SARS-CoV-2 and children

@CJEMetcalf

Age and COVID-19

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Are **contacts** more frequent among adults than children?

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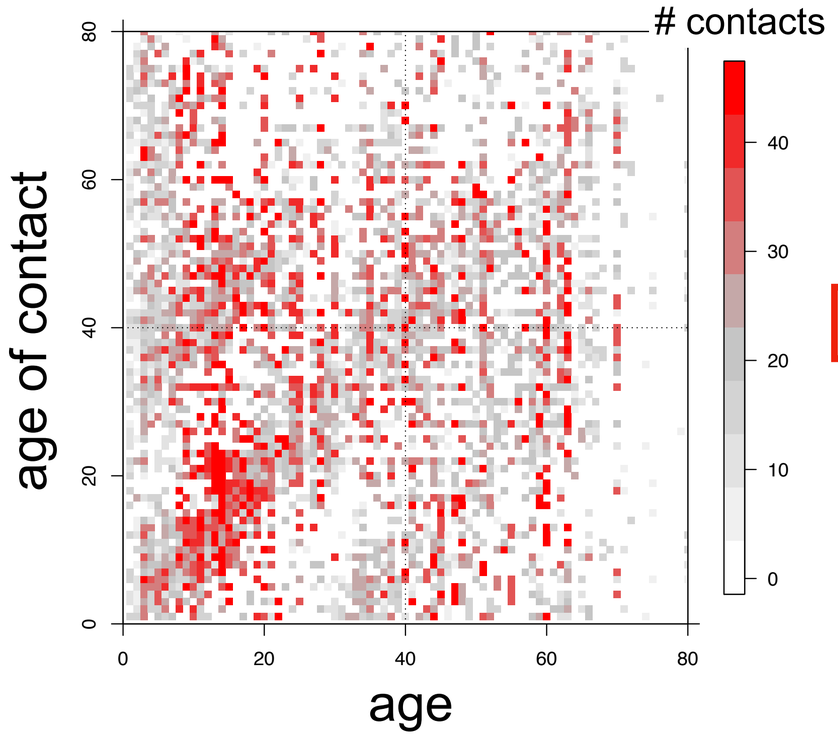

Not normally!

raw diary study data, Mossong et al. 2009

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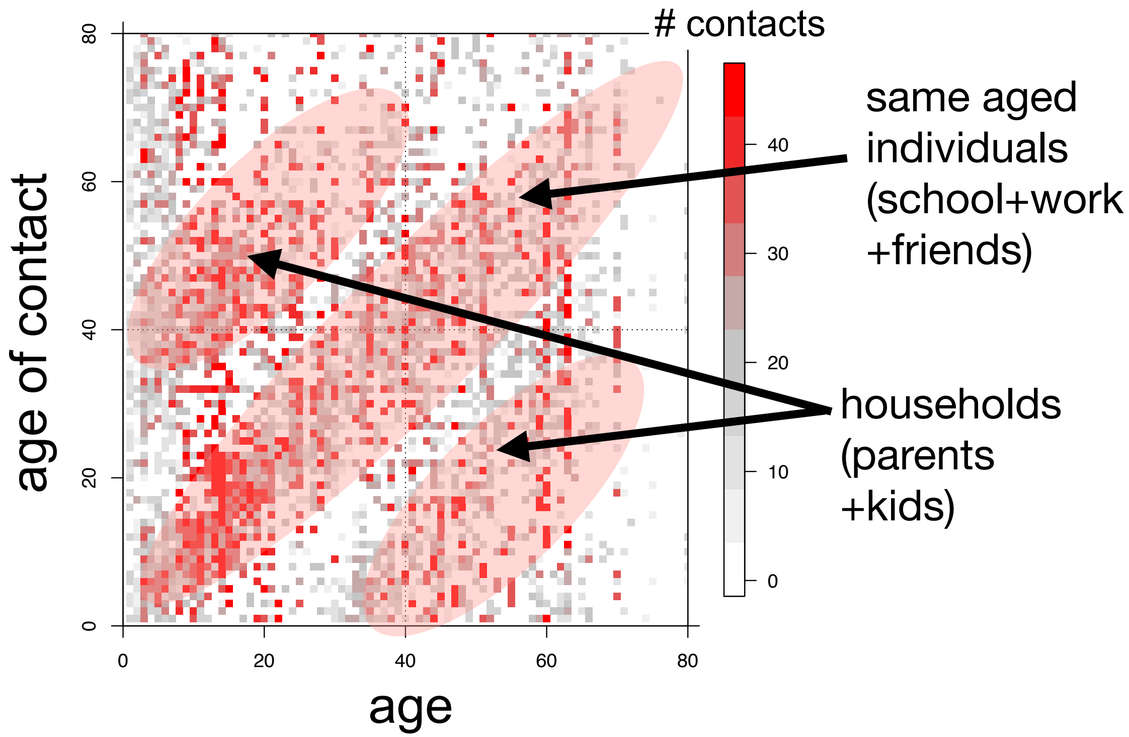

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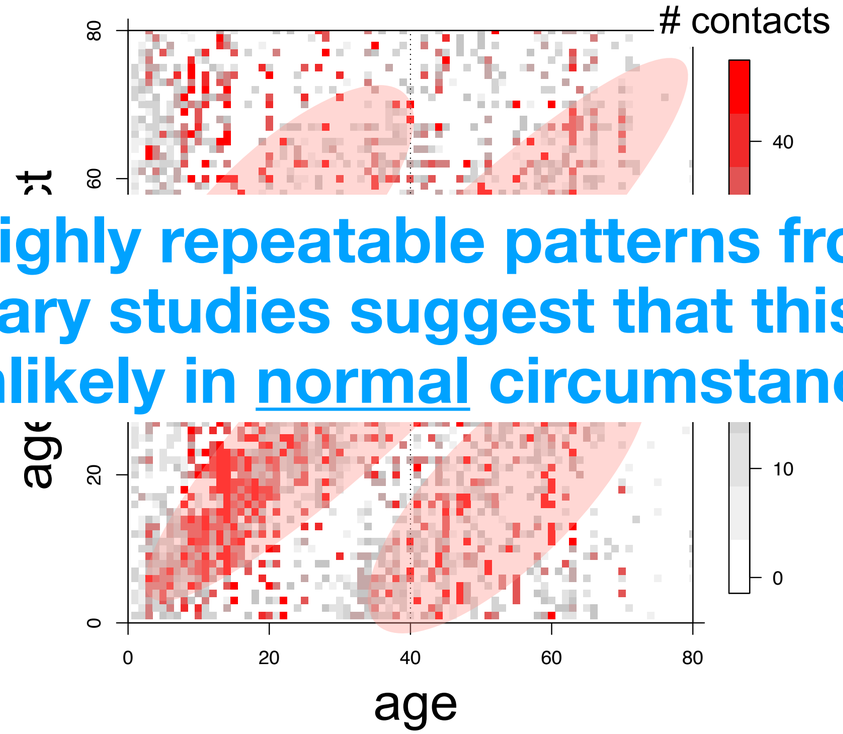

