Use of microbial risk assessment to inform the national estimate of acute gastrointestinal illness attributable to microbes in drinking water

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ABSTRACT

Microbial risk assessment (MRA) evaluates the likelihood of adverse human health effects that occur following exposure to pathogenic microorganisms. This paper focuses on the potential use of MRA to provide insight to the national estimate of acute gastrointestinal illness (AGI) in the United States among persons served by public water systems. This article defines MRA, describes how MRA is implemented, provides an overview of the field of MRA and discusses how MRA may be useful for characterizing the national estimate. Communities served by drinking water systems with relatively contaminated source waters, sub-standard treatment facilities, and/or contamination problems in their distribution systems are subject to higher risks than communities where such issues are less of a concern. Further, the risk of illness attributable to pathogens in drinking water in each community can be thought of as the sum of the risk from the treated drinking water and the risk from the distribution system. Pathogen-specific MRAs could be developed to characterize the risk associated with each of these components; however, these assessments are likely to under-estimate the total risk from all pathogens attributable to drinking water. Potential methods for developing such MRAs are discussed along with their associated limitations.

Key words | drinking water, microbial risk assessment, risk assessment, waterborne pathogens

OVERVIEW

The Safe Drinking Water Act amendments of 1996 required the US Environmental Protection Agency (EPA) and the Centers for Disease Control and Prevention (CDC) to conduct epidemiological studies on the occurrence of waterborne disease in major communities in the US and to estimate the annual amount of waterborne disease in the US among persons served by public water systems (national estimate). After consultation with CDC, EPA defined waterborne diseases as acute gastrointestinal illness (AGI) for the purposes of the national estimate. Thus, other potentially important waterborne diseases are not specifically included in the national estimate unless the symptoms associated with those diseases include AGI. This paper focuses on the potential use of microbial risk assessment (MRA) to provide insight to the national estimate. To that end, this paper defines MRA, describes how MRA is implemented, provides an overview of the field of MRA and then discusses how MRA methodologies may be useful for estimating AGI attributable to microbes in drinking water.

Risk analysis consists of three principal components: risk assessment, risk management and risk communication. Within this construct, risk assessment is the qualitative or...
quantitative characterization and estimation of potential adverse health effects associated with exposure of individuals or populations to hazardous materials and situations (NRC 1983; Hoppin 1993). The risk management component weighs policy alternatives in light of the results of risk assessment and, if required, selects and implements appropriate control options, including regulatory measures. The risk communication component is the interactive exchange of information and opinions concerning risk and risk management among risk assessors, risk managers, consumers and other interested parties (WHO 1999). This paper focuses on the risk assessment component of the risk analysis process.

MRA (also known as pathogen risk assessment) is a process that evaluates the likelihood of adverse human health effects that can occur following exposure to pathogenic microorganisms or to a medium in which pathogens occur (ILSI 1996). To the extent possible, the MRA process includes evaluation and consideration of quantitative information, however, qualitative information is also employed as appropriate (WHO 1999).

Quantitative risk assessment has been used since the 1970s to assess human health effects associated with exposure to chemicals (Hammond & Coppick 1990). The principles, processes and methods for carrying out risk assessments for chemical agents were formalized in 1983 by the National Research Council (NRC) resulting in a four step process or framework (NRC 1983). The steps outlined by the NRC include hazard identification, dose–response assessment, exposure assessment, and risk characterization. Many of the early MRAs employed the NRC conceptual framework to provide a structure from which the assessments could be conducted (Haas 1983a; Regli et al. 1991; Rose et al. 1991; ILSI 1996).

As the field of microbial risk assessment developed, it became clear that there were some complexities associated with modeling the infectious diseases that are unique to pathogens, such as person-to-person transmission of infection and immunity. Therefore, the conceptual framework for chemicals may not always be appropriate for the assessment of risk of human infection following exposure to pathogens (ILSI 1996). To address this concern, the EPA Office of Water sponsored a series of workshops to develop a conceptual framework to assess the risks of human infection associated with pathogenic microorganisms.

Those workshops resulted in a published framework (ILSI 1996) that was then tested through the conduct of two case studies (Soller et al. 1999; Teunis & Havelaar 1999) and subsequently revised (ILSI 2000). The EPA/ILSI framework for assessing the risk of human infection following exposure to water- and food-borne pathogens is comprised of three principal components: problem formulation, analysis, and risk characterization. At this time, both the NRC and EPA/ILSI frameworks are currently employed for the conduct of MRAs. Following is a brief summary of those frameworks.

**NRC risk paradigm for microbial risk assessment**

As applied to microbial risk assessment, the four steps comprising the NRC risk paradigm are summarized below:

**Hazard identification**

For microbial agents, the purpose of hazard identification is to identify the microorganisms or the microbial toxins of concern. Hazards can be identified from relevant data sources such as scientific literature, databases, and solicitation of expert opinion. Relevant information for the hazard identification often includes review of clinical studies, epidemiological studies and surveillance, laboratory animal studies, investigations of the characteristics of microorganisms, interaction between microorganisms and their environment, and studies of analogous microorganisms and situations (WHO 1999).

**Dose–response assessment**

The dose–response assessment provides a quantitative or qualitative description of the likelihood, severity and/or duration of adverse effects that may result from exposure to a microorganism or its toxin. Dose–response relationships can be developed for different end points, such as infection or illness, depending on the microorganism of interest. In the absence of appropriate dose–response data, risk assessment tools such as expert elicitations could be used to consider factors such as infectivity that may be necessary to characterize the host’s response to a dose of pathogens (WHO 1999).

There are several important factors related to both the microorganism and the human host in the dose–response
assessment. Relative to the microorganism the following may be important: the virulence and infectivity of microorganisms can change depending on their interaction with the host and the environment; genetic material can be transferred between microorganisms, leading to the transfer of characteristics such as antibiotic resistance and virulence factors; and/or low doses of some microorganisms can in some cases cause a severe effect (WHO 1999).

Relative to the human host the following may be important: genetic factors; increased susceptibility due to breakdowns of physiological barriers; individual host susceptibility characteristics such as age, pregnancy, nutrition, overall health, medication status, concurrent infections, immune status and previous exposure history; and population characteristics such as population immunity, and access to and use of medical care (WHO 1999).

**Exposure assessment**

An exposure assessment describes the magnitude and/or probability of actual or anticipated human exposure to pathogenic microorganisms or microbiological toxins. For microbiological agents, exposure assessments might be based on the potential contamination in water by a particular agent or its toxins, and on other exposure pattern information (for example, the frequency and/or duration of exposure).

Factors that must be considered for exposure assessment include the frequency of human exposure to the pathogenic agents and the associated concentrations of those pathogens over time. Other factors that could be considered in the assessment could include the potential impact of environmental conditions and/or water treatment reliability (WHO 1999) as well as factors influencing the patterns of exposure (such as socio-economic status, ethnicity, seasonality, population demographics, regional differences, and/or consumer preferences and behavior).

