QMRA in the Built Environment

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Outline

"Quantitative microbial risk assessment (QMRA) is a framework and approach that brings information and data together with mathematical models to address the spread of microbial agents through environmental exposures and to characterize the nature of the adverse outcomes. While most microbes are harmless or beneficial, some are extremely dangerous we call these Biological Agents of Concern (BAC). All BAC can cause serious and often fatal illness, but they differ greatly in their physical characteristics, movement in the environment, and process of infection. Ultimately the goal in assessing risks is to develop and implement strategies that can monitor and control the risks (or safety) and allows one to respond to emerging diseases, outbreaks and emergencies that impact the safety of water, food, air, fomites and in general our outdoor and indoor environments."

source: `http://qmrawiki.canr.msu.edu/index.php/Quantitative_Microbial_Risk_Assessment`

Epi vs. QMRA

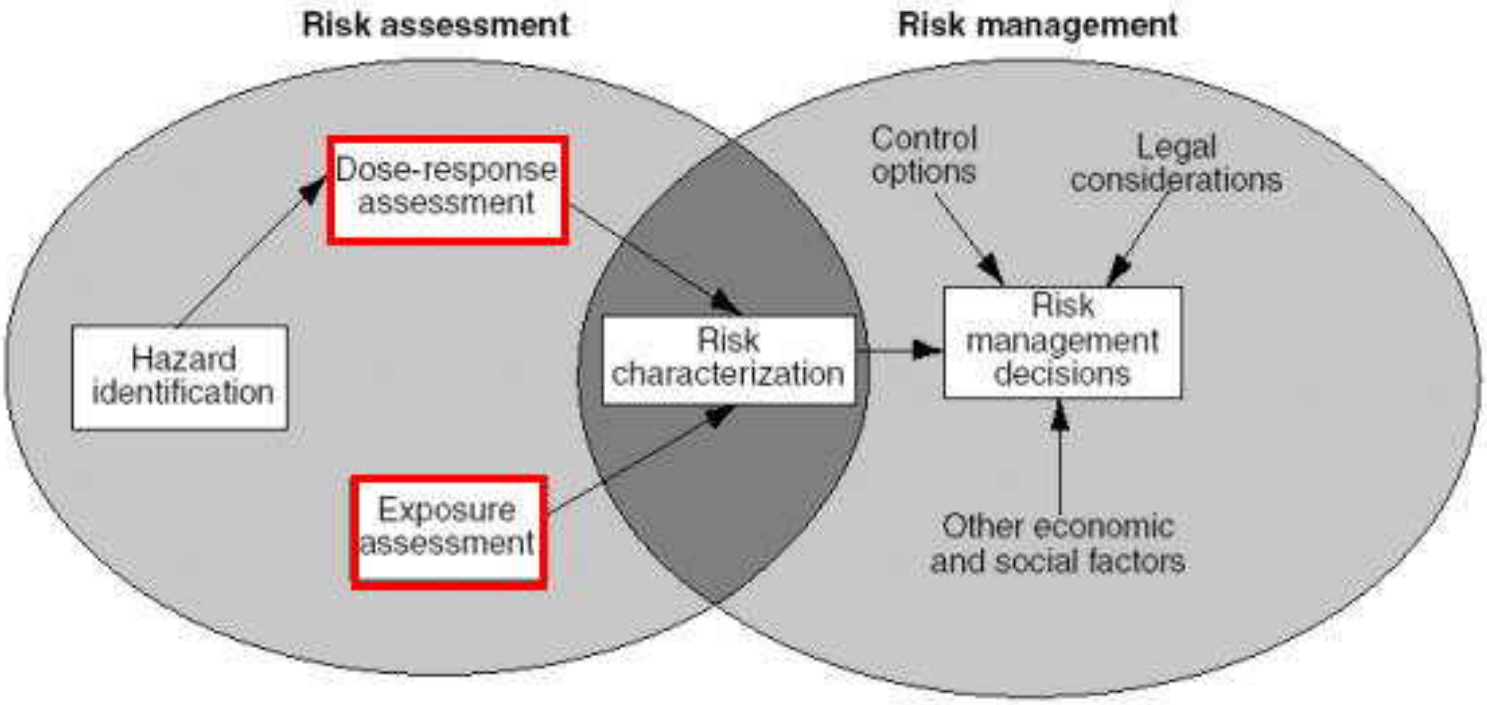
Epidemiology

- Focus on syndrome (often)
- Exposure variable can be qualitative
- Limited power unless effect $> 5\%$ above background

QMRA

- Focus on individual pathogen (often)
- Exposure variable is quantitative
- Can estimate low (as well as high) level incremental effects

Overall Risk Assessment Framework



Source: EPA Office of Research and Development.

