Transmission of Viruses in Droplets and Aerosols

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VIRGINIA TECH

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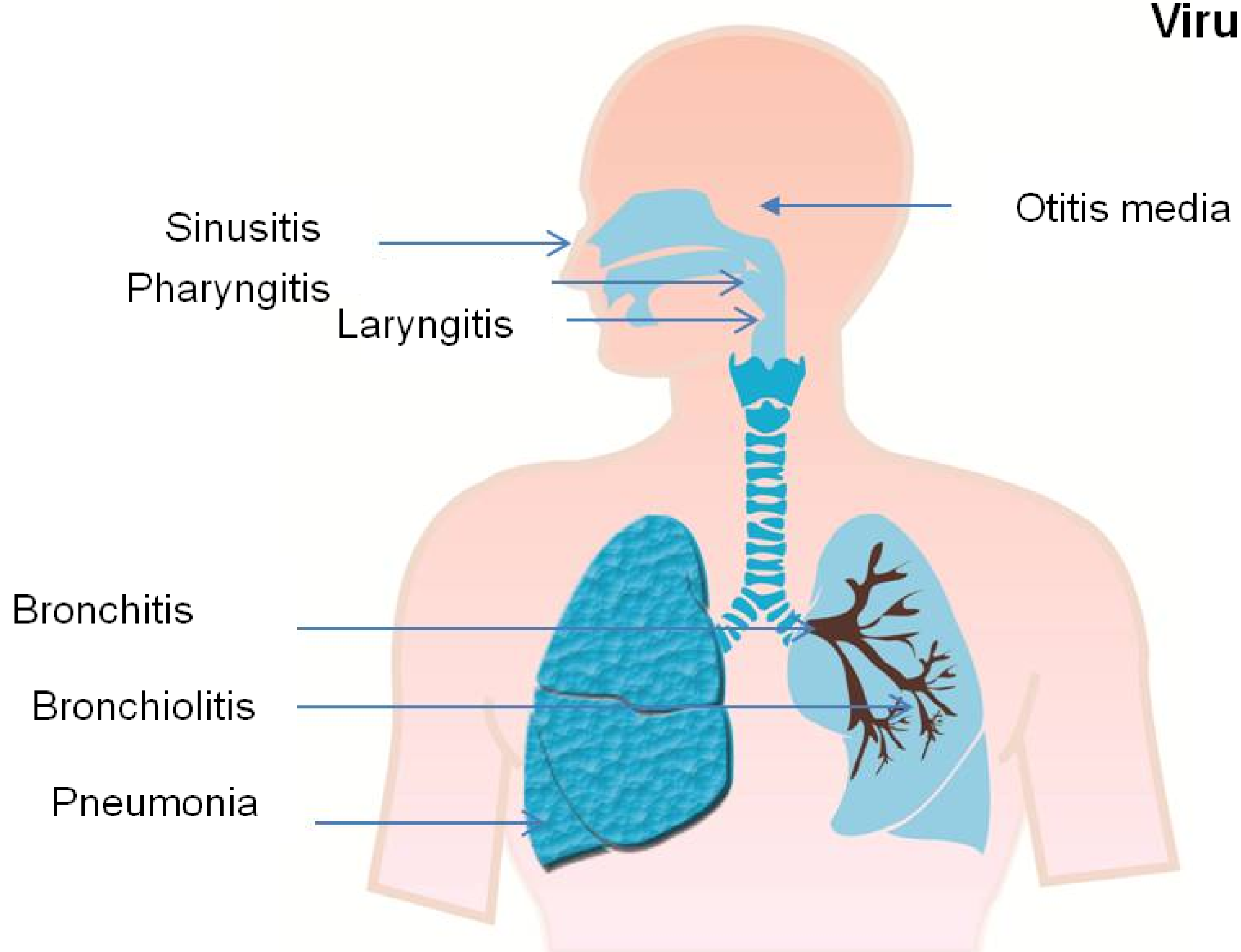
Topics

1. Respiratory viruses
2. Transmission modes
3. Size distributions and evaporation
4. Virus aerosol dynamics
5. Impact of temperature and humidity
6. Masks
7. SARS-CoV-2

https://phil.cdc.gov/Details.aspx?pid=11160

Viruses that infect the upper respiratory tract

- Rhinovirus
- Coronavirus
- Influenza virus
- Parainfluenza virus
- Respiratory Syncytial virus
- Herpesvirus
- Adenovirus
- Bocavirus
- Coxsackivirus

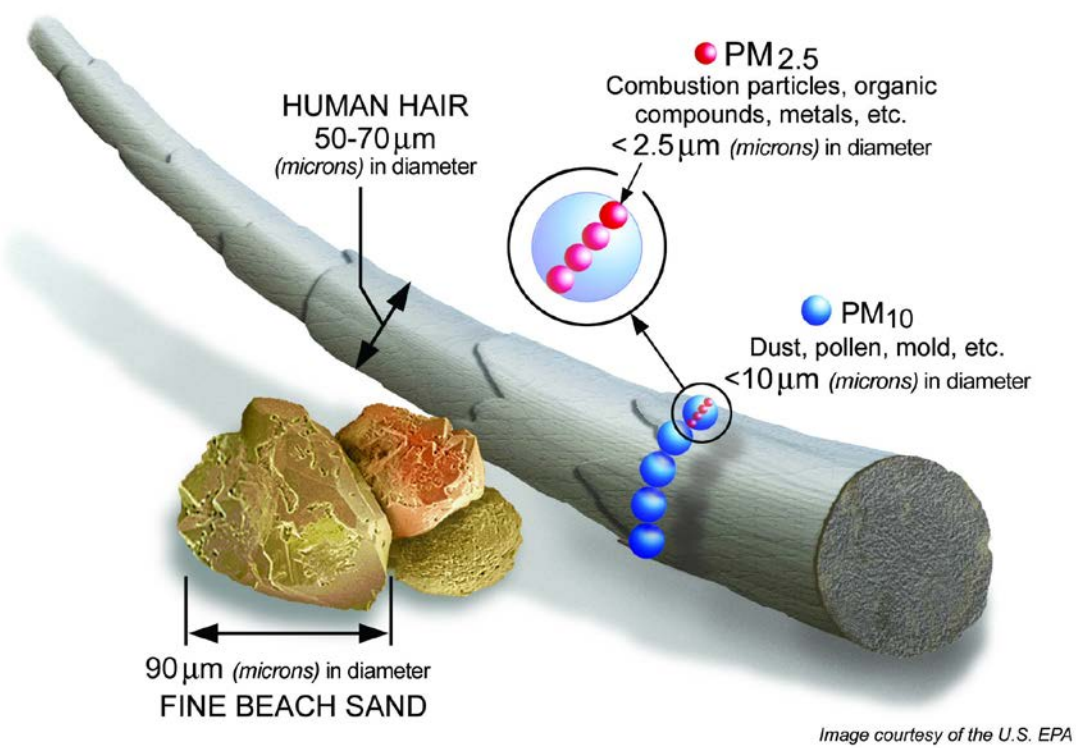


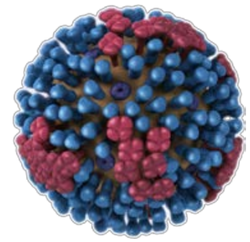
Viruses that infect the lower respiratory tract

- Influenza virus
- Parainfluenza virus
- Respiratory Syncytial virus
- Adenovirus
- Bocavirus
- Metapneumovirus

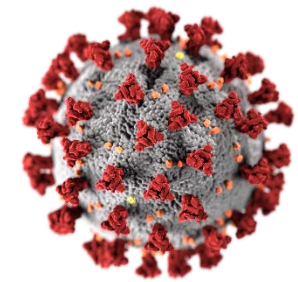
https://www.intechopen.com/books/respiratory-disease-and-infection-a-new-insight/pathogenesis-of-viral-respiratory-infection

Virus Size

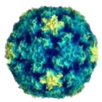




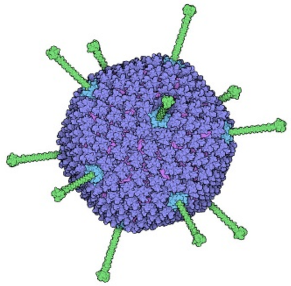
influenza
0.1 μm



SARS-CoV-2
0.12 μm



rhinovirus
0.03 μm

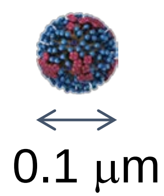


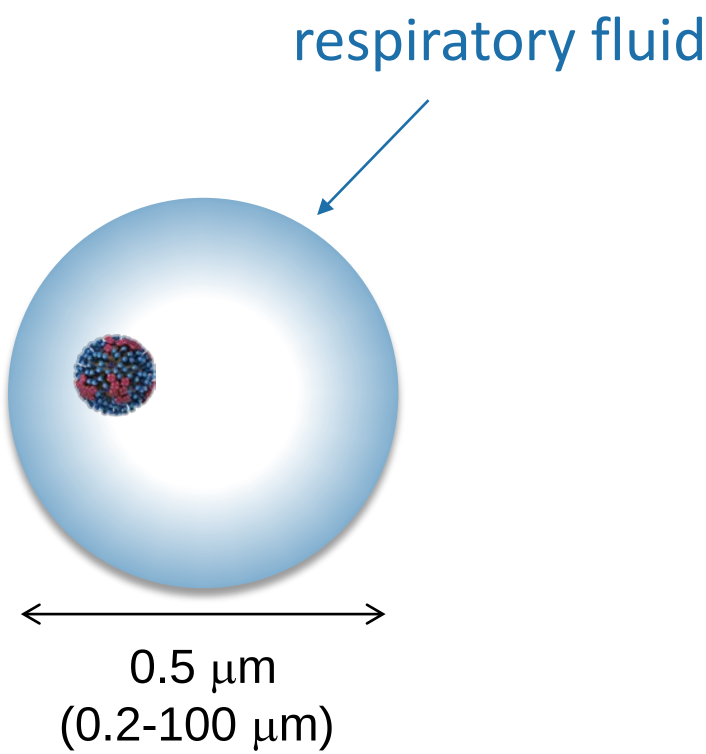
adenovirus
0.1 μm

https://www.cdc.gov/flu/resource-center/freeresources/graphics/images.htm, https://solutionsdesignedforhealthcare.com/rhinovirus, https://phil.cdc.gov/Details.aspx?pid=23312, https://pdb101.rcsb.org/motm/132

Size Matters

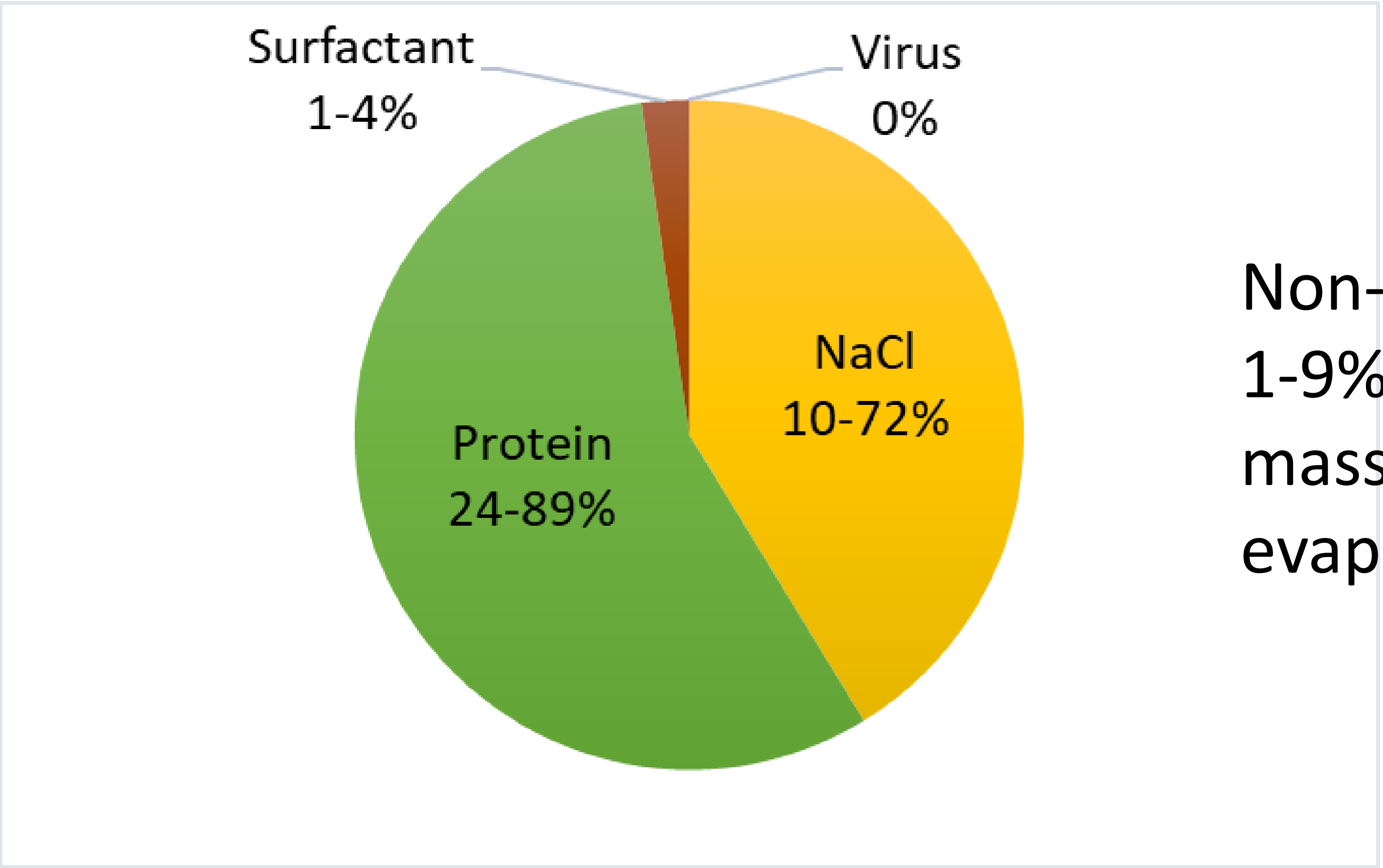
- Airborne virus is not naked!





- Size determines
  - Lifetime in the atmosphere
  - Where it deposits in the respiratory system

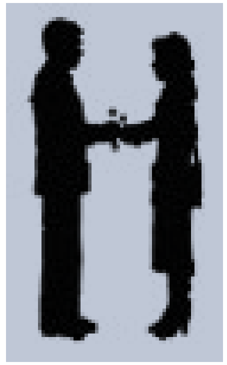
Droplet Composition



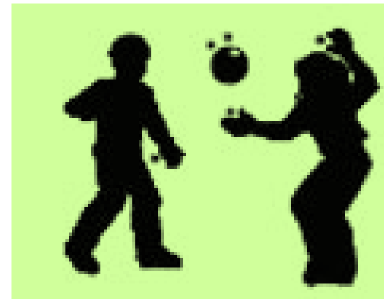
Non-volatiles are 1-9% of initial mass (before evaporation)

Vejerano and Marr, 2018, *J. R. Soc. Interface,* https://royalsocietypublishing.org/doi/10.1098/rsif.2017.0939; Marr et al., 2019, *J. R. Soc. Interface*, https://royalsocietypublishing.org/doi/full/10.1098/rsif.2018.0298

Modes of Transmission

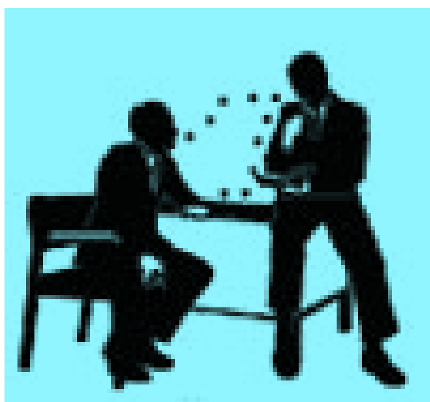


direct contact

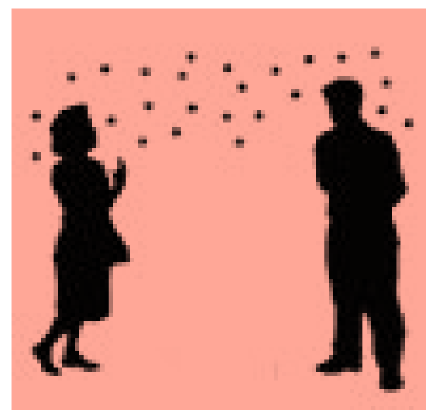


indirect contact

Defined as >5 μm and happening at close-range only (<2 m)



large droplets



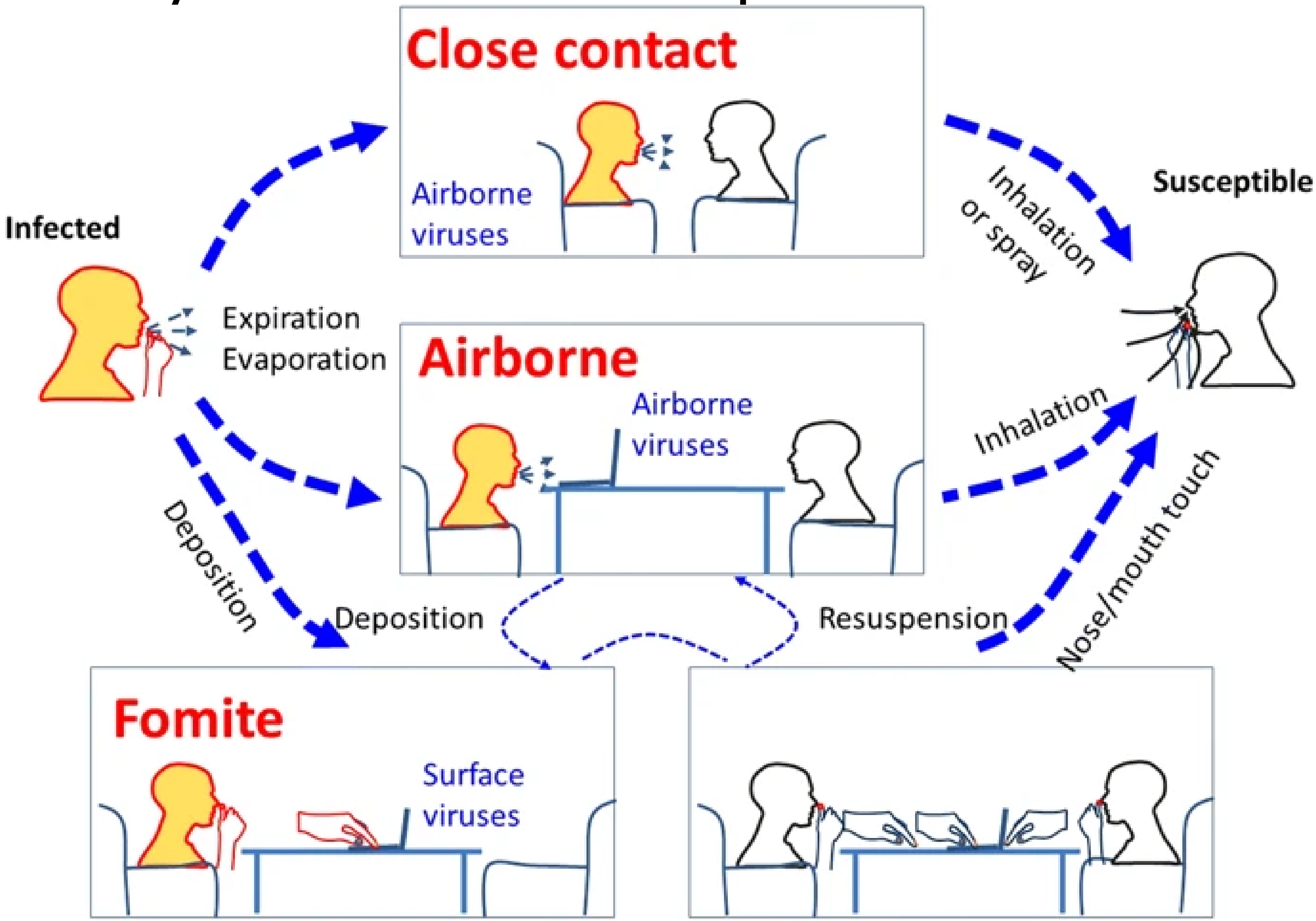
aerosols

Defined as <5 μm and happening mainly at long-distance (>2 m)

