Environmental Control of Transmissible Emerging Infections

Jim Koopman MD MPH
Josep M. Pujol PhD
Joseph N. Eisenberg PhD
Dept. of Epidemiology, Univ. of Michigan

Advancing Microbial Risk Assessment

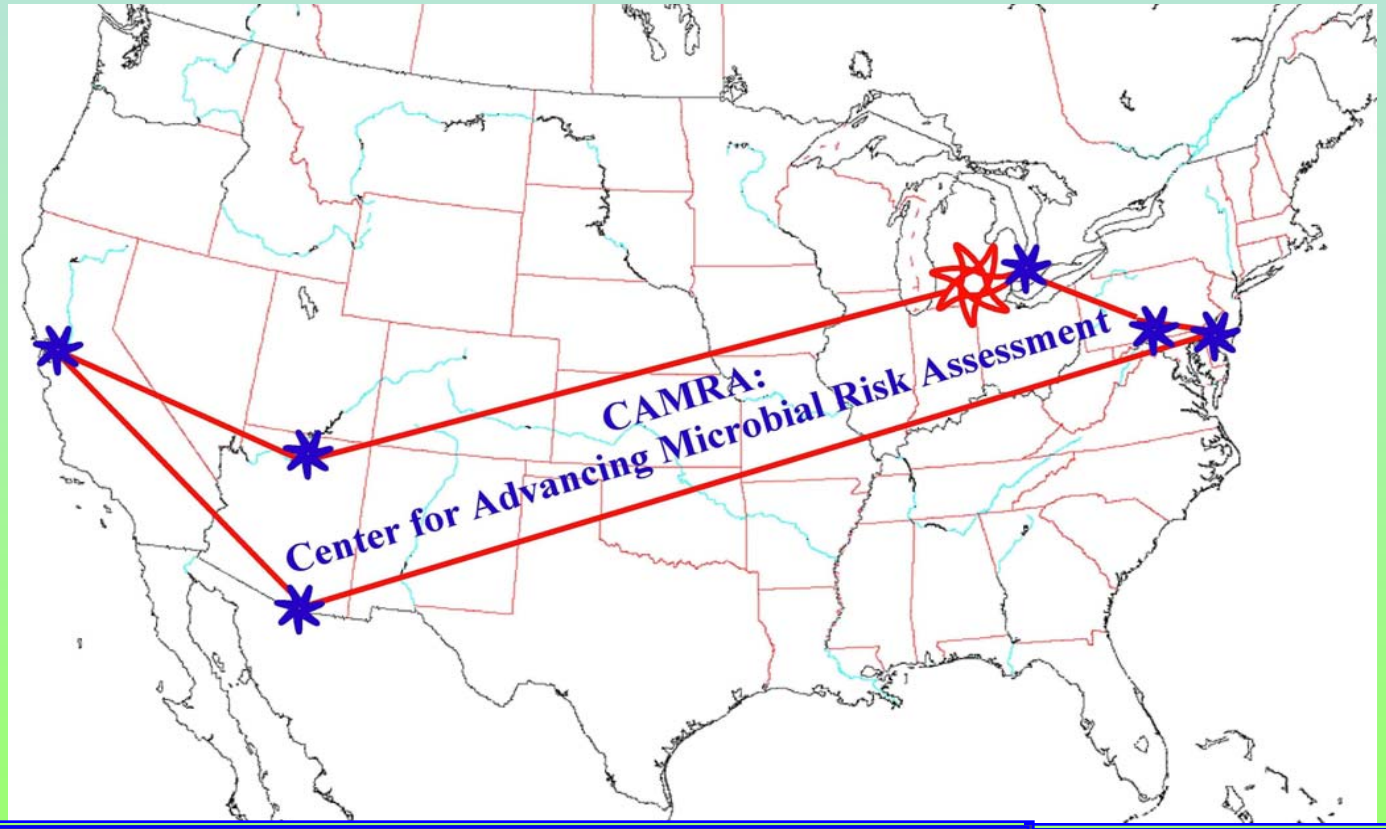
- What CAMRA is
- What our modeling core is doing
- Why we are doing it
- Issues our work raises so far
- Plans for the future