Highly repeatable patterns from diary studies suggest that this is unlikely in normal circumstances

raw POLYMOD data, Mossong et al. 2009

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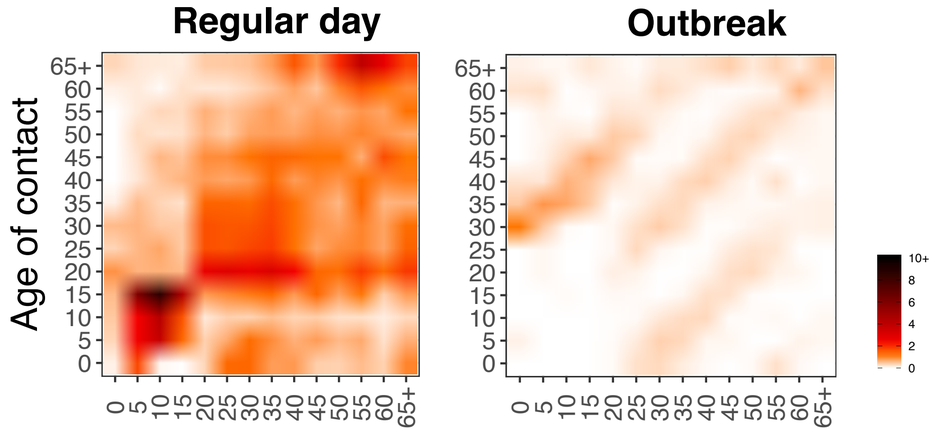

Diary studies in Wuhan
Striking reduction of contact among children during the outbreak

https://dash.harvard.edu/handle/1/42639493

https://science.sciencemag.org/content/early/2020/04/28/science.abb8001?rss=1

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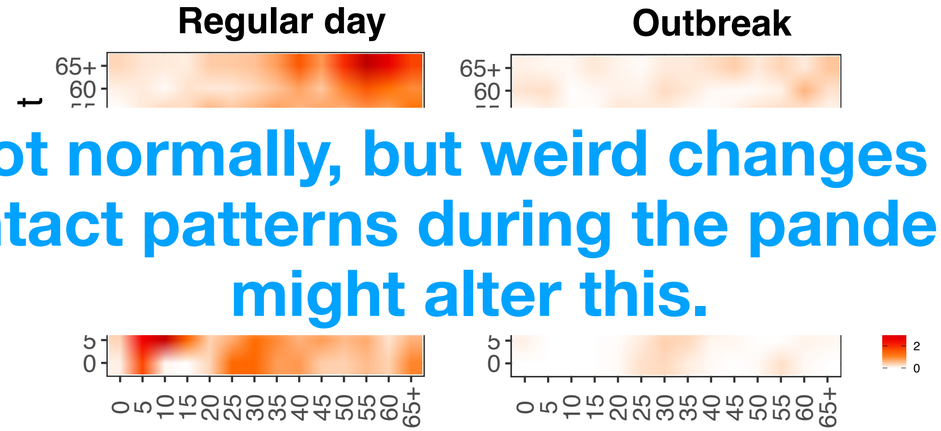

Not normally, but weird changes in contact patterns during the pandemic might alter this.

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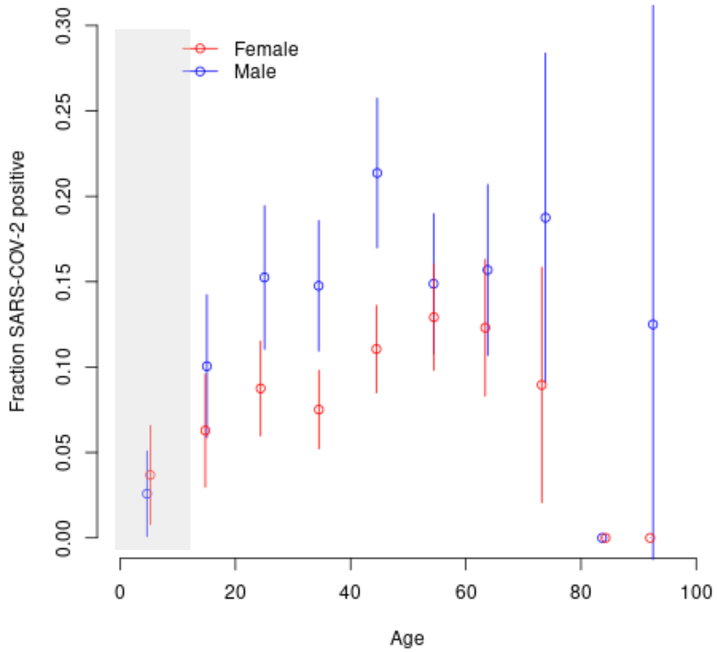

Iceland: children *seem* to get infected less.

https://dash.harvard.edu/handle/1/42639493

https://www.nejm.org/doi/full/10.1056/NEJMoa2006100

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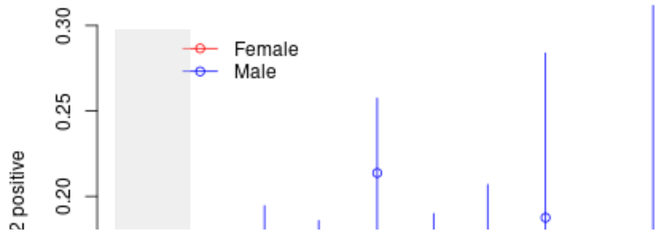
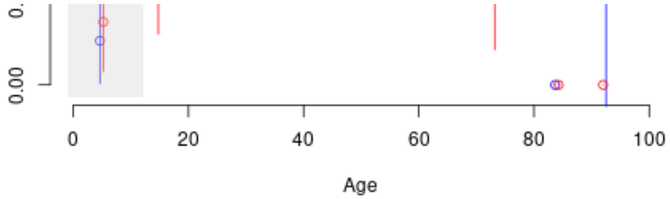


Iceland: children *seem* to get infected less.

But is it just contact? Genetics indicates lots of viral importation - perhaps cases are mostly travellers with less contact with children?



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	SARS-CoV-2 positivity	Unadjusted odds ratio (95% CI)	p value
Age (years)	..	..	<0·0001
0–17	23/499 (4·6%)	1 (ref)	..
18–39	84/666 (12·6%)	2·98 (1·85–4·81)	..
40–64	243/1316 (18·5%)	4·69 (3·00–7·28)	..
65–74	88/557 (15·8%)	3·88 (2·40–6·25)	..
≥75	149/764 (19·5%)	5·00 (3·18–7·90)	..

