QMRA and Its Applications to Bioaerosol Research

Amanda M. Wilson, PhD [1]
Kerry A. Hamilton, PhD [2,3]

[1] Department of Community, Environment & Policy, Zuckerman College of Public Health, University of Arizona, Tucson, AZ, USA; [2] Biodesign Center for Environmental Health Engineering, Arizona State University, Tempe, AZ, USA; [3] School of Sustainable Engineering and the Built Environment, Arizona State University, Tempe, AZ, USA

Talk Overview

01

What is QMRA?

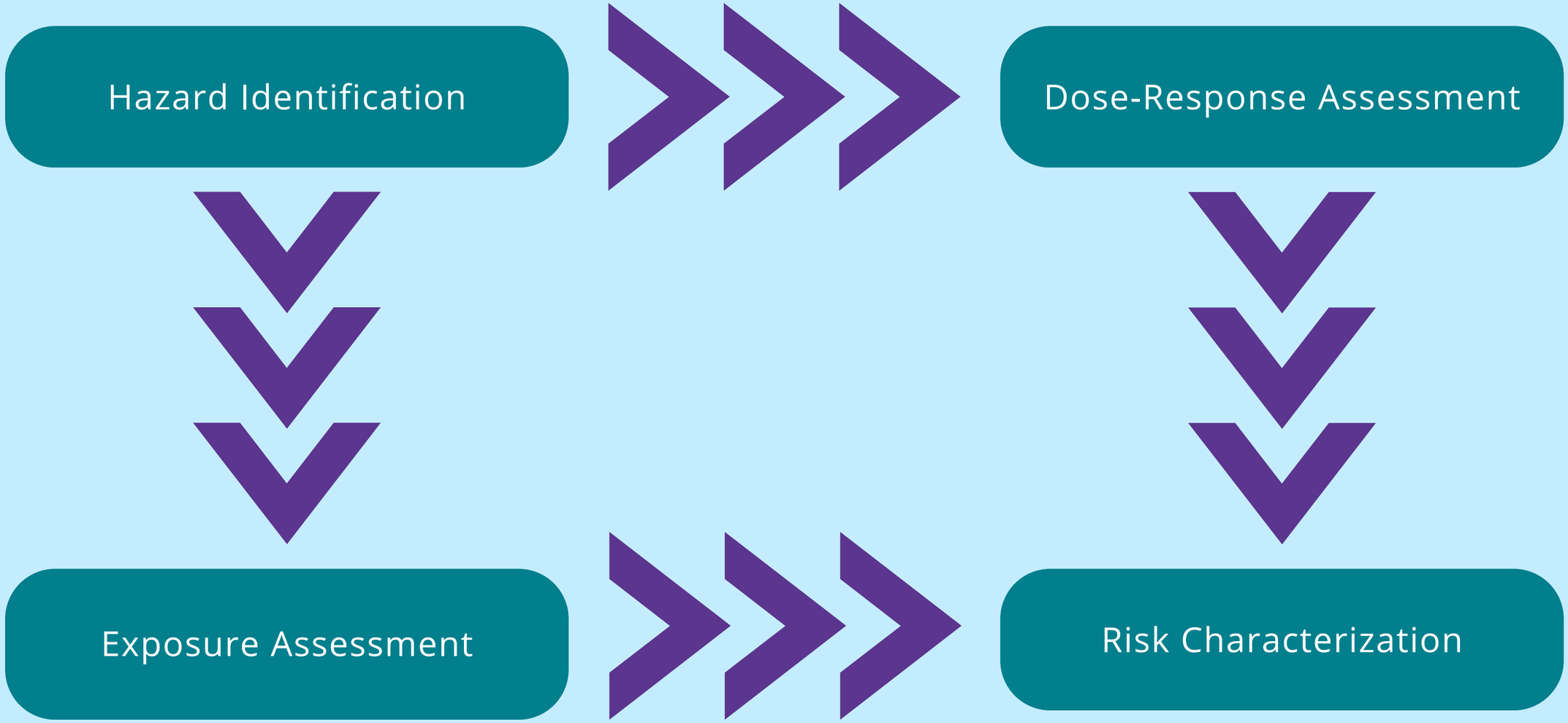
02

Examples of Bioaerosol QMRAs

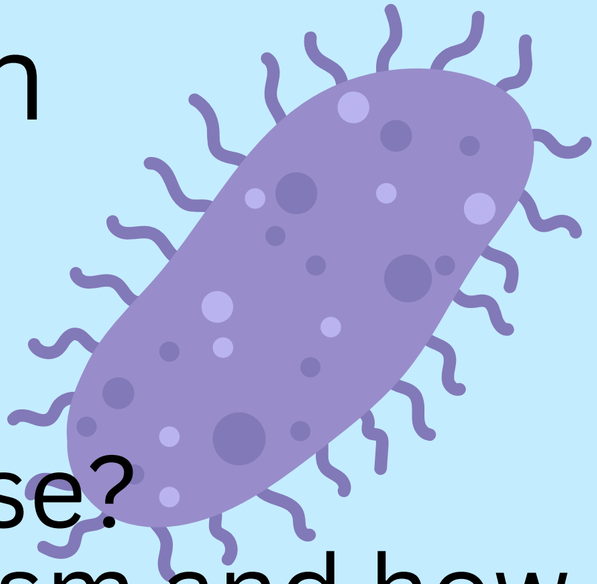
03

Opportunities to Learn More

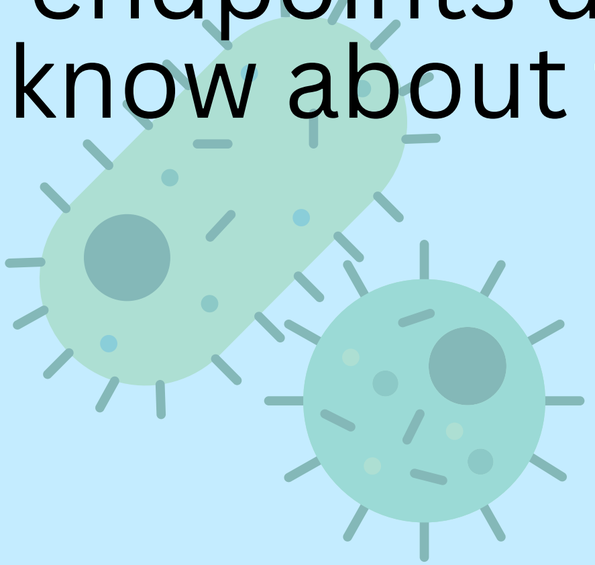
What is quantitative microbial risk assessment (QMRA)?

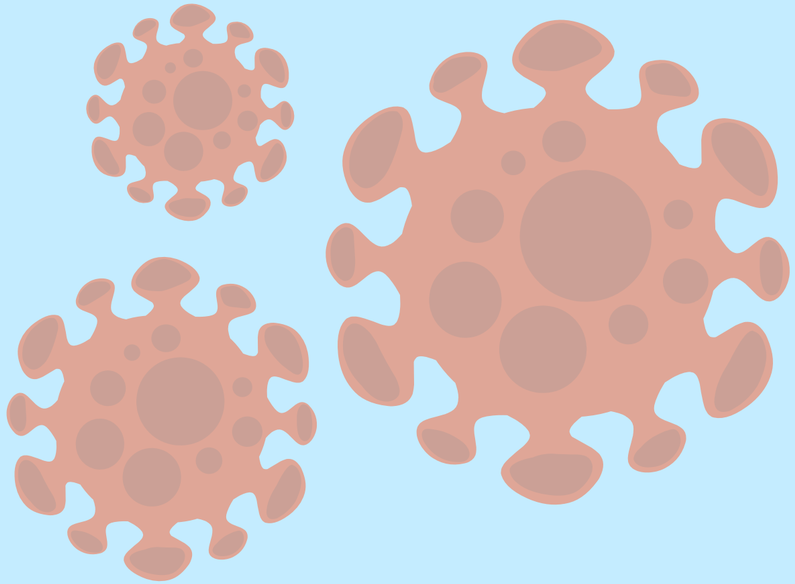


Hazard Identification



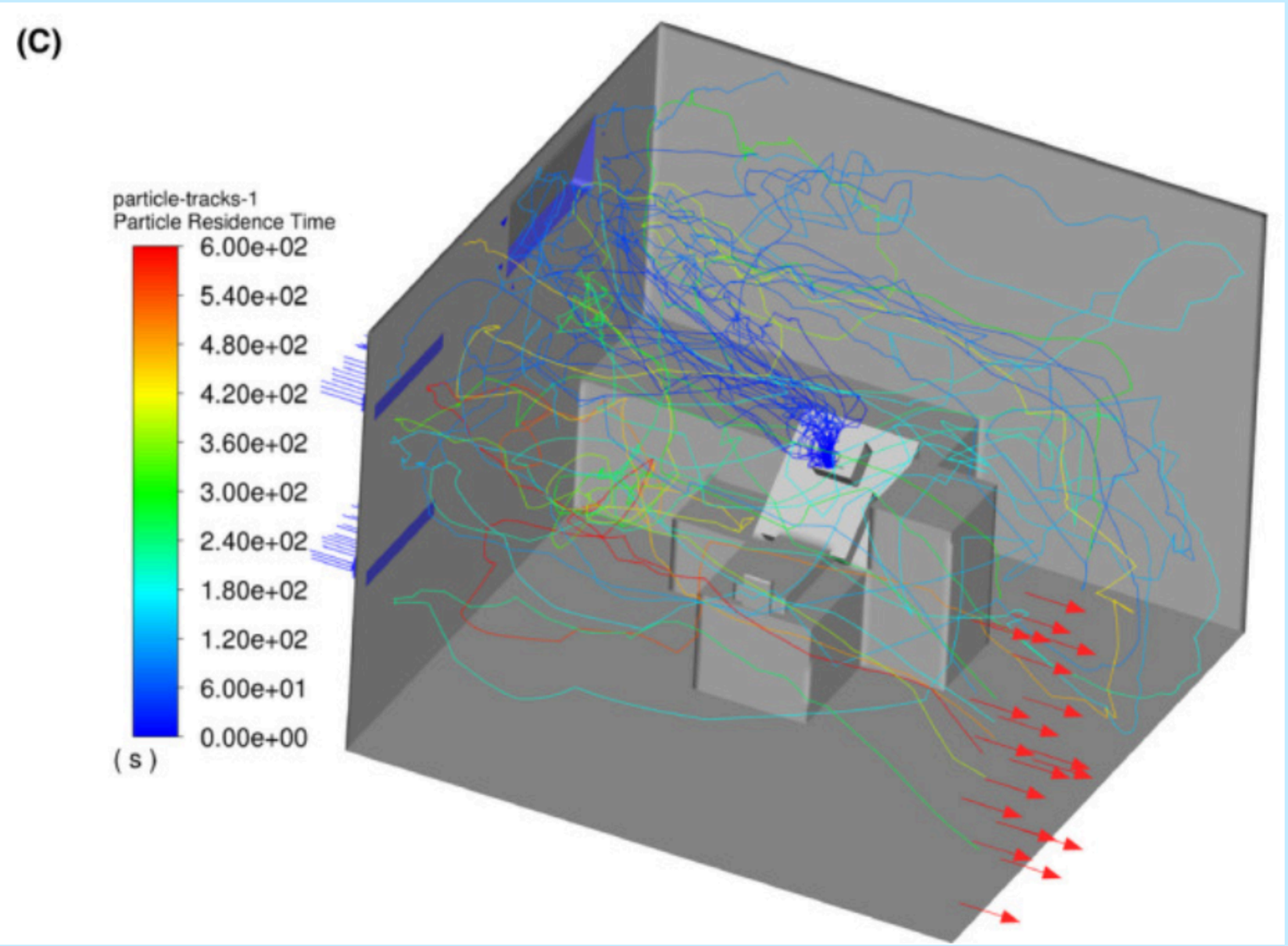
- What is the pathogen of concern?
- What health endpoints does it cause?
- What do we know about the organism and how it is spread?





Exposure Assessment

- Is the pathogen present and at what magnitude?
- How is it spread from the source to a susceptible person?
- At what rate does it decay in the environment?
- How do people behave in this environment that could result in a dose?
- How big do we think that dose is given what we know about the system?