**Risk characterization**

Risk characterization represents the integration of the hazard identification, dose–response assessment, and exposure assessment components to obtain a risk estimate. The risk characterization process results in a qualitative or quantitative estimate of the likelihood and severity of the adverse effects which could occur in a given population, including a description of the uncertainties associated with these estimates.

Risk characterization depends on available data and expert interpretation of those data. The weight of evidence integrating quantitative and qualitative data may permit only a qualitative estimate of risk. The degree of confidence in the final estimation of risk will depend on the variability, uncertainty, and assumptions identified in all previous steps (WHO 1999). Differentiation of uncertainty and variability may be important for subsequent risk management considerations. However, experience indicates that, for MRAs, it is possible that variability and uncertainty will be confounded to such an extent that it is difficult or impossible to consider them independently.

**EPA/ILSI paradigm for microbial risk assessment**

The EPA/ILSI MRA (ILSI 2000) is conceptually similar to the NRC paradigm for human health risk assessments (NRC 1983) and the ecological risk assessment framework (US EPA 1992). The framework emphasizes the iterative nature of the risk assessment process (Figure 1), and allows wide latitude for planning and conducting risk assessments in diverse situations (Soller et al. 1999). This framework consists of three principal components: problem formulation, analysis, and risk characterization. The analysis phase is further subdivided into the characterization of exposure and human health effects.

The problem formulation stage involves all stakeholders and is used to identify: (1) the purpose of the risk assessment, (2) the critical issues to be addressed, and (3) how the results might be used to protect public health. Once identified, initial descriptions of the exposure and potential health effects are described and then a conceptual model is developed. This conceptual model is used as a starting point for the analysis phase of the risk assessment and later as an interactive tool along with components developed in the analysis phase to initiate the risk characterization.

In the analysis stage information about both the exposure and the health effects is compiled and summarized. This compilation of quantitative and qualitative data, expert opinion, and other information results in exposure and host/pathogen profiles that explicitly identify the data to be integrated into the risk characterization and the
associated assumptions and uncertainties. These two elements, while separate, must also be interactive to ensure that the results are compatible.

The final stage, risk characterization, results in a statement of the likelihood, types, and/or magnitude of effects likely to be observed in the exposed population under the expected exposure scenario, including all of the inherent assumptions and uncertainties. Often, the risk characterization phase includes data integration through parameterization of a mathematical model, numerical simulation and interpretation.

**MRA METHODS**

Quantitative methods to characterize human health risks associated with exposure to pathogenic microorganisms were first published in the 1980s (Haas 1983a, b; Cooper et al. 1986). Over the last 20 years, the field of microbial risk assessment has been developing and maturing. Since that time, dose–response relations have been developed for various pathogenic microorganisms (Haas et al. 1999; McBride et al. 2002), and microbial risk assessment investigations have been carried out for a number of those pathogens in water, food and other...
media. This section reviews and summarizes the dose–response and risk characterization methods that have been most commonly employed in MRAs.

**Evaluation of dose–response relations**

The dose–response assessment provides a qualitative or quantitative description of the likelihood of adverse effects that may result from exposure to a microorganism or its toxin. For MRA, the adverse health effects most commonly of interest are infection and illness. Infection may be defined as the invasion, colonization and multiplication of a pathogenic microorganism (Teunis et al. 1996). Since humans may come into contact with a wide range of pathogen concentrations, it is therefore useful to develop a functional relationship between a quantitative measure of microorganism ingestion and the risk of infection. A dose is defined as a quantitative measure for the intensity of exposure of the host to the pathogen of interest. The units of dose are usually given as the number of organisms ingested. By studying the effects of various doses, it is possible to determine a dose–response relationship between the dose and the frequency of infection within the exposed population of hosts. Researchers have studied quantitative descriptions of the dose–response relationships of organisms to provide insight into the risk of becoming infected after the ingestion of a certain dose of organisms (Teunis et al. 1996).

Dose–response data from the results of clinical trials have been reported in the literature (McBride et al. 2002) for *Campylobacter* (Black et al. 1988), adenovirus 4 (Couch et al. 1966a, b, 1969), echovirus 12 (Akin 1981 as cited in Haas et al. 1999), Salmonella (McCullough & Eisele 1951a, b), Cryptosporidium (Dupont et al. 1995; Chappell et al. 1996; Moss et al. 1998; Okhuysen et al. 1998, 1999; Messner et al. 2001), *Giardia lamblia* (Rendtorff 1954a, b; Rendtorff & Holt 1954a, b), *Vibrio cholera* (Hornick et al. 1971), rotavirus (Ward et al. 1986; Regli et al. 1991), poliovirus (Lepow et al. 1962; Katz & Plotkin 1967; Minor et al. 1981), *Escherichia coli* O157:H7 (Powell et al. 2000), and coxsackieviruses B4 and A21 (Suptel 1965; Couch et al. 1965). Generally, these data were obtained from feeding studies of healthy adults. Thus, certain portions of the population including children, the elderly, and individuals with compromised immune systems are not well represented by these data.

Typically the reported dose–response data have been fit to models that relate the probability of infection to the mean dose ingested. In some cases, illness as an end-point was also investigated; however, the conditional modeling of illness given infection has proven to be difficult (Teunis et al. 1996). The most common models, although not the only models used to relate an ingested dose to infection, are the exponential and beta-Poisson models (Haas et al. 1999). Those models are summarized below.

The exponential model is based on the following assumptions (Haas et al. 1999): microorganisms are distributed in water randomly and thus follow the Poisson distribution for infection to occur, at least one pathogen must survive within the host the probability of infection per ingested or inhaled organism is constant.

Mathematically, the probability of infection \( (P_{\text{inf}}) \) as expressed by the exponential model is as follows:

\[
P_{\text{inf}} = 1 - e^{-rN}
\]

In the exponential model each microorganism has the same fixed probability \( r \) of surviving and reaching a host site at which infection may result. Under this model the dose required to cause infection in half the exposed population is \( N_{50} = -\ln(0.5)/r \). The dose–response relation for many protozoans and viruses tend to follow this model. The biological implication of this model is that differential susceptibility in the challenged population tends not to be strong (McBride et al. 2002).

The beta-Poisson model is based on similar assumptions to the exponential model except that the third assumption (that the probability of infection per ingested organism is constant) is relaxed. This model allows the probability of infection per ingested or inhaled organism to vary with the population. In this model the probability of surviving and reaching a host site (“\( r \)” in the exponential model) is beta distributed, and thus the model contains the two parameters \( \alpha \) and \( \beta \) of the beta distribution. The most commonly used approximation to the beta-Poisson model is as follows:

\[
P_{\text{inf}} = 1 - \left( 1 + \frac{N}{\beta} \right)^{-\alpha}
\]

Unfortunately, in this approximation to the beta-Poisson model, \( \beta \) does not have an obvious physical
interpretation. What can be said is that it is a shape parameter governing the steepness of the dose–response curve; the larger its value the steeper the curve (McBride et al. 2002). The derivation of the approximation to the beta-Poisson model requires that $\beta > \alpha$, and becomes poorer at small values of $\beta$ or large values of $N$. In practice this condition is not always met. The beta-Poisson is linear at low doses and is always shallower than the exponential model. However as $\alpha$ increases, the beta-Poisson model approaches the exponential model (Haas et al. 1999).

