Can we make better tests to quantify host infectiousness?

Turner-Warwick Lecture

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Conflicts of interest

None.

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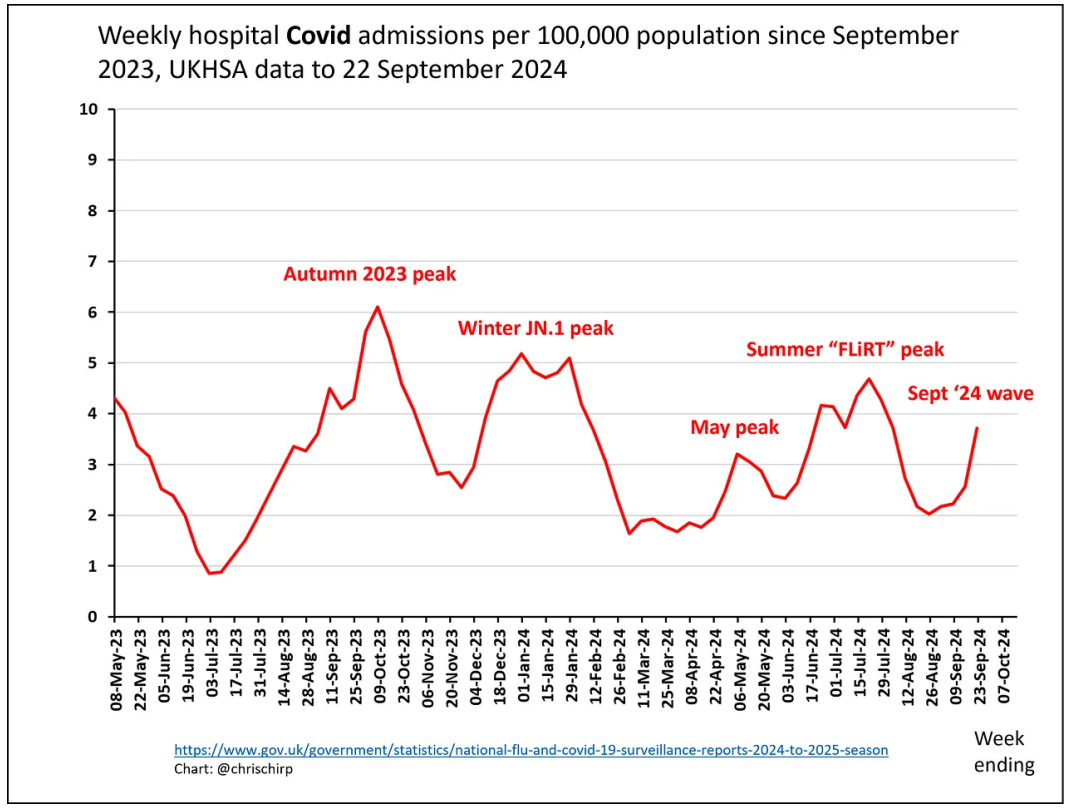
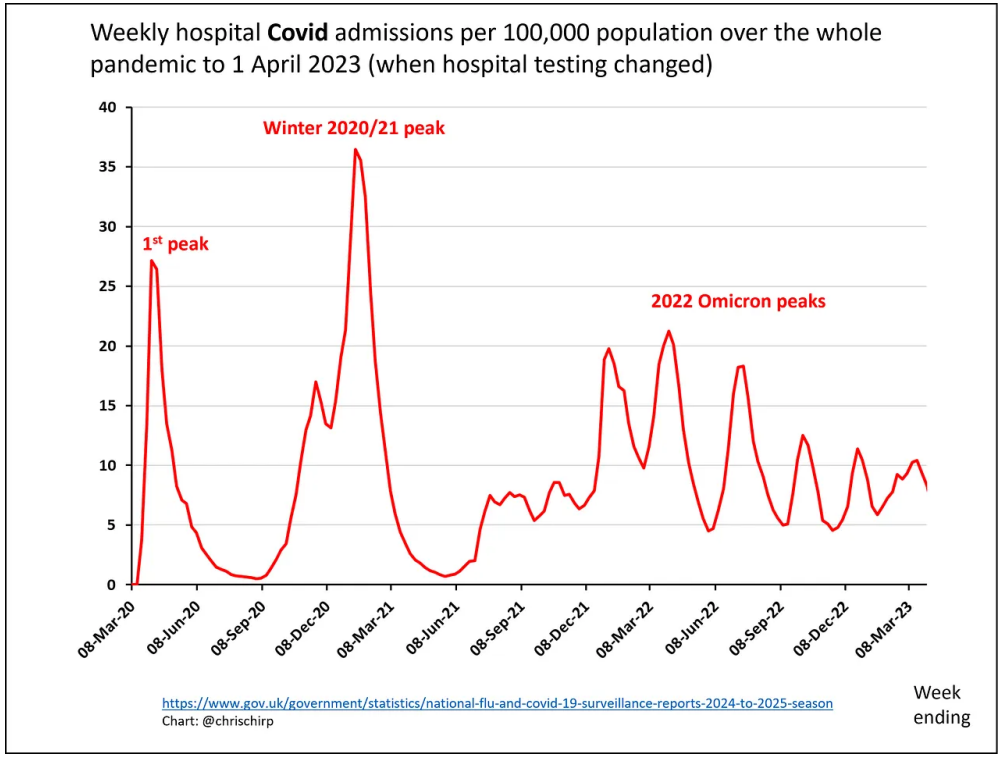
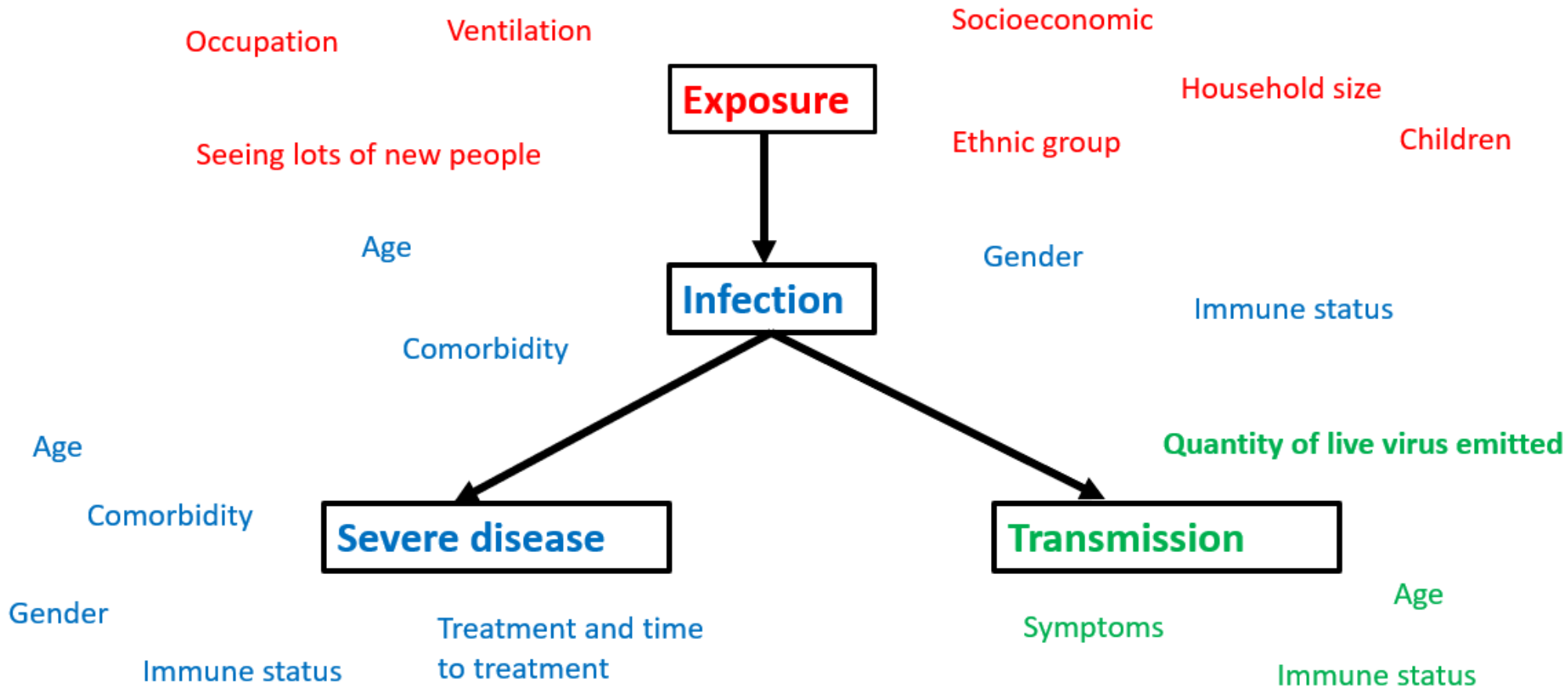
SARS-CoV-2 – do we still care about it?