Various mathematical approaches for modeling viral dispersion, including computational fluid dynamics

Wilson et al. (2021)

Dose-Response Assessment

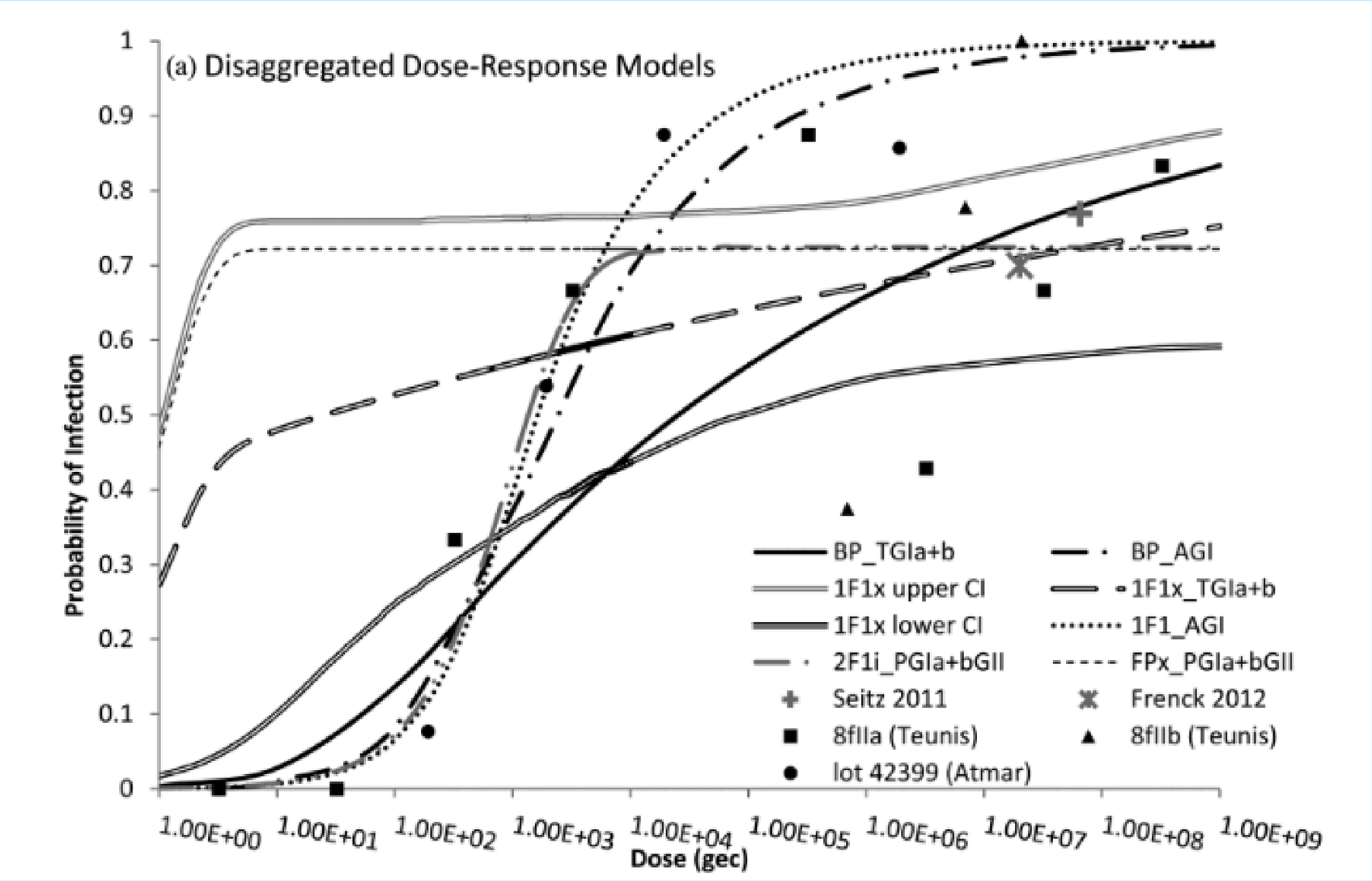
- Quantitative relationship between dose and probability of a health endpoint, usually infection with the pathogen of interest
- Considerations about which dose-response curve(s) may be best for our scenario in question

$$\text{Approximate beta} - \text{Poisson}: \quad P_{\text{infection}} \approx 1 - \left(1 + \frac{\text{dose}}{\beta}\right)^{-\alpha}$$

$$_1F_1\,\text{hypergeometric}: P_{\text{infection}} = 1 - {}_1F_1\left(\alpha,\ \alpha + \beta,\ -\text{dose}\right).$$

Van Abel et al. (2017)

Dose-Response Assessment



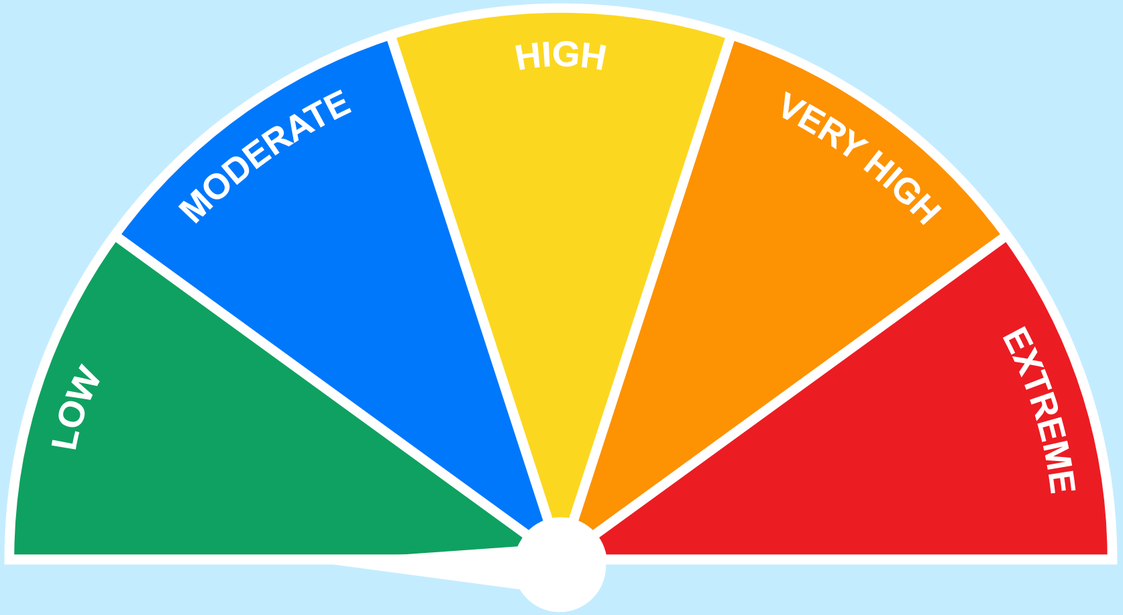
It can be hard to know which one to choose!

...and we don't have to choose just one.

Van Abel et al. (2017)

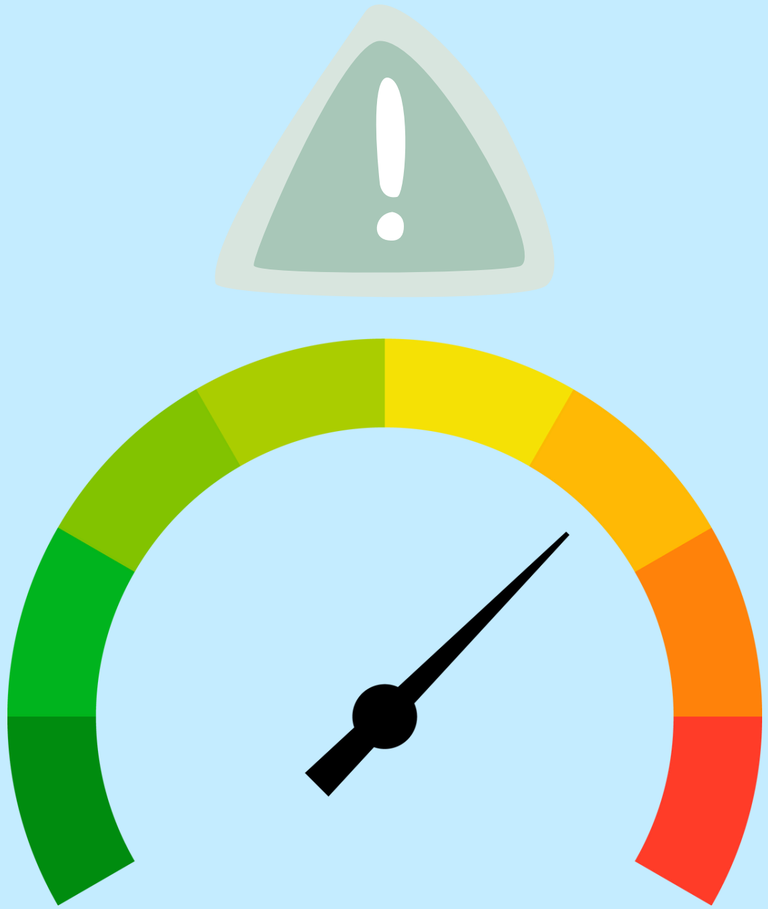
Risk Characterization

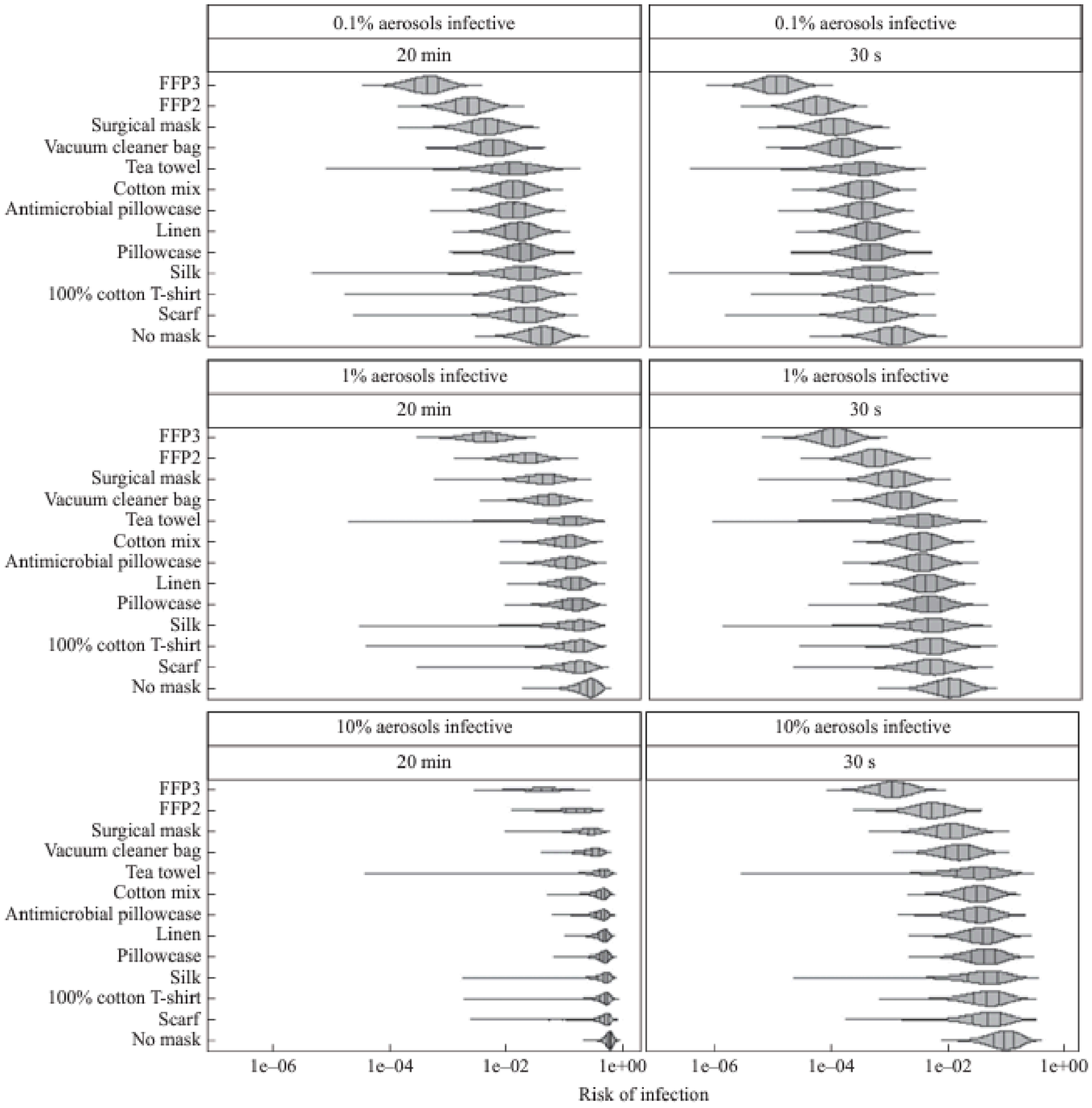
- We bring the pieces together to yield a quantitative probability of the health end point given what we know about the pathogen and the enviornmental conditions



What happens next?