This research is funded by
U.S. EPA - Science To Achieve Results (STAR) Program and U.S. Department of Homeland Security University Programs
Grant # R83236201

CAMRA

Center for Advancing Microbial Risk Assessment

Joan B. Rose
& Charles N. Haas
Michigan State Univ
Drexel Univ.
Carnegie Mellon Univ
Northern AZ Univ.
Univ. Arizona
Univ. Calif Berkeley
Univ. Michigan



Environmental microbiology with fate & transport modeling

Transmission system modeling

Dose Response

Policy & Behavior

to build a national network for microbial risk knowledge management

to develop models, tools and information that will be used in a credible risk assessment framework

CAMRA Modeling Activities

- Explore modeling & statistical needs using abstract models
  - human dissemination of contamination,
  - cumulative risk from pathogen uptake
  - environmental person to person transmission
- Realistically detailed models of
  - transmission in dorm trials of masks & hand wash for influenza control
  - norovirus outbreaks
- Statistical & model methods development

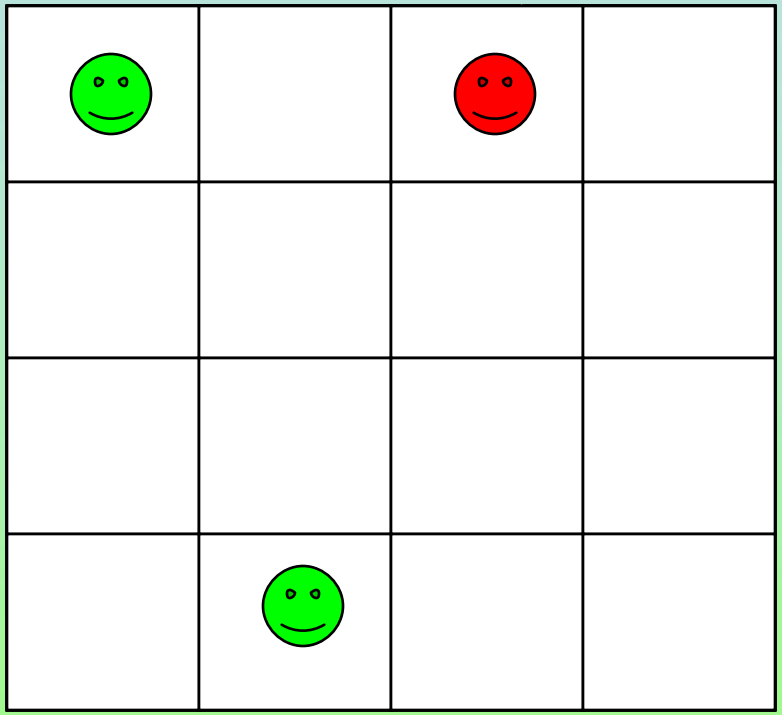
Why Focus on Environment To Model & Control Infection?

- Interventions often focused on the environment
  - Environment embedded in transmission system
  - Population effects of environmental interventions depend on unknown roles in system dynamics played by multiple routes of transmission
- Provides a causal model with greater predictive and explanatory power than contact models
  - Observing who was infected after what exposures on a population basis is too difficult

Major Findings to Date

- Environmental dynamics of human to human infectious agents are always far from equilibrium
  - Environmental sampling schemes & data analysis must take these dynamics into account
- Human movement patterns influence whether large droplet hand-fomite or aerosol transmission dominates
- Host immune particle dynamics might change major mode of transmission
- Density or frequency dependent contact transmission formulations are unrealistic for most pathogens

Transmission model



1) There are 3 people, 2 susceptible and one infected

2) The infected person sneezes. Droplets contaminate the surface and aerosolized pathogens start to spread.

3) The air contamination diffuses. At the same time the fomite and air contamination die-out at their respective rates.

4) Contamination reaches a susceptible person.

