An Introduction to Quantitative Microbial Risk Assessment

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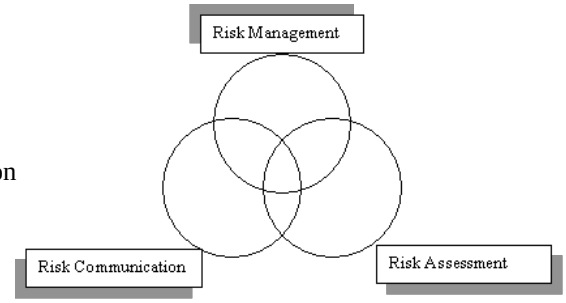
Outline

- Introduce QMRA
  - Components
  - Process
  - Summarize state of the science and limitations
- Provide examples of how QMRA has been used
  - National scale
  - Site specific scale
- Offer personal perspectives on how I think QMRA could be useful for AQWC development
- Answer questions

Risk Assessment

- Risk Analysis
  - Risk Assessment
  - Risk Management
  - Risk Communication



- Risk Assessment: characterization and estimation of potential adverse health effects associated with exposure of individuals or populations to hazardous materials or situations

Why Use Risk Assessment?

- Epidemiology can not always provide sufficient sensitivity to measure risks directly using human health data
  - For example: Recreational waters impacted by low occurrence, high severity pathogens due to wet weather events
  - There are <u>many</u> possible permutations of various sources of contamination and water characteristics: not practical to consider all via epidemiology
- To predict relative risks for future scenarios and/or evaluate efficacy of alternative management actions (treatment, other mitigation, etc.)

What is QMRA???

- Risk Assessment: A formal process of estimating human health risks due to exposures to environmental contaminants
- (Q)MRA: A formal process, analogous to chemical risk assessment of estimating human health risks due to exposures to microbial pathogens

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How are pathogens different from chemicals?

- Sources of Exposure
  - Chemicals – environmental
  - Microbes – environmental & infected individuals
    - Pathogens can be transmitted from person to person
- Health Effects

		Chemicals	Microbes
Timing of Exposure	Acute	Yes	Yes
	Chronic	Yes	Emerging
Severity of Illness	Less severe	No	Yes
	More severe	Yes	Emerging
Duration of Illness	Shorter	No	Yes
	Longer	Yes	Emerging
Immunity		No	Yes
Most common subjects of quantitative risk assessment			

Process Used to Conduct QMRA

- US EPA / ILSI Framework for Microbial Risk Assessment
  - Problem Formulation: Planning step to identify goals, regulatory and policy context, and develop conceptual models
  - Analysis: Technical evaluation of exposure and health effects data
  - Risk Characterization: Compilation of information from *Problem Formulation* and *Analysis* steps into a risk estimation and risk description

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Overview of QMRA
Considerations for Framing an Assessment

- Which pathogen(s) (*hazard identification*)?
- How many pathogens are individuals or populations exposed to (*exposure assessment)* and from what scenarios (hazardous events)?
- What are the adverse health effects of interest?
- What is the relation between exposure and health effects (*dose-response evaluation*)?
- How does variability (temporal, spatial, inherent) and/or uncertainty impact our understanding or interpretation of risk?
- Do properties that are unique to microorganisms or infectious diseases such as person-person transmission and/or immunity need to be accounted for?
- What methods are appropriate / needed to characterize risk?

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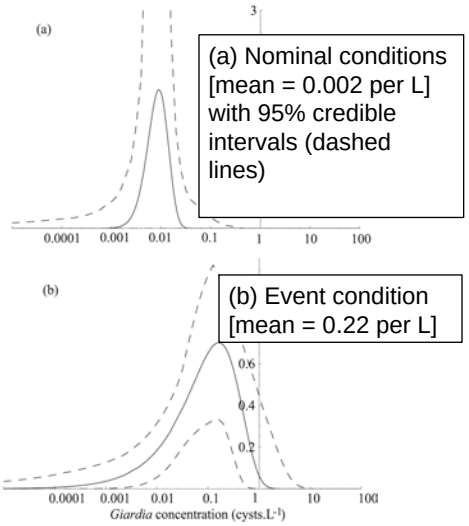
Representative Data Used in QMRA
Exposure assessment (*Giardia* concentration)

