, 95% Cl 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.66 [0.25, 0.80] 0.66 [0.27, 163.84] Not estimable 2.76 [0.35, 21.57] 1.67 [0.62, 4.45] 0.93 [0.65, 1.33] 2.90 [2.13, 3.96] 0.84 [0.35, 2.01]	M.H, Random, 95% Cl
i.2.1 Children therstone 2021 haw 2020 Dattner 2020 iang 2020 (orea Centers for Disease Control and Prevention .aws 2020 .aws 2020 .aws 2020 .ark 2020 Difang Bi 2020 Otosenberg 2020 Difang Bi 2020 Otosenberg 2020 Difang 2020 Subtotal (95% CI) Total events Heterogeneity: Tau ² = 0.42; Ch ² = 95.45, df = 14 (P < rest for overall effect: Z = 2.60 (P = 0.009) K.2.2 Adolescents therstone 2021 chaw 2020 Difang 2020 Screa Centers for Disease Control and Prevention .aws 2020 Corea Centers for Disease Control and Prevention .aws 2020 Difang Bi 2020	Events 5 4 149 149 40 60 133 5 11 5 1 1 0 47 354 0.00001) 7 7 8 291 1 1 1 1 1 1 1 1 0 33 45 6 6 5 5 5	Total 8 267 891 1 4 88 44 1072 1048 44 1072 1048 237 16 123 237 16 123 237 16 31 756 4759 (F=85 71 163 846 1 6 75 16 4759 1 1 1 1 1 1 1 1 1 1 1 1 1	Events 9 39 339 432 7 5 12 18 2800 421 2119 67 613 556 5606 7309 % 9 9 39 432 0 612 12 1219 67 612 613 613 613	Total 166 1317 978 111 5 2201 60 42556 9713 925 8379 811 182 3672 666 6437 127096 166 1317 978 1700 6 2201 00 9713 358379 811 187 978 1700 6 2201 187 197 187 197 187 197 187 197 187 197 197 197 197 197 197 197 19	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 4.3% 5.9% 4.3% 5.0% 3.9% 1.2% 56.9% 3.7% 4.6% 6.0% 0.9% 1.9% 4.6% 5.8% 4.0%	M-H, Random, 95% Cl 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.07, 41] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.16, 1.43] 1.69 [0.78, 3.68] 0.66 [0.57, 0.87] 8.76 [0.35, 21.57] 1.67 [0.62, 4.45] 0.93 [0.64, 1.33] 2.90 [2.13, 3.96] 0.84 [0.35, 2.75] 1.67 [0.57, 3.75]	M.H, Random, 95% Cl
i.2.1 Children therstone 2021 haw 2020 jattner 2020 iang 2020 Gorg 2020 Gorea Centers for Disease Control and Prevention .aws 2020 .aws 2020 bark 2020 bark 2020 bark 2020 bark 2020 bark 2020 Cosenberg 2020 Corea Centers for Disease Control and Prevention .aws 2020 Liu 2020 Corea Centers for Disease Control and Prevention .aws 2020 .iu 2020 Corea Centers for Disease Control and Prevention .aws 2020 .iu	Events 5 4 149 1 4 0 9 40 60 0 0 0 0 0 13 5 11 1 1 5 1 1 1 0 47 354 207 8 291 1 1 1 1 1 1 1 1 0 5 5 0 0 0 0 0 1 3 5 4 0 1 9 9 40 6 0 0 9 9 40 6 0 13 9 5 11 9 149 9 10 9 10 9 10 9 10 9 10 9 10	Total 8 267 891 1 4 884 1048 237 148 237 148 255 16 31 71 168 4759 711 168 78 71 163 71 163 71 163 846 78 846 78 167 24 819 457 85 212	Events 9 39 339 432 7 7 5 12 12 12 18 2800 421 18 2119 67 606 606 7309 9 9 9 432 0 6 12 18 12 12 18 4212 18 613 55	Total 166 1317 978 2201 600 42556 9713 922 58379 811 1822 3672 666 6437 127096 166 1317 978 170 60 9713 58379 811 3672 60 9713 58379 811 3672 666 6437 170 60 9713 58379 811 160 60 9713 170 60 60 80 80 80 80 80 80 80 80 80 8	2.3% 3.9% 6.0% 0.9% 1.2% 5.9% 4.8% 5.9% 1.2% 5.8% 5.8% 5.8% 5.8% 5.9% 1.2% 5.8% 4.6% 6.0% 0.9% 1.9% 4.0% 5.8% 5.8% 5.8%	M-H, Random, 95% Cl 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.24] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.66 [0.55, 0.80] 6.60 [0.55, 0.80] 6.60 [0.55, 0.80] 6.60 [0.55, 21.57] 1.67 [0.62, 4.45] 0.93 [0.65, 1.33] 2.90 [2.13, 3.96] 0.84 [0.35, 2.17] 1.39 [0.51, 3.75] 0.44 [0.03, 7.54]	M.H, Random, 95% Cl
i.2.1 Children therstone 2021 haw 2020 Dattner 2020 iang 2020 Gorg 2020 Gorea Centers for Disease Control and Prevention .aws 2020 .aws 2020 .atk 2020 .ath det Kather .aws 2020 .ath det Source .aws 2020 .ath det Source .aws 2020 .ath and Prevention .aws 2020 .ath 2020 .a	Events 5 4 149 1 4 0 9 40 60 0 0 0 0 0 13 5 11 1 1 5 1 1 1 0 47 354 207 8 291 1 1 1 1 1 1 1 1 0 5 5 0 0 0 0 0 1 3 5 4 0 1 9 9 40 6 0 0 9 9 40 6 0 13 9 5 11 9 149 9 10 9 10 9 10 9 10 9 10 9 10	Total 8 267 891 4 88 44 1072 1048 237 1123 237 148 25 161 756 4759 711 163 846 71 163 846 71 163 846 71 163 846 71 847 848 167 24 819 457 23 122 2	Events 9 39 339 432 7 7 5 12 12 12 18 2800 421 18 2119 67 606 606 7309 9 9 9 432 0 6 12 18 12 12 18 4212 18 613 55	Total 166 1317 978 111 5 2201 600 42556 9713 925 58379 811 182 3672 666 6437 127096 166 1317 978 170 60 9713 58379 811 3672 666 5 5 5 5 5 5 5 5 5 5 5 5 5	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 5.8% 4.8% 5.9% 1.2% 56.9% 3.7% 4.8% 6.0% 0.9% 1.9% 4.0% 5.7% 5.8% 4.0% 1.2% 0.8%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 1.57] 0.66 [0.27, 163.84] Not estimable 2.76 [0.35, 21.57] 1.67 [0.62, 4.45] 0.93 [0.65, 1.33] 2.90 [2.13, 3.96] 0.84 [0.35, 2.01] 1.39 [0.51, 3.75] 0.44 [0.03, 7.54] 1.67 [0.05, 58.28]	M.H, Random, 95% Cl
 12.1 Children 12.1 Children therstone 2021 haw 2020 battner 2020 cong 2020 corea Centers for Disease Control and Prevention aws 2020 awminarayan 2020 jui 2020 opez 2020 vark 2020 bitang Bi 2020 cosenberg 2020 tussell 2020 an der Hoek 2020 hang 2020 bitbotal (95% CI) otal events feat for Disease Control and Prevention aws 2020 an der Hoek 2020 hang 2020 bitbotal (95% CI) otal events feat coverall effect: Z = 2.60 (P = 0.009) k.2.2 Adolescents therstone 2021 chaw 2020 bittare 2020 corea Centers for Disease Control and Prevention aws 2020 aws 2020 bittare 2020 bittare 2020 corea Centers for Disease Control and Prevention aws 2020 aws 2020 bittare 2020 bittare 2020 bittare 3020 bittare 3020 bittare 3020 bittare 3020 bittare 3020 corea Centers for Disease Control and Prevention aws 2020 bittare 3020 core 3020 core 3020 core 4020 core 402	Events 5 4 149 149 600 600 133 5 111 5 11 0 47 354 5 0.00001) 7 7 8 291 1 1 1 1 1 1 1 1 0 33 45 5 5 0 0 2 2 430	Total 8 267 891 4 88 44 1072 1123 237 148 825 166 31 756 31 756 31 758 71 163 846 78 1 63 78 1 63 78 1 63 78 1 63 78 10 457 85 23 2 2648	Events 9 39 339 332 342 2 12 18 2800 421 18 2800 421 18 2119 67 606 7309 9 39 432 0 6 12 18 421 2119 67 613 55 4 3795	Total 166 1317 978 111 5 2201 600 42556 9713 925 58379 811 182 3672 666 6437 127096 166 1317 978 170 60 9713 58379 811 3672 666 5 5 5 5 5 5 5 5 5 5 5 5 5	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 5.8% 4.8% 5.9% 1.2% 56.9% 3.7% 4.8% 6.0% 0.9% 1.9% 4.0% 5.7% 5.8% 4.0% 1.2% 0.8%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 1.57] 0.66 [0.27, 163.84] Not estimable 2.76 [0.35, 21.57] 1.67 [0.62, 4.45] 0.93 [0.65, 1.33] 2.90 [2.13, 3.96] 0.84 [0.35, 2.01] 1.39 [0.51, 3.75] 0.44 [0.03, 7.54] 1.67 [0.05, 58.28]	M.H, Random, 95% Cl
i.2.1 Children therstone 2021 haw 2020 jattner 2020 iang 2020 Gorea Centers for Disease Control and Prevention .aws 2020 .aws	Events 5 4 149 149 600 600 133 5 111 5 11 0 47 354 5 0.00001) 7 7 8 291 1 1 1 1 1 1 1 1 0 33 45 5 5 0 0 2 2 430	Total 8 267 891 4 88 44 1072 1123 237 148 825 166 31 756 31 756 31 758 71 163 846 78 1 63 78 1 63 78 1 63 78 1 63 78 10 457 85 23 2 2648	Events 9 39 339 332 342 2 12 18 2800 421 18 2800 421 18 2119 67 606 7309 9 39 432 0 6 12 18 421 2119 67 613 55 4 3795	Total 166 1317 978 111 5 2201 600 42556 9713 925 58379 811 182 3672 666 6437 127096 166 1317 978 170 60 9713 58379 811 3672 666 5 5 5 5 5 5 5 5 5 5 5 5 5	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 5.8% 4.8% 5.9% 1.2% 56.9% 3.7% 4.8% 6.0% 0.9% 1.9% 4.0% 5.7% 5.8% 4.0% 1.2% 0.8%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 1.57] 0.66 [0.27, 163.84] Not estimable 2.76 [0.35, 21.57] 1.67 [0.62, 4.45] 0.93 [0.65, 1.33] 2.90 [2.13, 3.96] 0.84 [0.35, 2.01] 1.39 [0.51, 3.75] 0.44 [0.03, 7.54] 1.67 [0.05, 58.28]	M-H, Random, 95% Cl
