SARS-CoV-2 and children

Metcalf

Age and COVID-19

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

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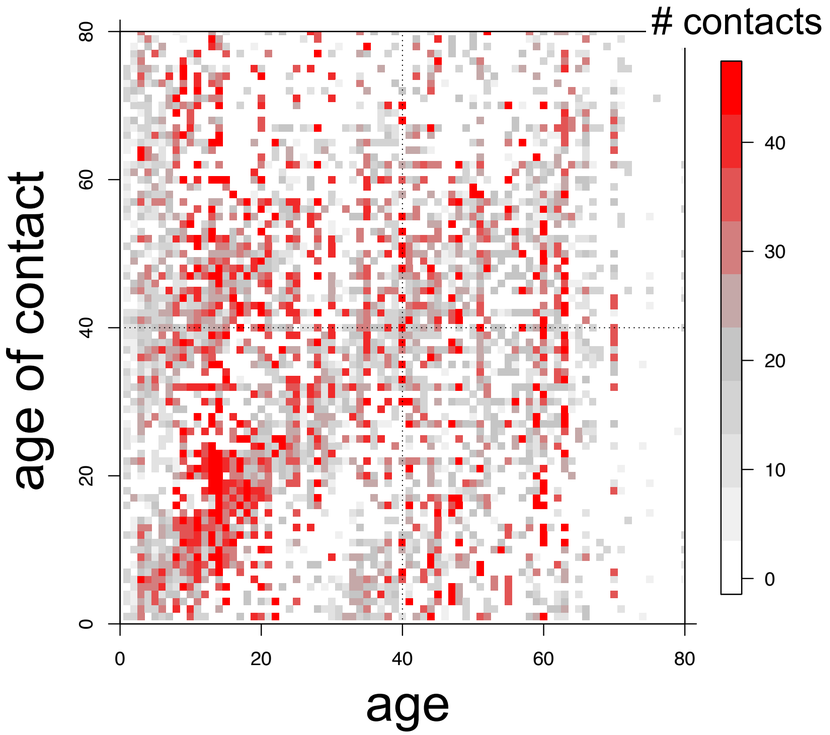

Not normally!

raw POLYMOD data, Mossong et al. 2009

Age and COVID-19

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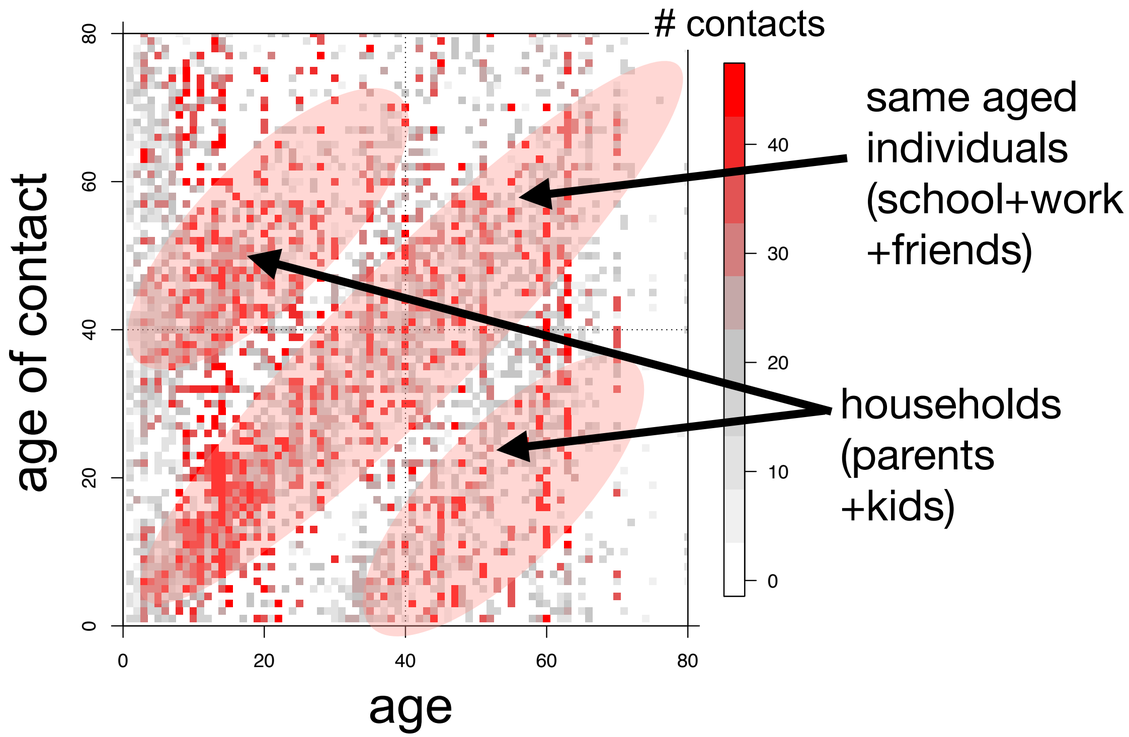