Count	Analysed Vol (L)
0	137.5
3	125
2	125
2	125
0	125
0	125
1	122.25

Nominal data

Count	Analysed Vol (L)
8	16.25
9	9.25
8	65
7	67.5
9	92.5
1	110
3	130.75
4	134
5	105
2	76.25

Event affected data

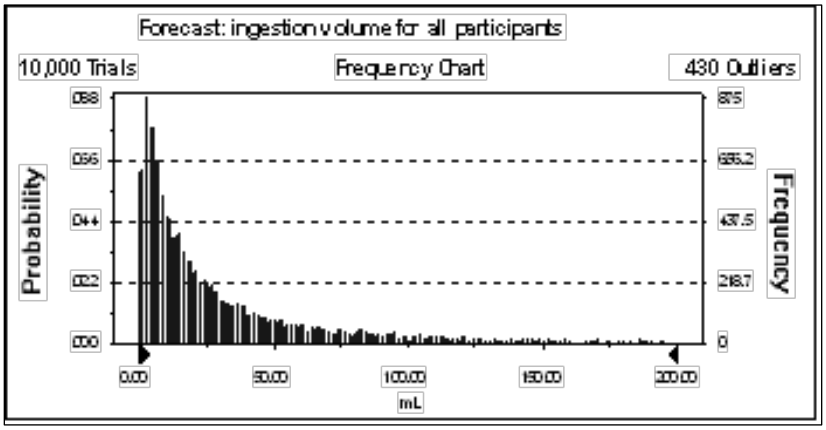


(a) Nominal conditions [mean = 0.002 per L] with 95% credible intervals (dashed lines)

(b) Event condition [mean = 0.22 per L]

Source: Petterson et al. 2007

Representative Data Used in QMRA
Volume of Water Ingested During Recreation

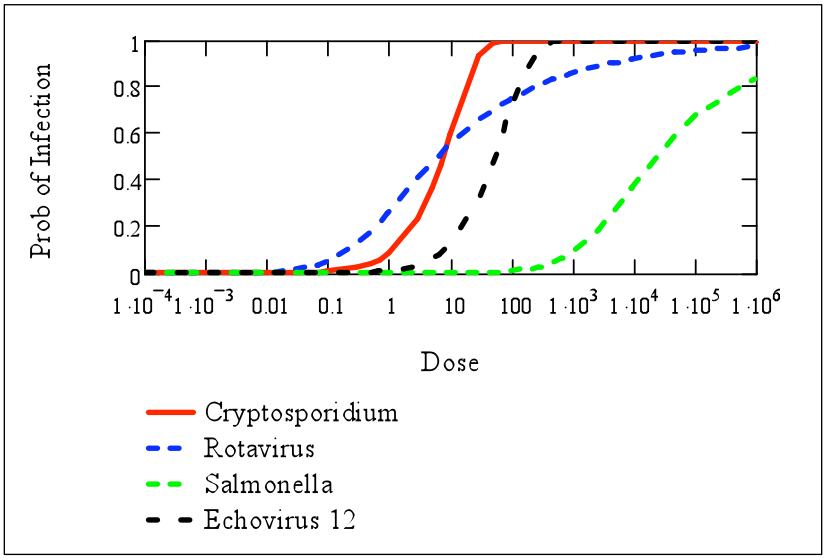


Source: Dufour et al. 2006

Representative Data: Dose response overview

- Provides a qualitative or quantitative description of the likelihood of adverse effects that may result from exposure to a microorganism or its toxin.
  - Infection
  - Illness
- Dose: intensity of exposure of the host to the pathogen (number of organisms ingested or inhaled)
  - Measured
  - Computed: concentration x volume