Many bacteria and some viruses are described by the beta-Poisson model. For organisms whose dose–response relations are described by this model, the biological implication is that there is substantial differential susceptibility in the challenged population (McBride et al. 2002). For a compendium of critically analyzed dose response curves, refer to Haas et al. (1999) or McBride et al. (2002).

New methods for dose–response assessment relying on Bayesian approaches have begun to appear in the literature over the last several years (Messner et al. 2001; Englehardt 2004; Englehardt & Swartout 2004). A detailed description of these methods is beyond the scope of this paper. However, it is noteworthy that these methods attempt to address a major limitation of likelihood-based approaches (that data validation is not possible for the doses of pathogens that are consistent with public health goals).

**Risk characterization methods**

A literature review was recently conducted to document the status, advantages, and limitations of different types of microbial risk assessment risk characterization techniques (Soller et al. 2004). The literature review of approximately 1100 citations indicated that at the broadest level there was a distinction between direct estimates of risk or illness using epidemiologic data and indirect estimates using models. Direct estimates entail collecting infection or disease outcome data, for example, prospective studies or outbreak investigations. Indirect estimates employ exposure data as input to numerical models to compute estimates of illnesses.

Based on the available literature, it appears that direct methods are most commonly used to assess the public health impact associated with a specific and known (or identifiable) exposure pathway. Those methods may not, however, provide the regulatory and management information for making decisions regarding changes in environmental conditions. For this purpose indirect methods can play a useful role. The literature review indicated that MRA methodologies vary primarily in the manner in which they address the unique properties of an infectious disease transmission system. The fundamental difference between these risk assessment techniques is that NRC paradigm models (static models) do not account for the properties that are unique to a dynamic infectious disease process (Table 1). In static models, the number of individuals that are assumed to be susceptible to infection is not time-varying, whereas in dynamic models that number is time-varying.

**Static microbial risk assessment models**

Assessments using a static model for evaluating microbial risk typically focus on estimating the probability of infection or disease to an individual as a result of a single exposure event. These assessments generally assume that multiple or recurring exposures constitute independent events with identical distributions of contamination (Regli et al. 1991). Secondary transmission and immunity are typically not considered, assumed to be negligible, or that they effectively cancel each other out. In this context, secondary transmission would increase the level of infection/disease in a community relative to a specific exposure to pathogens, and immunity would decrease the level of infection/disease in a community relative to a specific exposure to pathogens.

In static MRA models, it is assumed that the population may be categorized into two epidemiological states: a susceptible state and an infected or diseased state. Susceptible individuals are exposed to the pathogen of interest and move into the infected/diseased state with a probability that is governed by the dose of the pathogen to which they are exposed and the infectivity of the pathogen (Figure 2). In Figure 2, the solid lines represent the movement of individuals from one epidemiological state to another, and the dotted lines represent the movement of pathogens. Although humans may be exposed to pathogens from a number of potential environmental sources, static models typically employ the assumption that susceptible individuals are exposed to pathogens from the specific pathway under
Table 1 | Comparison of static and dynamic risk assessment models

<table>
<thead>
<tr>
<th>Static risk assessment model</th>
<th>Dynamic risk assessment model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Static representation (not varying in time)</td>
<td>Dynamic representation (time varying)</td>
</tr>
<tr>
<td>Direct exposure (environment-to-person)</td>
<td>Direct (environment-to-person) and indirect exposure (person-to-person)</td>
</tr>
<tr>
<td>Individual-based risk</td>
<td>Population-based risk</td>
</tr>
<tr>
<td>Potential for secondary transmission of infection or disease is typically not considered.</td>
<td>Potential for secondary or person-to-person transmission of infection or disease exists.</td>
</tr>
<tr>
<td>Immunity to infection from microbial agents is typically not considered.</td>
<td>Exposed individuals may not be susceptible to infection or disease because they may already be infected or may be immune from infection due to prior exposure.</td>
</tr>
<tr>
<td>Dose–response function is the critical health component.</td>
<td>The dose–response function is important; however, factors specific to the transmission of infectious diseases may also be important.</td>
</tr>
</tbody>
</table>

consideration for the investigation and do not include the potential interaction and implications of multiple routes of exposure.

The probability that a susceptible individual becomes infected or diseased is a function of the dose of pathogens to which that individual is exposed. When individuals are exposed to pathogens from an environmental source, they move with a given probability to an infected or diseased state. This probability dose–response function is labeled \( P_{\text{inf}} \) in Figure 2. The dose is typically calculated by estimating two quantities: the concentration of pathogens at the exposure site and the volume of water ingested. This dose quantity is then input into the dose–response function and the probability that an exposed individual will become infected or diseased is estimated.

![Figure 2](https://iwaponline.com/jwh/article-pdf/4/S2/165/396587/165.pdf)

The critical health effects information required for the static model, therefore, is summarized in the function that represents this probability of infection \( P_{\text{inf}} \), the pathogen-specific dose–response function. The probability of infection following exposure to a virulent pathogen depends on several host- and pathogen-specific factors. The interaction between a pathogen and the host can be viewed as a series of conditional events, in which each event must occur in order to result in infection. The infection status depends on a number of factors such as: (1) the number of organisms that enter the host; (2) the host’s ability to inactivate these organisms; (3) the number of organisms that can withstand the host’s local immune defenses, adhere to mucosal surfaces, and multiply in order to infect the host; and (4) variation in pathogen virulence and host susceptibility (Eisenberg et al. 1996, 2004). The probability of infection is often multiplied by the number of exposed individuals to estimate the expected number of infected individuals for the exposure scenario under consideration.

Dynamic microbial risk assessment models

In a dynamic risk assessment model, the population is assumed to be divided into a group of epidemiological states. Individuals move from state to state based on
epidemiologically relevant data (duration of infection, duration of immunity, etc). Only a portion of the population is in a susceptible state at any point in time, and only those in the susceptible state can become infected or diseased through exposure to microorganisms. The probability that a susceptible person moves into an exposed state is governed by the dose of pathogen to which they are exposed, the infectivity of that pathogen, as well as the number of infected/diseased individuals with whom they may come into contact. For both dynamic and static representations of the disease process, infectivity as a function of dose (estimated using a dose–response function) is an important factor in estimating risk. The dose–response function is important in a dynamic microbial risk assessment model; however, other factors such as person-to-person transmission, immunity, asymptomatic infection, and/or incubation period may also be important.