What Is Exposure Assessment

- **What pathogen are we interested in?**
- What is the dose (distribution)
- By what route(s)
  - Inhalation
  - Ingestion
  - Fornites ($\rightarrow$ mouth, $\rightarrow$ nose, $\rightarrow$ eye)
  - Dermal
- How often

How to Assess Exposure

- Direct concentration measurements
- Indirect concentration measurements (indicator correlations)
- Modeled concentrations
- Convoluted with intake distributions (or touch frequency, transference)

Probability distributions highly desirable

Model Basis

Biological Processes

- Ingestion/Inhalation – Retention
- *In vivo* transport and survival to reach an amenable target
- Successful multiplication – colonization
- Attain sufficient numbers to elicit infection or disease response

Modeling Concepts

- Models should consider discrete (particulate) nature of organisms (high variability at low dose)
- Models should be based on concept of infection from one or more 'survivors' of initial dose (birth-death models)

What is the dose?

- Average administered to a population
- Actual number an individual experiences
- Retention
- *In vivo* body burden after multiplication

What is a Response?

- Proportion of subjects administered a dose whom have discernible effects (excretion, infection, illness, death). Quantal.
- Probability that a single subject administered a dose will exhibit a discernible effect.

Other responses may be nonquantal (more attention is needed): rise in antibody levels, rise in fever ...

What we know from single dose bolus experiments - total outcome

- All data are consistent with exponential or beta-Poisson model (non threshold, low dose linear) based on ingested/inhaled *average* dose
- Different competent host species can often be pooled based on actual inhaled/ingested dose

$$p = 1 - \exp(-kd)$$

$$p = 1 - {}_1F_1\left(\alpha, \alpha + \frac{N_{50}}{2^{1/\alpha} - 1}, -d\right) \approx 1 - \left[1 + \frac{d}{N_{50}}\left(2^{1/\alpha} - 1\right)\right]^{-\alpha}$$

What is "d" In the Indoor Air Context

$$\int C(t)\, R(t)\, dt$$

where R is respiration rate

Example Organisms With Dose Response Data

Bacteria

- *E. coli*
- *Salmonella*
- *Legionella*
- *Bacillus anthracis*

Protozoa

- *Giardia*
- *Cryptosporidium*
- *Toxoplasma*

Viruses

- Norovirus
- Echoviruses
- Coronaviruses (e.g. SARS)
- Influenza

Other

- Helminths
- Rickettsiae

Missing: fungi

Legionella, Japanese Spa Outbreaks

Animal dose response, estimation from water concentration

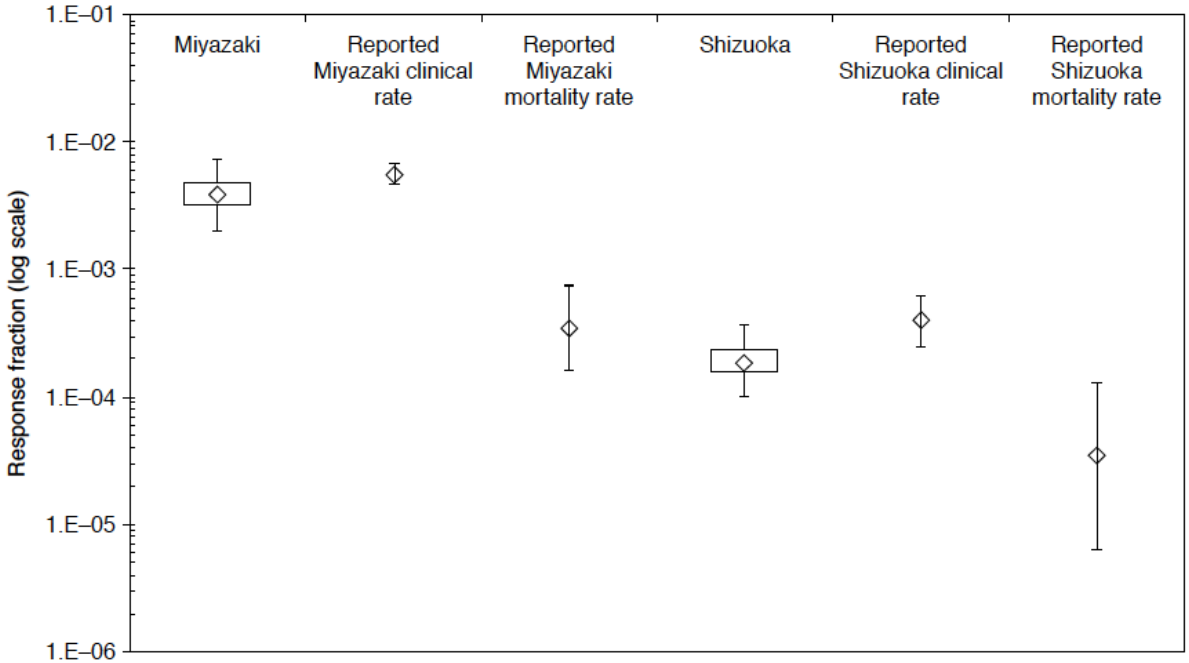


Figure 6 | Comparison of the calculated clinical severity infection risks with the reported clinical severity infection risks and mortality risks for the Miyazaki and Shizuoka prefecture outbreaks. Bar ends = 2.5 and 97.5th percentiles, box ends = 25 and 75th percentiles, ◇ = median.