UK government data
Chart made by @chrischirp on X

Respiratory viruses and transmission



Pan et al. *EClinicalMedicine* 2024

Rapid tests for infectiousness

A rapid test must be..

- **Accurate in assessment of host infectiousness**
- **Cheap, easy to perform, acceptable**
- **Scalable**

Implications:

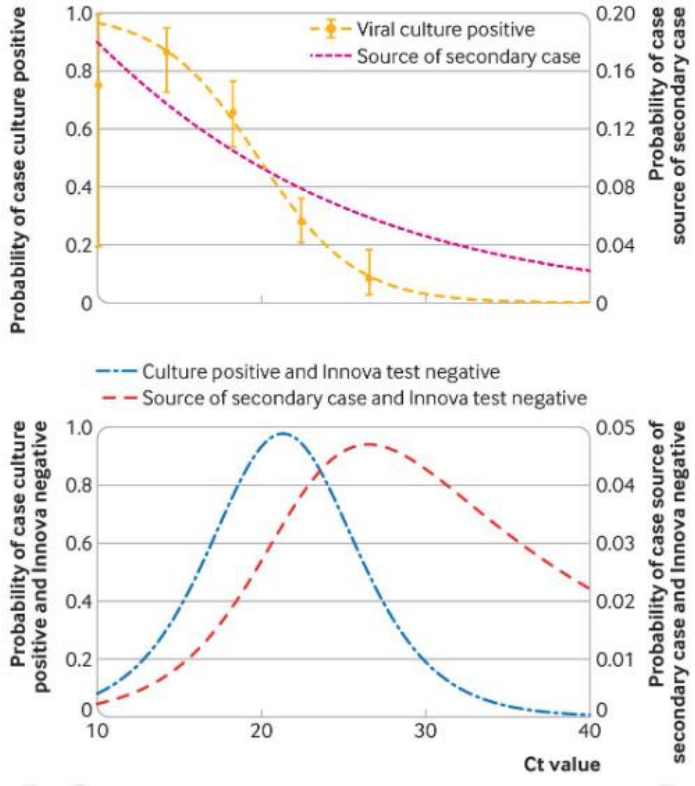
- Clinical assessment
- Rapid de-escalation
- Workplace (healthcare/care homes/schools)
- Used in indoor assessment models
- Human challenge studies
- Recruitment into studies with more complex methods of measuring exhaled breath
- Infectiousness as an outcome in observational studies/clinical trials

Pan et al, *The Lancet Microbe* 2021

Rapid tests for infectiousness

Viral culture is thought to be the gold standard for infectiousness, but it cannot be scaled as a public health test, however **excellent association** between **viral load** by PCR, **viral culture** and **lateral flow assays** in human challenge studies

There is **poor association** between **lateral flow tests** with **actual transmission** in real-world studies, especially in **asymptomatic cases**