UK: children also <u>*seem*</u> to get infected less (also potential role for contact).

https://dash.harvard.edu/handle/1/42639493

https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30371-6.pdf

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	n	positive	seroprevalance	p-value
Age				
5-19	214	13 (6.1%)	6.0, 95% CI (2.3-10.2)	0.12
20-49	538	45 (8.4%)	8.5, 95% CI (4.9-11.7)	-
50+	583	25 (4.3%)	3.7, 95% CI (0.9-6.0)	<0.001
Sex				
Female	715	40 (5.6%)	5.6, 95% CI (3.1-8.1)	-
Male	620	43 (6.9%)	6.9, 95% CI (3.3-9.9)	0.24

Geneva: children's risk similar? (schools closed, so probably ~ contact)

https://dash.harvard.edu/handle/1/42639493

https://www.medrxiv.org/content/10.1101/2020.05.02.20088898v1.full.pdf

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Contact tracing data

Estimates from Shenzhen: **No**

"children were as likely to be infected as adults (infection rate 7·4% in children <10 years vs population average of 6·6%).".

https://dash.harvard.edu/handle/1/42639493

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

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Estimates from Wuhan: **Yes**

"We find that children 0-14 years are less susceptible to SARS-CoV-2 infection than adults 15-64 years of age (odd ratio 0.34, 95%CI 0.24-0.49), while in contrast, individuals over 65 years are more susceptible to infection (odd ratio 1.47, 95%CI: 1.12-1.92).

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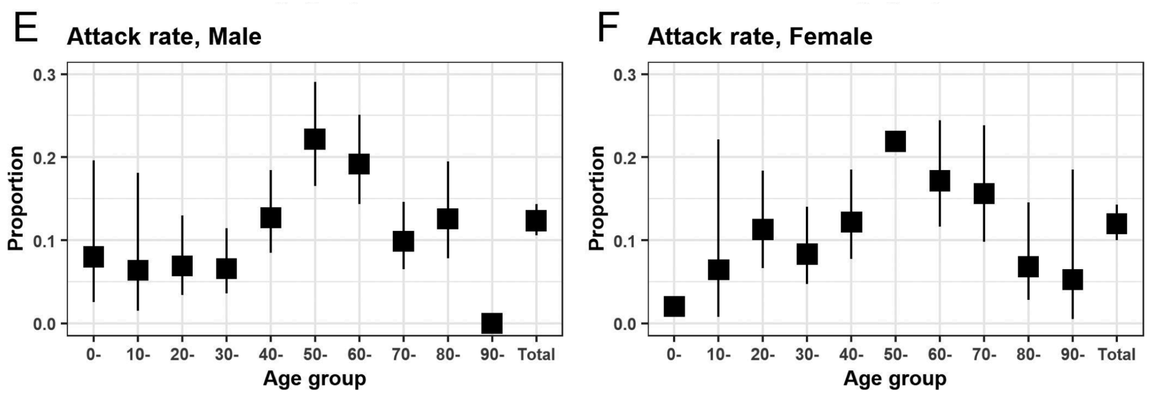
Estimates from Japan: **Yes**



https://dash.harvard.edu/handle/1/42639493

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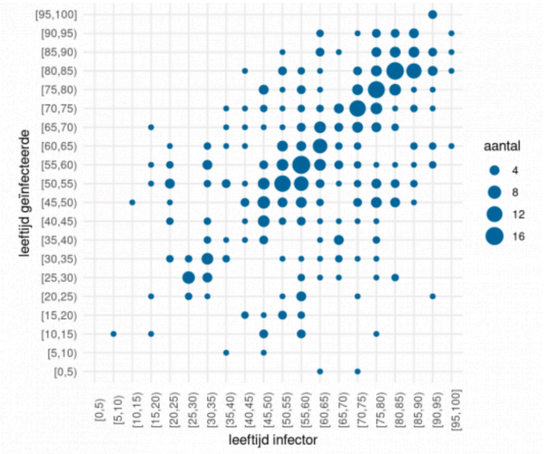
Estimates from Holland: **Yes?**



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https://www.rivm.nl/en/novel-coronavirus-covid-19/children-and-covid-19

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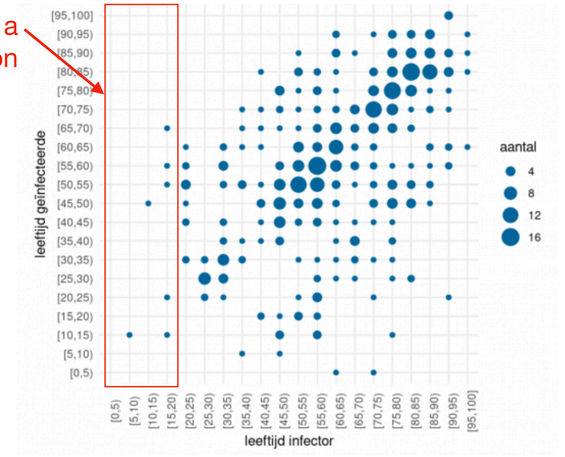
Estimates from Holland: **Yes?**

Children more rarely a source of infection



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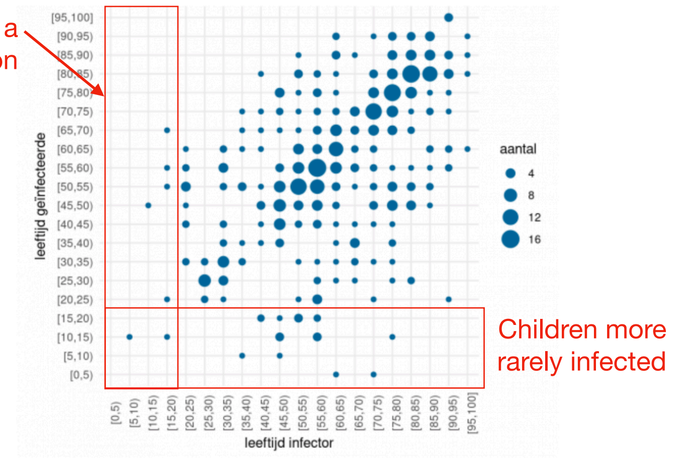