i.2.1 Children therstone 2021 haw 2020 pattner 2020 iang 2020 Gorg 2020 Gorea Centers for Disease Control and Prevention .aws 2020 .aws 2020 .ayser 2020 ark 2020 .ayser 2020	Events 5 4 149 149 600 600 133 5 111 5 11 0 47 354 5 0.00001) 7 7 8 291 1 1 1 1 1 1 1 1 0 33 45 5 5 0 0 2 2 430	Total 8 267 891 4 88 44 1072 1123 237 148 825 166 31 756 31 756 31 758 71 163 846 78 1 63 78 1 63 78 1 63 78 1 63 78 10 457 85 23 2 2648	Events 9 39 339 332 342 2 12 18 2800 421 18 2800 421 18 2119 67 606 7309 9 39 432 0 6 12 18 421 2119 67 613 55 4 3795	Total 166 1317 978 111 5 2201 600 42556 9713 925 58379 811 182 3672 666 6437 127096 166 1317 978 170 60 9713 58379 811 3672 666 5 5 5 5 5 5 5 5 5 5 5 5 5	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 4.3% 5.9% 4.3% 5.0% 3.9% 1.9% 4.6% 6.0% 0.9% 1.9% 4.0% 5.7% 5.8% 4.0% 1.2% 0.9% 4.0% 4.0% 4.3,1%	M-H, Random, 95% CI 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54.33] Not estimable 0.99 [0.06, 16.85] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 1.57] 0.66 [0.27, 163.84] Not estimable 2.76 [0.35, 21.57] 1.67 [0.62, 4.45] 0.93 [0.65, 1.33] 2.90 [2.13, 3.96] 0.84 [0.35, 2.01] 1.39 [0.51, 3.75] 0.44 [0.03, 7.54] 1.67 [0.05, 58.28]	M-H, Random, 95% Cl
 b.2.1 Children b.2.1 Children therstone 2021 braw 2020 patter 2020 patter 2020 corea Centers for Disease Control and Prevention aws 2020 awrinarayan 2020 u 2020 opez 2020 ark 2020 Diffang Bi 2020 Russell 2020 and et Hoek 2020 brand 2020 Subtotal (95% CI) Total events telerogeneity: Tau² = 0.42; Chi² = 95.45, df = 14 (P Test for overall effect: Z = 2.60 (P = 0.009) b.2.2 Adolescents therstone 2021 braw 2020 patter 2020 core centers for Disease Control and Prevention aws 2020 aws 2020 ark 2020 	Events 5 4 149 149 600 600 133 5 111 5 11 0 47 354 5 0.00001) 7 8 291 1 1 1 1 1 1 1 1 1 0 33 45 5 5 0 0 2 2 430	Total 8 267 831 4 88 44 1072 1048 237 123 237 148 25 161 756 4759 711 846 766 71 163 846 78 71 163 846 71 163 846 71 85 23 12 2 2648 17 = 85 22 2648	Events 9 39 339 332 342 2 12 18 2800 421 18 2800 421 18 2119 67 606 7309 9 39 432 0 6 12 18 421 2119 67 613 55 4 3795	Total 166 1317 978 111 5 2201 600 42556 9713 925 58379 811 182 3672 666 6437 127096 146 1317 978 17096 166 1317 978 127096 811 3672 666 577994	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 4.3% 5.9% 4.3% 5.0% 3.9% 1.9% 4.6% 6.0% 0.9% 1.9% 4.0% 5.7% 5.8% 4.0% 1.2% 0.9% 4.0% 4.0% 4.3,1%	M-H, Random, 95% Cl 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54, 33] Not estimable 0.99 [0.06, 10.68] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.66 [0.27, 163.84] Not estimable 2.76 [0.35, 21.57] 1.67 [0.62, 4.45] 0.39 [0.65, 1.33] 2.90 [2.13, 3.96] 0.84 [0.35, 2.01] 1.39 [0.51, 3.75] 0.44 [0.03, 5.24] 1.22 [0.74, 2.04]	M-H, Random, 95% Cl
i.2.1 Children therstone 2021 haw 2020 Dattner 2020 iang 2020 Gorea Centers for Disease Control and Prevention .aws 2020 .aws 2020 .ayez 2020 Jark 2020 Difang Bi 2020 Conserved State Stat	Events 5 4 149 149 600 133 5 11 1 5 1 1 1 0 47 354 0.00001) 27 8 291 1 1 1 1 1 1 1 1 0 33 45 5 6 0 2 2 430 0.00001) 784	Total 8 267 891 4 88 1072 1048 237 1123 237 148 255 166 31 756 31 756 31 756 71 163 846 78 1 63 78 1 63 71 163 846 78 1 63 24 819 457 22 2648 7407	Events 9 39 39 432 432 12 12 18 2800 421 18 2119 613 5 506 7309 9 39 432 0 6 12 18 421 2119 67 613 55 4 3795 41104 3795	Total 166 1317 978 111 5 2201 600 42556 9713 925 58379 811 182 3672 666 6437 127096 146 1317 978 17096 166 1317 978 127096 811 3672 666 577994	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 4.3% 5.9% 4.3% 5.0% 3.9% 1.9% 4.6% 6.0% 0.9% 1.9% 4.0% 5.7% 5.8% 4.0% 1.2% 0.9% 4.0% 4.0% 4.3,1%	M-H, Random, 95% Cl 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54, 33] Not estimable 0.99 [0.06, 10.68] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.66 [0.27, 163.84] Not estimable 2.76 [0.35, 21.57] 1.67 [0.62, 4.45] 0.39 [0.65, 1.33] 2.90 [2.13, 3.96] 0.84 [0.35, 2.01] 1.39 [0.51, 3.75] 0.44 [0.03, 5.24] 1.22 [0.74, 2.04]	M.H, Random, 95% CI
2.1 Children therstone 2021 haw 2020 Jattner 2020 Jattner 2020 Jattner 2020 Grea Centers for Disease Control and Prevention aws 2020 axminarayan 2020 Ju 20	Events 5 4 149 149 600 133 5 11 1 5 1 1 1 0 47 354 0.00001) 27 8 291 1 1 1 1 1 1 1 1 0 33 45 5 6 0 2 2 430 0.00001) 784	Total 8 267 891 4 88 1072 1048 237 1123 237 148 255 166 31 756 31 756 31 756 71 163 846 78 1 63 78 1 63 71 163 846 78 1 63 24 819 457 22 2648 7407	Events 9 39 39 432 432 12 12 18 2800 421 18 2119 613 5 506 7309 9 39 432 0 6 12 18 421 2119 67 613 55 4 3795 41104 3795	Total 166 1317 978 111 5 2201 600 42556 9713 925 58379 811 182 3672 666 6437 127096 146 1317 978 17096 166 1317 978 127096 811 3672 666 577994	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 4.3% 5.9% 4.3% 5.0% 3.9% 1.9% 4.6% 6.0% 0.9% 1.9% 4.0% 5.7% 5.8% 4.0% 1.2% 0.9% 4.0% 4.0% 4.3,1%	M-H, Random, 95% Cl 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54, 33] Not estimable 0.99 [0.06, 10.68] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.66 [0.27, 163.84] Not estimable 2.76 [0.35, 21.57] 1.67 [0.62, 4.45] 0.39 [0.65, 1.33] 2.90 [2.13, 3.96] 0.84 [0.35, 2.01] 1.39 [0.51, 3.75] 0.44 [0.03, 5.24] 1.22 [0.74, 2.04]	M.H. Random, 95% CI
2.1 Children therstone 2021 haw 2020 iang 2020 iong 2020 iong 2020 iorea Centers for Disease Control and Prevention aws 2020 axminarayan 2020 iu 2020 opez 2020 ark 2020 ark 2020 an der Hoek 2020 hang 2020 tussell 2020 an der Hoek 2020 hang 2020 ubtotal (95% CI) otal events teterogeneity: Tau ² = 0.42; Chi ² = 95.45, df = 14 (P < est for overall effect: Z = 2.60 (P = 0.009) .2.2 Adolescents therstone 2021 haw 2020 iu 2020 org 2020 org 2020 org 2020 org 2020 org 2020 org 2020 org 2020 org 2020 iu 2020 ark 2020 bit	Events 5 4 149 149 40 60 133 5 11 5 11 0 47 354 0.00001) 7 8 291 1 1 1 1 1 1 1 1 0 33 3 45 6 5 5 291 1 1 1 1 3 3 45 6 0 22 7 8 291 1 1 1 4 0 0 9 40 8 0 9 40 8 0 9 40 8 0 9 40 8 11 1 1 5 11 1 1 9 40 8 11 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Total 8 267 891 1 4 88 44 1072 1048 423 237 148 825 16 31 756 4759 71 846 78 846 78 819 457 823 122 2648 7407 1); I*= 8	Events 9 39 432 39 432 12 12 12 12 12 12 12 12 13 55 66 7309 % 9 39 432 0 613 55 4 3795 11104 8%	Total 166 1317 978 111 5 2201 600 42556 9713 925 58379 811 182 3672 666 6437 127096 146 1317 978 17096 166 1317 978 127096 811 3672 666 577994	2.3% 3.9% 6.0% 0.9% 1.2% 5.8% 4.3% 5.9% 4.3% 5.0% 3.9% 1.9% 4.6% 6.0% 0.9% 1.9% 4.0% 5.7% 5.8% 4.0% 1.2% 0.9%	M-H, Random, 95% Cl 1.30 [0.23, 7.38] 0.50 [0.18, 1.41] 0.25 [0.20, 0.32] 1.80 [0.06, 54, 33] Not estimable 0.99 [0.06, 10.68] 0.60 [0.24, 1.50] 0.55 [0.40, 0.76] 1.34 [1.01, 1.77] 0.49 [0.22, 1.05] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.57 [0.24, 1.39] 0.89 [0.46, 1.73] 0.27 [0.10, 0.74] 0.33 [0.04, 2.52] 0.17 [0.01, 2.90] 0.64 [0.47, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.57 [0.37, 0.87] 0.66 [0.27, 163.84] Not estimable 2.76 [0.35, 21.57] 1.67 [0.62, 4.45] 0.39 [0.65, 1.33] 2.90 [2.13, 3.96] 0.84 [0.35, 2.01] 1.39 [0.51, 3.75] 0.44 [0.03, 5.24] 1.22 [0.74, 2.04]	M.H. Random, 95% CI