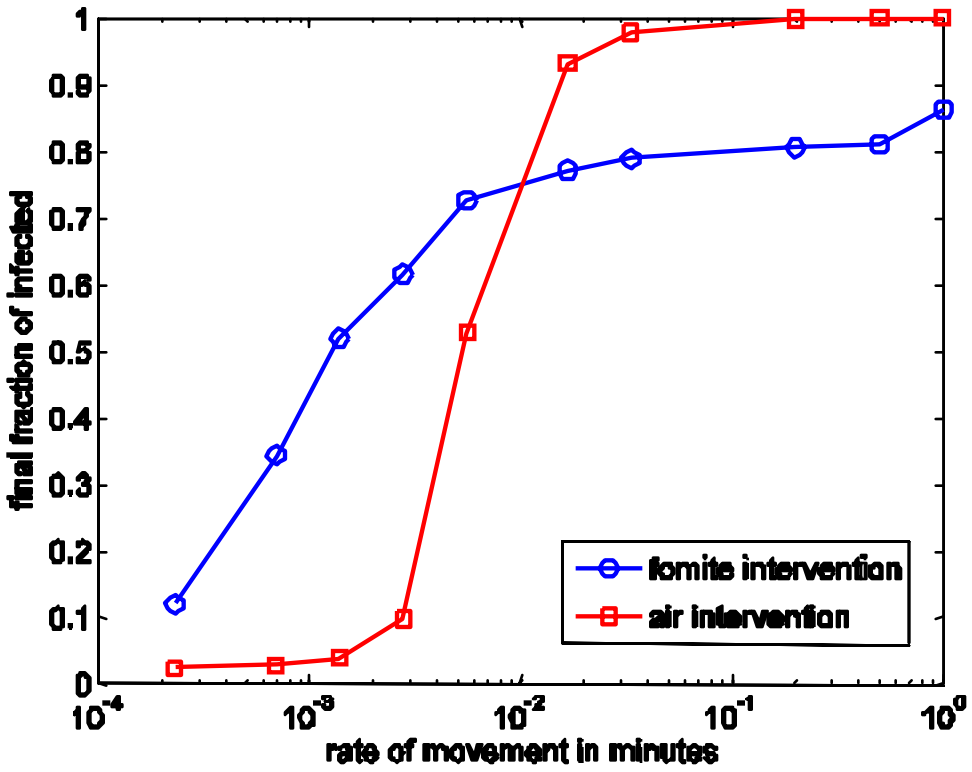
5) The contamination of the air dilutes in the whole area. The infected people move. One susceptible person becomes infected.

6) The contamination of the air dilutes as it disseminates. The infected people move.

7) The remaining susceptible person moves to the cell with fomite contamination. The contamination of the air is fully spread throughout the venue.

8) The person is infected. The concentration of fomite contamination in that person's cell is much larger than air contamination.

Results: the role of movement



Optimal Interventions depend on:

1. Disease
2. Venue
3. Patterns of movement within a venue

For Influenza:

1) Air intervention only effective if movement rate is < 1/180 (< 1 movement in 3h)

2) Fomite intervention more effective when movement is faster than one every hour.

3) Movement helps determine which transmission route dominates.

Cumulative Dose Response

- Risk of infection is classically characterized as a static function of dose.
  - Exponential model: $P_{inf} = 1 - e^{-\mu r}$
  - BetaPoisson model: $P_{inf} \approx 1 - (1 + \frac{\mu}{\beta})^{-\alpha}$
- Probability of infection only depends on dose. Therefore,
  - A dose of 100 pathogens over 2 hours has the same outcome as 100 doses of 1 pathogen in two hours
  - If that's true, what is the immune system doing for those two hours? Nothing at all?!

Cumulative Dose Model

- The state of the system is defined by *(I,P)*, number of pathogens and immune particles.

$$(I,P) \xrightarrow{\alpha_i + P\lambda_i} (I+1,P)$$

$$(I,P) \xrightarrow{I\gamma_i + PI\delta_i} (I-1,P)$$

$$(I,P) \xrightarrow{\alpha_p + P\theta_b} (I,P+1)$$

$$(I,P) \xrightarrow{PI\delta_b} (I,P-1)$$

$$\alpha_p = \begin{cases} \dfrac{D_e}{T_e} & t \le T_e \\ 0 & t > T_e \end{cases}$$