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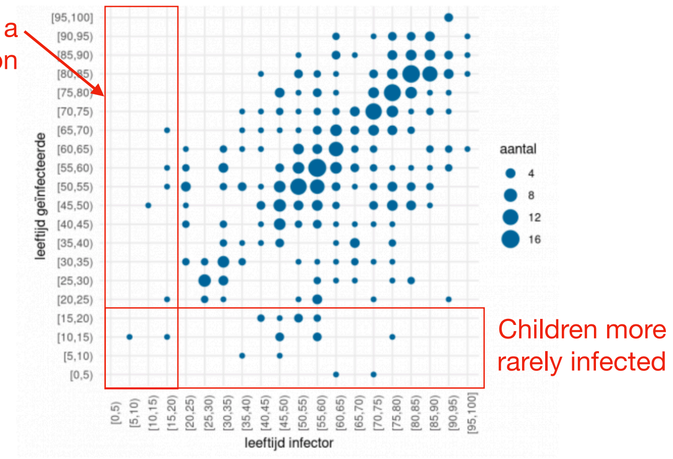

Children more rarely infected

But contact has also changed! (schools closed)

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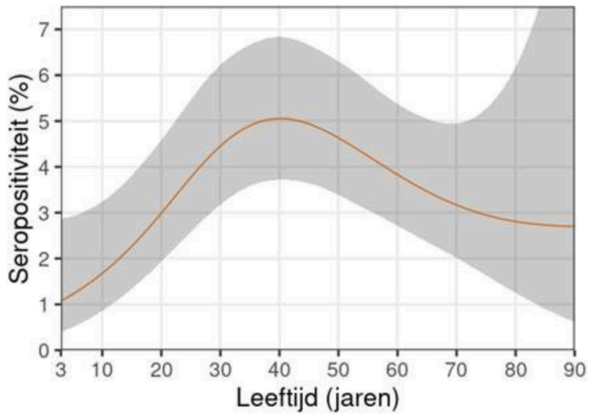

Children also seem to show less signs of having being infected (seropositivity lower)

https://dash.harvard.edu/handle/1/42639493

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Estimates from Spain (13th May): **Maybe?**

	Totales		
	Nº	%	IC 95%
Total	60897	**5,0**	4,7 - 5,4
Edad			
<1	268	**1,1**	0,3 - 3,8
1-4	1693	**2,2**	1,4 - 3,6
5-9	2857	**3,0**	2,3 - 4,1
10-14	3425	**3,9**	3,1 - 4,9
15-19	3221	**3,8**	3,0 - 4,9
20-24	2805	**4,5**	3,5 - 5,7
25-29	2606	**4,8**	3,7 - 6,1
30-34	3050	**3,8**	2,9 - 4,9
35-39	4000	**4,6**	3,8 - 5,6
40-44	5174	**5,3**	4,5 - 6,2
45-49	5330	**5,7**	4,9 - 6,7
50-54	5263	**5,8**	4,9 - 6,9
55-59	5187	**6,1**	5,2 - 7,2
60-64	4560	**5,9**	5,0 - 7,0
65-69	3568	**6,2**	5,1 - 7,4
70-74	2931	**6,9**	5,7 - 8,3
75-79	2161	**6,1**	4,8 - 7,7
80-84	1410	**5,1**	3,8 - 6,9
85-89	968	**5,6**	3,8 - 8,2

But not huge differences, and contacts, etc?

https://dash.harvard.edu/handle/1/42639493

https://www.mscbs.gob.es/gabinetePrensa/notaPrensa/pdf/13.05130520204528614.pdf

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If yes, mechanism? cross protection from other coronaviruses?

https://dash.harvard.edu/handle/1/42639493

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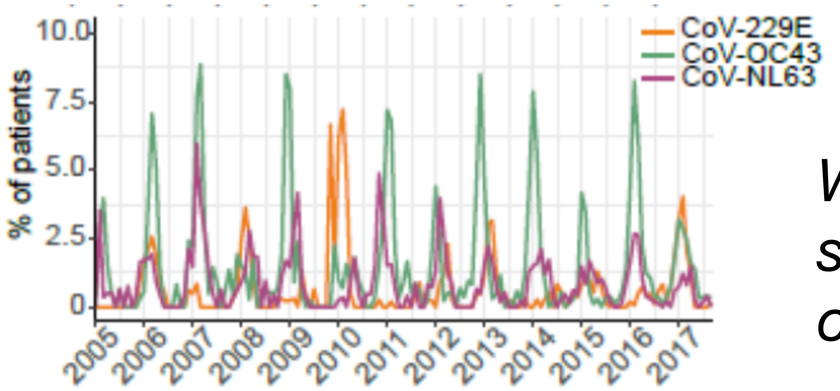

When big, is small, suggests cross protection

Scottish data: non overlap also observed over age (Many others exemplars too)

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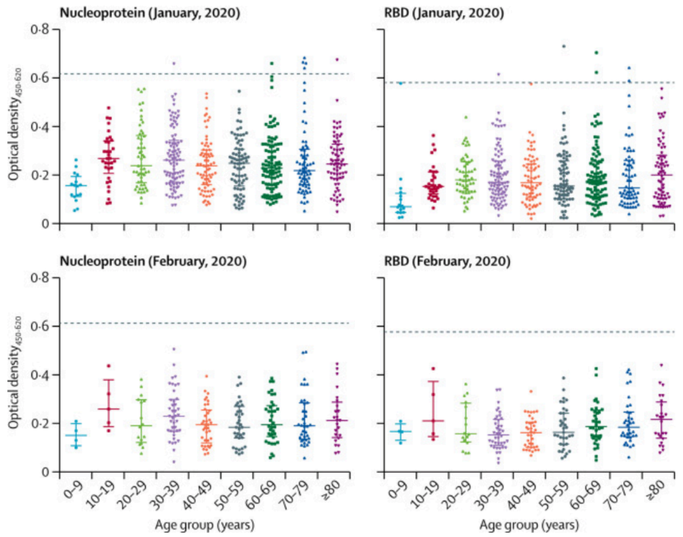

Hong-Kong multi-cohort study

https://dash.harvard.edu/handle/1/42639493

https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(20)30053-7/fulltext

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*Or: is that **children have less ACE2**, (the receptor the virus uses to bind) and thus are less prone to infection?*

https://dash.harvard.edu/handle/1/42639493

https://jamanetwork.com/journals/jama/fullarticle/2766524

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Are children **less prone to symptoms** on infection?

Children lacking from clinical registries; yet at least some evidence of infection.