Figure 4. Pooled odds of children and adolescents being an infected contact in community and household family clusters Panel A. Odds of children and adolescents being infected vs adults, by school status. Panel B. Odds of children and adolescents being infected vs adults, by age group (subset of studies in Panel A).

	Childr		Adult			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
4.2.1 Day care and presch	lool						
Heudorf 2021	78	3065	48	1062	4.7%	0.55 (0.38, 0.80)	
Lachassinne 2021	14	327	14	197	3.9%	0.58 [0.27, 1.25]	
Ladhani 2020	22	306	83	486	4.5%	0.38 [0.23, 0.62]	<u> </u>
Larosa 2020	0	156	0	204		Not estimable	
Link-Gelles 2020	17	30	16	22	2.9%	0.49 [0.15, 1.60]	
NCIRS (1)	0	84	0	18		Not estimable	
NCIRS (2)	0	369	3	70	0.9%	0.03 [0.00, 0.51]	
NCIRS (3) Okarska-Napierala 2020	7 8	406 28	6 5	128	3.0% 2.7%	0.36 [0.12, 1.08]	
Okarska-Napierala 2020 Torres 2020	8 18	28 147	5 39	25 235	4.2%	1.60 [0.45, 5.74]	
Subtotal (95% CI)	10	4918	39	235 2447	4.2 % 26.8%	0.70 [0.38, 1.28] 0.53 [0.38, 0.72]	•
Total events	164	1010	214	2111	2010/1	0.00 [0.00, 0.12]	•
Heterogeneity: Tau ² = 0.06		12 df=		18) [,] I ² =	31%		
Test for overall effect: Z = 3							
4.2.2 Primary school							
Armann 2020	11	1536	1	502	1.5%	3.61 [0.47, 28.06]	
Brandal 2020	2	234	1	58	1.2%	0.49 [0.04, 5.51]	·
Dub 2020	7	211	1	9	1.4%	0.27 [0.03, 2.51]	·
Fontanet 2020	45	510	80	1411	4.7%	1.61 [1.10, 2.35]	
Heavey 2020	0	1001	2	139	0.8%	0.03 [0.00, 0.57]	←─────
Heudorf 2021	71	2891	8	897	3.9%	2.80 [1.34, 5.83]	
Kriemler 2020	0	341	0	29		Not estimable	
Ladhani 2020	61	486	84	658	4.8%	0.98 (0.69, 1.40)	
Ladhani 2021	61	542	104	689	4.8%	0.71 [0.51, 1.00]	
_arosa 2020	1	266	0	204	0.8%	2.31 [0.09, 57.02]	
NCIRS (4)	1	179	4	39	1.4%	0.05 [0.01, 0.45]	
NCIRS (5)	2	778	1	80	1.2%	0.20 [0.02, 2.27]	•
NCIRS (6)	0	210	0	21	1.00/	Not estimable	
Sazblewski 2020 Ferree 2020	51	100	29	88	4.3%	2.12 [1.17, 3.83]	
Forres 2020 Johnn 2021	66 8	515 775	39 17	235 405	4.6%	0.74 [0.48, 1.14]	
/olpp 2021 /oon 2020	8 2	6320	0	405	3.6% 0.8%	0.24 (0.10, 0.56) 0.96 (0.05, 19.92)	· · · · · · · · · · · · · · · · · · ·
Subtotal (95% CI)	2	16895	U	6671	39.8%	0.85 [0.55, 1.31]	
Total events	389		371		001070	0.00 [0.00, 1.01]	
Heterogeneity: Tau² = 0.35 Test for overall effect: Z = 0			14 (P ≺ 0	1.00001)	; I² = 74%		
4.2.3 High school							
Fontanet 2020	92	240	79	421	4.8%	2.69 [1.88, 3.85]	· · · · · · · · · · · · · · · · · · ·
Kriemler 2020	1 30	327	0	37	0.8%	0.34 [0.01, 8.61]	
Ladhani 2021		274	105	690	4.6%	0.69 [0.44, 1.06]	
araaa 2020		670		204	1.0%	28.64 [1.75, 468.59]	
Larosa 2020	37	572	0	22			
NCIRS (7)	37 0	165	0	23	1.404	Not estimable	•
NCIRS (7) NCIRS (8)	37 0 5	165 2291	0 1	235	1.4%	Not estimable 0.51 (0.06, 4.40)	<u> </u>
NCIRS (7) NCIRS (8) NCIRS (9)	37 0 5 2	165 2291 600	0 1 1	235 96	1.2%	Not estimable 0.51 (0.06, 4.40) 0.32 (0.03, 3.54)	÷
NCIRS (7) NCIRS (8) NCIRS (9) Pray 2020	37 0 5 2 100	165 2291 600 127	0 1 1 16	235 96 41	1.2% 3.9%	Not estimable 0.51 (0.06, 4.40) 0.32 (0.03, 3.54) 5.79 (2.71, 12.35)	
NCIRS (7) NCIRS (8) NCIRS (9) Pray 2020 Sazblewski 2020	37 0 5 2 100 180	165 2291 600 127 409	0 1 16 29	235 96 41 88	1.2% 3.9% 4.5%	Not estimable 0.51 (0.06, 4.40) 0.32 (0.03, 3.54) 5.79 (2.71, 12.35) 1.60 (0.98, 2.60)	
NCIRS (7) NCIRS (8) NCIRS (9) Pray 2020 Sazblewski 2020 Stein-Zamir 2020	37 0 5 2 100 180 153	165 2291 600 127 409 1161	0 1 16 29 25	235 96 41 88 176	1.2% 3.9% 4.5% 4.6%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45]	
NCIRS (7) NCIRS (8) NCIRS (9) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Szablewski 2021	37 0 5 100 180 153 123	165 2291 600 127 409 1161 197	0 1 16 29 25 4	235 96 41 88 176 9	1.2% 3.9% 4.5% 4.6% 2.5%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98]	
NCIRS (7) NCIRS (8) NCIRS (9) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Szablewski 2021 Forres 2020	37 0 5 2 100 180 153	165 2291 600 127 409 1161	0 1 16 29 25	235 96 41 88 176	1.2% 3.9% 4.5% 4.6%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45]	
NCIRS (7) NCIRS (8) NCIRS (9) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stein-Zamir 2020 Stablewski 2021 Forres 2020 Subtotal (95% CI)	37 0 5 100 180 153 123	165 2291 600 127 409 1161 197 265	0 1 16 29 25 4	235 96 41 88 176 9 235	1.2% 3.9% 4.5% 4.6% 2.5% 4.2%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60]	
NCIRS (7) NCIRS (8) NCIRS (8) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Szablewski 2021 Forres 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69	37 0 5 2 100 180 153 123 16 739 3; Chi ² = 70	165 2291 600 127 409 1161 197 265 6628 0.11, df=	0 1 16 29 25 4 39 299	235 96 41 88 176 9 235 2255	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60]	
NCIRS (7) NCIRS (8) NCIRS (9) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stein-Zamir 2020 Stein-Zamir 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69 Fest for overall effect: Z = 0	37 0 5 2 100 180 153 123 16 739 3; Chi ² = 70	165 2291 600 127 409 1161 197 265 6628 0.11, df=	0 1 16 29 25 4 39 299	235 96 41 88 176 9 235 2255	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60]	
NCIRS (7) NCIRS (8) NCIRS (8) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stein-Zamir 2020 Stein-Zamir 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69 Fest for overall effect: Z = 0	37 0 5 2 100 180 153 123 16 739 3; Chi ² = 70	165 2291 600 127 409 1161 197 265 6628 0.11, df= .40)	0 1 16 29 25 4 39 299	235 96 41 88 176 9 235 2255	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; ² = 86%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38]	
NCIRS (7) NCIRS (8) NCIRS (9) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Szablewski 2021 Forres 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69 Fest for overall effect: Z = 0 Fotal (95% CI) Fotal events	37 0 5 2 100 180 153 123 16 739 739 3; Chi₹= 70 0.84 (P = 0.	165 2291 600 127 409 1161 197 265 6628).11, df= .40) 28441	0 1 16 29 25 4 39 299 10 (P < 0 884	235 96 41 88 176 9 235 2255 0.00001) 11373	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; I ² = 86%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38] 0.84 [0.62, 1.14]	
NCIRS (7) NCIRS (8) VCIRS (9) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stablewski 2021 Forres 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69 Fost for overall effect: Z = 0 Fotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.47 Fest for overall effect: Z = 1	37 0 5 2 100 180 153 123 16 739 0; Chi₹= 70 0.84 (P = 0. 1292 7; Chi₹= 17 11 (P = 0.	165 2291 600 127 409 1161 197 265 6628 0.11, df= 40) 28441 20.76, df .27)	0 1 16 29 25 39 299 10 (P < 0 884 = 33 (P <	235 96 41 88 176 9 235 2255 0.00001) 11373 0.00007	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; ² = 86% 100.0%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38] 0.84 [0.62, 1.14]	0.1 0.2 0.5 1 2 5 10 Favours children Favours Adults
NCIRS (7) NCIRS (8) VCIRS (9) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stablewski 2021 Forres 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69 Fost for overall effect: Z = 0 Fotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.47 Fest for overall effect: Z = 1	37 0 5 2 100 180 153 123 16 739 0; Chi₹= 70 0.84 (P = 0. 1292 7; Chi₹= 17 11 (P = 0.	165 2291 600 127 409 1161 197 265 6628 0.11, df= 40) 28441 20.76, df .27)	0 1 16 29 25 39 299 10 (P < 0 884 = 33 (P <	235 96 41 88 176 9 235 2255 0.00001) 11373 0.00007	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; ² = 86% 100.0%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38] 0.84 [0.62, 1.14]	0.1 0.2 0.5 1 2 5 10 Favours children Favours Adults
NCIRS (7) NCIRS (8) NCIRS (8) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stablewski 2021 Forres 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69 Fotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.47 Fotal roverall effect: Z = 1 Fotal for overall effect: Z = 1 Fotst for overall effect: Z = 1	37 0 5 2 100 180 153 123 16 739 0; Chi₹= 70 0.84 (P = 0. 1292 7; Chi₹= 17 11 (P = 0.	165 2291 600 127 409 1161 197 265 6628 0.11, df= 40) 28441 20.76, df .27)	0 1 16 29 25 39 299 10 (P < 0 884 = 33 (P <	235 96 41 88 176 9 235 2255 0.00001) 11373 0.00007	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; ² = 86% 100.0%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38] 0.84 [0.62, 1.14]	
NCIRS (7) NCIRS (8) NCIRS (9) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stablewski 2021 Forres 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69 Fost for overall effect: Z = 0 Fotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.47 Fest for overall effect: Z = 1 Fest for subgroup difference <u>Eootnotes</u>	37 0 5 2 100 180 153 123 16 739 0; Chi₹= 70 0.84 (P = 0. 1292 7; Chi₹= 17 11 (P = 0.	165 2291 600 127 409 1161 197 265 6628 0.11, df= 40) 28441 20.76, df .27)	0 1 16 29 25 39 299 10 (P < 0 884 = 33 (P <	235 96 41 88 176 9 235 2255 0.00001) 11373 0.00007	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; ² = 86% 100.0%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38] 0.84 [0.62, 1.14]	
NCIRS (7) NCIRS (8) NCIRS (9) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stein-Zamir 2020 Stein-Zamir 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69 Fost for overall effect: Z = 0 Fotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.47 Fest for overall effect: Z = 1 Fest for overall effect: Z = 1 Fest for subgroup difference <u>Footnotes</u> (1) april to July	37 0 5 2 100 180 153 123 16 739 0; Chi₹= 70 0.84 (P = 0. 1292 7; Chi₹= 17 11 (P = 0.	165 2291 600 127 409 1161 197 265 6628 0.11, df= 40) 28441 20.76, df .27)	0 1 16 29 25 39 299 10 (P < 0 884 = 33 (P <	235 96 41 88 176 9 235 2255 0.00001) 11373 0.00007	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; ² = 86% 100.0%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38] 0.84 [0.62, 1.14]	
NCIRS (7) NCIRS (8) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Szablewski 2021 Torres 2020 Subtotal (95% CI) Total events Heterogeneity: Tau ² = 0.69 Total (95% CI) Total events Heterogeneity: Tau ² = 0.47 Test for overall effect: Z = 1 Test for subgroup difference <u>Footnotes</u> (1) april to July (2) July to Sept (3) march to april	37 0 5 2 100 180 153 123 16 739 0; Chi₹= 70 0.84 (P = 0. 1292 7; Chi₹= 17 11 (P = 0.	165 2291 600 127 409 1161 197 265 6628 0.11, df= 40) 28441 20.76, df .27)	0 1 16 29 25 39 299 10 (P < 0 884 = 33 (P <	235 96 41 88 176 9 235 2255 0.00001) 11373 0.00007	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; ² = 86% 100.0%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38] 0.84 [0.62, 1.14]	
NCIRS (7) NCIRS (8) NCIRS (9) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stablewski 2021 Forres 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69 Fest for overall effect: Z = 0 Fotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.47 Fest for subgroup difference <u>Footnotes</u> (1) april to July (2) July to Sept (3) march to april	37 0 5 2 100 180 153 123 16 739 0; Chi₹= 70 0.84 (P = 0. 1292 7; Chi₹= 17 11 (P = 0.	165 2291 600 127 409 1161 197 265 6628 0.11, df= 40) 28441 20.76, df .27)	0 1 16 29 25 39 299 10 (P < 0 884 = 33 (P <	235 96 41 88 176 9 235 2255 0.00001) 11373 0.00007	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; ² = 86% 100.0%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38] 0.84 [0.62, 1.14]	
NCIRS (7) NCIRS (8) NCIRS (8) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stablewski 2021 Forres 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69 Fest for overall effect: Z = 0 Fotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.47 Fest for subgroup difference <u>Footnotes</u> (1) april to July (2) July to Sept (3) march to april (4) march to april (5) July to Sept	37 0 5 2 100 180 153 123 16 739 0; Chi₹= 70 0.84 (P = 0. 1292 7; Chi₹= 17 11 (P = 0.	165 2291 600 127 409 1161 197 265 6628 0.11, df= 40) 28441 20.76, df .27)	0 1 16 29 25 39 299 10 (P < 0 884 = 33 (P <	235 96 41 88 176 9 235 2255 0.00001) 11373 0.00007	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; ² = 86% 100.0%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38] 0.84 [0.62, 1.14]	
NCIRS (7) NCIRS (8) NCIRS (8) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stablewski 2021 Forres 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69 Fost for overall effect: Z = 0 Fotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.47 Fest for subgroup difference <u>Footnotes</u> (1) april to July (2) July to Sept (3) march to april (4) march to april (5) July to Sept (6) April to July	37 0 5 2 100 180 153 123 16 739 0; Chi₹= 70 0.84 (P = 0. 1292 7; Chi₹= 17 11 (P = 0.	165 2291 600 127 409 1161 197 265 6628 0.11, df= 40) 28441 20.76, df .27)	0 1 16 29 25 39 299 10 (P < 0 884 = 33 (P <	235 96 41 88 176 9 235 2255 0.00001) 11373 0.00007	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; ² = 86% 100.0%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38] 0.84 [0.62, 1.14]	
NCIRS (7) NCIRS (8) NCIRS (8) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stein-Zamir 2020 Stein-Zamir 2020 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.69 Fest for overall effect: Z = 0 Fotal (95% CI) Fotal events Heterogeneity: Tau ² = 0.47 Fest for subgroup difference East for subgroup difference <u>Footnotes</u> (1) april to July (2) July to Sept (3) march to april (4) march to april (5) July to Sept (5) July to Sept (6) April to July (7) april to July	37 0 5 2 100 180 153 123 16 739 0; Chi₹= 70 0.84 (P = 0. 1292 7; Chi₹= 17 11 (P = 0.	165 2291 600 127 409 1161 197 265 6628 0.11, df= 40) 28441 20.76, df .27)	0 1 16 29 25 39 299 10 (P < 0 884 = 33 (P <	235 96 41 88 176 9 235 2255 0.00001) 11373 0.00007	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; ² = 86% 100.0%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38] 0.84 [0.62, 1.14]	
NCIRS (7) NCIRS (8) NCIRS (8) Pray 2020 Sazblewski 2020 Stein-Zamir 2020 Stein-Zamir 2020 Stein-Zamir 2020 Subtotal (95% CI) Total events Heterogeneity: Tau ² = 0.69 Total (95% CI) Total events Heterogeneity: Tau ² = 0.47 Test for overall effect: Z = 1 Test for subgroup difference <u>Footnotes</u> (1) april to July (2) July to Sept	37 0 5 2 100 180 153 123 16 739 0; Chi₹= 70 0.84 (P = 0. 1292 7; Chi₹= 17 11 (P = 0.	165 2291 600 127 409 1161 197 265 6628 0.11, df= 40) 28441 20.76, df .27)	0 1 16 29 25 4 39 299 10 (P < 0 884 = 33 (P <	235 96 41 88 176 9 235 2255 0.00001) 11373 0.00007	1.2% 3.9% 4.5% 4.6% 2.5% 4.2% 33.4% ; ² = 86% 100.0%	Not estimable 0.51 [0.06, 4.40] 0.32 [0.03, 3.54] 5.79 [2.71, 12.35] 1.60 [0.98, 2.60] 0.92 [0.58, 1.45] 2.08 [0.54, 7.98] 0.32 [0.18, 0.60] 1.30 [0.71, 2.38] 0.84 [0.62, 1.14]	