Accounting for these additional factors when estimating risks associated with exposure to pathogenic microorganisms requires a more sophisticated mathematical model than the static model shown conceptually in Figure 2. When a dynamic disease transmission model is used, one can account for attributes specific to the transmission of infectious diseases. Depending on the infectious disease processes that are important, the dynamic model may include more or less components, and therefore vary in complexity. For example, a dynamic model may account for person-to-person transmission, immunity, incubation, and asymptomatic infection, as is illustrated in Figure 3 (Soller et al. 2004).

The solid lines in Figure 3 represent the movement of individuals from one epidemiological state to another, and dotted lines represent the movement of pathogens.

In Figure 3, the population is separated into six epidemiological states. A summary of the epidemiological states employed in the Figure 3 dynamic model is provided in Table 2. Rate parameters specifying the movement between epidemiological states are shown as Greek letters and are summarized in Table 3.

The model shown in Figure 3 is called a dynamic model because the number of people in each epidemiological state varies over time. The dynamic model is a more comprehensive mathematical rendering of the static model and under a specific set of assumptions the two models are equivalent. Comparison of Figures 2 and 3 indicates that the two models would be equivalent when: the background concentration of the pathogen (or equivalently the endemic level of infection/disease) in the population is zero; the duration of infection and disease approaches zero; and infection and/or disease do not confer immunity or the duration of immunity approaches zero.

In categorizing the epidemiological status of the population, individuals are considered infected if they are shedding pathogens in their feces. People are considered diseased if they exhibit any of the clinical symptoms related to the specific pathogen of interest, for example, diarrhea and/or vomiting.

Dynamic microbial risk assessment models can take two main forms: deterministic or stochastic. In the deterministic
form, the model is expressed as a set of differential equations that have defined parameters and starting conditions which determine the rate of transfer of individuals from one epidemiologic state to another. This type of model is most suitable for large populations of individuals randomly interacting with one another (Eisenberg et al. 1998; Soller et al. 2003). In the stochastic form, the model incorporates probabilities at an individual level and is evaluated by an iterative process such as Markov Chain Monte Carlo analysis. Stochastic model forms are most suitable for small populations with heterogeneous mixing patterns (Koopman et al. 2002).

Table 2 | Epidemiological states for a representative dynamic model

<table>
<thead>
<tr>
<th>Figure 3 label</th>
<th>Epidemiological states</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S</td>
<td>Susceptible</td>
<td>Individuals who are not infected and are not protected from infection</td>
</tr>
<tr>
<td>E</td>
<td>Exposed</td>
<td>Individuals who have been exposed to a pathogen, but are not yet infected</td>
</tr>
<tr>
<td>C1</td>
<td>Carrier 1</td>
<td>Individuals who are infected but do not have symptoms of disease</td>
</tr>
<tr>
<td>D</td>
<td>Diseased</td>
<td>Individuals who are infected and have symptoms of disease</td>
</tr>
<tr>
<td>C2</td>
<td>Carrier 2</td>
<td>Individuals who were diseased, no longer exhibit symptoms of disease, but are still infected</td>
</tr>
<tr>
<td>P</td>
<td>Post-Infected</td>
<td>Individuals who are neither infected nor symptomatic, and have resistance to infection</td>
</tr>
</tbody>
</table>

Table 3 | Rate parameters for a representative dynamic model

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$</td>
<td>Rate of movement from an exposed state to a carrier (infectious and asymptomatic) state or a diseased state (infectious and symptomatic). $1/\alpha$ corresponds to the latency period prior to infection for the pathogen of interest.</td>
</tr>
<tr>
<td>$\sigma$</td>
<td>Rate of movement from a carrier state to a post infection state. $1/\sigma$ corresponds to the duration of infectiousness, or equivalently, the duration of asymptomatic shedding of pathogen in feces.</td>
</tr>
<tr>
<td>$\delta$</td>
<td>Rate of movement from a diseased state (infectious and symptomatic) to an asymptomatic (carrier) state. $1/\delta$ corresponds to the duration of symptoms during infection.</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>Rate of movement from a post-infection state (not infectious, asymptomatic, and not susceptible to infection) to a susceptible state. $1/\gamma$ corresponds to the duration of immunity or protection from infection.</td>
</tr>
<tr>
<td>$\beta 1$</td>
<td>Rate of movement from a susceptible state to an exposed state due to exposure to pathogens from an environmental source (i.e. not person-to-person transmission). Function of the number of pathogens to which an individual is exposed and the infectivity of the pathogen of interest. The infectivity is described quantitatively through a dose–response function which is comprised of one or two dose-response parameters.</td>
</tr>
<tr>
<td>$\beta 2$</td>
<td>Rate of movement from a susceptible state to an exposed state due to exposure to pathogens from secondary (person-to-person or person-to-environment-person) transmission.</td>
</tr>
<tr>
<td>$P_{\text{sym}}$</td>
<td>Probability of a symptomatic response. Clinical data describing the proportion of infected individuals that develop symptoms.</td>
</tr>
</tbody>
</table>
Risk characterization model complexity

A variety of model forms can be employed to characterize infectious disease transmission and to evaluate the potential for effective interventions. Particular characteristics of each model form capture different aspects of the disease transmission system. However, it is unrealistic to presume that one model form is most appropriate for all waterborne microbial risk assessments. Soller et al. (2004) demonstrated, for exposures to microbes from reclaimed water applications, the selection of an appropriate model form (static or dynamic) could be identified based on as few as three to four model parameters. That investigation also clearly demonstrates that no model form will be appropriate for all possible combinations of potential pathogens of interest and exposures.

Occam’s Razor\(^1\) is a useful starting point in considering model complexity; however, the selection of a model type does involve tradeoffs. Biological or demographic “realism” can come at the cost of analytical complexity that distances the model from available data. Further, each model form involves certain types of assumptions that may or may not be realistic or appropriate for a particular situation. With the perspective that different model forms and accompanying analytical approaches may be necessary for different applications, Koopman et al. (2001) suggest an analysis strategy involving a hierarchy of models from simple to increasingly complex models which could be traversed to make microbial risk assessment analyses more realistic while remaining mathematically tractable. It seems quite reasonable to anticipate that the issue of model complexity for microbial risk assessments will be an area of future research that will receive substantial attention.

REPRESENTATIVE MRAS FOR WATERBORNE PATHOGENS

A number of microbial risk assessments have been carried out for waterborne pathogens including assessments employing both static and dynamic models. This section summarizes static and dynamic MRAs representative of those found in the literature with an emphasis on MRAs carried out for drinking water exposures.