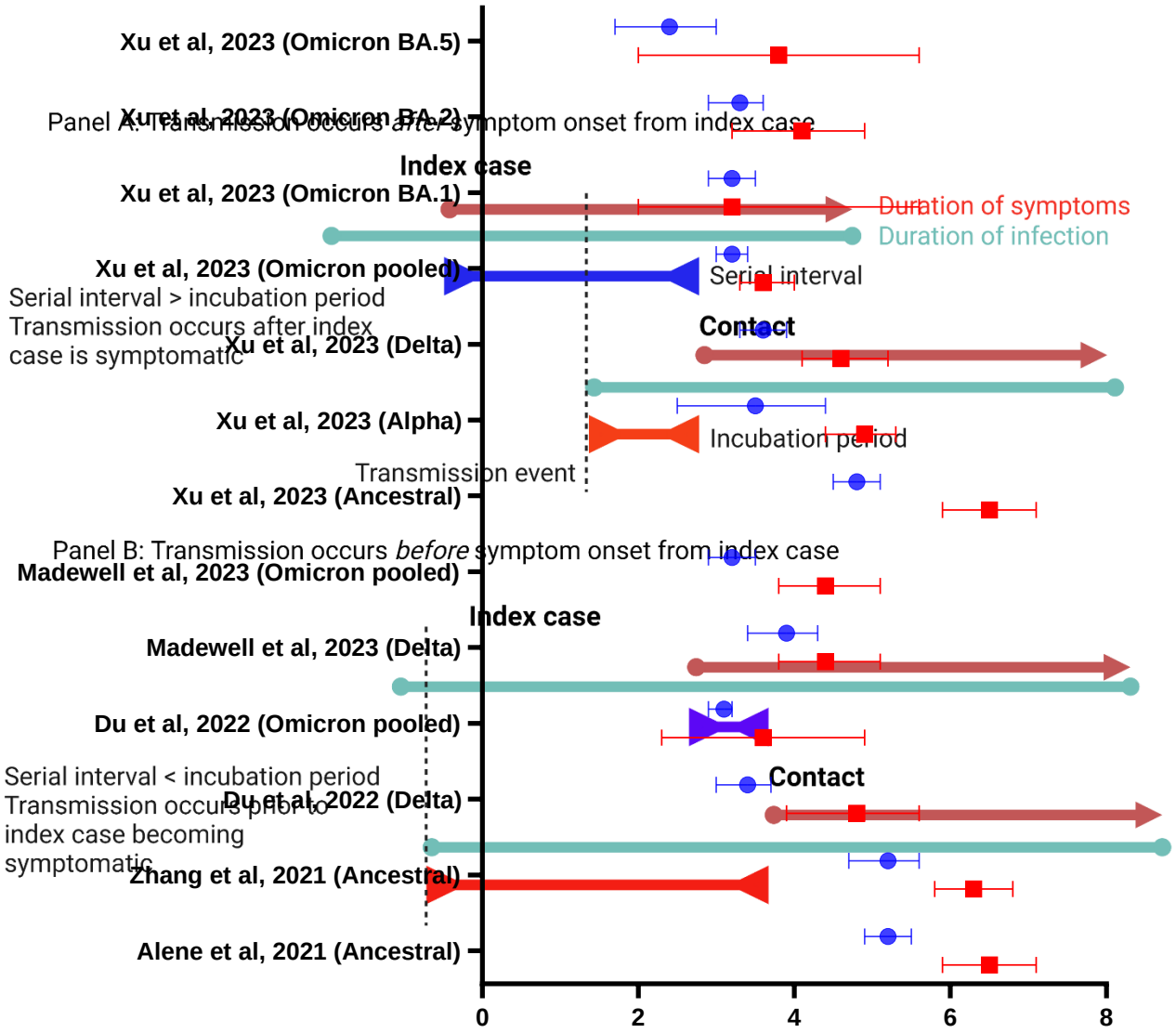


Innova LFTs missed up to 90% of source of secondary cases!

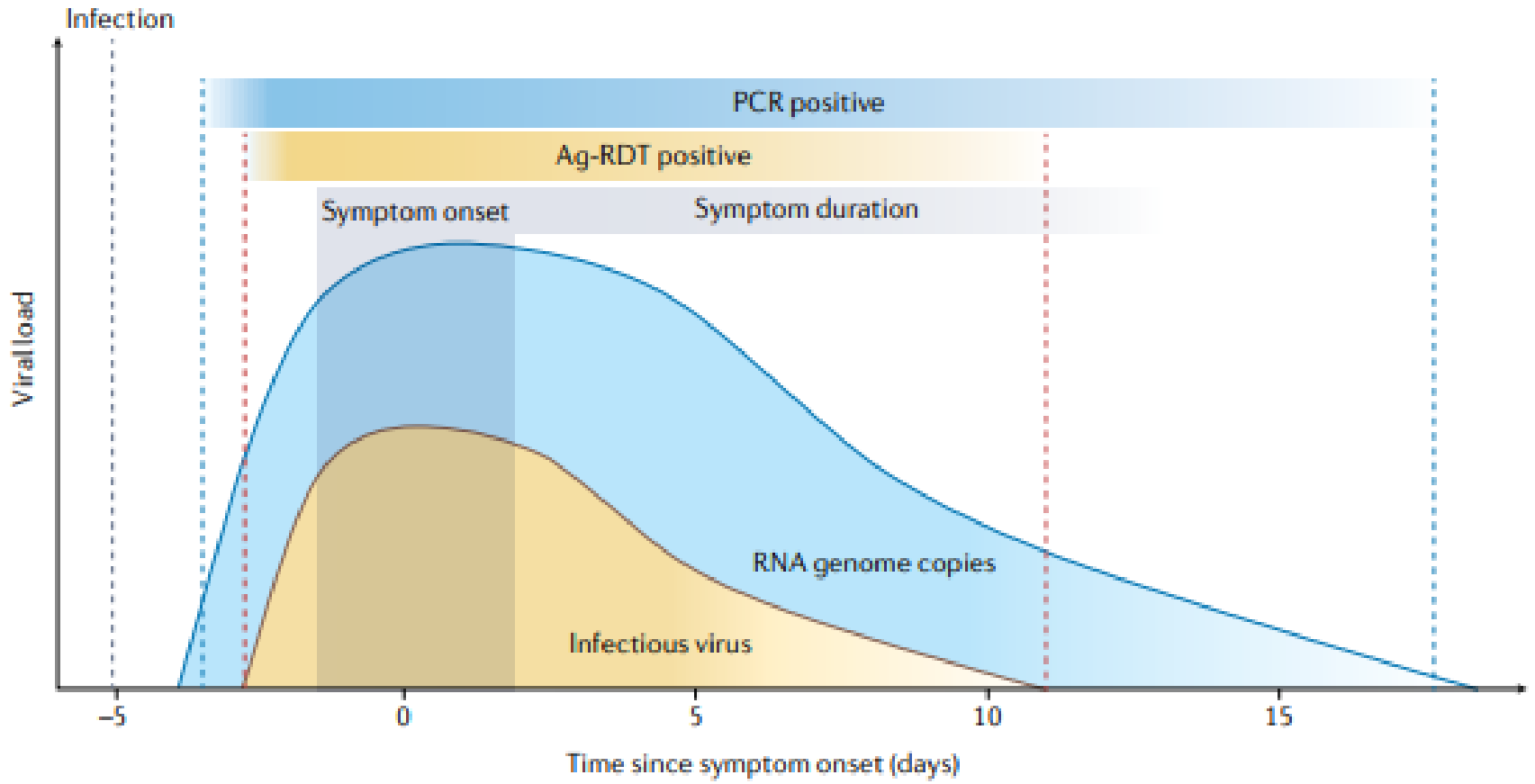
Killingley et al, *Nature Medicine* 2022

