What Have We Learned?
SARS-CoV-2 Transmission & Indoor Air: The Source Term

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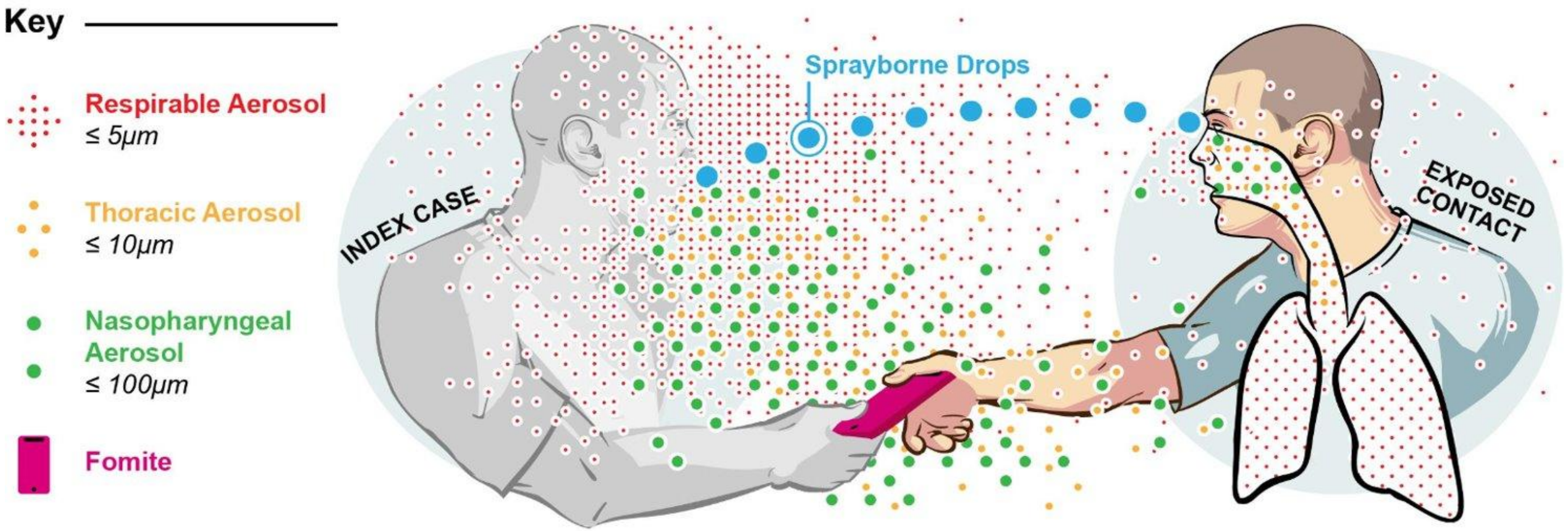
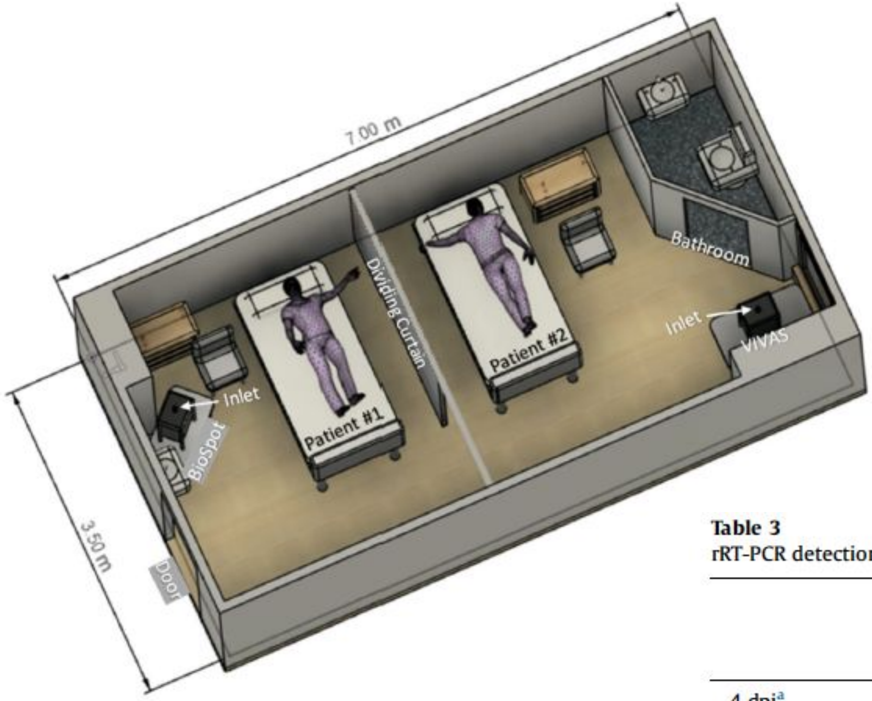
PUBLIC HEALTH

Transmission Modes of Respiratory Viruses



- **Inhalation**
  - Nasopharyngeal aerosols ≤ 100 μm
  - Thoracic aerosols ≤ 10-15 μm
  - Respirable aerosols (deep lung) ≤ 5 μm
- **Spray**
  - Ballistic drops (> 100 μm)
  - Direct hit on eye, nostril, or mouth
- **Touch**
  - Fomite to finger transfer
  - Finger to eye, nose, or mouth transfer

