Infectious Drops and Aerosols

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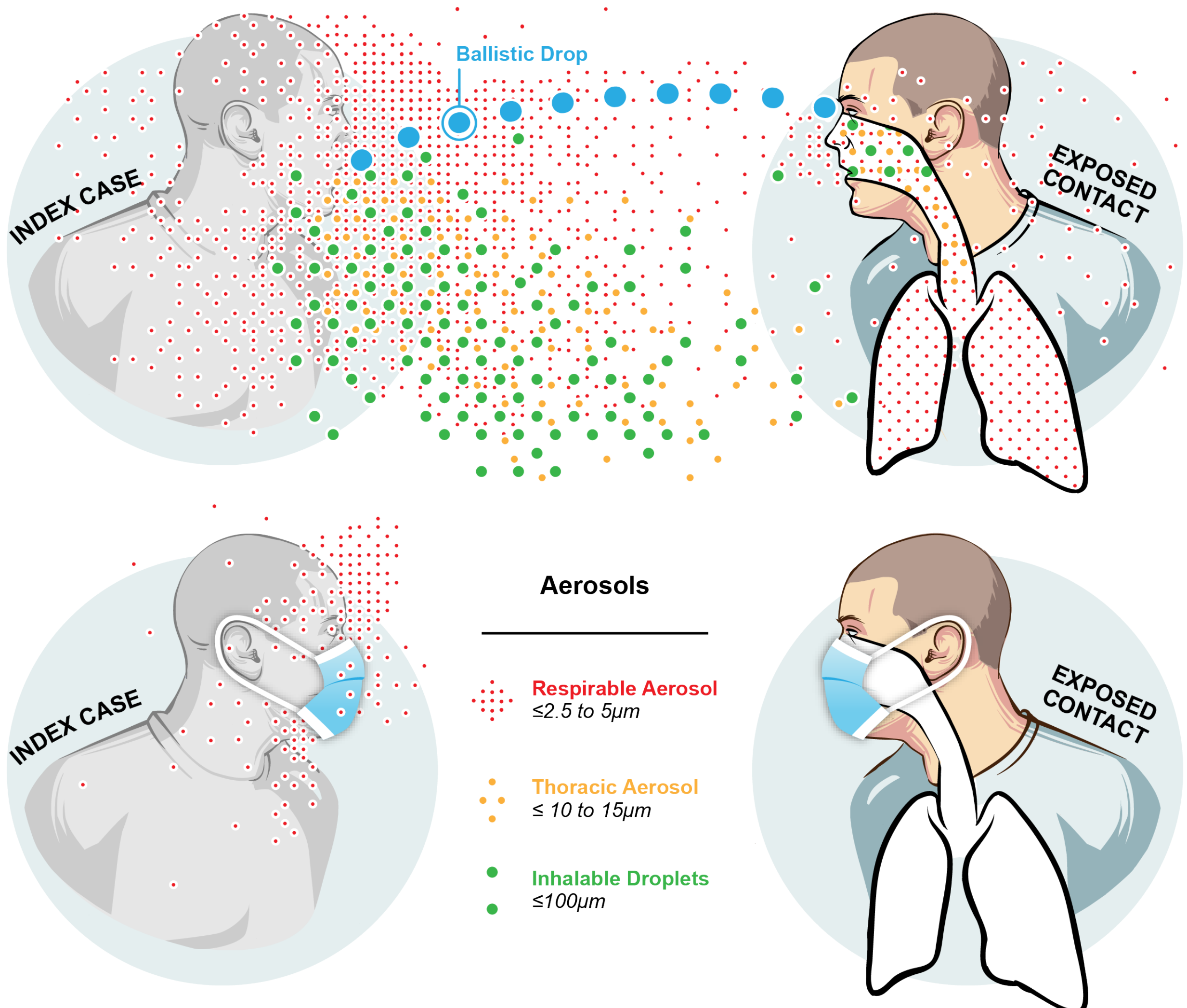
Transmission Modes of Respiratory Viruses

- Contact (direct and indirect)
  - Case to finger of contact
  - Fomite to finger of contact
  - Finger to eye, nose, or mouth
- Sprayborne
  - Ballistic drops (> 100 µm)
  - Direct hit on eye, nostril, or mouth
- Aerosol inhalation
  - Nasopharyngeal (Inhalable) ≤ 100 µm
  - Thoracic ≤ 10-15 µm
  - Respirable ≤ 5 µm



Comparison with Known Aerosol Transmitted Respiratory Infections

Tuberculosis

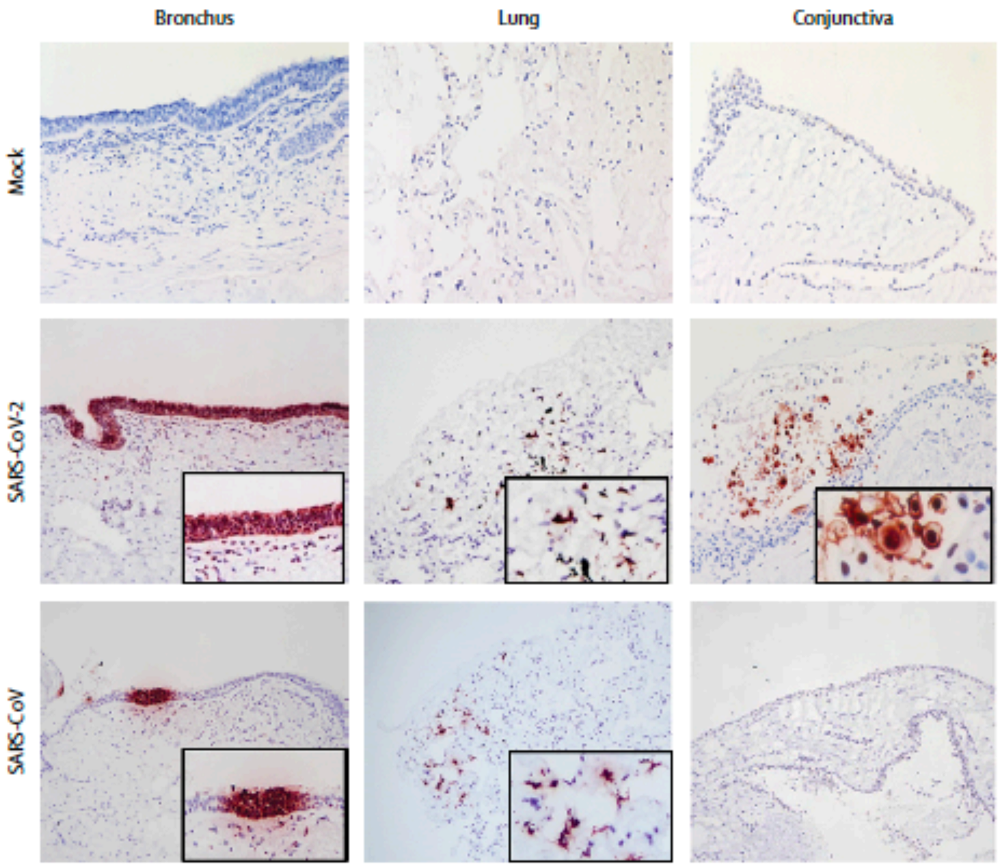
- Low rate of infectious dose generation (0.5 to 1.2 / hour) for months
- Target: alveolar macrophage
- Aerosol sampling: Negative (except cough box)
- Easily detected in surface samples
- R_0 0.2 (Netherlands) to 4.3 (China)
- Prolonged close contact
- Long-range transmission only evident in low prevalence settings
- Face masks masks effective as source control

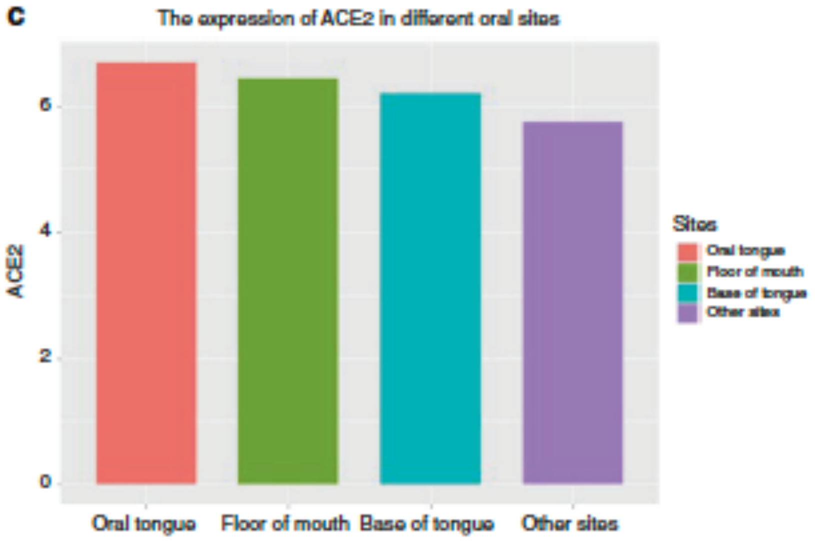
Measles

- High rate of infections dose generation (2 to 10 / minute) for days
- Target: airway dendritic cells & alveolar macrophage
- Aerosol sampling: RNA detected in aerosol – No culture evidence of infectious aerosols
- Easily detected in surface samples
- $R_0 > 15$
- Incidental contact
- Long-range transmission only evident in low prevalence settings
- Face mask?