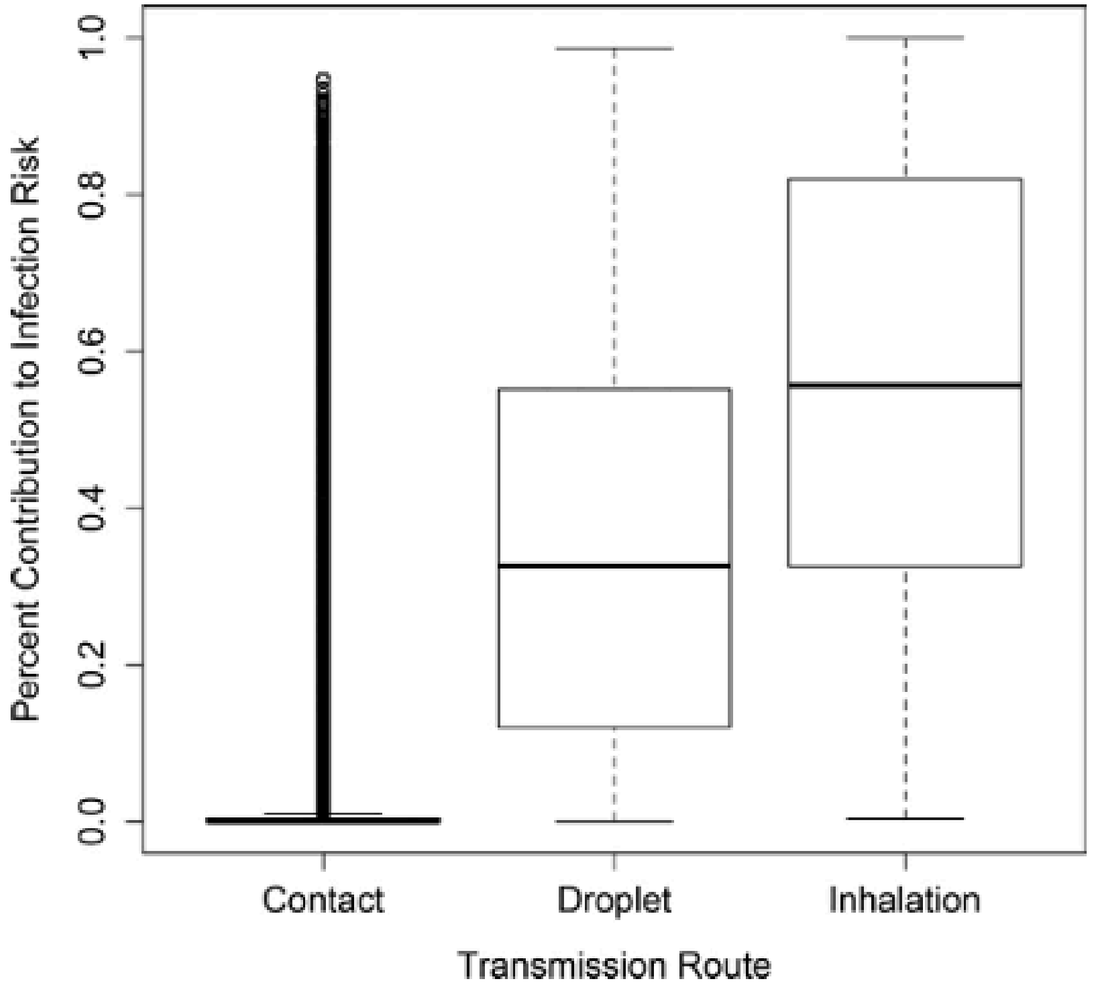
- May compare the risk to thresholds we deem acceptable
- Inform what concentrations would be needed to achieve the risk target
- Explore how interventions change the predicted risk
- Perform sensitivity analyses

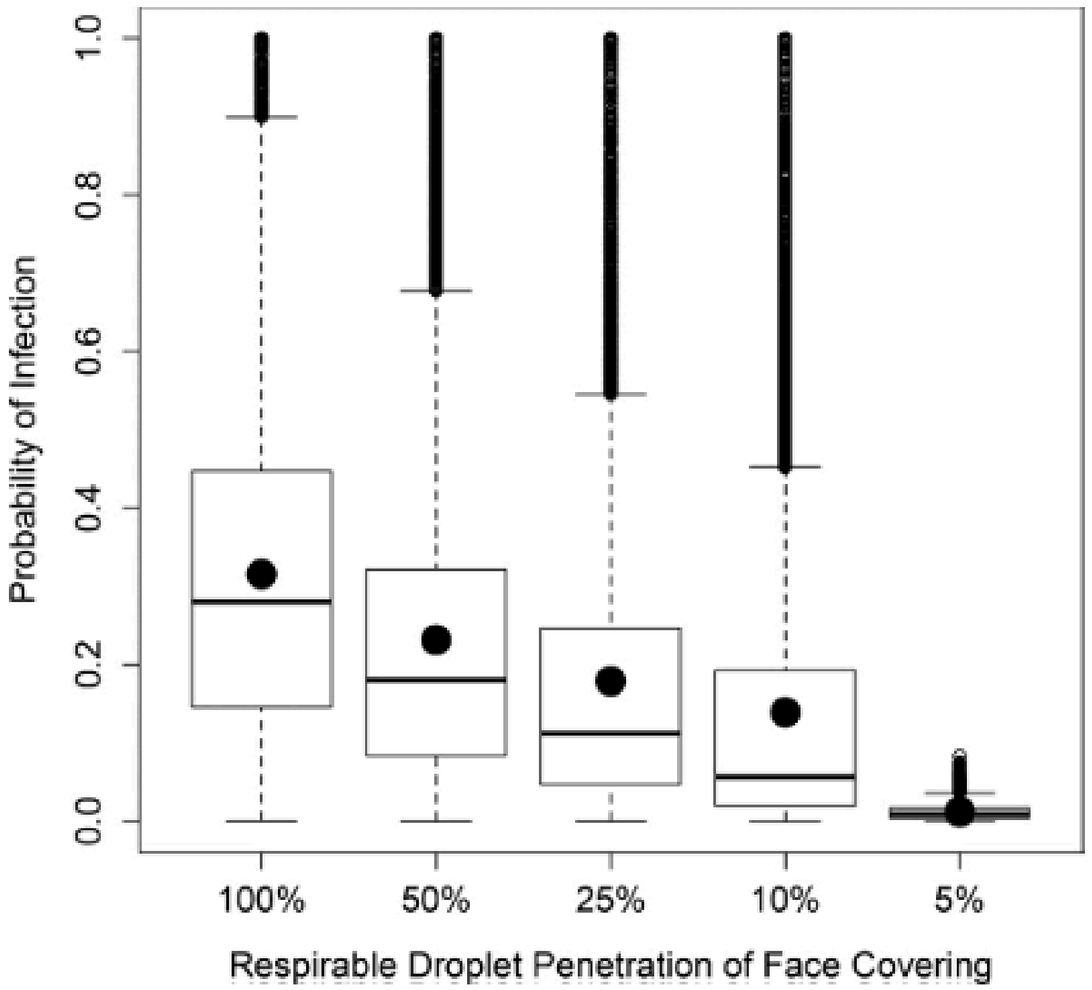




- Comparing different mask materials for COVID-19 risk reduction
- Explore different outcomes based on exposure duration and assumptions about relationship between genome copies and infectious virus

Wilson et al. 2020. PMID:32502581





- Compare relative contributions of exposure pathways to risk
- Relate intervention effectiveness to risk

Jones 2020. PMID: 32643585.

Environmental Science & Technology > Vol 53/Issue 8 > Article

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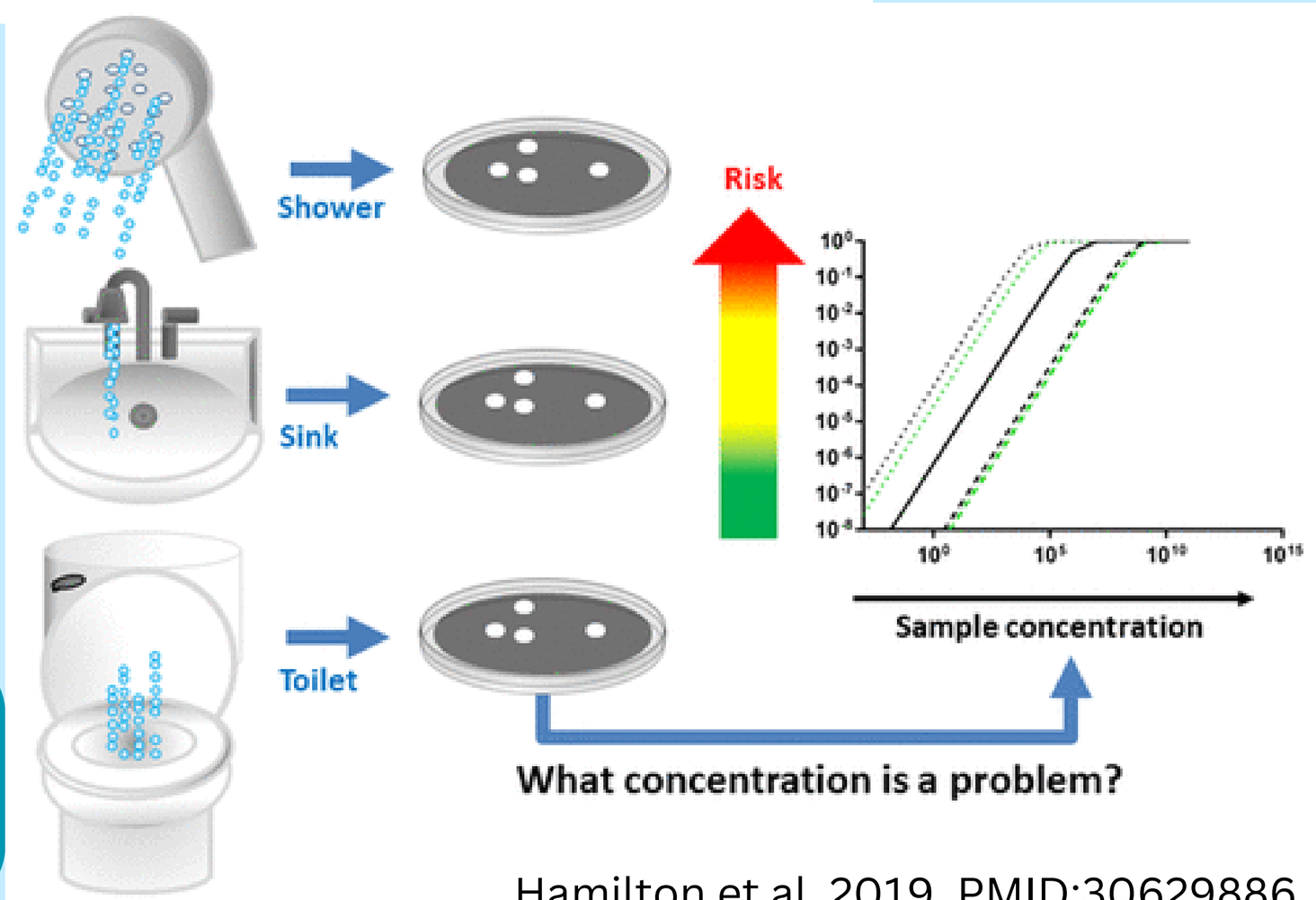
ARTICLE | January 10, 2019

Risk-Based Critical Concentrations of *Legionella pneumophila* for Indoor Residential Water Uses

Kerry A. Hamilton*, Mark T. Hamilton, William Johnson, Patrick Jjemba, Zia Bukhari, Mark LeChevallier, Charles N. Haas, and P. L. Gurian



- Compare risks or other outcomes (disability-adjusted life years) to acceptable thresholds to inform environmental hygiene standards

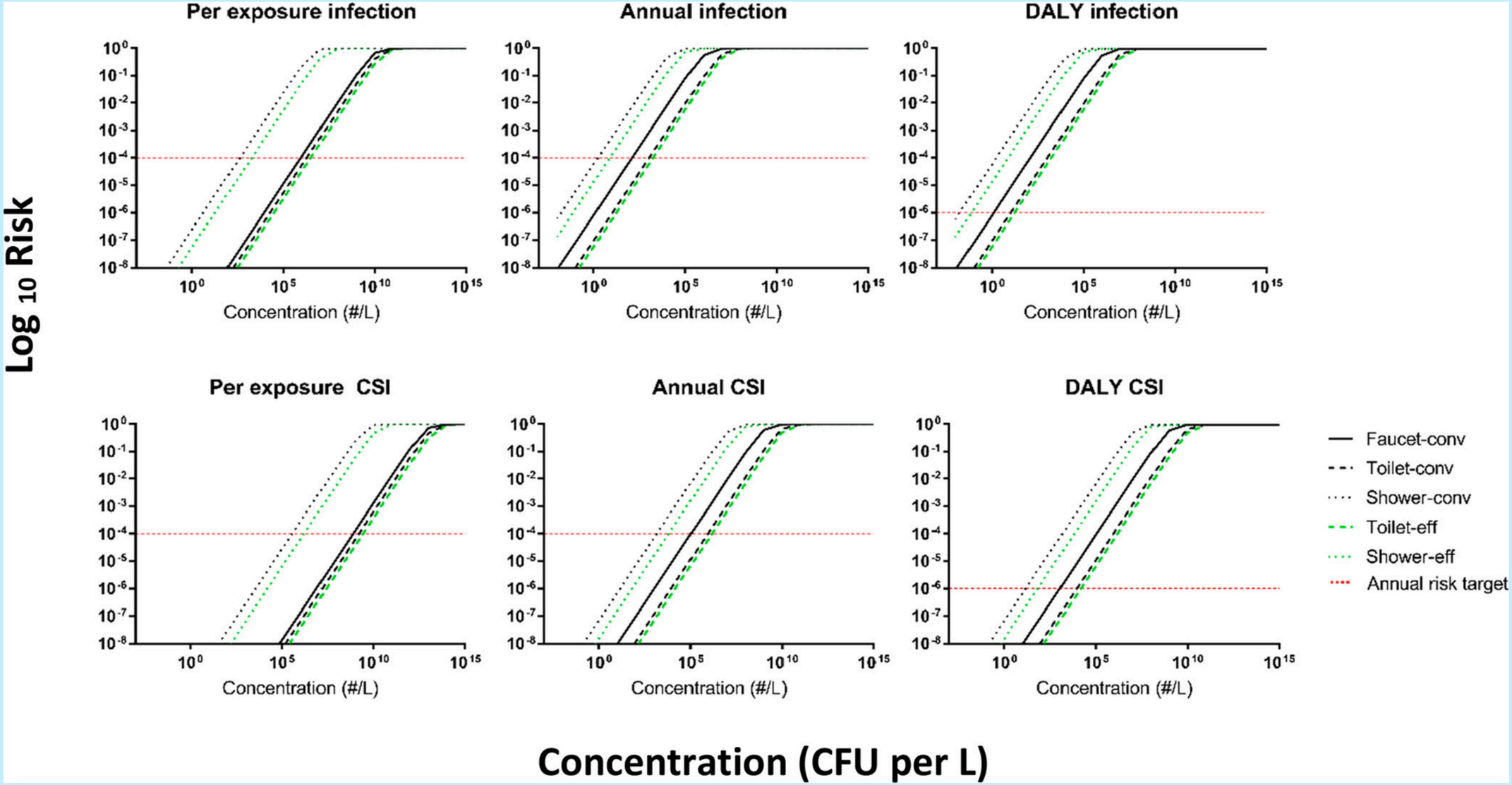
Hamilton et al. 2019. PMID:30629886.

$$\text{dose}_{\text{fixture}} = C_{\text{Leg}} Bt \sum_{i=1}^{10} C_{aer,i} V_{aer,i} \sum_{i=1}^{10} F_i D_i$$

Considers aerosol size profile per fixture type (i=aerosol size range)

$$\text{dose}_{\text{fixture}} = C_{\text{Leg}} PBtF_i D_i$$

Partitioning coefficient approach



Hamilton et al. 2019. PMID:30629886.