The origin of the 5-μm cutoff is not clear. This cutoff is not supported by modern aerosol science. This distinction has hampered our understanding of transmission.

http://www.phac-aspc.gc.ca/cpip-pclcpi/annf/v2-eng.php

Reality is More Complicated

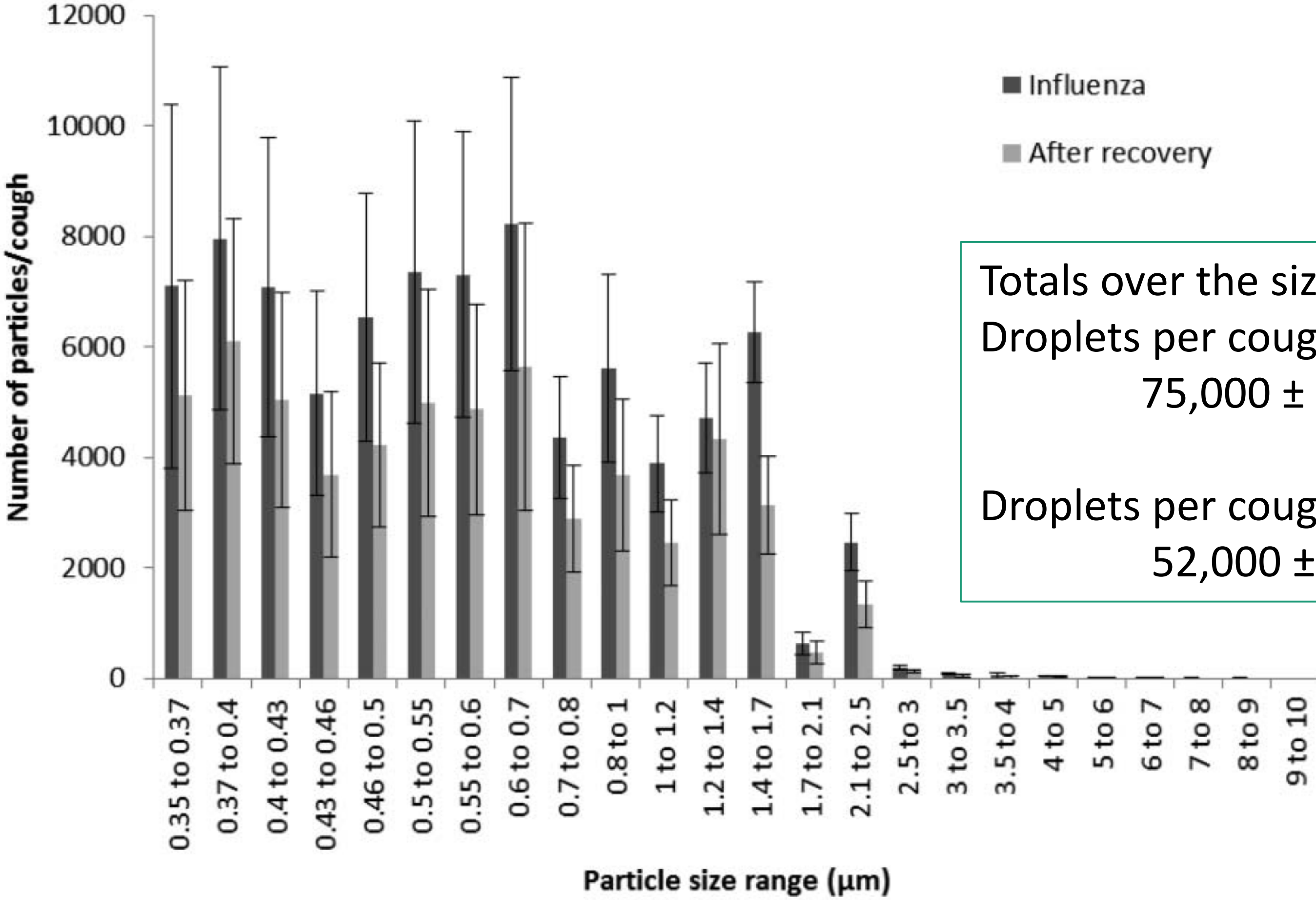


Tellier et al., 2019, *BMC Infect. Dis*, https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-019-3707-y

Droplets that are expelled into air can be inhaled, land on people's mucus membranes, or deposit onto surfaces, where someone can touch them or they can be resuspended into air.

How many droplets are there, and how big or small are they?

Number of Droplets Emitted



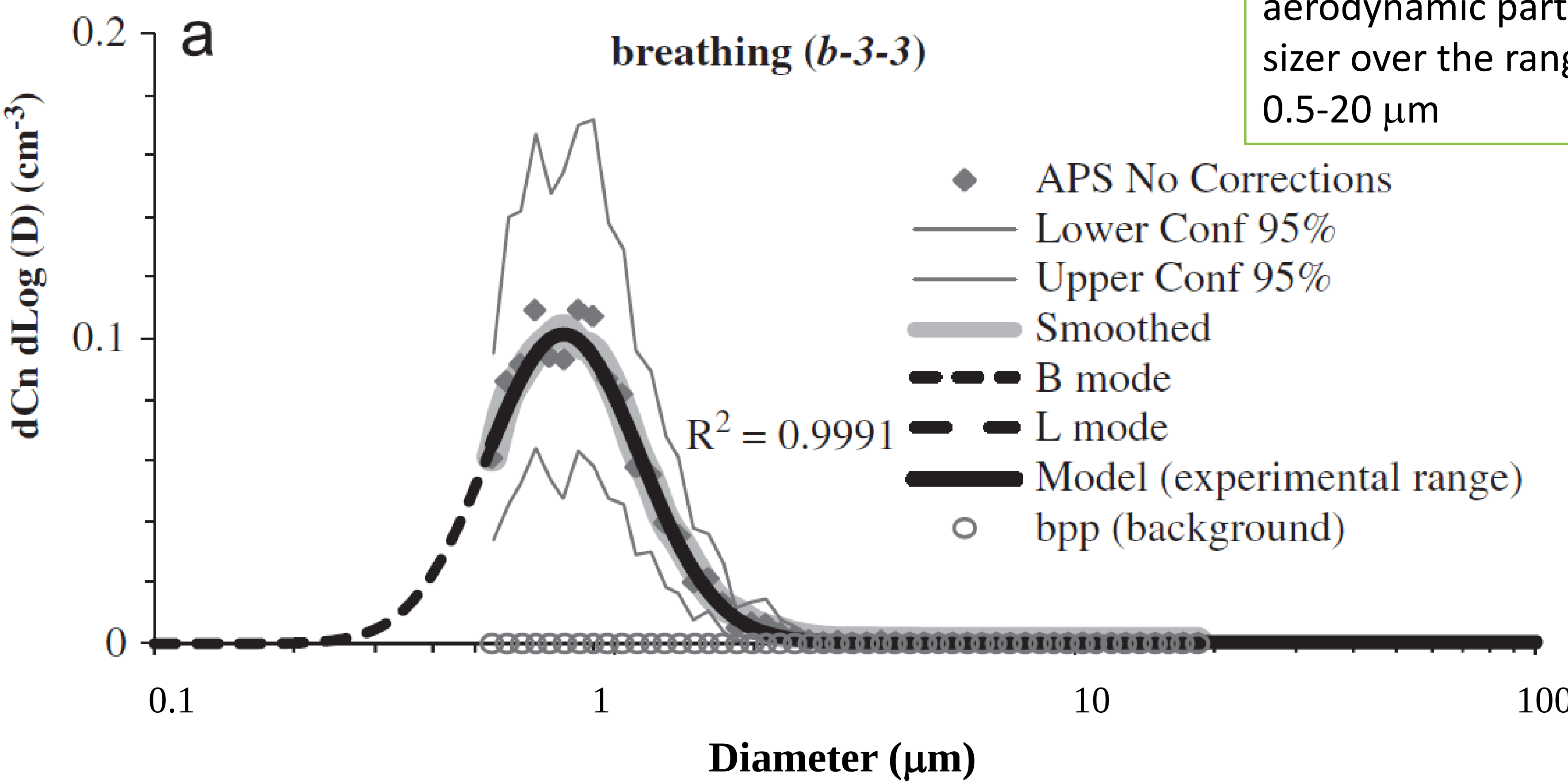
Totals over the size range 0.35-10 µm:
Droplets per cough when sick
75,000 ± 97,000

Droplets per cough after recovery
52,000 ± 99,000

Lindsley et al., 2012, *J. Occupat. Environ. Hyg.*, https://www.ncbi.nlm.nih.gov/pubmed/22651099

Size Distributions: Breathing

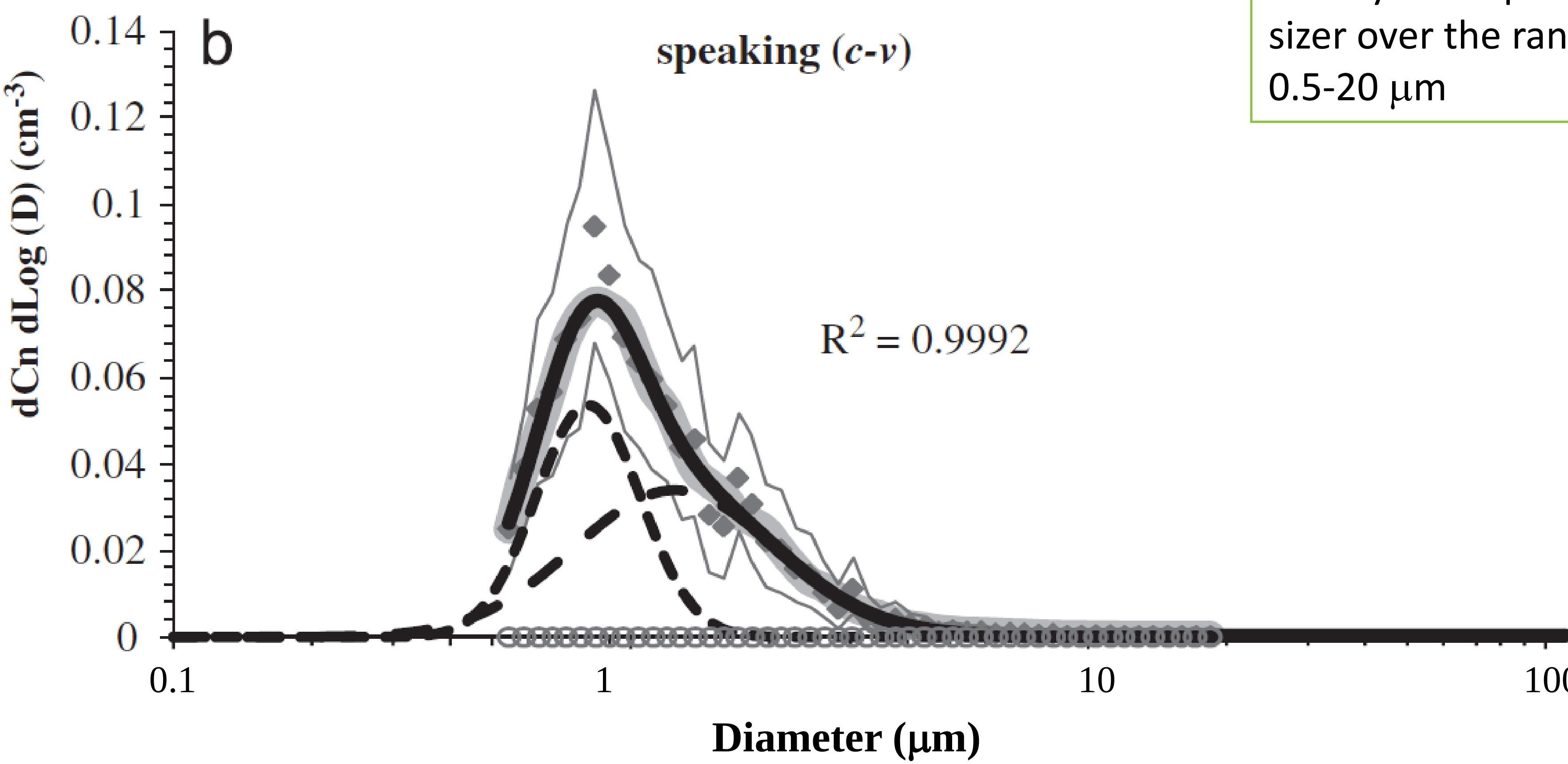
Measured by aerodynamic particle sizer over the range 0.5-20 μm



Johnson et al., 2011, *J. Aerosol Sci.*, https://www.sciencedirect.com/science/article/pii/S0021850211001200

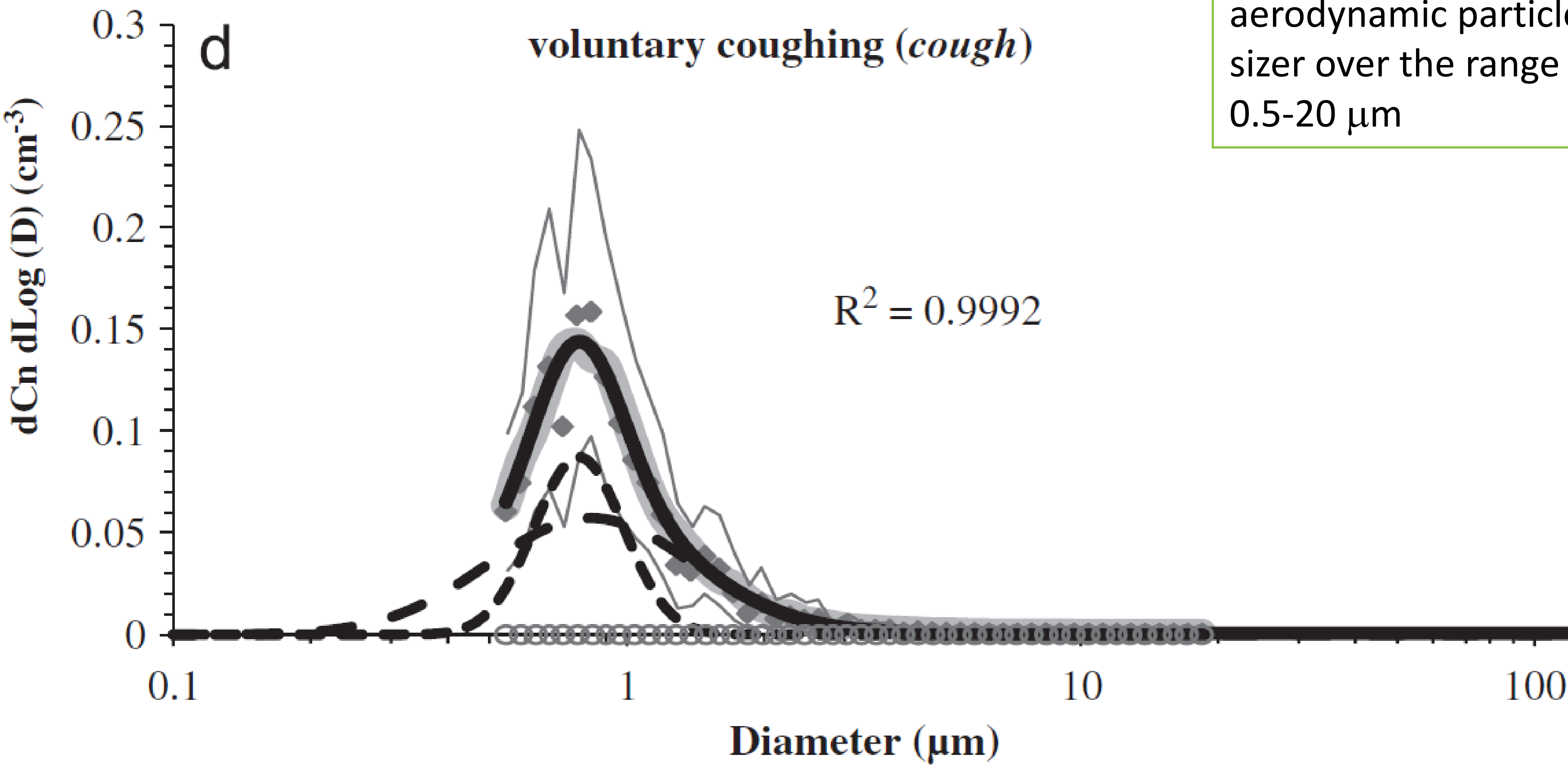
Size Distributions: Speaking

Measured by aerodynamic particle sizer over the range 0.5-20 μm



Johnson et al., 2011, *J. Aerosol Sci.*, https://www.sciencedirect.com/science/article/pii/S0021850211001200

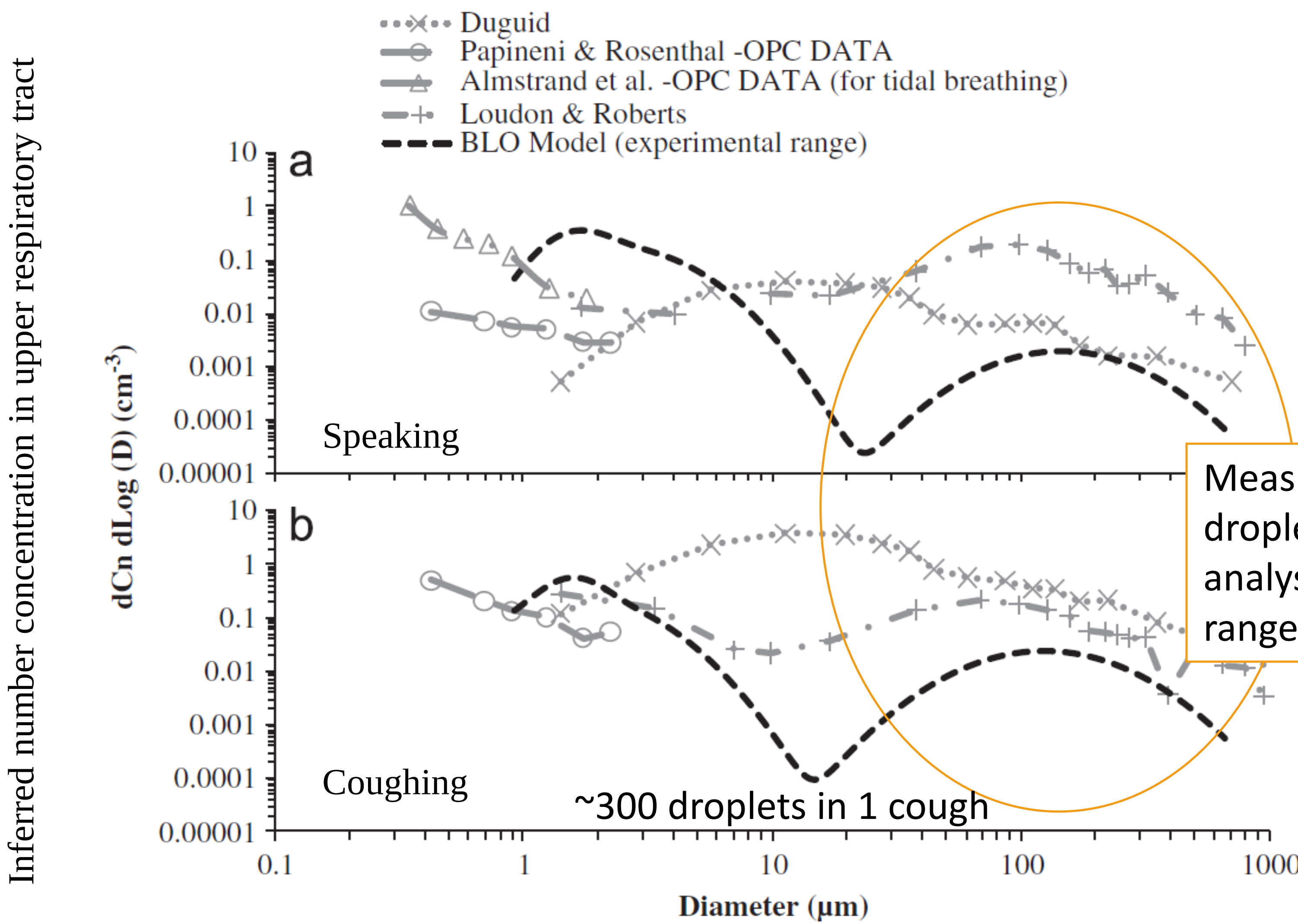
Size Distributions: Coughing



Measured by aerodynamic particle sizer over the range 0.5-20 µm

Johnson et al., 2011, *J. Aerosol Sci.*, https://www.sciencedirect.com/science/article/pii/S0021850211001200