Armstrong, T. W. and C. N. Haas (2008). "Legionnaires' disease: evaluation of a quantitative microbial risk assessment model." J Water Health 6(2): 149-166.

Mycobacterium tuberculosis - Aircraft

Risk Analysis

**Characterizing the Risk of Infection fro
tuberculosis in Commercial Passenger A
Quantitative Microbial Risk Assessmen**

Rachael M. Jones,[1,2]* Yoshifumi Masago,[3,4] Timothy Bartr
Mark Nicas,[1] and Joan B. Rose[3]

Markov-chain multi-zonal model given single passenger emitter

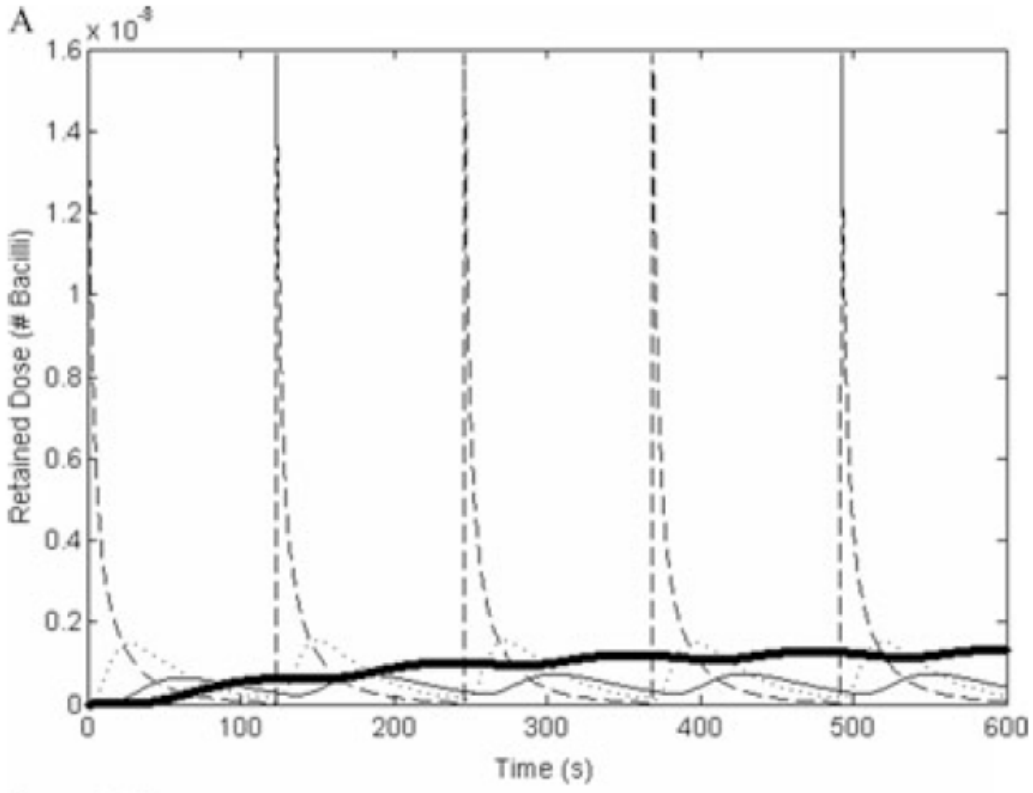


Fig. 4. Time series of retained dose at zone 8 (row 4, dashed line) zone 16 (row 8, dotted line), zone 24 (row 12, solid line), and zone 32 (row 16, dot-dash line) given emission of *Mtb* bacilli by a passenger seated in zone 8 (row 4) with the mean *Mtb* saliva concentration and mean cough rate given 100% efficacy of the HEPA filtration system (A)

- Absolute doses are not currently possible with *omics
- We expect pathogens to be rare, so they may be under-represented
- Issue of viability
- Could an ecological epidemiological study be done to assess whether some "pattern" is predictive of particular adverse infectious outcomes? Essentially use an indicator approach.
- We know fungi can be infectious pathogens, and need more effort both in deducing quantitative occurrence as well as in dose response (data mining, animal models)

Readings

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