Representative Data Used in QMRA Dose-Response Relations Based on Human Studies



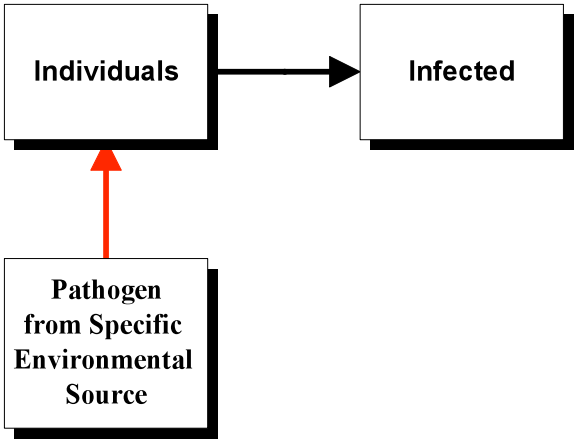
Overview of QMRA
Brief History

- Technical basis for infectious disease modeling is well documented in literature
  - First mathematical models to analyze the spread and control of infectious diseases were for measles (Hamer 1906) and malaria (Ross 1911)
- Quantitative methods to characterize the human health risks associated with exposure to pathogens published in 1970s (Fuhs 1975, Dudley 1976)
- Field of QMRA has grown exponentially
  - Waterborne: (Haas 1983; Regli 1991; Rose 1991; Gerba 1996; Crabtree 1997; Teunis 1997; Mena 2003)
  - Foodborne: (Farber 1996; Buchanan 1998; Buchanan 2000)

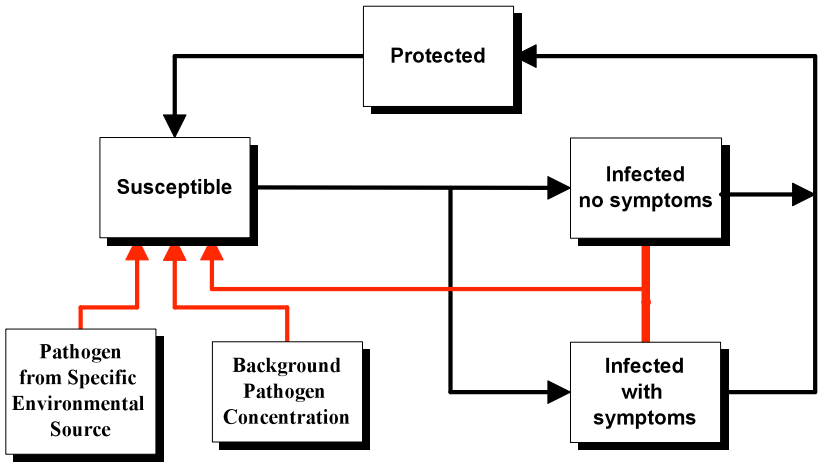
Overview of QMRA
State of the Science

- Two prevailing perspectives
  - Individual level (Static)
  - Population level (Dynamic)
- Individual level models
  - Estimate the probability of infection (illness) to an individual from a single exposure event
  - Assumes recurring exposures are independent
- Population level models
  - Exposures not necessarily independent, multiple routes considered
  - Account for immune status and person-person (and/or person-environment-person) transmission
  - Require more data

Individual Level QMRA Health Effects Model



Population Level QMRA Health Effects Model



Potentially Important Data for QMRA

Exposure Specific Factors

- Magnitude of exposure
- Frequency of exposure
- Proportion of population exposed

Pathogen Specific Factors

- Background level of infection
- Infectivity (dose response)
- Duration of incubation
- Duration of infection & disease
- Duration of immunity
- Probability of symptomatic response
- Person-person transmission potential

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Overview of QMRA
Current Research Focus – State of the Science

- Person-person transmission
- Inter-dependent exposure pathways
- Differential susceptibility in population
- "Super-spread" events
- Geographical and temporal variability
- Characterizing uncertainties
- *Cryptosporidium*, *E. coli* O157 and noroviruses
- Emerging, reemerging and zoonotic pathogens
- Pathogens with low occurrence but high severity

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Overview of QMRA Limitations

- Pathogen specific (by contrast: epidemiology studies generally focus on broad spectrum disease, and use water quality measurements of fecal indicator data)
- Easiest to conduct and clearest to interpret when comparing relative risk of two or more scenarios
- Characterization of exposure can be difficult due to uncertainty and variability
- Dose-response relations are needed, limited availability
- QMRAs are numerical simulation studies: best when anchored to observable data
- Subjectivity in model and parameter selection
- Differential susceptibility is important and we have very little quantitative information

QMRAs Have Been Used to Characterize Risks of Pathogens of Public Health Concern

- Viruses
  - Rotavirus
  - Poliovirus
  - Echovirus
  - Adenovirus
  - Hepatitis A
  - Coxsackie virus
- Parasites
  - *Cryptosporidium*
  - *Giardia*
- Bacteria
  - *Salmonella*
  - *Shigella*
  - *E. coli* O157
  - *Vibrio cholera*
  - *Campylobacter jejuni*