C. K. Navaratnarajah, A. R. Generous, I. Yousaf, R. Cattaneo, J. Biol. Chem. 295, 2771–2786 (2020); T. A. Yates *et al.*, *Lancet Infect Dis.* **16**, 227–238 (2016); W. E. Bischoff et al., J Infect Dis. 213, 600–603 (2016); Y. Ma, C. R. Horsburgh, L. F. White, H. E. Jenkins, Epidemiol Infect. 146, 1478–1494 (2018).

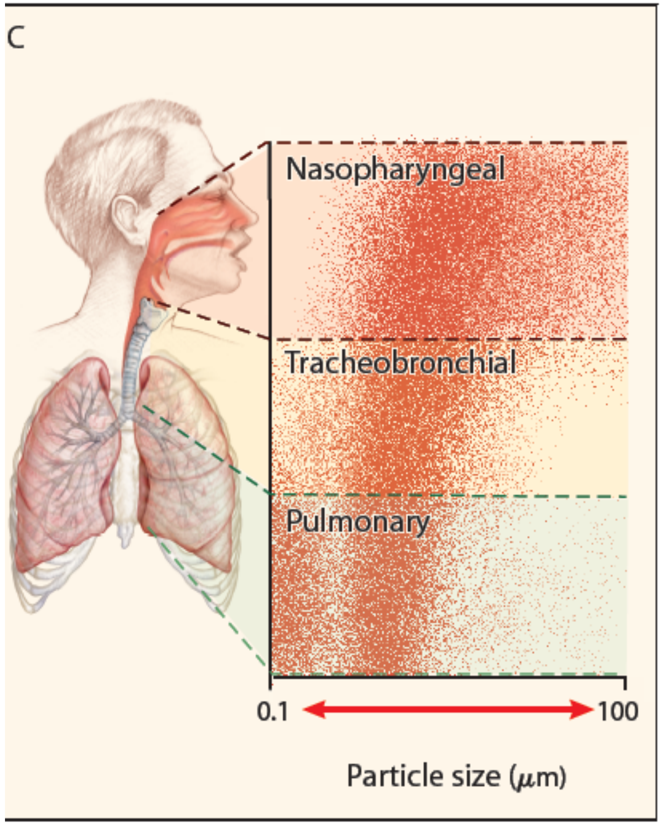
Where SARS Viruses Bind and Infect





K. P. Y. Hui *et al.*, *Lancet Respir Med* (2020), doi:10.1016/S2213-2600(20)30193-4.
H. Xu *et al.*, *Int J Oral Sci.* **12**, 8 (2020).

Total & Regional Respiratory Tract Deposition of Aerosols



- Aerosols
  - Liquid and/or solid particles suspended in air
- When inhaled
  - Large particles get stuck in the nose, mouth, and throat
  - Smaller ones penetrate into the large air tubes in the lung
  - Very small ones get into the deepest parts of the lung

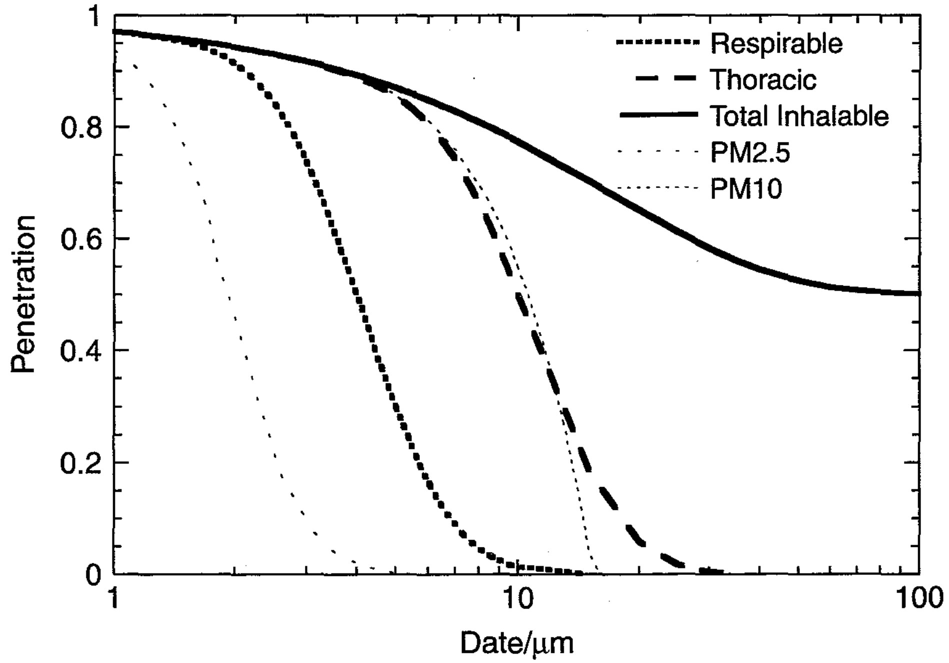
Roy C and Milton DK, New Engl J Med, 2004

Two ways to define droplets and particles that can carry respiratory viruses

Medical categories

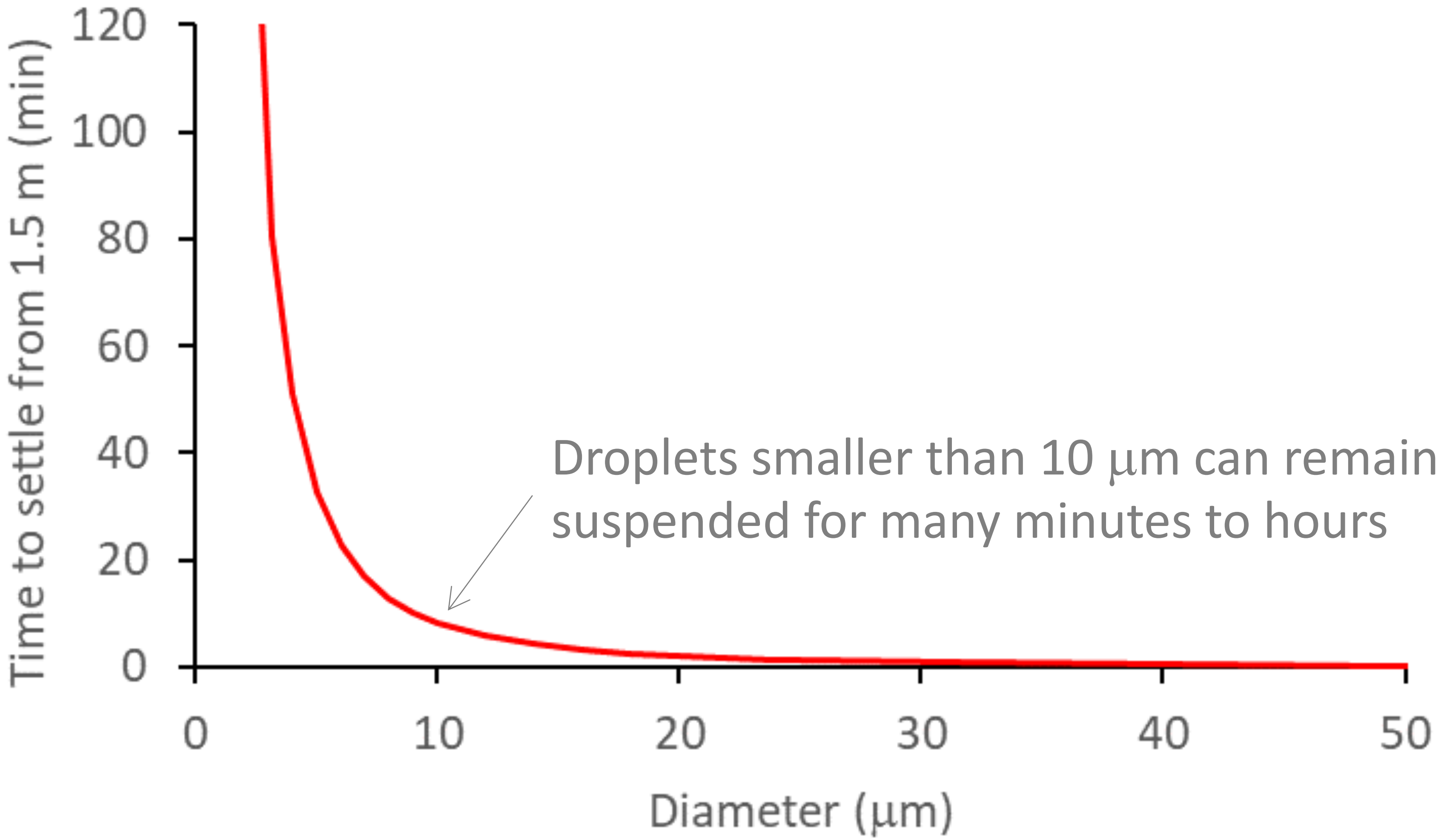
- Respiratory droplets
  - Droplets that do not travel very far
  - Mode of inoculation unclear but generally not thought to be 'inhaled'
  - Not considered "airborne infection transmission"
- Aerosols
  - Sometimes called droplet-nuclei
  - Less than 5 µm in diameter
  - Small enough to travel long distances and cause infection far from the source.
  - Considered the only cause of "airborne infection"