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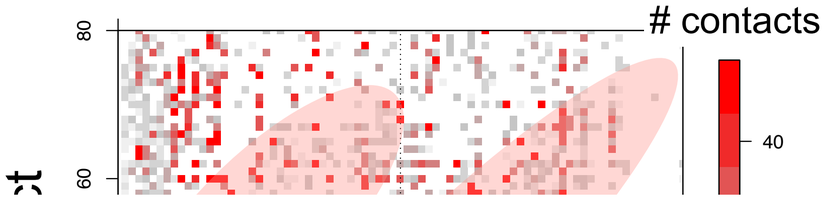
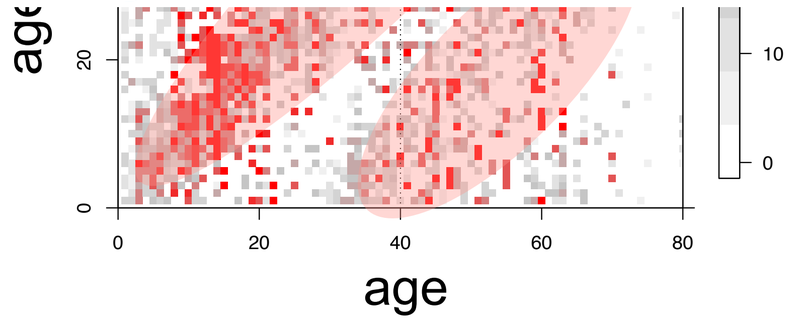


Highly repeatable patterns from diary studies suggest that this is unlikely in normal circumstances



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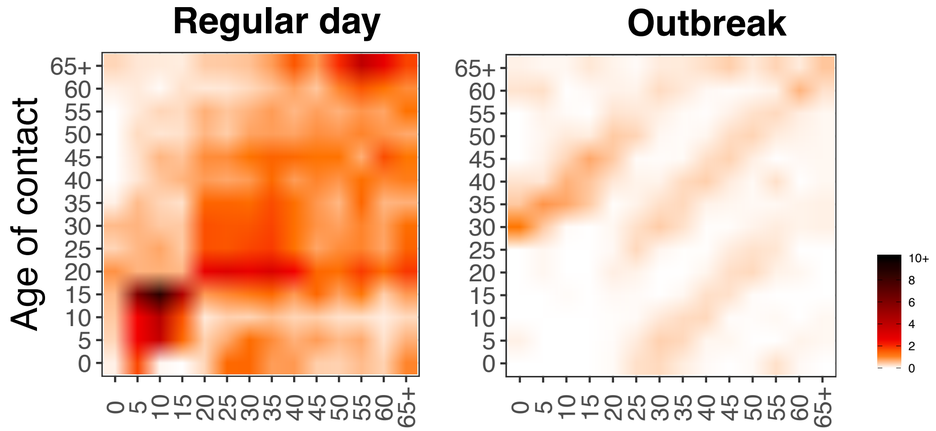

Diary studies in Wuhan
Striking reduction of contact among children during the outbreak

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

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

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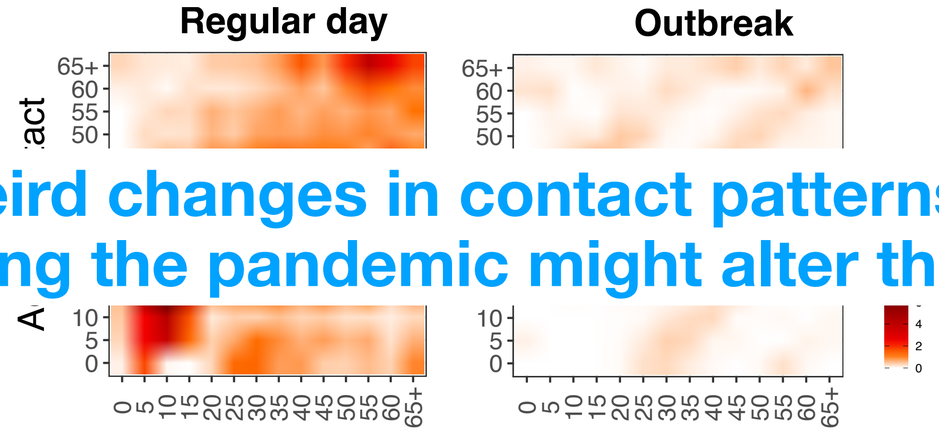

Weird changes in contact patterns during the pandemic might alter this.