Infectious SARS-CoV-2 in Hospital Room Air



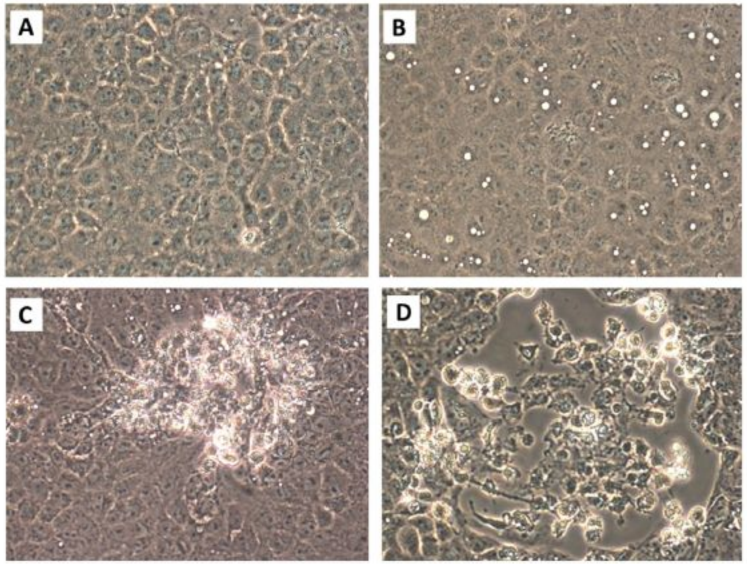


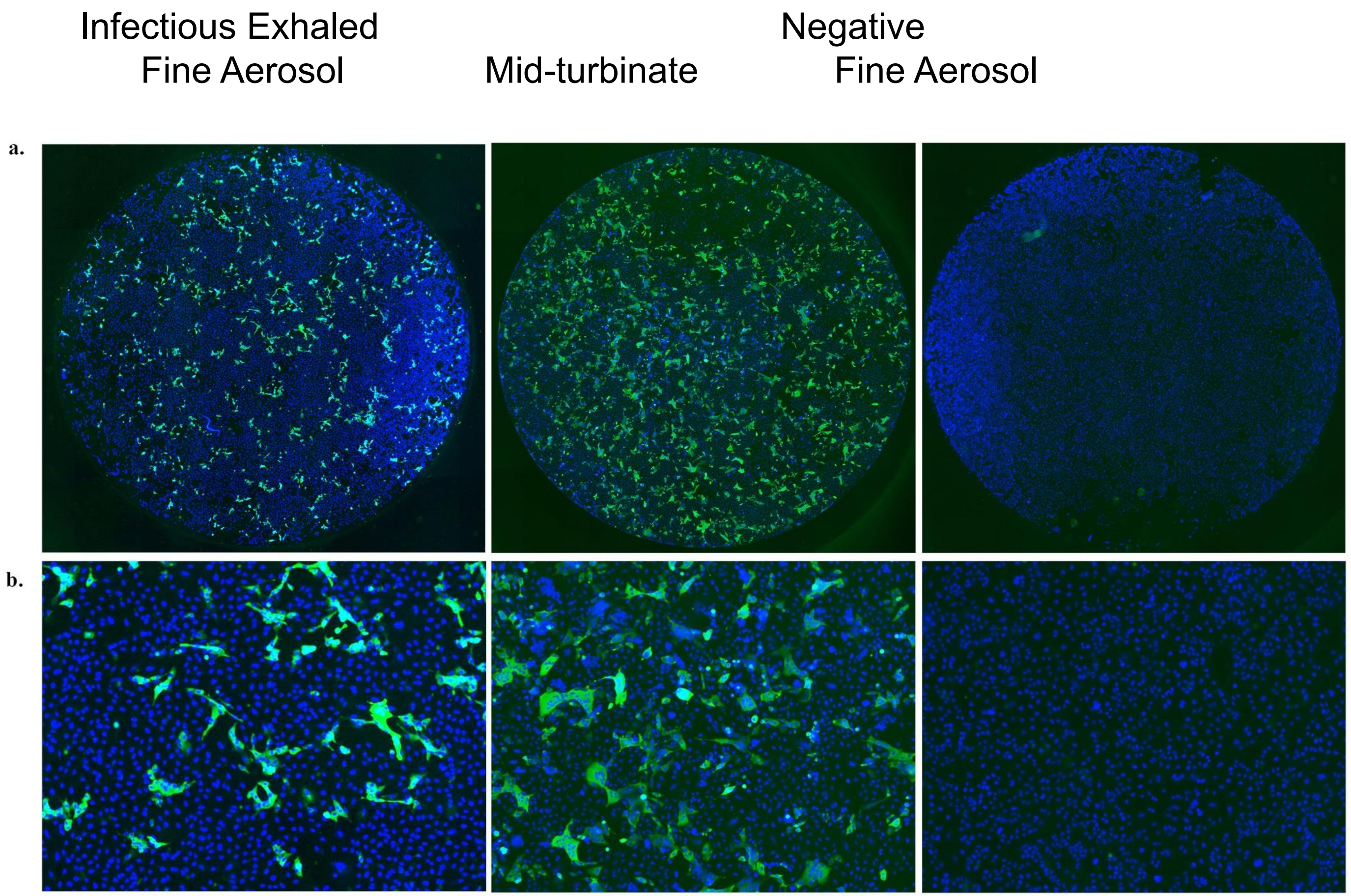
Table 3
rRT-PCR detection of SARS-CoV-2 N-gene sequences in air sample cultures.

	Air sampling interval					
	1-1 LLC[b] Vero[c]	1-2 LLC Vero	1-3 LLC Vero	2-1 LLC Vero	2-2 LLC Vero	2-3 LLC Vero
4 dpi[a]	38.1 38.4	ND[d] ND	ND ND	ND ND	ND ND	ND ND
7 dpi	35.3 35.9	ND ND	39.1 40.2	37.3 38.8	ND ND	ND ND
10 dpi	31.5 32.2	ND ND	33.7 34.8	32.8 33.2	ND ND	36.4 37.2

[a] dpi, days post-inoculation with material collected by air sampler.
[b] LLC, LLC-MK2 cell culture.
[c] Vero, Vero E6 cell culture.
[d] ND, Not detected.

J. A. Lednicky *et al.*, *Int J Infect Dis*. **100**, 476–482 (2020).

Culture results from representative samples

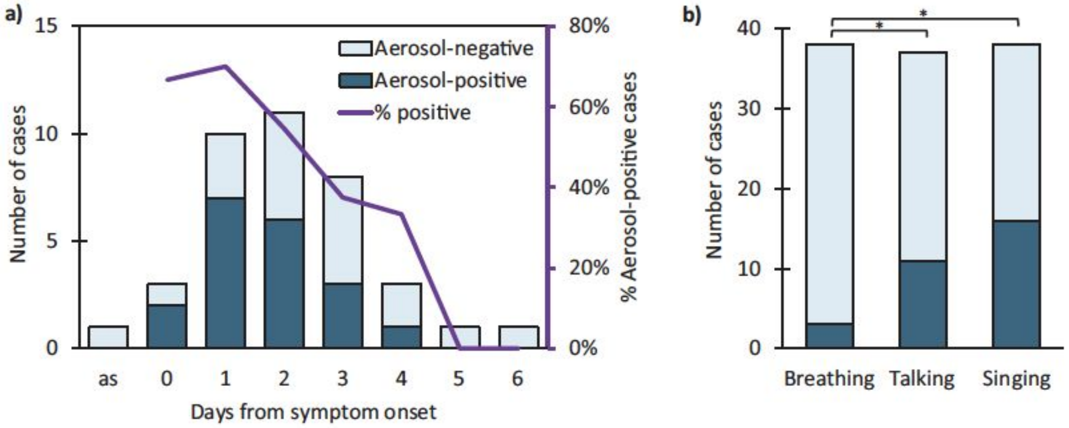


Example images from the focus assays as whole well images (**a**) and zoom in of the center of the well (**b**).

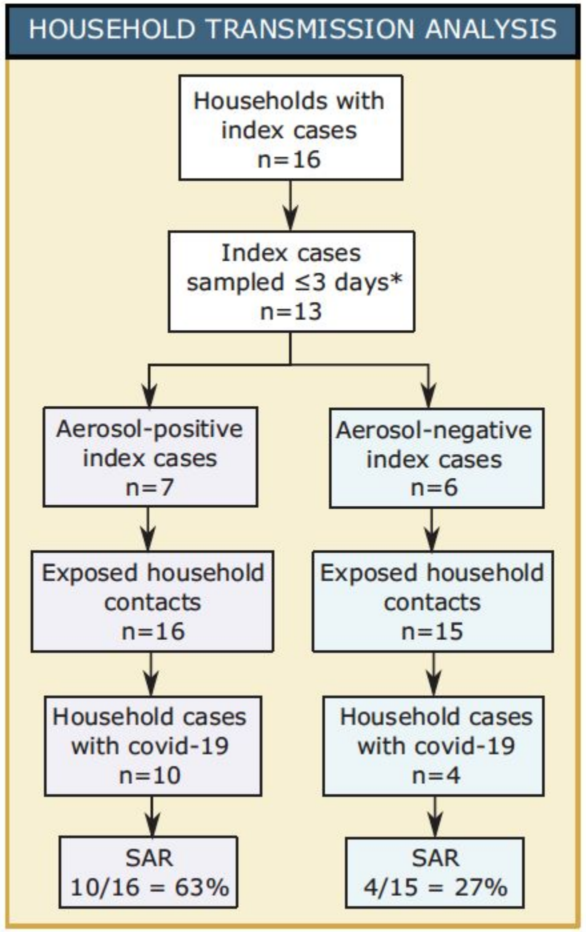
- Left, positive fine aerosol sample.
- Center, positive mid-turbinate swab sample.
- Right, negative fine aerosol sample.