Exposure science based categories



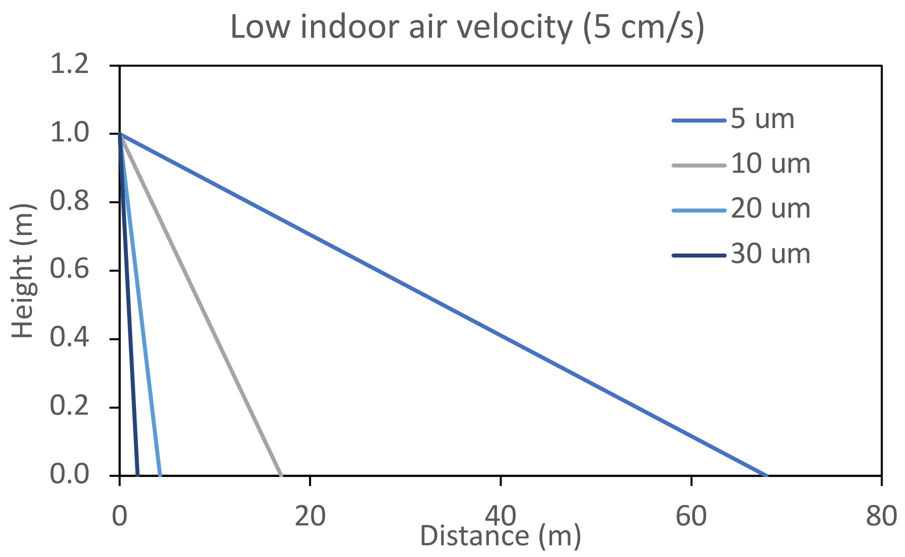
J. C. Volkwein, A. D. Maynard, M. Harper, in *Aerosol Measurement*, P. Kulkarni, P. A. Baron, K. Willeke, Eds. (John Wiley & Sons, Inc., Hoboken, NJ, USA, 2011, pp. 571–590.

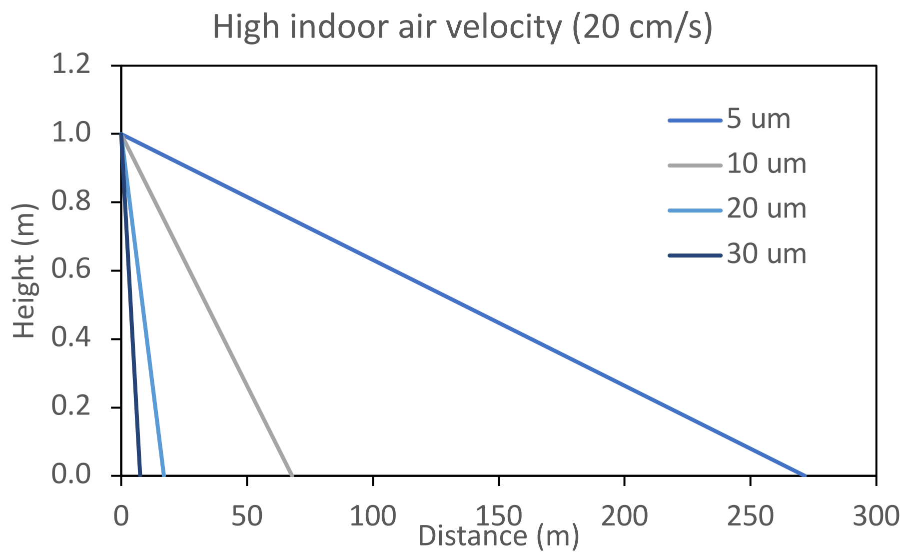
Settling Time of Droplets in Still Air



Indoor Air is not Still: Droplets Can Travel >>2 m Indoors

Travel distance of droplets released from a height of 1 m with directional airflow



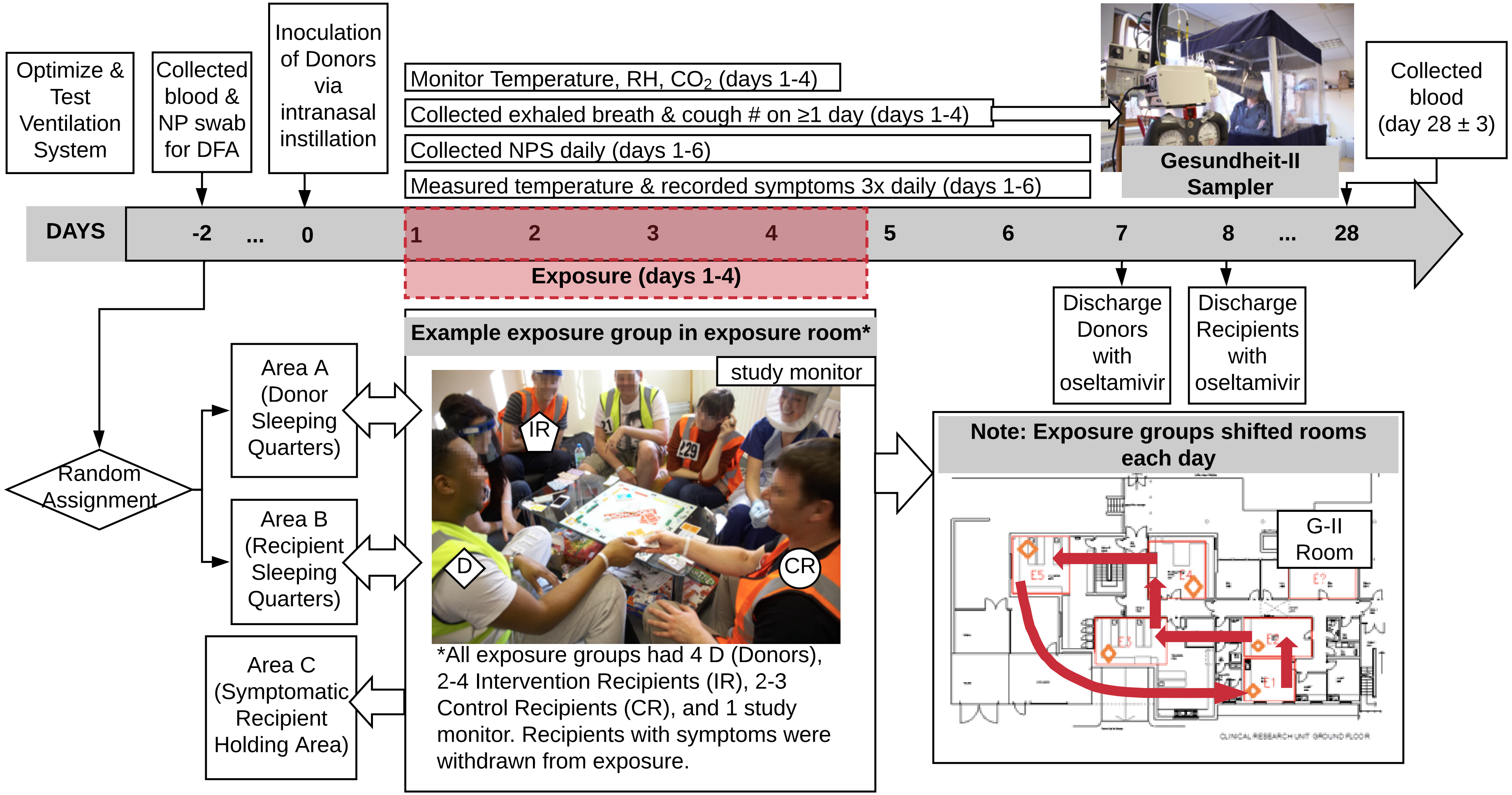


10 µm >15 to >60 m, 20 µm > 4 to > 15 m, and 30 µm > 2 to > 5 m, depending on air velocity.

Aerosol science does not support the idea that droplets > 5 µm fallout within 6 meters.

With turbulence distance traveled is less, but settling time is longer.