Corrected Size Distributions



Measured by droplet deposition analysis over the range 20-2000 μm

~300 droplets in 1 cough

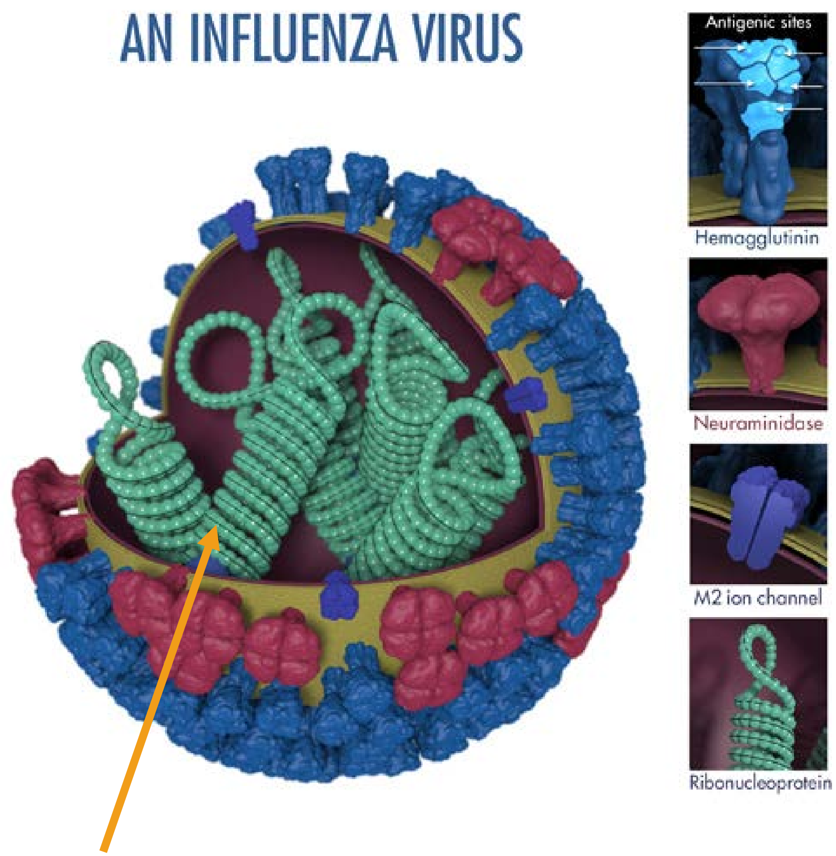
Johnson et al., 2011, *J. Aerosol Sci.*, https://www.sciencedirect.com/science/article/pii/S0021850211001200

Breathing, talking, and coughing release droplets that range from submicron to millimeter in size.

What size droplets carry viruses?

Virus Detection Methods

1. Total virus
    - Number of genome copies (GC) determined by molecular techniques (quantitative polymerase chain reaction, qPCR)
    - Reflects number of viruses with intact DNA or RNA
    - Does NOT indicate whether virus is infectious or not

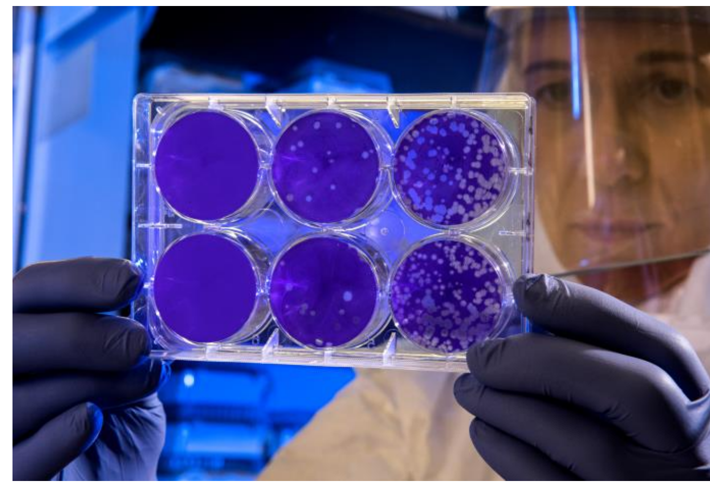


RNA is wrapped around the ribonucleoprotein

https://www.cdc.gov/flu/resource-center/freeresources/graphics/images.htm

Virus Detection Methods

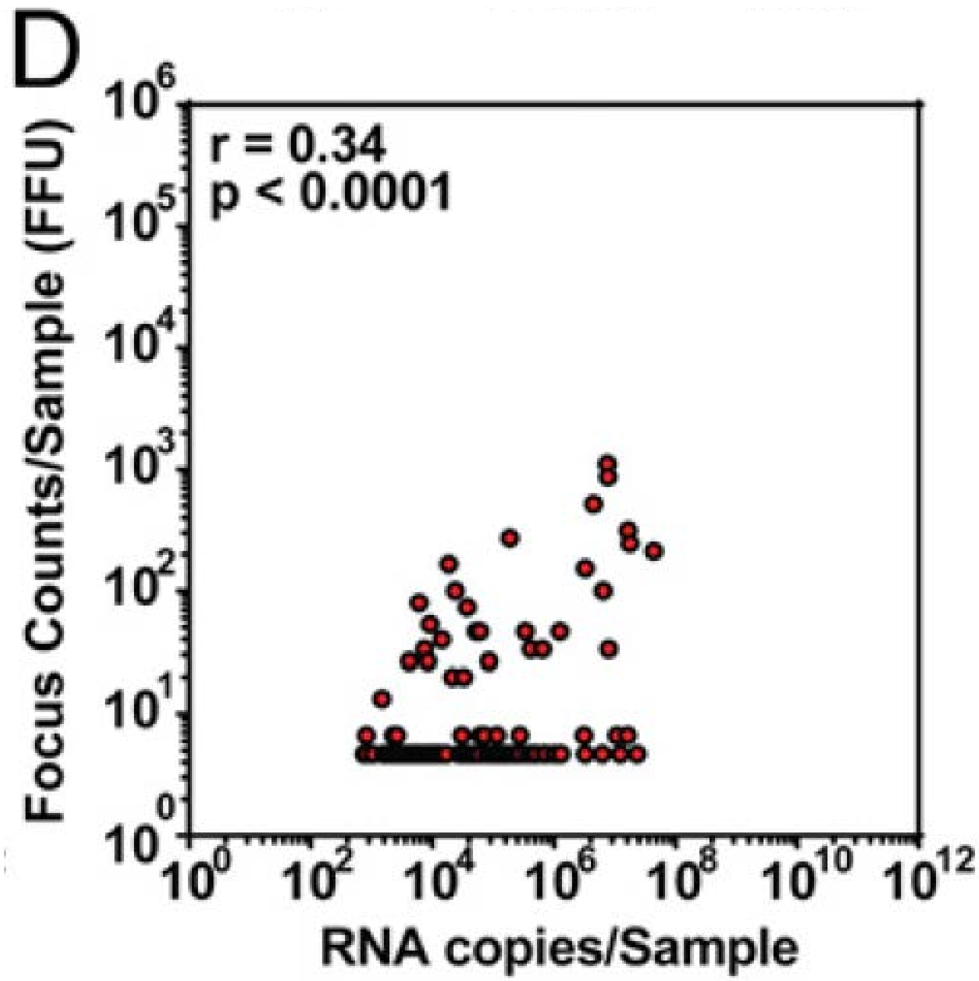
2. Infectious virus
   - Number of viruses that are able to infect cells determined by culture (growing)
   - PFU = plaque forming units, number of viruses capable of forming plaques on host cells, focus forming units (FFU) are related



   - $TCID_{50}$ = median tissue culture infectious dose, concentration at which half of cells are infected after being exposed to the sample

https://phil.cdc.gov/Details.aspx?pid=23213

Relationship Between the Two Methods for Flu Virus



There is a weak, but significant, correlation between virus RNA copies and infectious virus.

Yan et al., 2018, *PNAS*, https://www.ncbi.nlm.nih.gov/pubmed/29348203

Amount of Flu Virus in Coarse vs. Fine Droplets (Particles) in Exhaled Breath

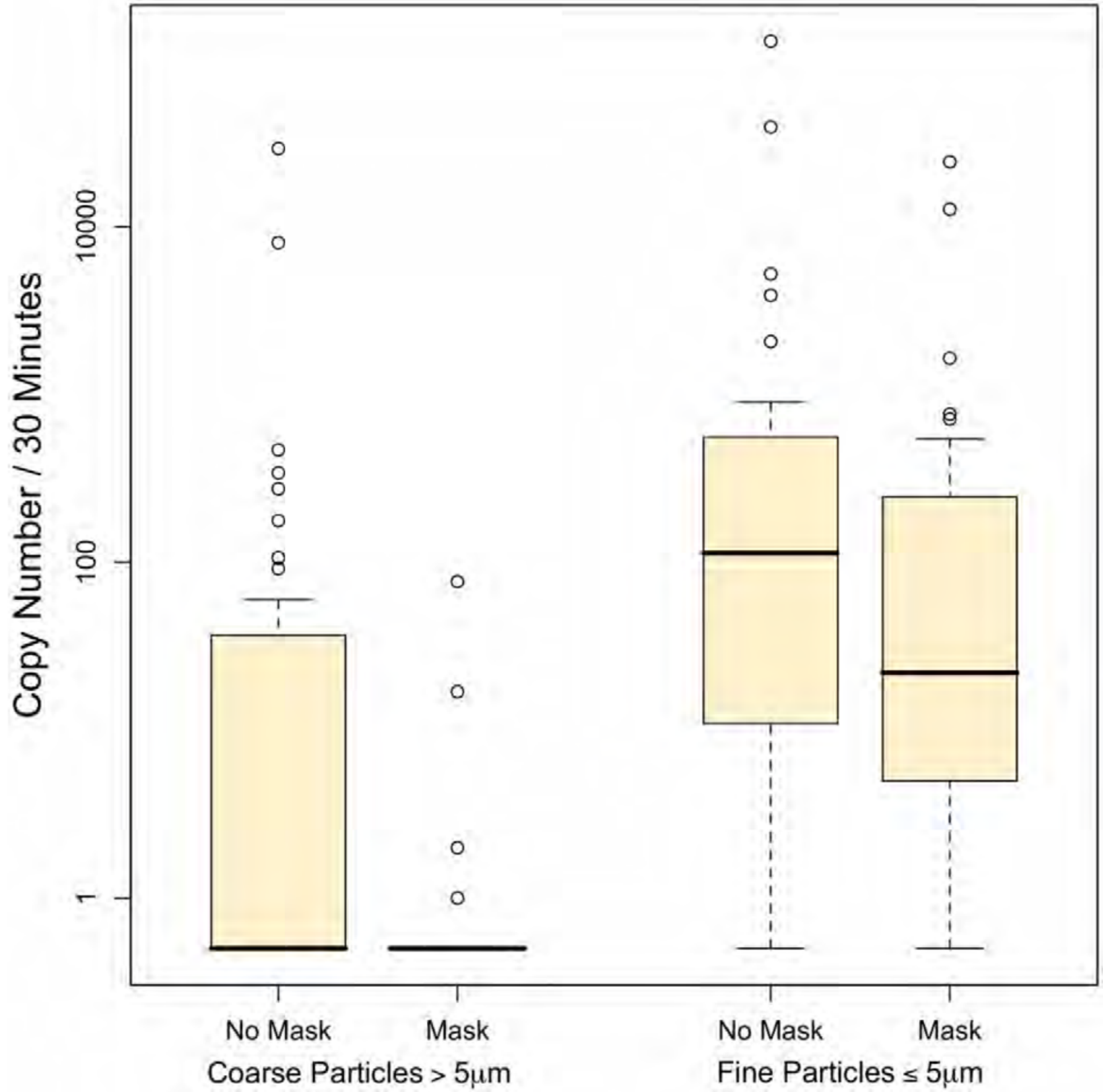
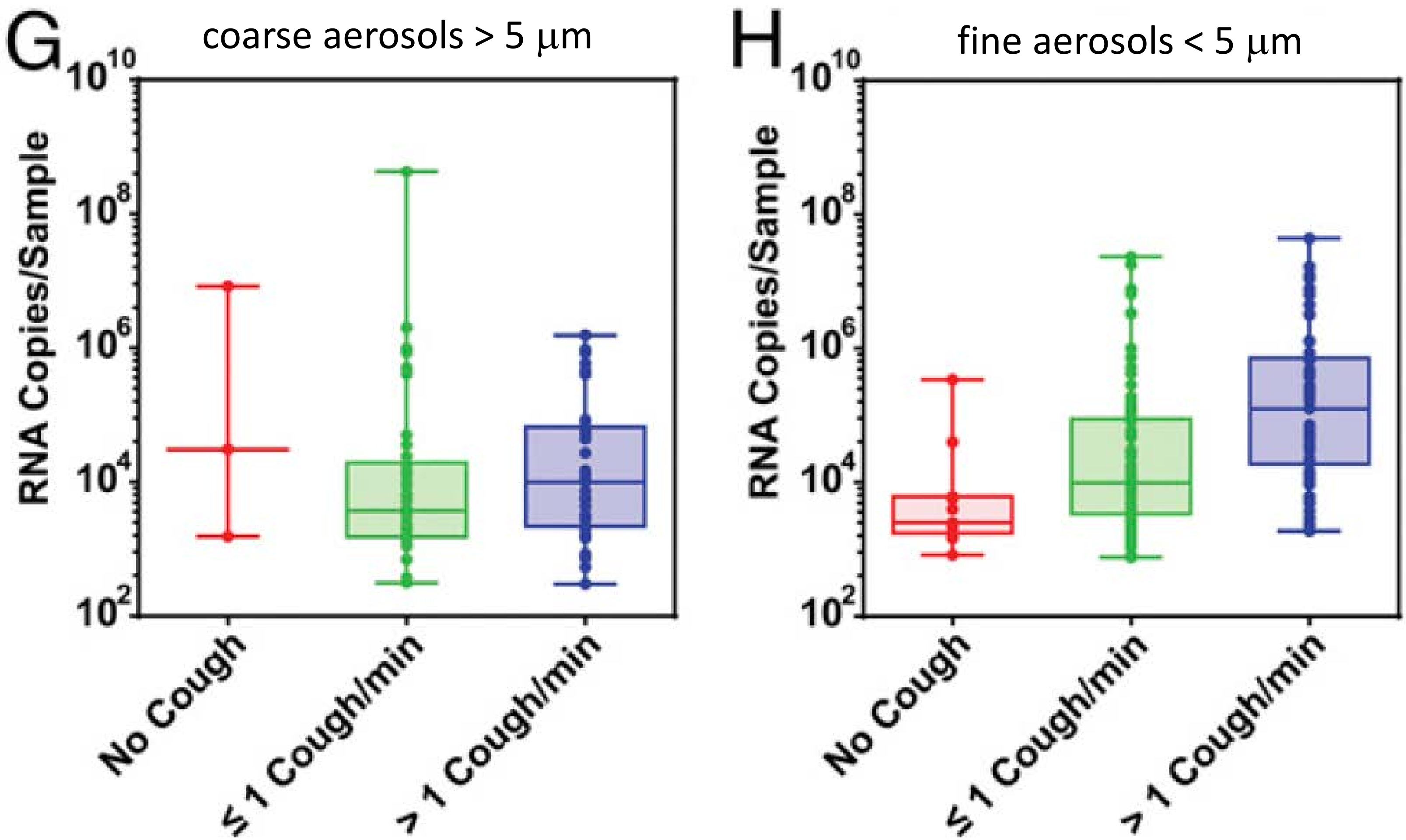


Figure 1. Influenza virus copy number in aerosol particles exhaled by patients with and without wearing of an ear-loop surgical mask. Counts below the limit of detection are represented as 0.5 on the log scale.
doi:10.1371/journal.ppat.1003205.g001

Milton et al., 2013, *PLoS Pathogens*, https://www.ncbi.nlm.nih.gov/pubmed/23505369

Flu Virus in Droplets (Aerosols)



30-min sample
recite alphabet at 5, 15, 25 min

Yan et al., 2018, *PNAS*, https://www.ncbi.nlm.nih.gov/pubmed/29348203

The majority of flu virus (RNA copies) is found in fine (<5 μm), rather than coarse (>5 μm), droplets/aerosols.

How do these droplets move around the indoor environment?