O. O. Adenaiye *et al.*, *Clin Infect Dis*, ciab797 (2021).

Vocalization – aerosol shedding – transmission

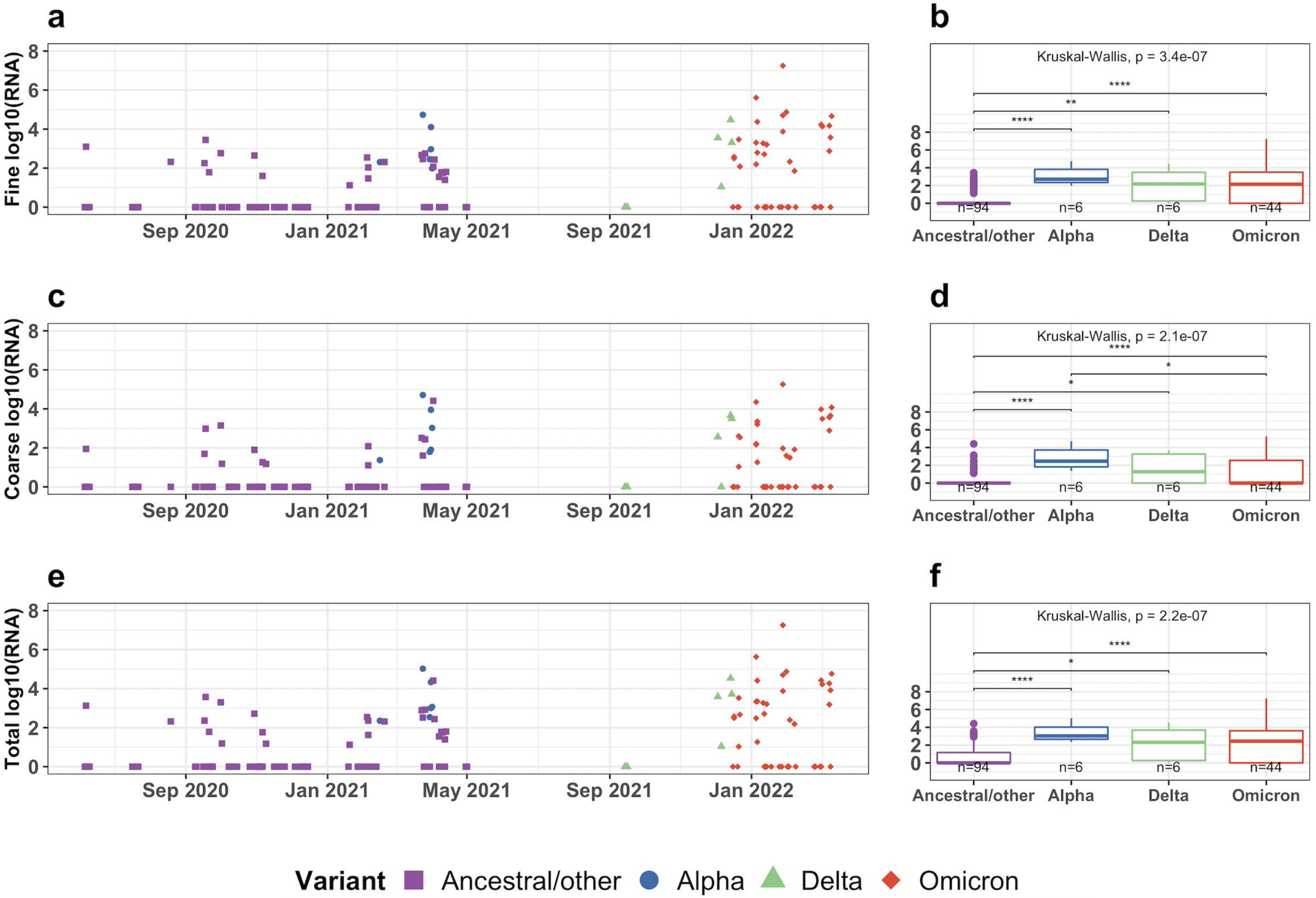


	Coarse Fraction	Fine Fraction	Total (% of column)
Three expiratory activities	4527.3 (14.6)	26 503 (85.4)	31 030.3*
Breathing[a]	897 (45.8; 2.9)	1062.3 (54.2; 3.4)	1959.3 (6.3)
Talking[b]	868.4 (6.9; 2.7)	11 787.5 (93.1; 38)	12 655.9 (40.8)
Singing[c]	2762 (16.8; 9)	13 653.2 (83.2; 44)	16 415.5 (52.9)



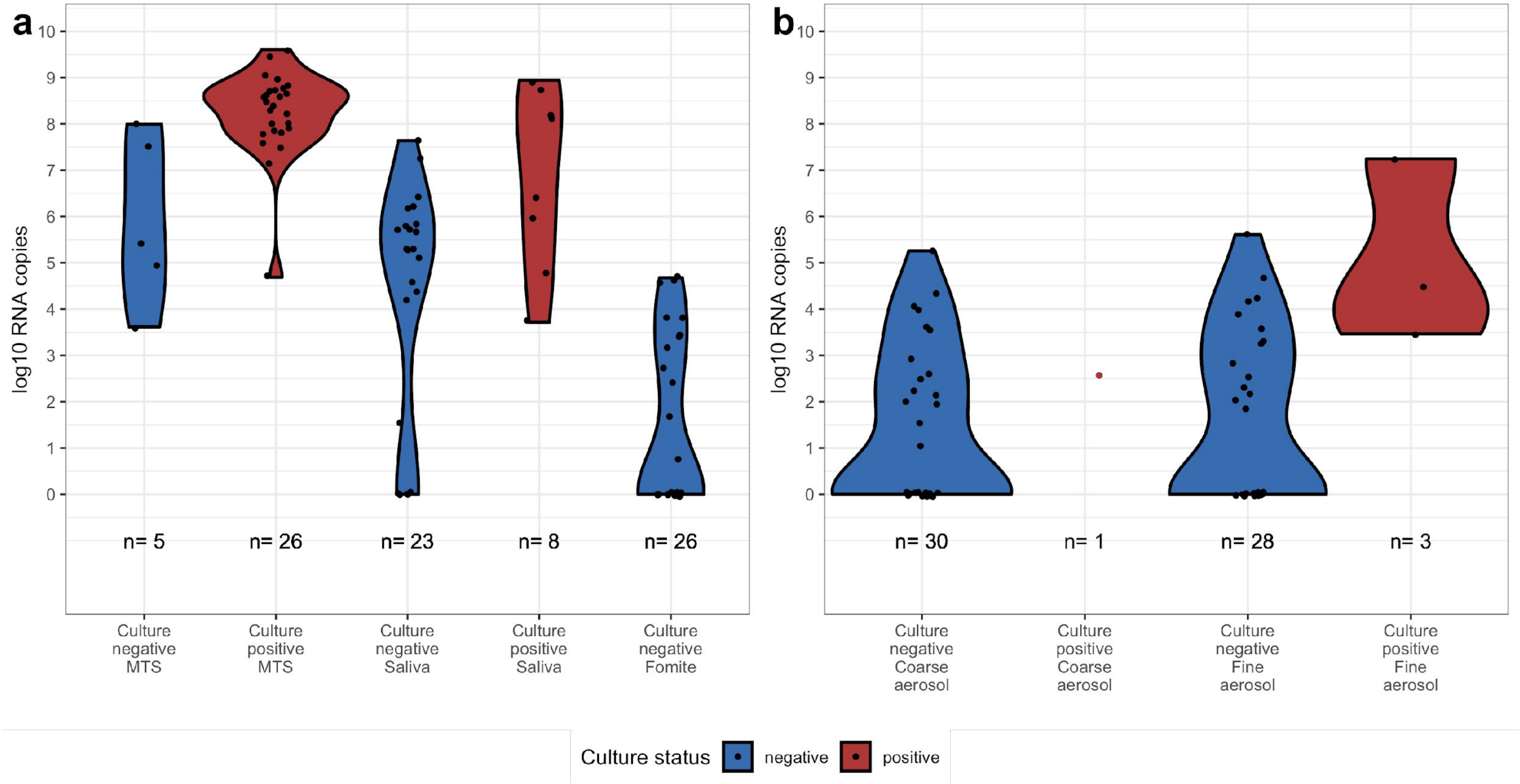
M. Alsved *et al.*, *Clin Infect Dis*, ciac202 (2022).
K. K. Coleman et al., Clin Infect Dis, ciab691 (2021).