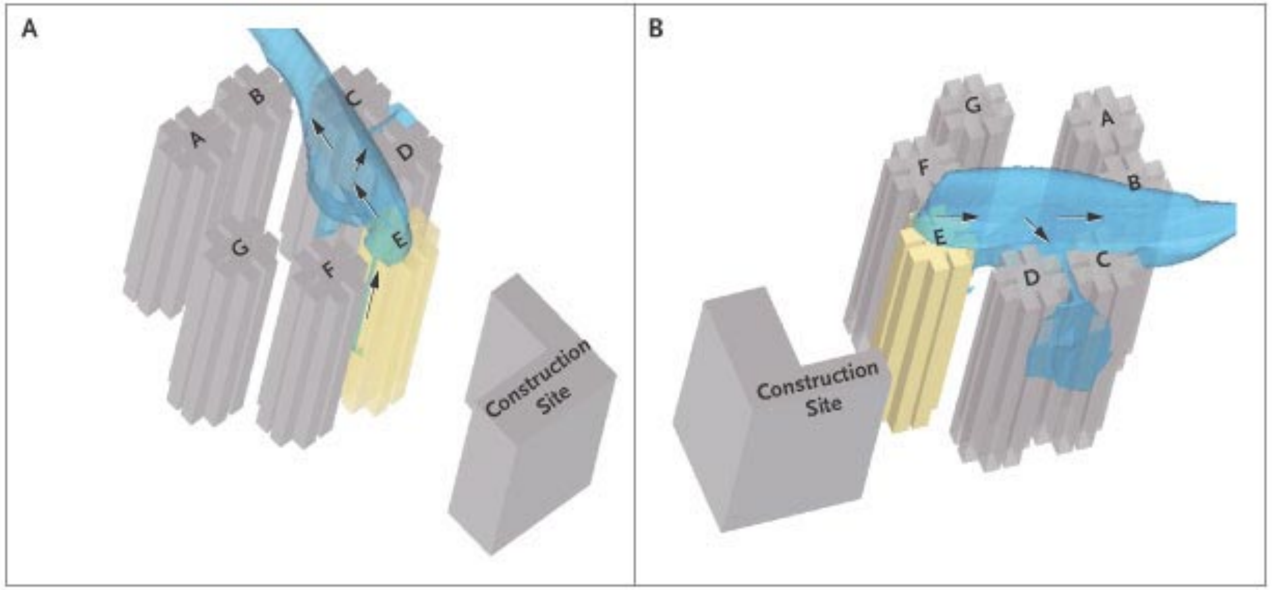
Randomized Controlled Transmission Study?



J. S. Nguyen-Van-Tam et al., PLOS Pathogens. 16, e1008704 (2020).

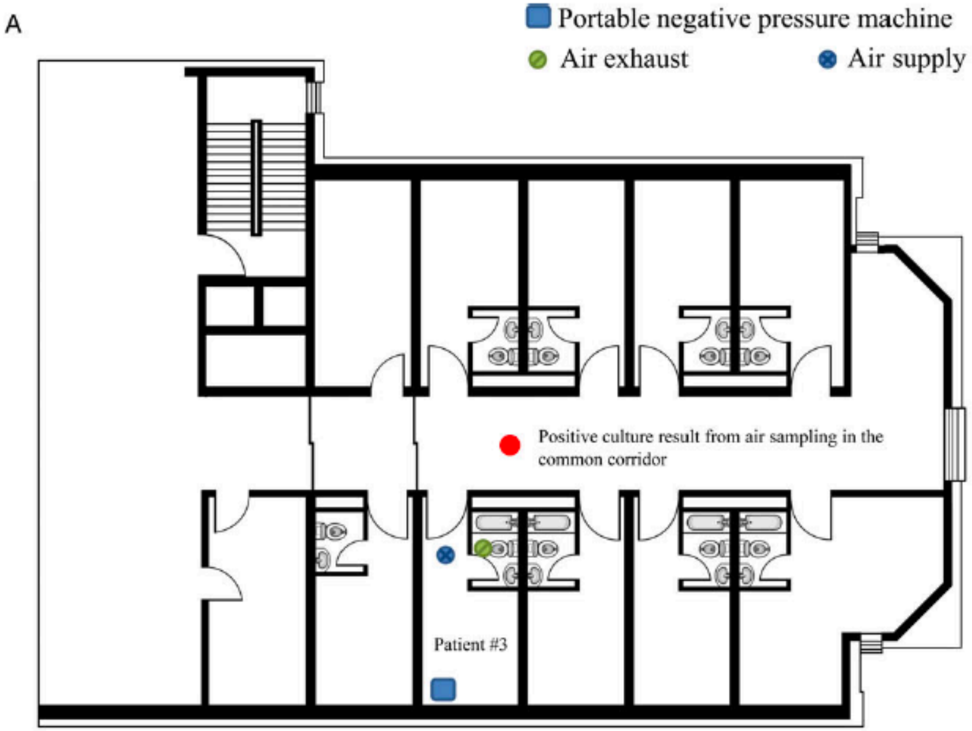
Aerosols in SARS and MERS

Amoy Gardens SARS Outbreak 187 Cases



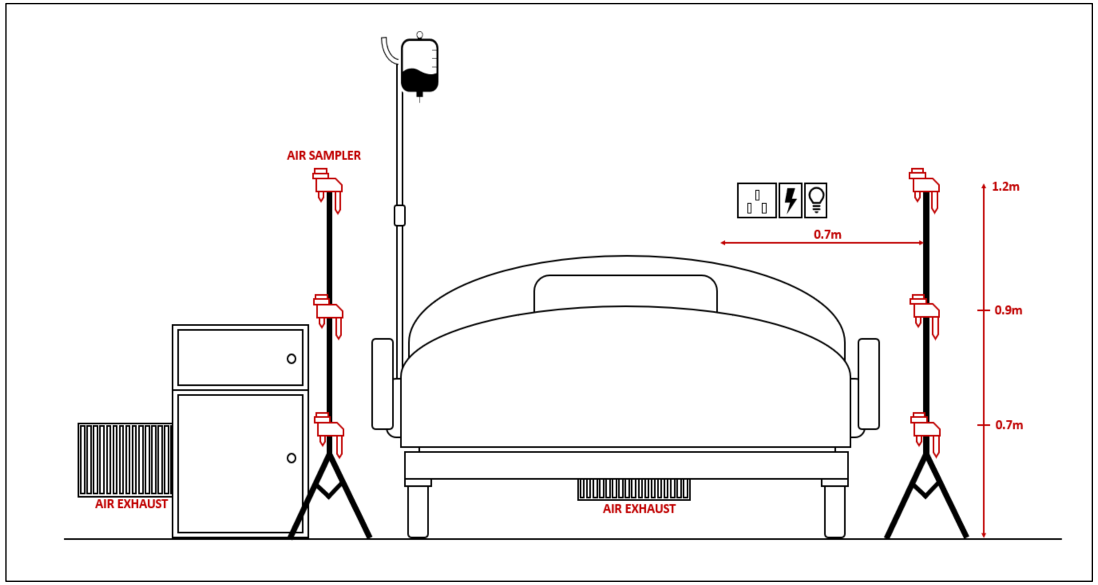
Yu, I. T.S. et al. N Engl J Med 2004;350:1731-1739

Infectious MERS-CoV in Hospital Corridor Air



S.-H. Kim *et al.*, *Clin. Infect. Dis.* **63**, 363–369 (2016).