Deeks et al, *BMJ* 2022

For SARS-CoV-2, serial interval<incubation period

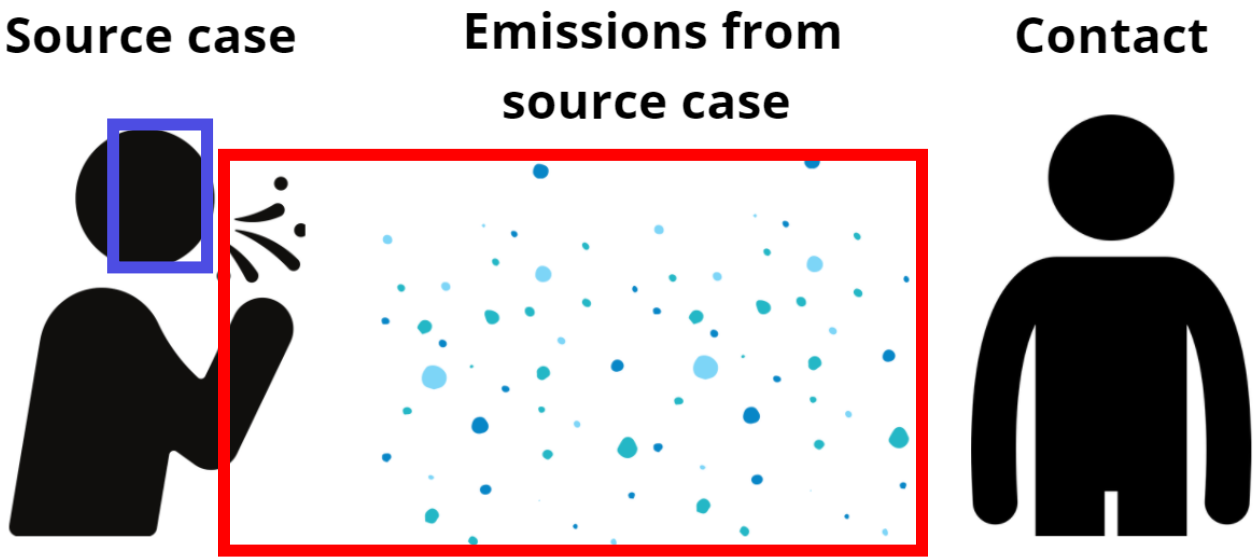


Viral load on swab does not peak pre-symptoms



Hypothesis

Are we actually sampling from the best compartment for infectiousness?



Nasopharyngeal swab: samples virus from within the host

Hypothesis:

1. **More abundant respiratory emissions relate to more frequent transmission**
2. **Sampling for infectiousness should reflect this**

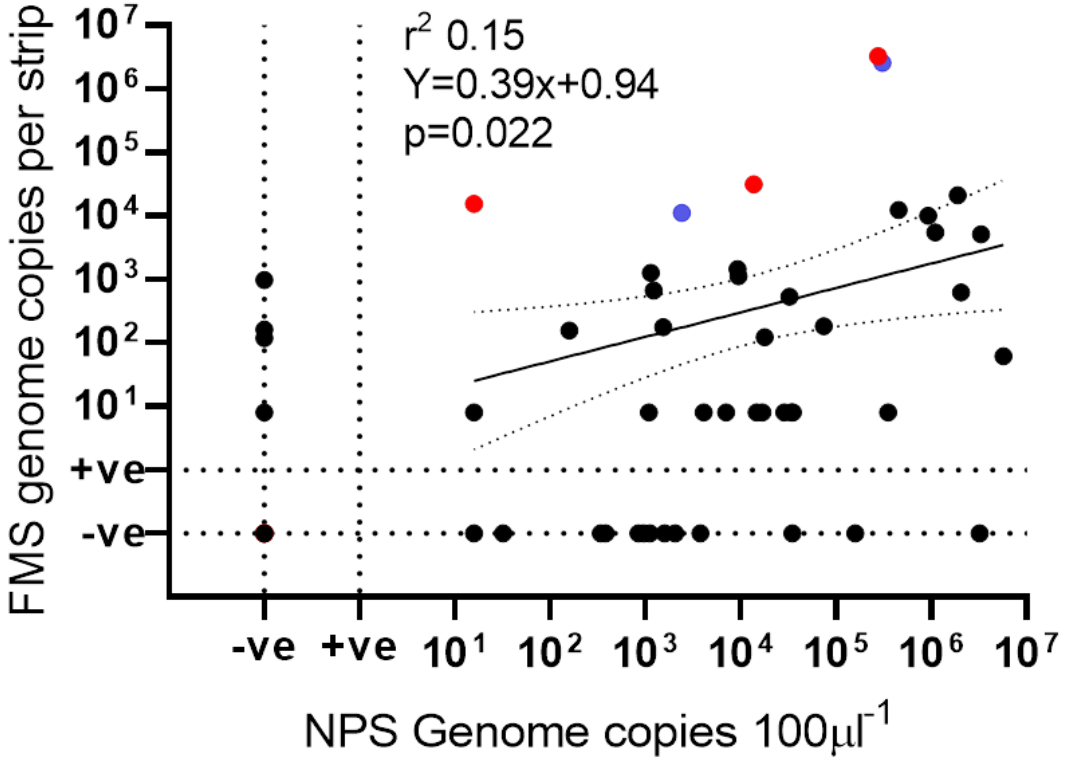
Facemask sampling captures exhaled virus

Facemask sampling (FMS)

Exposed sampling strips processed – positive for both **RNA** and **viral culture**