SARS-CoV-2 aerosol shedding over time by variant



J. Lai *et al.*, *medRxiv*, doi:10.1101/2022.07.27.22278121.

Viral load and culture results: Delta & Omicron infections among vaccinated and boosted participants



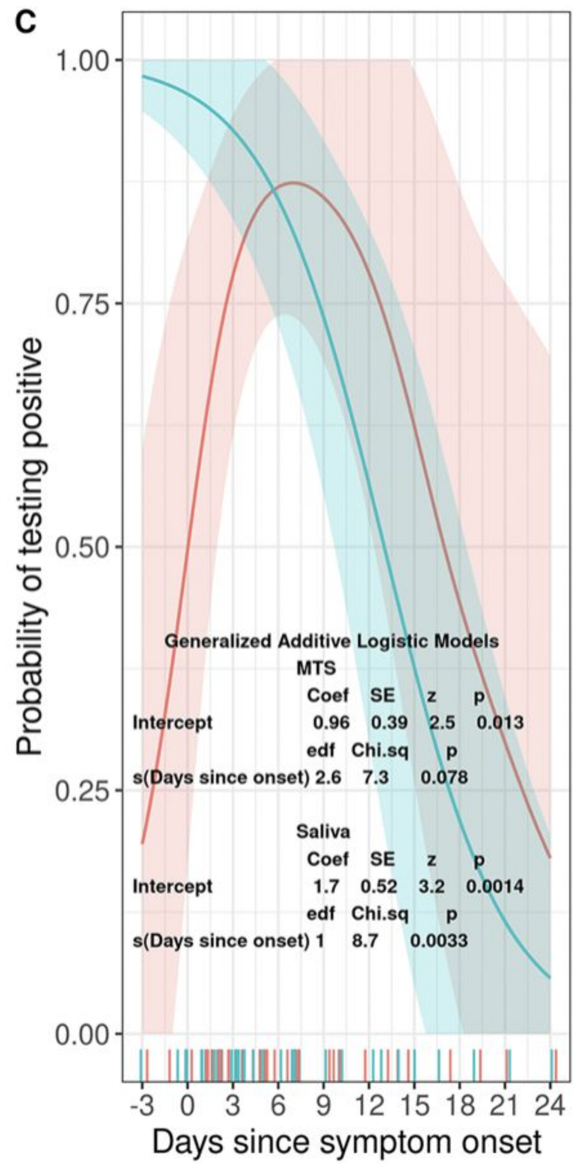
J. Lai *et al.*, *medRxiv*, doi:10.1101/2022.07.27.22278121.

Predictors of viral RNA load in EBA during Omicron infection

	Coarse Aerosol N=29, n=44[a]		Fine Aerosol N=29, n=44[a]	
	Unadjusted	Adjusted[b]	Unadjusted	Adjusted
Omicron BA.2	1.9 (0.058, 61)	8.6 (0.57, 130)	1 (0.034, 31)	2.7 (0.32, 23)
Days since last vaccine or booster	0.98 (0.96, 1)	-	1 (0.99, 1)	-
Age	2.6 (1, 6.4)	**2.6 (1.3, 5.4)**	2.3 (0.87, 6)	1.4 (0.75, 2.6)
Sex (Male)	2.6 (0.13, 53)	0.96 (0.1, 8.9)	6.1 (0.37, 100)	4.2 (0.76, 23)
Day post-symptom onset	0.33 (0.15, 0.71)	-	0.57 (0.25, 1.3)	-
Log mid-turbinate swab	9.4 (2, 44)	-	7 (1.7, 28)	-
Log saliva	64 (6.8, 610)	**54 (8.2, 360)**	39 (5.2, 290)	**22 (4.7, 100)**
Number of coughs	1 (0.97, 1.1)	-	1.1 (1, 1.2)	**1.1 (1, 1.1)**
Upper respiratory symptoms	1.9 (0.26, 14)	-	1.6 (0.24, 10)	-
Lower respiratory symptoms	1.6 (0.6, 4.2)	-	1.4 (0.54, 3.8)	-
Gastrointestinal symptoms	3.5 (0.86, 15)	-	2.1 (0.48, 8.9)	-
Systemic symptoms	13 (2, 80)	3.7 (0.85, 16)	21 (2.3, 190)	**12 (2.6, 55)**

Saliva PCR is more sensitive than nasal PCR for SARS-CoV-2 during early infection

Days since symptom onset [a]	Saliva Positive/N (Sensitivity %)	MTS Positive/N (Sensitivity %)	Odds Ratio[b] Saliva:MTS	Estimates[c] Saliva:MTS
All samples [d]	31/40(78)	28/40(70)	1.5 (0.54, 4)	0.083 (0.069, 0.099)
-3 through 2	10/11 (91)	5/11 (45)	12 (1.2, 130)	3.2 (2.8, 3.8)
3 through 8	16/18 (89)	17/18 (94)	0.47 (0.037, 6)	0.03 (0.026, 0.036)
9 through 24	5/11 (45)	6/11 (55)	0.7 (0.13, 3.8)	0.065 (0.057, 0.073)



J. Lai *et al.*, *Microbiol Spectr*, e0012822 (2022).

SARS-CoV-2 Time From Onset of Symptoms to Transmission (TOST)

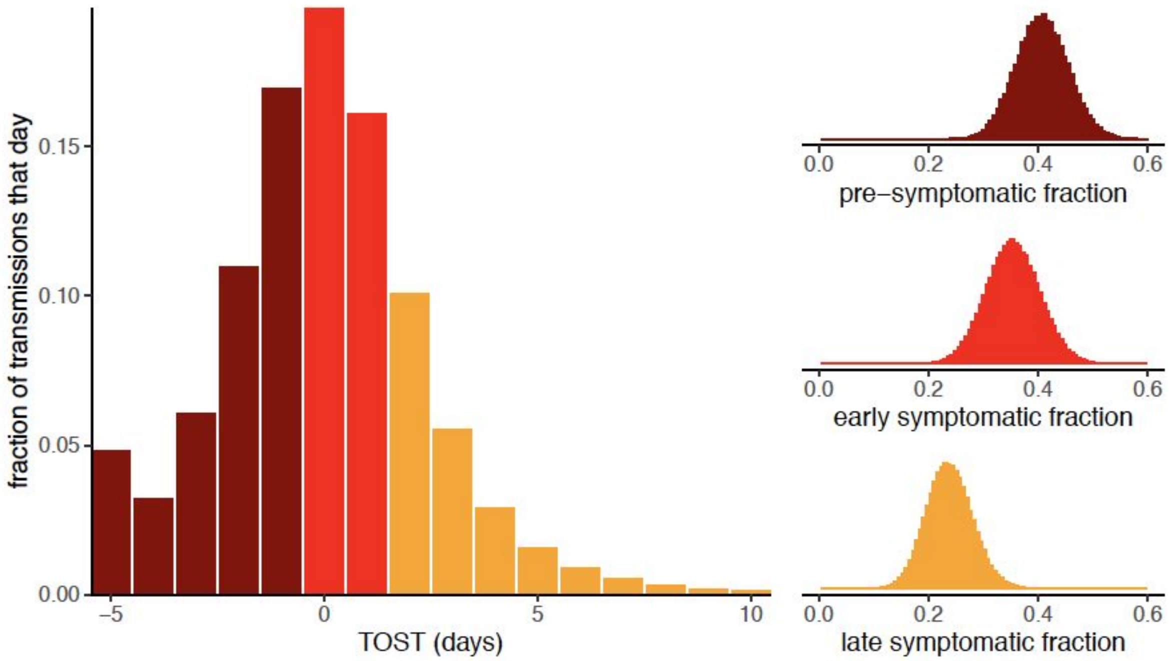
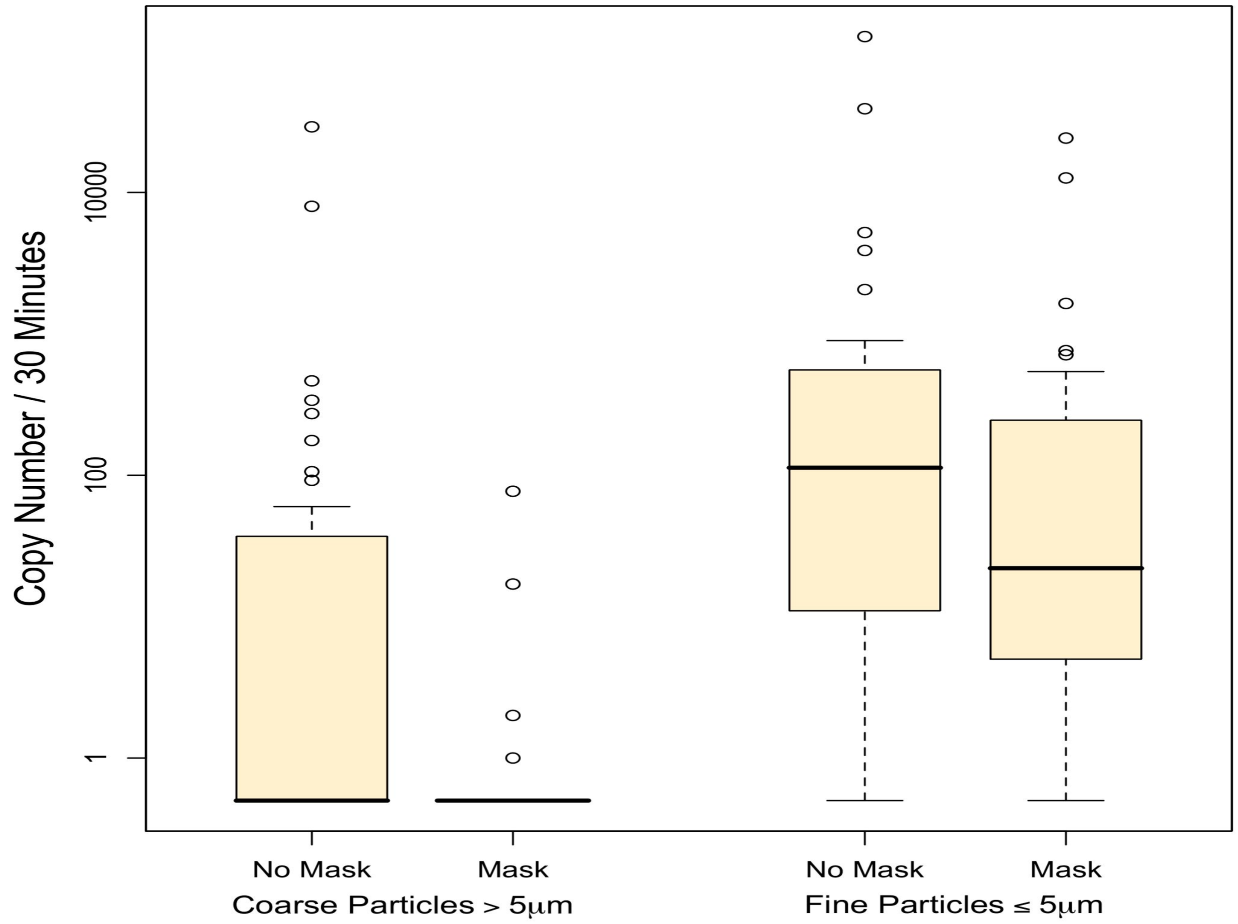