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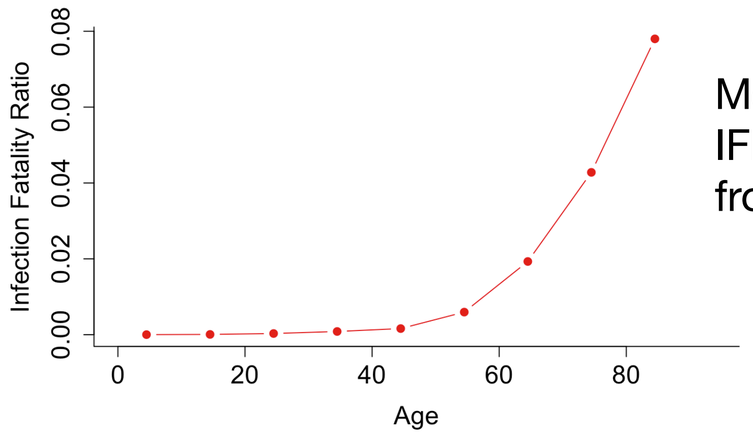

Model based estimates of IFR from integrating data from Hubei, Italy, etc.

https://dash.harvard.edu/handle/1/42639493

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30243-7/fulltext

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In this preliminary description of pediatric U.S. COVID-19 cases, **relatively few children with COVID-19 are hospitalized, and fewer children than adults experience fever, cough, or shortness of breath**. Severe outcomes have been reported in children, including **three deaths.**

https://dash.harvard.edu/handle/1/42639493

https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e4.htm?s_cid=mm6914e4_w

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In contrast with infected adults, most i**nfected children appear to have a milder clinical course. Asymptomatic infections were not uncommon.**

https://dash.harvard.edu/handle/1/42639493

https://www.nejm.org/doi/10.1056/NEJMc2005073

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*Recent evidence in Europe / the US of a **multi-system inflammatory condition** with some features similar to those of Kawasaki disease and toxic shock syndrome (relatively rare).*

https://dash.harvard.edu/handle/1/42639493

https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19

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Comorbidities matter:

Children hospitalized with COVID-19 commonly had **comorbidities**, infants had less severe disease, those with **obesity** were likely to receive mechanical ventilation, and elevated markers of inflammation at admission and during hospitalization were associated with severe disease.

https://dash.harvard.edu/handle/1/42639493

https://jamanetwork.com/journals/jamapediatrics/fullarticle/2766920

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Do older individuals **transmit more**, skewing onward transmission to their older contacts?

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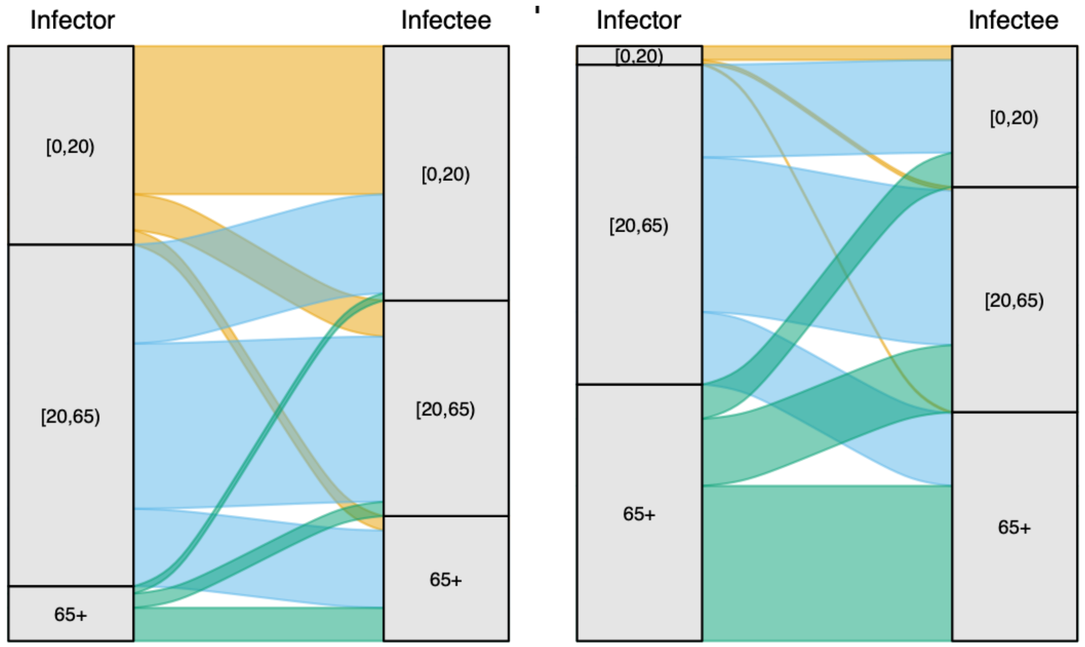
raw POLYMOD data, Mossong et al. 2009

assume transmissibility higher in older ages



relative contribution of age specific transmission pairs

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Do younger individuals **transmit less?**

Cluster of cases in the Swiss Alps

"The fact that an infected child did not transmit the disease despite close interactions within schools suggests potential different transmission dynamics in children."

Do older individuals **transmit more**, skewing onward transmission to their older contacts?

https://dash.harvard.edu/handle/1/42639493

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa424/5819060

Age and COVID-19

Why are there so few cases in children? To become a case requires:

1) **contact** with an infected person
2) **susceptibility** to infection
3) **symptoms** given infection
4) **transmissibility** of contact

Do younger individuals **transmit less?**

Children less likely to be index case in households

"We showed that **of the 31 recorded SARS-CoV-2 household transmission clusters there were only three incidences of children** being identified as the index case in the family."

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https://dash.harvard.edu/handle/1/42639493

https://www.medrxiv.org/content/10.1101/2020.03.26.20044826v1.full.pdf+html

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No evidence for onward transmission in **Irish Schools**

" […] examination of all Irish paediatric cases of COVID-19 attending school during the pre-symptomatic and symptomatic periods of infection (n=3) identified no cases of onward transmission […] within the school and other settings. These included […] choir practice"

Do older individuals **transmit more**, skewing onward transmission to their older contacts?

https://dash.harvard.edu/handle/1/42639493

https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.21.2000903

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Little evidence in **Australian Schools**

"In the 15 schools (10 high school and 5 primary schools) a total of 18 cases (9 students and 9 staff) were identified […] The public health staff identified 863 close contacts in these 15 schools. Of the 863 close contacts, only two students have been identified as secondary cases. "

Do older individuals **transmit more**, skewing onward transmission to their older contacts?

https://dash.harvard.edu/handle/1/42639493 http://ncirs.org.au/sites/default/files/2020-04/NCIRS%20NSW%20Schools%20COVID_Summary_FINAL%20public_26%20April%202020.pdf