Figure 5. Pooled odds ratios for children and adolescent contracting infection compared to adults, by educational setting.

infection (OR=0.53, 95% CI=0.38-0.75) in schools compared to community and households, which was consistently observed on disaggregation by age; children (<10 years) (OR=0.45, 95%=0.39-0.51); adolescents and high-schoolers (OR=0.63, 95% CI=0.56-0.72) (Figure S1 in the **Online Supplementary Document**).

Study quality assessment

The majority of included studies were considered of good or fair quality based on the scores generated by using quality assessment tools (Table S3 in the **Online Supplementary Document**). Out of the 29 population prevalence studies, 28 were of good quality while one was of fair quality. Twenty-five out of 31 contact-tracing studies were of good quality while six were of fair quality. For studies conducted in educational settings, eight were of fair quality and the remaining 22 were of good quality.

Studies were primarily downgraded for inadequate sample size and unclear description of study setting. However, potential biases were noted for some of the included studies, which could negatively affect their quality (eg, low response rate from the study population in contact-tracing studies [15,81,83,85], only symptomatic cases receiving tests [12,14,79,86,104]).

DISCUSSION

This systematic review provides a comprehensive assessment of COVID-19 risk of infection and transmission in children and adolescents compared to adults in household, community and educational settings and in the relationship of age and school contexts with risks of transmission. Consistent with previous reviews [105,106], we found an overall lower risk of infection among children and adolescents (0-19 years) in households and communities compared to adults. In educational settings, children attending daycare, preschool and primary school presented a lower risk of infection than that of adults.

Our review has several important strengths. Compared to existing reviews [105,106], most of which were conducted at an earlier stage of the pandemic, the present review provided the most up-to-date evidence of this research question. We have undertaken several pre-specified sub-group analyses as per data availability. The subgroup comparisons included assessment of active infection (PCR test), past infection (blood serology), school operational status and differential effects by age groups. It was also important to assess if the risk of community transmission was affected by school closure. Using a broad search strategy implemented in English, Chinese and Spanish databases, we summarize evidence from 90 studies from 31 different countries. We also attempted to reduce possible overlap in cases to prevent duplication. Compared to a previous systematic review by Viner et al [105], we report almost thrice the number of studies with disaggregation of analyses by age and settings. This review is primarily limited by the large heterogeneity across studies and the lack of uniform age- and test-specific evidence for transmission in different study settings. Lastly, the evidence of COVID-19 infection in children is rapidly evolving; therefore, evidence from this review should be cautiously interpreted and regularly updated. This review does not include modelling studies, which can forecast future transmission scenarios but under various assumptions about disease transmission and immunity [107].

Currently available epidemiological data have revealed two unique features of pediatric COVID-19 cases: a relatively low prevalence in this population and milder clinical features compared to adult patients [9,108]. Several studies and reviews have studied children and adolescents' susceptibility to SARS-CoV-2 infection and their role in transmission in different settings. Viner et al. examined studies on the prevalence of SARS-CoV-2 infection in children and young people (<20 years), and found that the pooled odds ratio of being infected among children vs adults was 0.56 (95% CI: 0.37-0.85) with substantial heterogeneity ($I^2 = 95\%$) [105]. Goldstein et al [109] reviewed data on detection of SARS-CoV-2 infection in different settings and suggested a significantly lower susceptibility of infection for children (<10 years of age) compared to adults. There was some evidence of robust spread of SARS-CoV-2 in secondary and high-schools (eg, high seroprevalence of anti-SARS-CoV-2 antibodies among high-school students in northern France [83], and an outbreak in an Israel high-school [13]), while the spread seemed to be more limited in primary schools [12,14,15,82,88-91]. Xu et al. conducted a living systematic review and reported that the SARS-CoV-2 infection attack rates were 0.15% (95% CI=0%-0.93%) among students and 0.70% (95% CI=0%-3.56%) among school staff, respectively [110]. These findings are largely consistent with the primary finding of the present study that children are not as susceptible to SARS-CoV-2 infection as adults, and while children are known to be "super spreaders" for influenza [111] and measles viruses [112], they play only a limited role in SARS-CoV-2 transmission in various settings.