Engage with communities to build risk tools for decision-making support

A35 ASTHMA AND COPD: EPIDEMIOLOGY, TREATMENT, OUTCOMES, AND SOCIAL DETERMINANTS / Thematic Poster Session / Sunday, May 19/09:15 AM-04:15 PM / San Diego Convention Center, Area B (Hall A-B2, Ground Level)

Developing a Risk Calculator Tool to Reduce Respiratory Viral Transmission in Classrooms

A. M. Wilson[1], Y. Jung[1], A. A. Lowe[2], M. P. Verhougstraete[1], D. Seong[1], M. Islam[3], Y. Son[3], L. B. Gerald[4]; [1]Community, Environment & Policy Department, Mel and Enid Zuckerman College of Public Health, University of Arizona, Tucson, AZ, United States, [2]Asthma & Airway Disease Research Center, University of Arizona, Tucson, AZ, United States, [3]School of Industrial Engineering, College of Engineering, Purdue University, West Lafayette, IN, United States, [4]Office of Population Health Sciences, Univ of Illinois Chicago, Chicago, IL, United States.

American Lung Association.

NASN National Association of School Nurses

Advantages of QMRA

- Useful for estimating the impact of interventions
- Can model scenarios that are difficult or unethical to observe
- Insights into how exposures may be occurring
- Translating environmental micro data to anticipated public health burden
- Useful for informing policy and economic analyses, such as cost-benefit analysis
- Faster and often cheaper than other means of evaluating disease risks (i.e., epidemiology)

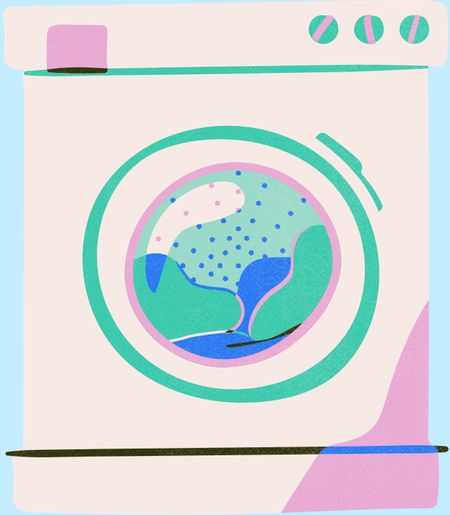
Disadvantages of QMRA

- Risk estimates may be small and, therefore, are difficult to validate (would have to observe many many people to see 1 case)
- Exposure models can be difficult to validate
- Assumptions are necessary in the face of missing data or lack of knowledge
- Uncertainty may be challenging to convey to media or lay audiences
- Usually requires a multidisciplinary team

Modeling Bioaerosol Exposures

Needed parameters include...

- Partitioning coefficient
- Aerosol size distributions
- Viability of pathogen in aerosols
- Description deposition and settling on surfaces
- Inhalation rate of workers
- Filtration effectiveness if wearing face covering
- Information about droplet spray
- Hand-to-surface and -face contact rates



Accidental Ingestion vs. Dietary Ingestion

Lung Penetration

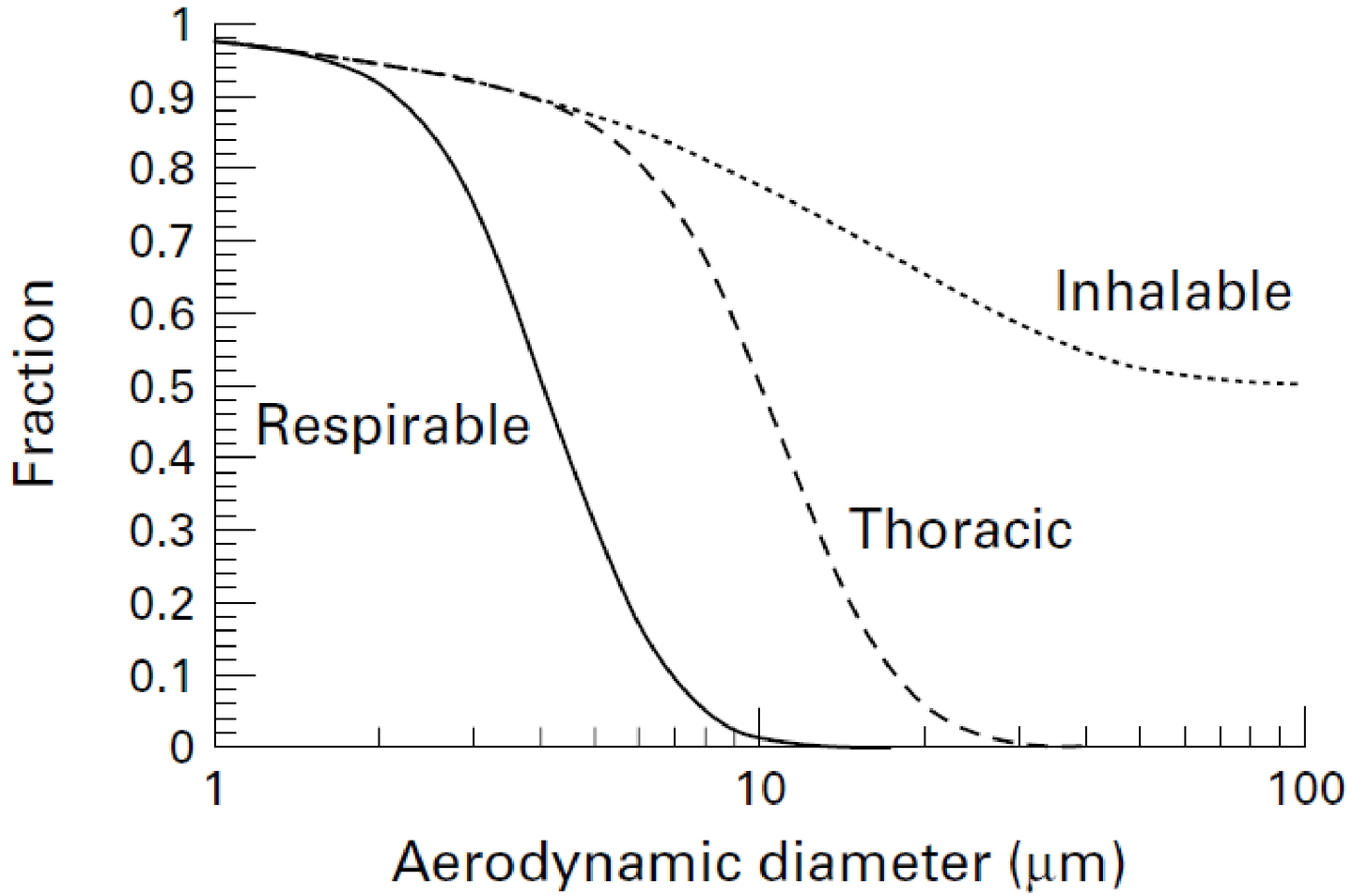


Figure 1 Inhalable, thoracic, and respirable sampling criteria.

The fraction of aerosols that reach regions of the lung depends upon the aerosol size.

Cherrie & Aitken (1999)

Wastewater Treatment Plant Example

Open Access Article

Protecting Wastewater Workers by Categorizing Risks of Pathogen Exposures by Splash and Fecal-Oral Transmission during Routine Tasks

by **Rasha Maal-Bared**

Quality Assurance and Environment, EPCOR Water Services Inc., EPCOR Tower, 2000, 10423-101 Street NW, Edmonton, AB T5H 0E8, Canada

Waste **2023**, *1*(1), 95-104; **https://doi.org/10.3390/waste1010007**

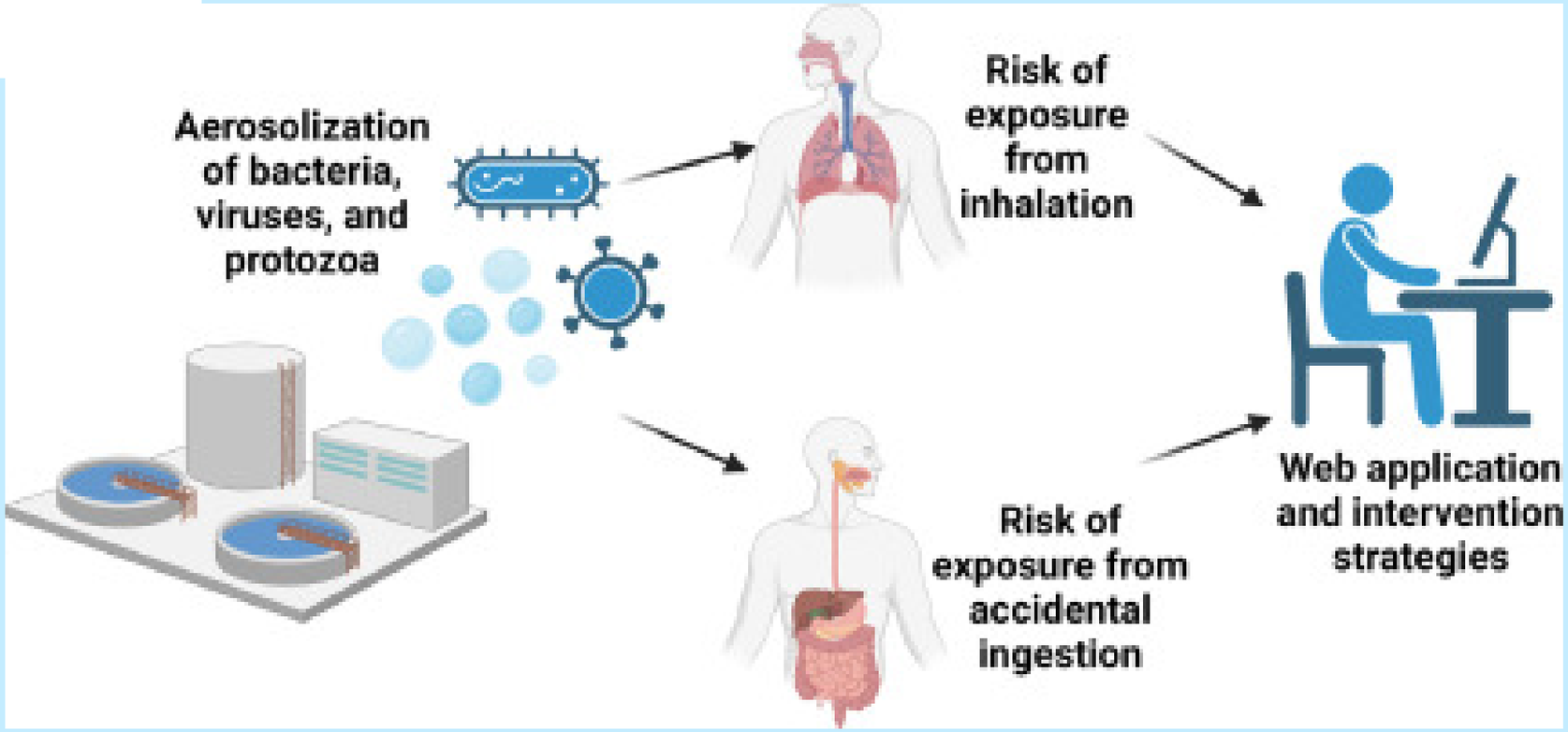
Table 2. Exposure Information including estimates for wastewater contact volumes and aerosol exposures for urban, municipal and industrial WWTP full time equivalents (FTE).