FMS RNA **poor association** with concomitant URTS VL

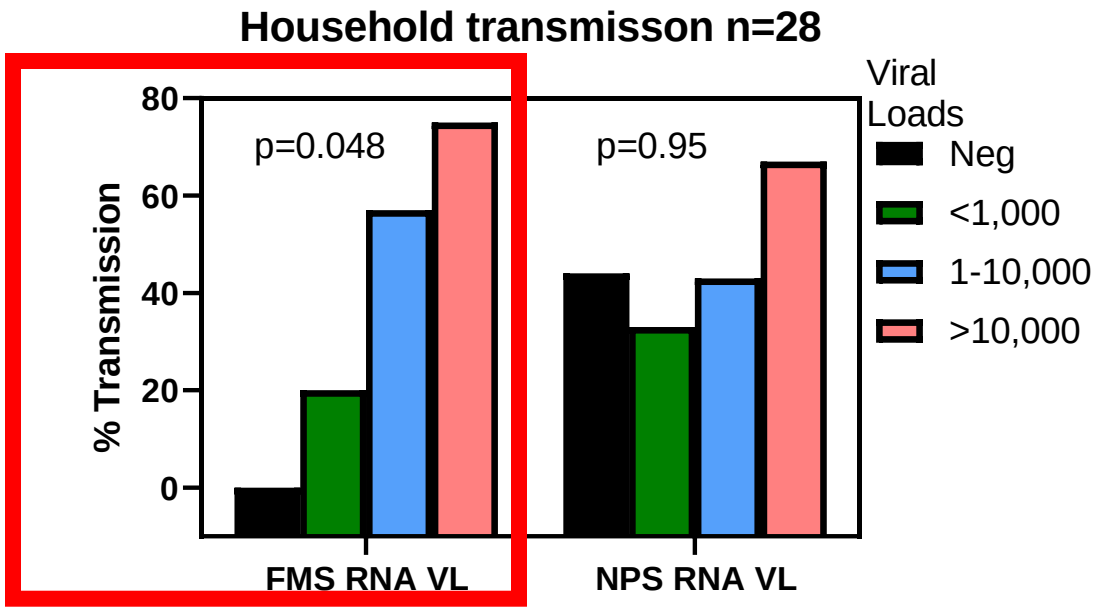
Positive for shorter periods, stable signal



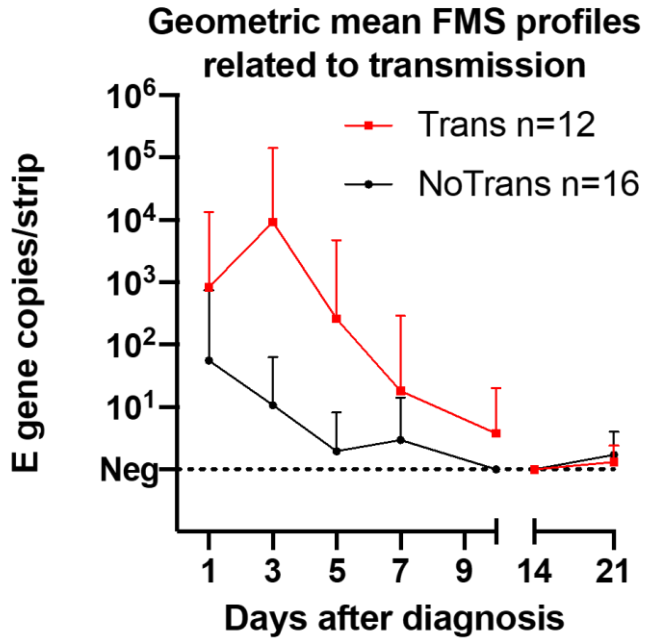
Williams C, Pan D et al *Journal of Infection 2021*

Facemask sampling relates to household transmission

We have shown that **FMS related to household transmission better than URTS**



Age adjusted OR of household transmission per log increase in copies/strip: 4.97; 95% CI, 1.20–20.55; $p = 0.02$ but not observed with peak NPS RNA VL



Consistently higher FMS VL in those who transmitted compared to those who did not

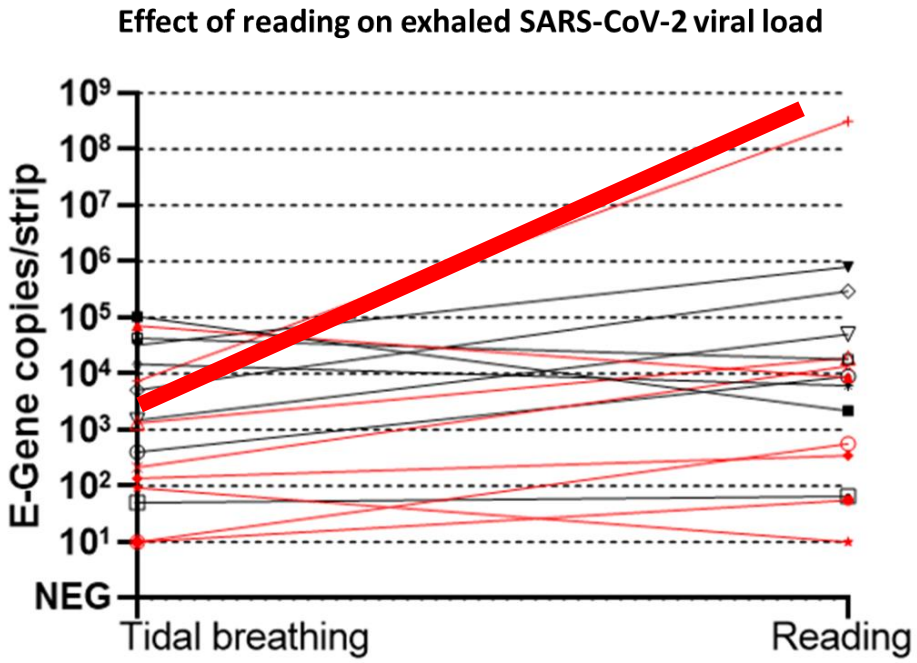
Pan et al, *Clinical Microbiology and Infection* 2022