Risk assessments employing static models

Static microbial risk assessment methods have been used to evaluate the potential public health effects associated with drinking water contaminated with a range of waterborne pathogens including both viruses and parasites. The methods employed in those assessments have varied from relatively straightforward assessments using point estimate values for model parameters to more complex assessments relying on stochastic (probabilistic) models. For example, in evaluating the public health impact from exposure to human rotavirus in drinking water, Gerba et al. (1996) used point estimate values for the concentration of rotavirus in drinking water (0.004/l and 100/l) based on surface water concentrations from previously published studies and an assumed 99.99% reduction of rotavirus through drinking water treatment. The volume of water ingested (2l/day and 4l/day) and beta-Poisson dose–response parameters \(a = 0.26, b = 0.42\) were also based on point estimate values. The probability of clinical illness was determined by multiplying the resulting probabilities of infection by 0.5. The probability of mortality was calculated by multiplying the probability of illness by 0.01% for the general population and 1% for the elderly. Yearly risks were calculated as a function of daily risks: \[ P = 1 - (1 - P_{\text{daily}})^{365}. \]

Crabtree et al. (1997) employed a static risk assessment model to evaluate the potential health effects associated with adenovirus from drinking water exposures. There are 47 types of adenoviruses with infections resulting in conjunctivitis, pharyngitis, pneumonia, appendicitis, bronchiolitis, and gastroenteritis. Adenovirus infections are usually acute and self-limiting. The MRA method employed was similar to that described above for rotavirus (Gerba et al. 1996). Point estimate values were employed for the concentration of adenovirus in drinking water (0.01/l and 0.001/l), the volume of water ingested (2l/day and 4l/day), and the exponential dose–response parameter \(r = 0.4172\). The risk of illness was determined by multiplying the probability of infection by 0.5. The probability of mortality was calculated by multiplying the probability of illness by

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\(^1\) Occam’s Razor states that one should make no more assumptions than needed. Put into everyday language, it says, given two equally predictive theories, choose the simpler (www.wikipedia.com).
0.01%. Annual risks were computed using a similar methodology as described above (Gerba et al. 1996).

Mena et al. (2005) employed static MRA methods to evaluate the public health risk associated with drinking waters contaminated with coxsackieviruses. Coxackieviruses are the most common non-polio enteroviruses found in domestic wastewater and in contaminated surface water, groundwater and drinking water (Mena et al. 2005). Most coxsackievirus infections result in mild febrile illness, although coxsackieviruses are also capable of causing a wide range of more serious illnesses. The methods employed were similar to those described above for rotavirus and adenovirus with point values used to estimate exposure and the exponential dose–response relation.

In addition to the point estimate virus specific assessments described above, static MRA methods have also been used (1) in assessments for viruses in which combinations of characteristics of different viruses have been assumed to determine appropriate level of drinking water treatment for viruses as a class of contaminants, and (2) in conjunction with Monte Carlo simulation techniques to account for variability and uncertainty in model parameters. For example, Regli et al. (1991) suggest that the enteroviruses (a subgroup of enteric viruses) for which a standard analytical method has been available for some time, could serve as an indicator of worst-case potential occurrence for any specific virus. Similarly, the dose–response relation for rotavirus has been used to derive upper-limit risk estimates for viruses in water as rotavirus is the most infectious waterborne virus for which dose–response information is currently available (Haas et al. 1993). Haas et al. (1993) accounted for uncertainties in exposure assessments (lognormal distribution for volume ingested) and the dose–response relationship (95% confidence intervals about the maximum likelihood estimate for α and β) for viruses in drinking water by applying Monte Carlo simulation techniques.

Static microbial risk assessment methods have also been used to evaluate the potential public health effects associated with drinking water contaminated with G. lamblia (Rose et al. 1991; Teunis et al. 1997) and Cryptosporidium (Perz et al. 1998; Teunis & Havelaar 1999; Makri et al. 2004). Rose et al. (1991) conducted a static risk assessment investigating the potential health risks associated with G. lamblia in drinking waters. The methodology employed was similar to that described above for rotavirus and adenovirus. Point estimates were used to characterize the volume of water consumed daily (2 L), average levels of cysts in surface waters (0.22–104/100 l), reduction of cysts due to drinking water treatment (99.9%), and the dose–response relation. Annual risks were computed as described above and source water concentrations corresponding to annual risks of 1/10 000 were derived.

Teunis et al. (1997) conducted an assessment of the risk of infection by Cryptosporidium and G. lamblia in drinking water from a surface water supply in which the major contributing factors to risk were each treated as stochastic variables. The stochastic variables investigated included the concentration of cysts (G. lamblia) and oocysts (Cryptosporidium) in raw water, the recovery of the detection method, the viability of recovered cysts or oocysts, the removal of organisms in the treatment process, and the daily consumption of unboiled tap water. A frequency distribution for the probability of infection was developed based on the results of the probabilistic simulations. The advantage of this stochastic approach was clearly evident in the results that indicated that the uncertainty in the estimated removal efficiency of the treatment process dominated the uncertainties in all other contributing factors.

In a similar investigation to that described above, Teunis & Havelaar (1999) conducted a case study in which the risk of human infection from Cryptosporidium parvum in drinking water was characterized. Exposure was assessed by considering the different stages from river water to consumed tap water. Oocyst counts in the river water were corrected for the performance of the detection method via a probabilistic process. Before treatment, the water was assumed to be stored in storage basins for several months. The removal and inactivation of oocysts during this process was modeled as a stochastic process. Assessment of the performance of a drinking water treatment process was modeled using spores from sulfite reducing clostridia as the surrogate organism. Inactivation by disinfection was estimated by using a process model from the literature. Consumption of unboiled tap water was modeled using the lognormal distribution based on a Dutch survey.
The daily ingested dose was then calculated by means of Monte Carlo simulation. For dose–response assessment, the beta-Poisson model was employed. The dose–response relations for infection and illness were used to generate, via Monte Carlo methods, distributions for the risk of daily, annual, and lifetime infection and illness.

A static MRA model was employed by Perz et al. (1998) to examine the potential role of tap water in the transmission of endemic Cryptosporidium parvum infection. Their model had two components: an exposure–infection component to relate low-dose exposure to infection; and an infection–outcome component to include the probabilities of clinical outcomes leading to case detection and reporting. A concentration of 1 oocyst/1000 L was assumed for the treated and distributed drinking water. The population was divided into four subgroups which included adults and children both with and without AIDS. The computed risks were used in conjunction with the 1995 New York City population to estimate the number of cases due to ingestion of tap water.

Makri et al. (2004) carried out a case study static MRA investigation to develop and test a predictive model for waterborne cryptosporidiosis risk on a regional scale, accounting for persons living with AIDS, and to determine if the model predicted regional patterns of cryptosporidiosis incidence. Similar to the investigations carried out by Teunis et al. (1997) and Teunis & Havelaar (1999), probabilistic simulations were employed to account for variability and uncertainty in model parameters. Analytic recovery, source water concentration, viability, consumption, dose–response relation, and the probability of illness given infection were all modeled as probabilistic distributions for the exposure component. The Monte Carlo routine resulted in daily and annual probability estimates of Cryptosporidium infection, illness, prolonged illness, and case detection. This study differs from prior work as it compares predictions based on water quality data with endemic cryptosporidiosis surveillance and accounts for differential susceptibility. When accounting for the different susceptibilities in the population, the model did over-predict disease incidence; however, the findings assume that the surveillance data used for comparison reflect actual waterborne cryptosporidiosis incidence.