Exposure Category	Urban			Municipal			Industrial		
	FTE	Liquid Contact (mL)	Aerosol Contact (h)	FTE	Liquid Contact (mL)	Aerosol Contact (h)	FTE	Liquid Contact (mL)	Aerosol Contact (h)
Type A	15%	3.00	-	14%	3.00	-	10%	3.00	-
Type B	10%	5.00	0.40	2%	5.00	0.40	3%	5.00	0.40
Type C	20%	0.001	0.80	6%	0.003	1.60	7%	0.004	1.60
Type D	7%	0.02	0.80	2%	0.02	0.80	3%	0.03	0.80
Type E	1%	0.09	4.00	<1%	0.06	4.00	<1%	0.09	4.00
Type E1	1%	0.01	-	<1%	0.02	-	<1%	0.02	-

Water Research
Volume 260, 15 August 2024, 121858

Quantitative microbial risk assessment (QMRA) tool for modelling pathogen infection risk to wastewater treatment plant workers

Ashley Heida [a b], Rasha Maal-Bared [c], Marc Veillette [d], Caroline Duchaine [d], Kelly A. Reynolds [e], Ahamed Ashraf [e], Olusola O. Ogunseye [e], Yoonhee Jung [e], Lester Shulman [f g], Luisa Ikner [h], Walter Betancourt [h], Kerry A. Hamilton [b i], Amanda M. Wilson [e]



Hazard Identification

Ingestion exposure pathway

- *Cryptosporidium hominis*
- *Escherichia coli*
- *Giardia duodenalis*
- Norovirus
- Rotavirus

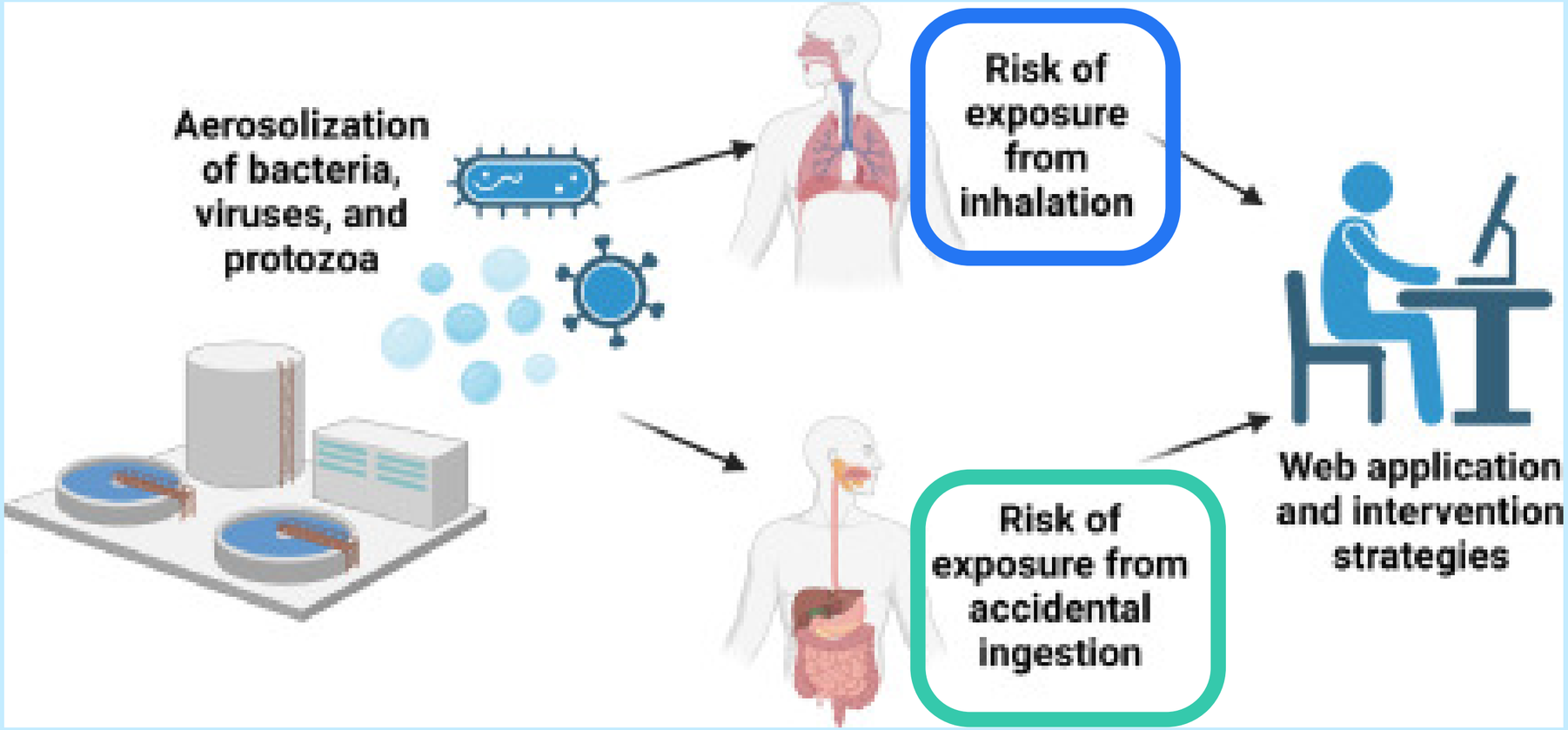
Inhalation exposure pathway

- Adenovirus
- Rhinovirus
- Influenza A virus
- *Legionella pneumophila*

Exposure Assessment: Pathogen Concentrations

- Collection in Canada over four seasons, 2016-2017
- Two plants
  - Small municipality
    - Serves ~20,000 people
    - 10 MLD
  - Large/urban
    - Serves ~1.1 million
    - 310 MLD
- Culturable sample collection
  - SAS Super 100 dual-head, single-stage multi-hole impactor (pbi International, Rockville, MD, USA)
- Molecular analysis sample collection
  - SASS 3100 high flow dry filter air sampler (Research International Inc., Monroe, WA, USA)
  - Electrostatic sampling filter was used

$$Dose = (C_{water})\,(PC)\,(F_{res})\,\left(e^{-\lambda t}\right)\,(I)\,(M)\,(t)$$



$$Dose = (C_{water})\,(V)$$

Dose Response

The risk for infection from each pathogen was calculated with a pathogen-specific dose-response. Three different dose-response model equations were used across the nine pathogens (Table 2). An exponential dose-response model (Eq. (3)) was used for *C. hominis*, *E. coli*, *G. duodenalis*, *L. pneumophila*, adenovirus, and rotavirus. A Beta-Poisson model (Eq. (4)) was used for rotavirus, rhinovirus, influenza A, and norovirus, and a fractional Poisson model (Eq. (5)) was also used for norovirus.

$$Risk_{\text{inf}} = 1 - e^{-k\ dose} \tag{3}$$

$$Risk_{\text{inf}} = 1 - \left(1 + \frac{Dose}{\beta}\right)^{-\alpha} \tag{4}$$

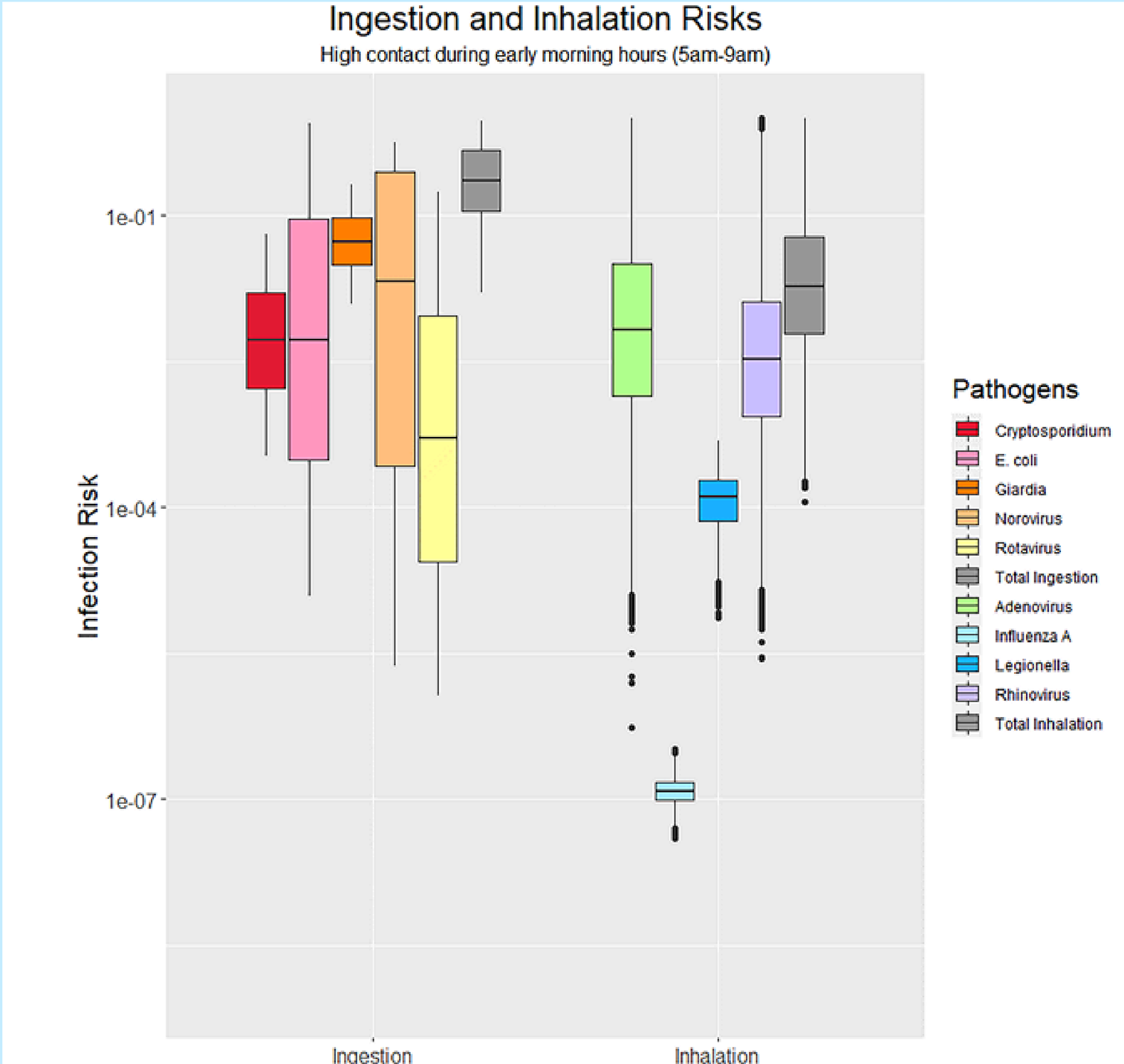
$$Risk_{\text{inf}} = P * \left(1 - e^{-\frac{Dose}{\mu_a}}\right) \tag{5}$$

Case studies

- Case Study 1: Individual pathogen infection risks given typical wastewater treatment concentrations
- Case 2: *C. hominis* and *L. pneumophila* risks for different tasks
- Case 3: Gastrointestinal and respiratory infection risks for exposure during peak vs. non-peak hours
- Case 4: Respiratory infection risks for masks, N95 respirators, and no personal protective equipment (PPE)

Risk Characterization (Case 1 Results)

- *G. duodenalis* had highest median risk, while rotavirus had the lowest
- Adenovirus had highest median risk, while influenza A virus had the lowest.



Other Findings

- Case 2: *C. hominis* and *L. pneumophila* risks for different tasks
  - Walking the plant posed highest risk
- Case 3: Gastrointestinal and respiratory infection risks for exposure during peak vs. non-peak hours
  - *G. duodenalis* highest risk during peak and non-peak hours
- Case 4: Respiratory infection risks for masks, N95 respirators, and no personal protective equipment (PPE)
  - N95s = 77% reduciton in median infection risks for *L. pneumophila*