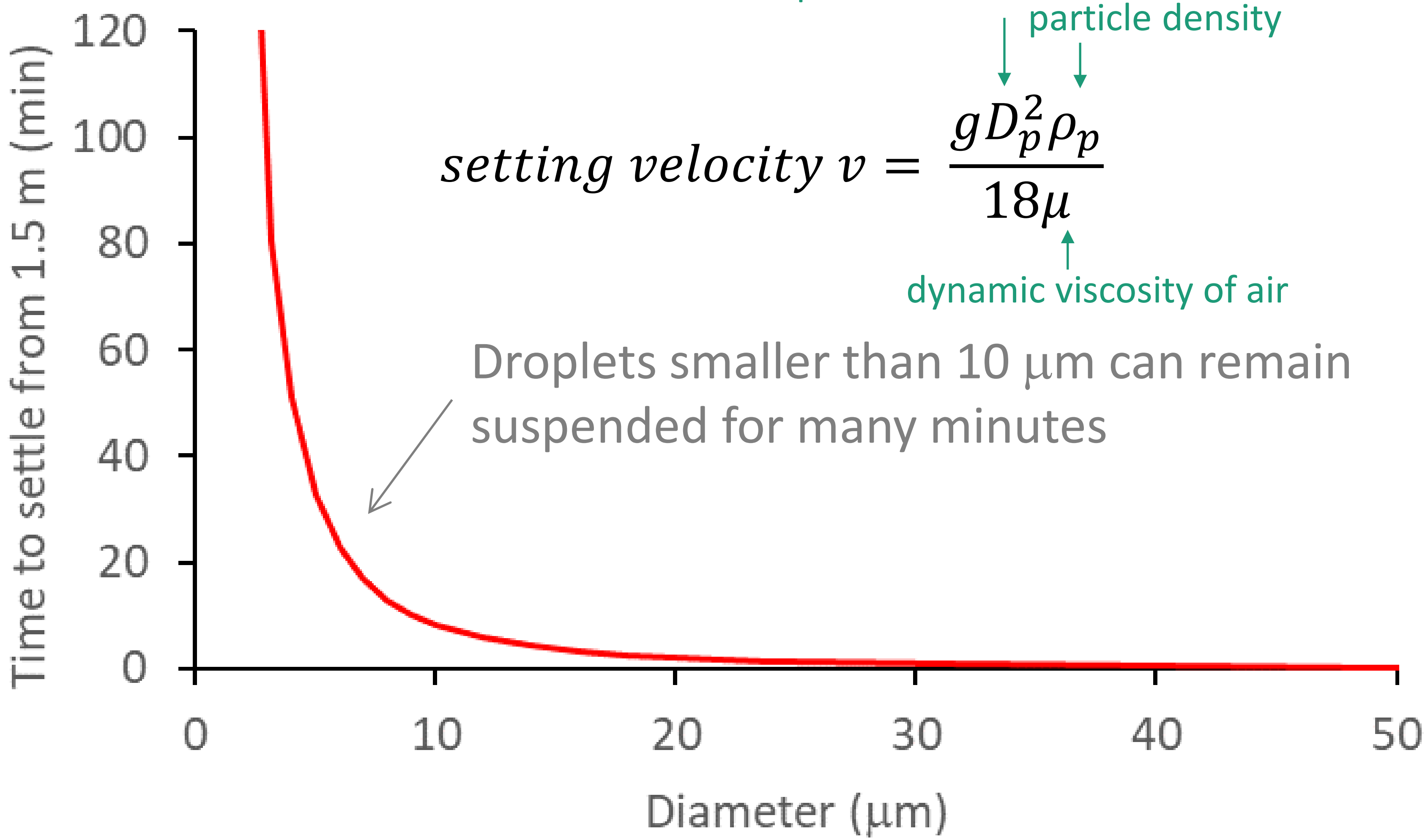
Settling Velocity and Time

particle diameter

particle density

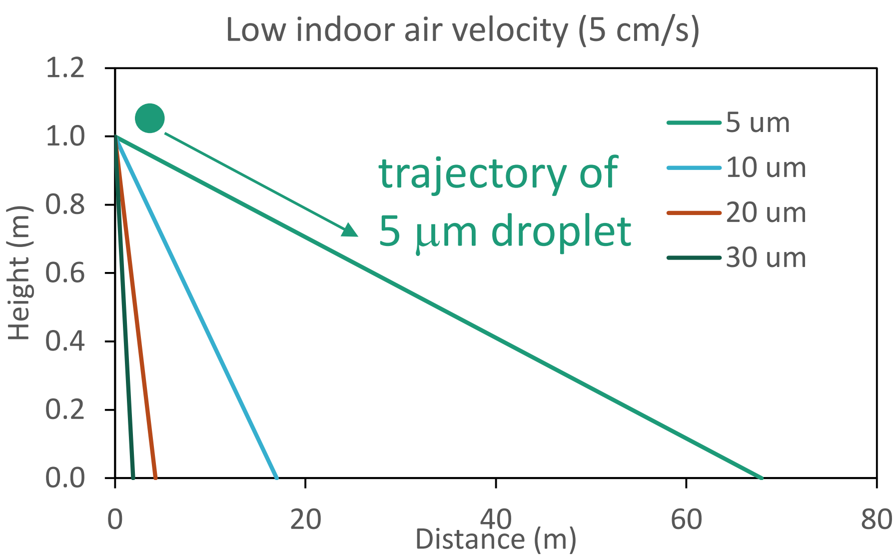
$$setting\ velocity\ v = \frac{gD_p^2\rho_p}{18\mu}$$

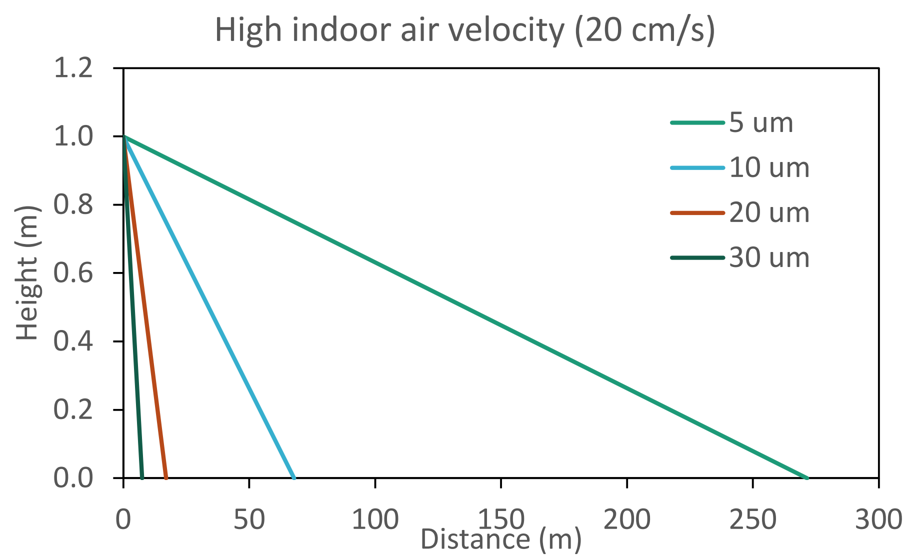
dynamic viscosity of air



Droplets Can Travel More Than 2 m

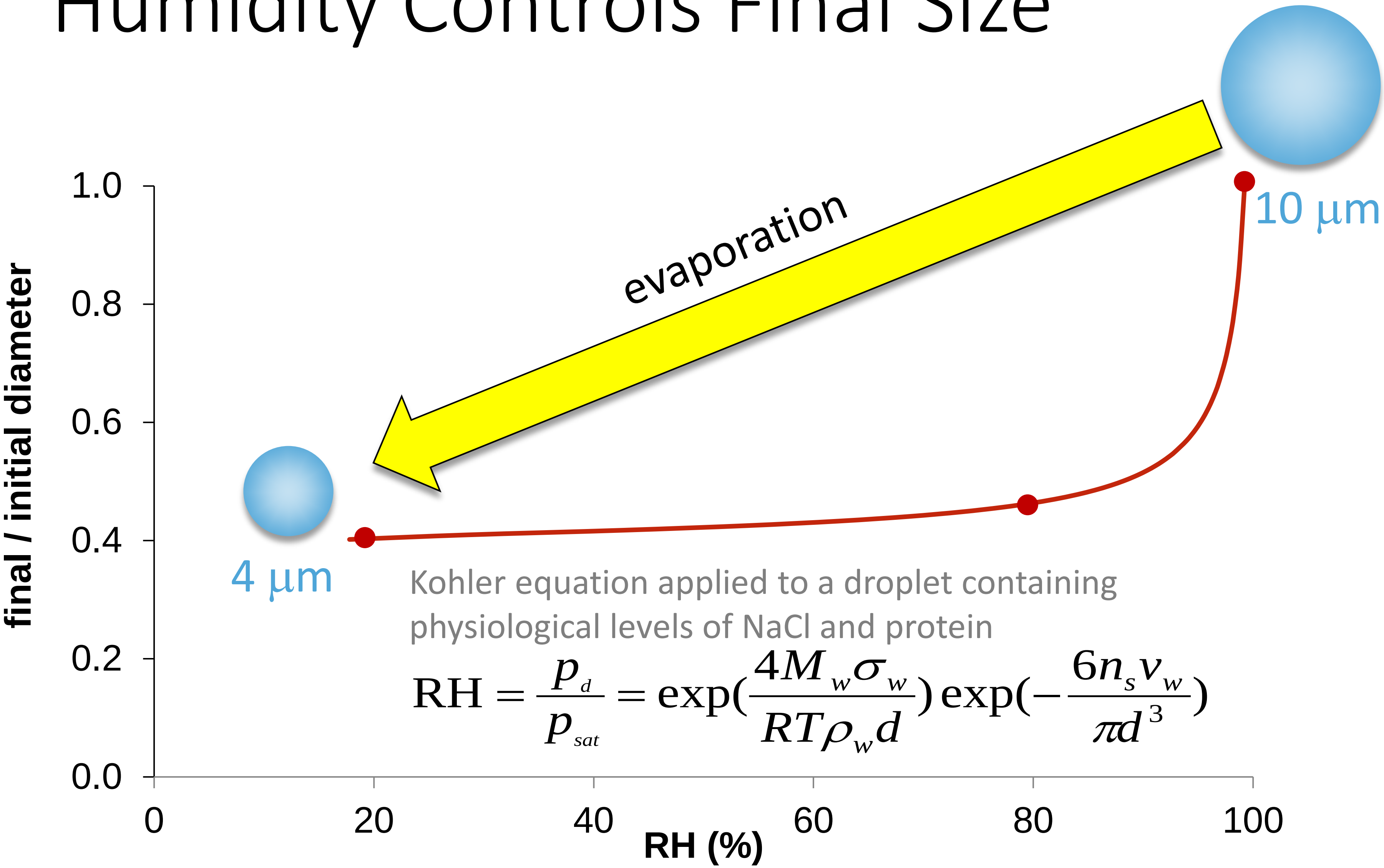
Position of droplets released from a height of 1 m





Nazaroff, 2020, personal communication

Humidity Controls Final Size

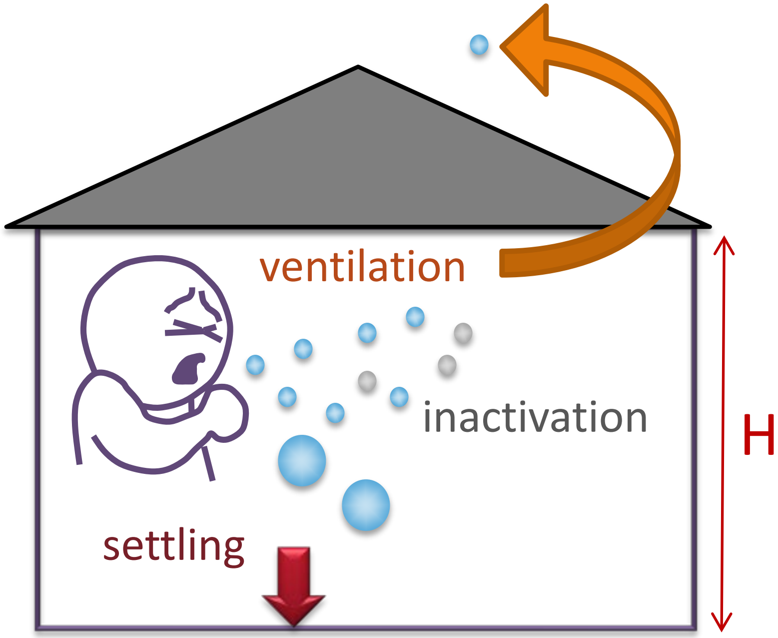


Kohler equation applied to a droplet containing physiological levels of NaCl and protein

$$\mathrm{RH} = \frac{p_d}{p_{sat}} = \exp\left(\frac{4M_w\sigma_w}{RT\rho_w d}\right)\exp\left(-\frac{6n_s v_w}{\pi d^3}\right)$$

Mikhailov, 2004, *Atmos. Chem. Phys.*, https://www.atmos-chem-phys.net/4/323/2004/

Virus Dynamics in Indoor Air



settling

ventilation (air-exchange)

inactivation

$$\frac{dC_d}{dt} = -\left(\frac{v}{H} + \lambda + k\right)C_d$$

↑

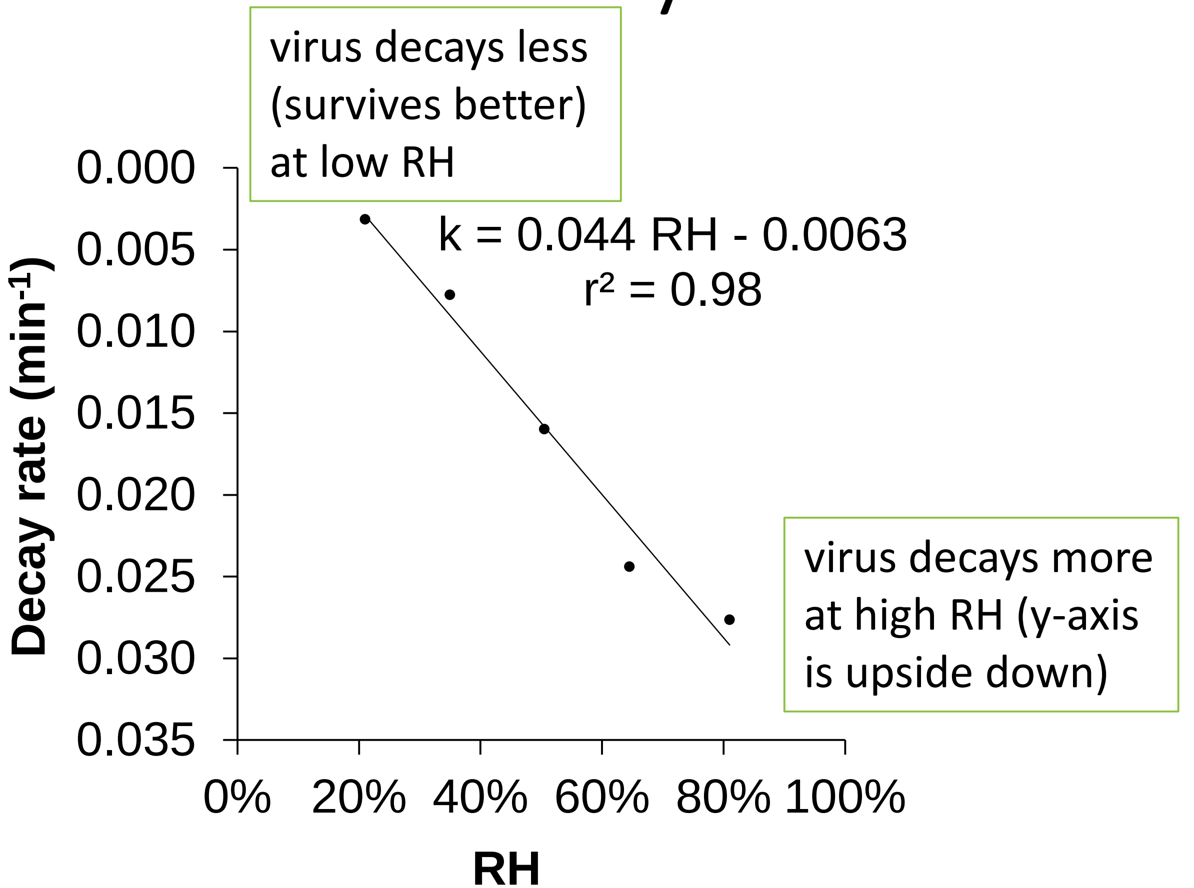
concentration of infectious virus in aerosols of <u>diameter *d*</u>

- Settling velocity *v* depends on diameter *d*
- Diameter depends on RH
- Inactivation rate *k* depends on RH

relative humidity (RH)

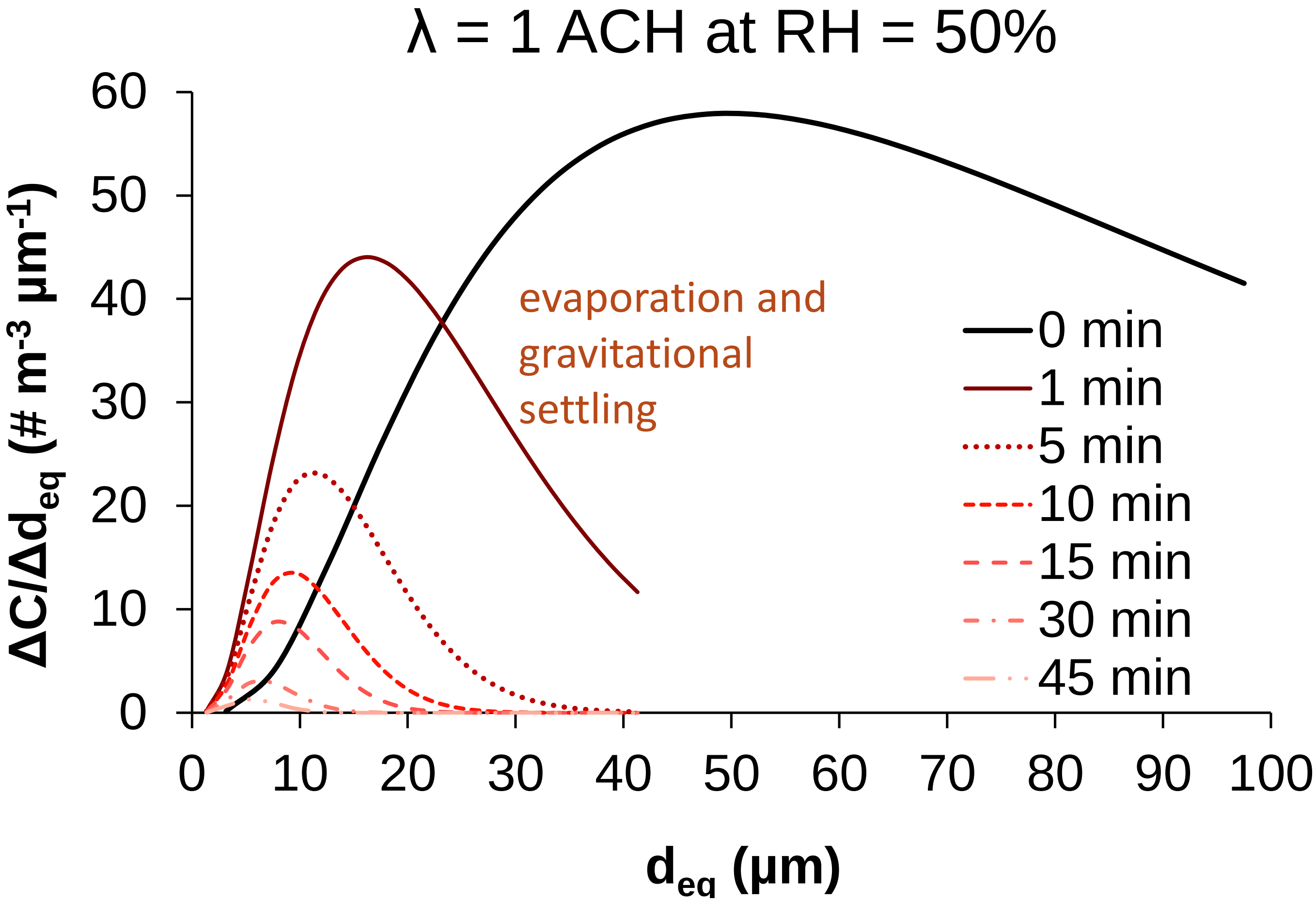
Yang and Marr, 2011, *PLoS One*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3123350/

Virus Viability vs. RH



Yang and Marr, 2011, *PLoS One*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3123350/

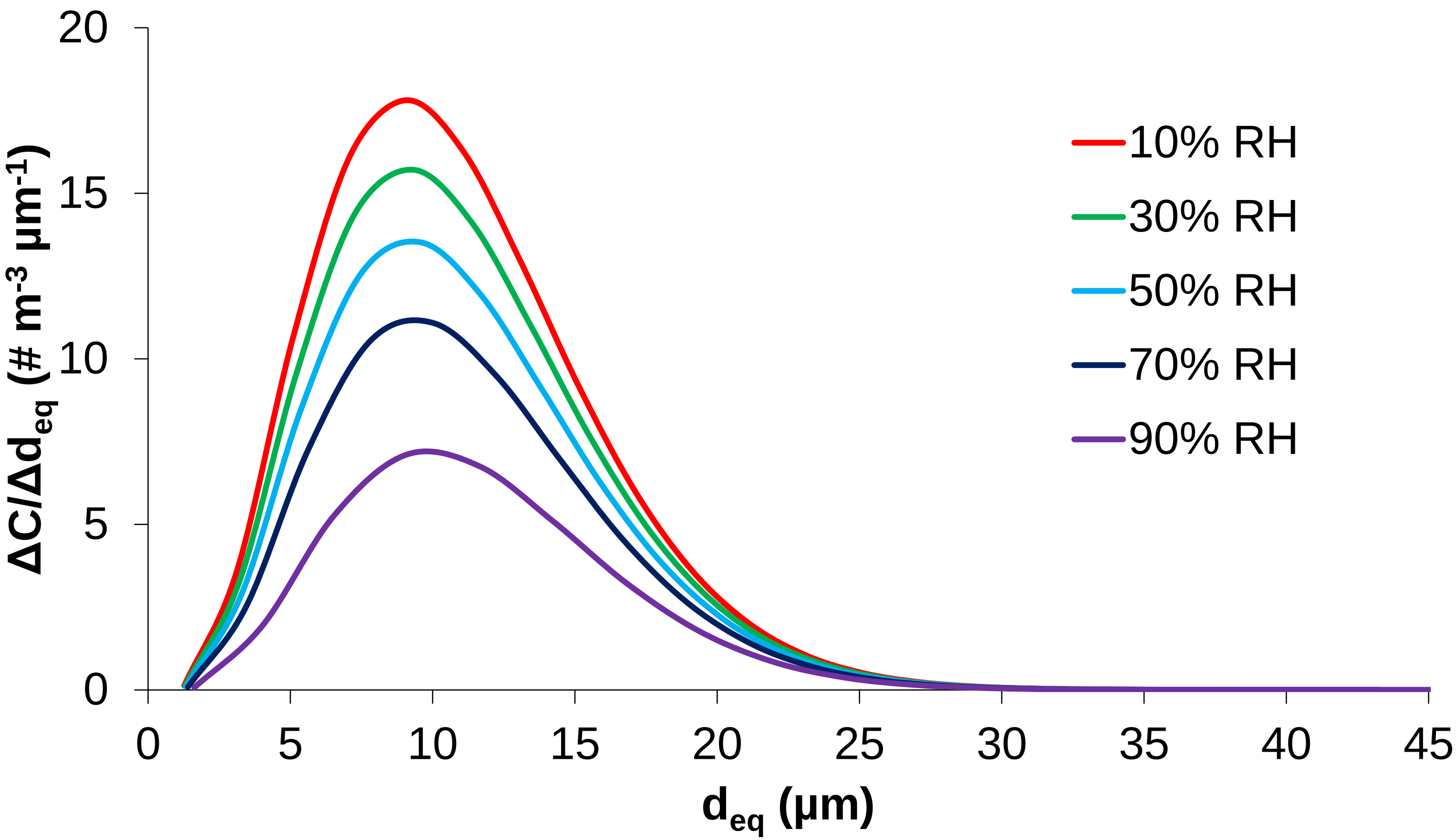
Virus-Aerosols From a Cough



There is a size shift due to loss of larger droplets by gravitational settling.

