ENVE 576
Indoor Air Pollution
Summer 2020

Lecture 13 - Airborne infectious disease transmission

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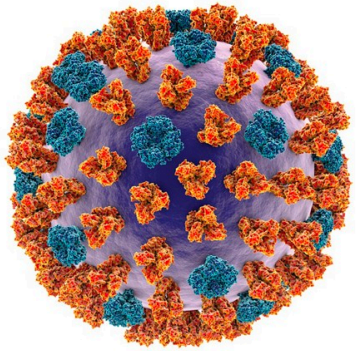
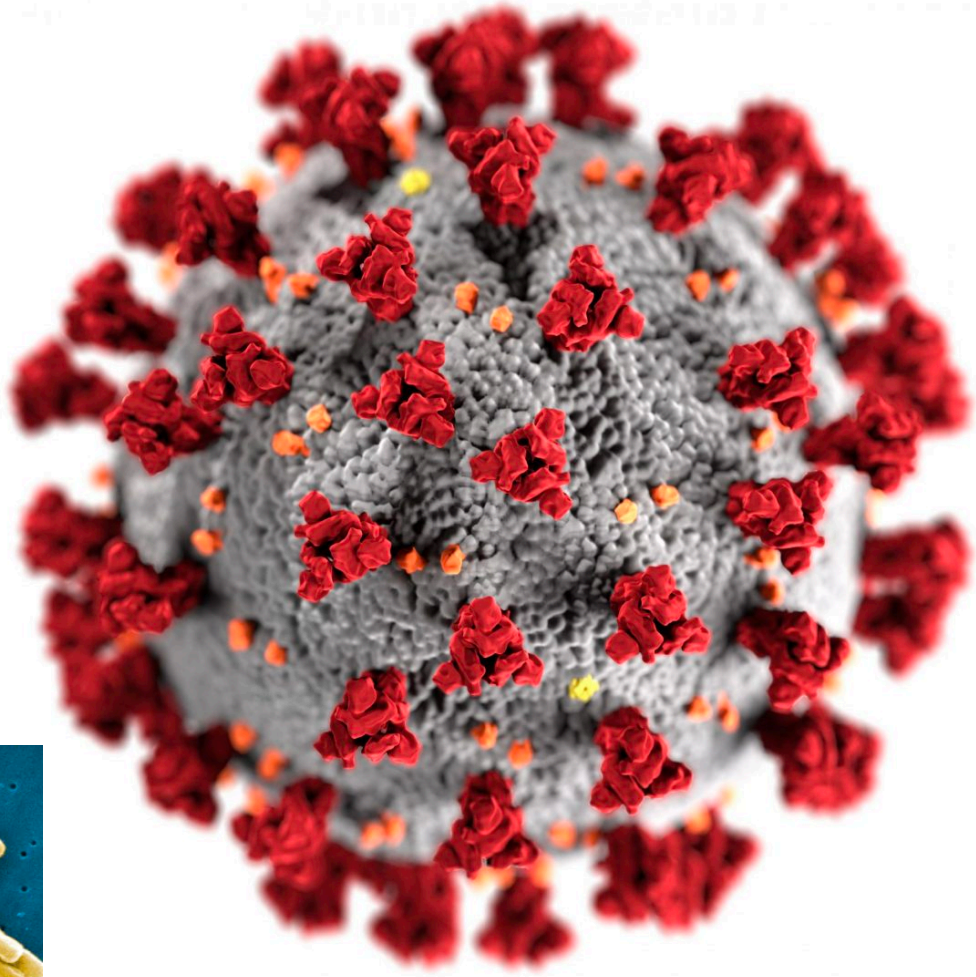
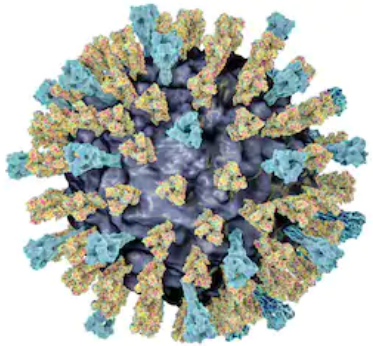
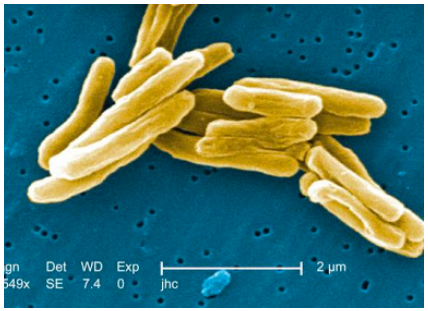
Introduction and motivation









Introduction and motivation

- Communicable respiratory illnesses have significant economic impacts in the U.S.
  - 43 common colds per 100 people
  - 26 cases of influenza per 100 people
  - Healthcare costs, absence from work, lost worker productivity
    - Total cost was ~$70 billion in 2000 Fisk **2000** *Ann Review Energy Environ* 25:537-566

- Transmission of respiratory pathogens is complex
  - Continuing debate about transmission modes for many pathogens
    - Inhalation (aerosols), direct contact (droplets or touch), fomites (surfaces)

239 Experts With One Big Claim: The Coronavirus Is Airborne **July 4, 2020**

The W.H.O. has resisted mounting evidence that viral particles floating indoors are infectious, some scientists say. The agency maintains the research is still inconclusive.

W.H.O. to Review Evidence of Airborne Transmission of Coronavirus **July 7, 2020**

The World Health Organization plans to update its advice after hundreds of experts urged the agency to reconsider the risk of aerosol transmission.

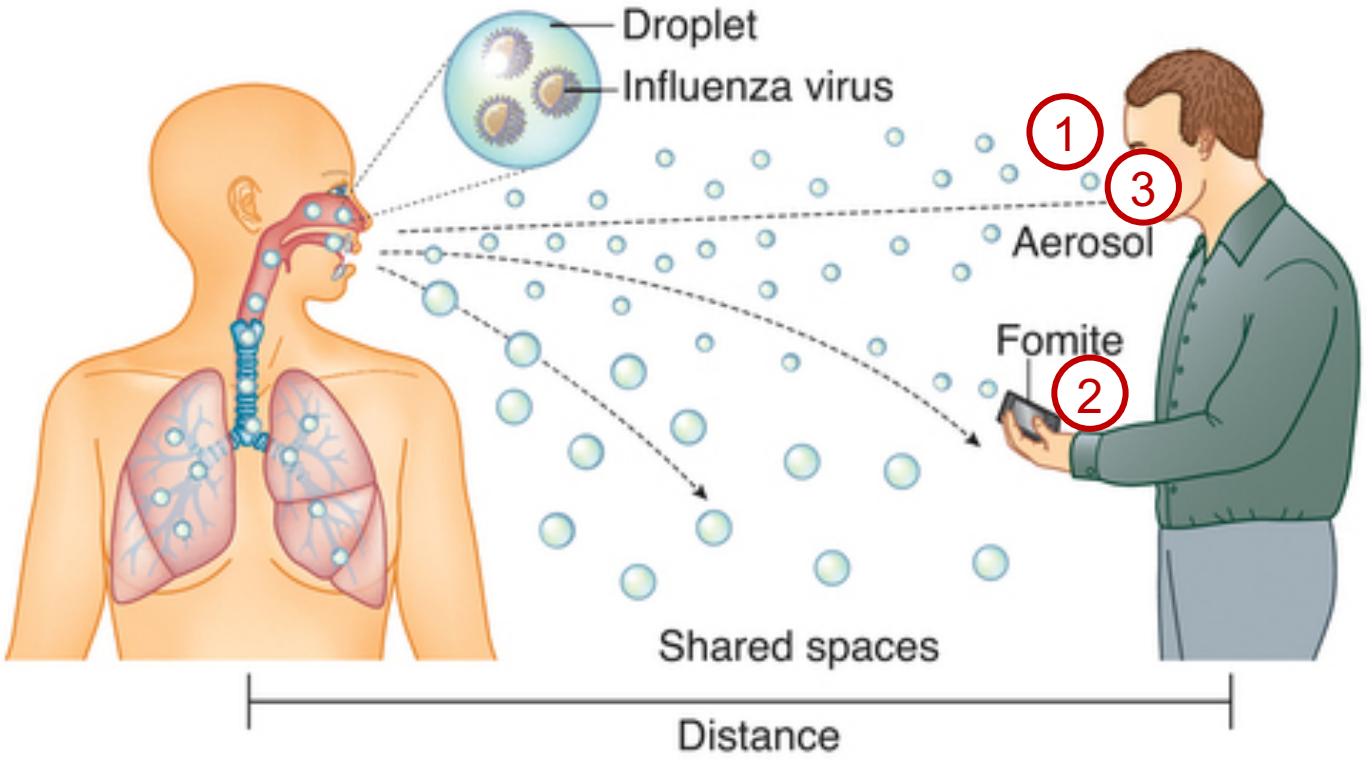
https://www.nytimes.com/2020/07/04/health/239-experts-with-one-big-claim-the-coronavirus-is-airborne.html
https://www.nytimes.com/2020/07/07/health/coronavirus-aerosols-who.html

Objectives for this lecture

- Explore modes of infectious disease transmission
- Infectious aerosols: particle sizes and emissions
  - Including viruses and bacteria within aerosols
- Methods of infection control
- Methods of estimating disease risks

MODES OF INFECTIOUS DISEASE TRANSMISSION

Primary modes of disease transmission

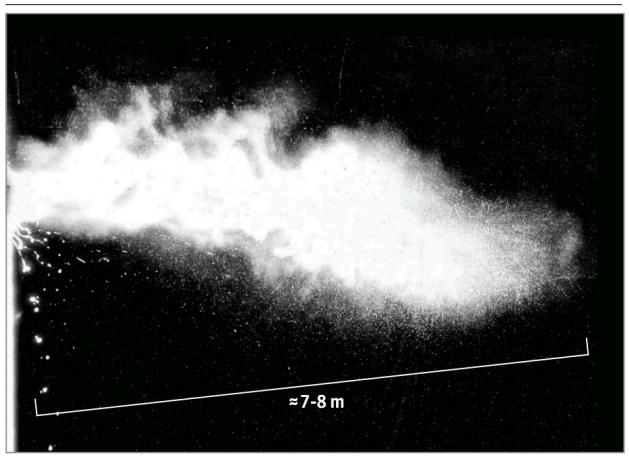


1. Direct contact with pathogen sources (i.e. aerosol/droplet deposition)
2. Contact with contaminated object surfaces (“fomites”)
3. Inhalation of airborne infectious aerosols (often longer distances)

Lakdawala and Subbarao **2012** *Nature Medicine* 18:1468-1470

Aerosols vs. droplets vs. fomites

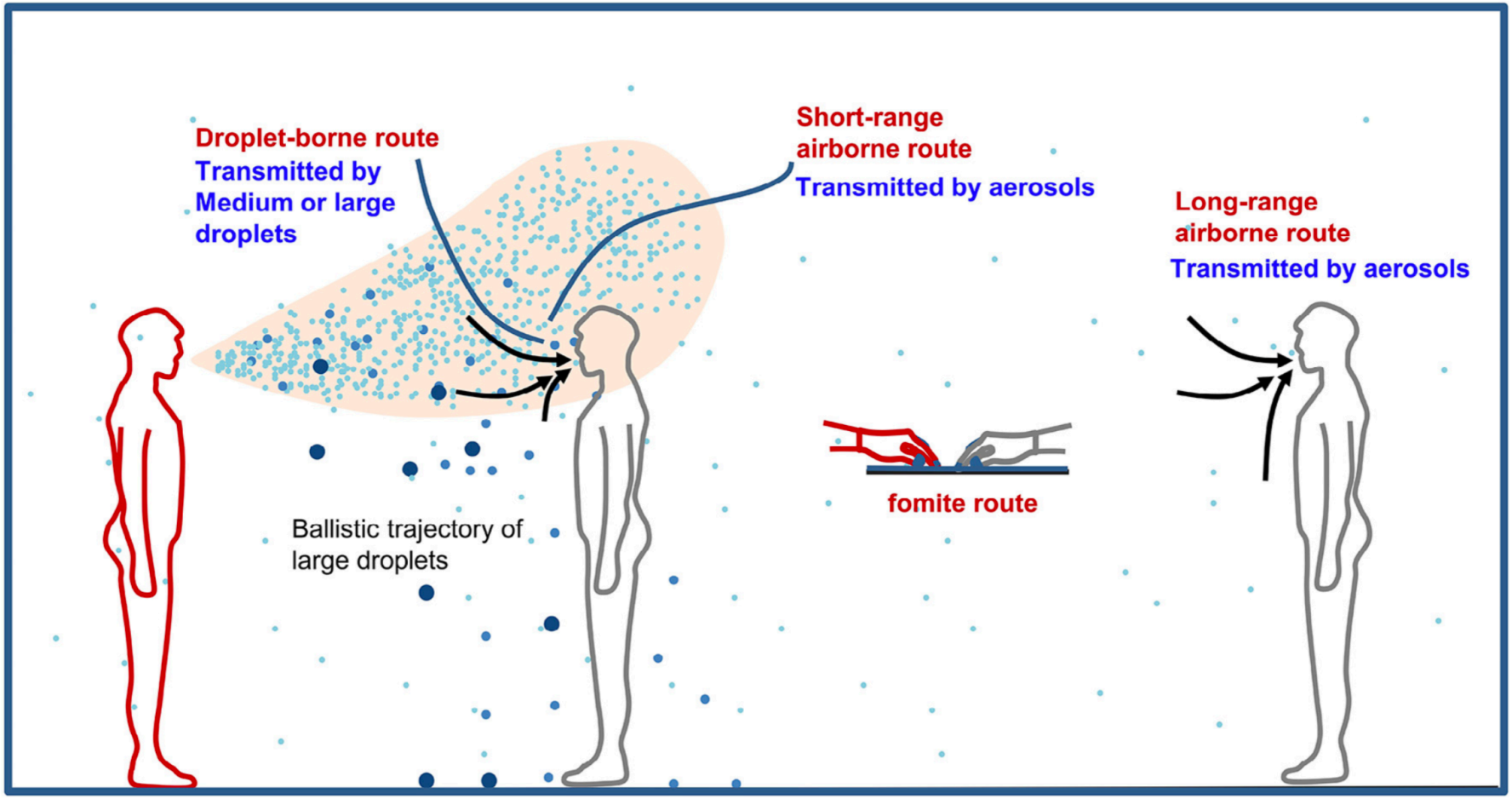
- Medical and public health communities commonly define:
  - Droplets as >5 μm (with transmission occurring only at close-range)
  - Aerosols as <5 μm (with transmission at long-range only)
  - Long-range/short-range cut-off distance ~1-2 m
    https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions



Bourouiba **2020** *JAMA* 323(18):1837-1838

- Reality is more complicated:
  - "Droplets" are much bigger than 5 μm
  - "Droplets" can travel farther than 1-2 m
  - Small particles ("aerosols") are also present at close-range

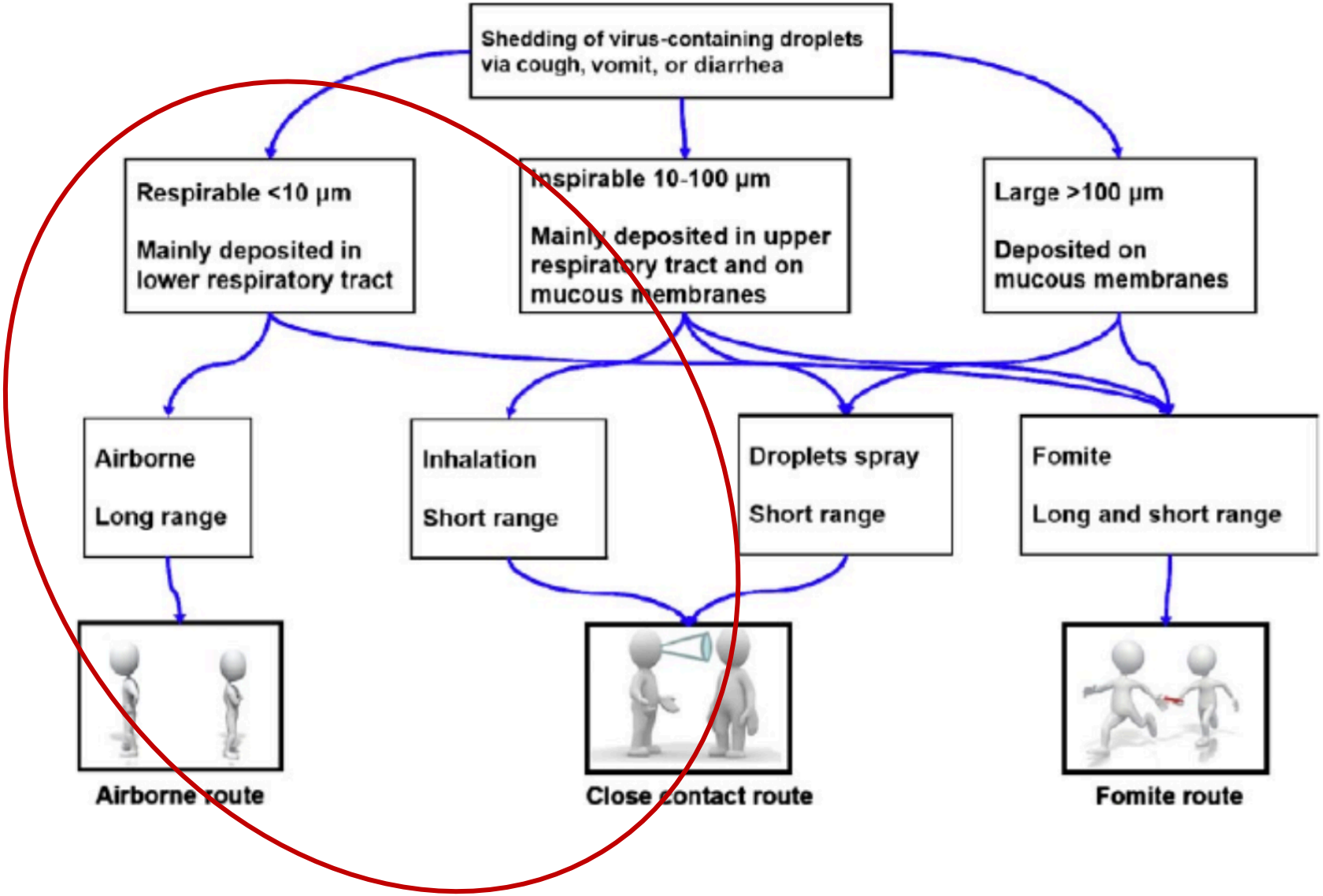
Aerosols vs. droplets vs. fomites



- Large droplets (>100 μm) : Fast deposition due to the domination of gravitational force
- Medium droplets between 5 and 100 μm
- Small droplets or droplet nuclei, or aerosols (< 5 μm): Responsible for airborne transmission

Wei and Li **2016** *Am J Infection Control* 44:S102-S103

Aerosols vs. droplets vs. fomites



Lei et al. **2017** *Indoor Air* 28:394-403

Diseases spread (in part) by airborne transmission

Disease	Organism	Clinical manifestations
Adenovirus	Adenovirus	Rhinitis, pharyngitis, malaise, rash, cough
Influenza*	Influenza virus	Fever, chills, malaise, headache, cough
Measles*	Rubeola virus	Fever, rash, malaise, conjunctivitis
Meningococcal disease	Neisseria meningitides	Fever, headache, vomiting, confusing
Mumps*	Mumps virus	Pain/swollen salivary glands
Pertussis	Bordetella pertussis	Malaise, cough, coryza, “whooping cough”
Parvovirus B19	Parvovirus B19	Rash, anemia, arthritis
Respiratory syncytial virus	RSV	Often asymptomatic
Rubella	Rubella virus	Fever, malaise, rash
Tuberculosis*	Mycobacterium species	Fever, weight loss, fatigue, night sweats, pulmonary disease
Varicella	Human herpes virus 3	Chicken pox

ASHRAE Position Document on Airborne Infectious Diseases (**2014**) – recently updated (but the table is gone ☹)

Evidence of airborne transmission

In China, Students in Crowded Dormitories with a Low Ventilation Rate Have More Common Colds: Evidence for Airborne Transmission

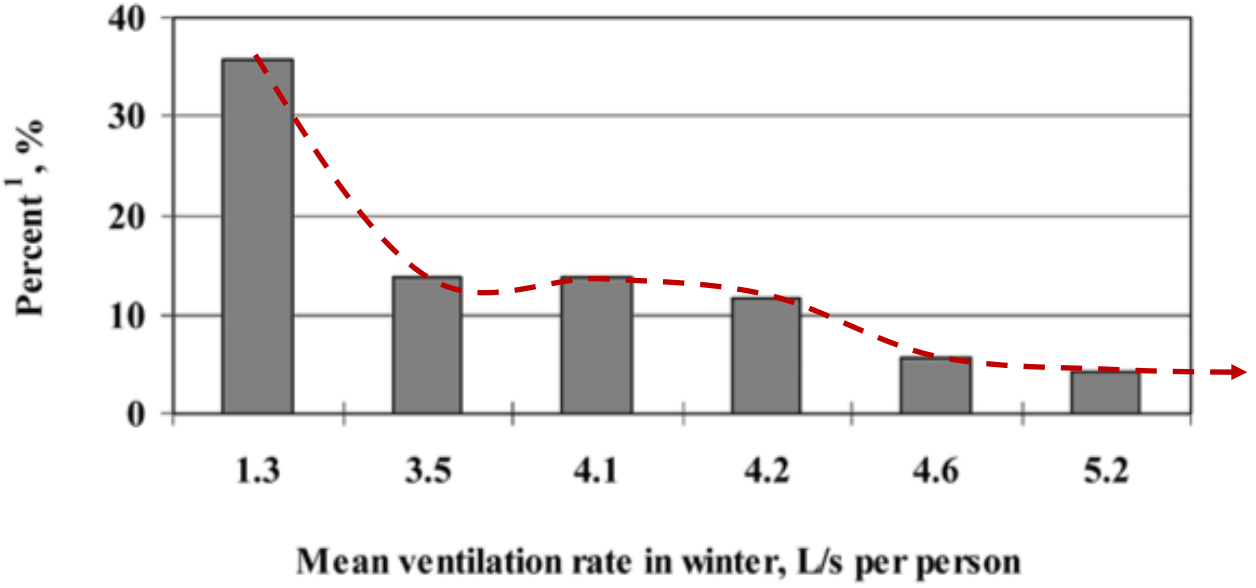


Figure 4. Associations between common cold infection rates and mean ventilation rate in winter in buildings constructed after year 1993. [1] Proportion of occupants with ≥6 common colds in the previous 12 months.

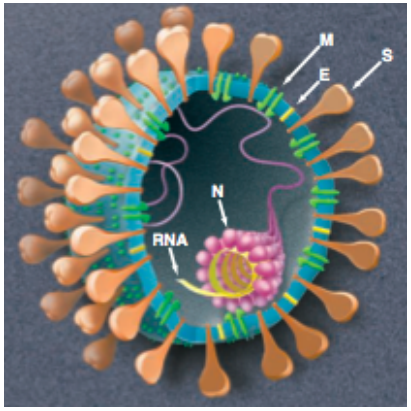
Sun et al. **2011** *PLoS ONE* 6:e27140

Evidence of airborne transmission

Severe acute respiratory syndrome (SARS)

- 10 years ago: global outbreak of SARS
  - In 8 months, 8100 people in 29 countries were infected
    - 774 died

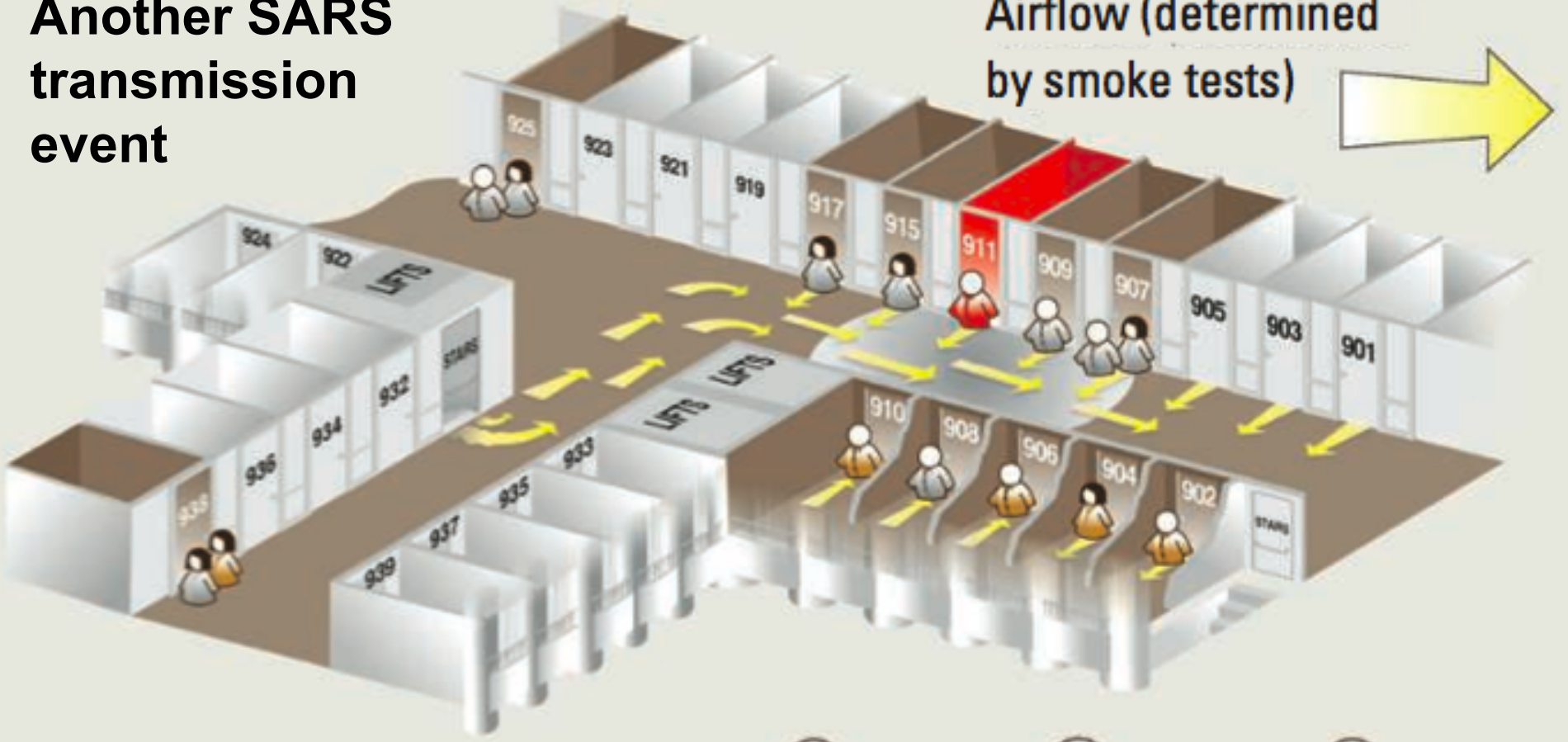
- In one high profile spreading event in Hong Kong, it became clear that transmission by airborne particles was substantial
  - One infected man suffering from diarrhea was linked to 300 SARS cases in one apartment building
  - Investigators concluded that diarrhea from the patient flushed into common plumbing system between units produced aerosols that traveled through piping and into other bathrooms
  - From there, both aerosol and subsequent person-to-person contact transmission likely occurred



SARS virus

Normile **2013** *Science* 339:1269-1273

Another SARS transmission event



Each room is indicated by its number (e.g. 911, index case); white numbers indicate affected rooms

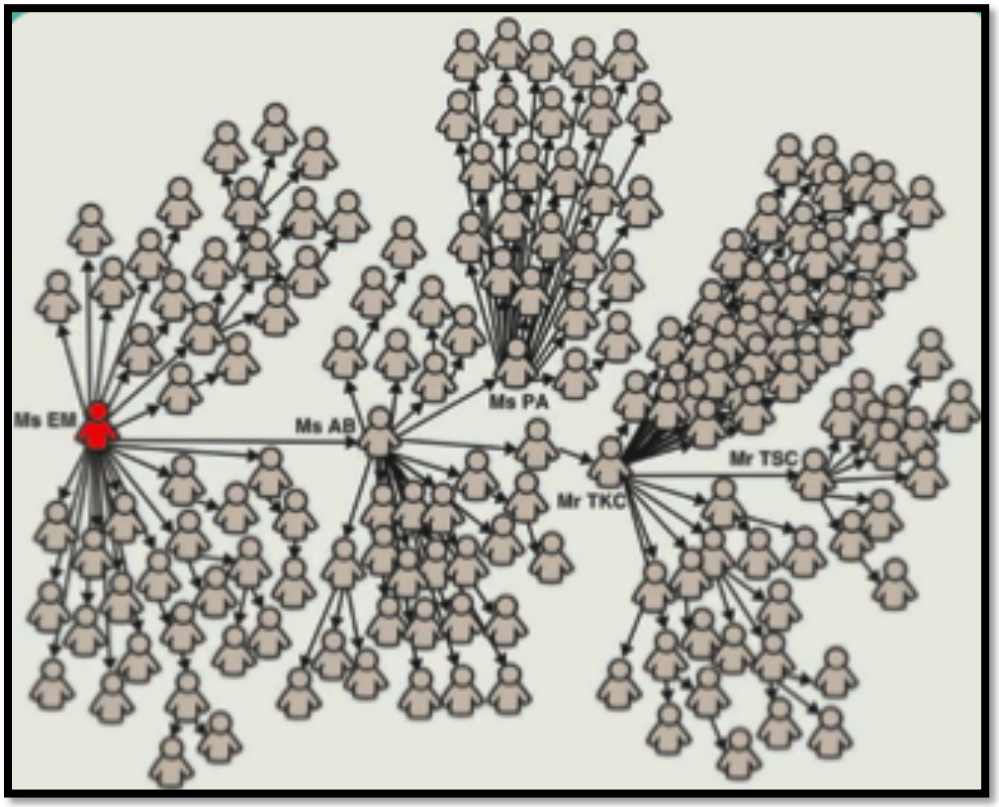
Index case
Prof LJL, 63, 21 infected

SARS case with further transmission

SARS case no further transmission

Normile **2013** *Science* 339:1269-1273

Importance of “super spreaders”



144 of Singapore’s 206 SARS cases were traced to 5 individuals

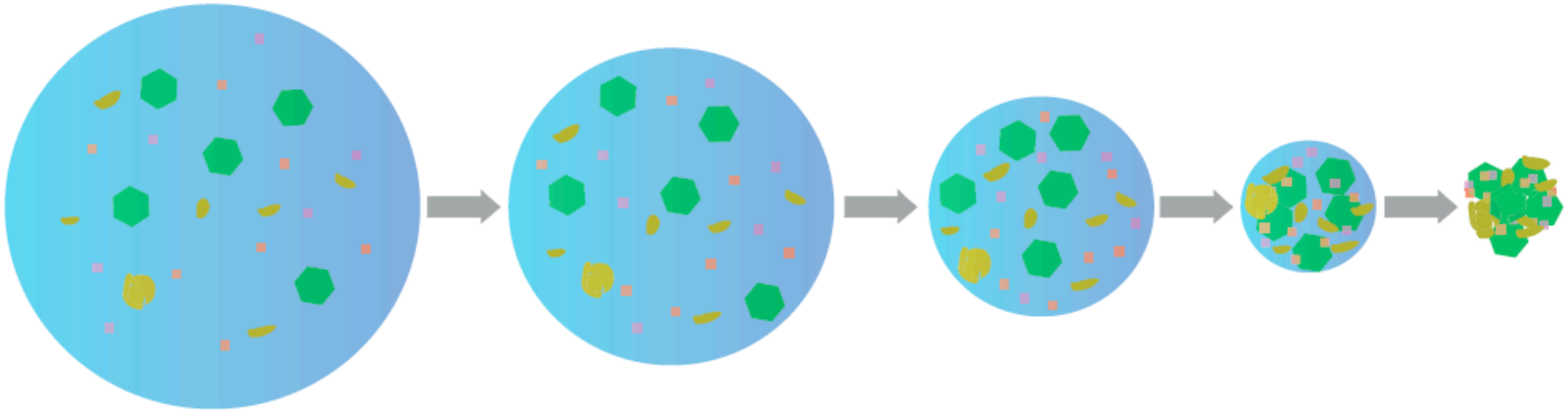
What makes a super spreader?

- Social/behavioral?
- Biological?
- Physical?