SARS-CoV-2 Aerosols in Containment Unit, Singapore

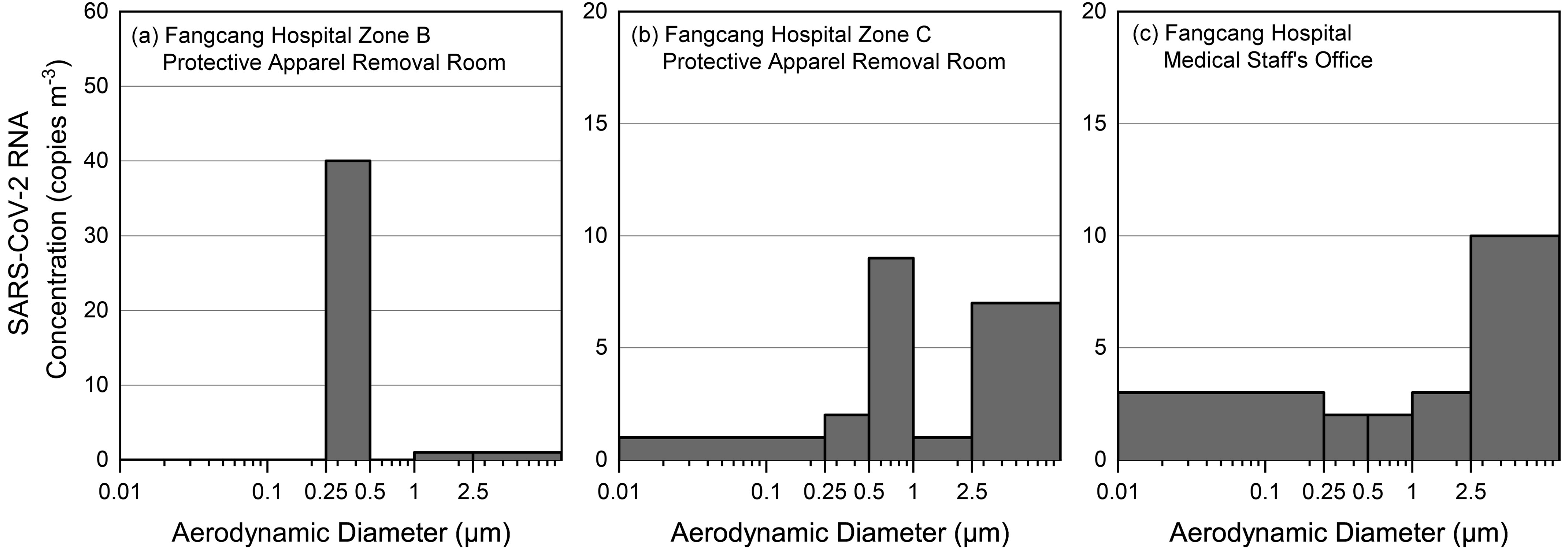


Patient	Day of illness	Symptoms reported on day of air sampling	Clinical Ct value*	Airborne SARS-CoV-2 concentrations (RNA copies m^{-3} air)	Aerosol particle size	Samplers used
1	9	Cough, nausea, dyspnea	33.22	ND ND	-- --	NIOSH SKC Filters
2	5	Cough, dyspnea	18.45	2,000 1,384	>4 µm 1-4 µm	NIOSH
3	5	Asymptomatic†	20.11	927 916	>4 µm 1-4 µm	NIOSH

Average breathing rate ~12-14 m^3 per day

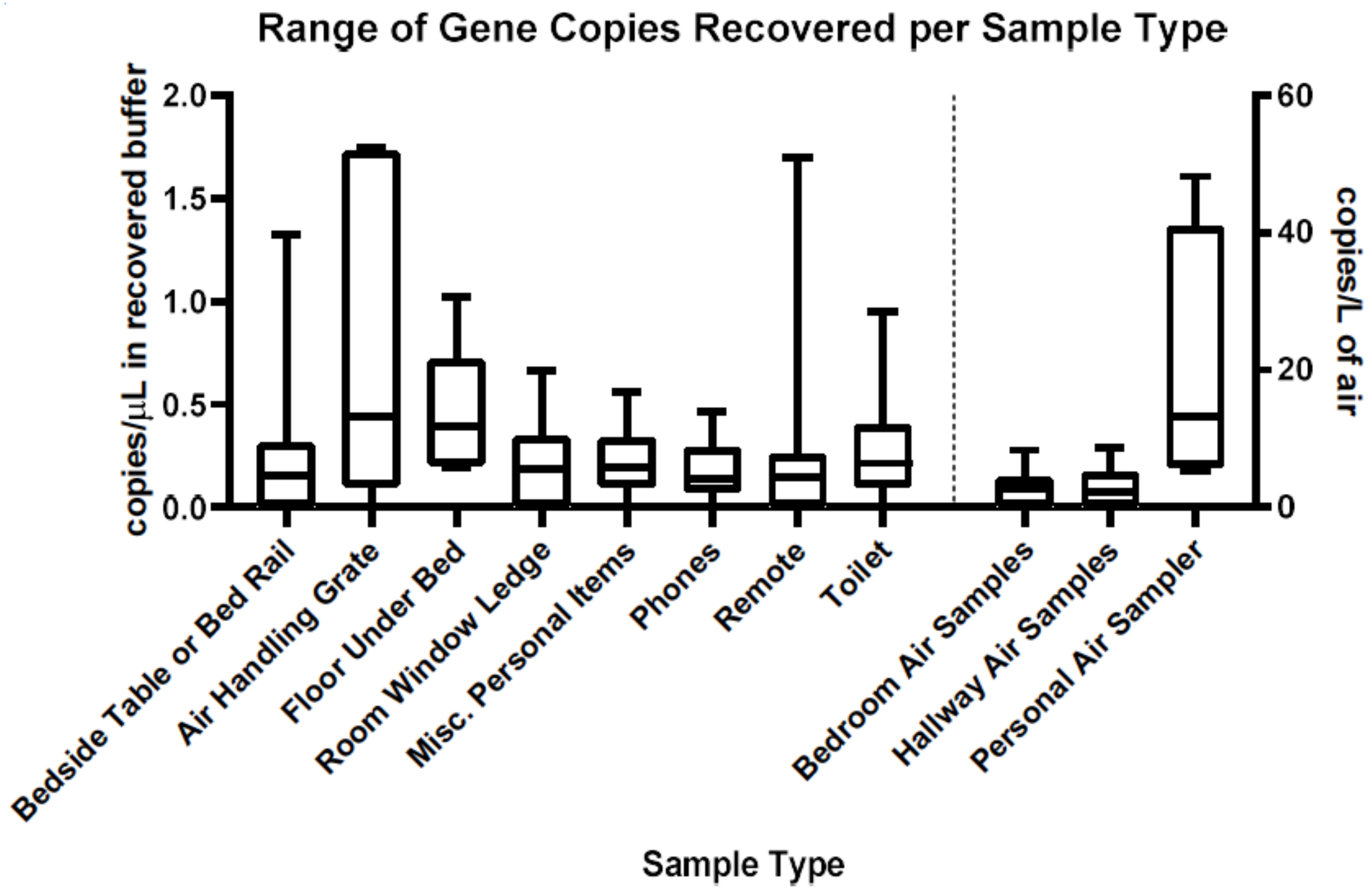
P. Y. Chia *et al.*, *Nature Communications*. **11**, 2800 (2020).

Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals



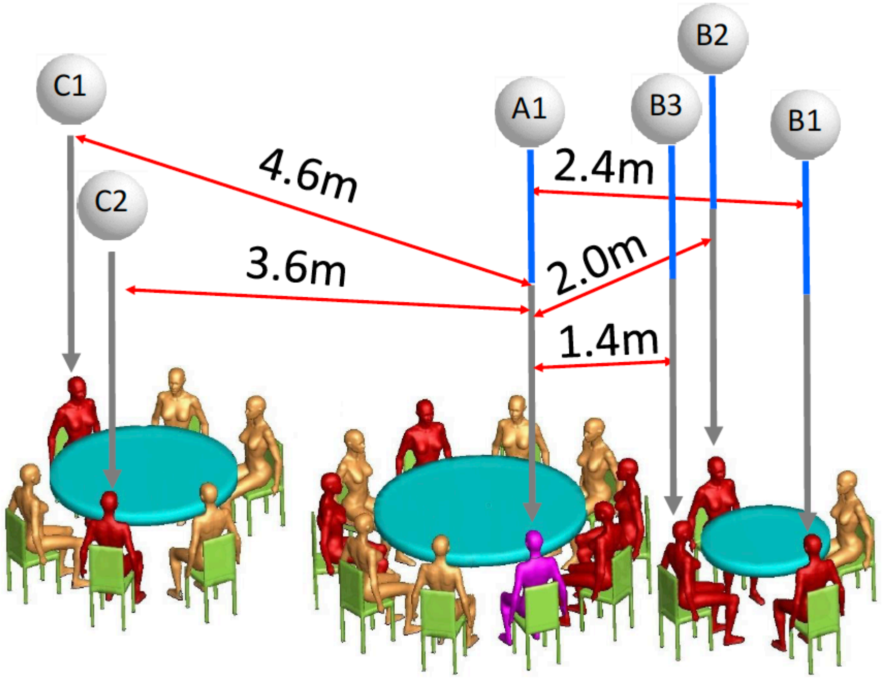
Y. Liu *et al.*, *Nature*, 1–6 (2020).