Figure 4: *Left: distribution of transmissions relative to the day of onset of symptoms. The left-most bin contains all transmission 5+ days before symptom onset. Right: posterior distributions of the fraction of all transmissions that occur before symptoms (pre-symptomatic, TOST<0), on the day of onset of symptoms or the following day (early symptomatic, TOST=0-1) or thereafter (late symptomatic, TOST>1), obtained from 10000 bootstraps from all pairs in the full dataset.*

L. Ferretti *et al.*, *medRxiv*, 2020, doi:10.1101/2020.09.04.20188516.

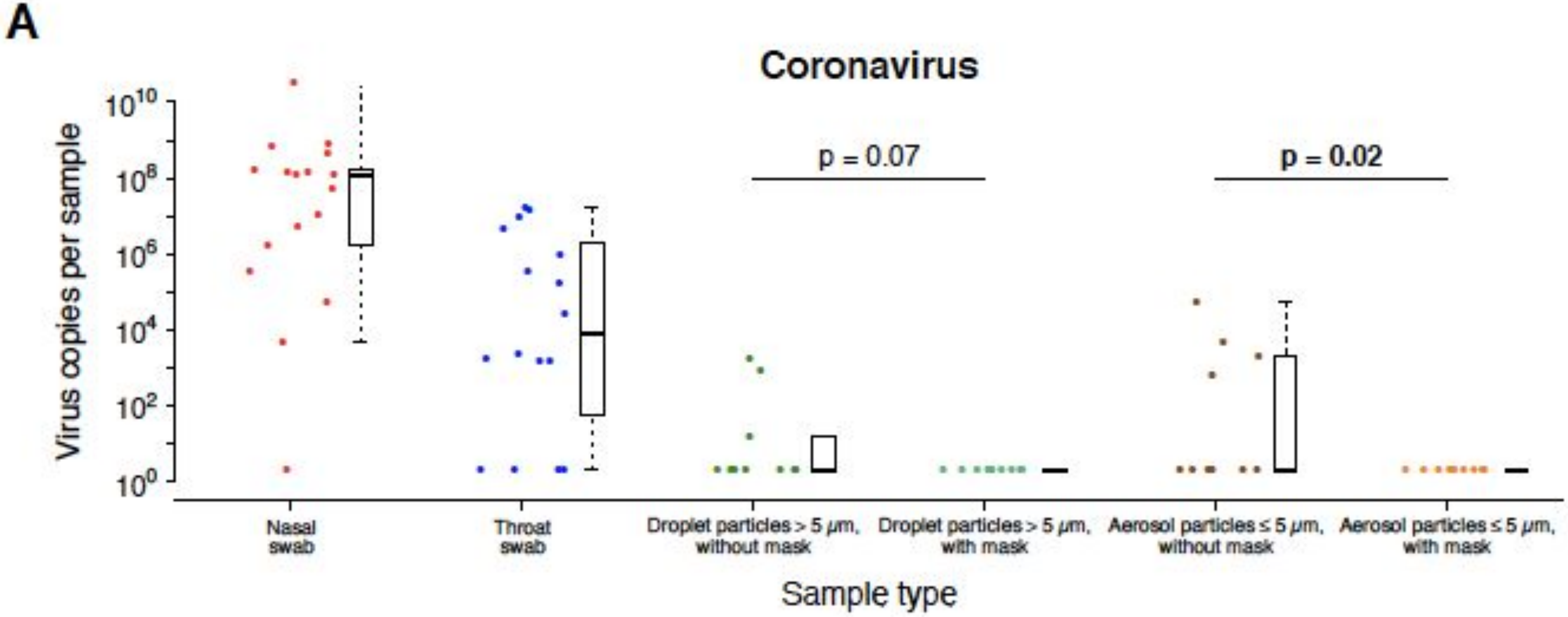
Masks as Source Control for Influenza Virus