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

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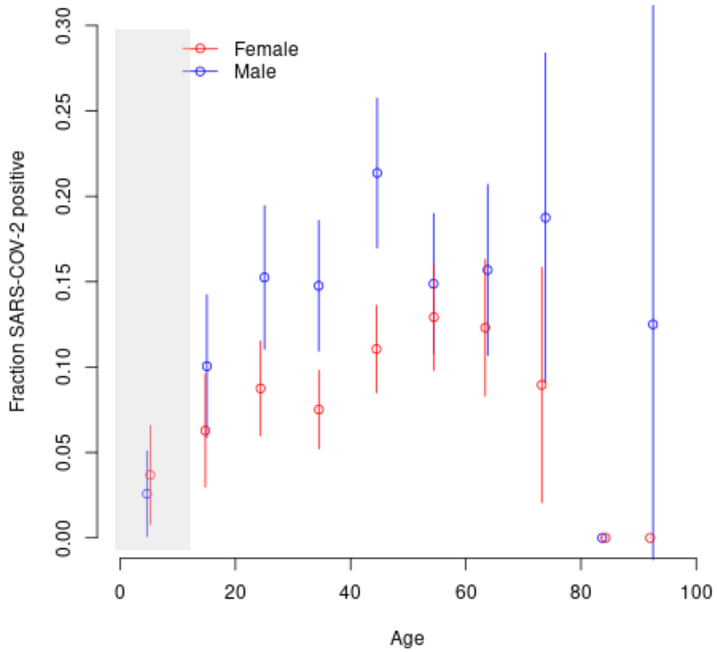

Iceland: children *seem* to get infected less.

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

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

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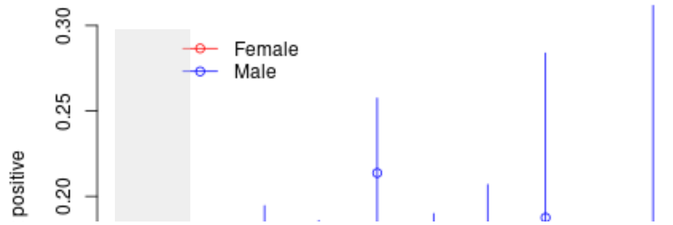
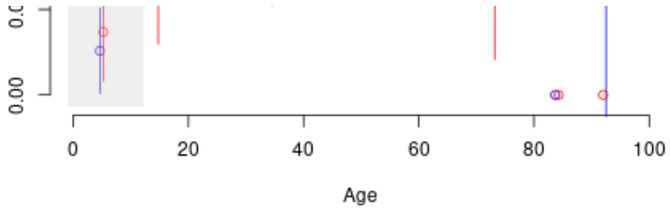


Iceland: children *seem* to get infected less.

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



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Are **children less susceptible** to infection?

	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 *seem* to get infected less.

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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Contact tracing data

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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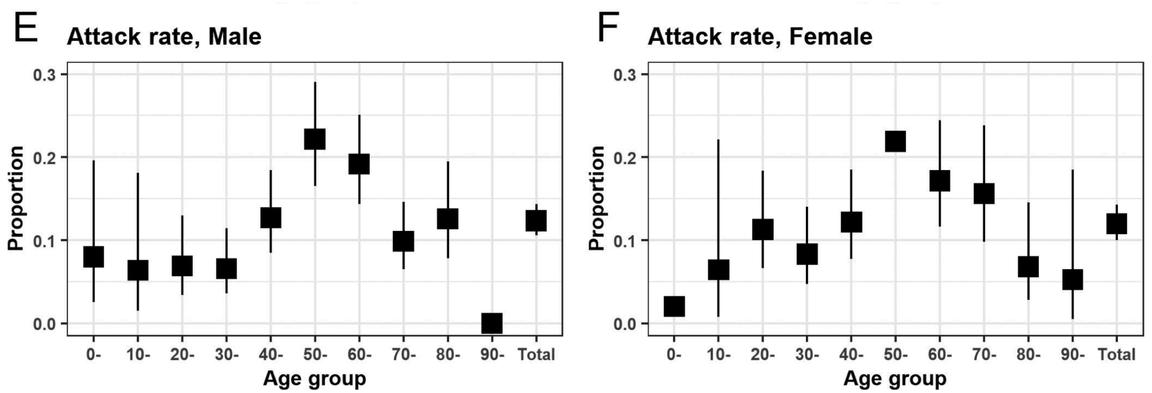
Contact tracing data

Estimates from Japan: **Yes**



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

https://www.medrxiv.org/content/10.1101/2020.03.09.20033142v1.full.pdf

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Are **children less susceptible** to infection?

If yes, mechanism? cross protection from other coronaviruses?

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

https://www.medrxiv.org/content/10.1101/2020.03.18.20037101v1.full.pdf

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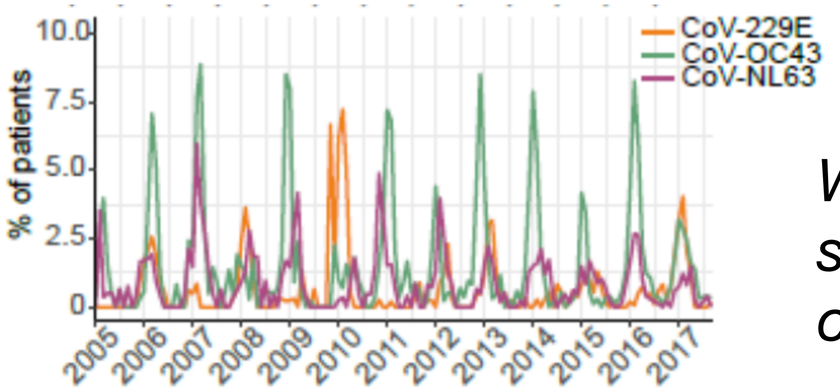