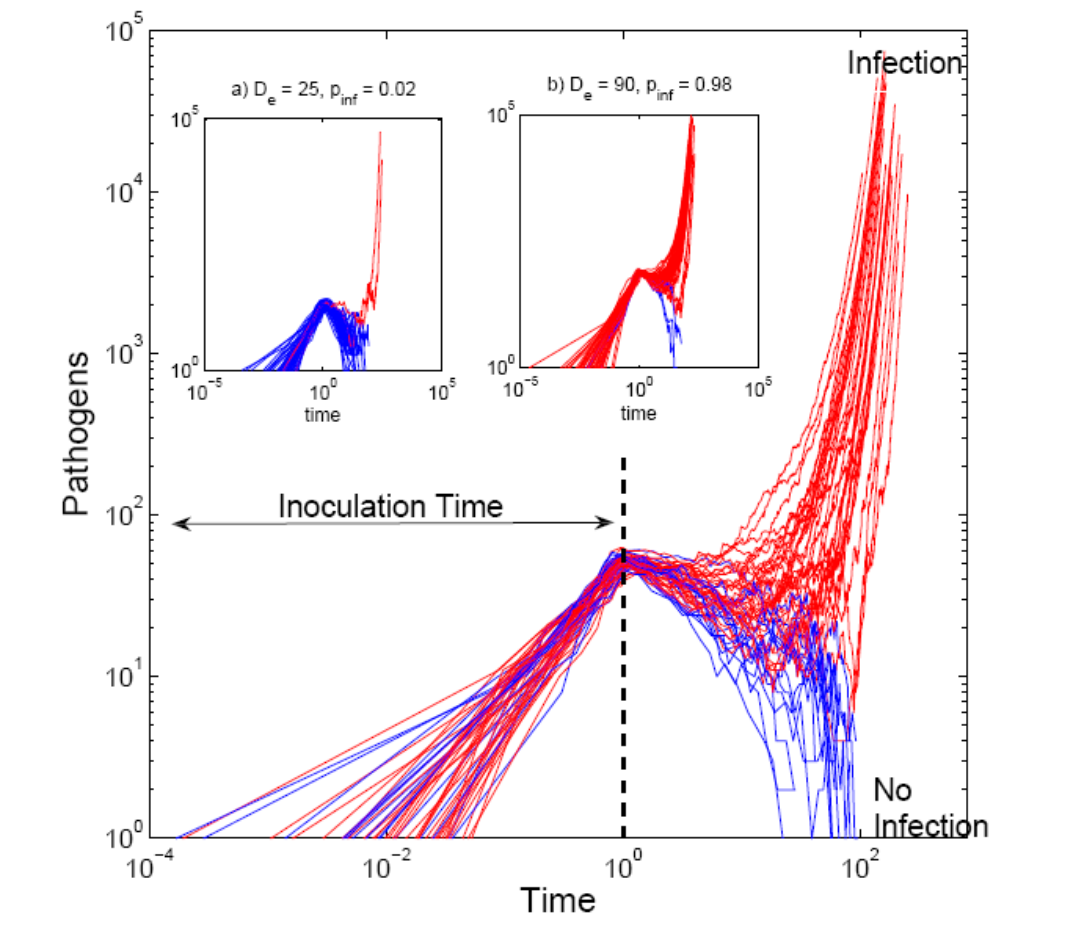
Immune particles have a baseline flux are both recruited and destroyed by pathogens. Pathogens have an input from the environment, grow, and are destroyed by immune particles.

CumDose-Model Dynamics

D_e=60,

T_e =1.0,

p_{inf} = 0.67



$$\{\theta_p, \delta_p, \alpha_i, \gamma_i, \delta_i, \lambda_i\} = \{0.15, 0.01, 0.4, 0.01, 0.005, 0.05\}$$

