

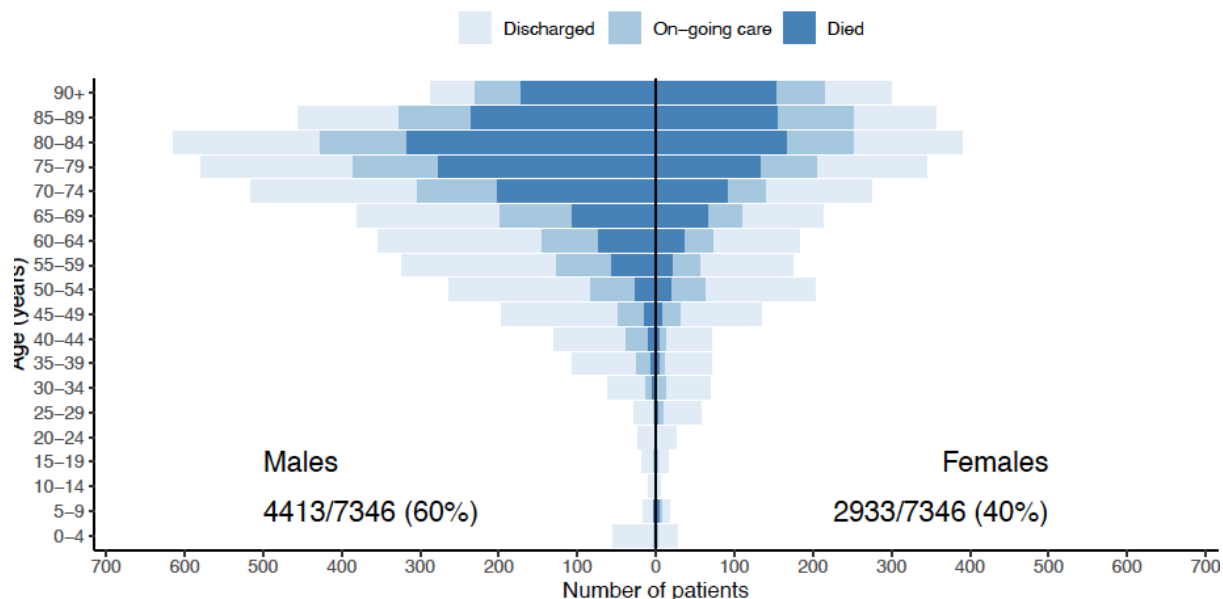
Susceptibility and Transmission in Children - updates from the last few weeks - 29-Apr-20

Russell Viner, Rosalind Eggo, + comments from others

The SAGE document “SAGE Subgroup: The role of children in transmission SAGE 26: 16 April 2020” concluded that there was some evidence that children had milder symptoms than adults but that evidence on susceptibility and transmission was as yet unclear and recommended consideration of additional data gathering.

Clinical data in the UK confirm previous reports that children have notably less symptomatic disease and of lower severity than adults. PHE data show that less than 5% of those <16y who have been tested for COVID-19 are positive in England, much lower than adults - although there are potential biases from testing indications. As of 26-4 there have been 6 deaths and around 400 hospitalisations in England with COVID-19 amongst <16y, with approx. 31 children <16y in paediatric intensive care.

ISARIC COVID-19 data (total n=16,749; 2.0% are <18y with 1.1% under 5y) are similar (Docherty et al <https://www.medrxiv.org/content/10.1101/2020.04.23.20076042v1.full.pdf>)



Below we update findings on transmission and susceptibility, based upon our knowledge of the literature and brief update searches of PubMed and medRxiv.

Summary:

- Evidence remains inconclusive on both susceptibility and transmissibility of children, but balance of evidence suggesting both may be lower.
- Serological studies are starting to be available on child infection history with some suggesting low rates of infection. These must be interpreted with caution based on exposure history (e.g. school closure) in the area they are drawn from, and also some suggestion that mild infections (more common in children) may be less likely to generate antibody.
- There is limited evidence about transmission from children, with some leaning towards lower transmission from children.

Reviews

1. Zhu et al. medrxiv <https://www.medrxiv.org/content/10.1101/2020.03.26.20044826v1.full.pdf>

Undertook a review of household transmission clusters of COVID-19 from studies from China, Singapore, Japan, S Korea and Iran, published up to March 2020. 3 of 31 (9.7%) household clusters identified to have a child as the index case. They note that this is in contrast to H5N1 influenza where 54% of clusters identified children as the index case. Concluded that children have not played a substantive role in intra-household transmission. Note that a sensitivity analysis attempted to account for missing asymptomatic children as the index; they concluded that only 6/28 (21%) could have been a child index.

School cluster or outbreak studies

2. Australian schools study 26 April 2020

A study was undertaken of all COVID-19 cases identified in schools in New South Wales (NSW; population 8 million) from March to mid-April 2020. COVID-19 is notifiable and contact tracing identified 18 cases (9 students, 9 staff) from 15 schools (high and primary). A total of 735 students and 128 staff were identified as close contacts. No staff/adults were identified as contracting COVID-19 from any case. In primary schools, 6 cases resulted in 168 contacts and in one potential child contracting disease. In high schools, 12 cases had 695 contacts; $\frac{1}{3}$ had contacts, all of which were negative. 75 high school contacts had serology 1 month after contact, with 1 student only (and no staff) having antibodies suggestive of infection. Small number of cases, unclear how many were tested, low transmission from all individuals in the study, school attendance was low due to encouragement to keep children at home (from March 23), unclear if there was also household contact tracing.