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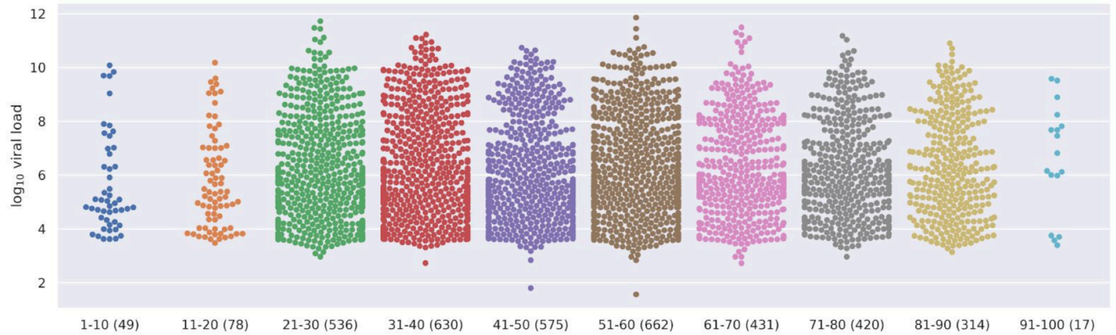

possibly lower viral loads? [but mapping to transmission uncertain, and #s small…]

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https://zoonosen.charite.de/fileadmin/user_upload/microsites/m_cc05/virologie-ccm/dateien_upload/Weitere_Dateien/analysis-of-SARS-CoV-2-viral-load-by-patient-age.pdf

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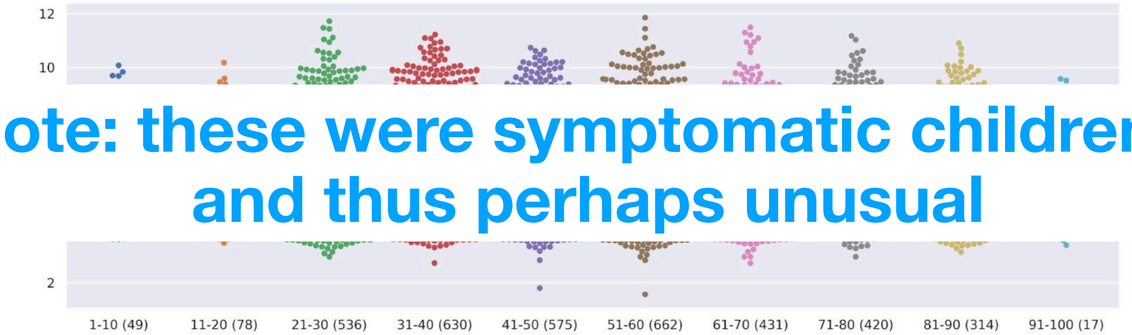


Note: these were symptomatic children… and thus perhaps unusual

possibly lower viral loads? [but mapping to transmission uncertain, and #s small…]

Do older individuals **transmit more**, skewing onward transmission to their older contacts?

https://zoonosen.charite.de/fileadmin/user_upload/microsites/m_cc05/virologie-ccm/dateien_upload/Weitere_Dateien/analysis-of-SARS-CoV-2-viral-load-by-patient-age.pdf

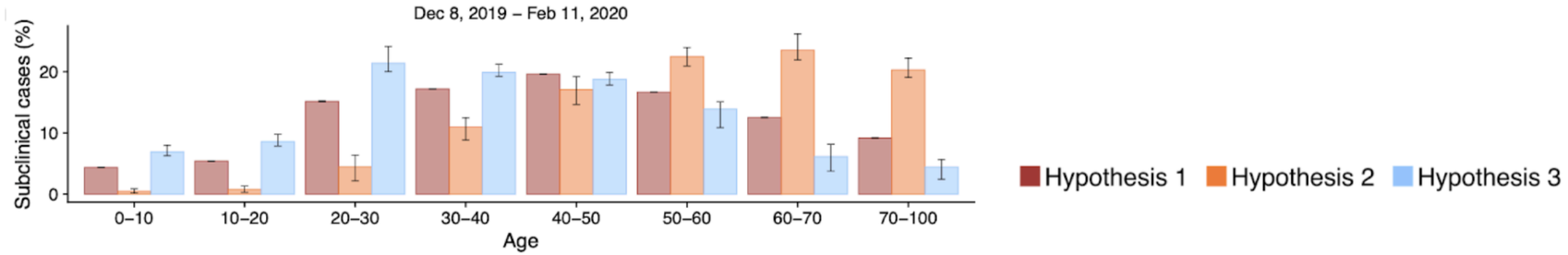
A formal test: age and COVID-19

Age-dependent effects in the transmission and control of COVID-19 epidemics

Authors: Nicholas G. Davies[1*], Petra Klepac[1^], Yang Liu[1^], Kiesha Prem[1], Mark Jit[1], CMMID COVID-19 working group, Rosalind M Eggo[1*]

Model fitting to test three hypotheses:
(1) age contact; (2) age susceptibility; (3) age symptoms

Found (2) & (3) better than (1); and (3) better than (2) overall, with key distinction being # subclinical infections that occur in adults (many more required for (2)).



https://www.medrxiv.org/content/10.1101/2020.03.24.20043018v1

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Discrimination between (2) and (3) hinges on late age subclinical infections being very high in (2) - little evidence to say this isn't the case, yet? + combination of (2) and (3) likely?

https://www.medrxiv.org/content/10.1101/2020.03.24.20043018v1

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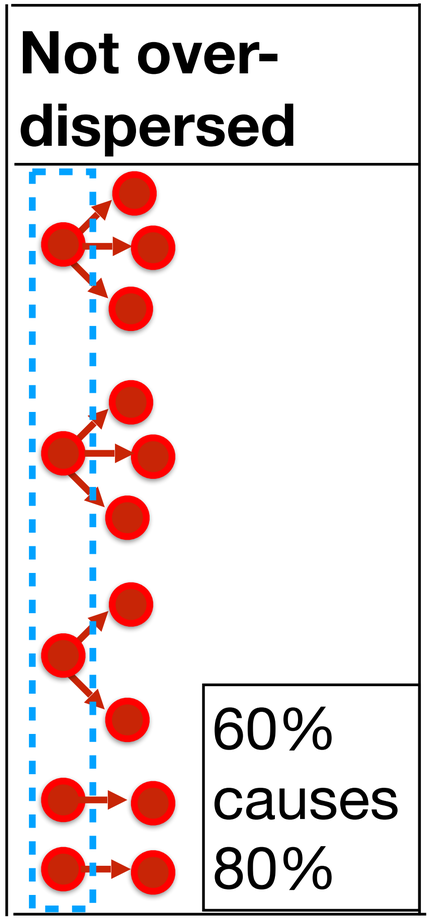
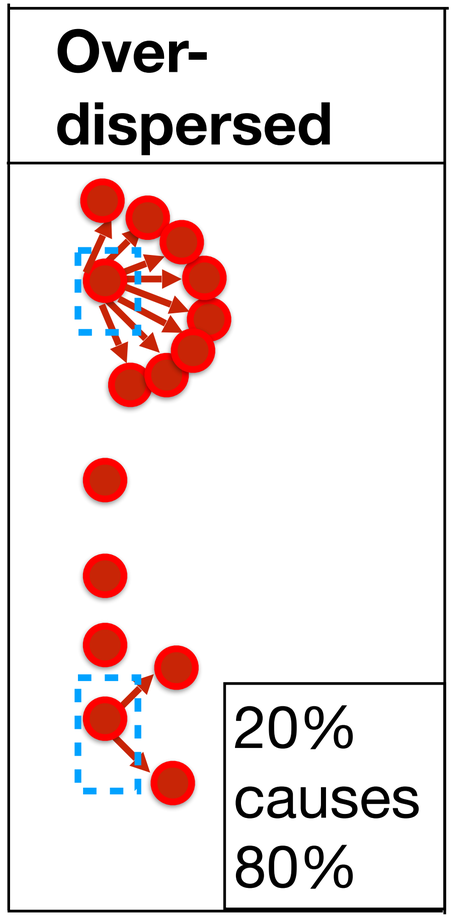
?possibility of higher transmission from older individuals.