Normile **2013** *Science* 339:1269-1273

Expulsion of respiratory droplets/aerosols

- When a person coughs, sneezes, speaks or even breaths:
  - Particles of liquid water, proteins, salts, and other matter are expelled
    - These are called droplets
    - These particles may contain smaller infectious organisms
  - Large droplets may rapidly deposit to surfaces and/or decrease in size as the surrounding liquid evaporates
    - Droplet nuclei remain after evaporation
    - Typically 40-50% smaller diameter (d_p) than original droplets
      - Still contain infectious organisms



Verreault et al. **2008** *Microbiology and Molecular Biology Reviews* 72:413-444; Nicas et al. **2005** *J Occup Environ Hyg* 2:143-154; Chen and Zhao **2010** *Indoor Air* 20:95-111; Yang and Marr **2011** *PLoS ONE* 6:e21481

Rapid evaporation of droplets brought to you by *Mythbusters*

Droplet evaporation is nearly instantaneous

(And dependent on relative humidity)

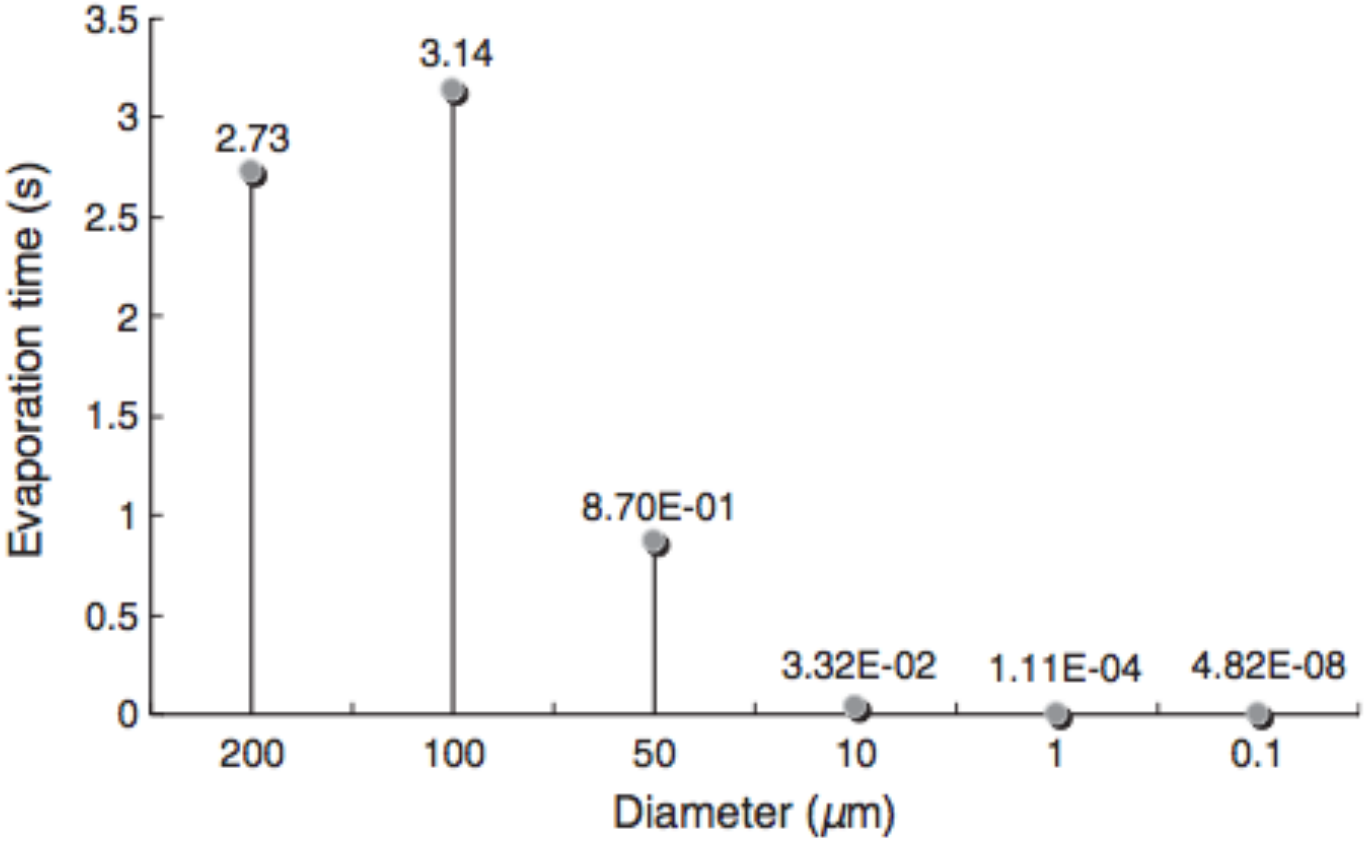


Fig. 5 The evaporation time of droplets with different diameters

Chen and Zhao **2010** *Indoor Air* 20:95-111

Disease transmission and droplet size

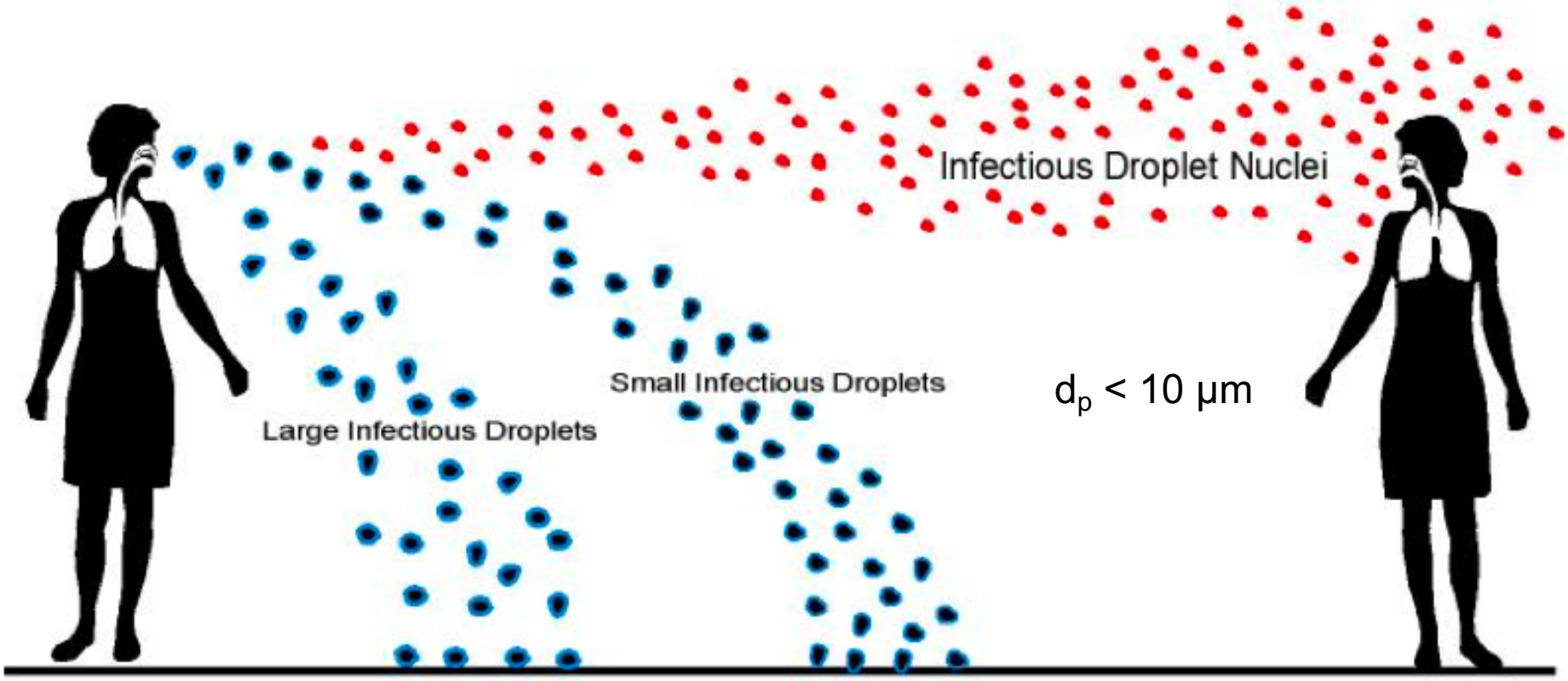
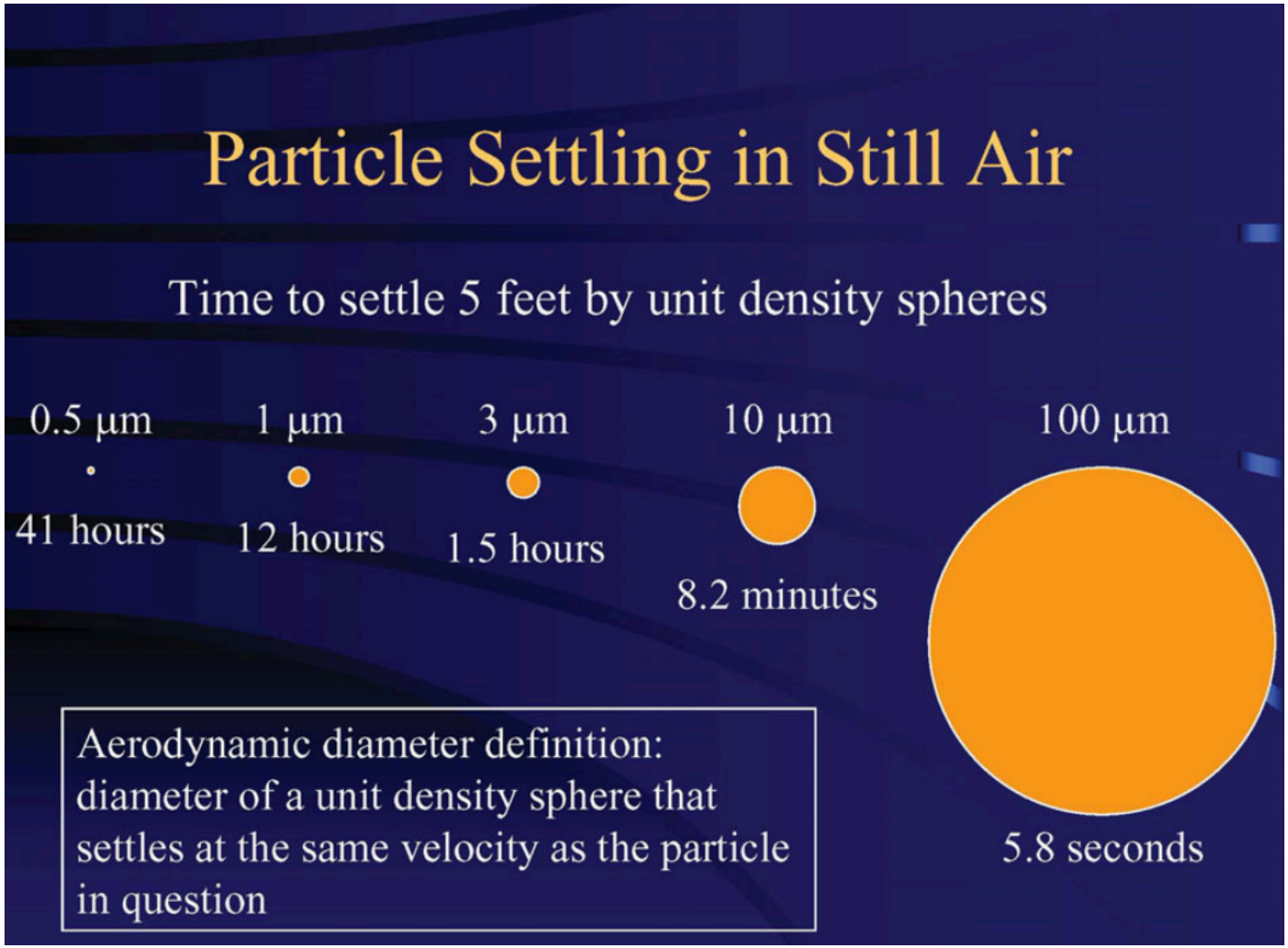


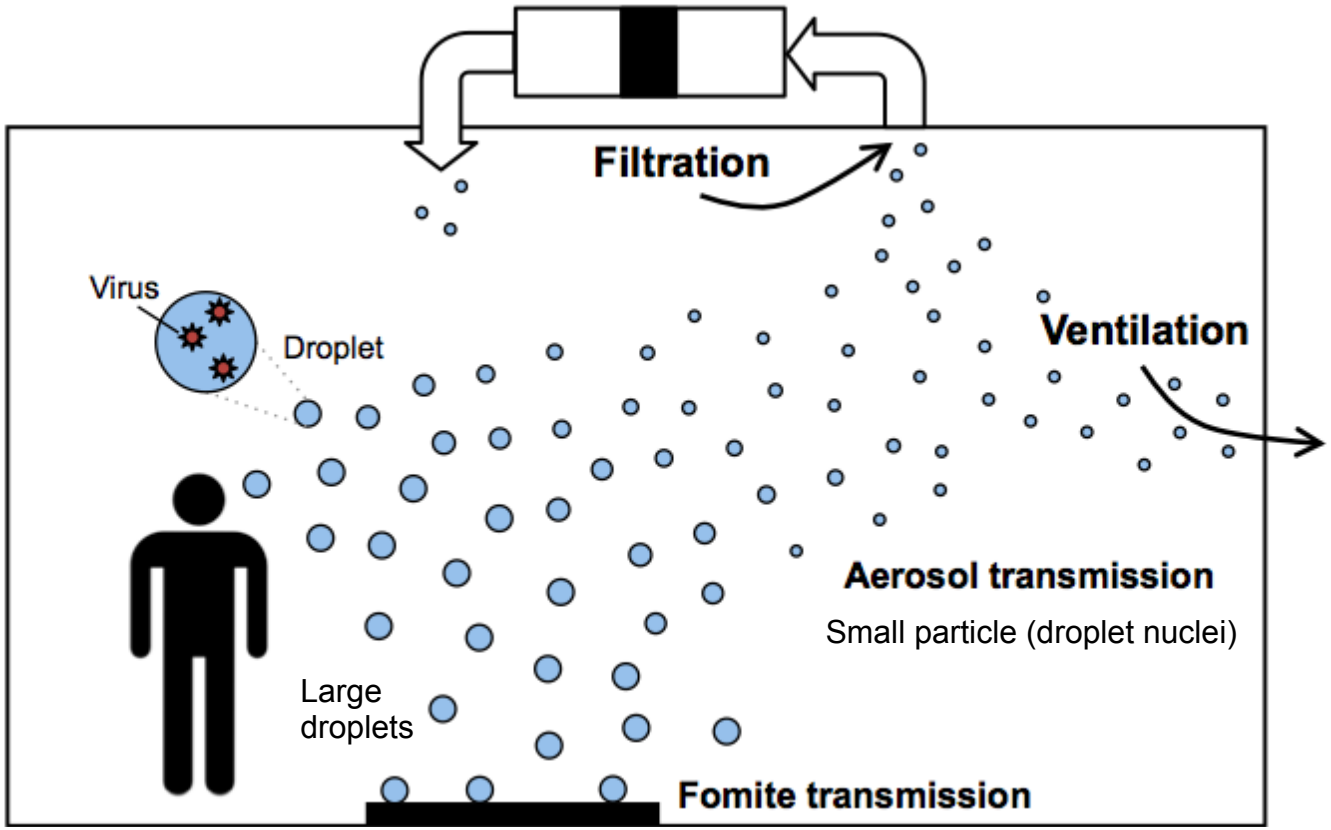
Figure taken directly from Welty **2009** presentation to FIC for IAQ, US EPA

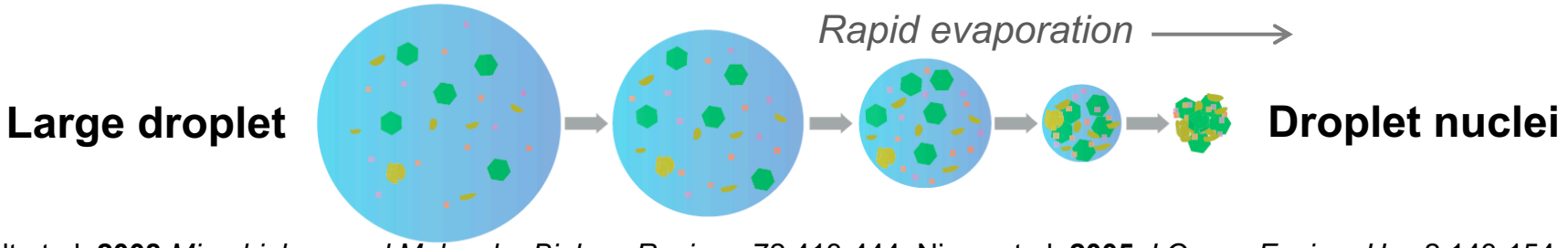
Droplet size and settling velocity



https://www.ashrae.org/file%20library/about/position%20documents/pd_infectiousaerosols_2020.pdf
https://www.cdc.gov/niosh/topics/aerosols/pdfs/Aerosol_101.pdf

Particle size is crucial for aerosol transmission





Verreault et al. **2008** *Microbiology and Molecular Biology Reviews* 72:413-444; Nicas et al. **2005** *J Occup Environ Hyg* 2:143-154; Chen and Zhao **2010** *Indoor Air* 20:95-111; Yang and Marr **2011** *PLoS ONE* 6:e21481; Lakdawala and Subbarao **2012** *Nature Medicine* 18:1468-1470

Droplet nuclei (aerosols) can mix rapidly

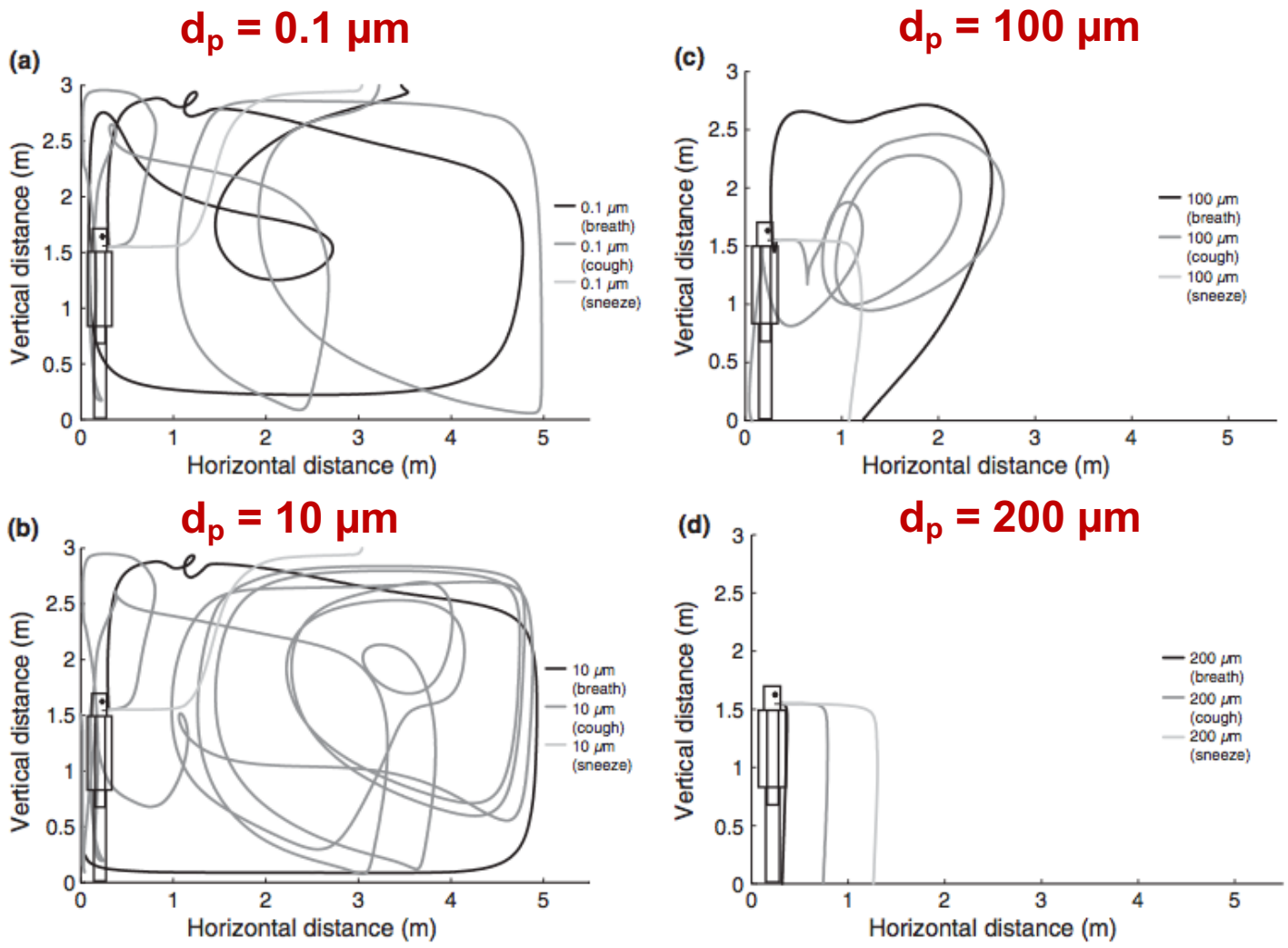


Fig. 13 Comparison of trajectories of droplets at different initial exhaled velocities. (a) initial diameter 0.1 μm, (b) initial diameter 10 μm, (c) initial diameter 100 μm, (d) initial diameter 200 μm. z = 2 m

Chen and Zhao **2010** *Indoor Air* 20:95-111

Evidence of airborne transmission

One of my favorite studies…

Aerosol Transmission of Rhinovirus Colds

Elliot C. Dick, Lance C. Jennings, Kathy A. Mink, Catherine D. Wartgow, and Stanley L. Inhorn

Rhinovirus infections may spread by aerosol, direct contact, or indirect contact involving environmental objects. We examined aerosol and indirect contact in transmission of rhinovirus type 16 colds between laboratory-infected men (donors) and susceptible men (recipients) who played cards together for 12 hr. In three experiments the infection rate of restrained recipients (10 [56%] of 18), who could not touch their faces and could only have been infected by aerosols, and that of unrestrained recipients (12 [67%] of 18), who could have been infected by aerosol, by direct contact, or by indirect fomite contact, was not significantly different ($\chi^2 = 0.468$, $P = .494$). In a fourth experiment, transmission via fomites heavily used for 12 hr by eight donors was the only possible route of spread, and no transmissions occurred among 12 recipients ($P < .00$ results suggest that contrary to current opinion, occurs chiefly by the aerosol route.

ments. Twenty-seven to 34 men >18 years of age were inoculated intranasally with 560–2,400 $TCID_{50}$ of safety-tested RV16 [5] by pipette and spray on two successive days. On the third day, eight men with the most severe colds (donors) played stud and draw poker with 12 antibody-free (no neutralization of virus by the undilute [1:1] serum specimen against a 20–25 $TCID_{50}$ challenge) men (recipients) between hours of 8 a.m. and 11 p.m. The ending hour was

Dick et al. **1987** *J Infectious Diseases* 156:442-448

Dick et al. **1987** *J Infectious Diseases* 156:442-448

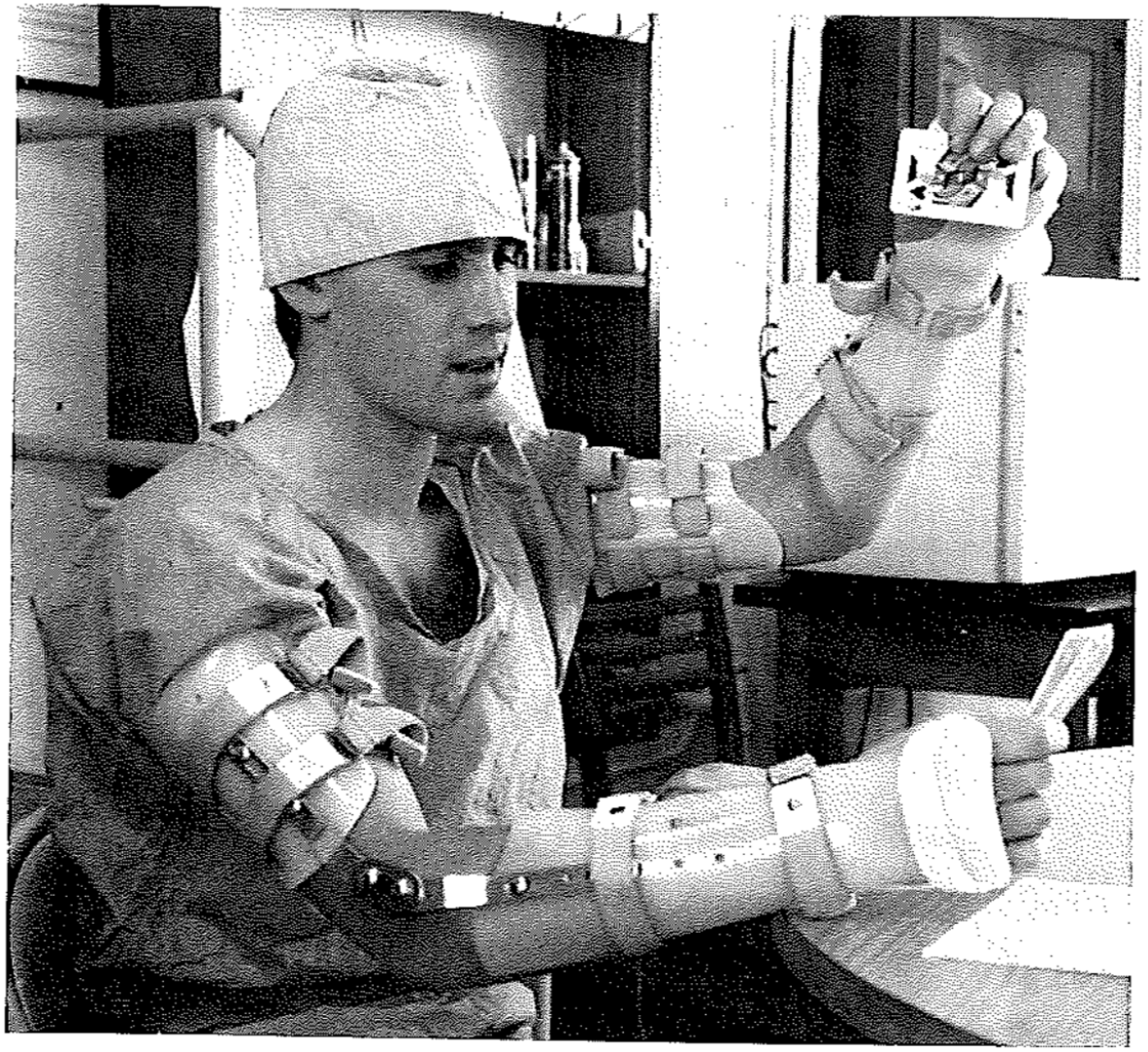


Figure 2. The arm braces used for restraining half of the recipients in experiments B and C. The braces allowed normal poker playing but prevented the wearer from touching any part of his head or face.

Dick et al. **1987** *J Infectious Diseases* 156:442-448

RESPIRATORY AEROSOLS/DROPLETS

Size distributions and pathogen presence

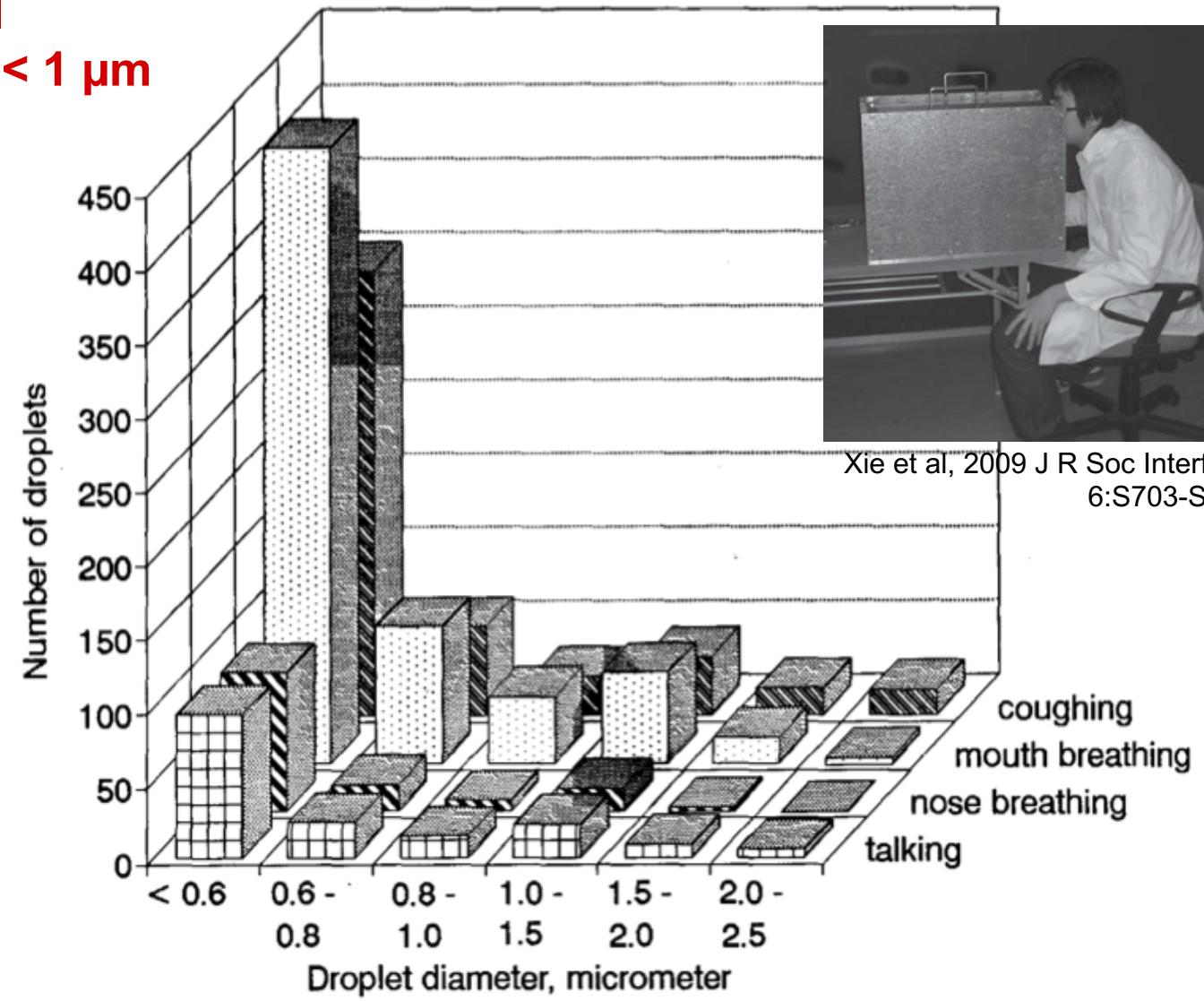
What particle sizes are emitted by humans?

- Commonly believed that droplet nuclei average 1-3 μm
  - Recent studies show that 80-90% of particles expelled during human activities are actually smaller than 1-2 μm

- When considering dynamics of infectious aerosols
  - It is crucial to consider particle sizes of infectious aerosols
  - Particle size governs transport, control (e.g. by filtration), deposition in respiratory tract, and resuspension ability

Emissions from coughing subjects

Nearly all particles < 1 µm

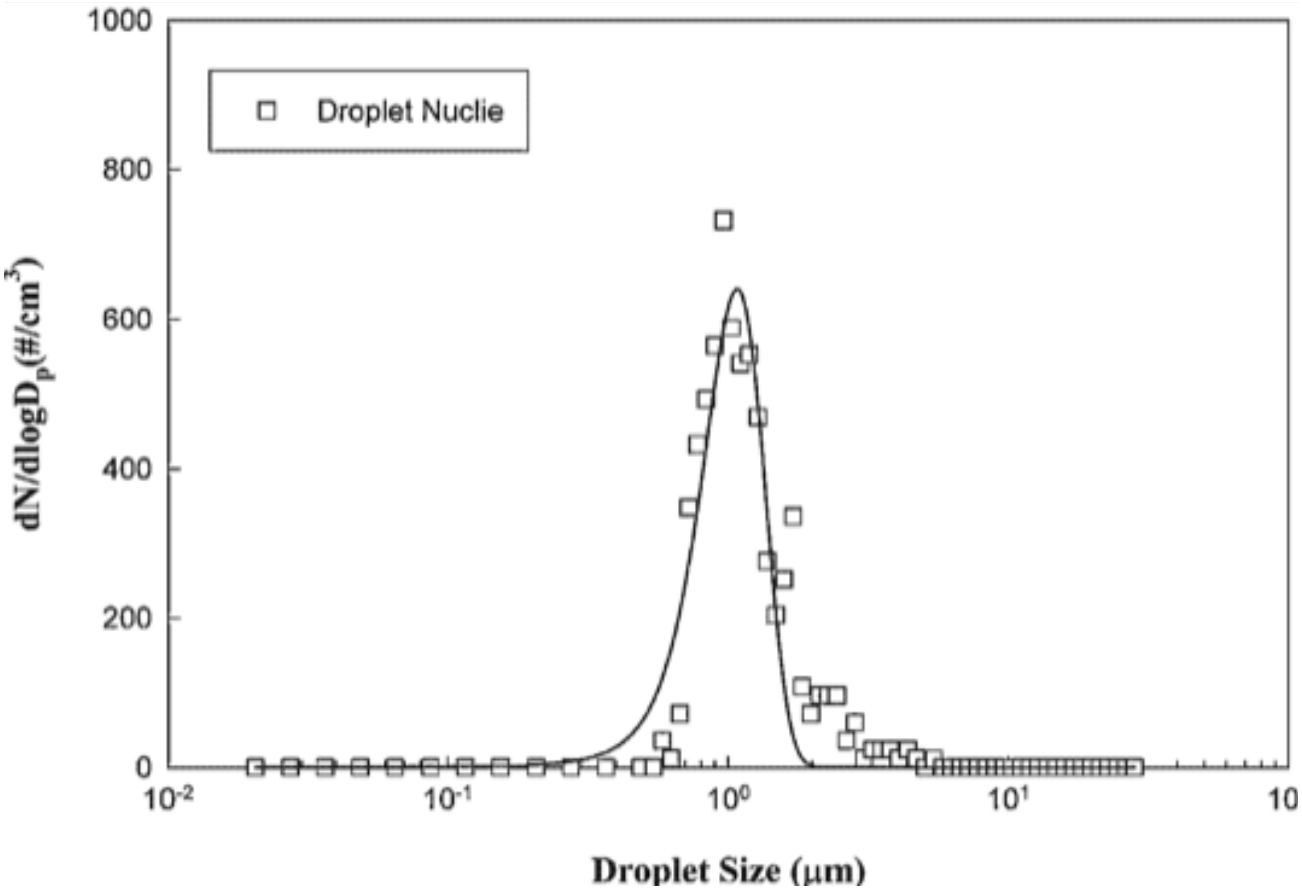


Xie et al, 2009 J R Soc Interface 6:S703-S714

Papineni and Rosenthal **1997** *J Aerosol Medicine* 10:105-116

More emissions from coughing subjects (n = 54)

- 82% of particles in the 0.7-2.2 μm size range

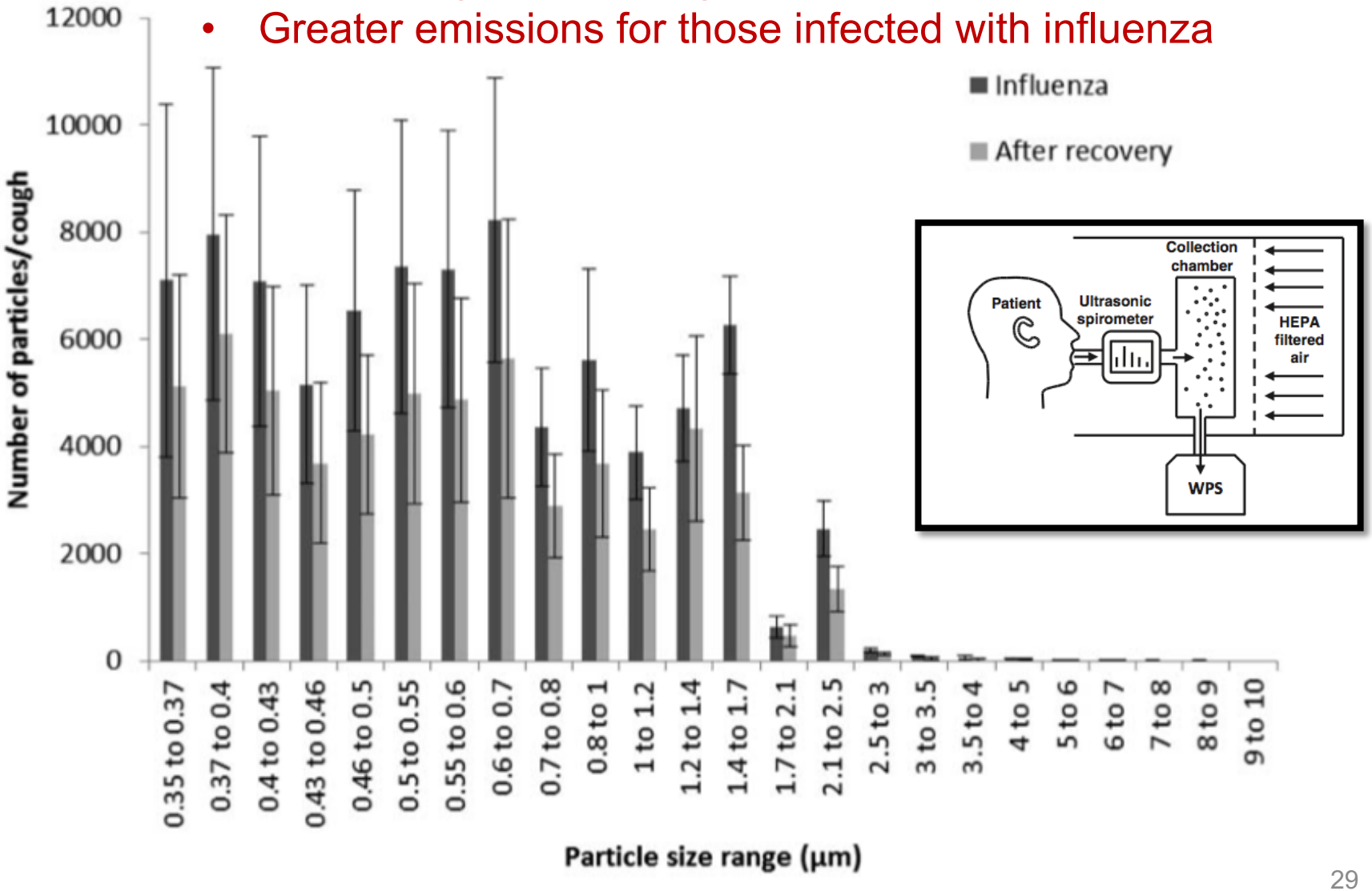


Yang et al., **2007** *J Aerosol Med* 20:484-494

Coughing subjects with and without influenza

Most emitted particles < 1 µm

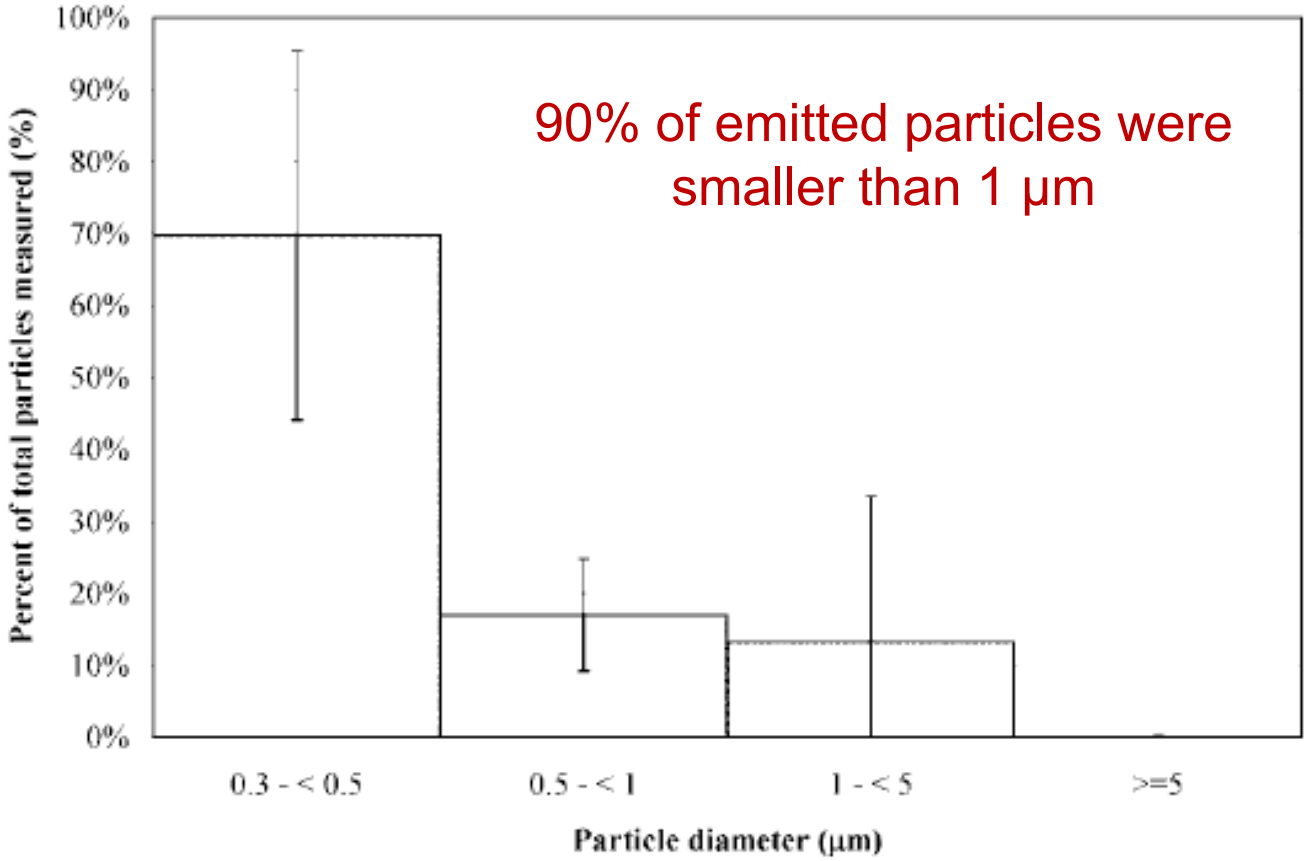
- Greater emissions for those infected with influenza