Risk assessments employing dynamic models

Dynamic microbial risk assessment methods have been used to characterize the potential public health effects associated with rotavirus in drinking water (Soller et al. 1999), obtain insight into the epidemic process related to drinking water treatment failures (Eisenberg et al. 1998), characterize risks from microbiological contaminants associated with recreational activities (EOA 1995a, b; Eisenberg et al. 1996; Soller et al. 2003, 2006), and estimate the bias associated with modeling the infectious disease process using a static model (Eisenberg et al. 2003; Soller et al. 2004). In all of these investigations probabilistic simulations were employed to account for variability and uncertainty in model parameters.

The fundamental difference between the investigations cited above and those described in the previous section is that the risk characterization perspective is shifted away from an individual to a population-based perspective in the dynamic MRA investigations. In these dynamic MRAs, the models simulate the epidemiologic status of a population over time as well as environmental variables such as pathogen density. In each investigation, a conceptual model for health effects was developed. Risk characterization was implemented by integrating the exposure and health effects components (models) via a parameterization step, and by running Monte Carlo simulations. The outputs from the simulations are distributions of predicted adverse health effects.

Soller et al. (1999) conducted a case study in which the risk of human infection from rotavirus in drinking water was investigated. This case study was implemented to evaluate the EPA/ILSI framework for microbial risk assessment and thus was not rigorous in terms of exposure. Nevertheless, the methods used are representative of other dynamic MRAs for waterborne pathogens. In this assessment the population was assumed to be served drinking water by a surface water treatment plant using conventional treatment and the watershed was assumed to be dominated by agricultural activity. A schematic diagram showing the important components in the investigation is presented in Figure 4.

The population was divided into four states as follows: (1) individuals susceptible to infection (S); (2) individuals
who are infectious but not symptomatic (i.e. carriers); (3) individuals who are symptomatic and infectious (diseased) (D); and (4) individuals in a post-infection state who are neither infectious nor fully susceptible due to (limited and short-term) immunity (P). A schematic of the conceptual health effects model for this case study is presented in Figure 5.

Rate parameters describe the movement of the population from one epidemiological state to another, and include $\beta$ (rate of acquiring infection), $\sigma$ (rate of recovery from infection), and $\gamma$ (rate of decline in immunity). The quantitative values for the rate parameters were determined through literature review.

Mathematically, the epidemiological status of the population was modeled as a series of ordinary differential equations. Using this approach and assuming that the primary (drinking water) and secondary (person-to-person) transmission processes are independent, the change in the fraction of the population in any state from one time period to the next was computed. For example, the relative change in state $S$ from one time period to the next due to primary infection was

$$\frac{dS}{dt} = -\beta_{SC}S - \beta_{SD}S + \gamma P$$

where: $\beta_{SC}$ is the rate at which the population moves from State $S$ to State $C$ due to primary exposure, $\beta_{SD}$ is the rate at which the population moves from State $S$ to State $D$ due to primary exposure, and $\gamma$ is the rate at which the population moves from State $P$ to State $S$.

The dynamic microbial risk assessment model tracks the number of susceptible, infected, diseased and immune individuals over time. Using data from the literature, each parameter in the model was described in terms of a probability distribution. Both exposure and health related variables were included in the Monte Carlo simulations. The health related variables accounted for probabilistically in the simulations included: beta-Poisson dose–response variables (95% confidence regions for $\alpha$ and $\beta$), volume of water ingested daily (lognormal distribution), person-to-person transmission potential, probability of a symptomatic infection, duration of incubation and latency, duration of infection, and duration of post-infection status (immunity). Example output from one simulation is

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**Figure 4** | Case study schematic, for Soller et al. (1999).

**Figure 5** | Conceptual health effects model (from Soller et al. 1999).
presented in Figure 6 that shows how the number of individuals in each epidemiological state changes over the course of the simulation, eventually reaching a steady state condition.

Eisenberg et al. (1998) combined information on the temporal pattern of disease incidence for the 1993 cryptosporidiosis outbreak in Milwaukee, WI with information on oocysts levels to obtain insight into the epidemic process. In this investigation, a dynamic model was constructed and possible parameter combinations were evaluated to find combinations consistent with surveillance data from the outbreak. Evaluation of the model output from this exercise indicated that a smaller outbreak likely occurred prior to the large reported outbreak. This finding suggested that, had surveillance systems detected the earlier outbreak, up to 85% of the cases might have been prevented. Further analysis using the incidence data resulted in three inferred properties of the infection process: (1) the mean incubation period was likely to have been between 3 and 7 days; (2) there was a necessary concurrent increase in Cryptosporidium oocyst influent concentration and a decrease in treatment efficiency of the water treatment facility; and (3) the variability of the dose-response function in the model did not appreciably affect the simulated outbreaks.

Soller et al. (2003) employed a dynamic MRA approach to provide insight regarding the potential public health benefit that may be provided by year-round tertiary wastewater treatment compared to summer season tertiary treatment and winter season secondary treatment in Northern California. The conceptual health effects model from that investigation is presented in Figure 7. Effluent from the treatment facility discharges to a river that is used by the public for recreational purposes. A hydraulic model of the river was coupled with a dynamic disease transmission model to integrate a wide array of disparate data to estimate the level of viral gastroenteritis under the two treatment scenarios.

This investigation demonstrated that the risk of viral gastroenteritis attributable to the wastewater treatment facility from recreation was related not only to treatment efficacy of the wastewater treatment facility (Figure 8), but also viral loading from people recreating in the river (Figure 9). The primary advantage of employing a simulation based approach in this type of investigation is the ability to evaluate the potential benefits of proposed management options (Soller et al. 2006). Although MRA methods inherently do not characterize the cumulative risk associated with all pathogens potentially present in an environment, this study illustrated that it is possible to synthesize a model organism that captures the salient features of a class of pathogens of interest, and thus frame an investigation in a manner such that practical risk management decisions can be made.

**MICROBIAL RISK ASSESSMENTS CONDUCTED BY EPA OFFICE OF WATER**

Drinking water is regulated in the United States by the Safe Drinking Water Act (SDWA). SDWA regulations specifically controlling microorganisms in surface water and groundwaters under the direct influence of surface water include the Surface Water Treatment Rule, Total Coliform Rule, Interim Enhanced Surface Water Treatment Rule, Long Term 1 Enhanced Surface Water Treatment Rule, Filter Backwash Recycle Rule, Long Term 2 Enhanced Surface Water Treatment Rule, and the Groundwater Rule (under development).

Benefit-cost studies have been prepared for every major rule developed by EPA’s Office of Water under the Safe Drinking Water Act (Regli et al. 1999). Microbial risk assessment has been used as a primary tool to characterize
the benefits portion of those analyses. This section provides an overview of the MRA methods that have been used to support those rules.