NCIRS, NSW

http://ncirs.org.au/sites/default/files/2020-04/NCIRS%20NSW%20Schools%20COVID_Summary_FINAL%20public_26%20April%202020.pdf

3. Fontanet et al. Cluster of COVID-19 in north France: A retrospective closed cohort study

<https://www.medrxiv.org/content/10.1101/2020.04.18.20071134v1.full.pdf>

Retrospective study using COVID-19 serology of a closed cohort from a cluster of secondary school students, their parents and siblings and staff of a French high school north of Paris, where coronavirus was known to be highly prevalent before lockdown in France. Infection defined by serology. 37% response rate for staff and students. One third of the cohort was 15-17y and 6% were <14y. 2.7% of <14yo and 40% of 15-17yo were seropositive, compared with 22% of 18-44yo and 20.5% of 45-64yo. Supports lower susceptibility in younger children but concerningly high in 15-17yo, although was a school cluster.

Contact tracing studies

4. Bi et al. Lancet ID.

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30287-5/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30287-5/fulltext)

Was pre-printed and just published (no major changes). Contact tracing study following indexes in Shenzhen, China. 1286 contacts, 391 secondary cases. Found no significant difference in attack rates in children. Fairly wide CIs. Low attack rate overall.

5. Zhang et al. (<https://www.medrxiv.org/content/10.1101/2020.03.19.20039107v1>)

Pre-print. Contact tracing study following indexes in Hunan Province, China. Contacts followed for 14 days, and swabbed (but not reported how often) to find symptomatic and asymptomatic cases. 57 clusters, 2278 contacts, 133 secondary cases. Estimate a decreased risk of infection in children, and decreased (nsf) probability of showing symptoms.

Table 2. Age-specific estimates of relative susceptibility to infection and relative probability of developing symptoms with COVID-19.

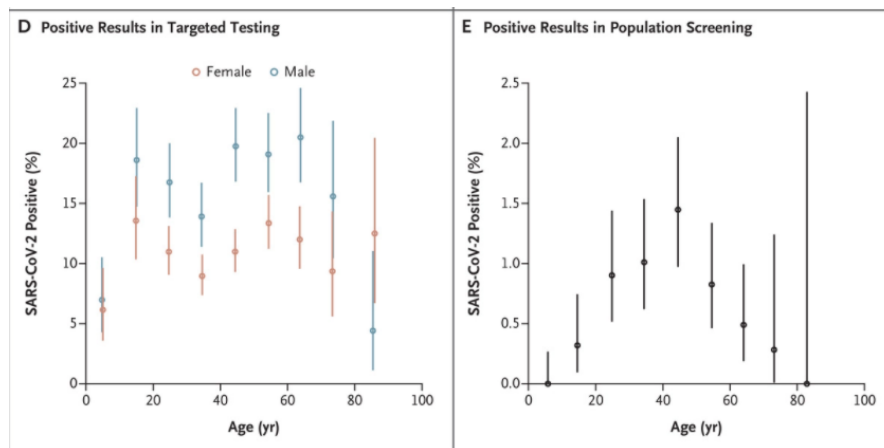
Age group (years)	Susceptibility to infection by age		Risk of developing symptoms by age	
	Relative risk ratio (95%CI)	p-value	Relative risk ratio (95%CI)	p-value
0-14	0.41 (0.18-0.93)	0.026	0.71 (0.40-1.25)	0.133
15-65	0.76 (0.46-1.24)	0.270	0.93 (0.77-1.13)	0.550
≥65	1	-	1	-

6. Jing et al. (<https://www.medrxiv.org/content/10.1101/2020.04.11.20056010v1>).

Contact tracing in Guangzhou. 212 index cases and 2075 contacts. The odds of infection among children (<20 years old) was only 0.26 (95% CI: 0.13-0.54) times of that among the elderly (≥60 years old). Unclear sampling frequency of contacts to detect asymptomatic infections.

Population based studies

7. Iceland study (Gudbjartsson et al NEJM) tests community members (population based and targeted strategies). Cases identified by virus testing. Finds much lower positivity in children. In the population-screening group, 0/848 children under 10y were positive; compared with 0.8% aged 11 or older. ~50% of community screening were symptomatic, so is not unbiased with regard to symptoms.



8. Riccardo et al. (<https://www.medrxiv.org/content/10.1101/2020.04.08.20056861v1>) Large study of cases in Italy. N=62,843, 15,940 of whom have a 5 category measure of clinical severity. Strong evidence of lower severity in younger ages, but the method of finding asymptomatic cases in this dataset is not clear (note similar patterns in UK data - however it is very likely that in the UK and Italy, very young children (i.e. <3y) are more likely to be tested compared with slightly older children). No evidence for transmission.