Respiratory Virus in an Ambulance Example

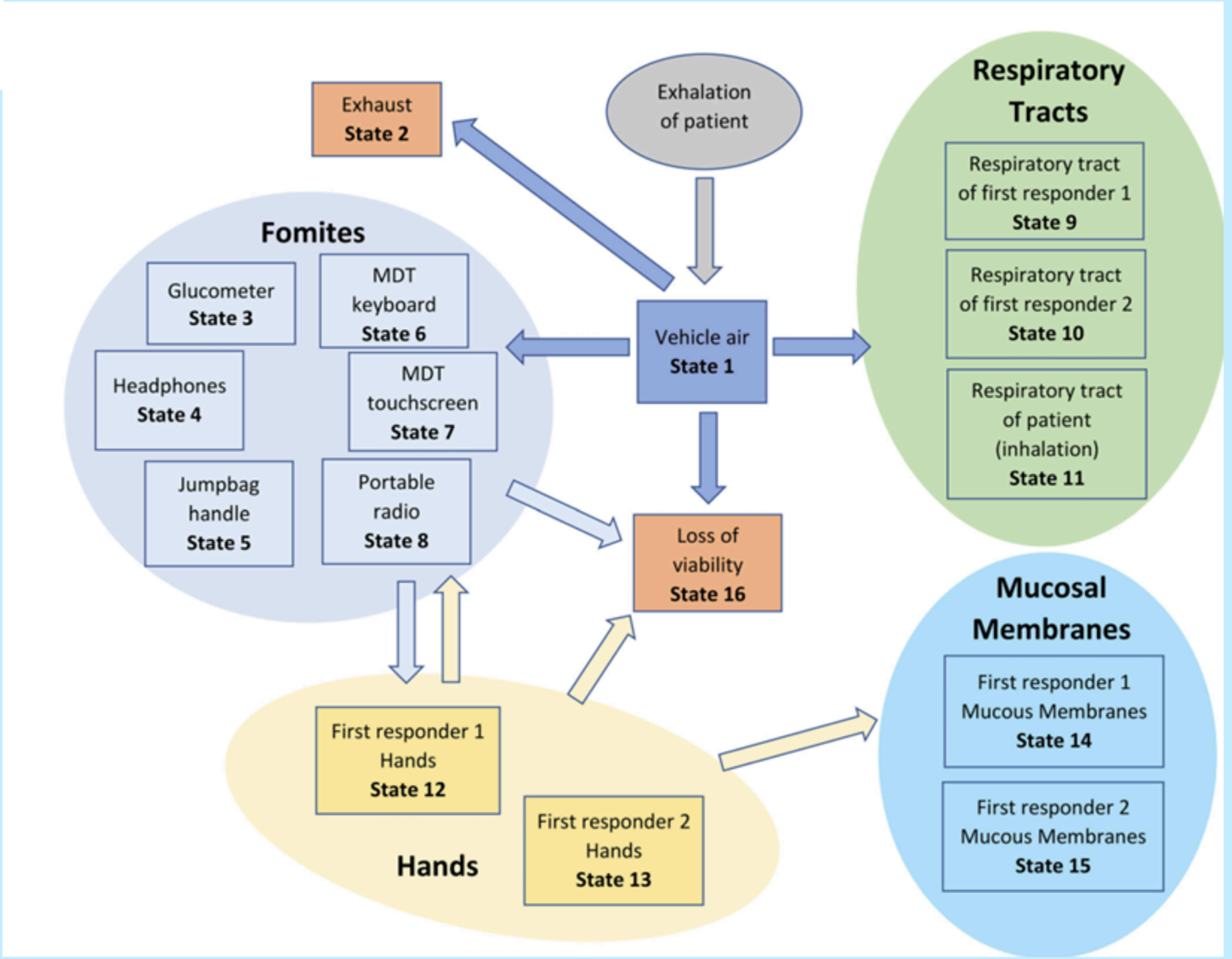
J Occup Environ Hyg. 2021 Jul;18(7):345-360. doi: 10.1080/15459624.2021.1926468.
Epub 2021 Jun 15.

Respirators, face masks, and their risk reductions via multiple transmission routes for first responders within an ambulance

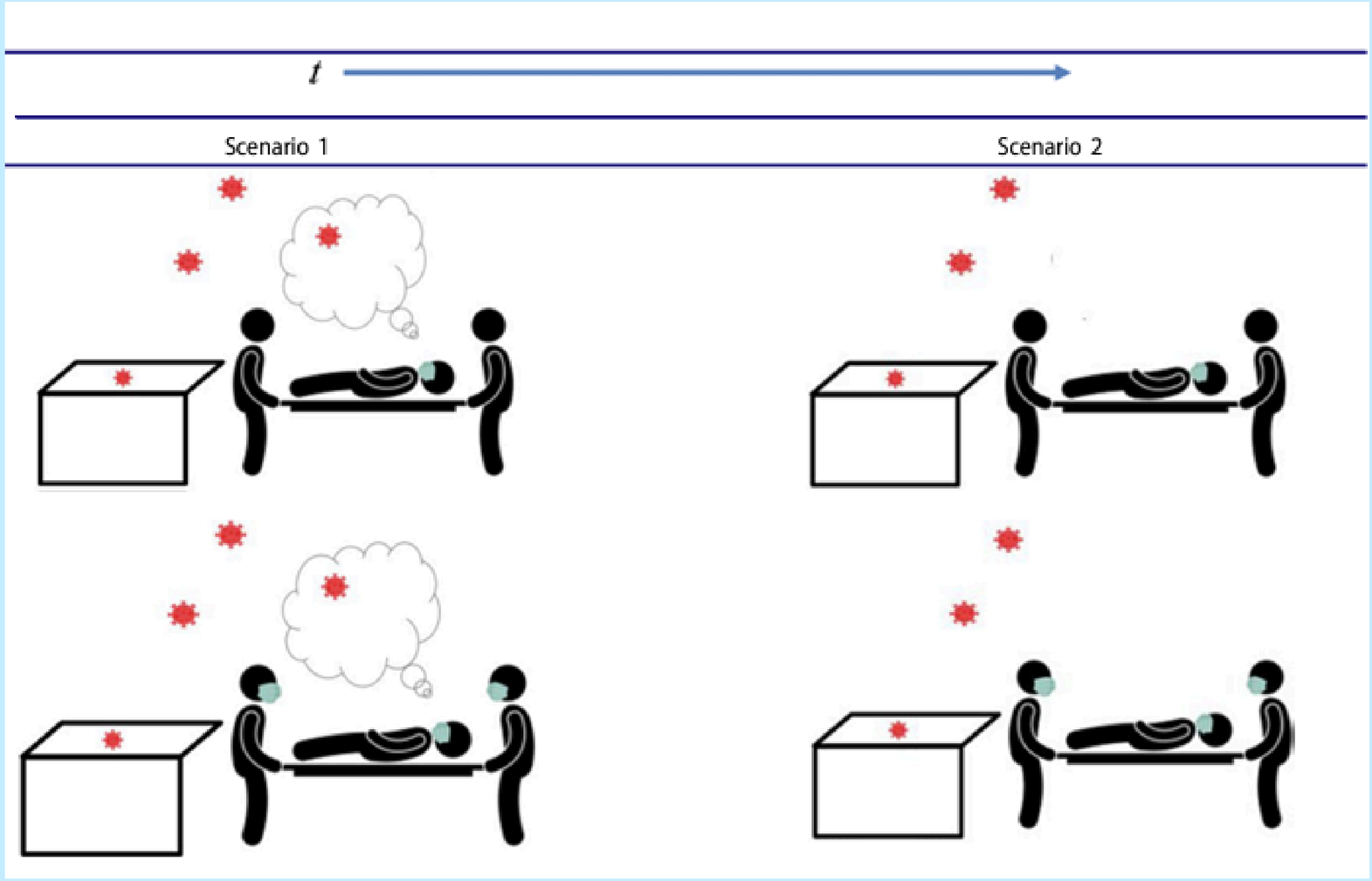
Amanda M Wilson [1 2], Rachael M Jones [1 2], Veronica Lugo Lerma [3], Sarah E Abney [3 4], Marco-Felipe King [5], Mark H Weir [6], Jonathan D Sexton [3], Catherine J Noakes [5], Kelly A Reynolds [3]

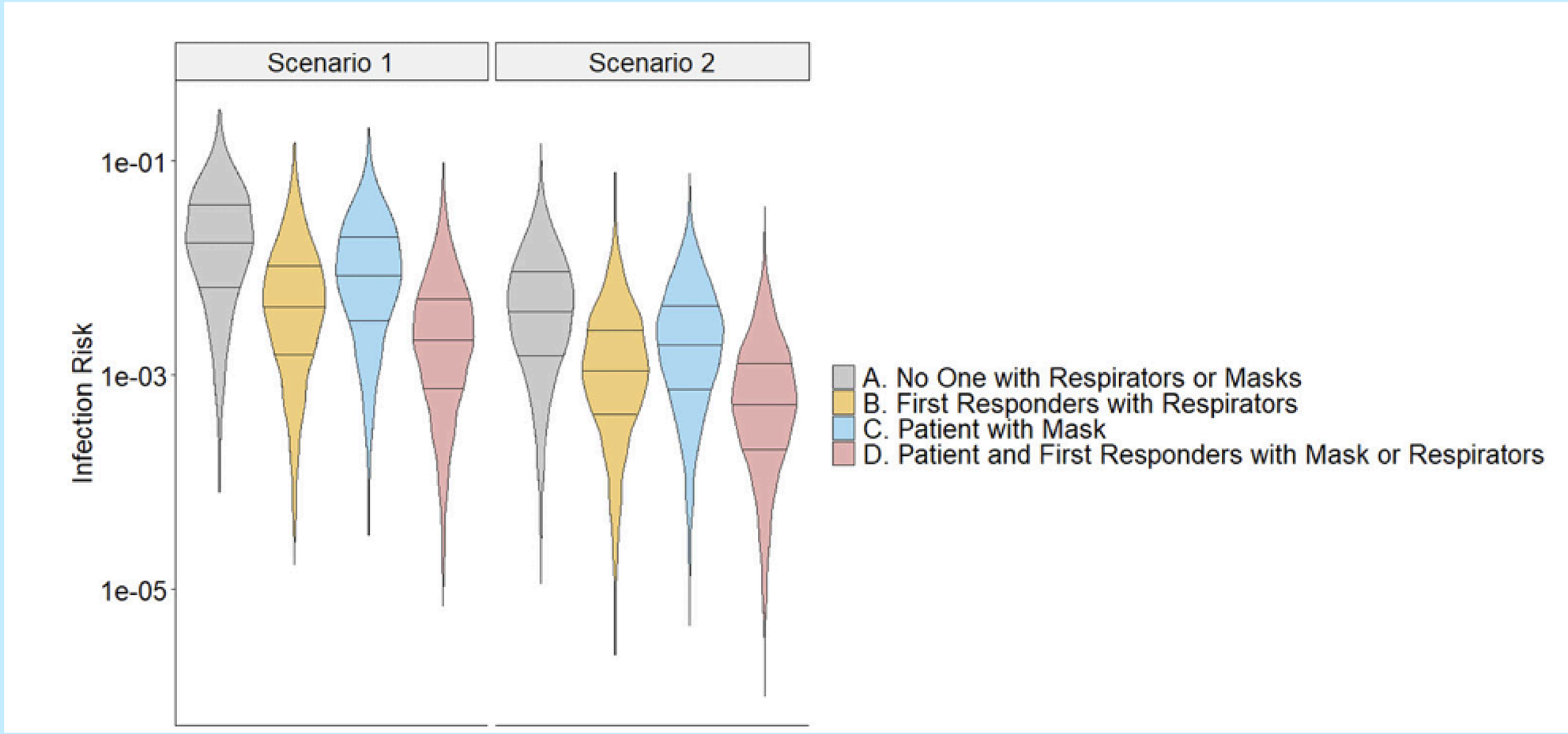
Compartment model to describe the "transition" of virus from one "state" to another per time step (fractions of a minute)

Aerosol source is the patient, or even lingering aerosols from a previous patient