Lindsley et al., **2012** *J Occup Environ Hygiene* 9:443-449

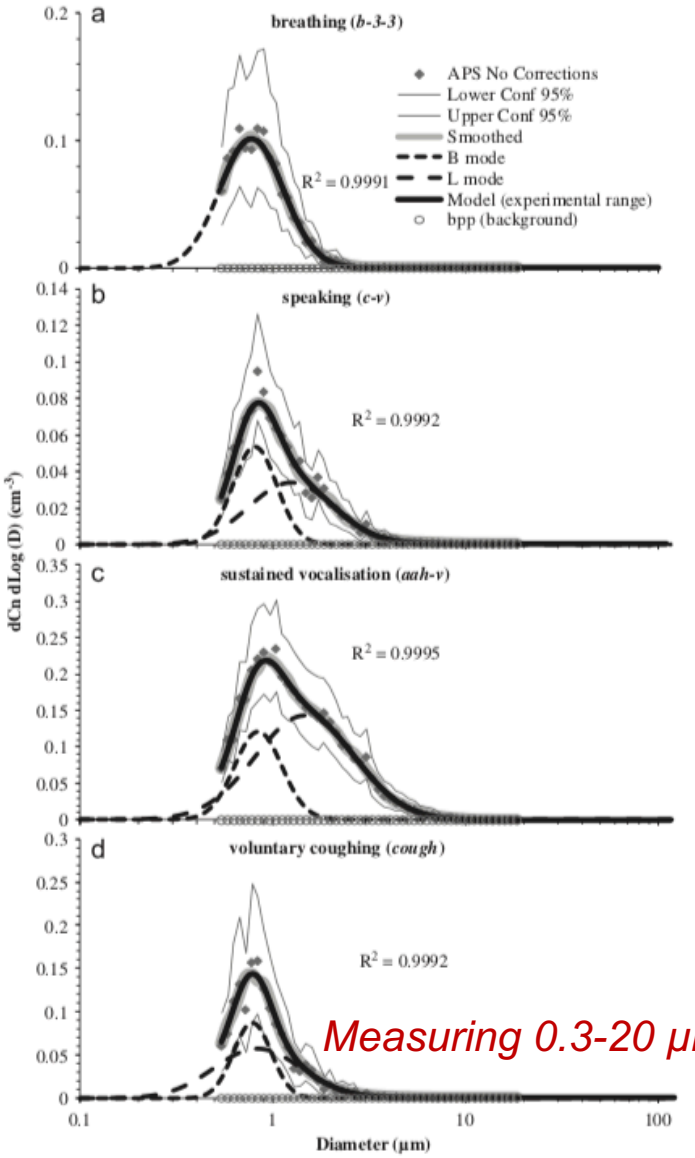
Emissions from breathing subjects

- Typically much smaller number concentrations than during coughing



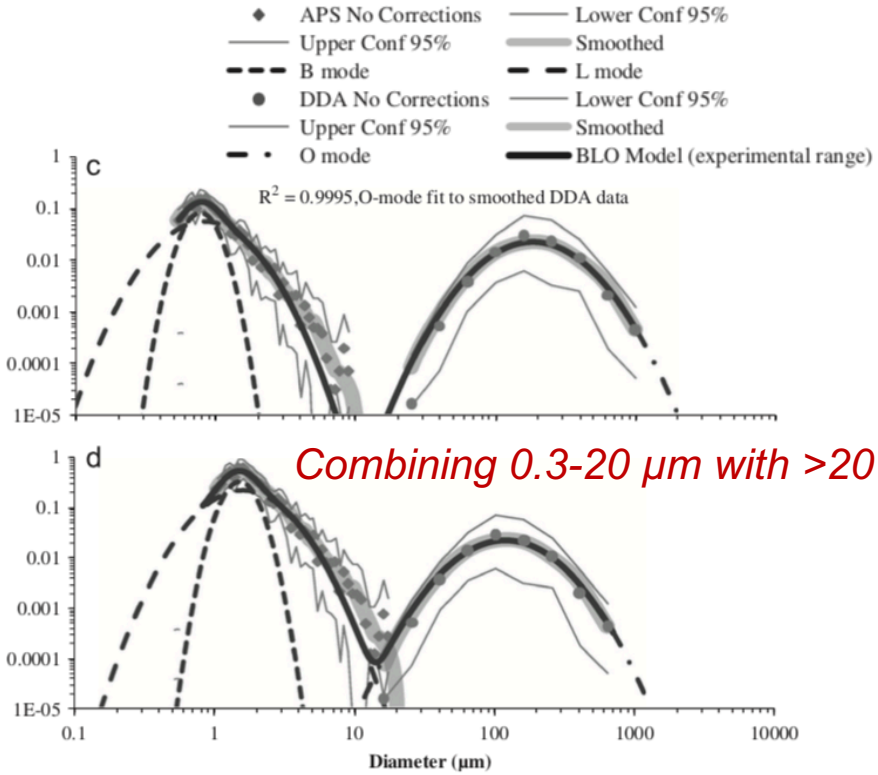
Fabian et al., **2008** *PLoS ONE* 3:e2691

Emissions from breathing, speaking, singing, coughing



Measuring 0.3-20 µm

Label	Description
b-3-3	Inhaling a normal breath volume via the mouth over a 3 s period, followed immediately by a 3 s full, deep exhalation via the mouth over a 3 s period. Repeated for 2 min
c-v	Alternately 10 s of voiced counting and 10 s of naturally paced breathing (2 min sample)
aah-v	Alternately 10 s of un-modulated vocalization (voiced "aah") and 10 s of naturally paced breathing (2 min sample). Mouth open throughout
cough	Coughing at an intensity and frequency, which the volunteer felt comfortable with. In practice, for most volunteers, the resulting cough intensity can be best described as a mild throat clearing cough (30 s sample)

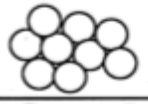
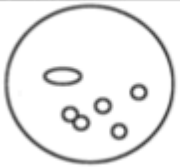


Combining 0.3-20 µm with >20 µm

Johnson et al., **2011** *J Aerosol Science*

What about infectious organisms within particles?

Shape and Aspect Ratios of Microorganisms

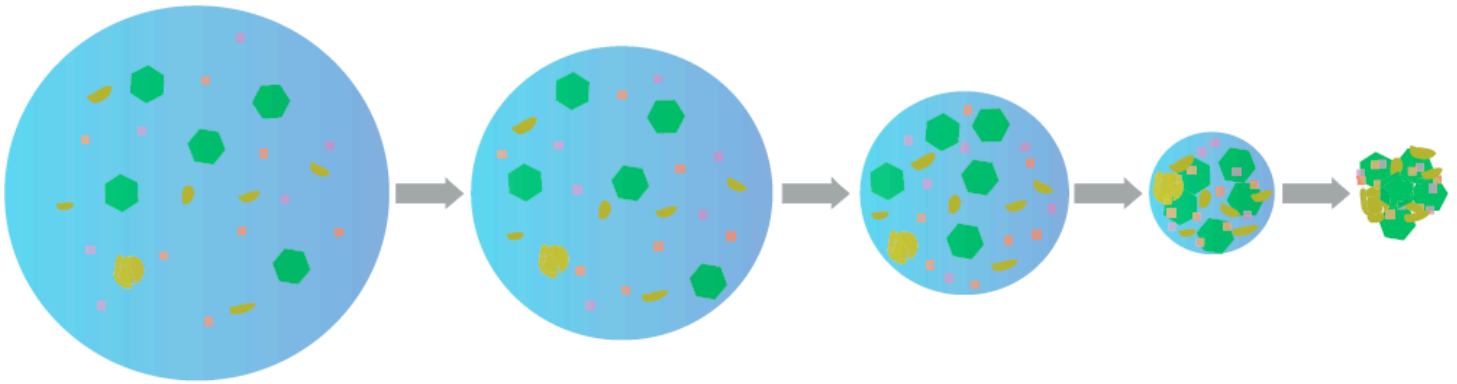
Shape	Type	Description	AR
	Icosahedral Helical	All respiratory viruses, whether icosahedral or helical, are so much smaller than filter fibers that they can be considered spherical for filtration calculations.	1
	Spherical	Most bacteria and spores are approximately spherical.	1
	Ovoid	Some bacteria and spores are ovoid.	1-3
	Rods	Bacteria classed as bacilli are rod-shaped.	1-10
	Diplo-cocci	Certain bacteria normally occur in pairs.	1-3
	Strepto-cocci	Some bacteria occur in strings (i.e. strepto-coccus) but are likely to break up on impact with filter fibers.	NA
	Staphylo-cocci	Some bacteria occur in bunches (i.e. staphylo-coccus) but are likely to break up on impact with filter fibers.	NA
	Flagella	Some bacteria have flagella, enabling motility.	NA
	Capsule	Some bacteria have hydrophobic capsules that can be shed or regenerated depending on the environment.	1-3
	Slime layer	Some microbes produce slime layers in addition to capsules that can be shed at any time.	1-3
	Droplets & Droplet Nuclei	Aerosolized droplets, typically 20-100 microns, may contain numerous microbes and other particles. These evaporate to condensation nuclei that may contain several viable microbes and residue. These will break up upon impact with filter fibers.	1-3

Pathogen	Mean size, μm
Influenza	0.098
Smallpox	0.22
C. burnetti	0.283
R. prowazeki	0.283
L. pneumophila	0.520
M. tuberculosis	0.637
C. diphtheria	0.700
S. pneumoniae	0.707
R. rickettsii	0.85
N. asteroides	1.12
Bacillus anthracis	1.12
H. capsulatum	2.24
Botulinum toxin	2.24
B. dermatitidis	12.6

Kowalski et al., **1999** *ASHRAE Transactions*

What about pathogens within respiratory aerosols?

- Most particles emitted during human activities are smaller than 1-2 μm
  - But particle volume scales with d_p^3
  - Does the amount of viral or bacterial material contained in droplet nuclei scale similarly?



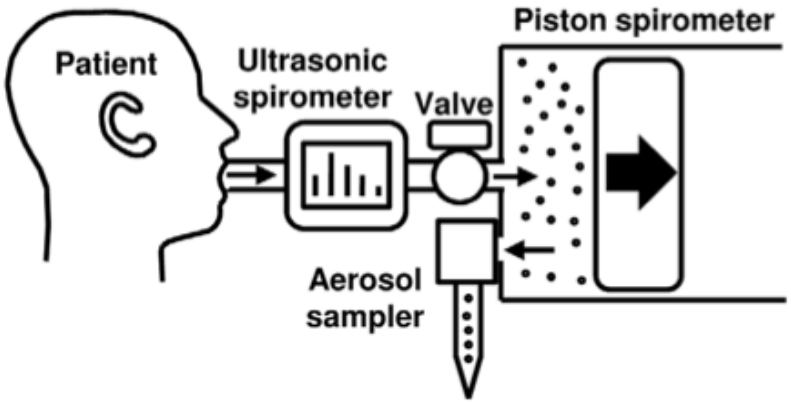
Virus detection methods

- Total bacterium or virus quantity
  - Number of gene copies (qPCR)
  - Intact DNA or RNA (infectious not known)

- Infectious virus
  - Number of viruses able to infect cells
  - Determined by culture (growth)
  - PFU = plaque forming units: the number of viruses capable of forming plaques on host cells
  - $TCID_{50}$ = median tissue culture infectious dose: the concentration at which half of the cells in a sample are infected after being exposed

Adapted from ”Viruses in Air,” presentation by Linsey Marr, Virginia Tech
https://twitter.com/linseymarr/status/1242245486196768773

Influenza RNA in size-resolved aerosol samples



qPCR reveals influenza viral RNA size distribution in human coughs:

- 42% < 1 µm
- 23% 1-4 µm
- 35% > 4 µm

Table 1. Influenza viral RNA detected in the NIOSH two-stage aerosol sampler.

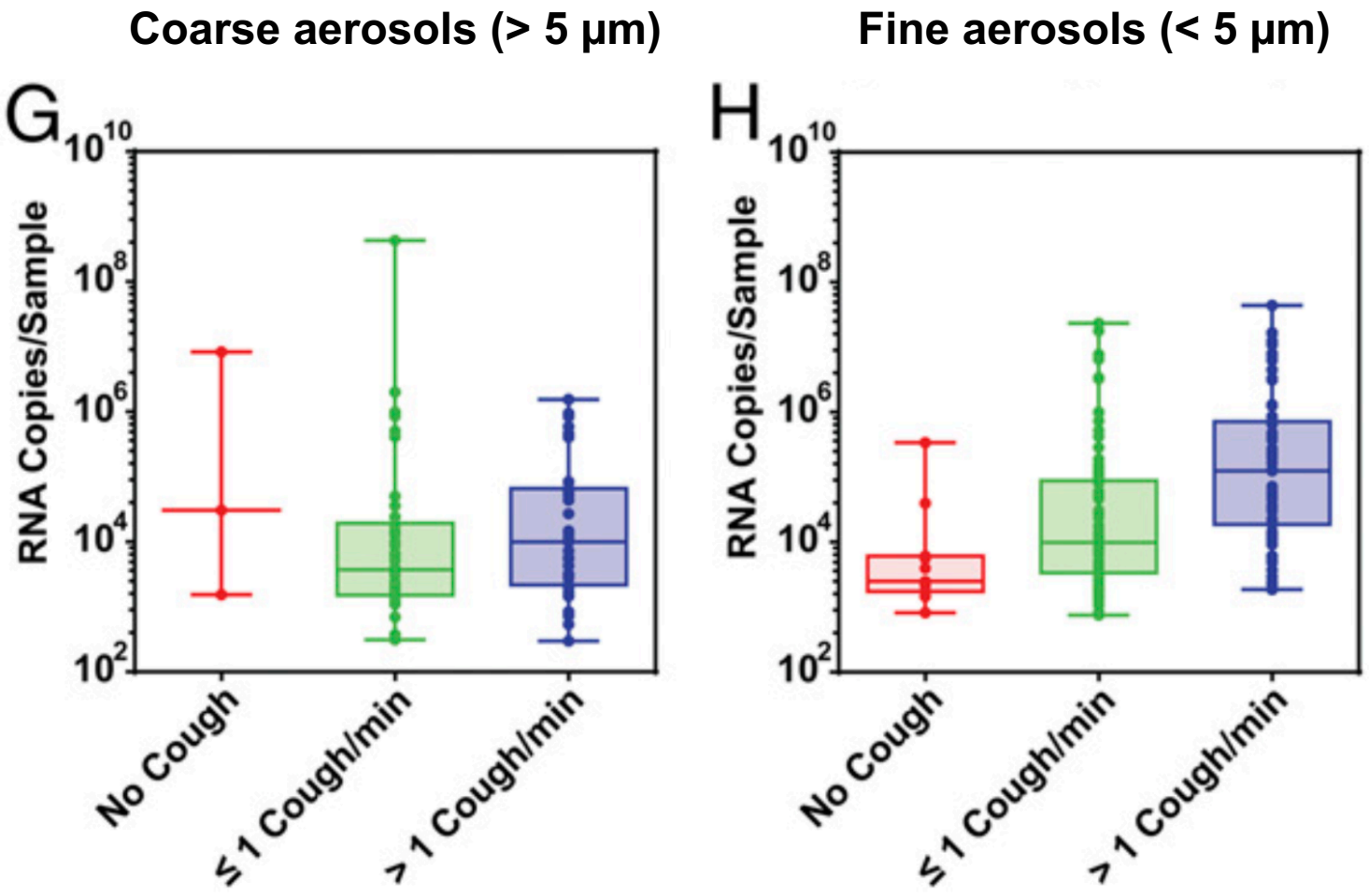
Aerosol particle size range (aerodynamic diameter)	*Median # of viral copies per cough*	*% of viral RNA contained in particles in this size range*	*% of subjects whose cough aerosol contained viral RNA-laden particles in this size range*
>4 µm	6.3 (SD 9.0)	35%	90%
1 to 4 µm	3.3 (SD 6.9)	23%	81%
<1 µm	3.7 (SD 23.7)	42%	75%
All particles	15.8 (SD 29.3)	100%	100%

Although ~90% of emitted particles (number concentrations) are < 1 µm

- Only ~40% of viral RNA is contained in that fraction

Lindsley et al., **2010** *PLoS ONE* 5:e15100

Influenza RNA in size-resolved aerosol samples



Yan et al., **2018** *PNAS* 115(5):1081-1086

Influenza RNA in size-resolved aerosol samples

Distribution of Airborne Influenza Virus and Respiratory Syncytial Virus in an Urgent Care Medical Clinic

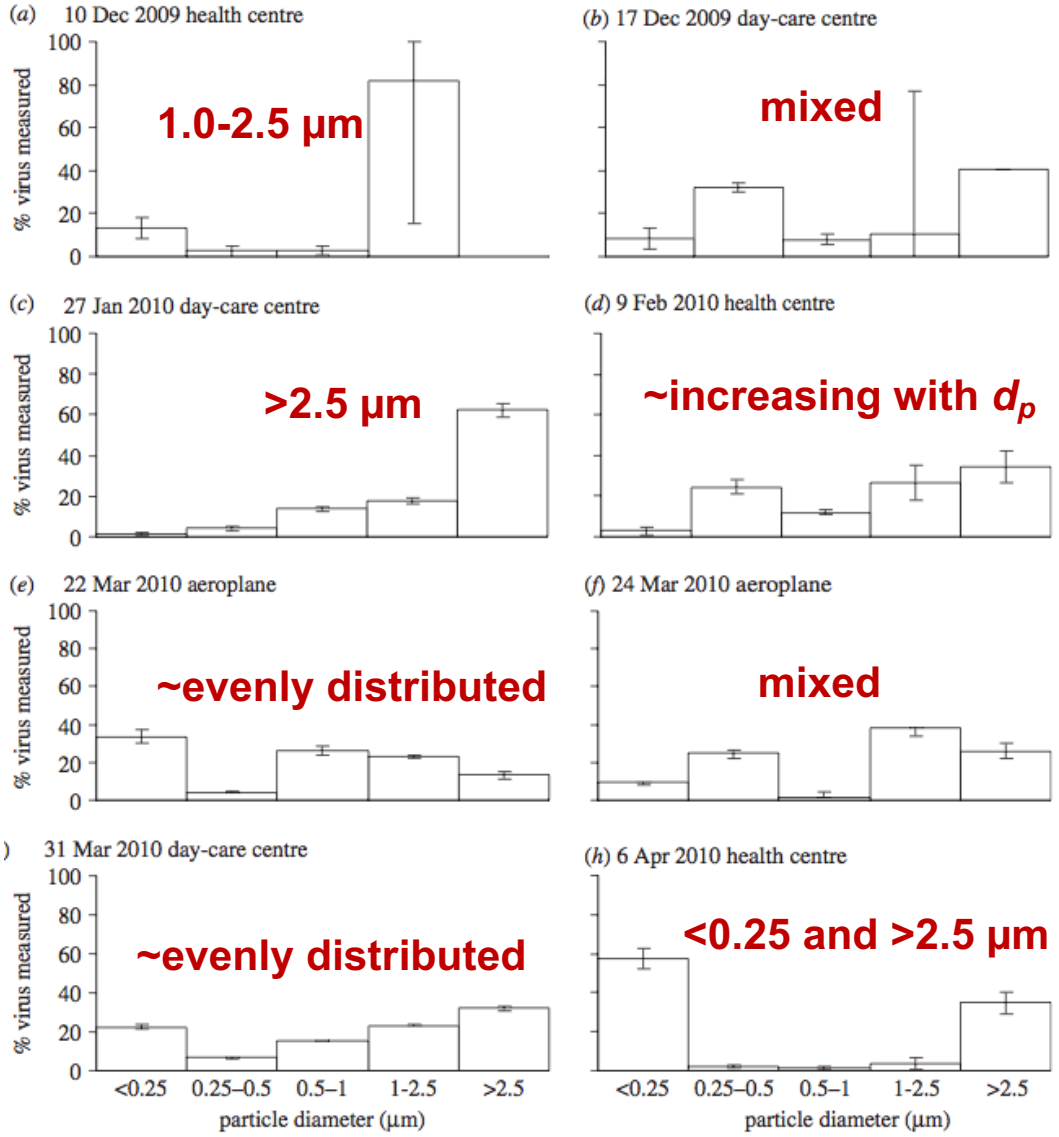
qPCR reveals influenza viral RNA size distribution in an urgent care clinic:

- ~10-20% < 1 µm
- ~20-40% 1-4 µm
- ~50-60% > 4 µm

Sampling Location	Distribution of viral RNA		
Personal samplers	< 1.7 µm 32%	1.7-4.9 µm 16%	> 4.9 µm 52%
Lower stationary samplers	< 1 µm 13%	1-4.1 µm 37%	> 4.1 µm 50%
Upper stationary samplers	< 1 µm 9%	1-4.1 µm 27%	> 4.1 µm 64%

Lindsley et al., **2010** *Clinical Infectious Diseases* 50:693-698

Influenza RNA in size-resolved aerosol samples



Yang et al., **2011** *J R Soc Interface* 8:1176-1184

Influenza virus *viability* in aerosols

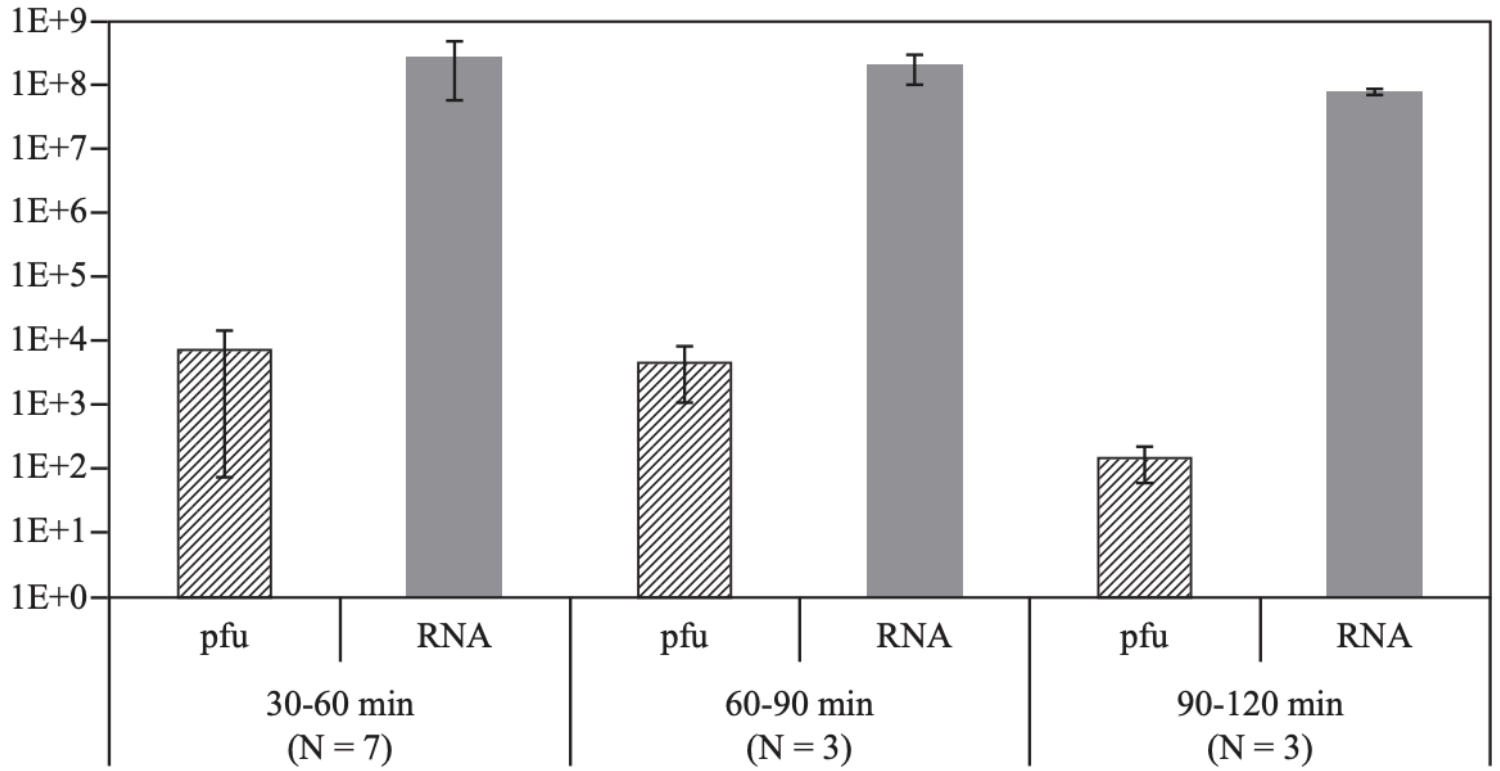
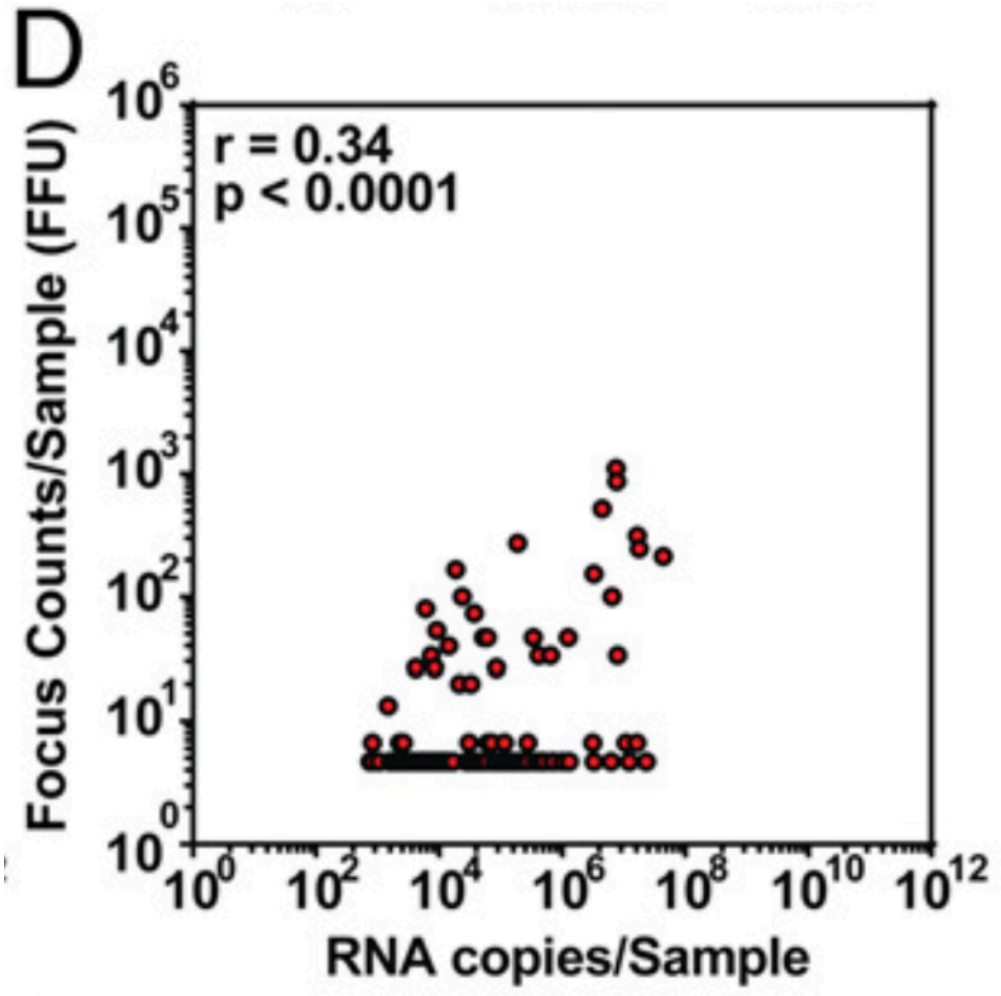


Figure 2. Quantification of viable virus (plaque-forming units, pfu/m^3) and viral RNA (copies/m^3) recovered from air-sampling after various suspension times, post-nebulization. Error bars represent mean $\pm$ 1 standard deviation.

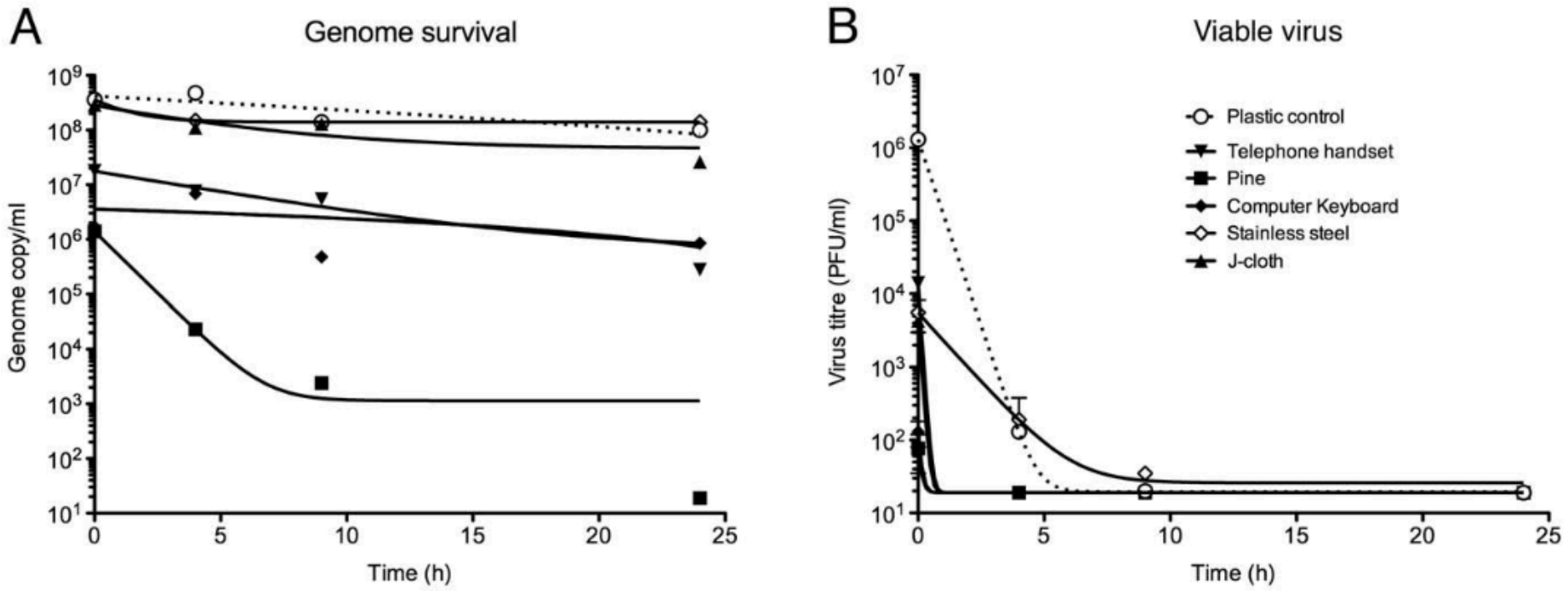
Brown et al., **2015** *J Hospital Infection* 91:278-281

Influenza RNA vs. influenza viability in aerosols



Yan et al., **2018** *PNAS* 115(5):1081-1086

Influenza virus *viability* on surfaces



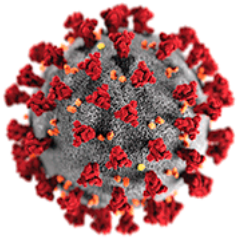
Conclusions/Significance: The genome of either virus could be detected on most surfaces 24 h after application with relatively little drop in copy number, with the exception of unsealed wood surfaces. In contrast, virus viability dropped much more rapidly. Live virus was recovered from most surfaces tested four hours after application and from some non-porous materials after nine hours, but had fallen below the level of detection from all surfaces at 24 h. We conclude that influenza A transmission via fomites is possible but unlikely to occur for long periods after surface contamination (unless re-inoculation occurs). In situations involving a high probability of influenza transmission, our data suggest a hierarchy of priorities for surface decontamination in the multi-surface environments of home and hospitals.

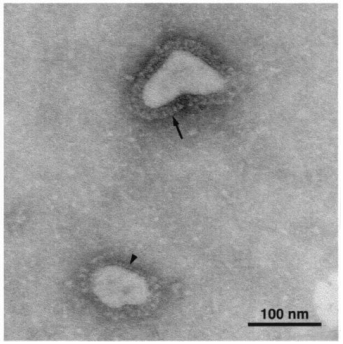
Greatorex et al., **2011** *PLoS ONE* 6(11): e27932

NOVEL CORONAVIRUS (SARS-COV-2)

SARS-CoV-2 and COVID-19

- Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus (SARS-CoV-2)
  - The problem is no one has immunity to a novel virus (yet)
- Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment
  - Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness
- There are no vaccines or treatments for COVID-19 (yet)
  - There are many ongoing clinical trials evaluating potential treatments





https://www.who.int/health-topics/coronavirus

How is SARS-CoV-2 spread?

- **WHO, March 2020**:

  "The virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes."

  https://www.who.int/health-topics/coronavirus

How is SARS-CoV-2 spread?

- **WHO, July 2020**:

Main findings

- Understanding how, when and in what types of settings SARS-CoV-2 spreads between people is critical to develop effective public health and infection prevention measures to break chains of transmission.
- Current evidence suggests that transmission of SARS-CoV-2 occurs primarily between people through direct, indirect, or close contact with infected people through infected secretions such as saliva and respiratory secretions, or through their respiratory droplets, which are expelled when an infected person coughs, sneezes, talks or sings.
- Airborne transmission of the virus can occur in health care settings where specific medical procedures, called aerosol generating procedures, generate very small droplets called aerosols. Some outbreak reports related to indoor crowded spaces have suggested the possibility of aerosol transmission, combined with droplet transmission, for example, during choir practice, in restaurants or in fitness classes.
- Respiratory droplets from infected individuals can also land on objects, creating fomites (contaminated surfaces). As environmental contamination has been documented by many reports, it is likely that people can also be infected by touching these surfaces and touching their eyes, nose or mouth before cleaning their hands.

https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions

How is SARS-CoV-2 spread?