Symptomatic patients have a lower SARS-CoV-2 cycle threshold (Ct) values, which corresponds to higher viral RNA levels. SARS-CoV-2 Ct values have been found to be almost linearly inversely correlated with its transmission [113]. Furthermore, a meta-analysis reported risk of asymptomatic transmission is significantly lower

than that of symptomatic transmission (relative risk = 0.58; 95% CI = 0.34-0.99) [114]. To contextualize, these findings might suggest that children may be less likely to transmit SARS-CoV-2 due to their lower prevalence of symptomatic and severe presentation during the infection [115].

School closures are an effective public health mitigation measure in reducing the community transmission of many respiratory infectious diseases, such as influenza [2,3], however, current evidence on the effectiveness of school closures in curbing the COVID-19 pandemic is inconsistent. Large experiences from Australia, USA and England demonstrated low transmission rates in schools and early childhood education services when these facilities were still open [90,91,116]. However, Auger et al. conducted a US population-based observational study between March 9 and May 7, 2020 and found that school closure was associated with a significant decline in the incidence of COVID-19 [117]. Majority of the school linked index cases report none or only a small number of secondary cases [91,93]. Reports investigating outbreaks have demonstrated a higher transmission by school-age children to other students or teachers, particularly when the mitigation measures were inadequately implemented in schools [104]. Reports from Sweden [118] and US [119] suggest a comparable increased risk of transmission from teacher to students and other staff members. These highlight the significance of focusing COVID-19 prevention protocols and vaccination strategies for the teachers, which may indirectly protect students who might not be immediately prioritized in the vaccine rollout. In the present study, we find overall that opening educational establishments may not predispose children and adolescents to a higher risk of SARS-CoV-2 infection compared to adults. On the contrary, children and adolescents were found to have more than 2-fold greater risk of infection in household and community settings than in schools. The school attendance may serve as a protective factor, which reduces children's chances of community contacts in a relatively isolated environment during school hours. It may also be attributable to the effective infections control measures applied in schools introduced by global and national guidelines.

Importantly, prolonged school closures have also been found to have negative impacts on the educational and social development of children including increasing mental disorders, worsening nutrition, lack of physical activities, substance abuse, child violence and abuse [106,120-124]. Lessons from the 2013-2016 Ebola pandemic suggested that youth, and young girls in particular, of poor households saw the largest increase in permanent school dropouts post-Ebola [125,126]. The disruption of education is particularly harmful to young children who are in the most sensitive window of learning, as the early education loss could permanently affect the development of one's foundational skills [127]. Alternative educational opportunities such as online distance learning may not be available to poorer or marginalized populations and are non-existent in many LMICs [128].

The decision to reopen schools is understandably a delicate balance between various factors, including the incidence of COVID-19 cases in the community, the concerns and choices of the parents and the public, the school-based mitigation strategies in place including vaccinations for teachers and the availability of resources. It is recommended that schools should only be reopened when the prevalence of COVID-19 at the community level is under a relatively safe threshold [129].

Safe reopening of schools is not possible without proper mitigation plans and strategies in place. Some of the measures, which are suggested by the present guidelines, include repeat testing, avoiding crowded/close contact environments, social distancing, wearing facial coverings, maintaining hand hygiene, and some protective measure of classrooms and environment, including limiting classroom size and ensuring adequate ventilation including open air classes where feasible [130]. Despite these recommended actions, there are major challenges in evaluating the effectiveness of such guidelines. It is even more challenging to ensure the most effective interventions to be properly implemented in schools. Mitigation strategies at schools may incur a considerable financial cost. For instance, it was estimated that an additional 20 billion USD would be needed for the nationwide implementation of recommended school-based mitigation strategies in the US [131]. There is currently limited data on and much need for collating evidence from safe school reopening strategies and experience across the world.

Given the highly contagious nature of SARS-CoV-2 and the new variants, a expanding vaccine eligibility for children and adolescents and addressing it's hesitancy is the most effective strategy for returning children to schools [116]. While some countries have prioritized vaccination of school teachers and staff to reduce occupational transmission, the evidence of effectiveness of vaccination strategies in adolescents is just emerging [132] and trials are being ramped up in younger children [133]. Given the potential serious complications of COVID-19 infection in subsets of children [134], vaccination research and implementation in children must be prioritized across the world.

REFERENCES

Funding: Supported by an unrestricted core grant from UNICEF (NY) through the International Pediatric Association and core support from the Centre for Global Child Health, Toronto.

Authorship contributions: OI designed the data collection instruments, collected data, carried out data analyses, and reviewed and revised the manuscript. JL conceptualized and designed the study, conducted the literature search, study screening, selection and data extraction and drafted the manuscript. KT and ZW drafted the initial manuscript, and reviewed and revised the manuscript. ZAB conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work. ZAB is the guarantor.

Conflict of Interest: The authors have completed the ICMJE Unified Competing Interest form (available on request from the corresponding author), and declare no conflict of interest

Additional material

Online Supplementary Document

- 1 World Health Organization. WHO Coronavirus Disease (COVID-19) Dashboard Data last updated: 2021. https://covid19. who.int/. Accessed: 5 April 2021.
- 2 Viner RM, Russell SJ, Croker H, Packer J, Ward J, Stansfield C, et al. School closure and management practices during coronavirus outbreaks including COVID-19: a rapid systematic review. Lancet Child Adolesc Health. 2020;4:397-404. Medline:32272089 doi:10.1016/S2352-4642(20)30095-X
- 3 Cauchemez S, Van Kerkhove MD, Archer BN, Cetron M, Cowling BJ, Grove P, et al. School closures during the 2009 influenza pandemic: national and local experiences. BMC Infect Dis. 2014;14:207. Medline:24739814 doi:10.1186/1471-2334-14-207
- 4 Cauchemez S, Valleron A-J, Boelle P-Y, Flahault A, Ferguson NM. Estimating the impact of school closure on influenza transmission from Sentinel data. Nature. 2008;452:750-4. Medline:18401408 doi:10.1038/nature06732
- 5 Litvinova M, Liu Q-H, Kulikov ES, Ajelli M. Reactive school closure weakens the network of social interactions and reduces the spread of influenza. Proc Natl Acad Sci U S A. 2019;116:13174-81. Medline:31209042 doi:10.1073/pnas.1821298116
- 6 Gemmetto V, Barrat A, Cattuto C. Mitigation of infectious disease at school: targeted class closure vs school closure. BMC Infect Dis. 2014;14:695. Medline:25595123 doi:10.1186/s12879-014-0695-9
- 7 Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiology of COVID-19 among children in China. Pediatrics. 2020;145:e20200702. doi:10.1542/peds.2020-0702. Medline:32179660
- 8 CDC COVID-19 Response Team. Coronavirus disease 2019 in children—United States, February 12–April 2, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(14):422-426. Medline:32271728
- 9 Irfan O, Muttalib F, Tang K, Jiang L, Lassi ZS, Bhutta Z. Clinical characteristics, treatment and outcomes of paediatric COVID-19: a systematic review and meta-analysis. Arch Dis Child. 2021;106:440-8. Medline:33593743 doi:10.1136/archdischild-2020-321385
- 10 Götzinger F, Santiago-García B, Noguera-Julián A, Lanaspa M, Lancella L, Carducci FIC, et al. COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study. Lancet Child Adolesc Health. 2020;4:653-61. Medline:32593339 doi:10.1016/S2352-4642(20)30177-2
- 11 Hoang A, Chorath K, Moreira A, Evans M, Burmeister-Morton F, Burmeister F, et al. COVID-19 in 7780 pediatric patients: a systematic review. EClinicalMedicine. 2020;24:100433. Medline:32766542 doi:10.1016/j.eclinm.2020.100433
- 12 Heavey L, Casey G, Kelly C, Kelly D, McDarby G. No evidence of secondary transmission of COVID-19 from children attending school in Ireland, 2020. Euro Surveill. 2020;25:2000903. Medline:32489179 doi:10.2807/1560-7917.ES.2020.25.21.2000903
- 13 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;25:2001352. Medline:32720636 doi:10.2807/1560-7917. ES.2020.25.29.2001352
- 14 Yung CF, Kam K-q, Nadua KD, Chong CY, Tan NWH, Li J, et al. Novel coronavirus 2019 transmission risk in educational settings. Clin Infect Dis. 2021;72:1055-8. Medline:32584975 doi:10.1093/cid/ciaa794
- 15 Fontanet A, Grant R, Tondeur L, Madec Y, Grzelak L, Cailleau I, et al. SARS-CoV-2 infection in primary schools in northern France: A retrospective cohort study in an area of high transmission. MedRxiv. 2020. doi:10.1101/2020.06.25.20140178.
- 16 Macartney K, Quinn HE, Pillsbury AJ, Koirala A, Deng L, Winkler N, et al. Transmission of SARS-CoV-2 in Australian educational settings: a prospective cohort study. Lancet Child Adolesc Health. 2020;4:807-16. Medline:32758454 doi:10.1016/ S2352-4642(20)30251-0
- 17 National Heart L, and Blood Institute. Quality assessment tool for observational cohort and cross-sectional studies. Available: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools. Accessed: 22 February 2021.
- 18 Institute TJB. Checklist for prevalence studies. Available: https://joannabriggs.org/sites/default/files/2020-08/Checklist_for_ Prevalence_Studies.pdf. Accessed: 22 February 2021.
- 19 Gudbjartsson DF, Helgason A, Jonsson H, Magnusson OT, Melsted P, Norddahl GL, et al. Spread of SARS-CoV-2 in the Icelandic population. N Engl J Med. 2020;382:2302-15. Medline:32289214 doi:10.1056/NEJMoa2006100
- 20 Canadian Blood Services. COVID-19 Seroprevalence Report August 19, 2020. Available: https://www.blood.ca/en/research/ our-research-stories/research-education-discovery/seroprevalence-COVID-19-inside-lab. Accessed: 22 February 2021.