CumDose-Model Dynamics

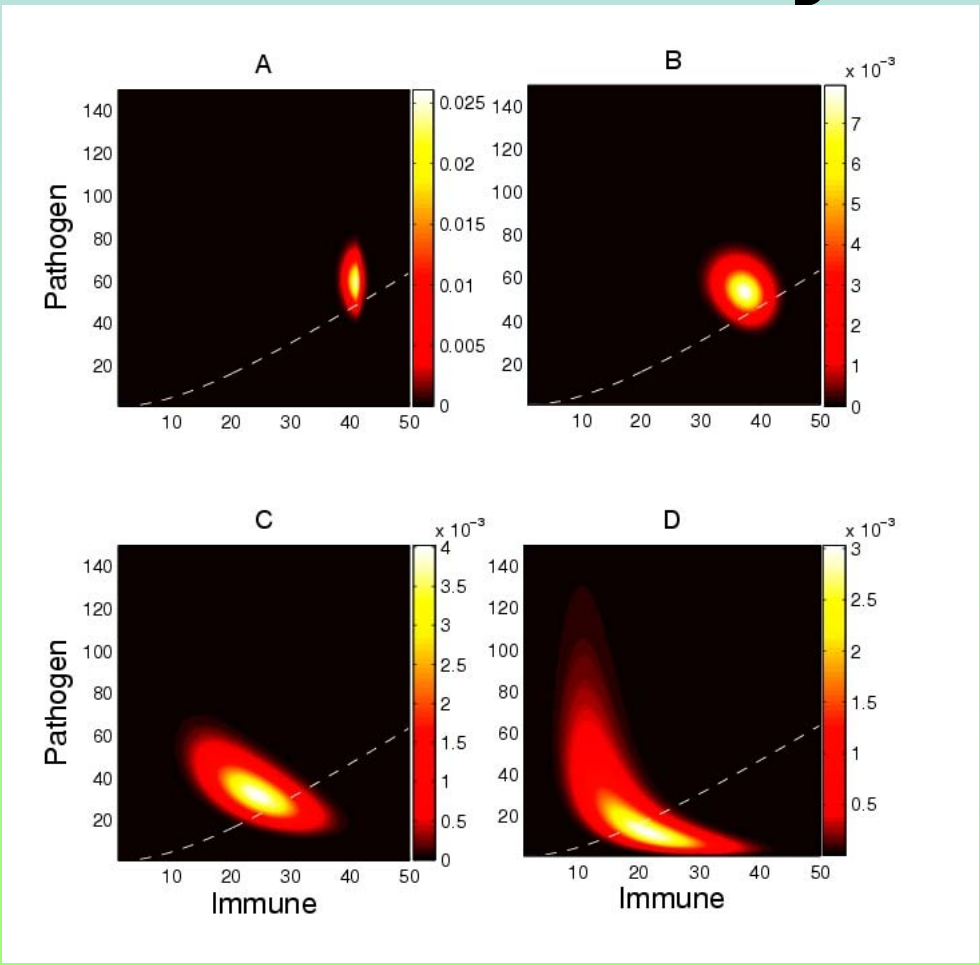
T_e =

0.1,

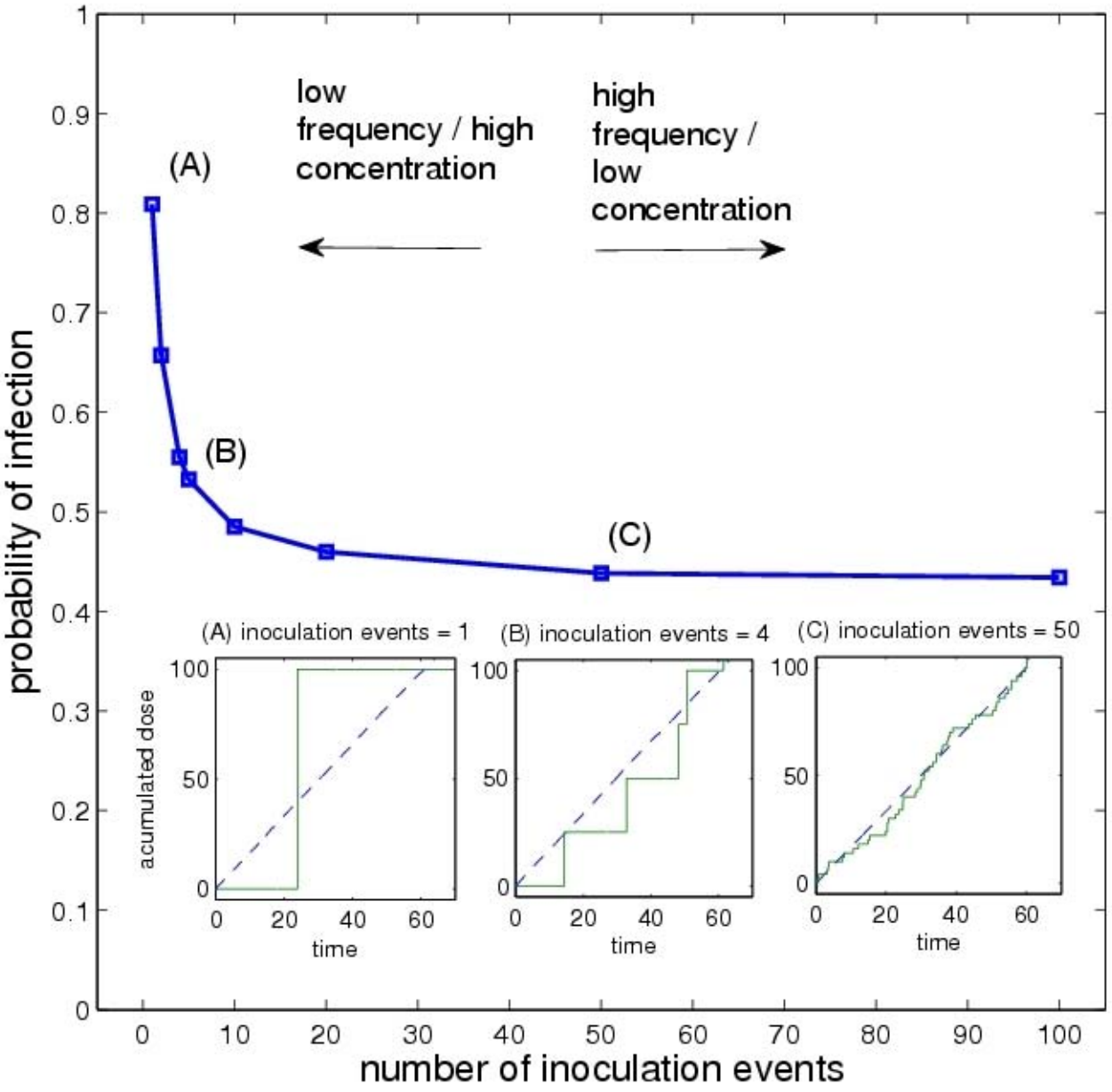
1.0,

10.0,

50.0



$$\{\theta_p, \delta_p, \alpha_i, \gamma_i, \delta_i, \lambda_i\} = \{0.15, 0.01, 0.4, 0.01, 0.005, 0.05\}$$