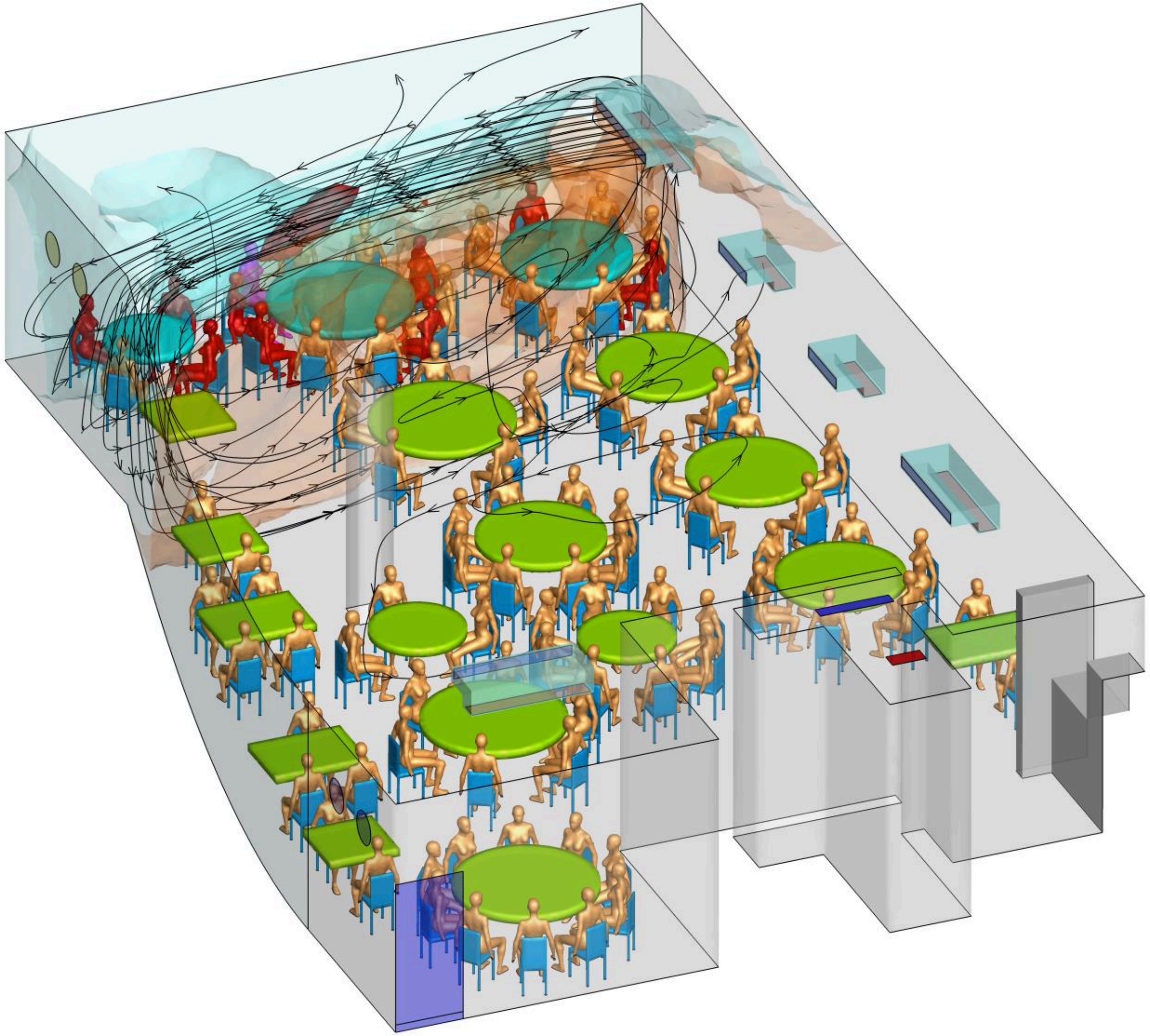
Aerosol and Surface Transmission Potential



J. L. Santarpia *et al.*, *medRxiv*, 2020, doi:10.1101/2020.03.23.20039446.

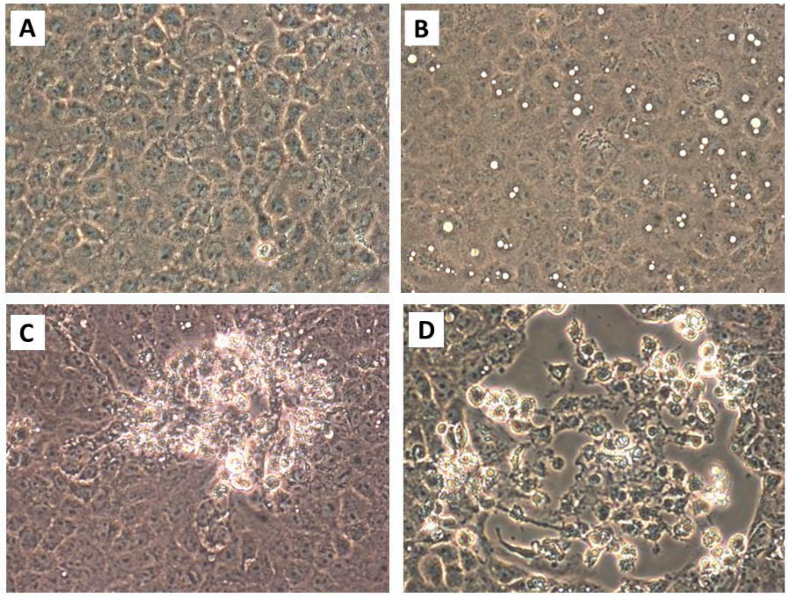
Transmission Distance

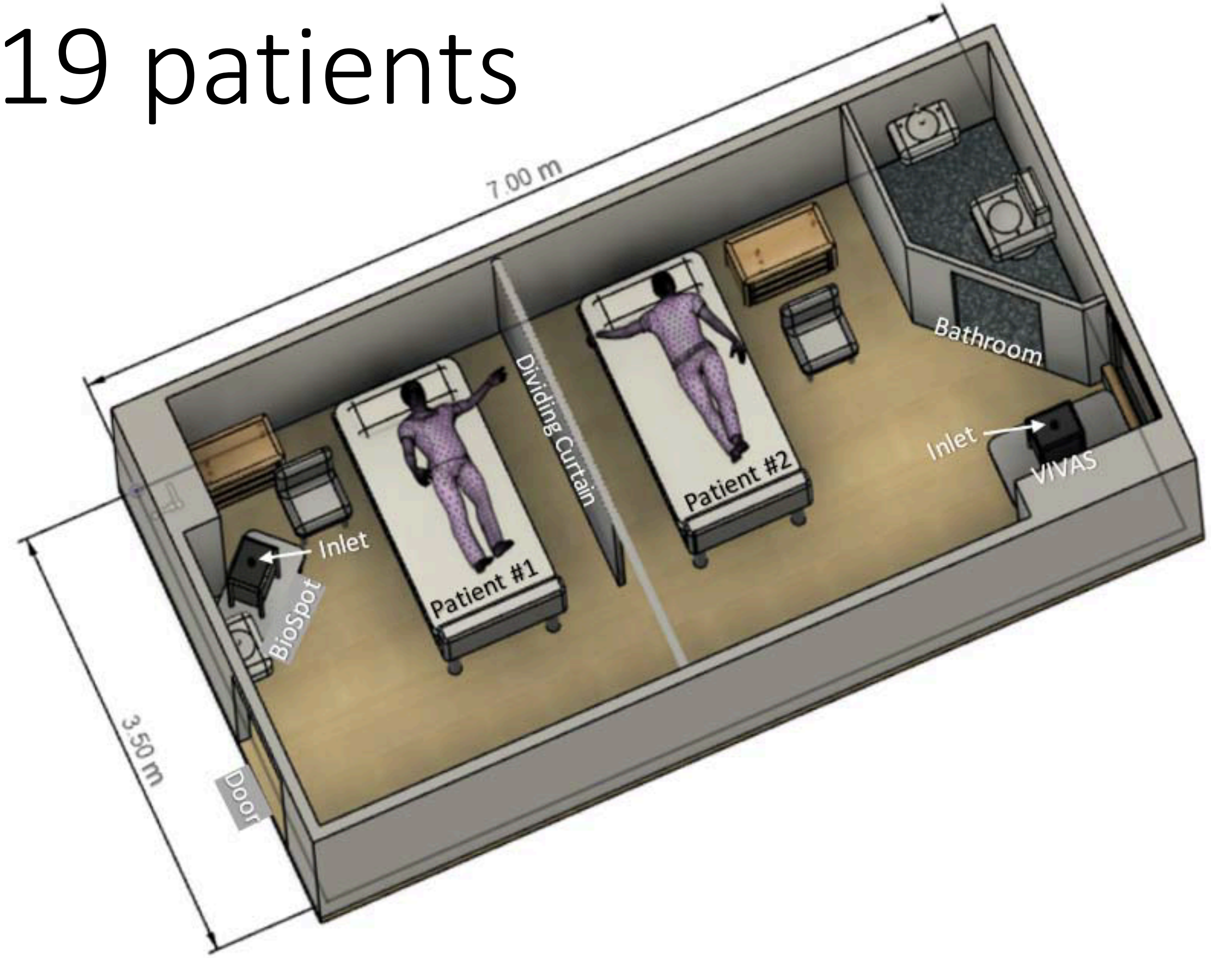




Y. Li *et al.*, *medRxiv*, 2020, doi:10.1101/2020.04.16.20067728.

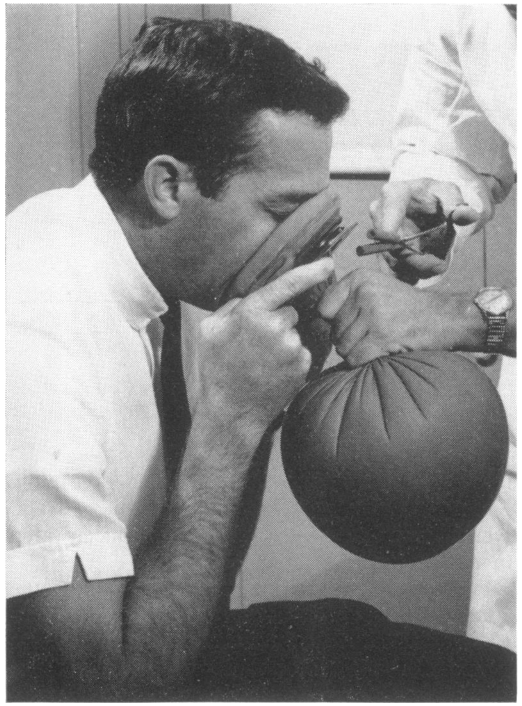
Viable SARS-CoV-2 in the air of a hospital room 1 with COVID-19 patients