- 21 Hallal P, Hartwig F, Horta B, Victora GD, Silveira M, Struchiner C, et al. Remarkable variability in SARS-CoV-2 antibodies across Brazilian regions: nationwide serological household survey in 27 states. MedRxiv. 2020. doi:10.1101/2020.05.30.20117531
- 22 Yousaf AR, Duca LM, Chu V, Reses HE, Fajans M, Rabold EM, et al. A prospective cohort study in non-hospitalized household contacts with SARS-CoV-2 infection: symptom profiles and symptom change over time. Clin Infect Dis. 2020. Online ahead of print. Medline:32719874 doi:10.1093/cid/ciaa1072
- 23 ICMR COVID Study Group. Laboratory surveillance for SARS-CoV-2 in India: Performance of testing & descriptive epidemiology of detected COVID-19, January 22-April 30, 2020. Indian J Med Res. 2020;151:424-37. Medline:32611914 doi:10.4103/ ijmr.IJMR_1896_20
- 24 National Institute for Public Health and the Environment. Children and schools. Available: https://www.rivm.nl/en/novelcoronavirus-covid-19/children-and-covid-19. Accessed: 22 February 2021.
- 25 Office for National Statistics. Coronavirus (COVID-19) infection survey pilot: England and Wales, 11 September 2020. Available: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/coronaviruscovid19infectionsurveypilot/11september2020. Accessed: 22 February 2021.
- 26 Pollán M, Pérez-Gómez B, Pastor-Barriuso R, Oteo J, Hernán MA B, Pérez-Olmeda M, et al; ENE-COVID Study Group. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. Lancet. 2020;396:535-44. Medline:32645347 doi:10.1016/S0140-6736(20)31483-5
- 27 Public Health Agency of Sweden. Förekomsten av covid-19 i Sverige 21-24 april och 25-28 maj 2020. Available: https://www.folkhalsomyndigheten.se/publicerat-material/publikationsarkiv/f/forekomsten-av-covid-19-isverige-21-24-april-och-25-28-maj-2020/. Accessed: 28 July 2020.
- 28 Bendavid E, Mulaney B, Sood N, Shah S, Ling E, Bromley-Dulfano R, et al. Covid-19 antibody seroprevalence in santa clara county, california. MedRxiv. 2020. doi:10.1101/2020.04.14.20062463
- **29** Biggs HM, Harris JB, Breakwell L, Dahlgren FS, Abedi GR, Szablewski CM, et al. Estimated community seroprevalence of SARS-CoV-2 antibodies—two Georgia counties, April 28–May 3, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:965-70. Medline:32701941 doi:10.15585/mmwr.mm6929e2
- 30 Bogogiannidou Z, Vontas A, Dadouli K, Kyritsi MA, Soteriades S, Nikoulis DJ, et al. Repeated leftover serosurvey of SARS-CoV-2 IgG antibodies, Greece, March and April 2020. Euro Surveill. 2020;25:2001369. Medline:32762796 doi:10.2807/1560-7917.ES.2020.25.31.2001369
- **31** Lavezzo E, Franchin E, Ciavarella C, Cuomo-Dannenburg G, Barzon L, Del Vecchio C, et al. Suppression of a SARS-CoV-2 outbreak in the Italian municipality of Vo'. Nature. 2020;584:425-9. Medline:32604404 doi:10.1038/s41586-020-2488-1
- 32 Menachemi N, Yiannoutsos CT, Dixon BE, Duszynski TJ, Fadel WF, Wools-Kaloustian KK, et al. Population point prevalence of SARS-CoV-2 infection based on a statewide random sample—Indiana, April 25–29, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:960. Medline:32701938 doi:10.15585/mmwr.mm6929e1
- 33 Nawa N, Kuramochi J, Sonoda S, Yamaoka Y, Nukui Y, Miyazaki Y, et al. Seroprevalence of SARS-CoV-2 IgG Antibodies in Utsunomiya City, Greater Tokyo, after first pandemic in 2020 (U-CORONA): a household-and population-based study. medRxiv. 2020. doi:10.1101/2020.07.20.20155945
- **34** Pagani G, Conti F, Giacomelli A, Bernacchia D, Rondanin R, Prina A, et al. Seroprevalence of SARS-CoV-2 IgG significantly varies with age: results from a mass population screening (SARS-2-SCREEN-CdA). MedRxiv. 2020. doi:10.1101/2020.06.24 .20138875.
- 35 Public Health Ontario. COVID-19 Serosurveillance Summary. COVID-19 Seroprevalence in Ontario: May 27 to June 30, 2020. Available: https://www.publichealthontario.ca/en/data-and-analysis/infectious-disease/covid-19-data-surveillance. Accessed: 22 February 2021.
- **36** Shakiba M, Nazemipour M, Salari A, Mehrabian F, Nazari SSH, Rezvani SM, et al. Seroprevalence of SARS-CoV-2 in Guilan Province, Iran, April 2020. Emerg Infect Dis. 2021;27:636. Medline:33349310 doi:10.3201/eid2702.201960
- 37 Streeck H, Schulte B, Kümmerer BM, Richter E, Höller T, Fuhrmann C, et al. Infection fatality rate of SARS-CoV2 in a super-spreading event in Germany. Nat Commun. 2020;11:5829. Medline:33203887 doi:10.1038/s41467-020-19509-y
- **38** 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;396:313-9. Medline:32534626 doi:10.1016/S0140-6736(20)31304-0
- 39 Sutton M, Cieslak P, Linder M. Notes from the Field: Seroprevalence Estimates of SARS-CoV-2 Infection in Convenience Sample—Oregon, May 11–June 15, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:1100. Medline:32790658 doi:10.15585/ mmwr.mm6932a4
- **40** Weis S, Scherag A, Baier M, Kiehntopf M, Kamradt T, Kolanos S, et al. Seroprevalence of SARS-CoV-2 antibodies in an entirely PCR-sampled and quarantined community after a COVID-19 outbreak-the CoNAN study. medRxiv. 2020. doi:10.1101/2020.07.15.20154112
- **41** Riley S, Eales O, Walters CE, Wang H, Ainslie KE, Atchinson C, et al. REACT-1 round 8 final report: high average prevalence with regional heterogeneity of trends in SARS-CoV-2 infection in the community in England during January 2021. medRxiv. 2021. doi:10.1101/2021.01.28.21250606.
- **42** Bignami-van Assche S, Boujija Y, Fisman D, Sandberg J. In-person schooling and COVID-19 transmission in Canada's three largest cities. medRxiv. 2021. doi:10.1101/2021.03.21.21254064.
- 43 Murhekar MV, Bhatnagar T, Selvaraju S, Saravanakumar V, Thangaraj JWV, Shah N, et al. SARS-CoV-2 antibody seroprevalence in India, August–September, 2020: findings from the second nationwide household serosurvey. Lancet Glob Health. 2021;9:e257-66. Medline:33515512 doi:10.1016/S2214-109X(20)30544-1