When big, is small, suggests cross protection

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

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

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

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

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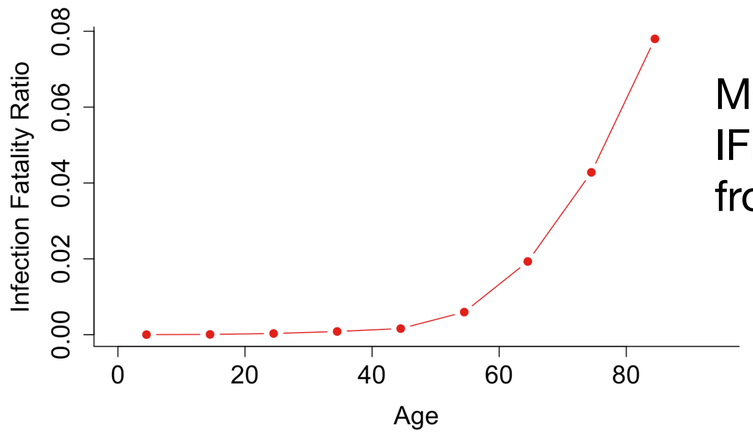

Model based estimates of IFR from integrating data from Hubei, Italy, etc.

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

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

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4) **transmissibility** of contact → Do older individuals **transmit more**, skewing onward transmission to their older contacts?

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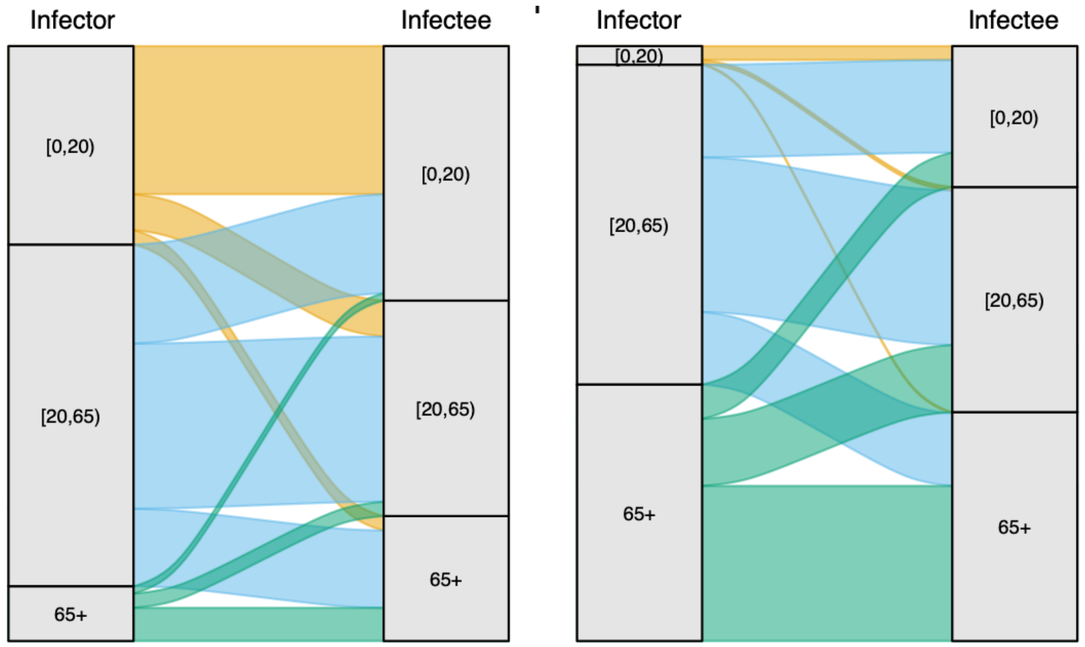
raw POLYMOD data, Mossong et al. 2009

assume transmissibility higher in older ages



relative contribution of age specific transmission pairs

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

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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

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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."

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

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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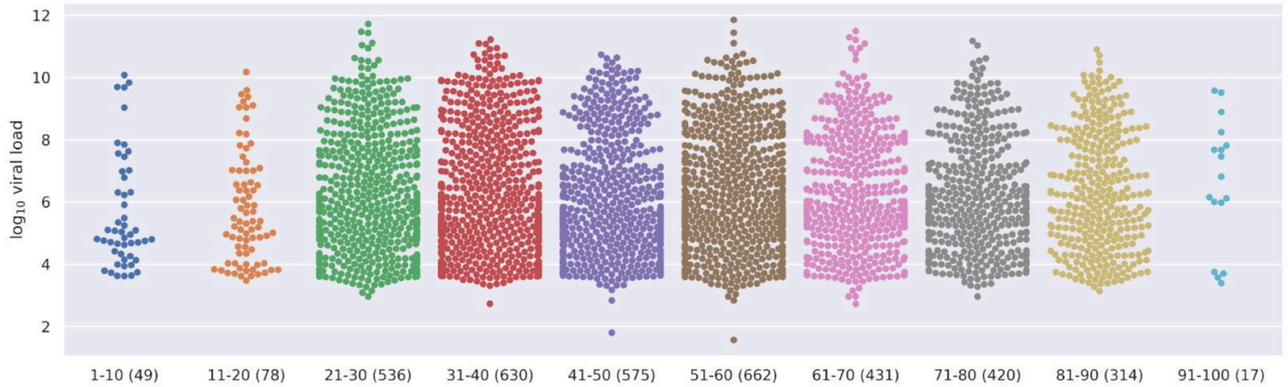
Or are the they **the same?**



Children have similar viral loads - so why not similar transmission?