Other advantages of FMS

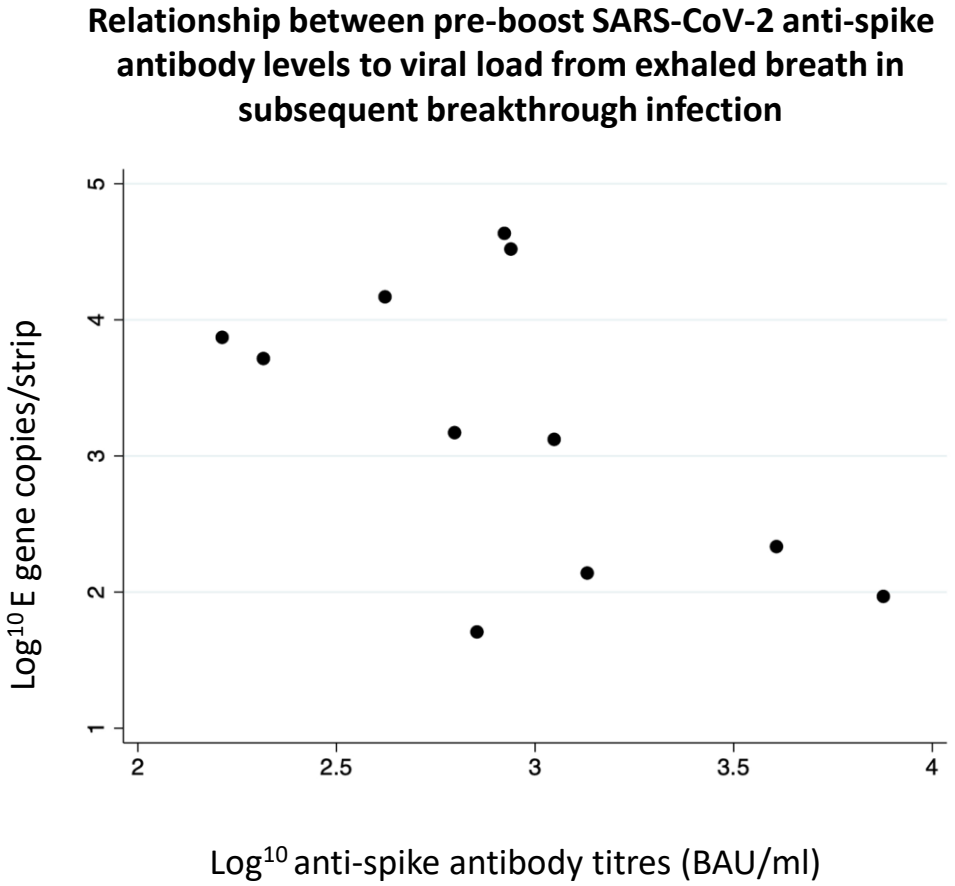
….but shouting does!

5310 to 315,000,000 copies/strip

Reading has no effect on FMS VL

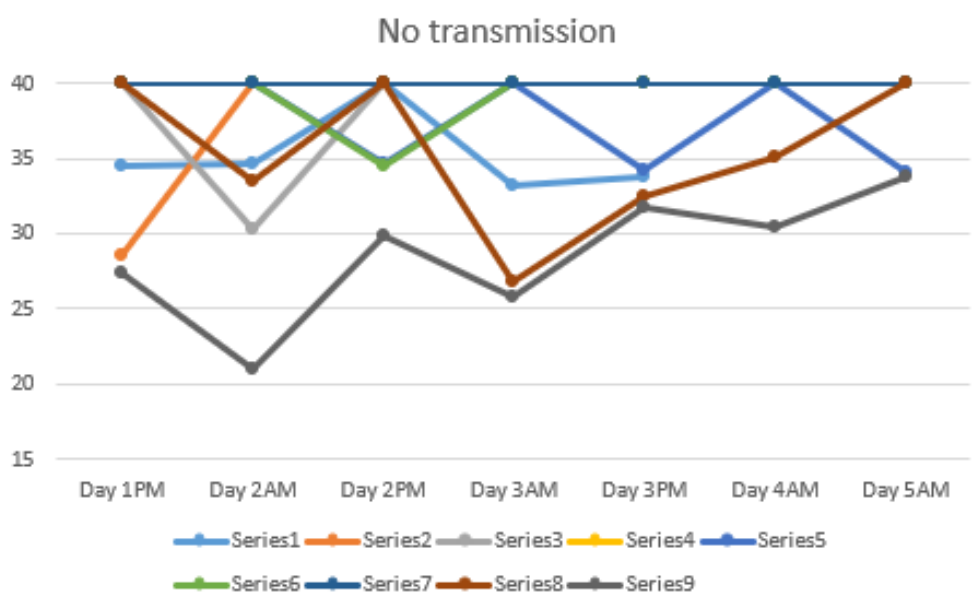


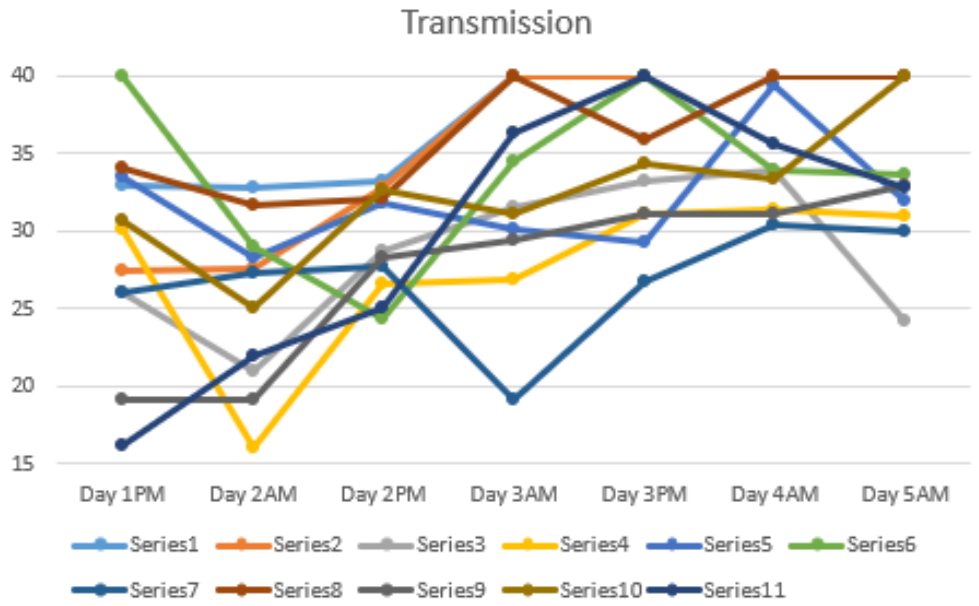
Pre-boost antibody titres negatively associated with exhaled VL on FMS following breakthrough



FMS relates to transmission even now

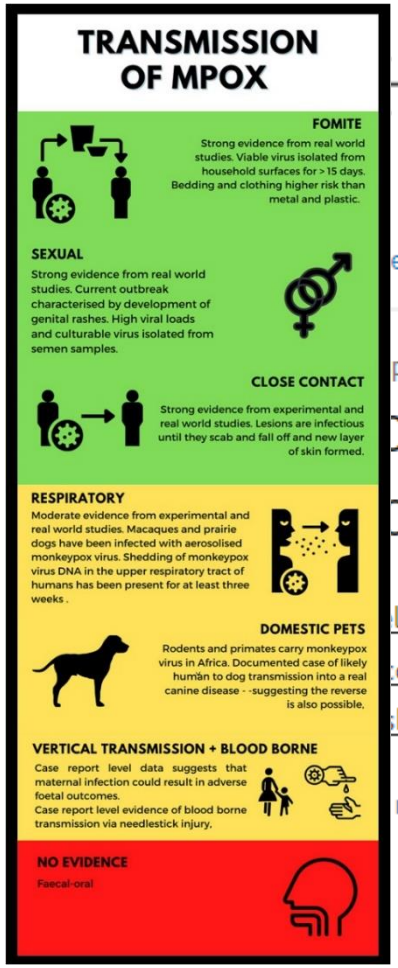
Even with more strict definitions of transmission (household emission + sequencing)
The same pattern emerges