2021 • Vol. 11 • 05013

- RESEARCH THEME 1: COVID-19 PANDEMIC
- 44 Smith BK, Janowski AB, Danis JE, Harvey IB, Zhao H, Dai Y-N, et al. Seroprevalence of SARS-CoV-2 Antibodies in Children and Adults in St. Louis, Missouri, USA. MSphere. 2021;6:e01207-20. Medline:33536325 doi:10.1128/mSphere.01207-20
- 45 González F, Vielot NA, Sciaudone M, Toval-Ruíz C, Premkumar L, Gutierrez L, et al. Seroepidemiology of SARS-CoV-2 infections in an urban Nicaraguan population. medRxiv. 2021. doi:10.1101/2021.02.25.21252447.
- 46 Gidding HF, Machalek DA, Hendry AJ, Quinn HE, Vette K, Beard FH, et al. Seroprevalence of SARS-CoV-2-specific antibodies in Sydney, Australia following the first epidemic wave in 2020. Med J Aust. 2021;214:179-85. Medline:33538019 doi:10.5694/ mja2.50940
- 47 Wiens KE, Mawien PN, Rumunu J, Slater D, Jones FK, Moheed S, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Juba, South Sudan: a population-based study. medRxiv. 2021. doi:10.1101/2021.03.08.21253009.
- **48** Chaw L, Koh W, Jamaludin S, Naing L, Alikhan M, Wong J. SARS-CoV-2 transmission in different settings: Analysis of cases and close contacts from the Tablighi cluster in Brunei Darussalam. medRxiv. 2020. doi:10.1101/2020.05.04.20090043.
- 49 Cheng H-Y, Jian S-W, Liu D-P, Ng T-C, Huang W-T, Lin H-H. Contact tracing assessment of COVID-19 transmission dynamics in Taiwan and risk at different exposure periods before and after symptom onset. JAMA Intern Med. 2020;180:1156-63. Medline:32356867 doi:10.1001/jamainternmed.2020.2020
- **50** Dattner I, Goldberg Y, Katriel G, Yaari R, Gal N, Miron Y, et al. The role of children in the spread of COVID-19: Using household data from Bnei Brak, Israel, to estimate the relative susceptibility and infectivity of children. PLOS Comput Biol. 2021;17:e1008559. Medline:33571188 doi:10.1371/journal.pcbi.1008559
- 51 James A, Eagle L, Phillips C, Hedges DS, Bodenhamer C, Brown R, et al. High COVID-19 attack rate among attendees at events at a church—Arkansas, March 2020. MMWR Morb Mortal Wkly Rep. 2020;69:632-635.
- 52 Jiang Y, Niu W, Wang Q, Zhao H, Meng L, Zhang C. Characteristics of a family cluster of severe acute respiratory syndrome coronavirus 2 in Henan, China. J Infect. 2020;81:e46-8. Medline:32335170 doi:10.1016/j.jinf.2020.04.028
- 53 COVID-19 National Emergency Response Center, Epidemiology and Case Management Team, Korea Centers for Disease Control and Prevention. Coronavirus Disease-19: Summary of 2,370 Contact Investigations of the First 30 Cases in the Republic of Korea. Osong Public Health Res Perspect. 2020;11:81-4. Medline:32257773 doi:10.24171/j.phrp.2020.11.2.04
- 54 Laxminarayan R, Wahl B, Dudala SR, Gopal K, Neelima S, Reddy KJ, et al. Epidemiology and transmission dynamics of COVID-19 in two Indian states. Science. 2020;370:691-7. Medline:33154136 doi:10.1126/science.abd7672
- 55 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;71:1943-6. Medline:32301964 doi:10.1093/cid/ciaa450
- 56 Liu T, Liang W, Zhong H, He J, Chen Z, He G, et al. Risk factors associated with COVID-19 infection: a retrospective cohort study based on contacts tracing. Emerg Microbes Infect. 2020;9:1546-53. Medline:32608325 doi:10.1080/22221751.2020.1787799
- 57 Lopez AS, Hill M, Antezano J, Vilven D, Rutner T, Bogdanow L, et al. Transmission dynamics of COVID-19 outbreaks associated with child care facilities—Salt Lake City, Utah, April–July 2020. MMWR Morb Mortal Wkly Rep. 2020;69:1319. Med-line:32941418 doi:10.15585/mmwr.mm6937e3
- 58 Mizumoto K, Omori R, Nishiura H. Age specificity of cases and attack rate of novel coronavirus disease (COVID-19). MedRxiv. 2020. doi:10.1101/2020.03.09.20033142.
- 59 Park YJ, Choe Y, Park O, Park S, Kim Y, Kim J, et al. COVID-19 National Emergency Response Center, Epidemiology and Case Management Team. Contact tracing during coronavirus disease outbreak, South Korea, 2020. Emerg Infect Dis. 2020;26:2465-8. Medline:32673193 doi:10.3201/eid2610.201315
- 60 Posfay-Barbe KM, Wagner N, Gauthey M, Moussaoui D, Loevy N, Diana A, et al. COVID-19 in children and the dynamics of infection in families. Pediatrics. 2020;146:e20201576. Medline:32457213 doi:10.1542/peds.2020-1576
- **61** Rosenberg ES, Dufort EM, Blog DS, Hall EW, Hoefer D, Backenson BP, et al. COVID-19 testing, epidemic features, hospital outcomes, and household prevalence, New York State—March 2020. Clin Infect Dis. 2020;71:1953-9. Medline:32382743 doi:10.1093/cid/ciaa549
- 62 Fore HH, Dongyu Q, Beasley DM, Ghebreyesus TA. Child malnutrition and COVID-19: the time to act is now. Lancet. 2020;396:517-8. Medline:32730742 doi:10.1016/S0140-6736(20)31648-2
- 63 World Food Programme. COVID-19 will double number of people facing food crises unless swift action is taken. 2020. Available: https://www.wfp.org/news/covid-19-will-double-number-people-facing-food-crises-unlessswift-action-taken. Accessed: 22 February 2021.
- 64 UNICEF. Situation tracking for COVID-19 socio-economic impacts. New York: UNICEF. 2020. Available: https://data.unicef. org/resources/rapid-situation-tracking-covid-19-socioeconomic-impacts-data-viz/. Accessed: 22 February 2021.
- 65 UNICEF. Yemeni children face deadly hunger and aid shortages as COVID-19 pandemic spreads UNICEF. 26 June, 2020. Available: https://www.unicef.org/press-releases/yemeni-children-face-deadly-hunger-and-aid-shortages-covid-19-pandemic-spreads. Accessed: 22 February 2021.
- **66** World Health Organization. Addressing violence against children, women and older people during the COVID-19 pandemic: key actions, 17 June 2020. Geneva: WHO; 2020.
- **67** World Health Organization. Nurturing care for early childhood development: a framework for helping children survive and thrive to transform health and human potential. Geneva: WHO; 2018.
- 68 Komorowski M, Aberegg SK. Using applied lung physiology to understand COVID-19 patterns. Br J Anaesth. 2020;125:250-3. Medline:32536444 doi:10.1016/j.bja.2020.05.019
- **69** Xie J, Covassin N, Fan Z, Singh P, Gao W, Li G, et al, editors. Association between hypoxemia and mortality in patients with COVID-19. Mayo Clin Proc. 2020;95:1138-47. Medline:32376101 doi:10.1016/j.mayocp.2020.04.006
- **70** Wang Y, Tian H, Zhang L, Zhang M, Guo D, Wu W, et al. Reduction of secondary transmission of SARS-CoV-2 in households by face mask use, disinfection and social distancing: a cohort study in Beijing, China. BMJ Glob Health. 2020;5:e002794. Med-line:32467353 doi:10.1136/bmjgh-2020-002794

Irfan et al

- 71 Gupta N, Saravu K, Varma M, Pm A, Shetty S, Umakanth S. Transmission of SARS-CoV-2 Infection by Children: A Study of Contacts of Index Paediatric Cases in India. J Trop Pediatr. 2021;67:fmaa081. Medline:33280033 doi:10.1093/tropej/fmaa081
- 72 Kim J, Choe YJ, Lee J, Park YJ, Park O, Han MS, et al. Role of children in household transmission of COVID-19. Archives of disease in childhood. 2020;archdischild-2020-319910. Medline:32769089 doi:10.1136/archdischild-2020-319910
- 73 Kong X-G, Geng J, Zhang T, Wang B, Wu A-Z, Xiao D, et al. Dynamic profiles of SARS-Cov-2 infection from five Chinese family clusters in the early stage of the COVID-19 pandemic. Sci Rep. 2020;10:22048. Medline:33328533 doi:10.1038/s41598-020-79035-1
- 74 Luo L, Liu D, Liao X, Wu X, Jing Q, Zheng J, et al. Contact settings and risk for transmission in 3410 close contacts of patients with COVID-19 in Guangzhou, China: a prospective cohort study. Ann Intern Med. 2020;173:879-87. Medline:32790510 doi:10.7326/M20-2671
- 75 Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. Lancet Infect Dis. 2020;20:911-9. Medline:32353347 doi:10.1016/S1473-3099(20)30287-5
- 76 Metlay JP, Haas JS, Soltoff AE, Armstrong KA. Household Transmission of SARS-CoV-2. JAMA Network Open. 2021;4:e210304. Medline:33635324 doi:10.1001/jamanetworkopen.2021.0304
- 77 Maltezou HC, Vorou R, Papadima K, Kossyvakis A, Spanakis N, Gioula G, et al. Transmission dynamics of SARS-CoV-2 within families with children in Greece: A study of 23 clusters. J Med Virol. 2021;93:1414-20. Medline:32767703 doi:10.1002/ jmv.26394
- 78 Atherstone C, Siegel M, Schmitt-Matzen E, Sjoblom S, Jackson J, Blackmore C, et al. SARS-CoV-2 transmission associated with high school wrestling tournaments—Florida, December 2020–January 2021. MMWR Morb Mortal Wkly Rep. 2021;70:141. Medline:33507895 doi:10.15585/mmwr.mm7004e4
- 79 Szablewski CM, Chang KT, Brown MM, Chu VZ, 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;69:1023-5. Medline:32759921 doi:10.15585/mmwr.mm6931e1
- 80 Desmet S, Ekinci E, Wouters I, Decru B, Beuselinck K, Malhotra-Kumar S, et al. No SARS-CoV-2 carriage observed in children attending daycare centers during the intial weeks of the epidemic in Belgium. J Med Virol. 2021;93:1828-31. Med-line:33230857 doi:10.1002/jmv.26689
- 81 Torres JP, Piñera C, De La Maza V, Lagomarcino AJ, Simian D, Torres B, et al. SARS-CoV-2 antibody prevalence in blood in a large school community subject to a Covid-19 outbreak: a cross-sectional study. Clinical Infectious Diseases. 2020; ciaa955. Medline:32649743
- 82 Dub T, Erra E, Hagberg L, Sarvikivi E, Virta C, Jarvinen A, et al. Transmission of SARS-CoV-2 following exposure in school settings: experience from two Helsinki area exposure incidents. medRxiv. 2020. doi:10.1101/2020.07.20.20156018.
- 83 Fontanet A, Tondeur L, Madec Y, Grant R, Besombes C, Jolly N, et al. Cluster of COVID-19 in northern France: A retrospective closed cohort study. medRxiv. 2020. doi:10.1101/2020.04.18.20071134.
- 84 Armann JP, Unrath M, Kirsten C, Lück C, Dalpke A, Berner R. Anti-SARS-CoV-2 IgG antibodies in adolescent students and their teachers in Saxony, Germany (SchoolCoviDD19): very low seropraevalence and transmission rates. 2020. doi:10.1101 /2020.07.16.20155143.
- 85 Brown NE, Bryant-Genevier J, Bandy U, Browning CA, Berns AL, Dott M, et al. Antibody responses after classroom exposure to teacher with coronavirus disease, March 2020. Emerg Infect Dis. 2020;26:2263. Medline:32597750 doi:10.3201/ eid2609.201802
- 86 Blaisdell LL, Cohn W, Pavell JR, Rubin DS, Vergales JE. Preventing and mitigating SARS-CoV-2 transmission—four overnight camps, Maine, June–August 2020. MMWR Morb Mortal Wkly Rep. 2020;69:1216-20. Medline:32881850 doi:10.15585/ mmwr.mm6935e1
- 87 Link-Gelles R, DellaGrotta AL, Molina C, Clyne A, Campagna K, Lanzieri TM, et al. Limited secondary transmission of SARS-CoV-2 in child care programs—Rhode Island, June 1–July 31, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:1170-2. Med-line:32853185 doi:10.15585/mmwr.mm6934e2
- **88** Surveillance NCIRS. COVID-19 in schools and early childhood education and care services-The term 1 experience in NSW. National Centre for Immunisazion Research and Surveillance (NCIRS); July 31, 2020 2020. Available: https://www.ncirs.org. au/covid-19-in-schools. Accessed: 22 February 2021.
- **89** Surveillance NCIRS. COVID-19 in schools and early childhood education and care services-The term 2 experience in NSW. National Centre for Immunisazion Research and Surveillance (NCIRS); July 31, 2020 2020. Available: https://www.ncirs.org. au/covid-19-in-schools. Accessed: 22 February 2021.
- **90** Surveillance NCIRS. COVID-19 in schools and early childhood education and care services-The term 3 experience in NSW. National Centre for Immunisazion Research and Surveillance (NCIRS); July 31, 2020 2020. Available: https://www.ncirs.org. au/covid-19-in-schools. Accessed: 22 February 2021.
- **91** Ismail SA, Saliba V, Bernal JL, 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;21:344-53. Med-line:33306981 doi:10.1016/S1473-3099(20)30882-3
- 92 Brandal LT, Ofitserova TS, Meijerink H, Rykkvin R, Lund HM, Hungnes O, et al. Minimal transmission of SARS-CoV-2 from paediatric COVID-19 cases in primary schools, Norway, August to November 2020. Euro Surveill. 2021;26:2002011. Medline:33413743 doi:10.2807/1560-7917.ES.2020.26.1.2002011
- **93** Larosa E, Djuric O, Cassinadri M, Cilloni S, Bisaccia E, Vicentini M, et al. Secondary transmission of COVID-19 in preschool and school settings in northern Italy after their reopening in September 2020: a population-based study. Euro Surveill. 2020;25:2001911. Medline:33303065 doi:10.2807/1560-7917.ES.2020.25.49.2001911