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

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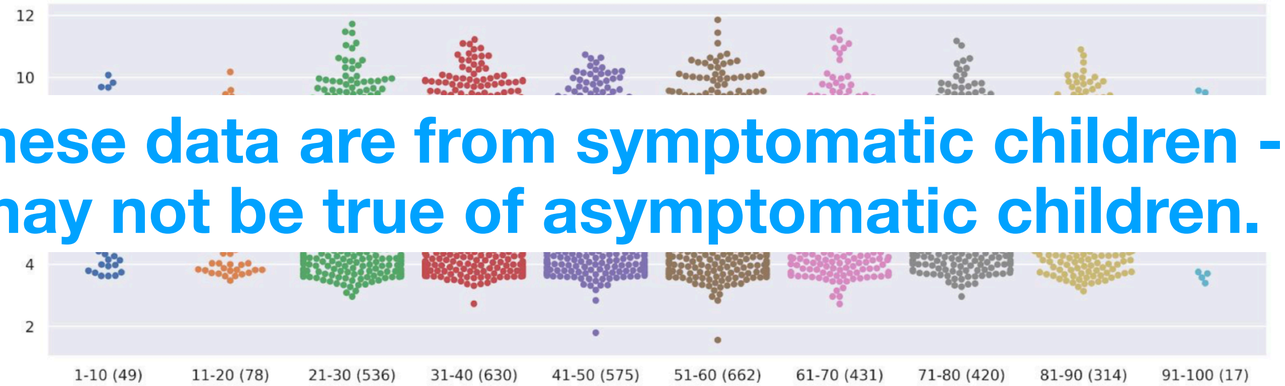

These data are from symptomatic children - may not be true of asymptomatic children.

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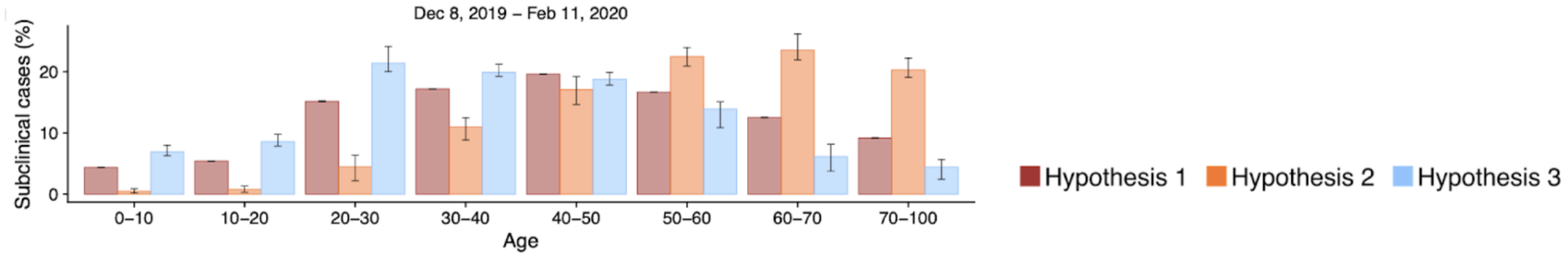
A formal test: age and COVID-19

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)).



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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?

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

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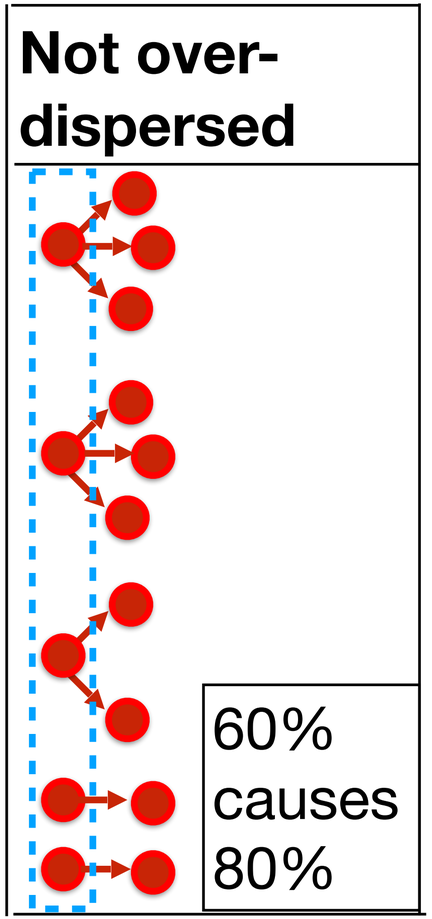
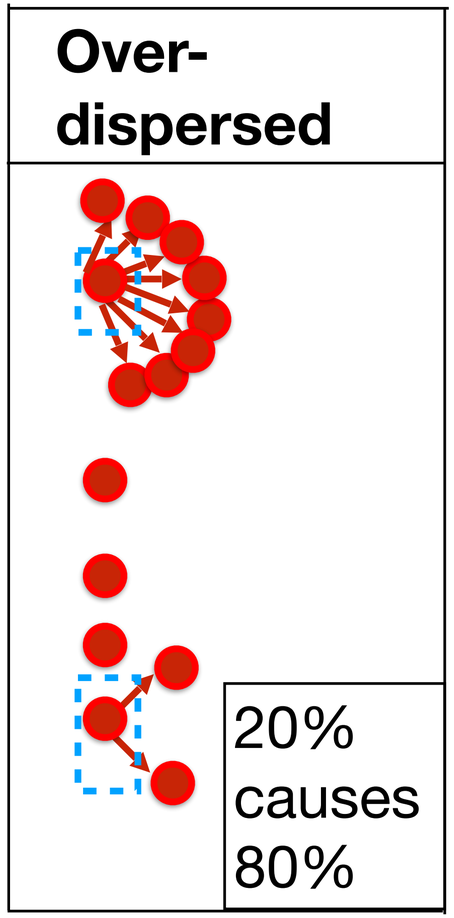
?possibility of higher transmission from older individuals.