- What changed?

239 Experts With One Big Claim: The Coronavirus Is Airborne

The W.H.O. has resisted mounting evidence that viral particles floating indoors are infectious, some scientists say. The agency maintains the research is still inconclusive.

W.H.O. to Review Evidence of Airborne Transmission of Coronavirus

The World Health Organization plans to update its advice after hundreds of experts urged the agency to reconsider the risk of aerosol transmission.

https://www.nytimes.com/2020/07/04/health/239-experts-with-one-big-claim-the-coronavirus-is-airborne.html
https://www.nytimes.com/2020/07/07/health/coronavirus-aerosols-who.html

ACCEPTED MANUSCRIPT

It is Time to Address Airborne Transmission of COVID-19 FREE

Lidia Morawska ✉, Donald K Milton

Clinical Infectious Diseases, ciaa939, https://doi.org/10.1093/cid/ciaa939
Published: 06 July 2020 **Article history** ▾

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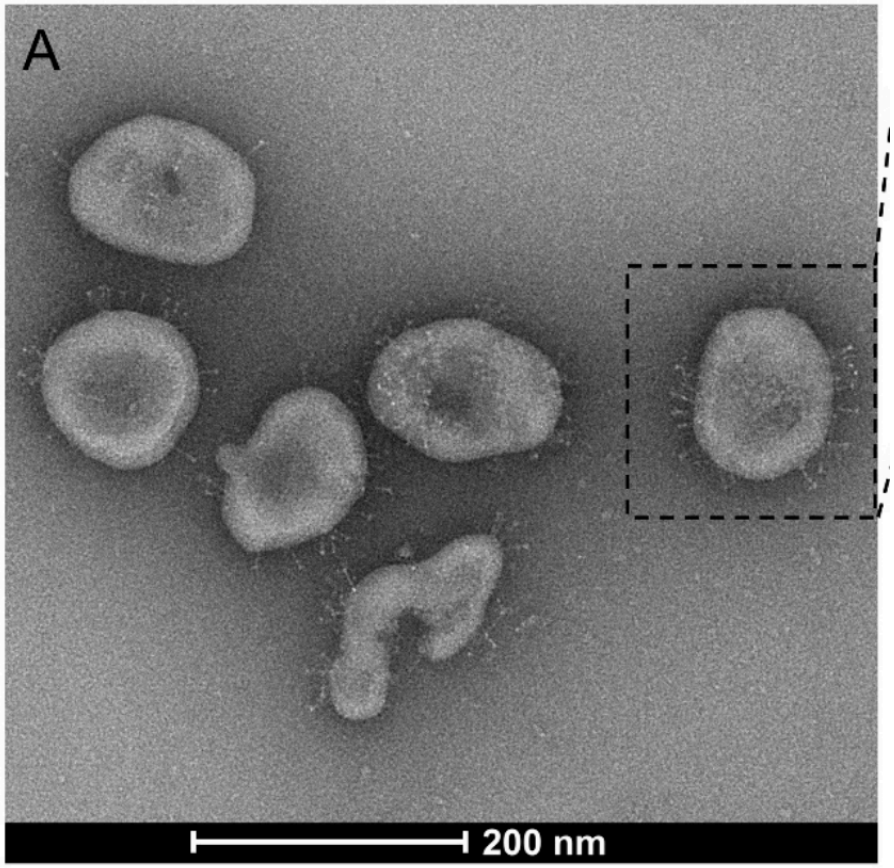
https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa939/5867798

How is SARS-CoV-2 spread?

- This novel coronavirus is ~120 nm in diameter
  - Influenza viruses are ~80-120 nm in diameter



https://www.biorxiv.org/content/10.1101/2020.03.02.972927v1

SARS-CoV-2 detection in Singapore hospital AIIRs

- AAIRs = airborne infection isolation rooms
  - Negative pressure, high air exchange rates

Understanding the particle size distribution in the air and patterns of environmental contamination of SARS-CoV-2 is essential for infection prevention policies. Here we screen surface and air samples from hospital rooms of COVID-19 patients for SARS-CoV-2 RNA. Environmental sampling is conducted in three airborne infection isolation rooms (AIIRs) in the ICU and 27 AIIRs in the general ward. 245 surface samples are collected. 56.7% of rooms have at least one environmental surface contaminated. High touch surface contamination is shown in ten (66.7%) out of 15 patients in the first week of illness, and three (20%) beyond the first week of illness ($p = 0.01$, χ^2 test). Air sampling is performed in three of the 27 AIIRs in the general ward, and detects SARS-CoV-2 PCR-positive particles of sizes >4 μm and 1–4 μm in two rooms, despite these rooms having 12 air changes per hour. This warrants further study of the airborne transmission potential of SARS-CoV-2.

Chia et al., **2020** *Nature Communication* 11:2800
https://www.nature.com/articles/s41467-020-16670-2

SARS-CoV-2 detection in Singapore hospital AIIRs

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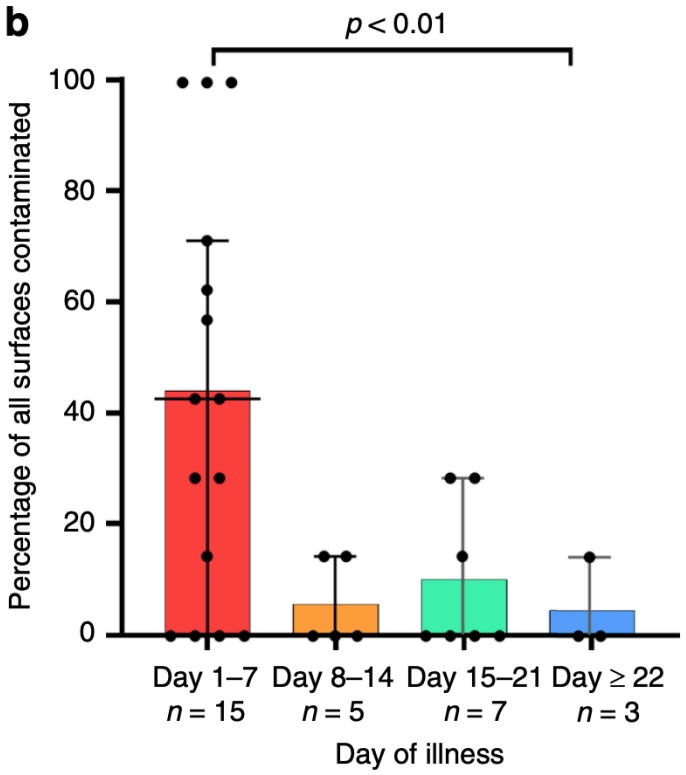
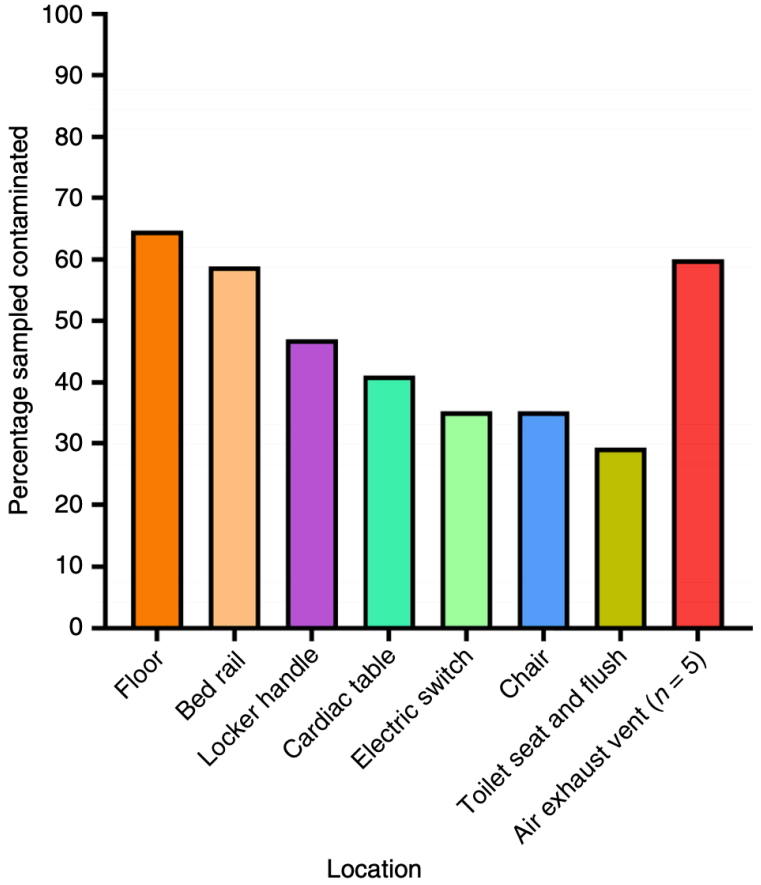




Chia et al., **2020** *Nature Communication* 11:2800
https://www.nature.com/articles/s41467-020-16670-2

Fig. 1 Percentage of contaminated swabs from surface samples, in rooms with any contamination. All sites were $n = 17$, except for air exhaust vents where $n = 5$.

SARS-CoV-2 detection in Singapore patient rooms

From January 24 to February 4, 2020, 3 patients at the dedicated SARS-CoV-2 outbreak center in Singapore in airborne infection isolation rooms (12 air exchanges per hour) with anterooms and bathrooms had surface environmental samples taken at 26 sites. Personal protective equipment (PPE) samples from study physicians exiting the patient rooms also were collected. Sterile premoistened swabs were used.

Samples were collected on 5 days over a 2-week period. One patient's room was sampled before routine cleaning and 2 patients' rooms after routine cleaning. Twice-daily cleaning of high-touch areas was done using 5000 ppm of sodium dichloroisocyanurate. The floor was cleaned daily using 1000 ppm of sodium dichloroisocyanurate.

Patient A's room was sampled on days 4 and 10 of illness while the patient was still symptomatic, after routine cleaning. All samples were negative. Patient B was symptomatic on day 8 and asymptomatic on day 11 of illness; samples taken on these 2 days after routine cleaning were negative (**Table 1**).

Ong et al., **2020** *JAMA* 323(16):1610-1612
https://jamanetwork.com/journals/jama/fullarticle/2762692

SARS-CoV-2 detection in Singapore patient rooms

Patient C, whose samples were collected before routine cleaning, had positive results, with 13 (87%) of 15 room sites (including air outlet fans) and 3 (60%) of 5 toilet sites (toilet bowl, sink, and door handle) returning positive results (**Table 2**). Anteroom and corridor samples were negative. Patient C had upper respiratory tract involvement with no pneumonia and had 2 positive stool samples for SARS-CoV-2 on RT-PCR despite not having diarrhea.

Only 1 PPE swab, from the surface of a shoe front, was positive. All other PPE swabs were negative. All air samples were negative.

There was extensive environmental contamination by 1 SARS-CoV-2 patient with mild upper respiratory tract involvement. Toilet bowl and sink samples were positive, suggesting that viral shedding in stool[5] could be a potential route of transmission. Postcleaning samples were negative, suggesting that current decontamination measures are sufficient.

Ong et al., **2020** *JAMA* 323(16):1610-1612
https://jamanetwork.com/journals/jama/fullarticle/2762692

SARS-CoV-2 detection in Wuhan hospitals

The ongoing outbreak of coronavirus disease 2019 (COVID-19) has spread rapidly on a global scale. Although it is clear that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is transmitted through human respiratory droplets and direct contact, the potential for aerosol transmission is poorly understood[1–3]. Here we investigated the aerodynamic nature of SARS-CoV-2 by measuring viral RNA in aerosols in different areas of two Wuhan hospitals during the outbreak of COVID-19 in February and March 2020. The concentration of SARS-CoV-2 RNA in aerosols that was detected in isolation wards and ventilated patient rooms was very low, but it was higher in the toilet areas used by the patients. Levels of airborne SARS-CoV-2 RNA in the most public areas was undetectable, except in two areas that were prone to crowding; this increase was possibly due to individuals infected with SARS-CoV-2 in the crowd. We found that some medical staff areas initially had high concentrations of viral RNA with aerosol size distributions that showed peaks in the submicrometre and/or supermicrometre regions; however, these levels were reduced to undetectable levels after implementation of rigorous sanitization procedures. Although we have not established the infectivity of the virus detected in these hospital areas, we propose that SARS-CoV-2 may have the potential to be transmitted through aerosols. Our results indicate that room ventilation, open space, sanitization of protective apparel, and proper use and disinfection of toilet areas can effectively limit the concentration of SARS-CoV-2 RNA in aerosols. Future work should explore the infectivity of aerosolized virus.

Liu et al., **2020** *Nature* 582:557-560
https://www.nature.com/articles/s41586-020-2271-3

SARS-CoV-2 detection in Wuhan hospitals

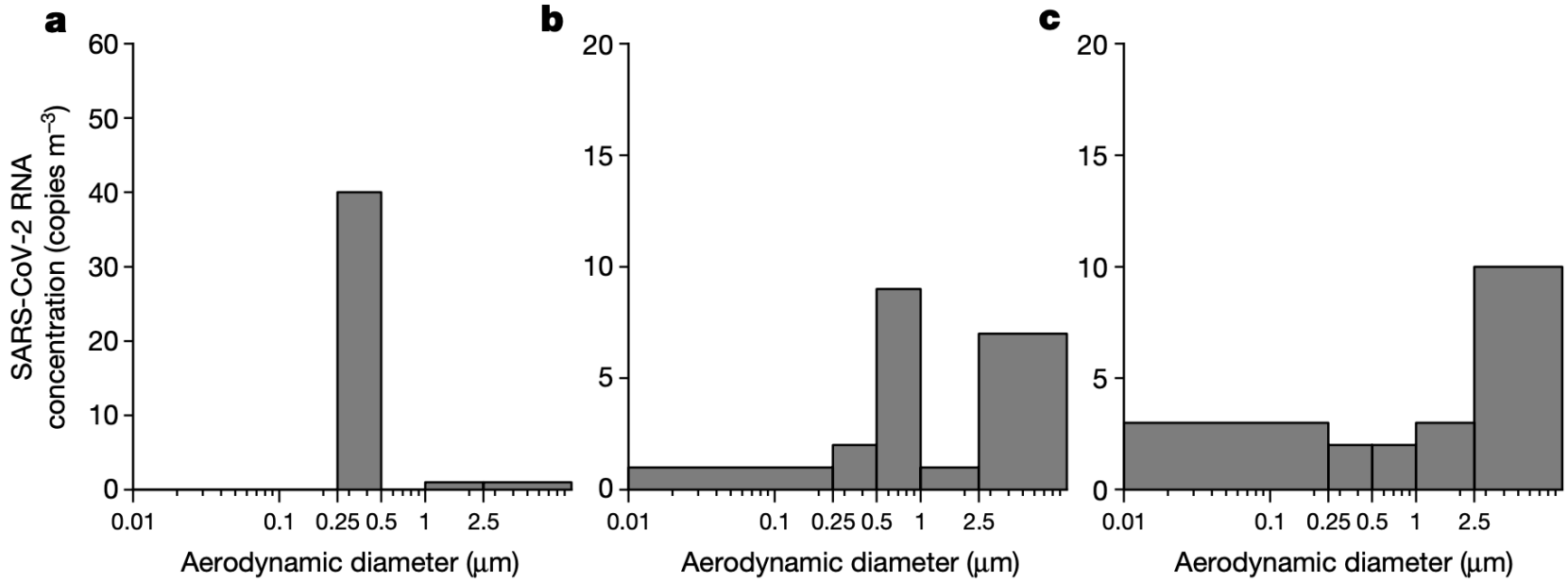
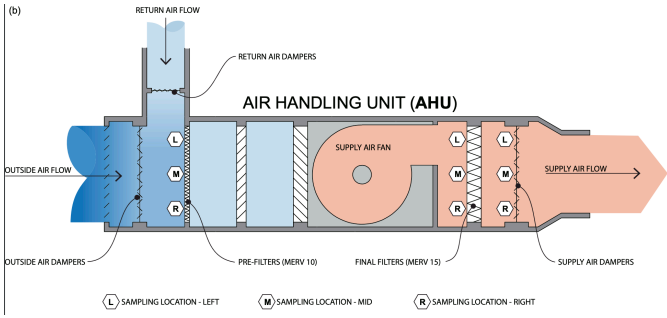


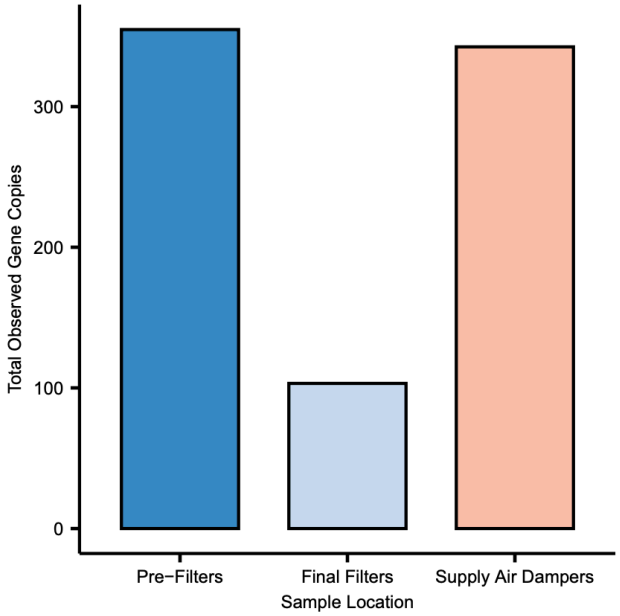
Fig. 1 | Concentration of airborne SARS-CoV-2 RNA in different aerosol size bins. a, Concentration of SARS-CoV-2 in a protective-apparel removal room in zone B of Fangcang Hospital. **b**, Concentration of SARS-CoV-2 in a protective-apparel removal room in zone C of Fangcang Hospital. **c**, Concentration of SARS-CoV-2 in the medical staff's office of Fangcang Hospital. The *x* axis represents the aerodynamic diameter on a logarithmic scale to cover the multiple magnitudes of measured aerosol diameters.

Liu et al., **2020** *Nature* 582:557-560
https://www.nature.com/articles/s41586-020-2271-3

SARS-CoV-2 detection in healthcare HVAC units

Available information on Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) transmission by small particle aerosols continues to evolve rapidly. To assess the potential role of heating, ventilation, and air conditioning (HVAC) systems in airborne viral transmission, this study sought to determine the viral presence, if any, on air handling units in a healthcare setting where Coronavirus Disease 2019 (COVID-19) patients were being treated. The presence of SARS-CoV-2 RNA was detected in approximately 25% of samples taken from nine different locations in multiple air handlers. While samples were not evaluated for viral infectivity, the presence of viral RNA in air handlers raises the possibility that viral particles can enter and travel within the air handling system of a hospital, from room return air through high efficiency MERV-15 filters and into supply air ducts. Although no known transmission events were determined to be associated with these specimens, the findings suggest the potential for HVAC systems to facilitate transmission by environmental contamination via shared air volumes with locations remote from areas where infected persons reside. More work is needed to further evaluate the risk of SARS-CoV-2 transmission via HVAC systems and to verify effectiveness of building operations mitigation strategies for the protection of building occupants. These results are important within and outside of healthcare settings and may present a matter of some urgency for building operators of facilities that are not equipped with high-efficiency filtration.





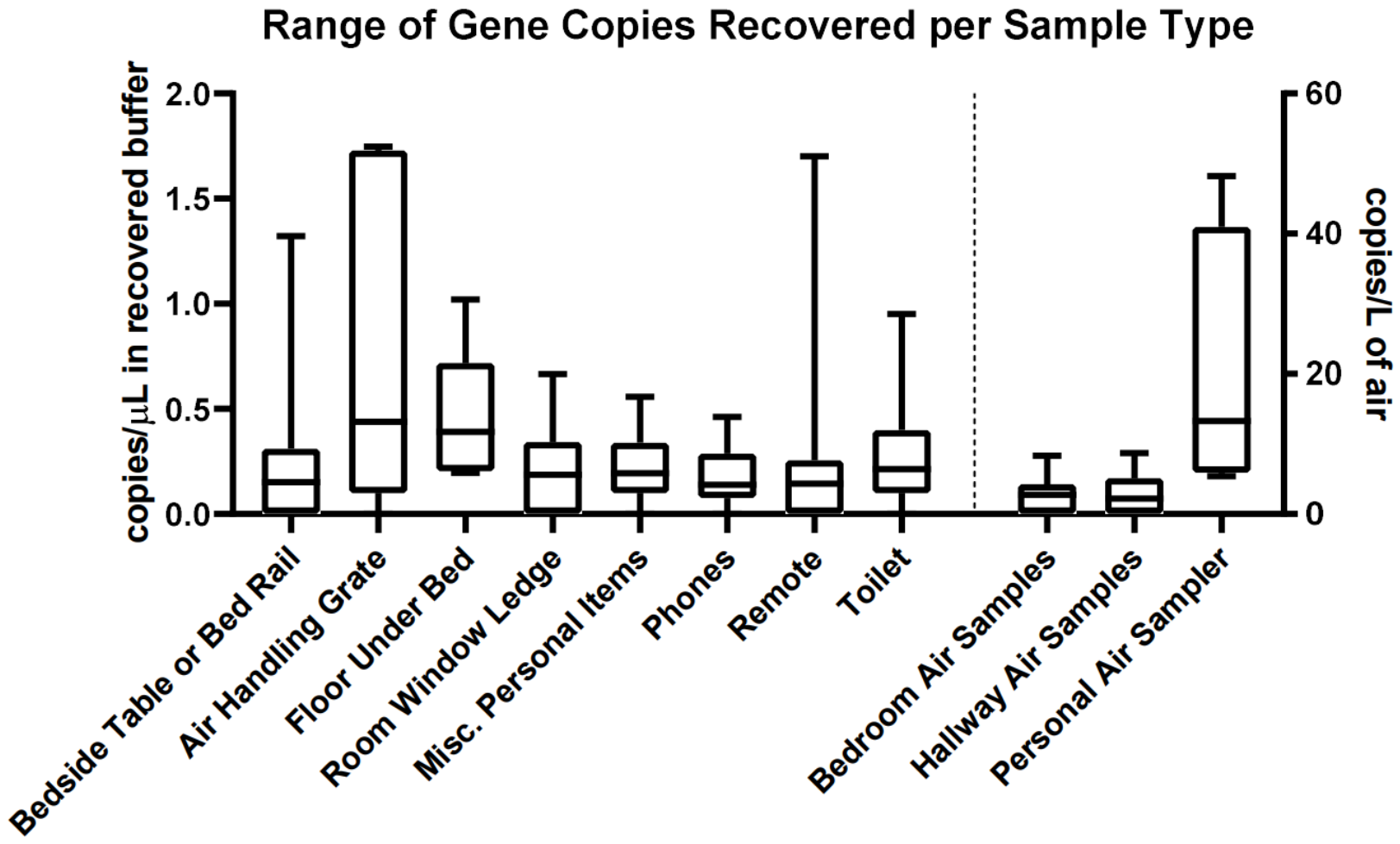
Horve et al., **20xx** *pre-print*
https://www.medrxiv.org/content/10.1101/2020.06.26.20141085v1

SARS-CoV-2 detection in a Nebraska hospital

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) originated in Wuhan, China[4] in late 2019, and its resulting coronavirus disease, COVID-19, was declared a pandemic by the World Health Organization on March 11, 2020. The rapid global spread of COVID-19 represents perhaps the most significant public health emergency in a century. As the pandemic progressed, a continued paucity of evidence on routes of SARS-CoV-2 transmission has resulted in shifting infection prevention and control guidelines between clasically-defined airborne and droplet precautions. During the initial isolation of 13 individuals with COVID-19 at the University of Nebraska Medical Center, we collected air and surface samples to examine viral shedding from isolated individuals. We detected viral contamination among all samples, indicating that SARS-CoV-2 may spread through both direct (droplet and person-to-person) as well as indirect mechanisms (contaminated objects and airborne transmission). Taken together, these finding support the use of airborne isolation precautions when caring for COVID-19 patients.

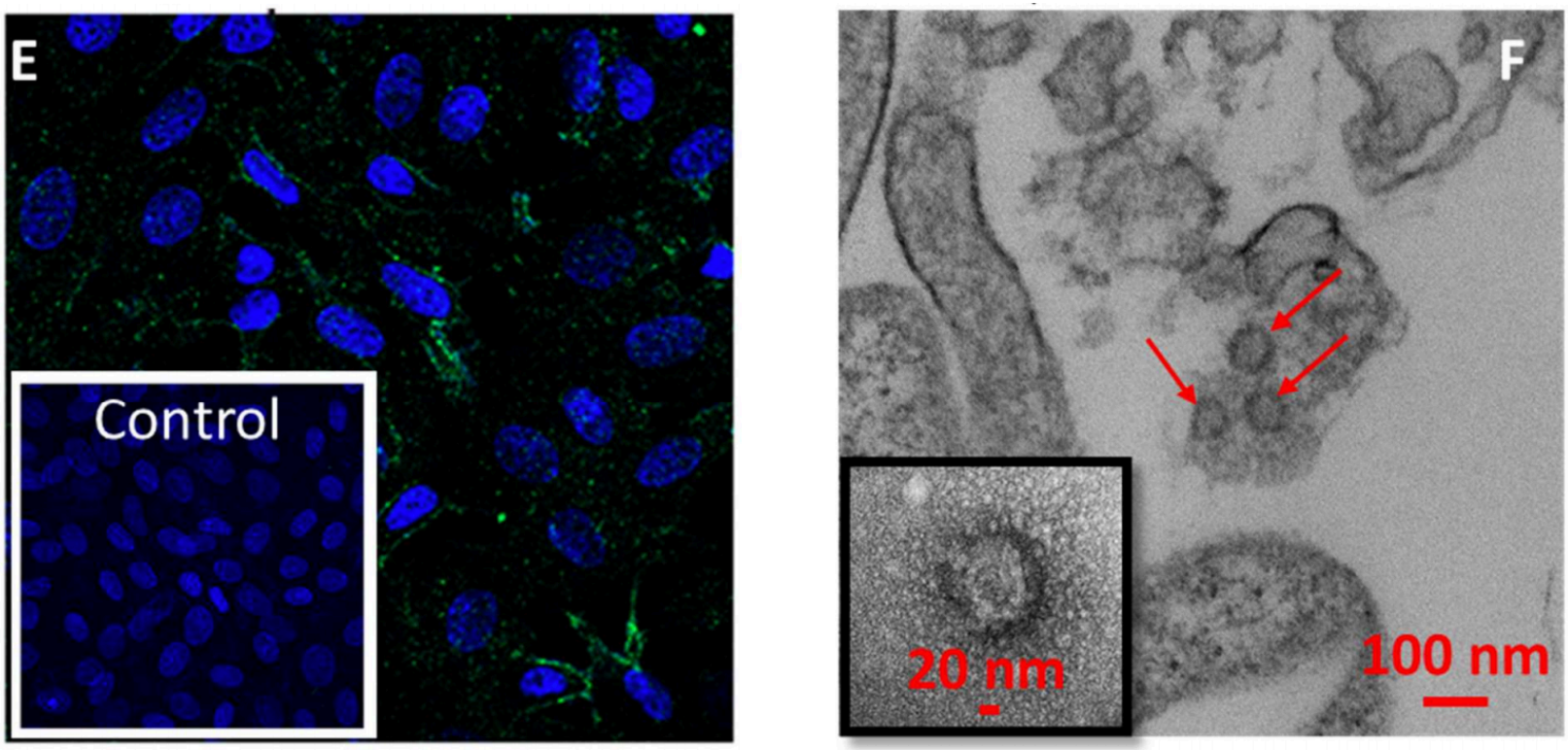
Santarpia et al., **20xx** *pre-print*
https://www.medrxiv.org/content/10.1101/2020.03.23.20039446v3

SARS-CoV-2 detection in a Nebraska hospital



Santarpia et al., **20xx** *pre-print*
https://www.medrxiv.org/content/10.1101/2020.03.23.20039446v3

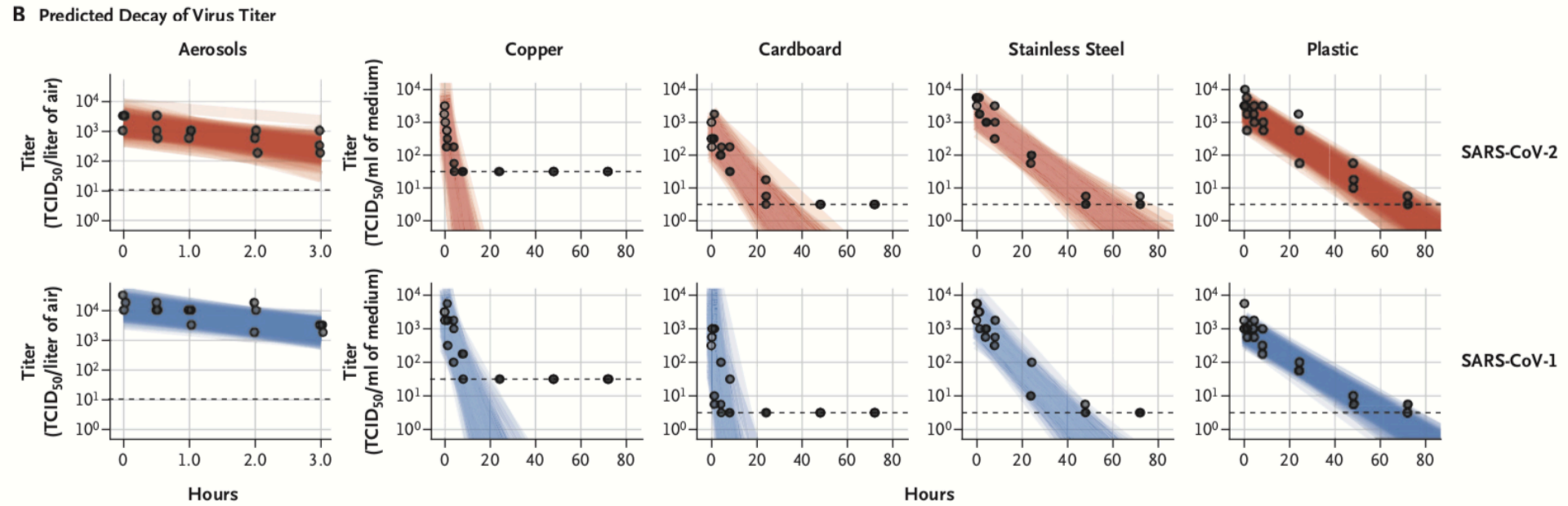
SARS-CoV-2 detection in a Nebraska hospital



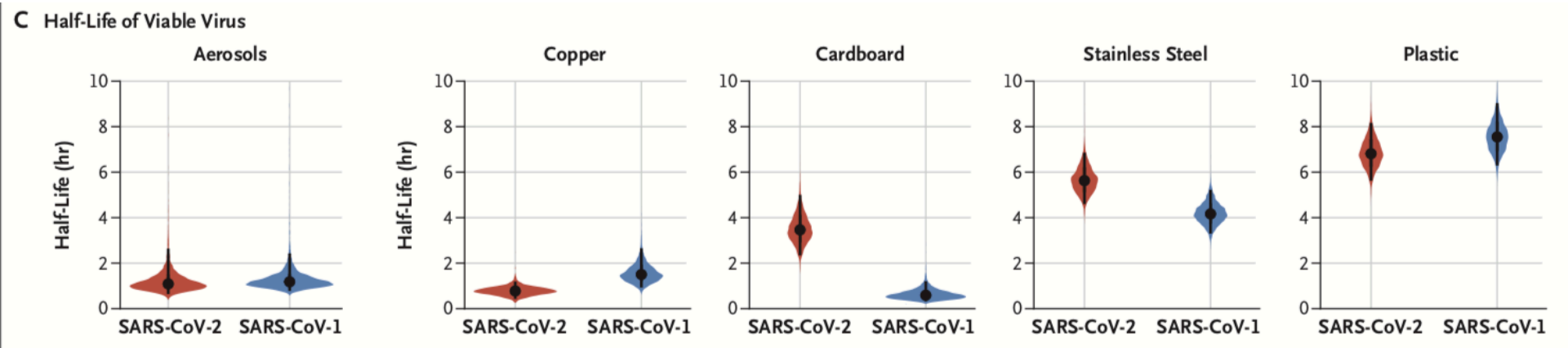
despite the withdrawal of supernatant for analysis (D). Immunofluorescent staining of the hallway air sample indicates the presence of SARS-CoV-2, after 3 days of cell culture (E), as compared to control cells (inset), which were not exposed to any environmental sample. TEM images of the lysates from the windowsill culture (F) clearly indicate the presence of intact SARS-CoV-2 virions, after 3 days of cell culture.