J. A. Lednicky *et al.*, *medRxiv*, medRxiv, doi:10.1101/2020.08.03.20167395.

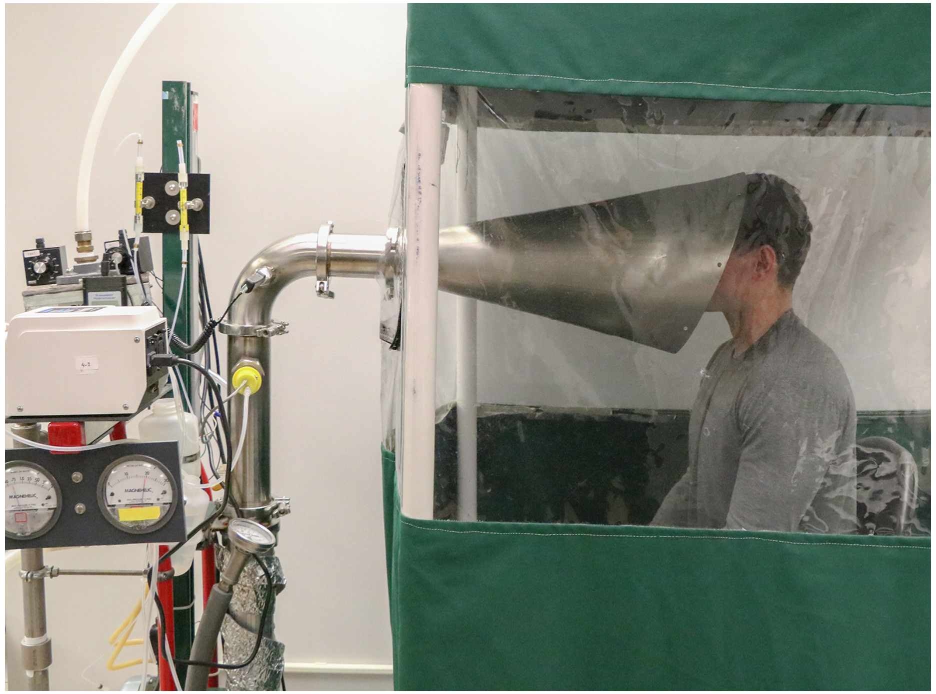
Human Cough and Sneeze Collectors 1960s



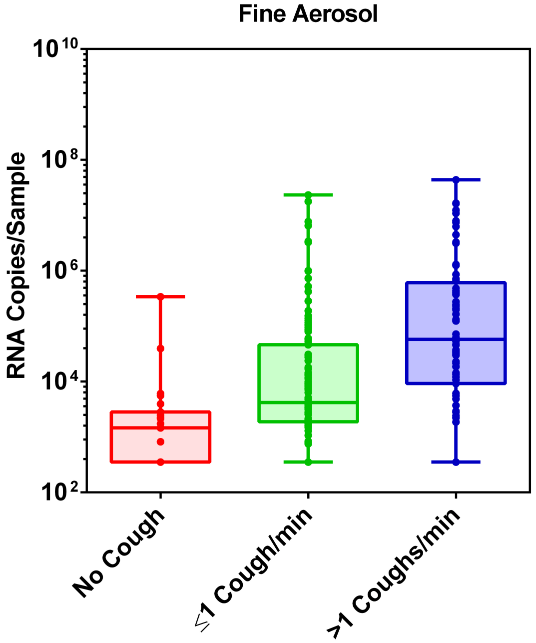
Gerone PJ, Couch RB, Keefer GV, Douglas RG, Derrenbacher EB, Knight V. Bacteriol Rev. 1966 Sep;30(3):576–88.

Gesundheit-II Human Bioaerosol Collector

- Coarse aerosol (> 5 and < 80 µm)
- Fine aerosol (> 0.05 µm and ≤ 5 µm)
- **Influenza virus was cultured from fine aerosol (~1/min)**
- **Influenza virus is present in exhaled breath** – even without coughing.