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

Transmissibility: 'Super-spreading events'?

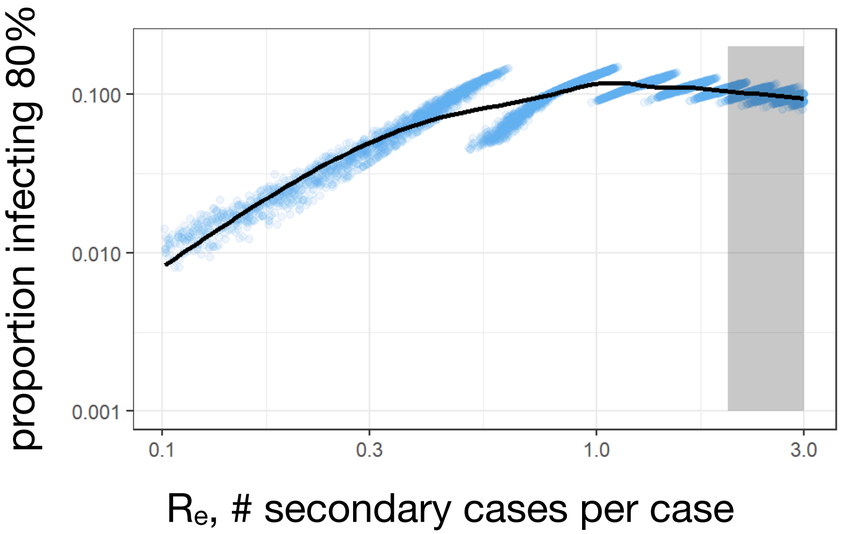


100% of introductions cause onward transmission



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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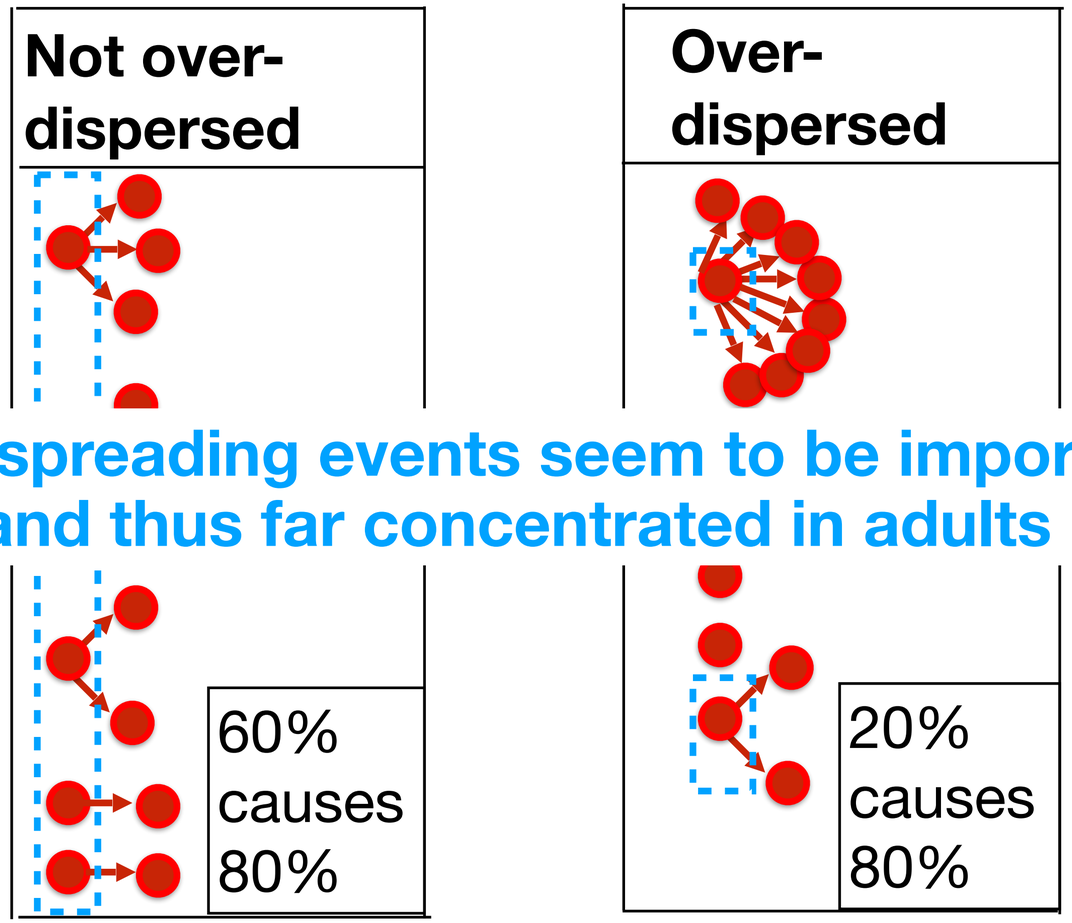