The Interim Enhanced Surface Water Treatment Rule (IESWTR) was published in the Federal Register on December 16 1998 and was the first part of a series of rules known as the “Microbial-disinfectant/Disinfection Byproducts Cluster” that are intended to control microbial pathogens while minimizing the public health risk of disinfectants and disinfection byproducts. The IESWTR sought to improve control of pathogens such as Cryptosporidium and to ensure that pathogen control was maintained while the Stage 1 D/DBP rule was implemented. Major features of the rule include a maximum contaminant level goal for Cryptosporidium, removal requirements through treatment for Cryptosporidium, turbidity performance and monitoring criteria, a disinfection benchmark requirement,

![Figure 7](https://iwaponline.com/jwh/article-pdf/4/S2/165/396587/165.pdf)  
Conceptual health effects model (from Soller et al. 2003).

![Figure 8](https://iwaponline.com/jwh/article-pdf/4/S2/165/396587/165.pdf)  
Relation between wastewater treatment efficacy and public health risk from recreational activities.

![Figure 9](https://iwaponline.com/jwh/article-pdf/4/S2/165/396587/165.pdf)  
Relation between gastroenteritis rate and viral loading from recreation.
and a sanitary survey for all systems using surface water. The economic benefits of the IESWTR are assumed to result entirely from the decreased probability of incidence of cryptosporidiosis as determined through MRA, and the avoidance of resulting health costs. Exposure to pathogenic protozoa such as Giardia or other waterborne bacterial or viral pathogens is almost certainly reduced by this rule, but was not quantified through MRA (Regli et al. 1999).

In the IESWTR analysis, a static risk assessment methodology was employed to quantify the number of infections, illnesses, and deaths of Cryptosporidium in drinking water. Data from human ingestion trials were used to derive the best fit value (k = 239) and 95% confidence interval (132–465) for the exponential dose–response function. The exponential dose–response parameter was then modeled as a lognormally distributed variable. The rate of daily water ingestion was assumed to be lognormally distributed with mean 1.95 l and a standard deviation of 0.81. Assumptions were made about the performance of existing drinking water treatment processes in removing oocysts to estimate Cryptosporidium concentrations in finished water. It was estimated that the existing standard treatment resulted in a normal distribution of reduction with mean of 2.5 logs and a standard deviation of 0.65 logs. An alternative removal distribution was also evaluated (mean 3.0 logs with standard deviation of 0.63 logs). The viability–infectivity of Cryptosporidium in finished water was modeled as a uniform distribution with a minimum value of 5% and a maximum of 15%. The percent of infections that result in symptomatic illness was modeled as a triangular distribution with mean 39%, low of 19% and high of 0.62.

The authors used the above data to calculate the expected number of annual infections. Monte Carlo simulations were carried out to estimate the probability distribution of the estimated number of infections and illnesses. This approach is fundamentally consistent with the approach developed earlier for Giardia and viruses in drinking water (Regli et al. 1991).

The proposed Long Term 2 Enhanced Surface Water Treatment Rule (LT2) was published in the Federal Register on August 11 2003 and the final rule was published on January 5, 2006. This rule was intended to reduce the occurrence of viable waterborne pathogens, particularly Cryptosporidium, in public drinking water delivered by surface water systems (US EPA 2003). The quantified health benefits estimated for this rule result from reducing the incidence of adverse health effects caused by drinking water containing Cryptosporidium. Similar to the IESWTR, microbial risk assessment was used to characterize the expected incidence of adverse health effects associated with exposure to Cryptosporidium and to estimate the benefits of actions taken to reduce the exposure.

The static risk assessment methodology, comprised of a two-dimensional Monte Carlo simulation model, was employed to quantify the benefit estimates of the LT2 by calculating the difference between illness and death estimated for the baseline condition (pre-LT2) and after implementation of the LT2. Benefit estimates are the predicted number of illnesses and deaths avoided because of the implementation of the regulatory requirement.

The risk assessment model is conceptually similar to that implemented for the IESWTR; however, the model is more sophisticated in its treatment of variability and uncertainty and more detailed in its exposure assessment. The LT2 risk model integrates dose–response and exposure assessment components into a Monte Carlo simulation model which is implemented in two steps.

The first step of the risk assessment model was structured as a two-dimensional Monte Carlo simulation. A two-dimensional simulation is used when the model includes both uncertainty and variability components in the inputs, and where it is necessary to clearly distinguish the influence of these elements in the model output. Uncertainty components included the dataset representing source water concentrations, the true distribution of source water oocyst concentration, the true distribution of pre-LT2 oocysts removal, the morbidity factor, the fraction of oocysts that are infectious, and the true mean of the exponential dose–response infectivity parameter. The form of the dose–response model employed was one that predicted the probability of acquiring one or more infections over the time period studied. Variability components included in the model were the source water concentration, pre-LT2 Cryptosporidium removal, log reduction achieved due to treatment, and the volume of water ingested daily. Of note is the fact that the volume of water ingested was assumed to have mean of 1.07 l per day (1.23 liters/day.
minus 0.16 liters/day, the mean consumption by those who reported bottled water as their main source of drinking water). Variability in individual consumption was reflected by calculating the individual risk reduction estimates; however, that variability was not reflected in the overall estimates of variability in illness.

By structuring the first step in the modeling process in this way, it was possible to characterize both the distribution of the individual annual risk of illness in the affected population and the overall population average annual risk of illness.

In the second step of the risk assessment model, the number of cases of illness and mortality and the confidence bounds on those estimates were computed for the various pre-LT2 and post-LT2 assumptions regarding *Cryptosporidium* in source water. During this second step, the number of illness cases was adjusted to account for secondary transmission. To account for uncertainty in the secondary spread factor, a triangular distribution was used with a low of 10%, a high of 40% and a most likely value of 25%. These estimates were derived based on a summary of available outbreak data.

The risk characterization process was implemented to describe the reduction in general population risk for unfiltered systems and filtered systems. Morbidity risk in the analysis was based on studies of infectivity and morbidity on healthy volunteers. No data were available to characterize differential infectivity or morbidity for the immunocompromised or other sensitive subpopulations. The mortality risk was based on data from the 1993 Milwaukee outbreak which indicated that all fatalities were in sensitive subpopulations. Thus, all of the quantified deaths avoided due to LT2 were presumed to be lives saved in sensitive subpopulations.

**USE OF MICRIBAL RISK ASSESSMENT TO INFORM THE NATIONAL ESTIMATE**

**Previous estimates of waterborne disease in the US**

Questions about the magnitude of waterborne disease and the importance of different risk factors associated with waterborne disease occurrence in the US have been a subject of interest for many years. A comprehensive review of this topic was completed and can be found in this issue (Roy et al. 2006). The following description is a very brief summary of previous estimates of waterborne disease in the US.