Influenza Virus RNA in Aerosol Particles
with and without a Surgical Mask



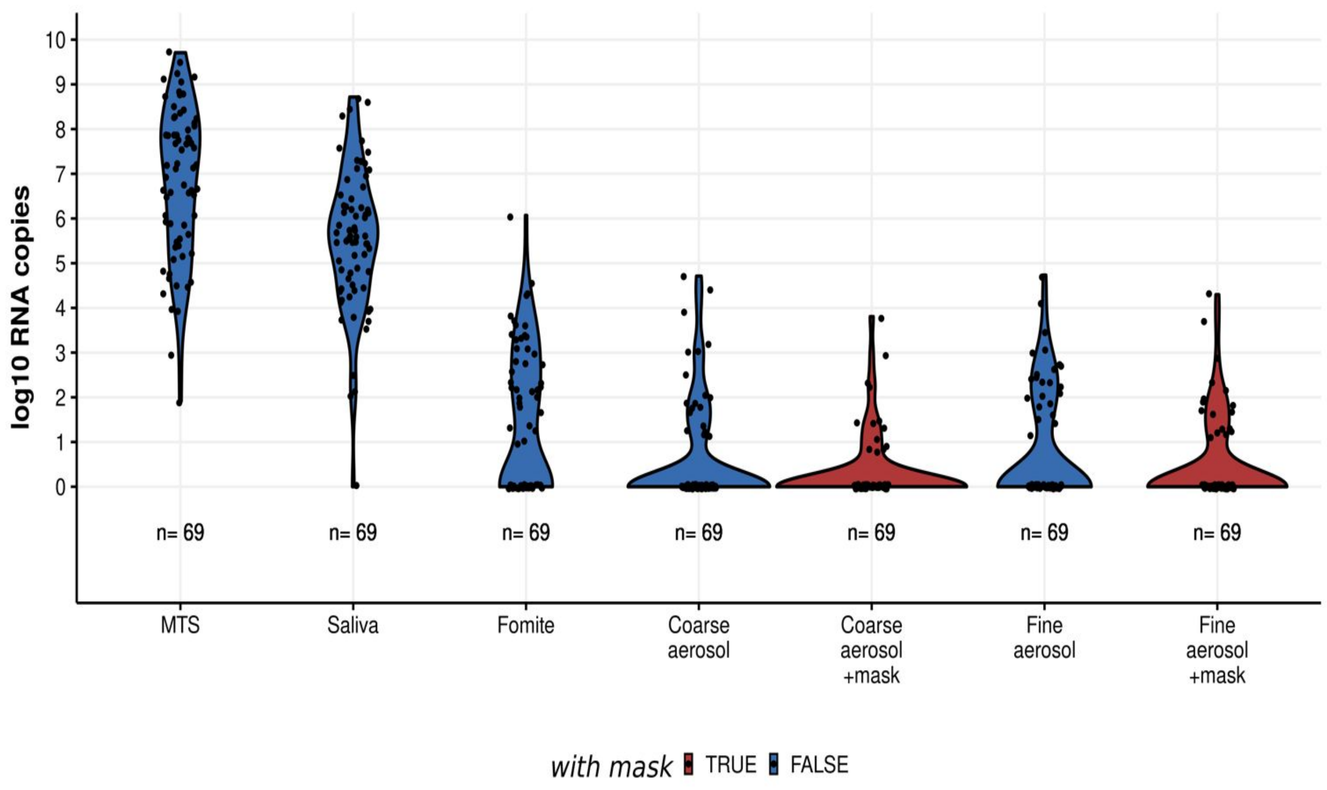
Milton DK et al. (2013) PLoS Pathog 9(3): e1003205.

Masks as Source Control for Seasonal Coronaviruses



N. H. L. Leung *et al.*, *Nature Medicine*, 1–5 (2020).

Mask as Source Control for SARS-CoV-2



	Coarse Aerosol (>5 µm)	Fine Aerosol (≤5 µm)
	Paired ± Mask N=46, n = 69	Paired ± Mask N=46, n = 69
	Estimate	Estimate
Alpha Variant	100 (16, 650)	73 (15, 350)
Face mask	0.23 (0.11, 0.49)	0.52 (0.28, 0.97)
Number of coughs	1 (0.93, 1.2)	1.1 (1, 1.3)
Alpha Variant x Face mask	0.62 (0.15, 2.7)	0.7 (0.2, 2.4)

Critical Evidence of Fine Particle Aerosol Transmission & **Inadequacy of Surgical Masks as PPE**

- Boston hospital infection control case – contact investigations
- Multiple instances of transmission to healthcare workers wearing surgical masks
- Viral sequence confirmed transmission from patient to masked worker

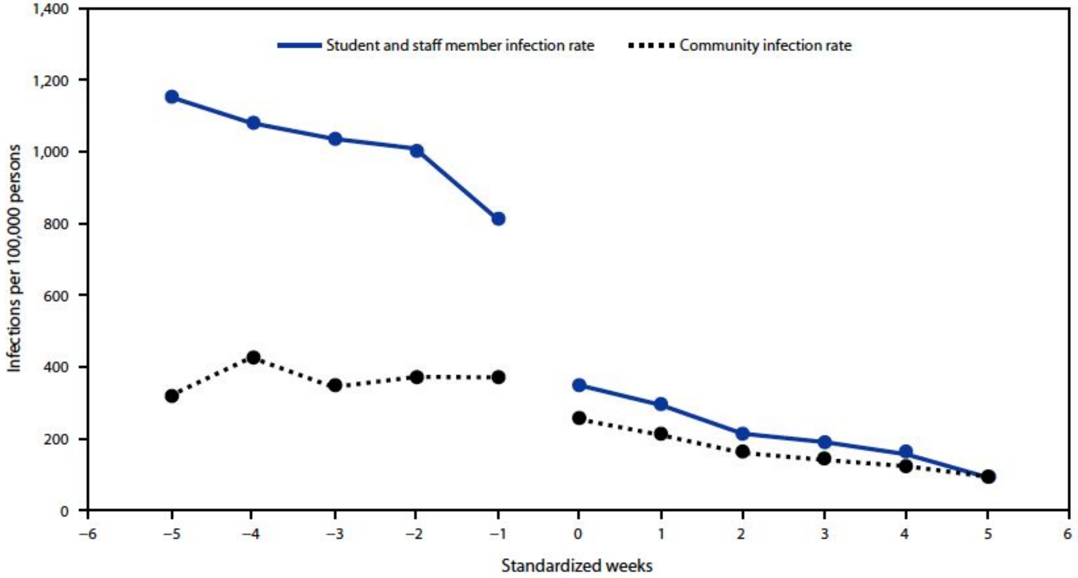
Table 1. Summary of Cases With Whole Genome Sequencing-confirmed SARS-CoV-2 Transmission Despite Use of Masks and Eye Protection

Case	Transmission Direction	Exposure Duration and Circumstance	Patient Consistently Masked?	Healthcare Worker Personal Protective Equipment
1	Asymptomatic hospitalized patient to 2 patient care assistants	4-hour and 8-hour sitter shifts	No	Masks and eye protection
2	Presymptomatic nurse to hospitalized patient	8-hour nursing shifts (non-ICU)	No	Mask and eye protection
3	Presymptomatic patient to physician	45-minute outpatient visit	Yes, except for brief oral exam	Mask and eye protection

Abbreviations: ICU, intensive care unit; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