Yang and Marr, 2011, *PLoS One*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3123350/

Infectious Concentrations vs. RH

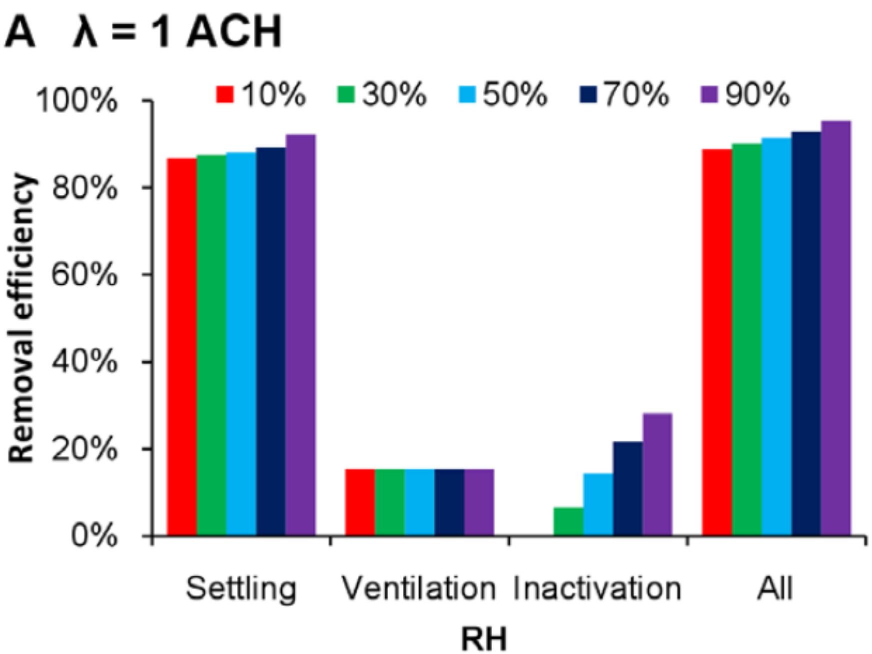


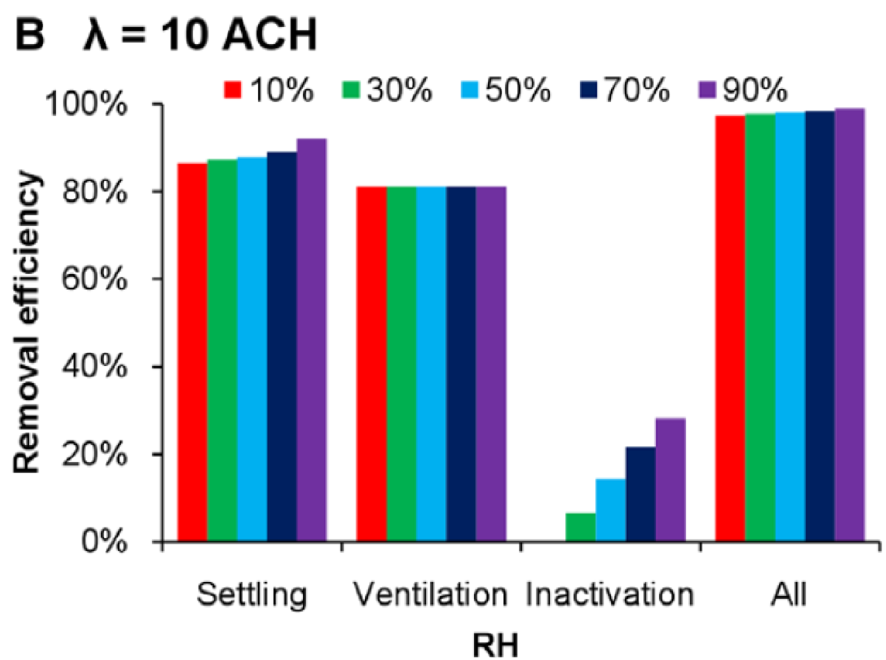
Concentrations are higher at lower RH mainly because lab-determined inactivation rate is lower.

Yang and Marr, 2011, *PLoS One*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3123350/

RH and Removal Mechanisms

- Settling: main removal mechanism, efficient for large but not small droplets
- Ventilation: effective for all sizes, important in public places
- Inactivation: effective for all sizes, important for small droplets



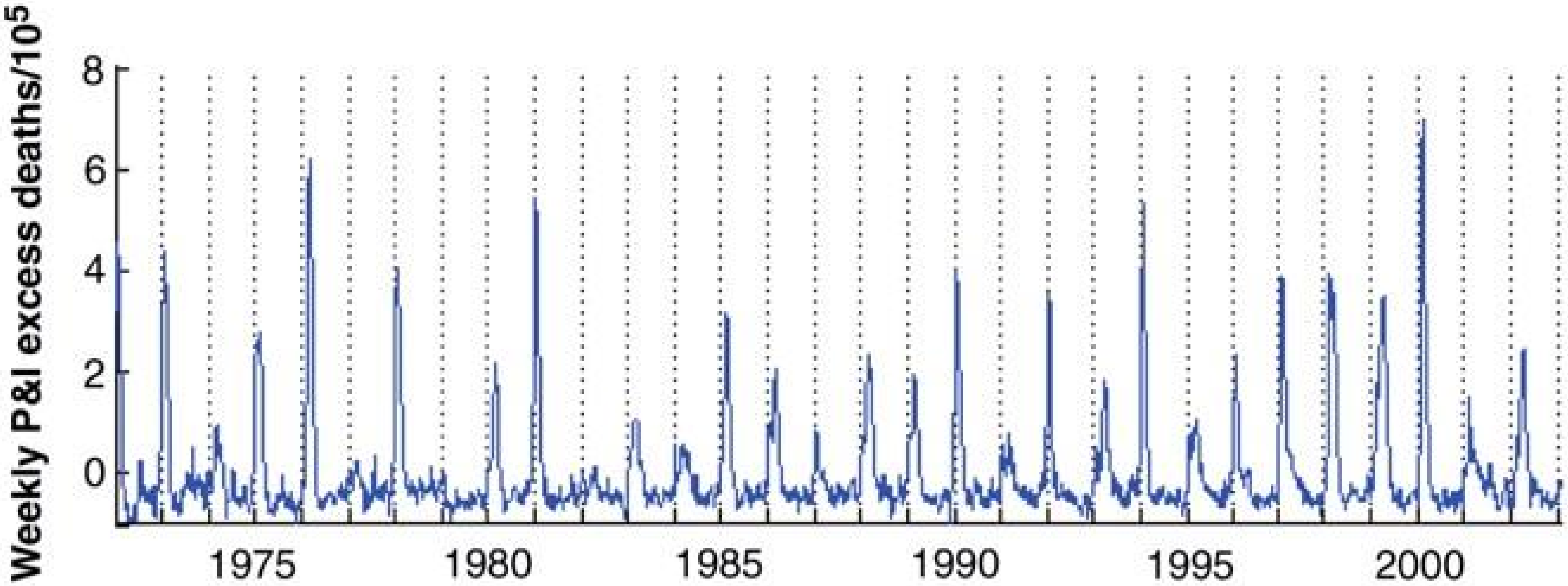


Yang and Marr, 2011, *PLoS One*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3123350/

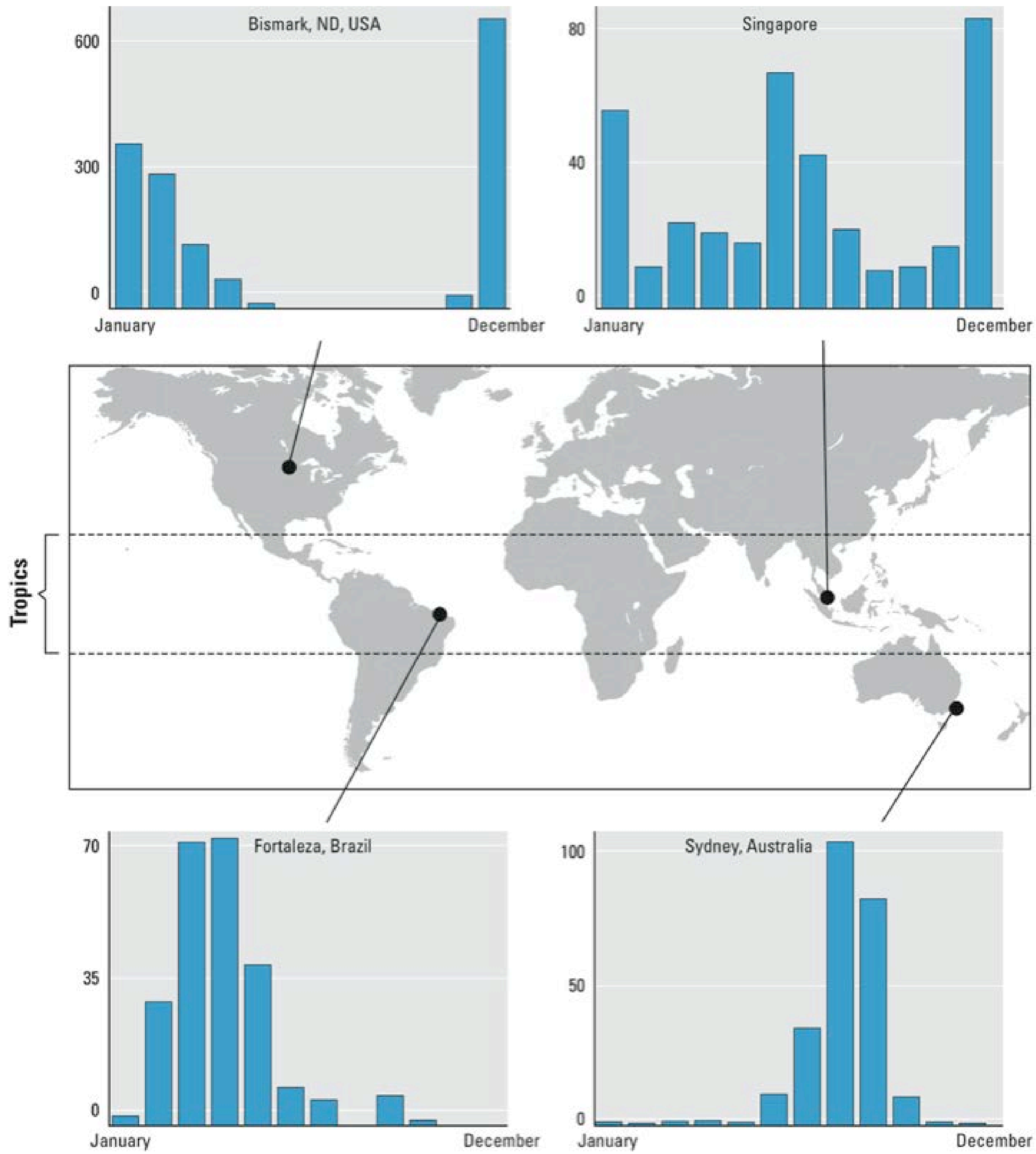
Viruses can be removed from indoor air by settling, ventilation, and inactivation; some of these processes depend on humidity.

How do temperature and humidity affect transmission?

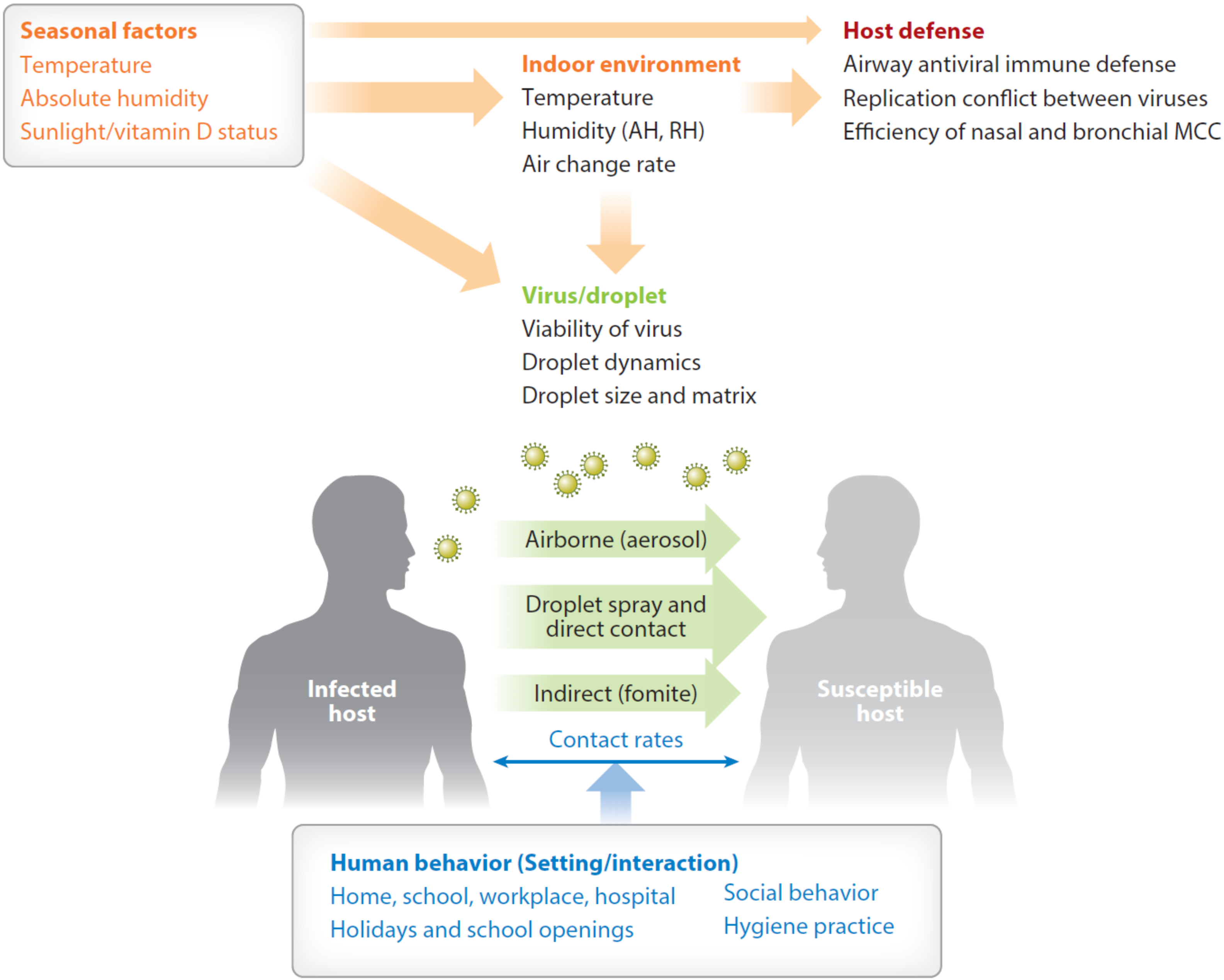
Seasonality of the Flu



Viboud et al., 2006, *Science*, https://science.sciencemag.org/content/312/5772/447



Tamerius et al., 2011, *EHP*, https://ehp.niehs.nih.gov/doi/10.1289/ehp.1002383



Moriyama et al., 2020, *Ann. Rev. Virol.*, https://www.annualreviews.org/doi/10.1146/annurev-virology-012420-022445

Virus Viability

- Temperature (T): In general, viruses survive better at lower T.
- Relative humidity (RH): Many, but not all, viruses in aerosols and droplets survive best at low RH (<40%). Some survive well at very high RH (>95%).
- Indoor T and RH are key because most transmission probably occurs indoors.