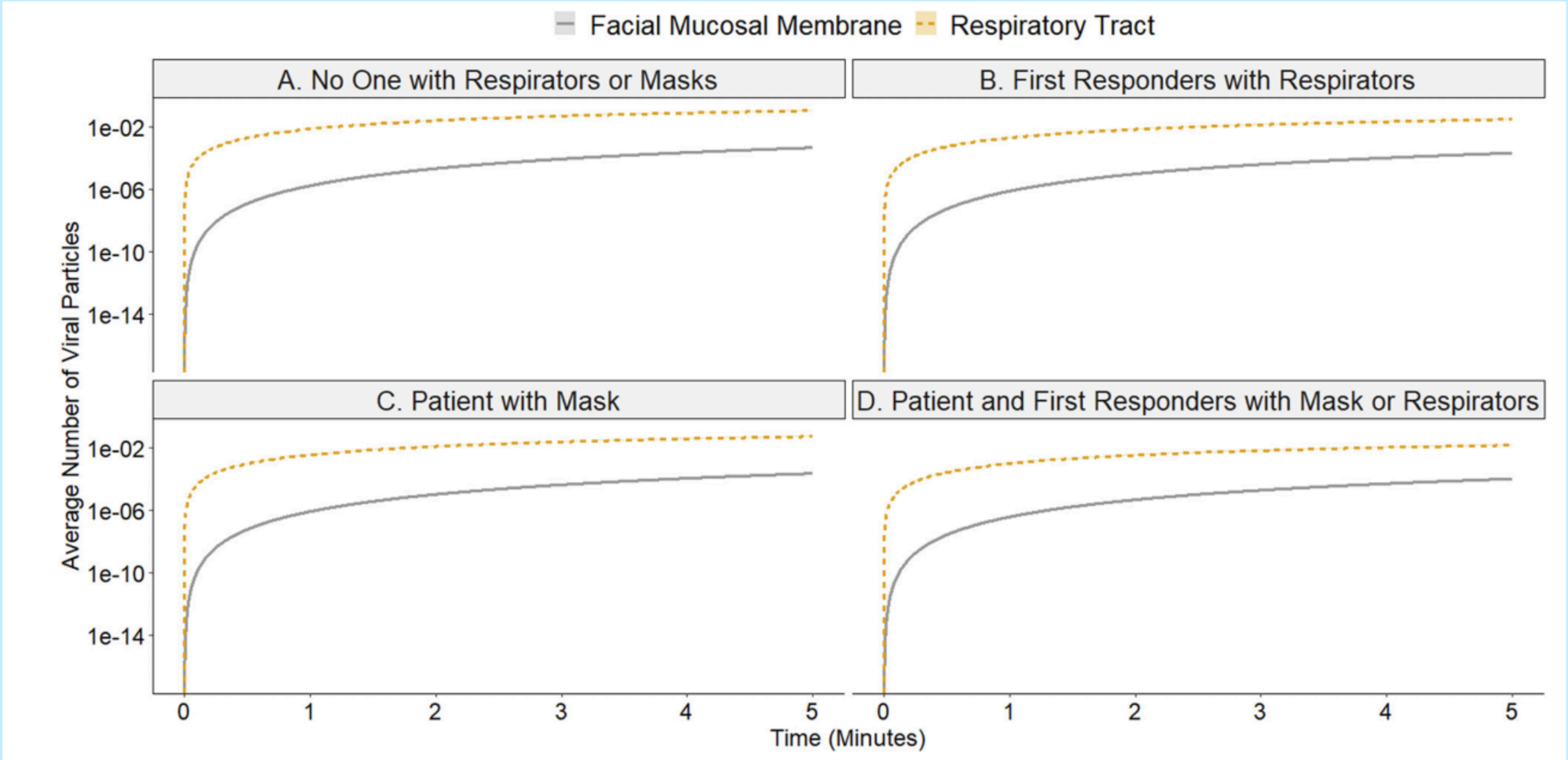


Sequence of Care Scenarios

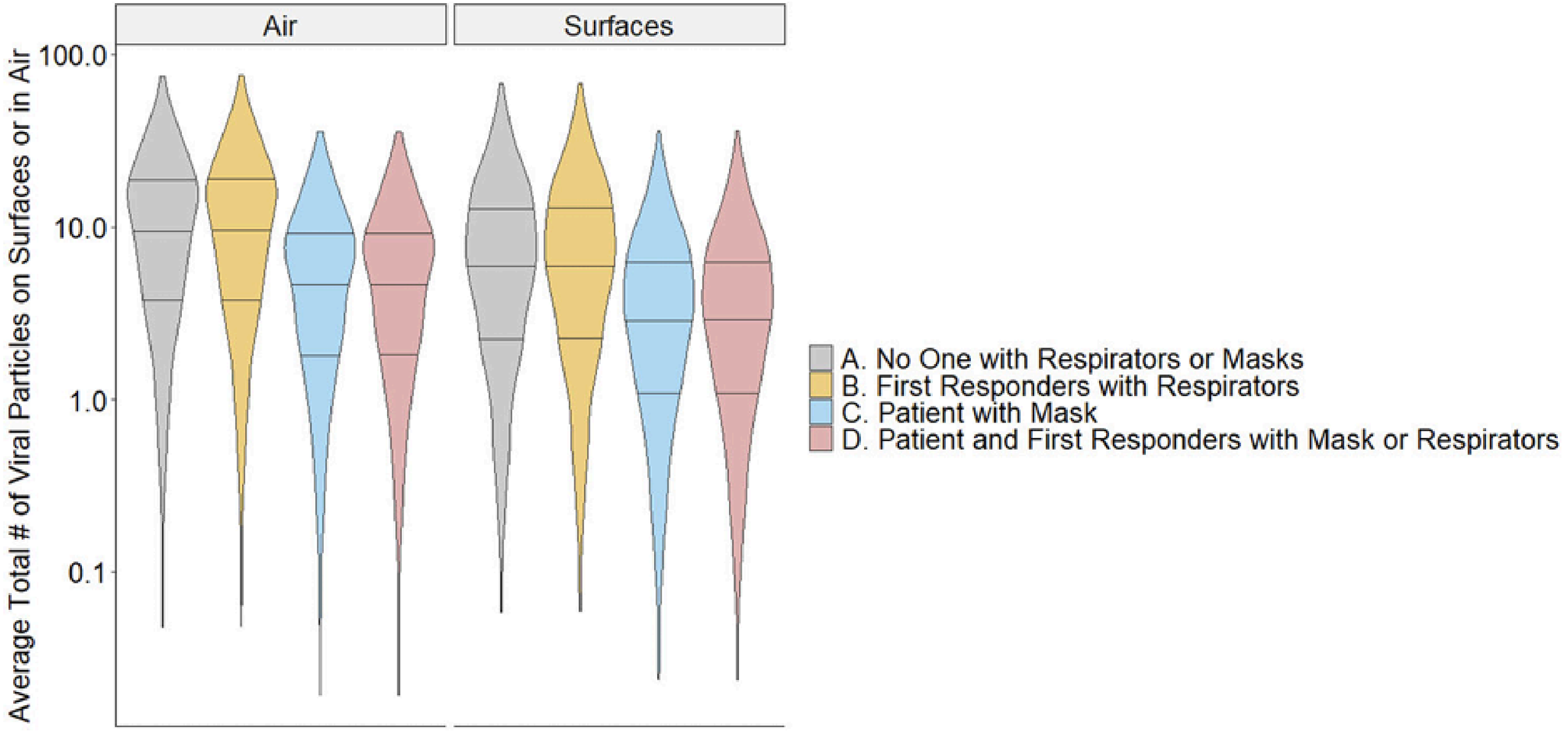




As expected, paired respirators/masks are the most effective. Second most effective is respirators used by first responders, even though source control is typically seen as the most important.



This model approaches a steady state concentration quickly over the course of simulated care with a patient



Reducing aerosol emissions from the source impacts the surface transmission pathway

Putting bioaerosol risks in context

Legionella vs. other considerations

1. Flushing
2. Water heater set point change
3. Flushing + water heater set point change

Water Quality Parameters	Intervention 1 - Flushing	Intervention 2 - Increasing water heater setpoint	Intervention 3 - Combined flushing and increasing water heater setpoint
Metals	Iron ↑ Copper ↑↓	Iron - no change Copper ↑	Iron ↑ Copper ↑↓
DBP (TTHM)	↑	↑↓	↓
Chlorine Residuals	↑	↑↓	↑
cATP	↓	↑↓	↓
L. pneumophila	↓	↑↓	↓

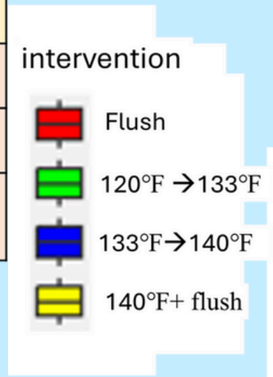
Key

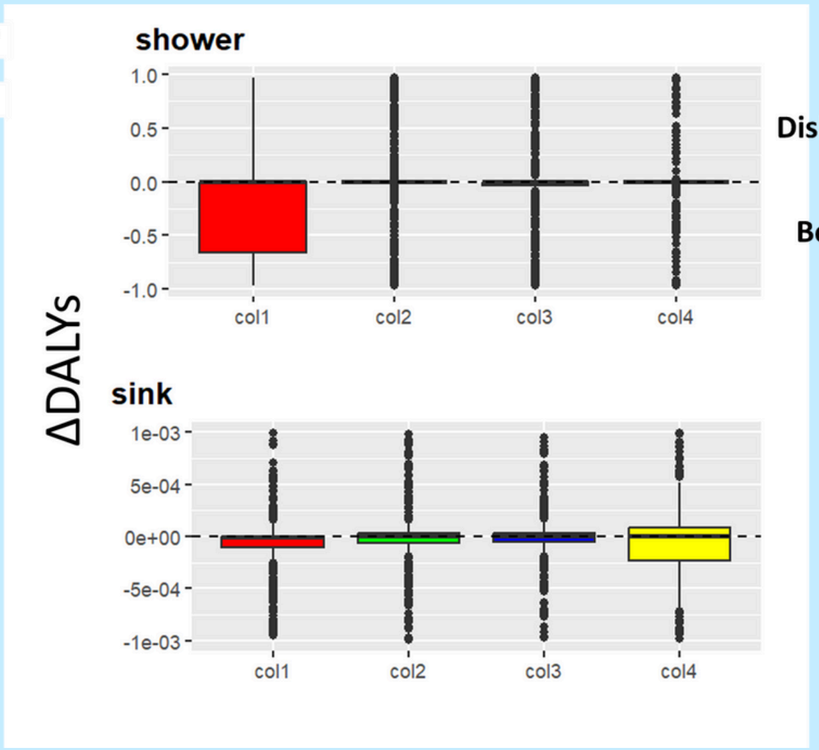
- ↑ Statistically significant increase in undesired water quality parameter
- ↑ Statistically significant increase in desired water quality parameter
- ↓ Statistically significant decrease in desired water quality parameter
- ↑↓ Mixed trends
- ↓ Decrease in concentration but not statistically significant

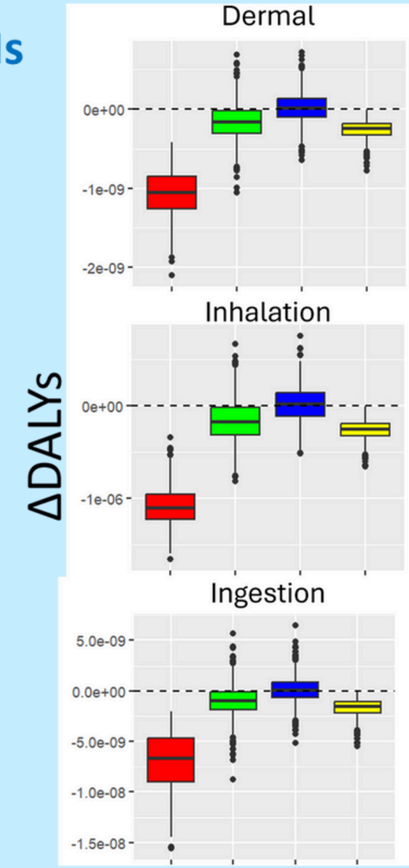
Joshi S et al. 2023 Water quality trade-offs for risk management interventions in a green building. *Environmental Science: Water Research and Technology*

Legionella vs. other considerations

Assessment	Exposure scenario	Exposure route	Contaminant	Endpoint
Microbial risk	Showering	Inhalation	*L. pneumophila*	Infection
	Faucet	Inhalation	*L. pneumophila*	Infection
Chemical risk	Showering	Inhalation	THMs	Bladder cancer
	Showering	Dermal contact	THMs	Bladder cancer
	Consumption of tap water	Ingestion	THMs	Bladder cancer