A number of different estimates of the national occurrence of waterborne disease were published in the 1970s and 1980s. These estimates are highly uncertain as they were not based on studies specifically designed to obtain such an estimate nor are they based on MRA methods. For example, Hauschild & Bryan (1980) estimated the annual incidence of both food- and waterborne disease in the US for 1974 and 1975 to be 1400 000 to 3400 000 cases, Morris & Levin (1995) estimated that 1.8 million cases of waterborne disease and 1800 deaths occur annually, and Bennett et al. (1987) estimated the annual incidence of waterborne disease to be more than 900 000 cases and almost 900 deaths.

Discussions on the magnitude of waterborne disease associated with drinking water supplies continued throughout the 1990s. Two epidemiology studies suggested that drinking water consumption might be responsible for approximately one third of all gastrointestinal illness (Payment et al. 1991, 1997). It is also noteworthy that a large waterborne disease outbreak in the city of Milwaukee, WI occurred under conditions that did not violate the drinking water regulations in effect at the time. That outbreak resulted in an estimated 403 000 cases of illness.

Mead et al. (1999) estimated the annual total number of illnesses in the US caused by known pathogens by adjusting for under- and non-reporting of illnesses. Based on their methodology, an estimated 38.6 million cases of GI illness occur annually due to known pathogens in the US from all exposures including food, water and other routes of exposure. Of those 38.6 million cases, it was estimated that 5.2 million cases are from bacterial pathogens, 2.5 million are from parasitic pathogens, and 30.9 million are from viral pathogens. The most recent CDC estimate of AGI from all types of exposures (e.g. food, person-to-person transmission, water, air, etc.) in the US is 195 million episodes per year (Imhoff et al. 2004). This estimate is based on data collected during 1998–1999 and translates to a rate of 0.72 illnesses per person-year (Imhoff et al. 2004). This CDC estimate is based on an analysis of random-digit
dialing (RDD) telephone survey results from a sample population of 29 million persons (~11% of the total US population) in 8 states during a 12-month period (Imhoff et al. 2004). This estimate is similar to an earlier CDC estimate of AGI in the US (0.75 illnesses per person-year from all sources) based on 1996–1997 data using the same RDD methodology, similar questions, and covering most of the same sample population.

**Microbial risk assessment methods for the national estimate**

In considering the national estimate of AGI specifically attributable to microbes in drinking water, it is reasonable to assume that communities served by systems with relatively contaminated source waters, sub-standard water treatment facilities, and/or contamination problems in their distribution systems are subject to a higher risk than communities where such issues are less of a concern. Further, the risk of illness attributable to pathogens in drinking water in each community can be thought of as the sum of the risk from pathogens present in the water as it leaves the drinking water treatment facility (treated water risk) and the risk from pathogens in the distribution system (distribution system risk).

Based on the discussions presented earlier in this paper, it seems reasonable that MRA methods could be used to provide some insight into the national incidence of AGI attributable to drinking water provided that appropriate data are available as input to MRA models. If it is assumed that the risk attributable to drinking water in each community is the sum of the treated water risk and the distribution system risk, it seems feasible that MRAs could be developed to characterize the risk associated with each of these components. It should, however, be recognized that MRA-based infection or illness estimates derived from pathogen-specific data will inherently under-estimate the total risk attributable to drinking water because the total risk will be a function of all pathogens present in drinking water whereas the MRA estimates will likely be based on data for specific pathogens. Thus, MRA methods may be most useful for providing a reasonable lower bound characterization of the national estimate.

**Risks from pathogens in treated drinking water**

To identify the types of MRA models that may be of most use for providing insight into the national estimate, it is necessary to consider treated water risk and distribution system risk separately. Characterizing the risk associated with pathogens in the treated water (at the point that the water enters the distribution system) could be accomplished either with a static model or a dynamic model as described previously in this paper. For example, if a static model were used, an assessment similar to those conducted by EPA for previous regulations (IESWTR or LT2ESWTR) may be appropriate. On the other hand, if a dynamic model were used, in addition to considering source water quality and drinking water efficacy, the relative importance of person-to-person transmission of disease and/or immunity to the pathogenic agent of particular concern could be investigated and characterized (Eisenberg et al. 2003; Soller et al. 2003).

At the present time, the potential bias associated with modeling treated drinking water risk as a static process compared to a dynamic process is unknown and has not been investigated. Previous work for exposure to pathogens from reclaimed water exposures indicated that there is a substantial potential for person-to-person transmission and immunity to impact the results of an assessment in a meaningful way relative to the results obtained using similar assumptions and a static model (Soller et al. 2004). However, since exposures to pathogens from a drinking water route of exposure may occur as frequently as daily for a large portion of the population, the results from the reclaimed water investigation (which investigated less frequent exposures and a smaller proportion of the population exposed) may not be applicable. Thus, in selecting a model for an assessment of the risk associated with pathogens in treated drinking water, it appears that some consideration of and/or justification for not including person-to-person transmission and immunity would be appropriate.

**Risks from pathogens in the distribution system**

Risks associated with exposure to pathogens from contamination in the distribution system of a public water supply
have not been quantitatively characterized to date via MRA. Given the various types of contamination events that result in distribution system risk, these risks are likely to occur sporadically in a community in both temporal and spatial dimensions. Thus, modeling and characterizing the risks from exposure to pathogens from contamination in the distribution system may require a different level of complexity in both the exposure and health effects components of a risk assessment compared to the risks from treated water at the point it enters the distribution system.

If it is assumed that pathogens enter drinking water distribution systems on a sporadic basis, and that those events have the potential to affect populations of varying size, it is reasonable to presume that MRA methods that are capable of accounting for intra- and inter-household disease transmission may be appropriate. If this is the case, stochastic dynamic models may be appropriate candidate MRA methods to characterize the risk associated with distribution system risk. Similar to the discussion presented above for treated water, the potential bias associated with modeling distribution system risk as a static process compared to a dynamic process is unknown at this time.

Potential risks associated with transient community water systems

In addition to the discussions presented above for treated water and distribution system risk, the potential exists for the transmission of infectious diseases to occur from exposure to microbes in drinking water when individuals visit areas served by transient community water systems such as a rest area or a summer camp, and then return home. In this type of situation the potential exists for propagation of infections derived from the transient drinking water system. The relative magnitude of the risk associated with this type of event compared to treated water or distribution system risk is unknown. Nevertheless, in considering the type of MRA methods that may be appropriate to characterize these types of events, it is clear that an MRA method that accounts for person-to-person transmission of disease would be necessary. Further, depending on whether the infectious agents in the transient system are the same as those present in the “home system”, some consideration of the relative distribution of the population’s epidemiological status may be necessary.

ACKNOWLEDGEMENTS

The author is grateful to Glenn Rice, Mary Rothermich, Stig Regli, Phil Berger, Gunther Craun and Rebecca Calderon for their assistance, support and review during the preparation of this manuscript.

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REFERENCES


EOA Inc 1995a Mamala Bay Study Infectious Disease Public Health Risk Assessment. Prepared for the Mamala Bay Study Commission.