Santarpia et al., **20xx** *pre-print*
https://www.medrxiv.org/content/10.1101/2020.03.23.20039446v3

SARS-CoV-2 survival in aerosols and on surfaces

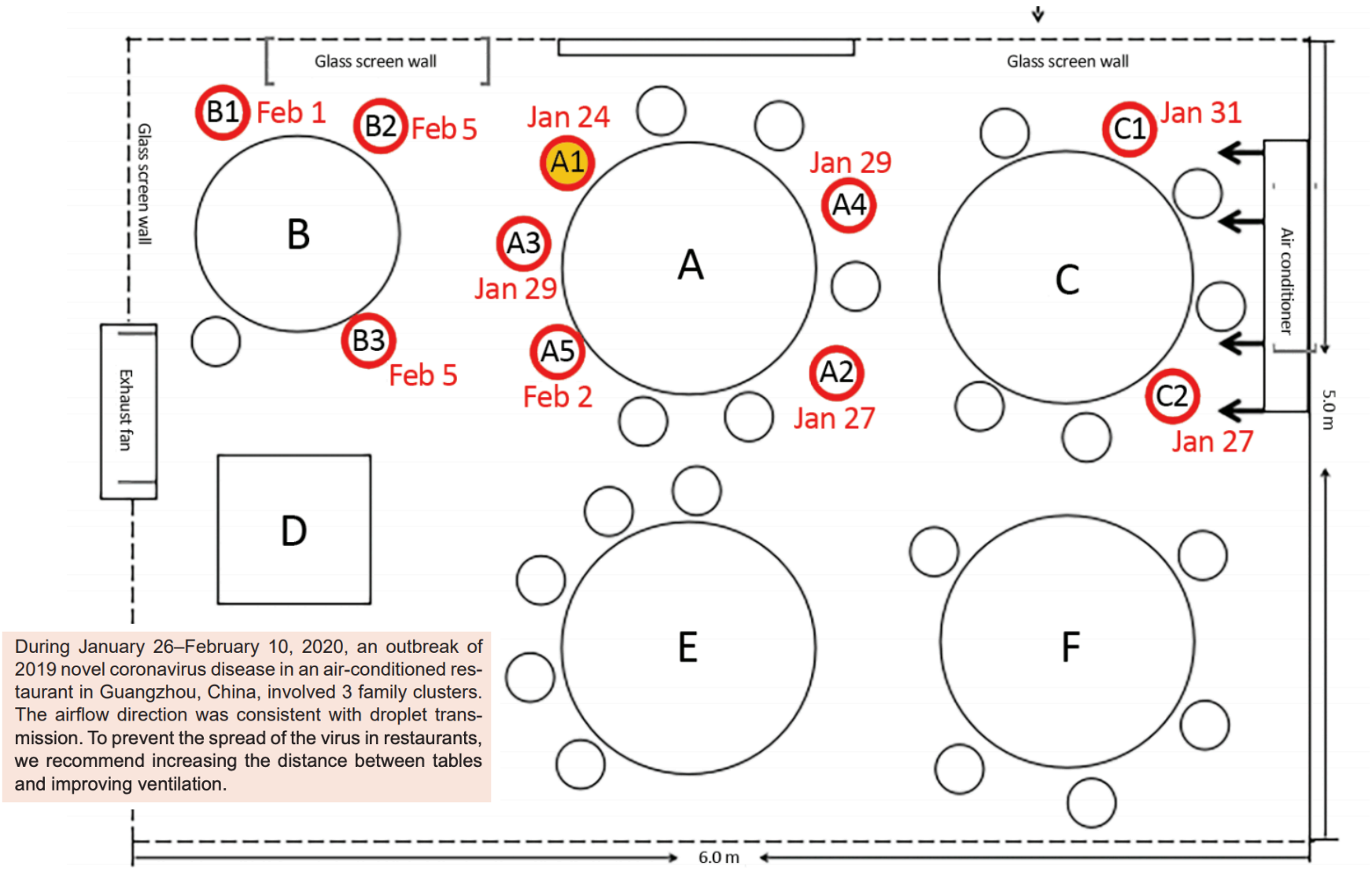


(>3 hrs) (>4 hrs) (>24 hrs) (>48 hrs) (>48 hrs)



van Doremalen et al., **2020** *NEJM*

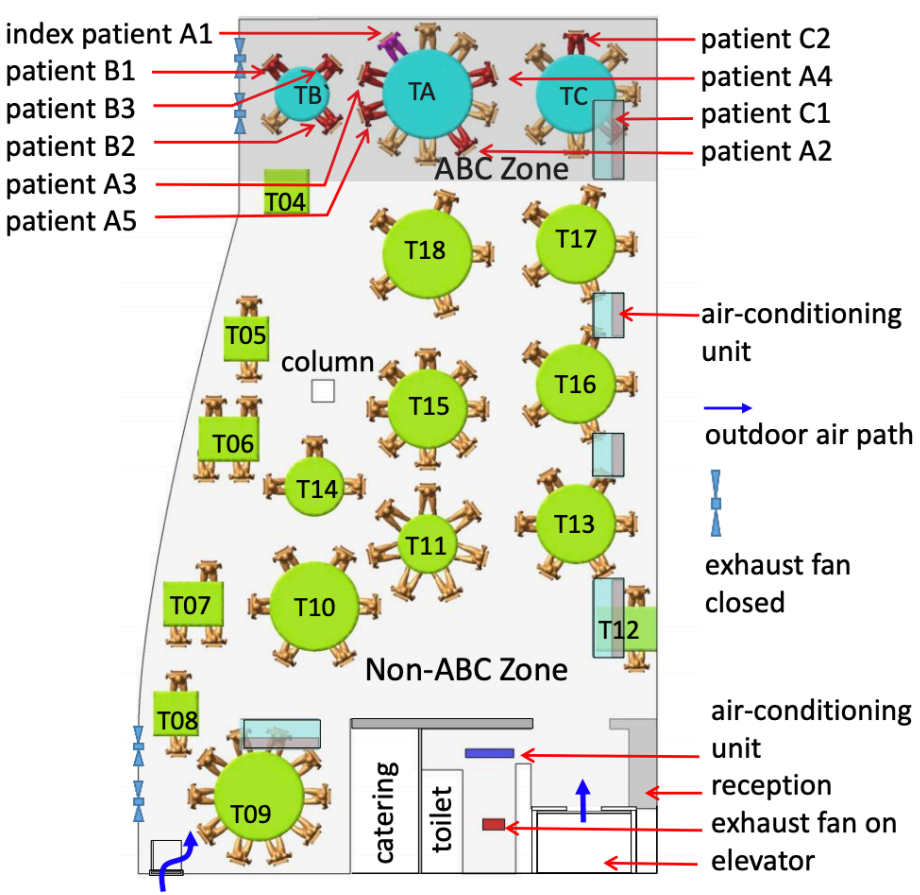
COVID-19 outbreak in a restaurant (Guangzhou)

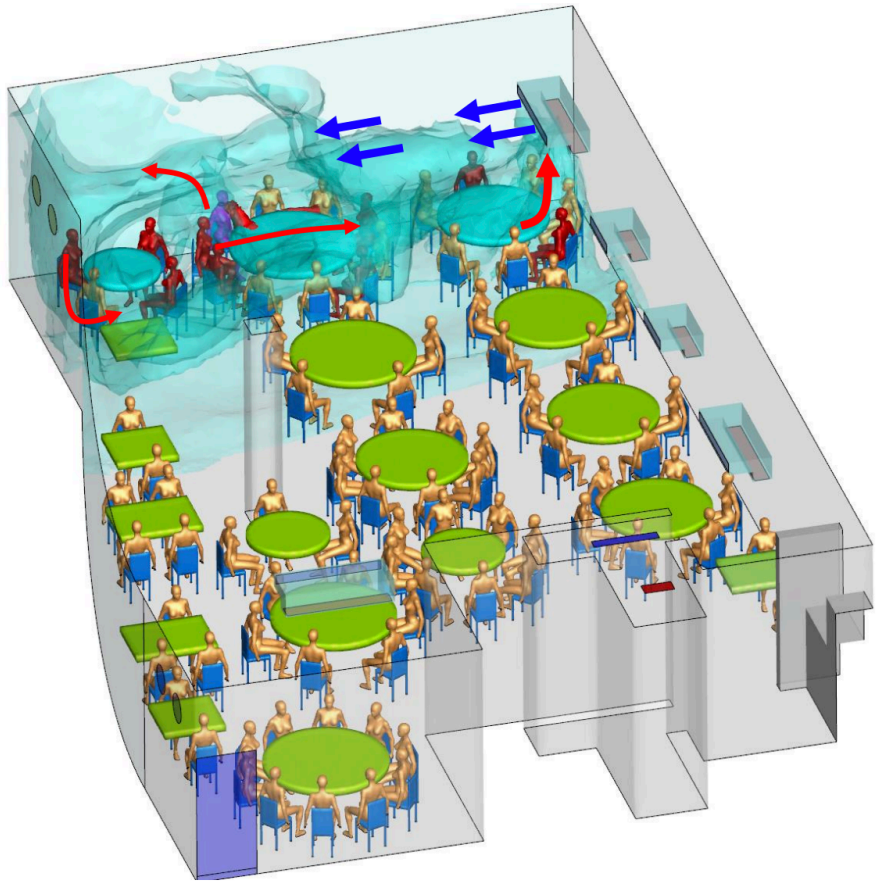


During January 26–February 10, 2020, an outbreak of 2019 novel coronavirus disease in an air-conditioned restaurant in Guangzhou, China, involved 3 family clusters. The airflow direction was consistent with droplet transmission. To prevent the spread of the virus in restaurants, we recommend increasing the distance between tables and improving ventilation.

Lu et al., **2020** *Emerging Infectious Diseases* 26(7):1628-1631
https://wwwnc.cdc.gov/eid/article/26/7/20-0764_article

COVID-19 outbreak in a restaurant (Guangzhou)





Conclusions: Aerosol transmission of SARS-CoV-2 due to poor ventilation may explain the community spread of COVID-19.

Li et al., **20xx** *pre-print*
https://www.medrxiv.org/content/10.1101/2020.04.16.20067728v1

COVID-19 outbreak in a choir practice (Skagit Cty, WA)

Summary

What is already known about this topic?

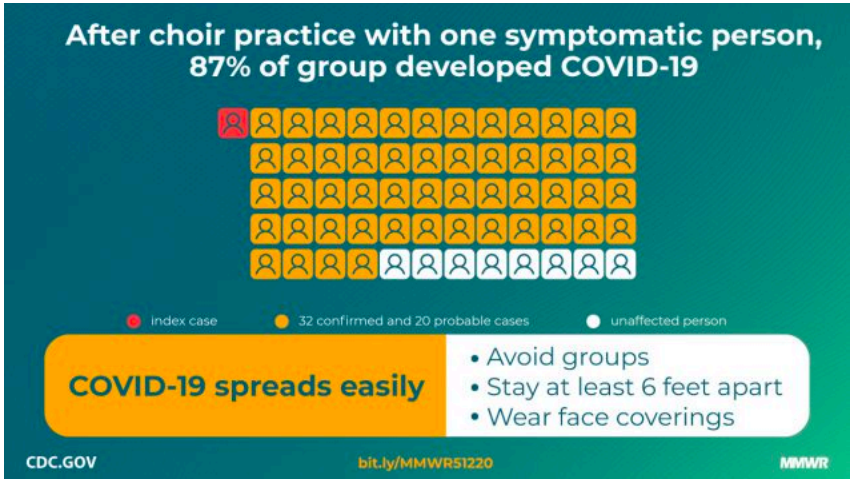
Superspreading events involving SARS-CoV-2, the virus that causes COVID-19, have been reported.

What is added by this report?

Following a 2.5-hour choir practice attended by 61 persons, including a symptomatic index patient, 32 confirmed and 20 probable secondary COVID-19 cases occurred (attack rate = 53.3% to 86.7%); three patients were hospitalized, and two died. Transmission was likely facilitated by close proximity (within 6 feet) during practice and augmented by the act of singing.

What are the implications for public health practice?

The potential for superspreader events underscores the importance of physical distancing, including avoiding gathering in large groups, to control spread of COVID-19. Enhancing community awareness can encourage symptomatic persons and contacts of ill persons to isolate or self-quarantine to prevent ongoing transmission.



Hamner et al., **2020** *CDC Morbidity and Mortality Weekly Report* 69(19):606-610
https://wwwnc.cdc.gov/eid/article/26/7/20-0764_article

INFECTION CONTROL STRATEGIES

Airborne infection control

Surface disinfection and hand hygiene

Procedural controls and isolation

Treatment, prophylaxis, and vaccination

Engineering controls and air disinfection

Engineering controls and disinfection

- Control of airborne infectious disease transmission
  - Studies suggest building characteristics such as outdoor air ventilation rates and lower occupant density can reduce respiratory illnesses 15-76%

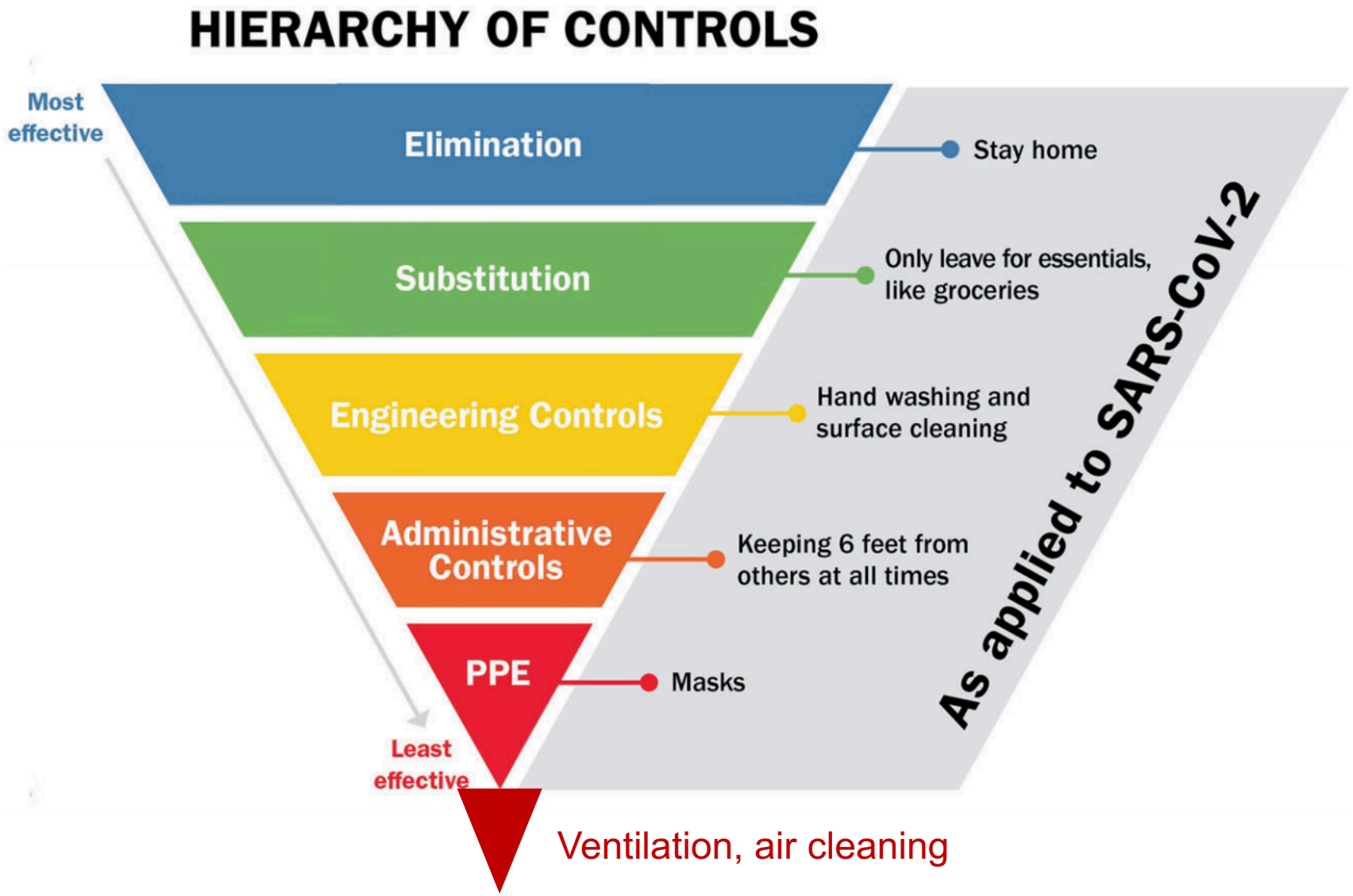
Langmuir et al. **1948** *Am J Hyg*; Brundage et al. **1988** *JAMA*; Drink a et al. **1996** *Am Geriatr Soc*; Fisk **2000**; Li et al. **2007** *Indoor Air*

- Aerosol engineering controls include:
  - Facemasks
  - Isolation rooms (dedicated HVAC) / flow control
  - Particle filtration (HVAC or stand-alone)
  - Ultraviolet germicidal irradiation (UVGI)
  - Humidity control

  - These only work for diseases that are primarily spread via airborne routes (not through surface contamination)

ASHRAE Position Document on Airborne Infectious Diseases (2014)

Hierarchy of controls for SARS-CoV-2



Deziel et al., **2020** *J Expos Sci Environ Epidem* 30:591-593
https://www.nature.com/articles/s41370-020-0225-3

Important notice for preventing COVID-19 outbreaks.

Avoid the "Three Cs"!

1. Closed spaces with poor ventilation.

2. Crowded places with many people nearby.

3. Close-contact settings such as close-range conversations.

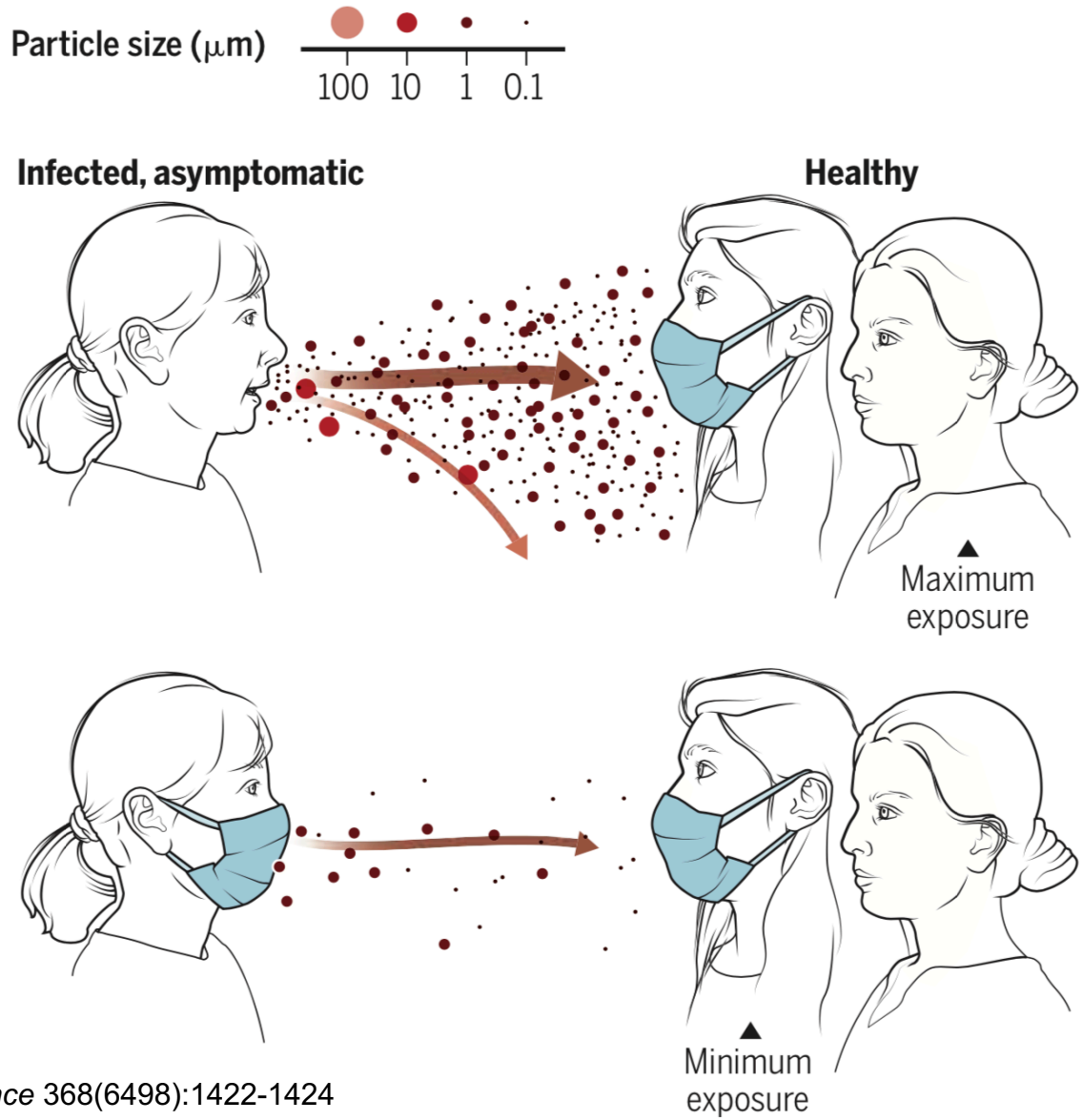
https://www.mhlw.go.jp/content/10900000/000615287.pdf

One of the key measures against COVID-19 is to prevent occurrence of clusters.

Keep these "Three Cs" from overlapping in daily life.

Masks reduce airborne transmission

Infectious aerosol particles can be released during breathing and speaking by asymptomatic infected individuals. No masking maximizes exposure, whereas universal masking results in the least exposure.



Prather et al., **2020** *Science* 368(6498):1422-1424

Masks can reduce airborne transmission

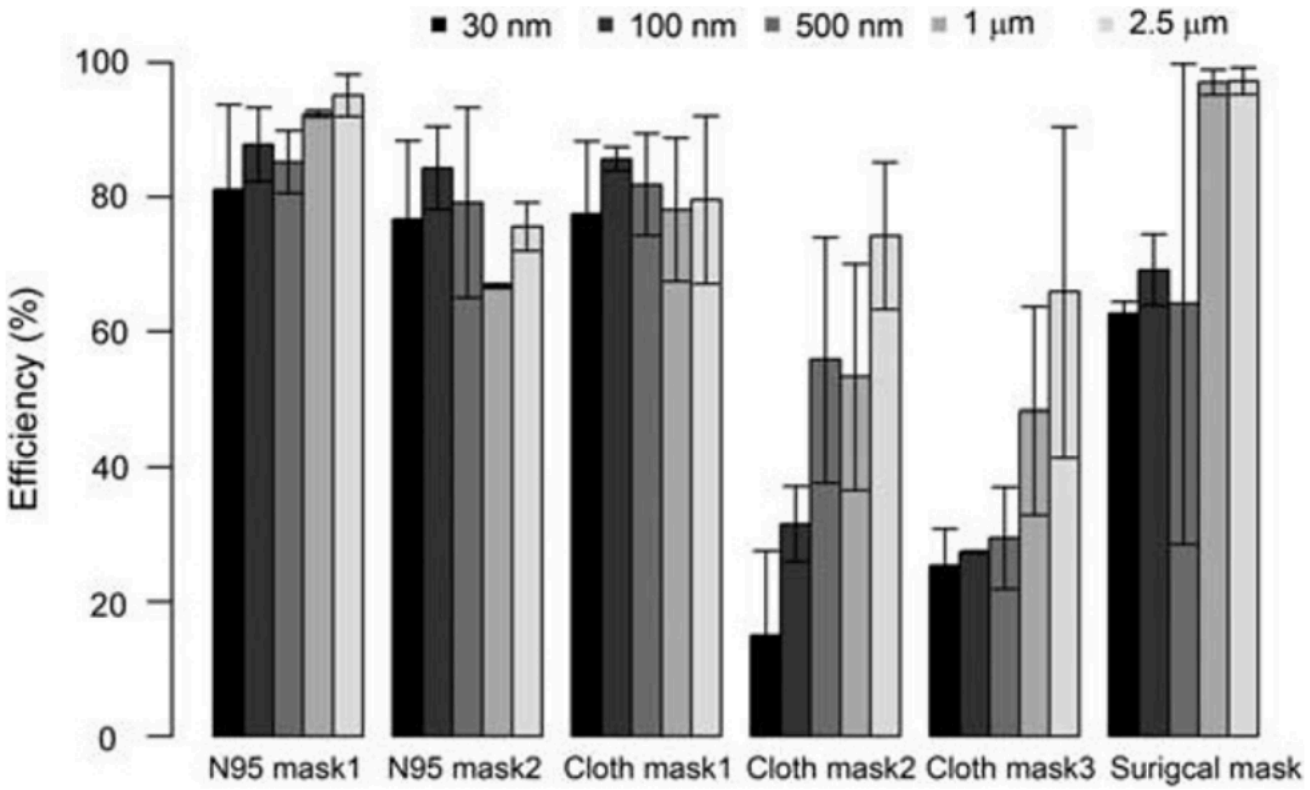
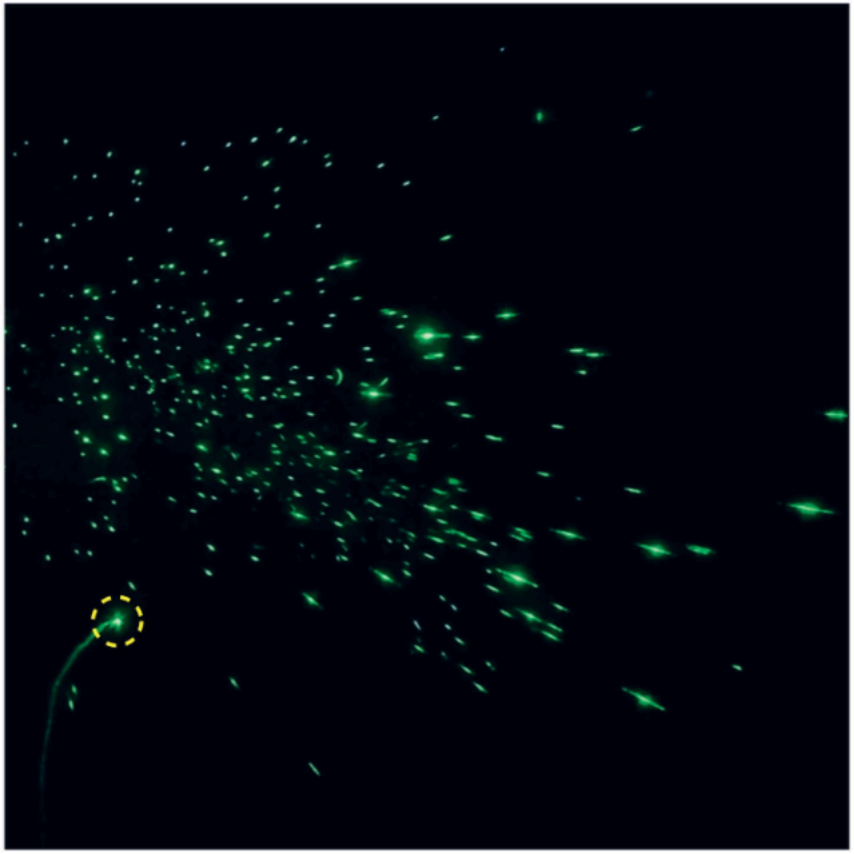


Figure 2. Efficiency of masks in removal of five polystyrene latex (PSL) particle sizes at a flow rate of 19 L/min. Error bars are the standard deviation from three experiments.

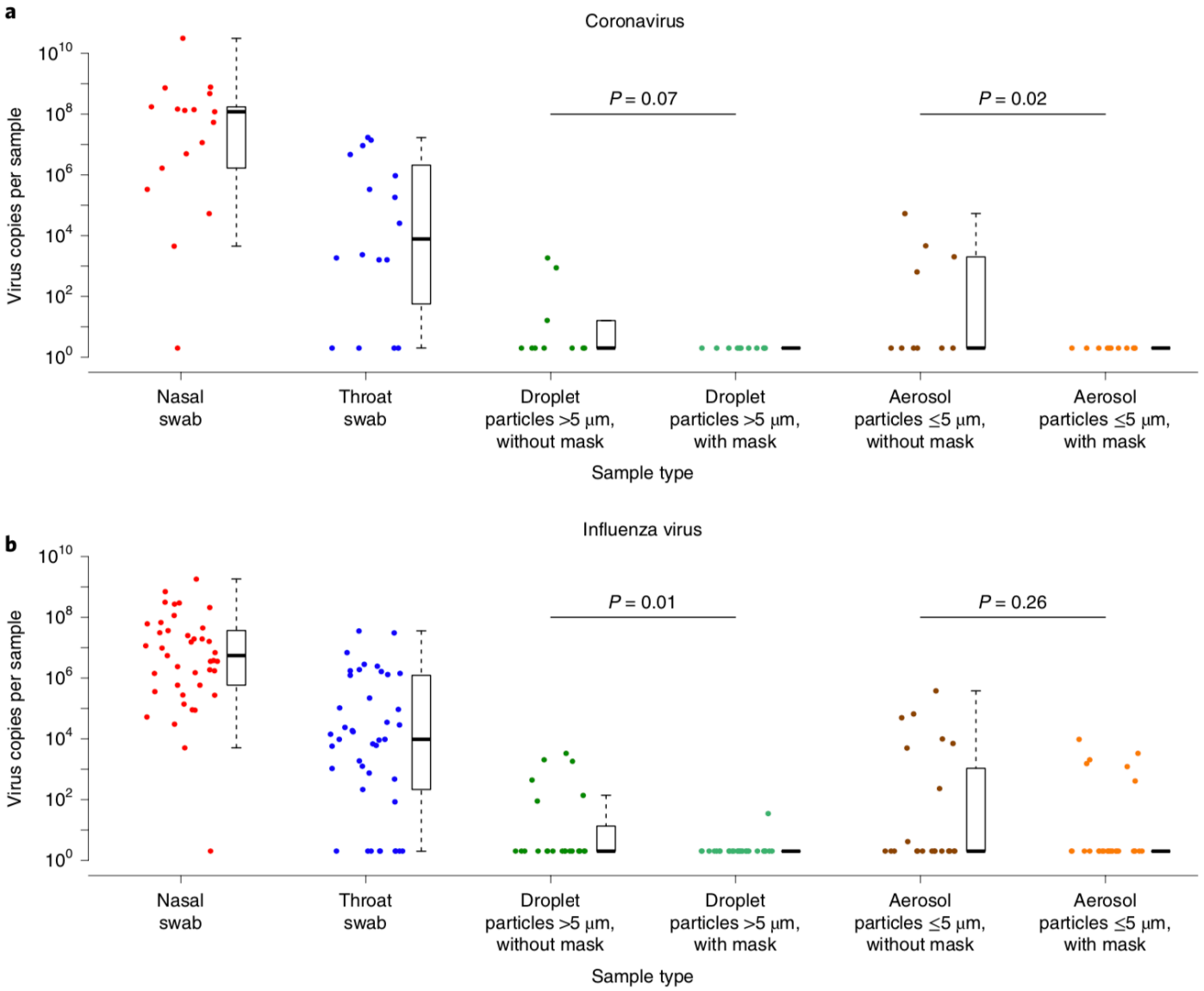
Shakya et al., **2017** *J Exp Sci Environ Epidem* 27:352-357

Masks can reduce airborne transmission



https://www.nejm.org/doi/full/10.1056/nejmc2007800

Masks can reduce airborne transmission



Leung et al., **2020** *Nature Medicine* 26:676-680

Masks can reduce airborne transmission

Absence of Apparent Transmission of SARS-CoV-2 from Two Stylists After Exposure at a Hair Salon with a Universal Face Covering Policy — Springfield, Missouri, May 2020

Early Release / July 14, 2020 / 69

Hendrix et al., **2020** *CDC MMWR* July 14, 2020
https://www.cdc.gov/mmwr/volumes/69/wr/mm6928e2.htm

ESTIMATING RISKS OF INFECTIOUS DISEASES

And quantifying modes of transmission

Featuring Guest Speaker:
Dr. Parham Azimi, Ph.D.
Postdoctoral Researcher
Harvard T.H. Chan School of Public Health
pazimi@hsph.harvard.edu

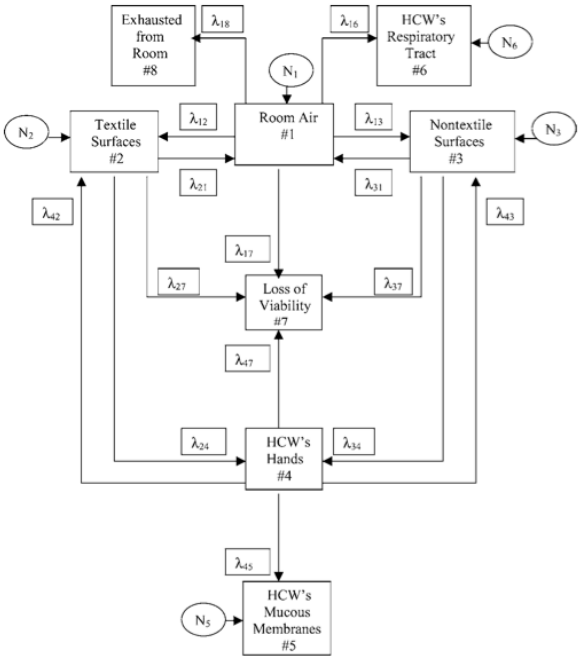
Methods of estimating infectious disease risks

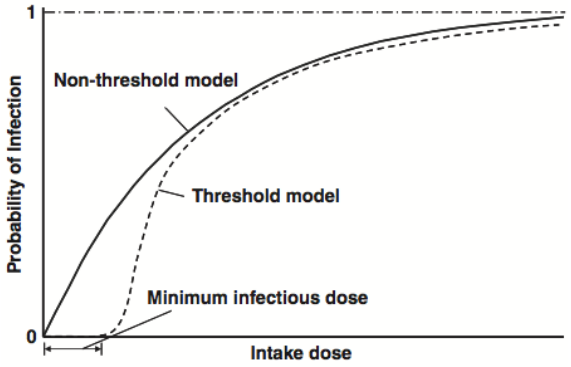
Wells-Riley model

$$P_{\text{infection}} = \frac{cases}{susceptiles} = 1 - e^{-\frac{Iqpt}{Q_{\text{oa}}}}$$

$P_{\text{infection}}$ = the probability of infection
cases = the number of infection cases
susceptibles = number of susceptible individuals
I = number of infector individuals
p = pulmonary ventilation rate of a person (m^3/hour)
q = quanta generation rate (1/hr)
t = exposure time (hr)
Q_{oa} = room ventilation rate with clean air (m^3/hour)

Markov chain combined with dose-response models





Wells-Riley model

$$P_{\text{infection}} = \frac{cases}{susceptiles} = 1 - e^{-\overline{\mu}}$$

- μ = average number of "quanta" breathed by a susceptible person, assuming probability of infection fits a Poisson distribution
- "quantum" = number of infectious droplet nuclei necessary to initiate infection based on the assumption that infection requires at least one organism
  - Function of type of infectious agent (more on that later)

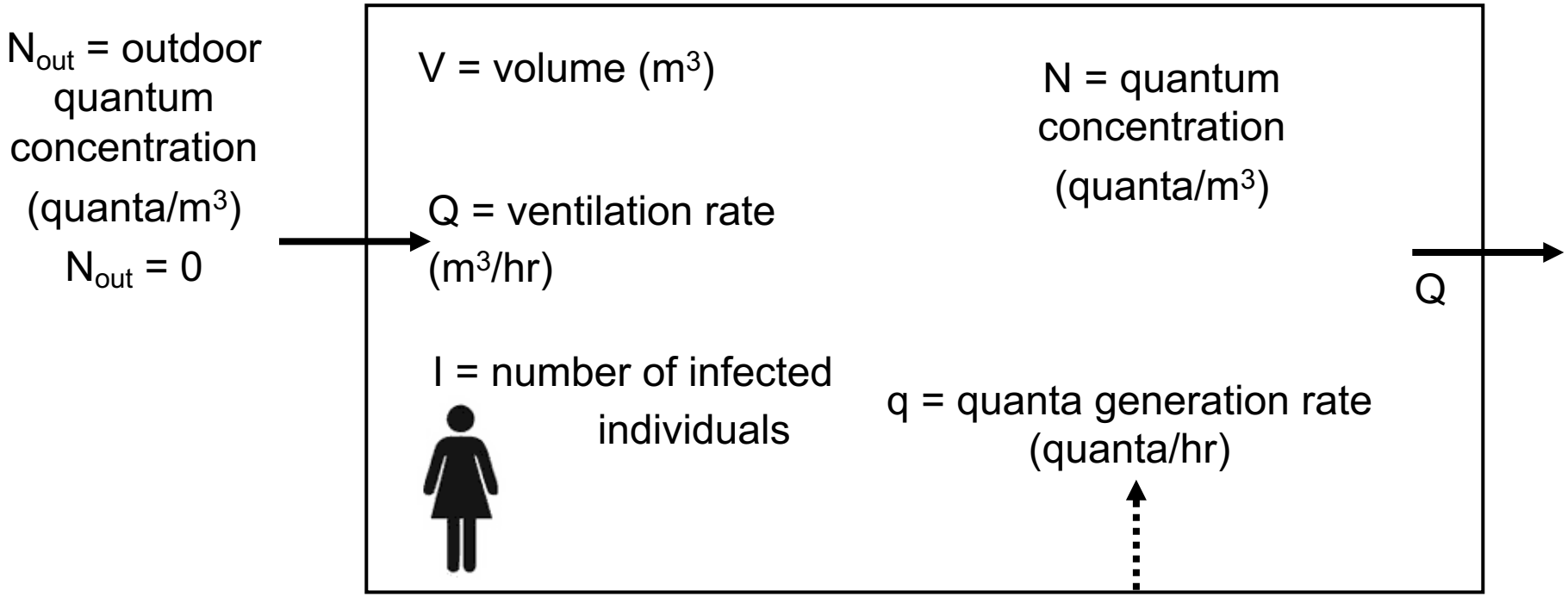
- If μ = 1 quanta breathed, risk of infection = $1 - e^{-1} = 1 - 1/e$ = ~63%

$$\overline{\mu} = p_b t \overline{N}$$

p_b = breathing rate (m^3/hr)
t = total time of exposure (hr)
$\overline{N}$ = average quantum "concentration"

Wells-Riley model

- Simplest mass balance on “quanta”, assuming:
  - Well-mixed space
  - AER is much greater than loss of agent viability, loss by filtration, loss by deposition



$$V\frac{dN}{dt} = Iq - NQ \quad \rightarrow \quad \overline{N}_{\text{at steady state}} = \frac{Iq}{Q}$$

Wells-Riley model

- Average # of quanta breathed:

$$\overline{\mu} = p_b t \overline{N}$$

p_b = breathing rate (m^3/hr)
t = total time of exposure (hr)
$\overline{N}$ = average quantum "concentration"

- Average quanta concentration:

$$\overline{N}_{\text{at steady state}} = \frac{Iq}{Q}$$

- Poisson risk model:

$$P_{\text{infection}} = \frac{cases}{susceptiles} = 1 - e^{-\overline{\mu}}$$

$$P_{\text{infection}} = \frac{cases}{susceptiles} = 1 - e^{-\frac{Iqpt}{Q_{\text{oa}}}}$$