The Effect of Time of Exposure

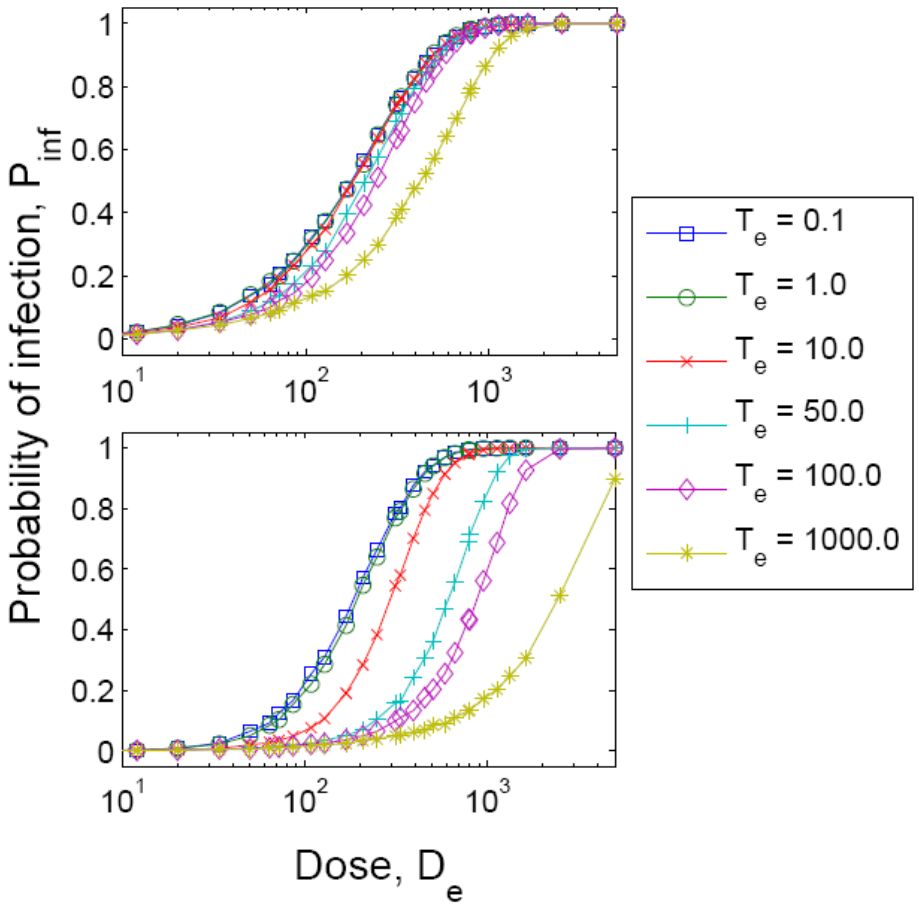


Figure based on parameter estimated for a fixed (rapid) exposure time (Te=1.0) and the model prediction with exposure time is increased

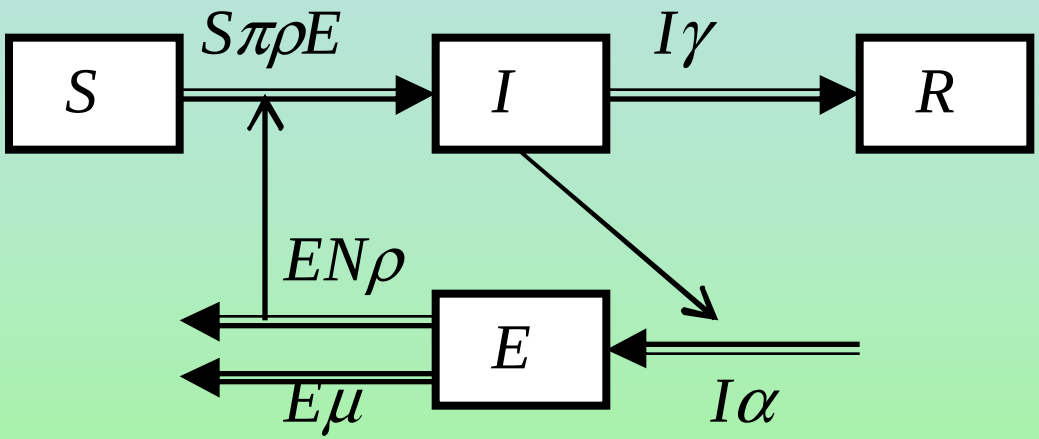
How does the dose-response curve change when the same dose is applied in different timing?

Depends on the parameter of the model, but the effect is always there.

We speculate that innate and established immune dynamics across a day of exposure might flip transmission between aerosol and large droplet hand-fomite

Dose response data with doses administered across time are needed to determine which mode of transmission prevails

Simple Environmental Transmission System Model



ρ = fraction of contamination picked up per time

π = Probability of infection per particle picked up

α = Rate of pathogen deposition by I

μ = Pathogen particle death rate

γ = Infection cure rate

$N = S + I + R$

Analytic Insights

- Effect of crowding is dependent upon environmental survival, deposit, & pickup rates and infectivity (+ movement)
  - Density & frequency dependent extremes are unlikely (Models like EPISIMS need to formulate venue person density dependence)
- Epidemic dynamics are likely to be different from Kermack – McKendrick SIR model

CAMRA Can Move Us From a Weak to a Strong Transmission Science