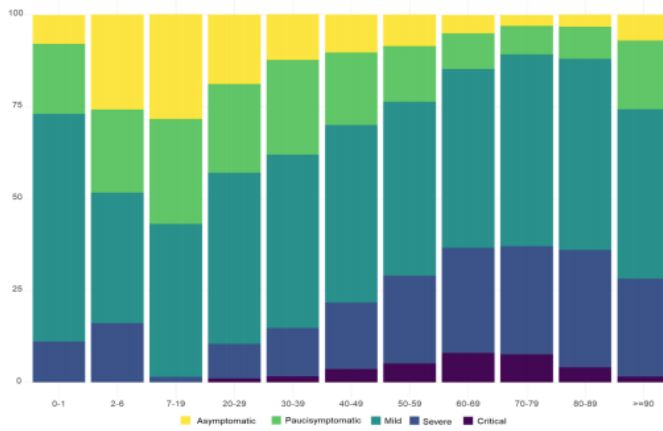
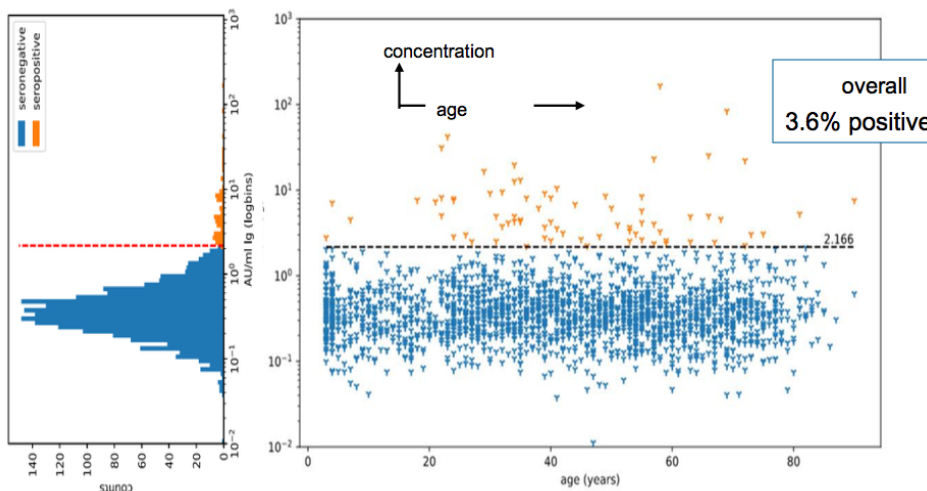


Figure 3 – Reported clinical severity of confirmed COVID-19 cases, Italy (N=15 940)

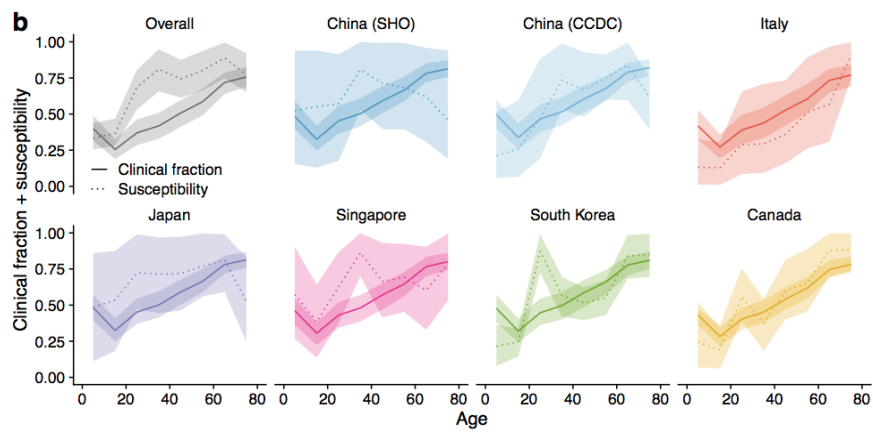
9. Lavezzo et al. (<https://www.medrxiv.org/content/10.1101/2020.04.17.20053157v1>) Study in Vo in Italy, where a high % of the town were tested with or without symptoms, twice. Town was in lockdown, so very low secondary transmission. This is also a modelling study. Low prevalence in children, but very low numbers of infection.

10. RIVM slide show, van Dissel, 22 April. Lower serological positivity in younger ages.



Modelling studies

11. Updated version of Davies et al. (screening on Medrxiv & under revision) During review we were requested to try to jointly fit varying susceptibility by age and varying clinical fraction by age. Originally these two were not jointly identifiable. Used a penalised likelihood fitting to Bi et al, Zhang et al, Riccardo et al, Iceland, and Vo to give lower susceptibility to infection in children (children approx 50% as susceptible as adults).



12. Wu et al. (<https://www.nature.com/articles/s41591-020-0822-7>) Nature Medicine. Modelling study using only data from Wuhan. Estimates “relative susceptibility to symptomatic infection” by age, which combines showing symptoms and being infected. Lower in under 20s. Wuhan also known for having a very extreme age profile compared to other epidemics, so numbers not likely to be reliable elsewhere.