$P_{\text{infection}}$ = the probability of infection
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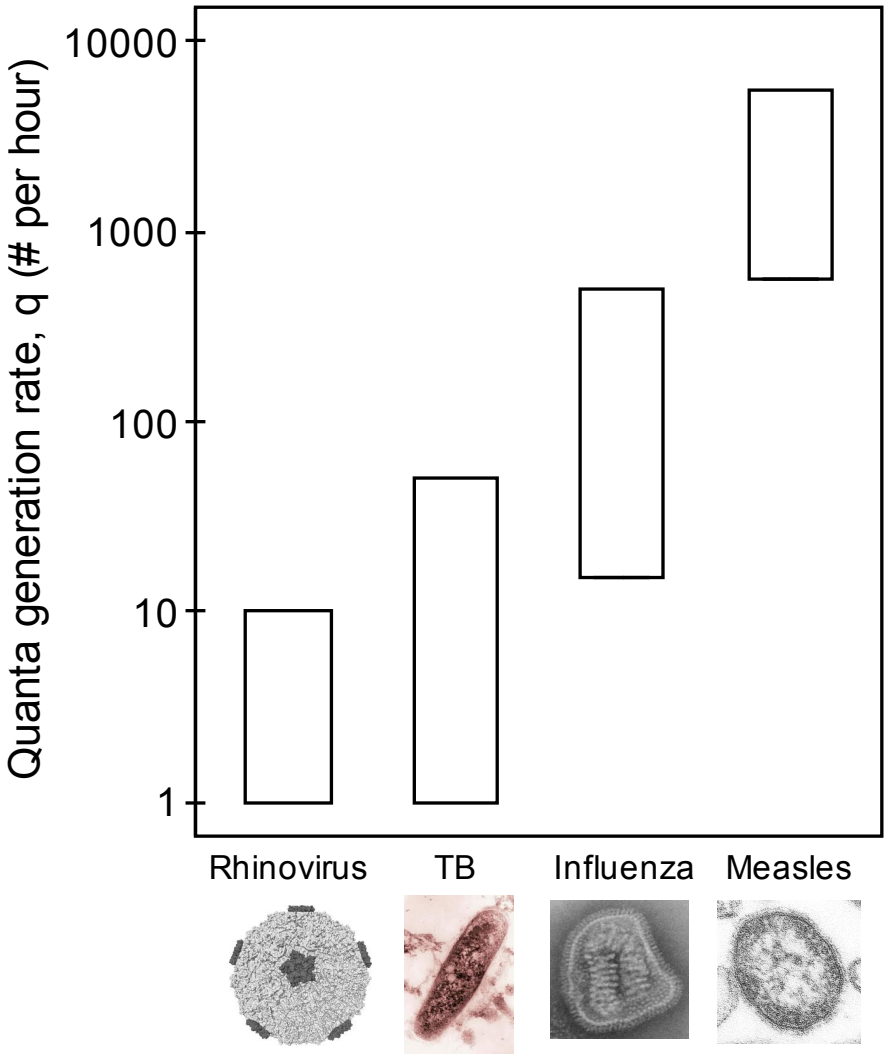
Q_{oa} = room ventilation rate with clean air (m^3/hour)

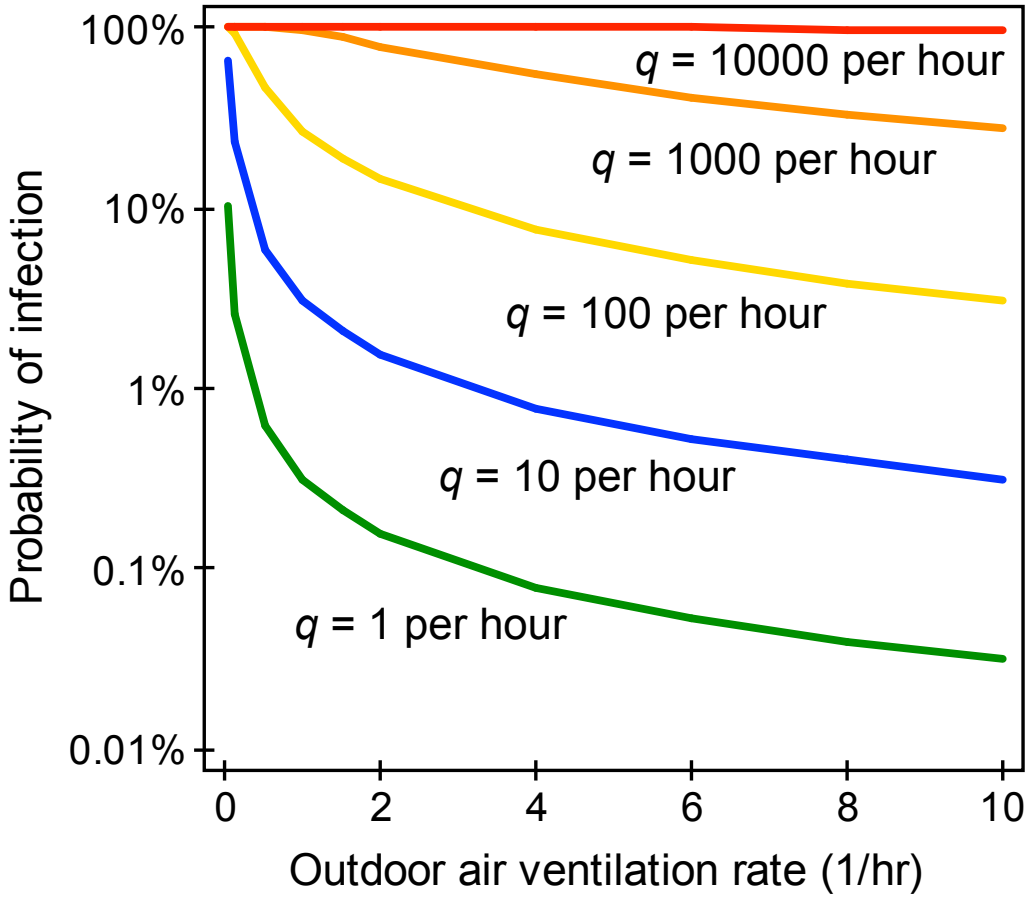
Concept of quanta generation

- The unit *quantum of infection* is not an actual physical unit
- It is a hypothetical infectious dose
  - Back calculated from epidemiological studies
- Accounts for emissions, transport, inhalation, infectivity, and susceptibility all in one term



Riley et al., 1978 *Am J Epidemiology* 107:421-432 (and many others for quanta estimates)

How do quanta generation and ventilation rates affect risk?

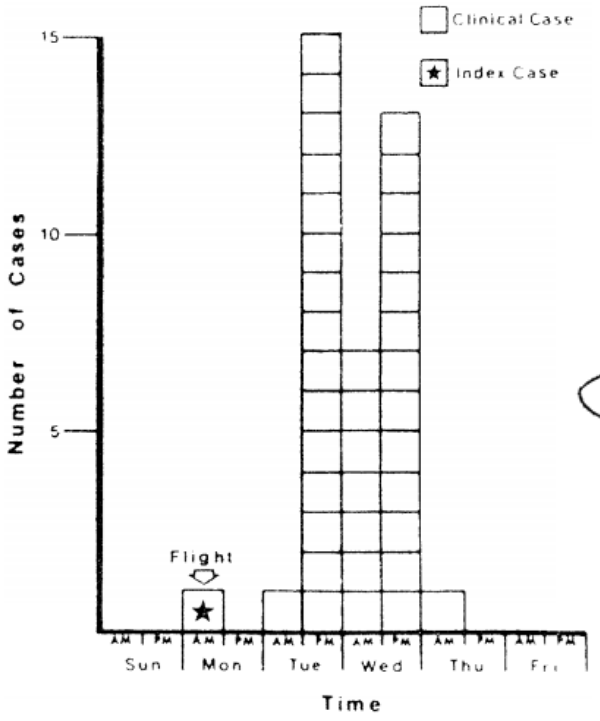


- Example 500 m^2 (5,300 ft^2) building with 1 infector
  - Containing adults with 0.48 m^3/hr breathing rate
- Depends strongly on value of *q*

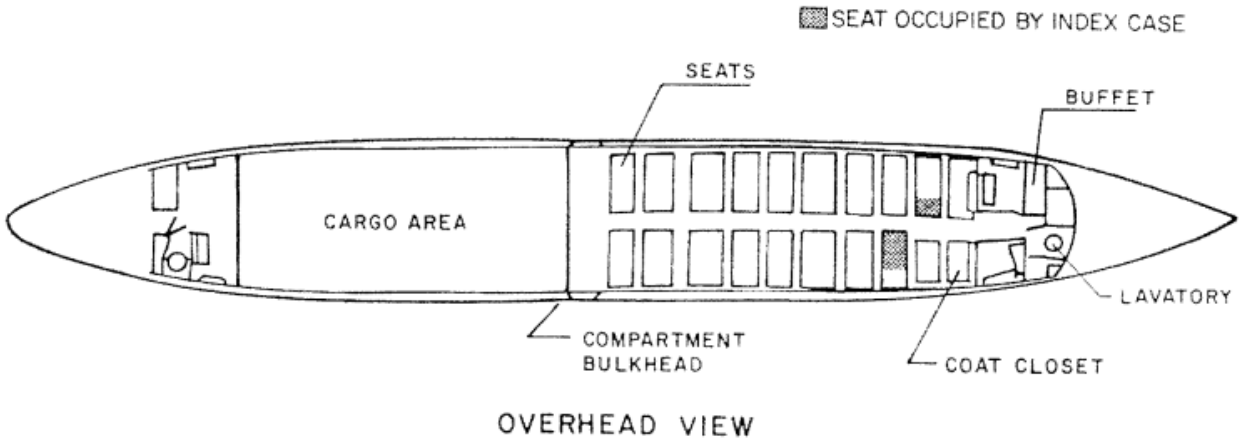
$$P_{\text{infection}} = \frac{cases}{susceptiles} = 1 - e^{-\frac{Iqpt}{Q_{\text{oa}}}}$$

Example of quanta generation rate back-calculation

- Passenger plane grounded for 4.5 hours
  - One known infector and 29 other uninfected passengers
    - 25 (86%) contracted influenza within 2 days
  - Rudnick and Milton made assumptions of breathing rates and air exchange rates to yield *q* of 15-128 per hour



$$P_{\text{infection}} = \frac{cases}{susceptiles} = 1 - e^{-\frac{Iqpt}{Q_{\text{oa}}}}$$



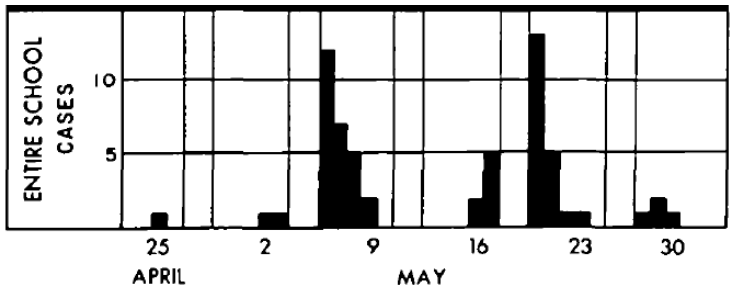
Buxton Bridges et al. 2003 *Clinical Infectious Diseases* 37:1094-1101; Rudnick and Milton, 2003 *Indoor Air* 13:237-245

Back-calculated quanta rates from one case study could be different

Looking at Riley et al. (1978) study after a measles outbreak in an elementary school in upstate New York:

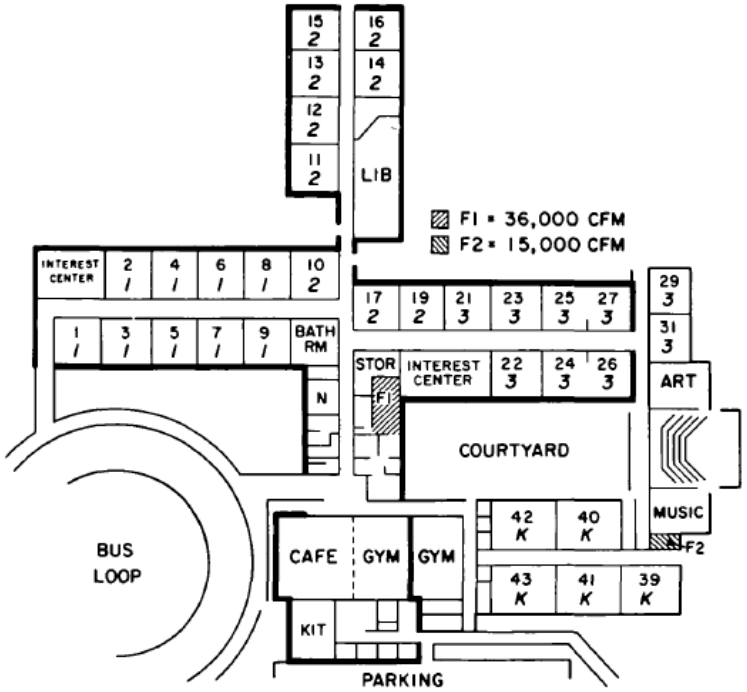
- 868 students
- 28 cases in the first generation of the outbreak
- Estimated the index case produce 93 quanta/min (5580 quanta/hr)

Riley et al. 1978 *American journal of epidemiology*, 107(5): 421-432.



Then other studies used the same outbreak to back-calculate quanta generation rate of measles for the models that they developed:

- Chen et al. (2006): 125 quanta/hr
- Rudnick and Milton (2003): 570 quanta/hr
- Azimi et al. (2020): 1925 quanta/hr



Chen et al. 2006 *Indoor Air,* 16: 469–481; Rudnick and Milton. 2003 *Indoor Air,* 13: 237–245;
Azimi et al. 2020 BMC Infectious Diseases, 20:497-519

WELLS-RILEY: MEASLES CASE STUDY

Nationwide transmission risk of measles in US schools

- U.S. was certified measles-free in 2000
- In 2019 number of measles cases broke the record of the nationwide annual number of cases since 1992
- We used a combination of:
  - Newly developed multi-zone transient Wells-Riley approach
  - Nationwide representative School Building Archetype (SBA) model
  - Monte-Carlo simulation

$$P_{infection} = \frac{Number\ of\ Infected\ Cases}{Number\ of\ Susceptible\ Individuals} = 1 - e^{-\mu}$$

Nationwide transmission risk of measles in US schools

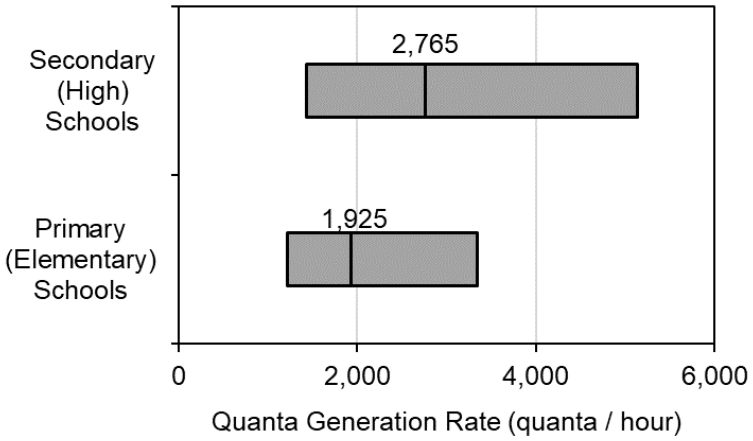
$$\bar{\mu} = \frac{1}{N_{total}} \times \bar{p} \times \sum_{i} \int_{0}^{\bar{t}_i} N_i(\tau).\, C_{quanta,i}(\tau) d\tau$$

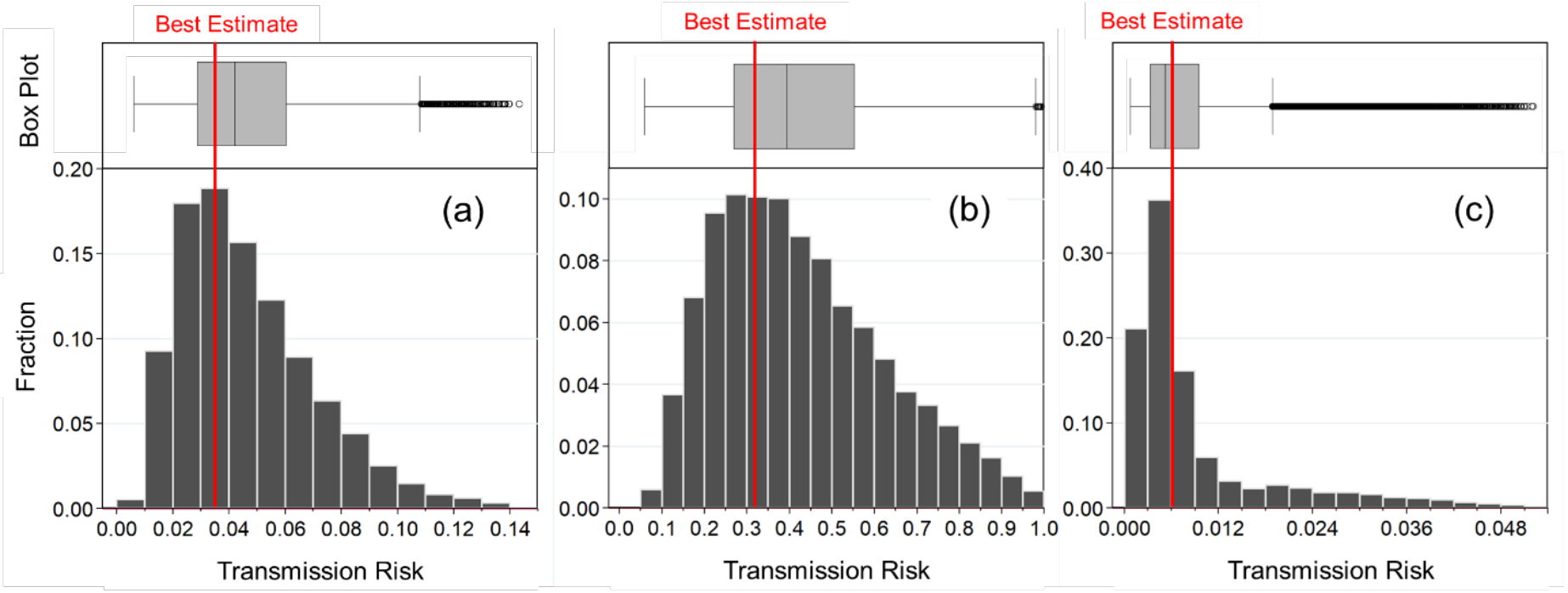
- N_{total}: Total number of students in the schools during the infection period
- $\bar{p}$: Average breathing rate of one student (m^3 / hour)
- $\bar{t}_i$: Average time that students spend in space *i* (hour)
- $N_i(\tau)$: Number of students in space *i* as a function of time
- $C_{quanta,i}(\tau)$: Concentration of quanta in space *i*, τ hours after the index case enters the space (quanta / m^3)

Summary of variables used in the model

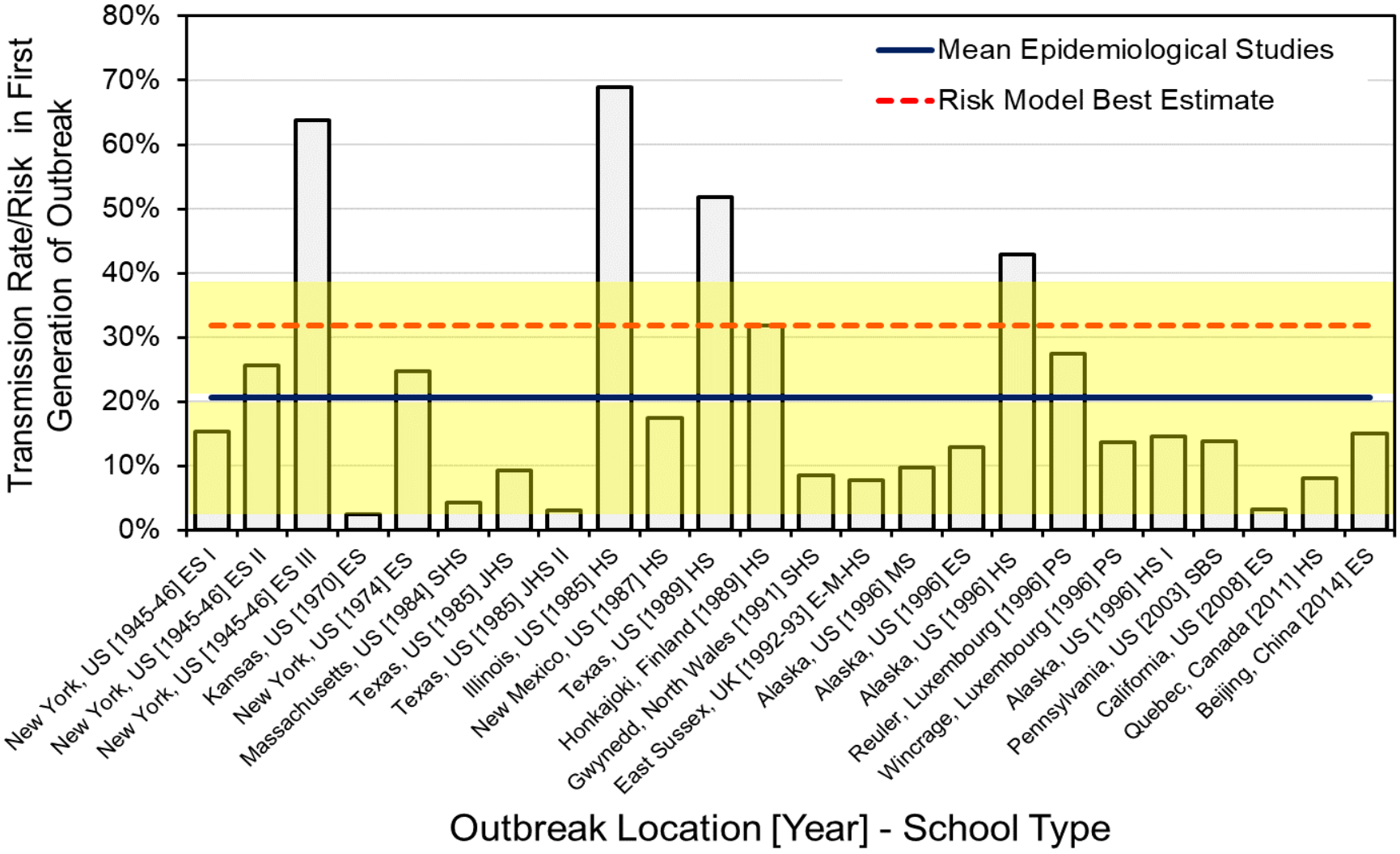
Parameter	Primary School Best-Estimate [Range]	Secondary School Best-Estimate [Range]
No. of educational institutions in US 2015-2016	88,665	26,986
No. of Index case/s	1	1
Quanta generation rate (quanta / hour)	1925 [1185 - 3345]	2765 [1430 - 5140]
No. of enrolled students before outbreak	513 [175 - 825]	854 [245-1394]
Infection period in school (day)	3 [2 - 4]	3 [2-4]
Portion of unvaccinated students	9% [8% - 10%]	9% [8% - 10%]
Portion of students with ≥ 2-dose vaccination	91% [90% - 92%]	91% [90% - 92%]
No. of students in infector's classroom	21 [18 -26]	23 [18-30]
Occupancy density of classroom (m^2/person)	4 [3-5]	4 [3-5]
Occupancy density of common area (m^2/person)	1.39 [1.04-1.74]	1.39 [1.04-1.74]
Average time spent in school (mins)	400 [375-425]	400 [375-425]
Average time spent in common area (mins)	20 [15-30]	30 [20-45]
Heating and cooling periods in US schools (day)	H: 200 & C: 90	H: 200 & C: 90
HVAC system type	10% - 63%	11% - 54%
HVAC recirculation rate in classrooms (per hour)	6.4 [3.3–8.5]	6.4 [3.3–8.5]
Outdoor air ventilation in classrooms (L/s-person)	6.7 [4.0 – 9.5]	6.7 [4.0 – 9.5]
Outdoor air ventilation in common area (L/s-person)	4.9 [4.7 – 5.1]	4.9 [4.7 – 5.1]
HVAC runtime for applicable systems	1	1
Air filter removal efficiency (%)	72% [44% - 86%]	72% [44% - 86%]
Infiltration rate (1/hour)	0.31 [0.12 – 0.49]	0.31 [0.12 – 0.49]
Deposition rate of measles bio-aerosols (1/hour)	1.7 [1.0 – 2.7]	1.7 [1.0 – 2.7]
Inhalation rate (m^3/day)	12.96 [11.34- 14.53]	15.53 [13.93- 17.45]

Back-calculated quanta and best estimates of transmission rate

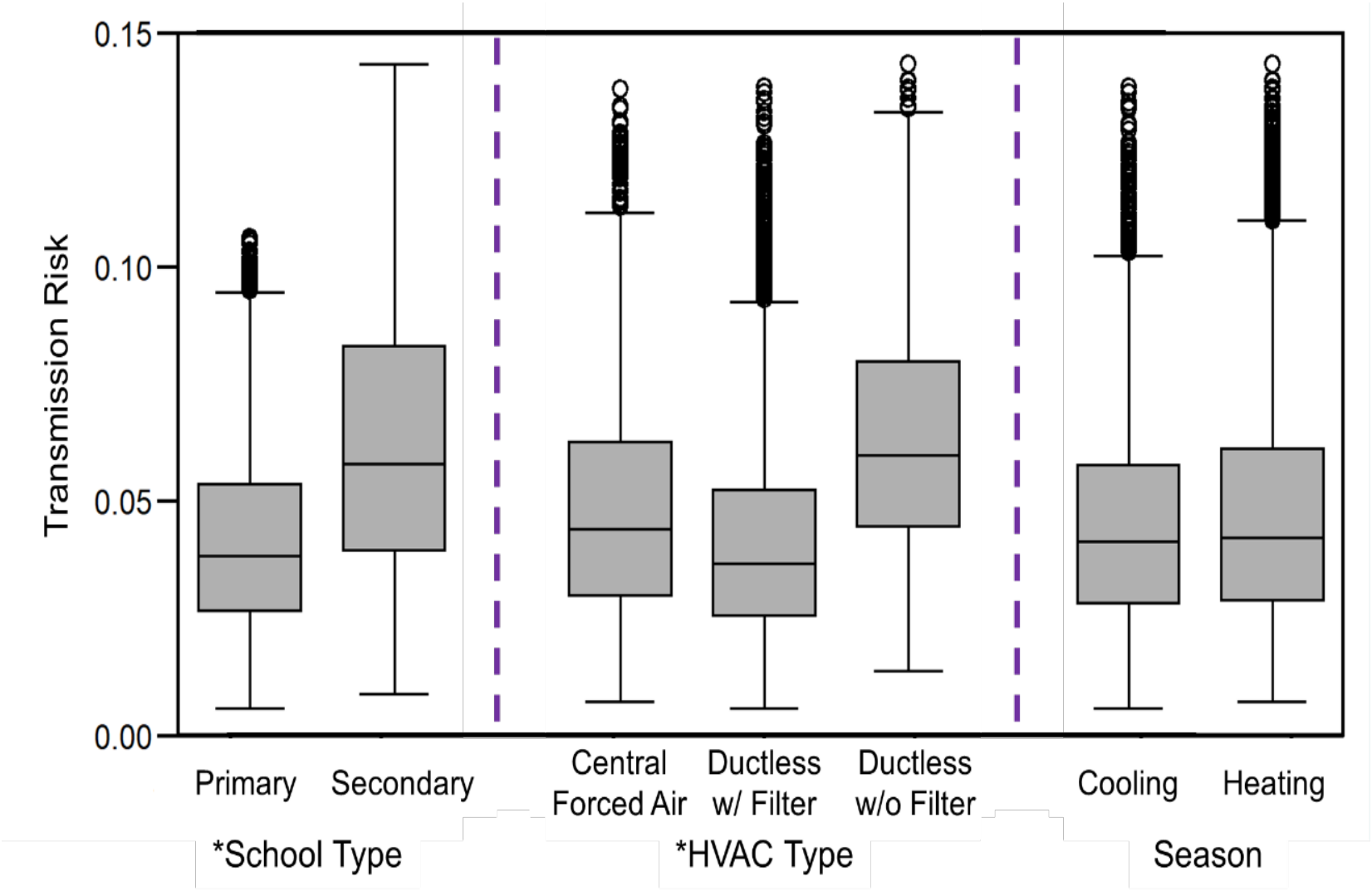




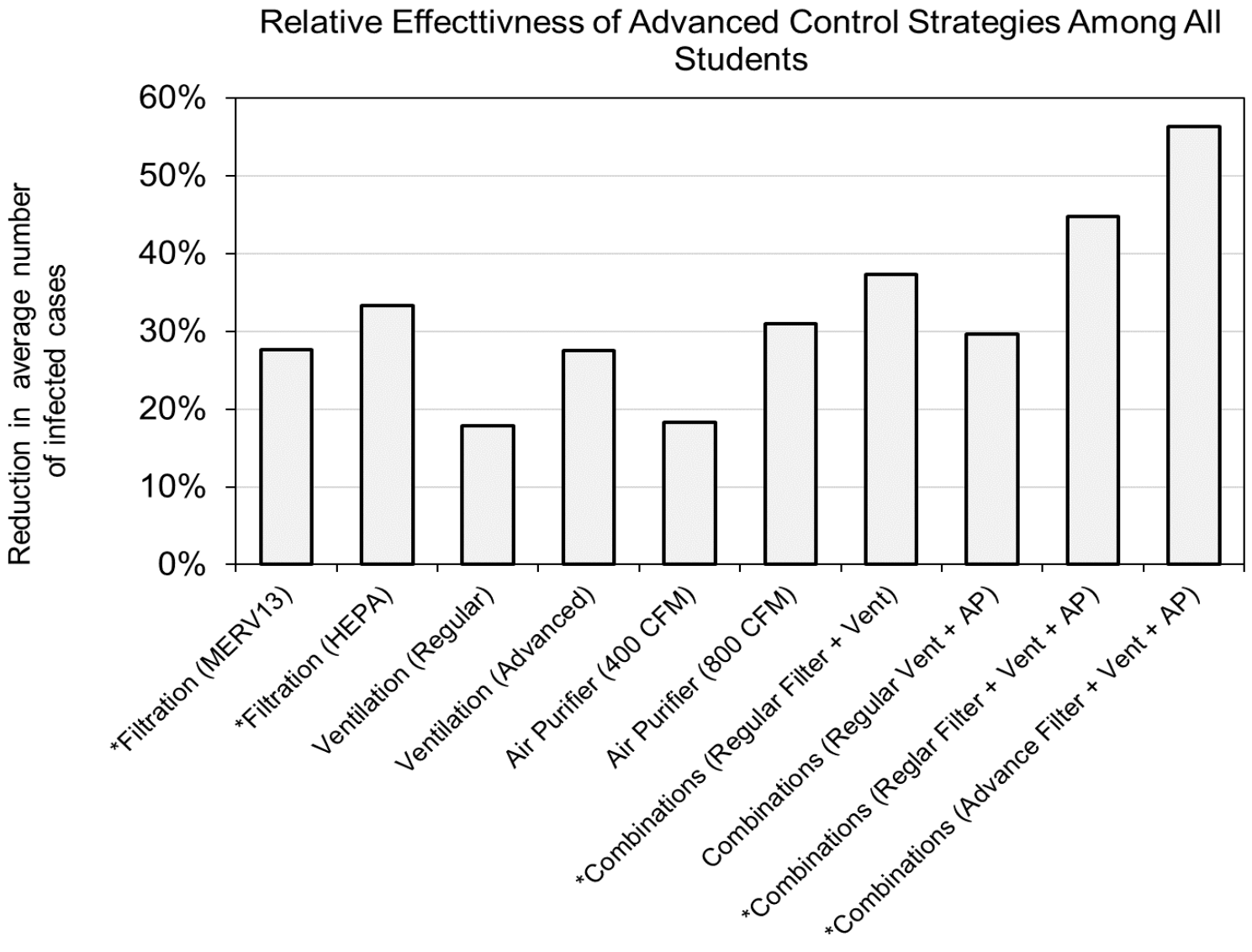
Comparing estimates of transmission risk with existing epidemiological studies



Impacts of HVAC system and school type on measles transmission



Relative effectiveness of advanced control strategies on measles transmission risk



Methods of estimating infectious disease risks

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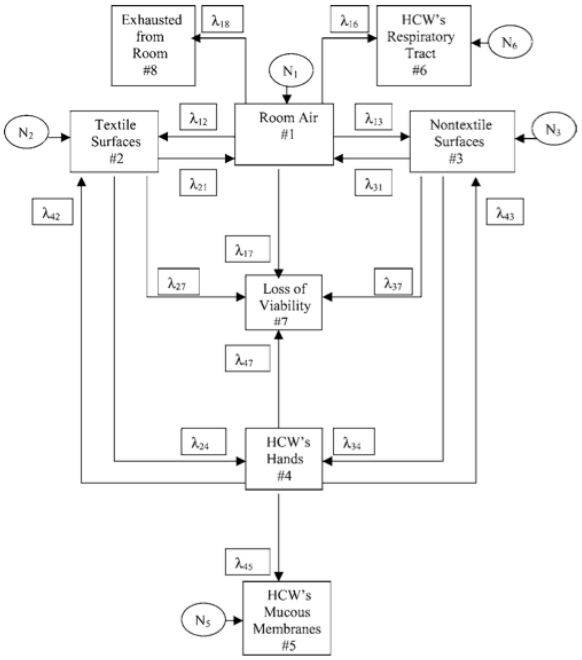
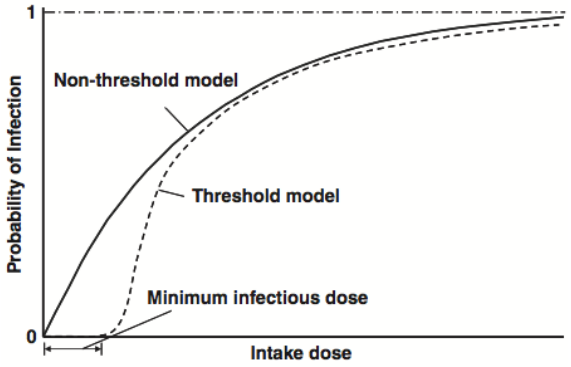




Mechanistic Transmission Model

Markov Chain	Dose Response	Monte Carlo
Estimate **intake dose**	Calculate **probability of infection**	Provide **statistical distribution**

Jones, R. & Adida E. (2011), *Risk Analysis*; Jones, R. (2009), *Risk Analysis*.

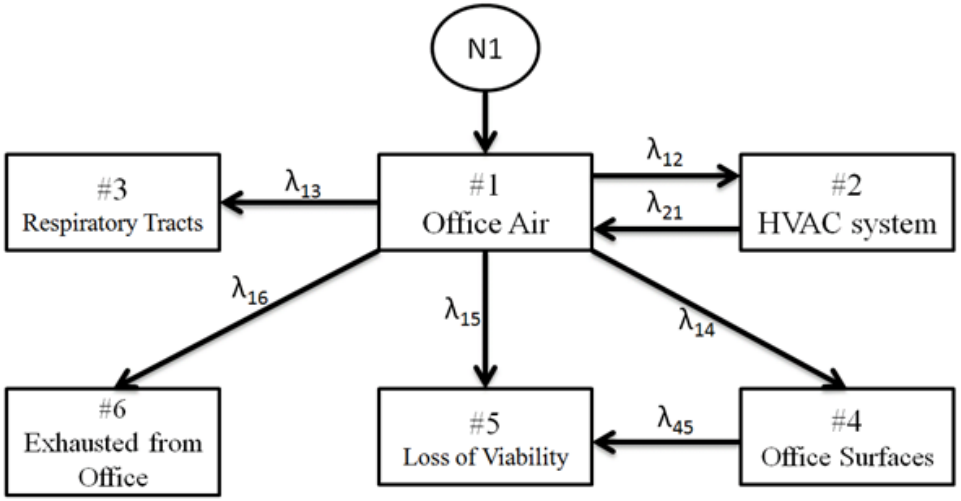
Application:

- **Estimating the transmission risk more precisely:** Bioaerosol characteristics (e.g. deposition, resuspension, inactivation, and size distribution), Building HVAC characteristics (e.g. outdoor air ventilation, filtration, and purification rates), human activity

- **Evaluating dominant transmission routes:** Could be used for unknown diseases such as COVID-19

Markov chain method

- Consider a hypothetical environment
- Define as many states as you like



In the next time step Δt,

- ✓ N_i pathogens are injected to state i
- ✓ A pathogen remains in state i with probability of P_{ii}
- ✓ A pathogen moves to another state j, with probability of P_{ij}

The λ_{ij} are first-order (exponential) transition rate constants from state i to state j with the inverse unit of time.