https://basc.pnnl.gov/resource-guides/thermostat-controls

SARS-CoV-1 in Droplets

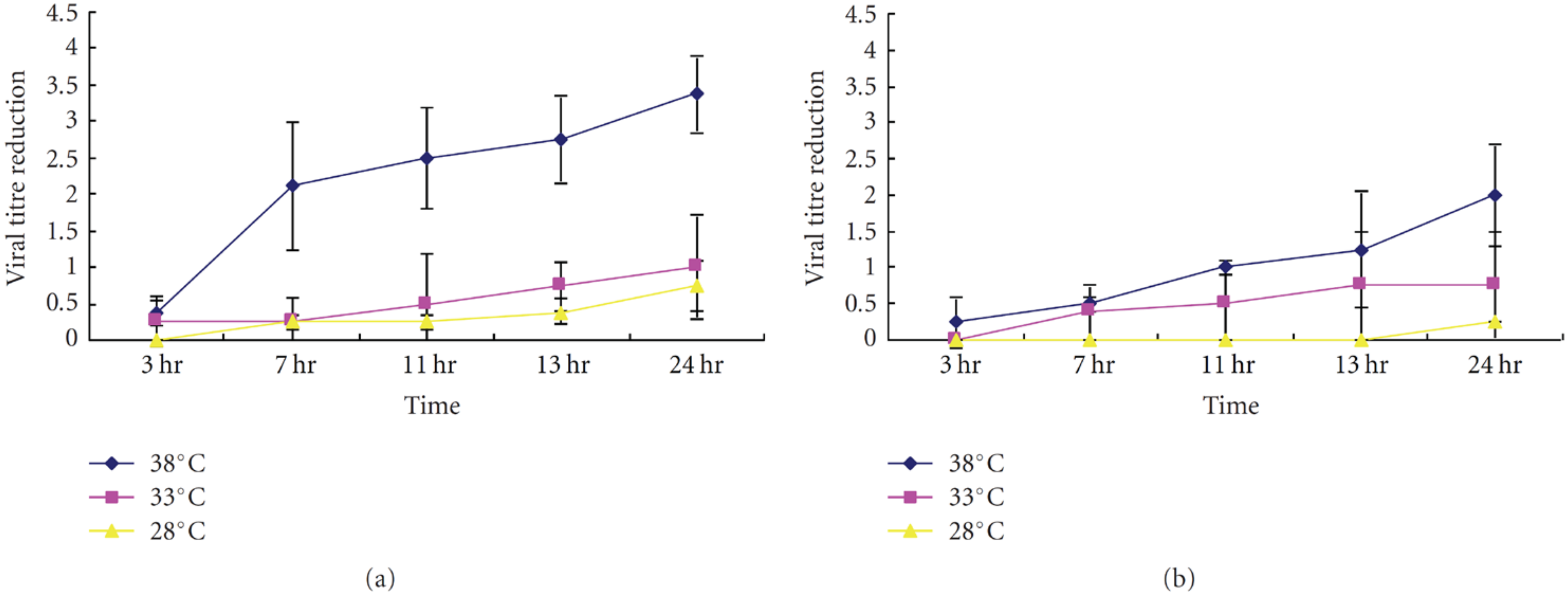
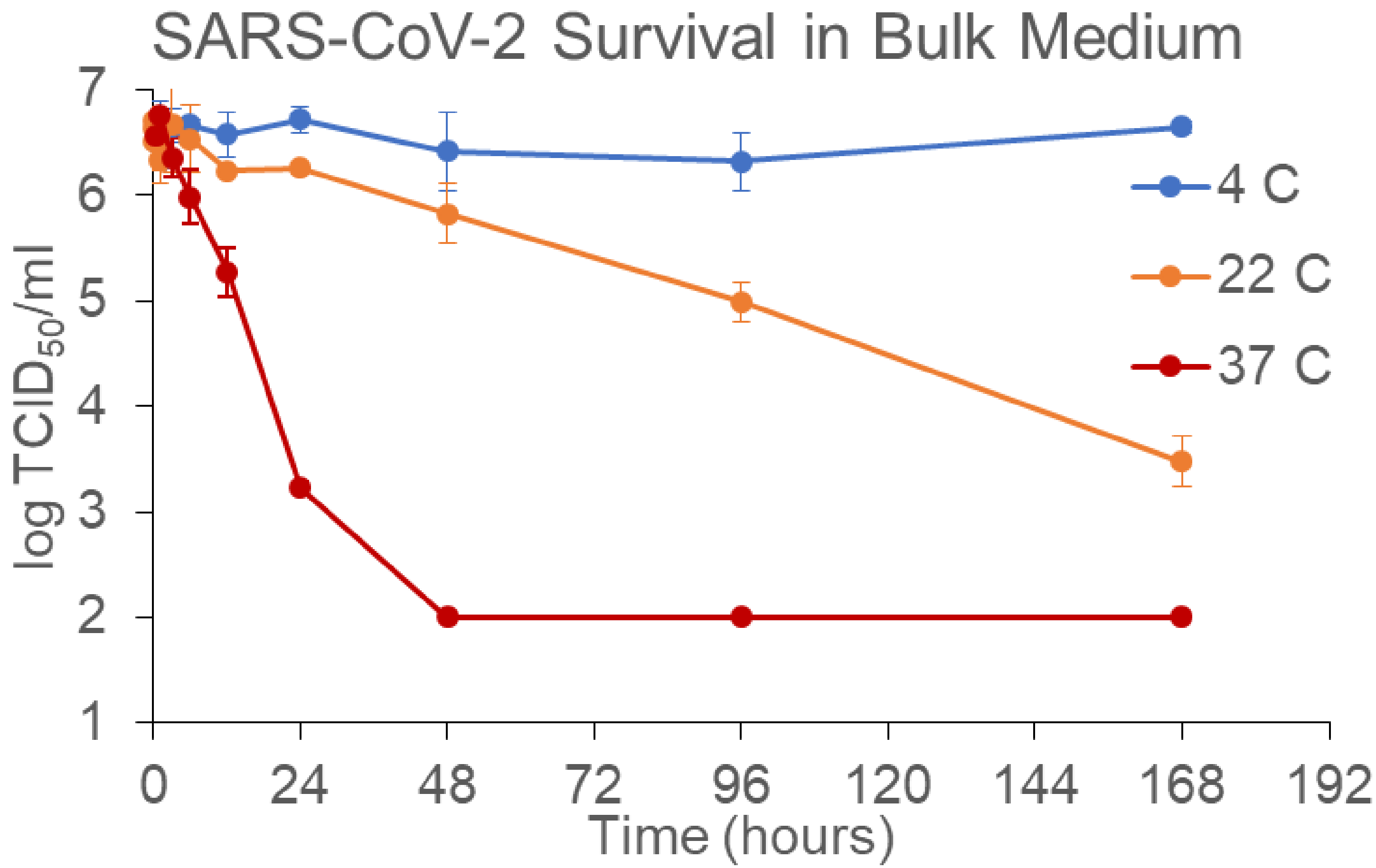


FIGURE 2: Infectivity of SARS Coronavirus ($10^5/10\,\mu$L) to different temperatures at (a) >95% relative humidity, (b) >80–89%.

Dried SARS-CoV-1 on plastic decayed faster at higher temperature and faster at >95% RH than at 80-89% RH. In another study, it decayed much more quickly at 56 and 60 °C than at 4 °C.

Chan et al., 2011, *Adv. Virol.*, *https://www.ncbi.nlm.nih.gov/pubmed/22312351*; Rabenau et al., 2005, *Med. Microbiol. Immunol.*, https://www.ncbi.nlm.nih.gov/pubmed/15118911

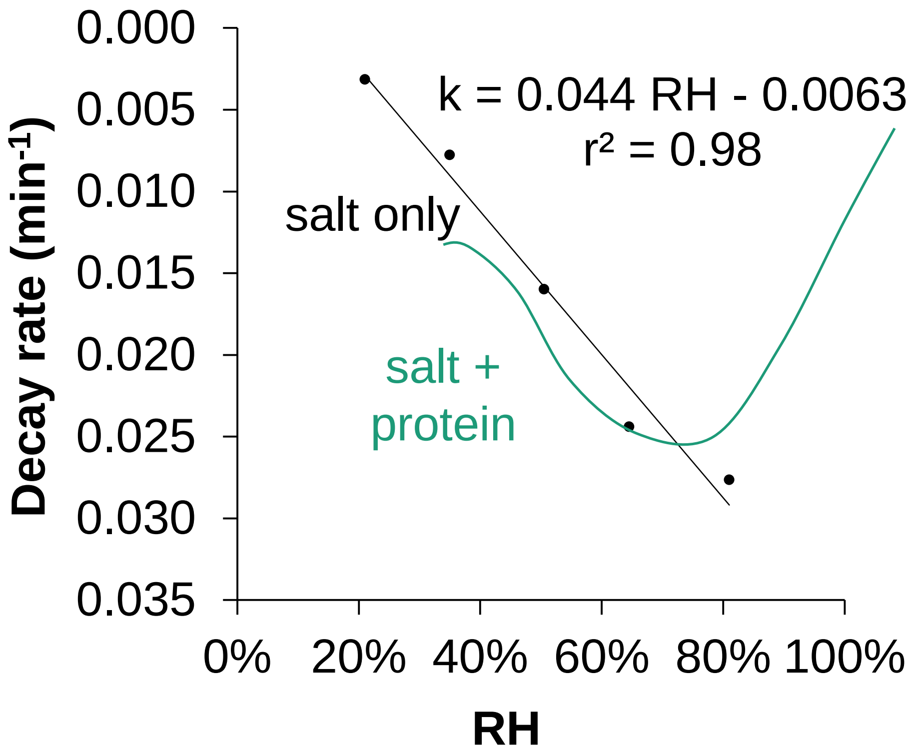
SARS-CoV-2 vs. Temperature



SARS-CoV-2 decayed fastest at 37 °C, moderately at 22 °C, and not at all at 4 °C in bulk solution.

Chin et al., 2020, https://www.medrxiv.org/content/10.1101/2020.03.15.20036673v2

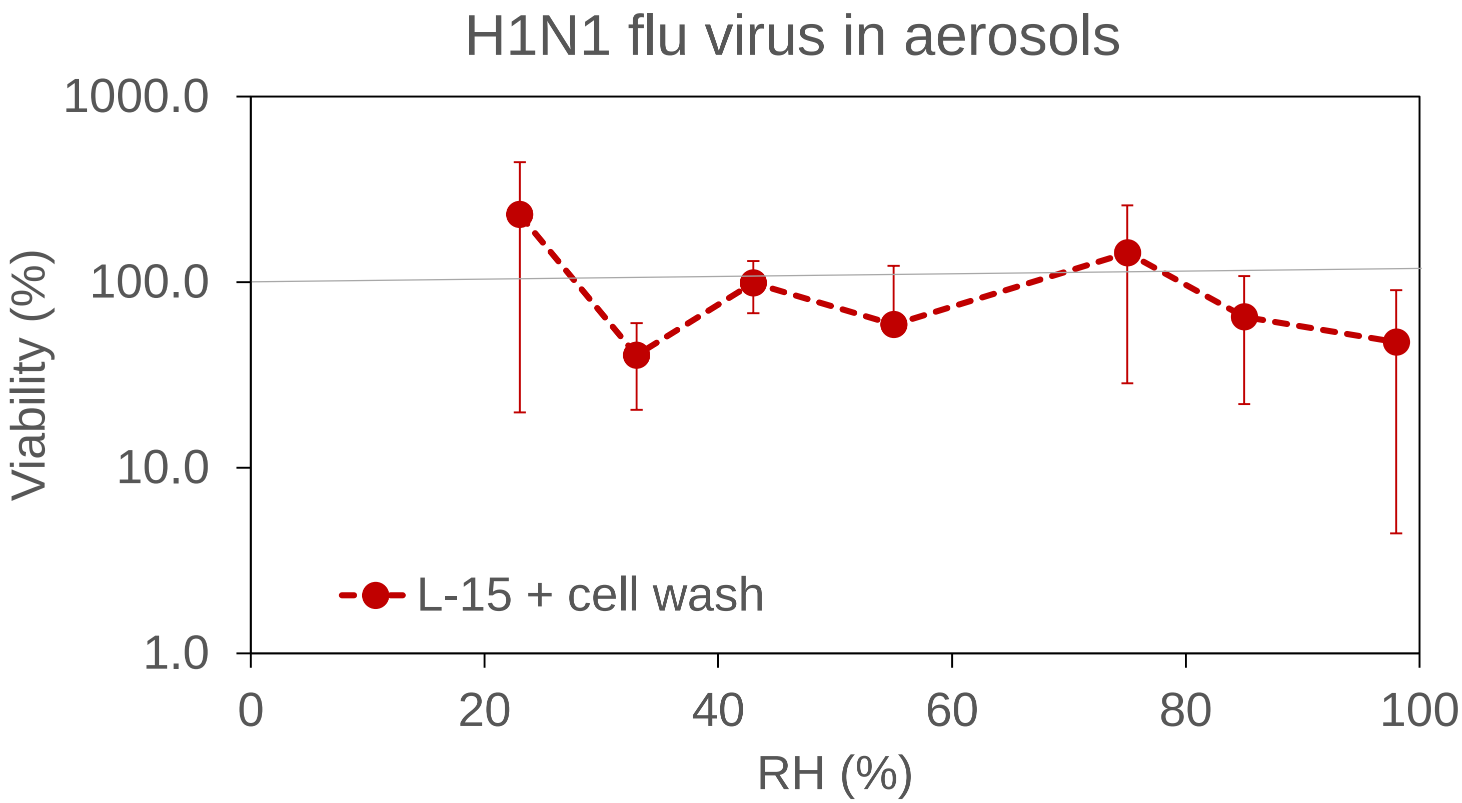
Virus Viability vs. RH



Conflicting results in the literature

Yang and Marr, 2011, *PLoS One*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3123350/

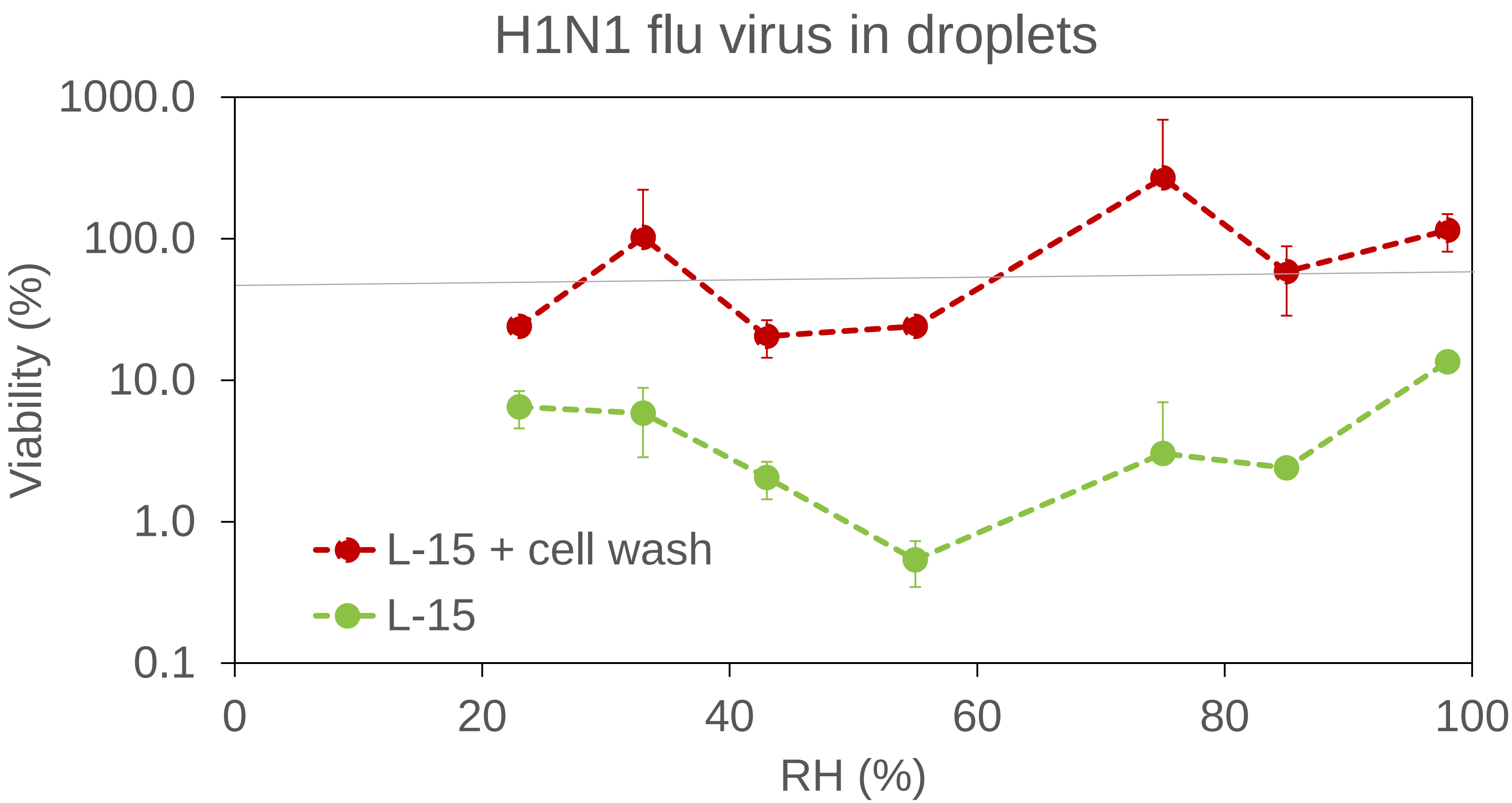
Flu Virus Remains Viable at All RH



Virus in L-15 medium + human bronchial epithelial cell wash maintains high viability across all RHs tested.

Kormuth and Lin et al., 2018, *J. Infect. Dis.*, https://academic.oup.com/jid/article/218/5/739/5025997

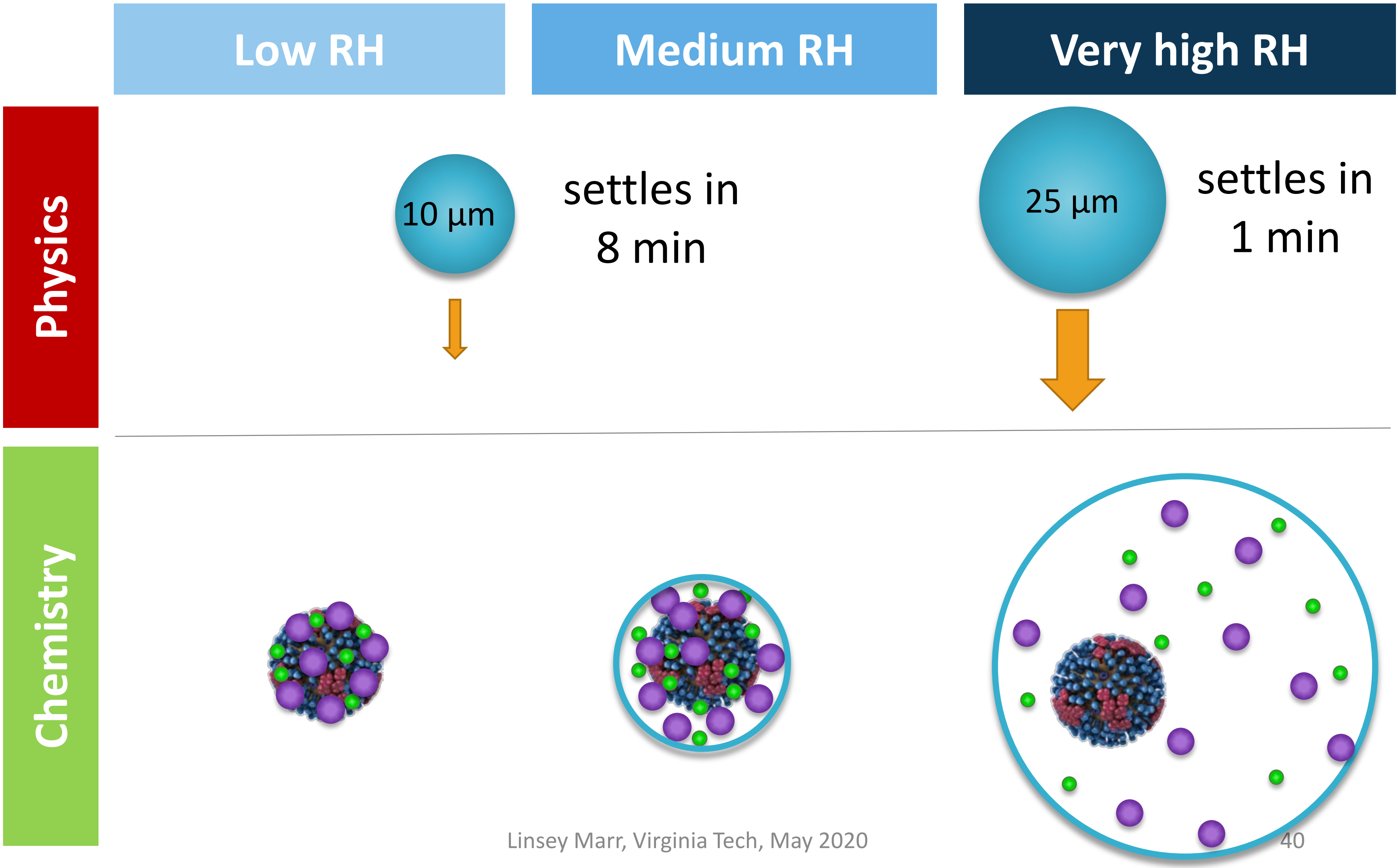
Respiratory Secretions Protect



Viability is lower without human bronchial epithelial cell wash. Also for bacteriophage Φ6.