Representative Examples of Large-Scale QMRAs Conducted by US Government Agencies

- US EPA – OGWDW
  - IESWTR and LT2 ESWTR benefits based on *Cryptosporidium* risk assessment
  - GWR benefits based on virus risk assessment
- FDA
  - *Listeria monocytogenes* in Ready-to-Eat (RTE) foods (FDA / USDA)
  - *E. coli* O157:H7 in Apple Cider
  - *Vibrio parahaemolyticus* in raw oysters
- USDA
  - *Clostridium perfringens* in RTE foods and partially cooked meats
  - *Salmonella enteritidis* in shell eggs and *Salmonella spp*. in egg products
  - *E. coli* O157:H7 in ground beef

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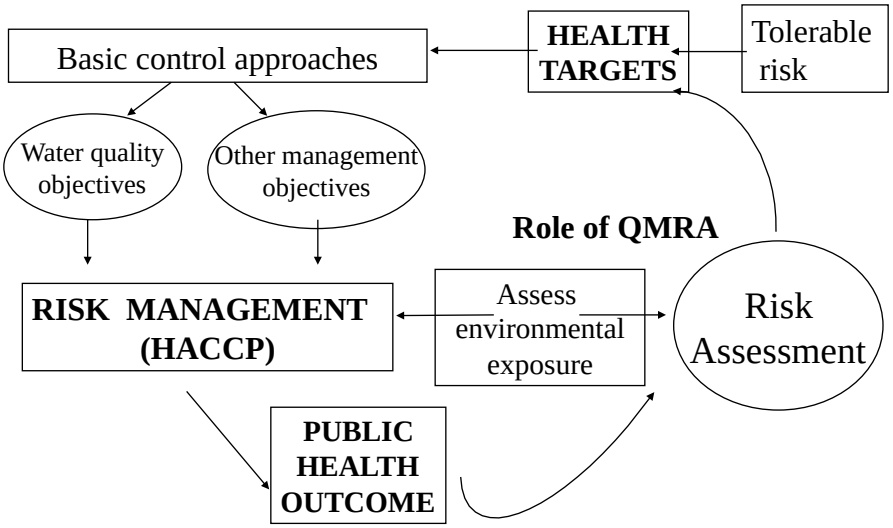
WHO harmonised approach for provision of safe water



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International Examples of QMRA Application

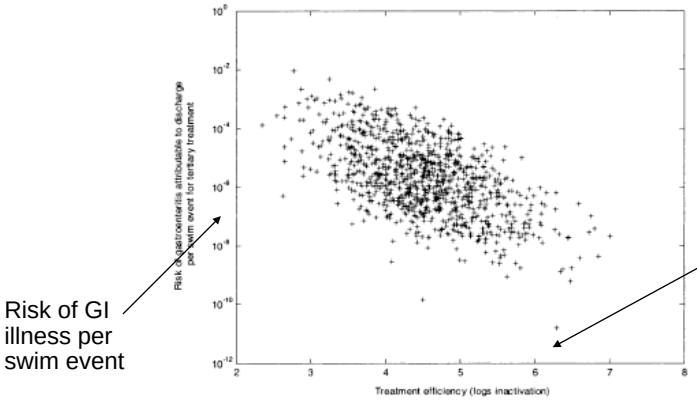
- MicroRisk EU project
  - Dutch water companies must meet < 1 infection per 10,000
  - Major Australian, French & English water companies must provide HACCP plans
- Urban Water Project (Sweden)
- Bather risk reduction from deepwater ocean outfalls (Sydney, Australia)
- Reopening of an urban freshwater recreational lake (Sydney, Australia)
- Setting disinfection level for sewage outfall (Auckland, Australia)

Site Specific Examples Use of QMRA in the US

City of Stockton, CA (Soller et al., 2003)

- Purpose: Evaluate the public health benefit of tertiary wastewater treatment compared to secondary treatment
- Background
  - WWTP discharges to San Joaquin River (SJR) – also used for recreation
  - QMRA used to determine if the addition of tertiary treatment would substantially reduce the risk the public faces via recreation in the SJR
    - → Existing flows
    - → Future flows