REFERENCES

- **94** Yoon Y, Kim K-R, Park H. young Kim S, Kim Y-J. Stepwise school opening online and off-line and an impact on the epidemiology of COVID-19 in the pediatric population. medRxiv. 2020. doi:10.1101/2020.08.03.20165589.
- 95 Okarska-Napierała M, Mańdziuk J, Kuchar E. SARS-CoV-2 Cluster in Nursery, Poland. Emerg Infect Dis. 2021;27:317. Medline:33035153 doi:10.3201/eid2701.203849
- **96** Kriemler S, Ulyte A, Ammann P, Peralta GP, Berger C, Puhan MA, et al. Surveillance of acute SARS-CoV-2 infections in school children and point-prevalence during a time of high community transmission in Switzerland. medRxiv. 2021. doi:10.1101 /2020.12.24.20248558.
- 97 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: prospective cohort study of 55 schools in Switzerland. BMJ. 2021.372:n616. Medline:33731327 doi:10.1136/bmj.n616
- 98 Ladhani S. Prospective Active National Surveillance of Preschools and Primary Schools for SARS-CoV-2 Infection and Transmission in England. SSRN, June 2020. Available: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3764198. Accessed: 22 February 2021.
- 99 Ladhani SN, Baawuah F, Beckmann J, Okike IO, Ahmad S, Garstang J, et al. SARS-CoV-2 infection and transmission in primary schools in England in June–December, 2020 (sKIDs): an active, prospective surveillance study. Lancet Child Adolesc Health. 2021;5:417-27. Medline:33740430 doi:10.1016/S2352-4642(21)00061-4
- 100 Szablewski CM, Chang KT, McDaniel CJ, Chu VT, Yousaf AR, Schwartz NG, et al. SARS-CoV-2 transmission dynamics in a sleep-away camp. Pediatrics. 2021;147:e2020046524. Medline:33504612 doi:10.1542/peds.2020-046524
- 101 Lachassinne E, de Pontual L, Caseris M, Lorrot M, Guilluy C, Naud A, et al. SARS-CoV-2 transmission among children and staff in daycare centres during a nationwide lockdown in France: a cross-sectional, multicentre, seroprevalence study. Lancet Child Adolesc Health. 2021;5:256-64. Medline:33571450 doi:10.1016/S2352-4642(21)00024-9
- 102 Heudorf U, Steul K, Walczok A, Gottschalk R. Children and COVID-19-Data from mandatory reporting and results of contact person testing in daycare centers and schools in Frankfurt am Main, Germany. Monatsschrift Kinderheilkunde. 2021;2021:1-11. Medline:33678906
- 103 Volpp KG, Kraut BH, Ghosh S, Neatherlin J. Minimal SARS-CoV-2 Transmission After Implementation of a Comprehensive Mitigation Strategy at a School—New Jersey, August 20–November 27, 2020. MMWR Morb Mortal Wkly Rep. 2021;70:377. Medline:33735161 doi:10.15585/mmwr.mm7011a2
- 104 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;69:1600. Medline:33119558 doi:10.15585/mmwr.mm6943a4
- 105 Viner RM, Mytton OT, Bonell C, Melendez-Torres G, 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;175:143-56. Medline:32975552 doi:10.1001/jamapediatrics.2020.4573
- 106 Merckx J, Labrecque JA, Kaufman JS. Transmission of SARS-CoV-2 by children. Dtsch Arztebl Int. 2020;117:553. Medline:32705983
- **107** Lu FS, Nguyen AT, Link NB, Lipsitch M, Santillana M. Estimating the early outbreak cumulative incidence of COVID-19 in the United States: three complementary approaches. medRxiv. 2020.
- 108 Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. JAMA Pediatr. 2020;174:882-9. Medline:32320004 doi:10.1001/jamapediatrics.2020.1467
- 109 Goldstein E, Lipsitch M, Cevik M. On the Effect of Age on the Transmission of SARS-CoV-2 in Households, Schools, and the Community. J Infect Dis. 2021;223:362-9. Medline:33119738 doi:10.1093/infdis/jiaa691
- 110 Xu W, Li X, Dozier M, He Y, Kirolos A, Lang Z, et al. What is the evidence for transmission of COVID-19 by children in schools? A living systematic review. J Glob Health. 2020;10:021104. Medline:33437465 doi:10.7189/jogh.10.021104
- 111 Tsang TK, Fang VJ, Chan K-H, Ip DK, Leung GM, Peiris JM, et al. Individual correlates of infectivity of influenza A virus infections in households. PLoS One. 2016;11:e0154418. Medline:27153194 doi:10.1371/journal.pone.0154418
- 112 Paunio M, Peltola H, Valle M, Davidkin I, Virtanen M, Heinonen OP. Explosive school-based measles outbreak: intense exposure may have resulted in high risk, even among revaccinees. Am J Epidemiol. 1998;148:1103-10. Medline:9850133 doi:10.1093/oxfordjournals.aje.a009588
- 113 Lyngse FP, Mølbak K, Træholt Frank K, Nielsen C, Skov RL, Kirkeby CT. Association between SARS-CoV-2 transmission risk, viral load, and age: a nationwide study in Danish households. medRxiv. doi:10.1101/2021.02.28.21252608.
- 114 Byambasuren O, Cardona M, Bell K, Clark J, McLaws M-L, Glasziou P. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis. JAMMI. 2020;5:223-34. doi:10.3138/jammi-2020-0030
- 115 Rostad CA, Kamidani S, Anderson EJ. Implications of SARS-CoV-2 Viral Load in Children: Getting Back to School and Normal. JAMA Pediatr. 2021. Epub ahead of print. Medline:34115097 doi:10.1001/jamapediatrics.2021.2022
- **116** Zimmerman KO, Akinboyo IC, Brookhart MA, Boutzoukas AE, McGann K, Smith MJ, et al. Incidence and secondary transmission of SARS-CoV-2 infections in schools. Pediatrics 2021. Epub ahead of print. Medline:33419869 doi:10.1542/ peds.2020-048090.
- 117 Auger KA, Shah SS, Richardson T, Hartley D, Hall M, Warniment A, et al. Association between statewide school closure and COVID-19 incidence and mortality in the US. JAMA. 2020;324:859-70. Medline:32745200 doi:10.1001/jama.2020.14348
- 118 Vlachos J, Hertegård E, Svaleryd HB. The effects of school closures on SARS-CoV-2 among parents and teachers. Proc Natl Acad Sci U S A. 2021;118:e2020834118. Medline:33574041 doi:10.1073/pnas.2020834118

- 119 Gold JA. 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;70:289-92. Medline:33630823 doi:10.15585/ mmwr.mm7008e4
- 120 Ziauddeen N, Woods-Townsend K, Saxena S, Gilbert R, Alwan NA. Schools and COVID-19: reopening Pandora's Box? Public Health in Practice. 2020;1:100039. doi:10.1016/j.puhip.2020.100039
- 121 Van Lancker W, Parolin Z. COVID-19, school closures, and child poverty: a social crisis in the making. Lancet Public Health. 2020;5:e243-4. Medline:32275858 doi:10.1016/S2468-2667(20)30084-0
- **122** Xie X, Xue Q, Zhou Y, Zhu K, Liu Q, Zhang J, et al. Mental health status among children in home confinement during the coronavirus disease 2019 outbreak in Hubei Province, China. JAMA Pediatr. 2020;174:898-900. Medline:32329784 doi:10.1001/jamapediatrics.2020.1619
- 123 Wang G, Zhang Y, Zhao J, Zhang J, Jiang F. Mitigate the effects of home confinement on children during the COVID-19 outbreak. Lancet. 2020;395:945-47. Medline:32145186 doi:10.1016/S0140-6736(20)30547-X
- 124 Dunn CG, Kenney E, Fleischhacker SE, Bleich SN. Feeding low-income children during the Covid-19 pandemic. N Engl J Med. 2020;382:e40. Medline:32227759 doi:10.1056/NEJMp2005638
- **125** Hallgarten J. Evidence on efforts to mitigate the negative educational impact of past disease outbreaks. 2020 Report 793. Reading, UK: Education Development Trust. 2020.
- **126** Government of Sierra Leone. National Ebola Recovery Strategy for Sierra Leone: 2015-2017. Freetown: Government of Sierra Leone; 2015.
- 127 Conto CA, Akseer S, Dreesen T, Kamei A, Mizunoya S, Rigole A, et al. COVID-19: Effects of school closures on foundational skills and promising practices for monitoring and mitigating learning loss. 2020. Available: https://www.unicef-irc.org/pub-lications/1144-covid19-effects-of-school-closures-on-foundational-skills-and-promising-practices.html. Accessed: 22 February 2021.
- 128 Eltahir ME. E-learning in developing countries: Is it a panacea? A case study of Sudan. IEEE Access. 2019;7:97784-92. doi:10.1109/ACCESS.2019.2930411
- 129 Levinson M, Cevik M, Lipsitch M. Reopening primary schools during the pandemic. N Engl J Med. 2020;383:981-5. Medline:32726550 doi:10.1056/NEJMms2024920
- 130 Coronado F, Blough S, Bergeron D, Proia K, Sauber-Schatz E, Beltran M, et al. Implementing mitigation strategies in early care and education settings for prevention of SARS-CoV-2 transmission—eight states, September–October 2020. MMWR Morb Mortal Wkly Rep. 2020;69:1868. Medline:33301431 doi:10.15585/mmwr.mm6949e3
- 131 National Academies of Sciences E. Medicine. Reopening K-12 schools during the Covid-19 pandemic: Prioritizing health, equity, and communities: National Academies Press; 2020. Available: https://www.nap.edu/catalog/25858/reopening-k-12-schools-during-the-covid-19-pandemic-prioritizing. Accessed: 22 February 2021.
- 132 Pfizer-BioNTech Announce Positive Topline Results of Pivotal COVID-19 Vaccine Study in Adolescents. March 31, 2021. Available: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-biontech-announce-positive-topline-results-pivotal. Accessed: 22 February 2021.
- 133 Couzin-Frankel J. Vaccine trials ramp up in children and adolescents. Science. 2021;371:874-5. Medline:33632828 doi:10.1126/science.371.6532.874
- 134 Jiang L, Tang K, Levin M, Irfan O, Morris SK, Wilson K, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. Lancet Infect Dis. 2020;20:e276-e288. Medline:32818434 doi:10.1016/S1473-3099(20)30651-4