Kormuth and Lin et al., 2018, *J. Infect. Dis.*, https://academic.oup.com/jid/article/218/5/739/5025997

How Might RH Affect Transmission?



Viruses in air and on surfaces survive better at lower temperatures. Survival varies with humidity and liquid composition.

How do masks work?

Types of Masks

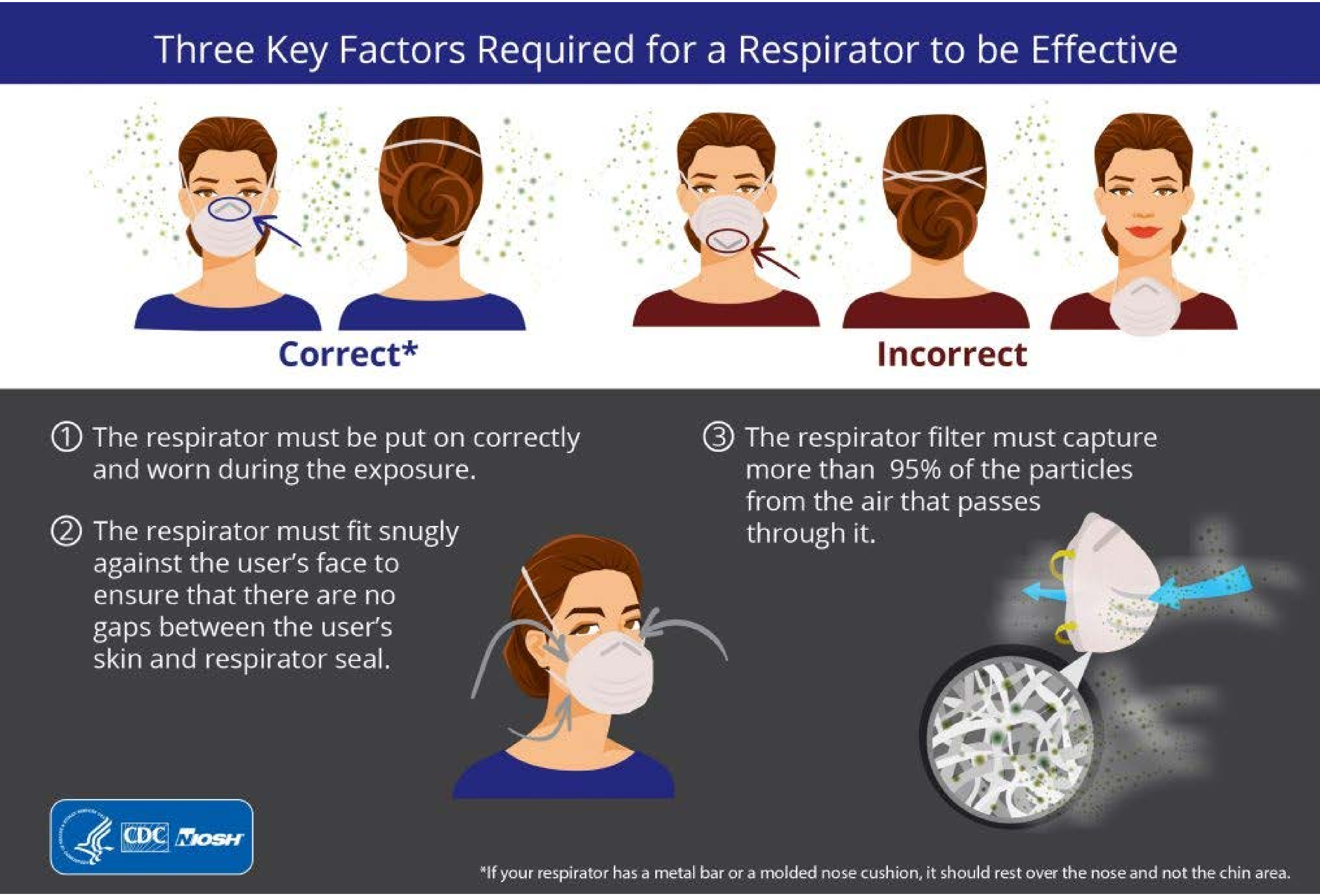
surgical mask

respirator

intended to keep the wearer from spraying droplets onto others

intended to reduce the wearer's exposure to inhaled particles

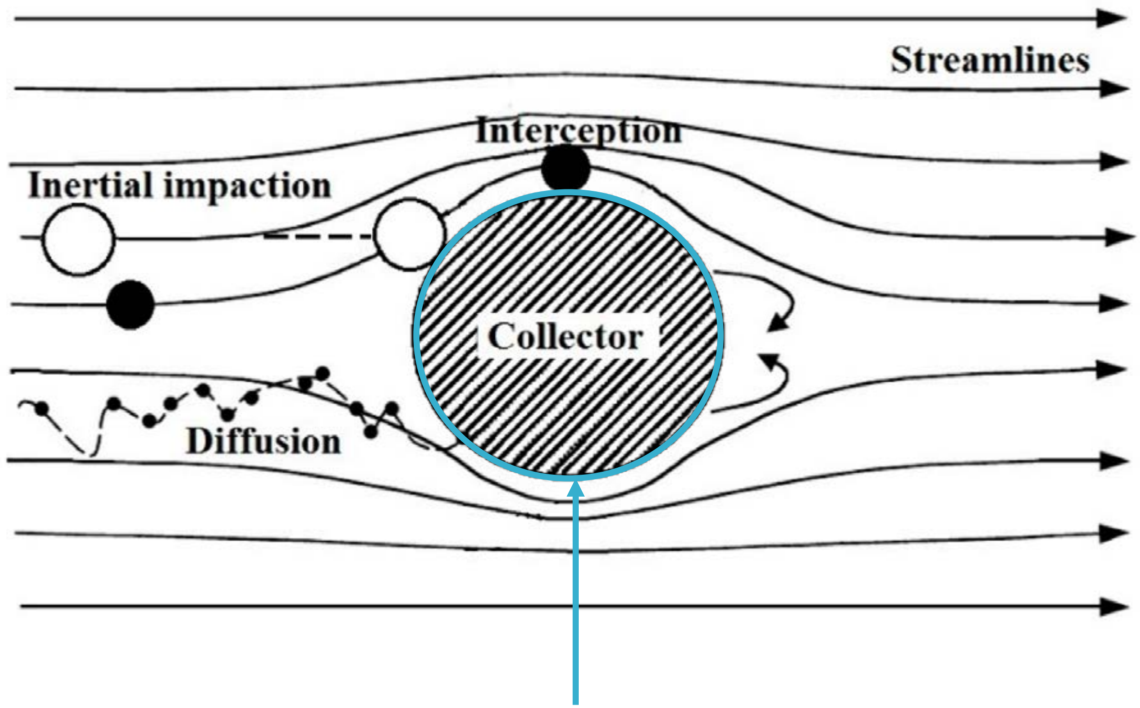
https://www.fda.gov/medical-devices/personal-protective-equipment-infection-control/n95-respirators-and-surgical-masks-face-masks



https://blogs.cdc.gov/niosh-science-blog/2018/01/04/respirators-public-use/

Filtration Mechanisms

- Impaction
- Interception
- Diffusion
- Not sieving!

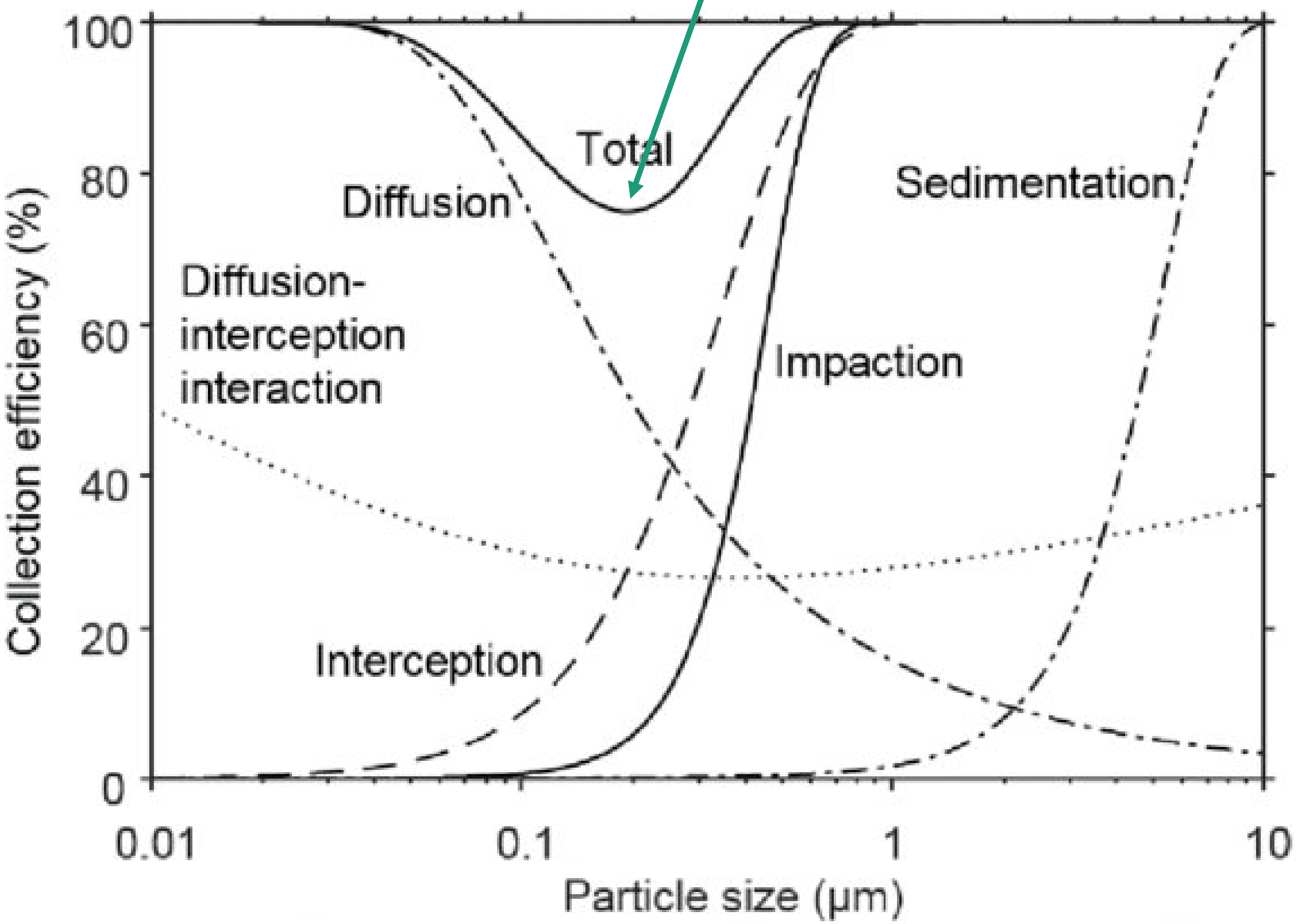


"collector" = single fiber in a filter

Bulejko, 2018, *Nanomaterials*, https://www.mdpi.com/2079-4991/8/6/447/htm

Filter Efficiency

minimum at 0.1-0.3 µm, where no collection mechanism works well



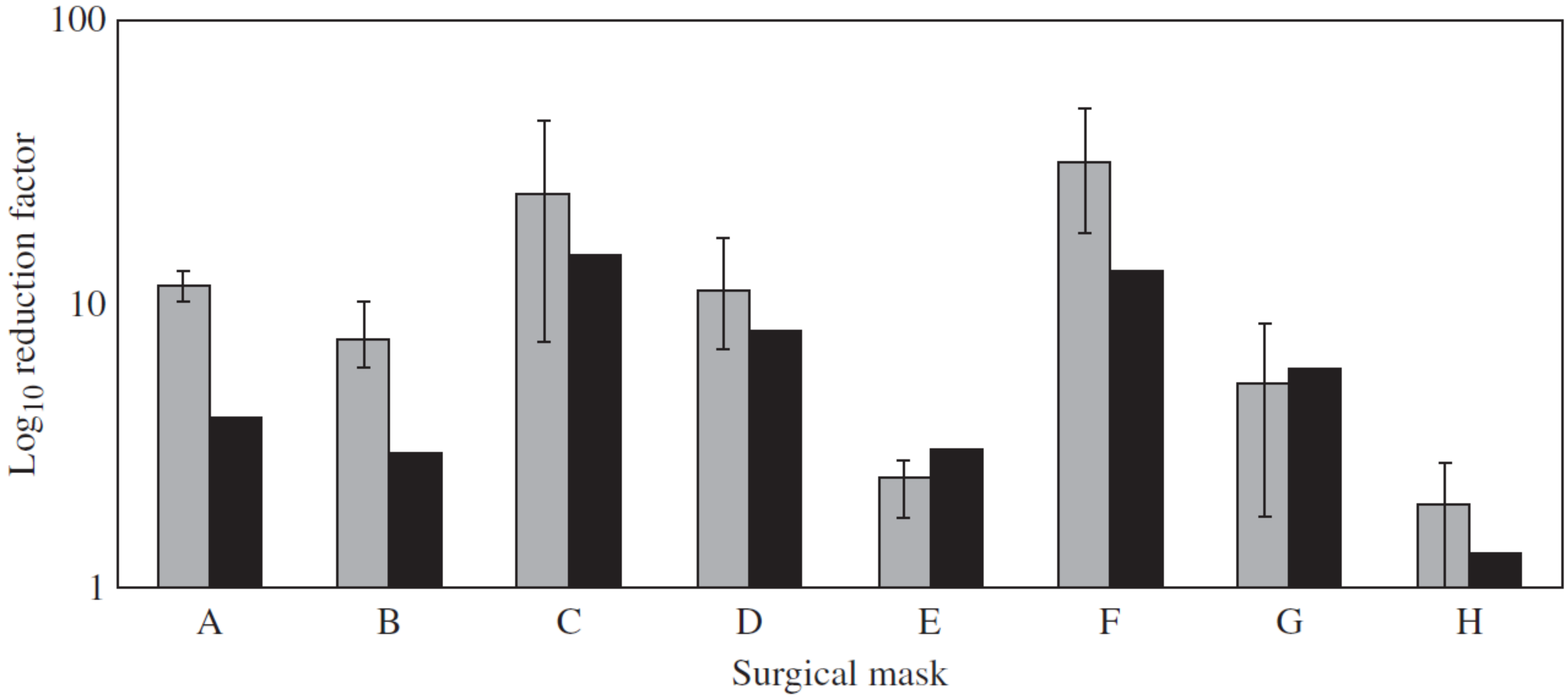
Lindsley, 2016, NIOSH Manual of Analytical Methods, https://www.cdc.gov/niosh/nmam/default.html

N95

- Removes ≥95% of 0.3 µm particles
- Removal efficiency is even better for particles >0.3 µm and particles <0.3 µm
- Removal efficiency depends on the size and density of the particle and should be the same whether the particle contains a virus or not

https://www.cdc.gov/niosh/npptl/default.html

Surgical Masks and Flu Virus

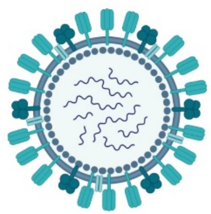
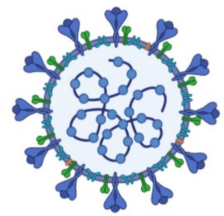
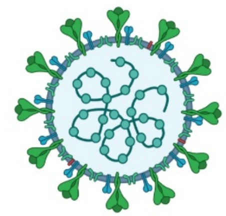
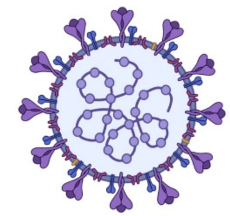


Different types of surgical masks reduced the amount of infectious flu virus measured behind the mask on a manikin by an average of a factor of 6 (range 1.1-55).

Booth et al., 2013, *J. Hosp. Infection*, https://www.ncbi.nlm.nih.gov/pubmed/23498357

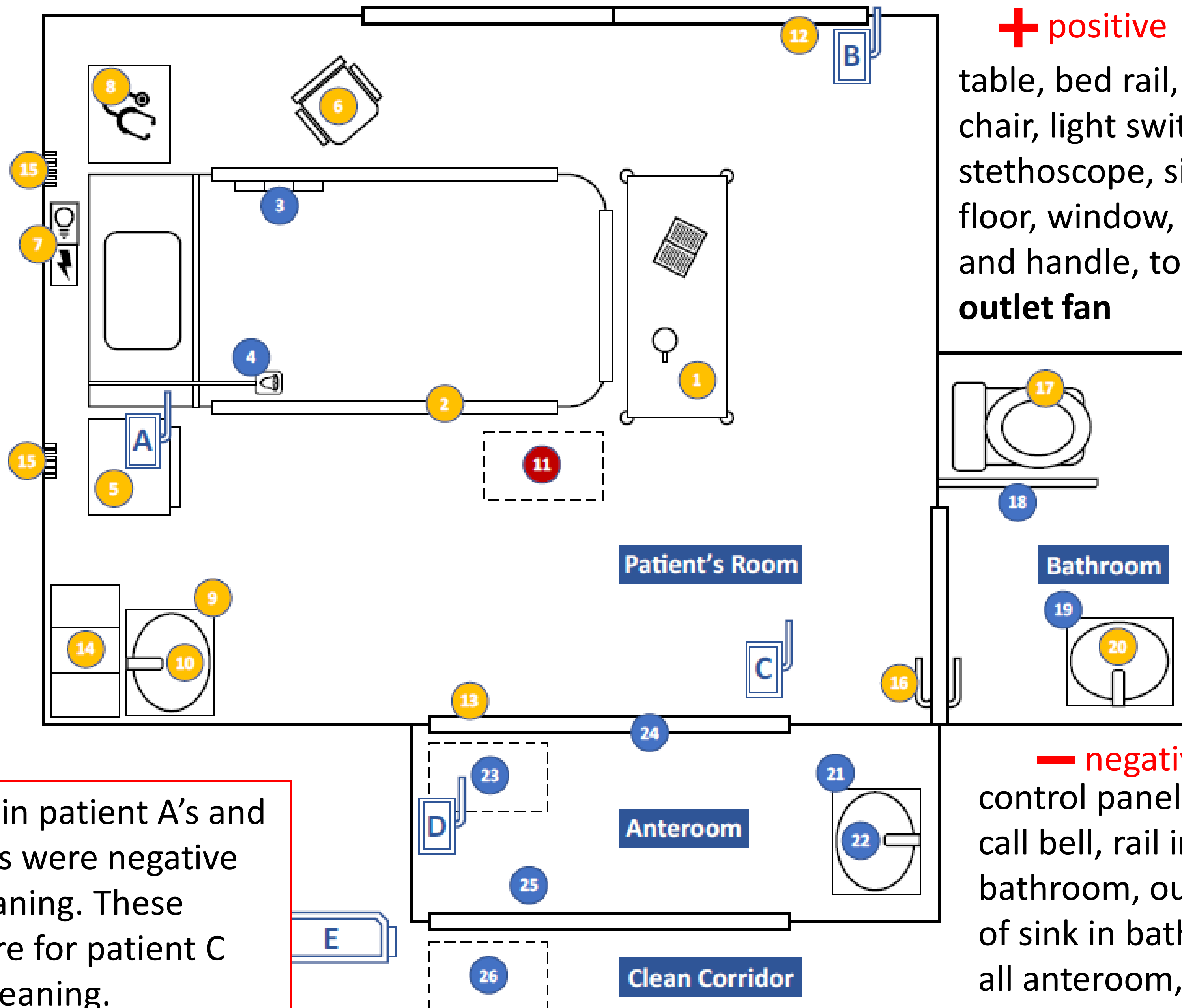
What do we know about SARS-CoV-2 in droplets/aerosols?