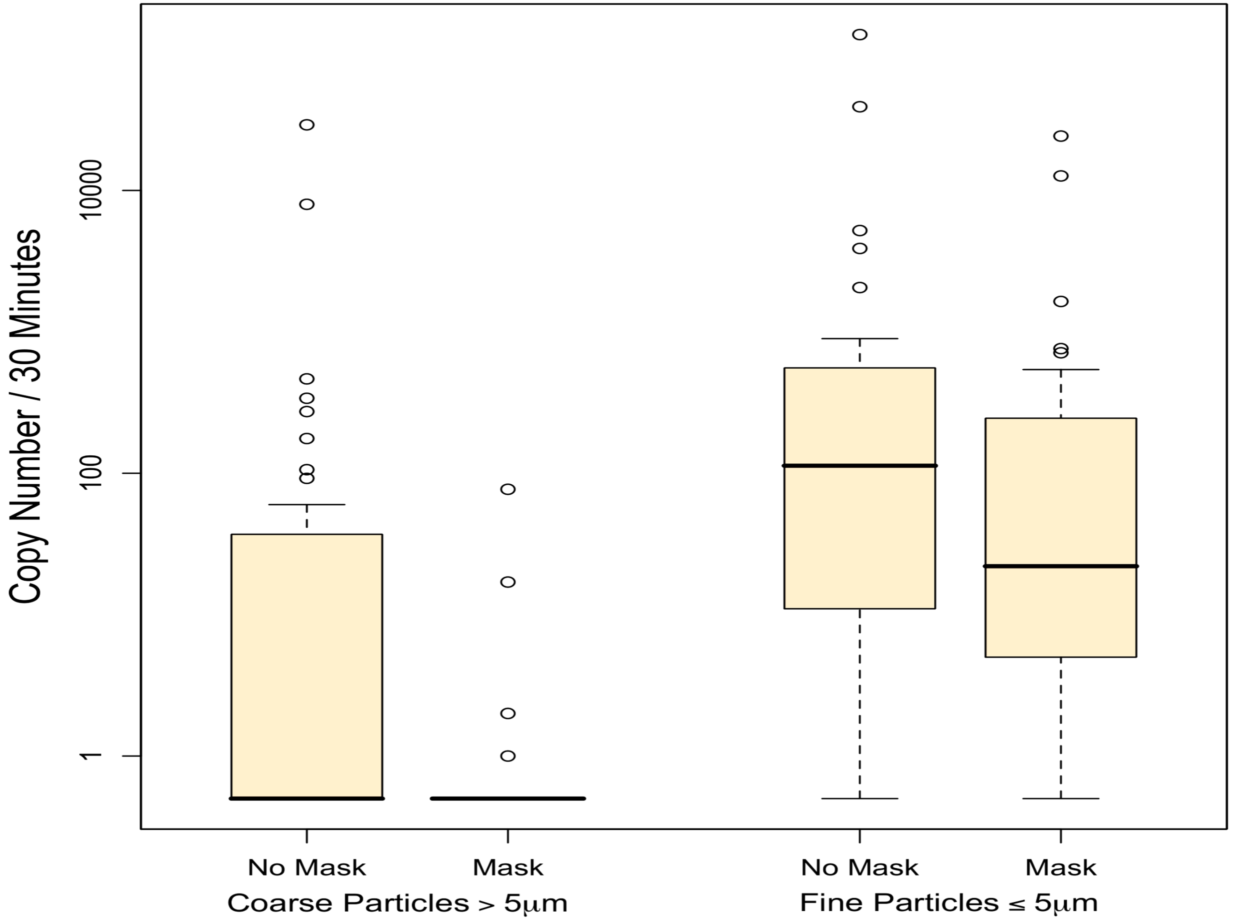
Influenza virus in exhaled breath



J. Yan *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **115**, 1081–1086 (2018)

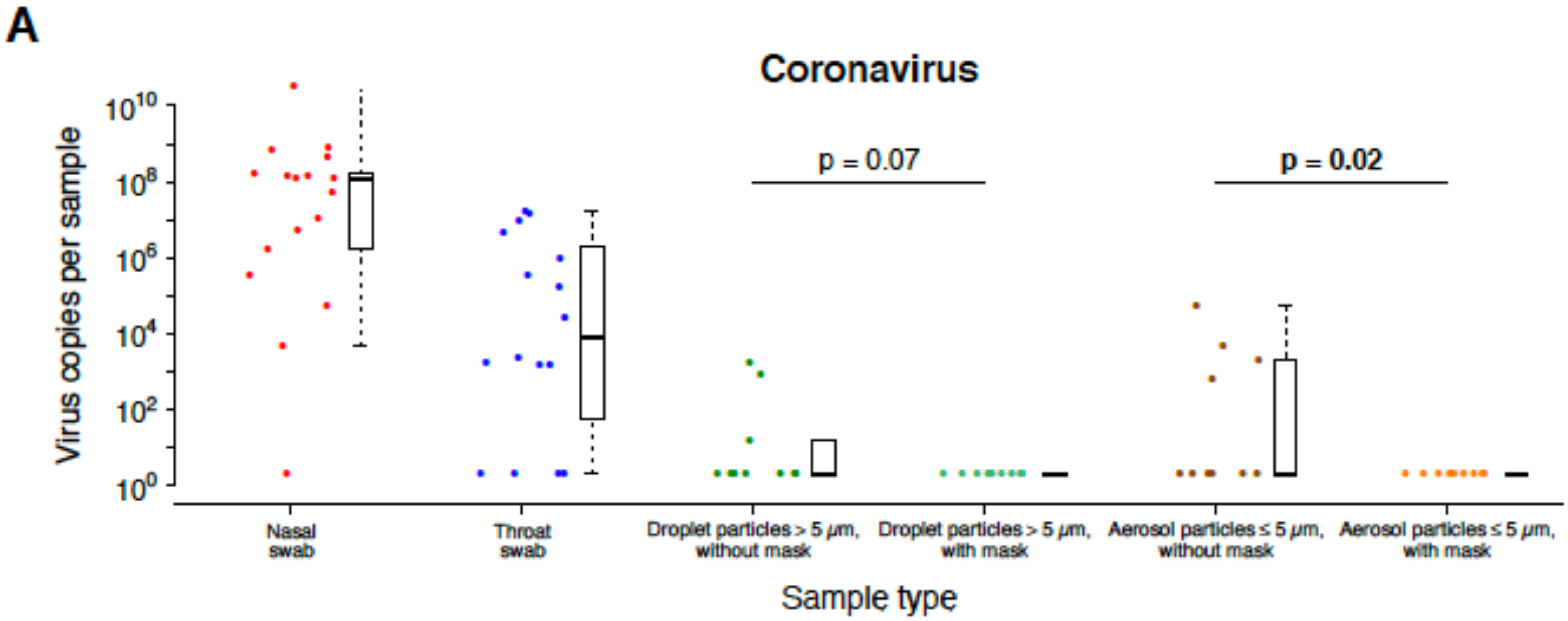
Masks as Source Control

Influenza Virus Copy Number In Aerosol Particles Exhaled By Patients With And Without Wearing Of An Ear-loop Surgical Mask



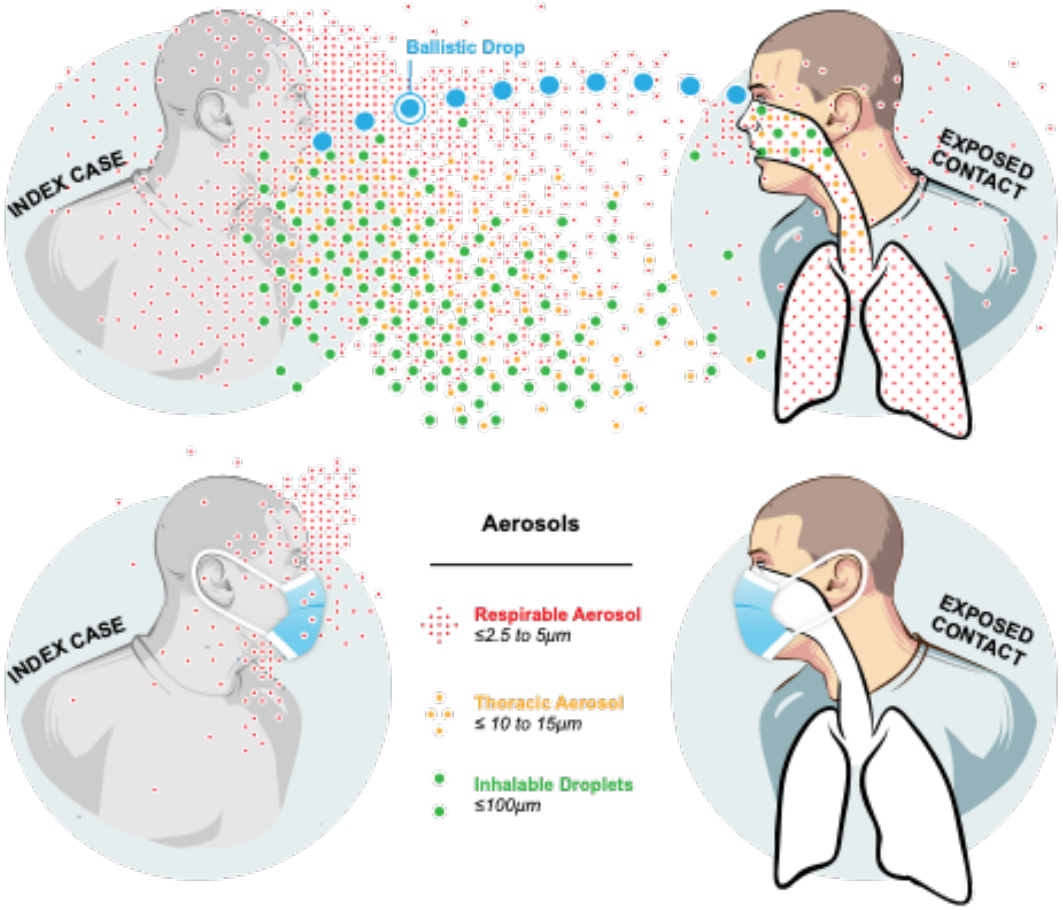
Milton DK et al. (2013) PLoS Pathog 9(3): e1003205.

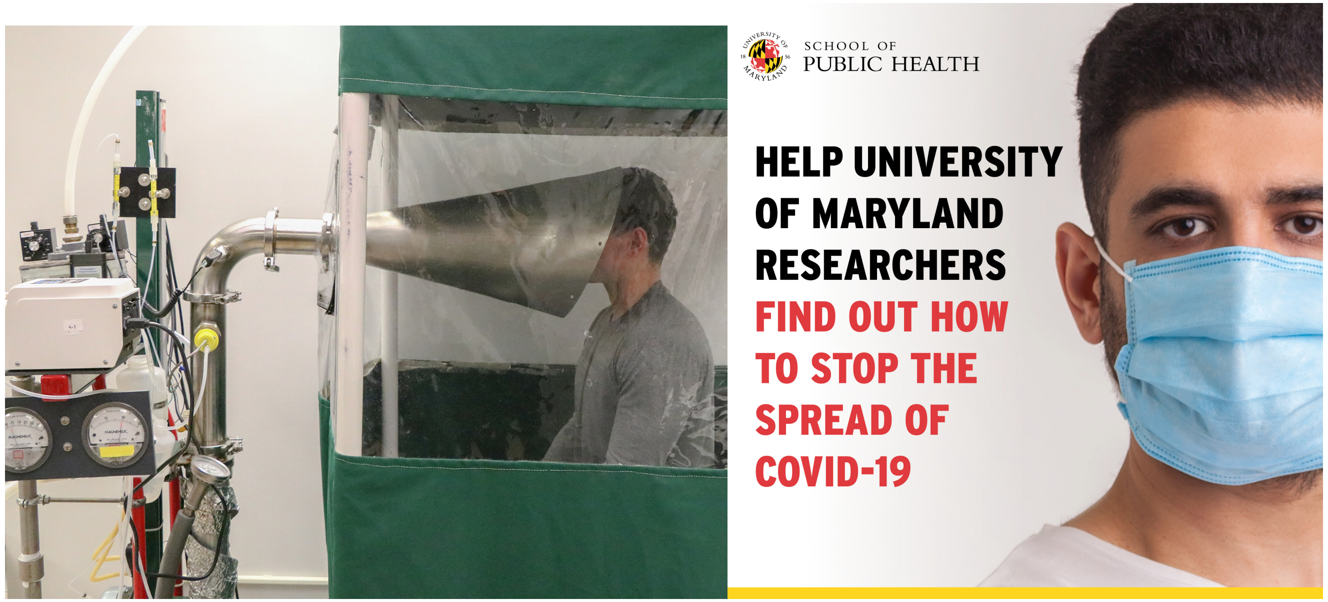
Masks as Source Control



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

Infectious aerosol generation and impact of face masks in SARS-CoV-2 infection





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