Markov chain method

For example the transition rates from indoor air
to outdoor is air exchange rate
to surfaces is deposition rate
to removed by HVAC system is filtration rate

The overall rate at which a pathogen can leave state i is the sum of the rate constants for removal from that state, denoted λ_i

$$\lambda_i = \sum_j \lambda_{ij}$$

Then…

$$P_{ii} = e^{(-\lambda_i \times \Delta t)}$$

$$P_{ij} = \frac{\lambda_{ij}}{\lambda_i} \times (1 - P_{ii})$$

$$\text{MM} = \begin{bmatrix} P_{11} & P_{12} & P_{13} & P_{14} & P_{15} & P_{16} \\ P_{21} & P_{22} & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & P_{44} & P_{45} & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

Markov chain method

Lets assume pathogens are not injected to the environment for a time period of T, then the presence probability of pathogens in each state can be calculated as $MM^{(n)}$

In which

$$n = T/\Delta t$$

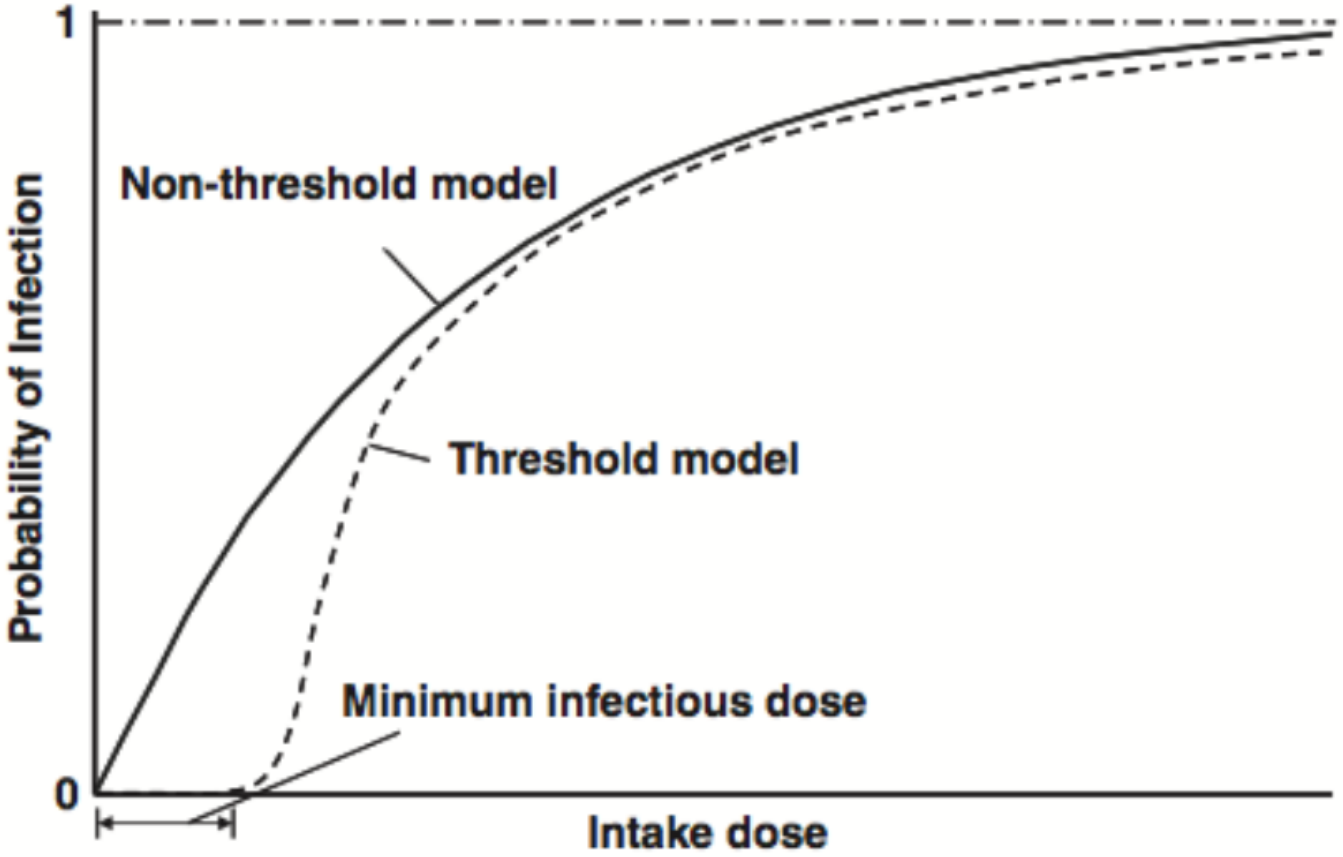
If we have K injections during the exposure in time periods of T

In each injection N_K pathogens enter to the environment

The presence probability of microorganisms in each state after exposure time can be estimated as $E(D_K)$

$$E[D_i] = (E[D_{i-1}] + N_i) \times MM^{(n)}$$

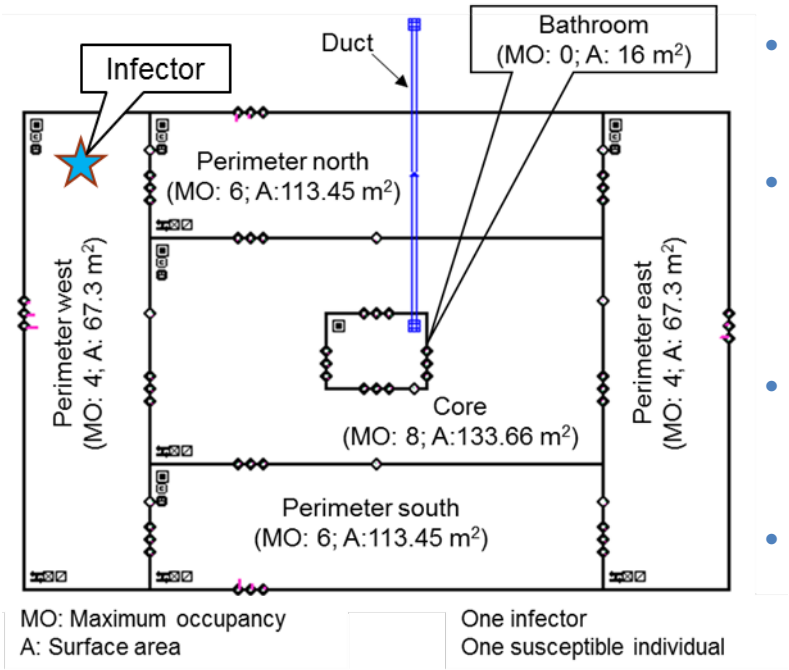
Dose Response Model



INFLUENZA AND COVID-19 CASE STUDIES

Defining a typical indoor environment (office) as the case study

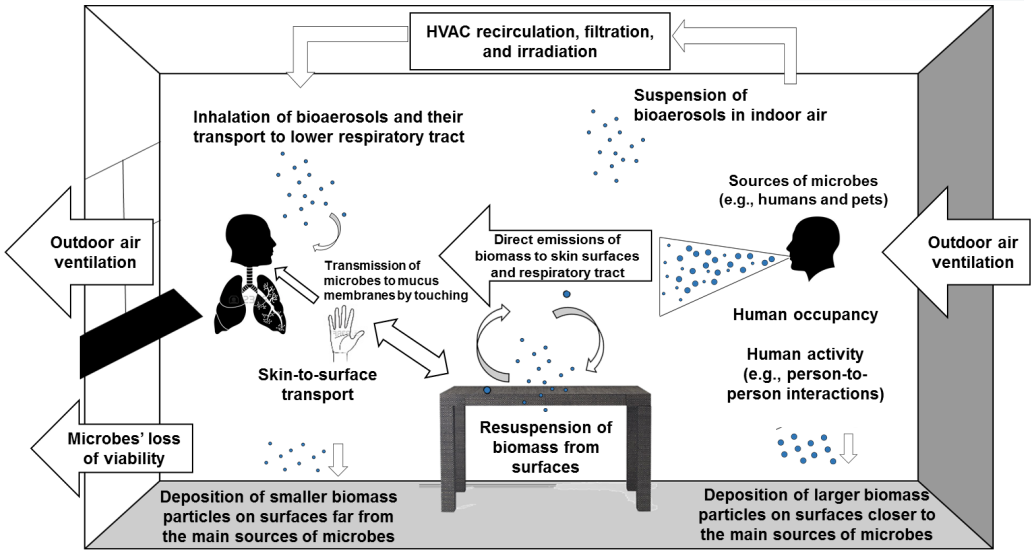
- In the existing Markov chain models some parameters have not been considered yet including the impacts of:
  - various control strategies (i.e. filtration, OA ventilation, RH control, and UV irradiation)
  - size distribution of influenza viruses in droplets and droplet nuclei
  - deposition and resuspension
  - human activities



- The flow rate of AHUs were assumed varied in different zones from 1188 to 1620 m^3/hour
- The assumed OA ventilation was 20%-35% higher than required OA ventilation rates based on ASHRAE 62.1-2010
- An exhaust fan provides a ventilation rate of 180 m^3/hour for the bathroom
- Susceptible and infector individuals stay in the office for 8 consecutive hours during a workday, from 8:00 AM to 4:00 PM

Defining the Markov chain model states and transmission pathways

1) Attic,
2) PerimeterWest air
3) PerimeterNorth air
4) PerimeterEast air
5) Core air
6) Restroom air
7) PerimeterSouth air
8) Ambient
9) Close Surfaces
10) Attic Surfaces
11) PerimeterWest Surfaces
12) PerimeterNorth Surfaces
13) PerimeterEast Surfaces
14) Core Surfaces
15) Restroom Surfaces
16) PerimeterSouth Surfaces
17) Finger Skin
18) Upper Respiratory Tracts
19) Lower Respiratory Tracts
20) HVAC Removal (i.e., filtration or UV sterilization)
21) Inactivation



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
1	0	TR	TR	TR	TR	TR	TR	TR	TR	TR	0	0	0	0	0	0	0	0	TR	TR	TR
2	TR	0	TR	TR	TR	TR	TR	TR	TR	0	TR	0	0	0	0	0	0	0	TR	TR	TR
3	TR	TR	0	TR	TR	TR	TR	TR	TR	0	0	TR	0	0	0	0	0	0	TR	TR	TR
4	TR	TR	TR	0	TR	TR	TR	TR	TR	0	0	0	TR	0	0	0	0	0	TR	TR	TR
5	TR	TR	TR	TR	0	TR	TR	TR	TR	0	0	0	0	TR	0	0	0	0	TR	TR	TR
6	TR	TR	TR	TR	TR	0	TR	TR	TR	0	0	0	0	0	TR	0	0	0	TR	TR	TR
7	TR	TR	TR	TR	TR	TR	0	TR	TR	0	0	0	0	0	0	TR	0	0	TR	TR	TR
8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	TR	TR	TR	TR	TR	TR	TR	0	0	0	0	0	0	0	0	0	TR	0	0	0	TR
10	TR	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	TR	0	0	0	TR
11	0	TR	0	0	0	0	0	0	0	0	0	0	0	0	0	0	TR	0	0	0	TR
12	0	0	TR	0	0	0	0	0	0	0	0	0	0	0	0	0	TR	0	0	0	TR
13	0	0	0	TR	0	0	0	0	0	0	0	0	0	0	0	0	TR	0	0	0	TR
14	0	0	0	0	TR	0	0	0	0	0	0	0	0	0	0	0	TR	0	0	0	TR
15	0	0	0	0	0	TR	0	0	0	0	0	0	0	0	0	0	TR	0	0	0	TR
16	0	0	0	0	0	0	TR	0	0	0	0	0	0	0	0	0	TR	0	0	0	TR
17	0	0	0	0	0	0	0	0	TR	TR	TR	TR	TR	TR	TR	TR	0	TR	0	0	TR
18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Key inputs for modeling influenza transmission (emission rate of viral IAV copies)

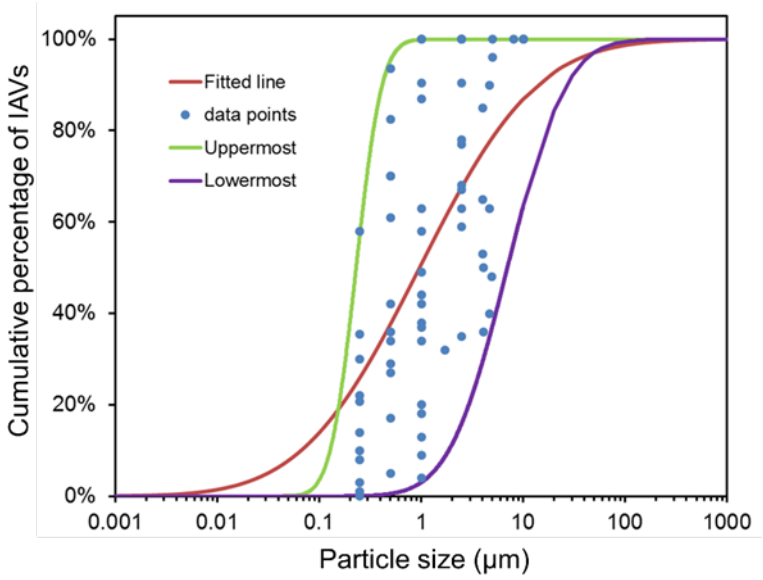
References	Min	Mean (SD)	Max	Activity	Description
Fabian et.al. (2008)	< 3.2 #/min	7.4 (7.3)[1] #/min	20 .0 #/min	breath	Collected onto Teflon filters, analyzed by qPCR
Lindsley et al. (2010)	> 0 #/cough	15.8 (29.3) #/cough	140 #/cough	cough	Collected by a three stage aerosol particle collection system, analyzed by qPCR
Bischoff et al (2013)	> 0 #/cough	31.6 (14.2)[2] #/cough	~1600 #/cough	all	Collected by aerosol samples for 20 minutes in 0.3 m distance from patient head
Milton et al (2013)	> 0 #/cough	6.3 (20.4)[2,3] #/cough	~1600 #/cough	all	Collected by an exhaled breath collection system for 30 minutes of normal breathing and 10 coughs at every 10 minutes for both fine and coarse particles without facemask
Lindsley et al. (2015)	0.8 #/cough	23.7 (35.8) #/cough	89.7 #/cough	cough	Collected by aerosol particle collection system (0.3-8 μm) for six coughs

- Emission rate of airborne influenza viruses from infected individuals
  - For breath: normally distributed with mean (±SD) of 7.4 (±7.3) per minute
  - For cough: normally distributed with a mean (±SD) of 19.3 (52.5) #/cough

Key inputs for modeling influenza transmission (size distribution of IAV copies)

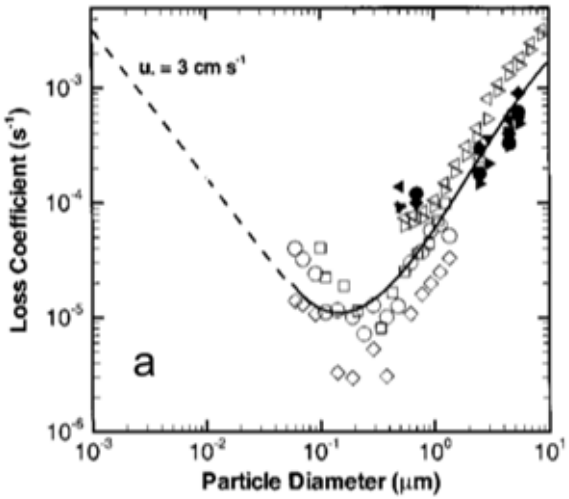
	<0.25 µm	< 0.5 µm	< 1 µm	< 2.5 µm	< 4 µm	<4.7 µm	< 5 µm	< 10 µm	Description
Fabian et.al. (2008)		70%	87%				100%		Human exhaled breath; Aerosol particle collection system
Blachere et al. (2009)			4%		53%				Hospital emergency department; Personal, upper, & lower samplers
Lindsley, Blachere, Davis, et al.(2010)			14%[1]		42%[1]				Urgent care medical clinic; Personal, upper, & lower samplers
Lindsley, Blachere, Thewlis, et al.(2010)			42%		65%				Human cough; Aerosol particle collection system
Yang et al. (2011)	18%	31%	41%	68%					Health center and airplane; Aerosol samplers
Cao et al. (2011)			34%		85%				Calm-air chamber; NIOSH bioaerosol sampler
Milton et al. (2013)							96%		Human cough and breath; Aerosol particle collection system
Lednicky & Loeb (2013)	19%	82%	97%	97%				100%	Single-family 4-bedroom apt.; Aerosol samplers
Bischoff et al (2013)						64%			Emergency department; Aerosol samplers

[1] The reported influenza virus size bins were < 1 µm, < 4.1 µm, and ≥ 4.1 µm for upper and lower stationary samplers and < 1.7 µm, < 4.9 µm, and ≥ 4.9 µm for personal samplers

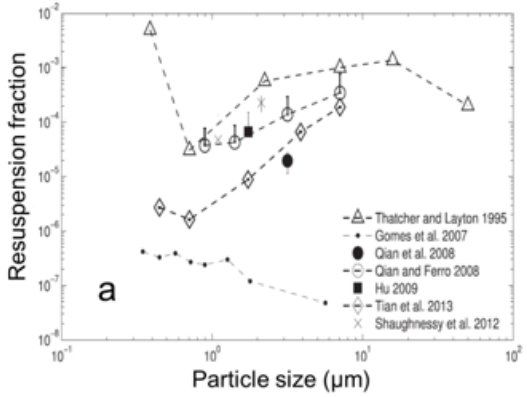


Key inputs for modeling influenza transmission (deposition and resuspension factor)

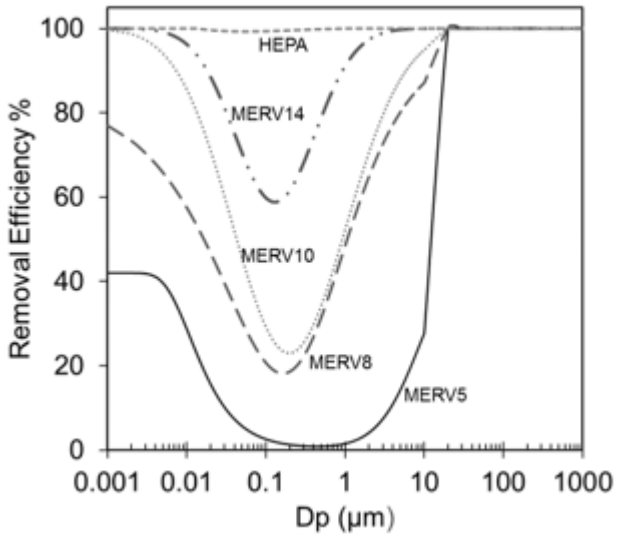
Size resolved deposition loss rate



Size resolved resuspension factor



Size resolved filtration removal efficiency



- Bulk deposition rate, resuspension factor and filtration efficiency of influenza

	Deposition rate (1/hr)	Resuspension factor	MERV5	MERV8	MERV10	MERV14	HEPA
Best fit curve	0.69	1.395×10^{-4}	18.3%	53.7%	59.9%	85.7%	99.8%
Uppermost curve	0.06	1.415×10^{-6}	1.3%	21.7%	26.1%	65.4%	99.6%
Lowermost curve	1.62	1.958×10^{-4}	44.5%	83.7%	88.1%	98.8%	100.0%

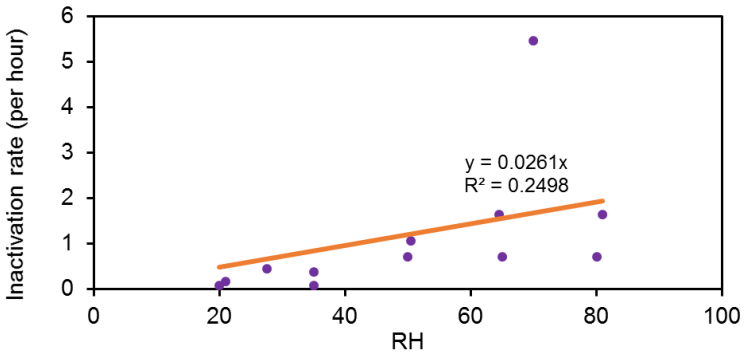
Key inputs for modeling influenza transmission (inactivation rate of IAVs)

Temperature (°C)	RH (%)	Inactivation rate (hr^{-1})	Media	Reference
7-8	23-25	0.12	Air	Harper (1961)[1]
7-8	51	0.08	Air	
7-8	82	0.59	Air	
20-24	20-22	0.16	Air	
20-24	15-40	0.44	Air	Hemmes et al (1960)[2]
20-24	34-36	0.38	Air	Harper (1961)
20-24	50-51	1.06	Air	
20-24	64-65	1.64	Air	
20-24	50-90	5.46	Air	Hemmes et al (1960)
20-24	81	1.64	Air	Harper (1961)
21-24	20, 35	0.07	Air	Harper (1963)[3]
21-24	50, 65,80	0.70	Air	
32	20	0.66	Air	Harper (1961)
32	49-50	2.02	Air	
32	81	2.62	Air	
Room temp	N/A	0.12	Pajamas	Bean et al. (1982)[2]
27.8-28.3	35-40	0.58		Boone and Gerba (2007)[4]
Room temp	N/A	0.45	Magazine	Bean et al. (1982)
27.8-28.3	35-40	0.77		Boone and Gerba (2007)
Room temp	N/A	1.02	Tissue	Bean et al. (1982)
Room temp	N/A	1.06	Handkerchief	Bean et al. (1982)
27.8-28.3	35-40	0.58		Boone and Gerba (2007)
Room temp	N/A	0.31	Bank notes	Thomas et al. (2008)[2]
Room temp	N/A	0.11	Steel	Bean et al. (1982)
17-21	23-24	0.70		Greatorex et al. (2011)[5]
27.8-28.3	35-40	0.08		Boone and Gerba (2007)
Room temp	N/A	0.10	Plastic	Bean et al. (1982)
17-21	23-24	3.29		Greatorex et al. (2011)
27.8-28.3	35-40	0.77		Boone and Gerba (2007)
Room temp	20	1.57	Glass	Buckland et al (1962)[2]
Room temp	20	1.29		Buckland et al (1962)[2]
Room temp	84	3.22		Buckland et al (1962)[2]
Room temp	84	2.40		Buckland et al (1962)[2]
Room temp	N/A	71.9	Human skin	Bean et al. (1982)

1. The inactivation rate is estimated by taking natural logarithm of initial percentage viability of viruses divided by percentage viability after one hour from Harper (1961).
2. Derived from Jones (2011), summary of inactivation rates.
3. Derived from Weber and Stilianakis (2008), summary of inactivation rates.
4. The inactivation rate is estimated from T90, which is the times required for the initial viral titer to decrease by 90%.
5. Estimated from changes in titre of viable influenza viruses on various surfaces after 4 hours

- Air temperature of 20 ºC and indoor air RH scenarios of 20%, 40%, and 60%

Inactivation rate of IAV in indoor air



- Inactivation rate of IAV on surfaces (log-normally distributed with a geometric mean of 0.6 and GSD of 3.1 per hour) and human skin (normally distributed with an arithmetic mean of 71.9 and SD of 23.4 per hour)

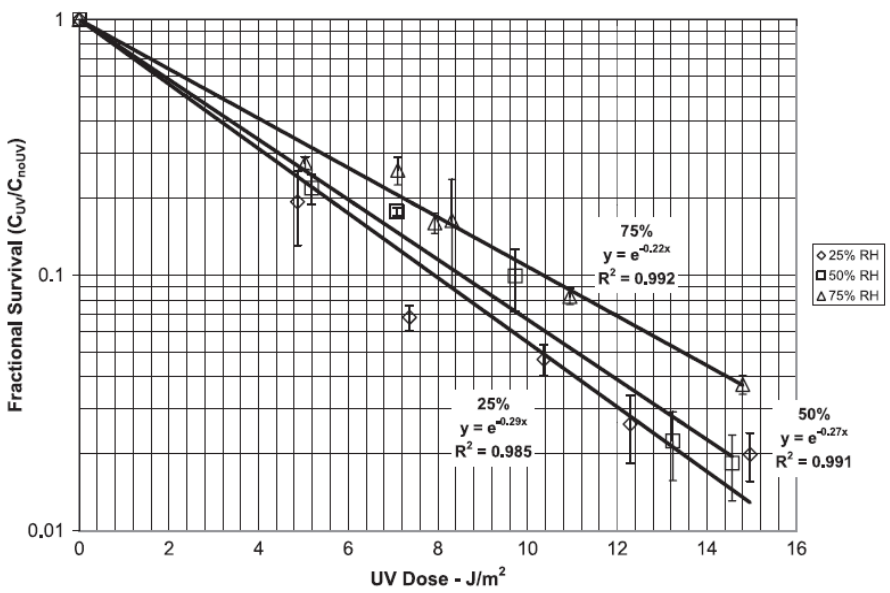
Jones, R. M., *Risk Analysis* (2011)

Key inputs for modeling influenza transmission (HVAC UV sterilization and transfer efficiency between surfaces)

HVAC UV sterilization

- Fractional survival of IAV passing through UV air cleaning as a function of RH and UV-C dose

$$F_{UV-C,RH} = \exp(-\delta_{RH} \times D_{UV-C})$$



McDevitt, J. J., *Applied and Environmental Microbiology* (2012)

Transfer efficiency rate estimation

- Transfer efficiency of IAV for hand-to-surface (log-normally distributed with a geometric mean of 0.079 and GSD of 1.4) and finger skin to the face (log-normally distributed with a geometric mean of 0.046 and GSD of 1.4)

Jones, R. M., *Risk Analysis* (2011)

Key inputs for modeling influenza transmission (human activities)

- Breathing frequency and breathing flow rate (assumed to be 15 breaths/min and 8 L/min, respectively)
- Coughing frequency (log-normal distributed with median of 38 coughs/hr and GSD: 1.5)
- Probability of touching office surfaces (log-normally distributed with median of 1.5 touches/min and GSD of 0.34) and face (have a Weibull distribution with λ of 1.28 and k of 1.95)
- Close distance contact time (uniformly distributed between 2% and 36%)
- Stepping frequency (75 step/min)
- Shoe flooring contact area (192 cm^2) and finger skin contact area (10 cm^2)
- proportion of walking time of employees (uniformly distributed between 10% and 30%)

Key inputs for modeling influenza transmission (probability of infection)

- The most common method of estimating α value is calculating it as a function of HID_{50}

$$HID_{50} = \ln(2) \div \alpha$$

- We used different probabilities of infection by a single influenza virus dose for upper and lower respiratory tracts ($\alpha_{URT}, \alpha_{LRT}$)
- We assumed the HID_{50} of influenza is uniformly distributed between 0.6 and 3 $TCID_{50}$ for lower respiratory tracts and between 30 and 320 $TCID_{50}$ for upper respiratory tracts
- The ratio between $TCID_{50}$ and PFUs of IAV was estimated to be 0.7 PFU/$TCID_{50}$
- Conservatively we assumed 50 IAVs are necessary to yield one PFU

Estimated IAV transmission risk

- Total probability of getting infected was calculated using a non-threshold dose-response model

$$P_{IAV,infection} = 1 - \exp\left[-\left(\alpha_{URT} \times N_{IAV,URT} + \alpha_{LRT} \times N_{IAV,LRT}\right)\right]$$

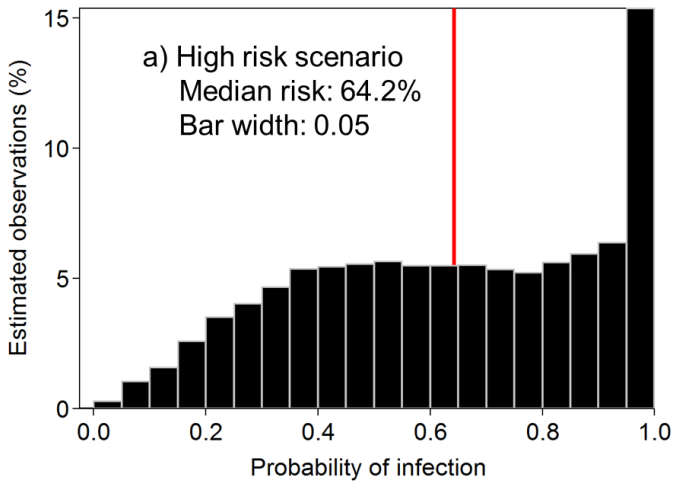
$N_{IAV,URT}$ = Number of viable influenza viruses in upper respiratory tracts (-)

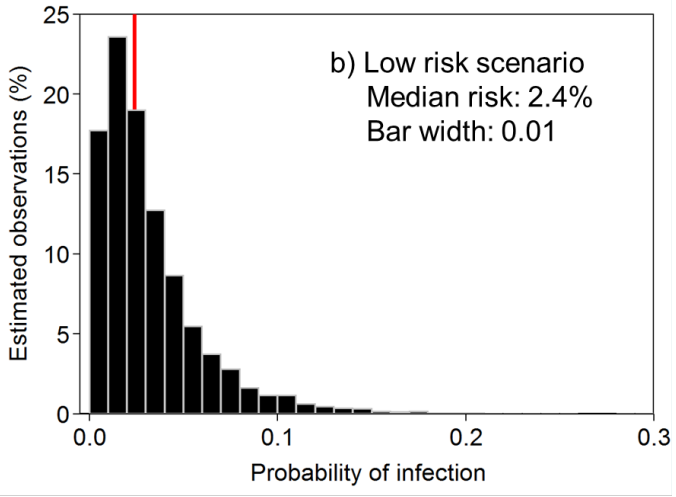
$N_{IAV,LRT}$ = Number of viable influenza viruses in lower respiratory tracts (-)

- We ran a Monte Carlo simulation with 10,000 repetitions to predict the statistical distribution of probability of infection using MATLAB

- Typical outcomes from the modeling procedure

- MERV 5
- RH = 20%
- Continuous direct contact

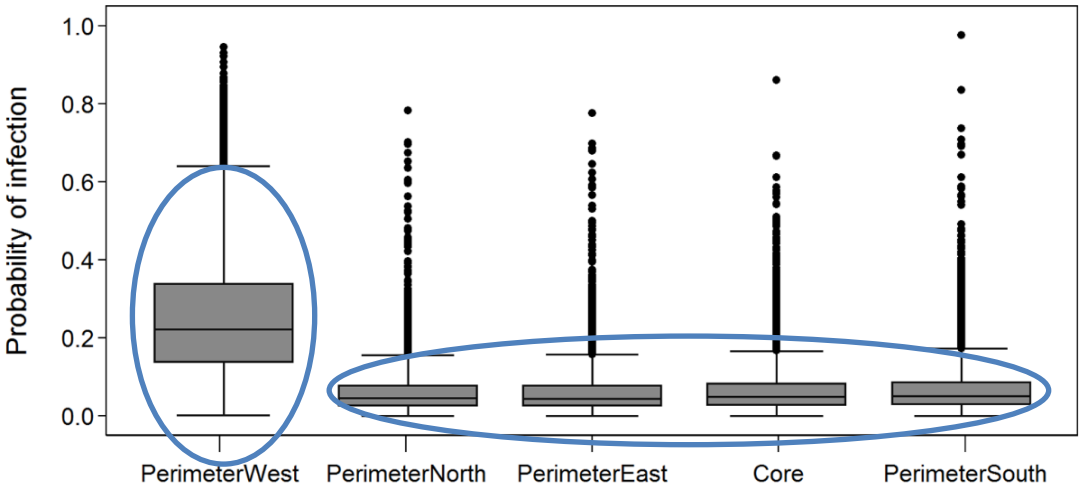




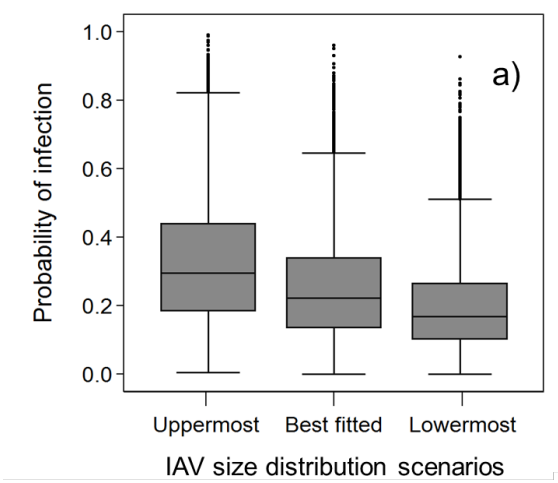
- HEPA
- RH = 60%
- No direct contact

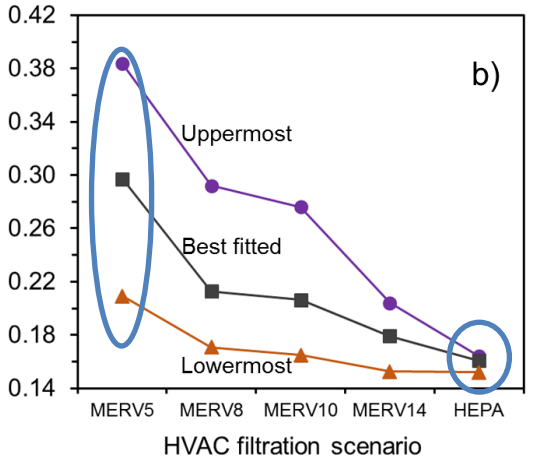
Impacts of location and IAV size distribution on transmission risk

- Impact of susceptible individual primary location
  - the infector spends at least 55% of their time in the PerimeterWest zone
  - The susceptible individual spends most of their time in various locations



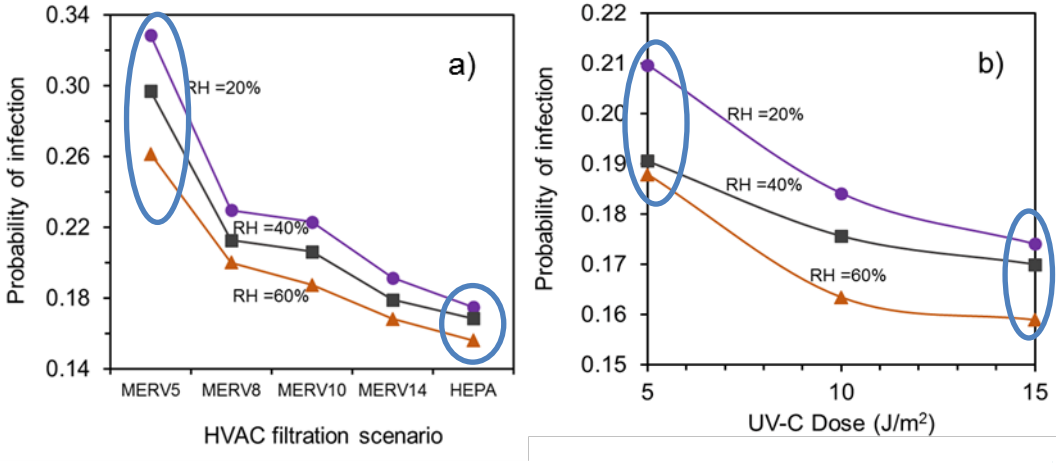
- Impact of IAV size distribution scenarios on a) range of infection transmission risk in the office when AHUs have MERV 8 filters, b) median IAV infection risk for various HVAC filtration scenarios