Epidemiological Comparison of Respiratory Viral Infections

Disease	Flu	COVID-19	SARS	MERS
Disease Causing Pathogen	 Influenza virus	 SARS-CoV-2	 SARS-CoV	 MERS-CoV
R_0 Basic Reproductive Number	**1.3**	**2.0 - 2.5** *	**3**	**0.3 - 0.8**
CFR Case Fatality Rate	0.05 - 0.1%	~3.4% *	9.6 - 11%	34.4%
Incubation Time	1 - 4 days	4 - 14 days *	2 - 7 days	6 days
Hospitalization Rate	2%	~19% *	Most cases	Most cases
Community Attack Rate	10 - 20%	30 - 40% *	10 - 60%	4 - 13%
Annual Infected (global)	~ 1 billion	N/A (ongoing)	8098 (in 2003)	420
Annual Infected (US)	10 - 45 million	N/A (ongoing)	8 (in 2003)	2 (in 2014)
Annual Deaths (US)	10,000 - 61,000	N/A (ongoing)	None (since 2003)	None (since 2014)

* COVID-19 data as of March 2020.

https://twitter.com/VirusesImmunity/status/1238475009712160769



\+ positive

table, bed rail, locker, chair, light switches, stethoscope, sink, floor, window, door and handle, toilet, **air outlet fan**

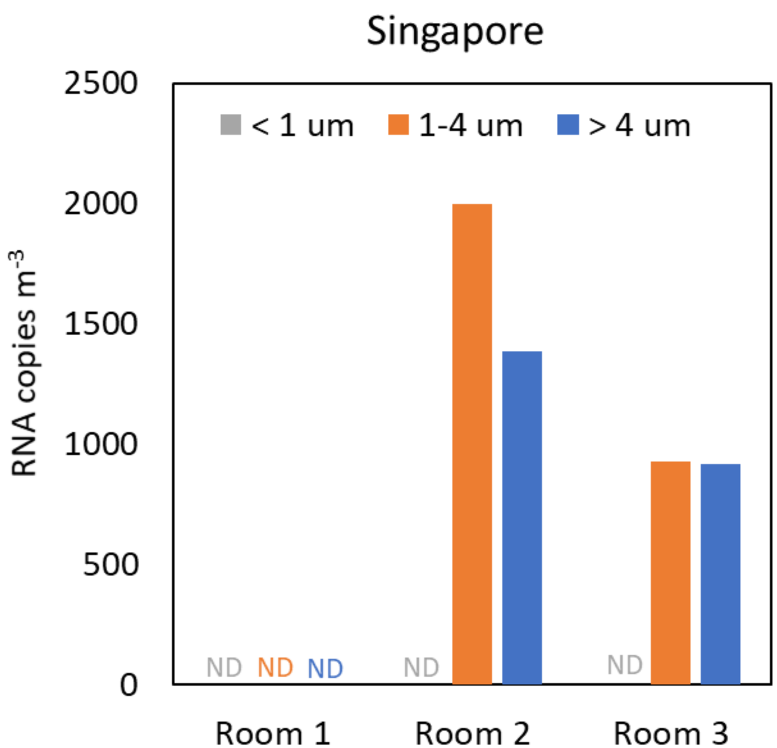
− negative

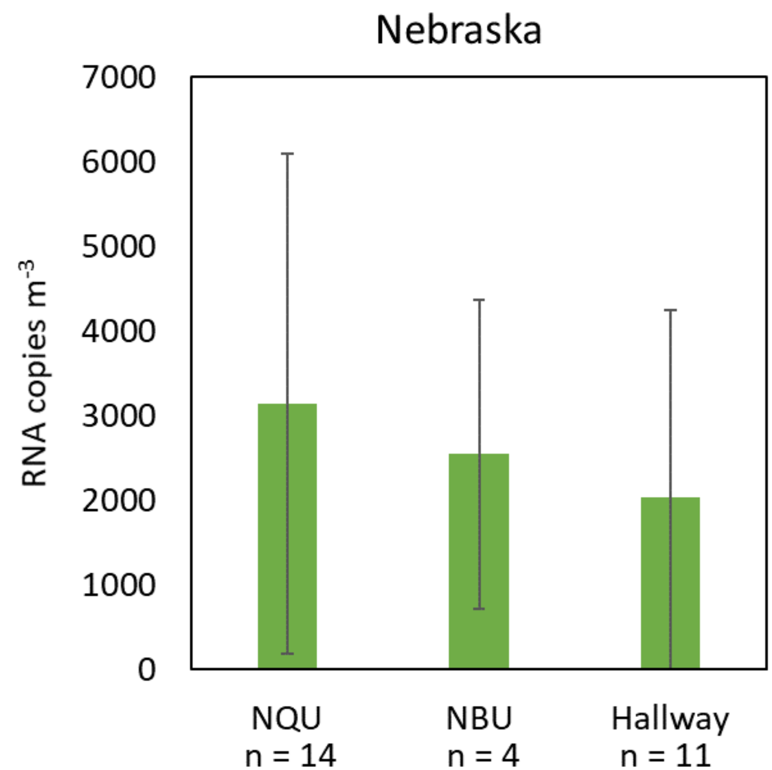
control panel on bed, call bell, rail in bathroom, outer rim of sink in bathroom, all anteroom, **air**

Samples in patient A's and B's rooms were negative after cleaning. These results are for patient C before cleaning.

Ong et al., 2020, *JAMA*, https://jamanetwork.com/journals/jama/fullarticle/2762692

Airborne Viral RNA in Hospitals





I estimate a viral RNA emission rate of 10,000 genome copies per minute in “small” droplets.

SARS-CoV-2 Size Distributions

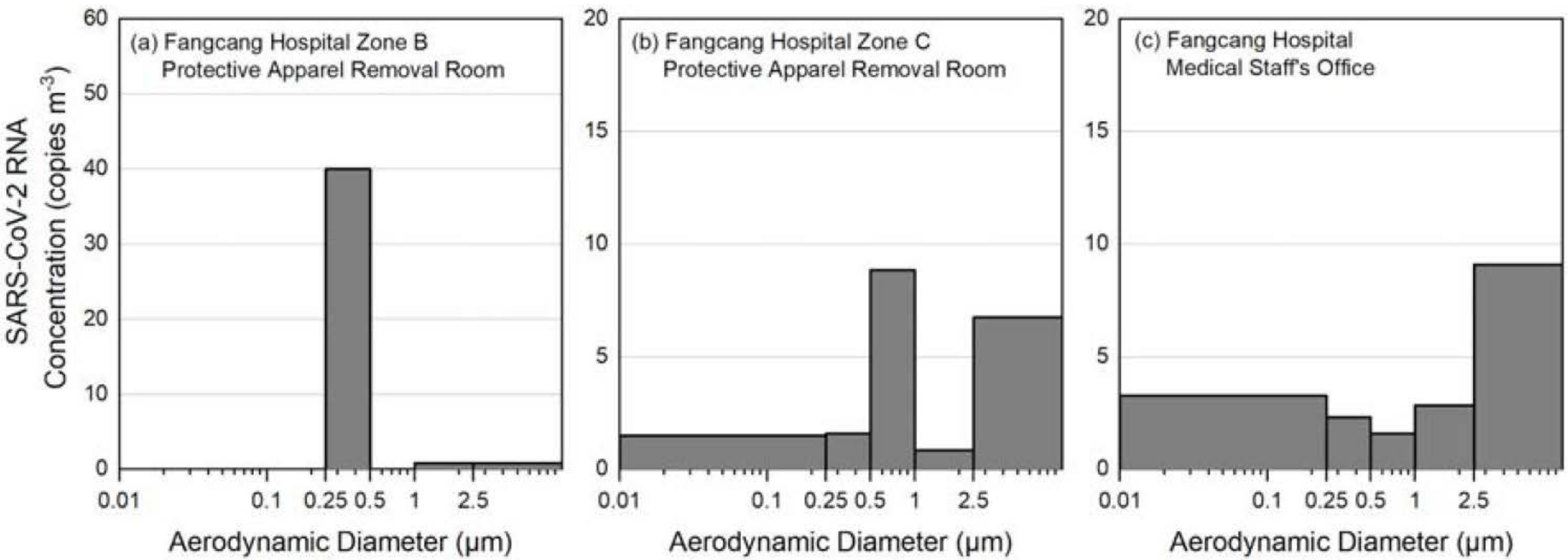
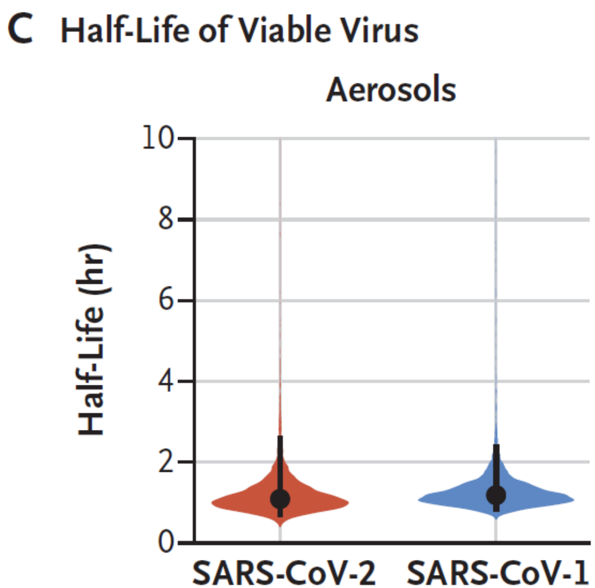


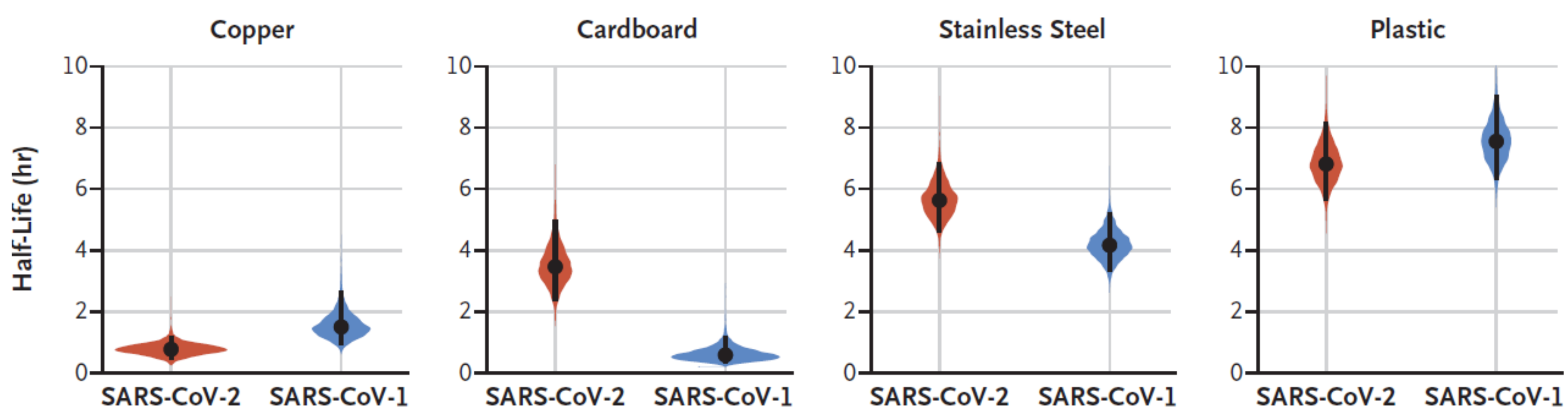
Figure 1 Concentration of airborne SARS-CoV-2 RNA in different aerosol size bins

Liu et al., 2020, *Nature*, https://www.nature.com/articles/s41586-020-2271-3

SARS-CoV-2 Survival in Aerosols

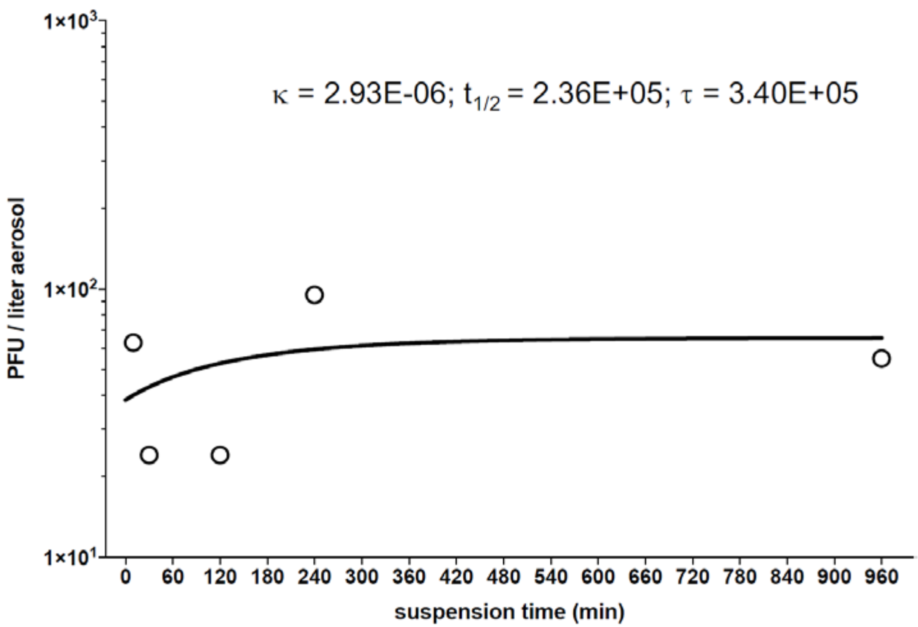


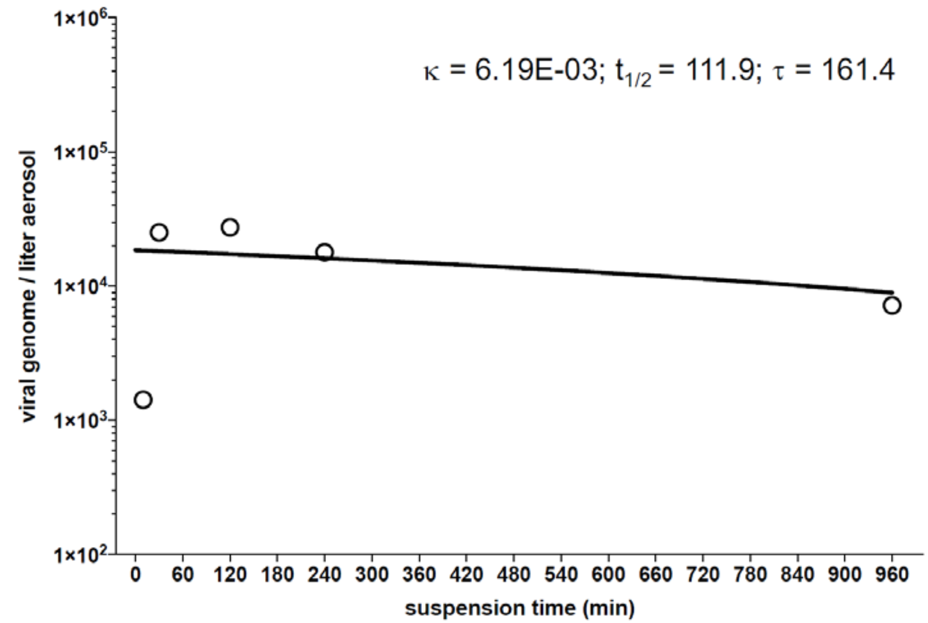
Half-life is 1.1 hours in culture medium at 65% RH.



van Doremalen et al., 2020, *NEJM*, https://www.nejm.org/doi/full/10.1056/NEJMc2004973

SARS-CoV-2 Survival in Aerosols

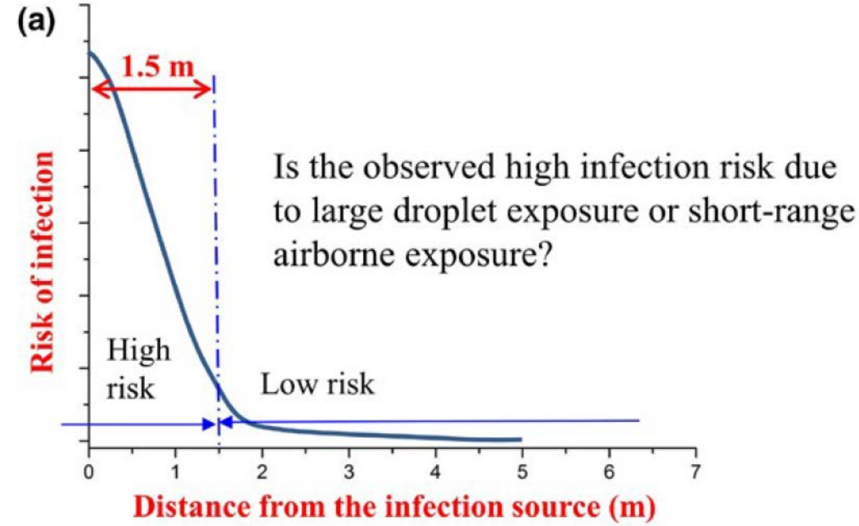




Virus survives 16 hours in aerosols in culture medium at 53% RH

Fears et al., 2020, https://www.medrxiv.org/content/10.1101/2020.04.13.20063784v1

Major Unknowns



- Which transmission route is dominant: direct contact, indirect contact with contaminated objects (fomites), inhalation of aerosols, deposition of droplets?
- How much virus is released in what size aerosols at different stages of infection?
- How well does SARS-CoV-2 survive in aerosols under real-world conditions?
- How are viruses inactivated in air and on surfaces?
- How well do homemade masks work for source control?

Liu et al., 2016, *Indoor Air*, https://onlinelibrary.wiley.com/doi/abs/10.1111/ina.12314

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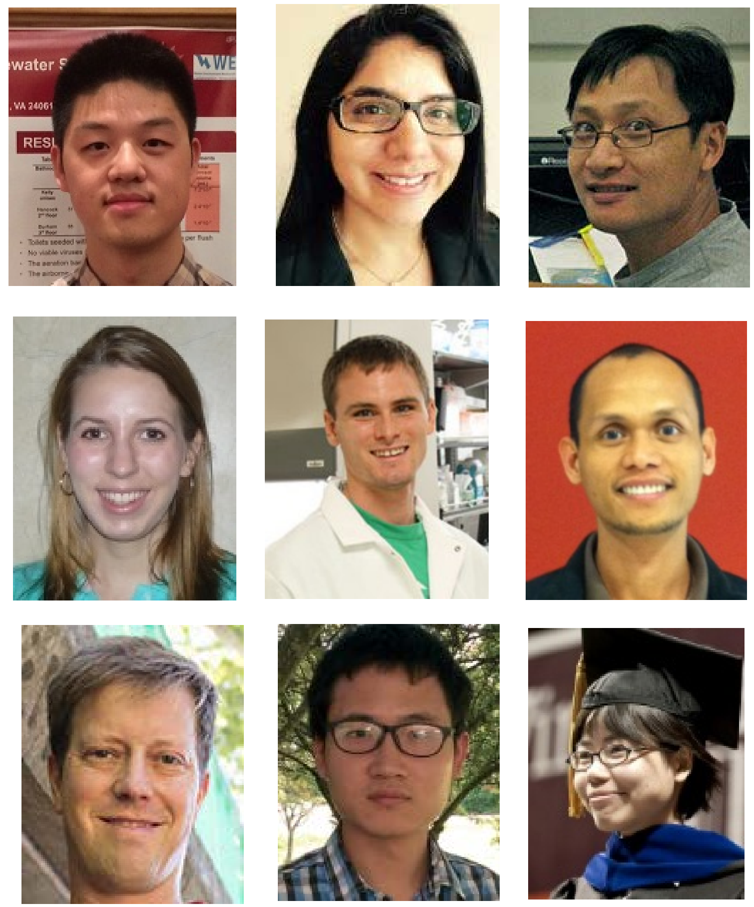

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NNCI nano