M. Klompas *et al.*, *Clin Infect Dis.* **73**, 1693–1695 (2021).

Layers: Ventilation, Filtration, and Masks



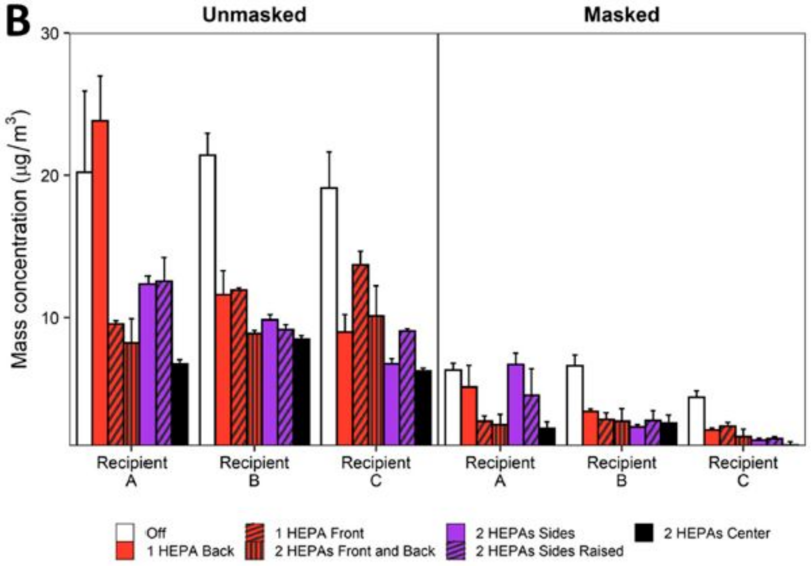
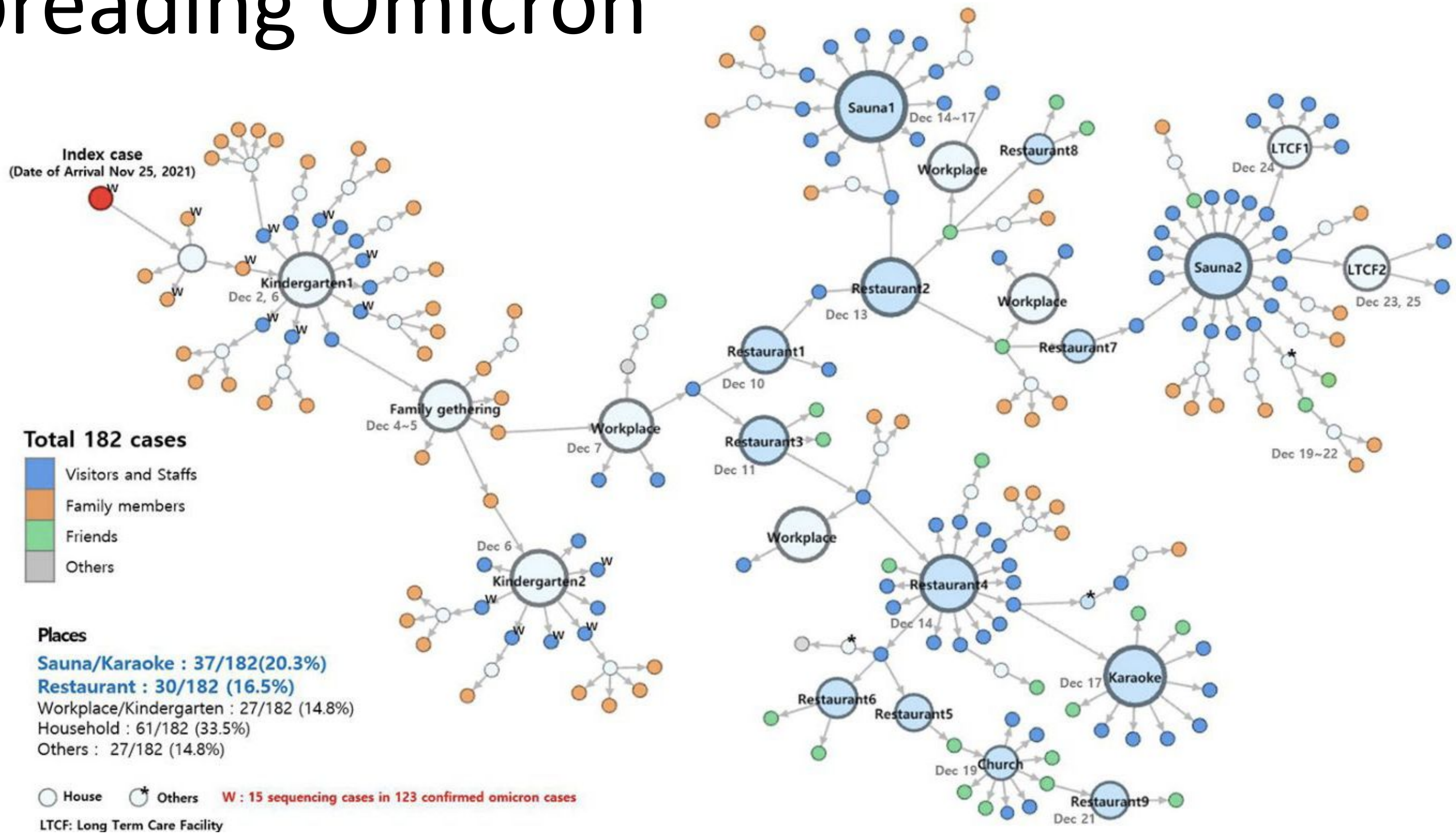


TABLE 2. COVID-19 incidence* and rate ratios in 123 elementary schools,† by type of ventilation improvement as a COVID-19 prevention strategy — Georgia, November 16–December 11, 2020

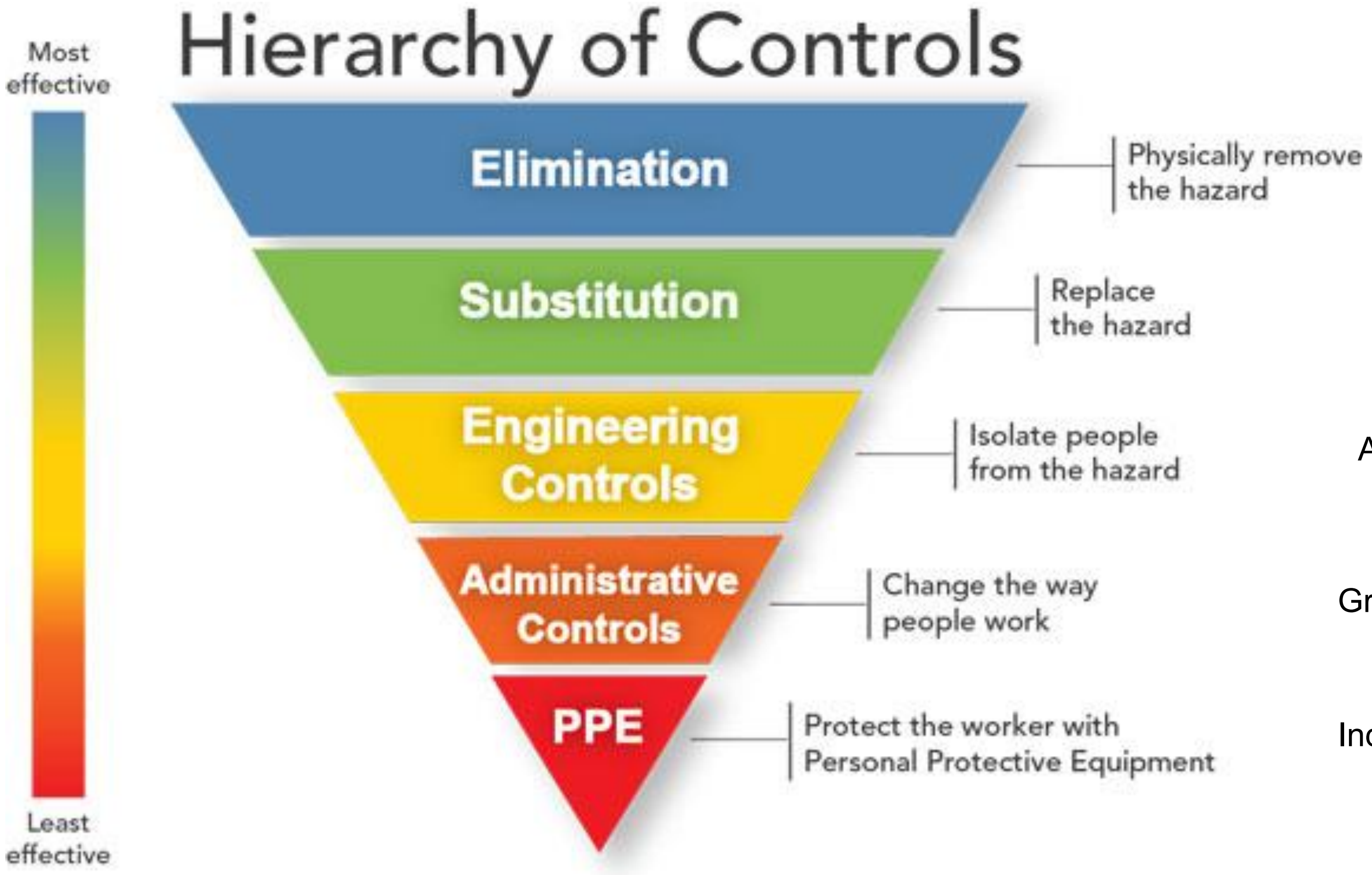
Ventilation improvement	No. (%) of schools	No. of enrolled students	No. of cases§	Cases per 500 students enrolled (95% CI)	RR¶ (95% CI)
Total	**123 (100)**	**66,499**	**417**	**3.13 (2.84–3.44)**	—
None**	37 (30.1)	21,844	183	4.19 (3.63–4.84)	Ref
Dilution only††	39 (31.7)	21,562	127	2.94 (2.48–3.50)	0.65 (0.43–0.98)
Filtration ± purification only§§	16 (13.0)	9,133	45	2.46 (1.84–3.29)	0.69 (0.40–1.21)
Dilution and filtration ± purification¶¶	31 (25.2)	13,960	62	2.22 (1.73–2.84)	0.52 (0.32–0.83)

J. Gettings *et al.*, *MMWR Morb Mortal Wkly Rep*. **70**, 779–784 (2021);
C. V. Donovan, *MMWR Morb Mortal Wkly Rep*. **71** (2022);

Superspreading Omicron



E.-Y. Kim *et al.*, *Emerging Infectious Disease journal*. **28** (2022), doi:10.3201/eid2804.220006.