Superspreading events seem to be important, and thus far concentrated in adults

100% of introductions cause onward transmission

40% of introductions cause onward transmission

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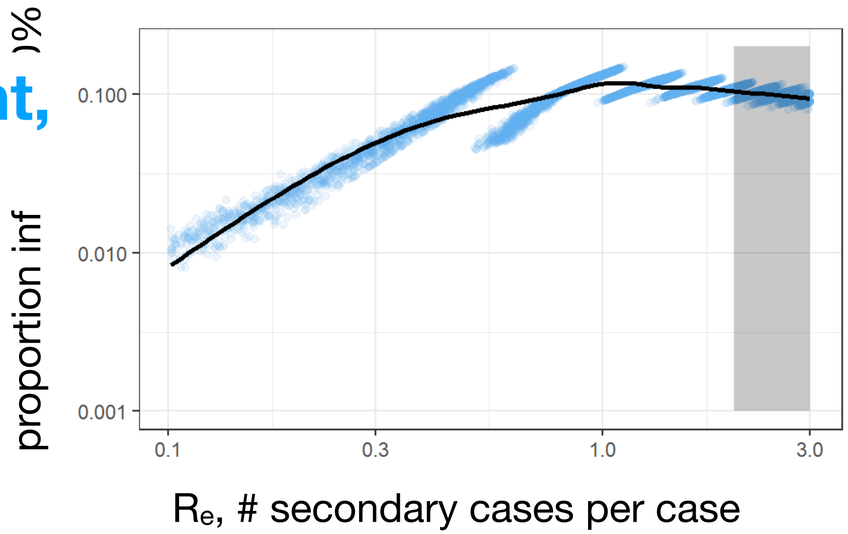
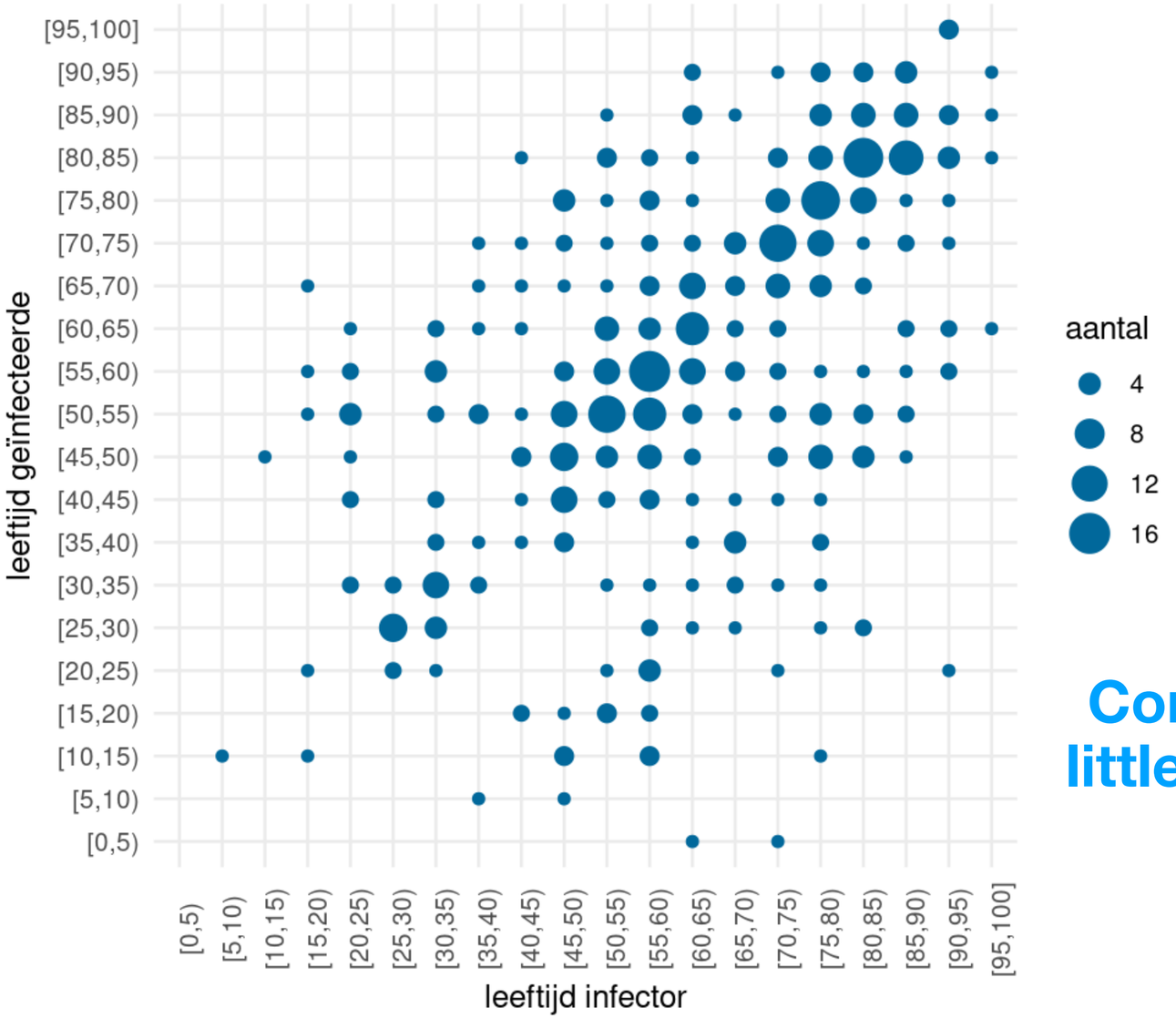