https://www.medrxiv.org/content/10.1101/2020.03.24.20043018v1

Transmissibility: 'Super-spreading events'?

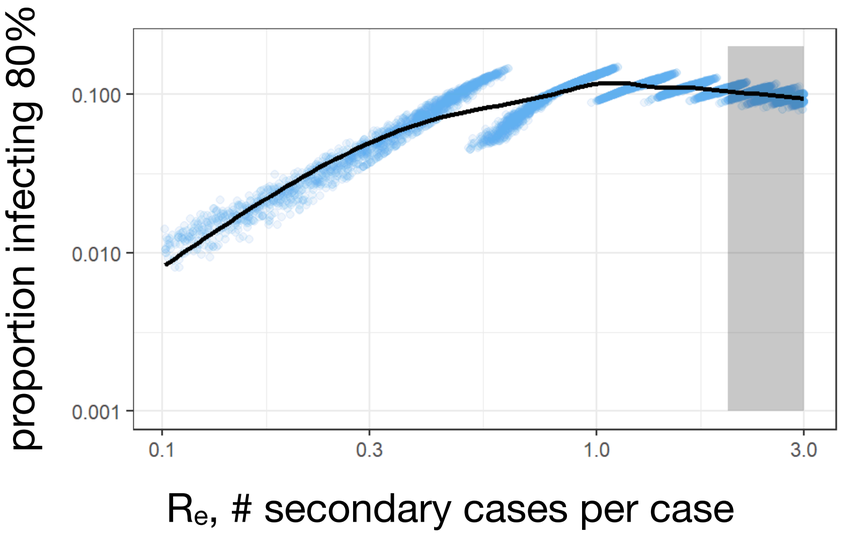


100% of introductions cause onward transmission



40% of introductions cause onward transmission

Map observed (165 introductions; 84 local cases)



https://hopkinsidd.github.io/nCoV-Sandbox/DispersionExploration.html

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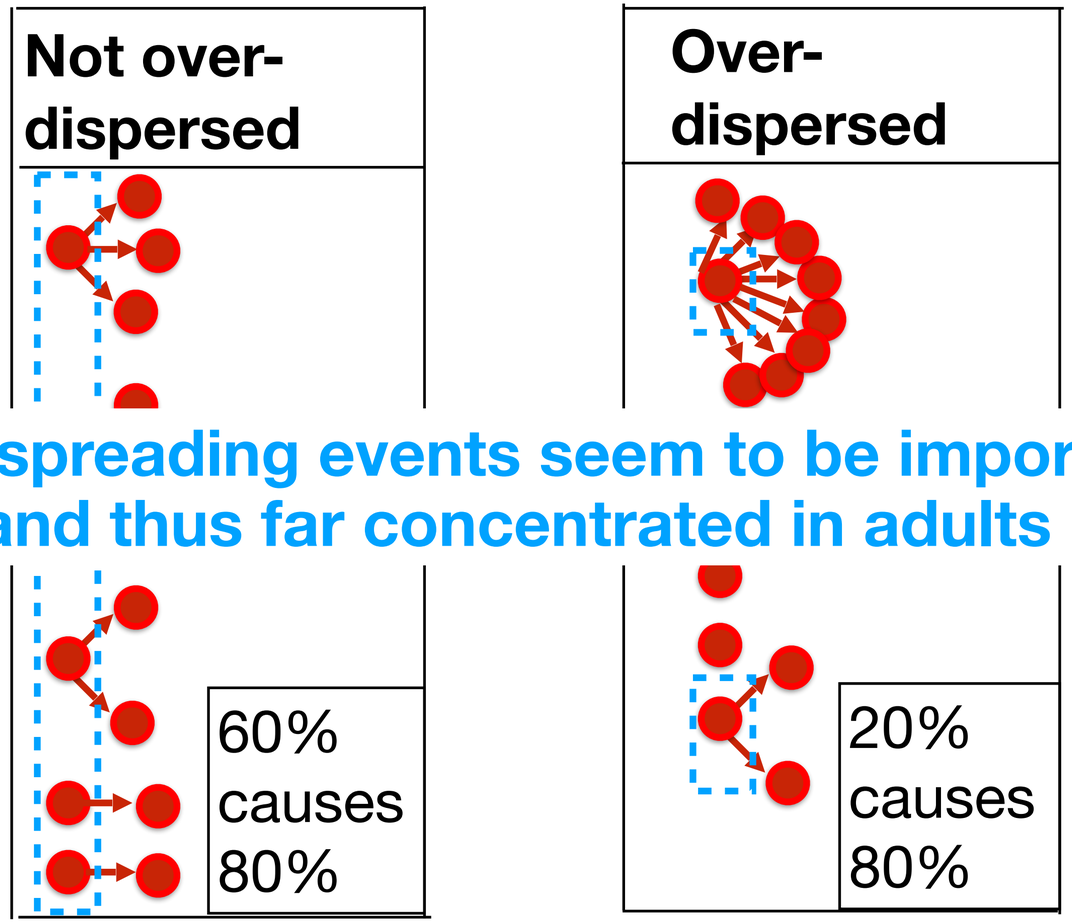