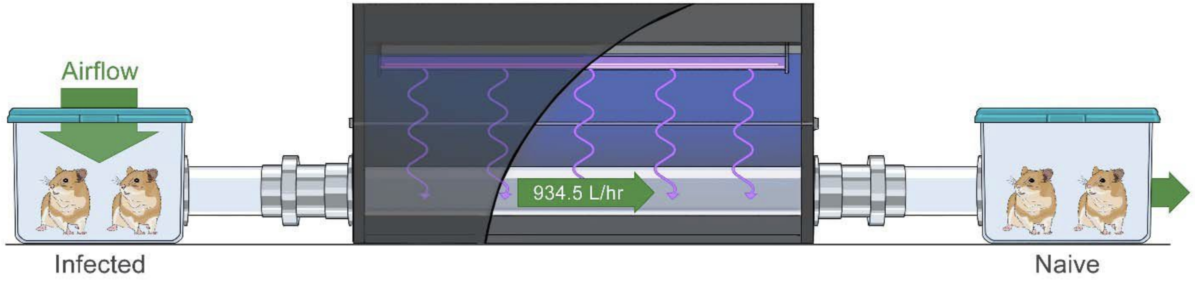


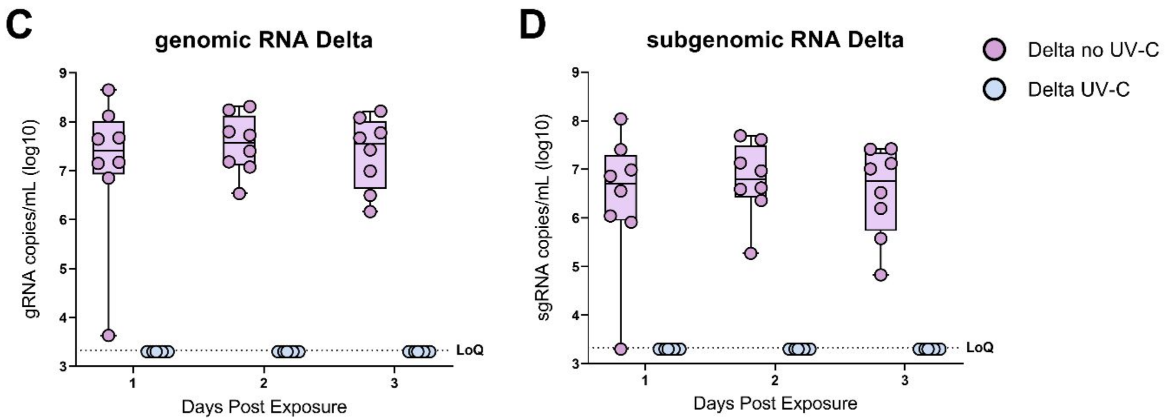
Automatic

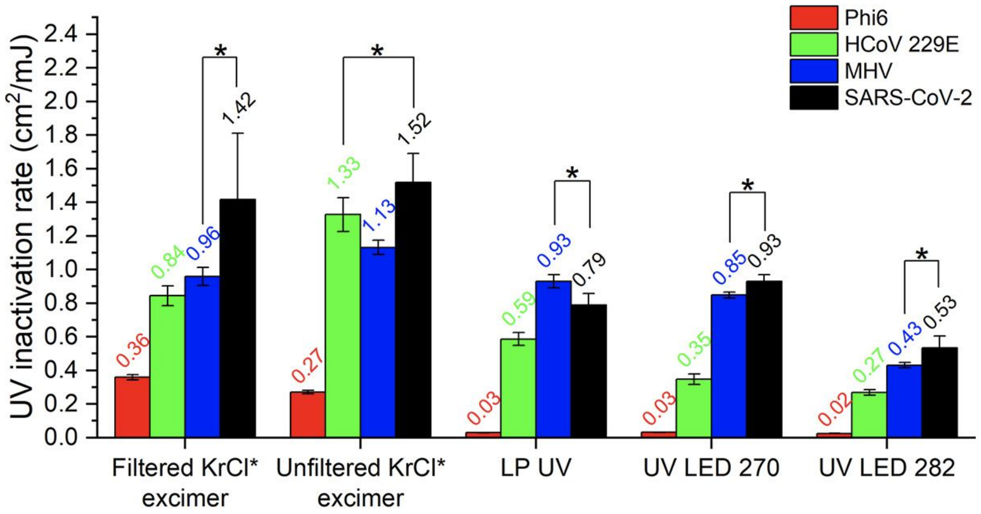
Group Behavior

Individual Behavior

Germicidal UV for prevention of COVID-19

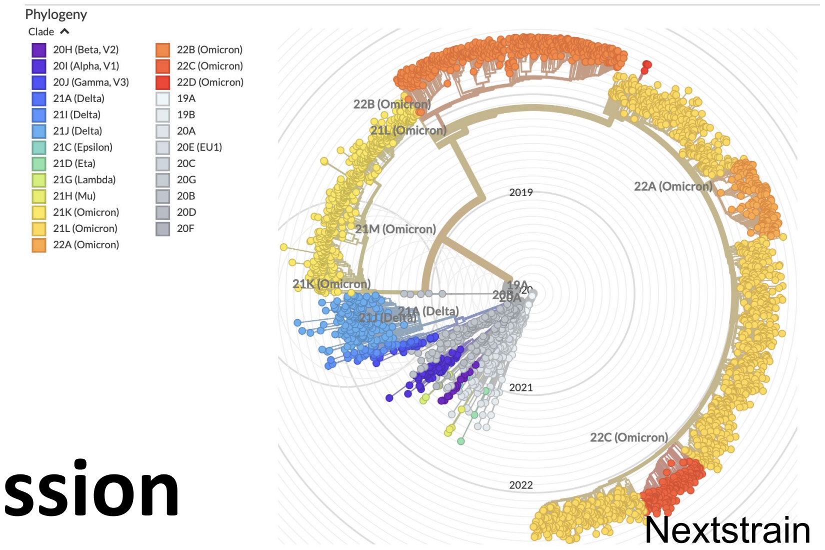






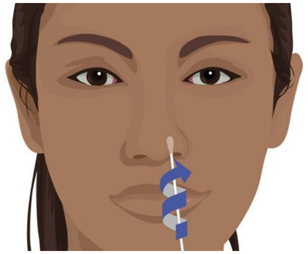
R. J. Fischer *et al.*, *bioRxiv*, doi:10.1101/2022.01.10.475722.
B. Ma, *et al.*, Appl Environ Microbiol. 87, e0153221 (2021).

Conclusions



- **Extensive evidence for airborne transmission**
  - Culture from room air and breath
  - More virus in <5 µm than ≥5 µm particles (all are aerosols)
  - Aerosol shedding associated with transmission
  - Highly contagious VOCs have higher aerosol shedding
  - Convergent evolution of high aerosol shedding phenotype

Conclusions



- **Testing and vaccination are insufficient to prevent transmission**
  - Nasal swabs and rapid antigen testing cannot detect early contagious cases
  - Vaccination and boosters do not prevent shedding of infectious aerosols
- **Layers including environmental interventions are key**
  - Superspreading remains a major factor sustaining transmission
  - Masks, ventilation, and filtration limit transmission
  - Germicidal UV holds tremendous promise to reduce transmission