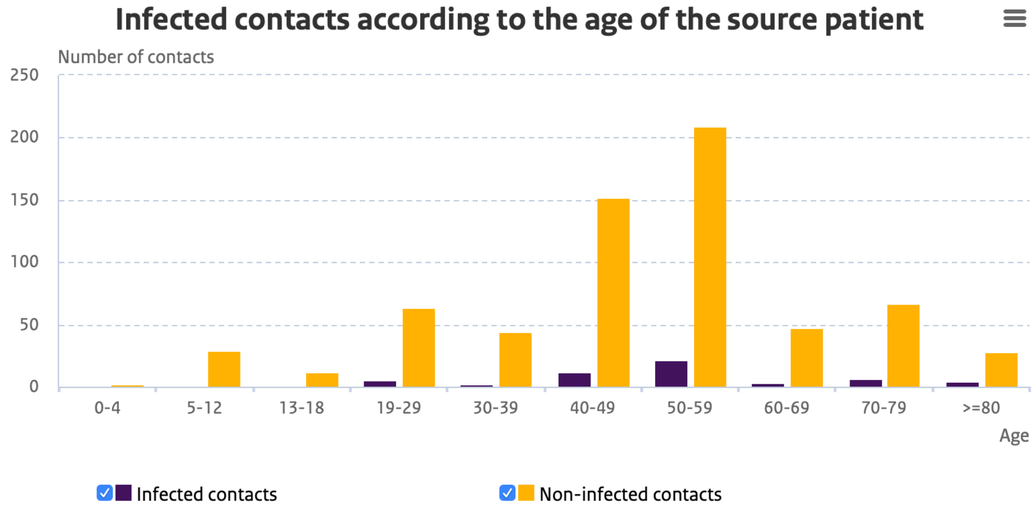
Recent data out of Holland

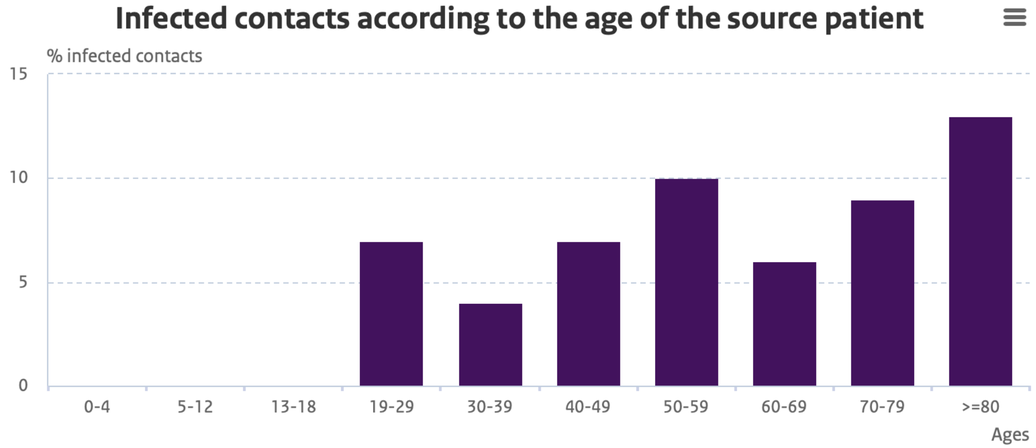


Contact tracing suggests very little transmission from children

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

Recent data out of Holland





But why do older individuals have so many contacts? something strange about this data?

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

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

Children:

-may be less susceptible,

-may be less likely to show 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.

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