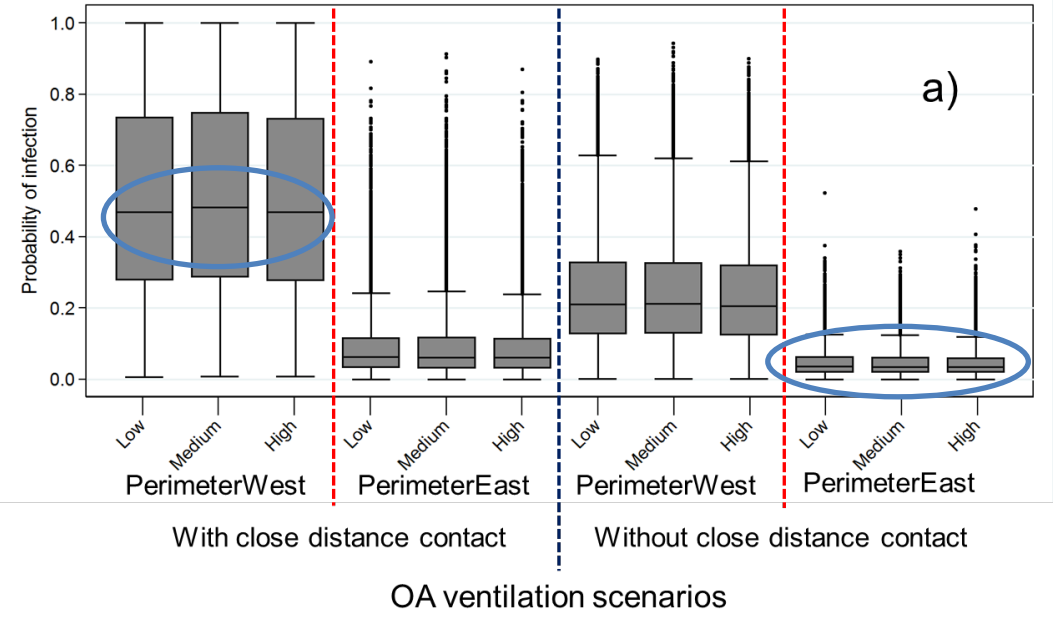
Impacts of various control strategies

- a) impact of indoor air RH scenarios (RH of 20%, 40%, and 60%) and HVAC filtration on the median of infection risk; b) Impact of indoor air RH, UV sterilization, on median infection transmission risk of IAV



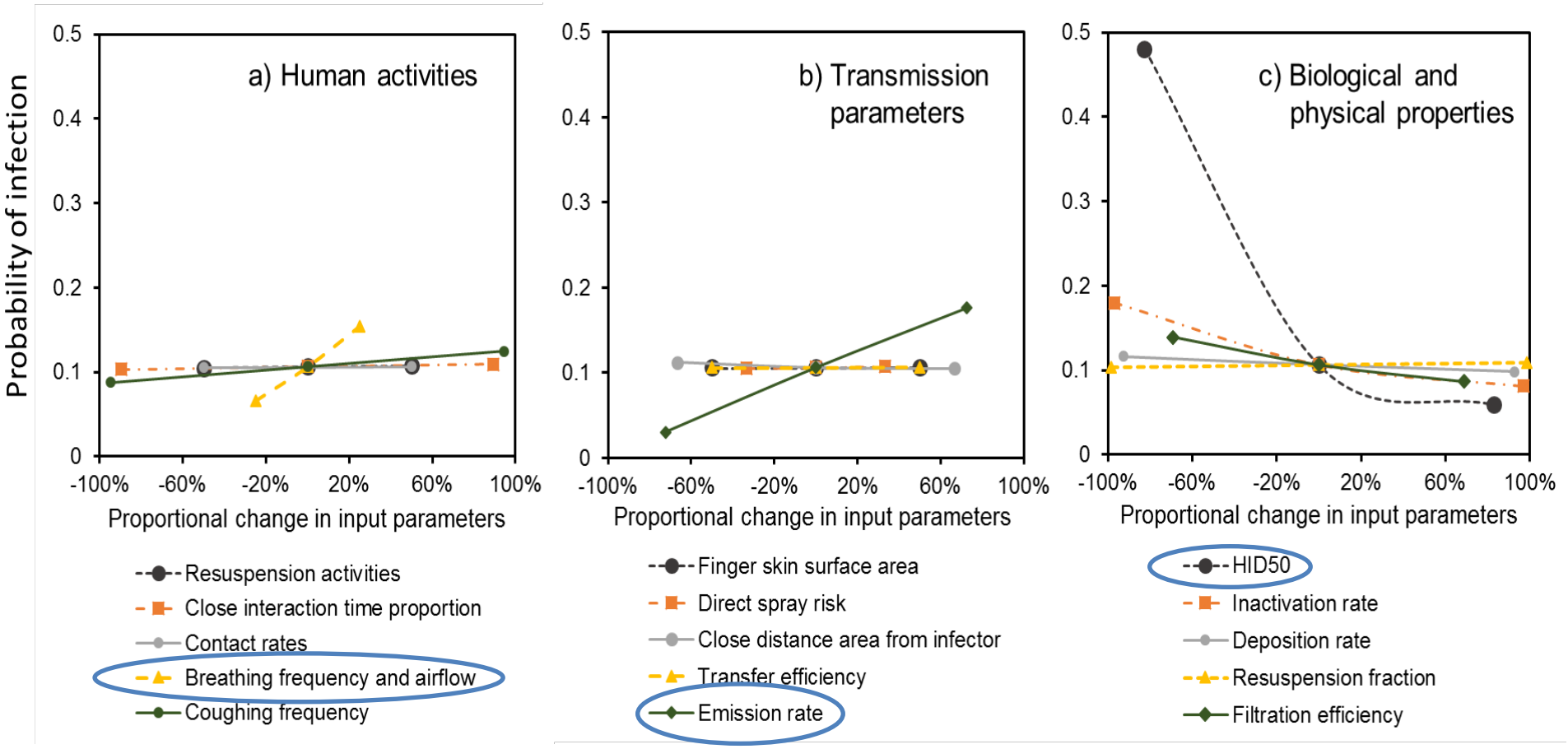
- Impact of outdoor air (OA) ventilation scenarios on absolute IAV transmission risk

- Low: 0.5x of default OA ventilation from the NIST model
- Medium: 1x of default OA ventilation from the NIST model
- High: 2x of default OA ventilation from the NIST model



Sensitivity analysis

- Sensitivity of the complex model to the input parameters



Comparison of the complex transmission model results with simpler single-zone models

- Last, the median IAV transmission risk (and 1st and 3rd quartiles) in the office was estimated ~8% (5% and 13%) using a simpler single-zone model assuming the whole indoor air office is well mixed and employees distributed uniformly
- We compared the results of the simpler single-zone model with a modified transient Wells-Riley model to back calculate quanta generation rate

$$P_{\text{infection}} = 1 - e^{-\frac{pIq}{V} \times \frac{Ct + e^{-Ct} - 1}{C^2}}$$

Gammaitoni, L., and Maria C. N., *Emerging infectious diseases* (1997)

C = the total loss/disinfection rate (e.g., $\lambda_{\text{ventilation}} + k_{\text{filtration}} + k_{\text{deposition}} + k_{\text{inactivation}}$, 1/hr)

- Median (1st and 3rd quartiles) results from the single-zone model yields a quanta generation rate of ~155 (90 and 267) per hour, ranging from ~163 (95 and 284) to ~149 (88 and 252) per hour when the rates were back calculated from the low and high risk scenarios, respectively

- The results were directly in line with the existing data on the quanta generation rate of influenza viruses gathered from epidemiology studies from the literature, which have varied from ~15 to ~500 per hour

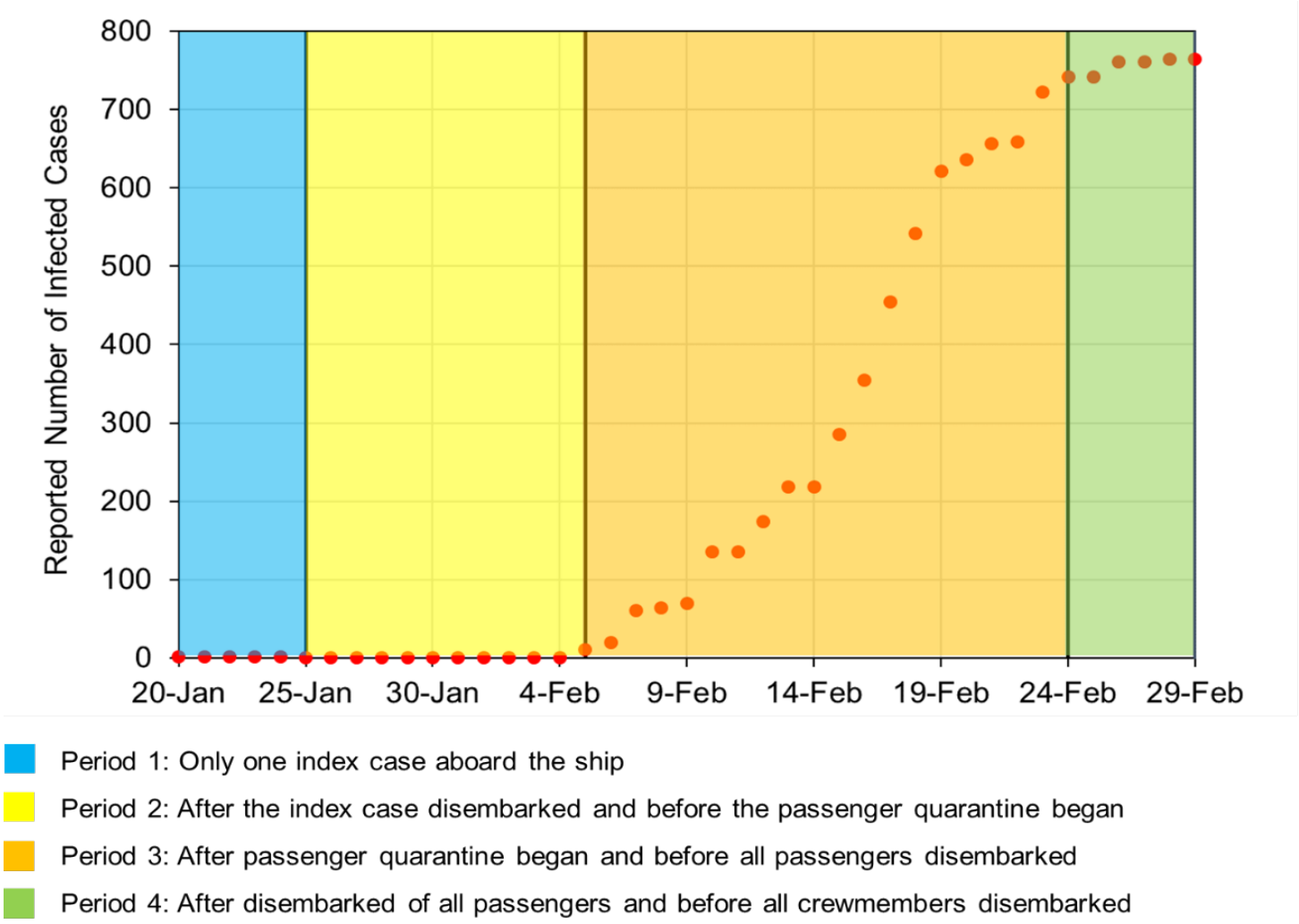
Evaluating COVID-19 Transmission Routes

Spanish Flu (1918 - 19)

COVID-19 (2019-Present)

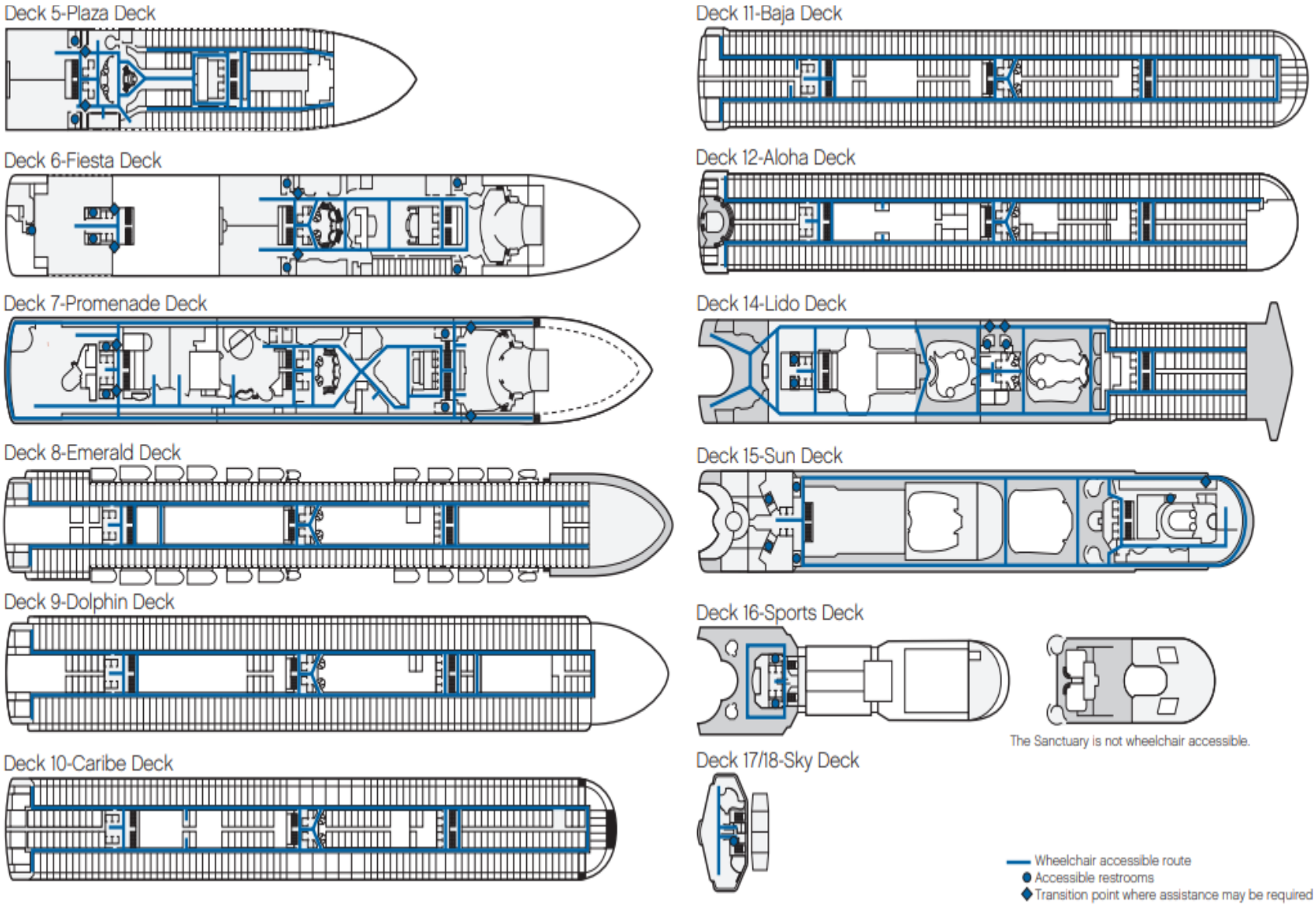
COVID-19 Outbreak in Diamond Princess Cruise Ship

Diamond Princess Cruise Ship Outbreak



Daily cumulative number of infected cases aboard the Diamond Princess Cruise Ship between January 20, 2020 and February 29, 2020

Generating a Markov Chain Model to Estimate the Intake Dose of SARS-CoV-2



Generating a Markov Chain Model to Estimate the Intake Dose of SARS-CoV-2

Transmission/Removal Rates Per Hour		Cabin Air	Common Area Air	Cabin Surfaces	Common Area Surfaces	Palm Skin Cabin-Mate	URT-Cabin-Mate	LRT-Cabin-Mate	Palm Skin other people	URT-Other People	LRT-Other People	HVAC System	Inactivation - Removal
		1	2	3	4	5	6	7	8	9	10	11	12
Cabin Air	1	0	0.5	0.64	0	0	0	0	0	0	0	9	0.69
Common Area Air	2	0	0	0	0.6	0	0	0	0	0	0	12	0.69
Cabin Surfaces	3	0	0	0	0	0	0	0	0	0	0	0	0.12
Common Area Surfaces	4	0	0	0	0	0	0	0	0	0	0	0	0.12
Palm Skin Cabin-Mate	5	0	0	0.58	8.7	0	3.6	0	0	0	0	0	0.8
Upper respiratory Tracts of Cabin Mate	6	0	0	0	0	0	0	0	0	0	0	0	0
Lower respiratory Tracts of Cabin Mate	7	0	0	0	0	0	0	0	0	0	0	0	0
Palm Skin Other people	8	0	0	0	8.7	0	0	0	0	3.6	0	0	0.8
Upper respiratory Tracts of Other people	9	0	0	0	0	0	0	0	0	0	0	0	0
Lower respiratory Tracts of Other People	10	0	0	0	0	0	0	0	0	0	0	0	0
HVAC System	11	0	0	0	0	0	0	0	0	0	0	0	0
Inactivation - Removal	12	0	0	0	0	0	0	0	0	0	0	0	0

Combining Markov Chain with an Epidemic Model

A modified version of the Reed-Frost epidemic model was used:

(i) Infection is spread from infected individuals to others by four main transmission pathways (long-range inhalation, short-range inhalation, direct deposition within close-range, and fomite),

(ii) a portion of susceptible individuals in the group will develop the infection and will be infectious to others (the portion of '*susceptibles'* who will develop the infection is estimated by the transmission risk model), restaurant crawling

(iii) Probability of coming into adequate contact with any other specified individual in the group within one time interval depends on the interaction behavior of the individual and is estimated using the Markov chain method,

(iv) Susceptible individuals in the cruise ship were isolated from others outside the cruise ship, and

(v) These conditions remain constant during one whole day of the outbreak.

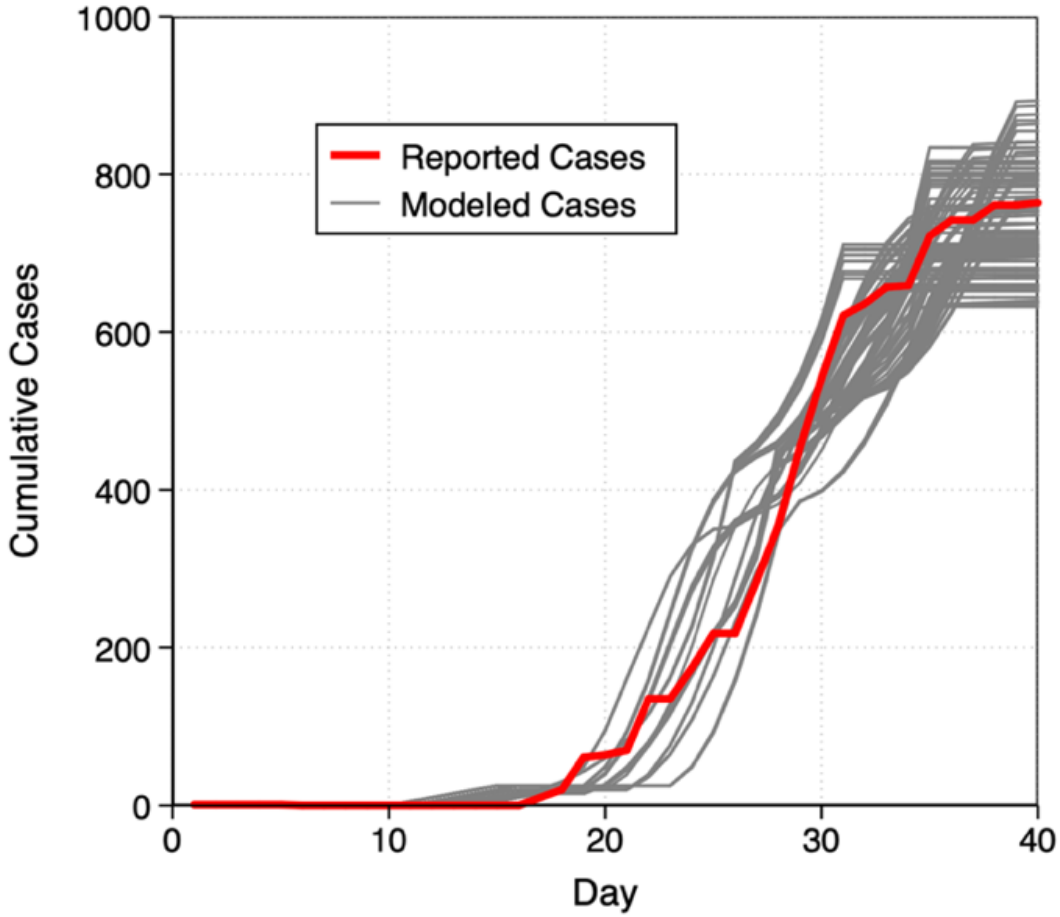
Selecting acceptable model iterations

The model approach resulted in a total of 21,600 model iterations

Model Inputs	Epidemiological Factors			Mechanistic Transmission Factors				
	Effective incubation period	Effective sub-clinical infectious period	Effective reproduction number for the index case	Symptomatic vs asymptomatic emissions	Ratio of aerosol vs. droplet emissions	Minimum close interaction time in cabins	Quarantine infection control efficiency	URT/LRT infectious doses
No. Scenarios	10	5	6	2	3	2	2	3
Range	6 – 15 (days)	1 – 5 (days)	1 – 6	0.544 1.0[35]	0.3:1 2.4:1, 1:1	8 or 12 hours per day*	Moderate High*	1:1 10:1 100:1*
Best Estimate (Mean ± SD)	11.9 ± 1.3	4.2 ± 1.1	0.78 ± 0.23	A/D = 1.3 ± 0.9	11.9 ± 4.0	3.9 ± 0.9	47.1 ± 46.9	Moderate

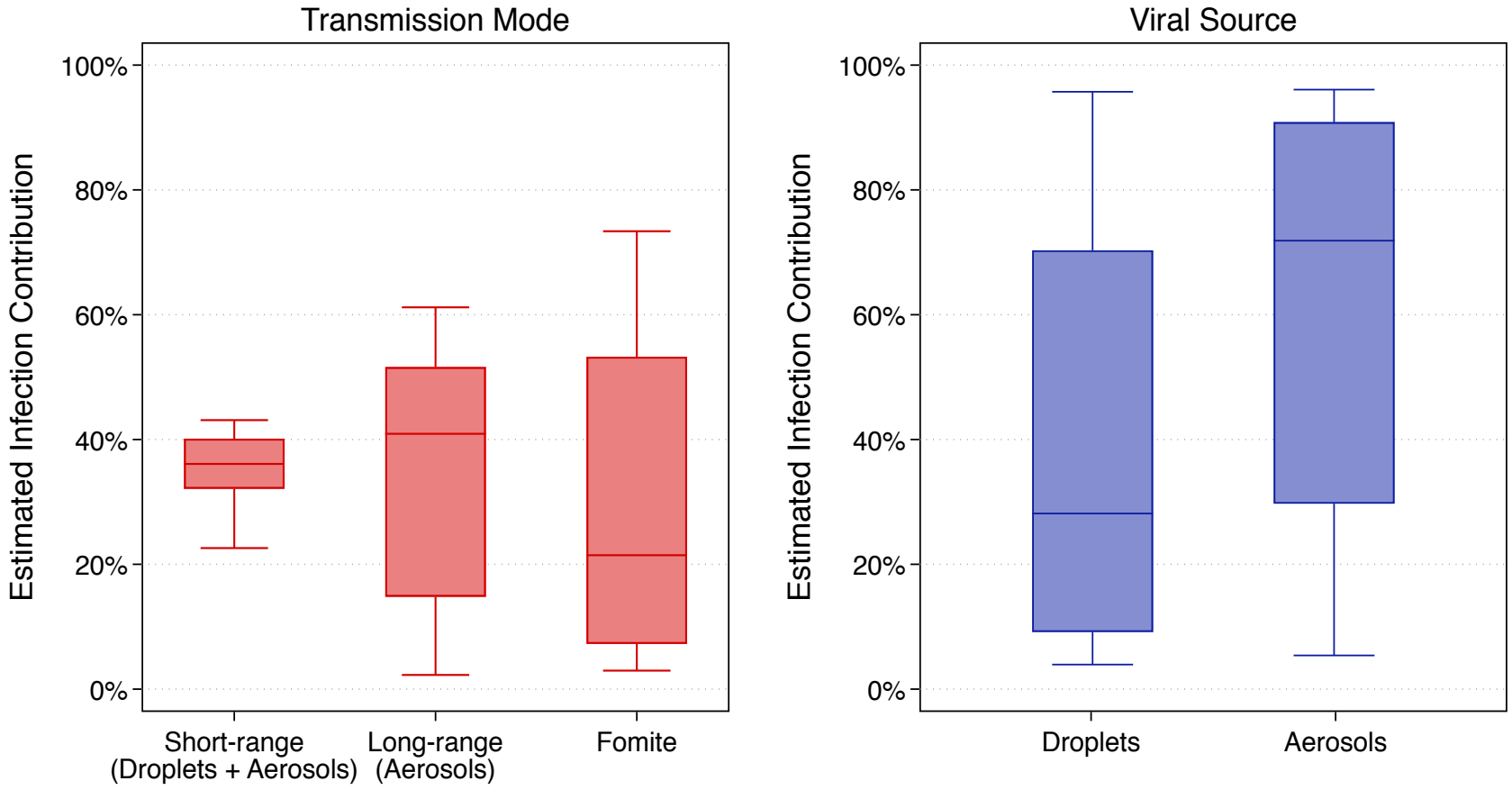
Summary of the ranges of 8 unknown or uncertain critical model input parameters that defined each model iteration

Results: Reported vs Modeled Cases



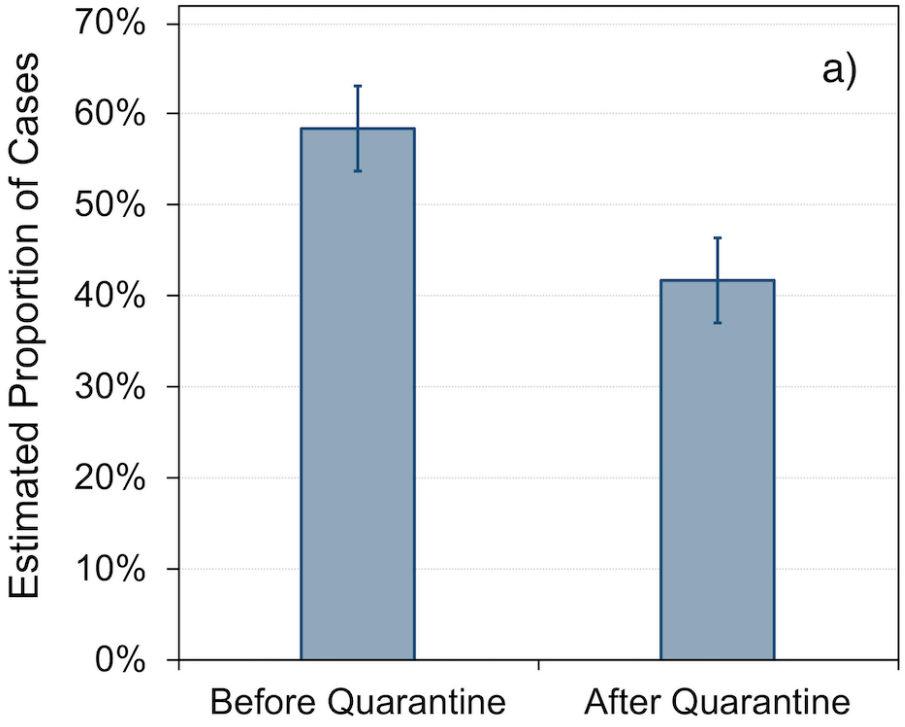
Reported (actual) and modeled (predicted) cumulative COVID-19 cases aboard the Diamond Princess Cruise Ship from January 20 – February 24, 2020. Modeled cases are from 132 model scenarios that met acceptable criteria (R^2 >0.95 for cumulative daily cases and R^2 > 0 for daily cases).

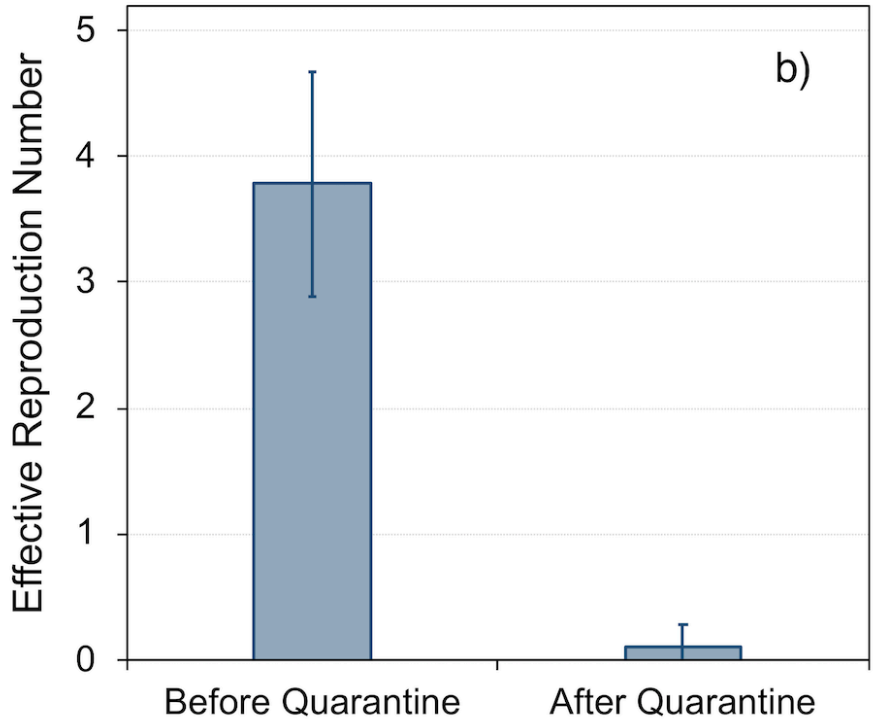
Results: Transmission Modes and Viral Sources Contributions



Estimates of the contributions of transmission modes and viral sources to infected cases aboard the Diamond Princess Cruise Ship over the entirety of the simulation period

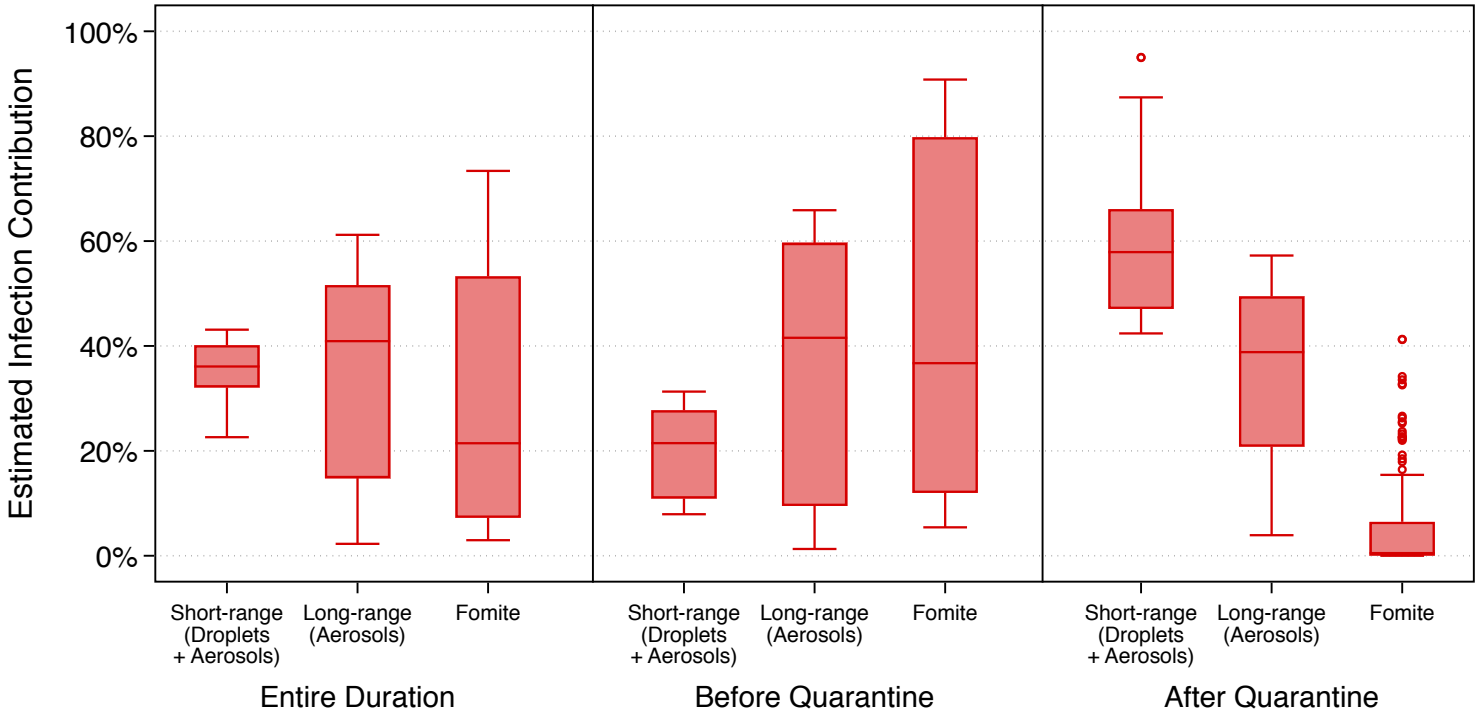
Results: Proportions of Cases and Reproduction Number





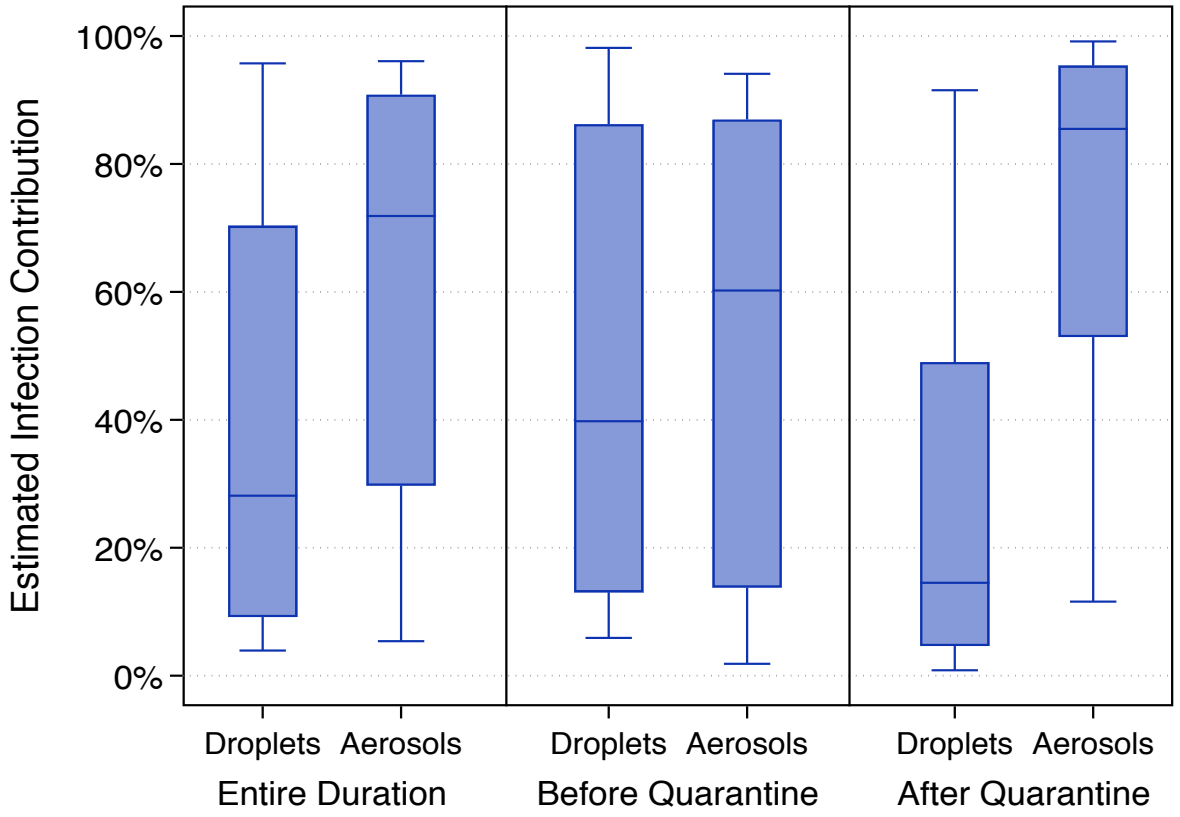
Mean (SD) estimates of (a) the proportion of cases and (b) the effective reproduction number before and after passenger quarantine

Results: Impacts of Isolation on Transmission Modes



Estimates of the contribution of multiple transmission modes to infected cases aboard the Diamond Princess Cruise Ship over the entirety of the simulation period as well as before and after quarantine measures

Results: Impacts of Isolation on Virial Source



Estimates of the contribution of droplets and aerosols to infected cases aboard the Diamond Princess Cruise Ship over the entirety of the simulation period as well as before and after quarantine measures