Negative results in mpox

Negative results for pathogens not spread by the airborne route (for example, mpox)



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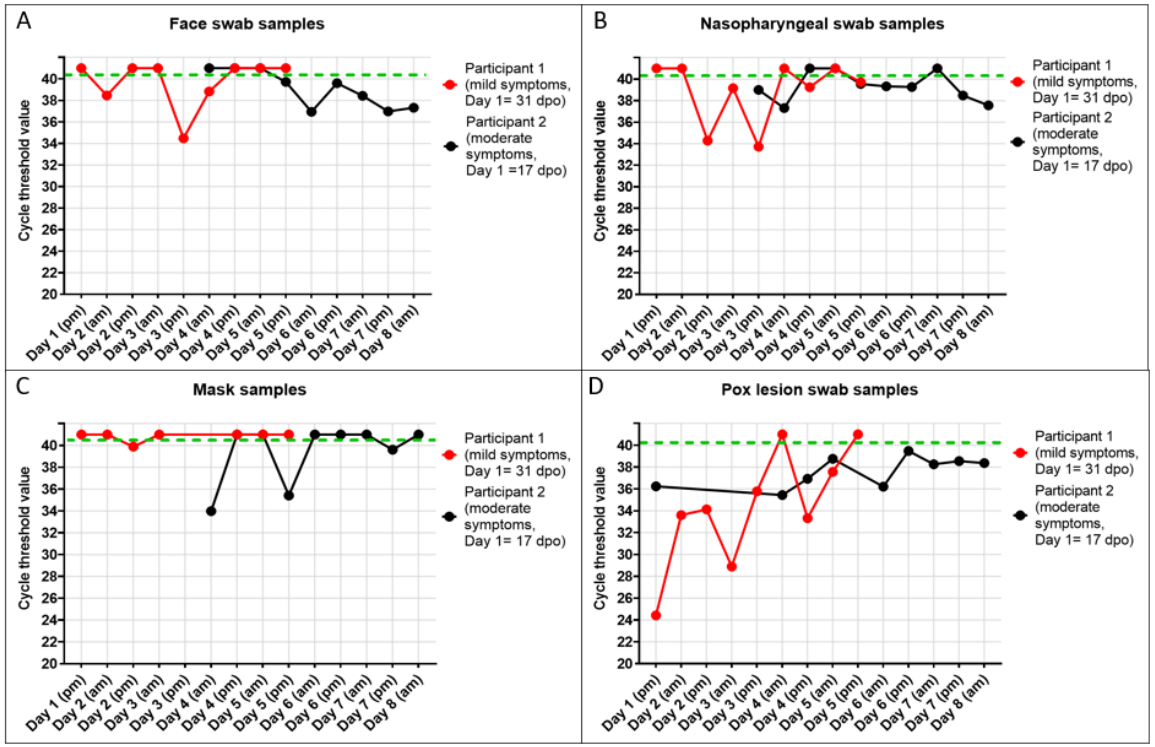