Superspreading events seem to be important, and thus far concentrated in adults

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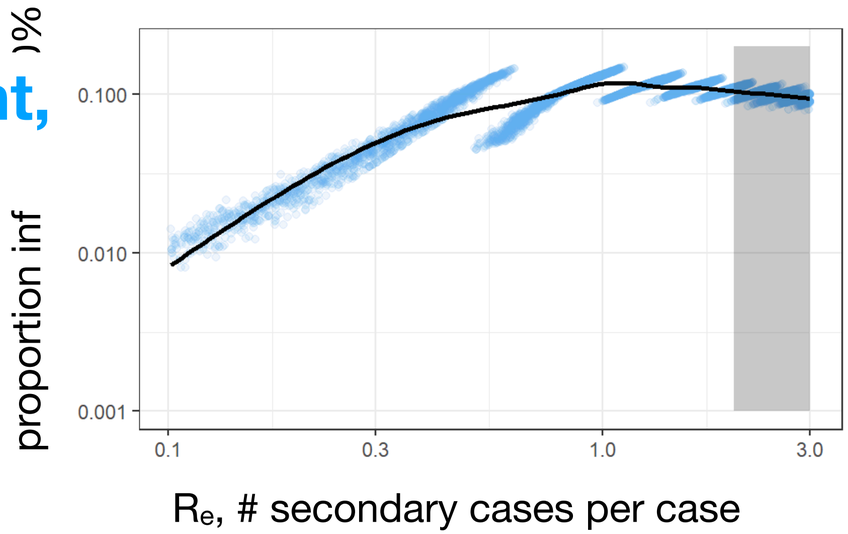
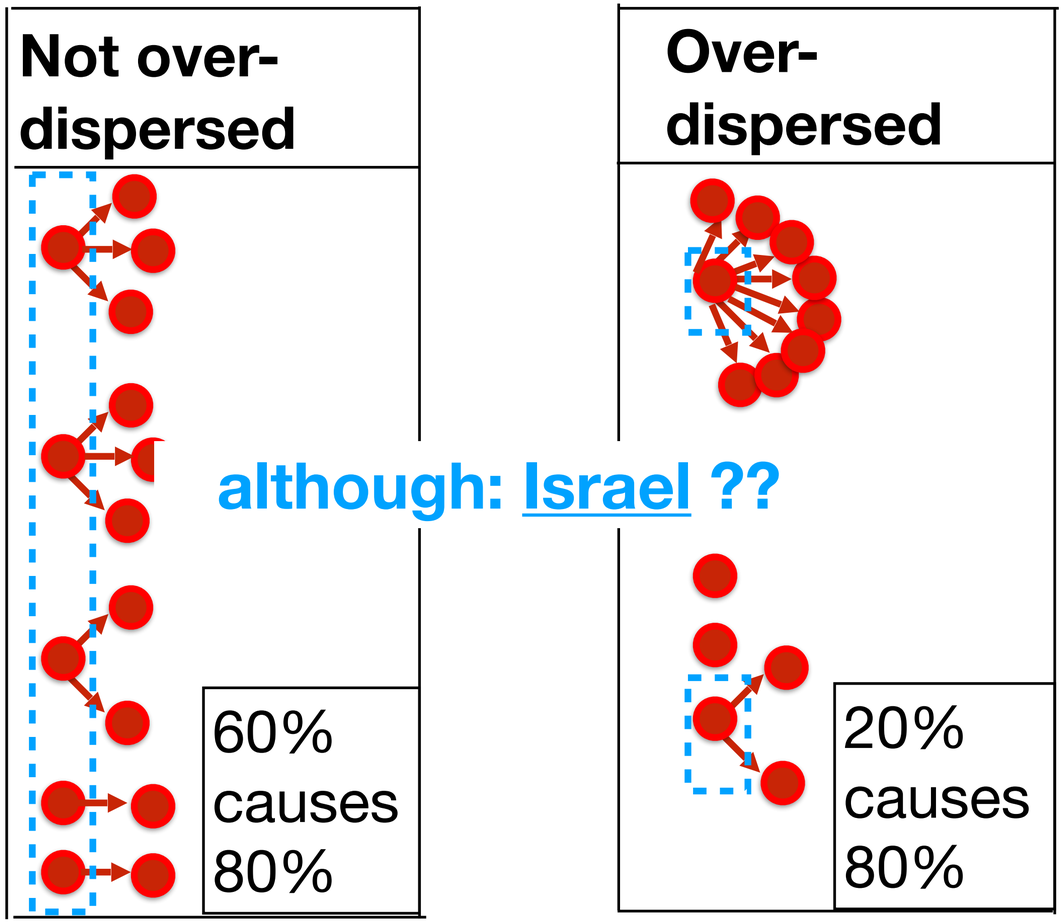
40% of introductions cause onward transmission

Map observed (165 introductions; 84 local cases)



Transmissibility: ’Super-spreading events’?



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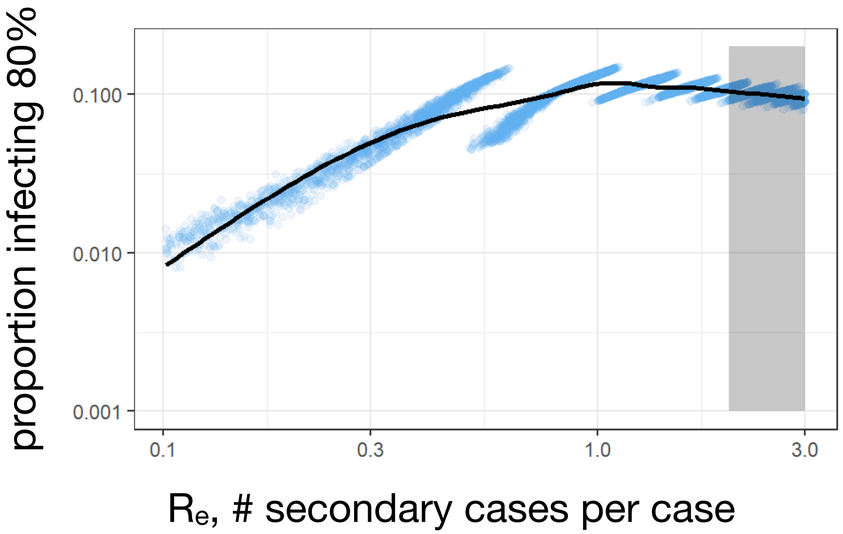

https://www.npr.org/sections/coronavirus-live-updates/2020/06/03/868507524/israel-orders-schools-to-close-when-covid-19-cases-are-discovered

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Children:

-may be less susceptible,

-may be less prone to symptoms,

-this may be associated with less transmission…

…but hard to say still; and contacts are still in flux (school closures, etc).

Implications of the age profile of the novel coronavirus.

James A. Hay[1], David J. Haw[2], William P. Hanage[1], C. Jessica E. Metcalf[3], Michael J. Mina[1,4,5,*]

https://dash.harvard.edu/handle/1/42639493

References not yet organized

https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30135-8/fulltext

https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.18.2000600

Hospital admission within age groups		
< 1 year	52	78.8
1–5 years	24	63.2
6–10 years	13	54.2
11–17 years	21	52.5
Total	110	65.1

higher severity in the very young

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2766670?widget=personalizedcontent&previousarticle=0

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7228213/