Site Specific QMRA Examples
City of Stockton, CA



- Benefit of additional treatment computed as difference between results for different types of treatment for each simulation

Representative Examples of How QMRA Has Been Used in the US

- Milwaukee *Cryptosporidium* outbreak (Eisenberg et al., 1998)
  - Ran QMRA in reverse to gain insights about conditions leading to outbreak
- *E. coli* outbreak from spinach in 2006 (Seto et al., 2007)
  - Modeled outbreak while it was occurring to estimate outbreak magnitude and potential effectiveness of additional interventions
- Numerous others in peer-reviewed literature
- These studies provide examples of how QMRA can be anchored to observable data or events

How Might QMRA be Useful to Support Recreational Water AWQC Development

1. National: Complementary approach to epidemiological studies for understanding health risks
   - Relative risks from various contamination sources
   - Identify detection limits that would be needed to monitor pathogens/indicators at levels of public health relevance
   - Characterize differential risks to sensitive subpopulations (e.g. children)
   - Relative risks of temporally varying inputs

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Perspectives: QMRA to Support Recreational Water AWQC Development

2. National: Understand risks associated with pathogens with low occurrence but severe health outcomes (for example: *E. coli* O157:H7, Hepatitis A, or *Cryptosporidium* in immunocompromised subpopulations)
   - ➢ Epidemiology studies are unlikely to be conducted due to ethical issues, and/or unlikely to provide adequate resolution due to low probability outcomes

4. National: Evaluate value of additional data
   - ➢ Sensitivity analysis can be used to identify which data are most likely to provide important insights relative to health

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Perspectives: QMRA to Support Recreational Water AWQC Development

4. Site specific implementation: Provide quantitative insight to managing control points
   - "What if" scenarios
     - → Alternative management scenarios
     - → Equivalency evaluation for new or alternative types of wastewater treatment
5. Site specific implementation: Provide ability to generate scientifically defensible, site specific criteria

Perspectives: What has been suggested for AWQC & how might QMRA be useful?

- Types of water that are being investigated or that have been recommended to be investigated:
  - Fresh vs. Marine
  - Temperate vs. Subtropical vs. Tropical
  - Non-flowing vs. Flowing

Perspectives: What has been suggested for AWQC & how might QMRA be useful?

- **Sources of contamination that are being investigated or have been recommended to be investigated:**
  - Untreated human: sewage
  - Untreated human: bathers
  - POTW effluent impacted
  - Urban runoff
  - Combination of urban runoff / animals
  - Agricultural: Cattle (grazing)
  - Agricultural: CAFOs (including but not necessarily limited to feedlot/dairy cattle, pigs and turkeys)
  - Wildlife
  - Birds

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Too many combinations of contamination and water type to base AWQC only on epidemiological data

	Freshwater						Marine					
	Temperate		Subtropical		Tropical		Temperate		Subtropical		Tropical	
Source	Non-flowing	Flowing	Non-flowing	Flowing	Non-flowing	Flowing	Non-flowing	Flowing	Non-flowing	Flowing	Non-flowing	Flowing
Septic or untreated												
POTW												
Unspecified urban runoff												
Combination urban runoff / animal												
Agricultural												
Wildlife												
Birds												

How many studies would each cell require to account for inter-site variability?

Final Thoughts

- QMRA is a well developed, scientifically accepted tool that could be useful to fill holes where no epidemiological data exist, until new epidemiological are developed, and/or where epidemiological studies may not be practical or appropriate
- QMRA is best when anchored to observable data in a robust manner
- For QMRA to succeed in context of new/revised AWQC, understanding the etiology of illness for important water type/ contamination source combinations will be important

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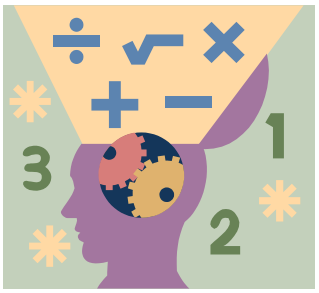
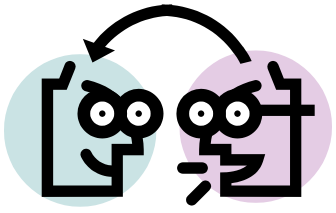
Questions / Comments / Closing Thoughts





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