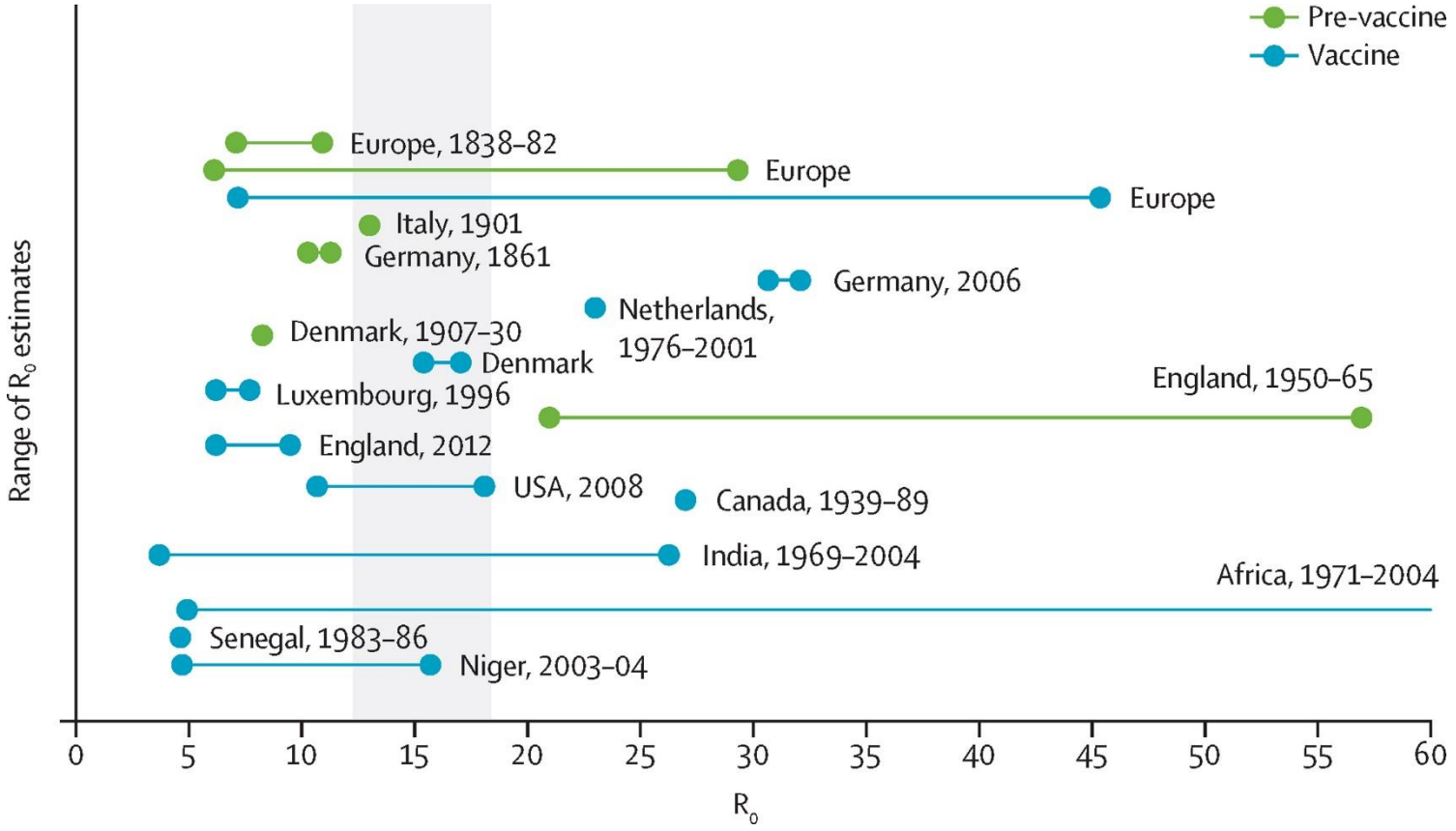
Pan et al *Lancet*

Pan et al *Journal of Medical Virology* 2023

Pan et al *Journal of Infection 2023*

Positive results in measles

First *ever* empirical evidence for exhaled measles in the literature



Guerra et al *Lancet infectious diseases 2018*

Screening

FMS also needs to be accepted by those who use it

What proportion of SARS-CoV-2 transmission is asymptomatic?

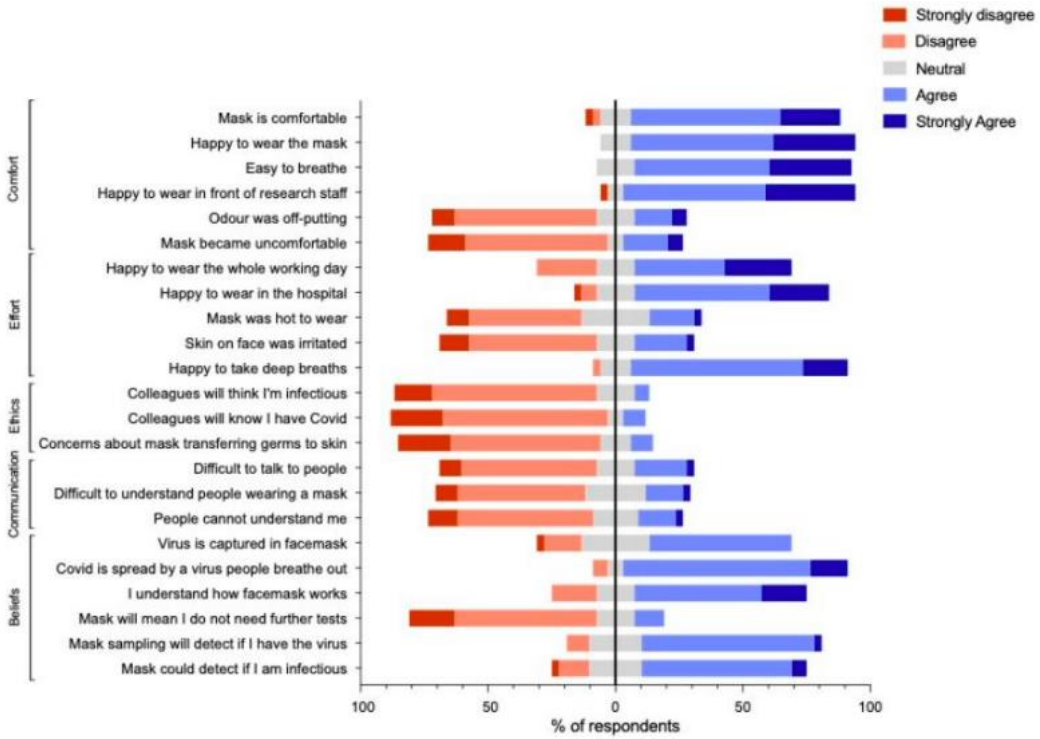
April 2023 – 202 samples from 188 participants; 5% prevalence of flu/SARS-CoV-2. **All 'asymptomatic'**

October 2022 – mock examinations – 36 participants and 6 patients (highly vulnerable); 1 participant was positive for SARS-CoV-2

Most HCWs are amenable but would like URTS to confirm diagnosis

HCWs don't like wearing facemasks but will do it if it protects patients

Longitudinal sampling of 50 participants in 2024 underway



Pan et al. *Future Healthcare Journal* 2024

Summary

1. **Not all sampling sites are equal**

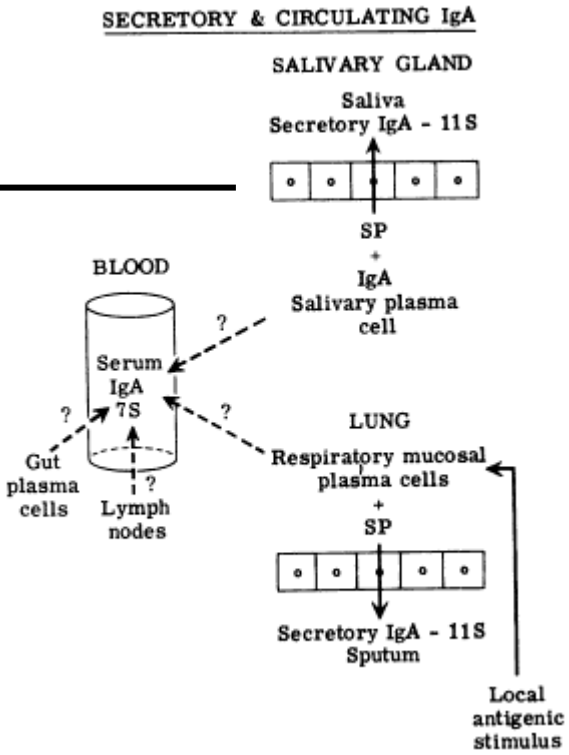
2. **FMS is positive for SARS-CoV-2 RNA in early disease and asymptomatics, and may relate to transmission in household contacts better than swabs**

3. **FMS is acceptable within healthcare settings (don't want to, but will do it if necessary to protect patients)**

4. **Findings from FMS is consistent with work done on other pathogens (mpox/measles/TB) and relation to transmission; work on SARS-CoV-2 replicable by other independent groups**

5. **Potential for FMS to be used within future vaccine studies**

Exhaled IgA?



Pan et al *Journal of Infection 2023*

Pan et al *Clinical Microbiology and Infection* 2022

Zhou et al *The Lancet Microbe* 2023

Gallichotte et al *American Journal of Infection Control* 2022

Williams et al *The Lancet Infectious Diseases* 2020

Williams et al *Clinical Infectious Diseases* 2023

Turner-Warwick. *Thorax* 1975

Thank you! Contact: dp440@leicester.ac.uk

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