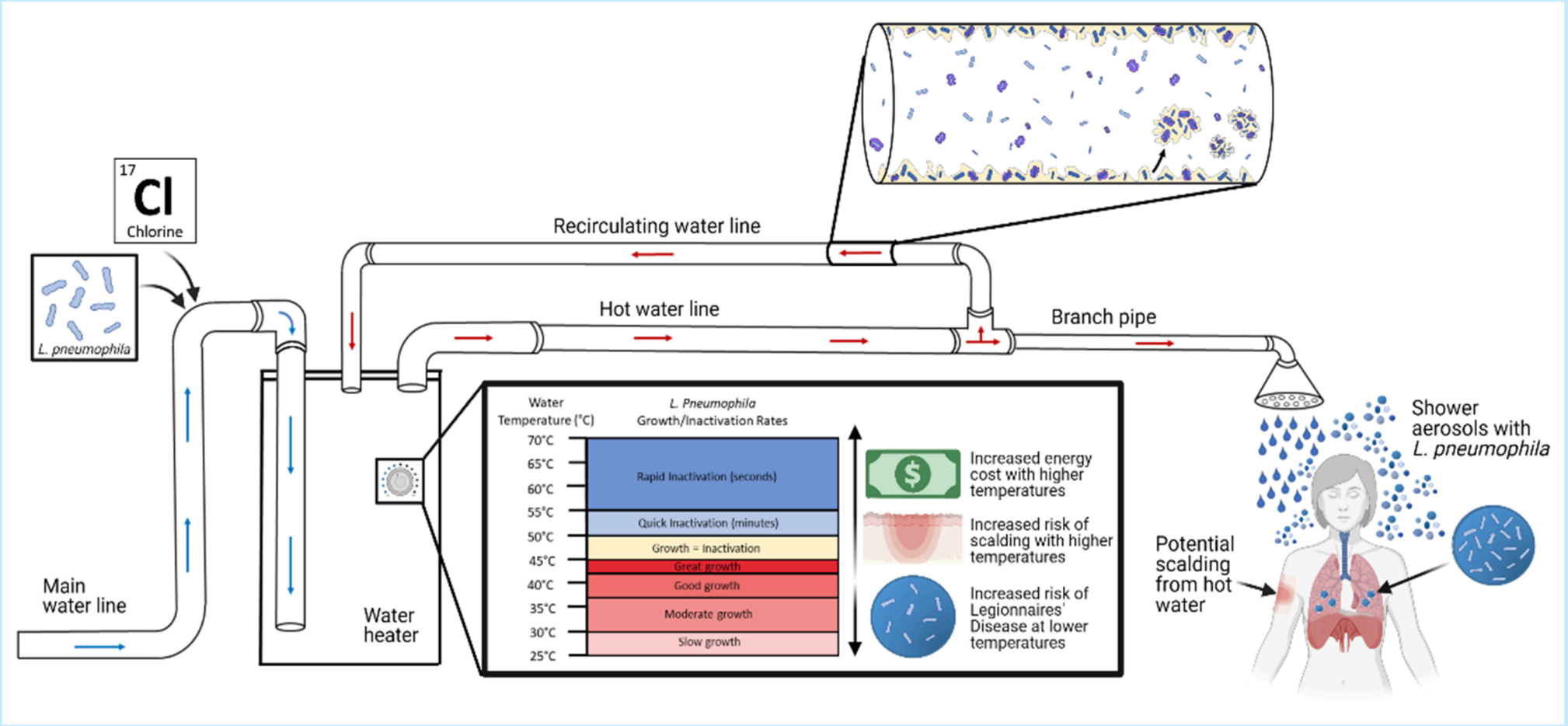






Quon et al. in prep

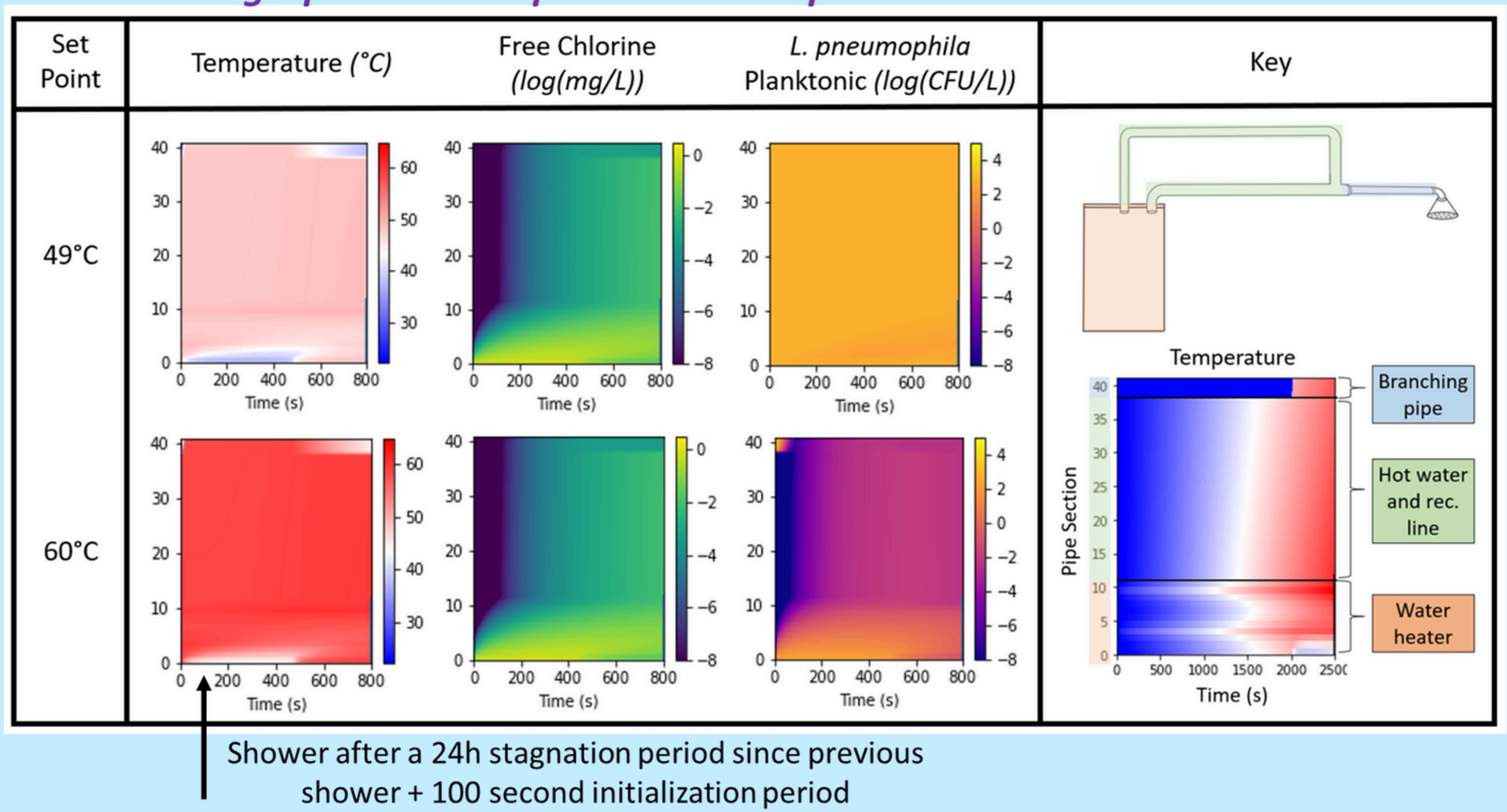
Legionella vs. other considerations



Heida, A et al. 2021. Computational framework for evaluating risk trade-offs in costs associated with Legionnaires' Disease risk, energy, and scalding risk for hospital hot water systems. *Environmental Science: Water Research & Technology*.

Mechanistic-machine learning testbed

The graphs are interpreted with respect to their numbered nodes

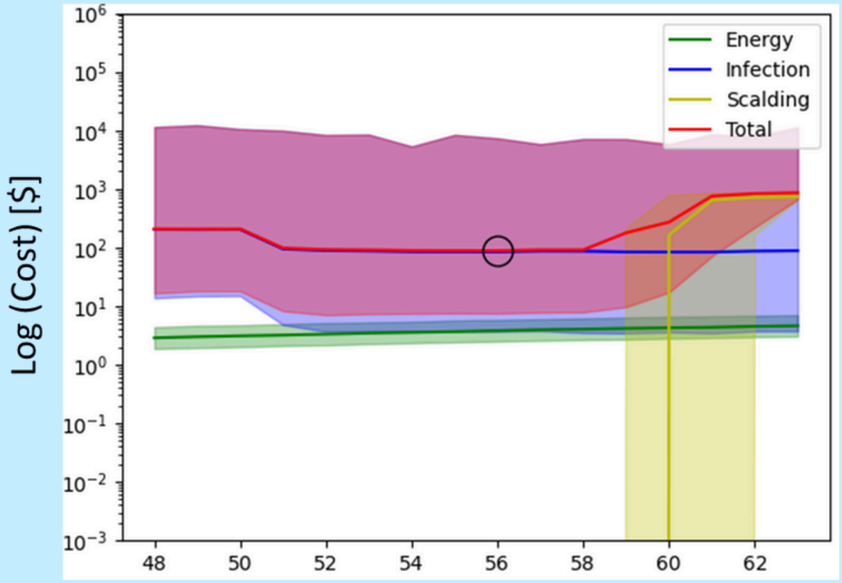


Heida, A et al. 2021 ESWRT

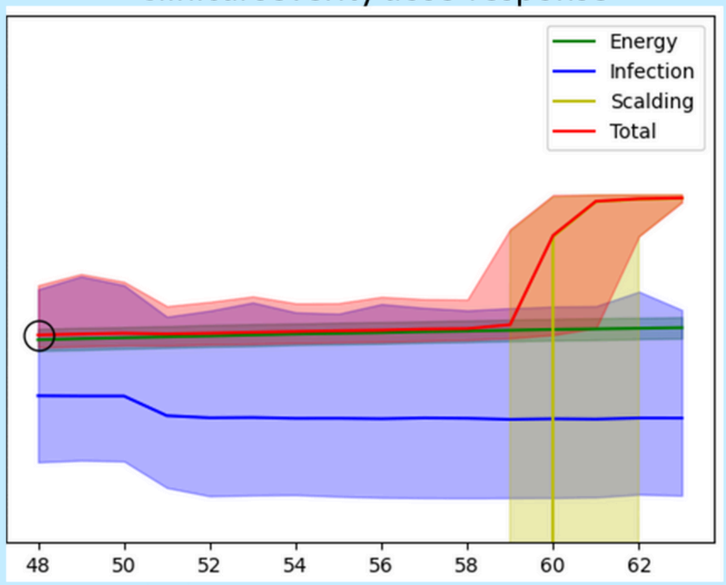
Minimizing a total cost function

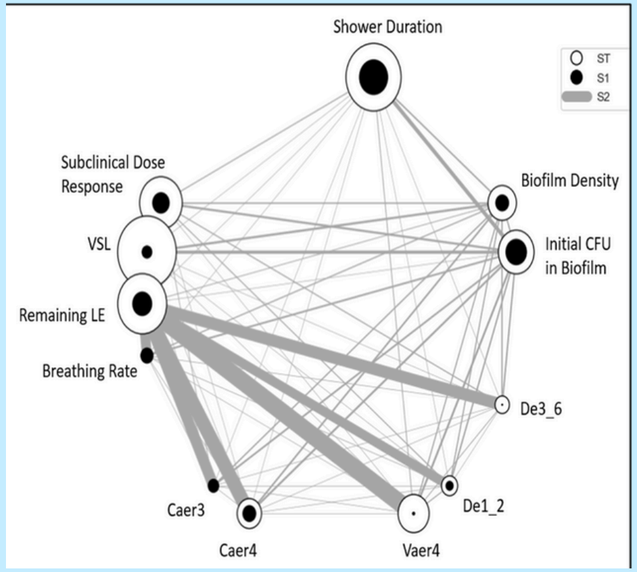
Total cost = infection cost + energy cost + scalding cost

Expected costs of infection, scalding, and energy for each set point tested.
Subclinical dose-response results in infection risk being the driving cost with 56°C as the optimal temperature.
Energy is the driving risk with a clinical-severity dose-response model.



Clinical severity dose-response





Temperature set point (°C)

Optimum at 56°C vs. 48°C

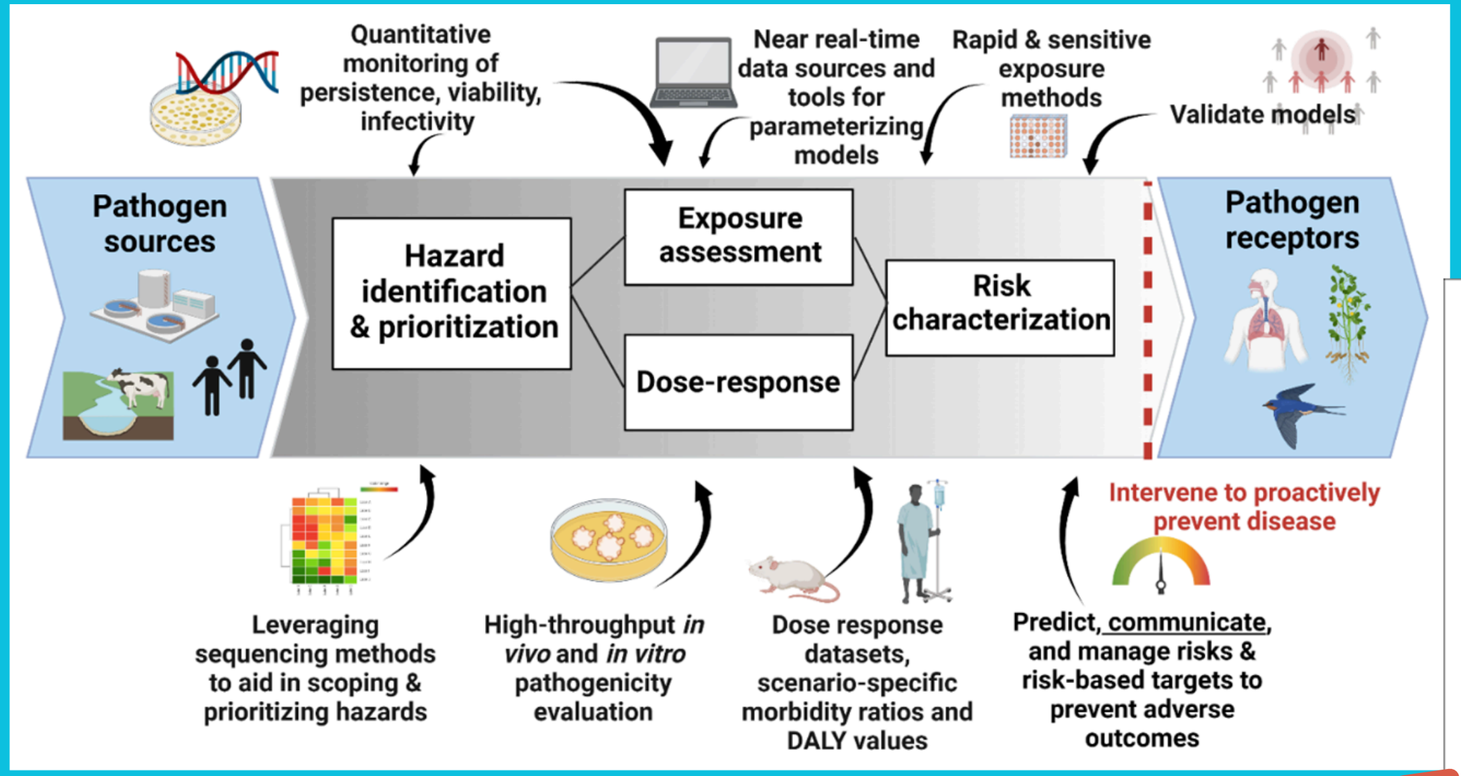
Heida, A et al. 2021 ESWRT

How/where to learn more about QMRA?

Opportunity to Learn More about QMRA…

https://camra.msu.edu/

QMRA roadmap- bioaerosols and beyond



Hamilton K et al. 2024 Key research priorities for advancing the field of Quantitative Microbial Risk Assessment (QMRA). *Risk Analysis* 1-16.

Ranked topics by workshop participants (n=28)

1. How do we make use of molecular data (on exposure) to assess risk?
2. Coupling of QMRA to disease transmission models for contagious agents
3. New/emerging applications: antibiotic resistant pathogens and genes
4. Communicating with those who really could benefit from the approach
5. How to describe exposures to pathogens with other stressors (either other pathogens or chemical or physical stressors)
6. More mechanistic models for dynamics of pathogens within hosts
7. How to describe repeated exposures?
8. Best practices for doing QMRA on Agent "X"
9. Emission rates of pathogens: is there a unified framework that can be developed?
10. New/emerging applications: animal pathogens
11. What about fungi?

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Questions/Discussion

amwilson2@arizona.edu

Kerry.Hamilton@asu.edu